Internship proposition 2025-2026

(One-page max)

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

Lab: Centre de Recherche Translationnelle en Transplantation et Immunologie (CR2TI)

Team: Team 3 "Integrative transplantation, HLA, Immunology and genomics of kidney injury"

Name and position of the supervisor: Sarah Bruneau, chargée de projets translationnels

Email of the supervisor: sarah.bruneau@univ-nantes.fr

Candidate (if internship filled): None

Title of the internship: Neddylation blockade as a new organ transplant preconditioning strategy

Summary of the internship proposal:

The number of patients waiting for a solid organ transplant has been rising constantly, while the number of transplantations performed every year remains fairly stable. To meet this ever-increasing demand for organs, transplants from donors with extended criteria (over 60 y/o, history of diabetes or high blood pressure…) and from donors after cardiac arrest are now being used. However, these "lower quality" grafts are highly sensitive to ischemia-reperfusion and are more immunogenic, and therefore display a lower survival rate. Lately, a lot of effort has therefore been put into improvement of transplant preservation strategies, not only to maintain graft viability, but also to improve its quality (so called "graft preconditioning"). *Ex vivo* injection of protective molecules into the graft presents the advantage of targeting the graft only and especially its endothelium, thus avoiding many of the limitations associated with systemic drug delivery. In our previous *in vitro* work, we have identified a powerful protective molecule for endothelial cells through its capacity (1) to block endothelial activation and proinflammatory responses, (2) to inhibit endothelial prothrombotic responses, and (3) to decrease hypoxia and hypothermia-induced endothelial cell death. Importantly, these effects are observed upon a simple pretreatment of endothelial cells for 3 hours at 4°C prior to stimulation with TNFα/IFNγ, which makes it perfectly applicable to a preservation method in hypothermic perfusion or even static cold storage, which are commonly used in the clinical practice. The objective of this project is to confirm these results obtained on human microvascular endothelial cells from the skin in human endothelial cells from other transplantable organs, and to test the protective effect of this molecule *ex vivo* on whole kidneys and pancreases to provide proof-of-concept for future clinical applications.

<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)