University of Basel

DBM Basel
Department of Biomedicine

MSC THESIS PROPOSAL

NCIL1RA & OA Cartilage Organoids

Project Background

Osteoarthritis (OA) is a highly prevalent degenerative joint disease that causes pain, reduced motility,and diminished quality of life for many individuals worldwide. Furthermore, with our society's ageing population, the incidence of this musculoskeletal condition is expected to rise in the coming years. OA is influenced by various factor such as age, ethnicity, gender, genetic traits, or abnormal joint loading (e.g.: due to obesity, joint misalignment, or injuries). A primary characteristic of OA is the chronic inflammation that accompanies the gradual deterioration of articular cartilage, leading to a loss of function of the joint. Current treatment options, however, primarily focus on palliative care; as a result, the underlying degenerative processes continue leading to the necessity of total joint replacement in advanced cases. Nasal chondrocytes (NCs), an autologous cell source presently in clinical trial (phase II) for the repair of focal cartilage defects, represent a promising cell therapy alternative against OA but their performance in chronic inflammatory environments remain to be tested. In this framework, we aim to develop a new approach combining the intrinsic regenerative capacity of NC-based constructs with the therapeutic release of the anti-inflammatory signal Interleukin-1 Receptor antagonist (IL-1Ra). NCs will be genetically modified with the IL-1Ra gene, which is a natural inhibitor for activation of pro-inflammatory mediators and will be induced to generate Nasal Tissue Engineered Cartilage. Assessing the therapeutic potential of an advanced therapeutic approach like IL1Ra-NCs requires a representative in vitro model recapitulating OA pathophysiology. We have successfully created an in vitro OA-cartilage organoid model by exposing human bone marrow-derived mesenchymal stromal cells (hBMSCs) macromass to OA-relevant cytokine levels. In this project IL1Ra-NCs will be cocultured with OA-cartilage organoids to evaluate their potential as a therapeutic solution in a chronic inflammatory/degenerative environment.

Significance

The project will for the first time investigate the ability of NCs combined with an anti-inflammatory strategy to revert the phenotype of degenerated/hypertrophic cartilage in an OA-cartilage organoid model.

Goal and Pillars

The goal of this MSc thesis is to genetically engineer NCs with IL1Ra and assess their therapeutic effect on OA cartilage organoids. **In Pillar 1**, the candidate will generate OA cartilage organoids and IL1Ra-NCs according to established protocols. **In Pillar 2**, the candidate will assess the regenerative potential of these constructs evaluating their capacity to fuse with degenerated cartilage and to revert its inflammatory/hypertrophic phenotype by heteroculturing IL1Ra-NCs with OA cartilage organoids in screw top tubes.

Methods

Cartilage organoids will be generated in a pellet culture model using hBMSCs in an established chondrogenic medium formulation and then exposed to various inflammatory and hypertrophic factors to induce OA traits. Simultaneously, pellets will be generated using IL1Ra transduced NCs. Thus generated OA-cartilage organoids and IL1Ra-NCs pellets will be cocultured in a custom-designed hetero-culture system. In the hetero-culture system, the ability of IL1Ra-NCs to act as a cell therapeutic will be assessed. The cell repair potential of IL1Ra-NCs will be evaluated using RT-qPCR, ELISA and histology.

Profile of the Master Student

Duration: atleast 6 months (flexible), Expected start: February 2025 (flexible).

Contact

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References

1. https://doi.org/10.1007/s00018-020-03567-y
2. https://doi.org/10.1016/S0140-6736(16)31658-0
3. https://doi.org/10.1126/scitranslmed.aaz4499
4. https://doi.org/10.1242/jcs.00527

Short Description

The goal is to coculture IL1Ra transduced Nasal Chondrocyte cell pellets with OA cartilage organoids to assess their potential as a treatment for osteoarthritis. You will evaluate the cartilage regenerative potential of IL1Ra transduced Nasal Chondrocyte cells to repair Osteoarthrit-