Unlimited Source Of Chondrocyte-Like Cells: How Far Are We?

Ewelina Stelcer[1], **Magdalena Richter**[2], Tomasz Trzeciak[2], Katarzyna Kulcenty[1], Marcin
Rucinski[3], Karol Jopek[3], Wiktoria Suchorska[1]

1. Greater Poland Cancer Centre, Poznan, Poland
2. Department of Orthopaedics and Traumatology, Poznan University of Medical Sciences, Poznan, Poland
3. Poznan University of Medical Sciences, Poznan, Poland

Keywords: Chondrocytes, Regenerative Medicine, Stem Cells, Articular Cartilage

Background

Stem cells (SCs) application is a promising approach to regenerative medicine, with the potential to treat numerous orthopaedic disorders, including osteoarthritis. The development of human induced pluripotent stem cells (hiPSCs) has increased the potential of SCs for new treatments. Human articular cartilage (AC) has a poor regenerative capacity. Therefore, extensive studies on AC regeneration, including the cell-based tissue engineering research, are carried out. However, more data are required to improve the understanding of key aspects of cell differentiation process, including the way specific chondrogenic processes affect gene expression profile of chondrocyte like cells.

Objectives

Based on the novel chondrogenic differentiation protocol, this study has two main aims: a) to investigate gene expression profile via high-throughput analysis of obtained chondrocyte-like cells and b) to examine most markers characteristic of functional chondrocytes in those cells.

Study Design & Methods

• Differentiation of hiPSCs throughout monolayer culture with the addition of defined growth factors (GFs) was carried out. • Global gene expression microarray was performed and analysed using GeneAtlasTMWT Expression Kit Assay and AffymetrixGeneAtlasTM Operating Software. • The expression of selected genes was confirmed by qRT-PCR.

Results

The differentiated hiPSCs acquired chondrocyte-like cell morphology. Based on microarray data, the obtained chondrocyte-like cells differentiated from hiPSCs, possess significantly decreased expression of genes characteristic for pluripotent SCs (e.g. LIN28, NANOG, NODAL). Particularly decreased expression of genes involved in SC population maintenance, Wnt signaling, somatic SC population maintenance and formation of primary germ layer pathways were observed. Furthermore, our cells demonstrate increased expression of genes specific for early chondrogenesis (inter alia limb development, limb morphogenesis, embryonic skeletal system development) such as HOXD13, HOXB6 and EYA1. Finally, the generated chondroprogenitors also show the expression of desirable markers such as type II collagen, COMP and aggrecan.

Conclusions

Our results obtained in this study show that hiPSCs were differentiated toward chondrogenic lineage via previously established protocol. The chondrocyte-like cells derived from hiPSCs lost pluripotency markers. Moreover, gene expression profile of obtained hiPSC-derived cells proved that that we generated theoretically unlimited source of human chondroprogenitors. This promising approach could be potentially used in articular cartilage regeneration.