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HUMAN DERMAL FIBROBLASTS IN TISSUE ENGINEERING

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Johan PE Junker, PhD student in the field of experimental plastic surgery. Born 1980 in the idyllic city of Nyköping, Sweden. He is the author of this doctoral thesis, as well as several articles in the field of tissue engineering and reconstructive surgery.

He is a firm believer of the positive effects of caffeine induced research and writing scientific papers accompanied by rock music. After nine years at Linköping University, he now sets sail towards greener pastures and a continued academic career.

The loss or failure of tissues and/or organs is one of the most frequent problems in modern healthcare. The field of tissue engineering applies the principles of biology and engineering in order to develop functional substitutes for damaged tissues. Tissue engineering contains elements of medicine, material science and engineering with major components in focus being cells, biomaterials and soluble factors. All three components may be required for the development of clinical treatments.

The usage of autologous tissue specific cells for clinical treatment is often not feasible due to poor growth kinetics or unstable phenotypes of the cells. Furthermore, lack of availability of healthy tissue that can be biopsied is a major problem in many applications. One approach to overcome this problem is to use adult stem cells which have the capacity to give rise to several different cell types. Although promising, adult stem cells have major impediments for use in several tissue engineering applications. The difficulties associated with harvest, culture and storage render problems in the development of clinically relevant procedures.

During the last years, the inherent plasticity of differentiated somatic cells has been demonstrated. One of the easiest human cell types to obtain, expand and store is the dermal fibroblast. Recent reports indicate that dermal fibroblasts can be induced to differentiate towards several distinct mesenchymal lineages *in vitro*.

The main aim of this thesis was to investigate the inherent stem cell plasticity of human dermal fibroblasts and explore their possible usefulness in tissue engineering applications. The papers included in this thesis employ routine and immunohistochemical staining, enzyme activity assay, analysis of low density lipoprotein incorporation, capillary-like network formation assay and full expression micro array analysis.

Fibroblasts were shown to differentiate towards adipocyte, chondrocyte, endothelial and osteoblast-like cell types *in vitro*. The differentiation from fibroblasts to myofibroblasts in burn scar tissue upon stimulation by mechanical tension was also demonstrated. Adipogenic, chondrogenic and osteogenic induced fibroblasts display the upregulation of several genes associated with adipocytes, chondrocytes and osteoblasts.

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