



Master Biologie Moléculaire et Cellulaire 'BMC',
Université de Paris - UFR Sciences du Vivant

Parcours : **Biologie et Développement Cellulaires 'BDC'**

<http://www.master2bdc.fr/>

Fiche de Projet de Stage M2, Année 2021-2022

Unité INSERM ou CNRS ou Université : Institut Necker Enfants Malades, U1151 Intitulé Equipe : Régulation hormonale du développement et des fonctions du cerveau ED d'appartenance : BioSPC (ED562) Responsable de l'Equipe : Franck Oury	Responsable du Stage : Anne-Sophie Armand Contacts Adresse : 156 rue de Vaugirard, 75015 Paris Email : anne-sophie.armand@u-paris.fr Tel : 01-40-61-53-58
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Titre du projet : Role of GPRC6A expressing cells in human prostate cancer.

Résumé du Projet de Stage (en 300 mots maximum, mots clés en gras)

In the team, we focus on the communication between organs and how ageing impact their interaction. Hormones are essential factors regulating physiological functions. Our studies focus on i) how these hormones regulate cognitive and metabolic functions; ii) What is their impact on brain ageing, iii) on age-related diseases?

In this project, we will focus on the bone-derived hormone, **Osteocalcin**, and one of its receptors, the G-coupled receptor, **GPRC6A**, in the progression and severity of prostate cancer. Prostate **cancer** is the most frequent cancer in men after 50 years of age, and the second cause of death by cancer in men. While prostate cancer is intrinsically an age related disease, the predication of its evolution is often erratic at early stages. Identifying predictive biological markers is hence needed to ameliorate the prognostic of patients with severe prostate cancer and guide treatments.

The tumor microenvironment plays a critical role in the pathogenesis and progression of cancers. Indeed, interactions between tumor cells and their **microenvironment** can influence cell survival, proliferation, resistance to therapy or increased metastatic spread. G protein-coupled receptors are important molecular players of these interactions. In this project, we will decipher the mechanistic role of one of them, GPRC6A, and its ligand, Osteocalcin, in the prostate tumor microenvironment and their impact in the progression and severity of prostate cancers. To do so, the candidate will perform cellular and molecular experiments on human cell lines and primary cells, as well as biopsies from patients with prostate cancer.

At long term, this project could give several tracks to ameliorate the diagnostic and provide the foundation for future therapies to prevent the progression and the severity of prostate cancer.

Publications de l'équipe relatives au projet de stage (max 5)

- 1- De Majo F, Hegenbarth JC, Rühle F, Bär C, Thum T, de Boer M, Duncker DJ, Schroen B, Armand A-S, Stoll M, De Windt LJ. **2020**. Dichotomy between the transcriptomic landscape of naturally versus accelerated aged murine hearts; **Sci Rep**. 10: 8136
- 2- De Risi M, Torromino G, Tufano M, Moriceau S, Pignataro A, Rivagorda M, Carrano N, Middei S, Settembre C, Ammassari-Teule M, Gardoni F, Mele A, Oury F, De Leonibus E. **2020**. Mechanisms by which autophagy regulates memory capacity in ageing. **Aging Cell**. 19:e13189.
- 3- Glatigny M, Moriceau S, Rivagorda M, Ramos-Brossier M, Nascimbeni AC, Lante F, Shanley MR, Boudarene N, Rousseaud A, Friedman AK, Settembre C, Kuperswasser N, Friedlander G, Buisson A, Morel E, Codogno P, Oury F. **2019**. Autophagy Is Required for Memory Formation and Reverses Age-Related Memory Decline. **Curr Biol**. 29:435-448.e8.
- 4- Obri A, Khrimian L, Karsenty G, Oury F. **2018**. Osteocalcin in the brain: from embryonic development to age-related decline in cognition. **Nat Rev Endocrinol**. 14:174-182.
- 5- Oury F, Ferron M, Huizhen W, Confavreux C, Xu L, Lacombe J, Srinivas P, Chamouni A, Lugani F, Lejeune H, Kumar TR, Plotton I, Karsenty G. **2015**. Osteocalcin regulates murine and human fertility through a pancreas-bone-testis axis. **J Clin Invest**. 125:2180.