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Morten Sager

Pluripotent Circulations

Putting Actor-Network Theory to Work on
Stem Cells in the USA, prior to 2001

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Any remaining defects in this work are my own responsibility.

Göteborg, November 2006.

Contents

Abbreviations

AAAS	American Association for the Advancement of Science
ACT	Advanced Cell Technology
APP	alternative point of passage
ALS	Amyotrophic Lateral Sclerosis
ANT	Actor-Network Theory
CRS	Congressional Research Services
DHEW	Department of Health, Education and Welfare
DHHS	Department of Health and Human Services
EAB	Ethics Advisory Board
ES cell	embryonic stem cell
HERP	Human Embryo Research Panel
hESC	human embryonic stem cell
HFTTRP	Human Fetal Tissue Transplantation Research Panel
ICM	inner cell mass
IVF	in vitro fertilization
ICS	Institute of Civil Society
JAMA	*The Journal of the American Medical Association*
JDRF	Juvenile Diabetes Research Foundation
NBAC	National Bioethics Advisory Commission
NAS	National Academy of Sciences
NEJM	*The New England Journal of Medicine*
NIH	National Institutes of Health
OPP	obligatory point of passage
OTA	Office of Techology Assessment
PNAS	*Proceedings of the National Academy of Sciences*
STS	Science and Technology Studies (or Science, Technology and Society)
SSK	Sociology of Scientific Knowledge

Introduction

This study starts off with a puzzle about how to understand *human embryonic stem cells* (hESCs). By using *actor-network theory* (ANT), this puzzle becomes a topic for a theory of science study. ANT is put to work on largely textual materials, often directly from US political settings, such as Congressional debates and national panels. Beginning in the time period November 1998 – August 2001, this study then goes backwards to understand processes in the 1980's and 90's that can be related to the later situation in hESC research and politics in the USA.

However, unlike most ANT studies, a meta-theoretical interest in some notions that have been central to ANT and related approaches, continually guides the empirical inquiries in this work. Such notions include *the circulatory system of science*, *obligatory point of passage*, and *boundary objects*. As the empirical case unfolds, the concepts in use are continually tested, elaborated and expanded, and hESCs and ANT both become topics for analysis. A more detailed aim of the study therefore runs: *To explore ANT in order to understand the sociotechnical reality of hESCs in the USA prior to August 2001 – in particular with regard to the public and political dynamics.* All the elaborations serve a more general aim, viz. *an exercise in seeing differently*.

Making sense of the specific aim requires a first theoretical chapter. In this Introduction I will be happy if I can resolve the possibly (and probably) lingering confusion about the study's main title. I will attempt this resolution by presenting my initial puzzles about stem cell research. Then I introduce *Theory of Science* – the home discipline of the author and this publication. Theory of science is a way of *seeing deliberately*, and *deliberating on how to see* science and politics. Other scholars have approached the subject of stem cell research from a variety of perspectives. The

chapter will clarify why one more study is needed. Finally, I offer an outline of the main arguments and chapters.

Starting off by describing my first experiences with stem cells and my struggle with how to turn this into a topic is not only pedagogically sane when introducing complicated matters such as stem cells and theory of science; it also reflects the process of research and will permeate the consequent use of methods, theory, and progress of investigation. Instead of reconstructing the empirical, theoretical and methodological boundaries – as if they were there from the start – the reader is invited to follow my own perplexity when approaching an empirical situation and some theoretical tools.[1] In this respect you are invited to a work in progress together with me: A doctoral student in theory of science who discovers stem cell realities by acquiring, using, and modifying theoretical tools.

Taking the first steps with stem cells

The title is itself confusing. In order to sort out the first half of *Pluripotent Circulations* I consult an on-line dictionary (Oxfordreference.com). There are two entries for the term "pluripotent". One states that "pluripotent" is an adjective "(of an immature or stem cell) capable of giving rise to several different cell types" (The Concise Oxford English Dictionary 2004a). A pluripotent cell can produce many different cell types. For this to make sense something has to be said about cell types ("immature or stem cells"), and how cells develop from other cells. The other entry on "pluripotent" in the same dictionary is a hyperlink to an explanation of the term "stem cell":

> A cell that is not differentiated itself but can undergo unlimited division to form other cells, which either remain as stem cells or differentiate to form specialized cells. For example, stem cells in the bone marrow divide to produce daughter cells that differentiate into various types of immune cells (e.g. monocytes, lymphocytes, mast cells). Also, stem cells in the intestine continually divide to replace cells sloughed off the gut lining. *Embryonic stem cells*, such as those taken from an early human embryo, are capable of differentiating into many or all of the various tissue cells found in a fully developed individual – they are described as *pluripotent*. (The Concise Oxford English Dictionary 2004b)

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[1] My view of the research process and mode of presentation thus in many ways resembles Law's Method Assemblage in his *After Method*, 2004.

"Differentiated", "specialized", or "mature" cells are the cells that make up most of what we usually see of our bodies, such as skin, hair, or eye cells, or various type of blood cells. Undifferentiated and immature cells are the mother and father cells of the specialized cells. One of the daily occasions when we can "see" the work of stem cells is when a wound is healing. The new cells that seal up the wounded tissue are produced by stem cells. However, new cells are continually being produced all over the body by various stem cells. All cells have come from stem cells.

"Pluripotent" was not mentioned in the above lines until the later third. It is only after the introduction of a specific type of stem cell that pluripotent is mentioned: "Embryonic stem cells". Unlike the first-mentioned stem cells, the embryonic stem cells are said to have the capacity to become "many or all of the various tissue cells found in a fully developed individual". According to the dictionary, pluripotent is used to signify this capacity in contrast to the capacity of other stem cells. Due to their "pluripotency" (the noun-form of the adjective "pluripotent") the cells can become many more cell types than other stem cells. On the University of Wisconsin website this is graphically presented as a flow from an in-vitro fertilized egg (i.e. an embryo resulting from the combination of an egg and a sperm outside of the body), to a Petri-dish, and then to specialized tissue cells.

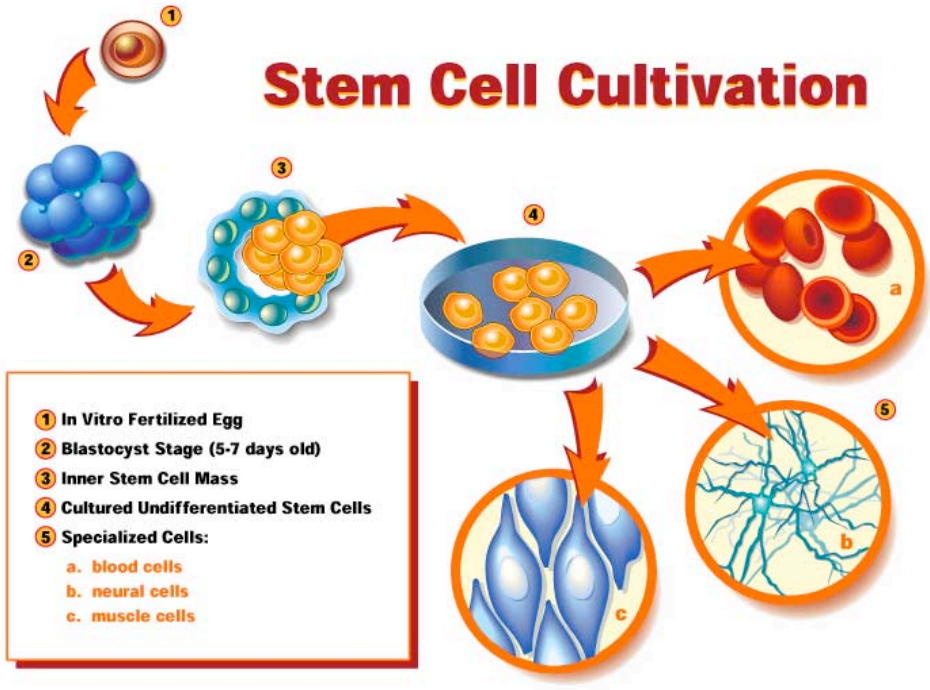

Figure 1: Stem Cell Cultivation. (Reprinted by permission of the University of Wisconsin. Copyright held by the University of Wisconsin Board of Regents).

While a full explanation of *Pluripotent Circulations* will not be available until the final chapter, a first, preliminary meaning can be derived from my initial experiences with stem cells. Those experiences are quite recent. It may be a comfort for the reader who happens to know little or nothing about pluripotency to learn that roughly five years ago (in late 2000, give or take six months) the author of this study had never heard of this property of stem cells (or of stem cells in general).[2] In retrospect, pluripotency and human embryonic stem cells became a part of my imagination – and soon more than that – mainly due to President Bush's decision in August 2001:

> Based on preliminary work that has been privately funded, scientists believe further research using stem cells offers great promise that could help improve the lives of those who suffer from many terrible diseases – from juvenile diabetes to Alzheimer's, from Parkinson's to spinal cord injuries. And while scientists admit they are not yet certain, they believe stem cells derived from embryos have unique potential. (Bush 2001)[3]

Bush used prime television time to inform the country about stem cells and a long awaited decision on federal funding for research on hESCs. In practice, no Federal funding had been possible. After two and a half years of debates, policy statements, panel deliberations, drafts, and guidelines, Bush announced his policy. Hearing this on the news in Göteborg, Sweden, carried a special meaning. When Bush declared his decision he referred to a number of stem cell "lines":

> As a result of private research, more than 60 genetically diverse stem cell lines already exist. They were created from embryos that have already been destroyed, and they have the ability to regenerate themselves indefinitely, creating ongoing opportunities for research. I have concluded that we should allow federal funds to be used for research on these existing stem cell lines, where the life and death decision has already been made. (Bush 2001)

Stem cells seldom come alone.[4] After being "derived from human embryos" (in the terms of the practising scientists) they are cultured in little

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2 It is difficult to recall ignorance, but five years is an honest guess.

3 When no pages are mentioned in references following upon quotations, it implies that full information is available in the bibliography. In this case there are no page numbers in the source.

4 Some would say it is *necessary* that the cells come alone. The need for purified populations has been crucial in the last few years' debates about the

plastic "batches". If the researchers are lucky and/or skilled the cells multiply, and new batches are filled with the solution in which the – for the bare eye – invisible cells are floating. These multiply and result in new batches of cells-in-solution that all stem from the same original cells and the same embryo. Each such pedigree of cells is called a line. Of the 60 stem cell lines mentioned by Bush, the largest joint number of lines existed in Göteborg, where I was living and doing graduate studies.

In the decision, these already existing lines were very important, since they "could lead to breakthrough therapies and cures" without having to destroy more of the human embryos that served as sources for the stem cells. Bush described his decision as a balancing act between the concern for these embryos and the possibilities to alleviate suffering. By not funding any new production of hESC lines no more embryos would be destroyed. By funding the already existing cell lines from laboratories (some thus situated also outside of the USA) the researchers would have sufficient numbers of cells to explore the therapeutic promises.

However, I would not stay beside the 24 important stem cell lines in Göteborg the coming year, but leave for the USA for a one-year stay at a center for philosophy of science. My advisors were sure to let me know that I could still redirect my dissertation work in theory of science to another subject – for instance the subject of stem cell research.

Upon my arrival I soon realized that such research was being done on the same campus half a mile away from my temporary office. Six months after hearing Bush's decision, I connected with the main researchers and was allowed to observe their work and listen in to their conversations. These cells were not stem cells from human embryos, but from adult bone marrow. However, the laboratory claimed that their stem cells had very similar capacities to the pluripotent embryonic stem cells. Another term for such capacities in adult stem cells is "plasticity". *High* plasticity means more potency, maybe even pluripotency. The alleged high plasticity of these cells attracted interest from other laboratories at the university, nationally, and internationally.

I interviewed people from these other laboratories, but mostly I followed one scientist in his daily business of doing research. I looked at his interaction with colleagues and his boss. I looked at the mundane tasks and often boring routines he had to perform in order to secure the life of

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appropriate criteria for assessing claims about adult stem cell plasticity, Weissman et al. 2001.

his cells. After a week there was "the journal club", a weekly event where the members of several groups of the stem cell lab gathered to discuss a current paper. People were a little upset. Two papers had challenged the results of the lab.

> Y: It doesn't happen in vitro. Can we rule out that it happens in vivo?
>
> X: Co-culture of adult and embryo cells in this paper […] that's my biggest concern.
>
> [---]
>
> X: It is a contrived system. No one has ever used such a system to prove plasticity. It's speculation! Reporters called me 2 weeks ago about this [before the publication].
>
> Z: Can they do that?
>
> X: They can't, but *Nature* can.
>
> Y: Burden of proof is on them. But, they put a question mark on a lot.
>
> A: Show the karyotype and you ward off such doubts?
>
> [---]
>
> X: They didn't do it in vivo.
>
> Y: So, it's a long step to that question mark. Dr. X, Do we have to change our routines?
>
> X: GFP + cells and put it in blastocyst. Stain both and get independent staining, not from both. That would do it.
>
> [---]
>
> B: FISH-analysis?
>
> X: The problem is you cut through tissue so some things could be on the other side.
>
> C: Tissue sections are hard.
>
> (Laboratory notes 2002)

The atmosphere was tense. Afterwards I went back to see what the papers said.

> the altered phenotype does not arise by direct conversion of brain to embryonic stem cell but rather through spontaneous generation of hybrid cells. The tetraploid hybrids exhibit full pluripotent character, including multilineage contribution to chimaeras. We propose that transdetermination consequent to cell fusion could underlie many observations otherwise attributed to an intrinsic plasticity of tissue stem cells. (Ying et al. 2002: 545)

If the first part of the quotation is too complicated, then focus on the latter. The laboratory I was visiting was just about to publish a paper about remarkable "plasticity of tissue stem cells". Ying et al. suggested that such observations could be due to a fusion of embryonic cells and adult cells. If so, the plasticity observations – and the adult cells – would basically be less valuable. In the other paper the speculative nature of the "fusion experiments" was admitted:

> Contribution of cell fusion to apparently transdifferentiated cells *in vivo* is currently pure speculation; however, our data raise a warning to the overzealous trend in stem cell research to conclude transdifferentiation or dedifferentiation of cells without careful examination of genotypes. (Terada et al. 2002: 544)

Usually, scientific papers are written and published to suggest something new, or at least combine some things already known in a new way. Studies aiming to falsify other results are quite uncommon (pace Popper). Here were two papers that, based on preliminary experiments, *speculated* on the inadequacy of *other findings*. At a conference a few days later in Colorado the main author of the first paper (Ying et al.), Austin Smith from Edinburgh, appeared and presented a paper. The room was full of excitement and people grabbed the microphones afterwards to ask questions. Jonas Frisén, neuro stem cell researcher, from Karolinska, Sweden, who had reported on plasticity himself asked:

> Frisén: Have you checked other plasticity work? If they show hyperploidity?
>
> Smith: No we haven't done that. As you know our interest is in embryonic stem cells…
>
> (Laboratory notes 2002)

Smith presented his results to challenge research, beyond an actual interest in plasticity and the adult stem cells. Furthermore it was not himself involved with the research.[5] What was this about?

As soon as I attempted to understand my observations in and around the laboratory, I realized that stem cell research in America needed more than a laboratory study. The laboratory was immersed in references and "context". Therefore I turned to politics.

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[5] Though, he was to be involved in it. On the same occasion he announced that his center in Edinburgh advertised a lectureship in adult stem cells, Laboratory notes 2002.

Returning to the political stage, which had awoken my interest from the beginning, merely looking at the social groups was not enough. The standard categories of American politics – pro-life vs. pro-choice – did not suffice.[6] The questions massed above my head: Why did the Republican pro-life President partly endorse research on embryos (although with strong restrictions), in spite of his election promises and pro-life opinion? The ethical and political disputes could not overshadow the achievements of the hESCs, possibly even "success". What was the big attraction of the hESCs and what was the role of plasticity in the lab I was visiting?

In the strictly biological sense pluripotent is an adjective: "(of an immature or stem cell) capable of giving rise to several different cell types" (The Concise Oxford English Dictionary 2004a). It is illustrated above (Figure 1) by the flow from embryos, to Petri-dishes, and to multiple tissue types. What attracted me about stem cells was, however, not only their *biological pluripotent* capacities. Equally interesting was that the pluripotency seemed to influence people and make them important. The cells had a *political pluripotency* (metaphorically speaking):

> The issue of research involving stem cells derived from human embryos is increasingly the subject of a national debate and dinner table discussions. The issue is confronted every day in laboratories as scientists ponder the ethical ramifications of their work. It is agonized over by parents and many couples as they try to have children, or to save children already born. (Bush 2001)

When approaching the issues of stem cell research a number of people played important roles, most visibly President Bush, but also ethicists, parents, and patients. Bush's decision was televised and watched by millions. I learned about it thousands of miles away. It even caught my advisors' imagination and made them suggest that I could still redirect my dissertation. In my contacts with the laboratory, I saw how pluripotency and plasticity were bringing researchers at the university and from outside laboratories together. Sometimes these meetings were more critical than approving. In any case, people's lives were redefined. The "political pluripotency" I had noticed, pointed toward other flows than those illustrated on the University of Wisconsin website. The stem cells I wanted to understand did not only flow from embryos to multiple tissue

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[6] Pro-life is a position and movement against abortion. Pro-choice is the opposite. See Chapter 2.

types of the human body, but also *circulated* between political bodies and multiple other actors in the wider society. There it is, the title: *Pluripotent Circulations* in one phrase sums up my initial perplexity, and interest in stem cell research in the USA as being both biological and political.

My first steps into stem cell research were prompted by seeing Bush on the news, which led me to the laboratory. Leaving the lab, my empirical concerns were to understand the struggles and reality that it was involved in. So much was already in place prior to Bush's decision. My curiosity soon homed in on the circulations that preceded it. This curiosity ultimately led me to the developments of assisted reproduction and fetal tissue research in the 1980's and 90's – although they may seem to be far from the 2001 situation. The historical inquiries of this study stop just before "my" laboratory became involved in the political and scientific dynamics subsequent to August 2001.[7] This study thus does not draw on the data from the participant observations (and it does not further analyze Swedish stem cell research and its importance for Bush's decision).

Turning stem cells into a topic

After these elementary observations on stem cells my question was how to turn them into a topic. This is an important question, since there are many possible ways to turn stem cell research in the USA into a topic. I am not a biologist, not even a natural scientist. I cannot approach stem cells by e.g. making a "southern blot" and then writing a paper based on the result.[8] My training is in theory of science.

There are several ways to define theory of science. In a first basic respect, theory of science is everywhere people see and do science. Etymologically, theory comes from the Greek *theoreia* whose meaning is, to see or comprehend. Seeing is thus in a derived sense theoretical. In line with, for instance, hermeneutics and paradigm theory, I believe that seeing always presupposes or works together with perspectives. This roughly amounts to what hermeneutics calls pre-understanding or pre-judgment or what the historian of science, Thomas Kuhn has called paradigm. In Karl Popper's words, observations are not neutral, but theory-

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7 For the temporal limitations of the study, see more in the next chapter.

8 *Southern blotting* is the detection of DNA fragments by gel-transfer hybridization. It is a common method in stem cell laboratories.

laden, theory-impregnated. In this sense, theory of science is pursued by every human being looking at science, whether or not s/he is aware of it.

There are also professionals trained in seeing or studying science who have therefore elaborated specific *theories of science* for this use. A number of disciplines have studied the (natural, human or social) sciences, for instance philosophy, sociology, history, and anthropology. Within studies of science there are two versions of theory of science, often side by side. First, analysts draw on and expand perspectives on science.[9] The integral elements of a specific perspective are related to each other explicitly. Usually there has been some fundamental idea about knowledge production, about the relationship between knowledge and reality, criteria for truth or truth-likeness, and methods for studying science. Second, when analysts juxtapose, contrast, and/or compare various perspectives and analyze the implications and effects of theories of science they pursue theory of science in another respect: as *meta-theory*, theorizing theories of science, *seeing* their *seeing* of science, as it were. A meta-theoretical inquiry is thus not only to analyze science – by applying various theories of science – but also to analyze the theories of science thereby applied.

Before turning my observations into a topic for a study in theory of science, I surveyed several already existing analyses. I distinguish between three groups of analyses: commentaries (on science, ethics, and politics), popular science writing, and academic work. The first group was found in collections of commentaries. Thus they presented a multitude of voices, rather than a coherent account. The commentaries include books and special issues of bioethics journals (e.g. *American Journal of Bioethics* 2001, *Yale Journal of Health, Law, and Ethics* 2001, Holland et al. 2001, Kiessling and Anderson 2003, Ruse and Pynes 2003, Snow 2003, Waters and Cole-Turner 2003). To me these commentaries were a probably necessary entrance to stem cell research and politics in the USA. However, as a theorist of science I could not avoid seeing their implicit theory of science. Although including diverse contributions from various commentators (such as ethicists, politicians, and scientists) they usually share one common way of seeing stem cell research. In spite of the

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[9] A thoroughly incomplete list of theories of science could contain logical positivism, hermeneutics and Critical Theory, and individual theorists such as Ludwick Fleck, Karl Popper, Paul Feyerabend, Imre Lakatos, or Thomas Kuhn.

diversity of views they usually divide the world into two realms: the closed realm of science and a more open-ended one of politics and ethics.

One example of this is James Thomson's chapter in a collection, *The Human Embryonic Stem Cell Debate: Science, Ethics, and Public Policy* (Holland et al. 2001).

> Human embryonic stem (hES) cells capture the imagination because they are immortal and have an almost unlimited developmental potential. After many months growing in culture dishes, these rather nondescript cells maintain the ability to form cells ranging from muscle to nerve to blood, and potentially any cell type that makes up the body. Their proliferative and developmental potential promises an essentially unlimited supply of specific cell types for transplantation in disorders ranging from heart disease to Parkinson's disease to leukemia. (Thomson 2001: 15)

Thomson, at the University of Wisconsin, is considered one of the main experts on hESCs. He headed one of the two groups that first announced the successful cultures of such cells. Here he starts in the public imagination, the effect of which is explained with reference to the immortal and developmental properties of the cells. These are harbored in the culture dishes, and from there Thomson takes the reader to the therapeutic promises for certain diseases. The powers and promises of these "nondescript cells" do not come from nowhere. Thomson anchors the powers of hESCs somewhere outside the laboratory and outside the scientist. The powers arrive at the scientists' culture dishes because of the early embryo.

> To understand hES cells, it is necessary to understand something about the basic properties of early human embryos. (Thomson 2001: 15)

> It is the developmental plasticity of early mammalian embryos that allows the derivation of embryonic stem (ES) cells. (Thomson 2001: 17)

The early embryo "allows" the scientist to get at the stem cells. If the early embryo were not so flexible in its developmental program, the scientist would kill the cells when removing them from the inner room of the developing embryo, the inner cell mass (ICM; see stage 3 in the above Figure 1). Fortunately, the flexibility (or the plasticity) allows an arrest of the cells' march toward maturity, in the scientist's culture dish.

> because of the developmental plasticity of mammalian embryos, if the ICM is taken out of its normal embryonic environment and cultured under appropriate conditions, ICM-derived cells can proliferate and replace themselves in-

> definitely, yet maintain the developmental potential to form any cell type. These pluripotent, ICM-derived cells are ES cells. (Thomson 2001: 17)

Thomson ties together the public imagination, the promises, and the therapeutic potential, with the scientists' culture dish and ultimately the embryo. Although he started with the former aspects, the direction is clear: All the promises and applications come from the cells. The latter are, in turn, the "pluripotent ICM-derived cells" from the early embryo. The movement is unidirectional and unilateral. The origin of properties and promises is the embryo that (or who) has allowed, and let go, of the cells into the hands and dishes of the scientists.

Most of the commentaries assume that the therapeutic promises are harbored in scientists' culture dishes because of the developmental features of the early embryo. The ethical appropriateness, or the comparative strength of hESCs may be challenged, but the nature and capacities of hESCs, as presented by Thomson above, are not denied or questioned. This is an indisputable reality of hESCs, based on cell lines in culture dishes, embryo development, and a unanimous community of scientists.

Another reality is more diverse and heterogeneous, at least on the surface. Thus, it is not enough to let one representative speak, as in the case of Thomson. There is not one voice here. The ethics usually contains questions about the status of embryos, when life begins, and how to balance the life of embryos and the lives of future patients. Erik Parens, associate at the Hastings Center in New York (a leading bioethics center) presents the arguments:

> The major argument for doing embryo research is that it promises to reduce human suffering and promote well-being. The *major* argument against using embryos for research is that they have the moral status of persons and thus should not be destroyed, no matter how great the human benefit. (Parens 2001: 40)

Parens bases the conflict over hESC research on two major arguments about how to use the hESCs that – in accordance with the scientific reality – are already there. David A Prentice, Professor of Life Sciences and Medical and Molecular Genetics, Indiana, who has advocated to slow down hESC research, claims:

> The real root of the debate is this: What does it mean to be human? As we look at different forms or stages of human life, to whom will we choose to assign value? Who will decide, and who will benefit, from these value choices? (Snow 2003: 20)

Parens and Prentice are in one sense saying the same thing. It comes down to people's views and stance on what it is to be human, and who is to benefit from the research. Representatives of religious communities suggest guidance for people based on religious faith and on philosophical thinking. Although much of this guidance relates to "how God is", "what humans are" or "what good actions are" many acknowledge they are explicitly oriented toward people and their decision-making capacities. Even when representatives have a firm position they do not deny that there are other disagreeing views. Frank E Young, an ordained evangelical minister who has served at the US Department of Health and Human Services (DHHS), participates in a third volume of papers and explains how political decisions should follow from some people's views:[10]

> Many people consider this research immoral, illegal, and unnecessary. Therefore, it is imperative to proceed cautiously. Federal funding of research using human embryos or pluripotent cells derived from them would be inappropriate until further resolution of the ethical issues has been achieved. (Young 2003: 213)

Young opposes the federal funding of hESC research. This had been a crucial political question for many years, linked to people's views. Bioethics Professor Arthur Caplan, also chairman of the advisory committee to the DHHS and the FDA, supported federal funding based on a tradeoff between the harm to embryos and the benefits and the good to patients.

> I do not think we are in the realm of absolutes. I think we need judgment. I think we need virtues. That is why we need public funding, public accountability, to make the right tradeoffs. (US Senate 1999b: 37)

Caplan explicates another reality of hESCs beyond the scientific: a realm of arguments, values, virtues, faith, judgment and people's decisions. Many actors would oppose calling the ethical disputes and the political controversies the reality of hESCs, but they maybe recognize them as the realities *in which* hESCs *are*. Those realities are sometimes related to the abortion wars, and the history of embryo research in general. Following the many accounts of the science, ethics and politics of hESCs the stem

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[10] Young is also a former commissioner of the federal supervisory authority, the Food and Drug Administration (FDA), and at the World Health Organization (WHO).

cells appear in at least two realms. While the ethics and politics are kept open-ended in the commentaries, the realm of science is closed. In the scientific realm hESCs are matters of fact, that via culture dishes in the scientists' laboratories, because of their particular properties, are finally conceived as getting to patients through transplantation therapies. In the ethical and political realm (or realms) hESCs are matters of opinion: people can express their opinions whether to use or fund the hESCs or not, and how.

The seeing implied in these commentaries thus divides the world. More than pluripotent *circulations*, pluripotency stays in the scientific realm separated from the political and ethical uncertainties. The commentaries usually separate stem cells that can be explained and represented (by scientists), from their application and reception (by ethicists, politicians, and patients).

This way of seeing stem cell science and politics is common, perhaps even a common sense one. At least it seems so, judging from a second group of accounts, viz. popular science writing. In contrast to the commentaries, the popular science texts, however, attend to the history of stem cells. Just as in the above commentaries, science is closed off from the uncertainties and disputes in the outside world. There may be disputes, but they are misunderstandings and deviances from the rational pursuit of science.

For natural reasons there was initially very little popular literature on the issue: The stem cells lived quite hidden from public interest until 1998. One of the first to give an easy-to-read introduction to general stem cell biology was Ricki A. Lewis's *Windows On the Life Sciences* (2001), of which stem cells were one of eight windows. Another popular-science writer, Ann B. Parson, goes as far back as the 1700's to understand what stem cells are in her historical account *The Proteus Effect* (2004). This is an interesting work, not least because of Parson's empirical material, which to some extent consists of interviews with (what are often considered to be) key stem cell researchers. Robin Marantz Henig's *Pandora's Baby* (Henig 2004) is a history of in vitro fertilization (IVF) about the "test tube babies" that "sparked the reproductive revolution" (following the book's subtitle). Thus it does not concern stem cells specifically until its final chapter, where a connection between IVF and stem cells is mentioned. Parson and Henig are two examples of popular science history relating to hESC research. To the extent that these authors uncritically take up and

convey definitions of stem cells they are part of the empirical material I draw on.[11]

These two groups of literature thus represent a similar way of seeing stem cell research and politics by dividing the realms of biological pluripotency and political/ethical uncertainties. In addition, stem cell research is analyzed without a theoretical awareness. The noted "division of realms" is *my* explication of their implicit theories of science. Within the *discipline* of theory of science there are other perspectives that would result in another topic of study. Furthermore, these perspectives are explicitly and deliberately applied to the analysis of scientific activity. One such "playing-ground for perspectives" is the field of Science and Technology Studies (sometimes Science, Technology and Society) or just STS. According to work done within STS, research can be as heterogeneous and open-ended as the ethics and politics above were. Since the 1970's this emerging inter-disciplinary field has gathered an increasing number of scholars and researchers studying science and technology. They have done so as if science were not a closed box, but one possible to open up. Approaches used in STS have, for instance, been the Sociology of Scientific Knowledge (SSK), the Social Construction of Technology (SCOT), Social worlds theory, and Actor-Network Theory (ANT).[12] This field has inspired meta-theoretical work at the home department of this study.[13] My work is congruent with these reflections on the theories of science used within STS.

Of the many approaches available, I will (in the next chapter) select to draw mainly on the theory of science presented by ANT, and more specifically Bruno Latour's version of this. This should be obvious from the subtitle of the book and it will add a second more theoretical dimension to the title. According to Latour, the capacities or powers of entities (whether cells or Presidents) are not *within* that entity, but happen as a

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[11] However, they usually fall outside of the empirical territory by not being *prior to 2001*. To the extent that these authors convey empirical material about the situation prior to 2001, I will use it as I use other materials. See more below, Materials and Methods in Chapter 2.

[12] For more full-length accounts of the many perspectives and tools used within STS, see Jasanoff, et al. 1995. For collections of seminal papers see Biagioli 1999, and for introductory works where SSK and SCOT also are outlined see Hess 1997, Sismondo 2004, Yearley 2005.

[13] For examples of this, see Bohlin 1995, Bragesjö 2004, Hallberg 2001, Kasperowski 2001, Landström 1998, Larsson 2003.

continuous movement between a number of things and people. Latour has spoken of these movements as circulations (1999b: Chapter 2). He has also spoken of the interplay between science and society as a circulatory system (1999b: Chapter 3). Seeing science in this way goes explicitly against any partition of science, ethics and politics.

The commentaries above are examples of what Bruno Latour calls "purification" and are part of a "modern" view of science and society. Purification, in short, is the analysis of knowledge and things in terms of either (1) the external reality of nature, (2) the social bonds, the "forces that structure society" (Latour 1993: 88), (3) signification and meaning "that make up the stories that we tell ourselves", "the great narratives that dominate us infinitely" (p. 88), or (4) the Existence (or Being) as opposed to all the existences. In relation to the phenomena at hand Latour seems to ask us to stop debating about the status of embryos or stem cells in terms of what they "really are" in the Bible or in the Petri-dish, or merely with reference to their social role, or as an issue of discourses shaping the meaning of "embryo", or in comparison with Being itself (God?) as opposed to the cold, disenchanted technoscience. Seeing science and politics as involved in circulations across those realms is one alternative to the "modernist purification". Circulations are thus not only a general metaphor, but can be part of a theoretically informed attempt to look differently on stem cells and their pluripotency – as a movement between a number of entities.

Putting ANT to work on stem cells in the USA thus amounts to seeing circulations. It is an attempt to avoid the separation of e.g. discourse and social bonds from "external reality". My fascination with stem cells was tied up with my observation that these cells seemed to make a difference among so many people. I called this the stem cells' "biological and political pluripotency". However, it is no surprise that many of the people that go out of their way to oppose or support such research have never encountered a stem cell in a petri-dish, in a laboratory or in a clinic. This suggests that I was wrong to assume that *stem cells* were making a difference among e.g. politician or ethicists – or I was merely using an imprecise figure of speech. The "political pluripotency" was not due to stem cells, but to the *representations*, or *receptions of* stem cells. However, when spending time in the laboratory it became clear to me that even laboratory personnel, who could be said to handle the stem cells in their daily business, were not dealing with them as you handle a spoon, a dog, or a friend. On a daily basis they claimed to pour stem cells

from one batch to the other, put them through machines, and even "see" the stem cells in a microscope. But, all of these meetings were *highly mediated by other things*. These machines and techniques were trusted means to handle cells – just as Bush and the ethicists trusted that what they learned about stem cells was correct when commenting and making decisions.

I am making a philosophical suggestion here, about reality. Batches are not necessarily closer to reality than political documents. They are all part of what will later be called *sociotechnical reality* – as opposed to biology separate from politics, or natural reality separate from social reality. Instead of drawing a line between what intermediaries are, and are not, giving access to the real stem cells, ANT talks of *articulations*. Articulations are the combinations performed of e.g. stem cells with other things or people, such as microscopic light or Federal funds. Bush is articulating stem cells with his televised speech, just as well as Thomson is articulating stem cells in his lab together with microscopes. Thus, in order to access the sociotechnical reality of stem cells and the pluripotent circulations I will be *analyzing the articulations of stem cells*. Much of the next chapter will be spent on explaining Latour's version of ANT, including the notion of sociotechnical reality, the role of articulations, and the concepts of obligatory point of passage and boundary objects.

In this study, I am not only fascinated by stem cells, but also with the view of science provided by ANT. In relation to many of the existing popular science texts and the collections (about science, politics and ethics) ANT provides another way of seeing hESC research and politics. An underlying aim of the whole study stems from being meta-theoretically aware and encountering stem cells via the lab and the literature: A drive to see stem cells differently. This aim is summarized in the title as a matter of pluripotent circulations.

Putting ANT to work on stem cell research and politics is an attempt to exercise a different seeing than the (perhaps commonsensical) seeing exemplified in the commentaries and popular science writing. The task is however not a straightforward one. My choice of empirical material and ongoing critique of ANT call for meta-theoretical elaboration of ANT.

Had I stayed in the lab, an ANT approach would have been natural. Latour has urged students of science and technology to follow the scientists. I did not do this. I went back to Bush's decision and tried to understand the situation prior to August 2001. More specifically, I attended to the role of stem cell research within a public and political dynamics

(and not as, e.g., within a laboratory dynamics). There are at least four reasons for this choice. The first reason came from my puzzles about the preceding dynamics. There seemed to be more to the struggles around plasticity and pluripotency than I could find in the lab. Second, the political ramifications of hESC research were tangible upfront – as in Bush's speech – and they attracted my interest. As I did come from Sweden, the heated public debates about the life sciences were something new. Third, because of the lack of Federal policies the stem cells existed in the US public and political debates just as much as (or more than) they existed in US laboratories during this period: hESCs were still quite modestly researched in the USA. There were only a dozen hESC lines out there. A final reason has to do with the underlying aim of seeing differently. To display the effects of another way of seeing, the most appropriate topic is a well-known one. When observing something never seen before, the very act of seeing, or the differences in seeing, are much harder to detect. It is when ex-patriots return to home ground after a time abroad that a change in seeing suddenly can be noticed. If ANT were to be applied to a completely new material the result would be a *completely different phenomenon*. The politics and public debates are therefore especially interesting to analyze from an ANT perspective. However, ANT has not been extensively used to cover a predominantly public and political dynamics. The empirical case thus requires an elaboration of ANT. This meta-theoretical task converges with another one.

ANT has been criticized within STS. One criticism has been that ANT studies have given a human-centered view of how research takes place.[14] Critics have argued that though such a view of science is sometimes called for, it is not always useful. They have suggested more distributed models for understanding the flows between the various participants in the production of knowledge. This critique thus also uses a flowing, circulatory metaphor. Taking this critique seriously will add to the notion of circulations already introduced. Furthermore, it constitutes a second meta-theoretical task that puts ANT on the operating-table.

The relevance and contribution of this study in relation to previous research

In relation to the existing popular science and commentaries on stem cell science, ethics, and politics, a *first area of relevance* for this study can now

[14] For the critique raised by proponents of SSK, see the next chapter.

be stated: The relevance consists in approaching stem cell research and politics in terms of a different seeing which does not divide the biological and political reality of stem cells. Furthermore, the ANT perspective is applied with a meta-theoretical awareness. The title indicates this by drawing on Latour's notion of circulations.

ANT is, however, not the only way to see stem cells differently. The discipline of *Theory of Science* as well as STS provide plenty of other perspectives. In addition, there are other approaches in academia. Stem cell research has triggered a number of academic studies. I will focus here on studies done in (or in the proximity of) STS. Thereby I am leaving a survey of, e.g., the bioethical literature to professional bioethicists. There have so far been relatively few STS-related publications on stem cell research, although the number is increasing. Some of these include scientometric studies of how words occur in media and scientific reports (Leydesdorff and Hellsten 2006), various "framings" of embryonic stem cells (Hviid Nielsen 2005, Nisbet et al. 2003), how the boundaries of human life and between politics, science, and ethics are managed (Leinhos 2005, Waldby and Squier 2003) and cross-disciplinary analyses on stem cells in global and/or national contexts (Salter et al. forthcoming, Koch and Høyer in press).

On-going projects that have not yet resulted in publications have been presented at conferences. There have been several sessions of papers devoted exclusively to stem cell research at conferences held by the Society for Social Studies of Science (4S), and the European Associations for the Study of Science and Technology (EASST). At the 2004 4S/EASST conference in Paris, there were three sessions of papers (4S/EASST Conference 2004: Sessions 19 and 114).[15] Few of these papers concerned American politics and hESC research (Gottweis 2004, Hogle 2004), and even fewer included a historical dimension. There is at least one UK-based project on the historical emergence of hematopoietic (i.e. blood-forming) stem cells (Brown et al. 2005). In her *Whose View of Life?,* historian of biology Jane Maienschein has traced the present-day "hopes and hypes" of stem cell research back to early cloning experiments and genetic research (Maienschein 2003). This is not strictly STS and not popular science, but a historical study written also for a non-academic reader.

There is to my knowledge no book-length study done within STS on the public and political dynamics of hESC research in the USA drawing

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15 *Three* since session 19 was a double session.

consistently on ANT. In popular science writing, authors have traced the historical emergence of stem cell research. This has not been done from an STS- and/or ANT-inspired perspective. In the present study I do not stop at the events immediately preceding 2001, but go backwards to events in the 1980's and 90's within assisted reproduction (in vitro fertilization) and fetal tissue debates. These processes were not directly tied up with stem cell research at the time. I have not seen any STS studies tying together those processes and the negotiations over stem cell research at the turn of the century. A *second area of relevance* for this study can thereby be stated: Within STS, it is one of the (so far) few book-length studies drawing on ANT to understand the historical emergence of the public and political dynamics of stem cell research at the turn of the 20th century.

A *third area of relevance* concerns the meta-theoretical contribution and elaboration of ANT-according-to-Latour. The empirical case challenges ANT's analysis of public and political processes. This study also makes ANT into a topic by considering the critique from more distributed approaches. It will thereby put the metaphors of circulations into more explicit use than earlier.

By now the title and subtitle should be a little less opaque. The detailed aim presented when starting this chapter (in the second paragraph) will need the next chapter to be fully understandable. (To explore ANT in order to understand the sociotechnical reality of hESCs in the USA prior to August 2001 – in particular with regard to the public and political dynamics.) However, by now it is clear that the aim is the result of my meta-theoretical interests oriented towards both actor-network theory as well as stem cell research and politics in the USA.

Outline

The four first chapters form *Part One*. More than being all-encompassing analyses, these chapters are exercises in how to understand the sociotechnical reality of hESCs 1998–2001.

The first part of Chapter 1, *A Meta-Theory Assemblage: Methods, Materials and Theories of Science* continues this Introduction, by assuming that hESC research and politics as a topic is not something given. It may be many things, depending on the perspective. By juxtaposing possible analysts, and adjacent constructions of topics, the added value of selecting ANT is suggested. After making this selection the second half of the chapter presents my modifications of ANT. Instead of being left alone, ANT beco-

mes a topic for meta-theoretical explorations. It is tossed, tried and turned by means of the existing critique. Lastly I present and justify my choice of empirical materials, i.e. political and public texts, and how to approach them.

In Chapter 2, *Attempting an Obligatory Point Of Passage: Federal Funding of Human Embryonic Stem Cells,* I approach probably the most striking phenomenon for a foreigner beginning to look at articulations of hESCs in the USA, viz. the issue of federal funding. Instead of seeing this merely as a struggle between the pro-life movement and liberals together with a biomedical lobby, the articulations of hESCs were of a specific kind, resembling the classic studies of Latour and Callon on obligatory points of passage (OPP). The references to the cells' capacities and therapeutic uses were closely linked to the Federal administration. To exercise seeing differently, I stress both useful similarities, as well as the discrepancies between this case and the classic ones.

Susan Leigh Star and James Griesemer presented an alternative approach to the OPP, to capture a less dominating coordination of actors. Chapter 3, *Outlining a Boundary Object Coordination: Diverse Actors and Multiple Uses*, draws on their approach. By looking for a distributed coordination of boundary objects, instead of the centralized OPP, other things are seen. Articulations of hESCs are thus not only dominant and excluding, but also enabling, and address many actors' needs without total transformation. Again, the analysis is drawing out what it would mean to see the hESCs from a specific perspective, viz. as boundary objects.

Chapter 4, *Theoretical Tensions and Innovations: A Boundary Package in Multiple Loops,* reflects a struggle to make place for the reality of hESCs as seen in the previous two chapters. While those chapters started from two specific and contrasting approaches fully applied as precise and sharp tools, this chapter searches for theoretical convergence – with due respect to the tensions. Whether seen with one or the other theoretical tool, three elements of hESCs are central: pluripotency, transplantation therapies and "spare embryos" are all aspects of the hESCs' flows among diverse actors. Thus combining the empirical findings in one theoretical space gives a preliminary answer to what the reality of hESCs was in the USA, 1998–2001, and ends the first part of the book.

In *Part Two*, this reality is unpacked in order to understand how the sociotechnical reality of hESCs came to be. A first step is to go backwards and look at the hESCs before they became laboratory objects, but were nevertheless entities in official reports and debates. Chapter 5, *A*

Project, its Problems and Prescriptions: The 1994 Human Embryo Research Panel, finds actors engaged in, but disappointed with, the negotiations of federally funded human embryo research. Their references to two of the three hESC elements suggest that the multiple flows of 1998–2001 were set in motion even before 1994. The observations also suggest a specific role for the hESCs, as a solution to the problems of federally funded human embryo research.

In Chapter 6, *Multiple and Partial Stabilizations: The Necessity of "spare embryos", and the Urgency of (Possible) Transplantation Therapies*, two of the elements in the reality of hESCs in 1998–2001 are unpacked. Instead of taking their stability in 1998–2001 (and already in 1994) for granted, I use the debates about in vitro fertilization and fetal tissue research to examine the flows of actors that enabled the stable references. These histories also challenge the traditional notion of stabilization as a gradual increase of linkages.

Drawing on the elements' stabilization the hypothesis from Chapter 5 about the role of hESCs is tested in Chapter 7, *Pluripotent Articulation: Relating hESCs to Embryos and Transplantation Therapies.* The study returns to the period of 1998–2001. Now the focus is not on patterns in circulations, but rather on how hESCs are configured by relating to embryos and transplantation therapies. A central locus for such configuration is the terminological definitions of pluripotency.

In Chapter 8, *Conclusion*, I briefly summarize and pull out some of the key contributions of the study.

1. A Meta-Theory Assemblage: Methods, Materials and Theories of Science

The Introduction laid out the need to see differently as a matter of turning the initial puzzles into a topic. This chapter will enact this on a larger scale by introducing the selected theory of science (ANT), the meta-theoretical interests, and the empirical materials. Together these three components constitute an *assemblage*. My use of this notion – *assemblage* – signals that the theories and questions will have to unfold and change during the confrontation with the empirical material.[16] It is important to redefine what *methods* can be. Methods are not used here to draw up roads with already prepared lanes for the investigation or for a reader. Obviously, an outline was already presented in the Introduction. But my methods, the meta-theory, and the initial material define each other as the study proceeds. They come in a "bundle-in-progress" that continues to bundle and re-bundle (in Law's words, 2004). This is not a methodological failure, but reflects the research process. Again, the reader is invited to follow the work in progress, as I approach the hESCs and the theoretical tools.

Among theories of science

In the Introduction I asked how the elementary puzzles of hESC research could become a topic for a study in theory of science. The answer is that I use ANT. The first part of this chapter further develops this answer by envisioning two other contrasting theories of science, and how they would turn the initial puzzles about stem cells into a topic. This is also a way to outline the added value of ANT in relation to other approaches. However, it must be made clear: The two contrasts are not gi-

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16 To this extent I am inspired by Law's Method Assemblage in his *After Method,* 2004. He in turn credits Deleuze and Guattari 1988 for the notion *assemblage*.

ven the same space or elaboration as ANT is. It will not be a symmetric account, but a pedagogical and heuristic juxtaposition of various approaches. A full comparison between ANT and other approaches will need a study of its own. This first part of the chapter mainly serves the purpose of outlining the characteristics of ANT.

A social realist analyst and topic

I have already announced what interests me, viz. the "biological and political pluripotency" of hESCs. Depending on what theory of science is used, those initial and quite common observations can be studied in different ways by an analyst. To see what happens with the object of study when a perspective is applied, I will draw on SSK and in particular Harry Collins's social realism (Collins 1985, Collins and Kusch 1998, Collins and Yearley 1992a).

The strong program in the sociology of scientific knowledge was launched in the 1970's by David Bloor (Bloor 1973, 1976). He introduced the symmetry principle as one of four main methodological principles: Apparently successful scientific beliefs as well as the "mistakes" can be explained with reference to the same factors. The content – not only the institutional environment – of scientific knowledge was thus opened for sociological analysis. One contribution of this *symmetry principle* was the introduction of an impartiality to the analysis of science. Some things are also left out of the analysis. By explaining beliefs, proponents have made clear that they explain scientists' *representations* or *beliefs* of natural reality, but they do not claim to thereby explain natural reality. The analyst's topic is thus representations of nature, not nature itself (Bloor 1999a: 92).[17]

SSK, as an acronym for the sociology of scientific knowledge, later came to include also the Bath school and the related Empirical Program of Relativism (EPOR) (Collins 1983), the program of discourse analysis (Mulkay et al. 1983), and the reflexivists (Ashmore 1989, Woolgar 1988).[18]

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17 Barnes, Bloor and Henry 1996 is a contemporary textbook written by some of the original proponents of the "Strong Program", covering many of the central theses.

18 See Yearley 2005 for the internal development of SSK, including the Bath School and the Strong Program.

Collins has proposed that social realism is central for SSK.[19] For instance, in a paper co-authored with Steven Yearley he stated:

> Natural scientists, working at the bench, should be naive realists – that is what will get the work done. Sociologists, historians, scientists away from the bench, and the rest of the general public should be social realists. Social realists must experience the social world in a naive way, as the day-to-day foundation of reality (as natural scientists naively experience the natural world). (Collins and Yearley 1992a: 308)

To explain scientific beliefs about nature, the analyst can draw on resources from social reality, such as professional or economic interests. Finding such factors is the sociologist's contribution to the study of science and technology.

By drawing on Collins's social realist version of SSK there are now a few important and decisive notions for turning hESC research into a topic: scientific beliefs, natural reality, and social reality. The first is the topic and the latter is the resource. Natural reality is left for the scientists (at their benches). Based on Collins's theory of science it is possible to envision a *social realist analyst* and the way s/he would turn hESC research into a *topic*. Such an analyst approaching hESC research would not be identical to Collins, but borrow traits from him. *The social realist* is thus my simplification, my temporary construction. It is more elaborate than the common strawman, but hardly doing full justice to how Collins or SSK would have approached hESC research.

One study that displays how *the social realist* would approach a topic related to hESC research is offered by Michael Mulkay. He pursues a sociological analysis in *The Embryo Research Debates* (1997) that fits the symmetry principle. In this book Mulkay analyzed the British parliamentary and related debates on human embryo research, between 1984 and 1990. Scientific results and expectations were brought in, by scientists and others, to argue for a specific regulation of embryo research. Ultimately the UK did get a liberal, and simultaneously very detailed, regulation of embryo research. Mulkay's study was in accordance with SSK by not taking sides. An asymmetric study would have referred to truths versus misconceptions of science. When Mulkay discusses the science of embryo research he lets the scientists speak for themselves without taking sides (Mulkay 1997: especially Chapter 7). Embryo research is not inclu-

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[19] This is Collins's position and not SSK's in general.

ded in his story in order to find out how truth or natural reality was unfolded to scientists or how falsity was ultimately seen through. Scientists' and others' representations of embryo research, whether regarded as true or false, were treated in the same way by Mulkay.

Mulkay exemplifies some aspects of a social realist analysis. However, he does not treat the construction of scientific beliefs. Mulkay did not chiefly study science, but *debates* about science. Within Mulkay's study *the social realist* could ask about the scentific beliefs. One such instance is the consensus among scientists about the benefits of embryo research (p. 106–112). Among the benefits most significant in the debates were the scientists' references to the control of genetic diseases through the selective screening of IVF embryos. Members of Parliament could refer to "the overwhelming weight of scientific and medical opinion".[20] A scientific consensus is a possible topic for *the social realist*, especially if there are cracks in the consensus. According to Mulkay the "major sources of authoritative scientific opinion" (p. 110) were the Royal Society, the Medical Research Council, the British Medical Association, and the Royal Society of Obstetricians and Gynaecologists. These all supported embryo research and the scientific testimonies in the Parliament were unanimous. However, Mulkay tentatively concludes from his conversations with scientists that they probably "were less unified in private than in their public testimony" (p. 198, note 61). *The social realist* would pick up on this and start interviewing people, learning about which results warranted the promises of genetic screening, and then see how professional or other interests affected scientists' beliefs. Typical questions would be: How were the societies and councils assembled? What people were assessing the future benefits and what relations did they have with embryo research? What were their interests?

From an overwhelming scientific consensus allegedly based on scientific facts *the social realist* would find cracks and social interests. This would be the contribution: To not a priori accept scientists' beliefs but to start looking for underlying social processes. While the scientists' subject and explanatory resources are natural reality, the social scientists' subject is made up of beliefs about natural reality analyzed by recourse to the social reality of groups and interests.

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[20] Lord McGregor in the parliamentary debates in 1989 quoted in Mulkay 1997: 111.

By using notions introduced in relation to SSK above, it is possible to analyze the implicit theory of science in Bush's and Thomson's accounts of hESCs (see Introduction). Bush refers to the problems and decisions that stem cell research actualizes. Because of the medical promise and the unique potential there is a need to federally fund the research. When Thomson comments on the popular imagination, he refers to the pluripotency of hESCs and the "the basic properties of early human embryos" (Thomson 2001: 15). Politics and ethics are affected by scientific research. In the terms introduced above social reality is affected by natural reality. The role of humans is to discover natural reality and to make ethical choices and political decisions, such as the one made by Bush. This distribution of work between humans and the natural reality of cells is tangible in a recently published history of stem cells. Science writer Ann Parson's *The Proteus Effect* (2004) goes as far back as the 1700's to understand stem cells. She describes how

> humans have gradually awakened to these distinctive, often camouflaged, cells in our midst and slowly come to recognize their worth [---] Stem cells are basic to the regeneration of every multicellular plant and animal, and as scientists discover more about them, these flexible worlds-unto-themselves should open our eyes to the presence of forces in Nature that are far greater than anything humans could imagine or invent. As neuroscientist Evan Snyder has aptly put it, "Even the dumbest stem cell is smarter than the smartest scientist." (Parson 2004: 8f)

In her thorough and fascinating history of stem cells, Parson is practicing a *theoreia* of science in which hESCs were there all the time in our midst, although camouflaged, as instances of natural forces. hESCs are defined as part of natural reality beyond social reality and human invention. It is an asymmetric analysis. There is no space for professional or economic interests in Parson's account of the unfolding of natural reality before the eyes of scientists, except for the cases where scientists were obstructed from finding the truth about stem cells.

It is unfair to let the contrast with the SSK-inspired *social realist* be borne by non-professional theorists of science. Many philosophers of science have developed more sophisticated versions of natural realism.

Common to these is usually that humans can attain knowledge *about natural reality* in various ways.[21]

One example is Ronald Giere's constructive realism. In his *Explaining Science* (1988) scientific knowledge is not a direct reflection of reality, but comes in models, which correspond to particular aspects of real systems. Giere admits that SSK and other constructivist approaches have contributed to the understanding of laboratories and the process of ongoing research. However, by denying the causal interaction between scientists and the natural world, SSK is missing out on something important. Giere also sees science as constructed, but not *socially* constructed. Giere's version of realism has lately come to focus on how cognition interacts with a complex reality by the distribution of discrete tasks to material, technological, and societal aids (Giere 2002, Giere and Moffatt 2003). Such distribution draws on cognitive rather than social constructs. Although highly involved, the cognitive capacities of humans result in true knowledge due to their interaction with the natural world. For Giere, the success of cognitive systems hinges on the interaction with real systems in nature, e.g. the real stem cells and the truth about them. This is the similarity between Parson's implicit theory of science and Giere's constructive realism: Both theories of science ultimately judge the success of science by reference to natural reality. In this sense natural reality is the ultimate resource, although mediated by many smaller ones, such as scientists' experiments and cognitive systems.[22]

Based on these similarities and Giere's attention to distributed cognition, I envision a second analyst. This *natural realist* is not any specific natural realist. It is an analyst envisioned in order to see how hESC research could be approached by means of a second theory of science. For *the natural realist* there is a stem cell that can be interacted with, or uncovered, by humans through experimental, conceptual, and cognitive designs with subsequent political and ethical decisions to be made. The object of study is science, uncovering and interacting with natural reality, with effects on a social reality. Pluripotency is a feature of nature captured by the scientists and affecting politics. Empirically the study amounts to talking to people who were there when "it" happened, or reading

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21 For collections on natural realist philosophers of science see Boyd et al. 1991, Sklar 2000.

22 Except for the already quoted papers, this paragraph's reproduction of Giere's position is based on his book (1988), mainly chapters 1 and 4.

scientific and news articles reporting on the events. A study could also involve experimental designs in detail, visits to the labs, and observations of the researchers. Nevertheless, the truth/falsity of claims about stem cells would ultimately refer to a natural reality "out there". In this respect natural reality is the ultimate resource for *the natural realist*.

For *the social realist* the main topic could be the parliamentary debates about hESC research, and the beliefs among scientists. Those beliefs would not be explained by recourse to natural reality, but by finding out what professional and other interests determined this consensus. Society is no longer merely affected by the research, but is a resource for understanding how representations have come about. The pluripotency of hESC research would reside in politics or social factors, rather than in any biological objects. Empirically, both analysts start in the same reality. Both of them could start in Bush's decision and Thomson's explanations, but then move in different directions. *The natural realist* would go from the research claims to the stem cells, and then assume asymmetry, i.e. humans would be right when contributing to cognitive systems or to the uncovering of natural reality, but wrong otherwise. *The social realist*'s analysis of hESC research would not move to the cells from the scientific claims, but to the social factors that influenced both (allegedly) true and false representations of the cells. With regard to the interests announced in the Introduction, *the natural realist* does not include Bush's decision in his construction of the topic, and *the social realist* explains biological pluripotency in terms of social causes. The purpose of *the natural realist* would be to explain science in terms of cognitive science, e.g. as a distributed cognitive system. *The social realist* would formulate the topic of this study as explaining beliefs about hESCs in terms of social reality.

An ANT analyst and topic

The third theory of science is actor-network theory (ANT).[23] It started out in the works by Bruno Latour, Michel Callon, and Madeleine Akrich

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[23] Bruno Latour has explicitly rejected the T of ANT.

> Far from being a theory of the social or even worse an explanation of what makes society exert pressure on actors, it always was, […] a very crude method to learn from the actors without imposing on them an a priori definition of their world-building capacities. (Latour 1999a: 20)

Also see Latour 2005: 141–156. As will be evident below, this study is not a typical ANT study.

in the 1980's.[24] Early on, it is possible to see common traits, but the later directions of research have multiplied. ANT has come to denote an open-ended cluster of ideas, methods, books, scholars, and more.[25] It is therefore difficult to claim any main streams or clear boundaries in ANT.[26] Steven Yearley has stated this eloquently in his guide to science studies, *Making Sense of Science*:

> In important ways Actor-Network Theory (ANT) resists summary. It did not set out from a fundamental and unchanging programmatic statement in the way that the Strong Programme or EPOR did. Moreover, Latour's leading methodological injunction is to "follow scientists around", which sounds attractively simple but is also beguilingly vague. Worse still, ANT is a conspicuously moving target. The two authors principally responsible for this approach, Latour and Callon, have followed by no means identical intellectual trajectories […]. (Yearley 2005: 55)

From this "conspicuously moving target" I choose to focus on Latour's production in this chapter.[27] In the rest of the study my ANT inspiration will also come from a few works by Callon.

I take two recurrent motifs to be central in Latour's version(s) of ANT. One concerns the notion of reality, and the other concerns agency. The first redefines the topic of investigation, and the second continues this motion, by emphasizing the wide range of roles played by all sorts of entities.

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24 Some central works from this period are *Laboratory Life* 1979, by Latour and Steve Woolgar; *The Pasteurization of France* [1984] 1988, and *Science in Action* 1987, both by Latour; Callon's "Some Elements of a Sociology of Translation" 1986b; and Akrich's "Beyond Social Construction of Technology" 1992.

25 For some signs of this diversity, see Lancaster University 2005, Callon 1992, Callon et al. 1986, Law 1986, Law and Hassard 1999, Mol 2002, Mol and Berg 1998.

26 For one story about the intellectual evolution of ANT set in an STS neighbourhood – including "Classic ANT", its close kinship relations, and determined dissenters – see Landström 1998.

27 For more about the debates relating to ANT see below on social worlds theory.

Sociotechnical reality

The natural and *the social realist* both pursue epistemological projects in a relationship to ontological sources or potencies. "Epistemological projects" since *the natural realist* examines the cognitive systems that interact with a natural reality that is knowable. His/her topic is the epistemic processes. *The social realist's* topic is beliefs, not natural reality. "In a relationship to ontological sources" since *the natural realist's* reality is the ultimate arbiter of the knowledge attained through cognitive systems. For *the social realist* there are two arbiters depending on whether you are a natural scientists or a sociologist, historian, or in the general public: The latter groups relate to social reality as *the* resource just as the natural scientists relate to natural reality as the resource.

In contrast to these epistemological projects, ANT assumes that the topic of study is reality, not knowledge; not social reality as opposed to a natural reality; not beliefs about natural reality in contrast to actual reality; and not cognitive systems that interact with a natural world out there. In order to understand how ANT can approach hESC research, a first step is to understand what ANT reality is. This will have implications for the ANT resources.

There is no other fundamental reality, or ontological source, except the one that is there to be studied in a number of elements and entities that make up science and society. In contrast to the social and natural reality of *the social* and *natural realists* this seems counterfactual, counterintuitive, or bizarre: Should there not be a reality out there to know? According to ANT, reality is out there all the time. It is just a matter of grabbing a hold. The reality that is *not* there, is an alleged reality *beyond* the reality we find when we are grabbing. It is not something we believe in or not. What is thereby rejected is the notion of a "reality being somewhere else" – but always available to be referred to by philosophers or sociologists (Latour 1999b: Chapter 1).

According to my view, ANT's notion of reality builds on three distinct, but intertwined themes: the *entanglement of texts and materiality*, the *reality-construction of knowledge-production*, and *sociotechnical transformation*. I will exemplify these three themes by drawing on three of Latour's case studies.

The first theme, entanglement of texts and materiality, is visible in *Laboratory Life,* by Latour and Woolgar (1979), and in "Circulating Reference" in *Pandora's Hope* (1999). In the former case study the authors observed that most of the laboratory work was centered on texts. These

texts were, however, based on inscriptions coming from (usually) machines, or *inscription devices*, that combined material substances and turned them into some sort of textual trace, such as a diagram or a graph.[28] By comparing inscriptions and using other inscription devices producing additional inscriptions, and by relating to other texts relating to other traces, the scientists may ultimately be allowed to produce statements about "a substance". The beliefs of scientific articles are the results of step-by-step transformations of mice, forests, and more.

Also "Circulating Reference" exemplifies this fundamental entanglement of signs and materials. According to Latour there was a referential chain leading from the forest of Boa Vista in the Amazon to the claims about "the forest of Boa Vista" in a scientific article:

> Notice that, at every stage, each element belongs to matter by its origin and to form by its destination; it is abstracted from a too-concrete domain before it becomes, at the new stage, too concrete again. We never detect the rupture between things and signs, and we never face the imposition of arbitrary and discrete series of well-nested elements, each of which plays the role of sign for the previous one and of thing for the succeeding one. (Latour 1999b: 56)

By pointing out how the signs are nested in matter, Latour and others have claimed that there are no essential differences between *words* and the *world*. Texts are entangled in materiality, and vice versa.

Another, and second theme, was also tangible in *Laboratory Life*. Natural or material reality is not the underlying cause of knowledge, but a consequence of the inscription devices:

> The central importance of this material arrangement is that none of the phenomena "about which" participants talk could exist without it. Without a bioassay, for example, a substance could not be said to exist. The bioassay is not merely a means of obtaining some independently given entity; the bio-

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[28] John Law has discussed the ramifications of Latour and Woolgar's study for the issue of realism in his *After Method,* 2004. Law neatly summarized and exemplified the workings of an inscription device like this:

> For instance, an inscription device might start out with rats. These would be sacrificed to produce extracts which would be placed in small test tubes. Then those test tubes would be placed in a machine, for instance a radiation detector, which would convert them into an array of figures or inscriptions on a sheet of paper. These inscriptions would be said – or assumed – to have a direct relation to the "original substance". (Law 2004: 20)

> assay constitutes the construction of the substance. (Latour and Woolgar 1979: 64)

Another way to phrase it, is that the scientific process of making knowledge is making reality. "Nothing is known – only realized" (Latour [1984] 1988: 159). When Latour asserts that there is only realization, not a reality to know, this is thus not to say that there is no reality out there. To know something, assumes a binary relation between a knower and something known. If knowledge-production is what *Laboratory Life* claims it is, then the things known are the things produced in the process. The "phenomena [say, a substance] *are thoroughly constituted by* the material setting of the laboratory" (Latour and Woolgar 1979: 64, their italics). Reality is not known, but comes to be.[29]

A third and final theme that helps understanding how reality is not somewhere else is Latour's study of Louis Pasteur (Latour [1984] 1988). I will use this study to make a third point that captures the two earlier ones on a larger scale. Not only are signs entangled in materiality, or material phenomena constructed by means of inscription devices, but scientific claims are also turned into a societal, natural and technological reality – or *sociotechnical reality* – of farming, veterinary, medical and everyday practices.[30]

Pasteur's finding on anthrax microbes became a finding about a sociotechnical reality, since the laboratory reality was spread "all over France"

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[29] There are centuries of debate about the relationship between reality and knowledge. Some accept these case studies as important and relevant and some don't. Some accept some of the claims but not the whole package. Ronald Giere, for instance, has picked up on the case study about Boa Vista, accepting every step of the analysis, Giere and Moffatt 2003: 307f. However, this does not make him accept the metaphysical interpretations: Reality is not the consequence but an independent determinant for cognitive interaction, Giere 1988: 110.

[30] I use this notion – *sociotechnical reality* and *transformation* – to characterize the process described in *The Pasteurization of France*, although (to my knowledge) never used by Latour himself in that text. However, Latour devotes a large part of Chapter 6 in *Pandora's Hope*, 1999, to the explanation of *sociotechnical.* He does so to make a point about the intertwinement of society, nature, technology (and more). This is precisely what I mean when using *sociotechnical reality* and *The Pasteurization* is my example of it. Another reason to use the notion is that it indicates the kinship between Latour's study and Thomas Hughes's work, 1983 (see section about the obligatory point of passage below).

transforming, or "Pasteurizing" the nation (Latour [1983] 1999: 264). There was reality in every step of the process. First, Pasteur and his co-workers picked up on the interests that were there among farmers and hygienists, and then went to the field to gather bits and pieces from the realities of cattle farming (Latour [1983] 1999: 260). Second, the laboratory conditions and methods enabled Pasteur and his disciples to see more of the microbes than out in the dirty and unordered farm situation. Third, by a series of operations Pasteur extended his lab to the outside world. In field trials, in the later transfer of vaccines, in new practices, such as disinfection and inoculation, the instruments and the phenomena in the lab were transferred to the farms. The "nature" of microorganisms and the "society around" the laboratory were constructed in the same process. Pasteur ensured his "scientific" reference to microbes by enabling the circulation of instruments, colleagues, veterinaries, political allies, farmers, sanitation (such as the pasteurization of milk) and public support.[31]

With each new flow of such things, the truth of his theories and the reality of the anthrax microbes increased. More than a discovery of microorganisms in nature, it was a sociotechnical transformation, or in Latour's term, a Pasteurization of France. Latour compares the transformative effects of the Pastuerization with socialist politicians:

> it is clear that in political terms the influence of Pasteurian laboratories reached further, deeper, and more irreversibly since they could intervene in the daily details of life – spitting, boiling milk, washing hands – and at the macroscale – rebuilding sewage systems, colonizing countries, rebuilding hospitals – without ever being clearly seen as a stated political power. (Latour [1983] 1999: 268)

Pasteur's research did not take place *in* a social and natural reality, but itself resulted in a societal and natural reality. According to Latour, research can perform a sociotechnical transformation that extends beyond changes attempted by means of political action.

As was mentioned above, *the natural* and *the social realists* have specific resources to approach the topic of hESC research. In the first case, the analyst accesses cognitive systems of the scientists. These systems have explanatory power because of their interaction with the ontological source of natural reality. In contrast, *the social realist* would access social reali-

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31 This particular metaphor of the reference and the flows is not from *The Pasteurization*, but from Latour 1999b.

ties that have explanatory power because of their influence on scientific beliefs. According to the ANT view, a sociotechnical reality is in the making, and cannot be used straightforwardly as a resource to explain hESC research; the latter is involved in a transformation of social and natural reality. In Chapter 3 of *Pandora's Hope*, "Science's Blood Flow", Latour presented two figures to explain this difference (Figures 2 and 3).

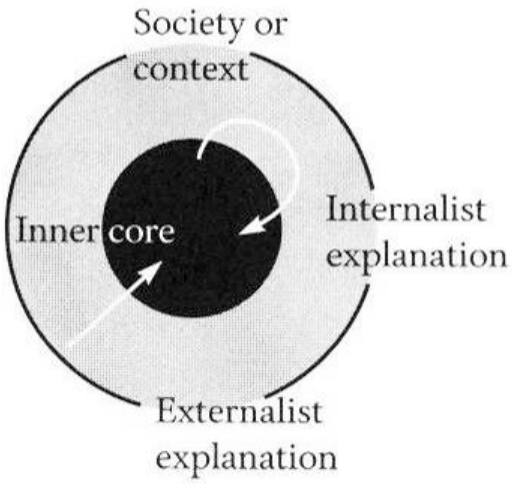

Figure 2: The common model for externalist and internalist explanations (Latour 1999b: 92). (With permission from Bruno Latour. Copyright by the President and Fellows of Harvard College.)

Latour has used this picture to describe "externalist" versus "internalist" histories of science. [32] It fits the two first analysts exactly. *The social realist* explains the inside by using resources from the outside context or society. *The natural realist* observes how science may affect society on the one hand, and on the other hand be hindered or furthered by society. The territory of *the social realist* is the corona and *the natural realist* would keep inside the core, maybe with reference to a natural reality inside the core, as a kernel.

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[32] The labels externalism and internalism have long histories, Shapin 1992. There is no reason to attach those labels to my *natural* and *social realists*. Nevertheless, I do keep close to Latour's argument in *Pandora's Hope,* chapter 3, 1999, in the following pages of my explanation. Below I will question and extend ANT's approach according to my meta-theoretical interests.

For the ANT analyst there is no way of saying a priori whether hESCs were the results of social or natural factors. Scientists move all around and manage a number of resources. They modify and draw on social and economic interests that feed back into their laboratories, or their conceptual work. For *the social realist* such interests would be highly interesting factors that explain the ultimate experimental design. But, it also seems reasonable when explaining the experimental design, to focus on specific laboratory materials, such as the use of growth media and laboratory techniques. These factors would typically be *the natural realist*'s first priority. Which is primary? The pre-existing interests, the social expectations, or the cognitive aids in the laboratory? According to ANT they mutually define and enforce each other. Neither social reality nor natural reality can be used as a privileged analytic resource. The analyst has to follow the scientists' trails wherever they lead, whether to allegedly social or natural places. What needs to be analyzed are the multiple flows or loops that scientists have to get going between labs and other parties (Figure 3).

This figure specifies the sociotechnical processes mentioned above. Flows of instruments and things, other scientists, allies (such as corporations and politicians), and the public all feed into the laboratory and the conceptual work. The latter is inextricable from the four other loops. According to Latour, the conceptual heart of scientific references is made up of the "links and knots" that tie the outer loops together. Together all these flows make up a circulatory system – "blood vessel after blood vessel". The system works better the more connected the blood vessels are. Science is dependent on these flows as the heart is dependent on its circulatory system of veins and arteries.

Seeing hESC research as sociotechnical reality thus in a sense robs the analyst of resources but leaves flows, trails.[33] The analyst is redefined, from having resources to having trails to follow which suggests that the acronym of ANT should be read as an animistic redescription of the analyst: He is an *ant* (Latour 2005: 9).[34]

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[33] I am using "trails" in Latour's commonsense use – not according to either Adrian or Charis Cussins's elaboration of the metaphor, Cussins 1996.

[34] On the use of gendered pronouns: For political reasons I have tried to envision a female ant, but failed, probably because of Latour.

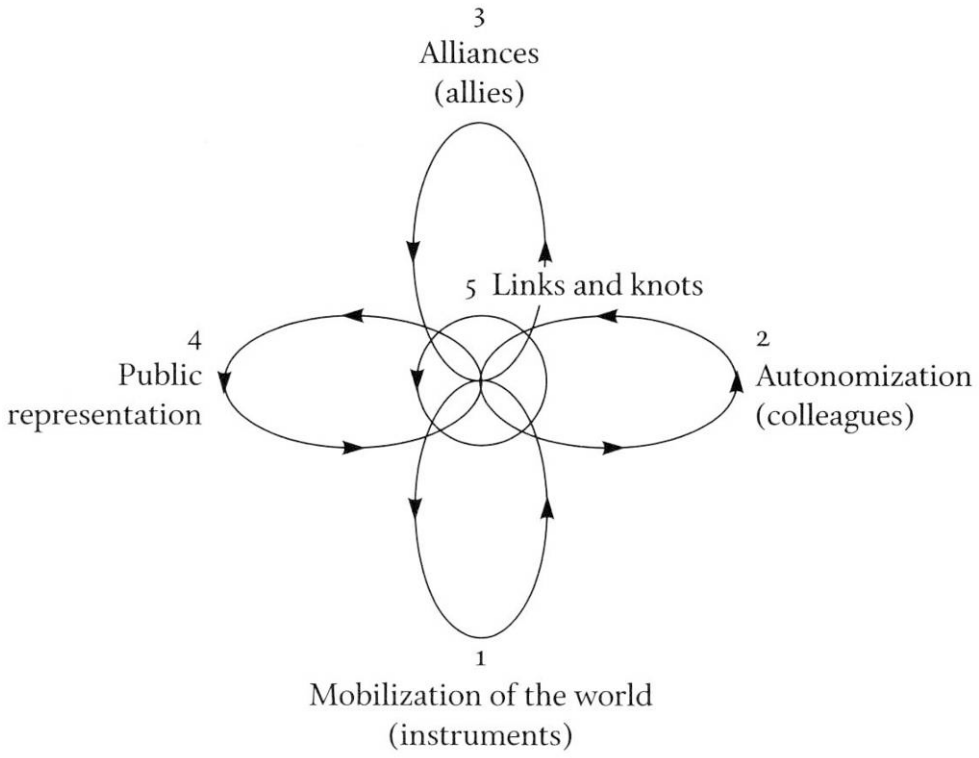

Figure 3: The five loops of the circulatory system of science (Latour 1999b: 100). (With permission from Bruno Latour. Copyright by the President and Fellows of Harvard College.)

From having a predetermined view of science and already defined resources at hand, the ANT analyst, according to Latour, becomes a much more myopic follower of trails, an *ant*.[35] If the *ant* wants to understand hESC research, the only resource consists in the traces out there of reality being articulated, in various settings: materials turning into signs, the reality-production of knowledge-production, and the transformation of society and nature.

However, the difference between the *ant* and the two other analysts is not about following trails or not. *The natural* and *the social realist* can follow scientists closely, too. They are also ants in this sense. But, whereas *the natural realist* stays within the cognitive systems, and *the social realist* exa-

[35] Henceforth I will italicize the an(t)imalized ANT analyst to distinguish him from the more mundane counterparts.

mines the social realities of the laboratories, the ANT analyst continues to follow the scientists as they cross those realms. Resources are thus not only about which factors to refer to, but say something about *where to go*, and where not to go. Resources thus have to do with realms and territories. Social and natural reality are not only a matter of resources but can be a matter of *territories*. What separates the ANT analyst from *the natural* and *the social realists* is not that the former follows trails and the others don't, but that the former follows the trails *also when they start criss-crossing* between natural reality, cognitive systems and social realities.

This has been a pedagogical account to explain what scientists are doing, according to ANT, and where the analysts could go. It has implications for my initial observations of the stem cells' "biological and political pluripotency". *The social realist* would explain biological pluripotency as a matter of social reality and human agency. *The natural realist* would analyze the political events as a consequence of (cognitive) laboratory systems capturing the biological and naturally real pluripotency. The *ant* would follow scientists moving in their laboratories, and from laboratories to the Congress, to the public, to colleagues. But, this raises the question: Which of these sites would account for the stem cells' pluripotency as biological and political phenomena? Critics have (in other words) asked: If everything is flowing, then where can the analyst place her/himself to get a perspective on the flows?[36]

Agency

As a response to natural and social realist approaches, respectively, ANT has talked about *human and nonhuman agency*. Sometimes this is called *generalized symmetry* – in contrast to the first symmetry principle that was introduced by Bloor (1976). There are many aspects of generalized symmetry and it has been opposed fiercely by critics.[37] This opposition will not be treated here. Instead the purpose is to understand the effects for the *ant*. Assuming human and nonhuman agency widens the analyst's attention.

A first thing has to be noted before anyone's mind runs off with the idea of nonhuman agency: It is not a principle saying anything positive about the world, such as for instance claiming that stones or nuclear par-

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36 This was basically what was asked in Collins and Yearley 1992a: 303.

37 For such critics see e.g. Bloor 1999a, 1999b, Collins and Kusch 1998, Collins and Yearley 1992a, 1992b.

ticles have intentions or reflexive capacities (Latour 2005: 70ff). However, baskets and hammers *make a difference* for humans fetching provisions or hitting nails. Baskets and hammers are thus

> *participants* in the course of action […] This, of course, does not mean that these participants "determine" the action, that baskets "cause" the fetching of provisions or that hammers "impose" the hitting of the nail. [---] Rather, it means that there might exist many metaphysical shades between full causality and sheer inexistence. In addition to "determining" and serving as a "backdrop for human action", things might authorize, allow, afford, encourage, permit, suggest, influence, block, render possible, forbid, and so on. (Latour 2005: 71f)

Generalized symmetry is useful since it tells the analyst not to turn around when the trails of research are leading to an object instead of people or social groups. In the hands of the analyst, generalized symmetry helps by paying attention to agency wherever it appears.

In some respects agency plays the same role as natural and social reality does for the two first analysts. Reality for these, signifies what makes a difference in the world, or "ontological potency". Seeing agency in humans and nonhumans is to accept the ontological force of – in principle – any entity of the circulatory system of science-and-society.

In the sense of being effective and active, agency is also tied up with ANT's reality. Seeing agency is seeing what *really* makes a difference. In Swedish or German this would be clear from the words that could be used for agency and reality: the Swedish *verkan* and *verklighet,* and the German *Wirkung* and *Wirklichkeit*. What is ontologically active, what really makes a difference to others, is real – whether it be humans, nonhumans or anything in between, below, and above. For reasons of simplicity: Instead of referring to all these kinds of entities (humans, nonhumans, etc) in the rest of the text, I will usually just call them *heterogeneous* elements or entities.

Agency is the ontological activity of something or someone affecting other entities. In spite of this similarity between ANT's use of agency and the other analysts' uses of social and natural reality their attitude toward this activity is radically different. Since agency in ANT is the result of scientific (or other) processes – such as the Pasteurization of France – it is a starting-point for the *ant*. *The social* and *the natural realists* study knowledge-production, and various sorts of reality come in to explain or account for this. Ontological activity is thus the end-point for the two latter theories of science, and the starting-point for ANT studies. ANT

starts in reality and agency and then finds out *how something has become real and active*. *The social realist* starts in knowledge and finds out *how this has become perceived as true* by finding out the social reality of those knowledge claims. *The natural realist* starts in knowledge claims and assumes that their references to a natural reality are there.

Imagine analysts following the trails of scientific work: Whenever *the natural realist* runs into social factors they motivate him to go and find cognitive factors. Whenever *the social realist* analyst runs into cognitive factors or nonhumans the attention is turned toward social factors. When the ANT analyst comes to an agency the first reflex, according to the generalized symmetry, should not be to turn away, but to stay curious and respectful. It thus becomes a matter of attitude. Latour claims that this attitude should extend to the explanations of pilgrims too:

> "I came to this monastery because I was called by the Virgin Mary." How long should we resist smiling smugly, replacing at once the agency of the Virgin by the "obvious" delusion of an actor "finding pretext" in a religious icon to "hide" one's own decision? [---] "As long as possible in order to seize the chance offered by the pilgrim to fathom the diversity of agencies acting at once in the world." (Latour 2005: 48)

The *ant*'s attempt to fathom the agency starts by examining the variety of factors that occur in relation to the acting entity, whether the Virgin Mary, anthrax microbes, or hESCs. In the latter case, pluripotency is not assumed to be something else – such as social or cognitive factors – but indeed something related to other elements playing a role in a net of relations. This role of Virgins, microbes or cells amid relations to heterogeneous elements is so important for ANT that it is part of its name. *Actor-network* is a term to signify how action happens in relation to other elements where neither the point of agency nor the surrounding relationships are reducible from the equation (Latour 1999a). Drawing on the metaphor of networks is obviously not the exclusive property of ANT.[38] What makes ANT unique is the heterogeneity of these networks' associations.[39] Actor-network is not an actor without a network, not an actor reducible to a network, and it is not a network without distribution of

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[38] Networks have been used to describe scientific theories at least since Pierre Duhem [1906] 1954, and others have been Willard V. O. Quine 1964, Mary Hesse 1974, and Collins 1985 (just to mention a few).

[39] *Association* is a theoretical term within ANT. For more about its connotations, see below.

agency to certain elements. ANT focuses on how things or people make a real difference in co-dependence with a network of heterogeneous elements. The term used to capture the investment of agency in an element is *delegation*.

Seeing agency in this manner is not to ask for *explanations*. Finding the relationships does not explain pluripotency but contributes to an understanding of its role.[40] Generalized symmetry about human and nonhuman agency helps the analyst to remain respectful of the phenomenon. In relation to my initial interests, in the "biological and political pluripotency" of hESCs, both of these issues can be studied as the reality and agency of stem cells, without reducing one to the other. Biological agency and political agency do not have to be reduced to another repertoire, at least not immediately. I raised the question above: Which of the many sites where hESC research takes place should account for the stem cells' pluripotency as biological and political objects? This question asked for something like an explanation. According to ANT's view of agency no single site is responsible for pluripotency. Viewing pluripotency through the ANT theory of science means "seizing the chance to fathom the diversity of agencies acting in the world at once".

I find the claim that science is involved in – and even the main vehicle for – sociotechnical reality an extremely interesting way of seeing hESC research and politics. It is interesting since it implies another way of topicalizing the two initial observations of hESCs, as biologically and politically pluripotent. The observations do not necessarily concern two distinct phenomena but interlocking flows of the same circulatory system. If so, then there is not a biology distinct from politics. Plainly put: Instead of a social and/or natural reality of hESC research this study draws on ANT and therefore the hESCs and their "biological and political pluripotency" is understood as *the sociotechnical reality of hESCs*. The initial puzzle has thus been turned into a first ANT-inspired research question:

(ANT-Question No 1) What is the sociotechnical reality of hESCs?

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[40] I am fully aware that ANT in general does not refer to *understanding*, probably because of this notion's hermeneutic connotations. ANT has preferred to speak of description in contrast to explanation, Latour 1988. However, I find the notion appropriate below Latour's lines about "fathoming the diversity of agencies", which to me implies precisely understanding.

This chapter has outlined the added value of viewing hESC research as sociotechnical reality *in relation to natural and social realist approaches*. ANT is merely one among several approaches – not least within STS – that account for the heterogeneity and intertwinement of science and society.[41] In this study however, ANT provides the main analytic assumptions. These assumptions are a first step in exercising how to see differently.

Whether the assumptions are defendable or not, there is a direct methodological consequence for the analyst. Since reality is all there is – everywhere – the analyst shifts, from studying knowledge to studying reality (wherever it is), from being an epistemologist to being an "ontologist", from being a sociologist of the social, or a philosopher of the cognitive, to becoming a sociologist of heterogeneous associations (Latour 2005: 9).

Some ANT concepts in use[42]

ANT scholars have coined specific words to capture sociotechnical reality *in becoming*. *Articulation* is one term which brings in linguistic and material connotations: linguistic in the sense of expressing something clearly; material in the sense of articulating a joint or a lorry. Turning materials into sign is articulation. The reality-production of knowledge-production whether in the laboratory or on a larger scale is also articulation.

Earlier terms used by Latour for the same basic phenomenon are e.g. construction, translation, and coordination. There is little need to start laying out the differences between the various notions. They are all metaphors for capturing various aspects of the process of discovery-invention-construction (Latour [1984] 1988, 1999b: Chapter 5, Latour and Woolgar 1979). According to Latour, articulations are the fundamental entity of the universe. I make no such fundamental claims when referring to articulations. My use is a little more modest. I look for articulations to capture the making of actor-networks, bits of sociotechnical reality, or *associations*.

Association is the term for an articulated connection – whether it is between matter and sign or between a laboratory and people's daily practices. To signify that in principle anything/anyone can connect with anything/anyone these associations are *heterogeneous*. By way of associations

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41 For more about alternative approaches and the added value of choosing ANT, see below.

42 Also see the Glossary (at the back) for definitions of the most frequently used terms.

the analyst attends to the connections made in articulations. The chain going from the Amazon to the scientific article could be said to consist of associations. Likewise the process going from inscription devices to diagrams, to comparisons, to statements and texts could be said to consist of associations. The Pasteurization of France was also accomplished by way of associations. Above, there was another metaphor, the one of loops in a circulatory system. Associations between heterogeneous elements enable the multiple flows.

The temporal connection of articulation, associations in actor-networks and the resulting sociotechnical reality may be tracked as a process of *stabilization*. As e.g. laboratory claims are more and more articulated, and more and more associated, they become stabilized. Sociotechnical transformation is the stabilization of facts and people, places and practices. This process and its results have many names in ANT. Elements can, for instance, be packaged in *black boxes* or *immutable mobiles*, in order to be moved to new places and used off the shelf. These are examples of "frozen articulations", or "congealed labor". An articulation is a unique event, and only contributes to a tiny bit of reality (Latour [1984] 1988: 162). To make it last, work has to be done. Black-boxing is one way of making articulations endure from one space or one time to the other (Latour 1987).

Such processes are reversible, although often at a high price. If the black-boxing is a congealment of labor, it requires energy and effort to "fluidize". In practice, this can often be impossible. It would by now be difficult, but not impossible, to reverse e.g. the use of electricity in Western societies. It may be the case that too many applications and practices are tied up with the use of electricity to make a reversal possible. Stabilization enables the extension of actor-networks, but also constrains future articulations. Anything can, in principle, be done, but many (if not most) things are too cost-demanding.

Although it is hard for actors to open and, even harder to reverse, an achieved stabilization, the *ant* can do something similar but on an analytic level. If an analyst follows the associations implied in a stabilization backwards he is *unpacking* the stabilized object. When Latour analyzed the impact of Pasteur and the microbes on France in the 19th century, he was thus unpacking sociotechnical reality. This is not the same as actors' attempts to reverse a stabilization, but it may speak to the same intuitions. The opening of today's black boxes may show that "it could have been otherwise" (Bijker 1995, Fujimura 1996, Law 2004). hESCs

could be effects of stabilization processes, examples of stable elements, entities that are repeatedly articulated together with certain other entities. This notion of unpacking and stabilization thus results in a second ANT-inspired question akin to the previous one:

> (ANT-Question No 2) How has the sociotechnical reality of hESCs come to be?

It should by now be clear that the implied "how" of such a question is not a strictly explanatory one (as if asked by the social realist), but neither is it merely descriptive. It is an unpacking "how" that searches description; not just any but a specific description to understand the stabilization processes and the emergence of agencies.

The first part of this chapter has transformed the preliminary observations in the Introduction into a preliminary topic by drawing on several theories of science. By juxtaposing three envisioned analysts I have suggested the added value of a sociotechnical approach. Unlike the social realism inspired by Collins, and the natural realism inspired by Giere, the ANT analyst's topic is the heterogeneous associations and the multiple flows of hESC research. My interpretation of ANT suggests that the documented biological and political pluripotencies of hESCs are not distinct phenomena, but involved in one circulatory system. The phenomena indicate a strong agency that, according to ANT, is the result of delegation in a network. It should be possible to unpack the stabilization of hESCs and find out when and how agencies have been delegated. Since the hESCs are the result of sociotechnical transformation, then the emergence of this reality can be tracked down – association by association, element by element. Starting with the "biological and political pluripotency" of hESCs, the analyst can assume that a stabilization of reality has occured. As new relations have been added, as other people, animals, objects, or arguments have participated, the sociotechnical reality of hESCs has increased and resulted in the "biological and political pluripotency". The analyst therefore goes backwards to track the addition of elements. This is unpacking. It should preferably *not* result in an explanation or a reduction of hESC research and politics to other processes (see Virgin Mary quotation above). Unpacking the sociotechnical reality of hESCs should instead outline the role of hESCs in a heterogeneous network.

Meta-theoretical modification of the *ant*

The above sections were enacting a zooming-in movement. It went from many theories of science to the construction of an ANT analyst. The next third of the chapter will zoom out again, but not to end up in the same place. The agnostic *ant* will not be the analyst of this study. He will be burdened with conceptual glasses and limitations before he is put to work on a specific material with specific questions.

After having focused on the *ant,* he will now become one component in a larger assemblage of methods and theories. The analyst can start out with puzzles and aims, but they will be specified and modified as it runs into empirical or theoretical issues. Research questions can be asked to get the *ant* going, but not too far in advance. Materials can be limited at the outset, as initial values, but not indefinitely. Since the study will move in an unpacking manner the methodological package has also to be flexible, like an assemblage. Who knows what is inside the next black box, and what then to ask?

Above, the *ant* was accessing sites, traveling from one flow to the other. Below, I will turn ANT into a theory, a perspective that can be applied and elaborated. This goes against the ANT as presented by Latour. According to him, it is not a perspective that can be used to understand a particular material. It is more like a tool that can be used to record and describe – not a theory to filter out, or discipline (Latour 2005: 55). The *ant* is thus not alone in this study. He will be guided by meta-theoretical interests and research questions on an ANT non-typic textual and public/political material. The purpose of the rest of this chapter is to explain in what way this is not a characteristic ANT study (if there is such a thing). Outlining this, will add to the analyst's theoretical, methodological and empirical presuppositions.

Most probably I am treating ANT in my own way (as a perspective) because of my training and assimilation of it. Whereas one of Latour's slogans for how to learn ANT is "sur le terrain" – get into the field, into the laboratories, follow the actors – I have learnt about ANT from a book and in a context where meta-theory is emphasized (Latour 1987). Theories of science at this department (of History of Ideas and Theory of Science at Göteborg University) are not merely introduced for students in order to be used, but to be juxtaposed, contrasted, and compared. More than any privileged resource the physical department of theory of science offers an *intellectual space* in which to theorize theories.

I have thus started by reading ANT, not by doing it. Many doing ANT may have started that way (probably most) and then assimilated the method. Instead of turning native as ANTer and *becoming* the *ant* sniffing on trails, I keep a conceptual, meta-theoretical distance to ANT in this study, treating it as one theory of science among others. When I approach ANT there are similarities with Manuel in the series *Fawlty Towers* claiming to know English since he "learnt it from a book". Another way to see it – more flattering, I think – is that I am a linguist approaching English, or a religious philosopher approaching religious practices, i.e. with a *meta-awareness*. This may disturb some believers, and may pollute or contribute to the actual practice. At least, I have now admitted my starting-point: "I learnt it from a book".

Some basic ANT concepts in use have already been mentioned above. Critics have pointed out that the alleged agnosticism of the generalized symmetry has often resulted in human-centered accounts with strategic actors (Fujimura 1995: 304, Star and Griesemer 1989). Finding associations is not innocent. In her *The Body Multiple* (2002), Annemarie Mol recognizes a necessary shift from the logical coherence of Foucault's *structures* to the material coherence of actor-networks achieved through associations. However, she also criticized the equality, or even "homogeneity", of actor-network associations. Coordination is "bivalent" – either on or off:

> Each new and successful association makes a network larger. But however great the difference between the coherence in a network and *logical* coherence, to talk of "associations" does have a homogenizing effect. Either an association is made or it isn't. An element is either inside or outside a network. Coordination is established or not. There are no distinctive *forms* of coordination. (Mol 2002: 65f)

Mol is putting her finger on what could be one of the most salient developments within ANT since the 80's and early 90's. Many scholars who accepted the basic tenets of "Classic ANT", have turned to multiplying their understandings of sociotechnical reality, heterogeneity, etc (Bijker 1995, Landström 1998, Law and Hassard 1999). I take Mol's question about *forms of coordination* seriously, as an interesting meta-theoretical challenge for this study.

Alternative forms of coordinations: OPP and boundary objects

One form of coordination that has been heavily criticized is the obligatory point of passage (OPP). In several case studies Latour, Callon, and Law have shown how OPP is one means to coordinate heterogeneous elements. One of these cases was *The Pasteurization of France*. The OPP was Pasteur's laboratory and his institute. In Callon's study about three scallops researchers, the OPP is the attempt and failure to achieve the same absolute degree of domination. Three researchers return from Japan with a new way to understand the scallops' reproductive processes. By formulating a new research problem for other researchers, by suggesting to fishermen a more lucrative method for scallops fishing, and lastly, inviting the scallops to reproduce themselves in new places the three researchers become the centre of an actor-network. They re-position the actors through their new understanding of the situation and themselves become an OPP for all actors – ultimately, however, without success. Callon and Law mapped a military aircraft project – the TSR 2 – in the UK. In this case the OPP was set up to protect a *local* sociotechnical network of production and a *global* one supplying funds. The OPP and the TSR 2 project eventually failed.

There are two features in the OPP stories that single them out in the ANT literature. One is the dominating degree of stabilization, and another is the mode of alignment through entrepreneurial activity and funneling of other actors.

Firstly, the OPP is an either-or. The attempt at a dominating stabilization can succeed or it can fail. There are no in-betweens. In this sense the Pasteurization of France draws on the socio-technical system presented in Thomas Hughes's work on the "Electrification of America". One of his articles is subtitled *The System Builders*:

> Not one of them [the system builders] was satisfied to solve a part of the problem, simply to invent, manage, or finance, for each believed that the invention would not become an innovation, the managerial structure would not evolve, and the financial means would not bring growth unless electric light and power were viewed as a coherent system. (Hughes 1979: 125)

The system story about the Electrification, just like the OPP story about the Pasteurization, suggests how a whole cloth comes into being without seams. One example of the systematic character of this growth was the mutual adjustment of the generators, the lamps and the system voltage (Hughes 1979: 139). The objects had to be stabilized together with the

infrastructures in which they could move. One could not be put in place without the others.

The system story and the OPP stories are examples of the simultaneous and total stabilization of objects and their networks. Both stories present similar models of what a network is and how it is built. They both concern huge transformations. To achieve any success, you have to achieve total success. Although impressive, not all innovations end up becoming the total transformation achieved through the electrification of America and the pasteurization of France, or the total failures in the cases of the scallops and TSR 2. Everything is either drawn in and connected through the network, or the network is not established.

Secondly, on agency, the OPP story seems to side with human actors rather than the nonhumans. The driving force in the OPP networks is the agency of human entrepreneurs. Latour describes a series of articulations in which new objects were shaped and spread to other actors, whether cows, farmers, or veterinaries. In spite of the symmetry between humans and nonhumans a central feature in Latour's story is the agency of Pasteur. The OPPs of Callon, Latour, and Law are dependent on entrepreneurial humans.

Some approaches have related explicitly to ANT, such as social worlds theory. This is a development within the Chicago School of symbolic interactionist sociology (Clarke 1990). Social worlds have been combined with ANT notions by virtue of their heterogeneity, fluidity, and inclination for mixing, intersecting, and segmenting. Similar to ANT, the social worlds perspective emphasizes "antideterminism", is interested in practices and does not stop at a specific scale of the objects of study (micro vs. macro) (Strauss 1978: 121). Such common orientations have been points of contact when scholars – such as Adele Clarke, Joan Fujimura, and Elihu Gerson – have productively drawn on the two perspectives (see also e.g. Fujimura and Clarke 1992, Star 1995a).

Susan Leigh Star and James Griesemer start from social worlds theory in their criticism of the OPP approach. The latter attributes too much of the network formation to entrepreneurial humans, they claim (Star and Griesemer 1989). They also observed that the OPP assumed a funneling of all actors through a specific interdefinition and problematization. For the network to be established, actors had to accept the OPP formulation of the situation, or be left on the shrinking outside of the actor-network. In a conference paper, Star pointed toward the crucial issue:

> How can two entities (or objects or nodes) with two different and irreconcilable epistemologies cooperate? If understanding is necessary for cooperation, […] what is the nature of an understanding that can cooperate across viewpoints? (Star 1989: 42)

Star suggested an alternative to the actor-network OPP that would account for the coordination of actors of different viewpoints and from diverse *social worlds* (1989). Together with James Grisemer, she elaborated the notion in a paper about the establishment of the Museum for Vertebrate Zoology (MVZ) in Berkeley, California. Actors were coordinated through the circulation of certain objects. These *boundary objects* retain their identity across various social worlds and actors, but are sufficiently plastic for specific usage in individual sites. In common use they are weakly structured, enabling communication between different actors. In individual use they are strongly structured contributing to the actors in question (Star and Griesemer [1989] 1999: 509).

Although the OPP and the *boundary objects* are both examples of how disparate elements can come together, the means, the agency, and the actor-networks and socio-technical reality resulting from the two models differ greatly. Boundary objects are positioned and travel between cooperating institutions and actors that are conjoined through the boundary objects. The resulting network does not depend on the common acceptance of one situation, one problem or the identities of the actors. Star and Griesemer talk about the loose coordination of actors as an *ecological system* (or in other places an *ecology of knowledge*). Around the boundary object(s) an ecology of social worlds, institutions, things and actors emerges, where no actor necessarily is more important than others.

> The ecological analysis does not presuppose an epistemological primacy for any one viewpoint; the viewpoint of the amateurs is not inherently better or worse than that of the professionals. The important questions concern the *flow* of objects and concepts through the *network* of participating allies and social worlds. (Star and Griesemer [1989] 1999: 507, their italics)

The ecology is not dominated through one site, in this case, but multiple sites define the situation through the boundary objects. Actors are not funneled through the definition of one or a few actors. The multitude of connected actors is in a sense explained through the role of the boundary objects. Actors, their interests, and material objects together make up a "boundary object". Instead of watching a few actors move other actors, the vantage point is the objects that enable cooperation between diffe-

rent actors. This has implications for the agency issues. Boundary objects are gateways to other worlds. Whatever the intentions of the original entrepreneurs, the objects and their flows are in focus. There are entrepreneurs in the boundary object story too, but they are not the driving force – the objects are. They are not primarily facts, artifacts, or black boxes, but coordinators.

As an alternative to the translations of human entrepreneurs of the OPP, Star and Griesemer point toward the coordinating effects of objects. Such an alternative is in full accordance with the eclectic nature of ANT. Latour has in any case not locked himself into any specific way to understand scientific work. Different metaphors have their own benefits and weaknesses. *Articulation*, for instance, "stresses the independence of the thing" brought forward and maintains the historical and material character of such events (Latour 1999b: 140). *Translation*, seizes on the gap between actors and their understanding of a situation, including their perceived interests, but risks becoming too linguistic and non-material. *Coordination*, similarly, is one figure of speech among many, with benefits and weaknesses. One benefit is that coordinated actors presumably have to be and remain relatively independent to be coordinated. Actors are not linked by having all of their interests, respectively, translated into terms of one institution or group. Rather, actors maintain their interests and their social worlds, but meet through and in the objects. One possible weakness could be that coordination has too little to do with an ontological event, is too far removed from the innovative aspect of scientific work. Henceforth *articulation* and *coordination* will be used when they are appropriate respectively, often interchangeably without assuming any fundamental differences between them. They both concern the combination of elements.

The ecology of knowledge also addresses the question about different kinds of networks and network building by leaving a space for *partial stabilization* in contrast to the total domination of the OPP stories. Wiebe Bijker refers to *boundary objects* in relation to his own notion of artifacts' *obduracy*. This latter notion is a direct answer to the ANT *stabilization*. When objects (or in Bijker's term: artifacts) are stabilized and less malleable, less fluid, they are more obdurate. Their obduracy is the result of the linkage of "different social groups to form a (new) semiotic power structure" (Bijker 1995: 285). To assess their obduracy is to assess the strength of the actor-network. To ascertain that objects are boundary objects is to say that the actor-network is not all encompassing and to-

tally dominant. Instead of Bijker's obduracy I will stick to *stabilization* or stability, but adopt the correspondence between the strengths of boundary objects and their actor-networks. In my usage the stability of boundary objects does not transform all actors, but continues to be modifiable, unlike the stabilization of a successful OPP.[43] The OPP is established – or not. When it is there, it has transformed everything. The black boxes also have this black-and-white character (Fujimura 1992). Star and Grisemer present a form of stabilization in shades. Various actors buy into the boundary objects while remaining in their social world. The social worlds are not totally dependent on the stability of the boundary objects, as in the case of Callon's scallop researchers. When they failed to become an OPP the particular actor-network failed too. Although Star and Griesemer's story has mostly omitted the dissenters, the mode of coordination does not require total acceptance or nothing. The boundary object is stabilized in proportion to the number of actors using it, and is, in these terms, a grey, nuanced or, preferably, a *multi-colored box*. The "composition of colors" is determined by the actors connecting to each other through the object.

Combining OPP and boundary objects

OPP and boundary objects have been presented as two *alternative* forms of coordination (Star and Griesemer 1989). From a meta-theoretical vantage point ANT could be challenged and complemented. The first third of this chapter introduced ANT on its own terms, and formulated the issue of stem cell research and politics as sociotechnical reality. This part has provided two ways in which to capture sociotechnical reality. Through the confrontation with the actual practices of ANT, and the critique, a meta-theoretically informed *research question* can be posed:

> (Meta-theoretical Question No 1) How can the notions of obligatory point of passage and boundary objects be put to use in order to understand the sociotechnical reality of hESCs?

This is most probably a far more "deductive" question than the approach that originally produced the notions. The OPP and the boundary objects were suggested in order to capture the phenomena of

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[43] Bijker equates obligatory point of passage and boundary objects, 1995: 285, which is contradictory to my own and Star and Griesemer's use of the concepts.

coordination. ANTish analysts have followed associations and the patterns have suggested the OPP and the boundary objects. According to Latour, what is needed is not more terms, but fewer. ANT notions should only be used to let "new actors define the world in their own terms using their own dimensions and touchstones" (Latour 1999a: 20). I start from the other end of the stick. Beginning with the notions, what phenomena will we see? That is the issue in part one of this study.

Obviously this question is not posed innocently beforehand. When writing this, I know the story.[44] But the above account is also true. I started by *learning ANT from a book* – including the OPP and the boundary objects. When approaching the stem cell situation in the US, those concepts functioned as paradigms, as glasses. It is a grave difference in approach, compared to the *ant* (-ideal). My fascination with the two notions in a sense equaled my fascination with stem cell research and politics. By approaching the latter by means of the former, new metaphors may result.

This is a second way that is opened up. It will only be hinted here to indicate a future possible rebundling waiting among the reeds, as it were. Combining the two notions is an opportunity to shift the central metaphor from networks to something else. Many have suggested other spatial metaphors than that of network: topical contextures (Lynch 1991), rhizome (Latour 1999a), choreography (Cussins 1996), and fluids (Mol and Law 1994). Concepts such as *regions*, *networks*, or *fluids*, are all possible topological presuppositions in analyses of science and society.[45]

A less sophisticated (but not necessarily less deep) way to formulate the role of metaphors is that they enable *another way of seeing*. The boundary objects come with another topology: "The important questions concern the *flow* of objects and concepts" (Star and Griesemer [1989] 1999: 507, their italics). These flows belong in the metaphor of ecology (of institutions or of knowledge). By juxtaposing boundary objects and OPP, a different metaphor for seeing science and society can be tried.

It is possible to ask about what happens if the flows and ecology of boundary objects are "metaphorically passed on" to the OPP. This question is justified since the OPP was originally presented within the network metaphor. It is, however, not impossible to envisage flows passing

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44 That is probably true for the original case studies too. Pure *ants* are hard to come by. Many of them are more than agnostic. I am just very open about my conceptual bias.

45 The notion of *topological presupposition* is borrowed from Mol and Law 1994: 642.

through one point of passage. Think of the reservoir at the service of a hydroelectric power station. Think of the heart's role in the body's circulation of blood. The latter was Latour's metaphor of flows, which I used to construct the *ant*. In doing so, I also applied it to *The Pasteurization of France* – one of the classic OPP stories.

Searching the literature, I have found one case where boundary objects and the OPP are *combined*. The paper is written by Véronique Vissac-Charles and exists in another version (both in French) co-authored by Latour (Vissac-Charles 1998, Vissac-Charles and Latour 1996). Both papers are based on two innovation projects, the processes of constructing an automatic apple-picker and an electric steel foundry.

Combining approaches from different traditions is typical for ANT. Vissac-Charles does not address the theoretical differences between the original approaches. She adopts the notions to her own use of it. There are however important differences that could become obstacles – especially if generalized symmetry is misunderstood. Paying attention to these differences can shed more light on the issue of agency.

While Star and Griesemer's approach puts nonhumans in focus by locating much of the coordination in the boundary objects, an important drawback and possible problem in the social worlds perspective (in relation to ANT) concerns the status of nonhumans. There is no ANT generalized symmetry in the former perspective. In spite of their focus on objects, Star and Griesemer do not place them on a level with humans. Boundary objects are, for instance, not identical to marginal people:

> Unlike the situation of marginal people who reflexively face identity and membership problems, however, objects do not change themselves reflexively or voluntarily manage memberships. (Star and Griesemer [1989] 1999: 519)

Boundary objects cannot change themselves as people sometimes can. Have Star and Griesemer thus contradicted the generalized symmetry? There are (at least) three answers: yes, no, and no. *Yes*, Star and Griesemer's approach does differ fundamentally from the generalized symmetry. *Social worlds* does assume a more commonsense distinction between people and things tangible in the above quotation.

No, the generalized symmetry is not contradicted, because proponents of the social worlds approach also wish to include all sorts of elements in analyses of science and technology (Clarke and Fujimura 1992, especially 5f). This is particularly obvious in the MVZ case study. By highlighting

the role of objects this is a good example of the practical thrust of generalized symmetry: What difference can objects make?

The second *no* depends on the varying importance of ontology in the two approaches. Social worlds theory does not discuss ontology and metaphysics in the way ANT sometimes does. The common goal of ANT and social worlds theory is to capture the role of *all elements*. ANT formulates this as (among other things) a matter of ontology. Social worlds theory drives the same point for sociological studies, but does not formulate it in the same ontological manner. Star is more *operational* than ontological when she explains the common interests and tools of ANT and symbolic interactionism (and social worlds theory) under the joint flag of *ecology of knowledge*:

> If one adopts an ecological position, then one should include all elements of the ecosphere: bugs, germs, computers, wires, animal colonies, and buildings, as well as scientists, administrators, and clients or consumers […] The advantages of such an analysis are that the increased heterogeneity accounts for more of the phenomena observed; one does not draw an arbitrary line between organism and environment, one can empirically "track" lines of action without stopping at species, mechanical or linguistic boundaries, and especially without invoking a reified conception of society. (Star 1995b: 13)

In this introduction to a volume presenting studies drawing on ANT and social worlds, respectively, Star aligns the two approaches without invoking the strict ontology of generalized symmetry. The main purpose of the ecological position is not ontological, but to "account for more of the phenomena" and to "empirically 'track' lines of action". Boundary objects are thus – paradoxically and contrary to the social worlds' distinction between people and things – good examples of the work nonhumans can achieve between diverse actors.

I have observed – and argued for – differences and compatibilities between social worlds theory and ANT to remove possible obstacles, before putting the notions to use. Other differences between the two approaches will be treated later (see Chapter 4). The combination of OPP and boundary objects not only requires clearing the way. It also opens a way – in fact, two. First, it may be an answer to Mol's inquiries about modes of coordination. Mol called for distinctive forms of coordination. There are already two such distinct forms out there, in the literature – the OPP and boundary objects. Considering that there is only (according to my searches) one case where they are combined, it is still an open and interesting question what such a combination may yield: What pheno-

mena are accessible if the notions of obligatory point of passage and boundary objects, respectively, are applied to the "same" situation, e.g. the case of hESC research and politics in the USA prior to August 2001?

The issue is still sociotechnical reality, but now with a focus on the mode(s) of coordination: An ecology of multiple viewpoints or a funneling through one group; entrepreneurial and strategic humans or flowing objects; total stabilization at stake or partial and relative stabilization? These questions should (hopefully) be answered in the coming chapters.

Politics and ANT

Juxtaposing the boundary objects and the OPP is one meta-theoretical issue. Another concerns politics, which is a feature overlooked in ANT. In spite of the assumed heterogeneity and intertwinement of science and politics, case studies have *de facto* treated explicit politics as a derivative or auxiliary factor in relation to where the real action lies, in laboratories and research. This is so even in cases where politics has obviously been crucial to the eventual success. The real sociotechnical action lies in local, constructive networks that are extended (Law and Callon 1995). ANT has made a point out of the politics of the laboratory, how the inside of labs is extended to the outside, micro is turned into macro. Latour was one such example (above), claiming that the Pasteurian laboratories "in political terms" exercised a more far-reaching influence "without being clearly seen as a stated political power" (Latour [1983] 1999: 268). [46]

There is thus a meta-theoretical reason for analyzing materials relating directly to explicit politics. Unlike many ANT cases the political and public dynamics in hESC research is worth studying "on their own merits". There seems to be an independent dynamic in public arenas. Actors envision future scenarios of what the research could be and become, reminiscent of Callon's *actor-worlds*. Callon's usage of this notion is informative (Callon 1986a). The French *Electricité de France* (EdF) envisaged a network for the construction of an electric vehicle (the VEL). Other actors were positioned by EdF. Renault was, for instance, marginalized as merely a producer of car bodies for the VEL. Still not an actor-network, the EdF and this new definition of other actors constituted an actor-world, according to Callon. What followed were several competing actor-worlds in which actors such as Renault tried to establish other inter-

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[46] To distinguish between the politics of the laboratory/things and stated political powers, I henceforth refer to the latter as explicit politics.

definitions between actors, and roles for themselves. EdF ultimately failed to establish the necessary associations. The actor-world did not become an actor-network. In Callon's case there is very little material, laboratory, or other construction-work going on. Alternative sociotechnical realities are envisaged, mainly by EdF and Renault. Associations are negotiated but very much as possibilities, rather than actualities.

Explicitly political actors, such as the state, were part in the actor-worlds negotiations, but without any great potential. This is from the 1980 version of the case study:

> Confronted by these actors, the state is powerless. It rarely has sufficient expertise to transform technical controversies into policy debate; it is undermined by internal divisions that prevent it from showing any coherent political will; it is trapped into deals that lead it to defend the most powerful groups. (Callon 1980: 358)

Similarly, politics was auxiliary in the TSR 2 project (Law and Callon 1995). The project started out by way of *sociotechnical scenarios* (somewhat resembling Callon's actor-worlds). In this case there was a strong political element, but it had little impact on the actual construction process. When the project was in motion there was an on-going coordination within and between two networks, one global and one local. Political parties, the cabinet, and funding decisions belonged in the global network. "[A] local network of designers, designs, production teams, management and subcontractors" was supposed to carry out the actual construction (Law and Callon 1995: 290). Because of a combination of political factors and construction issues, the project was ended six years after its inception. Politicians' concerns were vital, but mainly to endorse the project, or – eventually – not.

It is an important question for ANT, how to deal with the impingement from explicit politics on the sociotechnical reality.

> (Meta-theoretical Question No 2): How can ANT account for the role of explicitly political actors in sociotechnical network attempts?

In other parts of STS explicit politics is the main topic, but in ANT it has been neglected (Elzinga and Jamison 1995, Fuller 2000, Guston 2000, Rouse 1996). This is again an opportunity and maybe one that calls for new metaphors. Latour's circulatory system makes the flow to politicians as important as the flow to colleagues or instruments. His example is Frédéric Joliot's involvement in the production of the first artificial chain

reaction (Latour 1999b: Chapter 3). Political concerns were interacting more complexly here than in the case of the TSR 2. Joliot was put in motion by his friends in the Ministry of War, and the director of the French National Center for Scientific Research. They facilitated his contacts with a Belgian mining company producing radioactive material. Joliot was thus provided with research materials and funding. When Joliot later approached Raoul Dautry, the Minister of Armament, the latter offered support, but also made demands. Dautry stressed the need to first produce a bomb and then pursue the (civilian) experimental reactor. Explicit politics was in this case more than a mere supporter. It modified the sociotechnical network considerably.

Materials and methods

There are by now two meta-theoretical issues: The juxtaposition and combination of the OPP and of the boundary objects; the issue of political and public dynamics. To get started, one more thing is needed: an empirical material. I will first discuss the role of the material chosen in relation to the meta-theoretical questions and my use of ANT. Then I will account for, and elaborate on, the empirical materials chapter by chapter. On the way some things need to be said about the methods used; how I have read and used various kinds of texts.

ANT and textual materials

The reality of hESCs and treating hESCs as making a pluripotent difference can result in many studies. The main slogan of ANT, "Follow the actors!", usually means approaching the messy, dirty, nuts and bolts of research preferably in laboratories, at conferences, or at least interviewing somebody. There are, however, salient examples of ANT pursued on textual materials (Callon et al. 1986, Latour [1984] 1988). This study is based on texts (although with a whiff of laboratory and conference experiences). Many of the texts were produced in or addressed to political settings, such as the Congress or the White House. There are also texts from scientific journals or reports. Most of these texts concern the political and public dynamics *in the USA prior to August 2001*. Before accounting for exactly what texts I have studied and how I have found them, something about the role of textual materials from political settings in a study inspired by ANT.

There are three reasons for selecting a textual material that relates to a general public and political dynamics in the USA. The first reason follows from my meta-theoretical interest in ANT and politics. Two more reasons have to do with the empirical and theoretical advantages of the US situation.

Above, the neglected role of explicit politics in ANT was described. Approaching hESC research in the USA is an opportunity to elaborate these aspects of ANT. Explicit politics in the USA is not only an add-on, but an integral part of the dynamics, i.e. it does not only provide a yes or a no to hESC research. In the period 1998–2001, it is even possible to say that explicit politics and debates *constituted the predominant dynamics*, since hESCs were still quite scarcely researched in the USA. There were only a dozen hESC lines out there. This is not to say that there were no laboratory activities, but it justifies attending to the political and public dynamics. Similarly, this study only attends to corporate dynamics as they appear in a public and political setting. I have not gone to the economic reports of companies, or examined the movements on the stock exchange.

There is a second reason to focus on the public and political dynamics: The US situation is a space for uncertainties and alternatives. Obviously, those features exist in other countries too (Gottweis 2004). One reason for studying hESC dynamics in the US, and not e.g. in Sweden, is the visibility and production of alternatives. Whereas the USA has an adversarial way of negotiating public issues, Sweden has a more corporatist mode (Kulawik 2004). In the adversarial mode, issues are solved by public disputes where opponents and proponents voice their opinions. In a predominantly corporatist milieu, negotiations mostly stay in the hands of official or semi-official bodies. The uncertainties in the stabilization processes are thus more readily picked up in the American political context of strong proponents and opponents. The ethical controversies on embryonic and fetal research in the USA make the choices more visible, at least for a while. In Sweden the dispute on hESCs was started and ended in less than 9 months in 2001 (Kulawik 2004). These issues in the USA are thus non-issues in Sweden, or at least they are public issues for a shorter time. This is not to say that there are no alternatives or disputes, but they are harder to access.

Third, the US visibility of controversy, uncertainties, and alternatives corresponds to a theme in an on-going critical assessment of ANT. Some scholars have pointed out that a focus on the stabilization of particular actor-networks will risk losing sight of the margins, the in-betweens.

Actor-networks do not include everything. Some actors, things, and viewpoints are excluded (Fujimura 1996, Law 2004, Longino 1997, Star 1991). Analyzing the US situation is an opportunity to observe such exclusion.

After it has been decided to focus on the sociotechnical reality of hESCs as articulated in politics, public debates, and media reports the next necessary limitation is the time period. One obvious period that is not too close to the writing process is November 1998 to August 2001. It was begun by the announcements from two groups that they had cultured hESCs from humans (Shamblott et al. 1998, Thomson et al. 1998).[47] It was ended by George W. Bush's decision August 9 (2001) to fund the already produced hESC lines. Between these two events there were vivid debates in Congress, in media, and on the Internet.[48] My reference to *the political and public dynamics in the USA between 1998 and 2001* mainly concerns those debates. I suggest, however, that such debates should not be viewed as merely discourse, representations, or beliefs. Because of the ongoing sociotechnical transformations (including the entanglement of signs and matter), scientific texts as well as other texts are more than discourse. In this study *political, scientific, and other texts are assumed to be in the middle of sociotechnical reality,* that is*, parts of chains articulating reality*. This suggestion is similar to that of Callon, Law, and Arie Rip, in *Mapping the Dynamics of Science and Technology* (1986), although they focused on scientific texts:

> texts make possible the construction of linkages between existing entities and the formation of novel entities and, if persuasive, thereby constitute an important method for attempting to control the environment. (Callon et al. 1986: 11)
>
> A scientific text not only reveals the world-building strategy of its authors, but also the nature and force of the building blocks derived from the domain of science from which it draws and to which it contributes. The text thus pro-

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47 More specifically, Gearhart's group called their cells human embryonic *germ* cells.

48 These are two events in a continuous flow of associations. It is hard to claim that Bush's decision – to fund research on already existing hESC lines, but not on lines henceforth being derived – stopped the debates. However, after this point a tendency is visible. From the debates on the funding of hESC research the Congressional energy on hESC research related more to the issue of cloning, or nuclear transfer. That issue was present before August 9, but afterwards there was a shift in predominance. A policy for the federal funding of hESC research was in place and was being implemented.

> vides access to the dynamics of science, to the shared worlds that constitute a means of mutual (and evolving) control. (Callon et al. 1986: 12)

The above authors studied texts "in order to understand the power of the laboratory" (p. 11). I am more open-ended. It may be that the study of these texts leads to the laboratory, or not. Political and public texts are articulations of sociotechnical reality without necessarily indicating the power of the laboratory. Powers, potencies, agencies are interesting whether in the laboratory or elsewhere.

The empirical material of the study

For a fundamental understanding of stem cells, I have used a standard text-book recommended by medical students whom I have met in stem cell laboratories (Alberts et al. 1994). In order to get a general overview of the field I have consulted books on stem cell research, ethics and politics.[49] I have borrowed these books at university libraries, but mostly bought them on major Internet book stores.[50] Most of these are collections of papers by people considered to be authorities or crucial actors (such as Thomson, Gearhart, or President Bush). I have also examined the popular science writing, which has been scarce, due to the relative novelty. These materials are – in theoretical respects – far from ANT and would thus normally be considered as other analyses of the same situation or "reference literature". Since the topic is the public and political dynamics of hESC research they are also source material. Each collection is a summary of the actors, analysts, arguments and facts that are regarded as important. They are part of network attempts, the sociotechnical reality of hESCs.

Chapters 2 and *3:* To access Congressional politics I have used the Governmental websites on the Internet (http://www.gpoaccess.gov/ and http://thomas.loc.gov/) to download all of the Congressional hearings during this period that responded to the keywords "stem cells". This search resulted in six hearings held between December 1998 and September 2001, by a Senate subcommittee of the committee on appropriations for the departments of labor, health, and human services (DHHS), and education, and related agencies. There were six hearings, with in all

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49 See the introduction for specific references.

50 I have utilized the libraries of mainly two universities, Göteborg University and the University of Minnesota.

twelve occasions, and eleven of these fall within the temporal constraints (November 1998 to August 2001).

Another source of information available via Internet has been the national panels and reports from the period. President Clinton requested, in November 1998, a review of the ethics of stem cell research from the National Bioethics Advisory Commission (NBAC). In September 1999, this resulted in the report *Ethical Issues in Human Stem Cell Research* (Shapiro et al. 1999). The American Association for the Advancement of Science (AAAS) and the Institute for Civil Society (ICS) finished a report, *Stem Cell Research and Applications: Monitoring the Frontiers of Biomedical Research*, around the same time, in November 1999 (Chapman et al. 1999). A third national overview was pursued toward the end of the period, on June 22, 2001, by way of a workshop: *Stem Cells and the Future of Regenerative Medicine*. This was organized by two of the National Academies – the National Research Council (NRC) and the Institute of Medicine (IOM) – with the support of the National Academy of Sciences (NAS). The NAS is the central of these semi-official and advisory bodies. Apart from the resulting publication in 2002, I have listened to audio files from the workshop available on the Internet (*Workshop on Stem Cells and the Future of Regenerative Medicine* 2001). A final report that immediately preceded Bush's decision was the Report for Congress from the Congressional Research Service (CRS): *Stem Cell Research* (Johnson 2001). I acquired this from the library at the University of Minnesota, and it is available on the Internet.[51]

All of these hearings and reports are, as it were, an already sifted source. The committees prepare bills for the two Houses and in this respect may have a semi-legislative power (US Senate 2005). At their service they have a number of subcommittees. Public Congressional hearings are a source of information for the preparation of bills in Congress and for the interested public. In the selection of witnesses the committees or subcommittees are independent, but they are supposed to call advocates representing a wide range of opinions. However, it sometimes happens that committees or subcommittees are accused of being partisan in the selection process. Likewise, the reports are the result of selection processes. The members of the NBAC were appointed by the President. The AAAS is a federation of scientific societies and also individual members,

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[51] There were also other CRS reports during the period, in 2000. The 2001 report was especially interesting because of the proximity to Bush's decision.

which mentions first the furthering and facilitation of science in its self-description (Chapman et al. 1999: 38). [52] The ICS was created in 1995 to "renew civil society" and strengthen community initiatives, e.g. by providing grants for grassroot initiatives (p. 39). The NAS and its related bodies consist of "distinguished scholars engaged in scientific and engineering research" (*Workshop* 2001: iii). Speakers at the workshop were called by the NRC and IOM organizing committees. According to the website of the CRS (http://www.ncseonline.org/NLE/CRS/) it is "a branch of the Library of Congress providing nonpartisan research reports to members of the House and Senate". However, in spite of this declaration, the CRS report – just like the hearings, and the other reports – are sifted sources, one might say. The participants and scientific results are preselected in the bodies. I am not selecting the actors. They have already been selected.

In order to understand the Congressional dynamics and learn more about the actors that appear in the Congressional material I have looked for media reports in a few major American newspapers, i.e. *The New York Times* and *The Washington Post*, and in *Science* and *Nature*. The media material is also already sifted. A partisan background source to understand the political game and the panel deliberations is Ronald Green's *The Human Embryo Research Debates* (2001). Green is a bioethicist and was a part of the working group for the AAAS/ICS report. In 1994 he was also a member of the Human Embryo Research Panel (see below). Green is supportive of hESC research, which is visible in the account.

A short detour is required, in order to clarify the status of this heterogeneous material in an ANT-inspired study. The siftedness is not a problem, but necessary and deliberate. If anything the term *sifted* is a problem, because it could suggest that something more original has been slanted in a certain way, as a divergence or distortion. According to ANT there is no *original* reality, but *articulations* in which sociotechnical reality comes to be. More than sifted, the materials are articulations of a certain kind. Since the research question concerns the public and political dynamics of hESC research, articulations from highly public and explicitly political processes are needed. In this case the articulations are a textual material, and in a few cases also graphic material downloaded from web sites, Congressional hearings, or photocopied from review papers. These

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[52] The AAAS is probably the largest scientific organization in the world. It has existed since 1848 and is responsible for the journal *Science*.

are all articulations in one or two of the five loops of the circulatory system of science, viz. the loops to *allies* and the loops of *public representations*. The articulations enforce certain associations between entities. The purpose is not to cover all associations or loops, e.g. the collegial, or instrumental looops. According to ANT, reality is all over the place (see above). Although many case studies have focused on the move from materials to signs – and thus one or two loops – sociotechnical reality is articulated in multiple loops. Reality is multiple, and the universe is pluriverse (Latour 2005: 115–120).

Now the loops are not all that separate from each other. Asking for the public dynamics will also involve scientific materials and some data about corporate activities – in so far as these are part of the public dynamics. Therefore I have also approached scientific articles that are mentioned in hearings etc. The most important ones are Shamblott et al. 1998 and Thomson et al. 1998, but also overviews in which hESCs or non-human embryonic stem cells are discussed. They have been found via Medline searches on the keyword "stem cells". Of the many articles on stem cells I have selected reviews or articles by scientists who have appeared in hearings, reports, or in the media. These articles have, in general, been possible to download from journal databases accessible via university libraries, or have been available in the libraries' collections of scientific journals. I have also "Googled" to find additional material about, or from, the actors who appeared in public.

It is important to note what can and what cannot be claimed on the basis of this material. Although the study is based on empirical material it is controlled by my meta-theoretical interests in the concepts of obligatory point of passage, boundary objects, the metaphor of circulation, and the implication of politics for ANT. Empirical data has been gathered *in relation to* the conceptual explorations. This obviously affects the possible claims and contributions. There are no claims to cover the whole situation of debates between 1998 and August 2001 – whatever that might be.[53] Initially the contributions are more theoretical than empirical. So many commentators have already said so much about those debates, which posits no hindrance for the purpose. Seeing differently does not primarily require new facts, but a new perspective.

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[53] For one suggestion of what it might be (to cover most of the press/politics during this period), see Nisbet et al. 2003.

This choice of material and temporal limitation could be (and in fact was) made quite early. It is after this that it becomes difficult to state any pre-existing selections or criteria. Of course, I could make a rational reconstruction of such selection processes, but this would go against the method and purpose of the study.

For the later chapters (5–7) the empirical process has been guided by unpacking. Unpacking is similar to the job of a private detective finding a dead body in the library. The process goes backwards clue by clue, without knowledge of what sort of people, materials, relations the search will lead to. In ANT terms unpacking is to open black boxes and stable elements, and follow the associations and articulations (= clues) that have contributed to the stabilization (= corpse). Detective stories can run forward, but there is definitely a point in telling the story backwards without revealing the whole plot beforehand. The same pertains to this understanding of the public and political dynamics of hESC research.

Chapter 5: From 1998, I go backwards in order to see whether and how three elements of hESC research have appeared together earlier, in public and political dynamics. The unpacking searches for articulations that offered a "contrasting continuity" to the 1998–2001 situation; continuity, since without this, the two situations would not be connected in any sense; contrasting, since if the situations were totally similar there would be no point in speaking of two situations, or of unpacking.[54]

The task might seem impossible since hESC research is sometimes held to have dawned on a public awareness and the political process in November 1998. Going backwards from the debates in 1998–2001, there was one public and political event that many actors referred to: The Human Embryo Research Panel (HERP) convened in 1994. A copy of the report was ordered from an American library to Sweden. Some of the testimonies in the HERP sessions I found on the Internet. Although the report concerned what its title says, the hESCs existed as an articulated expectation between its covers. In order to capture the public dynamics in relation to the HERP, I searched the Internet by way of Google on the keywords "HERP", "human embryo research panel" or "embryo research".

I also searched the Congressional database for the keywords "embryo*" and "embryo research" to find out whether and how Congres-

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54 This phrasing is indebted to Fujimura 1996 and her traces of continuity, pp. 16 and 136.

sional debates handled the issue. There were a number of mentionings in Congress, but I found only one exchange in which several representatives had an animated discussion, in the House of Representatives, July 1996 (House of Representatives 1996).

Again, the aim has not been to cover all actors or all statements. My unpacking has been oriented toward contrasting continuity between the HERP situation and the articulations of hESCs, 1998–2001. This means that I have halted after finding enough to shed a contrasting light on the later situation and to guide me further back.

The study continues in order to understand why some commentators referred to IVF embryos and transplantation therapies as a solution to the disputes in 1994–1996. From the HERP the trails branch off backwards toward two different elements resulting in different material.

Chapter 6 (IVF and "spare embryos"): To capture the sociotechnical reality of "spare embryos" and understand their role after 1994, my first clue was Louise Brown, considered to be the first baby born by means of in vitro fertilization (IVF). Her scientific fathers were Robert Edwards and Patrick Steptoe. Consequently, I searched for publications by, or about, these. There were four sorts of documents: popular books, journal articles by scientists and by ethicists, political documents, and statistical reports. My first source was Edwards and Steptoe's autobiographical *A Matter of Life* (Edwards and Steptoe 1980). It is a partisan contribution in which the two authors represent themselves as successful pioneers – against all odds. However, their victors' voices guided me to what they saw as the main opponents and obstacles. These were textual linkages to other ethical and scientific references. That was also how I continued, by way of textual associations. Sometimes they were direct associations. Sometimes they were hints in a certain direction. I was an *ant* crawling from text to text. In this respect the search was not systematic, but networkish. Some of the associations led to the British debates; trails which I could not follow due to the US focus.

The main political documents were produced in the policy processes directly after the Supreme Court's 1973 interpretation of the constitutional implications of abortion (Roe vs. Wade 1973): the 1979 report issued by the US Department of Health, Education and Welfare (DHEW) and the earlier policy process visible in the Federal Register (FR) (US DHEW 1974, US DHEW 1979). In the FR proposed policies and public responses are notified. Especially the latter are interesting in order to understand the public dynamics. The Congressional activity increased to-

ward the end of the 1980's, when several national reports were produced and Congressional hearings held (House of Representatives 1987, House of Representatives 1988, Office of Technology Assessment 1988, US Congress 1989). All of these documents were possible to order from American libraries. Statistical data about the general use of fertility services were published by the National Center for Health Statistics on several occasions in the 1980's (Hendershot and Bauman 1981, Mosher and Pratt 1990). Although these statistics said something about the general reproductive status usually very little is said about the clinical realities. The latter became more and more important when I found out that the "spare embryos" were not there from the beginning. To find out where the procedures that produced them came from, I turned toward the scientific papers.

The two main journals for following the development of IVF techniques in the 1980's are *Fertility and Sterility* and *The Journal of In Vitro Fertilization and Embryo Transfer* (existing from 1984). The first is available at the Göteborg University library. The second I ordered from outside libraries. In this journal reports appear from the *Conferences on In Vitro Fertilization and Embryo Transfer* and the *Congress of Future Aspects in Human In Vitro Fertilization*. The former were held for the first time in 1980 and then followed by annual or biannual conferences at several locations (Jones Jr. and Schrader 1988, Seppälä and Edwards 1985). In the early 1980's there are a number of collections produced to capture the state-of-the-art and bring together the medical, ethical and social issues (Biggers 1984, Mazor and Simons 1984). Probably due to the federal non-involvement there were no systematic survey and statistics in the 1980's about the clinical use of various IVF techniques, such as excess production of embryos and subsequent freezing. In conference material I found an international survey (Van Steirteghem and Van den Abbeel 1988).

To compensate for this gap, I turned toward traces of IVF procedures in comments from bioethicists in articles and books. By way of defending IVF these authors articulated what they perceived as standard IVF procedures during the 1980's (Robertson 1986, Singer and Wells 1984, Steinbock 1992). These are treated for what they are: articulations of perceptions. As such, they are part of the public and political flows of IVF.

The situation is more clear after 1992, when the Fertility Clinic Success Rate and Certification Act required the Centers for Disease Control and Prevention to publish annually an Assisted Reproductive Technology suc-

cess rate report. These reports are available on the Internet (US DHHS 1998, 2000, 2001a, 2005).

Chapter 6 (transplantation therapies): In the inquiring about the importance of transplantation therapies in fetal tissue research, political texts were again basic. The one event that was mentioned repeatedly in the negotiations after 1994 and 1998 was President Clinton's change of fetal tissue research policy in 1993. Therefore I investigated the Congressional bills that accompanied this change, again via the Congressional web sites. By reading these debates I was also led on to earlier debates, in the media and in Congress. The "leads" were provided by the appearance of certain Senators or Representatives and the way they referred to earlier events. I also used free search motors, such as Google and Find Articles (www.findarticles.com) using the keywords "fetal tissue", "fetal tissue research", "fetal tissue transplantation". By means of the library databases I found commentaries and overviews on fetal tissue research from the period (Hanna 1991, Sobelsohn 1989, Vawter et al. 1990).

In actors' articulations, one landmark was the 1988 report from the Human Fetal Tissue Transplantation Research Panel (HFTTRP) (Adams 1988). This was acquired from the University of Minnesota library. My searches continued along two flows from the HFTTRP. One direction led to the media reports, and previous, political debates. The latter eventually led to the Supreme Court's decision on abortion, via the 1975 federal report *Research on the Fetus* (US DHEW 1975). This was ordered from US libraries. Another direction led to scientific trails of references. Within the report, as well as in other material, scientific work was referenced. These papers constituted what was regarded as the science of fetal tissue research for the panel's (and others') ethical deliberations. From public and political loops the material led to laboratory and collegial loops – still only by way of texts. I followed these flows from one citation and reference to the next. I was guided by the interest in alternatives and uncertainties (outlined above). To understand the centrality or marginality of uncertainties in the scientific material I kept close to the major journals such as *The Journal of the American Medical Association* (*JAMA)*, *The New England Journal of Medicine (NEJM)*, *The British Medical Journal* (*BMJ)*, and *The Lancet*. After a number of articles I found that some researchers occurred more frequently than others. Without scientometric measures I searched on these names specifically.

Chapter 7: When the study returns to the 1998–2001 dynamics, the same material as earlier appears again. Now the attention is radically dif-

ferent because of the unpacking performed in the preceding chapters. One group of materials is added. Due to the focus on the definition of the term pluripotency more material from scientific articles is included. I found articles on adult stem cells by drawing on my laboratory experiences from 2002 and onwards. In the field of stem cell research (adult and embryonic) there was by then a quite explicit canon of the adult stem cell findings that had appeared in 1998–2001. This was salient in conversations and at conferences. Apart from also being mentioned in the Senate hearings, these "plasticity" papers are often a part of the introduction or discussion sections in later papers.

At one point in Chapter 7 I recount a database search of scientific articles using the terms pluripotency and/or totipotency. This search is done in order to capture general tendencies in the scientific community. It is thus a step away from the interpretative work of finding associations and flows. For this mathematical exercise I used the reference program EndNote to search the database Medline/Pubmed accessed via the Göteborg University library. I searched the occurrence of the truncated terms "ES cell*" and "embryon* stem cell*" (thus covering ES cell and ES cells, embryonic and embryonal stem cells) in combination with "pluripoten*" and "totipoten*" (thus covering pluripotent, pluripotential, and pluripotency, etc) regardless of the context of use in articles. The search was conducted November 15, 2005.

The above account – although complicated as it stands – is by necessity a retrospective simplification of how I acquired and interpreted a body of empirical material. Common to all of these text studies is that the straightforward "Follow the Actors!" is modified. In the next chapters I will follow trails in texts, not in labs. Sometimes there are explicit links going from paper to paper, from report to report. More often I will have to reconstruct associations, trails, and flows of references, entities and actors from textual materials. This also accounts for the unsystematic acquisition of source material. The empirical work is interpretative, modifying itself while moving forwards/backwards – quite like an assemblage – and as such can only be assessed in retrospect, not defined beforehand.[55]

Many of us are used to thinking in terms of a temporal line going from the Beginning to the End. However, a crucial point in putting ANT to

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[55] I would guess that the same interpretative work has to be done when following human actors around in the laboratories; cf. the anthropologist of *Laboratory Life* by Latour and Woolgar 1979.

work is to let the *ant* create a new chronology by following associations. Instead of starting with a year-based linear chronology that the author – after doing the study – is able to reconstruct, it is integral to the ANT *seeing* of the world to let the *ant* do his work (i.e. start with the corpse in the library). Revelations and chronologies have thus been provided reluctantly and go against the *ant*'s approach, the methods of his moves.

The research questions

According to the notion of assemblage presented already in the Introduction it is hard to formulate research questions in advance. ANT is about unpacking or understanding a phenomenon. More than a soccer field this is a hike in the mountain. We still don't know what will be around the next corner – in the next black box. If the questions are posed beforehand it means the phenomenon is already known. Research questions thus come one by one. One of these resulted from applying ANT to the initial puzzle about stem cell research and politics.

> (ANT-Question No 1) What is the sociotechnical reality of hESCs?

ANT is used to find associations between heterogeneous elements in actor-networks. This was introduced above together with the notion of sociotechnical reality. However, this task is pursued in relation to the meta-theoretical interests. One question resulted from applying existing critiques of ANT.

> (Meta-theoretical Question No 1) How can the notions of obligatory point of passage and boundary objects be put to use in order to understand the sociotechnical reality of hESCs?

Another meta-theoretical question was raised because of focus on the public and political dynamics:

> (Meta-theoretical Question No 2): How can ANT account for the role of explicitly political actors in sociotechnical network attempts?

When these three questions are combined with the empirical material, the textual materials from 1998–2001, they make up the detailed aim that was mentioned in the Introduction:

To explore ANT in order to understand the sociotechnical reality of hESCs in the USA prior to August 2001 – in particular with regard to the public and political dynamics.

This is, in turn, one way to approach the basic, underlying aim to *exercise seeing differently*. All of these questions guide *part one* of the study, spanning the three next chapters (Chapters 2–4). After finding a first answer to the question the study continues with a second research question that relates to the general aim. In accordance with ANT, it is possible to unpack stabilized object and actor-networks to find out how socio-technical reality has come to be. This was formulated above as a second ANT-inspired research question.

> (ANT-Question No 2) How has the sociotechnical reality of hESCs come to be?

Together with the temporal focus above, this question is now specified.

> (Temporally limited ANT-Question No 2) How did the sociotechnical reality of hESCs in the USA 1998–2001 – and especially the public and political dynamics – come to be?

Obviously this is a very general question, and it would be impossible to answer without qualifications. Such qualifications exist after part one, meta-theoretically and empirically. What will then appear as central to the sociotechnical reality of hESCs (1998–2001) are the unhindered *flows* between actors, together with a specific combination of *elements* in hESC articulations. The flows will be the result of meta-theoretical elaboration. The three elements are the result of following the public and political articulations of hESCs. In *part two*, the analyses are thus guided by a second modified question:

> (Meta-theoretically modified Question No 2) How were the flows between actors and the three elements – frozen embryos, transplantation therapies, and pluripotency – of hESCs mutually stabilized?

PART I

2. Attempts to Establish an Obligatory Point of Passage: The 1998–2001 Negotiations of Federal Funding

Introduction

In November 1998 two laboratories announced that they had ”derived” and cultured pluripotent embryonic cells (Shamblott et al. 1998, Thomson et al. 1998). More than two and a half years later, on August 9, 2001, President George W. Bush addressed the American people from his ranch in Texas and became the first Republican President to approve of federal funding for embryo research. Bush's decision was one end-point (certainly not the last) of the negotiation process set in motion in November 1998. I approach this negotiation wondering: What were human embryonic stem cells (hESCs) during those two and a half years? Drawing on actor-network theory and theory of science the question becomes: What was the *sociotechnical reality* of hESCs during that time?

This question opens for theoretical and empirical issues. Empirically, the question concerns what associations and articulations made up this reality. Theoretically, three issues follow from this, according to Chapter 1. A first one is the network's degree of stabilization. Another is how entities are related to each other, i.e. the mode of coordination. A third concerns which actors were more or less responsible for coordination, i.e. how agency was distributed. Actors may be funneled to take a detour or remain in their worlds. Entrepreneurial humans may be positioned as an obligatory point of passage for the emerging actor-network, or boundary objects may coordinate people through the flexible uses involved in diverse practices.

In this chapter I focus on how one specific relationship is articulated, viz. the association between the Federal administration and hESC research. This relationship is probably the most controversial and conspicuous feature of hESC research in the USA, between November 1998 and August 2001. Before any other issues or elements are investigated the fede-

ral funding must be understood, or at least approached. Here, this is done in two parts. First the proponents of federal funding are given space, and then the opponents.

Associations of a new reality

In an attempt to understand the sociotechnical reality of hESCs in the USA 1998–2001 it is impossible to bypass the role of the government and Congressional politics. Even internationally, the disputes about whether to support hESC research with federal funds, or not, are well known. The Federal administration is either associated with, or dissociated from, hESC research.

A few words are needed about how this study treats the Federal administration. No individual is solely identifiable with it, not even the President of the USA. During this period, November 1998 to August 2001, there is great uncertainty about the role of the Federal administration in relation to hESC research. The President may do one thing, executive agencies such as the The National Institutes of Health (NIH) another thing and Congressional committees and individual senators a third, fourth and fifth thing.[56] All of those actors are closely tied to the Federal administration and may each articulate its role differently. Only at the end of the period (August 9, 2001), does Bush's decision define this role. There are some other decisions, but these are never put to work during the period. In order to understand the role of the Federal administration in this period of uncertainty it is useful to not deal mainly with decisions, but to treat the Federal administration as an aggregated actor that can be articulated in a number of ways, decisions included.

This way of dealing with the Federal administration differs from an exclusive focus on decisions and actual policies. If this were a study in political science one aim could have been to explain Bush's political decision.[57] However, the purpose of this analysis is not to explain political decisions, but to understand the sociotechnical reality of hESCs (which may, however, lead to improved understanding of political decisions). So many articulations of the stem cells are also articulations of

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56 The NIH is a part of the US Department of Health and Human Services and the main agency for Federal support of medical research.

57 It is probably too early and too difficult to pursue such a study at the present time, especially from Sweden. There are too many factors of Washington political power-games for a good answer to be found.

what the Federal administration is and should do. It is in this respect that the role of the Federal administration is crucial, and not only in official Presidential and Congressional decisions, but through others such as scientists, patients, politicians, corporations and bioethicists. Indeed Bush's decision and other decisions are interesting as articulations – among others – of what the Federal administration and hESCs are. Often the latter are also endowed with capacities and implications such that they were, in effect, also an actor.

In ANT terms there are alternative patterns in these articulations. In one cluster of articulations the Federal administration is made responsible for the hESCs as if it were the main actor. This responsibility is constructed together with the agency of hESCs.

Stem cell actions

As soon as the hESCs were announced they were associated with a federal course of action, and sometimes more than that. Sometimes the stem cells seemed to have direct political consequences, at least according to editorials in *Nature* and *The New York Times*:

> Last week's announcement on human embryo stem cells requires a change in the US law on embryo research. (*Nature* 1998: 97)

> The breakthrough in growing human stem cells in laboratory with private funding is not only a remarkable achievement, it is a rebuke to Congress for banning Federal funding of this exciting new research. (*The New York Times* 1998)

Although less explicitly President Clinton also responded to the stem cell reports from Thomson's and Gearhart's groups (and ACT's announcement of cloning experiments), in November 1998. He wrote a letter to the National Bioethics Advisory Commission (NBAC), asking for a report about the ethical and medical implications of the research.[58] In his letter Clinton presented the policy situation and mentioned the ethical concerns. He recapitulated the 1994 ban on federal funding of embryo research and the balance between the then-anticipated medical benefits and "immediate ethical concerns".

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[58] President Clinton's letter of November 14 was addressed to Dr. Harold T Shapiro, Chair of the NBAC. The commission first reported back to Clinton November 20 after consulting Dr. Ralph Brinster and Dr. Michael West. The more extensive report, delivered in September 1999, included a wider range of perspectives.

> Four years ago I issued a ban on the use of federal funds to create human embryos solely for research purposes. The ban was later broadened by Congress, which will prohibit any embryo research in the public sector. At that time, the benefits of human cell research were hypothetical, while the ethical concerns were immediate. (Shapiro et al. 1999: 88)

The research was already constitutionally and legally possible, with *private* funds. The specific ban on *federal* funding was due to Congressional action, and without support from the Republican-dominated Congress Clinton could not change this even if he wanted to.[59] According to the continuation of his letter he now did not have to enact a change on his own. The new developments in hESC research motivated a new review of the issues.

> Although the ethical issues have not diminished, it now appears that this research may have real potential for treating such devastating illnesses as cancer, heart disease, diabetes and Parkinson's disease. With this in mind, I am also requesting the Commission undertake a thorough review of the issues associated with such human stem cell research balancing all ethical and medical considerations. (Shapiro et al. 1999: 88)

Gearhart's and Thomson's announcements in November 1998 became a starting-point for renewed considerations and disputes on the ethics and policy of embryo research; at least this is the point of Clinton's request to the NBAC (US Senate 1999a: 14–16, 1999b: 66–68, Shapiro et al. 1999). According to the President the consequences of the stem cells had moved from "hypothetical" to a "real potential". He was joined by others. Apart from NBAC, the NIH also drafted guidelines for hESC research in 1999, and sought public comments between December 1999 and late February 2000. The NIH released the finalized guidelines in 2000 (NIH 2000). There were differences between the NBAC and the NIH in relation to how much the administration should be involved in the actual and original production of hESC lines. The NIH took the more restrictive line and claimed that federal funds should not be used to destroy embryos, but only for work on (already produced) cell lines. Those differences aside the two bodies were both in support of federally funded research on hESCs. They both argued for the responsibility of the Federal administration based on the capacities and promises of hESCs. It was no

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[59] The Dickey-Wicker amendment had been attached to the DHHS appropriation in 1996 (Public Law 194–99) and in 1998 was encoded in Public Law 105–78, § 513. See more about the Dickey-Wicker amendment in Chapter 7.

big surprise. Clinton had himself appointed the NBAC. The NIH is a federally controlled authority.

Faster than the NBAC and the NIH, Senators Tom Harkin and Arlene Specter acted. They were the leading senators in the Senate Subcommittee on labor, health and human services.[60] It is worth noticing the speed with which the Senate hearings were called. Only four weeks after the announcements by Thomson and Gearhart the Senate subcommittee gathered a first hearing on stem cell research and cloning technology.[61] In these hearings many of the central scientists, patient organizations, bioethicists, corporate and religious representatives, and Senators appeared. The opening remarks of Senator Specter, the chairman of the sub-committee repeated the formula:

> The subject matter on our hearing today arises from a provision of the legislation reported out by this subcommittee last year, which limits the use of Federal funds for research on human embryos. That is an issue which has come into sharp focus with very dramatic recent medical developments, warranting a closer analysis or perhaps a reanalysis of that question. (US Senate 1999b: 1)

The NBAC, the NIH guidelines and the subcommittee hearings were all official sites in which the two actors – the Federal administration and the hESCs – were articulated. In all of those sites the Federal administration was apparently deeply affected by the hESCs, which were usually articulated as a powerful actor. The absolute majority of the testimonies in the first three Senate hearings (December 1998 – February 1999) argued for the federal funding of hESC research.

Pluripotent agency

What are the powers of the hESC actors and how do they affect the Federal administration? They have effects in several steps. First, there are the fundamental capacities of the cells, sometimes articulated in images. The following is from Geron Corporation in the Senate hearings (US Senate 1999b: 61):

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60 Committee on appropriations.

61 It was the first of a total of three such occasions within two months, and twelve in the next two years.

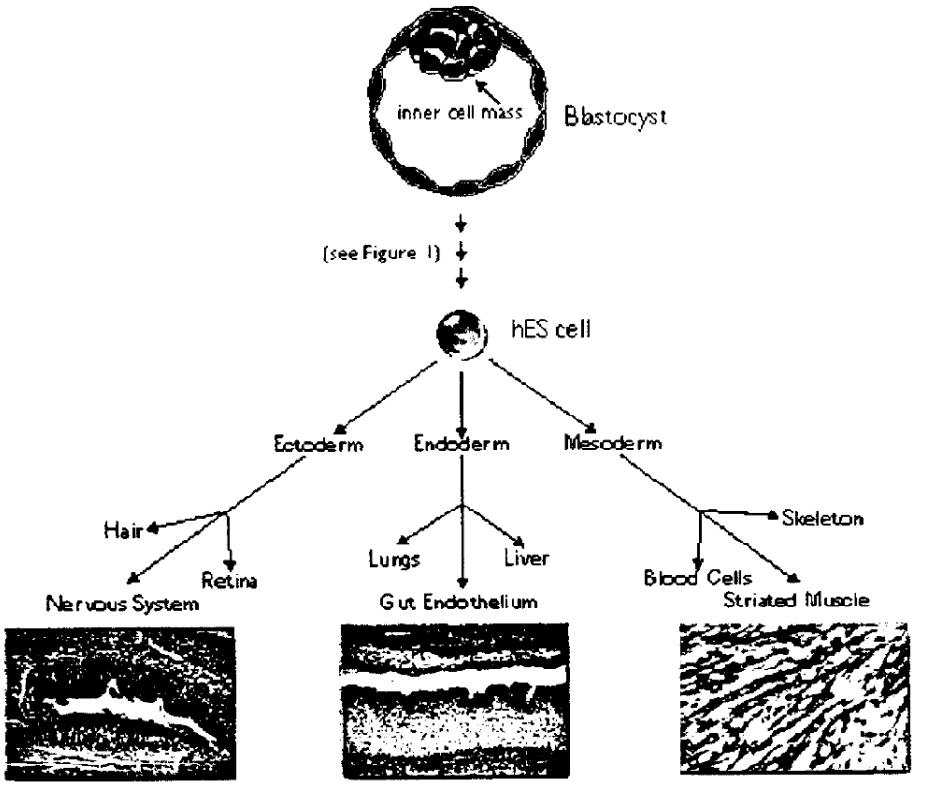

Figure 4: Differentiation (development) of hESCs into Three Germ Layers. Reproduced from (US Senate 1999b), by courtesy of Geron Corporation.

My introductory explanation of stem cells reproduced another (graphically more sophisticated) illustration from the University of Wisconsin web site (see Introduction). It was doing the same thing. Both cases feature the biological potential of the cells, their developmental potential and result in visible tissue types, such as muscles, nerve cells or blood cells. These tissues are transformable says the Subcommittee chairman, Senator Specter:

> The recent advances have shown that the stem cells have potential to grow into any kind of bodily tissue and have, at least reportedly, enormous potential on a wide variety of very serious ailments – heart disease, diabetes, Alzheimer's, cancer, spinal cord. (US Senate 1999b: 2)

The recent advances are the two reports from Thomson's and Gearhart's groups. This is from the latter:

> Human pluripotent stem cells, with their potential to differentiate into a wide variety of cell types in culture, would be invaluable for studies of some aspects

> of human embryogenesis and for transplantation therapies. (Shamblott et al. 1998: 13731)

The mentioned differentiation potential is one definition of pluripotency. Shamblott et al. link it directly to studies of human embryogenesis and transplantation therapies.

A pluripotent transformation of the USA

Pluripotency is extended from stem cells to therapies to individual patients and the whole nation. Actors are not merely articulating the use of stem cells in therapies. Through their use in transplantations the stem cells are capable of transforming people's lives, medicine and even the USA and the world. This is done by stressing the qualitative and quantitative change on an individual and collective level. Examples of the two most common needs linked to the use of hESCs in transplantation therapies come from Richard Pikunis and Doug Melton. Pikunis appears in the second hearing. He is a Parkinson patient, a lawyer, a doctor, and only 27 years old, and thus much younger than PD patients usually are. His account is touching, not least because of his age.

> it [the research on hESCs] holds my future in its hands. My son celebrated his first birthday and is learning to walk as I am slowly losing my ability to do so. I wake up every morning barely able to move until my medication kicks in. (US Senate 1999b: 103)

Pikunis does not *associate* himself with the stem cells, but *anchors* his life and his hope in them.

> Only you can help put an end to the human suffering associated with Parkinson's disease. Do not let me become a burden to my loved ones and society. Let me live my dream of an optimistic future with my wife and family. (US Senate 1999b: 104)

Dr. Doug Melton combines a scientific identity with a personal relationship to diabetes by being both a molecular biologist and the father of a diabetic son. He is involved in The Juvenile Diabetes Research Foundation (JDRF).[62]

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[62] JDRF is a patient organization devoted to patient support, advocacy and raising funds for research relating to type I diabetes. It was started in 1970.

> I am sorry to say that I cannot recall a night of peaceful sleep since Sam was diagnosed nearly 7 years ago, and I am unwilling to accept the enormity of the medical and psychological burden […] (US Senate 1999b: 99)
>
> today I look to science praying it will be able to save my life. (p. 102)

These are personal needs and conditions which the hESCs – by being used in transplantation therapies – are thought possible to relieve. By stressing the gravity of these conditions a possible reality is articulated. Apart from qualitative, there are quantitative articulations.

CEO of Geron Corporation, Thomas Okarma, presented one list of possibly affected people: 5 million congestive heart patients, 1 million cases of invasive cancer/year, atherosclerosis, 650,000 deaths/year, 1.4 million diabetes patients, 1 million Parkinson's patients, 500,000 stroke victims and 4 million Alzheimer's patients (US Senate 1999b: 53).[63]

To support stem cell research, in May 1999 34 patient organizations formed an umbrella organization *Patients' Coalition for Urgent Research* (CURe), with the explicit goal of supporting the federal funding of hESC research. According to their estimates more or less every second American could be affected by the research.

Cardiovascular diseases	58 million
Autoimmune diseases	30 million
Diabetes	16 million
Osteoporosis	10 million
Cancer	8.2 million
Alzheimer's disease	4 million
Parkinson's disease	1.5 million
Burns (severe)	0.3 million
Spinal cord injuries	0.25 million
Birth defects	150,000 (per year)
Total	128.4 million

(Perry 2000)

The fate of these numbers is an interesting history in itself. In several places they *became* the quantitative need for hESC research. The Ameri-

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63 Also see US Senate 1999b: 99, for quantitative articulations.

can Association for the Advancement of Science (AAAS) and the Institute for Civil Society (ICS) picked up on these numbers in their joint report where they stated "Virtually every citizen is affected directly or indirectly" (Chapman et al. 1999: 4). When Republican and Pro-life Senator Orrin Hatch wrote to President Bush and the Secretary of Health, Tommy Thompson, in June 2001, he used the same numbers – and formulations.

> Potentially, stem cell research can help virtually every American family. It has been estimated that over 128 million American [sic!] are afflicted with conditions that may benefit from embryonic stem cell research. (Hatch 2001b)

The AAAS/ICS report did refer to other sources, e.g. numbers from the American Diabetes Association estimating the cost of treating diabetes at $100–140 billion in the USA. (Chapman et al. 1999: 4). Whatever the source and the flow of numbers, these actors use them to articulate a total transformation of millions of lives. The actors are not merely discussing a therapeutic option, or a change in medicine. Patients' lives will be totally transformed, and the numbers of Americans affected are huge.

The missing link

Together with the articulation of hESCs as a powerful actor a specific agency is attributed to the Federal administration. The hESCs and the Federal administration are co-constructed. By bringing in the pluripotent transformation, a new reality was allegedly made possible because of the pluripotent stem cells – on one condition.

> But all of these benefits could be delayed or even denied to patients without a healthy partnership between the private sector and the Federal Government. [---] The only way to ensure that this research is conducted is to allow NIH to support it. But unfortunately, as the American Society for Cell Biology writes in a recent letter, the ban on human embryos research "has the effect of excluding the majority of the Nation's most prominent researchers who are supported by the NIH and limits the development of new therapies". [---] The research conducted by the distinguished scientists sitting before us today holds such hope and such potential for millions of people around the world who are sick and in pain that I believe it is morally wrong for us to prevent or delay our world-class scientists from building on this progress. (US Senate 1999b: 3)

The hESCs and their capacities are brought to bear on the Federal administration by extending pluripotency to the whole nation and the whole World, according to Harkin. At stake here is not hESCs but a new world, dependent on the condition of federal involvement. Harkin, the American Society for Cell Biology (ASCB), and other professional organizations, e.g. the Biotechnology Industry Organization (BIO), claim that the private sector lacks financial motivation for a lot of the fundamental research needed to advance treatments that will only be realized in the very long term. The pluripotent transformation of the USA may be obstructed if the Federal administration does not take its responsibility. What will happen then?

> Industry can target one or two or a couple and get it done in a reasonable time. The more difficult ones will just be left undone.
>
> Senator HARKIN. So you are saying, again, with this research there could be all kinds of breakthroughs later.
>
> Dr. THOMSON. Take diabetes as an example. [---] That is likely to be a more difficult cell to derive from embryonic stem cell. It requires a lot of basic research, and the Government has the job of doing basic research. (US Senate 1999b: 33)

Dr. Goldstein, a stem cell scientist, was asked about the time-line for treatments of Alzheimer's.

> Alzheimer's is a very tough problem, Senator, and I do not think we have a very good sense of how long it will be. I guarantee you that every day we delay is another day that the clock ticks and we are not making progress using this vital research need. (US Senate 1999b: 113)

Dr. Doug Melton, a molecular biologist, father of a diabetic son, and involved in the JDRF comments as a scientist and urges for federal funding with reference to "the research trenches":

> What I can see, speaking from the scientist's point of view in the trenches, is that there are many people with very good ideas about how to actively pursue this research, and we are anxious for Federal funding. (US Senate 1999b: 112)

Again and again federal funding is the missing link between pluripotency and difficult diseases, and more, since a pluripotent transformation is at stake. Thomson, Melton, Goldstein, Hatch and Okarma all claim that it is insufficient to keep hESC research in the private sector.

In addition to the hESCs and a transformed USA the Federal administration is articulated. There is a simultaneous construction going on here of hESCs, a new US reality, and the Federal administration. The path from pluripotency to cures of difficult diseases leads to a transformed USA, but on this path one actor is given a choice. Because of hESC pluripotency the Federal administration has been given an opportunity to act on these diseases for the benefit of the many. It is not only the hESCs that become a specific and powerful actor in these articulations. The Federal administration also becomes a powerful actor as a direct consequence of hESC pluripotency. The agency of the Federal administration is directly derivable from the agency of the hESCs. Only if the humans in decision-making positions allow federal funding can the capacities of hESCs be released. Here is a last example of how these articulations of stakes and the gravity of transformation are said to affect other elements too, for instance the source material. Bioethicist Arthur Caplan quotes his son on the ethical dilemmas:

> I think it is true that the goal of our public policy should be to tell that person in a wheelchair we are going to try and weigh tradeoffs morally ethically, between the hard choices that have to be made […] and that it is wrong in the end if we cannot come up with a policy that says we will not hold that person in a wheelchair hostage to our moral concerns about tissue that will otherwise be destroyed, tissues that are not going to be turned into human beings under any circumstances, or cells and tissues that, because we misunderstand or misdescribe them, are going to wind up being misclassified as potential people or possible human beings. (US Senate 1999b: 36)

This is the agency resulting from the cells' pluripotency and their pluripotent transformation: that if the use of embryos for producing hESCs is prohibited it is holding people hostage to moral concerns.

An obligatory point of passage

The all-encompassing transformation implied in hESC research according to these articulations resembles the three case studies by Latour, Callon, and Law and Callon in which a new actor-network appears all in a seamless web. A new system is set up in which knowledge, truth and society are remade, whether it be the Pasteurization of France, the interplay between scallops, fishermen and researchers, or the military aircraft TSR 2.

Apart from the resulting dominating actor-network the OPP cases display some common traits regarding the mode of coordination and the distribution of agency. The coordination builds on a *funneling* translation of actors' goals. All actors ultimately accept that a detour through the OPP (as a funnel) is the best way to achieve their goals. In the OPP the central group functions as an *entrepreneurial* force driving the actor-network with an almost Machiavellian agency, while other actors either accept or deny the suggested network-formation. This either-or response is closely tied to an extensive *sociotechnical transformation*. If the necessary actors accept the translation a new reality is established through the OPP. If someone or something does not collaborate the actor-network fails. These three features have thus characterized an OPP coordination according to Callon, Latour and Law: an extensive transformation achieved by funneling heterogeneous actors through one central and entrepreneurial actor (or group of actors).

In this case the USA is involved in a pluripotent transformation. Actors envision a sociotechnical reality of stem cells, and the stem cells are the human embryonic ones. Because of the capacities of hESCs the capacities and responsibilities of the federal government increase, and vice versa. The realization of hESC pluripotency in the USA for all the patients in need, is made possible because there is a Federal administration with strong means to funnel the actors. With money and laws the Federal administration has the capacity to stabilize a research practice and subsequently to spread its objects and facts. The network of research facilities and medical clinics that is maintained by federal means is a huge power for social transformation all by itself – even without hESCs. In this case its power is expanded through the power of hESCs; its agency is made even more important because of the agency of hESCs. Latour has used Archimedes motto – "Give me a place to stand and I will move the world" – to explain the power of the laboratory. With a lever and one stable spot one weak man could move a heavy world. In this case it is more than one weak man. The agency of the Federal administration is already considerable. A government can translate people's goals through the simple means of prohibitions and payrolls. It is therefore hardly an actor like any other. It is a center for stabilization with the capacity to force a number of actors to do or to not do certain things; to funnel other actors into a specific understanding of a situation. The already considerable agency of the Federal administration is reinforced by the pluripotent agency of hESCs. If the co-construction of hESCs and the Fede-

ral administration is successful then the stem cells will be supported by all tax-payers in the USA, by way of the administration's authorization of the research, and spread out to the whole country (or at least every second American) through the institutional network of research universities, publicly funded laboratories, and ultimately patients in clinics (Figure 5).

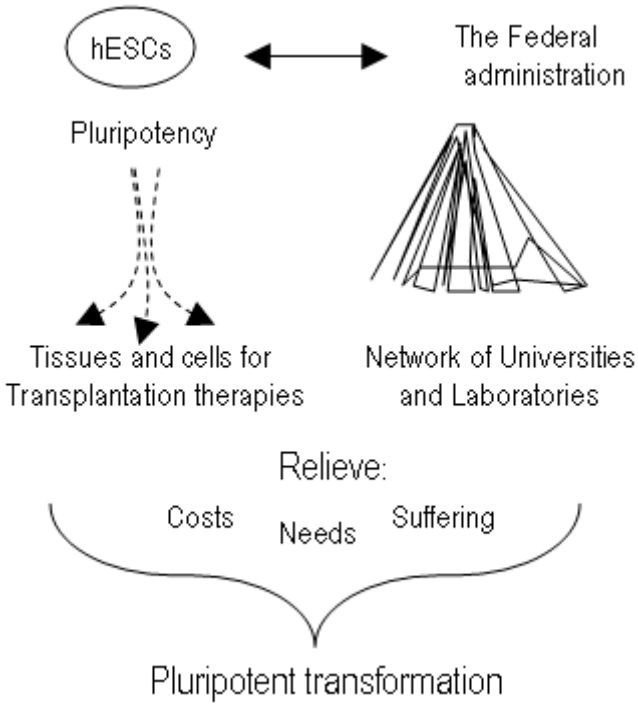

Figure 5: The pluripotent transformation envisioned together with the association of hESC research and the Federal administration.

Among numerous articulations this first part of the chapter has focused on the relationship between hESCs and the Federal administration. So far only the articulations proposing an association of the two entities have been investigated. A striking pattern has been the attempt to establish a transformation of the USA through the co-construction of two strong actors, the hESCs and the Federal administration. There is also a funneling aspect to this coordination as a result of the powerful center constituted by the combined agency of hESCs and the Federal administration. The stabilization at stake through a centralized funneling is typical for an OPP coordination.

Dissociations

An OPP attempt is not necessarily successful, or without resistance.[64] In Callon's study one linkage failed – the one to the scallops, which rejected the attempted OPP coordination. Law and Callon's military aircraft project ultimately failed since the proposed OPP could not be sustained. In the *Pasteurization* two physicians, Koch and Peter, and also the medical profession as a whole opposed the OPP. Koch could be marginalized, but the doctors had to be convinced through the distribution of vaccines and serums directly to the clinics, instead of forcing them to take a geographical detour to *l'Institut Pasteur*. Just as in other cases of OPP some actors in this case resisted the attempted actor-network. By following the opponents' arguments some things about the existing and attempted coordination may be revealed. The actors who objected to hESC research did so to stop the involvement of taxpayers' money in the usage of embryos in stem cell (and related) research.

Although the decision to allow federal funds for hESC research is political and is ultimately taken in Congress or the White House, non-politicians are very important. Some of the articulations from scientists and patient representatives were presented above. Individual persons supported or opposed federal funding as spokespersons for other actors. A senator's role as representative is obvious. S/he is elected and usually interacts continuously with voters from her/his constituency. But, other actors also "represented", as they opposed or supported federal funding. These acts of representation are dependent on the relationship between the individual actor and the group he/she/it represents and the strength of the group. Because of the lack of strong party structures in the USA social movements have achieved an important role, quite distinct from how the parliamentary systems of European countries have traditionally worked. Originally there was no direct connection between the two main parties and the abortion movements (whether pro or anti). In 1980 the Republican party created a "pro-life platform" and the Democratic party soon made "pro-choice" a major priority (National Right to Life 2005).

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64 A few words about resistance in OPP cases: As a result of the central actors' strength the other actors in classic OPP studies have been somewhat bivalent, or two-dimensional. In such studies actors exist in relation to the OPP. They can accept or reject a new understanding of a situation; accept or reject the offer to make a detour through the OPP to reach their goals. Their two-dimensional agency, "yes or no", is a consequence of the attempted funneling.

Still, parties are less important than social movements when it comes to public attention, and political pressure and action (Ferree et al. 2002). Congressmembers are in general more tied to their constituencies and social movements than to a party line. This is the importance of individual actors relating to the cells. They stand for whole clusters of other people and resources that may (or may not) be significant potential allies in the political game.

The pro-life movements have been well organized and capable of gathering people from, largely, diverse Christian viewpoints and denominations. The pro-life movement is a stretched-out network, ranging from state-by-state groups to well-funded national lobby organizations, such as the National Right to Life Committee (NRLC) and the National Conference of Catholic Bishops and its secretariat for pro-life activities. Some are tied to scientists and doctors, e.g. Do No Harm – the coalition of Americans for research ethics, and others explicitly address the political arena by forming Political Action Committees (PAC), such as the Republican National Coalition for Life (RNC/Life). The significance of single actors being called to hearings or interviewed in newspapers relates to the strength of the groups they represent. There is no way to cover all of the pro-life activities touching on the issue of hESC research, but many of the actors have been converging. Some of them will be mentioned, especially those showing up in Congress, the Senate hearings and in panels and major newspaper debates. For the most part, three main objections raised by opponents will be treated. All of these serve to dissociate the hESCs from the Federal administration, and from the envisioned pluripotent transformation. The first objection is legal, the second is moral, and the third is scientific.

Reactions to funneling

The opponents of federal funding did not deny the authoritative and central importance of federal funding, but they could claim that there were already legal obstacles to federal involvement.

> "There are no instances in which I feel the ban on federally funded research on human embryos should be lifted," says Dickey. "The language of this ban prevents taxpayer funding for bizarre experiments, such as cloning. Eventually, I could see the embryonic stem cell technology going in this direction." (Butler 1998: 104)

Congressman Jay Dickey had been instrumental in the then-existing ban on embryo research (the Dickey-Wicker amendment). Another pro-life actor in the hearings opposing the cells was Richard Doerflinger. He officially represented the National Conference of Catholic Bishops (NCCB) and its secretariat for pro-life activities.[65] In the dialogue below, Doerflinger is approached by Senator Harkin in the first Senate hearing on stem cells (December 1998). The issues are the legal and moral status of existing stem cell lines. They are not "organisms", Harkin claims, and the ban on federal funding thus should therefore not apply. Doerflinger disapproves of the question.

> Senator HARKIN. [---] I asked all of the scientists who were here before the question of whether or not these stem cells are organisms. And I believe the record will show they all said no, it is not an organism. [---] Let me ask the nonscientist. Mr Doerflinger?
>
> Mr. DOERFLINGER. Thank you. Stem cells are not organisms. However, two of the three experiments that were discussed here were not experiments on stem cells. They were experiments to get stem cells, by in one case creating and then destroying embryos [ACT], organisms, and in the other case taking embryos already in existence and destroying them [Thomson et al.]. (US Senate 1999b: 71)[66]

Doerflinger agrees about the status of the existing stem cell lines. They are, like any tissue outside of the body, not organisms. He shifts the focus. The problem is the "derivation" of stem cells, which destroys the

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65 The members of the NCCB (now: USCCB) are the Catholic bishops in the USA. It is driven as a corporation by a staff of 350 people. According to bioethics professionals, the USCCB is one of the most powerful lobby organizations in Washington, DC. This is also suggested by its presence in the hearings. According to the USCCB its purpose is:

> To unify, coordinate, encourage, promote and carry on Catholic activities in the United States; to organize and conduct religious, charitable and social welfare work at home and abroad; to aid in education; to care for immigrants; and generally to enter into and promote by education, publication and direction the objects of its being. (The US Conference of Catholic Bishops 2005)

66 The conversation is from a Senate hearing in December 1998, although the US Senate reference is from 1999. There is generally a delay between the actual hearings and their publication, cf. US Senate 2001.

source embryo.[67] Harkin disagrees, although he also (earlier in the hearing) recognizes that the research should be conducted "in an ethically validated manner" (US Senate 1999b: 4).

His second argument is that the ban should be lifted anyway and be replaced with guidelines to regulate the research on stem cells. His example is how guidelines were substituted for the fetal tissue research ban. Doerflinger again does not accept the suggested solution, and returns to the issue he represents.

> Mr. DOERFLINGER. I do not know, if I can respond to that question […]. I think guidelines may be appropriate in cases where you are dealing with tissue that is already tissue, it is already from someone who is already dead. What they are talking about is setting guidelines for how and when to make and destroy human embryos, and I do not think guidelines alone are sufficient for that. (US Senate 1999b: 73)

> If you ask are the stem cells an organism, the answer is no. If you take my heart out, it is not an organism, either. But the question is the experiment involves ripping out the cells from what was before a living organism. (US Senate 1999b: 73)

Doerflinger was invited as a representative of one of the most influential pro-life groups in Washington DC. The concerns of the NCCB and other pro-life actors were whether the source of the stem cells, which are embryos and organisms, are destroyed or not. They claimed that this was also the concern of the existing ban, and that they therefore were supported legally. When the Department of Health and Human Services, and its general counsel Harriet S. Rabb, shortly after the hearing reinterpreted the ban and drafted guidelines for federally funded hESC research this was opposed on legal ground not only by Republican congressmembers, but also eight Democrats in the House of Representatives. According to the totally 70 congressmembers the new interpretation "would violate both the letter and spirit of the Federal law" (Wade 1999b); the existing ban was the legal hindrance for using taxpayers' money for hESC research. The guidelines were not put into full use before the 2000 election, when they became an issue. George W. Bush promised to reverse the legal ruling by Rabb if he became President (Taylor 2001a).

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[67] Derivation is the process of pulling out the stem cells from the inner cell mass of the blastocyst/embryo. See Introduction: Figure 1, the arrow between step 3 and 4.

These disagreements about the existing ban point to the funneling aspect of the coordination process. Because of the fiscal and legal means of the Federal administration the latter may force actors. As already noticed (above) this is one of the features of governments. It may be used or not. Not only can they force actors through various means but such strength may also force other actors to react "bivalently", to either accept or reject the attempted coordination. As predicted from the OPP model Doerflinger and the 70 congressmembers play this role and reject the coordination. In so doing they say something about how the federal means were put (or attempted to be put) to use. Under the Clinton administration some actors reacted to what they saw as a funneling attempt. Among them there was an already existing understanding of what was allowed and what was prohibited. The suggestion to fund hESC research confronted many actors' understanding of embryo research; an understanding that, except for the legal aspects already treated, also included moral issues.

Doerflinger, together with other actors representing pro-life views, did not accept ethical guidelines for something that they found wrong in the first place: the use of embryos in research.[68] Senator Brownback expressed this view in the hearings in 2000. Brownback identifies embryos as humans. His example is the holocaust:

> You had the Nazis in World War II saying, of these people, they are going to be killed. Why do we not experiment on them and find out what happens with these experiments? They are going to die anyway.
>
> Senator SPECTER. But they were living people unlike the embryos.
>
> Senator BROWNBACK. These are living embryos. These are living embryos. And they are being treated in this case as property.
>
> Senator SPECTER. But the people whom the Nazis experimented with in the abhorrent way in the holocaust were living.
>
> Senator BROWNBACK. These are living embryos. You are taking living embryos. (US Senate 2001: 30)

The moral objection to federal funding of hESC research articulated by Dickey, Brownback, and Doerflinger was based on their views on the embryos. Whether moral or legal arguments, they all concern the OPP. Doerflinger, Brownback, Dickey and others rejected the attempt to open the federal resources for hESC research and thereby draw all taxpayers

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[68] See also David Prentice in US Senate 2001:61ff.

into supporting it. Just as in other OPP cases actors are given an either-or choice, to accept or reject the funneling from the central actors, in this case the Federal administration. The opponents of federally funded hESC research have confirmed the centrality of the Federal administration and its attempted legal and moral funneling. Together with the attempted domination, these two aspects reinforce the resemblance between hESCs in USA 1998–2001 and other cases of OPP.

Alternative pluripotency

Doerflinger devoted most of his time in the first hearing, in December 1998, to the legal and moral aspects (US Senate 1999b: 73). While those aspects responded to the funneling and central actor propelling the attempted domination (the Federal administration), the third line of arguments addresses the hESCs and stem cell science. In the first hearing Doerflinger briefly mentioned *alternatives* to hESCs. In his next appearance, three months after the first hearing, the alternative had increased in importance for him. hESC research is not necessary to achieve the sought-after therapeutic potential, he now maintains.

> This subcommittee has now held three hearings on one narrow avenue of research, precisely the avenue that raises the most obvious moral and legal problems, so far to the exclusion of all other alternatives, even when those avenues may be more promising. The use of adult stem cells, for example, is said to promise the complete avoidance of the tissue rejection problems that Dr. Varmus has noted still need to be solved using embryonic cells. I would urge the subcommittee to expand its vision, to explore the alternatives that will advance medical progress and the wellbeing of patients without demeaning human dignity. (US Senate 1999b: 132)

Adult stem cell (ASC) research is proposed as an alternative that may be more promising than hESC research. His appeal is supported by findings reported in *Science* and discussed in major papers like *The Washington Post* and *The New York Times*. Doerflinger refers to cells from the bone marrow:

> Their versatility was recently found to be even greater than once thought. For example, given the right environment bone marrow cells can be used to regenerate muscle tissue, opening up "a whole avenue of potential therapies that didn't exist before" for muscular dystrophies. (US Senate 1999b: 50)

In this case the authors believed that the cells responsible for muscle reconstitution were a species of *multipotent* mesenchymal stem cells (Ferrari

et al. 1998: 1530). The bone marrow is merely one tissue of the adult body that hosts cells that seem to have multi- or pluripotent abilities. Papers from 1998 and onwards in high profile journals (*Science*, *Nature*, *Cell*) accounted for a new kind of experiment. In these papers research groups marked and traced cells injected into an alien tissue. The conclusions and interpretations pointed to a hypothesis about somatic cell de- and transdifferentiation and an increased plasticity of specialized stem cells.[69] Doerflinger again:

> An adult body cell can be "de-differentiated" surprisingly easily and regressed all the way back to a stage at which it can provide the nucleus for a new developing embryo. The question is: Can this regression be done to a point short of this, so an adult cell becomes the basis for cells that are like embryonic stem cells but never came from an embryo? (US Senate 1999b: 50)

Doerflinger's answer is that there is enough scientific evidence pointing in that direction. There are scientific reasons for not allowing federal funds for hESC research.

Independent entities

The legal and moral concerns responded to the funneling of a central actor, the Federal administration, and thus confirmed my use of an OPP model for understanding the sociotechnical reality of hESCs in the USA 1998–2001. However, Doerflinger's appeals to alternative stem cells do not fit the OPP, at least not right away. There are three implications of the articulations of alternative stem cells and alternative pluripotency. One concerns the visions of a USA transformed thanks to pluripotent stem cells and federal intervention. Another concerns the character of the Federal administration and its relationship to hESCs. A third one concerns the stabilization of hESCs aside from their association with the Federal administration. The pluripotent visions, the Federal administration, and

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[69] These phenomena were hypothesized partly because of the success with the cloned sheep Dolly, Wilmut et al. 1997. In the creation of Dolly a somatic cell (from the udder of Dolly's genetic twin/mother) functioned as a nucleus in a denucleated egg. The somatic cell proved to have an ability to instruct the resulting cell (egg and nucleus) into becoming a seemingly normal sheep embryo; i.e. sufficiently normal for it to develop to term including the differentiation of all cells in a newborn lamb. A somatic cell thus displayed an unexpected versatility, raising hopes for the pluripotency of adult cells.

the hESCs are all much more independent than the classic OPP cases predict.

Pluripotent transformation

A first implication of Doerflinger's objections is the commonalities between the claims about alternative stem cells and the claims about hESCs. In fact there are shared commitments in the opposing claims about the best stem cells. Just like the supporters, the opponents articulate a pluripotent transformation. Pluripotency and its effects are not questioned per se. hESCs are also not questioned per se, *only the appropriateness of federal funding for this specific stem cell.* The importance of transplantation therapies based on pluripotent cells is sometimes questioned, but the arguments drawing on adult stem cells hinge on the very relevance of such therapies and the role of the federal government. By referring to alternative stem cells with equal or almost equal capacities to those of the hESCs, the pluripotent transformation may be possible with federal funds. There is still the crucial role of the Federal administration, but the pluripotent transformation of the USA does not stand or fall with the hESCs. This is an odd implication with respect to the OPP suggestion. In the classic ANT cases whole networks have been at stake. The scallops said no, and the OPP failed. The doctors said no, and they had to be enrolled in order to enable the total Pasteurization of France. Here, the hypothetical chain from pluripotent cells, to transplantation therapies, to patients all over the USA and the world, via the Federal administration, is dissociated from the hESCs. The latter are said to be merely one of several means to achieve the new medical treatments and their far-reaching consequences for many Americans. hESCs are one kind of stem cells, but not necessarily *the* stem cells of America.

The Federal Administration

While the first implication concerned the independence of the pluripotent transformation, the second implication relates to the independence of the Federal administration. Just as in the Pasteurization of France the coordination of actors in the hESC case is focused on a central actor with funneling capacities. In Latour's case the centrally organized coordination is dependent on an entrepreneurial activity in which nonhumans and humans (microbes and Pasteur) are wed to each other. The authority of the latter is entwined with the significance of the for-

mer. Thus in this and other OPP cases the authority and centrality of the OPP is not an isolated human actor, already in power. The centrality of the OPP is the result of successful entrepreneurial action, not an already existing feature. One point of the OPP-transformation is that it is achieved by sociotechnical engineering, in which heterogeneous actors are coordinated.

Pasteur and the Pasteurians built the new actor-network in close connection with the introduction of the new nonhuman agent, the microbes. By introducing a new agent a new source of political power was created, Latour claims. Because of their control over these agents Pasteur and the Pasteurians became a new political, economic and scientific authority (Latour [1984] 1988: 52–58). Attempts to oppose Pasteur and attempts to oppose the theory of germs accordingly addressed the same OPP. There is no way to separate Koch's and Peter's resistance to Pasteur from their resistance to his microbes. They simultaneously challenged the authority of Pasteur and the "microbic furia", Latour claims (pp. 29–31). Louis Pasteur was "Pasteur of the Microbes" meaning that while he was shepherding the microbes they also defined his identity.[70] If the microbes had been successfully challenged, then Pasteur's authority would have been challenged too.

In contrast, Doerflinger's (and others') attacks on the exclusivity of hESC pluripotency is combined with an acknowledgement of the funneling capacities of the central actor, i.e. the Federal administration. Accordingly, the central human actor is dissociated from the central nonhumans. It is true that the responsibility attributed to the Federal administration because of the pluripotency of hESCs is an attempt to turn the former into a sort of entrepreneur for the latter. Some actors attempted this because of the already dominating and funneling capacities of the Federal administration. The moral and legal objections also built on this fact – that there is a human strategic agency that is not dependent on the agency of the hESCs. It may also be true that Presidential and Congressional candidates were in part dependent on the stem cell issue (among other issues) in campaigns and elections. In this sense the hESCs may have directly affected individual people's position and influence. However, even if George W. Bush's, Al Gore's or some Senators' status as actors was affected by the hESC issue (e.g. in the 2000 Presidential and Congressional elections), the power of the Federal administration that

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[70] In a paraphrase of the title of his Chapter 2, Latour [1984] 1988: 59.

they sought, was not threatened by the hESCs. As already mentioned, the responsibility may have been increased depending on the hESCs, but the total federal budget, structure, or existence was not at stake. In Latour's case the identity and agency of Pasteur were close to inseparable from the role and agency attributed to the microbes. This does not correspond to the hESC case. The authority of the Federal administration does not stand or fall with the success of hESCs, as did Pasteur. With or without hESCs the administration is a central actor in USA.

Hence, I suggest that Doerflinger's objections not only dispute the articulations of hESCs as the only way to a pluripotent transformation, but also disturb my attempt to apply the OPP model to the 1998–2001 situation. Particularly the notion of a central entrepreneurial actor whose fate is tied to the fate of the negotiations. A political, already existing actor, such as a government or Congress, cannot immediately be juxtaposed with a scientist or a group of researchers achieving economic, political and social transformation through the extension of e.g. laboratory objects. In the case of hESC research neither Clinton nor Senators Harkin and Specter were entrepreneurs in the Pasteurian sense. They were indeed strategic, and central for future stabilization, with the capacity to funnel other actors into a transformation of medicine and society. A Federal administration can translate people's goals by the simple means of money and laws, but these capacities were not dependent on, or uniquely bound up with, the hESCs.

This is an interesting observation considering ANT's view of actors. According to ANT, actors' identities are defined in networks of other entities, by and by, association by association. A main point of case studies has been that the importance of stated political powers have been less powerful than sociotechnical network formations (Callon 1980, Latour [1983] 1999). In this case the negotiations presuppose that the Federal administration is a strong independent actor. It is, however, not an absolute independence. Above, it was obvious how a specific responsibility for alleviating suffering was ascribed to the Federal administration.

Human embryonic stem cells

There were other possible entrepreneurs linked to the hESCs. Thomson and Gearhart with their respective co-workers were, together with Geron corporation, closest to the stem cells before the public announcement in November 1998. In this sense they were entrepreneurs, much like Pasteur, the scallops researchers or Hughes's system-builder Edison. The

first scientific articles correspond to Edison's visions. When Thomson et al. published their results in 1998, little of what was claimed about the potentiality of hESCs had been realized in laboratories, in clinics, or with patients:

> Screens based on the in vitro differentiation of human ES cells to specific lineages could identify gene targets for new drugs, genes that could be used for tissue regeneration therapies, and teratogenic or toxic compounds. [---] The standardized production of large, purified populations of euploid human cells such as cardiomyocytes and neurons will provide a potentially limitless source of cells for drug discovery and transplantation therapies. Many diseases, such as Parkinson's disease and juvenile-onset diabetes mellitus, result from the death or dysfunction of just one or a few cell types. The replacement of those cells could offer lifelong treatment. (Thomson et al. 1998: 1146f)

Three "coulds" and one "will" in four sentences of this quotation say something about its vision-casting character. James Thomson was the leading scientist in the team and he was in this sense an entrepreneur. He found the hESCs too important to not try to derive and culture them (Whitaker 2002). Just like Pasteur Thomson has had a unique consultative role in questions about the nature of the stem cells. In panels and hearings he has been the obvious "representative" for the cells. In this sense he has been defined through the hESCs, and he has "shepherded" them, but not to such a large extent outside of the culture dishes, as did Pasteur. He has not pursued apologetics on behalf of the cells. Geron contacted him. He has consistently answered to questions about the hESCs, rather than enrolling other actors himself. In these respects Thomson is no entrepreneurial builder of actor-networks.

Geron Corporation consisted of entrepreneurs who saw the financial potential of hESCs. Just like Pasteur, Geron's existence is interdependent with the success of hESCs. Initially, they tied the cells exclusively to the company and tried to earn a profit on the distribution (Thomson 2002). This strategy of funneling actors through Geron was however limited and later changed. In Senate hearings they advocated public involvement in the research, claiming that private resources would not be sufficient. Also the procedures were not specific enough to keep the hESCs as an exclusive property of Geron.[71] Other laboratories in the USA and elsewhere were producing their own hESCs.

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[71] Cells are usually not patentable per se. In this case Geron only had the ownership of the actual hESC lines, not the procedures or the specific kind of cell.

Neither Thomson nor Geron alone thus took on a Pasteurian role in the stabilization of hESCs. They were also only a few compared to the many that immediately appeared and articulated the cells. Patient organizations, ethicists and politicians argued for the benefit of cells for society as a whole. As early as a month after the announcement, so many and diverse actors were arguing for their own particular uses of the stem cells. The visions in November 1998 did not come from scientists or corporations alone. No specific group of people became the entrepreneurs or the representatives of the cells.

The Federal administration was central but not an entrepreneurial actor dependent on, and driving, the stabilization of hESCs. Clinton and Senators quickly responded to Thomson's and Gearhart's articles, but to respond is not to be a *primum movens* behind the stem cells. Thomson and Geron had such entrepreneurial functions, but the first didn't sell his cells and the second did sell them, but ultimately did not successfully claim exclusive rights to the future fate of the cells. Around the world and around the USA the hESCs popped up in laboratories independently of Geron. The absence of any major representatives or entrepreneurs of the cells, and the absence of any site or group exclusively claiming the rights to them co-incide with a third implication of Doerflinger's objections in the Senate hearings: The hESCs at this time were already somewhat independent of any specific actor. Even the fiercest opponents of hESC research did not question the scientific qualities of the hESC reports or the existence of the cells. Legal, moral or scientific concerns could be used to oppose the federal funding, but nobody questioned the quality of hESC research. Next to – not together with – the Federal administration, the most central actor in the whole situation may well have been the hESCs themselves.

Above (in the first part of the chapter and in Figure 5), the entities of the sociotechnical network were few and tightly fitted to each other in order to achieve the pluripotent transformation. In this section and in the below Figure 6 the network is more complex. The entities are not dependent on one association, but exist somewhat independently.

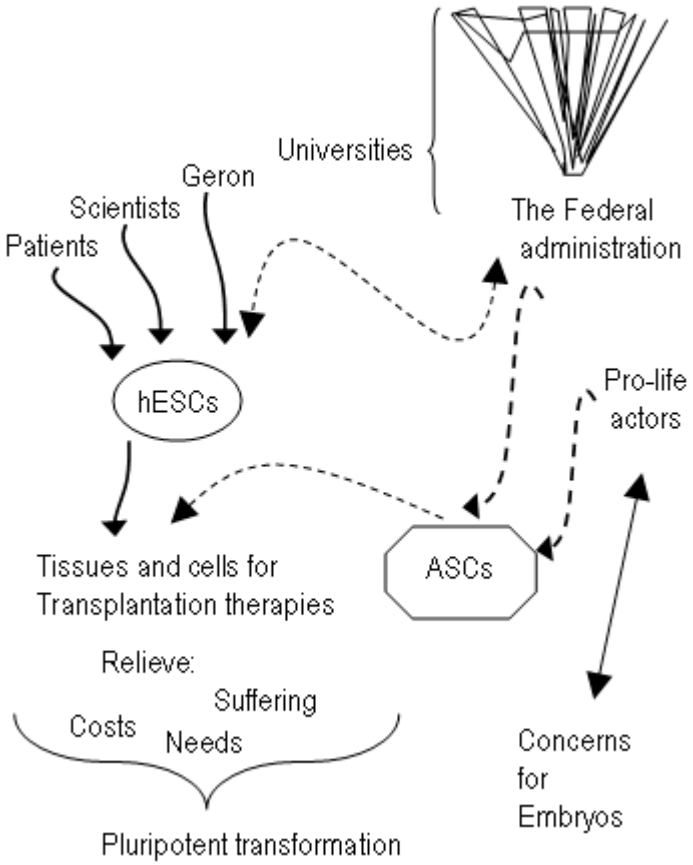

Figure 6: Increased complexity of associations between independent entities.

The hESCs, the pluripotent transformation, and the Federal administration are affected by their prospective associations. However, the network as a whole does not stand or fall with the success of any specific point of passage. In this sense it was not a an OPP coordination. In other respects it was.

I have related the case of hESCs closely to the classic OPP case studies, as if the latter were theoretical black boxes to take down from the shelf. Although the hESC case does not fit these cases exactly, important traits in the coordination of entities have been brought up. The negotiation of federal funding of hESC research bore some similarities with the classic OPP cases. Actors articulated a pluripotent transformation of America reminiscent of the pasteurization of France: a seamless vision of federal funding, stem cell research, applications, patient needs, and economic effects. Through one center, consisting of the combined agencies of hESCs and the Federal administration, a number of actors can be funneled by the means of money, laws and pluripotent promises. Oppo-

nents confirm the funneling character of the coordination. These are all OPP-like traits. However, opponents also point to the seams in the cloth: the independence of the Federal administration, the hESCs and the envisioned transformation. Unlike the classic cases the new actor-network attempted through the OPP does not stand or fall in its entirety. Specific associations are negotiated, but not a whole network. No specific group had their identity or fate defined exclusively in relation to the agency and fate of the cells, as in the classic OPP cases. There was no center, or instead, there were many centers.

The failure of the OPP

Even when accepting an OPP-like cordination a last empirical and analytical blow to the suggested parallell was dealt by George Bush's decision at the end of the selected period, 1998–2001. In the first part of the period Clinton was approaching the end of his term and a new election was coming up in 2000. The new NIH guidelines for federally funded research on hESCs were not put to work on the eve of the election. hESC research was thus not federally funded during the Clinton period. George W. Bush promised to make a decision when he was elected President. On August 9, 2001 he signed an executive order to allow federal funds to some hESC lines, but not all. hESCs were thus not endorsed in the wholesale manner suggested by the proponents (and the opponents) of federal funding. The hESCs were kept as one option to be investigated but not in a full scale as *the* option for research leading to transplantation therapies. Only some hESC lines could be funded and no new hESCs could be produced with federal support or even in buildings thus funded. Bush used his agency to associate with hESC research, but only partially, and without the total authorization hoped for by supporters. Adult stem cells were the main option, receiving more than 8 to 10 times more than hESC research in the following two budgets (for 2002 and 2003).[72] Federal funding of hESCs was envisaged as a funneling of actors into a dominating network thereby authorizing and stabilizing the hESCs, but this did not happen, because of Bush's decision.

The OPP-like traits of the coordination attempt – i.e. a funneling and dominating coordination – did not *empirically* succeed in 2001 or later (in 2006). Bush's decision meant that hESCs did not achieve a dominating position in combination with a centralized and funneling coordination of

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72 One reason for this was the lack of hESC research proposals.

actors. Empirically, the end of the story was not an OPP. In the *analytical* respect, Bush's decision added to the discrepancy between OPP cases and the coordination of actors in the hESC case. If this had been an OPP in the sense described by Callon, Latour, and Law, the hESC coordination would have stood or fallen with the success, but it didn't. Yes, the federal funding was important, but nothing in the later history indicates that hESCs will disappear because of the merely partial support from the Federal administration. In 2003 24.8 million federal dollars were used for hESC research, which scarcely implies their disappearance. Linda Hogle has shown how new organizational forms, including partnership between state government, private enterprises and foundations, have emerged strongly, equaling or exceeding the federal support, to enable more research on hESCs (Hogle 2004). Thus, the sociotechnical reality of hESCs cannot ultimately be captured empirically or analytically in terms of the OPP model, at least not as this has been used by Callon, Latour, and Law.

Summary

This chapter has focused on the negotiations of federally funded hESC research. A number of OPP-like traits have been found in these negotiations. According to Harkin, Specter, Hatch, Okarma of Geron, and others the hESCs are the saviors for almost every (or at least every second) American and are thus *the* Stem Cells of America. Bringing out the domination efforts are one result from my application of the OPP model. Another one is the occurrence of funneling, due to the powerful means of the Federal administration as a central actor. These aspects were there, although without the marked entrepreneurial traits.

However, there have been three negative results of the attempt: Firstly, there is no Pasteur of the hESCs. The coordination is not explicable with reference to a central entrepreneurial actor whose fate and role are irreversibly bound up with the cells. Although the Federal administration (and individual politicians) and its responsibility (as articulated by some actors) are affected by the hESCs, its centrality and general capacities are independent of any particular stem cell. Secondly, the envisioned pluripotent transformation does not stand or fall with the success of hESCs. Proponents and opponents of federally funded hESC research endorse transplantation therapies of pluripotent stem cells. Thirdly, as the opponents display, and the later history too, the quality of hESC research, the existence or capacity of the cells are not threatened *per se* because of the

failed attempt to establish domination. More than an either-or, the sociotechnical reality of hESCs is of a relative kind. But, not only is it relative, it is also multiple and pluralist in virtue of divergent and contradictory articulations.

Initially in this chapter the first research question of the study – to understand the sociotechnical reality of hESCs – was put forward in terms of the degree of stabilization, the mode of coordination, and the distribution of agency. After my attempt to apply the OPP model the reality of hESCs is marked by (at least seemingly) contradictory features. Firstly, the hESCs' degree of stabilization: The stem cells do exist and link up to other (non-federal) actors without totally dominating or totally failing, as conditioned in the OPP model. Simultaneously, they are involved in a total pluripotent transformation of the USA, although not necessarily as the only and exclusive stem cell. How could the hESCs' degree of stabilization be mapped while paying attention to the relative existence and the total transformation at stake? Secondly, the stabilization of hESCs is not tied to the performance of any central and entrepreneurial human actor, as in the classic OPP cases. All the while the funneling capacity of the Federal administration is there and is a non-dismissable factor in the negotiations in hearings and elsewhere. Understanding the coordination of hESCs will have to account for the non-entrepreneurial features and the funneling potential of the Federal administration. Thirdly, in the understanding of the coordination, the agency of humans and nonhumans is distributed much more and in much more complex patterns than in the classic OPP studies. There is no central site to go to in which a human agency is at work master-minding other actors including nonhuman ones. In addition, actors disagree about the agency of nonhumans, struggling over which cell is most pluripotent.

3. Outlining a Boundary Objects Coordination: Diverse Actors and Multiple Uses

Introduction

Even if the Federal administration was one important actor of the reality of hESCs 1998–2001, it was evidently not the only actor relating to the cells. The funding at stake certainly framed many of the interactions, but as we saw after Bush's partial commitment to fund hESC research there was more to stem cell research than this relationship. This chapter is to a large extent based on the same source material, but instead of focusing on the articulation of hESCs and the Federal administration the attention is focused on the associations already established, already there. An actor negotiating federal funding is not only attempting to stabilize a specific linkage between hESCs and the administration, but simultaneously articulating his/her relationship to hESC research. This chapter asks about the sociotechnical reality of hESCs in relation to the latter, existing associations rather than the former, attempted ones.

The attempts to understand the federal negotiations as an OPP effort narrowed down and specified some characteristics of the political and public dynamics of hESCs between 1998 and 2001. The stabilization is not total, but relative and partial. Funneling is part of the mode of coordination, but there is no entrepreneurial center exclusively linked to the stem cells. With respect to agency no human is masterminding everybody else and the relative capacities of nonhuman actors (the hESCs compared to adult stem cells) are disputed. Alternative (or complementary) models are needed to capture the sociotechnical reality of hESCs, 1998–2001.

The first part of this chapter continues the previous chapter's observations of relatively independent entities by examining the many diverse actors that were in fact linked to hESC research. The second part asks:

What is the nature of this reality, of these linkages between actors? How are the actors coordinated?

A relative reality

It is true that in many articulations the hESCs, their pluripotency and a possible pluripotent transformation were allegedly dependent on federal funding. The same articulations, however, are also traces of an already existing actor-network of hESCs. Although the advocacy for federal funding certainly influenced these linkages they also have a life of their own.[73] As much as possible, the Federal administration as the crucial linkage is now left out of the picture.

What is conspicuous in the established linkages to hESCs is the diversity of actors and their commitments to the stem cells. During the period 1998–2001 scientists, corporate representatives, patients, bioethicists, politicians and administration officials testified in Senate hearings. It is possible to see two things in these articulations. Their references to the hESCs, pluripotency, embryos and transplantation therapies or other uses, may be of an "absolute" nature, i.e. as being certain, indisputable or urgent. However, the articulations they perform by linking to the cells are not as absolute, meaning that they hope for effects and in some cases transformation, but can either *manage without* hESCs or *do not commit themselves fully* to the research. This last clause is important, since it contradicts the "new reality" articulated in their reference to the hESCs and a pluripotent transformation (see Chapter 2). Articulating stem cells makes them real in relation to other actors or elements, but this can happen in two ways: Both by actors' references to the cells *and* through their linkages to them.

Scientists

The first publications on successful production of hESCs came from John Gearhart's group at Johns Hopkins (Shamblott et al. 1998), and James Thomson's group at the University of Wisconsin (Thomson et al. 1998). Here the authors accounted for the "derivation" and culture of human pluripotent embryonic stem cells, which form the basis for subsequent research on the cells. There is no need to state that the two

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[73] Since Bush's decision in 2001 this has also been apparent. States and private initiatives have tried to increase hESC research without Federal support. In the state of California, citizens, in a 2004 referendum, approved a $3 billion funding of hESC research over 10 years, Finkelstein 2004.

groups at Johns Hopkins and the University of Wisconsin were strongly linked to the hESCs. An important question is, however, to what extent the cells were successful outside of the two laboratories.

The articles, like most scientific articles, point towards other scientific linkages. Most of the papers are devoted to the technical details and results of experiments. Each compound or substance that is used, connects to companies, earlier research and other laboratories. Just the fact that the papers had been published in high-prestige journals was a recognition. However, many published papers are never further quoted or picked up by others. In this case other scientists did in fact endorse the stem cells and even produced them on their own. Thomson and Gearhart were the first – but not alone (Freed et al. 1999, Pesce et al. 1999, Smith 2001a).

A year later, the journal *Science* hailed stem cells, including human embryonic ones, as the breakthrough of the year (Vogel 1999).[74] The American Association for the Advancement of Science (AAAS) endorsed hESCs (Chapman et al. 1999) and two years later the NIH issued a report on hESCs in which 50 stem cell scientists were interviewed and 1.200 papers were reviewed (US DHHS 2001b).

At the same time, in early summer 2001, the National Academy of Sciences gathered a workshop on stem cells in which scientists explained the value of hESCs (*Workshop on Stem Cells and the Future of Regenerative Medicine* 2001). Both the report and the workshop (and its subsequent publication) were hugely supportive of hESC research, not least in relation to adult stem cells. In all of these reports and conferences scientists expressed their support for hESCs. It is, in fact, hard to find resistance to the hESCs among stem cell scientists. They may advocate federal funding or not, but they do hail the cells as a scientific achievement. How about non-scientists?

Business

Many companies were (and are) engaged in hESC research. Other scholars in the STS community are specifically engaged in mapping how the corporate sector is re-structuring and transforming in order to adopt stem cell technology (Hogle 2004, Waldby 2004). Two of the companies should be mentioned here since they were the most visible initially and were invited to the hearings. Other companies responded to the possibi-

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[74] The designation concerned stem cells, both human embryonic and adult.

lities in hESC research, for instance through the Biotechnology Industry Organization (US Senate 1999b: 104).

Advanced Cell Technology (ACT) had appeared a lot in relation to cloning technologies. Its CEO, Michael West, had driven much of Geron's investments in stem cell technology before coming to ACT. Geron Corporation was a biotech company that had specialized in the derivation of hESCs and had vested interests in both Thomson's and Gearhart's projects. The importance of Geron was partly due to the restrictions put on human embryo research in the USA. Because of the restrictions on the federal funding of human embryonic research, Thomson had to set up a whole laboratory separate from his usual facility. At the time nothing from the federally financed buildings or materials could be utilized for embryonic research. With financial support from Geron Corporation, and an alumni foundation at the University of Wisconsin (WARF), Thomson did the hESC work in the parallel facility. Gearhart's group also worked with funds from Geron. Without the support from Geron the actual work on hESCs would at least have been delayed. The corporate linkages are more dependent on the success of hESCs than the others. However, they were established without federal support, and continued to be so. The very coming to being of hESCs bears witness of corporate interest in the cells without the total endorsement from the administration.

Patients

Among patient advocates the most famous examples may be Michael J. Fox and Christopher Reeve. Fox suffers from PD and Reeve was paralyzed because of a horseback riding accident, and died in October 2004. These patients related to the hESCs in a particular way. By already being icons of successful persons and famous TV and movie stars they are familiar to people (with or without diseases) watching TV and movies. Many people know them and may be more easily moved by their situation and their advocacy. By appearing as patients and suffering and advocating hESC research Fox and Reeves not only linked as individuals but probably linked many in the public to the research.

Both of them inspired, headed and donated to research foundations, the Christopher Reeve Paralysis Foundation and the Foundation for Parkinson's Research, respectively. They also gathered together other organizations to enforce their demands for federally funded hESC research. When Reeve testified in the hearings in 2000 he did so with the support of more than 100 professional and patient organizations (US Senate 2001).

Other patient representatives who supported hESC research represented the Alliance for Aging Research, the Juvenile Diabetes Research Foundation, Project ALS, and Paralyzed Veterans of America.

Except in two cases the patients in stem cell hearings supported the research completely. In many cases their lives (allegedly) hinged on federal support of hESCs; Michael J Fox was one of these. However, when he appeared in a hearing on Parkinson's disease he did not even mention stem cells (US Senate 2000). In one setting hESC research was necessary and urgent. In another setting, although still a context of negotiation, hESC research was invisible. There are other examples of how various modes of articulation co-exist.

The previous chapter accounted for Patients' CURe and their activities in gathering many of the patient organizations below one lobbying roof. For this purpose the coalition presented estimates of large numbers of potential patients. Virtually every American was somehow to be affected by hESC research. Interestingly, CURe also wanted to combine these great expectations for every other American with 'tempered optimism'.

> In general, the patients and their advocates who are active for CURe display tempered optimism when it comes to appraising the chances of anyone's health benefiting soon from applications of stem cell research. (Perry 2000)

Many of the organizations had existed for several decades, e.g. the American Diabetes Association for six decades (American Diabetes Association 1990), JDRF for three decades (US Senate 1999b: 100). They have million-dollar budgets and have been funding and doing research since long before the hESCs arrived. Although zealously arguing for hESC research their research portfolios were not dependent on hESCs. They were strong lobby actors, but also somewhat independent of federal funding. There is a doubleness between their articulations and their actual linkages (which are also articulations).

In spite of the massive mobilization (34 patient organizations cooperating) others did not want to join. Soon after the coalition was founded the American Cancer Society withdrew its sponsorship, either because of Catholic pressure or due to families who returned pledges, or both (Wade 1999a). There were also examples of individual patients who distanced themselves from hESCs (US Senate 2001: e.g. Owen, 23ff and Heagy, 93ff). Not all patients or patient organizations were enthusiastic about hESCs. "Patients" was not a homogeneous category. Putting together

Patients' CURe was a part of a homogenizing movement for the purpose of putting pressure on law-makers (Perry 2000).

Bioethicists

In the hearings Arthur Caplan, Eric Meslin, and Glenn McGee supported hESC research. Elsewhere a large community of bioethicists also endorsed the stem cells (*American Journal of Bioethics* 2001, Green 2001, Holland et al. 2001). Another actor, also appearing in the hearings either indirectly or directly through consultation, was the National Bioethics Advisory Commission (NBAC). James Childress, commissioner on NBAC, testified. After its report was issued the Commission functioned as an aggregated actor, subsuming 17 bioethics professionals and numerous consultants in one document and one set of recommendations (Shapiro et al. 1999). It is one striking example of how a lot of bioethicists supported federally funded hESC research in one way or the other, and vice versa, how bioethicists were sustained by the controversy.

Mary Leinhos has claimed that the NBAC was set up much like a boundary organization, making room for negotiations of the boundaries between science and politics, and between philosophical ethics and public policy (Guston 2000, Leinhos 2005). One of her observations is that the NBAC's recommendations largely reflected the views of the scientific community and the Administration and less those of pro-life opponents (which could have to do with the fact that the Commission was appointed by President Clinton). According to Leinhos the NBAC recommendations served the mutual interests of science, government, and their mediators (the commission, and the field of bioethics), and specifically the latter by continuing the call for their services, and legitimating the bioethics concepts and techniques deployed (Leinhos 2005).

Politicians and temporality

With respect to politicians, dissociation from the issue of federal funding is impossible. However, some linkages to politicians, in spite of the stakes of federal funding, did contribute to the relative reality of hESCs and not the dominating versus avoiding coordination displayed in the previous chapter.

The support from some, such as President Clinton and the Subcommittee Senators Specter and Harkin, was clear from the previous part of this chapter. They followed a pattern of polarization between Democrats

and pro-life Republicans. However, not all of the pro-life congressmembers were against the research and refused to give up their pro-life identities. In a letter sent to George W. Bush in 2001, Orrin Hatch pointed out these associations between pro-life Republicans and hESC research.

> Mr. President, once you have considered the complexities of the questions at hand, I hope you will conclude, as other pro-life, pro-family Republicans such as Strom Thurmond, Gordon Smith, Connie Mack, and I, that the best course of action is to lead the way for this vital research. (Hatch 2001a)

Hatch was thus not alone. Except for the Senators mentioned in the quotation Nancy Reagan, former First Lady, wrote to Bush in support of hESC research. Senator Bill Frist was considered an important supporter, partly because of being one of the few in Congress with medical training (and partly because of being considered close to the President) (US Senate 2002: 14–18, Smith 2001b, Taylor 2001b). Below is Frist's suggestions for hESC research policy in early summer 2001:

1. a ban on the creation of embryos for research purposes;
2. the continuation of the present ban on federal funding of the derivation of embryonic stem cells;
3. a ban on all human cloning;
4. an increase in adult stem cell research funding;
5. funding for embryonic stem cell research only from blastocysts that would otherwise be discarded;
6. a rigorous informed consent process;
7. a limited number of stem cell lines;
8. a strong public research oversight system;
9. ongoing, independent scientific and ethical review; and
10. strengthened and harmonized fetal tissue research restrictions.

(Frist 2001: 172)

With this manifesto Frist articulated support for hESC research without giving in to a domination attempt. It was a moderate endorsement. The suggestions were echoed in Bush's August decision partially committing himself (and the Federal administration) to hESC research, but on strict conditions. Just *because* the administration ultimately did not *fully* embrace all hESC research with federal funds, they did contribute to a relative reality. In comparison to the domination attempt these partial endorse-

ments are especially interesting. The partial acceptance from Bush and Frist – although concerned with federal funding – do not 'fit' into the domination attempt, since they denied giving the research a blank check (to perform the pluripotent transformation).

There is a temporal aspect to the pro-life support for hESC research that must be noted. The domination attempts and the alternatives were there almost from the beginning of the period, in 1998, which is true for most of the linkages to the actors presented above. However, the group of pro-lifers mentioned by Hatch, and others "came out" as the time went on, until August 2001, when Bush made his partial commitment to the research. In this sense hESCs were "more" a relative reality by August 2001 than in 1998, when pro-life politicians had still not come out in partial support. Their "coming out" constitutes a temporality in a situation that has so far provided two diverging patterns of coordination, one polarized, either-or, and another more relative, e.g. both pro-life and hESCs. So far, the most tangible *dynamics* is the slight tilting, no radical shift, from an OPP-kind of coordination to partial connections, a more relative reality.

Many other actors also supported hESC research. The purpose and claims here are not all encompassing, but meant to indicate the diversity of actors contributing to a relative stabilization of the stem cells. This stabilization differed significantly from the articulations in the previous chapters by prevailing even though the sought-for domination were not immediately realized, and by in practice being less unconditional. Patients were a big support, but paradoxically the size of organizations also indicated that they had been thriving before and without hESC research. Paradoxically the corporate interest in the stem cells and in federal funds (see the previous chapter) proved a relative stabilization that did not hinge on the administration's decision. Pro-life politicians' partial commitments also contributed to a relative reality of hESCs and not a dominating, either-or kind. There was more to the stem cells than the attempt to achieve federal funding and set in motion a "pluripotent transformation of America".

A boundary objects coordination

After observing these many associations to the hESCs, the question is how this coordination of diverse actors should be understood. None of the supportive actors could (or in the case of Bush chose to) themselves funnel all the other actors. None of them were themselves in the center

or could claim to be the sole "source of the general movement" (Latour 1987: 118). So was there any "source" or cause of the coordination? According to the actors their associations were due to the hESCs. They explained their linkages to the hESCs with reference to the hESCs.

Should the actors be taken at their word? [75] In the absence of any central human entrepreneurial actor the actors' articulations are worth a try. In addition actors' explanations to some extent converge with Star and Griesemer's case study of the Museum of Vertebrate Zoology (MVZ) (Star and Griesemer 1989). In the MVZ case diverse actors collaborated without agreeing about every detail of the situation, i.e. without accepting the same translation. The collaboration happened through the flow of certain objects, "boundary objects", without any central entrepreneur making everybody agree. Multiple uses of the boundary objects spoke differently to various actors and practices without moving anyone out of their path or imposing one single view on the world. The circulating objects "did the job" rather than any human. These similarities suggest that the diverse actors were coordinated by the hESCs as boundary objects. A way to approach the suggestion is to ask what such an understanding would imply.

The materiality is notable in Star and Griesemer's approach. Material traces bear witness to the coordinating process achieved by the "flow of objects and concepts through the network of participating allies and social worlds" (Star and Griesemer [1989] 1999: 507). Between November 1998 and August 2001 hESCs existed in culture-dishes in a few laboratories. Although the hESCs were successfully linked to other actors and uses, they could obviously still not be materially circulated. Materially they could not coordinate actors.

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[75] A certain justified puzzlement may arise concerning the following of actors: Can the analyst be fooled by this recommendation and start believing the actors' truths? Will the analyst be limited to the actors' definitions of the situation? Yes (to the latter version of the question) and no (to the former one). Yes, the analyst has to follow the actors since s/he does not have any other-worldly access or capacity. But, no: To follow the actors' associations does not necessarily mean being fooled into believing that this reality is necessarily the only or the final version of things. The purpose is not to find the Truth or prove the actors to be right/wrong, but to see how one or several realities are stabilized among actors, without claiming it/them as the final answer about reality.

The 1998–2001 situation is marked by coordination on a very general level. Initially we are not talking about coordination through the flow of the hESCs themselves (they still existed mainly in Thompson's and Gearhart's laboratories). But, this provokes the questions: In what sense are the cells then boundary objects? In what sense do the cells "flow through the network of allies"? The materiality of boundary objects should not be understood narrowly. Also "concepts", "platonic objects" or "ideal types" are boundary objects that flow through the network.

> This is an object such as a diagram, atlas or other description which in fact does not accurately describe the details of any one locality. It is abstracted from all domains, and may be fairly vague. However, it is adaptable to a local site precisely because it is fairly vague; it serves as a means of communicating and cooperating symbolically – a "good enough" road map for all. (Star [1989] 1999: 518)

In the above sections diverse actors testified about their uses of something that they all called "human embryonic stem cells". Their particular reasons shifted, but they all referred to the same word. This is a first trace of coordination. The term "human embryonic stem cells" is used in communication across a variety of practices, much as Annemarie Mol has described the use of the term "atherosclerosis" between groups in a hospital:

> But "atherosclerosis" is the word they use when they want to talk to one another. The term is a coordinating mechanism operative in conjunction with the various distributions. It bridges the boundaries between the sites over which the disease is distributed. It thereby helps to prevent distribution from becoming the pluralizing of a disease into separate and unrelated objects. (Mol 2002: 117)

The term "human embryonic stem cells" thus participated in diverse actors' articulations. However, this is a slender linchpin for making a full analogy with the boundary objects of Star and Griesemer. In addition to the already mentioned vague qualities, another complementary set of characteristics is needed to serve cooperation.

> Boundary objects are both plastic enough to adapt to local needs and constraints of the several parties employing them, yet robust enough to maintain a common identity across sites. They are weakly structured in common use, and become strongly structured in individual-site use. They may be abstract or concrete. They have different meanings in different social worlds but their

> structure is common enough to more than one world to make them recognizable means of translation. (Star and Griesemer [1989] 1999: 509)

If the hESCs do coordinate actors they should not only be vague and weakly structured but also be more constraining and defining ("strongly structured") in individual-site use. There should be more to it than a name used by diverse actors. hESCs should be adaptable "to local needs and constraints". One cell should take part in multiple practices and thereby coordinate actors. This is exactly what is indicated already in the first reports, and was soon reciprocated by other, diverse actors.

Multiple uses

While the first part of the chapter outlined some of the actors, this part will look at the specific uses that spoke to actors. As early as in the November 1998 papers in *Science* and *The Proceedings of the National Academy of Sciences,* the stem cells' multiple uses had been articulated. The hESCs are associated with "outside" actors, i.e. non-scientists. In the abstracts, the introductions and the conclusions, the stem cells are said to be suitable for certain uses.

> These cell lines should be useful in human developmental biology, drug discovery, and transplantation medicine. (Thomson et al. 1998: 1145)

Transplantation therapies together with basic research in developmental biology ("human embryogenesis"), and drug discovery/screening, are the three most frequently mentioned uses in scientists' accounts. These three areas are not only scientists' concerns. They can be, and are repeatedly, linked to many people's lives. Thomson et al. indicate the linkage from the usage in developmental biology to that with people.

> Human ES cells should offer insights into developmental events that cannot be studied directly in the intact human embryo but that have important consequences in clinical areas, including birth defects, infertility, and pregnancy loss. (Thomson et al. 1998: 1146)

Developmental biology is usually seen as *basic* science, as opposed to *applied*, which is regarded as the more user-oriented form of research. In Thomson et al.'s paragraph the use of developmental biology does not remain within the scientific world. Birth defects, infertility and pregnancies happen to people, not merely to cells or things in a biomedical lab.

That's the message.[76] In the quote that I used above (p. 96) to display the entrepreneurial and prospective character of Thomson's work, the uses of hESCs in drug screening/discovery and transplantation therapies were explained in several steps. First, the in vitro differentiation of hESCs forms a base for screens, which "could identify gene targets for new drugs, genes that could be used for tissue regeneration therapies, and teratogenic or toxic compounds" (Thomson et al. 1998: 1146). Thomson's and Gearhart's articles are the first step towards differentiation, which will then be useful in the screening performed by companies and in university laboratories. In the next step the engineers are connected via their role in the "standardized production of large, purified populations of euploid human cells such as cardiomyocytes and neurons" (p. 1146f). The anticipated result, such as a limitless source of cells, speaks to drug companies and transplantation doctors. And, lastly:

> Many diseases, such as Parkinson's disease and juvenile-onset diabetes mellitus, result from the death or dysfunction of just one or a few cell types. The replacement of those cells could offer lifelong treatment. (Thomson et al. 1998: 1147)

The beneficiaries of transplantation, we learn, are Parkinson's and diabetes patients. Lifelong cures are on the line.

There are many uses of hESCs implicated in the seminal articles. The uses picked out are, however, not arbitrary. Each of the uses appeals to other actors, whether scientists or non-scientists. Other scientists, corporations, bioethicists, politicians and patients did confirm their own need of the three uses indicated in the original papers.

General responses

The three uses were regularly picked up in many review articles (e.g. Odorico et al. 2001, Smith 2001a). Sometimes they were repeated as a formula by actors, for example as below in Senator Harkin's words:

> I want to thank Dr. West for his commitment to a public discussion of the ethical implications of stem cells research and to commend Doctors Thomson and Gearhart for their groundbreaking accomplishments. From enabling the development of cell tissue transplantation to improving and accelerating pharmaceutical research and development, to increasing our understanding of hu-

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[76] The reason that the early developmental events cannot be studied without the hESCs is of course that the events usually take place in the womb under extremely precarious conditions.

man development and cancer biology, the potential benefits of this work are awe-inspiring. The cell lines they have isolated and kept alive could reduce the demand for organ donors and pave the way for many life-saving therapies. (US Senate 1999b: 2f)

The NIH issued a graphic illustration in order to explain the use of hESCs, which confirmed the three uses (Figure 7).[77]

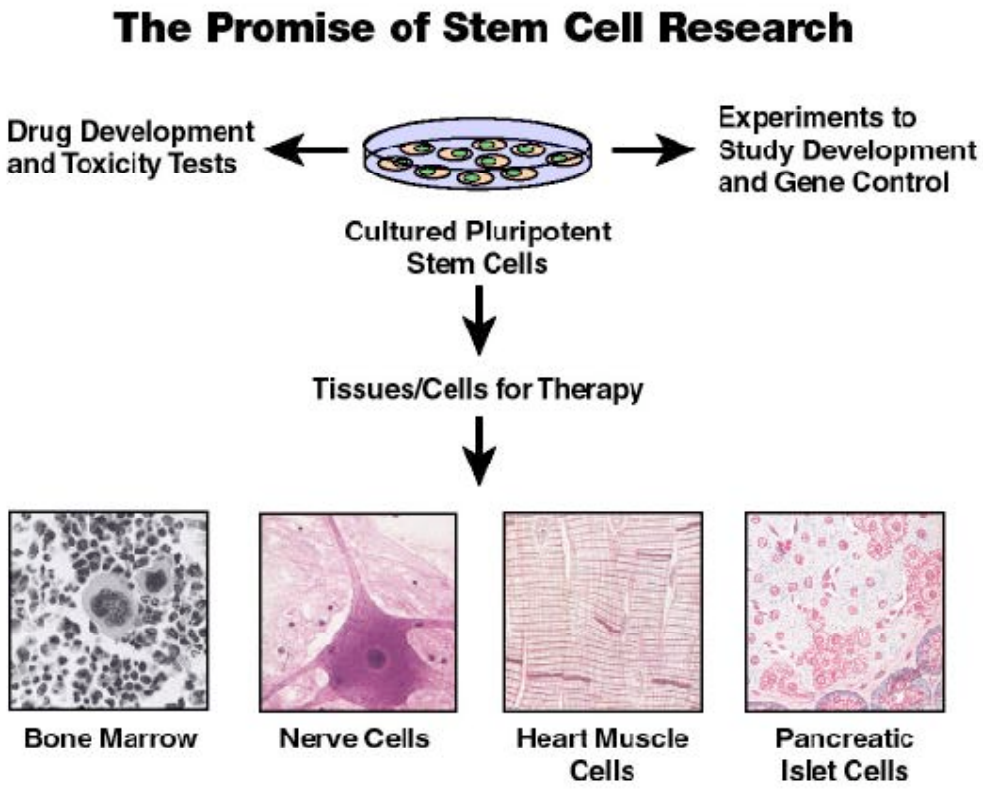

Figure 7: Illustration of three uses of pluripotent stem cells (NIH 1999).

The stem cells are in the center and can be turned to a number of uses, via tissue differentiation. The hESCs are doing the job, coordinating the actors because of their plasticity and capacity to adapt to local needs.

Six months after Gearhart's and Thomson's respective reports *Cells Tissues Organs* featured a special issue on the use of ES cells (human and nonhuman) as a developmental model. In one of the papers an illustration (Figure 8) described the uses and technologies that were linked to pluripotent embryonic stem cells (ES) or embryonic germ (EG) cells (Prelle et al. 1999).

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77 It is now not available on the NIH web site. It has been used in (at least) two other presentations of hESCs, Lewis 2001, Terpstra 2002: 13.

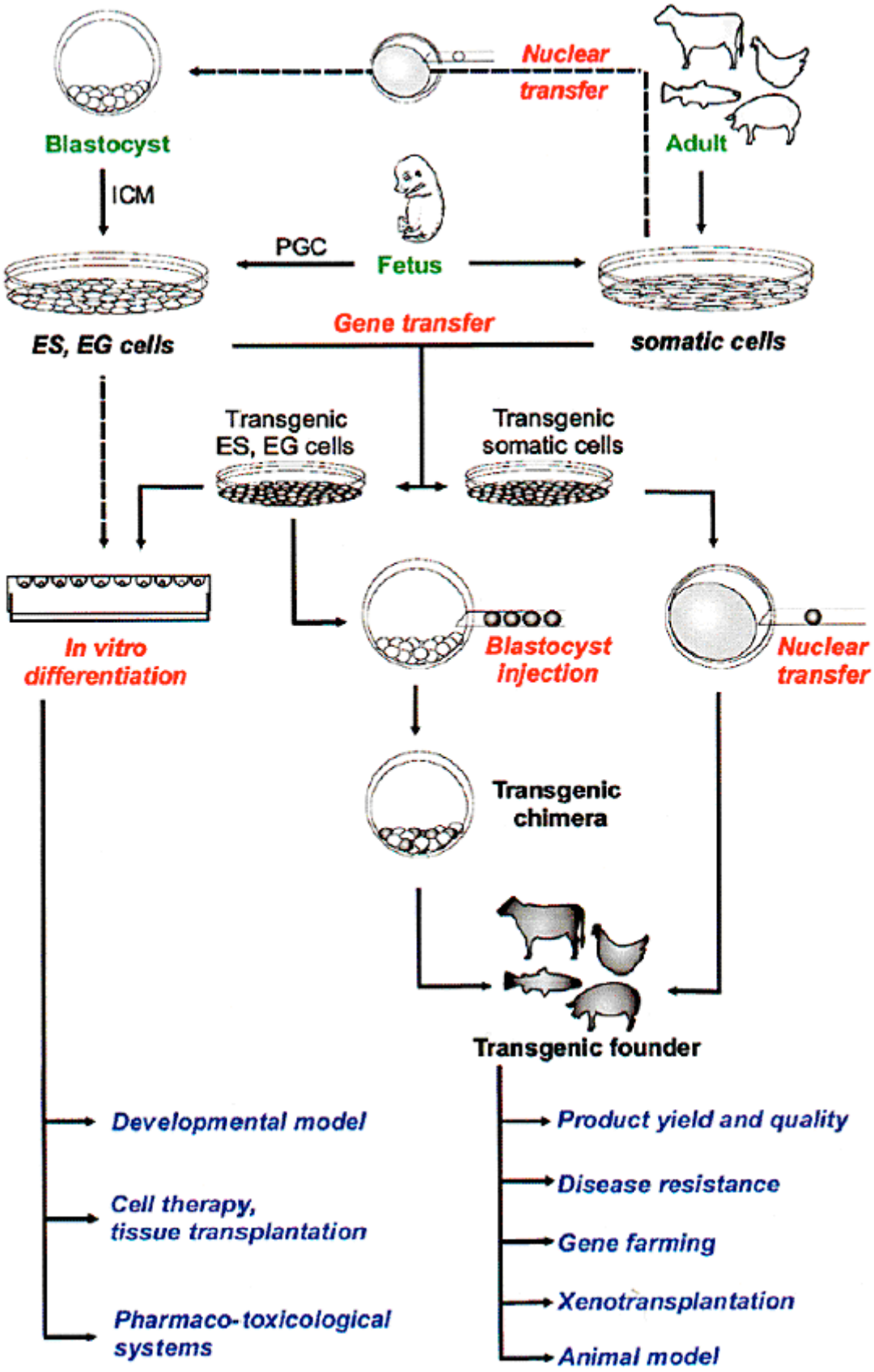

Figure 8: The uses of stem cells (Prelle et al. 1999).
(By courtesy of S. Karger AG, Basel.)

Just as in the NIH illustration the path from ES cells to uses is articulated. This time the three uses of hESCs are one small part of a larger map. Apart from the uses for humans the arrows lead to applications in animals.

As the stem cells flow from one application to the next, specific technologies are included, such as gene therapy and nuclear transfer. Although the latter picture is more complex they are both articulations of three uses that follow from the hESCs: transplantation therapies, drug testing and developmental biology.

The National Bioethics Advisory Commission was one striking example of how a lot of bioethicists linked themselves to hESC research by responding to the three suggested uses of the cells:

> It is the potentially unique versatility of the ES and EG cells derived, respectively, from the early stage embryo and cadaveric fetal tissue that presents such unusual scientific and therapeutic promise. Indeed, scientists have long recognized the possibility of using such cells to generate more specialized cells or tissue, which could allow the generation of new cells to be used to treat injuries or diseases, such as Alzheimer's disease, Parkinson's disease, heart disease, and kidney failure. Likewise, scientists regard these cells as an important – perhaps essential – means for understanding the earliest stages of human development and as an important tool in the development of life-saving drugs and cell replacement therapies to treat disorders caused by early cell death or impairment. (Shapiro et al. 1999: 1)

There was awareness of the ethical controversy, but in the end the medical and scientific promises echoing the three first uses also indicated above, in the original scientific articles, motivated the NBAC's endorsement of hESC research (Leinhos 2005).

The specific element in the business articulations of the hESCs and their relationships to actors is the expected profits. Geron and ACT are no charity organizations. They are accountable to stockholders. The monetary dimension of the cells is not exclusive to the business world. Politicians and patients mention money more in statements. Geron and ACT representatives emphasize the need of hESCs for other actors, though their own activities, to some extent, have to be profit-oriented. When Thomas Okarma, vice president of R&D at Geron, appears in the hearings in a Senate subcommittee he confirms the scientists' (Thomson, Gearhart, and West) characterization of the hESCs and the multiple uses (US Senate 1999b: 51). This is natural. Geron was associated with the stem cells

via the scientists and can earn money if others accept the hESCs' multiple uses.

Business actors, bioethicists, and politicians thus concurred with the multiple uses indicated by scientists. Even if there were multiple definitions of what a hESC is, the multiple uses were a general structure shared between actors, in graphic and textual form. Some actors were specifically involved with one or two of the uses.

Developmental biology

One trace of how scientists related to the cells because of their use in developmental biology comes in illustrations. Figure 9 from Austin Smith's review of research on (non-human) embryonic stem cells (ES cells) and hESCs, draws on the parallel between ES cells and embryonic development (Smith 2001a). The grey arrows between the ES cell culture dish and the inner cell mass and epiblast indicates the embryonic stage that the ES cells are perceived to equal.

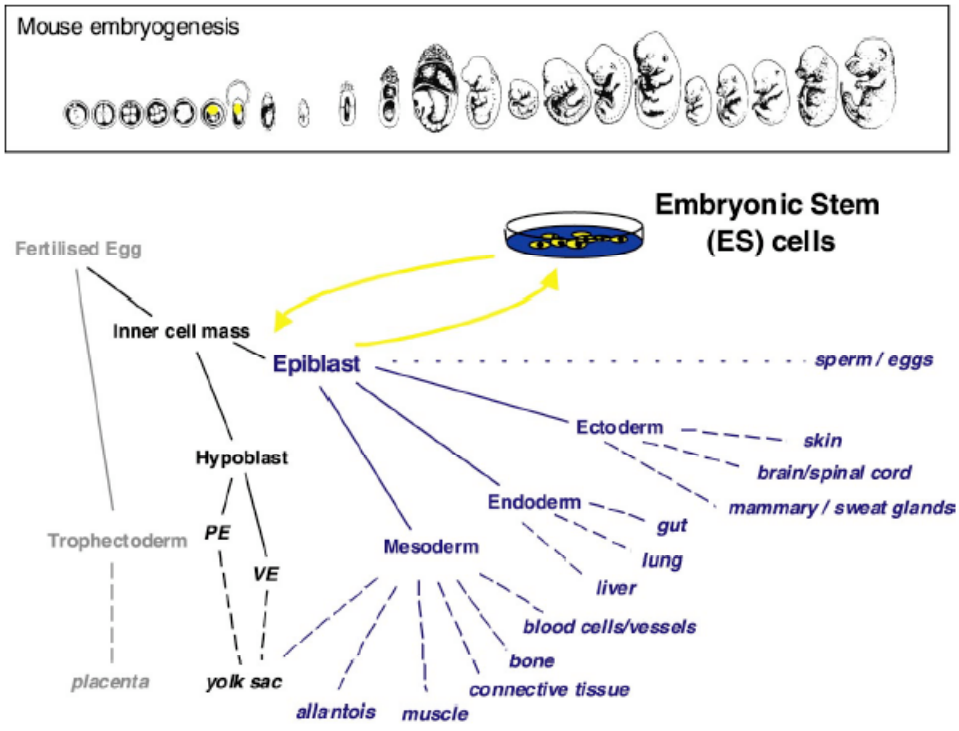

Figure 9: The parallel between mouse embryogenesis (development) and embryonic stem cell development (Smith 2001a). (Reprinted, with permission, from the *Annual Review of Cell and Developmental Biology,* Volume 17, © 2001 by Annual Reviews, www.annualreviews.org).

According to Smith's illustration the developmental potential of ES cells is not equal to the fertilized egg, but to the inner cell mass or epiblast.[78] The illustration builds on the general structure of the flowing cells, but instead of multiple *uses*, the cells result in multiple *tissues* that parallel embryonic development. Another example again comes from the issue of *Cells Tissues Organs* on ES cells as a developmental model. Although this issue mainly concerned non-human ES cells the guest editors Anna Wobus and Kenneth Boheler explicitly assumed that their use for developmental biology would soon be extendable to hESCs. Article after article approached specific practices in which ES cells were involved. Wobus and Boheler introduced these articles.

> The first two chapters are dedicated to molecular mechanisms regulating self-renewal and differentiation of ES cells […] and the expression pattern of Oct-4, a key regulator of totipotency during the mammalian life cycle […] The following articles review the present knowledge of ES cell-derived neurogenesis […], adipogenesis […] and hematopoiesis […] on tissue-restricted gene and protein expression. To study developmental aspects of ion channel formation and signalling cascades during early developmental stages, one chapter is devoted to confocal imaging and patch clamp analyses of differentiated cells derived from ES cells […] The use of differentiation factors and signalling molecules for selective differentiation of ES cells will become more and more important; therefore, the effects of retinoic acid on stage-dependent differentiation of ES cells is summarized […] Another article describes the use of ES cells in an in vitro embryo toxicity screening system, which is already part of a validation study of the European Union […] Two chapters summarize the attempts to establish pluripotent cell lines from species other than mouse […], including the most recent strategies to introduce genetic modifications into livestock by nuclear transfer […] (Wobus and Boheler 1999: 130)

What is remarkable about this outline is that it conveys the multiple uses of the same type of cell, ES cells. Wobus and Boheler articulate the multiple uses of ES cells as they lay out the content of the special issue by presenting chapter by chapter. In respective chapters, the cells' significance for understanding the development of specific tissue-types is dealt with. The "molecular mechanisms regulating self-renewal and differentiation" concern the pluripotent state that ES cells are arrested in. Oct-4 is a transcription factor expressed by cells as long as they are toti- or pluripotent. The development of ES cells into specific tissues such as neu-

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78 In the Introduction this stage of the embryonic development was called blastocyst (step 3 in Figure 1).

ral, fat and blood cells (neurogenesis, adipogenesis, and hematopoiesis) is treated in the following chapters. Each of these cell-types visible in the illustrations above are articulated by Wobus and Boheler in textual form. Each cell-type require specific practices. *Cells Tissues Organs* is a scientific publication and the contributing authors are all scientists. All of the articles address specifics of ES cells. Irrespective of specialties the various scientists all use the same type of cell.

Basically all of these uses and practices also apply to the hESCs. When Wobus and Boheler extend the use of ES cells as a developmental model to hESCs, this concurs with other scientists, e.g. Smith. When Thomson and Gearhart explain the capacities of the hESCs they link this explicitly to the earlier work on non-human ES cells. According to Gearhart their reported experiments are just the application of already established knowledge of ES cells:

> I want to emphasize that this technology was first developed in the mouse and we adapted it to the human. We did not have to work it out in the human per se, just adapt it. (US Senate 1999b: 12)

Transplantation therapies

Patients are constantly included in actors' articulations. All actors refer to possible patients and to all who may need new drugs, or suffer from infertility, pregnancy loss, or neuro-degenerative and cardio-vascular diseases, and cancers. When the patients appear themselves they do not contradict the "formula" of the three uses. However, one usage is more important than the others for patients: transplantation therapies. In effect, the transplantation therapies are not only one usage. Transplantation therapies are one concept that opens for a number of ailments and ways of dealing with those conditions.

Even if Reeves, Fox, diabetes patients and relatives, and another 100 patient and professional organizations, all support hESC research they are not all hoping for the same treatment, but multiple treatments that allegedly result from the use of hESCs for transplantation therapies. In the previous chapter Pikunis and Melton articulated the needs for Parkinson's disease and juvenile diabetes. In the laboratory, or in the clinic, there are huge differences between therapies for Parkinson's disease, Alzheimer or heart disease. As the hearings unfold the many therapeutic practices are all assumed to be approachable by means of the hESCs. For all

of the supportive patients the transplantation therapies are central although articulated differently dependent on the patients' conditions.

Although the use of hESCs in drug screening may be thought to appeal to companies, transplantation therapies are presented as the major reasons for corporate involvement. When Okarma in hearings 1998–1999, and at a workshop in 2001, explained why Geron sponsored the initial hSEC research the major reason was transplantation therapies, and not drug screening (US Senate 1999b, Okarma 2001). This was also the focus of ACT, although with a greater emphasis on cloning technology. The Biotechnology Industry Organization supported hESC research with reference to the uses of hESCs in developmental biology and in transplantation, but sidestepped the drug discovery aspect (US Senate 1999b: 104).

In the NBAC's recommendations the multiple uses were repeated. However, when other bioethicists appeared at the hearings, such as Arthur Caplan, the transplantation therapies were the main issue and those in need of such therapies the main justification for federal funding (US Senate 1999b: 36). Coming from the opposite side of the pro-life/pro-choice camp, Republican Senators linked to the cells because of their use in transplantation therapies. Here Republican Senator Thurmond explains his support for hESC research:

> There is great optimism that lifesaving therapies might be produced. Cells and tissue capable for transplantation could include insulin producing cells to cure diabetes, heart cells to rebuild damaged hearts, or new brain cells for victims of Parkinson's disease or other neurological disorders.
>
> As a father of a daughter with juvenile diabetes, I know first-hand the devastating nature of this disease. In addition, during my service in the Senate, I have heard the personal pleas of thousands of constituents who are affected by various diseases and disorders. (US Senate 1999a: 19)

Thurmond is one among many. Not only do patients pick out this one usage from the multiple uses indicated by scientists. Senators, businesses, and bioethicists explain their own interests in the cells by referring to the cells' use in transplantation therapies.

Ethical use of IVF embryos

There is a fourth use of hESCs that in particular addresses the previously mentioned pro-life actors in Congress and in the White House. IVF and the remaining embryos contributed to coordination in three ways in 1998–2001. A number of actors opposed the use of already existing embryos,

but would not come out in *opposition* to the practices of producing and storing the embryos. It was thus a case of non-opposition to their existence. Another linkage between embryos and pro-life actors was the explicit endorsement of using already existing embryos in research to achieve important medical treatments. This was justified with the necessity of producing extra embryos for IVF. A third was the endorsement of hESCs already produced from supernumerary embryos.

Non-opposing contribution

Some opponents questioning the use of embryos in research did not question the practice of in vitro fertilization (IVF) that had produced the embryos. Instead they avoided the issue. In a hearing in 2000 Senators Brownback and Specter had a conversation. Brownback brought up the holocaust to oppose research on embryos and Specter objected that the experiments during World War II were on living people. Brownback responded that "[t]hese are living embryos. You are taking living embryos". In their conversation the moral status of embryos and the issue of IVF stands out bluntly. Embryos as living persons confront the IVF practice.

> Senator SPECTER. Let me ask you, Senator Brownback, do you oppose in vitro fertilization?
>
> Senator BROWNBACK. I have not thought through that one, and I am not prepared here today to talk about that particular issue. The issue in front of us is you have a live embryo.

Brownback tries to separate the IVF issue from the hESC issue. He is not willing to take a stand on the former, only on the latter. Specter's final argument in the exchange with Brownback refers to IVF and what is thereby presupposed.

> Senator SPECTER. I raise the in vitro fertilization issue – and you are correct. It is not before us. We are exploring the matter today, but we are going to have an opportunity to discuss it on the Senate floor at greater length. But I raise the in vitro fertilization issue because there are some who do object to that, and it is a consequence of in vitro fertilization that these embryos are created. There might be an argument that every one of these embryos is entitled to life. But the process of in vitro fertilization is to have a large group and then to use some but not to use others. So, this is something we will be getting into. (US Senate 2001: 30)

Brownback is not alone in trying to avoid definite statements on the issue of IVF (US Senate 2001: 74). Many oppose the use of embryos for stem cell production, but Specter's point here is not dealt with: "But the process of in vitro fertilization is to have a large group and then to use some but not to use others". It is not brought up in any elaborate way in the hearings.[79] Doerflinger and the official Catholic doctrine are clear on their dissociation from IVF (US Senate 1999b: 144f), but the lobby organization he represents has not acted in any way against the procedure (Wade 2001). The case is similar with other pro-life actors.[80]

Supportive contribution

Toward 2001 other pro-lifers did not only "not oppose" IVF but explicitly found it justified to use it in hESC research. This is the second sort of contribution from embryos to coordination. Next time Brownback appears, in 2001, he is involved, together with three other pro-life sena-

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79 Dr. Prentice's testimony in US Senate 2001: 74, and Dr. Caplan's testimony in US Senate 1999b: 39, both bring up the IVF industry as a part of the "spare embryo problem", but without going into the problem in depth, or providing any solutions. William L Pierce, PhD Senior Fellow, Discovery Institute for Public Policy is an exception when he suggests an unpacking of IVF in the 2001 hearings:

> IVF techniques themselves could be changed to provide that reproductive medical experts no longer extract more ova than can be safely fertilized and implanted, without freezing. Let's urge those contemplating IVF to take a different approach, one that may impact consenting adults rather than embryos who cannot give consent. (US Senate 2002: 72)

80 Observed by Nicholas Wade of the New York Times:

> Douglas Johnson, the legislative director of the National Right to Life Committee, said that in-vitro fertilization "is outside of our purview." His committee has not taken a position against fertility clinics, Mr. Johnson said, because "we don't get into passing judgment on the conception of any person."
>
> Richard Doerflinger, the chief lobbyist for the National Conference of Catholic Bishops, said that the church's moral opposition to in vitro fertilization "has been pretty clear from the outset, but in terms of political action we have to choose the issues that are raised for us."
>
> Sean Tipton, the public affairs director of the American Society for Reproductive Medicine, said, "We have not seen any opposition from the Catholic bishops to put a stop to in vitro fertilization." (Wade 2001)

tors, in a conversation with Senator Harkin and explicitly refrains from opposing IVF.

> Senator HARKIN. You are not opposed to in vitro fertilization?
>
> Senator FRIST. No, sir.
>
> Senator HARKIN. Senator Smith?
>
> Senator SMITH. No, sir.
>
> Senator HARKIN. Senator Hatch?
>
> Senator HATCH. No, sir.
>
> Senator HARKIN. Senator Brownback?
>
> Senator BROWNBACK. No.
>
> Senator HARKIN. No. I guess my question is that obviously in vitro fertilization is going on right now.
>
> Senator FRIST. Yes, sir.
>
> Senator HARKIN. So there will be, as you point out, left-over embryos, in essence.
>
> Senator FRIST. Thousands and thousands and thousands.
>
> (US Senate 2002: 31)

Harkin's orchestration of bipartisan support for IVF is persuasive. However, Frist, Hatch and Smith were not as hard-pressed as Brownback. They were among the pro-life actors who not only accepted IVF, but deliberately linked it to hESCs in order to justify their own support of the research in spite of "pro-life values". Some of the strongest articulations of hESCs come from these pro-lifers. They represented pro-life values and voters.

However, keeping an identity as a "pro-life congressmember" is not a straightforward thing. Pro-lifers outside of Congress are keeping track of and classifying votes in Congress as being more or less pro-life (Taylor 2001b). To maintain a pro-life identity these congressmembers referred not only to the therapeutic promises and the pluripotent properties of hESCs, but also to a specific source of cells, the embryos resulting from in vitro fertilization. One clear example of this is Orrin Hatch:

> I am proud of my strong pro-life, anti-abortion record. I commend the Bush Administration for its strong pro-life, pro-family philosophy. In my view, research on stem cells derived from embryos first created for, but not ultima-

> tely used in, the process of in vitro fertilization, raises questions and considerations fundamentally different from issues attendant to abortion. (Hatch 2001b)

Hatch had credibility thanks to his Senate voting record. In his separation between abortion and embryo research he draws on "the embryos first created for, but not ultimately used in, the process of in vitro fertilization" as elements that are stable in virtue of their actual material existence. The embryos are already there and, together with human actors, can take some of the responsibility for the endorsement of hESC research. Senator Bill Frist was also pro-life and is one of the few medically trained in the Senate.

> Senator FRIST. We are getting pretty technical there. In my own mind, IVF involves the creation of surplus – and these words are hard for people, discarding, disposing, and surplus. But that is the nature of in vitro fertilization today. You have to, and so you are going to have 10 or 15. People elect either to freeze them or to discard them immediately. (US Senate 2002: 31–32)

Frist not only appealed to frozen embryos, he appealed to "the nature of in vitro fertilization". Again, as in Specter's lines above, IVF is an already defined technology here and "people" can only elect to either freeze or discard. The options are limited because of the technology. In this sense the process of IVF is a "black-boxed" or "frozen" element. When articulated together with embryos it changed their meaning and status. The resulting number of embryos was regarded as a pre-given, as "already there". The IVF practice was in place and producing a specific and inevitable outcome that was used by some actors when they supported the hESCs.

Minimal contribution

The third sort of contribution to the coordination was offered by President Bush, in his August 9 decision (2001), as he explained his own task.

> My administration must decide whether to allow federal funds, your tax dollars, to be used for scientific research on stem cells derived from human embryos. A large number of these embryos already exist. They are the product of a process called in vitro fertilization, which helps so many couples conceive children. When doctors match sperm and egg to create life outside the womb, they usually produce more embryos than are planted in the mother. Once a couple successfully has children, or if they are unsuccessful, the additional embryos remain frozen in laboratories.

> Some will not survive during long storage; other are destroyed. A number have been donated to science and used to create privately funded stem cell lines. And a few have been implanted in an adoptive mother and born, and are today healthy children. (Bush 2001)

Bush accepted the process of IVF as producing "additional frozen embryos". But, he also mentions an alternative fate for the embryos. Destruction and donation to science are not necessary end destinations, following Bush's articulation. "A few" of the embryos had been implanted in an adoptive mother and then born. According to Bush, frozen embryos were not sufficient to justify support of hESC research.

> I have concluded that we should allow federal funds to be used for research on these existing stem cell lines, where the life and death decision has already been made. (Bush 2001)

All remaining embryos must *not* be used for hESC research. However, in the cases where the embryos had already been destroyed to produce lines of hESCs, federal funds could be used. Much media space has been used to debate Bush's decision as a balancing act between pro-life and the pressure for future cures. This is not the place to add to those speculations. Whatever the intentions, tactics or strategery on Bush's part, the frozen embryos did occupy a responsible role in his support for hESC research. As he explained his decision IVF was a black box producing additional embryos in the process of "helping so many couples conceive children". Although Bush only supported hESC research on embryos whose fate had already been sealed, the practice of IVF was explicitly linked to the embryos. He was not supporting the deliberate creation of embryos for research. For some pro-lifers his decision was still not sufficiently restrictive, but representative of a "moderate pro-life position", according to Jameson Taylor, pro-life author. Here in a newsletter from Children of God For Life (an associate of the American Life League).

> Perhaps the most disturbing upshot of the embryonic stem cell (ESC) debate has been the shameless co-option of pro-life language by a number of so-called pro-life politicians. (Taylor 2001b)

Taylor's critique is interesting because it highlights how the hESCs became a part in the creation of a new position among ("so-called") pro-lifers. The moral status of embryos was a hot and fluid issue. In spite of this, embryos contributed to the coordination of diverse actors, at least according to some actors' articulations. Heated polarization was some-

what cooled down as actors, especially from the pro-life side, used the frozen embryos and the black-boxed IVF procedure to explain their own support for the cells (although this stance did draw heated criticism from "less moderate" pro-lifers). The use of already existing embryos as source for hESCs was a reason for coordination.

Boundary object implications

All of these multiple uses are held together in the hESCs. Through the hESCs as mediators a scientist interested in developmental biology can join hands with patients and pro-life Senators. From the original articles to the hearings the hESC articulations were picked up, confirmed and sent on to other actors. The cells are not doing the same things for businesses, patients, politicians, ethicists and scientists. Patients endorse the cells because they promise cures to diseases such as Parkinson's and Alzheimer's. Corporations support hESC research since they expect a profit via transplantation therapies. Bioethicists gain more influence as a profession because of the ethical problems connected with the stem cells. Scientists obviously benefit from all of the uses which speak to other actors, but more uniquely from the use in developmental biology. Pro-life politicians attempted to stay pro-life with various references to the already existing embryos.

Applying the boundary object approach has implied a relative reality, and another mode of coordination and distribution of agency. Unlike the OPP cases a sociotechnical reality can be analyzed without supposing any central human entrepreneur and without a totally dominating coordination. The Museum of Vertebrate Zoology (MVZ) was not dependent on an expansionist agenda. Not all actors, all museums or all of California had to be remade to make the museum work. The collectors', and the trappers' and the university administration's concerns did not have to be reframed or remade. By managing repositories, coincident boundaries or standardized forms, i.e. the boundary objects, each actor could remain partially in control, with partial jurisdiction over the coordination. These objects transcended and travelled across the boundaries of diverse social worlds and actors.

The hESCs were involved in a coordination in which many of these features were repeated. As in the MVZ case, diverse actors in 1998–2001 could endorse the hESCs without having to be remade. Patients, corporations, politicians, bioethicists, and scientists, all could have the hESCs serve their purposes to get well, make money, satisfy voters or remain in-

fluential. No central human entrepreneur managed these actors. Instead the hESCs were the main character, and although the stem cells were not entrepreneurial, these nonhumans were the center of associations, the main factor.

However, this does not necessarily mean that it was a *centralized* coordination. After the failed domination attempt (in one respect ended with Bush's decision) the hESCs were still linked to diverse actors who continued to realize them. Rather than seeing how a total (pluripotent) transformation is at stake – or not – the boundary object approach considers each association to, and each use of, the hESCs. More than a systematic, seamless change and total alignment of actors, multiple practices are facilitated and coordinated through the flow of hESCs. The cells were thus involved in a *distributed coordination*. They were boundary objects in relation to the diversity of actors that was bridged. Scientists, pro-life or pro-choice politicians, patients, bioethicists and corporations could meet in a new space made up of the hESCs.

This changes the notion of reality in two ways. From one tightly defined singular reality, the hESCs are involved in a relative and multiple reality. In the above, the reality of hESCs is not an either-or but the number and nature of various linkages. Each possible use that was envisioned, welcomed and associated with actors, adds to the reality of hESCs. In the previous chapter there were two alternatives: The reality of hESCs either became all-encompassing, or failed. A success would allegedly have created a pluripotent transformation, a US of the human embryonic stem cells, and in this sense a singular, seamless whole (see Figure 5, Chapter 2). Instead of the whole and unified reality resulting from a totally successful OPP, the hESCs are involved in a reality as multiple as the many uses of hESCs among diverse actors, but not necessarily fragmented and pluralist.[81] In this sense the reality of hESCs was more than one, but less than many, to use Marilyn Strathern's and Annemarie Mol's phrase (Mol 2002: 82). The hESCs did not require actors to agree. Bush still does not agree with Specter, Caplan and Thomson, but they could all associate to

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[81] I use and define these words very much in accordance with Annemarie Mol's study of atherosclerosis:

> This, then, is what I would like the term *multiple* to convey: that there is manyfoldedness, but not pluralism. In the hospital *the body* (singular) is *multiple* (many). (Mol 2002: 84)

the hESCs. Because of the multiple uses of hESCs the actors hung together without making up a unified whole.

Summary

This chapter has answered two issues that lingered from the previous chapters: One concerning relative reality and one concerning the absence of any central entrepreneurial human actors. In contrast to the OPP model the boundary-object approach gave space for a partial stabilization in terms of a number of linkages, without achieving total domination. This relative reality was not dependent on any strong human entrepreneurial activity, but due to a distributed kind of coordination. Diverse actors were coordinated by the multiple uses of the hESCs. Without agreeing totally or systematically, actors could collaborate through the hESCs. Just as in Star and Griesemer's case the hESCs combined a general common identity and specific uses in individual sites.

There are now two answers to the question about the sociotechnical reality of hESCs in 1998–2001, building on two diverging models positing two modes of coordination and two ways of approaching reality. Too many "twos" answering one question about *the reality of*, in the singular.

4. Theoretical Tensions and Innovations: A Boundary Package in Multiple Loops

Introduction

This chapter is a (mostly) theoretical interlude taking stock of the previous chapters and reloading for the following chapters. The first part makes a break in the Chapter 3 analysis of hESCs as boundary objects, to see how the partial connections, and relative reality of flows can be reconciled with the OPP approach used in Chapter 2. In the previous chapters hESCs have been involved in two kinds of sociotechnical network attempts and two modes of coordination that have been presented as two separate processes. It is now time to see if and how these (at least apparently) different sets of hESCs hang together.

To do so, the chapter starts in the theoretical tensions between the ANT obligatory point of passage and the boundary object from social worlds theory. There are fundamental differences between the two approaches that may be put to good use by applying Latour's concept of multiple loops. In order to flesh out such a concept, several modes of coordination have to be utilized. OPP and boundary objects can be such modes, but this requires a more localized application of the concepts.

In the rest of the chapter, the similarity between boundary objects and hESCs are challenged. The stem cells are clearly involved in a boundary object-like coordination, but this does not immediately turn them into boundary objects. This challenge will not concern the basic mode of coordination observed by way of the multiple uses, the partial connections, and the relative reality. However, I will claim, these traits can be present without a total similarity between the hESCs and Star and Griesemer's boundary objects. The solution will be an innovative addition to the notion of boundary objects. Lastly, the requirements for future analysis will be outlined.

Theoretical tensions

From Chapter 3 one lasting observation is that by 2001 hESCs had become a boundary-transcending object and a meeting-point for diverse actors. In relation to Chapter 2, the observation of a boundary-transcending position is both coherent and puzzling; coherent, since already in Chapter 2 there was more than disputes to the hESCs. In order to fight, two parties usually have to share some assumptions and some views, while disagreeing about others. The commonalities – such as the acceptance of transplantation therapies and need for pluripotent cells – between all parties were in a sense boundary-transcending and point toward coherence between the two chapters. Still, the observation of hESCs as objects of boundary-transcending coordination was puzzling, since the negotiation of federal funding in Chapter 2 clearly involved high stakes, and a mode of coordination marked by funneling, domination, and exclusion. In one chapter the hESCs were objects of dispute and in the other chapter an object of coordination. Two new questions have resulted from the exploration of how to put the two approaches to use, in order to understand the sociotechnical reality of hESCs and especially the public and political dynamics.

How can the observation of a total transformation at stake be reconciled with the observation of partial stabilization?

How can the observation of funneling through hESC research be reconciled with the open-ended coordination of ecological flows?

A first answer turns on timing and involves actuality vs. potentiality. The hESCs as a meeting-point were most visible at the end of the period, in 2001, as an actually achieved coordination – a partial stabilization. It was at this time that Bush endorsed some hESC lines supported by a number of pro-life members of Congress. However, as early as in 1998 the hESCs were articulated much like a boundary object together with funneling and exclusion, traits of a potential and attempted coordination. In this respect OPP was present, but not achieved. Actuality vs. potentiality is nevertheless only one aspect, and does not exhaust the puzzle of hESCs as objects of disputes and objects of coordination.

Although Latour and Callon's OPP did not match every detail of the negotiations of federal funding (in Chapter 2) their notion did capture some things not covered in Chapter 3. The latter built on actors who were not dependent on the cells and who, because of the multiple uses, supported research on the cells. However, it is impossible to sidestep the role of the federal government, its centrality for American research and

its subsequent potentially funneling effects on the fate of medicine. In the articulations from both opponents as well as proponents a strong either-or was tangible; domination or failure was at stake. While these aspects corresponded to the OPP, the relative stabilization of hESCs among diverse actors suggested the boundary-object approach. Before this work can continue to map the reality and the stabilization of hESCs these observations and the theoretical tools need to be reconciled.

Combining the two previous chapters raises the questions: Can the phenomena be saved? Can the hESCs be involved in both kinds of co-ordination? In principle yes, as two separate perspectives on the hESCs. Boundary objects and OPP come from two distinct approaches, social worlds versus actor-network theory. They could be presented alongside each other as theoretical "frames" for how the understanding of hESCs. However, in this study I have already started to combine the two models within one framework. The previous chapter drew on the boundary object approach. It was done in terms of an ANT study, not a social worlds or a symbolic interactionist one. At the end of Chapter 3 it was furthermore indicated that the actors' articulations of the hESCs as a boundary object happened in a situation of advocacy and in the face of a potential OPP, i.e. the high stakes of a federal funding with funneling and dominating consequences, and definite opposition from pro-life actors. Not only are the two perspectives thus presented alongside each other, but together, as two *co-existing* – and even *co-producing* – modes of coordination.

Stressing divergence: heterogeneity and diversity

One way to consider the differences between ANT and social worlds is to analyze the notions of diversity and heterogeneity. The hESCs as boundary objects are said to coordinate *diverse actors*. In what sense is it meaningful to speak of actors as *diverse* at all in an ANT study? Chapter 2 was in fact structured according to diversity: scientists, corporations, patients, politicians. According to ANT, actors are *heterogeneous*, implying that their identities are not given. Identity is only achieved through hard work, enrollment, alignment and maintenance (Callon 1986b: 24). The reference to diverse actors comes from Star and Griesemer's article and has to do with the social worlds in which actors move, work and are active in practices. The boundary objects are used in order to explain how actors can cooperate, not within the same social world but between different ones. Applying the boundary object approach thus actualizes a difference be-

tween social worlds perspective and actor-network theory in terms of diversity and heterogeneity.

The social worlds perspective adds the influence of collectives to the processes of articulation. What are these collectives? In one oft-quoted passage Anselm Strauss defined social worlds:

> In each social world, at least one primary *activity* (along with related activities) is strikingly evident, i.e., climbing mountains, researching, collecting. There are *sites* where activities occur: hence space and a shaped landscape are relevant. *Technology* (inherited or innovative means of carrying out the social world's activities) is always involved [---] In social worlds at their outset, there may be only a temporary division of labor, but once underway, *organizations* inevitably evolve to further one aspect or another of the world's activities. (Strauss 1978: 122)

Talk of specific activities, sites, technology and organization is not alien to ANT. What has been alien to ANT is the *analytical presupposition* of delimited units of the world in which these things take place collectively and somewhat uniformly. According to Adele Clarke "[s]ocial worlds form fundamental building blocks of collective action and are the principal affiliative mechanisms through which people organize social life" (Clarke 1990: 18). Social worlds are not only units in the world but also the unit of analysis (p. 20), in fundamental contradistinction to the actor-networks of ANT. The analytic advantage of the latter is precisely the doing-away with prejudices about how and where which actors are aligned around what activities. This has been called heterogeneity, and the scientists of such a world have been called heterogeneous engineers – because of their management of heterogeneous elements in contrast to so-called "purely scientific" ones (Law 1987, Law and Callon 1995).

Heterogeneity is also part of an ontological distribution among all actors in a somewhat "democratic" way.[82] In social worlds, and for a

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[82] In Latour's own terms:

> The ontological activity that is no longer capitalized at the two extremities may be redistributed among all the actants. It was the necessity of the dual system of appeal either to nature or to society that in the Kantian framework caused all the agencies to be assigned to two and only two lists. Now that we are freed from this necessity, we are allowed to have *as many poles as there are actors*. This irreductionist principle is probably the most counterintuitive consequence of science studies but it is a necessary and a coherent one. [---] Dignity, activity, and world-making abi-

study of social worlds, boundaries are important. In actor-networks and in ANT, there are no boundaries, only links that are established or not. In one respect Star and Griesemer's talk of the coordination of diverse actors is an ANT *tautology*. What actors are not diverse in a heterogeneous world? In another respect diverse actors are *contradictory* to ANT, since the notion presupposes the opposite of heterogeneity, viz. fundamental similarities between some actors (the actors who share the same social world). According to this reading of the two perspectives there is thus a difference between the diversity of social worlds and the heterogeneity of actor-networks.

Just as in the case of agency and generalized symmetry (see Chapter 1) it is a good idea *not to build theoretical contradictions* that the respective practitioners (of the theories) themselves do not stumble on. The social worlds theory resembles ANT precisely in virtue of their heterogeneity, "antideterminism", and their interest in practices (Strauss 1978: 121). From the vantage point of ANT it is possible to understand the main feature of boundary objects (that they "coordinate diverse actors") as merely saying that actors – who, in ANT, are never *a priori* similar or identical – are coordinated. Boundary objects are then basically nodal objects with a capacity to align people and things through their combination of flexibility and integrity. There is little need to import the notion from Star and Griesemer at all, if this is all it says. I want to claim that this is *not* all it says. Another interpretation of boundary objects may challenge ANT and answer questions (about actors' differences, the strength of actor-networks and the epistemology of articulations/translations) raised by Latour's still undeveloped concept of the circulatory system of science. However, in order for this to happen the theoretical presuppositions underlying boundary objects have to be considered. The reference to diverse actors typically belongs to the social worlds perspective more than ANT. "Diverse actors" is a reference to actors from distinct social worlds, units that do not have independent and primary existence in an ANT world, at least not at the outset.

> lity are reclaimed by those actants that are, nevertheless, fully nonhuman, and fully real. Mere intermediaries in the Modern Constitution, they become full-blown mediators in the non-Modern, more democratic, one. (Latour 1992: 283)

Seeking convergence: multiple loops

In his *Pandora's Hope* (1999), Latour suggests that it is not enough to look at one chain of translations in which a reference can move back and forth. You also have to take into account the multiple loops of objects and references among various sorts of actors. Thus more and more actors are tied together through multiple flows. Latour's example is Joliot's work to establish a chain reaction during the second world war (see more above in Chapter 1). Five activities have to be linked together, Latour claims.

> All at the same time, Joliot must get the reactor to work; convince his colleagues; interest the military, politicians, and industrialists; give the public a positive image of his activities; and, last but not least, understand what is going on with these neutrons that have become so important to the parties he has interested in their fate. (Latour 1999b: 99)

The treatment and the example resembles Star and Griesemer's case study, and other social worlds studies, in one respect. Latour refers here to actors who are not chiefly heterogeneous but diverse. Actors' identities are not made anew in network attempts, but are already part of larger clumps. Actors are lumped together as politicians, military, public, colleagues, etc. *The circulatory system* may be meant merely as a heuristic, pedagogical device to understand actors' movements in a heterogeneous world. Here the concept will, however, be taken more seriously, viz. as a means for better studying the linkages between actors who are diverse in specific and collective ways, restricting the (in principle) unpredictable and "agnostic" ANT view of reality presented above in Chapter 1 (Cf. Callon 1992, Latour 1999a).

To talk of multiple loops instead of a myriad of links is to back off from fundamental heterogeneity and inch towards diversity. Not all actors are equal from the outset. All linkages do not carry the same weight. Recruiting politicians and federal funding may for instance differ from recruiting a bioethicist. Different resources are set free. Different sorts and numbers of other actors may come with a politician in contrast to a bioethicist.

The circulatory system of science is presented in Chapter 3 of *Pandora's Hope* as a direct continuation of Chapter 2 "Circulating Reference: Sampling the Soil in the Amazon Forest", in which one chain of circulation is mapped out. The Amazon soil is transferred and transformed to the pedologists' boxes and color codes, and ultimately to a diagram describing

the movement of the forest's boundary. Although circulation is the issue of both chapters there are important analytic implications of going from *one* chain of translation to *multiple* loops. Latour wants to say that the scientific work of transforming earthly material to diagrams (or neutrons to chain reactions) is neither different nor separable from the handling of ministers and militaries. They all require translation and articulation.

> Was it one thing to persuade a minister to provide a stock of graphite, and quite another to persuade a neutron to slow down enough to hit a uranium atom so as to provide three more neutrons? Yes and no. For Joliot it wasn't very different. In the morning he dealt with the neutrons and in the afternoon he dealt with the minister. (Latour 1999b: 89f)

Stressing the principle of similarity cuts up the traditional epistemological gap between words and the world into many small heterogeneous transformations. For each transformation there is matter and form, a piece of the world and words. The form of one transformation then becomes the matter for the next. No fundamental difference between the world and words then exists, but many minor differences bridged through the articulation of linkages. "Knowledge about" is a new "reality of". "Realization of" is not a platonic *insight* but the *becoming real.* Apart from epistemology (or, in effect, ontology) the multiple loops are doing a sociological job. Instead of separating internal and external factors, the scientists' work of convincing neutrons and convincing ministers are inextricably bound together. Understanding science is understanding society. Following scientists will take the analyst to neutrons and ministers. While the principle similarity of each linkage in the chain of translations is an important contribution to an age-old epistemological puzzle and a quite old sociological squabble, the stress on similarity is but one aspect of multiple loops. Latour answered "Yes and no" in the above lines but barely manages to keep the two answers together. The "yes" relates to the similarity and intertwinement of "persuading neutrons" and "persuading ministers" outlined above. The "no" has to do with the different preoccupations of the scientists. In Joliot's case: the work with "colleagues, the military, politicians, industrialists, the public and neutrons".

After the earlier unpredictability concerning the identity of actors, Latour's model raises a question: Why refer to such clumps of actors as politicians, the public, and colleagues, with their specific resources, competences and realms and not stick to linkages among heterogeneous actors? Without establishing a pre-determining scheme to be followed, *mul-*

tiple loops is more than talk of heterogeneity in general. Managing the clumps are necessary for Joliot to "be a good scientist" and to "guarantee the reference for what he says".

> It is impossible, by definition, to give a general description once and for all of the unpredictable and heterogeneous links that explain the circulatory system that keeps scientific facts alive, *it must nevertheless be possible to outline the different preoccupations that all researchers will hold simultaneously if they want to be good scientists.* Let us try to enumerate the various flows that Joliot must take into account simultaneously and that together guarantee the reference for what he says. (Latour 1999b: 99, my italics)

Instead of merely talking of heterogeneous actors and links "the various flows" are introduced because the differences between scientists' preoccupations are important. For Joliot to succeed, his ideas have to be transformed into public trust, political decisions, financial resources, heavy water, etc. Each of these transformations entailed its specific challenge, Latour claims. That's what makes the work of multiple loops so difficult and important. If politicians and the public could be treated just like neutrons or atoms there would be less point in "enumerating the various flows" that have to be managed in order for a new reality to take shape.

Accessing politicians, the public, or colleagues is important because politicians, the public and colleagues possess specific resources not possessed by other actors. This suggets that the very diversity between resources and competences is crucial for the actors to achieve success and stabilization for their projects. Multiple and diverse loops in that case will affect the analysis of stabilization and reality. Stabilization is the result of actors linked up to each other. Accordingly, is stabilization measured by counting up the total number of actors? Or, may there be a difference between linking up to one person or one piece of technology rather than another person or piece of technology?

Maybe one actor can make up for ten other actors. How do you tell which actors are important? Critics of ANT has pointed out that the analysis of an actor-network's strength is a purely retrospective and circular assessment: The winner had the strongest chain of associations (Yearley 2005: 64). But, why was it stronger? Because it won out. There is thus no way to tell the difference between linkages with respect to the strength of associations (just as there has been no difference in various forms of articulations). With multiple flows and the related notion of diversity some of this analytic weakness might be met. Actors are important not just as one more linkage, but with regard to their diversity – in competence, re-

sources and position. Analytically, there has been no difference in principle between aligning other colleagues and aligning politicians. However, the strength of a chain of associations differs if all of the actors are colleagues, versus if some are colleagues and some are politicians. Linking some actors to an object "realizes" the object more (i.e. makes it more real) than associating to other actors depending on what loops are working or not.[83] This is why Latour "enumerate[s] the various flows that Joliot must take into account simultaneously and that together guarantee the reference for what he says". A project's strength is directly proportional to not only the number of heterogeneous associations, but also to the diversity of the associated actors and their resources.

Especially in Chapter 3 the diversity of actors attached to the hESCs was visible. It is possible to say that the hESCs did circulate among these actors. That was one of the reasons for bringing in the boundary object approach. If not as batches, the hESCs circulated in diverse actors' articulations. Plainly put: Actors referred to hESCs. In the hearings, the diverse range of actors indicates the many aspects of the hESCs. Accordingly, the hearings were a place where multiple loops of the hESCs could be established, manifested and articulated – in particular in relation to one crucial actor, the Federal administration. While the laboratory established the reference "human embryonic stem cells" by linking them to a corporation and to other laboratory work (such as the earlier ES cells with the adjacent markers, procedures and tools) the hearings stabilized the reference by giving diverse actors the opportunity to articulate and circulate the "human embryonic stem cells".

Managing multiple loops: modes of coordination

However, if the different activities needed to manage diverse actors are so important, then why are these preoccupations all subsumed under the rubric of translation and articulation? The new concept of multiple loops does not correspond to the traditional ANT understanding of how actors are linked together. In spite of the "different preoccupations" that are needed for the continuity of the scientific reference in multiple loops the process is still one and the same thing: translation. This is where Latour does not fully relate his two answers to each other. He says that "yes", persuading ministers and neutrons is the same thing (that is, tran-

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83 NB: The "socio-technical weight" of actors is still constructed, difficult to assess and never straightforwardly pre-given.

slation). And, "no", they are not the same thing since the scientists are not limited to a scientific core, but pursue politics and public relations as well, in multiple loops. There thus seems to be a gap between the acknowledgment of diversity and the understanding of how diversity is handled by actors. In the theory chapter I quoted Annemarie Mol's call for *forms of coordination*. Coordination and associations are said to be either on or off.

> Each new and successful association makes a network larger. But however great the difference between the coherence in a network and *logical* coherence, to talk of "associations" does have a homogenizing effect. Either an association is made or it isn't. An element is either inside or outside a network. Coordination is established or not. There are no distinctive *forms* of coordination. (Mol 2002: 65f)

I suggest that an advantage with the multiple loops is that distinctive forms of coordination may become visible. Various loops require, or favor, specific forms of coordination. Some things are needed for analyzing actors who are handling multiple loops. One goal must indeed be to *not separate* the activities into "scientific" and "political" ones. If negotiating with neutrons is fundamentally different, epistemologically speaking, from handling politicians then the ghost of internalism-externalism may be revived. In a version of internalism, knowledge may then be determined through the former process (slowing down the neutrons) while the latter merely provides context (funding or not funding). In contrast the externalist may regard the political processes as the real causes for the underdetermined handling of neutrons. Considering this dichotomous ghost any fundamental differences between the activities of scientists are probably a bad idea.[84] In this respect they should be "the same thing" (see Latour's quote above). In order to capture the diversity of

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[84] Latour has presented one such significant difference between two construction processes, yielding different results: hard and soft facts Latour 1987: 208–210. Unfortunately these concepts get worryingly close to externalism and internalism. Hard facts are namely the usual technological and scientific way to form an alliance and result in short, limited networks. Soft facts are less techno-scientific and leave a wider margin of negotiation which on the other hand gives more stretched-out networks. Except for the distinction between scientists and non-scientists reminding one of internalism-externalism there is another drawback. The two notions refer to different facts (hard vs. soft) and actor-networks (short vs. long) and not different modes of constructing the *same* reference/fact in multiple circulations.

multiple loops the epistemological significance of activities cannot be decided beforehand. Latour agrees about this. The actor-network analyst should remain agnostic. Latour has subsequently shifted the signification of such processes with the explicit intention of not entailing how they can happen. In order to keep an open-endedness and keep away analytic prejudgment he has played around with different terms such as translation, articulation, construction, and production. These two goals should be set for matching multiple loops and the analysis of how actors handle them: First, the non-separation of science, politics and other areas, and second, the diversity and open-endedness of possible activities.

It may be that the multiplicity of terms does not meet the need to understand the management of diversity. While the concept of translation has been, and still is, formulated as non-prejudiced in theory, it has been less broad in practice. Callon, Law and Latour all practiced the translation model in case studies in which actors were linked together in one network. The actors were aligned by reformulating their goals so as to make them take a detour through one institution or one group of entrepreneurs, i.e. the obligatory point of passage. The model assumed that all actors, whether politicians or microbes, were negotiated by the same funneling movement. Thus, they (Callon, Law and Latour) avoided internalism-externalism by showing how the effective processes were not either on the inside or on the outside, but in the very tying together of various actors, whether perceived as "social", "political", "economic" or "cognitive". But in contrast to the theoretical open-endedness, translation in the OPP model did in fact lock the way actors were handled. One group of entrepreneurs was the main agents. Other actors and their goals were displaced as they became part of the new, dominating and totally transforming actor-network. Although there were many heterogeneous negotiations they all participated in one general pattern of coordination.[85]

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[85] OPP may impose a shape on the network but there are still various translations achieving this shape. While OPP is a result and a pattern for network building there are many tiny negotiations establishing the linkages that end up in the OPP formation. It is true that the recruitment of actors in Pasteur's France drew on the OPP, but still each negotiation was pursued differently, Latour [1984] 1988. Each translation required its own challenge. Farmers, politicians, hygienists, veterinarians had to be enrolled in different ways – albeit always with the goal to funnel them through one institution. In spite of the differences the OPP does in fact impose one similarity in all the coordi-

All loops do not work like this. Actors sometimes exist in networks or worlds that constrain the way they can be associated to other networks. What if the linkages between actors did not totally transform them all and in equal manner? Again, with reference to Mol: Studying an actor-network as the associations of *heterogeneous* actors from the perspective of one single network formation may have a *homogenizing* effect, unsuitable for a reality of many networks and different kinds of associations:

> it may be that, at least in each empirical study, it is possible to follow the associations made within a single network. But what if there are two or more networks? How then to articulate the difference between associations *within* and *between* networks and – more important still – might it be the case that different networks hang together in different ways, are there different *kinds* of association? (Mol 2002: 70f)

If multiple loops are meant to capture such differences, then the totally transforming and hegemonic character of the OPP model fall short – at least on its own. In Chapter 1, I explained the notion of multiple loops with reference to Latour's *The Pasteurization of France*. The biggest problem probably arises when the translation model is elevated to be the main, or the only, way to understand how actors behave and coordination happens. There is now no need to do this, since there are other available ways sketched in the literature.

Mol exemplified how the disease atherosclerosis was enacted in many hospital practices, such as calibrating test results through correlation studies, thus creating common measures for incommensurable tests (p. 84). Another form of coordination is to *add up* test results that do not conflict or if they do, establish hierarchies for which test is most important. Also terms can be a mode of coordination. The disease is named differently depending on whom you talk to implying that none of the places and none of the practices have *the* privilege to define what atherosclerosis is for all the others. The disease is distributed on many practices, and multiplied, but still hangs together (p. 117). Mol's description of atherosclerosis and its multiplicity hanging together, without "pluralization" and separation, reminds of Star and Griesemer's boundary objects. Diverse actors are coordinated without consensus through the flow of objects to multiple practices. The diversity of social worlds fits Mol's multiplicity.

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nation work: All actors are changed and they become so through the activities and conditions of the Pasteur Institute.

A dialectic of boundary objects and points of passage

In the previous chapters the OPP model and the boundary object approach were both applied to the case of hESC research. I suggest that both of these accounts were correct, but concerned specific loops. *OPP and boundary objects signify the modes of coordination in different loops*. This combination of OPP and boundary objects requires that the former does not concern all of the circulatory system of science and society.

In the classic studies by Latour, Callon, and Law, the OPP was *the* mode of coordination. The OPP was a pattern for the attempt to form an actor-network out of heterogeneous entities. When I suggest that the OPP merely concerns one loop, and not all of the loops, I localize and relativize this mode of coordination to make it fit multiple reality.

This is also what Vissac-Charles suggested in her study of two innovation projects: Rather than the description of one single network, the OPP is a pattern that emerges as several networks are combined, at the "butoir", the gateway (Vissac-Charles 1998). Unlike the original OPP the notion here does not signify the stabilization of a whole network at once, but the association of two networks. Similar to the original cases, Vissac-Charles's OPP is an either-or with a lot at stake. The negotiations thus concern association or not, rather than differentiated or partial commitments.

Crucial to her analysis is, however, also the delimitations of a project. It has an inside and an outside, and the construction of the boundary between them is essential. A project can interact directly with another network through a boundary object. Nevertheless, the object will also relate in a more indirect way to other, longer stretched-out networks, Vissac-Charles claims. In those cases the object will be the recipient of *prescriptions* from these other worlds, and vice versa: The object will convey *prescriptions* for the surroundings.[86] Such mutual, two-way prescriptions for the project and for the surrounding worlds are obligatory points of passage in Vissac-Charles's terms (Vissac-Charles 1998: 299). The boundary object and the OPP are mutually connected. If you choose a certain boun-

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[86] Vissac-Charles's use of prescription refers to the notion of inscription presented by Akrich 1993. I will not elaborate on the full import of Akrich's (or Vissac-Charles's) notion of prescriptions. For the purposes below it is sufficient to note that the configuration of boundary objects among some actors results in the OPP instructions or restrictions for other actors. Thus the two modes of coordination are linked to each other.

dary object you are also committed to a certain OPP. There is thus a choice, the configuration of the former actualizes and shapes the latter, the modifications of the former redefine the corresponding OPP.

Vissac-Charles's approach can be used as one way to address the management of multiple loops. This is applicable to the case of hESCs. The hESCs are involved in an OPP *and* in a boundary object coordination. They coordinate certain actors within a project. For these actors the stem cells can mean a number of things and be turned into multiple uses. hESCs are real in proportion to the links to scientists, corporations, bioethicists, and patients. In November 1998 there are also a number of actors on the outside. The Federal administration is positive, but still at the time (probably, depending on the interpretation) prohibited from funding the research. Because of this, the large institutional network of university departments is on the outside (including laboratories, tools, and scientists). Also on the outside are the actors who explicitly position themselves as opponents. The Senate hearings are summoned in order to negotiate the boundary between hESCs and the outside. By bringing in the outside, another kind of association is at stake, including the funneling and domination of federal funding, together with the staunch uncompromising mode of the pro-life opposition. It is in this way that hESCs become an obligatory point of passage.

The localized OPP

A combination of Vissac-Charles's approach and Latour's multiple loops provokes two questions: What is the relationship between the two "hESCs" – the hESCs as involved in a boundary-transcendent coordination and those of the OPP-like coordination? And, what do these two concepts now mean, in contrast to their original meaning? As already described above, Vissac-Charles uses the notion of OPP differently than in the earlier works by Latour and Callon. More than the description of a single network, the OPP denotes a pattern emerging in the combination of several networks at the gateway (or "butoir"). The notion thus does not signify the stabilization of a whole network at once, but two adjoining networks. As with the original notion, Vissac-Charles's OPP does signify high stakes in an either-or mode. Negotiations aim for successful assso-ciation – or not – instead of degrees of commitment.

Following Vissac-Charles, the OPP has two faces relating to two sides of a relationship. Inside and outside actors have to accept the prescriptions entailed in the OPP, respectively. From "the inside" (i.e. among suppor-

ters) the hESCs were intentionally articulated in relation to federal funding. This choice underlies the hearings. Senators Harkin and Specter are frank about their intentions to insert hESC research into the federal institutional and financial network, as are the majority of testimonies. They are there to negotiate the association of federal funds to hESC research.

> The subject matter on our hearing today arises from a provision of the legislation reported out by this subcommittee last year, which limits the use of Federal funds for research on human embryos. That is an issue which has come into sharp focus with very dramatic recent medical developments, warranting a closer analysis or perhaps a reanalysis of that question. (US Senate 1999b: 1)

The OPP in Vissac-Charles's version is thus no longer a group of researchers (cf. Callon), an institution, or a laboratory (cf. Latour). It is a passage from one network to another, a checkpoint on the common boundary of two networks that somehow do not communicate or cooperate as directly as do the inside actors. Vissac-Charles describes the OPP-boundary object dialectic in her case study of the automatic apple-picker Magali.

> For instance, the boundary objects "vision" and "arm" of Magali create the obligatory point of passage "flat trees". This means that for the alliance with apple cultivators the robot can only pass through this type of tree, but reciprocally, the apple cultivators will have to agree with a kind of flat tree to connect to Magali. *At each obligatory point of passage you can find corresponding alternatives:* you passed through the flat trees but you could have passed through the round trees etc… (Vissac-Charles 1998: 300, her italics, my translation)[87]

In Vissac-Charles's case the OPP is not as potentially dominating as the federal funding of hESC research. The farmers can choose other solutions. In the USA, taxpayers will not be able to avoid funding hESC re-

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87 Because of the lack of authorized translation I attach the original quotation:

> Par example les objets frontières "vision" et "bras" de Magali créent le point de passage obligé "arbres plats". Ce qui veut dire que pour s'allier à des arboriculteurs le robot ne peut passer que par ce type d'arbre mais réciproquement, les arboriculteurs devront se rallier à une forme d'arbre plate pour se connecter à Magali. *A chaque point de passage obligé on peut faire correspondre des alternatives:* on est passé par des arbres plats mais on aurait pu passer par des arbres en boule etc... (Vissac-Charles 1998: 300)

search if federal funding is allowed (unless they stop working or stop paying taxes). In addition, the latter has an authorizing and stabilizing effect for future stem cell research that is not covered in Vissa-Charles's study.

The obligation of the OPP is two-way and consequently has two mirror images on each side of the passage. For the project there is an obligation: The configuration of the boundary object creates a specific passage. Inside actors link to the outside through this particular object (robot for flat trees). The inside-actors cannot reach the farmers who use round apple trees. For the surrounding actors, the OPP prescribes that only certain actors can pass, and in certain forms (flat trees). The farmers must have flat trees to use the resources of Magali. The OPP is not a group of researchers or an institution, but the configuration of the gateway between two networks, between an inside and an outside. On the one side the OPP may involve a group of actors (apple cultivators) and on the other side there may be an object.

This is the answer to the above question of how the boundary object and the OPP can not only co-exist in the same study, but also *co-produce* each other. Settling for a specific boundary-object, or in this case the object of a distributed coordination, will simultaneously create an OPP. And vice versa, the presence of a specific outside network may shape the distributed coordination of "inside actors". While coordinating some actors in a distributed coordination the hESCs are also articulated as an OPP for the outside, consisting of pro-life actors and the Federal administration. Articulations of hESCs are both *prescriptions* for action and *descriptions* of multiple uses and existing flows. But, vice versa, the federal network is constraining what sort of research is possible. The existing regulations are a narrow gateway for hESCs. In 1998–2001 many claimed that hESC research could not pass through the gateway without a legal change.

The ban on federal embryo research is the OPP from the one side. It "has come into sharp focus" – in the words of Senator Specter (US Senate 1999b: 1) – because of the development of hESCs, i.e. the other side of the OPP. The OPP is not an object (e.g. the hESCs), or an institution (e.g. the Federal administration). It is the *point of contact* between a network already involved in hESCs and a network (still) "on the outside". If this definition sounds vacillating, it is correct. It is vacillating in the oscillating sense. Since the OPP notion is applied here to capture

how flows are interacting it should be a vacillating definition. OPP is used more locally and more fluidly than in the original sense.[88]

Applying the localized vacillating dialectic of boundary objects and OPP to the hESCs says something about how different the loops of hESCs are in relation to corporations, individual scientists with private funding, patient organizations, and bioethicists on the one hand and on the other hand in relation to the huge stakes and "bivalent" association of the Federal administration in the context of abortion disputes. The loops on the inside are all contributing with their linkages and it is difficult to assess whether one linkage is gravely more important than another. However, the outside circulation of federal funding is of another magnitude, not comparable to the other linkages. Its degree of stabilization is more far-reaching.

In my answer to the questions that started off this chapter, I suggest something similar to Vissac-Charles. However, now the OPP and boundary objects are applied to the loops of the circulatory system of science and society. Boundary objects and OPP says something about how different the loops of hESCs are. The differences appear between corporations, individual scientists with private funding, patient organizations, and bioethicists on the one hand, and on the other hand the huge stakes and "bivalent" association of the Federal administration in the context of abortion disputes. The loops on the inside all contribute with their linkages and it is difficult to assess whether one linkage is substantially more important than another. However, the outside flow of federal funding is of different magnitude, not comparable to the other loops (see Figure 10). Its degree of stabilization is more far-reaching. That is, unless the Federal administration decides to commit merely partially, as Bush did in August 2001.

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88 Vissac-Charles is not alone in using OPP in this localized fashion, Epstein 1996, Law and Callon 1995.

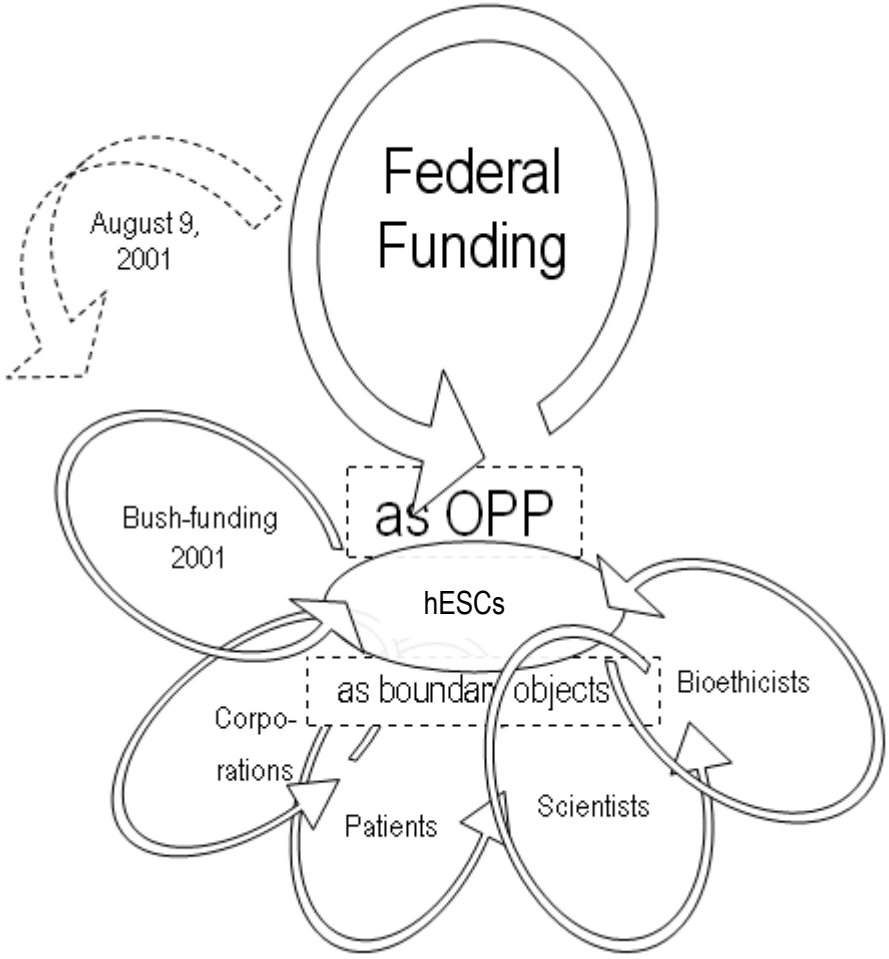

Figure 10: The hESCs as OPP and boundary objects in multiple loops.

The magnitude of stabilization at stake was also evident when federally funded hESC research was opposed. If federally funded hESC research was an attempted OPP, then what did opponents attempt, for instance Doerflinger?

> This subcommittee has now held three hearings on one narrow avenue of research, precisely the avenue that raises the most obvious moral and legal problems, so far to the exclusion of all other alternatives, even when those avenues may be more promising. The use of adult stem cells, for example, is said to promise the complete avoidance of the tissue rejection problems that Dr. Varmus has noted still need to be solved using embryonic cells. I would urge the subcommittee to expand its vision, to explore the alternatives that will advance medical progress and the wellbeing of patients without demeaning human dignity. (US Senate 1999b: 132)

According to Vissac-Charles, each OPP has corresponding alternatives: "At each obligatory point of passage you can find corresponding alternatives: *you passed through the flat trees but you could have passed through the round trees etc*…" (p. 300) Although of an "absolute" character the OPP is not necessarily the only alternative. This tallies with one of the few dogmas of the patchy field of science and technology studies, often in the words of interactionist sociologist Everett Hughes: "things could have been otherwise" (Fujimura 1996: 148).[89] Vissac-Charles's assertion about alternatives is a consequence of the contingency of nature and society. She does not take the final step to actually speak of alternative points of passage (APPs). I suggest that it is useful to not only speak of OPPs, but also of APPs. Such APPs are not mentioned in Callon and Latour, but fit well with the general scheme of actor-network theory.

The alternatives to the OPP may be more or less stable or important. If all the available points of passage are disputed and less stable the network will split up (Vissac-Charles 1998: 300).[90] In spite of the obligatory appearance of the OPP, "things can be otherwise". Next to the OPP, an APP is suggested. Both passages concern the circulation of hESCs and federal funds. The two chapters have thus by means of the elaborations in this chapter resulted in a model of multiple loops and multiple modes of coordination. By means of this model the second meta-theoretical question is answered:

> (Meta-theoretical Question No 2): How can ANT account for the role of explicitly political actors in sociotechnical network attempts?

ANT can account for the role of explicitly political actors by attending to the different modes of coordination that follows from specific actors. In the case of the Federal administration its influence may call for the use of an OPP model, whereas other actors are coordinated in other ways. In

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89 Facts and claims within natural science are not taken as being dictated by nature herself. There are few necessities in the development of science, scholars have claimed. Here are a few examples that share this dogma: Bloor 1976, Cartwright 2000, Collins 1985, Giere 1999, Knorr Cetina 1999, Latour 1999b, Longino 2002.

90 The Human Genome Project is one example of a split network. Instead of focusing on the federal funding, which wouldn't go fast enough, Craig Venter chose to carry on by himself Fortun 1998. In the case of HGP it does not mean the abandonment or failure of the project but a modification of its course.

the case of hESC research the association to the Federal administration at first bore OPP-like traits (funneling and total transformation). Nevertheless, also the Federal administration can choose to connect in a more partial manner, as Bush did in 2001. There are no necessities here, but possibilities more or less actualized in various cases of coordination.

A strong boundary object

Above, the two chapters were reconciled in one model of multiple loops. It required localizing the OPP as one mode of coordination co-existing with boundary objects. In this final part of the chapter, the flows of the boundary object will be modified (the lower loops in Figure 10). I will do this by adding to the analysis in the previous chapter.

It does make sense to see the reality of hESCs in terms of the associated actors and the possible uses, instead of an either-or depending on the success of a central entrepreneurial actor. However, in spite of these contributions there are four implications that challenge the analysis of hESCs as boundary objects. The first concerns the central status of hESCs in the analysis, resulting in a strong role for nonhuman agency. A second implication relates to the unit of analysis in Star and Griesemer's case study. They did not investigate the stabilization of an object, but an institution, a museum. Thirdly, the hESCs have more content and agency than boundary objects have. A fourth problem is the role of the diverse actors and the multiple uses that are thought to address them. Together these make up glitches between the boundary object approach and the hESC case as it has been presented so far. Each problem also relates to central STS discussions about explanations. There are thus two issues at stake when the above analysis is scrutinized: the analogy with the boundary object approach and the explanatory value. While the problems may be terminal for the relationship between Star and Griesemer's approach and the hESC case, they may also point out where to go next in the analysis of the sociotechnical reality of hESCs.

By seeing the hESCs as boundary objects involved in a distributed coordination a new center is created. A responsibility and an agency are attributed to the hESCs. In contrast to the OPP model the preceding section did not explain the associations with reference to a skillful human but to the possible uses of a non-human object, the hESCs. Even if it is a distributed coordination, if one pays close attention to the multiple practices of diverse actors, the hESCs become an analytic and explanatory center.

In one respect this is contrary to Star and Griesmer's intentions. Their ecological viewpoint is antireductionist and thus they do not strive to find *the cause* behind coordination (Star and Griesemer [1989] 1999: 507). The sites are many and the translations too. No over-arching translation can explain coordination, they claim. But they also have clear explanatory ambitions.

> We see two major factors contributing to the success of the museum: *methods standardization* and the development of *boundary objects*. (Star and Griesemer [1989] 1999: 508)

> Museum workers managed both diversity and cooperation through *boundary objects* […] (Star and Griesemer [1989] 1999: 509)

By finding the boundary objects, *a factor contributing* to coordination is discovered. By drawing on the boundary objects analysis two things about the hESC case are suggested. The hESCs coordinated actors much as boundary objects did in the Museum of Vertebrate Zoology. An explanation of an achieved coordination is thus offered, and it is done in terms of the central role of the hESCs. However, both of these suggestions can be challenged: Were the hESCs boundary objects? And does the analogy with Star and Griesemer's case constitute an explanation? These questions will be explored below.

The lack of management and project of hESCs

To approach the question about boundary objects it is necessary to understand exactly in what way these were "a major factor contributing to the success of the museum" studied by Star and Griesemer. The boundary objects are not as "unproblemized" as the hESCs have been in this chapter. It is true that the boundary objects have an explanatory *role* and are one of the main factors, but it is the *management* of boundary objects that coordinates actors, in contrast to the translation of interests through one OPP. The nonhumans – repositories, ideal types, coincident boundaries and standardized forms – coordinated diverse actors by being suitable for multiple uses. However, the flow of boundary objects among diverse actors did not happen because of their inherent capacities. No, it happened because they were crafted, managed, and maintained – by humans – in order to fit the actors of distinct social worlds. Thus the boundary objects did not "do the coordination" by themselves. Their agency was in fact quite weak, compared to the managing humans.

There may be management of the hESCs, but if so, the previous chapter did not described it. In this respect the hESCs are not boundary objects. If there is no management going on in either the actual, empirical case or in the analysis, the boundary object analogy breaks down. What is left is a powerful object with the capacity to coordinate many actors through its multiple uses.

A second failure of the analogy concerns the purpose of the boundary objects. They "contributed to the success *of the museum"*. Boundary objects are important, but not the units of analysis and not the end product. "The unit of analysis is the whole enterprise…" (p. 507). The management of boundary objects is a mechanism to understand how an institution or a project is successful amid diverse actors. So far, no institution or project has been presented in which the hESCs were part. The previous chapter served to describe and understand a partial stabilization of hESCs: The coordination of diverse actors and their associations to the hESCs. But, if this is the project, then the hESCs are boundary objects in the project of coordinating actors around hESCs. The hESCs are the means (boundary objects) and the end (the project). That seems to be a circular explanation.

However, it is not primarily an explanation (in the strictly causal sense) but an analysis or *understanding* of how coordination happen. And, it is not that circular – more circulatory. The boundary-object approach made tangible the flow of hESCs among diverse actors by bringing out the *multiple uses* of stem cells which enabled the coordination. Multiple uses were in turn made possible by the capacity of pluripotency. Multiple uses in biology and medicine were complemented with the ethical use of frozen embryos. More than a *circular explanation*, the multiple uses enabled a *circulatory understanding* by indicating the flows of hESCs among diverse actors.

The elements of the hESC package

This indicates a third failure of the boundary object analogy. Even if there may exist an underlying project of coordination drawing on hESCs, the latter are more than mere means. In Star and Griesemer's case study the coordinating objects are barely constraining actors. That's their advantage. Ideal types, repositories, standardized forms, and coincident boundaries, determine the *forms* of cooperation, by being weakly structured in common use and open-ended about the ultimate *content*. Such boundary objects are initially empty – more than black – boxes to be filled by

diverse actors. They are forms more than content. hESCs are not empty boxes, or merely forms or means. Seeing hESCs as boundary objects (in Star and Griesemer's sense) is thus dissatisfactory for analytical and empirical reasons.

Empirically, they have already, in this account, proven to be more than empty. The stem cells are indeed plastic and flexible, but considering the strong opinions this is not all there is to them. They are not only weakly structured in common use, but also constraining and defining. hESCs are clearly more than malleable boxes. They are flexible, i.e. pluripotent, but they are also constraining actors in specific ways quite unlike boundary objects. They are defined and constrain actors by way of three elements.

When examining the actors' articulations of the hESCs, it is not as simple as in the Figure 10 above. hESCs are being circulated, but together with a number of elements. Three of these seem to be more crucial and more closely linked to the hESCs than many others. This was clear in both of the preceding chapters. Except for referring to the hESCs, as a common term central for their linkages, the hESCs that are circulated among actors are pluripotency, transplantation therapies, and "spare embryos". There are others too, but I shall focus on those three here since they are not limited to one specific group, but appear in the articulations from diverse actors.

In Chapter 2, as actors extended the cells from the laboratories to people, businesses and medicine, they did so by referring to pluripotency. Because of pluripotency, they explained, hESCs can do a lot of things for patients. The alternative stem cells questioned the uniqueness of hESCs' pluripotency. In Chapter 3 the point was that pluripotency resulted in multiple uses. Apart from transplantation therapies, actors relate most easily to developmental biology. The third use in drug screening was not endorsed in more detail by many actors at the time. Whether in the OPP/APP-mode or in the boundary object mode of coordination, pluripotency was a stable linkage in two ways. Pluripotency was stable by being a resource for proponents and opponents. Nobody questioned that there was such a thing as pluripotency. It was stably linked to the hESCs, but maybe also linked to a different type of stem cell.

Another agreement between opposing actors in 1998–2001 was the urgency and the possibility of transplantation therapies. When Doerflinger and others suggest adult stem cells in the hearings they do so because they accept the need for transplantation therapies. Some dispute this very need, but they are substantially outnumbered by the references to alter-

native paths to reach the same goal. Alternative paths or not, hESCs are thought to result in such therapies. Whether actors agree about federal funding or not, the hESCs are articulated in relation to transplantation. Central to the analysis drawing on boundary objects in Chapter 3 was the stem cells' transformation into multiple uses among diverse actors. However, the stem cells are not doing these multiple things to anybody yet, but they are circulated as expected mediators of multiple use. What are seen are still merely the references to multiple uses. Out of the multiple uses one use is more prominent than the others, viz. transplantation therapies.

A last flow of the hESCs is the circulation of their *source material*, i.e. the already existing embryos. In Chapter 2 the "spare embryos" were articulated in two ways in relation to the hESCs. Caplan exemplified the trade-off between "spare embryos" and the "man in the wheel-chair". Doerflinger exemplified the other articulation, but in the same mode of coordination: "But the question is the experiment involves ripping out the cells from what was before a living organism" (US Senate 1999b: 73). Embryos, whether "spare" or "living organisms", are involved in a struggle and alternative, contradictory understandings. In Chapter 3 another dimension of embryos was highlighted. They could contribute to the coordination in three ways. Some actors did not oppose IVF or the resulting left-over embryos, but still opposed their use in research. Others, notably some pro-life people in Congress, endorsed IVF and the resulting embryos, and therefore found hESCs in these embryos acceptable. Bush acknowledged the existence of already existing embryos, the IVF treatments, and hESCs from already discarded embryos. I called this a minimal contribution. As this element of hESCs circulates it is configured differently, but two aspects remain very stable. In all of these cases, when actors refer to the hESCs and their sources, they refer to the already existing or "spare" embryos. In most cases IVF and its production of such embryos is not questioned. The IVF overproduction of embryos is a stable element linked to the hESCs via the "spare embryos".

It is notable how the elements play different roles. In spite of differences on the use of embryos in research, most actors agree about the value of transplantation therapies and of pluripotency. The "spare embryonic" element in articulations of hESCs is an element of disputes in the OPP/APP, but contributes to making the stem cells a boundary-transcending meeting-point, especially for some pro-lifers. These three

elements were, in 1998–2001, more or less stably linked to the hESCs by the actors.

When the multiple loops, the distributed coordination and the three elements are combined, the hESCs were not necessarily one boundary object, but rather like a boundary *package*: The hESCs were involved in flows, but as a composite boundary object consisting of at least three elements.[91] Latour posits multiple loops holding together one reference. There is still one reference here, but as soon as it is approached, it consists of other elements. The hESCs are still involved in multiple flows, but as a composite entity.

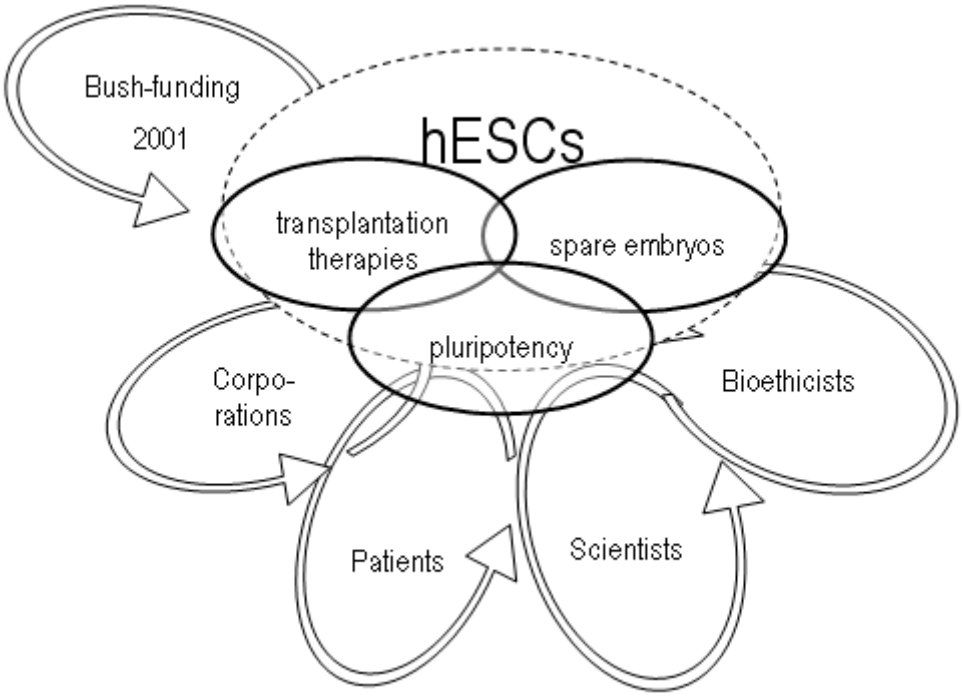

Figure 11: The multiple loops of the composite boundary object hESCs.

[91] I use package here in a commonsense meaning, although inspired from the standardized packages of theory and methods in Fujimura 1992, 1996. However, Fujimura's packages are much more structured than the boundary packages of hESCs ever were during the examined period.

Not only did the hESCs facilitate a distributed coordination, the stem cells were in addition themselves *distributed objects* consisting of three elements. In relation to patients, the transplantation therapies because of pluripotency were the great motivation, and in relation to scientists, pluripotency opened up for new studies in developmental biology. For corporations transplantation therapies and the economic gains were a major reason, and pro-life politicians could refer to the embryos that were already there the quite accepted practice of IVF. hESCs were thus distributed in multiple flows by way of being composed of three elements.

Analytically, the hESCs could be treated as mere coordinators. Merely seeing hESCs as coordinators turn the phenomena – such as the "biological and political pluripotency" – into intermediaries for other agencies, for the *really* real. This treatment is drawing close to a social explanation. Biological representations are explained by means of social reality. The focus of this study is sociotechnical reality, including the multitude of agencies in the world. Boundary objects do have agency, but of a weak kind. Agency is what makes a difference. Star and Griesemer's boundary objects are making a difference, but more as communicators and placeholders than as constraining, defining objects with a specific content. From the theoretical choices made here the weak boundary objects offer a too limited kind of agency to account for the observed pluripotent agency of hESCs. I suggest that what we see is a strong composite boundary object, a boundary package.

The absence of management, the lack of any explicit project, and the strong agency of hESCs are glitches between Star and Griesemer's case of boundary objects and the hESC case of 1998–2001. If the purpose is to understand the sociotechnical reality of hESCs, the coordination and the distribution of agency, then the study does not stand or fall with the total similarity with earlier studies. Quite the opposite: hESCs provide an interesting case of boundary-transcending flows and a strong composite object.

Risks for future unpacking analysis

Harry Collins and David Bloor have each, on repeated occasions, accused ANT of "giving back" power to Nature, objects or scientific rationality (Bloor 1999a, 1999b, Collins and Kusch 1998, Collins and Yearley 1992a, 1992b). By granting agency to nonhumans, ANT undoes what social constructivism, e.g. the Sociology of Scientific Knowledge (SSK), has achieved: the sociological explanation of scientific facts. According

to Collins the student of science and technology should do what s/he can, i.e. investigate social reality, in order to understand the natural reality represented by scientists. The analyst should not refer to natural objects in an unproblematic way, pretending to have the skills needed to interpret them. Uses should also be relativized, representatives of the Social Construction of Technology (SCOT) have claimed (Bijker 1995). Just like scientific facts, the application of facts or objects should be relativized, and not be used as explanatory resources in an unproblematic way. To carry out natural realist or "diffusionist" explanations in terms of the capacities or uses of hESCs is the scientists' task and competence.

To start with, the purpose of this work is not to *explain* in the causal sense suggested in SSK, but to *understand, analyze*, or *unpack* the reality of hESCs and how it came to be. Using OPP or the approach of boundary objects can be ways to see this reality differently. As this study continues, the explanatory import comes through re-describing, finding linkages between elements and actors, tracing stabilization, unpacking and seeing differently – not in finding causes. Still, the SSK critique is very useful for identifying how the analyst risks "reifications", i.e. taking things for granted. I use SSK here as a help in improving my understanding.

Instead of involving boundary objects in the first place, the coordination of actors could have been sociologically and politically explained. There is a strong convergence among the human actors on the uses of hESC research, but this feature is in one respect not surprising. In fact, informed observers in November 1998 predicted a convergence among some actors on hESCs, for instance *The Washington Post* reporter, Rick Weiss.

> With the therapuetic potential of embryonic cells suddenly very real, advocates are calling for a reexamination of that ban, saying the development of life-saving applications will be hindered if federal dollars remain off-limits.
>
> Such a reexamination would pit antiabortion forces and other strong proponents of the funding ban against a powerful biomedical research lobby that has in recent years become popular with Congress and the public. (Weiss 1998)

The exact meaning of the "biomedical research lobby" is not further defined by Weiss, but there was a pre-existing coordination between various research supporters. A coordination of scientists, politicians and patients had been initiated in the public negotiations of fetal tissue transplantation starting ten years earlier, in the late 80's. In these negotiations there had been polarization too, between two camps that agreed inter-

nally, but not with each other. Patient organizations pooled their resources, and collaborated with scientists and politicians, around a therapeutic concept involving fetal tissue. Pro-lifers opposed. There were thus positions and alliances already shaped. These were not unique to the debates on hESCs.

"Antiabortion forces" and a "powerful lobby" – these are stuff for sociological analysis of the reality of hESCs. Instead of attributing responsibility to the hESCs the diverse actors' interests and social positions could have been examined. What does it add to understand an already existing coordination of actors in terms of boundary objects (or packages)? And, what is the analytic role of the hESCs in the polarized American society in which allies had already been recruited?

If the coordination of actors merely followed a predictable political pattern, if the match was total between the abortion disputes and the hESC coordination, then an analysis drawing on the boundary object approach would say very little. However, the abortion debates were *not* identically repeated. Actors did not follow that pattern exactly. The major divergence was the pro-life actors who associated themselves with the hESCs even if they did not all fully support hESC research as a dominating and totally transforming activity. As the disputes of the previous chapter displayed, there was a polarization in the debates about hESCs. By examining the boundary-transcending features of the hESCs a third range of options comes into view in a space where actors can endorse the cells without agreeing about the total transformation. According to the analysis of this chapter the space is due to the hESCs and their multiple uses. Whether this is an explanation or not, it is one positive result from applying the boundary objects approach: To get into view a space between and across the already existing boundaries between diverse actors. If it is not an explanation of the coordination, it still describes the relationships between actors via boundary-transcending objects.

Already existing diverse actors and uses

However, the boundary-transcending feature is not enough to make the hESCs boundary objects, at least not as Star and Griesemer defined them. As important as this contribution may be, it constitutes a fourth divergence between this chapter and the approach of Star and Griesemer. Their case study on the success of the MVZ was pursued as an *ecological analysis* in line with Everett C. Hughes's ecology of institutions. A central feature is that the institution "chooses its environment" (Star and

Griesemer [1989] 1999: 506). In the creation of an institution the sources of funds, clientele and personnel are chosen, created and not given beforehand, much as in actor-network theory. ANT has criticized earlier social explanations in terms of interests. Instead of assuming pre-existing social forces, such as interests, society should also be relativized. If not, the analyst becomes a natural relativist, but remains a social realist. Accepting the multiple uses of hESCs among diverse actors whose identities are already given is thus not only a misfit between Star and Griesemer's case and the hESCs, but also constitutes a serious analytic weakness in relation to the frames of this work.

The boundary-transcending space created by the hESCs is due to the multiple uses that speak to diverse actors. In contrast to the ecology of institutions and the boundary-object approach, there is no sign, in the above analysis, of how this environment is chosen. Diverse actors are already there, and the multiple uses of hESCs address their needs. According to ANT "uses" and "actors" are not given beforehand, but are constructed. What is not answered by noting diverse actors and multiple uses, are how the identities of diverse actors were created and how the multiple uses became mutually recognized as uses. Even if the hESCs in 1998–2001 clearly occupied a role and a space between diverse actors in the midst of a polarized American society it does not immediately make the cells boundary objects (or packages). Furthermore the empirical material provides a tiny slice of articulations. It offers a snapshot account of an actor-network and distributed coordination. Due to this snapshot the *process* leading up to the flows of coordination are omitted.

Noting the central role of hESCs and their multiple uses in the coordination of diverse actors is, in spite of these objections, not trivial. By applying the boundary-objects approach instead of the OPP model the partial stabilization, the relative and multiple reality, and the distributed coordination have been brought out. These aspects of the hESCs stand. However, in comparison with Star and Griesemer's case study and in relation to the theoretical issues of the literature these aspects are less of an *explanation* and more of an *observation* that needs to be unpacked. Such unpacking does not necessarily have to agree with Star and Griesemer, as long as it does not claim to do so. The boundary object approach is one tool, among many, to understand coordination. But, according to the theoretical commitment of this study, an understanding of hESCs should try to avoid dividing reality into a natural and social realm. Rather than making human or nonhuman actors unproblematic resources, they are the ones

in need of analysis. Where does the future investigation go to better understand the emergence of hESCs, their multiple uses, and the identities and linkages of the diverse actors?

Stabilizing movements

In ANT there is no outside explanation, no reduction of events to things that the actors themselves are not associated with. Following the actors, as is recommended by Latour, serves this purpose: to find the associations. This is why the actors were followed as they took the analysis back to the hESCs. It was the actors who attributed the responsibility for their linkages to specific uses of the stem cells. Sometimes they did more, directly referring to the multiple uses for other and diverse actors, almost as if they had read Star and Griesemer. Some of the illustrations (without the terms) could function as generic maps for the flows of boundary objects. Thus, the "boundary object-like explanations" of the coordination are offered by the actors. I have not intruded on the actors, only juxtaposed their explanations with Star and Grisemer's case. Based on this precedent I drew the implications for the reality of the hESCs, the modes of coordination and the distribution of agency. It is recommended in ANT to listen to the actors' explanations, since they are usually doing as much sociology, or even socio-technology, as the analyst. If this is taken seriously (and actors are recognized as sociologists), SSK has asked, what then distinguishes the analyst from the actors? If the analyst merely follows the actors' twists and turns, what then is the critical potential?

ANT is less naïve than its recommendations may at first seem. To see what sort of understanding this chapter amounts to, two movements in the coordination of actors should be distinguished. Going back to Latour's study again, coordination was allegedly achieved by positioning Pasteur and his laboratory as an OPP. Latour's concept works by capturing two related movements in the building of facts and the coordination of actors.

> So as not to be confused, we should distinguish the recruiting of allies so as to build a fact or a machine collectively, from the *attributions of responsibility* to those who did most of the work. By definition, and according to our first principle, since the construction of facts is collective, everyone is as necessary as anyone else. Nevertheless, it is possible, in spite of this necessity, to make everyone accept a few people, or even one person, as the main cause for their collective work. [---] The two movements must be carefully distinguished […]: the recruitment of allies supposes that you go as far and make as many com-

> promises as possible, whereas the attribution of responsibility requires you to *limit* the number of actors as much as possible. (Latour 1987: 118–119)[92]

Pasteur and his institute were an OPP as a result both of Pasteur's entrepreneurial activities and of other actors' (chiefly the hygienists') attribution of responsibility.[93] OPP is Latour's term, but all it does is to capture those two movements of the actors. Both movements were centered on Pasteur and his *Institut,* and were thereby mutually reinforced. Because of Pasteur's skills in recruiting allies he could be attributed responsibility for what others wanted done and hence enable their recruitment of allies.

The OPP cases differ. When Star and Griesemer contrast their model with that of Latour, Callon and Law, they only point to the OPP as a way to recruit allies. The boundary objects are then another way of doing this. This juxtaposition fits Callon's and Law's cases, but less Latour's since his OPP (Pasteur and the Pasteur Institute) resulted from both of the movements and their mutual reinforcement. What is overlooked when treating the boundary objects as an alternative mode of coordination is the existence of the second movement, the actors' possibilities to attribute responsibility.

While Latour is very explicit about the OPP as a combination of Pasteur's behavior and others' creation of *The Pasteur,* Star and Griesemer only focus on actors' collaboration without any attributions of responsibility. Interestingly, the previous chapter captured the latter movement in

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92 To streamline Latour's extract I omitted the part of it that directly addresses Pasteur's role in the two movements.

> Pasteur, for instance, not only recruited many sources of support, but also strove to maintain his laboratory as the source of the general movement that was made up of many scientists, officials, engineers and firms. Although he had to accept their views and follow their moves – so as to extend his lab – he also had to fight so that they all appeared as simply "applying" his ideas and following his leads. (Latour 1987: 118)

What Latour does not mention here is the use the hygienists made of Pasteur as the authoritative source of the movement, [1984] 1988. Also, Latour focuses on the separation of the two movements and slightly overlooks what I call their *mutual reinforcement*.

93 In the rest of this section I will follow Latour's use of *attribution of responsibility*. In relation to the terminology introduced in Chapter 1, and in the Glossary, attribution of responsibility would fall under the notion of *delegation*. Actors are delegating agency to Pasteur, or to hESCs, when attributing responsibility.

terms of a boundary object coordination. Rather than *someone,* actors attributed responsibility to *something(s)*, viz. the hESCs.[94] Just as many actors, especially the hygienists in late 19th century France made Pasteur a saint, the hESCs are attributed responsibility for the multiple uses and the subsequent coordination of actors.

In 19th century France there were strategic gains in the hygienists' attributions of responsibility to Pasteur. He was an authority. Likewise there may be strategic gains as diverse actors explain their own linkages to the multiple uses of hESCs. Considering the domination at stake, and the polarization, the strategic gains may have been even greater in the USA 1998–2001. Attributing responsibility to an object may be the best option to recruit allies, as there were few human actors that could rise above the pre-existing polarization.

In a pluralist society – and in relation to federal funding: a polarized landscape – diverse actors cannot hope to change each other fully, or make everybody follow one person. Thus it may be strategic to gather around an object that speaks to multiple needs and uses. It becomes important to create a society and nature, for instance socially diverse actors and natural, naturally existing objects. When the hearings are set up, a society in miniature is created by calling in representatives of business, bioethics, patients, and scientists. The same happens in media, in panels, and reports. Diverse actors are continually appearing to represent groups of actors or social worlds. A natural reality is also set up that relates directly to this sociology. The multiple uses of hESCs are articulated not only by scientists, but by other actors too. For all of these actors there are natural and technological causes behind their linkages. Together they are performing a socio-technical explanation of their coordination, attributing the responsibility to the hESCs and their multiple uses.

This does not mean that actors are lying or fooling the onlooker. Even if the actors thus enact social and natural realist explanations, nothing stops the analyst from going further. Attribution is related to the actual recruitment, at least in the case of Pasteur. He could be attributed responsibility because of the associations with microbes and other things that he had already achieved. Pasteur's agency could be reinforced be-

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94 Latour explicitly talks of attribution of responsibility to *someone*, not *something*. I dispose of this application of *a*symmetry between humans and nonhumans and assume, in full accordance with ANT, that something can be made responsible as well as someone.

cause it was already strong. The recruitment of allies and the attribution of responsibility mutually reinforced each other, producing the OPP. Was there a similar mutual reinforcement in the hESC case? If so, then the hESCs could be attributed responsibility *because of an already achieved recruitment of allies*. The actors' 'boundary object-like' explanations point the way for further analysis.

After the criticisms from SSK about natural realism, and the ANT dissociation from social realism, it is clear what kind of understanding is desirable. Human and nonhuman actors – such as the hESCs, diverse actors, and multiple uses – are not resources, but objects of explanation. The big question, after following the diverse actors' attribution of responsibility to the hESCs, is how and why these nonhumans could coordinate so many actors. Instead of taking for granted the multiple uses of hESCs, the question is where these uses came from. Instead of taking for granted the actors' needs for those uses, the question is where their needs came from. Asking those questions is necessary in order to avoid both social realism and a naïve, natural realism, which is also to take Collins's and Bloor's challenges seriously.

Summary

This chapter has taken stock of the previous Chapters 2 and 3. From Chapter 2, the OPP attempt left loose threads of which some were picked up by the application of the boundary object approach in Chapter 3. The observation of a relative, non-centralized and distributed stabilization fitted the latter approach. In this sense the hESCs were involved in a boundary object-like coordination. The funneling and central role of the government as well as the claims of wholesale transformation of American medicine were still best subsumed in the OPP model. While this could be conceived as separate actor-networks or separate treatments of distinct patterns of hESC articulations such a separation is difficult to uphold in relation to the empirical case. There was not only co-existence of the two patterns, but perhaps even co-production. Actors' partial commitments and the relative stabilization of the hESCs may have been part of the OPP attempt. In any case the same actors were involved in both patterns.

Theoretically an answer to this puzzle amounted to stressing the divergence between the two approaches. The OPP totally transforms and moves *heterogeneous* actors, while boundary objects coordinate *diverse* actors who are already engaged in practices and social worlds. In *Pandora's Hope*

Latour steps back from fundamental heterogeneity and speaks of clumps of actors contributing to the stabilization process through *multiple loops*. Annemarie Mol has emphasized the need for several modes of coordination instead of homogenizing networks of associations. OPP and boundary objects may be such modes of coordination. To combine the two modes in the same study they must be used more localized than in earlier case studies. They could, via Vissac-Charles's example, be used to capture the connection points between networks – or multiple loops.

In the final section the analogy with Star and Griesemer was questioned, as was the explanatory value of the analogy. Star and Griesemer looked for the mechanisms behind the success of a large *institution*, the Museum of Vertebrate Zoology. The *management* of boundary objects was a main factor in this success, by establishing the appropriate *environment* for the museum: the participating actors from diverse social worlds. So far, the analysis has neither included any management of the hESCs nor any purpose of the coordination (e.g. a larger institution or project).

The observations in Chapter 3 also called for an innovative addition to the boundary object. More than being merely forms and means for coordination the hESCs have a strong content, constraining and restricting actors. This was evident when acknowledging the sources, the uses, and the capacities of the stem cells. It seems to be more of a boundary *package* than a boundary object. The partial stabilization and distributed coordination are boundary object-like traits. The coordination of diverse actors is brought out by drawing on Star and Griesemer's case. Amid polarized actors the hESCs constitute a meeting-point, a space for collaboration, whether or not the stem cells were boundary objects.

Besides discrepancies between the MVZ and the hESCs the unproblematic treatment of hESCs, their multiple uses and the diverse actors is open to criticism. In line with Collins's and Bloor's critique the analysis may treat hESCs in a natural realist manner. In contrast to the ANT intentions of this study human actors are treated in a social realist manner. Both natural and social realism are probably consequences of following the actors' attribution of responsibility.

After acknowledging the critique the question arises: What is the way out of this trap? Since there are no realities in ANT other than the articulations and the association of actors, there is only one way out: To continue following the actors. This recommendation is further specified by the notion of boundary package. The boundary-transcending coordination comes with a package. Actors probably would not be able to attribute

responsibility for their linkages to the hESCs and their multiple uses, unless a collective work had already been done.

PART II

5. A Project, its Problems, and Prescriptions: The 1994 Human Embryo Research Panel

Introduction

Discerning multiple loops, the two modes of coordination and actors thus associated with the cells is one way to capture the reality of hESCs in 1998–2001. In spite of disputes and varying modes of coordination the cells were involved in successful flows among actors. This was especially tangible in Chapter 3 as the boundary-transcendence of hESCs was outlined. The hESCs were picked up by several groups of actors, and ultimately, in 2001, by pro-life politicians. More than an extensive *analysis* the previous chapters' use of OPP, boundary objects, and multiple loops still merely amounts to *observations* of a reality in need of further inquiries. In other words, the second ANT question – to understand how the sociotechnical reality of hESCs in USA, in 1998–2001 (in particular the public and political dynamics) came to be – still remains unanswered. After part one, this question now implies:

> (Meta-theoretically modified Question No 2) How were the flows between actors and the three elements – frozen embryos, transplantation therapies, and pluripotency – of hESCs stabilized?

The next three chapters will be devoted to answering that question. One way to unpack the reality of hESCs could be to look more closely at how diverse actors were linked to the hESCs between 1998–2001. So far, only very public articulations, e.g. testimonies in hearings, have been presented as traces of associations. It would be possible to go into the details of lobbying activities, funding initiatives, and the relationships between me-

dia, politicians, scientists, patient organizations and bioethicists.[95] However, when faced with the negotiations of hESC research one phenomenon soon jumps out. Many of the linkages that were described in Chapter 2 and 3 were articulated a few weeks or even days after the stem cells were introduced to the public. When the cells were announced as successful laboratory cultures in November 1998, the *linkages to diverse actors were there already*.

Although George W. Bush or the pro-life people of Congress had not yet come out in support of the cells, Chapter 2 displayed how actors teamed up around the cells immediately. Within a month from their introduction they were circulated among actors as if they had been there for a long time. Demands for political action were voiced on the day of the announcement. Hearings were organized within few weeks. Proponents articulated the cells almost in chorus; how appropriate the source material was and the urgency of the medical promises. Later support from pro-lifers did not differ significantly from these articulations. The difference lay in the degree of support, not in the understanding of *what the hESCs were* and why they were worthy of support. Most actors agreed about the package described in Chapter 3; that the three elements were intimately linked to the hESCs. To understand this early and rapid coordination of actors and the configuration of the package it is not enough to look at the events between 1998 and 2001. Associations made from 1998 and after, are only one part of the story. Another part must be the associations already forged. Pre-existing coordination and configuration of the hESCs therefore define the question that, in this chapter, will help me approach the stabilization of hESCs: What previous coordination of actors was there, and what previous traces were there of the elements of the hESC package?

To better understand how the multiple flows of hESCs were established this chapter starts by going backwards to a point where the cells were still not laboratory objects, but nevertheless public entities.[96] In 1994 the hESCs were debated, although not separately, when they were a part of the deliberations of the Human Embryo Research Panel (HERP).

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95 To some extent this will be done in Chapter 7, mostly in relation to the response within the scientific community and the management of scientific taxonomy.

96 Although some scientists have in fact claimed that they had hESCs but did not fully characterize them, Parson 2004: 132.

The first part of the chapter looks at these negotiations. The resulting mode of coordination could hardly have been more different in relation to the 1998 and, in particular, the 2001 situation. In striking contrast to 2001, the negotiations of HERP did not result in partial stabilizations and an open-ended, boundary-transcendent coordination of actors, but in a total resistance to further research on embryos. This provokes a question: How could the mode of coordination change so completely between 1994 and 1998? One suggestion comes from the actors' own attempts to improve the coordination after HERP. For those supportive of embryo research the outcome was regarded a problem in need of a solution. In their diagnoses of the perceived failure of HERP, two elements featured: embryos and therapeutic benefits. In relation to the change of coordination between 1994 and 1998, actors' calls to reconfigure the benefits and source of embryo research are interesting, since the changes called-for correspond to the later articulation of hESCs and are thus an actually achieved improvement in coordination.

A human embryo research project

Before 1994 the future use of hESCs was hypothesized, but such propositions were occasional and unsystematic (Bongso et al. 1994, Hollands 1991, Pedersen 1994). Even in (non-human) ES cell research there was no major emphasis on the development of human ES cells. In the research literature more time, energy and space were devoted to bovine ES cells for use in the cattle industry, or for developmental biology (Müller and Dzierzak 1994, Nakano et al. 1994, Schmitt et al. 1991, Trounson 1994). This covert existence changes in 1994 when human ES cells were suddenly discussed more publicly for the first time in the USA. The public attention was due to the NIH panel, the Human Embryo Research Panel.

Human embryonic stem cells were but a minor part. Quantitatively, in a word count, the share of hESCs was minimal. The 26-page chapter on the scientific and medical issues had one page on human embryonic stem cells. Of the four papers that were presented to the panel, that on scientific aspects comprised 50 pages, of which three concerned hESCs (Van Blerkom 1994). Obviously this cannot be any *exact* measure of the role of ES cells in the deliberations. An ES cell biologist, Professor Brigid Hogan, had been named science co-chair of the panel. The page number is, however, a reminder that the HERP concerned research on embryos,

which, among other things, included human ES cells. This was not least true for the subsequent legal developments.

Embryo research moratoriums

IVF research had been ineligible for federal funding since 1980 because of the absent Ethics Advisory Board (EAB). [97] This constituted a de facto moratorium on all embryo research. When Bill Clinton was installed as President in 1993 he lifted a then-existing moratorium on fetal tissue research. The Congress passed the NIH revitalization act together with new laws to enable federal funding on fetal tissue research from elective abortions (US Senate 1993b). It has been suggested that very few in Congress may have understood that a paragraph on embryo research was actually included in the act. The paragraph itself did not stick out.

> The provisions of section 204(d) of part 46 of title 45 of the Code of Federal Regulations (45 CFR 46.204(d)) shall not have any legal effect. (US Senate 1993b: Title I, Subtitle A, Part III, Section 121, Paragraph [c])

"45 CFR 46.204 (d)" concerned the protection of human subjects. It was the requirement of an EAB approval for any project receiving federal funding, i.e. a crucial element of the de facto moratorium. According to Joseph Palca, of the National Public Radio, the removal of the paragraph was a new way to solve an old policy problem.

> For research administrators, it's been frustrating not to be able to support a promising medical technology. Quietly, persistently, officials from NIH, particularly from the National Institutes of Child Health and Human Development, lobbied to end the moratorium. Their strategy was to convince their superiors in the Department of Health to reinstitute the Ethics Advisory Board.
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> In 1988 the plan nearly worked. The assistant secretary of health told Congress there would be a new board, but plans for a new charter stalled, and when the Bush administration came into office, plans for a board were put back on the shelf. (Palca 1994)

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[97] Since 1979, federal funding of embryo research had required the approval of a national Ethics Advisory Board. The EAB was set up in 1978. It was allowed to review one research proposal (from Dr. Pierre Soupart), Quigley and Andrews 1984. However, this board only considered one research application before it was disbanded and never reinstituted, Office of Technology Assessment 1988, US DHEW 1979, Fletcher 2001.

The "new solution" in 1993 was to simply remove the requirement for an EAB approval. According to Palca "[l]anguage doing that was slipped into the NIH Revitalization Act of 1993". Whether Palca is right about the "slipping into", or not (the inconspicuous nature of the paragraph does support Palca's description), the legal change on fetal tissue transplantation was used to remove the main obstacle for federal funding of IVF, the EAB requirement, and to de facto legalize federal embryo research. While there had been public debates and scientific disputes, that had mobilized new actors for or against fetal tissue research for several years, no such deliberations had preceded the legal change on embryo research. A new law was literally packaged *within* the changing policies on fetal tissue transplantation, but very surreptitiously so.

There was no debate in Congress on 45 CFR 46.204 (d). Commentators have suggested that very few in Congress knew about the lifting of the de facto moratorium at all (Engel 1994, Palca 1994, Tauer 1997). Palca wrote in the March/April issue of the Hastings Center Report to comment on the fact that NIH officials – in the absence of any EAB requirement – had decided to let another panel develop guidelines for future embryo research, now that it was legally possible.

> The panel is supposed to give a new set of guidelines to the director of NIH next June. After that, the government should start supporting a much broader portfolio of research in the new world reproductive technology. Quite an achievement for one small sentence. (Palca 1994)

The achievement was however still not brought to a successful close. The attempt to implement a new embryo research policy together with the fetal tissue research policy suggested that the two sorts of research could be treated together and as, in some respects, the same. It was also built on the assumption that research on embryos could be included in the federal research portfolio without evoking substantial pro-life opposition. In spite of these implications the administration did feel a need for specific guidelines distinct from existing fetal tissue guidelines. By setting up the Human Embryo Research Panel for this purpose an external, explicit deliberation of the tacitly changed policy could be brought into the open. Such a process of deliberation could involve a number of actors, including some with pro-life views.

The Human Embryo Research Panel – and problem

The HERP had its first meeting, in February 1994, less than a year after the new fetal tissue policy had been passed and signed. The open hearings of the panel from February through June gave anyone inclined an opportunity to voice his/her opinions. Some were patients, some were representatives of professional and other organizations. Most were opponents of embryonic research (Tauer 1995). Soon after the first hearings pro-life communities had been alerted about the new panel. According to Randy Engel, former director of the US Coalition for Life, "the national alarm was set off" (Engel 1994). Some 30–50.000 (depending on the source) written responses were sent to the panel (Charo 1995a, Green 2001: 59–60, Schwartz and Devroy 1994). Philosopher participant of the panel, Carol Tauer, assumed that these were "linked to organized campaigns […] since the wording was identical on hundreds of them" (Tauer 1995: 31). This was an election year for Congress. Congressman Robert Dornan, a conservative Republican, sent a letter in June to NIH Director Harold Varmus promising to block the recommendations of the panel through legislative action (Carmen 1996). Dornan already had thirty colleagues in the House of Representatives behind his promise. The pro-life rejection together with Congressional support was potentially dangerous in an election year.

The charge of the panel was research on the preimplantation embryo. Usually this means research on fertilized eggs that have still not been implanted.[98] Three primary ethical considerations justified research on such embryos according to the "pluralistic ethical framework" accepted

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98 More specifically: the "extracorporeal" or "ex utero preimplantation embryos".

> The Panel's charge encompasses only research that involves extracorporeal human embryos produced by in vitro fertilization or from other sources, or parthenogenetically activated oocytes. Research involving in utero human embryos, or fetuses, is not part of the charge, since guidelines for such research are embodied in Federal laws and regulations governing human subjects research. [---] Throughout this report, "ex utero preimplantation embryo" or "preimplantation embryo" refers to a fertilized ovum in vitro that has never been transferred to or implanted in a uterus. (NIH 1994: ix)

"In utero" signifies "in the uterus". Parthenogenetical activation is a way to make an egg divide without the actual fertilization of a sperm.

by the panel: 1. The promise of therapeutic benefits. 2. The difference in moral status between preimplantation embryos and an infant or a child. 3. Although the embryo does not equal a child it still "possesses qualities requiring moral respect" enforcing the need for an ethical and scientific review of human embryo research that will be provided through federal funding (NIH 1994: x).

Based on the pluralistic framework balancing the benefits and the moral status of embryos, the panel recommendations were issued in three categories. One kind of research was judged to be unacceptable for federal funding, e.g. reproductive cloning and preimplantation genetic diagnosis for sex selection (NIH 1994: xix). Another kind was said to warrant additional review and included the deliberate creation of embryos for research purposes. This could be done to

> answer crucial questions in reproductive medicine and that it would therefore not be wise to prohibit altogether the fertilization and study of oocytes for research purposes. […] the health needs of women, children, and men must be given priority. (NIH 1994: xii)

Some of the research that would possibly answer such "crucial questions" concerned the maturation of oocytes and "investigations into the process of fertilization itself". They would serve to increase efficiency and safety in the IVF procedures (p. xviii).

A third category involved the studies deemed acceptable for federal funding, such as research on the fertilization process and "studies aimed at improving the likelihood of a successful outcome for a pregnancy" (p. xvii). In this category also fell the creation of embryos for studies "potentially of outstanding scientific and therapeutic value".

> An example of studies that might meet this second condition is research to ensure that specific drugs used in reproductive medicine, such as those for inducing ovulation, have no harmful effect on oocytes and their developmental potential and do not compromise the future reproductive health of women. (NIH 1994: xii).

In relation to these three categories there were two versions of the hESCs. They were placed in the two latter categories depending on the source material. Research on stem cells from "embryos resulting from IVF for infertility treatment or clinical research that have been donated with the consent of the progenitors" were acceptable for federal funding (p. xvii), while "the development of embryonic stem cells from embryos fertilized

expressly for this purpose" was not ruled out, but warranted additional review (p. xviii).

What happened to these recommendations? Opponents objected to the panel's view of embryos and its recommendations (Human Embryo Research Panel 1994). On October 12, 1994, the Advisory Committee (the ACD) to the Director of the NIH received the panel report and its recommendations, which included research on hESCs. In the November elections the Republicans gained majorities in the Senate and in the House, which strengthened the thrust of Dornan's promise to block votes to turn the panel recommendations into effective policy. On December 2 the ACD decided to recommend the director of the NIH, Harold Varmus, to accept the panel guidelines. The same day, before Varmus could make a decision of his own, Clinton had issued a statement that "federal funds should [not] be used to support the creation of human embryos for research purposes" (Marshall 1994a: 1634). In fact, Clinton probably had decided this beforehand. Bioethicist Alta Charo accounts for the White House response to the Republican mid-term election sweep, and the public reaction:

> William Galston, deputy director of Clinton's Domestic Policy Council […] reported that many White House senior staffers had been debating the Panel's work since early summer, and that a consensus had formed among the political advisors that creating embryos for research exceeded the public's (and their) tolerance for exotic research. (Charo 1995a: 14)

The President heeded their advice. Post hoc, Patricia King concurred with Clinton's decision, since it "was in tune with the public mood" (Marshall 1994a: 1635). King regretted not having stressed the point more forcefully in panel discussions in order to improve the chances of public acceptance (Carmen 1996: 102). Another anonymous panel participant said that the "panel would have been more sensitive in matters of language and expression" had it known the results of the November elections (Schwartz and Devroy 1994).

In spite of Clinton's rejection of embryo creation for research purposes, opposition was strong against all of the panel recommendations, including research on hESCs (Frazier O'Brien 1994, Hoke 1994). None of the panel recommendations was ultimately realized. The public reactions and the political strength of these objections obliterated the panel report also for use by the original proponents of embryo research. In 1995, the

following year, a general ban on human embryo research was passed in Congress and signed by Clinton (i.e. the Dickey-Wicker amendment).

In relation to the legal outcome and explicit politics the difference between 1994 and 2001 could scarcely have been greater. Formally and technically, embryo research was, beginning in 1994, allowed. The HERP's task was merely to outline what kinds of embryo research should be funded and not. However, the response did not concern what *kinds* of embryo research were appropriate or not, but opposed *all* embryo research. What started out as an attempt at an open-ended policy process ended in a wholesale rejection, ultimately even by liberal, democrat politicians.[99] By 1996, laws precluded publicly funded research on hESCs. In 2001, research on hESCs was endorsed not only by proponents of embryo research, but also pro-life representatives critical of other sorts of embryo research.

The difference between the two situations did not only concern which actors were coordinated, but *how* they were coordinated. During 1994–1996: from open-ended coordination to polarization. Ultimately there were two sides. On one side there were the panel recommendations with their "pluralistic ethical framework" and on the other side total restrictions of funding protecting the "sanctity of life".[100] During 1998–2001: in spite of polarization and attempts to establish either an OPP or an APP a boundary-transcendent coordination was strengthened by August 2001. Some actors in 1994 (e.g. the senders of "hate mail") insisted that it was

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[99] At least there was an expressed desire for public participation. Panel chairman Steven Muller formulated his view of the process of public policy development in a media report:

> Proper public policy develops through a public process rooted in public participation. Public participation involves a multitude of interests, many in conflict with one another. The public process which produces public policy, therefore, must strive for a balance among divergent interests, a balance sufficient to obtain and justify public support. (Hoke 1994)

After confronting some of the letters received by HERP from opponents Muller found the public education for such public participation wanting.

[100] Here congressman Dickey, in 1996, when he defended the current policy (of the Dickey-Wicker amendment) against the proposed Lowey amendment:

> Mr. Chairman, this is not a bill about research or science; it is an attack on the sanctity of life. It is an attack on the moral conscience of our Nation. (House of Representatives 1996: H7339)

an either-or and this became the prevailing mode of coordination, at least legally. Vice versa, by 2001, some crucial actors supported hESC research and a pro-life position without posing an either-or.

Diagnoses and prescriptions

Clearly, from the vantage point of the HERP the resulting coordination of actors was a failure. Federal funding was not allowed. Actors were in fact coordinated, in one respect: to *prohibit* further federal research funding. In relation to the successful flows of hESCs among diverse actors in 1998 and in 2001 the flows were much thinner in 1994. This evokes a question: How could this difference in mode of coordination be understood? An answer is given by the actors. Obviously, actors at the time did not know about this retrospective difference, but their actions assumed a gap between the actual situation and a more desirable future situation. Basically, some were dissatisfied with the mode of (non)coordination resulting from HERP and made "diagnoses" (to use a medical metaphor) of the perceived failure of coordination.

For the actors supportive of embryo research the outcome was regarded as a problem in need of a solution. Even during and immediately after the panel deliberations in 1994, even proponents of embryo research criticized the HERP recommendations. The policy development was seen as the failure of an attempt or a project (of sorts). Palca (above) described how scientists had been trying to lift the de facto moratorium in the 1980's. Following Palca, the project was thus a long-standing one relating to the lack of federal involvement. By 1994 many scientists were eager to receive funding for embryo research (Hoke 1994, Marshall 1994b). I interpret this as a kind of project, although of a quite distributed kind, and less organized or delineated than a "project" would usually imply.

During and after the death of HERP, actors made diagnoses of the failed coordination. There were two points of criticism. It had been too much to recommend the deliberate creation of embryos for research; better to go for research on already existing embryos, or "spare embryos". And, the research had not been linked to sufficiently pressing benefits.

Calls for the "spare embryo"

Criticism of the recommendations was made evident within the final report. There were three dissenting opinions. Patricia King, Carol Tauer,

and Bernard Lo all expressed satisfaction with the work of the panel, but disagreed on specific points. Tauer and King both objected to the deliberate creation of embryos for research purposes (NIH 1994: A-3f and B-3)[101]. Tauer explained why:

> Because the issue of developing embryos for research is so morally sensitive and because of my concern that clear restrictions may be difficult to maintain. [---] While there may be therapeutic reasons for developing cell lines of a vast variety of human genotypes, stem cell research studies do not require that cells be utilized from such a variety of genotypes. It would be only after research has demonstrated that the differentiated cells are therapeutically beneficial that one would want to ensure that people of different ethnic backgrounds are not deprived of therapy because of problems in matching transplantation antigens. (NIH 1994: B-3)

Tauer here articulates different source material for hESC research. She does not accept the need for the genomic variety following from creating embryos specifically for research. Considering the "moral sensitivities" embryos remaining from IVF are a sufficient source for hESCs.

Post-hoc, other commentators followed suit. In 1996 George Annas, Arthur Caplan and Sherman Elias attributed the impotency of the panel to its inability to realize the political constraints and possibilities (Annas et al. 1996). By adopting its "pluralistic ethical framework" on the status of embryos the panel didn't recognize "the deep moral reservations about such research held by many Americans, including the President".

> Thus, many people, like President Clinton, could approve of research using "spare" embryos created by in vitro fertilization without approving of the creating of embryos for that specific purpose. Provided with reasonable grounds for distinguishing research on spare embryos from research on embryos created solely for the purpose, even the Republican-dominated House of Representatives might have made the distinction. The House Appropriations Committee, for example, voted 30 to 23 in July 1995 to bar all federal funding for research on human embryos. A proposed amendment to permit such funding for research on spare embryos failed by a tie vote (26–26). It seems plausible that a more nuanced rationale for this distinction could have persuaded at least 1

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[101] The panel recommendations were consistent with the primary considerations. If the decisions are based on the partial respect for embryos and the potential benefits, then there are reasons to accept cloning or the derivation of hESCs from created embryos. Tauer accepted the basic tenets but still objected to the deliberate creation of embryos out of respect for tax-payers' sentiments.

> of the 26 members who voted against the amendment to vote for it. (Annas et al. 1996)

Annas et al. describe a political landscape in which some, but not all, research on human embryos could be politically pursued. The proposed argument focuses on embryos as the result of procreative activity. In the quote the example from the House Committee paints a political landscape in which some things are more feasible than others. Although contentious, embryo research would probably be fundable if it were done on "spare embryos", the argument goes, instead of creating new embryos deliberately for research.

Also other dissenting actors opposed the panel because of its inability to get things done in a perceived biopolitical landscape. The HERP's considerations on the status of embryos were criticized for being merely ethical and not sufficiently political, or "biopolitical" (Carmen 1996, Charo 1995a). The status of embryos, according to these commentators, is not a purely bioethical issue, but an issue of social and political relations and sensitivities.[102]

Subsequent Congressional action from research proponents seems to agree with the diagnosis. When changes to the Dickey-Wicker amendment were attempted, through the proposed Lowey amendment in 1996, the research creation of embryos was totally abandoned in favor of research-

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[102] No national panel, Ira Carmen claimed, can settle the ethical disputes about the status of embryos. Just as the President acted to manage political and public reactions the HERP should have included the "realities of the Washington political game" in their deliberations, Carmen 1996. Alta Charo of the panel, afterwards suggested that instead of calling the panel deliberations bioethical, they were a species of political ethics.

> If the Panel had more explicitly acknowledged how much of its work was an exercise in political compromise, rather than definitive moral reasoning, its report might well have engendered less bemusement and outrage. [---] Indeed, by writing a report grounded in political ethics rather than bioethics, the Panel might have demonstrated an appreciation of the sincerity and passion of research opponents, even while their outrage must yield to the needs of those awaiting the experimentation's benefits. It is their pain, rather than any dubious consensus on the status of embryos, that is actually being balanced against the claims of infertile couples, parents of children with birth defects, people seeking a cure for cancer, and third world women in desperate need of new contraceptive choices. (Charo 1995a: 12)

ing the "necessary and inevitable spare embryos". The following is from the debate in the House of Representatives, July 11:

> Mr PORTER: Mr. Chairman, the creation of spare embryos is a necessary and inevitable part of in vitro fertilization and it seems to me, at the very bottom line, that given the potentials for addressing and overcoming and preventing human disease, their use in research gives meaning to their existence which would otherwise simply not exist. They would be discarded in the normal course of events. (House of Representatives 1996: H7340)[103]

Porter, Lowey and other proponents of the bill did not succeed at that time. In this respect it was not sufficient to re-articulate the embryo to coordinate actors and the diagnosis was not "right".

Not all the proponents agreed about the diagnosis. The aftermath of the panel focusing on the recommendation to fund embryo creation was unwelcome and hard to understand for former panel members. Brigid Hogan comments here on Annas et al.'s claims in the NEJM editorial:

> "This doesn't reflect how we stressed the benefits of donated eggs and sperm [from couples undergoing in vitro fertilization, donated for research]." (Benowitz 1996)

Opponents of embryo research also disagreed. Congressman Roger Wicker (of the Dickey-Wicker amd.) did not support a claim about the political viability of "spare embryos" and even offered numbers to disprove it.

> Mr WICKER As a matter of fact, 76 percent of Americans oppose funding for the type of research that the Lowey amendment would sanction. This goes to the very profound questions of human life and to very sensitive questions of bioethics. (House of Representatives 1996: H7340)

Wicker did not even accept the "necessity and inevitability" of "a spare-embryo circumstance", and attacked the underlying distinction.

> Proponents of the Lowey amendment say there is a distinction between spare embryos and embryos created for research purposes. But the leading experts say there is no distinction. Let me quote Dr. Robert Jansen of the National Health and Medical Research Council. He says, "It is a fallacy to distinguish between surplus embryos and specially created embryos in terms of embryo research. The reason I say this is that any intelligent administrator of an in vitro program can, by minor changes in his ordinary clinical way of doing

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[103] Also see other proponents in House of Representatives 1996.

> things, change the number of embryos that are fertilized." (House of Representatives 1996: H7340)

The diagnosis focusing on the specific creation of embryos for research came from actors who wanted federally funded embryo research, not from pro-lifers, and it is hard to see any clear-cut support for the claim about the political viability of spare embryos.

Taking a step back it is important to realize what these traces of actors are saying. The shift to already existing embryos did not necessarily correspond to a reality of pro-lifers out there. It may have or it may not have corresponded. Annas et al offered voting numbers, but none of the others refer to any data that supported the conclusion that research on "spare embryos" would be more acceptable public policy. Correspondence or correctness is not the primary issue when following these actors. Whether they were right or not, they *had similar perceptions* of how research on embryos could become more acceptable. There was not one embryo to do research on, but at least two. One that linked strongly to pro-life opponents and a skeptical public. Another that – the critics hypothesized – might be more acceptable. Embryo research might be politically feasible, but not the creation of embryos for research purposes. It has to be research on already existing embryos. Pro-life actors disagreed and *could* disagree with the panel since it recommended research on embryos created deliberately for research, the diagnosis said. Not all agreed and apparently, pro-lifers could and did disagree also after the focus on "spare embryos", in 1996. Accordingly, the critics here were not primarily right or wrong, but left traces of a "diagnosis" living among and coming from the supporters of embryo research.

A very clear example of this is the journal *Science*'s reports from the panel work. While the panel was still deliberating, in August 1994, Eliot Marshall reported from one of the meetings and referred to the recommendation to create embryos for research.

> Those attacks [from the right-to-life movement] may well focus on what is likely the most controversial element in the panel's report. Although the 19-member panel is still at work, *Science*'s interviews of key panel members reveal that the panel's version of the guidelines permit creation of a limited number of human embryos for research purposes. (Marshall 1994b: 1024)

In this section the right-to-life movement "may well focus" on the creation of human embryos for research. In the next section, associate director for the Catholic Secretariat for Pro-Life Activities Richard Doer-

flinger "seized on this issue to denounce the entire NIH rule writing effort". The tentative "may well focus" from one section to the next is turned into "seized on". Marshall offers some quotes from Doerflinger's testimony, but no support for the conclusion that the research creation of embryos was the particular thorn in Doerflinger's flesh (Marshall 1994b: 1024). In fact, there is no support for this conclusion in the testimony (Human Embryo Research Panel 1994). The pro-life associate director questions research on already existing embryos and the specific creation of embryos equally.

I have found no evidence that pro-lifers in fact seized specifically on the creation of embryos. There may be such evidence or not. I have not come closer than the voting records referred to by Annas et al. There may also be such a thing as "political sensitivity". Again, evidence or sensitivity are less important than the fact that actors supportive of embryo research delegated a coordinating agency to the source material. These actors assumed an improvement of coordination by shifting to "spare embryos".

Spelling out benefits

Another point made by the proponents of embryo research (but critical of the HERP) was the vagueness of the benefits. While Clinton was only rejecting a part of the panel's recommendation, on December 3, an unidentified member of the panel stated in *The Washington Post*:

> One member of the panel who asked not to be identified said that […] "Even the name 'Human Embryo Research Panel' turned out to be a red flag for antiabortion groups […]" Yesterday, members of Varmus's advisory committee briefly discussed the idea of coming up with a name that stressed the importance of the research to fertility and other medical advances […] (Schwartz and Devroy 1994)

Later Jonathan Van Blerkom, biologist and author of one of the commissioned papers, concurred with this analysis of the panel's perceived failure.

> he contends that the panel's inability to spell out the specific benefits from human embryo research – particularly regarding treating disease – contributed to its demise. (Benowitz 1996)

However, several benefits had been clearly spelled out in the panel deliberations and the report. In the report there were a number of (allegedly) important uses for the research. The research portfolio that justified fe-

deral funding was quite extensive and featured in several places in the report. In the introduction specific kinds of research were enumerated.

> Studies aimed at improving likelihood for a successful outcome for a pregnancy.
>
> Research on the process of fertilization
>
> Studies on egg activation and the relative role of paternally derived and maternally derived genetic material in embryo development (parthenogenesis without transfer).
>
> Studies in oocyte maturation or freezing followed by fertilization to determine developmental and chromosomal normality.
>
> Research involving preimplantation genetic diagnosis with and without transfer. Research involving the development of embryonic stem cells, but only with embryos resulting from IVF for infertility treatment or clinical research that have been donated with the consent of the progenitors.
>
> Nuclear transplantation into an enucleated, fertilized or unfertilized (but activated) egg without transfer for research that aims to circumvent or correct an inherited cytoplasmic defect.
>
> Research involving the use of existing embryos where one of the progenitors was an anonymous gamete source who received monetary compensation. [---]
>
> A request to fertilize ova where this is necessary for the validity of a study that is potentially of outstanding scientific and therapeutic value. (NIH 1994: xvii–xviii)[104]

This portfolio concerns only research acceptable for federal funding. There were other lists for research that warranted additional review and for research that was deemed ineligible for federal funding. When the applications were listed in Chapter 1, there were eight of them.

> The process of embryo implantation, the maintenance of early pregnancy, and the prevention of early spontaneous miscarriages.
>
> Basic knowledge about normal early human development and the origin of certain birth defects.
>
> The preimplantation diagnosis of genetic or chromosomal abnormalities leading to severe inherited diseases.

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[104] The two last applications were recommended for federal funding, but needed "special consideration" by a national ad hoc body that would have functioned for at least 3 years following the acceptance of new guidelines.

> The origin of chromosomal abnormalities associated with infertility and with childhood cancers.
>
> Understanding the process of oocyte maturation and how eggs may be affected by environmental agents, including cryopreservation of oocytes from women undergoing chemotherapy or irradiation.
>
> The development of new contraceptives.
>
> Cancer and the process of metastasis.
>
> The development of pluripotent embryonic stem cell lines for generating differentiated cells for transplantation and tissue repair. (NIH 1994: 2)

Were the applications badly spelled out? At least they were meticulously spelled out. Six are applications that relate to pregnancy and infertility. Also included are the service to developmental biology and cancers (in two places). One concerns transplantation and tissue repair. In the second chapter on "Scientific and Medical Issues in Preimplantation Embryo Research" again a list was presented – now in 13 applications (p. 7f). Of these, six related to infertility and pregnancy and four to issues in developmental biology. Three points regard therapeutic use, viz. ES cells for transplantation, cancers and "the use of nuclear transplantation to circumvent disorders due to maternal inheritance of cytoplasmic defects" (p. 8).

Within the report there were plenty of benefits. Van Blerkom (above) criticized the panel for its "inability to spell out the specific benefits […] – particularly regarding treating disease". Depending on what you would label as disease, the latter part of that critique may correspond to the HERP report. If infertility is not a disease, then there was indeed proportionally less about benefits relating to cancer or tissue repair. In the paper Van Blerkom wrote for the panel, there seem to be similar proportions. One application concerning "diseases" was mentioned, viz. transplantation therapies. It was done in connection with embryonic stem cells.

> For example, it may be possible to establish cells lines [sic] from early embryos to serve as stem cells for bone marrow transplantation, as hepatic stem cells for the treatment of liver dysfunction, or neuronal stem cells that can be used in the treatment of nerve and spinal cord injuries. Indeed, some have suggested that organ transplantation may be replaced as the appropriate therapy in cases where the tissue could be reestablished by stem cell therapy. (Van Blerkom 1994: 48)

Although "spelled out" here as promising – "this approach has the potential to offer a new strategy for the treatment of a wide range of

human diseases" (p. 49) – Van Blerkom did not in his 49 pages, say more than these ten lines about the specific benefits for treating diseases. Apart from the three pages on stem cells there were three more pages on the significance of embryo research for preimplantation diagnosis. More than *treatment* of disease this is a technique to *avoid* the development of embryos carrying genetic disorders. Most part of the paper concerned embryo research on infertility and developmental biology.

The HERP did not only articulate the possible benefits of embryo research within its report. In ensuing commentaries and debates, possible uses were mentioned. A lot of attention was devoted to the various recommended sources for research such as donated or expressly created embryos of various maturity, eggs and parthenotes[105] (Marshall 1994b). In the media and in Congress the most specific benefits related to either preimplantation genetic diagnosis of embryos, or understanding the process of fertilization for improved IVF techniques[106], contraceptives, and pregnancies. More vaguely, future progress was promised in basic developmental biology and cancer research.[107] In an article in *The Scientist* five applications are mentioned: preimplantation genetic diagnosis, developmental biology, cancer pathology, cancer, and transplantation therapies (Hoke 1994). Only the latter would qualify as being directed towards treating disease. Analyzing these articles, the emphasis is not on disease treatment, but more on basic biology:

> "We're not going to be curing anybody of these tumors by doing research," Hogan says. "On the other hand, the basic biology is extremely interesting. Studies in mice and in humans show that choriocarcinoma arises with a particularly high frequency when there are only paternal genes present. And, so, the question is why. Presumably, this is because of imprinting problems, in

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105 Eggs dividing for a limited time as if fertilized although without being so.

106 Brigid Hogan, science co-chair at the panel explained the possible benefits for IVF through studies of egg maturation.

> research on human egg maturation, which requires that eggs be fertilized to test their viability. These studies – if they were allowed to proceed – would help improve the efficiency of in vitro fertilization, making the process safer and less expensive. (Marshall 1994a: 1635)

107 These promises appeared in numerous accounts, e.g. Annas et al. 1996, Benowitz 1996, Carmen 1996: 101, Charo 1995a, Fletcher and Waldron 1996, Frazier O'Brien 1994, Hoke 1994, Marshall 1994a, Schwartz and Devroy 1994.

> the sense that certain genes are going to be either active or inactive, oncogenes are going to be active, or tumor suppressors are going to be inactive in those cells." (Hoke 1994)

While the basic biology was "extremely interesting", the therapeutic expectations were low "we are not going to be curing anybody of these tumors". When Hogan, later in the article, mentions transplantation therapies through the use of ES cells the tone is again very modest:

> "So, the idea would be that maybe, down the line, you could use these for making blood cells for transplantation, and maybe some kinds of neuronal stem cells or muscle stem cells." (Hoke 1994)

Annas, Caplan and Elias claimed that "[e]mbryo research will not receive needed support unless it is linked more directly to research on fertility" (Annas and Elias 1989). Based on the actual lists of applications in the report (above), it is hard to agree with this analysis straight away. Fertility research had been present in the report. In July, 1996, it was a central theme, making one suspect that the congressmembers had read the May editorial by Annas et al. At least they concurred in action with the advice.

> Mr. WAXMAN. Early-stage embryo research is vital as it has the potential to address treatment and prevention of infertility, people who want children, want to bring in life into this world.
>
> It could lead to cures for childhood cancer and genetic disorders such as cystic fibrosis, muscular dystrophy, mental retardation and Tay-Sachs. It could lead to the reduction, if not the elimination, of miscarriages. (House of Representatives 1996: H7340)[108]

Although all of the speakers supportive of embryo research mentioned these diseases and fertility research the "spelling out" failed. The opponents responded in concert that the promises of benefits were not scientifically proven, and not sufficiently urgent or relevant for federal funds. Representative Weldon from Florida, as others, recycled Hogan's quote to make the points.

> Mr. WELDON. I think it is inappropriate to use taxpayers funds for this kind of a purpose, and it is a very dubious scientific benefit, contrary to some of the claims that have been made by the gentleman from California as well as others. I can even quote from people who were involved in studying this

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[108] See also Mrs. Johnson, Mr. Fazio and Ms. Pelosi in House of Representatives 1996.

> issue. Dr. Brigid Hogan, a scientific expert on the NIH Human Embryo Research Advisory Panel, said: "We are not going to be curing anybody of these tumors by doing research. On the other hand, the basic biology is extremely interesting." That is what we are talking about funding here, a very controversial, ghastly subject according to many Americans, including myself, and it is just going to be very, very interesting. Furthermore, we have a quote from Daniel Callahan, president of the Hastings Center, which is an IVF institute [sic].[109] He said: The NIH advisory panel "report notes that four countries already allow embryo research and that it has been going on for some years in private laboratories in this country. Yet not a single actual benefit derived so far from that research is cited to back the claims of great potential benefits from having even more of it." (House of Representatives 1996: H7342)[110]

When proponents referred to the scientific needs and criticized the pro-life opposition for setting up a "Flat Earth Society" the ball was sent back.

> The gentlewoman, my good friend from California, Ms. PELOSI, talks about the Flat Earth Society. That is interesting because the science is on our side. As I recall, there are two medical doctors, M.D.'s, on our side. I have not seen any M.D.'s or even Ph.D.'s, although there may be a hidden Ph.D. over there in English literature or something, but the science is from our side. (House of Representatives 1996: H7343)

Mr. Hyde refers here to the number of MDs among the opposition to embryo research. The history of embryo research was also used to oppose it. Representative Tom Coburn called out for some scientific evidence.

> I understand this is a complex issue, but after 17 years of research not one person in this body can stand up and tell me one positive medical outcome that has come from this research. There is none in the scientific literature, there is none projected. We hear: could, might, may. The fact is there is no proof, there is no scientific study at this time of any quantifiable benefit. (House of Representatives 1996: H7342)

Following the HERP some diagnosed the perceived "failure" of the panel recommendations in relation to the articulation of what embryo research could signify for disease treatment. Again, as to research embryos, it is not easy or even necessary to assess whether the diagnoses were

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109 The Hasting Center is a bioethics center – not an IVF institute – which could change the credibility of Callahan's quote as used by Weldon.

110 See also Mrs. Vucanovic, Mr. Coburn and Mr. Hyde in the House of Representatives 1996.

correct or not, whether a better spelling out would have improved coordination of actors.

Reading the report and related commentaries, the critics seem to be right – at least if benefits for infertility are excepted from the category of "disease treatments". Cancer and tissue replacement were marginal compared to the benefits for genetic diagnosis and the improved understanding of developmental biology, infertility and pregnancy. In these respects therapeutic benefits were not made central. Scientific results were also lacking. The opponents called the "therapeutic cards" offered by proponents and referred to the want of scientific evidence. The proponents referred to the expectations from scientists. These had been already detailed in the panel report. Were the benefits not sufficiently urgent, or perceived as such? Why could they not induce enough support in Congress? These are questions for a political historian or a political scientist, and thus beyond the approach of this study. The issue is not to decide whether benefits were a crucial factor for the outcome of the negotiations, i.e. the *validity* of the proponents' self-criticism. Quite the contrary is interesting here, viz. the fact that *some actors did understand* the situation *in this way*. Calls for more urgent benefits were their "prescription" (coherent with the above observed diagnoses) for how to proceed and succeed with the project of federally funded human embryo research.[111]

There were two comments from the proponents of embryo research that added an extra dimension. Again, something was lacking in the articulation of possible benefits. Mark R Hughes, professor of genetics, obstetrics and gynecology, and pediatrics at Georgetown University and at the NIH recapitulated the fetal tissue debates. Hughes

> notes that some interest groups, such as those supporting research for Parkinson's disease have argued successfully for funding. "Unfortunately, those arguments are not as politically compelling regarding the embryo research." (Benowitz 1996)

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[111] *Prescription* is not used here as Madeleine Akrich would use it, but in a more commonsense, although metaphoric way, Akrich 1987, Akrich and Latour 1992. However, an analysis drawing on her notion of *script* – including the related inscription, de-scription, pre-scriptions – is fully compatible with many of my observations and conclusions of how actors contributed to the shaping of the later reality of hESCs. In Akrich's terms the actors' diagnoses are close to de-scriptions.

To compel actors, applications that can bring in patient groups are needed, according to Hughes. Eventually he added that he thought there would never be a compromise "the two sides are so diametrically opposed". Another similar point came from Annas et al. They also referred to earlier negotiations on fetal tissue research, but, in contrast to the resigned Hughes, they wrote in the hope of breaking the "gridlock".

> Research on fetal-tissue transplantation did not garner public support and federal financing until supporters persuaded Congress that it might benefit the treatment of major diseases, such as Parkinson's disease. (Annas et al. 1996)

The authors outline a "method" for getting public support. However, Parkinson's disease was not regarded as an alternative in the case of embryo research. Their version of the same methodology applied for embryo research was to call for fertility research (see above). Both comments pointed out the force of patient and interest-group mobilization. Neither of them at the time saw that treatments of Parkinson's disease could be an option, but they called for a similar linkage between embryo research and "major diseases". In relation to the panel report this suggestion may have been justified – depending on what a major disease is. Cancer and tissue repair were mentioned, but such references were usually tentative and marginal in relation to the other research interests. Both of the commentaries were right about the absence of any obvious target group "representing" the urgency of embryo research. In the panel sessions, in the subsequent commentaries, and in congressional debates few, if any, patients or patient organizations were represented.

The HERP and the later role of hESCs

It is time to recapitulate the purpose and the observations of this chapter. In an attempt to understand the coordination of diverse actors that was strong already in 1998, only a few weeks after the introduction of hESCs, this chapter went backwards. hESC had been articulated earlier, in the negotiations of federally funded embryo research in 1994. The crucial question is: What do the traces found there say about the preexisting coordination, the multiple flows and the package of hESCs?

Prescriptions fulfilled

By looking at the earlier articulation of hESCs, a number of things are found. Firstly, the 1994 negotiations resulted in a completely different co-

ordination of actors. The only boundary-transcendence in 1994 was the agreement between a pro-life Congress and the Democrat President to *not* fund the creation of research embryos. Secondly, the many proponents were not happy about this and voiced criticism during and after the panel, highlighting two elements of human embryo research. They made diagnoses and prescriptions to not repeat the perceived failure of – what can be understood as – a project of federally funded human embryo research. The prescription: No creation of research embryos, and more salient benefits in terms of "major diseases", e.g. Parkinson's disease where there are interest groups that can persuade Congress. Coming from 1998 and the previous chapters the actors' diagnoses and prescriptions are extremely interesting, since they have a "prophetic" tinge. Put less mysteriously: The prescriptions seem to have been followed and effective in the subsequent negotiations in 1998.

When the hESCs were announced in the two articles in November 1998 they were made from spare embryos and one of the expected uses was transplantation therapy, e.g. for treating degenerative diseases such as Parkinson's disease and juvenile diabetes. Creating embryos deliberately was not an option for either of the two major reports (NBAC and AAAS/ICS) or by the embryo-research proponents testifying in Senate hearings.

As Chapters 2 and 3 outlined the elements seem to have done the job. Patient organizations mobilized and presented statistics and individual patients telling their stories of life with diseases. Some pro-life representatives in Congress did ultimately accept the use of embryos remaining from IVF treatments. This changed the whole mode of coordination. From a no-go and strict boundaries after 1994, the hESCs provided a sort of common, boundary-transcendent ground.

Going back to 1994 thus reveals an ongoing project and actors engaged in managing it to coordinate diverse – or in some cases even more than diverse: polarized – actors. While some resigned and claimed that it was "all political" and others tried to formulate an "ethical framework" some pursued the "project management" by re-articulating two elements of human embryo research. Their advice was to focus on spare embryos and disease treatments. This was tried in Congress 1996, but failed. It was not enough to (in Van Blerkom's words) "spell it out" differently. Increased coordination came with the *re-articulation* of an object. As the hESCs were articulated in the laboratory, and in public debates, they contained or embodied (or maybe more correctly "en-celled") the two elements in the prescribed configuration. The mode of coordination

expectedly changed from polarization to boundary-transcendence together with the articulation of hESCs in terms of the two elements.

Seen this way the role of hESCs as boundary packages is strengthened. It is strengthened, since some of the missing pieces outlined at the end of the previous chapter have come into view. hESCs were not merely coordinating actors in hESC research, but also in a long-standing project of federally funded research on human embryos. Diverse actors were not coordinated by direct negotiations, or by force, but through an object that addressed their needs. The 1994-1996 "prescriptions" from some actors suggest that the coordination of hESCs were due to the source materials and the therapeutic benefits. Spare embryos spoke to some pro-life actors. Transplantation therapies mobilized patient groups who appeared in Congress.

Unfulfilled purposes

Initially, this chapter moved backwards in order to unpack the reality of hESCs. While the OPP, the distributed coordination and multiple loops were interesting conceptions of hESCs, they did not constitute an analysis *per se*, but more observations in need of unpacking. Instead of going deeper into the actor-networks between 1998 and 2001 the early coordination of diverse actors suggested that events before November 1998 played a role in the multiple flows of hESCs. These purposes guided the initial research question of the chapter about previous coordination of actors, and previous traces of the elements of the hESC package.

Retrospectively the actors' diagnoses and prescriptions in terms of the elements of "spare embryos" and therapeutic benefits suggest that the hESCs were an answer to a "management problem" – the management of a project of federally funded human embryo research: The 1998–2001 hESC package consisted of the two elements and it did improve coordination.

At the moment however, this suggestion, based on the analogy with the boundary object case, is premature because of several serious gaps. So far the analysis has conjectured two things that follow from Star and Griesemer's case. Coordination was achieved by the *management of hESCs* in relation to two elements that *had a potential for coordination* (according to some actors in 1994 and after). The italicized words represent assumptions that are still barely more than that.

First, the management aspect: Noting that the hESCs made from already existing embryos and useable for transplantation therapies corresponded to some actors' diagnoses of a political landscape in 1994 is interesting. This in itself, however, does not imply that the hESCs were used by actors in a way reminiscent of boundary objects. To make hESCs analogous to boundary objects some sort of management is needed. It could very well be that the scientific discovery and the biological entity without any relation to the HERP events accidentally happened to have a political significance and transform the negotiations of federally funded human embryo research. If so, this is still worthy of note, but also of another history. Such interesting and important histories are already written by biologists and popular science writers (Lewis 2001, Smith 2001a).

These histories trace the origin of the hESCs to the work by Stevens and Pierce on teratocarcinoma, embryonal carcinoma cells and ES cells. The histories are based on the chain of material developments, assays, experiments which are described in articles that are traceable in the references-section of review articles, and also in most research articles. hESC stabilization would then include the discovery of Stevens's mouse strain 129 (Stevens and Little 1954), the later genetic modifications of these mice (Stevens 1959), the collaboration with Pierce and his group (Pierce 1975), the embryoid body assay (Stevens 1960), proofs of multipotentiality of single EC cells (Kleinsmith and Pierce 1964), perhaps the disputes with the British tumor pathologists about the existence of embryonal carcinoma (Pugh 1983, Pugh and Smith 1964, Willis 1967), the move from mice re-transplantations to cultures in Petri-dishes, the production of chimeras from EC cells injected in blastocysts (Mintz and Illmensee 1975), Martin's, and Evans and Kaufman's derivation of ES and EK cells in 1981 (Evans and Kaufman 1981, Martin 1981) which most hESC researchers today go back to. Such a chain could also be described as the establishment of a reference, much as Latour studied the transformation of earth from Boa Vista to the scientific articles in *Pandora's Hope*, Chapter 2.

However, this study assumes that "scientific discovery" is articulated by the combination of more elements than fill up a Petri-dish, and that "biological entities" not only circulate in human bodies, but in Congressional, corporate and other bodies too. It assumes the multiple flows of *Pandora's Hope* Chapter 3, rather than the single circulation of reference in its Chapter 2. Most importantly, as I have formulated the thesis about the role of hESCs, more is intended than the accidental correspon-

dence between a "discovery" and the diagnoses of a failed negotiation. To save the thesis there has to be some management of the hESCs in relation to these two elements (and not only in relation to mice, teratomas, and British tumor pathologists in the 1960's and 70's). If there was a management, then the hESCs would to some extent, in some respects have *changed* between 1994 and 1998 to accommodate "spare embryos" and transplantation therapies. If, instead, the hESCs were identical on those two occasions there was basically no "management" to speak of, not the one I have conjectured. To prove that the hESCs functioned as a sort of boundary object, i.e. a boundary package, traces of such modifications would have to be found.

Second, the elements' potential for coordination: If coordination was achieved by the management of hESCs in relation to the two elements, the latter would need to have some recognized potential. Much points in this direction. Obviously, patient organizations and Geron hoped for transplantation therapies and some pro-lifers did refer to embryos that would be discarded anyway. According to these actors the elements had a coordinating potential. Also the 1994 critics claimed that the elements would have such a potential. But, nothing so far explains *why* the elements could contribute in this way. The hESCs are unpacked in terms of the elements, but the latter are not unpacked. Spare embryos and transplantation therapies are analytic black boxes, regarded by actors as, respectively, necessary, versus possible and urgent. It was informing to see that these elements were deliberately called for in 1994 and after, but the observation still opens for accusations of natural, social and technological realism. Recalling some of the articulations, "spare embryos" existed out of necessity (as it were) from IVF procedures. Even opponents of human embryo research accepted the possibility and urgency of transplantation therapies. Nothing so far has explained why spare embryos or transplantation therapies were rarely questioned in 1998–2001. Where did this stability come from? Patients' and corporations' interests and others' acceptance of transplantation therapies are taken for granted. Pro-lifers' acceptance of the existence of IVF and "spare embryos" too. Some stabilization was visible already in 1994 as actors reached out for the elements as resources for coordination, but these resources have not been followed further backwards.

As long as these two assumptions – about coordinating effects and management – have not been defended, the purposes of this chapter and the present study remain unfulfilled. What is needed is an unpacking of

IVF embryos and transplantation therapies, and traces of how the hESCs were changed to fit those two elements. If not, this chapter amounts to not more than an interesting observation about the correspondence between the 1998-2001 coordination around hESCs and some commentaries during 1994–1996.

Summary

To approach the configuration and the coordination of the hESCs in 1998–2001, I went backwards in this chapter to the 1994 national panel about human embryo research (the HERP). I examined the HERP in order to find traces of the elements of hESCs and a pre-existing coordination of actors. The direct result of the HERP was legal restrictions of human embryo research. Another result was that proponents of federally funded research criticized the negotiations. My interpretations of these actors were that they were involved in a distributed project, by means of making diagnoses and prescriptions for how to improve the outcome of future negotiations. Without any central entrepreneur, or any neatly delimited project, there was an on-going common movement (without being an organized "social movement"). Actors were assuming a project, viz. the need for federal funding of human embryo research. Interestingly, attempts to improve coordination involved both the uses, and the material sources, that were later part of the articulations of hESCs. Like in 1998–2001 "spare embryos" and transplantation therapies were brought up, although less consistently and not primarily in relation to hESCs. The latter only existed as anticipated paper entities at the time.

These observations prompted a hypothesis about the boundary package. By being made of "spare embryos" and being useable in transplantation therapies the object fitted an already existing project. Thus hESCs were coordinating actors that were mobilized in a previous, failed project. The package could coordinate actors by being a package of at least two elements that were somehow already stabilized. To test this hypothesis, the next chapter will go further backwards to see how these elements had been stabilized and what circulations they were part of.

6. Multiple and Partial Stabilizations: The Necessity of "Spare embryos", and the Urgency of (Possible) Transplantation Therapies

Introduction

Earlier chapters have observed the prominent role of "spare embryos" and transplantation therapies in diverse actors' references to hESCs. Even before the hESCs some of the critics of the HERP referred to these two elements as possible meeting-points for otherwise disagreeing actors. What remains unanswered however is the stabilization of the elements in 1998–2001, the reasons for the post-HERP actors and those involved in the hESC management to reach out for the elements. What role did the two elements have in the multiple flows of hESCs?

A lot of the articulations in 1998–2001 indicate that "spare embryos" and transplantation therapies did contribute to the multiple flows of hESCs 1998–2001. From both proponents and opponents of hESC research, the transplantation therapies were accepted as urgent and medically possible, and the production of non-implanted embryos as a necessary part of IVF. *Medical possibility, urgency* and *necessity* were definitely there in the actors' articulations of hESCs. They may have contributed to the coordinating role of the stem cells and the changed mode of coordination. However, in line with ANT (and for that matter social worlds theory) urgency and necessity should not be treated as essential features but as constructed outcomes (Clarke and Fujimura 1992, Latour [1984] 1988). Instead of accepting what the actors accepted, and thus treating the *uses* and *sources* of hESCs as analytic black boxes (i.e. unproblematic resources) this chapter asks how the urgency and necessity, commonly accepted by actors, came about.

Many routes could be taken. By 2001 transplantation therapies were articulated as one part of a new approach to medicine, called regenerative medicine. Ann Parson has shown how this "bold new era in medicine" was prepared through the developments in various fields within brain and memory research, hematopoietic stem cell research, IVF and ES cell research (Parson 2004). It is a fascinating history of the convergence of several scientific investigations. However, just as the envisioned history about hESCs starting with Stevens's mice (see Chapter 5), Parson's account does not trace multiple loops of science-and-society. She follows scientific paths running together as a purely cognitive and technological development. Other paths for such an account could be organ transplantation, xeno-transplantation and the emergence of banks for blood transplantation.

This chapter does not intend to understand merely the cognitive or technological content of transplantation therapies or IVF, but how these elements were able to become resources for the coordination of diverse actors, i.e. not only "scientific" ones. I thus assume that the medical possibility and urgency of transplantations, or the technological necessity of IVF, are not categories decided only in laboratories or in conferences. And vice versa, their political significance and effects are decided not only in panels or in policies. The aim is to understand the multiple flows of hESCs among patients, pro-lifers, corporations, etc.

Unpacking urgency and necessity also approaches a related question resulting from Chapter 5. IVF embryos and transplantation therapies were resources as early as 1994 since the actors at that time could suggest coordinating potential of the two elements in relation to the perceived "gridlock". Why did actors reach out for the two elements in attempts to improve the coordination? It is not enough to say, in retrospect, based on the 1998–2001 negotiations, that "they were right". What was entailed in those references at the time? These two sets of questions concerning the unpacking of urgency and necessity, and some actors' references to "spare embryos" and transplantation therapies converge. They are answered similarly – by unpacking.

Urgency and necessity are not treated as givens, but as constructed through the inclusion of some entities and the exclusion of other entities. A fundamental assumption is that it could have been otherwise. This

means that at some points entities, that were later excluded, offered alternatives and uncertainties to what later became necessary and urgent. The same process applies to the establishment of the references to the two elements. A reference according to Latour is what is linked to and holds together several other entities. This is how I use "reference" in this chapter.[112] Referring to something in an attempt to coordinate actors is thus to appeal to already existing linkages, entities held together. If some entities are held together, some entities are *not* held together. Thus, the flip side of unpacking the reference concerns candidate entities for inclusion which were not ultimately included in the reference.

In the first part of this chapter the reference to "spare embryos" necessarily resulting from IVF treatments is unpacked. How did they become an element that was possible to refer to and how inevitable was their necessity? And, vice versa, what possibilities were not made necessary? In the second part the element of transplantation therapies is unpacked. When, where and how could this element become a reference for actors, and on top of that a commonly recognized and urgent medical possibility? And, vice versa, was there a time and a place where urgency and possibility were less stable?

"Spare embryos"

Two central differences between the hESCs of 1994 and those that were involved in public debates after 1998 concerned the embryo. Between 1994 and 1998, the proponents changed the articulation of embryo research in bioethical discourse and in policy proposals. The research creation of embryos was thrown out and "spare embryos" became the sole source material.

Why did the supportive actors shift toward the already existing embryos and totally remove references to the research creation of embryos? The HERP had offered good arguments for allowing the research creation of embryos. If the preimplantation embryos are not persons or equal to children, then it makes no difference for the moral status whether they are already created for procreation or specifically created for research, the reasoning went. Clinton directly opposed the creation of embryos when the recommendations were published, and in 1996 there was only talk of doing research on already existing, "spare", embryos. Recapi-

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112 This use of reference builds on the entanglement of signs and matter presented in Chapter 1, based on Latour and Woolgar 1979, Latour 1999b: Chapter 2.

tulating representative Porter's statement in the House of Representatives, July 11:

> Mr PORTER: Mr. Chairman, the creation of spare embryos is a necessary and inevitable part of in vitro fertilization and it seems to me, at the very bottom line, that given the potentials for addressing and overcoming and preventing human disease, their use in research gives meaning to their existence which would otherwise simply not exist. They would be discarded in the normal course of events. (House of Representatives 1996: H7340)[113]

In the later hESC negotiations many actors repeat the same formula, for instance Senator Specter: "But the process of in vitro fertilization is to have a large group and then to use some but not to use others" (US Senate 2001: 30). This first part of the chapter asks why there were "spare embryos" as a "necessary and inevitable part of IVF" to be used by (among others) Porter in 1996 and in the later negotiations of federally funded hESC research.

The conception of IVF: context, conditions

In the early 1970's work on IVF was controversial. *The Lancet* rejected a paper by Edwards and Steptoe because of the ethical problems. Others critical were theologians, ethicists, scientists (such as James Watson and Max Perutz), politicians (such as the Labour Government Minister of Health in 1972) and institutions (The British Medical Research Council) warned of the consequences and still unknown risks for the resulting fetuses and children (Edwards and Steptoe 1980: 117, 120, Kass 1971, Ramsey 1972a, 1972b). The US Department of Health, Education and Welfare (US DHEW) began considering IVF in 1973. The public response was mostly critical (US DHEW 1974). The resulting regulation prohibited support of IVF research "until the Ethics Advisory Board has advised the Secretary as to its ethical acceptability" (US DHEW 1979). In this critical landscape IVF did not only come into existence but, 15–20

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[113] Also see other proponents in House of Representatives 1996. Their distinction between embryos created expressly for research and "spare" embryos was challenged (e.g. H7340).

years later, became a factor in the negotiations of hESC research. How did this happen?

The first baby born from an in vitro fertilized egg, Louise Brown, was born in 1978, through the efforts of embryologist Robert Edwards and gynecologist Patrick Steptoe. The former worked with fertilizing eggs in vitro. The latter handled the collecting and transferring of embryos (or embryo transfer, ET). The successful birth of a healthy and living baby was itself an argument for the IVF procedure. However, not all ethical uncertainty about the procedure was solved by these now actually existing babies. In the USA the status of IVF remained disputed in spite of Louise Brown.

A poll carried out in August 1978 asked 3.000 people in the USA about IVF:

> Some people oppose this type of operation because they feel it is "not natural". Other people favour it because it allows a husband and wife to have a child they could not otherwise have. Which point of view comes closer to your own? (Singer and Wells 1984: 31) [114]

60% of respondents were supportive of the IVF and ET operation, while 27% opposed it. 13% had no opinion. Among persons with enough knowledge to explain the procedure the degree of support was even higher: 75% (US DHEW 1979: 88). When the respondents were asked about the destruction of embryos, only 45% would allow it and 40% opposed it. 14% were unsure (Singer and Wells 1984: 32). In other parts of the world the status of IVF was also disputed.[115]

The newly appointed Ethical Advisory Board considered IVF and embryo transfer. One research proposal, from Dr. Pierre Soupart, was

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114 The polling question quoted by Singer and Wells was used in a joint poll by Harris and Gallup. This poll was also used in the 1979 report (see below), US DHEW 1979: 88-89. The two organizations interviewed 1500 people each – only women (Harris) and men and women respectively (Gallup). The figures among Catholics differed somewhat: 39% allow, 48% would not, 12% unsure.

115 According to Singer and Wells there was high approval in British and Australian polls in the early 80's – around 70% pro in several polls 1981–1983. However, the opposition in the UK was sufficiently strong to stop further research on embryos in the mid-80's, Mulkay 1997.

recommended funding (Quigley and Andrews 1984). In a 1979 US DHEW report the EAB declared that IVF and ET research was "ethically defensible – but still legitimately controverted":

> the Board wishes to emphasize that it is not finding that the ethical considerations against such research are insubstantial. Indeed, concerns regarding the moral status of the embryo and the potential long-range consequences of this research were among the most difficult that confronted the Board. (US DHEW 1979: 100, emphasis by the EAB)

The Department then received comments from around 13.000 members of the public and 80 member of Congress. Most of them were negative to federal funding of IVF research, "particularly", explained Robert Windom, assistant secretary of health, "if the procedure were to involve the intentional destruction of human embryos or increase the risk of embryos being otherwise harmed" (House of Representatives 1988: 9, Norman 1988).

After the adverse public reactions to the EAB's recommendations of federally funded IVF the Reagan administration did not appoint and fund a new Ethical Advisory Board (see Chapter 5). Without an EAB, research proposals could not be federally funded. The federal policy during the Reagan and Bush administrations (1980–1992) was therefore a de facto moratorium. How did this policy – or maybe lack of policy – affect IVF? When the Federal administration stayed out of IVF, other actors became important.

An IVF population: the infertile, clinics, researchers, materials

While increasing numbers of babies were obvious results of IVF, other actors also resulted from the new technology, viz. the infertile, IVF clinics, researchers and embryos. In the constrained context of IVF one group of people was said to be especially important. The *infertile population* was a part of the IVF research in several ways. The research material, the expectations and the motivations came from them. In 1980 Edwards and Steptoe published their book, *A Matter of Life*, where they biographically recall and discuss their work on IVF and embryo transfer. The first lines of the first chapter read:

> She did not realize I was a medical student. Despite my youthful appearance she called me, "Doctor", then briefly lost control. "What have I done wrong,"

> she cried, "not to have a family of my own?" Perturbed I tried to comfort here and in a moment she managed to continue, "I would have liked to have a large family but I've been married seven years […]" her voice trailed off. (Edwards and Steptoe 1980: 11)

Infertile couples are essential in Edwards and Steptoe's self-reconstructive narrative.[116] They were also essential as donators of the raw research material – eggs and sperms. Couples willing to donate were not hard to find, although Edwards's contacts with gynecologists were crucial, in order to draw on couples' willingness.[117] The group of infertile grew in importance together with the increase of IVF treatments, babies and clinics. Here the group is present in a 1984 anthology, *Infertility: Medical, Emotional, and Social Considerations*.

> As infertility is discussed more openly, the stigma and mythology associated with it should decline, thus minimizing the controversy and blame that have surrounded the issue. As the infertile population becomes more outspoken and visible, they will hopefully be recognized as a constituency worthy of social compassion and political responsiveness to their needs. (Simons 1984: 69)

Harriet Simons hoped for increased recognition of the constituency of the infertile population. If "social compassion and political responsiveness" meant federal funding in the USA, the hope was not fulfilled. The Federal administration kept their money and their regulation away from IVF. However, the infertile constituency was recognized in terms of an increase in IVF clinics. The one went hand in hand with the other. The first provided money, eggs, and sperm. The other became the support for infertile couples. According to Robert Edwards at an IVF conference in 1984 the "alleviation of infertility is increasingly accepted as an urgent social and clinical need":

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116 IVF is not a technology that presupposes *couples*, but in some narratives – e.g. in Edwards and Steptoe's – and in some debates infertile couples are the perceived benefactors of the IVF treatment. For instance, by the year 2000 more than 80% of reporting IVF clinics provided their services for single women, US DHHS 2000: 49, 2001a: 63.

117 Robert Edwards:

> We soon discovered that patients needed to be restrained from volunteering too much. Patients would offer themselves for a second laparascopy or even to come into Oldham General Hospital twelve times a year if necessary! (Edwards and Steptoe 1980: 88)

> I imagine that we all agree that many aspects of the procedure are now fully accepted by society as ethical. [---] This is very different from the situation 15 years ago, when virtually everything about the procedure was questioned. We were accused of overpopulating the world, immorally collecting eggs and spermatozoa, opening a Pandora's box of biological tricks, and jeopardizing ethical standards. The infertile couple had no supporters. Those debates are now well behind us, however, and the alleviation of infertility is increasingly accepted as an urgent social and clinical need. (Edwards 1985: 1)[118]

Whether Edwards's characterization is completely correct or not, the increasing numbers of babies and clinics pointed toward a growing circulation of technology, knowledge, money, people, eggs and sperms.

In the USA there was no political recognition of the infertile population in terms of federal funds, but in terms of treatments performed the constituency grew in importance. The first clinic in the USA was established in 1979. In 1980 visits to infertility services were still below one million a year. By 1985 yearly visits had risen to nearly two million per year (Office of Technology Assessment 1988: 5). According to Gena Corea IVF clinics in scientifically developed countries (Australia, Japan, Israel, Western Europe, and the USA) amounted to one hundred by 1984[119] (Singer and Wells 1984: 13). By the early 1990's IVF treatments were practiced at 68 locations in the UK. In 1992 there were an estimated 200 IVF clinics in the USA (Hartz et al. 1992). Approximately 20.000 babies had then been born through IVF-ET and related techniques (Mulkay 1997). Twenty years after the first successful birth the number of clinics had grown to more than 400 (Hoffman et al. 2003). Clinics and newborn babies (and children, teenagers, and young adults) added to the importance of the infertile population. Another measure of the constituency's strength is the *perceived gravity* of infertility. The National Center for Health Studies was motivated to comment on the popular perceptions of an "epidemic" of infertility (in its statistical report *Fecundity and Infertility in the United States, 1965–88*):

> In some popular descriptions of infertility, it has been suggested that there are 9 or 10 million infertile couples, that 1 in 6 couples is infertile, that infertility is increasing rapidly, or that there is an "epidemic" of infertility in the United States. [Mosher and Pratt refer to four works between 1980 and 1987] The

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118 The conference proceeding was published in 1985, but the conference was held in 1984.

119 Corea was cited in Mulkay 1997: 1.

> findings of this report indicate that these perceptions are inaccurate, but the increased use of infertility services, the increased number of childless older women with impaired fecundity, and other factors […] may help to account for the perception that infertility is increasing or that it is more common than it actually is. (Mosher and Pratt 1990: 1)

The perception of an infertility epidemic coincided with the rise of IVF and ET as treatments for infertility. The report suggests that the perception was due to the new techniques for treating infertility, an increase in physicians trained to treat infertility, and increased news coverage. The epidemic perception and the number of clinics and doctors grew together with research, in spite of the missing federal US dollars. Edwards's earlier references to the support for infertile couples were reciprocal. The researchers were not only benefactors, but benefited themselves. IVF research grew as a professional community after 1978. Together with the other editor of the proceedings, Markku Seppälä from Helsinki, Edwards opened the 1984 conference proceedings with a reflection on the scientific field. Or, maybe more appropriately, the scientific field*s* that had been provided with a joint interest, and a meeting-point, thanks to IVF research.

> In addition to offering new hope, this technique has brought about a vast increase in knowledge of early reproductive phenomena. Indeed, human *in vitro* fertilization has already opened the door to a reproduction revolution […]. The Helsinki Congress was third in the sequence begun in Kiel (West Germany) in 1980 and followed, by the Second Congress, in Annecy (France) in 1982. Scientific meetings on *in vitro* fertilization have grown progressively larger each time. In Helsinki, more than 500 scientists working on embryology, developmental biology, endocrinology, and andrology were brought together with clinicians to exchange information and to present 235 scientific papers on various aspects of *in vitro* fertilization. (Seppälä and Edwards 1985: xi)

The vast increase in knowledge of early reproductive phenomena had a very material side. By connecting to and empowering the infertile population, researchers now had access to eggs, sperms and embryos in a scale never before experienced. IVF was an event, something happening to the infertile *and* to the IVF researchers. Disputed or not, politically recognized as a constituency or not, the new-born babies and their parents, the new clinics, researchers, and scientific conferences were human and material links adding to the IVF and the embryos. The infertile population grew in importance and achieved totally new ways of reaching its goals. Material and cognitive resources for researchers in several disci-

plines increased. Except for the linkages mentioned here, two technological links contributed to IVF.

Creating "spare embryos"

Edwards and Steptoe's first successful IVF birth utilized an egg from Mrs Brown and sperm from Mr Brown. The egg was extracted through laparascopy as a result of Mrs Brown's normal ovulatory cycle. After fertilization in vitro (i.e. in a Petri-dish) the fertilized egg was returned to Mrs Brown's womb. There were alternatives to, and soon many developments of, the "protocol" of Edwards and Steptoe. There had been other attempts, e.g. by Landrum Shettles in New York and an Australian group headed by Alan Trounson. Since the IVF treatments were kept in the private realm in the USA different clinics could choose to adopt different protocols in helping couples to conceive. No uniform or centralized regulation guided the growing number of American IVF clinics.

In the beginning the success rate varied a lot and was never higher than the natural cycles, which are said to result in successful pregnancies in 20–25% of cases (Soules 1985). In 1986 some IVF centers had still not achieved one pregnancy (Robertson 1986: 1035). Edwards and Steptoe had utilized the spontaneous ovulation cycle of Mrs Brown. They had cautioned that the use of drugs to stimulate ovulation would hamper the likelihood for implantation. Since the 1960's there had been drugs for stimulating the release of women's eggs in order to facilitate pregnancies and to control ovulation (Schwartz and Jewelewicz 1981, Steptoe and Edwards 1970). The "superovulation hormones" were, by the late 1970's, frequently used in cattle reproduction (Seidel 1981). Soon after Louise Brown these hormones were used to improve the low success rate of IVF. By 1984 Kerin and Seamark, from a department of obstetrics and gynecology, could write in a medical anthology of IVF and embryo transfer:

> The use of ovarian stimulants to manipulate and control the human ovulatory cycle is now an accepted practice in the more successful groups for IVF and ET even though the first successes with IVF and ET were obtained in spontaneous ovulatory cycles. (Kerin and Seamark 1984: 99)

The stimulants were used either to decide the timing of ovulation (and extraction) or to have more oocytes released. The latter usage enabled the implantation of several embryos, which could increase the chance for successful pregnancies without repeating the invasive extraction proce-

dure. The method was adopted by several clinics. In 1986, law Professor and bioethical commentator John Robertson described superovulation as a requirement for the "standard IVF regime".

> The standard IVF treatment regime requires that the ovaries be stimulated to produce several eggs, because the chance of pregnancy is very small if only one fertilized egg is transferred to the uterus. (Robertson 1986: 948)

In 1978 Louise Brown was born from a normal cycle-egg. By the mid-1980's superovulation was "an accepted practice" or even "required" for the "standard IVF treatment" according to inside actors and commentators.[120] With this development there also came a well-known problem, acknowledged since earlier use of superovulation (outside of IVF). In the cases where several eggs were released, fertilized and implanted there could be multiple pregnancies causing increased abnormality in fetuses and, sometimes, maternal health-risks (Schenker et al. 1981). In IVF there were suggestions on how to solve the problem of multiple pregnancies. One was from Trounson's group in Australia. Clomiphene citrate and gonadotrophins were common stimulants to induce ovulation:

> The widespread use of clomiphene citrate and exogenous gonadotrophins for *in vitro* fertilization (IVF) in humans, frequently results in the production of multiple embryos. Replacement of more than two embryos increases pregnancy rate but may result in multiple pregnancies with increased pre- and postnatal abnormality. Preservation of embryos from a limited time allows fewer embryos to be replaced on several different occasions and thus the problems of multiple pregnancy can be minimized, the effectiveness of a single IVF procedure increased and embryos replacement in adverse maternal conditions avoided. (Trounson and Mohr 1983: 707)

If, Trounson et al. suggested, the fertilized oocytes could be preserved instead of implanted all at once, the risk of multiple pregnancies would decrease. In the paper they presented the successful implantation of an embryo that had been "cryopreserved", that is, frozen. The pregnancy had been terminated prematurely, after 24 weeks. Trounson et al. claimed that the termination was not associated with the cryopreservation process. This theoretically opened for the possibilities indicated in the above quotation, although it was in no way standard

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120 Without any more exact numbers being found, the articles on superovulation at the time did not discuss it as possibility, but compared the efficiency and effects of various sorts of drugs, Kerin and Seamark 1984, Vargyas et al. 1984.

treatment at the time. The next year (in the medical anthology already visited) Kerin and Seamark spelled out not only the hoped-for possibilities, but also the current state of science:

> Excess embryos may be frozen and stored and hopefully with further technical developments, transferred successfully in a subsequent ovulatory cycle where the trauma of laparoscopy has not been involved. The stimulated and controlled ovulatory cycle also reduces the pressure of intense monitoring for timing oocyte recovery, provides a chance of obtaining a number of oocytes and if minor errors in timing do occur, final maturation in vitro prior to insemination is possible. (Kerin and Seamark 1984: 10)

Although the whole process from cryopreservation to pregnancies were in no way standardized in the mid 1980's (House of Representatives 1987: 12, Robertson 1986: 949), clinics started to store embryos for later use and for research, not least outside of the USA (Singer and Wells 1984). One reason for the cryopreservation of embryos was to avoid discarding excess embryos resulting from the superovulation drugs. Bioethicists Peter Singer and Deane Welles (then at Monash University Centre for Human Bioethics, Australia) describe how "The Queen Victoria Hospital Ethics Committee accepted the freezing of embryos because this is less drastic than throwing them out" (Singer and Wells 1984: 100).

Superovulation and *cryopreservation* were thus technologies that enabled the storing of "spare embryos". The superovulation technology creates the spare embryo. Cryopreservation stores it. The solution chosen by The Queen Victoria Hospital in Australia was a way to solve the problems of superovulation. In so far as clinics thus chose to utilize the two technologies, IVF could produce ethical dilemmas. Notice the modalities used in the quotations. Kerin and Seamark stated that "[e]xcess embryos *may* be frozen and stored" (my italics), and Trounson et al above discussed it as an *option* for IVF treatment. Somehow this possibility was turned into "necessity".

Creating necessity

The "necessity" did not follow from these technological possibilities. After 1994 IVF did in fact, by "necessity" as it was, produce scores of stored embryos. Just ten years earlier the "necessity" was still not there.

It was the result of technological possibilities, policy structures, and clinicians and patients in IVF.[121]

By the mid-80's, the IVF practices had come to engage a number of the actors mentioned above, including the two technologies of super-ovulation and cryopreservation. One should stress IVF practice*s* – not practice in singular: The IVF technique was not *one* technique at the time. For instance, it was still not true what was said ten years later by Porter: "the creation of spare embryos is a necessary and inevitable part of in vitro fertilization" (House of Representatives 1996: H7340) – or fifteen years later by Specter: "But the process of in vitro fertilization is to have a large group and then to use some but not to use others" (US Senate 2001: 30). There was no definite and standardized process.[122] George W. Bush could not at this time have formulated his two fundamental questions concerning the existence of frozen embryos, as he did in his August 9 decision, 2001:

> As I thought through this issue, I kept returning to two fundamental questions: First, are these frozen embryos human life, and therefore, something precious to be protected? And second, if they're going to be destroyed anyway, shouldn't they be used for a greater good, for research that has the potential to save and improve other lives? (Bush 2001)

Bush could not have asked the two questions in the mid-80's. There were not at that time hundreds of thousands of frozen embryos around.[123]

One actor still not engaged in any significant way was the Federal administration. Embryo research was technically possible but not federally funded. It was technically possible in the private sector. Any researcher could in principle – with private funds – do any research s/he wanted to within in vitro fertilization. The ethical and legal restrictions in the USA

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121 Considering that this is an ANT study and "necessities", as everything else, are assumed to come to be through articulations, I will drop the quotation marks henceforth. Necessity (without inverted commas) thus refers to the articulated necessity. The same is obviously true for "spare embryos", but the (still) politically charged role of this term justifies the keeping of the quotation marks, in order to keep a reification of "spare embryos" at bay. Analytic symmetry thus results in typographical asymmetry.

122 In fact this was not even true in 2001, but the process Specter describes was one of several IVF processes.

123 In 2002 the number of frozen embryos was around 400.000, Hoffman et al. 2003.

were few and amounted to informed consent, and compliance with general regulation, state laws and the local institutional review boards.[124] This was for good and for bad. In 1985 Michael Soules, at an obstetrics and gynecology department wrote in a *Fertility and Sterility* editorial about how the competition was probably a cause for exaggerated success rates from clinics:

> Competition appears to be the root of the problem. In the United States, literally hundreds of IVF programs sprang up between 1980 and 1982. [---] The widespread practice of exaggerating the IVF pregnancy rate appears to be a marketing ploy to lure prospective infertile couples into becoming active IVF patients. Aware of the high cost (at $3000 to $6000 per attempt), general nonavailability of third-party reimbursement, and the odds of achieving a viable pregnancy, many eligible infertile couples and their physicians have assumed a wait-and-see attitude toward IVF. [---] While inflation of the IVF pregnancy rate is an expedient stop-gap solution to this stalemate, this practice amounts to deception and exploitation of patients and is deplorable. (Soules 1985: 513)

Federal dollars and regulations were not a pre-condition for a new reality of IVF, embryos, the infertile, IVF researchers, clinics and doctors, but their absence had effect on how IVF was carried out. According to Soules, the competition between private IVF programs affected how data was presented to physicians and patients.

Private commissions and professional organizations (AMA, AFS and NABER)[125] presented guidelines but none of these were compulsory (US Congress 1989, Cohen 1996, Quigley and Andrews 1984). A hundred flowers could blossom, depending on the patients/clients' and professionals' wishes. There was a space for clinical and research alternatives.

Superovulation and cryopreservation as possible technologies were being developed in the USA together with the strong desires of infertile people, and unregulated but client-dependent IVF clinics. IVF empowered and was enforced by hopeful-parents-to-be, new parents and their newborns, clinicians, and researchers. Its shape was determined by its benefactors and beneficiaries and the landscape in which they all moved, i.e.

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124 In the case of fetal tissue research it was the Universal Anatomical Gift Act for treatment of cadaveric tissue.

125 The full names of organizations presenting guidelines were the American Medical Association (in 1983 and in 1989), the American Fertility Services (in 1982) and the National Advisory Board on Ethics in Reproduction (in 1996).

an American policy-structure which meant the absence of regulation because of the non-involvement of federal dollars. In 1987–1989 there were hearings in the House of Representatives to evaluate the need for, and appropriateness of, federal funding and regulation. No decision was taken until the formal (but quiet) lifting of the de facto moratorium in 1993.

By then, important decisions had already been made between clinics, patients, and IVF researchers. Of several ways to pursue IVF one type of IVF had produced stocks of frozen embryos. In the absence of federal interventions, a new reality had been established. Since the public sector would neither allow IVF in, nor definitely prohibit it by law, embryos had to be produced – literally and metaphorically – in the private sector.

In the early 1980's Professors of Obstetrics and Gynecology at Harvard Medical School, Machelle Seibel and Melvin Taymor, wrote in support of IVF:

> Many opponents to IVF persist in objections that are based upon the erroneous information that in the process a number of embryos are formed, that only one is reimplanted, and that the others are discarded. This may have been the original approach of Steptoe and Edwards and in procedures which may still exist in other countries, but it is not the procedure now followed by the majority of centers. If one uses the natural cycle, only one egg is available for fertilization and implantation. Even if one utilizes fertility medications and attains two or more eggs and fertilizes more than one egg, all of these fertilized eggs are reimplanted. The argument against IVF based upon the discarding of embryos is thus invalid. (Seibel and Taymor 1984: 214)

Except for the "erroneous guess" about the original approach of Steptoe and Edwards it is interesting that the natural cycle and reimplantation of all fertilized eggs were regarded as the norm, and as an argument for IVF. In the Congressional debates in 1996, 1998 and later, superovulation and cryopreservation were taken for granted as a part of IVF and used as an argument for hESC research. Seibel and Taymor renounced those technologies in order to argue for IVF. The technologies were thus in 1984 in no sense necessary for IVF to do its job as a mediator of infertility and research interests. Quite the opposite. Superovulation and cryopreservation were a threat for the emerging IVF treatment. Many clinics did not adopt the new techniques and chose to implant all the oocytes that had been fertilized, some because of lack of resources. Small clinics did not have resources to test and assess innovations (because of insufficient statistical data) (Kerin and Seamark 1984). Other clinics did

not use cryopreservation because of ethical, religious, political and publicity interests:

> To allay opposition on ethical grounds, some centres, such as the one in Norfolk, Virginia, will fertilize only as many eggs as the patient is willing to have transferred to her womb […]. (Singer and Wells 1984: 25)[126]

In spite of the lack of regulation most clinics would not store embryos. Right-to-life groups and collaborating hospitals demanded uterus transfer of all fertilized eggs:

> Discard of unwanted embryos raises the question of embryo status and the substantive limits on the gamete providers' dispositional authority. No law now requires that all fertilized eggs and preimplantation embryos be transferred to a uterus. However, a de facto policy against discarding embryos currently exists. To avoid controversy with right-to-life groups and gain hospital approval, most American IVF programs claim to transfer all fertilized eggs to a uterus. (Robertson 1986: 977)

In a footnote Robertson describes how this is in practice taken care of at IVF clinics:

> A typical IVF program will base acceptance into the program upon agreement that all embryos be transferred to the woman regardless of the embryos' condition. [---] To avoid the dilemma described here, many programs will not aspirate more than five or six eggs, or will not fertilize more eggs than they plan to place in uterus. (Robertson 1986: 977, note 125)

This situation lasted. Bonnie Steinbock observed, in her *Life Before Birth,* the same phenomenon in 1992.

> To avoid adverse publicity and controversy with right-to-life groups, most American IVF programs do not fertilize more eggs than they plan to place in the uterus. This avoids the problem of what to do with surplus embryos, but at a price. (Steinbock 1992: 198–199)

The price, according to Steinbock, is multiple pregnancies and, if implantation fails, one or several more extractions of eggs from the woman.

As late as 1992 the "necessary" production of "spare embryos" was still optional, according to Steinbock, but the hints of necessity were al-

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126 As early as in 1984 right-to-life groups were objecting to production of surplus embryos. 44% approved in an Australian poll, 33% disapproved, the rest had no opinion or needed to know more, Singer and Wells 1984: 101.

ready there. Robertson (in the previous section) claimed that "The standard IVF treatment regime requires" superovulation, "because the chance of pregnancy is very small if only one fertilized egg is transferred to the uterus" (Robertson 1986: 948). Steinbock thought the price for avoiding the surplus embryo problem too high for the women participating.

It is difficult to assess exactly how the saliency of cryopreservation increased. An international survey based on data from 24 IVF centers in ten countries up to December 1986 found that almost all of them (22) pursued cryopreservation (Van Steirteghem and Van den Abbeel 1988). Unfortunately these results say little about the frequency of embryo freezing, and also little about the US situation. Of the 24 centers only two were in the USA, and circumstances can be assumed to have varied between countries such as the USA, Israel, Australia, Norway and Spain. Van Steirteghem and Van den Abbeel's survey thus may say something about the international spread of cryopreservation techniques, but little about the actual use of them in the USA.

The situation is more clear after 1992, when the Fertility Clinic Success Rate and Certification Act required the Centers for Disease Control and Prevention to annually publish an Assisted Reproductive Technology success rate report (US DHHS 2005). Based on such data a JAMA publication in 1999 showed that in transfers initiated in 1996 of "the most common type of ART treatment: fresh, nondonor IVF" (Schieve et al. 1999: 1833) cryopreservation of excess embryos was done in less than half of the cases.[127] Of the 35.554 procedures studied less than a third (29,88%) involved cryopreservation of excess embryos (p. 1834). Frist's and others' description of embryo storage as part of a "standard treatment procedure" thus refers to a 30% usage rate.

"Standard" could also mean that this is a procedure that is done almost everywhere, which according to the annual national surveys is very true. As of January 2000, 90% of the clinics *provided* cryopreservation (US DHHS 2000) and according to the report for 1999 (US DHHS 2001a)

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[127] These procedures did not include use of donor eggs (n = 5.162); transfers to surrogate mother (n = 688); transfer of already frozen embryos (n = 9.290); transfers into a woman's fallopian tubes rather than uterus (n = 4.117); transfers to both the uterus and the fallopian tubes (n = 619); transfers of both fresh and thawed embryos (n = 125); procedures that did not progress to embryo transfer (n = 8.890) and cycles for which patient age was either missing (n = 79), younger than 20 years (n = 6), or older than 44 years (n = 194), Schieve et al. 1999: 1833.

99% of the clinics provided cryopreservation (the latter probably concerns January 2001 and not 2000). Since the 2000 report the rate of clinics that have provided it has been around 97–98% (US DHHS 2005).

Use of superovulation drugs was clearly the predominant way to carry out IVF by 1998–1999. In the report summarizing the IVF clinics' results in 1996, which was the one available for actors in the Senate hearings 1998–1999 it was said that "Nationally, fewer than 1% of ART cycles in 1996 were unstimulated. However, in a very few clinics, 25% or more of cycles were unstimulated" (US DHHS 1998: 28).

When procedures are investigated or studied the concern is the efficiency of various procedures (Kerin and Seamark 1984), the fecundity and need of fertility services among the population (Mosher and Pratt 1990) or the role of women in the treatment processes (Cussins 1996). Such debates could show whether the application of superovulation and cryopreservation was motivated by a concern for women's health or by financial constraints, and who the affluent actors were.

There may be such traces or there may not. What is obvious from my observations is that the policy landscape, together with the technological developments enabled a "selective necessity" and an "ontological proliferation" of actually existing embryos. A lot of clinics could and did choose to superovulate and cryopreserve, resulting in the overproduction and storage of embryos.[128] There was no formal regulation stopping clinics from doing this. As mentioned, the Federal administration and Congress had neither interfered nor supported, but left IVF in the private sector. When the "spare embryos" – produced by so-called necessity from IVF – entered the debates after HERP they were the result of these permissive clinics, not those that had reimplanted all embryos. The "spare embryos" were the result, not of the IVF process, but of the IVF process *as pursued* by certain clinics, patients and researchers. The selection of this process in a policy and a technological landscape had necessary effects. Was there a necessity in 1994 or in 1998–2001? No, since alternative processes had been known to work. Yes, since the actors assumed the necessity, and few directly questioned it. In any case there were thousands of frozen embryos. They were undoubtedly there in the world. The clinics and the patients had

[128] By 1989, over 700 pregnancies resulting from the transfer of nearly 11.000 cryopreserved embryos were reported worldwide, Gelety and Surrey 1993: 606.

determined a specific "status" of embryos as an already existing, remaining, excess, surplus or spare status. The Federal administration had handed the dilemma to everybody who would participate in superovulation and cryopreservation as aspects of IVF.

A first answer to the introductory question – how "spare embryos" became an element that actors could refer to and the *inevitability of* the assumed *necessity* – can now be offered. In spite of the pluralism implied in the US situation, the two IVF techniques gradually populated freezers with embryos that were there of necessity. The domination is mediated not mainly by any technological black-boxing, but through an "ontological proliferation". Superovulation and cryopreservation did not dominate in clinical use, or in the legal sense (at least not according to Steinbock's comment). There was pluralism. But enough clinics' use of the techniques produced lasting entities in freezers. A literally ontological production stabilized the existence of embryos. "Spare embryos" became a reference-point for actors. According to this history this was due to a lack of regulation, technological possibilities and the choices of clinics and infertility patients. It was also due to the marginalization of at least one other possibility that did not become necessary, in fact, was barely possible.

Non-creation of spare oocytes

Except for the clinical and legal option of just bypassing the new technology and pursuing the IVF process without excess embryos, alternative routes existed. One such possibility was the freezing of eggs (oocytes), instead of embryos. Oocytes do not have the ethical status of embryos. Few have moral problems about discarding human eggs. But there were other problems, according to researchers. Oocytes were relatively harder to handle than embryos, they claimed.

> The preservation of human gametes rather than embryos is a little more acceptable to some groups within the community. However, the preservation of human oocytes is extremely difficult. [---] We are continuing to investigate the possibility of freezing human oocytes but there is a scarcity of properly mature oocytes for these studies. (Trounson 1984: 127)

Suddenly there is a scarcity of oocytes, in spite of the development of super-ovulation techniques and interested infertility patients. Trounson did not succeed but another Australian, Christopher Chen, in 1986, did, as did later two West German groups (Chen 1986, 1998, Diedrich et al. 1986, 1988, Van Uem et al. 1987). In spite of the initial success the tech-

nology did not come into extensive use. Others continued to develop the technique and showed promising results, but without establishing a routine treatment based on cryopreserved eggs instead of embryos (Gelety and Surrey 1993, Hesla 1993). Timothy Gelety and Eric Surrey reported the state of science on the cryopreservation of embryos and oocytes in 1993. Several studies had been successful, but there were also question marks from other studies. Looking at the abstract of their article the need for further refinements dominates and the successes are merely mentioned. In the editorial overview John Hesla has omitted all signs of progress in the research. Only problems remain. "Finally, the authors describe the problems associated with cryopreservation of unfertilized oocytes" (Hesla 1993: 584). Successful studies were thus presented in Gelety and Surrey's main text, but did not survive to the Editor's Corner.

Oocyte cryopreservation did not manage to disturb the proliferation of "spare embryos". In 1998–2001 the possibilities of using fewer oocytes or freezing oocytes instead of embryos, are barely visible in the debates, and not at all in the Senate debates.[129] Could this have been otherwise? What would have happened to the necessary production of IVF and the "spare embryos" had cryopreservation of oocytes been successful? Would the innovation have influenced the reality of IVF? IVF mediated the infertile population, newborn babies, and reproductive researchers. The usual justification for freezing embryos was the better chance of pregnancies, less risk of multiple pregnancies and fewer extraction procedures for the woman. This justification was based on the needs of the clients, especially the women. In Edwards's introductory 1984 speech he talked about the research on the "spare embryos":

> Research on the spare embryos growing *in vitro* raises difficult ethical issues, which are still being hotly debated in my country. I have no doubt that we must do this research, to help improve our methods, and to introduce new concepts in stem cell biology, although obviously there must be limitations. (Edwards 1985: 1)

In this quotation he does not bring up cryopreservation as such, but *research on spare embryos*. Neither does he address the infertile or the public. He addresses colleagues at the Third World Congress of *in Vitro* Fertilization and Embryo Transfer sponsored by the International Federation

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[129] Some years later (2005) the situation is again different. Federal funds are allocated to "embryo adoptions" as an alternative destiny for IVF embryos, Nightlight Christian Adoptions 2005.

of Gynecology and Obstetrics. In this world of IVF and ET scientists Edwards displays other motives than those encountered earlier. Superovulation together with cryopreservation of embryos involved scores of ”spare embryos” that would give access to early developmental processes. Edwards mentions improvement of methods and stem cell biology. If IVF was not producing ”spare embryos” the possibility of such investigations would decrease significantly. The mediation performed by IVF would decrease, at least for the audience listening to Edwards's speech.

Soon after Trounson's successful (although terminated) pregnancy following embryo freezing in 1983 and before the procedure became routine, researchers expressed hope and stressed its *advantages* in articles and books. After successful pregnancies following oocyte freezing, editors and review authors kept emphasizing the *problems* – without adding expectations or hope for the procedure. The successful cryopreservation of eggs required extensive research from the professional group that may have benefited the least from it. Had the cryopreservation of oocytes been successful, there might have been thousands ”spare embryos” (and one necessity) less, in the later negotiations of embryo research. Had the Federal administration been involved such research could have been prioritized. In the concluding chapter the paradoxical effect of the Federal administration's non-involvement and *laissez-faire* – which indirectly resulted in the ”spare embryos” – will be elaborated more extensively. Before that, let us take a look at another example of how stabilization occurred in the constrained context of pro-life sensitivies.

Transplantation therapies

After the introduction of the hESCs, the appropriate *path* to transplantation therapies is more discussed, and less the relevance of the therapeutic concept (see Chapter 2). Its possibility and urgency are assumed in both the OPP as well as the APP suggestions and were referred to and accepted as real. When the need for hESC research is questioned the *therapeutic* needs are still accepted. Here is an example from Senator Brownback testifying in the Senate hearings (April 2000):

> My final point is that the human embryonic stem cell research is unnecessary, and this is a key point because I want to see people healed, which is what the chairman is after, which is what the ranking member is after. We want to see these diseases no more hit our people or anybody else across the planet. That is our heart and that is our objective, and on that we all agree. That is why I am saying this is not necessary. We can go on the areas of legitimate research

> into adult stem cells which do not create the moral and ethical difficulties […]. (US Senate 2001: 18)

Proponents and opponents of hESC research all articulated the need "to see these diseases no more hit our people or anybody else across the planet". It was a common "heart and […] objective". Such a common heart is an issue for unpacking: Where did it come from and how was it stabilized? In the political debates from 1988 to 1993 a number of actors ultimately endorsed the possibility and urgency of research on *fetal tissue* in *transplantation therapies*. This was a stabilization of linkages that endured until the concept was again actualized in public and political debates in relation to hESCs. However, the response from the scientific community calls for a notion of stabilization that allows for different degrees of stabilization among various actors. While being stable in relation to some actors, in some circulations, the element was, and still is, unstable and uncertain in relation to others.

From animals, to patients, to politicians

The first studies articulating the concept of transplanting fetal tissue came in the late 1970's (Björklund and Stenevi 1979, Markowski and Lawler 1977). Apart from neural studies papers on the transplantation of fetal islet cells also were presented in the mid-80's (Lacy 1984). Lacy and other researchers (Fiandaca et al. 1988, Strömberg et al. 1988, Tuch et al. 1988, Weiss 1988) were supported by patient organizations, but no *general* public or explicitly political attention was given to the concept. Not until 1987–1988.

At this time several suggestions about the potential of cell transplantations to brains surfaced, both for human patients and in animal models (Lindvall et al. 1987, Madrazo et al. 1987). Brain tissue from (electively or spontaneously) aborted fetuses was transplanted into Parkinson's disease (PD) patients, allegedly resulting in improvements. These coinciding reports roused public and scientific opinion (Joynt and Gash 1987, Lewin 1987). Thus, when the Director of the NIH, Dr. James Wyngaarden, in 1988, received an application for the transplantation of fetal tissue into PD patients a moratorium was issued on all such research and an advisory panel was convened (*The Lancet* 1988b, Adams 1988, Weiss 1990).[130]

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[130] The application was submitted by Irwin Kopin. By then 116 (non-therapeutic) research projects utilizing fetal tissue were already funded by the NIH

A number of scientists, patient organizations, bioethicists, and prolifers testified before the panel in 1988 (Adams 1988). At least seven patient organizations appeared before the panel.[131] Ultimately the panel recommended federal funds for the research, based on a review of the scientific literature.

> There is sufficient evidence from animal experimentation to justify proceeding with human clinical trials in Parkinson's disease and juvenile diabetes. (Adams 1988: 14)

The articles, justifying the need to move to human trials, all articulated a therapeutic concept based on transplanting fetal tissue. In January 1988, Wyngaarden accepted the panel's recommendation. In spite of, and against, the panel's advice the Bush administration said no and the moratorium was extended.[132] Privately funded research was still not illegal. A major reason for the moratorium was the anticipated link between fetal research and an increase in abortion incidence. The former was supposed to encourage or justify the latter (Vawter et al. 1990: 14).

Patients were a crucial group in the articulation of the therapeutic concept, not least for the actual surgery. According to science journalist Georgina Ferry they did exert pressure, at least on scientists. She asked why patients were so willing to risk brain surgery when the results were still meager and suggested an answer herself.

> Why are people queuing up to be guinea pigs in experiments that may not do them any good, and even do harm? For a start, they have no other hope. The search for an alternative drug treatment to L-dopa is going very slowly […]. Parkinson's patients face the prospect of years, maybe decades of declining physical competence, perhaps ending in mental deterioration as well. Anything

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amounting to $11.2 million in the fiscal year of 1987, Office of Technology Assessment 1990: 171–173.

131 Juvenile Diabetes Foundation International, American Diabetes Association, American Paralysis Association, Huntington's Disease Society of America, National Spinal Cord Injury Association, Parkinson Support Groups of America, United Parkinson Foundation.

132 More precisely, Wyngaarden's memorandum was not acted upon until October 1989, when the new Assistant Secretary of Health advised the new DHHS Secretary, Louis W. Sullivan, a continuation of the ban. In November Sullivan continued the temporary moratorium indefinitely, Office of Technology Assessment 1990: 171–173.

> that offers the smallest chance of changing that future seems worth trying. (Ferry 1988: 58)

Ferry's Q&As concern patients lining up for the first trials. According to others, patients were not so visible. In late 1989, neuroscientist Fred H. Gage complained about the ban and the lack of patient pressure:

> "None of the reasons for the ban had anything to do with bad science or good science or whether or not it's reasonable to pursue this work on scientific grounds," Gage says. "I can't believe that patients with degenerative diseases are not up in arms. It doesn't seem real. But then, I'm a scientist." (Weiss 1989)

This would definitely change during the coming years.

Patient mobilization

During the extended moratorium advocates for and against fetal tissue research mobilized. Public actors called for more research, stressing the urgency of cures.[133] Among these were 32 medical research and educational organizations that early in 1990 wrote to the Secretary of Health and Human Services (the DHHS), Louis W. Sullivan. Here they are reported in the *The New York Times*:

> "It is clear to us that the potential for good to result from this research outweighs the concerns about the impact on the abortion rate in this country, concerns that are at best speculative," They added, "Continuing the moratorium ignores the suffering of millions of Americans." (Hilts 1990: C6)

The New York Times reporter Philip Hilts also reported that Democrat representative Ted Weiss sent the DHHS a letter. Weiss in this questioned the legal basis for an indefinite moratorium, which in practice served as a

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[133] One such actor was professor of medicine (and a member of the fetal research ethics commission of 1974) Robert J. Levine:

> Now it seems likely that transplants of human fetal cells will ameliorate such devastating maladies as Parkinson's disease and juvenile diabetes. Even this incomplete list should serve to demonstrate the enormous value of fetal research. Moreover, there is by definition no other way to secure the benefits of such research, since federal law allows it only when a particular benefit cannot be realized by other means. The opponents of fetal research are demanding, in other words, that society relinquish all claim to such benefits. (Levine 1989: 96)

legal ban, but without due process including public notice, solicitation of public comment and the establishment of a rule. A Public Health Service document was quoted:

> "We have chosen to make the moratorium indefinite rather than permanent" because "a permanent prohibition of this research would require formal rule-making procedures and thus would require extensive formal public comment and would be rather easily susceptible to litigation which could reverse this action." (Hilts 1990: C6)

By yearly extending the moratorium litigation could be avoided. After "a legislative battle" following the next expiration of the moratorium (November 5, 1990) the pressure on the moratorium became acute (Roberts 1993). Lobbyists had convinced some well-known pro-life senators of the urgency of fetal tissue research and the possibility of – institutionally and legally – separating the research from abortion practices.

One pro-life Senator, Strom Thurmond, decided to vote for lifting the ban on funding the research in the explicit hope that his grandchild would some day be helped by the research. Senator John McCain, also with a pro-life voting record, was convinced by Anne Udall to vote for the use of tissue from aborted fetuses. Udall was the daughter of Senator Mo Udall, a friend of McCain who had died of Parkinson's Disease (*The Tribune Papers* 2000). A journal issued by the American Diabetes Association, *Clinical Diabetes*, in the Summer of 1992 reported on its activities.

> Still, the American Diabetes Association plans to continue lending support to fetal tissue research even though the bill's chances of being passed this year look slim. ADA is hopeful that by shoring up the support of those in Congress who already support the bill and aggressively lobbying those representatives who voted against the bill, fetal tissue research may become a reality, and the real business of finding a cure for diabetes can begin in earnest. (*Clinical Diabetes* 1992)

These are all traces of how patient advocates lobbied people in Congress. Other pro-life congressmembers followed suit, and bills that in practice would lift the ban were passed in the Senate and in the House of Representatives in April and May 1992, respectively (Vawter 1993: 82).[134] In parallel with this intermediate victory for fetal tissue research pro-life actors came together. Between the passing of the Senate bill and the

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[134] The House had passed a bill (by vote of 274 to 144) already in July 1991 based on the Research Freedom Act introduced by Henry Waxman in 1990.

House vote, a number of pro-life organizations ran the following advertisement in the congressional newspaper "Roll Call":

> Does fetal tissue research have anything to do with abortion?
>
> Ask NARAL: The National Abortion Rights Action League (NARAL) intends to score H.R. 2507, a bill to provide taxpayer funding of abortion-dependent fetal research, in their annual congressional roll call scorecard.
>
> Ask Ted Kennedy: On April 5, 1992, Ted Kennedy told a cheering pro-abortion rally on Capitol Hill that Senate passage of H.R. 2507 proved "your message is getting through, in a very important and significant way. Make no doubt about it."
>
> Ask Laurence Tribe: Harvard Law Professor Laurence Tribe testified that medical demand for fetal tissue gives Congress constitutional authority to pass the so-called "Freedom of Choice Act" to ensure a nationwide policy of abortion on demand.
>
> Abortion advocates agree: H.R. 2507 has everything to do with abortion.
>
> A congressional vote to fund abortion-dependent fetal tissue research would give the abortion industry something it's never been able to achieve on its own: respectability.
>
> Such a vote will make the abortion industry look good, but make Congress look awfully bad. Especially when Congress can use these funds for other, equally promising, research methods that do not require an unprecedented alliance with the abortion industry.
>
> 63 percent of Americans oppose spending tax dollars for transplant research that uses tissue from induced abortions (January 1992 Wirthlin poll).
>
> Americans want limits to abortion on demand. So why does Congress think now is the time to begin collaborating with the very industry that performs and profits from it?
>
> Why should Congress give the abortion industry a good name and taxpayer dollars? Vote No on H.R. 2507! (Charo 1995b)[135]

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135 Alta Charo quotes from the congressional newspaper *Roll Call*, May 12, 1992. The advertisement came from a number of organizations: The Committee on Research Ethics, National Rights to Life Committee, Southern Baptist Christian Life Commission, Christian Coalition, Doctors for Life, American Association of Pro-Life OB/Gyns, National Association of Pro-Life Nurses, United States Catholic Conference, American Association of Pro-Life Pediatricians, American Academy of Medical Ethics, Black Americans for Life, Pharmacists for Life, Catholic Women's Institute, Christian Action Council, Knights of Columbus, American Life League, National Conference of Catholic Wo-

The supporting organizations are visible in the footnote, and say something about the pressure exerted. The quotation exemplifies how abortion and fetal tissue research were related among the pro-lifers. Ted Kennedy is quoted using fetal tissue research as a way to pursue the abortion issue, or alternatively a way to enroll pro-choicers for the research (assuming that the information provided in the ad is correct).

Possibility assumed

Apart from displaying the number of actors coming together the advertisement bears the trace of a possibility assumed. Little or no medical and scientific uncertainty was attached to the concept of therapeutic transplantation of fetal tissue in the ad. It can be used to "give the abortion industry […] respectability". In opposing the research the advertisement assumes that transplantation therapies are a medically possible path. It is thus an implicit or "bracketed acceptance" of the concept's perceived medical potential. Otherwise transplantation therapies could not give abortion respectability.

This articulation by opponents could have been strategic and directly related to the pro-life sensitivities of the expected addressees. On the other hand *this* was *the* strategy chosen instead of disputing the medical feasibility or necessity, or pointing towards viable alternatives to fetal tissue (Weiss 1989). It was the main strategy of pro-life opponents of the research from the start, visible in relation to the panel deliberations (Adams 1988: 39–73, Weiss 1988). It was the strategy chosen by the Federal administration as early as 1989, after the panel report and subsequent advice. Instead of engaging in what the medical possibilities and routes to take might be, the therapeutic concept was rejected as such, with reference to the possible effects on abortion rates.

This is one answer to "when, where and how transplantation therapies were accepted as *possible* and *urgent*". The concept was accepted as possible by both proponents and opponents, although through "implicit ac-

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men, Ad Hoc Committee in Defense of Life, University Faculty for Life, Value of Life Committee, Life Issues Institute, Concerned Women for America, National Association of Evangelicals, Capitol Hill Women for Life, Women Exploited by Abortion, Jewish Anti-Abortion League, Women for Faith and Family, Women for Women, Fortress International, Family Research Council, Professional Women's Network, Traditional Values Coalition, American Victims of Abortion, Presbyterian for Life, Scientists for Life, Feminists for Life, Eagle Forum, Jews for Morality.

ceptance". However, before 1992, the urgency was still not accepted. Now, in 1992, President Bush concurred in action with the advertisement above, utilized his veto and sent the bills back to the Congress floor. However, unlike the earlier strategy, he did partially endorse the therapeutic concept. In contrast to 1989–1991, he now accepted the urgency of fetal tissue research claimed by patient advocates.

Urgency established

Bush's proposal was that such research could be realized without recourse to elective abortions. This had been suggested in the scientific literature already (Garry et al. 1992, Thorne and Michejda 1989). If a bank were set up that would collect tissues resulting from spontaneous abortions (miscarriages) and ectopic pregnancies there might be enough to pursue the research potentials. Funds were allocated to investigate the possibilities of these sources and for setting up a fetal tissue bank.

A compromise bill, that would give the administration a year to pursue such investigations, was however blocked in Congress. Several Parkinson's and diabetes patient organizations, and medical educational organizations filed suit against the Bush administration asking for a court decision on the lawfulness of the federal funding ban on fetal tissue research (*The New York Times* 1992). After the election of Bill Clinton the fetal tissue bank and the lawsuit fell by the wayside. While still a President-elect Clinton was approached by a number of senators:

> One must only look at the benefits fetal tissue transplantation research can bring to our ability to develop lifesaving therapies for diseases such as diabetes, Alzheimer's disease, Parkinson's disease, and other genetic and neurological disorders to realize the value of this research. In light of recent studies indicating the possibilities of fetal tissue transplantations in treating patients with Parkinson's disease, it has become more urgent for the federal government to be involved in supporting these efforts. (US Senate 1993a)

The letter was signed by several pro-life senators, among them Bob Dole, Mark O Hatfield, and Strom Thurmond. Therapeutic urgency ruled. January 22, on his second full day in office, President Clinton lifted the five-year old ban on the federal funding of fetal tissue research.

Two months later the US Congress had passed the NIH Revitalization Act, issuing funds for the NIH. The new laws made it possible for publicly funded scientists to pursue research on fetal tissue. However, when looking for the stabilization of transplantation therapies the legal change

is but one linkage, albeit important. Equally important for the unpacking was how the legal change was one more trace of how actors assumed the medical and scientific certainty of the therapeutic concept – even those actors who had opposed lifting the ban a year before. The Republican Senator Hatwell on the Senate bill for fetal tissue research in 1993 stated:

> Many were surprised by my support for this important research. Most expected that as a pro-life Senator I would be compelled to treat fetal tissue research as an abortion issue, and thus oppose it. Well, I do view this as a pro-life issue but not as an abortion issue. I strongly believe that we must look beyond abortion to the research benefits fetal tissue holds, remembering to consider the sanctity of all life. (US Senate 1993b: 1582)

In the words of Hatwell the fetal tissue holds "research benefits". The sanctity of life is a pro-life phrase often used to explain the value of unborn life. Here it is turned around to explain the value of fetal tissue research. When the pro-life congressmembers accepted the ethical feasibility of the research it was accepted as beneficial, and with a high degree of certainty. That is, no medical or scientific problems figured. Orrin Hatch had a well-known and consistent pro-life voting record as a Utah Republican and Mormon Senator, and he had earlier opposed federally funded fetal tissue research. His opposition did not concern the scientific and medical possibilities.

> Some may question how I, who led the charge against the bill last year, could be a strong supporter of the measure this year. In fact, earlier this month someone stopped me and inquired about my so-called dramatic reversal on the validity of fetal tissue research.
>
> I was surprised at this question, Mr. President, because nowhere in the debate did I ever criticize the scientific validity of fetal tissue research. In fact, I stated that some of the literature indicated it is quite promising. I also stated that I was a strong proponent of fetal tissue research. (US Senate 1993b: 1572)

Hatch's support for fetal tissue research related to alternative sources. These quotations are included because they display so clearly *how* pro-lifers in Congress were embracing fetal tissue research. They did so by referring to its "validity" and its relevance for "lifesaving therapies for diseases such as diabetes, Alzheimer's disease, Parkinson's disease". Clinton and Congress joined hands in supporting fetal tissue research. Even in the face of coordinated pro-life organizations (e.g. in the "Roll Call" above) the concept of transplanting tissue to treat degenerative di-

seases was politically strong because of links to pro-life politicians, patient organizations and individual patients.

This thus answers the initial questions about "when, where and how transplantation therapies became a reference for actors". The legal change with the help of pro-lifers in Congress is a testimony of the strength of the therapeutic concept among specific actors, at the time, in 1992–1993. Transplanting cells to cure Parkinson's disease and diabetes was linked to politicians and patients, and these actors together achieved federal funding. It is in glaring contrast with the negotiations on human embryo research only a year later (around the HERP). In 1994 and later critics and commentators complained about too few benefits. When Hughes and Annas et al. referred to the compelling force of serious diseases such as Parkinson's disease they were referring to the coordination of actors in the fetal tissue negotiations. Many of the actors in 1993 were still around when the hESCs were announced five years later. Hatch, Thurmond and the patient organizations, especially for diabetes and Parkinson's disease were still supportive of transplantation therapies now linked to another body of contentious research material. Articulating hESCs in terms of transplantation therapies thus drew on an already existing stabilization, linked them to a reality that was there especially among some crucial politicians and patients. This is probably why opponents in 1998–2001 (see Chapter 2) mainly bring up alternative sources instead of questioning transplantation therapies as such.

Validity questioned

Stabilization, however, need not be global or everywhere. In the multiple reality Annemarie Mol describes, one reference may be involved in different practices with only a few points of contact without making up one unified or single whole. Latour claims that a reference is dependent on the circulations it can enable, hold together and draw on (Latour 1999b: 99).

Transplanation therapies circulated as a stable element among some actors. Patient groups and politicians are good to draw on for public support and funding. In the practices of "garnering support" and lobbying, transplantation therapies were a strong element. It was as such this element could contribute to the negotiations on hESCs. In other practices and circulations transplantation therapies were not a strong element. While the above section thus gave one answer to the stabilization of transplantation therapies relating to a specific "when" and "where" and cer-

tain "whos", lower stabilization existed in other sites and among other actors and requires a different answer and ultimately a distinct theoretical apparatus.

As seen above there had been experiments supporting some sort of expectation from the therapeutic concept. In 1985 a review of potential applications of neural transplantation states:

> Mammalian neural transplantation has recently been recognized to be a valuable technique for studying normal development and regeneration in the central nervous system. In addition, the ability of grafted neurons to reinnervate damaged regions of the host brain and to ameliorate some neuroendocrine deficits, cognitive disorders and motoric dysfunctions in young adult rodents has *suggested* that transplantation therapy *may be effective* in treating human neurodegenerative diseases and neurotransmitter deficiencies related to aging. (Gash et al. 1985: 131, my italics)

Notice the italicized "suggested that transplantation therapy may be effective". Some sort of expectation, a "suggestion", was supported by many scientists, but there were important uncertainties about the concept during the whole period. The same year (1988) a state-of-the-art review in *The Lancet* attempted to slow down the rush for clinical trials:

> However, there are no confirmed accounts of definite sustained functional improvement in MPTP […] induced parkinsonism in primates after implantation of embryonic brain tissue. [---] Surely what is needed now is not more operations, but careful long-term follow-up, with positron emission, tomographic scanning and neurophysiological and clinical evaluation, of patients who have already received grafts. (*The Lancet* 1988a: 1087)

Uncertainties and the alternatives were there together with therapeutic expectations in many of the articles from leading scientists and in review articles in leading journals. Here, *Science* called for "patience rather than patients":

> This committee, together with the apparent failure to replicate the reported success from Mexico City should serve to raise a public and scientific awareness of the questions attendant to the use of embryonic cell grafting in PD patients. [---] We should not repeat the experience of the adrenal autograft experiments wherein far more human than nonhuman primates were operated upon as a result of a single unconfirmed report of two patients. (Sladek and Shoulson 1988: 1387)

The Lancet and *Science* are not marginal sites, but major journals and, as such, vessels for stabilization. Again, there is stabilization in particular circulations, not everywhere. In an envisioned circulation of scientific facts and credibility these journals, together with professional entities, were toning down the certainty of fetal tissue transplantation as a therapeutic concept ready for trials in patients. Others in agreement with this were the American Medical Association, which analyzed the scientific literature as of June 1989:

> Fetal tissue transplantation has been attempted for a limited number of clinical disorders, including Parkinson's disease, diabetes, immunodeficiency disorders, and several metabolic disorders. Fetal tissue has intrinsic properties – ability to differentiate into multiple cell types, growth and proliferative ability, growth factor production, and reduced antigenicity – that make it attractive for transplantation research. At this time the results from fetal tissue grafts for Parkinson's disease and diabetes have not demonstrated significant long-term clinical benefit to patients with these disorders. (American Medical Association 1990: 565)

"Fetal tissue has intrinsic properties" but results had "not demonstrated significant long-term clinical benefit". In 1991, articles that outlined the therapeutic concept of fetal tissue transplantation, emphasized its experimental nature:

> Although animal experimental data are very promising and clinical trials have given encouraging results, it must be underscored that there exists at present no treatment for Parkinson's disease based on intracerebral transplantation. It is important that patients and relatives are informed that this research is still at an experimental stage and that widespread clinical trials with transplantation in Parkinson's disease are not warranted at this time. (Lindvall 1991: 25)

Lindvall was (and still is) one of the leading authorities on fetal neural transplantation from Sweden. Other leading figures and organizations concur with the characterization of Lindvall and *The Lancet*.[136] The report

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136 Here WJ Freed, in a review for *Restorative Neurology and Neuroscience*:

> Only recently, a few controlled studies have obtained evidence for positive effects of SN grafts in primate models of Parkinson's disease. In the few clinical studies reported thus far, there are indications that some clinical improvements can be produced by SN grafts, although there is little or no evidence that the clinical changes found so far are larger than the changes that have been seen after adrenal medulla grafts. The possibility of a role of striatal injury in the clinical changes has not been resol-

on Neural Grafting from the Office of Technology Assessment, largely devoted to the therapeutic concept of fetal transplantation, recognized the tentative character of the research and the need for more animal work (trials and models): "no definitive statement about the actual usefulness of neural grafting as a therapeutic procedure can be made at this time" (Office of Technology Assessment 1990: 84). This view had been voiced already in the panel by two experts, e.g. Dr. Thomas Gill, from the University of Pittsburgh (Adams 1988: 46). Some research groups were cautious, not because they didn't believe in the therapeutic concept, but because they feared the adverse effects of rushing ahead with human experiments prematurely.[137]

Separate circulations

Not much happened with these scientific uncertainties. They were not in step with the political process, or vice versa. In articulations from patients and politicians or even pro-lifers the medical possibilities (although ethically disputed) were real.

The uncertainties did not to any major extent "leak" into those circulations, and when they did, they weren't soaked in. Somehow there seemed to be a quite clear "separation" of crucial scientists and scientific institutions in one circulation from another one of patients and politicians.

The circulations of this chapter are thus not necessarily loops in one circulatory system, but can exist separately as *multiple circulations*. My multiple circulations may, or may not, come together and become a circulatory system. Unlike loops the circulations are not centered on one locus

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> ved. It is noteworthy that nearly all of the studies of SN transplantation in rodents, primates, and humans have employed methodologies similar to those developed in the course of the first few reports on SN transplantation, and that the effects obtained by these methods are limited, even in rats. The possibility is raised that fundamental advances in SN transplantation techniques may be important for the development of a more efficacious clinical procedure. (Freed 1991: 109)

[137] Ferry mentions a British group comprising Deborah Clarke (Oxford), Steve Dunnett (Cambridge) and David Marsden (London). Marsden is quoted as saying "Before it will be justified in this country, we have to prove viability of transplants from human material to primates", Ferry 1988: 58. Other examples are Bakay and Barrow 1988, Joynt and Gash 1987, Sladek and Shoulson 1988: 1387.

or person (in Latour's case, Joliot, his reactor and the work on the chain reaction was at the heart of the loops).

One possible reason for the clear division of multiple circulations could be the perceived stakes. The moratorium was prohibiting federal research, which was immediately, in 1989, perceived as a very definitive constriction for researchers and ultimately for patients believing in the new therapeutic concept.

> But while Yale has granted permission for as many as 20 such operations, lack of federal support may prevent Redmond's team from ever reaching that goal. "People think Yale is rich," Redmond says. "But we're continually operating on the brink of not being able to proceed." and [sic] with most scientists having better things to do than go scrambling for private contributions for their next fetal transplant, Redmond already sees researchers avoiding such experiments to escape the attendant hassles. (Weiss 1989: 378)

In another report, H. Fred Voss, from a company specializing in fetal-cell research, Hana Biologics, estimates the numbers of diabetes and Alzheimer's patients that could benefit at 2 million, respectively (Weiss 1988). For the pro-life movement it was exactly this thought that was abhorrent – the thought of a cultural and economic integration of abortion into the treatments of millions of people. For James Bopp Jr., attorney, and one of the two dissenting members of the 1988 panel, it was the needs estimated by, and possibly mediated through, companies as Hana Biologics that were the threat.

> The economic implications of this scenario are astounding says James Bopp Jr. […]. "Hana Biologics estimates that the potential market in treating diabetes and Parkinson's disease through the use of fetal tissue from induced abortions exceeds $6 billion," says Bopp. "Thus a vast, new and lucrative market would be created for fetal issue from induced abortion" – a market whose gross revenue would exceed that of abortion clinics by 30 times, according to his controversial calculations. "The likely result is increased number of abortions, changes in abortion procedures, and delayed abortions to facilitate acquisition of more useful fetal tissue," Bopp contends. (Weiss 1988: 296)

It was this industry that was pointed out in the Roll Call advertisement from 1992 (above). These quotations are included to focus on the polarization from both sides, which drew on radically different resources. Bopp Jr. does not primarily attack the uncertainties of the research, but the mere possibility of combining abortion with therapeutic and adjacent economic interests. Bopp's emphasis was not due to ignorance about the

uncertainties. In his dissenting statement for the panel report 1988 he gave several references to the uncertainty in the professional literature. He used three lines and a footnote for this aspect (Adams 1988:46). The rest of his 26-pages statement relates to abortion. Abortion was *the* issue, not scientific uncertainty.

Scientific validity and ethical appropriateness were held apart, treated separately. This was inherent in the strategy of President Bush and his Secretary of Health, Sullivan, in 1989. Still, some actors did highlight the uncertainties, e.g. Bopp Jr. or Thomas Gill. In 1992 Bush and pro-life people in Congress shifted and accepted the urgency of the therapeutic concept, voiced by patients and others. Although Bush and some of the pro-life people would stick to the abortion concerns and would therefore propose other tissue sources, these suggestions also did not question the scientific and medical possibilities and the urgency of therapies. Recall Hatch's and Hatwell's articulations above. According to them, they had not doubted the scientific validity, but had ethical objections relating to abortion.

For Redmond and other discontented researchers the medical possibilities are the issue and the scientific uncertainties are what fuels the need for federal funding. When discussing alternative routes, such as genetically engineered cell-lines the certainty of fetal tissue is accentuated, as here by Fred Gage: "It certainly is clear that fetal neuronal transplants are more effective than any of the other cell types at present" (Weiss 1988: 296). Experts were approached about the scientific uncertainties as the 1988 panel convened. According to Bopp Jr. none of them discussed these (Adams 1988: 45f).

It was thus correct – even in the face of scientific uncertainties – to say in the section before the previous one that right from the beginning of the controversy and until the change of the funding policy the medical possibility and the scientific validity were (implicitly or explicitly) assumed and in this sense stabilized *among pro-life opponents* and *proponents*. Among these actors the uncertainties were either insignificant, toned down or neglected. Among other actors – such as some participating researchers and commentators in *The Lancet*, *Science*, and the OTA – the concept was not stabilized in the same way. During the period 1988–1993 what was increasingly stabilized was the urgency of the therapeutic concept. What finally changed with the political recognition were the economic conditions for exploring it. This stabilization among specific actors endured

until the concept was again actualized in public and political debates in relation to hESCs.

Summary

This chapter approaches actors' references to "spare embryos" and transplantation therapies in 1998–2001 (and to some extent after 1994). My account thus unpacks the necessity of "spare embryos" and the possibility and urgency of transplantation therapies in terms of a number of actors, technologies, policies, and rejection strategies. Many of these linkages stayed in place until the hESCs were negotiated.

In the first case, a necessary IVF technique was created through the influence of willing clients, i.e. hopeful parents-to-be, clinics in competition, technological possibilities and regulatory absence. While the necessity seems to be questionable because of alternative IVF processes, the so-called necessary technology had already produced actually existing frozen embryos. The status of these – as frozen and as bound to be discarded – could also, in principle, be questioned. Frozen embryos could be thawed and donated, or "adopted". After 2001, George W. Bush to some extent opened this black box of perceived necessity and the inevitable fate of "spare embryos" by funding adoption programs. Without evaluating the success of this attempt to – metaphorically speaking – thaw the frozen fate of "spare embryos", it just proves that irreversibilities are hard work and are seldom definite.

In the second case, the medical possibility and urgency of transplantation therapies were the result of negotiations of whether to federally fund research using tissues from elective abortion. From the start of the (explicitly) political disputes the major issues among politicians, patients and pro-lifers, opponents or proponents, was not the scientific validity of the expectations, but the ethical appropriateness. While many of these actors focused on the latter, to either support or reject federal funding, the many uncertainties of the medical concept among scientists did not significantly affect the political disputes. To understand the stabilization of transplantation therapies, multiple circulations have to be taken into account. In the circulation of political and public support the therapeutic element was strong. In the circulation of experimental results and collegial credibility it was weaker.

None of these histories is saying that the elements were not really real, or *social* constructions as opposed to naturally real. They were involved in construction, but they were also – and increasingly so – real. What this

chapter says is that technological necessity is the result of contingent processes that are not inevitable and may be reversible.

Furthermore, medical possibility and urgency are not always the result of stabilization among medical researchers or the circulation of scientific results and collegial support. In this case the possibility and urgency of transplantation therapies were more established among politicians and patients than among scientists. Noticing this particular circulation and the fact that many of the same actors re-emerged in relation to the articulation of hESCs answers another question from Chapter 3 about the selection of environment. Star and Griesemer's notion of boundary objects was formulated within the ecology of institutions as one way to analyze how an appropriate environment was selected for the project, providing funds, clientele and personnel.

The stabilizations of IVF necessity and therapeutic urgency have implications for the understanding of how the reality of hESCs in USA 1998–2001 developed. In relation to the multiple loops of hESCs this chapter unpacks two of the elements and display the flows they were part of. What remains unanswered is how the two elements that were separate before 1994 became a part of the multiple loops of hESCs. This will have to be answered in the next and final chapter.

7. Pluripotent Articulation: Relating hESCs to Embryos and Transplantation Therapies

Introduction

A bold hypothesis ended Chapter 5. Actors were coordinated by means of the management of hESCs in relation to two already stabilized and useful elements – "spare embryos" and transplantation therapies. While the previous chapter displayed the stabilization of the two elements and the coordination of actors, nothing has been said about whether and how there was management of the hESCs. Management implies some deliberate change. This chapter therefore examines whether and how the configuration of hESCs were changed between 1994 and 1998–2001.

The first part looks at how the articulations of hESCs were changed, especially their "*E*", that is, their *embryonic* character. This included a tuning of the source of hESCs and a calibration of the stem cells' capacities. The second part looks at how the lin k between hESCs and transplantation therapies was negotiated. Again, the stem cells' capacities are an issue.

The "embryonic" of hESCs

The most obvious change between 1994 and 1998 in the articulation of hESCs was probably the shift from being a reference on paper – in the panel report, as vague expectations in quoted interviews, and in the discussion-sections of scientific articles – to being a reference in laboratories and regarded as "existing" in scientific journals – moved from batch to batch, linked to markers, fetal calf serum and mouse feeder cells, being viewed in microscopes, photographed and transferred to prestigious scientific journals.

One obvious change concerns the scientific work and the political staging. The recognition of Thomson's and Gearhart's respective papers was tied to a change of articulation. When hESCs were articulated in 1998 they were no longer related to the Federal administration *together with other kinds of human embryo research*. This becomes clear when comparing chapters 2–3 to Chapter 5. Whereas in 1994 the stem cells were a minor part of a whole package of human embryo research being considered for federal funds, they were the main or only issue in 1998–2001. The HERP recommendations concerned the federal funding of *human embryo research*. The negotiations in 1998–2001 concerned the federal funding of *hESC research*. Chapter 2 described how the change, according to some actors, was prompted by the announcement of the successful cultures of hESCs:

> If there was ever a good time to reopen the congressional debate on the ban on federally funded research on embryos, it must surely be now. (*Nature* 1998: 97)

The announcement of the laboratory work did indeed reopen the debate. What this part of the chapter suggests is that hESCs were changed not only by virtue of appearing in Petri-dishes and becoming the main issue of negotiation. The change of articulation of hESCs was not merely a matter of media and political actors reacting to a sudden and remarkable discovery by scientists. Something happened to the hESCs as they shifted from being an expectation and a reference on paper. When the stem cells were articulated again in 1998 as laboratory cultures – and as the main character of a new negotiation – their biological capacities and their source material were modified.

Human *spare embryonic* stem cells

From being a circulating entity in panel reports, the media and in public and Congressional debates, hESCs were articulated materially, first in one laboratory, and then others. What sort of embryo was used for the laboratory production of the hESCs when they became entities in laboratories? To enable the work on hESCs, Thomson's group needed embryos.

> Fresh or frozen cleavage stage human embryos, produced by in vitro fertilization (IVF) for clinical purposes, were donated by individuals after informed consent and after institutional review board approval. (Thomson et al. 1998: 1145)

The embryo of hESCs in the laboratory was not just any embryo, but "donated by individuals" and approved by the local institutional review board (IRB). A similar paragraph occurs in the paper from Gearhart's group (but then with 5- to 9-week fetal tissue resulting from therapeutic termination of pregnancy). The two groups did not have to use those sources. Both ultimately received private funding and, in principle, nothing *prohibited* them from creating their own source embryos. Despite this, neither of them chose to create research embryos.

In practice, the disputes about embryos infringed on their freedom of action. Thomson mentioned IRB approval above. Since they were both still employed by their respective universities (University of Wisconsin and at Johns Hopkins) they had to comply with the local ethical review boards. The review processes and Thomson's and Gearhart's choices of source were affected by the opposition to embryo research (Parson 2004: 150f, 166f).

In *The New York Times* the embryonic source was articulated as follows:

> One research team used cells from fertilized eggs that would otherwise have been discarded after treating infertile couples, and the other used cells from already aborted fetuses. They literally created a major advance from cells that would otherwise have been wasted. (*The New York Times* 1998)

Such cells-to-be-discarded are obviously different from the research-created embryos articulated by the HERP. Other actors also pursued this alternative articulation of "embryos". Senator Harkin is a politician drawing on the argument of the already existing embryos:[138]

> It seems to me the height of morality to say that in order to help someone's life to prevent Alzheimer's or ALS or to regenerate neurons, to help people with juvenile diabetes, it seems to be the moral thing to do would be to use what we have there in these in vitro cells that are left over, the 100,000, to permit the kind of ethical guidelines structure that we set up so that scientists can use those to help make lives better. (US Senate 1999b: 34–35)

The same use of embryos is present in bioethicist Caplan's argument:

> To those who say this is still permitting the use of human embryos for a purpose that is disrespectful, research and the consequent destruction of the embryo, it seems appropriate to ask why continued freezing is not just as disrespectful. It is also appropriate to ask why, even if regrettable and sad, it would

[138] See also e.g. Senator Specter, US Senate 2001: 30, 50.

> not be worth permitting the donation of spare embryos for research that might lead to cures and benefits in much the same way that we allow families to donate their loved ones, organs and tissues under the most tragic of circumstances to aid others? Spare embryos would seem to be a legitimate and morally defensible source of human embryonic stem cells. (US Senate 1999b: 39)

Again, as in 1994, Clinton asked for advice, this time, not on embryo research, but on hESCs. With regard to embryos there was one difference between the reports of the National Bioethics Advisory Commission (NBAC) in 1999 and the HERP in 1994. The NBAC *did not approve of any federal funding for the deliberate creation of embryos*.

> Recommendation 3: ES Cells from Embryos Made Solely for Research Purposes Using IVF
>
> Federal agencies should not fund research involving the derivation or use of human ES cells from embryos made solely for research purposes using IVF. (Shapiro et al. 1999: 5)

The NBAC then recalls the HERP recommendations to (in exceptional cases) federally fund the creation of embryos for research purposes and mentions two reasons for doing so. Ultimately the NBAC distances itself forcefully from HERP's stance:[139]

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[139] Philosopher Francois Baylis does not embrace my conclusion about a forceful distance between the two federal reports on the point of embryos. Instead he notes the big difference in "packaging". "The NBAC's recommendations […] are similar to those developed by the NIH Panel […]." Emphasizing the packaging of similar recommendations misses the centrality of the distinction between the two "embryos", the deliberately created one and the one remaining from infertility practices.

> This policy-making "mistake," such as it is (assuming that the goal is to secure federal funding for human embryo research), is not repeated by the National Bioethics Advisory Commission (NBAC) in its 1999 report on "Ethical issues in human stem cell research." The NBAC's recommendations on the use and derivation of human embryonic stem cells are similar to those developed by the NIH Panel 5 years earlier, but they are noticeably more carefully packaged to better ensure their political viability. This suggests that NBAC is mindful of the political reality aptly described by Dan Brock […]: "An important part of the policymaker's job is to 'sell' a position or policy to others in the policy and political process […], including the public. That makes the 'packaging' of a policy proposal often extremely important to its fate". (Baylis 2000: 141)

> Nevertheless, we have concluded that, either from a scientific or a clinical perspective, there is no compelling reason at this time to provide federal funds for the creation of embryos for research. At the current time, cadaveric fetal tissue and embryos remaining after infertility treatment provide an adequate supply of research resources for federal research projects. (Shapiro et al. 1999: 5)

Only hESC research using embryos remaining after infertility treatments should be funded. In practice that meant making an exception to the ban on embryo research. hESCs should not, according to the NBAC, be regarded as embryo research in the legal sense.

The American Association for the Advancement of Science (AAAS) and the Institute for Civil Society (ICS) were even more cautious in their joint report. To further shield the federally funded research from contact with embryos, only research on already "derived" lines of hESCs was recommended.

> Public funding should be provided for embryonic stem cell and embryonic germ cell research, but not at this time for activities involved in the isolation of embryonic stem cells, about which there remains continuing debate. [---] Although the derivation of human stem cells can be done in an ethical manner, there is enough objection to the process of deriving stem cells to consider recommending against its public funding. (Chapman et al. 1999: viii)

The authors explained this stance a little later on in the report, where it outlined the controversies on the status of embryos. Could perhaps disputes be bridged?

> The zone of agreement is somewhat widened, however, when we recognize that some who adamantly oppose the destruction of embryos or fetuses can accept the view that research on the cellular materials remaining from such acts is not always unethical. (Chapman et al. 1999: 9)[140]

Thomson's production of hESCs, Harkin's and Caplan's emphasis on "in vitro cells" and "spare embryos", and the NBAC's and AAAS/ICS's recommendations all agree on the matter of hESCs from already existing

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[140] Where did this position or zone come from? The report refers to Catholic thinking (p. 10). Similar justification had been put forward by Carol Tauer and in Catholic ideas such as Shannon and Wolter 1990, and their "ensoulment theory".

embryos. All exclude the research creation of embryos, at least for federal funding. [141]

Without addressing "intentions" or "strategies", there were at least significant differences between the two occasions. The actors were also aware of the HERP recommendations, the subsequent resistance and regulations and acted accordingly. Thomson and Gearhart started their work on human ES/EG cells while the Dickey-Wicker amendment was being put into effect. As was mentioned in the previous section, Caplan had criticized the HERP precisely on the issue of research creation of embryos. According to Caplan, this was one reason for the panel's failure to produce new guidelines for embryo research (Annas et al. 1996). Considering the cautiousness of the AAAS/ICS report, and the NBAC's direct reference to the 1994 panel on the creation of research embryos, one can assume a "learning process" from one occasion to the next. This was probably the case since there was an overlap between the members of HERP and the two later groups. One ethicist, Ronald Green, participated in the HERP and the AAAS/ICS panels. Alta Charo, Bernard Lo, and Thomas H. Murray were all members of the HERP and the NBAC. Whether it was tuning or learning, many of the 1998–1999 articulations on the particular point of the embryo source for hESCs differed from that previously put forward by the HERP. The research creation of embryos was no longer an option. The embryo of human embryonic stem cells was "spare", frozen and already there from in vitro fertilization treatments.

Degrees of "embryonic"

Another issue concerned the subsequent regulations, viz. the status of the hESCs themselves – not their sources, but their embryonic potential. Nicholas Wade, science reporter for the *The New York Times*, summarized the legal importance of this factor, a few days after the announcement of the stem cells in November 1998.

> NIH officials said they believed that Congress's intent was to ban research on any entity with the potential to grow into a human being, and that, as the human embryonic stem cells cannot do so, they would be exempt from the ban. (Wade 1998)

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[141] Some actors did mention deliberately created embryos, in relation to cloning or nuclear transfer. However, until 2001 this issue was secondary to the hESCs.

From 1996, the Dickey-Wicker amendment had been a "legal black box" precluding any attempts to use embryos in federally funded research.[142] Anything that could be placed in the box was excluded from federal funds. However, nowhere in the paragraphs were hESCs mentioned explicitly. The debates following HERP had, as had the panel discussions, concerned research on embryos in general and not on hESCs in particular. According to the legal text it was a matter of whether they were "entities that had the potential to grow into a human being", and, concluded Wade, "as the hESCs cannot do so" they would be outside of the box. There was however one complication:

> "Assuming the cells are not totipotent, reservations go only to the source," said Kevin T. FitzGerald, a geneticist and jesuit priest at Loyola University Medical School.
>
> If they are totipotent, he said, he would conclude that their use could not be justified. But he noted the complexity of the issue, saying, "We are getting closer and closer to the lines of demarcation of the beginning of human life." (Wade 1998)

FitzGerald would have reservations if the cells were totipotent because this is the term that had been used to denote the potential of embryonic cells that would later develop into the whole organism. Totipotent were the cells that make up the embryos after a few divisions, or the cells of the inner cell mass of the blastocyst that form after a few days. Wade again:

> The cells of the inner cell mass are called "totipotent", meaning that each can form any tissue of the body. Both Dr. Thomson and Dr. Gearhart proved by a standard test that their cells are "pluripotent," meaning they can form many body tissues. The cells may also be totipotent, but the two researchers were

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142 For precise references to the Dickey-Wicker amendment, see p. 76. It prohibited the use of federal funds for

> research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury of death greater than that allowed for research on fetuses in utero under 45 CFR 46.208(a)(2) and section 498(b) of the Public Health Service Act (42 U.S.C. 289g(b)). (Sugarman et al. 1998: 159)

"Human embryo" was then defined as including "any organism […] that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells", Sugarman et al. 1998: 160.

> unable for ethical reasons to perform the standard test for totipotency. – Dr. Gearhart, whose cells were derived from a different tissue, the embryonic germ cells, but are probably equivalent to Dr. Thomson's, said he thought they would probably prove totipotent if the test were permissible. (Wade 1998)

According to these definitions pluripotency means that the cells can form many body tissues, while totipotency is the capacity to form all of the tissues of the body. hESCs, said Gearhart, are probably totipotent. But totipotency is the capacity of the cells of the early embryo to, under the right conditions, develop into all the tissues of the organism and thus equal an embryo and "an entity with the potential to grow into a human being". In case Gearhart's assessment was confirmed by others, the hESCs would thus not be admissible for federally funded research.

Terminological calibration: pluripotency and totipotency

Wade's article was published on November 10. In the hearings three weeks later, NIH director Harold Varmus explained the features of hESCs in relation to embryos:

> There are many issues to be raised about the cells that we're talking about today, but one of those questions is whether these cells have the ability to give rise to a complete human being. The answer to that from a scientific perspective is no. (US Senate 1999b: 7)

Considering the Dickey-Wicker amendment, and the opposition to federally funded research on hESCs, the affirmation and emphasis are understandable. Varmus's point was repeated over and over again.[143] It was imperative to separate the hESCs from embryos. In order to pursue this separation, the concepts of pluripotency and totipotency were used as a "terminological calibration" of the relationship between embryos and hESCs.

On November 10 (in Wade's article), Gearhart conjectured that hESCs are totipotent. On December 2 he had removed this conjecture, and his use instead conforms with the designation of hESCs as pluripotent. Totipotency is now only used to denote the early cells of the embryo that can

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143 Eg. in the next testimony by Gearhart:

> The most important point I think to be reinforced is the fact that, although these cells can form many different cell types, they are unable by themselves to form an embryo or a human being. (US Senate 1999b: 11)

each become an embryo, while pluripotency is exclusively used for hESCs. A hierarchy of stem cells and developmental potential is presented. Varmus again:

> Cells from the very earliest embryo […] are totipotent stem cells. They are "totally potent" or totally capable of forming all cells of the body, including the cells required to support embryonic and fetal development. Each cell of this early embryo has the potential to develop into a human being. (US Senate 1999b: 8)

If the embryo is developed a bit further it forms a blastocyst containing the inner cell mass, Varmus explained:

> The cells in the inner cell mass are not totipotent. Rather, they are pluripotent. Pluripotent stem cells are more "committed" than totipotent stem cells. Unlike the fertilized egg, or the early embryo, or the intact blastocyst, neither the disaggregated inner cell mass nor the pluripotent stem cells derived from it […] will produce a human being even if returned to a woman's uterus. (US Senate 1999b: 8)

The distinction between hESCs and embryos is defined by the distinction between pluripotency and totipotency. The two distinctions occur frequently and consistently together. In one of the quotes from Varmus's testimony above, one specific resource is drawn on to separate pluri- and totipotency. Here, totipotent cells, like embryos,

> are "totally potent" or totally capable of forming all cells of the body, *including the cells required to support embryonic and fetal development.* (US Senate 1999b: 8, my italics)

Pluripotent stem cells, on the other hand, are thought not to give rise to the "extra-embryonic structures" that support embryonic development, such as the trophectoderm, trophoblasts, and, later, the placenta. What Varmus said out loud was more quietly confirmed by other testimonies. In Gearhart's and Thomson's testimonies, hESCs are described as giving rise to a number of adult tissues. None of these two pioneer hESC scientists mentioned that trophectoderm and extra-embryonic tissue could be possible results of hESCs (US Senate 1999b: 13 and 17).[144]

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144 This denial later appears in other texts. In 2004, Professors D G Jones and C R Towns, of a New Zealand department of anatomy and structural biology, do not include trophectoderm as one of the cell types possibly produced by ES cells, Towns and Jones 2004: 412.

These articulations (by withholding) stand in contrast to Gearhart's earlier statement that "they would probably prove totipotent" (see quotation above). They also differ from Thomson's original *Science* article of November 6:

> After undifferentiated proliferation in vitro for 4 to 5 months, these cells still maintained the developmental *potential to form trophoblast* and derivatives of all three germ layers […]. (Thomson et al. 1998: 1145, my italics)

Articulating hESCs as pluripotent and not totipotent, as developmentally less capable than embryos, was picked up in the legal and policy recommendations. On January 15, 1999, a memorandum was issued by Harriet Rabb, General Counsel at the Department for Health and Human Services (DHHS). Her interpretation and that of the DHHS was that research on already produced hESCs would not fall under the embryo research ban since "human embryonic stem cells are not a human embryo within the statutory definition" (NIH 2005). The DHHS definition was justified with reference to the fact that "the cells do not have the capacity to develop into a human being even if transferred to the uterus". A few days later, and referring to Rabb's memo, the NIH director Harold Varmus announced that the NIH was preparing guidelines for the federal funding of research on hESCs. These guidelines would still not allow "the use of such funds in the derivation of the cells" (US Senate 1999b: 123).[145]

The New York Times reporter Gina Kolata contrasted the position of the DHHS and the NIH – and their dissociation of hESCs from embryos – by asking scientists for their opinion. Dr. Lee Silver, geneticist at Princeton dismissed the distinction between embryonic stem cells and embryos, at least based on "the capacity to develop into a human being". "Metaphysically, it's all the same", Kolata quotes Silver:

> He thinks research with human embryo cells should be permitted but is offended, he said, by all the winking and nodding by scientists who do not want to admit the true potential of these cells to become a baby, if anyone wanted to try. (Kolata 1999)

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145 The reason: Derivation of cells would fall under the Dickey-Wicker amendment as a case of "research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury of death greater than that allowed for research on fetuses in utero", Sugarman et al. 1998: 159.

Kolata also recalled experiments pursued in 1993 that could be interpreted as challenging the DHHS ruling and Varmus's subsequent intentions. Andràs Nagy and Janet Rossant (and others) had, in these experiments, produced "live offspring which were completely ES cell-derived" (Nagy et al. 1993: 8424). "If", Kolata suggested, "you can grow a mouse from a single embryo cell, you should in theory be able to grow a human from a single human embryo cell".

> Nagy said that he saw no reason why a human embryonic stem cell could not become a human being. "I don't think there's a theoretical or practical impossibility of creating a completely stem-cell derived human being, if one wanted to do that." (Kolata 1999)

In Kolata's article Nagy and Silver are associating – not dissociating – hESCs and embryos by referring to the cells' developmental potential. However, others questioned what this reference to developmental potential denotes. Nagy's and Rossant's claim that most of the resulting offspring were "completely ES-cell derived" did not mean that only ES cells had been involved in the reproductive process. The cells were not implanted in the uterus on their own, but were combined with "developmentally compromised tetraploid embryos" (Nagy et al. 1993: 8424). In analyses of the the offspring's genetic set-up, a specific version of a gene (GPI-BB) from the tetraploid embryos did not show up. In this sense the mice were indeed 100% the result of the ES cells.[146] On their path to developmental maturity the latter had needed support from the tetraploid embryo cells, which were eventually dropped, or "selected against" (p. 8424). Just like the embryo itself, the cells had the capacity to develop into a whole human being. Unlike the embryo, the cells needed some embryonic support, critics claimed.

This is also what Thomson said when approached about the issue (Thomson 2003). The silence on the production of extra-embryonic tissues was so deafening that when results were presented on trophectoderm differentiation of hESCs at a conference in 2003, one delegate expressed surprise: "Have these cells always produced trophectoderm? Since when?" (Informant A 2003). Before the hearings the central actors included references to the creation of extra-embryonic cells that could support a

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[146] That is, at least 98% of the individual mice did not contain any tetraploid genes. "A minor contribution (<2%) from tetraploid cells cannot be excluded", Nagy et al. 1993: 8426.

growing embryo, such as trophoblast, and used the term totipotent, together with pluripotent, to describe the stem cells. In the hearings (December 1998 – January 1999) these articulations of the stem cells were changed and the hESCs were consistently described both as pluripotent and as a possible source of all adult tissue types.

This was a marked difference from the 1994 negotiations and the pre-1998 situation. *In HERP both terms occurred.* The report featured pluripotency, while Van Blerkom used totipotency (NIH 1994, Van Blerkom 1994: 47). The two terms were used quite interchangeably before 1998. ES cells could be named toti- or pluripotent.[147] Totipotency and pluripotency could be attributed to non-embryonic stem cells, such as hematopoietic or blood-forming stem cells (Diukman and Golbus 1992). This was also the case after 1998, but to a much lesser extent.

The distinction between pluri- and totipotency was increasingly adopted in the scientific literature. Disciplining scientists participating in US Senate hearings was, however, easier than disciplining the strongly growing numbers of worldwide ES cell researchers. Scientific articles did not completely stop using totipotency for ES cells, but the use diminished. Gearhart and Thomson did their "calibration" in late 1998 and early 1999. Having scientific articles published takes approximately 6 months (from the journal receiving the article to acceptance and publication).

In a search for articles that combine the words embryonic stem cells or ES cells and totipotency, totipotential, totipotent versus pluripotency, etc, there is a dramatic increase for the use of pluripotent terminology compared to the increase in use of totipotent terms (because of a general increase in ES cell articles there is a general increase in the use of both terms).

Even before the negotiations in 1998–1999 the number of ES cell articles mentioning pluripotency (and related words) was approximately 4-5 times more frequent than articles mentioning totipotency. There existed thus a preference for the pluripotency-terms. However, it is a *highly preferred* choice afterwards. The explosion of "pluripotency" in relation to "totipotency" comes in and after 1998.

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147 In several articles totipotency is used for ES cells or in discussions of prospective human ES cells, Cherny et al. 1994: 569, Harris and Mansson 1988: 9, Müller and Dzierzak 1994: 47, Pesce et al. 1999. Other articles use pluripotency for ES or EC cells, Evans 1986, Jacob 1982, Martin and Lock 1983.

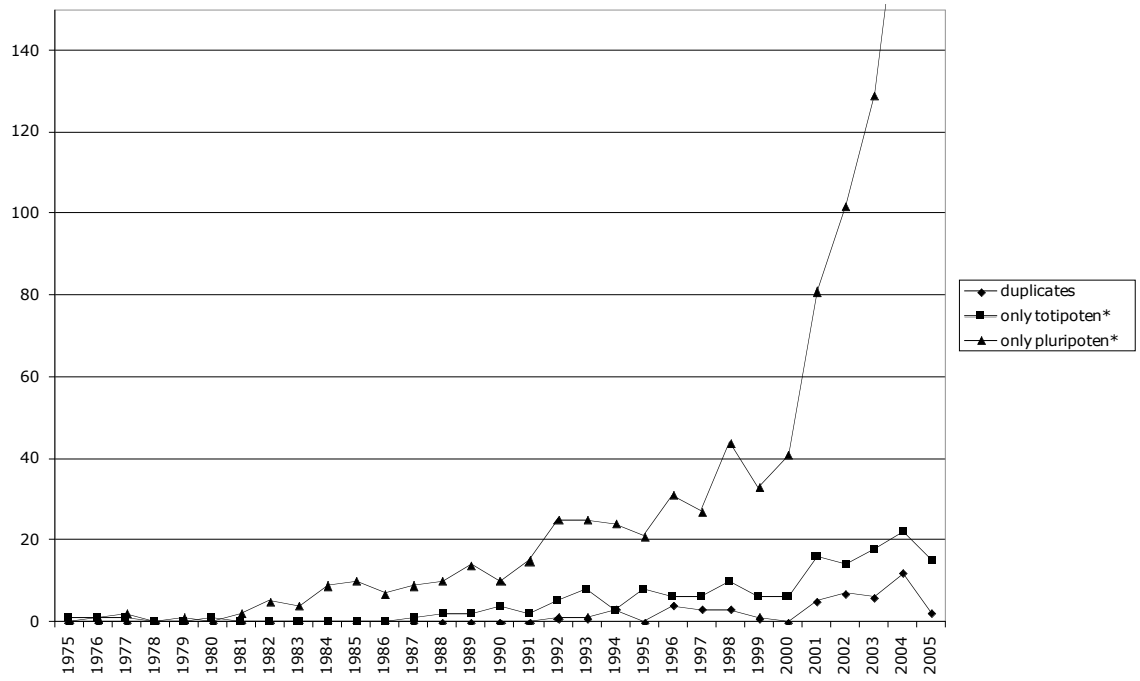

Figure 12: Distribution of "pluripoten*" and "totipoten*" in ES cell articles 1975-2005. (Medline search conducted November 15, 2005.)

The three curves display the year-by-year number of Medline articles about ES cells (or embryonic/embryonal stem cells) using (1) exclusively the term pluripotency, pluripotent(ial) (i.e. "pluripoten*"), which is the highest curve, (2) exclusively totipotent terms (i.e. "totipoten*"), which resulted in the middle curve, and (3) both terms ("duplicates"), which correspond to the lowest curve. The data do not consider the context of use, but merely the tendency within the scientific community in its use of the terms in articles where also ES cells occur.

To put it starkly, and rather provocatively, this means that the *pluripotent* ES cells (i.e. articles) in retrospect started an exponential increase in relation to the *totipotent* ES cells at the time of the negotiations of federal funding of hESCs. Not all scientists were influenced by this terminological calibration, but there was a definite tendency that appears to coincide with the negotiations about the newly produced hESCs. However, this also shows that Gearhart's change, from claiming totipotency to pluripotency, was not "mere politics", but coherent with the most current practice in journals.

Year	Total number of articles	(3) Both terms	(2) Only totipoten*	(1) Only pluripoten*
1975	1	0	1	0
1976	2	0	1	1
1977	3	0	1	2
1978	0	0	0	0
1979	1	0	0	1
1980	1	0	1	0
1981	2	0	0	2
1982	5	0	0	5
1983	4	0	0	4
1984	9	0	0	9
1985	10	0	0	10
1986	7	0	0	7
1987	10	0	1	9
1988	12	0	2	10
1989	16	0	2	14
1990	14	0	4	10
1991	17	0	2	15
1992	31	1	5	25
1993	34	1	8	25
1994	30	3	3	24
1995	29	0	8	21
1996	41	4	6	31
1997	36	3	6	27
1998	57	3	10	44
1999	40	1	6	33
2000	47	0	6	41
2001	102	5	16	81
2002	123	7	14	102
2003	153	6	18	129
2004	220	12	22	186
2005	258	2	15	241
TOTAL	1317	48	158	1111

Table 1: Distribution of "pluripoten*" and "totipoten*" in ES cell articles 1975–2005. (Medline search conducted November 15, 2005.)

The terminological calibration, as presented here, is not a case of external forces *invading* science and *causing* a change. Distinguishing between early (8-cells and 16-cells cleavage stage) embryonic cells and (inner cell mass) stem cells by terminological calibration *coincided* with the negotiation about whether or not to include hESCs in the ban on embryo research. Making a clear-cut distinction between hESCs and embryos *cor-*

relates with the attempts to achieve federal funding for hESC (and not embryo) research.[148]

Nor am I suggesting that it was a tactical deceit or a strategic move in order to manage the naming of hESCs. I am instead noting a historical conjunction of "scientific" and "political" events, in which a *dissociation* from embryos could be made and might have had significant effects. By dissociating hESCs from embryos, scientists and others could make a strong case for federal funding. Previously, the main issue had been precisely to *associate* the two.

The parallel between the development of embryonic stem cells and embryonic development had been one of the attractions of the stem cells. This was especially the case within the field of developmental biology, but also for the other envisioned uses, for instance in livestock. Such use built on the successful involvement of embryonic stem cells in the production of new individuals with genetic modifications. This point was made on the back cover of the 1999 special issue of *Cells Tissues Organs* to convey the importance of ES cells.

> Pluripotent mouse embryonic stem (ES) cells have been widely used to create mutant mice that pass genetic modifications to their offspring through germline transmission. ES cells also have the capacity to differentiate in vitro into cells of endodermal, ectodermal and mesodermal lineages. (Wobus and Boheler 1999: back cover)

In fact, this affiliation with embryonic development had been one of the recurrent motifs and aims in the elaborations of experimental models since

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148 Notice the choice of words: "Correlate" and "coincide" are not causal relationships. Terminological calibration did not necessarily affect the negotiations or vice versa. It is a sufficiently interesting observation that the terminological calibration occurred while the hESCs were articulated as a laboratory entity and possible for federally funded research. An alternative (or complementary) historical separation of the two terms comes from the guest editors of the special issue of *Cells Tissues Organs*.

> The results of the nuclear transfer technology employed by Campbell and Wilmut [1997] led us to use the terms "totipotent" for zygotes and blastomeres of early cleavage stage embryos, and "pluripotent" for cells and cell lines derived from either the inner cell mass or primordial germ cells. (Wobus and Boheler 1999: 130)

Nevertheless, in the 1999 special issue other papers had still not adopted the distinction.

the 1950's that preceded and ultimately resulted in the production of ES cells. Researchers had been busy proving embryo-likeness. The linkages with embryonic potential or embryonic cells had played a major part quite early on in Leroy Stevens's and Barry Pierce's respective work on a particular tumor form, often occuring in the testis: teratoma or teratocarcinoma. Stevens and Pierce were both active in US laboratories during the 1950's, 60's, and 70's.

The specific characteristic of teratoma tumors is the development of a variety of tissue types, such as teeth, hair, or nerve cells. Stevens's and Pierce's research came to focus on which cells were responsible for this variety of tissues. One of the experimental procedures (or "assays") that was developed and frequently used by Stevens and Pierce involved the production of "embryoid bodies" (EBs) (Kleinsmith and Pierce 1964, Pierce et al. 1960, Stevens 1959, 1960). After transplanting teratoma cells into the abdomen (the peritoneal cavity to be more precise) of mice, the EBs appeared. These consisted of cells from all of the three germ layers of the embryo (although in an inversed arrangement). Stevens and Pierce observed this similarity between, on the one hand the development of a particular teratoma cell (or cells), and on the other hand the development of embryos. Their hypothesis was that one very potent type of cell in the teratoma was responsible for all of the various tissue types. The successful transplantation of *single cells*, resulting in EBs, settled the issue for Pierce and Stevens. In line with earlier teratoma terminology, they called this cell type "embryonal carcinoma cells", or EC cells. According to Stevens and Pierce, these cells – that grew into teratomas – came from the "primordial germ cells", i.e. the germ cells of the embryo (Pierce 1975, Stevens 1967). There were thus two teratoma-related cells and both had embryonic potential. Embryonal carcinoma cells were the most potent cells within the teratoma tumor. Those EC cells had, in turn, originated from embryonic (or, more correctly, primordial) germ cells.

British pathologists in the 1960's and early 1970's did not embrace the hypothesis that there was anything like an "EC cell" within teratoma tumors (Collins and Pugh 1964: 1, Pugh and Smith 1964: 28). In their classification systems they "discarded the term 'embryonal carcinoma"', since "[i]t has led to much confusion" (Collins and Pugh 1964: 5). Earlier in the same article, the same authors dismissed the germ cell origin:

> It does not seem to us very realistic to trace the histogenesis of adult neoplasms to so primitive a past as the earliest somite embryo. (Collins and Pugh 1964: 1)

The British resistance to embryonal carcinoma and to the primordial germ cell origin were in both cases also *resistance against the association* between these cells and the embryo. When Pierce's and Stevens's claims were adopted and developed within a wide research community this happened precisely through *a series of associations* with the embryo (Sherman and Solter 1975).

Several experimental models presented in this community of teratoma researchers established the potential participation of EC cells in normal embryonic development (Mintz and Illmensee 1975). The production of "embryonic stem cells" (ES cells – or for a while "EK cells") at two places in 1981 was achieved in direct relation to the EC cells (Evans and Kaufman 1981, Martin 1981). Both of the papers situated the produced cells as an extension of the embryonic relationships established in the earlier research on EC cells and teratoma. For these researchers, ES cells were articulated as the direct linkage from embryos to cell cultures in a dish (Evans and Kaufman 1981, Martin 1981). The cells could not only participate in embryonic development, but could be taken from an embryo. ES cells were later compared favorably to the EC cells, precisely on the basis of the former's more embryo-like character (Doetschman et al. 1985). In spite of these developments, there were still, in the early 1980's, disagreements over the classfication issues mentioned above.[149]

This demonstrates how the association with embryos had been perceived as essential: first for Stevens and Pierce and their embryonal carcinoma cells; later for the community that developed these cells and produced the ES cells in direct relation to EC cells and the embryos.

There is no systematic use of totipotency and pluripotency for EC or ES cells in the developments outlined above. Both terms were used. One regularity exists. Embryos are never described as pluripotent, but always as totipotent. This suggests that the latter term was used to stress the association between the embryos and the cells in question (whether EC

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[149] Two workshops were held in 1980 and 1981 to "get the leading clinicians and investigators in the field of testis cancer to "talk to each other", Donohue 1983: vii. Roger Pugh, one of the British pathologists who discarded the term embryonal carcinoma 1964, attended the meeting. His contribution was "Pathology of Testicular Tumors – A British Perspective", Pugh 1983. He admitted that "there is no denying the weight of experimental evidence supporting the germ cell theory" (which had been related to the notion of embryonal carcinoma), but still "a great deal of work yet remains to be done to clarify the early stages of tumor induction in the human testis" (p. 2).

or ES cells). A terminological mixture of totipotency and pluripotency thus underlines the importance of embryo-association for the development of ES cells. To EC and ES cell researchers, a major point had been to prove the similarity between the stem cells and embryonic features and development. In a new political context the stem cells suddenly needed dissociation from embryos. What was needed this time was to avoid political consequences from the identification of hESCs with embryos or early embryonic cells (with the potential to become an embryo).

Successful calibration

As the circulation of federal funds was at stake, the reference to the capacities of hESCs thus had a specific role. Making them "more pluripotent and less totipotent" would remove the cells from the category of entities that could grow into a whole organism. Was this, then, a successful management of terms? There are at least two answers. One relates to the immediate negotiations of federal funding in 1998–2000. The other concerns the ultimate negotiation and decision in 2001.

The non-embryo status of hESCs (and also the lack of potential to develop into a whole organism) had no immediate legal effect. One example of this was Doerflinger's opposition to federally funded hESC research voiced in the first Senate hearing in December 1998 (US Senate 1999b: 71-73), quoted above in Chapter 2. Drawing on the pluripotent definitions of hESCs, Senator Harkin suggested that the Dickey-Wicker amendment did not apply to research on hESCs, since they were not organisms. Therefore, Harkin claimed, the ban does not apply to hESCs. Doerflinger agreed about the "organism-status" of the cells, but this success for the taxonomic calibration did not imply any immediate legal success. Doerflinger still opposed Harkin's interpretation of the Dickey-Wicker amendment and sidestepped the issue of the exact status of hESCs, since the research *still required the destruction of embryos*. Irrespective of the terminological calibration that dissociated embryos and hESCs, Doerflinger enforced their close association in the hearing, based on the production/destruction process.

The same pattern of dissociation attempts, resistance and re-affirmed association is visible in the January 1999 reaction to Harriet Rabb's legal interpretation of the relationship between hESCs and embryos. Rabb's memo was indignantly and immediately opposed by bipartisan (Republican and Democrat) congressmembers and the Secretariat for Pro-Life Activities at the National Conference of Catholic Bishops (Wade 1999b).

They re-affirmed the close association between hESC and embryo research and claimed that Rabb's interpretation went against the spirit of the existing law. In these alternative interpretations of the law, toti- and pluripotency were of little significance. Instead, the focus was on the very process by which hESCs were created from "spare embryos". However, Rabb's attempt (to enable NIH funding) was based not only on the separation of the cells from the production process, but also on the status of hESCs as non-organisms. While the legal separation of hESC research from the "spare embryonic" source failed in 1999, the new articulation of the stem cells' status – correlating with the distinction between toti- and pluripotency – prevailed.

The distinction was picked up in textbooks and among bioethicists, as well as in the lay press (Maienschein 2003, Parson 2004, Towns and Jones 2004). In this example from the 1999 July-August issue of the *American Scientist*, Shirley Wright re-articulates totipotency as a matter of producing trophoblast:

> Despite their potential, isolated embryonic stem cells cannot develop into a mouse if returned directly to the uterus because the cells have lost their capacity to form trophoblast cells, which are necessary for implantation. Under these conditions they are considered to be *pluripotent*, rather than totipotent. (Wright 1999: 354)

It is interesting to note how Wright continues the explanation. After claiming that the stem cells are not totipotent – since they cannot form trophoblast – she points to their "totipotent properties".

> However, if the embryonic stem cells are first added to a donor tetraploid embryo that is unable to develop normally and the resulting embryo is transferred to a mouse uterus, a normal mouse is born that is totally derived from the cultured embryonic stem cells. This indicates the incredible totipotent properties of these cells. (Wright 1999: 354)

Wright thereby (intentionally or not) captures the ambiguity of many attempts to articulate the cells' properties. The cells are not totipotent, but have "incredible totipotent properties".

Most importantly, this was articulated in official hierarchies on stem cells. Varmus was at the NIH and the distinction was used in the NIH's information about stem cells (NIH 1999). The AAAS/ICS report adopted the distinction as it had been articulated in the hearings (Chapman et al. 1999: 33). On August 1, 2001, the terms and the distinction were pre-

sented by the Congressional Research Service which serves to provide unbiased information for Congress:

> The earliest embryonic stem cells are referred to as *totipotent*, indicating that they can develop into an entire organism because they can produce both the embryo and the tissues required to support it in the uterus. Later in development, embryonic stem cells lose the ability to form these supporting tissues, but are still able to develop into almost any cell type found in the body. These *pluripotent* embryonic stem cells are the current focus of intense research interest. (Johnson 2001: 1)

August 1 was eight days before Bush's policy decision and he adopted many of the definitions in the report (Bush 2001). As he concluded his decision the status of hESCs was crucial:

> I have concluded that we should allow federal funds to be used for research on these existing stem cell lines, where the life and death decision has already been made. (Bush 2001)

In this respect the calibration was successful. hESCs were not identical to embryos in their developmental potential in Bush's decision. Had they been, his statement – "the life and death decision has already been made" – would have made little sense. Had the hESCs been on an equal footing with embryos, there would still be "a life and death decision" to be taken.

Pluripotent therapies

The hESCs did change in significant ways in relation to *how* embryonic and *what* embryonic they were: *pluripotent* and *spare embryonic* as opposed to totipotent and made from deliberately created embryos. This aspect of the hypothesis from Chapter 5 is answered. A second aspect concerned the management of hESCs in relation to transplantation therapies.

The hESCs became important in the argument for the benefits of human embryo research. This was a major point in Clinton's and others' later articulations, examplified in Clinton's letter to NBAC chair Shapiro that we saw in Chapter 2 (Shapiro et al. 1999). According to Clinton, the benefits of hESCs were the reason for a review. But was there any tuning of the hESCs to fit the expectations in regard to potential benefits from transplantation therapies? If the hESCs had been tuned, we should be able to find traces of change between the hESCs of 1994 and 1998. Trans-

plantation therapies were one of the uses linked to hESCs in 1994, together with the use for developmental biology.

However, the very focus on hESCs resulted in a proportional increase in the importance of transplantation therapies. In the HERP, the hESCs contributed with only one application to lists of 8, 9 or 13 possible applications. Now, in 1998, transplantation therapies from hESCs were the predominant in the three commonly articulated uses. By enlarging the role of hESCs, an important re-articulation of federally funded human embryonic research was brought about. It was a partially successful attempt to separate the negotiation of federal funds for hESCs from the earlier negotiations of human embryo research.

Another re-articulation of hESCs took place, as it were, in between chapters 2 and 3 of this book: Chapter 2 presented some articulations of hESCs as a new possibility, heralding a pluripotent transformation. In opposition to this attempt, some actors referred to other cells with equal potential and promise. In Chapter 3, Bush and some pro-lifers ultimately endorsed the hESCs with reference to the higher potential and promise of transplantation therapies. As Orrin Hatch put it:

> It is my understanding that, at the present time, the view that adult stem cell research is sufficient or even scientifically preferable to embryonic stem cell research is not the predominant view within the biomedical research community.
>
> While I have great admiration for, confidence in, and strongly support America's biomedical research enterprise, and I believe that our policy should be made on the best science available, I am hardly one who invariably follows the lead of what some may term "the science establishment." (Hatch 2001b)

There is, then, a time gap between the two chapters and in articulations of pluripotency and transplantation therapies: on the one hand, the articulations of the pluripotent transformation and the opposition (in Chapter 2), and on the other hand Bush's and some other pro-lifers' recognition of the pluripotent possibilities (in Chapter 3). Something happened in between. It was not just a matter of some people changing their minds, and not just a result of negotiations in the White House or among congressmembers. The reference to hESCs was de-stabilized for a time. This dynamic and chronological gap is the scene for management of the link to transplantation therapies. While the embryonic management was started before 1998 and finished by the end of 1999, the management of hESCs and transplantation therapies continued until Bush's decision in

2001 (and after, in fact; although this falls outside of the scope of this study).

Undisputed existing linkages

hESCs were linked to transplantation therapies in articles and in reports. As stated above, however, this did not constitute any major change in their articulation. This was the main envisioned use of hESCs even in 1994, due to their differentiation capacities, whether they were called pluri- or totipotent (Van Blerkom 1994: 46ff). The graphic articulation of this linkage was issued by the NIH in 1999, as presented in Chapter 3, Figure 7. Cultured pluripotent stem cells resulted in multiple uses.

Few people questioned the expected benefits from hESCs. In this respect, there was little difference between the supporters and opponents of hESC research. There were patients who challenged the therapeutic needs by playing down the urgency of the envisioned cures, such as Mary Jean Owen. Testimonies such as hers – pushing the need to recognize debilitating diseases and weaknesses – were, however, among the exceptions of the hearings (US Senate 2001: 23–34).[150]

When hESCs were announced in 1998, few actual studies had been conducted to prove the possibility of transplantation therapies using (non-human) ES cells. When the NBAC explained the use of hESCs in transplantation therapies, the main references were the same as Van Blerkom used in his commissioned paper in 1994 (Shapiro et al. 1999: Chapter 2, Van Blerkom 1994: 47). Those articles were merely tangential in relation to transplantation therapies using ES cells. Only one article expressed this explicitly (Hollands 1991). For one of the two most frequently mentioned applications, Parkinson's disease, two more references are used, both from 1999. One of these is a not-peer-reviewed paper, but a conference presentation of transplantations of fetal tissue cells to Parkinson patients. Another is a study of mouse ES cells differentiating into neurons and then transplanted.

In spite of the scarcity of scientific studies on transplantation therapies relating to ES cells, the possibility of transforming hESCs for transplantation therapies was not questioned. One element of this certainty was the differentiation capacity. Its scientific name was pluripotency (or totipotency). It was this capacity that ensured the usefulness of hESCs for

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150 Other strategies may have dominated outside of the hearings and outside of public debate, but this is not covered here.

transplantation therapies. Articulations of hESCs and transplantation therapies went *via* pluripotency. This has in previous chapters become clear as a matter of textual and graphic articulations. One such example was Figure 1 in the Introduction. In the illustration the differentiation capacities are involved in flows symbolized by big orange arrows, and the web site explains how these are tied to the medical possibilities:

> Embryonic stem cells are of great interest to medicine and science because of their ability to develop into virtually any other cell made by the human body. In theory, if stem cells can be grown and their development directed in culture, it would be possible to grow cells of medical importance such as bone marrow, neural tissue or muscle. (University of Wisconsin 2005)

The actors' combination of pluripotency and transplantation therapies was already displayed in Chapter 2 and above in Bush's decision. Below are two other examples from the hearings, first from Okarma (from Geron Corporation) and then the Biotechnology Industry Organization where they explain the applicability of the cells.

> The potential, however, is realizable and portions of it can be reduced to practice based upon prior knowledge gained from animal stem cell work and the convergence of available complementary technologies developed by both the biotech industry and the academic community. (US Senate 1999b: 51)

> It is anticipated that these cells will be differentiated into blood, skin, heart, or brain cells and may be able to treat cancers, spinal cord injuries, heart disease and potentially many other diseases. (US Senate 1999b: 104)

Doug Melton, representing the Juvenile Diabetes Research Foundation, is even more assertive as he moves from the stem cells' potential to the differentiation of cells specific for his needs.

> These stem cells then have the potential to develop into any tissue organ in the body, and they could no doubt be directed to make pancreatic islet or beta cells. (US Senate 1999b: 99)

All of these examples are articulations of the relationship between hESCs and transplantation therapies via pluripotency. Taken one by one, none of these linkages, between hESCs and transplantation therapies and pluripotency, was questioned.

Michel Callon has used "interessement maps" to picture how the relationships between entities can be established, intersected and restructured (1986b). This section will draw on Callon's simplified imagery of entities and relationships to lay out the role of pluripotency in the complex landscape of possible associations involving hESCs and transplantation therapies. In Melton's, Okarma's and others' articulations, the transplantation therapies are enabled through the pluripotent capacities of hESCs:

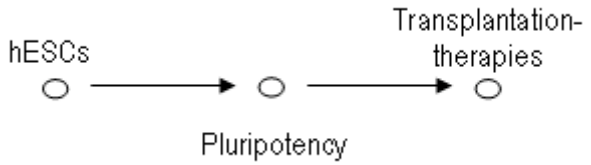

Figure 13: Interessement map of hESCs, pluripotency, and transplantation therapies.

Some of the articulations above concerned the first arrow and some both arrows (e.g. Figures 7 and 8 in Chapter 3). Treated separately, none of these changes during the period in question. Nobody questioned the *existence* of linkages between pluripotency and hESCs. They were, if anything, too potent rather than lacking in potency. As was described above, there was work done to *downplay* the stem cells' capacities, since they might take the hESCs uncomfortably close to the legal definition of an embryo. Nobody questioned their great potential, although they named it differently, as either totipotency or pluripotency.

To perceive a management in these relationships between hESCs and transplantation therapies, they cannot be treated separately, as if it were solely a matter of existing associations or not. The relationships were not questioned in an absolute sense, but in a relative actor-network sense. Recall the challenges to federal funding of hESCs mentioned in Chapter 2. The opponents pointed towards findings about "adult stem cells" as an alternative path to transplantation therapies. Here from Republican Congressman Dickey (first) and from Mary Jane Owen, Executive Director of the National Catholic Office for Persons with Disabilities (second) in Senate hearings in 1999 (November) and 2000 (April):

> numerous reports over just the last few months have shown remarkable discoveries about the versatility and possible uses of stem cells found in adults. (US Senate 1999a: 10)

> there are many other sources of these vital human tissues which give clear indication of their potential for positive results. [---] Exciting possibilities lie ahead in making use of self-contributed stem cells […]. (US Senate 2001: 26–27)

Sometimes references were more specific and elaborate. In one of the January 1999 hearings, Doerflinger quoted an article in *The New York Times* where NIH researcher Dr. Ronald McKay explains the results of Dr. Vescovi's group.

> Almost the first visible structures in animal embryos are three primary sheets of cells, known as the ectoderm, mesoderm, and endoderm, from which all the tissues of the adult body develop. [---] Dr. Vescovi's work defies the widely held assumption that cells in the three lineages are permanently committed to their fate.
>
> "It is that trinity that is now being challenged," said Ronald McKay, a brain cell expert at the National Institutes of Health. Dr. McKay said the new result showed that differentiation, the commitment of a cell to a specific fate, is not irreversible. (US Senate 1999b: 141, Original quote from *The New York Times* Jan 22, 1999, by Nicholas Wade)

The differentiation into the three germ layers was the main trademark of the pluripotency of hESCs. If Vescovi's results were correct, these capacities might not be unique to hESCs. Adult stem cell research was, in general, not used to question the scientific quality of hESC research. None of the actors disagreed about the basic findings: the stem cells' capacities to differentiate and self-renew. In Chapter 5, these challenges to the federal funding of hESCs were treated in terms of an alternative point of passage.

While accepting pluripotency and its significance for transplantation therapies, and without questioning the capacities of hESCs, the APP was still a challenge to the *relative relationship* between hESCs and transplantation therapies. The image above oversimplifies the relationship in question. The fit between hESCs and transplantation therapies was never as simple as the NIH, UW, Melton or Okarma articulated it. When the relationship between transplantation therapies and human embryonic research was first raised, it was within a "project" of achieving federal funding. The actors prescribed (see Chapter 5) that the benefits would be a

solution to the perceived problems. When the hESCs, and their relationship to transplantation therapies, were announced, they were immediately linked to other actors too. Clinton's letter was one example. If the earlier scheme is extended with his words then the following is a possible result:

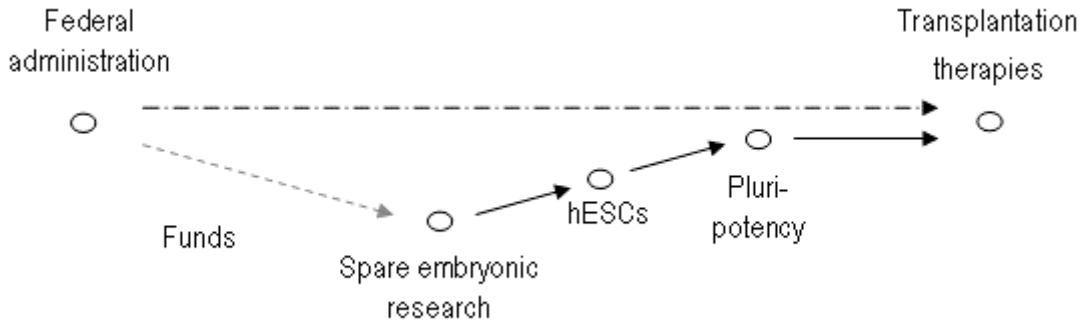

Figure 14: Interessement map of the hESCs, spare embryonic research and the Federal administration.

In the figure above, the threefold relationship is extended with the entities that are entailed in the "project" of the federally funded human embryonic research. This funding is still uncertain throughout the whole period, hence the shaded dotted arrow. Clinton indicated that the Federal administration would have an interest in transplantation therapies for Parkinson's disease etc, which is visualized in the broken arrow from the administration to transplantation therapies. The reference to "hESCs as pluripotent and therefore apt for transplantation therapies" does not correspond to an a-historical reality, but to a sociotechnical reality of other elements and actors. It is articulated, and thus made real in relation to the Federal administration. It is not uttered in a vacuum. In fact it is uttered in a very particular and explicitly political site, on the Capitol. And the actors do it in relation to an on-going project, whether they are deliberately part of the project or not. Chapter 5 showed that there is such a project and that large number of actors were involved in it, from the HERP panel to the retrospective critics. It is this "reality of links" that the articulations of alternative stem cells enter. They are thus competing and competitive articulations; not only establishing associations, but linking in competing ways with already existing actors and linkages. The effect that the competing articulations of adult stem cells have

on the relationship between hESCs and transplantation therapies is obvious: The former may obliterate the need for the latter.

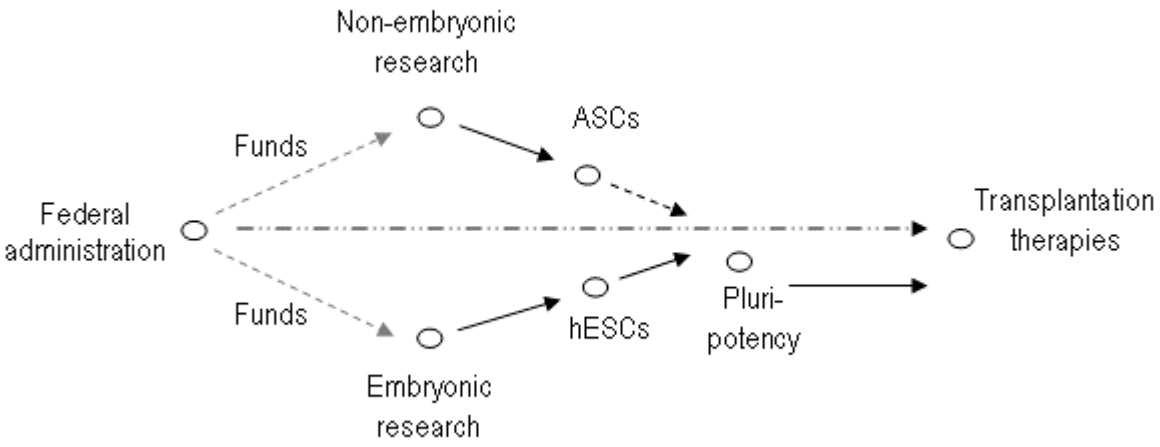

Figure 15: Interessement map of hESCs and possibly pluripotent (highly plastic) ASCs.

The prescriptions after 1994 were based on the assumption that the benefits of federally funded human embryo research needed to be spelt out. The pluripotency of hESCs linked the stem cells to transplantation therapies for diseases such as Parkinson's and juvenile diabetes. What was questioned by the adult stem cell claims was the *uniqueness* of the linkage between pluripotency and hESCs. There could be ways of achieving cells and subsequent therapies, opponents claimed, without having to use embryos. The plasticity (pluripotency) claims for adult stem cells (ASCs) gave the Federal administration's "funds-arrow" an alternative path if it wanted to reach the end-point – transplantation therapies. Paradoxically, the promise of adult stem cells built on the already stabilized relationship between pluripotency and transplantation therapies. Since this was stable, it was sufficient merely to link the ASCs to pluripotency.

The alternative path was the drama of the OPP and APP in Chapter 2 and Chapter 4. In those chapters this was a way to understand how hESCs were associated or dissociated from the circulation of federal funds. As this chapter continues the story, the spotlight is set on how hESCs and transplantation therapies were managed in the face of obliteration, or at least a significant reduction. If federal funding were to be directed to adult stem cells, then research would be done using hESCs to a much

lesser extent. There were still (by 1999; to my knowledge) no studies on transplanting hESCs. To many scientists American research is the engine of global research, and the engine of the engine is the NIH budget (consisting of federal funds). If adult stem cells were to be the only research promoted to achieve transplantation therapies, the reality of hESCs and transplantation therapies would, at the very least, decrease significantly.

Although strongly stabilized, the hESCs' pluripotency could be, and was for a period, destabilized by a comparative juxtaposition with other stem cells. However, the effect of this "comparative destabilization" of the exclusive pluripotency of hESCs was that "spelling out" benefits would no longer suffice. Pluripotency had to be reached solely through embryonic research, or no funds would be available. Merely *existing linkages* were not enough after the competing articulation of adult stem cells. To make an association in this landscape required keeping competing associations away. The association between hESCs and transplantation therapies through pluripotency was already there, and was stable, but had to be stabilized *in competition* with adult stem cells.

Mobilizing stem cells – and scientists

In actor-network theory there are no categorical differences in terms of strength of elements or linkages. What is usually called an "ethical argument" may be a stronger element than a "scientific object" through its linkages to a number of other actors, or vice versa. There is no way of saying that something "ethical" is stronger than something "scientific". Now, articulating adult stem cell pluripotency was a way of opposing the association of hESCs and the Federal administration, without appealing to explicitly political or explicitly ethical elements. The strength of adult stem cell pluripotency was dependent on which other elements and linkages of the network had to be moved or could be enrolled. Articulating alternative pluripotency suggested a network configuration without federally funded embryo research, *without therefore having to depend* on the mobilization of actors for the embryos. Instead, scientists, laboratories and experiments were enrolled *through* the adult stem cells. Note that the articulation of adult stem cells as alternatives came not from the active scientists, but from bioethical or political actors. However, the scientists' work was enlisted in the articulation. A whole bunch of actors was thus activated without lobbying for a specific embryo status or the displacement of other elements of the network: transplantation could still be endorsed.

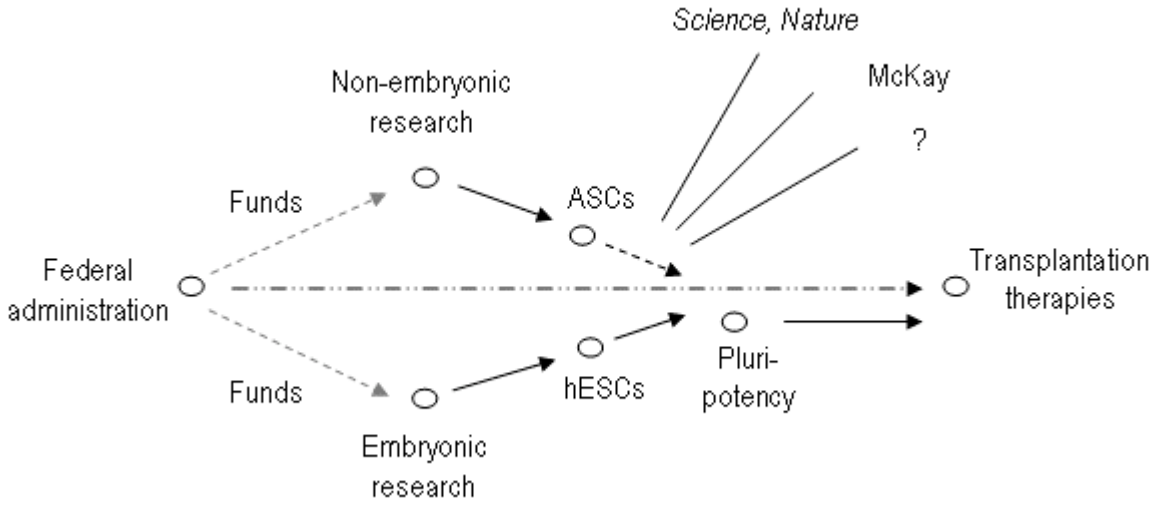

Figure 16: Supportive linkages for an association between ASCs and pluripotent capacities (high plasticity).

To start with there were strong allies for adult stem cell plasticity. Ron McKay was (is) situated at the NIH and – at least in the quotation above – articulated a linkage between high differentiation potential and adult stem cells. His articulation constituted important support because of his position at the NIH and his position in the field. Nicholas Wade of the NYT contacted him for a reason. In contrast to many of the scientists responsible for the articles on adult stem cell "plasticity", i.e. high differentiation potential, McKay appears at numerous neural stem cell conferences as a keynote speaker and is well-published and frequently quoted in scientific articles. He was co-author to some of the earliest studies on neuronal differentiation and transplantation in mice (Brustle et al. 1999).

Although the papers on adult stem cell plasticity were published in high profile journals (*Nature* and *Science*) the experiments and the scientists were very little entrenched in traditional stem cell disciplines or existing practices (Bjornson et al. 1999, Ferrari et al. 1998, Gussoni et al. 1999, Petersen et al. 1999). "Adult stem cells" were not a field or a discipline and still precariously linked to other actors, although some pro-lifers adopted them. Dickey referred above to stem cells in adults. The term "adult stem cells" was used towards the end of the period but usually in reports, or political, popular or media accounts. There were no departments or institutions explicitly doing research on "adult stem cells". Indeed, blood stem cells had been used experimentally and therapeutically for more than

thirty years (Thomas and Blume 1999, Till and McCulloch 1980). Neural stem cells were being revived after Altman's attempts in the 60's (Altman 1962). These were stem cells in adult humans, but not named "adult stem cells". The term appears in relation to the experiments on plasticity, and in relation to embryonic stem cells.

Vescovi, Ferrari, Bjornson and others were not recognized as "adult" blood- or neural stem cell scientists before the experiments indicating plasticity. As McKay was quoted as saying, to many scientists the phenomena challenged a dogma. Neural and especially blood stem cells were not challenging in themselves, but their connection to an embryonic-like differentiation potential was. Despite this, McKay was not skeptical in the quotation from January 1999.[151] There was however what I would prefer to call an *inversed proportionality* in progress. The opponents' use increased as the scientists' expectations decreased. In 1998 and 1999 many scientists and journals were positive about adult stem cells. As the importance of adult stem cells increased in the opponents' arguments, the scientists' statements and the journals' peer-reviewing become more and more cautious in relation to the capacities and promise of adult stem cells, in particular in relation to hESCs (*Workshop on Stem Cells and the Future of Regenerative Medicine* 2001).

Disciplining scientists – and cells

The attempted association to alternative stem cells eventually affected how differentiation capacities were articulated. Pluripotency was not only an element defined by ES cell research and hESC research. From being an interesting phenomenon in journals and among scientists it became *relative* and evaluated in relation to hESCs, and involved in a funneling, exclusive coordination. Dr. Goldstein is a professor in cellular and molecular medicine at UCSD:

> some have argued that so-called "adult stem cells", derived from adult tissues are of equivalent promise, less ethically compromised, and should therefore be pursued exclusively. But it is far too early to know if adult stem cells have the same potential as embryonic stem cells, whether they can be harvested in sufficient quantities to treat diseases, and whether they can grow indefinitely as can embryonic stem cells. In fact, it is likely to take years to find out if adult

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151 It is interesting to note that today (2005) McKay is in charge of the NIH's efforts to characterize embryonic stem cells.

> stem cells will be useful for treating many diseases that may be treatable sooner with embryonic stem cells. (US Senate 2001: 44)

Goldstein distinguishes the relative certainty and potential of hESCs by recalling the "past 20 years using mouse embryonic stem cells" and the use of such cells "in a variety of 'proof of therapeutic principle' experiments in several animal models of human disease" (US Senate 2001: 43).

The history of plastic adult stem cells is more brief. According to one researcher, it was Ian Wilmut's successful experiments with Dolly, that raised expectations about adult cell versatility (Verfaillie 2002). Dolly was a result of two cells, one of them a somatic, adult cell that thereby displayed the unexpected capacity of giving rise to and participating in tissue development.

When some of the "adult stem cell scientists" eventually appeared in hearings, they did associated their cells with differentiation into all three germ layers, or something close to it. In this respect the attempts to find nonhuman support for alternatives to hESCs did succeed, yet in the end they did not. No scientist involved in the plasticity research used it to put adult and embryonic stem cells on an equal footing The substitution of hESCs in favour of adult stem cells was eventually opposed outright by leading scientists responsible for the findings. The following is from Dr. Diane Krause in the 2001 hearing.

> This interpretation is not only stunningly premature, but potentially undermines the development of adult stem cell therapeutic options. In fact, the progress made in studying adult human stem cells relies on what has been learned from embryonic stem cell studies. – It is my testimony that these two areas of research together will lead to effective and safe treatments for life-threatening diseases. (US Senate 2002: 52)[152]

There are doctors who argue against hESCs, but they were not specifically working on the highly plastic adult stem cells (Do No Harm 2005, US Senate 2001). Between 1998 and 2001, scientists called to hearings and quoted in the press became increasingly unanimous on the relative biological advantage of hESCs. By the summer of 2001 scientific journals, such as *Nature*, had raised the bar for a publication of plasticity findings and similar claims about de- or transdifferentiation. (De Witt 2003, Verfaillie 2002). The judgments delivered by stem cell scientists at the National Academy of Sciences (NAS) workshop in June 2001 were un-

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[152] Also see Darwin Prockop's response in US Senate 2001: 87–92.

equivocal (*Workshop on Stem Cells and the Future of Regenerative Medicine* 2001): Adult stem cells were not equivalent to hESCs. The professional mobilization is marked in the figure by the bold arrow "cutting off" the linkage between adult stem cells and pluripotency (plasticity) and thereby disabling a path from the Federal administration via non-embryonic research to pluripotent cell transplantations.

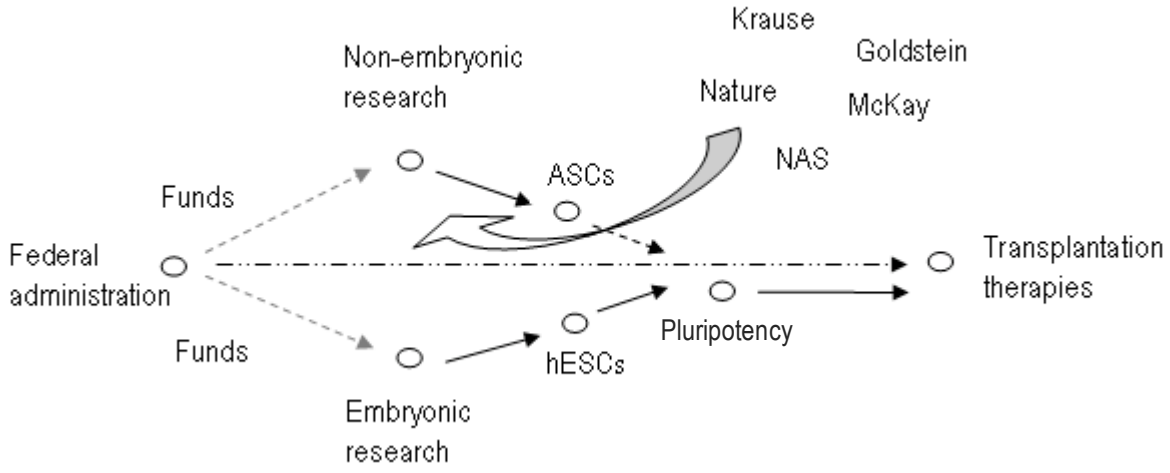

Figure 17: The association between ASCs and pluripotency is cut off.

Terminological calibration: pluripotency and multipotency

This mobilization of stem cell professionals was paired with a terminological calibration of the differentiation capacities of stem cells. Professionals not only used their own credibility, but also the terms pluripotency and multipotency to distinguish between various cells.

Before 1998, there were two types of pluripotent stem cells, hematopoietic stem cells and embryonic ones. Then, at the same time as the hESCs went public, two things happened to the concept of pluripotency. The concept before and after 1998 was not exactly the same. The first difference has already been discussed: the distinction between pluripotency and totipotency. Before 1998, both totipotency and pluripotency could be used to describe the developmental capacities of ES cells. This was less so after 1999 (see above). The second difference concerns the exclusivity of pluripotency in relation to the earlier usage of the term for another type of stem cell. Pluripotency had been developed for *blood stem*

cells since the 1960's (Becker et al. 1963, McCulloch and Till 1964, Till 1982, Till and McCulloch 1961, 1963).

From 1960 to the mid 1980's, blood stem cell researchers experimented on and defined what they called "pluripotent stem cells", in splendid isolation from the work on "pluripotent cells" in teratomas that later contributed to the ES cells. The succession and the hierarchies of stem cells presented were limited to the blood system. Pluripotency for blood stem cells could thus be used by hematopoietic researchers, without regard to the pluripotency defined by teratoma researchers. This double set of terms gradually changed in the 1980's and 90's as ES cells were applied increasingly to existing models of hematopoietic differentiation. As researchers of various stem cells started collaborating, the similarities between stem cell systems became visible and joint hierarchies were furnished. When the hESCs were announced and discussed in public in 1998, such hierarchies became important. Harold Varmus stated:

> There is a hierarchy of stem cell types. Some stem cells are more committed than others. Some stems [sic] cells – the pluripotent stem cell we are discussing today – have the ability to become many, but not all, of the cells [sic] types in the human body. (US Senate 1999b: 8)

In 1998 the pluripotency label was not only used to distinguish between embryos and hESCs, but also hESCs from other adult-derived stem cells. To perform this distinction, pluripotency was increasingly reserved for hESCs in contrast to other stem cells. One example is the AAAS/ICS report where adult stem cells are multipotent, and not pluripotent (Chapman et al. 1999: 4). Around 1998 there is a shift in blood stem cell terminology in the literature. Pluripotency is still used occasionally to describe adult stem cell potency, but more often the term multipotency is used.

Hematopoietic research, especially in the 1980's, had resulted in the classification of several populations of blood stem cells. These had been distinguished as ranging from pluripotency to more committed stem cells. A group of reviewers described these populations in 1997:

> Multipotent hematopoietic progenitors in mouse bone marrow can be purified in three distinct populations that differ according to self-renewal potential. Long-term, transiently, and non-self-renewing populations form a lineage of multipotent progenitors. Although the cells in these populations are similar in many ways, they undergo transitions from long-term to no self-renewal potential and from pluripotency to perhaps the earliest stages of lymphoid commitment. (Morrison et al. 1997: 218)

In 2000 and 2001, one of the authors (Weissman) again contributed to reviews on stem cells (Reya et al. 2001, Weissman 2000). This time pluripotency was not mentioned in relation to blood stem cells at all. Instead multipotency was used exclusively to characterize the capacity of blood stem cells, and other adult stem cells.[153] Sometimes no specific term at all was used to describe the less potent adult stem cells (Edwards et al. 2000: 3).[154]

The terminological calibration of pluripotency and multipotency is combined with a hierarchization of stem cells. From the very outset, the concepts of "stem cell" and "pluripotency" have been connected to the notion of a cell family tree, with the stem cell being part of the imagined stem of the tree, carrying the potential to differentiate into many of the branches. More differentiation capacity equals a higher rank in the hierarchy (or closer to the primary stem). As the unique pluripotency of hESCs was challenged, the hierarchization of stem cells made clear the relative capacities of various stem cells. The hESC is assumed to be higher in the stem cell hierarchy. The hESC occupies, as it were, a patriarchal, or even Holy Grail-like, position at the top of the stem cell pedigree (Whitaker 2002). This was salient in the graphic articulations (see above). Here is Fischbach from the NIH in the hearings:

> Now, there is a hierarchy of stem cells. I think the consensus of scientific opinion is that cells proliferate and differentiate when isolated from the adult nervous system, but there is a common view that cells proliferate more plenti-

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153 Even in cases where pluripotent stem cells (PSCs) are found in non-embryonic tissues they are separated from the allegedly non-pluripotent blood stem cells. The lines below, about the stem cells in the umbilical cord blood (UCB), would probably have been nonsensical before 1998, since hematopoietic stem cells (HSCs) were then pluripotent stem cells.

> It is not clear from either the preclinical or clinical models if this differentiation into nonhematopoietic tissues represents the dedifferentiation of HSCs into PSCs, or if PSCs exist alongside HSCs in the marrow compartment. If the former proves correct, then UCB will also likely be a source of PSCs. If the latter is the case, then these PSCs must also exist alongside HSCs in UCB for the potential of UCB to be realized. (Snow 2003: 51)

154 The distinction between hPSCs (human pluripotent stem cells) and their adult-derived, lineage-restricted counterparts, such as hematopoietic progenitors, lie mostly in their range of differentiation.

> fully, and they have a wider range of choices, if taken from the fetal or embryonic tissue […]. (US Senate 2001: 53)

Fischbach drew on the image of stem cell order, and the adult stem cells were subordinate to the hESC. These references set the comparison of hESCs and other cells outside of human decision-making or opinion. None of the scientists dismissed an interesting scientific potential of adult stem cells (just as none of the opposing actors dismissed the hESC on scientific grounds). Also, nobody claimed that there was total agreement about the state of the art (Bartelemez 2001, Weissman and Baltimore 2001). A small degree of uncertainty was retained, but they never totally let go of references to "a wide consensus", "the common view", etc. Still, stem cell scientists' testimonies were coherent: other cells lacked some of the differentiation capacity of the hESCs. Graphically, the terminological calibration enacts a separation of "application paths" of adult versus embryonic stem cells:

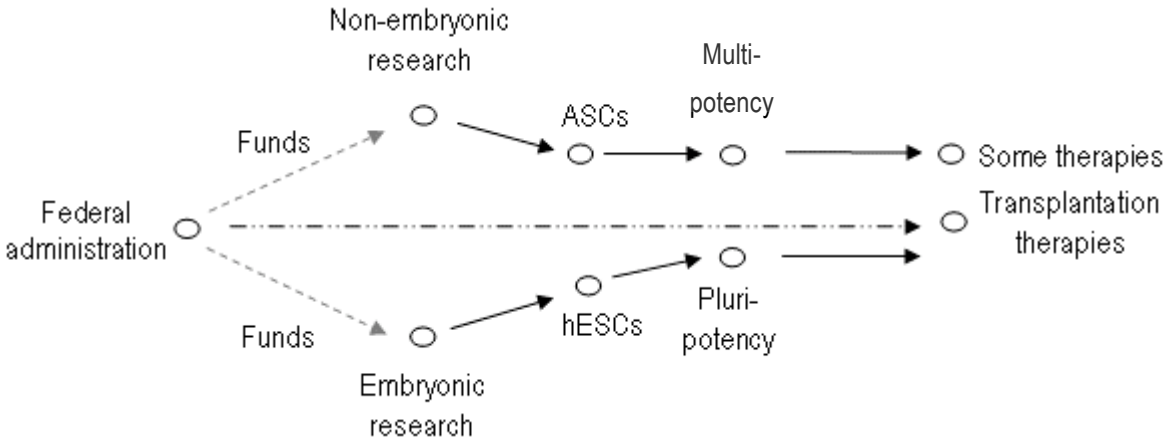

Figure 18: The diversion of ASCs.

With the separation between totipotency and pluripotency at one end of a developmental spectrum, and between pluripotency and multipotency at the other end, the hierarchy was in place and could be circulated. The following is from an account from 2003 in *Whose View of Life?*, by philosopher of biology Jane Maienschein:

> Whereas a *totipotent* cell can become an entire organism, including all the different cell types, a *pluripotent* cell has the capacity to become any one (but not all) of the cell types that make up the body. *Multipotent* cells are a little more

> specialized and can become one of several, but not of any, cell types. (Maienschein 2003: 254)[155]

New allies are good for network attempts as long as they do not betray you. It is impossible to say anything definite about the actions of "adult stem cells". Whatever the nonhumans' actions were, a hierarchy of stem cells was successfully installed that put them into neat terminological boxes.

Seeing management

By the summer of 2001, hESCs thus occupied a unique position in a circulation of standardized terms, journal criteria, and collegial recognition. Although influential, the scientific circulation does not determine Presidential decisions. When Bush announced his decision, August 2001, he referred to hESCs and acknowledged their "unique potential".

> Based on preliminary work that has been privately funded, scientists believe further research using stem cells offers great promise that could help improve the lives of those who suffer from many terrible diseases – from juvenile diabetes to Alzheimer's, from Parkinson's to spinal cord injuries. And while scientists admit they are not yet certain, they believe stem cells derived from embryos have unique potential. (Bush 2001)

After paying attention to alternative stem cells he returns to the capacities of hESCs:

> However, most scientists, at least today, believe that research on embryonic stem cells offer [sic] the most promise because these cells have the potential to develop in all of the tissues in the body. (Bush 2001)

Although Bush mentions alternatives, the promise of hESCs is outstanding. Based on this recognition, Bush did not unconditionally endorse all hESC research, but allowed funds for already existing cell lines. The reference to hESCs was managed in relation to transplantation therapies and embryos, but still did not achieve full federal funding.

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155 It should be mentioned that Maienschein, in contrast to the for-granted, realist attitude in the above quote, in other publications takes a more analytic, relativist stance towards the use of the same concepts, e.g. in Maienschein 2002.

Summary

In this chapter, I have argued that hESCs were part of a longstanding project of federally funded human embryonic research. As prescribed by actors after the failed coordination of 1994, *the hESCs were managed in relation to the embryonic source and the therapeutic benefits*. hESCs were now materially and discursively made from ”spare embryos”. The research-creation of embryos was not a viable, although still legal, option for most of the actors supporting hESC research. Another adjustment was made by calibrating the use and meaning of pluripotency. By distinguishing the term from totipotency, the risk of hESCs being legally or morally classified as embryos was avoided. By distinguishing the term from multipotency, the uniqueness of hESCs and transplantation therapies could be defended in the face of alternative stem cell articulations. In both cases of pluripotency-calibration, scientists were the main actors. The package “pluripotent hESCs from spare embryos” was made uniquely apt for transplantation therapies by means of these circulations of criteria, credibility, and collegial recognition. This composite entity played an important role in the political circulation and negotiations of the federal funding of hESCs.

This chapter thus shows how hESCs as pluripotent, made from ”spare embryos” and suitable for transplantation therapies, were not necessary, or the only way to construct the package and the actor-networks of cells, scientists, legislation, politicians, corporations, and others. The particular configuration was made in relation to one project, its perceived problems and prescriptions. In an attempt to achieve federal funding for human embryonic research, the hESCs were made less totipotent, less linked to the research creation of embryos, and less equivalent to adult stem cells. In this sense, hESCs were made real in direct relation to the public and legal repercussions from the HERP’s recommendations. It is altogether an example of how laboratories, scientific evaluations and terminology are connected with bioethical reports, specific social groups, and political decision making. The reality of hESCs is not separated into biological, ethical and political realms, but is constituted by circulations among scientists, patient organizations, IVF cycles, pro-lifers, bioethicists, politicians and corporations.

8. Conclusions

As promised in the Introduction, the road that this work has taken has not been straight. Just like an assemblage in progress, the research questions, concepts, new phenomena and issues have been added piece by piece to the understanding of stem cells. It is now possible to summarize this exercise in seeing the reality of hESCs differently.

I started this study with a puzzle about how to understand hESCs. Some things about the stem cells attracted my interest, viz. their alleged biological capacities and political effects. The puzzles were turned into a topic by using ANT, which assumes that biological capacities and political effects are part of the same sociotechnical reality.

Sociotechnical reality was defined as coming to be in articulations and in the flows between various entities. In order to capture what was really making a difference, I brought up the notion of agency held by ANT as something appearing among heterogeneous elements. The obligatory point of passage and boundary objects were two models used to capture the distribution of agency and map the stabilization of sociotechnical reality.

In Chapter 2, I attempted to apply the OPP model to understand the negotiations of federal funding of hESC research. Even if the match was not total, the OPP model highlighted the funneling coordination, the assumed total transformation, and an "either-or": Either the Federal administration gets involved or the cures for serious diseases will not be realized. Opponents accepted the need for cures, but suggested that other stem cells could make the cures happen.

In Chapter 3, I suggested that there were traits in the negotiations of hESC research that resembled the boundary object approach. Diverse actors were coordinated around the hESCs by partial connections, without being totally aligned. Actors' explanations for their support of hESCs refered to the multiple uses of the stem cells, within pharmacological re-

search, developmental biology, and transplantation therapies. These uses were made possible through pluripotency. Another important use had to do with the source. Although some objected to the use of "spare embryos", others, who were pro-life, supported federal funding of hESC research which used this source.

Chapter 4 brought out the meta-theoretical tensions resulting from applying both of these models to the same situation. Both enabled an understanding of the sociotechnical reality (especially considering the political and public dynamics) of hESCs in the USA, 1998–2001, in terms of agency and coordination.

Common to the two analyses was that actors articulated the hESCs with reference to the pluripotent capacities and the ensuing urgent and multiple uses of the stem cells. However, there were also striking differences. In the OPP case the hESCs were objects of disputes and involved in total transformation and funneling. In the boundary object coordination actors were partially connected to the hESCs even without a total federal effort behind hESC research. In the first case sociotechnical reality was presented as an either-or. In the second case the hESCs were relatively real through the flows among many actors already.

One solution to these apparent contradictions was to distinguish between actuality and potentiality. The OPP was a pattern in the negotiations of *future* linkages. The boundary object coordination *was there* as early as 1998. It was furthermore strengthened towards the end of the period, in 2001, when pro-life politicians supported federally funded research on hESCs.

A second solution was more extensive and suggested different roles of hESCs in relation to specific loops. I drew on Latour's circulatory system and suggested that OPP and boundary objects were modes of coordination in different flows within one circulatory system of science and society. Among non-dominating actors there was a distributed mode of coordination. In relation to the Federal administration, the hESCs were involved in an OPP funneling – in sharp competition with adult stem cells positioned as an alternative point of passage. The combination of OPP and boundary objects was thus a solution to the second meta-theoretical question about how to approach explicit politics in ANT: One way to account for dominant actors with high stakes involved is to consider an OPP-like mode of coordination. Typical cases would be negotiations where whole countries, states, or a Federal administration are engaged.

However, seeing hESCs as boundary objects in analogy with Star and Griesemer's case was problematic. I pointed to the glitches between the two cases. Whereas the hESCs were involved in the flows typical of the boundary objects, they were more strongly structured than boundary objects. Spare embryos, pluripotency, and transplantation therapies were elements that constrained the implications and uses of the hESCs in specific ways. hESCs were involved in flows, not merely as coordinators, but also as objects configured in a specific way, constraining and defining other actors. They were boundary objects, but due to the three elements the hESCs had a stronger agency than in Star and Griesemer's case. I suggested that these boundary-transcending composite entities were more appropriately called *boundary packages*.

In three ways, then, part one is an exercise in different seeing. *First*, the two models helped me not to separate "biological and political pluripotency". The OPP and the boundary object approach brought out the connections between stem cells, their capacities, multiple uses and various actors. Biological pluripotency was "seamlessly" conjoined to other flows. This did not question the notion of biological pluripotency, but insisted on the potential and actual flows in which the stem cells were involved. *Second*, I suggested an integrated model drawing on Latour's *circulatory system*, Vissac-Charles's combination of OPP and boundary objects, and my own focus on the public and political dynamics. My integrated model is an exercise in *seeing* existing notions within ANT (and related approaches) *differently*. Instead of assuming that sociotechnical reality is coordinated homogeneously, two modes of coordination (at least!) can co-exist. *Third*, I suggested a new way of seeing the coordination of diverse actors through a boundary object with stronger agency. My boundary package is both a coordinator in flows to diverse actors and a strongly structured combination of elements.

In part one the actors were taken at their word about the uses (transplantation therapies), the material sources ("spare embryos"), the pluripotent capacities, and the environment (the flows to diverse actors of patients, politicians, scientists, and more). These aspects of the hESCs were *connected to each other* in part one of the study, but not *unpacked*.

Part two of this study was devoted to understanding how the sociotechnical reality of hESCs came about in 1998–2001. Unpacking the heterogeneous elements of hESCs would be to unpack the sociotechnical reality of hESCs. I thereby assumed that neither the configuration of

hESCs (and the three elements) nor their flows among actors were inevitable but had come to be.

To approach these two aspects of the sociotechnical reality of hESCs, I went backwards to search for articulations of hESCs before the successful cultures of hESCs were announced to the public. One such site for public and political debates about hESCs was the 1994 national panel about human embryo research (the HERP). In these debates and their aftermath I found a pre-existing project distributed among proponents of federally funded research. Such actors were making diagnoses and prescriptions to improve future negotiations. Interestingly, these attempts to improve coordination involved both the uses and the material sources that were later part of the articulations of hESCs. Like in 1998–2001 ”spare embryos” and transplantation therapies were brought up, although less consistently and not primarily in relation to hESCs. The latter only existed as anticipated paper entities at the time.

These observations prompted a hypothesis about the boundary package. Being made of ”spare embryos” and being useable in transplantation therapies, the object fitted an already existing project. Thus hESCs were coordinating actors that were mobilized in a previous, failed project. The package was able to coordinate actors since it was a package of at least two elements that were somehow already stabilized.

I tested this hypothesis by going further backwards to see how these elements had been stabilized and what circulations they were part of. I found that the two elements were already stabilized and, as such, were already involved in coordination among specific actors.

My suggestion was that multiplication, stabilization, and coordination were “sticking” to the IVF and frozen embryos that were part of prescriptions after 1994, and, after 1998, part of articulations of hESCs.

The stabilization of transplantation therapies and the coordination of patients, scientists, and politicians during the debates in 1987–1993 happened together. Crucial for this coordination was the appearance of a “moderate pro-life” group. This group included many of the congressmembers that later supported federally funded hESC research. In addition, I showed that this stabilization did not include all scientists. There were alternative spaces, other possible paths of stabilization that were not pursued.

The uses (transplantation therapies), the sources (”spare embryos”), and the environment (the diverse actors of patients, politicians, scientists, and more) were not there inevitably, but were mutually and gradually sta-

bilized. In the final empirical chapter, the pluripotency ascribed to the hESCs was also unpacked.

Actors' calls for "spare embryos" and transplantation therapies after the HERP indicated pre-existing anticipation and coordination attempts. Chapter 6 displayed the mutual stabilization and coordination related to the two elements. These accounts suggested that the coordination of politicians, scientists, and patients around the hESCs was due to the pre-existing flows of "spare embryos" and transplantation therapies. However, nothing was said in Chapters 5 and 6 about how these elements were combined with the hESCs.

Chapter 7 approached the question of how the articulations of hESCs included the two elements. The answer to this question was that "spare embryos" and transplantation therapies were "fitted" to the hESCs in several ways. Already existing frozen embryos became an element of hESCs by being used in the production process and in bioethical articulations of hESC research. By dismissing deliberate creation of embryos for research, the source of hESCs became almost exclusively "spare embryos".

The hESCs' position between legally protected embryos and the developmental capacities needed for transplantation therapies was correlated to terminological definitions; the pluripotency of hESCs was situated between the totipotency of embryos and the multipotency of adult stem cells. Through the handling of "spare embryos" and the term pluripotency, the hESCs were "hooked on" to the already existing, stabilized, and flowing elements of transplantation therapies and "spare embryos".

In part two of the study seeing differently was exercised by suggesting that the sociotechnical reality of hESCs was a result of the management of pre-existing elements and their flows among actors. In these pre-existing processes "spare embryos", transplantation therapies, pro-life supporters of research using fetal materials, and pluripotency were fitted to each other. The articulations of hESCs were not an inevitable result of biological research or stable social interests, but a combination of heterogeneous elements that could have been otherwise.

A few more points need to be made concerning *the analytic contributions* that follow from this analysis. They are at least four: the strong boundary object, the analytic tool of multiple circulations, the ensuing modification of stabilization processes, and a fourth contribution that follows from opening up the black boxes of IVF and transplantation therapies.

Drawing on Star and Griesemer's approach helped me see the coordination among diverse actors and the multiple uses. It also made me look

for a project and active management of the hESCs. I found something reminiscent of a project in the HERP debates. I also found traces of management in the terminological calibration of pluripotency and the material and discursive use of ”spare embryos”. The real work done by means of the notion of *boundary package* was tangible both above and in part two. By observing the three integral elements of hESCs, two things were assumed in the ensuing analysis; the *configuration* of the package happened together with the *coordination* of actors. The boundary package is the result of those two processes. In the stabilization of the elements of the *package*, coordinating flows across *boundaries* were established. Thus, the notion helped to keep a double view of the stabilization of each element, and their flows.

In Chapter 4 the metaphor of circulatory system of multiple loops was brought in to clear up the theoretical incoherence between the OPP and the ecological approach. In Latour's model there are interlocking loops. His example was Joliot's chain reaction, where the flows are *concentric feedback loops* managed by one person. In the case of hESCs, there were loops to diverse actors centered on the stem cells. I argued that agency was much more distributed in the hESC circulatory system than in Joliot's. These observations challenged the notion of a centered circulatory system. In the case of hESC research, there were interlocking flows, but they were not managed by one human or protecting one space.

During the later chapters, the circulatory system became even more distributed. This called for a modification of Latour's circulatory system and loops to capture the distributed dynamics. When unpacking the ”spare embryos” and the concept of transplantation therapies, I suggested that distinct and *multiple circulations* were found that had developed totally independently of hESCs. The elements in the hESC package came with already existing linkages. In the hESC case, ”spare embryos” were linked to a number of actors, but when they were combined with hESCs in laboratories and in the panel reports, there was no easy transfer. Some used IVF practices and ”spare embryos” as an argument for hESC research, while others opposed the use of ”spare embryos” but did not oppose IVF. Something a little more fluid was needed, without giving up to a boundless, amorphous topology. Circulations were appropriate because of their combination of fluidity and restrictions. Circulations exist in vessels, veins and canals, but under the right conditions they can be redirected or break through. Circulations also move and exist like niches

in ecologies. Like *niches* they are not necessarily hegemonic. They can move separately even if joined to other circulations.

I have called these flows *multiple* circulations, not only to signify that there are many of them, but also to put flesh on Latour's (and others') talk of multiple reality. This was tangible when I mapped the stabilization of multiple circulations in the later chapters.

Within IVF research there were two distinct processes, or stabilities: one within Congressional politics, and one within IVF clinical practice. Since 1980 there has been insufficient political support for publicly funded IVF research. Attempts have been made to change the policy, but they have failed. This constituted a stability in the federal, explicitly political arena. In another arena a different process took place. From the mid-1980's, excess embryos were frozen because of the development and increasing use of superovulation drugs and cryopreservation. This was a quantitative kind of stabilization that happened in isolation from the political processes. The sociotechnical reality of IVF was thus not one circulatory system but made up of multiple quite distinct circulations. In the federal circulation, IVF was a problematic technique that could not be publicly funded. Here ethical and political concerns were formulated in relation to, as it were, an already existing technology. However, the technology was not only "already existing" but was also being constructed and configured in a specific way. In the clinical circulation, the flow of newborns, "new-parents", and frozen embryos was increasing each day at a number of clinics. Ultimately, unsuccessful efforts were made to change the federal policy but the two circulations were kept separate.

Paradoxically, this separation was shown to be a co-productive factor in the stabilization processes. After the announcements of successful cultures of hESCs in 1998, the clinical IVF practices contributed to the sociotechnical reality of hESCs because they had stabilized and multiplied frozen embryos away from federal regulations. The two, previously separated, circulations were suddenly entangled in each other. The "standard, necessary treatment" that had resulted in some hundred thousands of frozen embryos was a discursive and material resource in the negotiations of hESC research. The clinical circulation did not change the political process concerning IVF, but it did contribute to the political process concerning hESC research.

I showed how the stabilization of IVF only makes sense if the circulatory system is split up into multiple circulations that are stabilized sepa-

rately and may or may not be combined at some point. Although transplantation therapies offered a different situation, something like multiple circulations was needed to capture the dynamics.

Transplantation therapies were also stabilized differently in distinct circulations. They were a scientific and medical possibility among patients, politicians, and corporations. The expected improvements in the original patients did not last, if they showed up at all. Immunosuppression was (and still is) a big problem. In relation to actual treatment programs, the degree of stabilization is to this day (2006) quite low. Transplantation therapies were, I suggested, just *less real* in these circulations of experimental and clinical results among scientists.

The disparities between scientists, on one hand, and patients and politicians, on the other, made visible the fact that neither stabilization nor reality is monolithic but multiple. While stable in relation to some actors, the element of transplantation therapies was, and still is, unstable and uncertain in relation to others. The multiple measurement of stabilization, one for each discernable circulation, is an important benefit from seeing the reality of multiple circulations.

In both cases, I have shown how it could have been different. It was the Federal administration's non-involvement and *laissez-faire* that indirectly resulted in the "spare embryos". "Standard" IVF developed in a "hands-off" landscape where a hundred flowers could blossom under the influence of clinical competition and certain technological possibilities. Had the Federal administration chosen not to "wash its hands" (like Pilate) but been involved, alternative procedures might have prevented the stores of frozen embryos. The result could have been new knowledge about oocyte-freezing. Without hundreds of thousands of embryos, the negotiation of hESCs in 1998–2001 might have been played out very differently.

The Federal administration could have adopted an involvement strategy in the fetal tissue research too. With serious participation the scientific uncertainties and the editorial calls for more animal experiments and patience (rather than patients) could have prevailed. Now, there was an either-or articulated as the perceived consequences of abortion rates. President Bush (Sr.) proposed banking of tissues from spontaneous abortions. If this proposal had been tried from the beginning, the patient mobilization might have been different. With the moratorium in place, the tone and intensity of mobilized organization and individuals grew. Scientific uncertainties were not highlighted. The medical possibility was

bracketed and implicitly assumed. Therefore, by 1998, and as early as 1994, transplantation therapies were an element already linked to a circulation of public and political support.

However, these scenarios of "it could have been otherwise" do not mean that "anything goes". These alternative scenarios implicitly assume both cross-roads and path-dependencies. By locating cross-roads in the over-production of embryos and oocyte-freezing, I am assuming that IVF could not have been stopped as such. I am in fact assuming the development of IVF in conferences, clinics, and among thousands of patients. By locating cross-roads in the banking of alternative fetal tissue, I am assuming the push for transplantation therapies. Unpacking can find alternatives and forks in the paths of stabilization, but in so doing many dependencies and stabilities are implicitly assumed.

To conclude my conclusion in a few sentences: the coordination of diverse actors and the articulations of hESCs in terms of "spare embryos", transplantation therapies, and pluripotency have evolved together. The hESCs are composite objects consisting of at least three elements involved in multiple flows to diverse actors, i.e. *pluripotent circulations*.

Glossary

Actor can be two things: An entity exercising agency as a result of its position in a network. As such, "actor-ship" is the main topic of the study; understanding the emergence, distribution and location of agency. More often, the *term* actor in this study refers to any human entity analyzed, for instance politicians, scientists, ethicists, pro-lifers. Nonhuman entities are usually referred to as elements, or entities. Terminologically separating human and nonhuman entities thus is clearly inconsistent with ANT. It is a consequence of taking seriously the implicit asymmetry of generalized symmetry (see below). The main task of this study is not to claim an equality between humans and nonhumans, but to display the emergence of reality and agency in which nonhumans are important elements.

Actor-networks are more than networks of associations. It is not hard to find networks. What makes a network an actor-network is that the analyst attends to how the *agency* is distributed and relocated irrespective of whether the network entities are human or nonhuman. This character of actor-networks is emphasized in the thesis of *generalized symmetry* (see below). An entity that displays potency, such as the hESCs, can be understood by tracing the network(s) packaged within the entity. In this sense agency is a network effect without being *reducible* to the network (thus: irreducible). Otherwise actors would be not be actors but placeholders for other more fundamental actors.

Agency (see *Actor* and *Actor-networks*).

Articulation is the ontological movement in which the world and its *entities* or *elements* come to be by being associated (see *association*) while also being methodologically accessible e.g. through texts. Instead of seeing textual statements as representations of a reality out there, the use of articulation indicates that statements participate in making things real (which may ultimately be unsuccessful). A person can thus *be articulated*

and actively *pursue articulation*. An example of the former is a pro-life Senator who is said to have betrayed the pro-life cause. S/he risks becoming a little less pro-life through this articulation. S/he may also claim that adult stem cells are pluripotent, and be pursuing articulation. Other related terms for this are *translation* and *construction*. The most utilized alternative will be *coordination* (see below). Its function is however similar, viz. to combine and align disparate elements (usually humans) with each other.

Association, or *linkage*, is what is achieved by articulation (see also *dissociation* below). Together with articulation it is the most fundamental unit of analysis. Potency or agency is the result of associations. An association can occur in texts as the combination of one entity with another. It can happen in practice when a scientist puts cells into the brain tissue of a patient, or of a mouse; when a corporation makes contact with a particular scientist to fund him/her; when a patient organization decides to support an umbrella organization lobbying for more funds to stem cell research; or when a pro-lifer claims that fetal-tissue research has effects on the abortion rates. There are no a priori realms that delimit which entities can be associated with each other. Together, associations make up networks of actors (see actor-network above).

Boundary objects: Through the management of boundary objects and their flows, diverse (human) actors can collaborate in spite of diversities and without full alignment, i.e. the actors can remain in their respective worlds. Coordination without full alignment is possible because of the plasticity of boundary objects, together with a common identity that is not negated by specific uses in diverse practices. The resulting network is more or less stabilized depending on the number of participating actors. Coordination through boundary objects does not assume a central entrepreneurial force, funneling and transforming actors as does the notion of obligatory point of passage (see below).

Circulations: see *Multiple Circulations*.

Coordination is used here as in Star and Griesemer's case study (1989). Its function is similar to articulation, viz. to combine and align disparate elements (usually humans) with each other. Whereas articulation emphasizes the ontological event of combining entities, coordination does have such innovating, transforming and ontological effects, but the emphasis is on actors that remain in their worlds. Without total consistency I use coordination more often in relation to humans who can collaborate in

spite of differences. I use articulation in relation to both humans and nonhumans.

Dissociation is the noun (and *dissociate* the verb) that is the opposite of association. Articulations may dissociate elements from each other, as for instance when embryonic stem cells are defined as being of less developmental potential than embryos, or when fetal-tissue research is regarded as separate from the act of abortion.

Generalized symmetry is the programmatic placing of humans and things (or "nonhumans") on an equal footing with regard to their roles in actor-networks. In ANT all entities in a network can be actors depending on the delegation of agency. Classic examples of how agency is delegated from humans to nonhumans is the construction of a traffic light or a speed-bump. By constructing these in a particular way, humans are affected and restricted in more powerful ways than if they were only told to slow down. Delegated agency is thereby delegated back from nonhumans to affect human behavior. However, few examples of delegation in fact *start* in nonhumans delegating to humans. Although being placed on an equal footing theoretically, humans and nonhumans do differ in most ANT cases. Basically humans seem to be much more suitable for delegation than nonhumans because of humans' greater capacities to delegate to nonhumans. The master-delegator is human. Generalized symmetry also denies that either nature or society are the causes of knowledge, truth, or reality. Instead it is the analyst's job to follow how nature and society become categories, distributed as an effect of other processes.

Modes (or forms) of coordination, or *modes of articulation*. Two modes of coordination are fundamental in this study: obligatory point of passage and boundary objects. When these concepts are applied to the case of hESC research the two modes are seen to be co-existent and less clearcut than in previous studies. Therefore I (usually) choose to talk of boundary object-like, or boundary-transcendent coordination, versus an OPP-like, funneling, or exclusive coordination. The point is to see how coordination, articulations, and associations can happen in many ways. An association with the Federal administration is not the same as associating the cells with another ethicist, one more company, or another tissue-type. Depending on the mode of coordination (and on what circulation), associations come to have different implications.

Multiple circulations are one way to acknowledge that articulations occur in different places and in pre-existing activities with specific traits. The notion is derived from (Latour's) *Pandora's Hope* Chapter 3, and it is also

suggestive of Star and Griesemer's understanding of flows of boundary objects between social worlds. In contrast to these other examples of flows, multiple circulations are not necessarily concentric, focused on one project or on one human, but may be independent of each other. Multiple circulations may open for marked analytic differences between the stabilization of an object in different arenas. For instance, fetal-tissue transplantation is not necessarily flowing or coordinating in the same way in laboratories versus Senate hearings. Entities are linked to each other in a topography of already existing actor-networks with their own dynamics, structures and currencies. In this respect multiple circulations remind one e.g. of *social worlds*, but without the clear boundaries of the latter.

Obligatory point of passage (OPP) is one of two main models (in this study) for how elements are articulated and coordinated, how agency is distributed and actor-networks are built. In the classic case studies a number of actors were all funneled through one definition of a situation in which a small group of entrepreneurs was positioned as an OPP. The resulting actor-network is either a total success, and subsequently of a dominating character, or a total failure. Many things affect the success of an OPP attempt. A weakening aspect is the articulation of alternative points of passage (APP).

Politics is often treated in ANT as the *politics of things,* i.e. the values and political implications congealed in stable objects, thus invested with a specific agency, competence or politics (see *Actor* and *Actor-networks*). I refer instead to *explicit politics* which corresponds to the commonsense understanding of political activity that should be considered (just as scientific activity) in order to understand the reality of hESCs. While both activities deal with chains of humans and nonhumans (and without reinstating a total separation) explicit politics is more specialized in managing voices and the agency of humans (e.g. in hearings), while the decisive skill of scientific activities takes care of nonhumans (e.g. in laboratories).

Reality or *sociotechnical reality* is a result of articulation and stabilization. There is no one underlying causal reality, not a social versus a natural reality, neither is there a chaos of the myriad of realities of all articulations. Reality is not "out there" but right here in the associations and articulations of entities. One of Latour's well-known examples is how the Amazon forest, step by step, through visits, soil samples, use of international standards for soil quality, is ultimately transferred to the claims in a scientific article. Nowhere in that chain is it possible to say where reality stopped and became a representation. Asking for the reality of hESCs is

to ask for the entities associated with the cells. Two aspects of how reality come to be are combined in this study. One is the *relative reality* that varies relative to the number of linked elements. Rather than an either-or, reality is gradually stabilized. This aspect can be related to the notion of *multiple circulations*. Gradual increase of reality in one circulation does not necessarily imply the same degree of stability, or the same combination of entities, in all places. The relative reality is thus c*ompartmentalized and multiple*.

Reference: Not of a referent "out there", but what holds together a number of flows and is held together by a number of flows. The sciences do not establish a reference by isolating themselves, but by establishing successful flows, or circulations, in which the reference is used or supplied with money, public, collegial, or instrumental support. A reference to hESCs as pluripotent thus makes possible many other flows and is made possible through certain flows. In Chapter 7 this is salient, as the reference to pluripotency connects a circulation of fetal-tissue transplantation among patients and politicians to hESCs, while being defined by the circulation among scientists.

Representation in its traditional meaning is the opposite of articulation since it builds on a separation of words about the world, and the world, in which articulations are continually creating bridges between elements that may be more linguistic or more material. Actors can still represent other actors by speaking for them, whether they are pro-life voters or stem cells. Representations are thus not true or false but more or less faithful to the ones spoken for. This notion is necessary to understand how a few individuals out of 300 million Americans can produce articulations that significantly add to or subtract from the reality of hESCs.

Stabilization: Elements combined into articulations may result in chains, black boxes, or network nodes with a lot of invested agency. The more elements in the chain the more stable the object. Where a natural realist may talk of something existing or not, or being true or not, this study maps a successive stabilization. Such processes can be reversed, but it takes hard work to unpack them. Since the articulation of one object may happen in many circulations its successive stabilization may be the result of several chains or *multiple circulations* originally distinct from each other.

Unpacking is the crucial analytic activity of this study. It consists in finding out what has happened in the stabilization of an element, or an actor, i.e. what entities have been combined to form a new entity. One

example is “spare embryos”, which are the result of not only a sperm and egg, but of infertile clients visiting private, unregulated clinics where specific technologies are used in order to extract and fertilize more eggs than used in one treatment cycle and then to freeze the surplus embryos.

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