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Department of Anatomy and Cell Biology

Seminar Series

Alexandre Drubac, Ph.D.

Assistant Professor
Sainte-Justine Hospital Research Center -
Dept. of Pathology & Cellular Biology
Ophthalmology Dept., University of Montreal

Hosted by: Craig Mandato, Ph.D.

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11:30 am -12:30 pm

Room 1/12 - Strathcona Anatomy and Dentistry Building

"TGFb signaling function in the neurovascular heterogeneity and integrity"

Neuron's physiology strongly depends on angiogenesis, the growth of new blood vessels, and the development of a highly selective blood-brain/retina barrier (BBB and BRB, respectively). Sprouting angiogenesis and BRB/BBB develop simultaneously, and defects in those processes contribute to the onset and progression of neurovascular diseases such as ischemic retinopathies (IR) and cerebral ischemic stroke (IS). Therefore, retina and brain revascularization have therapeutic potential, and endothelial tip cells (guiding new vessel growth) are primary targets for angiogenic therapies. However, no treatments currently promote vessel regrowth with limited permeability breakdown. Thus, my lab aims to characterize the mechanisms coupling angiogenesis and BRB/BBB formation to ultimately propose new therapeutic strategies to improve revascularization and neuronal function in ischemic diseases of the central nervous system (CNS).

We have recently uncovered a neurovascular paradigm in which transforming growth factor β (TGFβ) signaling governs specialized tip cell (or D-tip cell) differentiation, sprouting, BRB formation, and mouse neuroretina vascularization. While retina and brain vascularization have shown similarities, the role of TGFβ-induced D-tip cells in brain angiogenesis and the underlying mechanisms are still unknown. The brain vascular network acquires structural and cellular heterogeneity across brain regions to maintain neuronal homeostasis and function. While the brain vasculature expands during a critical postnatal period, it remains unclear whether brain regions use different angiogenic mechanisms. Here, we identify a spatial and temporal regulation of the thalamus angiogenesis in the neonatal brain. Histological analysis of developing brains revealed that the thalamic area showed a higher vascular density and endothelial cell number than other regions. Combining spatial and endothelial single-cell RNAseq (scRNAseq) transcriptomic analysis, we provide a molecular atlas of developing brain regions and a comprehensive list of region-specific angiogenic regulators. We found that TGFβ signaling is crucial for thalamic vascularization during a critical postnatal period. Therefore, our projects focus on deciphering TGFβ signaling mechanisms controlling brain EC specification and vascular integrity in development and ischemic diseases