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Jérôme Robert, Ph. D.
Department of Pathology and Laboratory Medicine
Faculty of Medicine
University of British Columbia

Development of a human cerebrovascular model to study Alzheimer's disease in vitro (présentation en anglais)

Résumé
Alzheimer's Disease (AD) is the leading cause of senile dementia with over 44 million affected persons and an economic burden of over $600 billion. Amyloid plaques, consisting of deposited beta-amyloid (Aβ), and neurofibrillary tangles consisting of hyperphosphorylated tau proteins are neuropathological hallmarks of Alzheimer's Disease (AD). As cardiovascular risk factors increase dementia risk, major pathways that regulate Aβ clearance from the brain involve the cerebrovasculature, and most AD patients have vascular amyloid deposition (cerebral amyloid angiopathy (CAA)), it is now clear that cerebral vessels play a major role in AD pathogenesis.

I will present a novel human experimental platform to investigate the cerebrovascular contribution to AD, in which three dimensional perfusible cerebral blood vessels are engineered in a scaffold-directed flow bioreactor system from primary human endothelial cells (EC) and smooth muscle cells (SMC), with or without astrocytes. I will discuss as proof-of-principle relevant to Alzheimer's disease, that circulating high-density lipoprotein (HDL), a major player in cardiovascular health, reduces Aβ-mediated endothelial activation and also reduces Aβ accumulation in the vascular wall of our bioengineered tissues, thereby helping to explain more about the associations between cardiovascular disease and Alzheimer disease. Taken together, these results establish the utility of human engineered cerebral vessels as a highly innovative *in vitro* platform to study key mechanistic questions relevant to AD.

Biographie
Jerome completed his graduate studies in the labs of Arnold von Eckardstein and Simon Hoerstrup at the University of Zurich (Switzerland) in 2013 where he studied lipoprotein interaction with endothelial cells and developed a unique model of atherosclerosis in the dish. He went on and did his postdoctoral training in the lab of Cheryl Wellington at the University of British Columbia (Vancouver, Canada) where he studied the role of lipoproteins on cerebrovascular health in the context of dementia. In 2015 Jerome received the financial support of the Weston Brain Institute to develop a brain blood vessel equivalent to study Alzheimer's disease. He aims now to use this model to better understand how cardiovascular risk factors, including the gut microbiome might influence dementia.