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

Lab: INCIT, Inserm UMR1302

Team: Team 3 ("anti-tumor immunosurveillance and immunotherapy")

Name and position of the supervisor: Anne Jarry, CRHC Inserm

Email of the supervisor: anne.jarry@univ-nantes.fr

Candidate (if internship filled): Zoé Pineau Grimaud

Title of the internship: Role of the NLRC5/PRMT5/MHC-I axis in the modulation of the T cell response in colorectal cancer

Summary of the internship proposal:

Colorectal cancer (CRC) is a heterogeneous disease at the molecular and immune levels, making it difficult to predict treatment responses. In the majority of CRC, immunotherapy using immune checkpoint inhibitors (ICI) is ineffective as monotherapy. There is a need to better understand the mechanisms involved in acquired resistance to ICI and to identify new biomarkers of response in the various subgroups of CRC. This project focuses on the inflammasome component NLRC5 (NLR family CARD Domain containing 5) that bridges innate and adaptive immunity. NLRC5 not only participates in the formation of inflammasome complexes by activating caspase-1 but also can translocate into the nucleus where it transactivates genes coding for the antigen presentation machinery including MHC-I.
Our team recently showed that a high expression of NLRC5 in tumor cells is a favorable prognostic factor that favors a cytotoxic T cell response and can be a valuable biomarker in CRC. Conversely, a loss of NLRC5 in tumor cells, that can result from the action of the epigenetic modifier PRMT5 (protein arginine methyltransferase-5), could lead to tumor immune evasion.
The major aim of this M2 internship is to better characterize the involvement of PRMT5 in the modulation of the NLRC5/MHC-I axis and of the T cell response in CRC. Descriptive and functional studies will be performed using human samples from cohorts of CRC patients as well as *ex vivo* co-culture models (tumor cell lines, wild type or genetically engineered, co-cultured with CD8 T cells or T cell clones derived from CRC tumor fragments).

Bilonda-Mutala L et al. Cancers (Basel), 2021, 13(2):189. doi: 10.3390/cancers13020189.

Option(s) linked to the project:

☐ Clinical Research Profile (Recherche Clinique)
☐ Data Analyst Profile (Recherche et Analyse de Données Biologiques)
X Experimental Biology Profile (Recherche Expérimentale)

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