

Open PhD student position:

Bone marrow endothelial cell mechanosensing in the process of platelet formation



PhD Student Research Position:

“Involvement of bone marrow endothelial cell mechanosensitive channels on megakaryocyte transendothelial passage”.

A PhD student position is available in **co-direction between Strasbourg (France) and Freiburg (Germany), funded for 3 years.**

Platelets are small circulating cells vital to prevent hemorrhages. The mechanisms of platelet formation are far from being fully understood. In particular, the role played by the mechanical and cellular microenvironment in the bone marrow stroma, how endothelial cells interact with platelet precursor for their final maturation and transmigration within the blood vessel are essential steps still unresolved to understand normal and defective platelet production.

Platelets are produced by megakaryocytes (MK). MK extend protrusions, named proplatelets, that pierce through the sinusoidal bone marrow endothelial cells (sBMEC) lining the sinusoid vessels to enter the blood circulation.

Little is known about how sBMEC control local permeability while being constantly crossed by marrow cells and proplatelets. Our lab recently published that mouse proplatelet extension is preceded by MK forming podosomes that push on the sBMEC to create transendothelial pores. The response of sBMEC to the MK pushing force and the factors that control whether proplatelet invasion occurs via a transendothelial or inter-endothelial route are unknown. Physical forces are known to exquisitely regulate the function of endothelial cells from different vascular beds. However, despite that aging and a number of pathologies (bone marrow cancers) or treatments (chemotherapy) strongly alter the biophysical properties of the blood bone marrow barrier, the importance of its biomechanics in platelet production remains fully unknown.

This collaborative and interdisciplinary project therefore proposes to evaluate how sBMEC respond upon down-regulation of mechanosensitive channel expression and how this impacts MK differentiation/maturation and proplatelet formation.

Mission. The recruited PhD student will be in charge of 1) characterizing the mechanosensitive channels in sBMEC, 2) studying the impact of those channels on sBMEC stiffness and 3) evaluating their

roles on the crosstalk between MKs and SBMEC. 4) In collaboration with a post-doctoral researcher currently developing a model of *in vitro* transendothelial migration, the PhD student will evaluate the impact of pharmacological modulation of the channels in the process of proplatelet transmigration. He/she will also benefit from the help of a technician for cell culture and analyses.

Techniques that will be used: primary cell sorting (sBMECs, hematopoietic progenitors) and culture, qRT-PCR analysis, electrophysiology, immunofluorescence and imaging.

Requirements. We are looking for a self-motivated student with a Master's degree or equivalent in a discipline relevant to biomedical research such as biology, biophysics and physiology.

Solid experience in cell biology and cell culture is required, and research experience with biomechanical or biophysical methods, such as electrophysiology, would be welcome.

Scientific curiosity and the desire to actively shape your own research project will be highly seen.

Excellent communication skills in English (B2 or higher), as well as the desire to work as part of an English-speaking institute will be required.

Location. The institute in France is located in Strasbourg (France), directly in the city center (UMR_S1255, Inserm-EFS-University of Strasbourg). The institute in Germany is located in Freiburg (Institute for Experimental Cardiovascular Medicine, Universitätsklinikum Freiburg, Universitäts-Herzzentrum).

Interested candidates should apply as soon as possible but date of arrival is open to discussion.

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