Internship proposition 2025-2026

(One-page max)

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

Lab: Inserm U1229 Regenerative Medicine and Skeleton (RMeS)
Team: REJOINT, group StratOA

Name and position of the supervisor: Marie-Astrid Boutet, CRCN, group leader; and co-supervisor Mathilde Le Mercier, PhD student.

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Candidate (if internship filled): /

Title of the internship: Characterization of the pathogenic role of synovial macrophages in osteoarthritis.

Summary of the internship proposal:

Osteoarthritis (OA) is the most common rheumatic disease affecting over 500 million people worldwide. OA is an incurable and debilitating joint disease that leads to cartilage degradation, bone remodeling, and synovial tissue inflammation (synovitis).

Synovitis has been shown to play an important role in OA initiation and progression. OA synovial tissues can be divided into 3 groups (or synovial pathotypes), based on histopathological analyses of the synovial cellular infiltration. Single-cell RNA sequencing and spatial transcriptomic analyses from control and OA synovial tissues revealed that **macrophage populations are diversely represented across OA synovial pathotypes**. We hypothesize that the pathotype-specific targeting of macrophage populations could represent a new therapeutic strategy to treat OA.

In this context, we now aim to **better characterize the role of a population of resident synovial macrophage** through the generation of in vitro models to study their crosstalk with other joint cells (e.g., fibroblasts, chondrocytes) and **assess the effects of modulating specific molecular targets**.

Specifically, we propose to:

- Validate the spatial localization of these cells on synovial sections from a large biocollection of FFPE OA synovial samples by multiple immunofluorescence,
- Generate a robust in vitro model of this macrophage population, and validate their phenotype using different readouts (RT-qPCR, ELISA or bioplex, immunofluorescence),
- Develop co-culture protocols to study the interaction between these macrophages and other joint cells present in OA synovial tissue and cartilage,
- Study the effects of siRNA to modulate specific molecular targets.

Overall, this work will help **better understand OA physiopathology and contribute to the development of novel personalized therapeutic strategies**.

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

☒ Experimental Biology *(Recherche expérimentale)*
☐ Clinical Research *(Recherche clinique)*
☐ Research in data analysis (Recherche en analyse de données)