Master 2 research internship in Integrated Structural & Cell Biology in Grenoble

Supervisor(s):
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Host laboratory:
Lab : BioSanté, INSERM U1292

Host group/team:
Mechanisms of Angiogenesis in Biological Barrier (MAB2)

Title of the M2 research internship:
How C- and N-terminal tails affects PROKR1 and PROKR2 biochemical, structural and cellular behaviour.

Project summary:
Prokineticin receptors (PROKR1 and PROKR2) are G protein-coupled receptors (GPCRs) involved in several physiological and pathological processes, including immunity, pain, inflammation, and cancer. Both receptors are activated at the nanoscale level by two secreted prokineticin peptides (PROK1 and PROK2) and are often expressed in the same tissue. However, their activation leads to different cellular responses, suggesting that ligand-receptor pairing may depend on several parameters, including the availability of the receptors at the plasma membrane. This availability might be associated with intrinsic structural changes, which may affect the receptors' cellular localization, trafficking, plasma membrane insertion, and oligomerization. Analysis of human *PROKR* genes has shown that they are located on two different chromosomes, and their primary sequences are highly conserved, with nearly 85% identity. Sequence variation is mostly concentrated in the extracellular N- and intracellular C-terminal tails, suggesting that these regions may affect the cellular behavior of PROKR1 and PROKR2. However, the mechanism by which these tails contribute to biosynthesis, cellular trafficking, membrane stability, activation, and oligomerization of both receptors remains unknown.
Hence the objectives of our project are :
i) Examine the effects of C- and N-terminal tail modifications on PROKR receptor trafficking and cellular localization.
ii) Assess the impact of these modifications on receptor oligomerization and plasma membrane insertion.
iii) Investigate how the tail regions contribute to receptor activation, signaling, and functional outcomes (e.g., receptor-mediated signaling pathways).
iv) Characterize how the N- and C-terminal sequences affect the interaction of the receptors with their ligands (PROK1 and PROK2) and G-protein coupling.
This experimental program will help elucidate how specific structural regions (the N- and C-terminal tails) of PROKR1 and PROKR2 contribute to receptor biosynthesis, trafficking, oligomerization, and function, which may have important implications for understanding their roles in physiological and pathological processes.

Keywords :
Inflammation, Trafficking, Membrane Stability, Oligomerization, Function, Prokineticin

Relevant publications of the team:
1. Antagonization of Prokineticin Receptor-2 Attenuates Preeclampsia Symptoms. Benharouga et al., J Cell Mol Med. 2025 Jan;29(2): e70346.
2. EG-VEGF maternal levels predict spontaneous preterm birth in the second and third trimesters in pregnant women with risk factors for placenta-mediated complications. Benharouga et al., Sci Rep. 2023 Nov 14;13(1):19921.
3. Therapeutic Potential of Targeting Prokineticin Receptors in Diseases. Benharouga et al., Pharmacol Rev. 2023 Nov;75(6):1167-1199.