Internship proposition

(One-page max)

**Master 2 GP Immunology & ImmunoIntervention ($I^3$)**

**2024-2025**

**Lab: UMR1229 RMeS**

**Team: 1 REJOINT**

**Name and position of the supervisor: Christelle Darrieutort-Laffite (PU-PH) et Frédéric BLANCHARD (DR Inserm)**

**Email of the supervisor: Christelle.DARRIEUTORT@chu-nantes.fr ; Frederic.blanchard@univ-nantes.fr**

**Candidate (if internship filled): Blanche Quéré**

**Title of the internship: Study of macrophage-tenocyte interactions within the tendon**

**Summary of the internship proposal:**

Tendinopathies are very common diseases, triggered by excessive loads and repetitive movements. Their individual and societal impact is significant, linked to symptoms chronicity and lack of curative treatment. The main component of tendons is type I collagen (60-85% of dry weight), and the remaining extra-cellular matrix comprises proteoglycans, glycosaminoglycans, glycoproteins and other types of collagen. Tenocytes, the main cells of the tendon, regulate the production and turnover of extra-cellular matrix components in reaction to several mechanical or molecular stimuli. Tissue-resident macrophages (TRMs) are present within tendons, but little is known about their role and origin. Recent findings have shown that subpopulations of tenocytes and their healing properties may differ in healthy and injured tendons and that there is an aberrant regulation of the interleukin-6 (IL-6) pathway in the latter. The interactions of tenocytes and immune cells could lead to pathological pathways of differentiation of tendon progenitor stem cells, but also to abnormal TRM phenotypes.

The objective of the study is to better characterize, within the tendon, the interactions between macrophages and stromal cells which result in the deviation of normal healing towards a chronic inflammatory response causing degeneration of the tendon tissue. Better understanding of these mechanisms could lead to new therapeutic approaches in tendinopathy. Considering the data available at this stage, our working hypothesis is that chronic tendon inflammation, particularly via aberrant activation of the IL-6 pathway, would divert the differentiation of progenitors towards osteo-chondrogenic or fibrotic pathways rather than tenogenic.

Thus, the study of these interactions will be carried out both in vitro and then in vivo on a murine model. The use of monocytes extracted from the blood of healthy volunteers combined with tenocytes extracted after digestion of human rotator cuff tendons will allow us to study their interactions under different culture conditions. A murine model of partial rupture of the patellar tendon will be used to study immune cells and stromal cells characteristics and location during the various stages of the normal healing process, by histology, IHC and scRNAseq in the lesion zone, and functional measurements will be taken (catwalk analysis).

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

☐ Clinical Research *(Recherche clinique)*

☐ Data analyst *(Recherche et Analyse de Données Biologiques)*

X Experimental Biology *(Recherche expérimentale)*