Healing Cartilage
-Aspects on Regenerative Methods

Akademisk avhandling

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av

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The thesis is based on the following studies,
referred to in the text by their Roman numerals:

I. Enochson L, Sönnergren H, Mandalia V, Lindahl A. (2012) Bipolar radiofrequency plasma ablation induces proliferation and alters cytokine expression in human articular cartilage Chondrocytes. *Arthroscopy*. 28(9), 1275-1282

II. Enochson L, Brittberg M, Lindahl A. (2012) Optimization of a chondrogenic medium through the use of factorial design of experiments. *Biores Open Access*. 1(6), 306-313

III. Enochson L, Stenberg J, Brittberg M, Lindahl A. GDF5 reduces MMP13 expression in human chondrocytes via DKK1 mediated canonical Wnt inhibition. (*Submitted, Osteoarthritis and Cartilage*)

IV. Boreström C, Simonsson S, Enochson L, Bigdeli N, Brantsing C, Ellerström C, Hyllner J, Lindahl A. Footprint free human iPSCs from articular cartilage with redifferentiation capacity – a first step towards a clinical grade cell source (*Submitted, Stem Cells Transl Med*)

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Abstract

Articular cartilage has poor intrinsic capacity to heal and defects can cause severe pain for the patient. If the healing process is not assisted the damage might deteriorate and lead to the onset of osteoarthritis. Autologous chondrocyte implantation is a successful method in treating focal cartilage defects, with good clinical outcome. Low cellularity of the tissue and low proliferative capacity of the chondrocytes are limitations to the treatment.

The aim of the present thesis was to improve assisted articular cartilage healing and to evaluate how an eventual osteoarthritis progression could be halted. In particular, we investigated how anabolic chondrogenic processes in chondrocytes and chondrocyte derived induced pluripotent stem cells can be improved, thereby optimising the use of autologous cells in articular cartilage regenerative therapies and methods. Further, we studied if the application of plasma-mediated ablation can induce an anabolic response in the chondrocytes. Finally, we investigated how GDF5 signalling, a pathway implemented in the development of osteoarthritis, affects cartilage homeostasis.

The results indicated that plasma-mediated ablation induces an anabolic response in chondrocytes. ECM production by the chondrocytes was improved by optimizing the standard chondrogenic medium through the use of factorial design of experiments. We were able to demonstrate that GDF5 can contribute to the redifferentiation process, and has potential in inhibiting degenerative processes in the cells. Finally, the reprogramming of chondrocytes into induced pluripotent stem cells showed that these cells could be useful tools in the determination of cell signalling pathways in tissue regeneration and disease.

In conclusion, the methods investigated in this thesis can be used to improve the regenerative capacity of the articular chondrocytes and the thesis sheds further light on the intricate problems of healing cartilage.

Keywords: Cartilage, regeneration, osteoarthritis, induced pluripotent stem cells, factorial design, growth factors

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