







UMR-INSERM U1096 Endothelium, Valvulopathy and Heart Failure (EnVI) Institute for Research and Innovation in Biomedicine (IRIB) Normandy University Faculty of Medicine and Pharmacy of Rouen

## Cardio-immunology PhD Candidate position 2021-2024 Faculty of Medicine, Normandy University, Rouen, France

Workplace : Rouen, Seine-Maritime, France

**Title :** Impact of co-signaling pathways in cardiac lymphatics in cardio-onco-immunology: focus on myocarditis induced by treatment with immune checkpoint inhibitors.

We are looking for a PhD candidate for a 3-year fully funded scholarship for training in the **Inserm U1096 Laboratory** (<u>http://www.insermu1096.fr/</u>) at the Faculty of Medicine in Rouen (France) under the supervision of Dr. Ebba Brakenhielm and Dr. Virginie Tardif. The successful applicant will become part of a unique multidisciplinary training and research environment and be responsible for: 1/ Carrying out a research protocol, collecting and analyzing data, 2/ Disseminating the results in international peer-reviewed scientific journals and conferences and 3/ Completing a PhD dissertation within 3 years

**Project Summary** Cardiac inflammation is a common trait in many cardiovascular diseases, including myocardial infarction (MI) and myocarditis. We previously showed that insufficient cardiac lymphangiogenesis aggravates cardiac inflammation post-MI (Henri et al <u>Circulation</u> 2016). Conversely, we recently demonstrated that cardiac-infiltrating immune cells, notably T lymphocytes, suppress cardiac lymphangiogenesis (Houssari et al <u>ATVB</u> 2020). A major regulator of immune responses is the family of co-signaling molecules, such as PD-1. These molecules are the targets of immune check-point inhibitors (ICI) that have emerged as promising treatments to increase anti-tumor immunity in cancer patients. However, they may lead to significant adverse effects, due to a dysregulated immune response, notably in the heart with development of severe myocarditis. In this project, we will address **the molecular interactions between lymphocytes and cardiac lymphatics**, known to express inhibitory co-signaling molecules, such as the PD-1 ligand PDL1. The objectives are to I) investigate co-signaling molecule expression profiles (RNASeq) in T cells and cardiac lymphatics during auto-immune or ICI-induced myocarditis in patients and mouse models, and II) determine the impact of lymphangiogenic therapy on co-signaling pathways and anti-cardiac immune responses.

This project will allow, for the first time, the investigation of how co-signaling pathways in lymphatics may limit myocardial inflammation by decreasing both the activity and transit time of infiltrating lymphocytes in the heart, with the aim to identify new treatment strategies to prevent or reduce myocarditis.

This transdisciplinary and translational project is part of the 2021 *Normandy Region Chair of Excellence* project, directed by Dr Virginie Tardif, which is set to deepen our understanding of the cellular and molecular mechanisms involved in regulation of immune responses in the heart. The project will be developed in the setting of a dynamic international, national and regional research network (ANR-PRC 2019-2022, *RESIST-HF*; RIN SingleC 2019), and the FHU CARNAVAL consortium led by the host laboratory.

<u>Applicant Profile</u> Applicant is expected to have completed a MSc with top scores, and have a strong background in immunology, preferably with special interest in cardiac physiology. He or she should have experience in experimental approaches such as flow cytometry, RT-qPCR, western blot, and immunohistochemistry. Previous experience with animal care and handling will be appreciated. Speaking English is mandatory.

- <u>Theoretical knowledge</u>: the candidate should have strong knowledge in **immunology and molecular biology** as well as basic knowledge in integrated physiology, especially cardiac function and vascular cell biology.
- <u>Practical skills</u>: the candidate should be familiar with cell culture, cell biology (immunohistochemistry, westernblot) and molecular biology (RNA extraction and RTqPCR) technics. Skills in cell sorting and immune cell culture are highly appreciated.

The complete application file should be sent to Ebba Brakenhielm. It will include: - a cover letter discussing your interest in the position, - a detailed CV, - a full record of your academic tracks, - a letter of recommendation. The interview of the 10 candidates with the most adapted profile will take place by videoconference.

## Contact:

Application must be sent before May 15<sup>th</sup> 2021 to Ebba Brakenhielm and Virginie Tardif. <u>Beginning of PhD :</u> October 2021

Contact : > Ebba BRAKENHIELM ; ebba.brakenhielm@univ-rouen.fr; +33 2-35-14 83 70

> Virginie TARDIF ; <u>virginie.san-martin-tardif@inserm.fr</u>