Internship proposition 2026-2027

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

Lab: **RmeS INSERM 1229**
Team: INFLAMED (REGOS group)

Name and position of the supervisor: prof C. Nich and A. Gaudin

Email of the supervisor: christophe.nich@chu-nantes.fr, alexis.gaudin@univ-nantes.fr

Candidate (if internship filled):

Title of the internship: Role of Specialized Pro-Resolving Mediators in the Modulation of the Macrophage–Osteoclast Axis in Debris-Induced Periprosthetic Osteolysis

Summary of the internship proposal:

Background

Periprosthetic aseptic osteolysis is a major cause of late implant failure and is driven by chronic inflammation induced by prosthetic wear debris, leading to sustained macrophage activation, osteoclastogenesis, and progressive bone loss. Increasing evidence suggests that this condition reflects an impaired resolution of inflammation rather than excessive inflammation alone. Specialized pro-resolving mediators (SPMs), such as lipoxins and resolvins, actively orchestrate the resolution phase of inflammation while preserving host defense. Their role in periprosthetic osteolysis remains largely unexplored.

Objectives

This Master's project aims to investigate the effects of selected SPMs (Lipoxin A4, Resolvins) on debris-induced inflammatory responses along the macrophage-osteoclast continuum, with particular emphasis on osteoclast precursors. Specifically, the project will assess:

- Macrophage activation and polarization, with characterization of inflammatory (M1-like) and pro-resolving (M2-like) phenotypes following exposure to wear debris and SPMs;
- Commitment and differentiation of osteoclasts from monocyte/macrophage precursors, evaluated through classical osteoclastogenesis assays (TRAP staining, multinucleation, resorption activity);
- Inflammatory and pro-resolving mediator profiles, including key cytokines and regulators of bone resorption (RANKL/OPG balance);
- Key molecular pathways involved in inflammation resolution and osteoclast differentiation, focusing on NF-κB inhibition and PPAR-γ activation.

To increase the exploratory and translational value of the project, a targeted transcriptomic approach (focused gene expression panel related to inflammation resolution and osteoclastogenesis) may be considered on selected conditions, depending on feasibility.

Methodology (Overview)

- In vitro macrophage and osteoclast-precursor models (THP-1–derived macrophages and monocyte-derived cells) stimulated with clinically relevant prosthetic wear particles (PE or PMMA)
- Treatment with selected specialized pro-resolving mediators (Lipoxin A4, Resolvins)

- Evaluation of inflammatory and pro-resolving responses using cytokine-, gene-, and protein-expression analyses (ELISA, RT-qPCR)
- Macrophage–osteoclast differentiation and macrophage–bone cell co-culture systems to assess osteoclastogenesis and resorptive activity
- Exploratory targeted transcriptomic analyses (focused gene panels related to inflammation resolution and osteoclast differentiation) on selected experimental conditions

Expected Outcomes

Identification of pro-resolving effects of SPMs on wear-debris-induced macrophage activation and inflammation

Modulation of osteoclast-precursor commitment and reduction of osteoclastogenic signaling, contributing to restoration of inflammatory homeostasis

Mechanistic insights into resolution-based therapeutic strategies for limiting periprosthetic osteolysis and informing future omics-driven investigations

Profile(s) linked to the project:

X Experimental Biology *(Recherche expérimentale)*

☐ Clinical Research *(Recherche clinique)*

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