

# Postdoctoral position: Heart targeting agents for therapeutic delivery

## OFFER DESCRIPTION

### Job environment

Organization/company: INSERM

Research field: Biological sciences › Cell Biology - Chemistry › Biochemistry

Researcher profile: from First Stage Researcher (R1)

Application deadline : 12/09/2020 00:00 - Europe/Brussels

Location: France › University Paris-Saclay, Faculty of Pharmacy › Châtenay-Malabry - Inserm UMR-S1180  
(<https://inserm-u1180.cep.u-psud.fr/index.php/en/>)

Type of contract: Temporary – 2 years

Job status: Full-time

Hours per week: 35 equivalents

Desired starting date: March 2021

Salary: Salary will be determined based on years of experience post-degree according to established institution guidelines. Benefits included according to INSERM guidelines.

### The project

Cardiovascular diseases are the leading cause of morbidity and mortality worldwide. Heart failure (HF) is one of the main cardiovascular diseases and is defined as the inability of the heart to meet the body's circulatory demand. HF constitutes a major health problem, affecting about 1-2% of the adult industrialized-countries population. In spite of huge progress in its treatment over the last decades, no definite cure exists for HF and 5-years mortality remains as high as ~50%. Regardless the causes of HF, a common feature is the persistent activation of the  $\beta$ -adrenergic/cAMP signaling cascade that leads to chronic Protein Kinase-A (PKA) activation responsible for adverse cardiac remodeling, cardiac myocyte death and fibrosis replacement. Hence,  $\beta$ -blockers are a cornerstone therapy for HF. However, they cause severe side effects and are effective in only ~50% of HF patients. Thus, a major improvement to avoid  $\beta$ -blockers side effects and more generally of any therapeutic molecules developed for HF treatment, would be to deliver efficiently and rapidly the biologic agent directly to the myocardium in a tissue-specific manner. Such strategy would improve the treatment of cardiovascular diseases (*i.e.* hypertrophic cardiomyopathies, acute or chronic HF, rhythm disorders) and abolish or minimize undesirable side effects.

The team has designed and engineered heart homing peptides (HHP) that preferentially bind to and internalize in cardiomyocytes. We believe that our HHP will offer a new class of therapeutic when coupled to a medicine-cargo to treat HF. Therefore, the project aims at developing an efficient heart-targeted drug delivery liposomal-based platform that will encapsulate a therapeutic (*e.g.* PKA-inhibitor (*i.e.* PKI)) and grafted with our HHP.

The candidate will have to:

- 1/ Characterize the efficacy and specificity of PKI-coupled HHP in pharmacological models (*i.e.* *in vitro* & *ex vivo*);
- 2/ Develop original delivery systems conjugated with HHP to improve cardiac delivery *in vivo*;
- 3/ Assess the efficiency of specific cardiac therapeutic vectors (*i.e.* HHP targeted-liposomes) in the delivery of PKI as therapeutic in a pathophysiological model of HF.

To fill full these objectives, the candidate will have to combine cell biology (cell culture, immuno-histo & -cytofluorescence, FRET live cell imaging with bio-sensors, flow cytometry), with biochemistry/chemistry approaches (immunoblots, mass spectrometry, RT-qPCR, functionalized liposomes synthesis) but also *ex vivo* and *in vivo* studies on small animals (isolated perfused hearts *ex vivo*, echocardiography).

### Missions and related activities

- To design and conduct the research project
- Data dissemination (internally and in scientific meetings)
- Reading and writing articles, reports, protocols, grant proposals
- Participating in the laboratory and team collective life
- Work with and supervise graduate students
- Develop collaborations

Level of responsibility: Autonomous work performed at the interface of two laboratories (Inserm UMR-S1180 and Cnrs UMR 8612) under the direction of Dr Guillaume Pidoux (Inserm UMR-S1180).

Specific constraints: Work with small animals

### Requirements

- A PhD degree or equivalent in cell biology and/or biochemistry
- Knowledge in:
  - o Cell biology and biochemistry
  - o Cell signaling
  - o International research environment
  - o Good oral and written English communication skills (B2 minimum)
  - o Cardiac physiology would a plus
- Expertise/Methodology in:
  - o Basic cell biology and biochemistry techniques (*e.g.* cell culture, immunoblots, immunofluorescence, RT-qPCR)
  - o Biochemistry or biotechnology or formulation
  - o Results interpretation and analysis
  - o Computer skills (Level 3: familiar with computer practice)
  - o Animal experimentation degree would be a plus (training possibilities by the host structure)
  - o Technical approaches in cardiac function analysis would be a plus
- Skills
  - o Autonomy
  - o Creativity
  - o Scientific rigor
  - o Ability to report and share results
  - o Communication skills
  - o Teamwork
  - o Adaptability
- Thematic and geographic mobility: Strongly recommended but not essential

Applications, in English, should include i/ a cover letter, ii/ a detailed CV (publications, presentations), iii/ a brief description of past research programs (max. 2 pages) and iv/ the names of 2 references. Questions regarding position or full application should be sent as a single PDF before **December 9, 2020** to Guillaume Pidoux at [guillaume.pidoux@inserm.fr](mailto:guillaume.pidoux@inserm.fr) with the subject POSTDOC CARDIOTARGET 2021.