



Internship proposition
One page max
M2 I3/OHNU 2024-25



Lab: CIRI²NA INSERM UMR1307 & CNRS UMR6075, Nantes

team: Team 12 *"Manipulation of Lymphocytes For Immunotherapy"*

Name and position of the supervisor: Dr Emmanuel SCOTET, Research Director

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Candidate:

Title of the internship: Characterisation of intra-tumoral human $\gamma\delta$ T cells for cellular engineering purposes

Summary of the internship proposal:

Human $\gamma\delta$ T lymphocytes, sensors and sentinels against various stresses, react naturally against a broad spectrum of tumor cells. These potent effects result in direct cytolytic activity and regulation of the functions of other immune cell types. Due to their unique and remarkable properties, such as significant conservation, no alloreactivity and their effector and regulatory functions, $\gamma\delta$ T cells are currently the subject of particular attention for potential clinical applications, particularly in the implementation of anti-tumor immunotherapies. However, numerous studies also indicate quite unexpected phenotypic and functional diversities within sub-populations of human $\gamma\delta$ T cells as well as the modulatory effects of the tumor environment. The establishment of novel effective immunotherapies based on these T cells first requires a better understanding of the mechanisms involved in their recruitment, their localization, their biology and their dynamics within human solid tumors. Knowing how their functions are impacted in the tumor ecosystem can subsequently make it possible to define specific strategies for manipulation by molecular engineering allowing (ie. counter inhibitory effects) and thus improve their therapeutic effectiveness.

The research program carried out by the student during this internship will be focused on the identification of the molecular & cellular mechanisms which control the functional polarization of human T cells, and on the understanding of the mechanisms used by the tumor ecosystem to switch effector $\gamma\delta$ T cells towards a regulatory phenotype or promote the recruitment and development of sub-populations of regulatory T cells. The final objective of this research program (beyond the internship) will be to next exploit these informations to generate, by molecular engineering, or select "super-reactive tumor-killing" T cells for immunotherapeutic purposes.

Option(s) linked to the project:

- Clinical Research Profile
- Data Analyst Profile
- Experimental Biology Profile