Master 2 research internship in Integrated Structural & Cell Biology in Grenoble

Supervisor(s):
Claire Bouvard, claire.bouvard@cea.fr

Host laboratory:
BioSanté, BAL team
https://biosante-lab.fr/en

Title of the M2 research internship:
Characterization of the effects of cardiac and hepatic Bmp10

Project summary:
Bone Morphogenetic Proteins (BMPs) are a group of signaling molecules that belongs to the Transforming Growth Factor-β (TGF-β) superfamily of proteins. BMPs play crucial roles in all organ systems. Our team has shown that BMP9 and BMP10 are crucial for the development and homeostasis of the cardiovascular and lymphatic systems. Moreover mutations in this signaling pathway are associated with two rare vascular diseases, namely pulmonary arterial hypertension (PAH) and hereditary hemorrhagic telangiectasia (HHT). We recently found that a BMP9-BMP10 heterodimer was present in the blood and was responsible for most of the BMP activity that we could measure in vitro. BMP9 is produced by hepatic stellate cells and BMP10 is produced by cardiomyocytes and hepatic stellate cells. Hepatic stellate cells might be the source of the BMP9-BMP10 heterodimer. We generated liver specific and cardiac specific knockout mice in order to 1) confirm whether the source of the heterodimer is the liver or not, and 2) to study the role of cardiac BMP10 versus hepatic BMP10. For this purpose we will use in vitro assays to study BMP signaling and in vivo assays to study the role of BMPs in angiogenesis (retina model), lymphatic vessel formation and cardiovascular homeostasis. To analyze blood and lymphatic vessels we have access to the microlife imaging facility.

Keywords:
signaling, vascular biology, mouse model

Relevant publications of the team:

Tillet E, Ouarné M, Desroches-Castan A, Mallet C, Subileau M, Didier R, Lioutsko A, Belthier G, Feige JJ and Bailly S. A heterodimer formed by bone morphogenetic protein 9 (BMP9) and BMP10 provides most BMP biological activity in plasma. Journal of Biological Chemistry, 2018, 93(28): 10963-10974

Claire Bouvard, Ly Tu, Martina Rossi, Agnès Desroches-Castan, Nihel Berrebeh, Elise Helfer, Caroline Roelants, Hequn Liu, Marie Ouarne, Nicolas Chaumontel, Christine Mallet, Christophe Battail, Andreas Bikfalvi, Marc Humbert, Laurent Savale, Thomas Daubon, Pascale Perret, Emmanuelle Tillet, Christophe Guignabert, Sabine Bailly. Different cardiovascular and pulmonary phenotypes for single- and double-knock-out mice deficient in BMP9 and BMP10. Cardiovascular Research, Oxford University Press (OUP), 2021, ⟨10.1093/cvr/cvab187⟩

Ouarné M, Bouvard C, Boneva G, Mallet C, Ribeiro J, Desroches-Castan A, Soleilhac E, Tillet E, Peyruchaud O and Bailly S. BMP9, but not BMP10, acts as a quiescence factor on tumor growth, vessel normalization and metastasis in a mouse model of breast cancer. Journal of Experimental & Clinical Cancer Research, 2018, 37(1): 209

Agnès Desroches-castan, Emmanuelle Tillet, Claire Bouvard, Sabine Bailly. BMP9 and BMP10 : Two close vascular quiescence partners that stand out. Developmental Dynamics, Wiley, 2021, ⟨10.1002/dvdy.395⟩

Agnès Desroches-Castan, Emmanuelle Tillet, Nicolas Ricard, Marie Ouarné, Christine Mallet, Lucid Belmudes, Yohann Couté, Olivier Boillot, Jean-Yves Scoazec, Sabine Bailly, Jean-Jacques Feige.

BMP9 is a paracrine factor controlling liver sinusoidal endothelial cell fenestration and protecting from hepatic fibrosis. Hepatology, Wiley-Blackwell, 2019, ⟨10.1002/hep.30655⟩