**Stage Master M2 par l’Institut Cancer et Immunologie (ICI)**

**(ICI-MS2 2021)**

**Titre du Project**

Investigating the impact of SIRPα conformational flexibility on immune checkpoint function

**Équipe/Plateforme**

Chef(s) d’équipe ou responsable(s) scientifique(s) de plateforme : iSCB Team, CRCM

Nom, Prénom : MORELLI, Xavier ; COLLETTE, Yves

E-mail : [xavier.morelli@inserm.fr](mailto:xavier.morelli@inserm.fr); [yves.collette@inserm.fr](mailto:yves.collette@inserm.fr)

**Superviseur**

PI du sujet (Nom, Prénom) : MILLER, Thomas ([thomas.miller@inserm.fr](mailto:thomas.miller@inserm.fr))

**Résumé du Projet**

The SIRPα-CD47 axis is an immune checkpoint used by many types of cancer to evade immune detection and destruction. Recently, we discovered that SIRPα exists in 2 major protein conformations, a CD47-bound closed form, and a novel open form incapable of CD47 binding. Our therapeutic goal is to create small molecules that stabilize this open form and inhibit CD47 interaction. Toward this goal, we propose to perform structure-function studies on SIRPα to identify residues that impact this conformational change and associated immune checkpoint function. We have preliminarily identified candidate amino acids using our x-ray structures and phylogenetic analysis. The student will study the impact of these amino acids on SIRPα conformation using molecular dynamics simulations to select mutants for further biochemical study of SIRPα-CD47 binding and SIRPα structure. They will then study their impact on immune checkpoint function by creating macrophage cell lines engineered to express SIRPα mutants.

**Desired skills:** molecular biology, biochemistry (protein expression & purification), mammalian cell culture, data analysis (excel, prism), presentation with powerpoint, attention to detail, intellectual curiosity.