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Expression of Tissue Antigens in Human Pluripotent Stem Cells and Alterations During Differentiation

Potential application in regenerative medicine for treatment of terminal cell and organ failure

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Hörsal Arvid Carlsson, Medicinaregatan 3, fredagen den 16:e juni, klockan 09.00.

av
Karin Säljö

Fakultetsopponent:
Docent Martin Johansson
Lunds Universitet

Avhandlingen baseras på följande delarbeten:

I. Barone A, **Säljö K**, Benktander J, Blomqvist M, Månsson JE, Johansson BR, Mölne J, Aspegren A, Björquist P, Breimer ME, Teneberg S. Sialyl-lactotetra, a novel cell surface marker of undifferentiated human pluripotent stem cells. *Journal of Biological Chemistry 2014; 289*, 18846-18859

II. **Säljö K**, Barone B, Vizlin-Hodzic D, Johansson BR, Breimer ME, Funa K, Teneberg S. Comparison of the glycosphingolipids of human-induced pluripotent stem cells and human embryonic stem cells. *Glycobiology* 2017; 27: 291-305

III. **Säljö K**, Barone A, Mölne J, Rydberg L, Teneberg S, Breimer ME. HLA and Histo-Blood Group Antigen Expression in Human Pluripotent Stem Cells and their Derivatives. *Manuscript, submitted*

SAHLGRENSKA AKADEMIN
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Potential application in regenerative medicine for treatment of terminal cell and organ failure

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ABSTRACT

The major limiting factor in the treatment of patients with end-stage organ failure is the insufficient number of human organs available for transplantation. An unlimited access to human cells, tissues and organs would also open up possibilities to treat several chronic diseases, such as diabetes, neurological and cardiovascular diseases, affecting millions of patients worldwide. Cells and tissues derived from human pluripotent stem cells (hPSC) could potentially fulfill these ambitions. However, there are several biomedical barriers to overcome before this can be a clinical reality. One of the most important concerns is the immunogenicity of the conceivable cell or tissue grafts derived from hPSC when exposed to a non-self recipient.

This thesis explores the expression of immunogenic tissue HLA and blood group antigens in several hPSC cell lines and their derivatives. This characterization was performed by several complementary analytical techniques, such as flow cytometry, immunohistochemistry, PCR, as well as biochemical characterization of glycosphingolipid molecular structures and protein bound antigen composition. The results demonstrate that pluripotent stem cells express various cell surface immunodeterminants including HLA, AB(O)H and related histo-blood group antigens. Moreover, we identified significant alterations of antigen expression patterns during endodermal, mesodermal and ectodermal differentiation. Consequently, our results indicate that all hPSC-derived cells intended for clinical applications should be characterized regarding their individual tissue antigen profile in accordance with the standard selection criteria used in allotransplantation. Furthermore, we identified a novel cell surface marker of undifferentiated stem cells, sialyl-lactotetra, which can be used as a verification and selection tool for pluripotency, as well as a potential exclusion measure in heterogeneously differentiated cell cultures to prevent tumor formation.

In conclusion, this thesis adds new knowledge regarding cell surface antigen expression in hPSC of relevance both for basic science and for future clinical applications within transplantation and regenerative medicine.

Keywords: Pluripotent stem cells, Differentiation, Histo-blood group antigens, HLA, Tissue antigens, Cell surface antigens, Sialyl-lactotetra, Transplantation, Regenerative medicine.

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