Internship Proposition
(one page max)

Master 2 GP Immunology & ImmunoIntervention (I^3)
2025-2026

Lab: CR2TI, UMR1064 (Center for Research in Transplantation and Translational Immunology), Nantes

Team: Team 4 : Deciphering organ immune regulation in inflammation and transplantation (DORI-t)

Name and position of the supervisor: Richard Danger, CRCN

Email of the supervisor: richard.danger@univ-nantes.fr

Candidate (if internship filled): NA

Title of the internship: Characterizing double-negative B cells in long-term kidney transplanted patients

Summary of the internship proposal:

Kidney transplantation is the treatment of choice for end-stage chronic kidney disease with an excellent average survival of around 14 years, notably thanks to long-life immunosuppressive drugs. However, constant immunosuppression can lead to subclinical chronic inflammation and increased risks of infection or cancer, and sometimes insidious deterioration of graft function. We recently identified a significant increased frequency of double negative (DN) IgD-CD27- B cells in long-term immunosuppressed transplant recipients (LTTs) (Brinas F et al. Eur J Immunol. 2024). We are now seeking to determine whether if these DN B cells are only a marker of an altered immune state, such as exhaustion, as reported in the literature, or if they actively contribute to long-term graft outcomes, through their regulatory properties.

Building on our findings, the next step in this project is to conduct a more in-depth characterization of this specific DN B cell population. This characterization will consist in an in-depth phenotypic analysis using spectral flow cytometry and a detailed functional analysis. The functional analysis will aim to investigate their activation potential including proliferation capacity to various stimuli (e.g., BCR stimulation, TLR agonists), their cytokine production (pro-inflammatory vs. regulatory) and antigen presentation efficiency. We will also examine how different immunosuppressive regimens may affect the generation and maintenance of this B cell population. Finally, we will perform a transcriptomic analysis to identify the molecular pathways governing their development and function.

Understanding the role of these DN B cells would improve the understanding of long-term graft maintenance and enable us to develop more personalized and effective immunosuppression strategies, aiming to maintain graft stability while minimizing long-term side effects, thereby significantly improving patients' quality of life and survival.

Option(s) linked to the project:

☐ Clinical Research Profile (Recherche Clinique)☐ Data Analyst Profile (Recherche et Analyse de Données Omiques)

☒ Experimental Biology Profile (Recherche Expérimentale)

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