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

Supervisor(s):
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Host laboratory:
BioSanté, https://biosante-lab.fr/en

Host group/team:
BAL: BMP in Angiogenesis and lymphangiogenesis

Title of the M2 research internship:
Liver or cardiac BMP10 : circulating forms and vascular functions

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 two members of the BMP family, 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. We generated liver specific and cardiac specific Bmp10-knockout mice to discriminate the functions of the different sources of BMP10. For this, we analyze circulating forms of these BMPs using ELISA or BMP signaling with luciferase reporter assays. Vascular development is assessed using angiogenesis model of the retina followed by immunofluorescence /confocal microscopy. Finally, blood vessel permeability/disorganization will be studied by the use of fluorescent tracers in adult mice. Altogether, the project includes various techniques from protein expression (qPCR, western blot), to mouse tissue imaging. The intern will not directly handle mice but should not disagree with animal experimentation.

Keywords:
vascular disease, BMP, mice models

Relevant publications of the team:

Desroches-Castan A. , Tillet E. ,. Bouvard C., Bailly S. BMP9 and BMP10: two close vascular quiescence partners that stand out. Dev Dyn. 2021 Jul 9. doi: 10.1002/dvdy.395. Review

Tillet E, Ouarné M, Desroches-Castan A, Mallet C, Subileau M, Didier R, Lioutsko A, Belthier G, Feige JJ, Bailly S. A heterodimer formed by bone morphogenetic protein 9 (BMP9) and BMP10 provides most BMP biological activity in plasma. J Biol Chem. 2018 Jul 13;293(28):10963-10974.

Desroches-Castan A, Tillet E, Ricard N, Ouarné M, Mallet C, Belmudes L, Couté Y, Boillot O, Scoazec JY, Bailly S, Feige JJ. Bone Morphogenetic Protein 9 Is a Paracrine Factor Controlling Liver Sinusoidal Endothelial Cell Fenestration and Protecting Against Hepatic Fibrosis. Hepatology. 2019 Apr 9. doi: 10.1002/hep.30655

Desroches-Castan, A., Tillet, E., Ricard, N., Ouarne, M., Mallet, C., Feige, J. J., and Bailly, S. (2019) Differential Consequences of Bmp9 Deletion on Sinusoidal Endothelial Cell Differentiation and Liver Fibrosis in 129/Ola and C57BL/6 Mice. Cells 2019 Sep 13;8(9):1079. doi: 10.3390/cells8091079.

Bouvard C., Tu L., Rossi M., Ouarne M., Helfer E., Perret P., DaubonT., Desroches-Castan A., Roelants C., Chaumontel N., Humbert M., Mallet C., Bikfalvi A., Saval L., Tillet E., Guignabert C., Bailly S. (2021) Different cardiopulmonary phenotypes for single- and 1 double-knock-out mice deficient in BMP9 and BMP10. Cardiovasc. Res, 2021 Jun 4:cvab187. doi: 10.1093/cvr/cvab187.