

Jason Fernandes

PhD Candidate

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Education:

BSc (Honours)- Immunology and Infection, University of Alberta (2018)

PhD- Medical Microbiology and Immunology, University of Alberta (2019-current)

Academic Background and Interests:

In 2018, I completed a BSc (Honours) in the IMIN program at the University of Alberta. Through my coursework I gained a passion for science and an appreciation for the exquisite beauty life has at the molecular level. This was further reinforced in lab of Dr. Maya Shmulevitz (MMI), whom was an excellent mentor and critical to my early development as a scientist. I completed my undergraduate research studies in her lab and was pleased to have my work published as co-first author in the *Journal of Virology*.

For my graduate studies I moved to Dr. Christopher Power's lab where I am now a PhD candidate studying the biology of cell death in the brain:

In response to mutation, infection, inflammation and/or other forms of cellular stress, most cells in the body can activate a highly regulated 'kill-switch' that leads to their self-destruction. This has varying consequences that depend on the stimulus, the form of cell death that is activated and the cell type. Akin to a pre-emptive controlled burn of a forest, *apoptotic* death can be triggered to safely rid the body of problematic (e.g. pre-cancerous) cells. However, under specific circumstances more hazardous forms of cell death can arise and release highly inflammatory stimuli. Similar to how a burning ember can rapidly grow into a raging wildfire, this process can damage neighboring cells and further enhance the spread of inflammation. I think cell death is an incredibly fascinating process and my research focuses on gaining a mechanistic understanding of how one of these hazardous cell death forms - termed *pyroptosis* (Greek for 'fiery death') - is regulated in the brain. Specifically, I have been investigating how pyroptosis is regulated in neurons in several diseases, including multiple sclerosis, HAND (NeuroHIV) and NeuroCovid.

Neuronal death is the hallmark of neurodegenerative diseases such as HAND. However, the capacity for neurons to undergo pyroptosis is poorly understood. In our recent publication in *Brain*, I demonstrated that a protein expressed by HIV can trigger a unique form of pyroptosis in neurons that involves activation and cross-talk between both pyroptotic and apoptotic pathways. My findings were bolstered through the use of brain tissue from HAND patients, a non-human primate model of HAND and a high-throughput cell culture/microscopy protocol that I developed to measure injury in primary human neurons. These findings provide a mechanistic characterization of how pyroptosis is regulated in human neurons and uncovered novel drug targets that are likely applicable to several neurodegenerative diseases.

Publications:

- 1) Fernandes, J.P, Cristi F., Eaton, H., Chen P., Haeflinger S., Bernard, I., Hitt, M., and Shmulevitz., M. Breast tumor-associated metalloproteases restrict reovirus oncolysis by cleaving the $\sigma 1$ cell-attachment protein, and can be overcome by mutation of $\sigma 1$. (2019). *Journal of Virology*. 93(22): DOI: 10.1128/JVI.01380-19
- 2) Chen, P.A., Shrivastava, G., Balcom, E.F., McKenzie, B.A., Fernandes, J., Branton W.G., Wheatley, B.M., Petruk, K., van Landeghem, F.K.H., and Power, C. (2019). Absent in melanoma 2 regulates tumor cell proliferation in glioblastoma multiforme. *Journal of Neuro-Oncology*. 144:265-273
- 3) McKenzie. B.A., Fernandes, J.P, Branton, W.G., Doan, M.A.L., and Power C. Activation of the executioner caspases-3 and -7 promotes microglial pyroptosis in models of multiple sclerosis(2020). *Journal of Neuroinflammation*. 17(253):
- 4) Saito L.B., Fernandes J.P., Smith M.J., Doan M.A.L., Branton W.G., Schmitt M., Wuest M., Monaco M.C., Major E.O., Wuest F., Power C. Intranasal anti-caspase-1 therapy preserves myelin and glucose metabolism in a model of progressive multiple sclerosis(2020). *Glia*. DOI: 10.1002/glia.23896
- 5) Roczkowsky A., Limonta D., Fernandes J.P., Branton W.G., Clarke M., Hlavay B., Noyce R.S., Joseph J.T., Ogando N.S., Das S.K., Elaish M., Arbour N., Evans D.H., Langdon K., Hobman T.C., Power C. COVID-19 Induces Neuroinflammation and Suppresses Peroxisomes in the Brain(2023). *Ann Neurol*. 2023 Sep;94(3):531-546. doi: 10.1002/ana.26679.
- 6) Branton, W. G., Fernandes, J. P., Mohammadzadeh, N., Doan, M. A. L., Laman, J. D., Gelman, B. B., Fagrouch, Z., Kondova, I., Mooij, P., Koopman, G., & Power, C. (2023). Microbial molecule ingress promotes neuroinflammation and brain CCR5 expression in persons with HIV-associated neurocognitive disorders. *Brain, Behavior & Immunity*, 107, 110–123. doi:0.1016/j.bbi.2022.09.019
- 7) Pollock N.M., Fernandes J.P., Woodfield J., Moussa E., Hlavay, Branton W.G., Wuest M., Mohammadzadeh N., Schmitt L., Plemel J.R., Julien O. Wuest F., Power C. Gasdermin D activation in oligodendrocytes and microglia drives inflammatory demyelination in progressive multiple sclerosis (2024). *Brain, Behavior & Immunity*. 2024 Jan:115:374-393. doi: 10.1016/j.bbi.2023.10.022
- 8) **Fernandes J.P., Branton W.G., Cohen E.A., Koopman G., Kondova I., Gelman B.B., Power C. Caspase cleavage of gasdermin E causes neuronal pyroptosis in HIV-associated neurocognitive disorder (2024). *Brain*. 2024 Feb 1;147(2):717-734. doi: 10.1093/brain/awad375.**

Awards:

EndMS Doctoral Studentship (2024-current)
University of Alberta FoMD 75th Anniversary Graduate Student Award (2023)
EndMS Master's Studentship (2020-2022)
Walter H. Johns Graduate Fellowship (2019)
CIHR Canada Graduate Scholarships-Masters (CGS-M; 2019)
URI Undergraduate Researcher Stipend (2018)
AIHS Summer Studentship (2016, 2017)