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Edificio Norte, 4ªPlanta
28046 - Madrid

INPhINIT "la Caixa" Fellowship Programme

**POSITION**

**1. Project Title/ Job Position title:**

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

**2. Area of Knowledge:**

Life Sciences

**3. Group of disciplines:**

Human Biology, Microbiology, Molecular Biology, Genetics, Cellular Biology, Genomics and Proteomics, Biochemistry

**4. 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.

**5. Job position description**

Role: The candidate will be in charge of performing the experimental activities of the project, in collaboration with other members of the group. He/she will be trained accordingly and mentored through the completion of his/her PhD thesis. 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).

Responsibilities

Set up and perform experiments, maintain experimental resources (as cell lines, reagents, etc.) according to protocols, analyze & interpret results and contribute to the development of experimental strategies with accuracy and honesty.

Keep updated the laboratory notebook and properly store and manage the data produced during the project.

Collaborate with colleagues and participate in team activities (such as meetings, seminars, workshops, etc.) across the research group and wider scientific community while keeping up to date with current knowledge and recent advances.

Participate in knowledge exchange with several stakeholders, to promote the value of research in public health and to contribute to the dissemination of his/her research results in the principles of EU's Open Science policy.

Undertake any other duties of equivalent standing as assigned to him/her.

Skills

MSc Degree in Life Sciences: Biology, Medicine or Pharmacy.

Previous laboratory experience is desirable.

Motivation, critical thinking and problem-solving oriented skills.

Good interpersonal skills, including team working.

Good communication skills, willingness to engage in public presentations and ability to transmit complex concepts in a clear way.

Good time and workload management skills, including both initiative and flexibility.

**GROUP LEADER**

1. **Title:** Dr.
2. **Full name:** Francesc R. Garcia-Gonzalo
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4. **Research project/ Research Group website (Url):**
http://www.idipaz.es/PaginaDinamica.aspx?IdPag=246&Lang=EN

**OTHER RELEVANT WEBSITES**

www.garcia-gonzalo.com/