Internship proposition 2025-2026

(One-page max)

Master 2 GP Medicine 4R (Repair, Replace, Regenerate, Reprogram)

Lab: Inserm U1229

Team: REJOINT, Group HEAL

Name and position of the supervisor: Catherine LE VISAGE, Group Leader

Email of the supervisor: Catherine.levisage@inserm.fr

Candidate (if internship filled):

Title of the internship: A 3D model of an intervertebral disc for the evaluation of regenerative therapies

Summary of the internship proposal:

Low back pain, the leading cause of disability worldwide, is mainly linked to degeneration of the intervertebral discs. The degeneration process is characterized by catabolic events that lead to the degradation of the extracellular matrix and the loss of disc cells, ultimately altering the morphology and biomechanics of the disc, which results in pain and disability. Current treatments - drugs for the early degenerative stages and surgery for the more advanced stages - aim solely to control pain but do not treat the underlying degenerative processes. In contrast, regenerative medicine seeks to reverse the degenerative process and restore the integrity and function of the intervertebral discs. The main therapeutic strategies under development include biomolecules, biomaterials, cells, or their secretome. However, evaluating these new strategies relies on in vitro models, which do not accurately replicate the complex structure of a disc, and on pre-clinical models in large animals, such as sheep, which share physiological, anatomical, and biomechanical similarities with humans.

Therefore, this project aims to develop a clinically relevant in vitro model using biomanufacturing techniques to replicate the macro- and microarchitecture of the intervertebral disc, thereby reducing the need for animal experimentation. We have previously designed an in vitro intervertebral disc model that recapitulates the native cellular organization and phenotype of disc cells (Carrot et al., Int. J. Bioprint., 2025).

In this 3D model, we will evaluate the ability of human mesenchymal stromal cells and their extracellular vesicles to promote extracellular matrix synthesis and slow the degenerative process. Briefly, we will implement potency assays to assess the interactions between MSCs and MSC-derived EVs with ovine NP and AF cells, aiming to predict their biological efficacy in IVD regeneration. To address their functionality and regenerative potential, human MSCs and MSC-derived EVs will be injected into the NP compartment of the 3D bioprinted model via a transannular pathway. This evaluation will be carried out in parallel on ovine discs to validate the relevance and robustness of this new 3D model.

Techniques used in the project: Primary cell culture (bovine NP cells, Human mesenchymal stromal cells, ovine disc cells), Bioprinting, Ex-vivo organ culture of ovine IVD, cells / extracellular matrix evaluation (Histology, RT-qPCR, Elisa).

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Profile(s) linked to the project:

X Experimental Biology *(Recherche expérimentale)*

☐ Clinical Research *(Recherche clinique)*

☐ Research in data analysis (Recherche en analyse de données)