## **Internship Proposition**

(one page max)

## Master 2 GP Immunology & ImmunoIntervention (I3) 2025-2026

Lab: CRCI2NA

Team: Team 12

Name and position of the supervisor: RETIERE Christelle, EFS DR, head of

EFS research lab, PhD and HDR

Email of the supervisor: Christelle.retiere@efs.sante.fr

Candidate (if internship filled): Amélie TOULET

Title of the internship: Development of CAR-engineered NK cells as a treatment for acute myeloblastic leukaemia

Summary of the internship proposal: Acute myeloblastic leukaemia (AML) represents 1% of all cancers, with over 20,000 new cases diagnosed annually in Europe. The standard treatment is hematopoietic stem cell allograft transplantation (HSCT), but unfortunately, the relapse rate remains high. The development of new approaches to improve the prognosis of AML patients is of the utmost importance. Natural Killer (NK) lymphocytes represent a promising approach to targeting AML. In contrast to LT, NK cells do not require antigenic specificity to exert their natural cytotoxic function. The objective of this project is to develop an innovative solution to enhance the targeting of NK cells against AML while preserving their intrinsic capacity to differentiate between healthy and leukemic cells. Our approach, in contrast to CAR-T, involves imparting NK cells with CD33 specificity in maintaining self-recognition. This strategy has the potential to enable NK cells to spare healthy CD33+ hematopoietic progenitors while targeting leukemic cells. To achieve this, the candidate will be required to decline actual CAR constructs that have been developed into lentiviral expression plasmids in other immunogenetic contexts. The efficacy of the CAR-NK cells will be assessed using degranulation assays by flow cytometry against AML cell lines and primary AML cells. The quantification of the level of leukemic cell death will be carried out by means of real-time imaging (IncuCyte) using EGFP+ targets, which have been engineered in the laboratory. The generation of effective AML specific CAR-NK cells represents a pioneering domain within the field of immunotherapy in hematology.

## Option(s) linked to the project:

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□ Experimental Biology Profile (Recherche Expér@univ-nantes.frimentale)

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