Internship proposition
One page max
M2 I3/0HNU 2024-25

Lab: CRCI²NA, Centre de Recherche en Cancérologie Immunologie Intégrées Nantes-Angers

Team: PETRY 10 Plasticity of Ecosystem from the Tumor after Radiotherapy

Name and position of the supervisor: Sophie Fougeray, MCU, and Claire Pecqueur, DR (Head of the team)

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Candidate: None

Title of the internship: Identification of new CAR-T cell targets and characterization of tumor metabolic pathways influencing CAR-T cell efficacy in pediatric diffuse high-grade glioma.

Summary of the internship proposal:
Pediatric diffuse high-grade gliomas (PDHGG) are primary brain tumors that are among the most lethal cancers in children. These high-grade tumors comprise diffuse midline gliomas, including diffuse intrinsic pontine gliomas (DIPG) with a histone H3 K27M mutation. The median survival of patients with H3K27M-mutated DIPG is 11 months following diagnosis. Current treatments, including radiotherapy or chemotherapy, are insufficiently effective, and the long-term prognosis of patients remains poor. Therefore, new approaches need to be developed. The use of immunotherapy based on T lymphocytes genetically modified to express a chimeric antigen receptor (CAR) seems a relevant approach as they demonstrated their efficacy in certain malignant hemopathies. However, these CAR-T cells capable of recognizing and destroying cancer cells need to be optimized for solid tumors. Our aim is to develop CAR Vδ2 T cells targeting several tumor antigens, and to better understand the mechanisms of DIPG escape that may limit the efficacy of this immunotherapy. The objectives of the project are therefore (i) to identify new CAR-T cell targets expressed by tumor cells *in vitro* (2D and 3D) using flow cytometry; (ii) to evaluate the efficacy of CAR-T cells targeting antigens that we aim to identify using T cell activation assay; (iii) to characterize the metabolic pathways within DIPGs that may be involved in immunosuppression and loss of CAR-T cell efficacy, using Seahorse.

Option(s) linked to the project:

☐ Clinical Research Profile
☐ Data Analyst Profile
X Experimental Biology Profile