Internship proposition

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

Lab: INSERM UMR 1229 / RMeS - Regenerative Medecine and Skeleton

Team: Groupe BIODIV: “Stem cells and axial skeleton development” in

REJOINT Team "Regeneration and pathophysiology of joints"

Name and position of the supervisor: Anne CAMUS , CR CNRS, HDR

Email of the supervisor: Anne.Camus@univ-nantes.fr

Candidate (if internship filled):

Title of the internship:

Study of notochordal cell differentiation and maturation for intervertebral disc regeneration

Summary of the internship proposal:

Low back pain is one of the most common musculoskeletal disorders. Although aetiology is complex and not fully understood it is often associated with degeneration of the intervertebral disc (IVD). The disc ensures the function of a "mechanical stress absorber" within the vertebral column. During embryogenesis, Notochordal cells (NC) play major roles in vertebral column formation. Whereas NC disappear during the formation of the vertebrae, some NC persist in the fully formed disc and exert significant influence over its physiology. The loss of the NC with disc aging and degeneration has been correlated with IVD structural integrity deterioration. There is currently no effective treatment. This is largely due to a lack of basic molecular and cellular knowledge controlling disc development, growth, maturation, and homeostasis, during embryogenesis and at different stages of life [1, 2].

Precise understanding of normal tissue development and maturation, including cell-cell communication, cell-matrix interaction, gene regulation and growth factor control are critical in contributing to the identification of symptom-modifying factors or to the emergence of new therapeutic targets. This project combines fundamental studies on notochordal cells using innovative human induced pluripotent cells (hiPSC) differentiation systems [3, 4]. The major objective is to understand the regulation of the proliferation and the maturation of stem cell-derived notochord-like cells generated with our recently published hiPSC differentiation protocol using 3D culture and instructive bioinspired hydrogels [5, 6]. The impact of applying mechanical constraints and biochemical microenvironment mimicking pathological situations will be analysed in this *in vitro* model. The project will involve cell culture (2D; 3D-organoid), and characterization of cell phenotypes and functions (quantitative expression analysis: RT-QPCR, high-throughput transcriptomic analysis, single cell technology, fluorescence optical microscopy, imaging analysis). [1] Clouet *et al. Adv Drug Deliv Rev.*, 2018; [2] Bach *et al.*, *Front. Cell Dev. Biol.,* 2022 ; [3] Colombier *et al., Cells*, 2020 ; [4] Warin *et al., iScience*, 2024 ; [5] Paillat et al., Eur Cell Mater., 2023; [6] Lagneau et al., *Bioactmat.*, 2023.

<u>Profile(s) linked to the project:</u>

X Experimental Biology *(Recherche expérimentale)*