**Role of Hedgehog signaling in maintaining endothelium integrity**

The loss of vascular integrity (i.e. abnormal vessel permeability, endothelial activation…) is associated with the pathogenesis of many vascular and cerebrovascular diseases including retinopathy, dementia, heart failure, inflammation and post-traumatic oedema (observed after ischemic stroke or myocardial infarction). Our recent data identified Desert Hedgehog (Dhh) as a critical regulator of endothelial integrity. More specifically, we have recently demonstrated that Dhh signaling is essential for endothelial cell intercellular junction integrity and immune quiescence. We hypothesized that the loss of Hh signaling consecutive to obesity, type 2 diabetes, hypertension or aging might be triggering endothelial cell dysfunction and promote cardiovascular and cerebrovascular diseases.

More specifically, the objectives of this PhD project are (1) to characterize signaling pathways mediating Desert Hedgehog (Dhh) regulation of blood vessel integrity, (2) to evaluate the pathophysiological consequences of endothelial cell specific invalidation of Hedgehog signaling and (3) to test whether restoring Dhh-induced signaling may be used to prevent vascular diseases.

This project will involve both *in vitro* (cell culture …) and *in vivo* (evaluation of vessel permeability in mouse models) assays in which loss of function (blocking antibodies, siRNA, dominant negative, conditional KO mice) and gain of function (transfections, gene therapy, small molecule agonist) strategies will be used.

## Contact

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Financement

Funding: 3 year- PhD fellowship from the FRM (starting 01/10/2017)

Recent papers of the group

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