McGill University - Imperial College London Student Exchange

Training opportunity within the McKinney Laboratory at the Bellini Life Science Complex, McGill University

Dr Anne McKinney's laboratory has focused on studying excitatory synapse formation and maintenance under physiological and pathological conditions such as epilepsy and Alzheimer's Disease. She has made seminal contributions to the field including that AMPA receptor activation is necessary for dendritic spine maintenance. The McKinney lab uses a multidisciplined approach transgenic animals, electrophysiology, EM, immunohistochemistry and 4D imaging to address their questions of interest. It is also one of the few laboratories which combine high resolution 4D imaging with electrophysiology. One area of particular relevance for the McGill-Imperial student exchange program is related to the involvement of lipid metabolism in synaptic dysregulation in Alzheimer's Disease.

Background: Alzheimer's disease (AD) is the most prevalent form of dementia leading to a progressive cognitive decline that currently cannot be cured. The typical signs of AD include upregulation of inflammatory markers, early synapse loss followed by neuronal death, intracellular neurofibrillary tangles and accumulation of extracellular senile plaque that is made up mainly of amyloid-β peptide (Aβ). Based on this evidence, researchers have shown the abnormal accumulation of oligomeric Aβ as an important process in AD progression. However, another hallmark of AD, namely an increase of "adipose inclusions", suggests aberrant lipid metabolism in the brains of AD patients has largely been overlooked. This disruption in lipid homeostasis may aggravate the interference of synaptic connections induced by aberrant oligomeric Aβ accumulation. Large-scale epidemiological studies have also revealed several AD risk factors related to lipid homeostasis, such as the ε4 allele of the apolipoprotein E (APOE) gene. There is also a prevalence of AD in the obese population and a significant reduction of AD in long-time statins users to lower blood cholesterol. All indicate the importance of lipid dysregulation in AD progression.

Opportunity: This project aims to (i) to investigate how an imbalance in lipid homeostasis and the formation of lipid deposits in response to oligomer Aβ induce adverse morphological and functional changes in hippocampal dendritic spines in Aβ-model of AD and (ii) to test nanodelivery systems with drug designed to correct and induce circuitry repair. We have already preliminary data showing that there is change in lipid composition in AD hippocampus and modifying lipid composition can prevent structural and functional changes induced in AD. We will now investigate the mechanisms involved.

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