UFR CHIMIE & BIOLOGIE Université Grenoble Alpes

Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2026-2027

Laboratory/Institute: Grenoble Institut Neurosciences - GIN **Director:** E. Barbier
Team: BVasC **Heads of the team:** S. Bailly & N. Ricard

Name and status of the scientist in charge of the project:
Agnès Desroches-Castan (Research Engineer,Inserm, **HDR**) and Louane Despas (PhD student)

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Program of the Master's degree in Biology:

☐ Microbiology, Infectious Diseases and Immunology ☐ Biochemistry & Structure
☒ **Physiology, Epigenetics, Differentiation, Cancer** ☒ **Neurosciences and Neurobiology**

Title of the project: Deciphering the mechanism involved in brain hemorrhages induced by ALK1-NRP1 deletion

Objectives (up to 3 lines):

The aim of this internship is to understand how defects in the axon guidance signaling pathway can lead to brain microhemorrhages in a mouse model of a rare vascular disease (Rendu-Osler) in order to propose new therapeutic approaches.

Abstract (up to 10 lines):

ALK1 is a receptor mainly expressed on endothelial cells, which is necessary for proper vascular quiescence. Indeed, mutations of *ALK1* are involved in a rare autosomal dominant vascular disease named Rendu-Osler or HHT (hereditary hemorrhagic telangiectasia) characterized by brain vascular malformations. In a mouse model where *Alk1* is deleted in endothelial cell (*Alk1*^{iECKO}), RNAseq analysis revealed crosstalk with the axon guidance semaphorin/neuropilin (NRP1)/plexin signaling pathway. Interestingly, we observed that invalidating NRP1 with anti-NRP1 antibody in our *Alk1*^{iECKO} mouse model induces brain hemorrhages within a week. The objectives of this internship are to:
1) Characterize by electron microscopy and immunofluorescence the brain vascular defects induced by this treatment.
2) Decipher the molecular signaling leading to brain hemorrhages using brain primary endothelial cells.

Methods (up to 3 lines):

Microscopy techniques including Transmission electron microscopy, immunofluorescence.
Cell culture, molecular biology (RNA extraction and qPCR), and biochemistry (Western blot, proteomic)
Mouse model.

Up to 3 relevant publications of the team:

Desroches-Castan A, Koca D, Liu H, Roelants C, Resmini L, Ricard N, Bouvard C, Chaumontel N, Tharaux PL, Tillet E, Battail C, Lenoir O, Bailly S. BMP9 is a key player in endothelial identity and its loss is sufficient to induce arteriovenous malformations. Cardiovasc Res. 2024. doi: 10.1093/cvr/cvae052. PMID: 38502919.

Al Tabosh T, Liu H, Koça D, Al Tarrass M, Tu L, Giraud S, Delagrange L, Beaudoin M, Rivière S, Grobost V, Rondeau-Lutz M, Dupuis O, Ricard N, Tillet E, Machillot P, Salomon A, Picart C, Battail C, Dupuis-Girod S, Guignabert C, Desroches-Castan A, Bailly S. Impact of heterozygous ALK1 mutations on the transcriptomic response to BMP9 and BMP10 in endothelial cells from hereditary hemorrhagic telangiectasia and pulmonary arterial hypertension donors. Angiogenesis. 2024. doi: 10.1007/s10456-023-09902-8.

Hermann R, Shovlin CL, Kasthuri RS, Serra M, Eker OF, Bailly S, Buscarini E, Dupuis-Girod S. Hereditary haemorrhagic telangiectasia. Nat Rev Dis Primers. 2025. doi: 10.1038/s41572-024-00585-z.

Requested domains of expertise (up to 5 keywords):

Cellular biology, physiology, signaling.