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POSITION

Project Title/ Job position title

Project Title:

Installing the Cellular Antenna: Molecular Mechanisms of G protein-coupled Receptor Accumulation at the Primary Cilium.

Job Position Title:

PhD Student position in the laboratory of Dr. Garcia-Gonzalo.

Area of Knowledge

Life Science Panel

Human Biology, Microbiology, Genetics, Cell Biology, Genomics and Proteomics, Biochemistry

Research Project/Research Group Description

Cilia are microtubule-based cell membrane protrusions emanating from a specialized centriole known as basal body. Cilia perform two main functions: as motors and sensors. In multicellular organisms, these functions are segregated in different cell types. Thus, some cell types harbor motile cilia that propel extracellular fluid, whereas others contain primary cilia that act as signaling platforms that process optical, mechanical or chemical signals. Congenital defects in ciliary genes cause ciliopathies, human diseases that vary widely in prevalence, severity, genetics and symptoms. Some ciliopathy symptoms are due to defects in Hedgehog (Hh) signaling, a ciliary signaling pathway essential for embryonic development and adult stem cell function, and whose ectopic activation leads to cancer. Besides their well-established roles in ciliopathies and cancer, cilia also play important roles in other ailments, such as diabetes and Alzheimer's disease.

Several G protein-coupled receptors (GPCRs) localize to cilia, including HTR6, a serotonin receptor involved in neuropsychiatric diseases. In this project, we will use site-directed mutagenesis to establish which HTR6 residues are necessary and sufficient for ciliary targeting. We will then use proteomics to identify proteins that interact with HTR6 ciliary targeting sequences (CTSs), and will study how these interactions are regulated by HTR6 agonists and antagonists, and by phosphorylation. We will also test if, as occurs with other ciliary GPCRs, HTR6 ciliary targeting depends on TULP3, a phosphoinositide (PIP)-binding adaptor protein that connects ciliary trafficking complexes to the ciliary membrane. If so, we will check if TULP3 interacts with HTR6, and if this interaction is PIP-dependent.

In summary, we will combine cell biological, genetic, biochemical, pharmacological and proteomic approaches to elucidate the ciliary targeting mechanisms of a GPCR involved in brain function.

Job position description

The selected candidate will perform his/her PhD in our laboratory, investigating the molecular mechanisms of HTR6 ciliary localization. The candidate will be a highly motivated and responsible individual, with good interpersonal and organizational skills, and previous laboratory experience, preferably in areas related to this project.

The project will involve a variety of disciplines, including cell biology (mammalian cell culture, fluorescence microscopy), genetics (site-directed mutagenesis, CRISPR-based genetic modification), biochemistry (immunoprecipitation, protein purification, Western blotting), pharmacology (agonist and antagonist treatments) and proteomics (interactomics and phosphoproteomics).

GROUP LEADER

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Research project/Research group website: www.garcia-gonzalo.com/
http://www.idipaz.es/PaginaDinamica.aspx?IdPag=246&Lang=EN