Sciences de la Vie et de la Santé
Master BCPP, Universités Paris Descartes – Paris Diderot

Spécialité : **Biologie et Développement Cellulaires**
http://www.master2bdc.fr/
Fiche de Projet de Stage M2, Année 2021-2022

Unité INSERM ou CNRS ou Université : **UMR S1138** **Intitulé Equipe : Médecine Personnalisée, Pharmacogénomique et Optimisation Thérapeutique (Dir. P. Laurent-Puig)** **ED d'appartenance : MTCI** **Responsable de l'Equipe : Sophie Mouillet-Richard**	**Responsable du Stage : Sophie Mouillet-Richard** **Contacts** Adresse : Centre de recherche des Cordeliers 15 rue de l'Ecole de Médecine 75006 Paris Email : sophie.mouillet-richard@parisdescartes.fr Tel : 01-44-27-54-19

Titre du projet : The cellular prion protein and the mesenchymal subtype of colorectal cancer, interactions with the tumour microenvironment

Résumé du Projet de Stage

Colorectal cancer is a heterogeneous disease that can be classified into several subtypes. The CMS4 subgroup, which corresponds to a mesenchymal phenotype with a strong stromal infiltration, is associated with a poor prognosis and a resistance to treatment. The actors and the signalling pathways orchestrating the CMS4 phenotype are poorly characterised. Our lab has recently documented an overexpression of the **cellular prion protein** (PrP^C) in this subgroup, associated with a poor prognosis. We further showed that PrP^C controls the expression of a set of genes that are specific to this subgroup, through a control on the YAP/TAZ and TGFß pathways. This protein appears as a good candidate to contribute to the dialogue between cancer cells and their microenvironment. This hypothesis is notably supported by preliminary in silico results substantiating a correlation between the expression of the PrP^C-encoding gene *PRNP* and a signature of **cancer-associated fibroblasts** (CAF), which constitute a major component of the tumoral microenvironment.

The project aims at deciphering the contribution of the cellular prion protein PrP^C to the **dialogue cancer cells–microenvironment** in colorectal cancer. We have identified several **cytokines** under the control of PrP^C in the conditioned medium of cancer cells, including TGFß. The goal will be to study their involvement in the conversion of normal fibroblasts into CAFS, by combining several cell biology approaches. (RT-qPCR, western blot, immunofluorescence, real-time cell analysis with the xCELLigence technology…). A second axis will aim at deciphering how CAFs in turn influence cancer cells and how the two cell populations behave in co-culture. The M2 student will be trained by an experienced scientist and an engineer and the project can be extended to a PhD.

Publications de l'équipe, relatives au stage proposé

LE CORRE D, GHAZI A, BALOGOUN R, PILATI C, APARICIO T, MARTIN-LANNERÉE S., MARISA L., DJOUADI F., POINDESSOUS V., CROZET C., EMILE J.F., MULOT C., LE MALICOT K., BOIGE V., BLONS H., DE REYNIES A., TAIEB J., GHIRINGHELLI F., BENNOUNA J., LAUNAY J.M., LAURENT-PUIG P. & MOUILLET-RICHARD S. (2019): The Cellular Prion Protein Controls the Mesenchymal-like Molecular Subtype and Predicts Disease Outcome in Colorectal Cancer. **EBiomedicine** 46:94-104.

MOUILLET-RICHARD S & LAURENT-PUIG P (2020) : YAP/TAZ signalling in colorectal cancer : lessons from consensus molecular subtypes. **Cancers**. 12 :3160.