POSTDOCTORAL FELLOWSHIP

OPEN POSITION

DESCRIPTION

TITLE : The LSR as a new target for the identification of molecules with anti-inflammatory properties (CIBLSR)

Brief description of project

The lipoprotein receptor, the LSR (lipolysis stimulated lipoprotein receptor), identified and characterized by the Qualivie team of URAFPA (Stenger *et al*, 2012a), is a key player in peripheral and central lipid homeostasis. Studies in our laboratory have revealed a link between LSR, lipid-related disorders and pathologies including obesity, atherosclerosis (Yen *et al* 2008; Akbar *et al*, 2016), and brain aging and neurodegerative diseases (Stenger *et al,* 2012b; Pinçon *et al*, 2015, Xie *et al*, 2018), pointing towards LSR as a potential therapeutic target for these pathologies often associated with inflammatory processes. The main objective of this project is to develop an innovative *in vitro* screening LSR-based assay for the discovery of new molecules from bio-sources with targeted anti-inflammatory activity, and to identify and validate the candidate molecules in cell and animal models of these pathologies.

Objectives and Tasks:

Objective 1: The first objective is aimed towards developing an *in vitro* method to screen molecules that interact with LSR, based on surface plasmon resonance technology (Biacore®). Pilot studies using a functional soluble form of LSR attests to the feasibility of this approach. LSR purification will be achieved by immunoprecipitation of native LSR, or by expression cloning with tags allowing purification. Upon validation of the assay using known LSR ligands, screening of candidate molecules will be initiated, with analysis of real-time interactions with the receptor. Candidate molecules identified will be confirmed in binding assays using isolated cell membranes that express the multimeric LSR complex.

Objective 2: In the second objective, selected candidate molecules will be tested in appropriate cell models expressing LSR in order to characterize the properties and mechanisms of action of the drug candidate and potential effects on LSR-dependent pathways related inflammatory processes. *In vivo* studies using mouse models for the different pathologies described above will provide the means for testing the therapeutic potential of the candidate molecules.

Partners

This represents a collaborative project between the URAFPA QUALIVIE and IMoPA UMR 7365 CNRS-UL EMS teams. QUALIVIE provides expertise on the LSR receptor, biochemistry, and the cell and animal models of inflammation-related pathologies (obesity, atherosclerosis, Alzheimer's disease) required for the validation of the candidate molecules identified by *in vitro* screening. EMS provides expertise in protein engineering and *in vitro* characterization of interactions (Biacore®). Equipment platforms of UL are available for the biochemical characterization and the screening of molecules by surface plasmon resonance (UMS2008 IBSLor CNRS-Ul-INSERM, SCmass UL).

Missions

The post-doctorate will be responsible for developing and validating the *in vitro* screening method in Objective 1, including expression of LSR in the heterologous system, optimization of LSR purification, interaction studies of candidate molecules with LSR *in vitro* and in membrane binding studies. S/he will also conduct the cell culture studies to validate the effect of the molecules selected from the previous screening (Objective 2), and will participate in the management of the project, the analysis and the valorization of the results in the form of communications, articles, and/or patents.

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References cited

Akbar *et al.* (2016) Physiol Genomics. 48:928-935.

Pinçon *et al.* (2015) J Alzheimers Dis., 45:195-204.

Stenger *et al.* (2012a) *In* Chemical Biology, D. Ekinci, ed., Rijeka, Intech, 267-292.

Stenger *et al*. (2012b) J Neurochem., 123 :467-476.

Xie *et al.* (2018) Neurobiol. Aging 69 :292e1-292e5

Yen *et al.* (2008) J. Biol. Chem., 283, 25650-9.

Skills :

Protein and lipid biochemistry, Protein-ligand interaction, Protein production and purification, Cell biology.

Scientific contacts: Catherine CORBIER (catherine.corbier@univ-lorraine.fr) ; Frances YEN POTIN (frances.yen-potin@univ-lorraine.fr)

TERMS AND TENURE

The candidate will conduct the research at UR AFPA (EA3998 USC INRA 0340, *Unité de Recherche sur l'Animal et les Fonctionnalités des Produits Animaux*) with the Qualivie team (Frances Yen Potin, team leader) and at IMoPA (UMR 7365 CNRS-UL Ingénierie Moléculaire et Physiopathologie Articulaire), Team 3 : Enzymologie Moléculaire & Structurale (EMS; codirected by Pr Kira Weissman et Pr Sandrine Boschi-Muller) (researchers involved : Dr Hortense Mazon et Pr Sandrine Boschi-Muller).

Financial support for this project is provided by the Lorraine University of Excellence (LUE) Impact Biomolecules project.

Length of contract: 18 months.
The target start date for the position is **February 2019, with some flexibility on the exact start date**.

HOW TO APPLY

Applications are only accepted through email. All document must be sent to catherine.corbier@univ-lorraine.fr ; frances.yen-potin@univ-lorraine.fr and aya.khanji@univ-lorraine.fr

Deadline for application is January 7, 2019. Applicants will be interviewed by an *Ad Hoc* Commission on January 22, 2019 (videoconference).

JOB LOCATION

Nancy, Lorraine, France

REQUIREMENTS

Applicants are requested to submit the following materials:

- A cover letter applying for the position
- Full CV, including academic records and list of publications
- Statement of Research
- Two Letters of recommendations