JONATHAN & JOSHUA MEMORIAL FUND

Neil Donison is a senior PhD candidate in Dr. Michael Strong's Lab at Robarts Research Institute, Western University, London, Ontario. Neil's research investigates the cellular and molecular mechanisms of neurodegeneration associated with traumatic brain injury and other related diseases, including amyotrophic lateral sclerosis (ALS), chronic traumatic encephalopathy, and Alzheimer's disease.

One of the primary hallmarks of traumatic brain injury and neurodegenerative diseases is the accumulation of a protein within the brain, called tau. Under disease conditions, tau protein is modified, termed phosphorylation, which results in an increased propensity to aggregate. The accumulation of phosphorylated tau protein can lead to cell death and is closely associated with impairments in cognitive function. The phosphorylation of tau protein at a specific site on the protein, Thr175, has been identified as a critical cellular event. When Thr175 tau is phosphorylated, it initiates a cascade that results in various cellular changes and, ultimately, the formation of toxic aggregates. The presence of phosphorylated Thr175 tau is found in the brains of patients with chronic traumatic encephalopathy, ALS and Alzheimer's disease and is initiated within the first 10-days following traumatic brain injury. Targeting Thr175 tau is an ideal candidate to reduce tau aggregation, cell death and cognitive impairments.

Neil's research explicitly aims to identify the protein(s) responsible for initiating this cascade; that is, identifying which protein is responsible for phosphorylating tau at Thr175. To identify candidate proteins that may be involved, the expression of different proteins (known to phosphorylate tau) were examined following traumatic brain injury. Multiple proteins, including JNK, ERK, p38 & LRRK2, were shown to be increased within the first 10-days post-injury. The increase in these proteins is closely aligned to the increase in the phosphorylation of Thr175 tau and thus classified as candidate proteins. Multiple cellular approaches will be used to determine if these proteins directly play a role in the phosphorylation of Thr175. Once the protein is identified, it will be targeted (via therapeutic inhibition) to reduce the phosphorylation of Thr175 tau, hoping to improve outcomes following traumatic brain injury. Further, this therapeutic approach may be applied to other neurodegenerative diseases associated with tau aggregation to reduce cognitive impairment.