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

Parcours : **Biologie et Développement Cellulaires 'BDC'**
http://www.master2bdc.fr/
Fiche de Projet de Stage de M2, 2024-2025

Unité INSERM ou CNRS ou Université : Institut Necker Enfants Malades, U1151 **Intitulé Equipe :** Neurobiologie intégrative **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

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)

Hormones are essential factors ensuring proper regulation of our physiological functions by mediating dialogue between organs. Increasing evidence suggest that changes in their circulating levels during **aging** may directly contribute to the development of age-related diseases. In the proposed project, we will focus on a 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 (TME)** plays a critical role in the pathogenesis and progression of prostate cancers. Indeed, interactions between tumor cells and the TME 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 TME and their impact in the progression and severity of prostate cancers.

At long term, this project could provide novel biomarkers to ameliorate the diagnostic and the foundation for future therapies to prevent the development/progression and/or treat aggressive prostate cancer.

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

1- *Iskandar K, Foo J, Liew AQX, Zhu H, Raman D, Hirpara JL, Leong YY, Babak MV, Kirsanova AA, Armand A-S, Oury F, Bellot G, Pervaiz S.* ***2024****. A novel MTORC2-Akt-ROS axis triggers mitofission and mitophagy-associated execution of colorectal cancer cells upon drug-induced activation of mutant KRAS.* ***Autophagy****. DOI: 10.1080/15548627.2024.2307224.*

2- *De Majo F, Martens L, Hegenbarth JC, Rühle F, Hamczyk MR, Nevado RM, Andrés V, Hilbold E, Bär C, Thum T, de Boer M, Duncker DJ, Schroen B, Armand A-S, Stoll M, De Windt LJ.* ***2021.*** *Genomic instability in the naturally and prematurely aged myocardium.* ***Proc Natl Acad Sci USA.*** *118: e2022974118.*

3- *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*

4- *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.*

5- *Glatigny M, Moriceau S, Rivagorda M, Ramos-Brossier M, Nascimbeni AC, Lante F, Shanley MR, Boudarene N, Rousseaud A, Friedman AK, Settembre C, Kuperwasser 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.*