Internship proposition
One page max
M2 I3/0HNU 2024-25

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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Candidate:

Title of the internship: **Targeting metabolic competition initiated by tumor stromal fibroblasts to improve treatment response of triple-negative breast cancer cells**

Summary of the internship proposal:

Triple-negative breast cancers (TNBC) have a poor prognosis, notably due to the absence of targeted therapies and a high recurrence rate. The stroma of these cancers is enriched in cancer-associated fibroblasts (CAFs), which provide a favorable environment for tumor development.
Our results indicate that CAFs, by generating a nutritionally restrictive microenvironment (glucose depletion), induce the anti-apoptotic protein MCL-1 in cancer cells, making them more resistant to cell death. To dissect the mechanisms underlying this resistance, we carried out a comparative transcriptomic and proteomic analysis of cancer cells subjected to an apoptosis inducer under restrictive nutritional conditions (presence or absence of CAFs-conditioned medium). This allowed us to identify the possible involvement of the ER stress response, mitochondrial activity and Wnt signaling in the limiting effects of CAFs on cancer cell death.
The aim of the project is to identify the different players in these pathways responsible for treatment resistance, with a view to pharmacological targeting and improving response to breast cancer treatments. Experiments will be carried out in different culture models, including CAFs (primary cultures from patient excisions) and cancer cells (primary patient cell lines or organoids). To highlight the role of the various players in the protective effects of CAFs, their expression will be repressed by CrispR-Cas9 gene silencing. Effects on cell survival will be measured by flow cytometry (annexinV) and videomicroscopic analysis (culture on collagen matrix).

Option(s) linked to the project:
☐ Clinical Research Profile
☐ Data Analyst Profile
✓ Experimental Biology Profile