CRCI²NA
CANCER & IMMUNOLOGY

Master 2 internship proposition

Lab: CRCI2NA

Team: 7b: Cell Plasticity in Development and Cancer (DevCan) (https://crci2na.univ-nantes.fr/en/research/https-crci2na-univ-nantes-fr-en-research-team-7b-cell-plasticity-in-development-and-cancer-devcan)

Name and position of the supervisor: Eloïse GRASSET, chercheuse CNRS

Email of the supervisor: Eloise.grasset@univ-nantes.fr

Candidate: This project is suited for a candidate with a strong background in cell biology and immunology. Additionally, the research involves the use of murine models to study tumor dissemination in vivo, requiring the candidate to be comfortable working with mice. While prior authorization for animal experimentation would be an advantage, it is not a prerequisite.

Title of the internship: **Deciphering the impact of the immune microenvironment on cancer cell state and metastastic colonization.**

Description:

Triple-negative breast cancer (TNBC), which accounts for 15% of all breast cancers is a heterogeneous disease characterized by the absence of estrogen, progesterone receptors, and no amplification of the human epidermal growth factor receptor. This lack of expression has impeded the development of targeted therapies for TNBC. Currently, chemotherapy and immune checkpoint blockade are the leading treatment options. However, TNBC often recurs and metastasizes, and there is no curative treatment once it spreads to distant organs, highlighting the need for a better understanding of the molecular mechanisms behind TNBC metastasis.

We recently identified a novel mechanism of metastatic colonization implicating the epithelial-mesenchymal-transition (EMT) in TNBC (unpublished). Our preliminary data indicates that the immune system delayed this novel process without blocking it. Understanding and addressing this novel process of cancer cell colonization is crucial, as it renders cancer cells undetectable by clinical radiologic imaging until the emergence of large metastases.

The objective of this internship is to decipher the impact of the immune microenvironment on TNBC cell state and metastatic colonization.

To assess the impact of immune cells on cancer cell colonization in the lungs, we will inject fluorescent cancer cell clusters into the tail vein of immunocompetent mice, and collect the lungs at several time points. We will specifically analyze the immune cells in close proximity to the cancer cells by using multiplex immunofluorescence staining. Briefly, we will design a panel using specific immune markers to identify various immune cell types: F4/80 for macrophages, Ly6G for neutrophils, CD11c for dendritic cells, NKp46 for NK cells, CD19 for B lymphocytes, and CD4/CD8 for T cells. Additionally, we will use EMT markers, including E-cadherin, EpCAM, pan-Cytokeratins, vimentin, and alpha-SMA. In a second step, I will investigate the metastatic colonization of cancer cells in mice with established primary tumors. Previous studies have shown that primary tumors can significantly influence metastasis by creating pre-metastatic niches. To explore this, we will first inject non-fluorescent cancer cells into the mammary fat pad of mice. Three weeks later, we will introduce fluorescent cancer cells via the tail vein. By injecting cancer cells into the tail vein, we can monitor their arrival in the lungs and analyze their colonization over time, using the same methodology as in the previous step.

This project will advance our understanding of TNBC metastatic colonization, potentially revealing therapeutic vulnerabilities against metastatic disease.