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

Lab: CR2TI

Team: 4

Name and position of the supervisor: Nicolas Degauque CRCN / Sophie Brouard DRCE

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Candidate (if internship filled): Elina Deneele

Title of the internship: Regulation of the immune-metabolism of TEMRA CD8 by B cells and its involvement in kidney graft survival

Summary of the internship proposal:

The etiologies of kidney transplant failure vary depending on factors such as duration after transplantation and age of kidney transplant (KT) recipients. By combining single cell proteomic profiling and functional assay of CD8 subsets, we demonstrated that antibody-mediated rejection (ABMR) is associated with an accumulation of cytotoxic effector memory expressing CD45RA (TEMRA) CD8 T cells in the periphery and in the kidney allograft. In contrast, we have shown that GZMB regulatory B cells (GZMB-Bregs) accumulate in operationally tolerant KT patients and are able to prevent the proliferation of CD4 and CD8 T cells in vitro, including TEMRA CD8 T cells. The mechanism of regulation of TEMRA CD8 by GZMB-Bregs remains unclear as well as the impact of KT outcome on the TEMRA CD8 / Bcell crosstalk. One potential mechanism of regulation is the induction of T cell suppression through metabolic competition and inhibition of the mTOR pathway. The mTOR pathway is known to integrate environmental cues and nutrient availability to modulate the immune function of CD8 T cells. The objectives of the internship are (1) to define the modulation of the metabolism of TEMRA CD8 by GZMB-Bregs first in healthy volunteers (HV) and (2) according to the clinical characteristics of KT outcome, (3) to characterize the mTOR pathway of TEMRA CD8 before and after culture with GZMB-Bregs, non B regs and activated B cells. Clinical samples from HV, KT recipients with stable graft function or biopsy-proven rejection (ABMR, mixed rejection) from the DIVAT biocollection will be used. Using cell culture assays and multiplex spectral flow cytometry, we aim to better understand the role of CD8 T cells in the process leading to kidney transplant rejection by investigating crosstalk with the B cell population.

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