Internship Proposition
(one page max)

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

Lab: Center for Research in Transplantation and Translational Immunology

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

Name and position of the supervisor: Fabienne Haspot, CRCN INSERM, HDR

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Candidate (if internship filled): Maeva Durand

Title of the internship:

KIR3D3L+ T cell population: description and function upon HHLA2 ligation

Summary of the internship proposal:

HHLA2 is a surface ligand from the B7 family that regulates cell-mediated immunity by binding to T and NK cell receptors. CD28H and KIR3DL3 are receptors of HHLA2. However, while CD28H activates T and NK cells, KIR3DL3 has the opposite effect. HHLA2 is overexpressed by some epithelial tumor cells.

Scientific and technical challenges impact fundamental research on these three molecules. First, none of them are express in rodents. Then, KIR region is highly polymorphic with extensive sequence identity which challenge the specificity of any anti-KIR3DL3 mAbs. Furthermore, while CD28H expression on immune cells has been well established, KIR3DL3 is barely detectable. Additionally, obtaining cells expressing naturally and stably express HHLA2 needs to be confirmed.

We have previously developed genetically modified cells which stably express functional HHLA2 molecule. Using these cells, we have observed that upon ligation, CD28H is endocytosed suggesting a potential tumor immune escape mechanism. Yet nothing is known on KIR3DL3 fate upon its interaction with HHLA2. We will take advantage of the only anti-KIR3DL3 specific ab described to date (clone CH21) which we have access.

During your fellowship, you will develop genetically modified Jurkat cells to obtain Jurkat-KIR3DL3+ cells. You will first characterize KIR3DL3 fate upon HHLA2 ligand and further evaluate the behavior of the Jurkat-KIR3DL3+ cells. Using a specific anti-KIR3DL3 mAb, you will evaluate the consequences of KIR3DL3 ligation on Jurkat activation. Finally, you will confirm your observation with naturally expressing KIR3DL3 cells within the blood and tissue of healthy volunteers.

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