Internship proposition
One page max
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Lab: Centre de Recherche en Cancérologie et Immunologie Intégrée Nantes-Angers (CRCI2NA) UMR INSERM 1307, CNRS 6075 Nantes Université, Université d'Angers

team: Team 7 "Stress adaptation and tumor escape" (P Juin)

Name and position of the supervisor: Frédérique Souazé, PhD CR INSERM

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Title of the internship: **Impact of MCL-1 expression in cancer-associated fibroblasts on extracellular matrix in breast cancer progression**

The tumor microenvironment is composed of different cell types such as immune cells, endothelial cells and cancer-associated fibroblasts (CAFs). In breast cancer, a positive correlation has been established between the proportion of CAFs within the tumor and a negative prognosis. Indeed, these cells have numerous tumorigenic effects by promoting treatment resistance, invasion, and the development of cancer cell metastases through enhanced remodeling of the extracellular matrix (ECM) among other mechanisms.

Our previous works have identified the anti-apoptotic protein MCL-1 as a factor in the treatment resistance of luminal breast cancer cells under the influence of CAFs (Louault et al., 2019). Subsequently, we have shown that CAFs consistently overexpress MCL-1 compared to normal fibroblasts and that specific targeting of this protein, through pharmacological inhibition and gene silencing by CRISPR/Cas9, leads to actomyosin cytoskeleton remodeling associated with reduced invasive and migratory capacities of these cells (Bonneaud et al., 2022). A global proteomic analysis of the matrisome in MCL-1 knockdown CAFs reveals alterations in matrix protein production compared to CAFs with MCL-1 expression. Additionally, we observed remodeling of in vitro ECM derived from CAFs Kd MCL-1 in this context.

The proposed project aims to identify whether the matrix resulting from these modifications have pro- or anti-tumor properties. Our main objective is to determine how the ECM generated by CAFs (+/- MCL-1 knockdown) impacts cancer cell invasiveness and resistance to treatment. We will analyse the phenotype of cancer cells after culture on ECM and observe cell invasion by videomicroscopic analysis. A better understanding of the role of MCL-1 in influencing CAF phenotypes and the subsequent aggressiveness of cancer cells should make it possible to guide patients' therapeutic choices according to their response to chemotherapy.

Option(s) linked to the project:

☐ Hematology
☒ Oncology
☐ Immunology-Cancerology
☐ Nuclear Medicine

Option(s) linked to the profile:

☐ Clinical Research Profile
☐ Data Analyst Profile
☒ Experimental Biology Profile