Characteristic Markers of the WNT Signalling Pathway Are Differentially Expressed in Osteoarthritic Cartilage

A. Thorfve\textsuperscript{1, 2}, T Dehne\textsuperscript{3}, A. Lindahl\textsuperscript{1, 2}, M. Brittberg\textsuperscript{4}, A. Pruss\textsuperscript{5}, J. Ringe\textsuperscript{3}, M. Sittinger\textsuperscript{3}, C. Karlsson\textsuperscript{1, 2}

Corresponding Author: anna.thorfve@medic.gu.se

\textsuperscript{1} Institute of Laboratory Medicine, Department of Clinical Chemistry and Transfusion Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden \textsuperscript{2} BIOMATCELL VINN Excellence Center of Biomaterials and Cell Therapy, Gothenburg, Sweden \textsuperscript{3} Tissue Engineering Laboratory and Berlin-Brandenburg Center for Regenerative Therapies, Department of Rheumatology and Clinical Immunology, Charité-Universitätsmedizin Berlin, Germany \textsuperscript{4} Department of Orthopaedics, Sahlgrenska University Hospital, Gothenburg, Sweden \textsuperscript{5} Institute of Transfusion Medicine, Tissue Bank, Charité-Universitätsmedizin Berlin, Germany

Introduction

Gene expression profiling of osteoarthritic (OA) bone has demonstrated dysregulation of several WNT-related genes. The lack of knowledge concerning WNT signalling in OA cartilage prompted us to perform a comprehensive gene expression analysis of WNT markers in human articular cartilage obtained from healthy donors compared to that of OA patients [1].

Materials and Methods

Microarray analysis of cartilage biopsies from 5 OA- and 5 control donors (ND) was performed. Results were verified by qRT-PCR and immunohistochemistry. Statistical analysis was performed using the Mann-Whitney U test and Wilcoxon paired signed rank test.

eFig.1. Schematic summary of the results obtained from the microarray analysis demonstrating WNT signalling in OA cartilage. Genes whose expression in OA cartilage results in a repressed (red boxes) or activated (green boxes) WNT signalling. +/-: positive or negative fold change in the microarray analysis.

Results

The microarray analysis demonstrated WNT signalling significantly regulated between OA- and ND cartilage [Fig.1]. Both real-time PCR and immunohistochemistry verified the microarray results.

Discussion and Conclusions

Both the canonical and planar-cell-polarity WNT signalling pathways were inhibited while the Ca\textsuperscript{2+}/WNT pathway was activated in OA cartilage. Activation of the Ca\textsuperscript{2+}/WNT signalling pathway and its effector molecules in OA cartilage could thus to some extent explain the increased apoptosis detected in OA chondrocytes as well as the altered matrix composition seen in OA cartilage. Our study provides a basis for future studies on the function of numerous newly identified genes in OA pathogenesis and on their suitability as drug targets in OA.

References


Acknowledgements

We acknowledge BIOMATCELL VINN Excellence Center of Biomaterials and Cell Therapy, Region Västra Götaland, Swedish Research Council and EU’s sixth framework programme. We would like to thank Anja Wachtel and Sven Schurig for excellent technical assistance.

Disclosures

The author(s) declare that they have no competing interests.