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

Lab: Tocheva Lab

Team:

Name and position of the PI: Anna S. Tocheva, PhD; Assistant Professor

Email of the PI: anna.tocheva@mssm.edu

Candidate (if internship filled):

Title of the internship: DIFFERENCES IN PD-1 SIGNALING DRIVEN BY FUNCTIONAL T CELL DIVERSITY

Summary of the internship proposal:

Our immune system relies on first line (innate) and second line (adaptive) immune responses that protect us from infections and prevent tumor growth. Innate immune cells process invading pathogens and tumor cells to activate naïve T cells, which mature into a diverse population of memory cells with complementary functions. Memory T cells can recognize and eliminate infected and tumor cells, but in rare occasions may cause significant damage to our own tissues, including autoimmunity. Consequently, to prevent unwanted inflammation and tissue damage, T cells express inhibitory receptors that recognize environmental ques and suppress T cell functions. The surface receptor programmed cell death protein 1 (PD-1) is a key inhibitory receptor, which is expressed soon after T cell activation to limit excessive inflammation. Tumors have evolved to bind PD-1 and prevent T cells from recognizing and killing the tumor cells. To help T cell recognition and killing, new cancer treatments are designed to block PD-1 and greatly benefit some patients. However, a significant proportion of cancer patients fail to respond to this treatment. In order to improve therapies targeting PD-1, it is imperative to uncover its basic biology and signaling mechanisms in human T cells. ***Despite its critical role in immune regulation, little is known about the basic biology and differences in PD-1 signaling between functionally distinct human T cell populations.*** **Therefore, we propose to dissect PD-1 signaling in functionally different naïve and memory human T cells.**

To do this, we have developed laboratory assays to study PD-1 signaling specifically in human T cells. Specifically, the candidate will work closely with a third year PhD student and for this 6-month project, they will determine PD1 signaling differences between naïve and memory CD4 and CD8 T cells in modulating (1) T cell proliferation and cytokine production and (2) T cell metabolism. They will use methods for (1) isolating human naïve and memory T cell subsets; (2) measuring cytokine production via ELISA; (3) evaluating T cell proliferation via CFSE dye dilution, Edu incorporation and flow cytometry; (4) cell metabolism using Seahorse assays

Option(s) linked to the project:

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

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