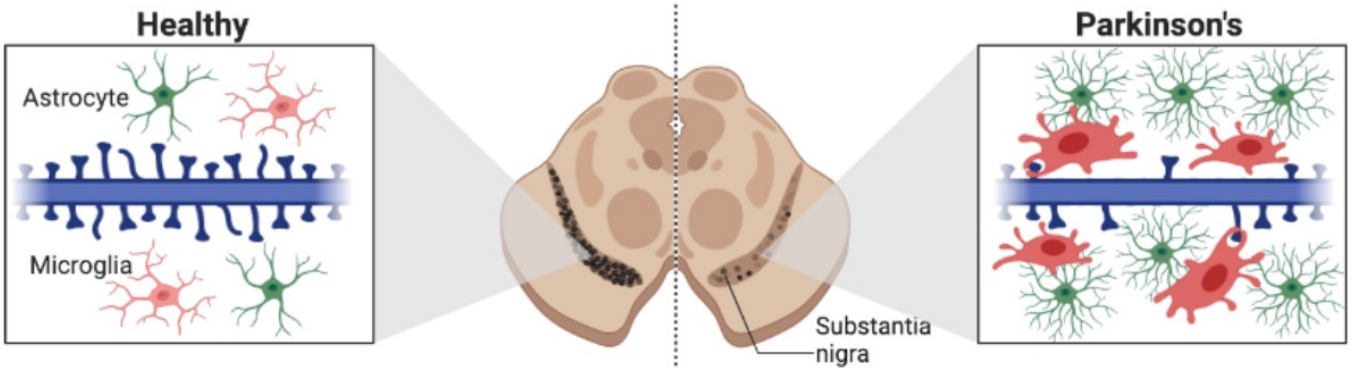
Centre for Neuroscience and Regenerative Medicine

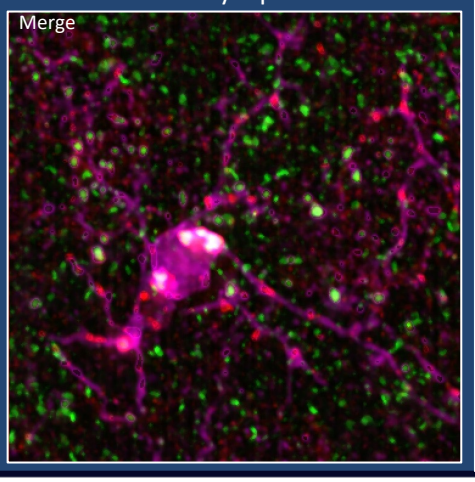
ST VINCENT'S CENTRE FOR APPLIED MEDICAL RESEARCH

Project: Investigating microglia driven synapse loss in a mouse models of Parkinson's disease and L-Dopa induced Dyskinesia

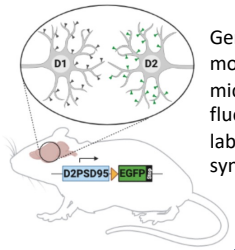


Neuroinflammation is a well characterized hallmark for Parkinson's disease (PD)[1] and recent evidence from our lab suggests its involvement in L-Dopa induced dyskinesia (LID)[2], a side effect of L-Dopa treatment in PD. Furthermore, we and others have evidence that synapse loss also contributes to PD and LID[3]. The current project will try to understand if microglia and astrocytes actively contribute to synapse loss in this disease and if anti-inflammatory treatments have anti-dyskinetic potential and protect synapses. For this project we have pharmacological (PLX3397) and genetic (CD11bDTR – all microglia; CD86DTR – proinflammatory microglia) tools to eliminate microglia or microglia subtypes, respectively. Furthermore, we have genetically modified mice with fluorescently labeled synapses that we will utilize to assess synapse loss via superresolution microscopy in various PD and LID phenotypes with / without treatment .

Synaptic material (PSD95) within lysosomes (CD68) of microglia in LID, suggests that microglia "eat" synapses and contribute to synapse loss in disease

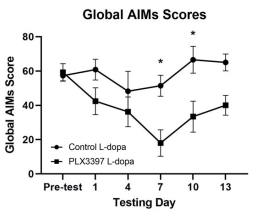


Models and Techniques that you will use

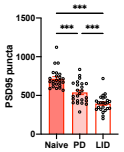


Genetically modified mice with fluorescently labeled synapses

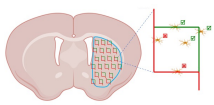
L-Dopa injections to induce LID and behavioral scoring to see effect of treatment

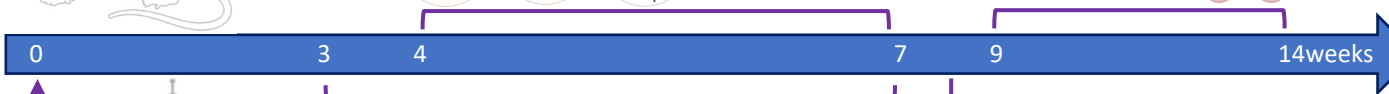


Analysis: Superresolution microscopy to quantify synapse loss



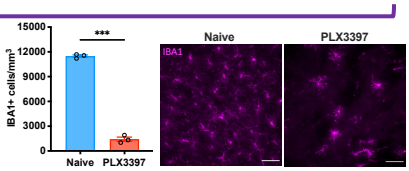
Stereology to quantify cell population





6-OHDA toxin stereotaxic brain surgery to model PD

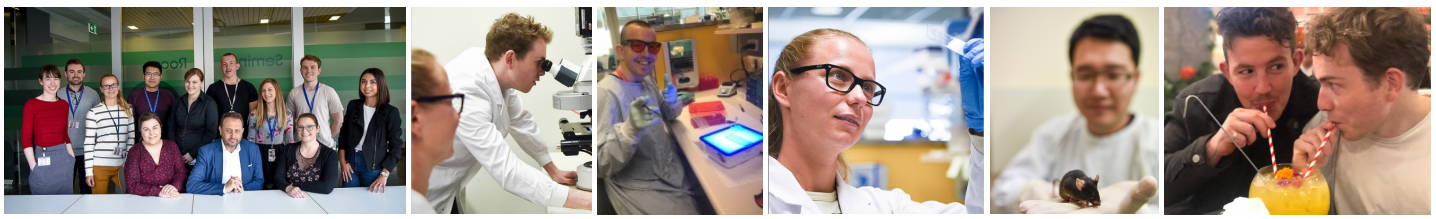
Microglia elimination using either a pharmacological (PLX3397) or genetic approach (DTR mice)



Tissue collection and processing

- Perfusions
- Sectioning
- IHC

Our Team – 4 Postdocs – 2 Research Assistants – 5 PhD students – 1 Honours student – 2 Internship students



1 - Stayte, S., Rentsch, P., Li, K. M., & Vissel, B. (2015). Activin A protects midbrain neurons in the 6-hydroxydopamine mouse model of Parkinson's disease. PloS one, 10(4), e0124325.
2 - Rentsch, P., Stayte, S., Egan, T., Clark, I., & Vissel, B. (2020). Targeting the cannabinoid receptor CB2 in a mouse model of l-dopa induced dyskinesia. Neurobiology of Disease, 134, 104646.
3 - Fieblinger, T., & Cenci, M. A. (2015). Zooming in on the small: The plasticity of striatal dendritic spines in l-DOPA–Induced dyskinesia. Movement Disorders, 30(4), 484-493.