Proposition de Stage de M2

Conventions : Sorbonne Université, Université Sorbonne Paris Nord, Université Paris Saclay, Muséum National d'Histoire Naturelle, Institut Pasteur

Année Universitaire 2020-2021

Equipe d'Accueil : Biologie vasculaire dans l'infection l'inflammation et le cancer

Intitulé de l'Unité : Institut Cochin Inserm U1016

Nom du Responsable de l'Unité : PO Couraud

Nom du Responsable de l'Équipe : S. Bourdoulous

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Responsable de l'encadrement : C . Faure

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9 Parcours de M2

(plusieurs parcours peuvent être choisis)

- Biologie moléculaire, cellulaire et fonctionnelle de l'hématopoïèse ☐
Responsables: S. Giraudier, N. Dulphy, E. Lauret

- Biomolécules, biologie et pathologie moléculaires ☐
Responsables: JM. Dupret, F. Rodrigues-Lima

- Biologie et développment cellulaires ■
Responsables: A. Guichet, A. Benmerah

- Inflammation et maladies inflammatoires ☐
Responsables: R. Monteiro, L. Mouthon, D. Ledoux

- Biothérapeutiques: Conception et applications ☐
Responsables: I. Garcia-Verdugo, JM. Sallenave

- Immunologie et Immunopathologies ☐
Responsables: M. Viguier, E. Tartour

- Microbiologie ☐
Responsables: I. Martin-Verstraete, X. Nassif

- Virologie ☐
Responsables: S. van der Werf, F. Rozenberg

- Microbiologie et génie biologique ☐
Responsables: O. Dussurget

Titre du sujet de recherche :

Regulation of HER2 by miR-429/DNAJB6 axis in HER2+ breast cancers

Résumé du projet (environ une demi-page)
Abnormalities of the HER2 tyrosine kinase receptor are responsible for 25% of breast cancer cases. Anti-HER2 therapies encounter numerous limitations due to their toxicity and resistance mechanisms, highlighting the urgent need for new therapeutic strategies against these cancers. In this context, a differential analysis of the miRnome of breast cancer cell lines revealed a pathological increase in the expression of miR-429 in HER2+ mammary tumors, associated with a poor clinical prognosis. MiR-429 loss of function experiments revealed an unsuspected role of this miRNA in enhancing membrane expression and activation of HER2 promoting cell proliferation and survival. These results demonstrate that miR-429 is a key regulator of HER2. To decipher the molecular mechanism of this regulation, we have identified by a proteomic approach several proteins potentially targeted by miR-429.
During the internship, the trainee will analyze:
- The correlation between the expression of HER2 and some interesting candidates in breast cancer cells and breast biopsy sections with known HER2 status.
- The consequences of their overexpression on HER2 expression and activation and, subsequently, on HER2-dependent proliferation and survival.
- The presence of a miR-429 binding site in the 3'UTR region of the target candidates and, if applicable, the direct targeting by miR-429.
This project will lead to the characterization of a novel miR-429-regulated pathway involved in HER2-dependent breast tumorigenesis, that could pave the way to novel therapeutic strategies. The trainee will acquire a solid experience in a large variety of techniques (cell cultures, transfections, biochemical analyses, in situ hybridization, proliferation assays, fluorescence microscopy, molecular biology…) and will beneficiate from the stimulating environment of the Institut Cochin.

Brevets de l'équipe relatifs au stage proposé
Treatment of HER2-dependent cancer using an agent that modulates the activity of a miRNA. Faure C., Bourdoulous S., Domingot A. (Brevet PCT/EP2018/079212).
Diagnosis and/or prognosis of HER2-dependent cancer using one or more miRNA as a biomarker. Faure C., Bourdoulous S., Domingot A. (Brevet PCT/EP2018/079215).

Ce projet s'inscrit-il dans la perspective d'une thèse :

oui ■
non ☐

si oui type de financement prévu : Allocation de l'école doctorale ou de la LNCC

Ecole Doctorale de rattachement :BioSPC