

# Master program in Cancer Biology

## Internship proposal form 2024

MASTER 1

MASTER 2

<b>Title</b>	Exploring the role of the phosphatidylserine-GAS6-AXL (PGAX) axis in the development of "drug tolerant persisters" during chemotherapeutic treatment of triple-negative breast cancers
<b>Host laboratory</b>	IRCM - Team « Genetic and phenotypic plasticity of cancer »
<b>Name of the PI</b>	Claude SARDET
<b>Supervisor</b>	Isabelle JARIEL-ENCONTRE
<b>E-mail- Contact</b>	Isabelle.jariel@inserm.fr
<b>Description (10 lines)</b>	<p>Chemotherapy tolerance/resistance and subsequent tumor recurrence remain an unsolved problem in many cancers, including triple-negative breast cancer (TNBC). Recent publications suggest that a Darwinian mechanism of selection of genetic mutations or epigenetic modifications cannot explain all the mechanisms leading to resistance to therapies. Various studies have led to the definition of so-called "drug tolerant persisters" (DTPs) characterized by a transient phenotypic state of tolerance to therapies, without additional mutations. The phenotypic plasticity of DTPs would allow a single genotype to give rise to several phenotypes in response to external stresses, such as genotoxic drugs, without clonal selection. The signals that lead to the appearance of DTPs remain poorly understood. Based on the literature and recent laboratory data, we propose to explore the role of the Phosphatidylserine-GAS6-AXL (PGAX) axis in the development of DTPs during chemotherapeutic treatment of TNBC. Our hypothesis is that a small number of particularly plastic cells expressing higher levels of AXL and GAS6 would be more apt than others to become DTPs thanks to their ability to activate the PGAX survival pathway in response to PhosphatidylSerine (PS) exposed by the majority of other cells that entered apoptosis following chemotherapeutic treatments. This project should establish whether targeting the PGAX axis in conjunction with chemotherapies could prevent/diminish tumor recurrence in TNBC.</p>
<b>Duration (2 to 6 months)</b>	6 months