Internship Proposition
(one page max)

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

Lab: CRCI2NA

Team: team 12

Name and position of the supervisor: FERRON Enora, EFS CR, PhD

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Candidate (if internship filled): JORE Alexia

Title of the internship: Biological characterization of KIR2DL5 and targeting of the KIR2DL5-PVR axis in the development of NK cell immunotherapies in acute myeloblastic leukemia

Summary of the internship proposal:
The treatment of acute lymphoblastic leukemia (ALL) has been particularly improved with the advent of CARs ("Chimeric Antigen Receptor") targeting specific ALL antigen as CD19. However, CARs have been observed to demonstrate an ineffective targeting of the leukemic cells of and acute myeloblastic leukemia (AML) patients due to the absence of a specific antigen. Natural Killer (NK) cells possess intrinsic anti-leukemic cytotoxicity and represent a promising alternative for the development of immunotherapies. The activation of NK cells relies on a balance between inhibitory receptors, which bind to HLA class I molecules, and activating receptors, which bind to ligands overexpressed by leukemia cells. Within a leukemic context, the reduced expression of HLA class I molecules leads to a "missing-self" effect, thereby rendering leukemic cells susceptible to lysis by NK cells. Furthermore, the aberrant expression of activating receptor ligands has been demonstrated to result in robust activation of natural killer cells. It has been demonstrated that the interaction between KIR2DL5 on NK cells and PVR on leukemic cells significantly inhibits the degranulation capacity of NK cells. However, the precise function of KIR2DL5 in NK cell biology or in a leukemic context remains to be elucidated. The objective of this internship is to deeply decipher the KIR2DL5 ligands and its functional role on NK cell biology, to finally develop a strategy of NK cell immunotherapy based on the KIR2DL5-PVR axis. This internship combines cell biology (flow cytometry, real-time imaging of cytotoxicity (IncuCyte)) and molecular biology (CAR construct, lentiviral productions, NK cell transduction), with strong expertise on NK cells. The procurement of an efficacious CAR-NK KIR2DL5 represents a pioneering domain within the realm of immunotherapy, with the potential for application in both leukemic and solid cancer patients who exhibit characterised by the expression of PVR

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