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

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Host laboratory:
Biologie et Biotechnologie pour la Santé
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Title of the M2 research internship:
Targeting of EG-VEGF protein through structural drug-designed screening to inhibit its proangiogenic effects in inflammatory diseases.

Project summary:
Lung inflammatory-associated diseases, such as cystic fibrosis (CF) are associated with increased neovascularization and exacerbated inflammation. Recently, we demonstrated that the new pro-angiogenic factor EG-VEGF is highly expressed in CF lung epithelial cells (LEC) and it upregulates their inflammatory mediators. EG-VEGF is a circulating ligand that exerts its actions via two receptors, PROKR1 and PROKR2. We have also demonstrated that EG-VEGF inflammatory effects are attenuated upon LEC treatment with two non-peptide PROKRs antagonists, suggesting a potential promise for the treatment of lung inflammatory-associated diseases. Nevertheless, the actual antagonists are not very specific. An alternative approach will be to consider a direct antagonization of the ligand EG-VEGF.
The objective of the proposed project is to resolve the three-dimensional structure (TDS) of EG-VEGF protein that will be used to identify, using molecular docking, the molecules that bind EG-VEGF and disrupt its interaction with its receptors. The promising molecules will be tested in vitro using our recently developed cellular models.
The master2 student will in charge, within our team, of the following tasks.
- In vitro tests of molecules of interest In vitro studies will be performed on the lung epithelial cells (LEC) and lung endothelial cells (EC). A series of in vitro tests, including, toxicity, proliferation, migration, and invasion, will be performed in the absence or presence of EG-VEGF.

To study angiogenic and inflammatory processes, we will use both normal and CF bronchial epithelial cells as well as lung explant model developed by our group. This model offers the possibility to test the effects of the identified molecules on a system that encompasses multiple cell types.

Keywords:
EG-VEGF structure, lung inflammation, drug screening

Relevant publications of the team:
Alfaidy N, Brouillet S, Rajaraman G, Kalionis B, Hoffmann P, Barjat T,Benharouga M, Murthi P. The Emerging Role of the Prokineticins and Homeobox Genes in the Vascularization of the Placenta: Physiological and Pathological Aspects. Front Physiol. 2020 Nov 12;11:591850.

Kouadri A, El Khatib M, Cormenier J, Chauvet S, Zeinyeh W, El Khoury M, Macari L, Richaud P, Coraux C, Michaud-Soret I, Alfaidy N, Benharouga M. Antioxid Redox Signal. 2019. 31(1):59-74 (IF 6.8).

Traboulsi W, Sergent F, Boufettal H, Brouillet S, Slim R, Hoffmann P, Benlahfid M, Zhou QY, Balboni G, Onnis V, Bolze PA, Salomon A, Sauthier P, Mallet F, Aboussaouira T, Feige JJ, Benharouga M, Alfaidy N. Clin Cancer Res. 2017. 23 (22):7130-7140. (IF 9.2).

Sergent F, Hoffmann P, Brouillet S, Garnier V, Salomon A, Murthi P, Benharouga M, Feige JJ, Alfaidy N. Hypertension. 2016. 68 (1): 148-156. (IF 6.5).

Chauvet S, Traboulsi W, Thevenon L, Kouadri A, Feige JJ, Camara B, Alfaidy N, Benharouga M. Am J Physiol Lung Cell Mol Physiol. 2015. 309 (3): L314-322. (IF 4.5)

Micoud J, Chauvet S, Scheckenbach KE, Alfaidy N, Chanson M, Benharouga M. Biochim Biophys Acta. 2015. 1853(10 Pt A): 2420-2431. (IF 5.3)