University of Basel

DBM Basel
Department of Biomedicine

MASTER OF SCIENCE – THESIS PROPOSAL

INVESTIGATING THE EFFECT OF GDF5 KNOCKDOWN ON CARTILAGE HOMEOSTASIS.

Background

Osteoarthritis (OA) is a leading cause of disability, with no disease-modifying treatments available. Growth and differentiation factor 5 (GDF5) is a major OA risk locus and plays a crucial role in joint development and cartilage maintenance. Its expression declines during OA progression, correlating with increased catabolic activity and matrix breakdown. GDF5 exerts anabolic, anti-catabolic, and potentially anti-inflammatory func4ons, yet the mechanisms leading to its misregula4on in OA, and the contribution of inflammation to this process, remain poorly defined. We hypothesise that decreased GDF5 expression disrupts the balance between anabolic and catabolic signalling pathways, thereby promoting cartilage degradation, and that inflammatory cues drive this loss of GDF5. The objective of this project is to establish whether loss of GDF5 expression in human articular chondrocytes and chondroprogenitors induces catabolic effects or impairs chondrogenic differentiation.

This project offers MSc students the opportunity to investigate GDF5 function in human chondrocytes using cutting-edge gene-editing and tissue-engineering techniques, combining molecular biology with translational research.

Methods

Primary articular chondrocytes and chondroprogenitors (N=3 donors) will be isolated from knee joint specimens and expanded. GDF5 knockout (KO) will be achieved using CRISPR-Cas9 or shRNA delivered via electroporation, with potential AAV-mediated knockout considered later depending on project progression. KO effciency will be validated by qPCR and protein analysis. KO and control cells will be cultured in 3D chondrogenic microspheroids in the presence and absence of inflammatory cytokines. Resulting tissues will be analysed by histology (Safranin O for glycosaminoglycans, GAG, immunofluorescence), GAG/DNA quantification, to assess extent of extracellular matrix deposition and degradation, and by qPCR to quantify expression of key catabolic and anabolic genes.

Specific Requirements

Experience with cell culture, RT-PCR and histology would be helpful.

Time plan

Duration: 6 months (flexible), Expected start: 2026 (flexible).

Supervision & contact

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https://biomedizin.unibas.ch/en/research/research-groups/martin-lab/

References

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