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:
MAB2: Mechanisms of Angiogenesis in Biological Barriers

Title of the M2 research internship:

PMN transmigration in cystic fibrosis: Roles of EG-VEGF and cellular prion (PrPC) proteins in inflammation.

Project summary:
In cystic fibrosis (CF) patients, the infiltration of the lungs by neutrophils (PMN) and the role of these cells in exacerbating the inflammatory response are well documented. PMN infiltration primarily uses the transmigration pathway across the endothelial and epithelial barriers that are impaired in CF. Several pro-inflammatory and pro-angiogenic factors released by CF epithelial cells participate via their receptors in the PMN infiltration process. We have recently demonstrated that the cellular prion protein (PrPC) is directly involved in the protection of epithelial junctions in CF and that a new pro-angiogenic and pro-inflammatory factor, named EG-VEGF, as well as its two receptors PROKR1 and 2 would be involved in the destabilization of these barriers.
Our project aims to characterize the role of EG-VEGF/PrPC, in relation to CF, in the transmigration process, and to propose therapies targeting the circulating ligand EG-VEGF to curb PMN infiltration in CF.
Two approaches will be used:
Clinical approach: In collaboration with the Lung Department and the CRCM of the Grenoble CHU, we propose to measure circulating EG-VEGF in healthy and CF patients.
In vitro approach: Healthy lung (16HBE14o- (HBE)), CF (CF14BEo- (CFBE)), and human lung endothelial cells will be used. Cell biology (coculture, trans-barrier resistance measurement, proliferation, migration, chemotaxis), biochemical (ELISA, Western Blot, RT-qPCR), and cell imaging techniques will be used.
Our study will be performed in the absence or presence of EG-VEGF. Similar experiments will be performed in the presence of a structural designed ligand-receptor inhibitory drug, wish has been recently identified using molecular docking on the in silico solved structure of EG-VEGF.
The work will be carried out at CEA-Grenoble in Health Department/BioHealth laboratory. The candidate will benefit from a close supervision and will work in close collaboration with the members of the MAB2 team. All the techniques are available in the lab

Keywords:
drug design, EG-VEGF/PrPC, lung inflammation

Relevant publications of the team:

Biomedicines. 2022 Jan 24; 10(2): 252.

Biochim Biophys Acta Mol Basis Dis. 2021 Dec 1; 1867(12):166244.

Cancers (Basel). 2021 Jun 15; 13(12):2999.

Front Physiol. 2020 Nov 12; 11: 591850.

Antioxid Redox Signal. 2019 Jul 1; 31(1): 59-74.

Methods Mol Biol. 2018; 1710: 317-324.

Clin Cancer Res. 2017 Nov 15; 23(22): 7130-7140.