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

Lab: INCIT, UMR1302

Team: Team 3 - "Anti-tumor Immunosurveillance and Immunotherapy"

Name and position of the supervisor: Nathalie Labarrière, DR Inserm, Head of Team

Email of the supervisor: nathalie.labarriere@univ-nantes.fr

Candidate (if internship filled): Alexia Boucard

Title of the internship: Cross-reactivity of anti-tumor TCRs: implications for immunotherapy

Summary of the internship proposal:

One of our team's areas of research is improving the therapeutic efficacy of immunotherapy approaches in solid tumors, such as adoptive transfer of T lymphocytes (ACT) in melanoma patients. In collaboration with a network of clinicians at Nantes University Hospital, our team has already set up several immunotherapy trials based on the injection of cytotoxic T lymphocytes specific to melanoma antigens (1). Very recently, it has been reported that the most persistent T-cells in patients after adoptive transfer possess TCRs capable of recognizing multiple antigenic epitopes (2), which would limit tumor escape, enabling T-cells to attack the tumor by targeting multiple HLA/peptide complexes. We have a collection of T-cells with characterized TCRs (specificity and sequence (3)), and have already demonstrated the cross-reactivity of some of these T lymphocytes to epitopes from the intestinal microbiota (4), and recently for other tumor antigens.
The aim of this M2 internship is to finely characterize the cross-reactive lymphocytes in terms of functional avidity, TCR sequences and to explore their reactivity against tumor lines from different origins expressing the target antigens. Validation of the cross-reactivity of these lymphocytes will be finalized by genomic deletion of antigens in tumor lines.

1. Dréno B *et al*. **Phase I/II clinical trial of adoptive cell transfer of sorted specific T cells for metastatic melanoma patients**. *Cancer Immunol Immunother*. **2021** Oct;70(10):3015-3030. doi: 10.1007/s00262-021-02961-0.
2. Dolton *et al*., **Targeting of multiple tumor-associated antigens by individual T cell receptors during successful cancer immunotherapy.** *Cell*. **2023** Aug; 186: 3333-3349. doi.org/10.1016/j.cell.2023.06.020
3. Simon S, *et al.* **PD-1 and TIGIT coexpression identifies a circulating CD8 T cell subset predictive of response to anti-PD-1 therapy**. N. *J Immunother Cancer*. **2020** Nov;8(2):e001631. doi: 10.1136/jitc-2020-001631.
4. Fluckiger A, *et al*. **Cross-reactivity between tumor MHC class I-restricted antigens and an enterococcal bacteriophage**. *Science*. **2020** Aug 21;369(6506):936-942. doi: 10.1126/science.aax0701.

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