Internship Proposition
(one page max)
Master 2 GP Immunology & ImmunoIntervention (I^3)
2024-2025

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): Pierre Braud

Title of the internship: Endothelium protection during organ preservation: A new means to achieve graft preconditioning

Summary of the internship proposal: Long-term kidney and pancreas allograft survival in allotransplantation is mainly limited by the occurrence of immunological events (chronic antibody mediated rejection) and aspecific fibrosis, the latter favored by the use of organs from extended criteria donors and ischemia-reperfusion injury (IRI). The graft endothelium is highly sensitive to IRI, which causes chronic damages and favors graft immunogenicity by increasing the expression of HLA I and II, adhesion molecules, and proinflammatory molecules. In pancreas transplantation, early allograft loss due to thrombosis remains a major issue and is associated with IRI. Lately, a lot of effort has been put into improvement of kidney 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 upon TNFα/IFNγ stimulation, (2) to inhibit the expression of the prothrombotic molecule Tissue Factor, and (3) to increase the expression of the cytoprotective molecule HO-1 and of the complement inhibitor CD55. 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 test the protective effect of this molecule ex vivo on whole pig kidneys and pancreas to confirm our in vitro results.

Option(s) linked to the project:
☐ Clinical Research Profile (Recherche Clinique)
☐ Data Analyst Profile (Recherche et Analyse de Données Biologiques)
☑ Experimental Biology Profile (Recherche Expérimentale)

Form to be sent by email to : gpi3@univ-nantes.fr