Development of innovative therapeutic strategies for osteoarthritis: exploring thermosensitive hydrogels, hiPSC-derived cells and cell-products, and novel drugs in preclinical models

Sayedipour, S.S.

Stellingen behorende bij het proefschrift getiteld

Development of innovative therapeutic strategies for Osteoarthritis:

Exploring thermosensitive hydrogels, hiPSC-derived cells and cell-products, and novel drugs in preclinical models.

1- To facilitate the clinical translation of P407-based hydrogels for intra-articular delivery, a formulation consisting of 25% P407 supplemented with a self-assembling peptide is necessary **(This thesis)**.

2- The translational value of intra-articular biomaterials is defined less by their material novelty and more by their compatibility with clinical constraints such as injectability, reproducibility, and localized persistence **(This thesis)**.

3- Owing to their comparable therapeutic efficacy, superior reproducibility, and manufacturing advantages, hiMSCs clearly outperform autologous hBMSC therapies and are well positioned to support next-generation cell-based treatments **(This thesis)**.

4- Disease-modifying activity mediated by hiMSC-derived extracellular vesicles confirms their therapeutic benefit in osteoarthritis therapy, and positions hiEVs as a credible cell-free therapeutic strategy **(This thesis)**.

5- To speed the clinical translation of hiMSCs and hiEVs, serum-free culture conditions provide a practical xeno-free manufacturing strategy without compromising therapeutic efficacy **(This thesis)**.

6- Across preclinical osteoarthritis models, Iopanoic acid repeatedly demonstrated disease-modifying activity, supporting modulation of T3 signaling as a therapeutic strategy in osteoarthritis **(This thesis, Houtman, Evelyn, et al. 2023)**.

7- Combining advanced biomaterials with biological or pharmacological interventions is essential for achieving disease-modifying osteoarthritis therapies, as single-component approaches are insufficient **(This thesis, Huang, Huirong, et al.2022)**.

8- Clinical trial success rates are higher when therapeutic strategies are grounded in well-defined etiopathophysiology properties, supported by human genetic evidence **(Nelson et al., 2015; King et al., 2019)**.

9- Integration of mechanistic insight by spatial transcriptomics, establishes a rational framework for potency assays in advanced osteoarthritis therapeutics **(Zhou, Qiongfei, et al. 2025)**.

10- Scientific precision is not limited to experiments; it reflects a mindset of clarity, responsibility, and respect for truth **(Own proposition)**.