Problem: Stroke is the second leading cause of death worldwide. The pharmacological tools available to reduce brain injury and treat patients with stroke are extremely limited. Two of the most important and non-modifiable risk factors for stroke are age and gender, with the risk for stroke doubling every decade after age 55 years, and affecting men to a larger extent than women until later in life where the rate of stroke increases in elderly women.

Attempts to accurately model the patient human population with ischemic neuronal damage have identified transient receptor potential M2 (TRPM2) as a molecule significantly associated with cause and control of certain diseases, including stroke. Non-specific TRPM2 inhibitors, such as clotrimazole (CTZ), have been shown to reduce neuronal death in in vitro cortical and hippocampal neurons and reduces injury in male animals following focal and global cerebral ischemia. Additionally, inhibition of TRPM2 ion channels with clotrimazole (CTZ) or genetic knockdown has been shown to reduce infarct size in males, but not females, following stroke. While TRPM2 appears to be a viable target for therapeutic interventions for stroke in males, preclinical studies have been limited by the lack of a specific inhibitor.

Technical Solution and Key Value Propositions: A University of Colorado research group led by Dr. Paco Herson has generated peptides and peptide constructs that are fused to a cell-permeable sequence, and specifically inhibits TRPM2 channel activity. Dr. Herson’s pre-clinical studies have shown the inhibitor’s neuroprotective properties in vivo and have also demonstrated the reversal of ischemia-induced impairment of synaptic plasticity following delayed administration of the inhibitor in addition to an improvement in synaptic and memory function, thereby providing benefit independent of extent of initial injury. Most current drugs only have neuroprotective effects and are mostly used for preventative care. This technology provides novel methods of treating or preventing neurological damage or injury, or enhancing the restoration of neurological function. It also has applications in global cerebral ischemia following cardiac arrest, TBI, and neurodegenerative diseases such as Alzheimer’s.

Data Update:
Dr. Herson has published related scientific findings in the following article: “Sirtuin-2 mediates male specific neuronal injury following experimental cardiac arrest through activation of TRPM2 ion channels.” Exp. Neurol. doi:10.1016/j.expneurol.2015.10.014 (Jan. 2016).

Key Documents and Sources:
“Peptide-Based Methods for Treating Neurological Injury.” Provisional patent application filed February 22, 2016; available under CDA.