INSTITUT DES SCIENCES DU VIVANT FREDERIC JOLIOT

DEPARTEMENT MEDICAMENTS ET TECHNOLOGIES POUR LA SANTE (DMTS)

SERVICE D'INGENIERIE MOLECULAIRE POUR LA SANTE (SIMoS)

Join the CEA SIMoS Team: Postdoctoral Fellow Position in Cardiovascular Pharmacology and Physiology

Work location
CEA Saclay- Ile-de-France – France

Main scientific field
Pharmacology et Physiology

Secondary scientific fields
Health, human medicine

Key words
G protein-coupled receptor signaling pathways, beta-arrestin recruitment, internalization, aqueous diuresis, arterial blood pressure,

Function
Research and Development

Employer

Environment

The CEA is a public research organization at the forefront of research, development and innovation. The Department of Medicines and Technologies for Health (DMTS) is part of the Frédéric Joliot Institute of Life Sciences. The DMTS comprises 3 departments, including the Molecular Engineering for Health Department (SIMoS). SIMoS focuses on the identification and preclinical development of bioactive molecules, using pioneering technologies in the fields of medical imaging, diagnostic advances and therapeutic innovations. The candidate's project will be carried out at SIMoS in the Experimental and Molecular Pharmacology laboratory, directed by Dr Denis Servent, under the supervision of Dr Catherine Llorens-Cortes.

Position and tasks

Scientific project

The project, funded by the French Federation of Cardiology and the Paris-Saclay University (SPRINGBOARD), aims to develop and define the functional role of biased agonists of the apelin receptor (Apelin-R). The Apelin-R is expressed in the brain, kidneys, vessels and cardiomyocytes. Apelin-17 (K17F, composed of 17 amino acids) has a subnanomolar affinity for Apelin-R and by activating it, K17F has aquaretic, vasodilatory and positive inotropic effects. Deletion of the C-terminal phenylalanine of K17F (K16P) does not alter the peptide's ability to inhibit cAMP production and has no effect on diuresis. Conversely, this deletion strongly reduces the peptide's ability to 1) recruit beta-arrestin, 2) induce Apelin-R internalization, 3) reduce blood pressure (BP) or 4) increase left ventricular ejection fraction (LVEF), making K16P a biased agonist favoring Gi protein-coupling versus beta-arrestin recruitment. Based on these data,

our aim is to develop biased agonists of Apelin-R that are resistant to enzymatic degradation. Their half-life, the Apelin-R signaling pathways that they activate and their *in vivo* efficacy on diuresis, BP and LVEF will be evaluated. (*See the articles cited below on one of the metabolically stable K17F analogues*.)
The *in vitro* part of the project is already well advanced. One of the main tasks will be to measure blood pressure in alert rats after subcutaneous administration of the various metabolically stable apelin analogues and to assess their effects on diuresis, water intake and urinary electrolytes in rats placed in metabolic cages. For blood pressure measurement, he/she will be able to learn from a member of the laboratory.

Certification in animal experimentation - Project Designer + diploma in experimental surgery are required.
The budget finances a full-time postdoctoral position at CEA, Centre de Saclay, SIMoS, for one year, starting no later than September 2025. A potential prolongation will depend on securing additional funds

This work will be carried out in collaboration with Dr Dominique Bonnet (Equipe Chémobiologie et Pharmacognosie pour la Santé, Laboratoire d'Innovation Thérapeutique - UMR 7200 CNRS-Université de Strasbourg, Faculté de Pharmacie) for the design and synthesis of biased agonists of Apelin-R and with Dr Pierre Couvineau (Equipe Granier-Mouillac: Pharmacologie et biologie structurale des protéines membranaires, Institut de Génomique Fonctionnelle, UMR 5203 CNRS - U 1191 INSERM, Montpellier) for the identification of Apelin-R signaling pathways activated by these agonists.

1.Gerbier et al., 2017 **Faseb J**; 31:687-700. doi: 10.1096/fj.201600784R

2 Flahault et al., 2021 **Front. Pharmacol**. 12 :715095. doi.org/10.3389/fphar.2021.715095

3. Flahault et al., 2021 **Nat. Commun.** 12(1): 305. doi: 10.1038/s41467-020-20560-y

4. Girault-Sotias et al. 2024 **Can J Cardiol** S0828-282X(24)01258-3. doi: 10.1016/j.cjca.2024.11.034

Geographic Mobility: National

Teleworking: Occasional

Date of beginning of function: Septembre 2025

Profile

Qualifications

Candidates should have a PhD. A background in cardiovascular pathophysiology is recommended. Experience in measuring arterial blood pressure in alert rats will be appreciated. Independence and strong motivation are essential. The position will require skills in *in vitro* and *in vivo* pharmacology, physiology, data analysis and scientific communication.

Objectives

Our offer

We are offering the opportunity to contribute to a scientific project bringing together several areas of expertise (peptide chemistry, pharmacology and physiology). The post-doc will benefit from all the laboratory's expertise as well as a large number of core facilities. Our collaborative network will offer many opportunities for professional development. The salary will depend on qualifications and professional experience and is calculated in accordance with CEA scales.

Application Process

Send your application by **April 30th** to c.llorens-cortes@college-de-france.fr or catherine.llorenscortes@cea.fr with the subject line: "Application to postdoctoral fellow position." Please include the following: CV + Cover letter + Letters of recommendation