

FORMULAIRE STAGE Recherche-M2 BBSG
(période de stage : du 5 janvier 2016 au 3 juillet 2016)

Titre du stage :

Structure-based drug design of compounds modulating PDZ domain-containing proteins

Laboratoire (intitulé, adresse, site web) :

Centre de Recherche en Cancérologie de Marseille (CRCM)
27 Boulevard Lei Roure BP30059
13273 Marseille (<http://crcm.marseille.inserm.fr>)

Equipe :

integrative Structural & Chemical Biology (<http://iscb.cnrs-mrs.fr>)

Maitre de stage : Philippe ROCHE

E-mail : philippe.roche@inserm.fr

Téléphone : 04 86 97 73 35

Descriptif du stage :

The focus of our research group is to identify, to understand, to validate and to target protein-protein interaction interfaces critically involved in tumor cell signaling and epigenetics, and to develop strategies to modulate these protein-protein complexes with small molecules. PDZ domain-containing proteins play a major role in numerous biological processes and are involved in the development of cancers mainly through interactions with the C-terminal residues of protein partners. The major goal of this project is to develop small molecule compounds able to modulate (inhibit) PDZ domain-mediated protein interactions using *in silico* structure-based or fragment-based approaches. The selected compounds will then be experimentally evaluated using *in vitro* and *in vivo* assays within the teams of biologist partners at the CRCM.

The student will only be involved in the computational part of this project (he/she will not perform the experimental validation). The student should have a good knowledge in structural biology. Although programming skills is not compulsory, it would be a strong plus.

Recent references:

- Sperandio O, Villoutreix BO, Morelli X and Roche P. (2015) Les chimiothèques ciblent les interactions protéine-protéine. *Med Sci (Paris)* **31**: 311-318.
- Zhang X, Betzi S, Morelli X and Roche P. (2014) Focused chemical libraries - design and enrichment: an example of protein-protein interaction chemical space. *Future Med Chem.* **6**: 1291-1307.
- Higueruelo AP, Jubb H, Blundell TL (2013) Protein-protein interactions as druggable targets: recent technological advances. *Curr Opin Pharmacol.* **13**:791-796.