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

Lab: CRCI2NA, Inserm1307, CNRS6075

Team: Team 7 “Stress adaptation and tumor escape”

Name and position of the supervisor: Sophie Barillé-Nion, CR Inserm

Email of the supervisor: sophie.barille@univ-nantes.fr

Candidate: no

Title of the internship: **Analysis of chemotherapy-induced secretomes in breast cancers**

Summary of the internship proposal:

How malignant cells respond to chemotherapy is essential for better comprehending the impact of anticancer drugs on the antitumor immune response. Recently, we established that in breast cancer cells, the ratio of the BCL2 family proteins NOXA and MCL-1 determines the mode of chemo-induced cell death (analyzed through videomicroscopy for apoptosis and pyroptosis) and the composition of the secretome released during cancer cell death (analyzed via proteomic approaches).

We identified that the production of inflammatory cytokines IL-1β and IL-18 during chemo-induced pyroptotic cell death, in addition to being influenced by the NOXA/MCL-1 ratio, relies on the intrinsic expression of the pore-forming protein Gasdermin E (GSDME). These cytokines are known to be secreted by immune cells following an inflammatory caspase-dependent maturation step and through mechanisms dependent on Gasdermin D (GSDMD) or GSDME. However, such processes have not yet been reported in cancer cells, and our preliminary results suggest alternative mechanisms that we propose to explore.

Furthermore, since cell death-associated secretomes possess immunomodulatory potential, we will first define their direct effect on natural killer (NK) cells, which are known to be modulated by IL-18 and contribute to the tumor-induced immune response.

The candidate will be trained in cellular biology, biochemistry, and gene editing to become autonomous during his/her internship.

[1] NOXA/MCL-1 axis determines cell-death decision between apoptosis and pyroptosis and the inflammatory secretome of breast cancer cells treated with anti-mitotics. Dumont A et al, doi: https://doi.org/10.1101/2023.10.06.561231

Option(s) linked to the project:
O Clinical Research Profile
O Data Analyst Profile
X **Experimental Biology Profile**