Market Need: Neuronal cell death and death of brain tissue associated with stroke, leads to a long term and debilitating loss of neurons, which results in cognitive impairment and loss of movement control. In 2010, the prevalence of stroke was estimated at 2.6% in the United States, and was the fourth leading cause of mortality. In Canada, stroke prevalence was about 1.1% in 2009, affecting 315,000 people. In 2008, total healthcare costs, including hospital care for stroke survivors, lost productivity, and premature mortality was estimated at $34.3 billion in the United States alone. Between one-third and two-thirds of stroke survivors require some form of rehabilitation due to loss of function disabilities. In 2007, sales of stroke management products in the U.S. were approximately $4.5 billion. Current stroke medications do not reduce brain damage by acting directly on neurons; rather, drug therapy is focused on administering blood thinners and anti-coagulants to increase blood flow whereby reducing the size of the clot. Therapeutics aimed at preventing and reducing stroke related neuron death would greatly mitigate patient disability and associated costs.

Technology Description: Our scientists have identified a previously unrecognized molecular pathway involving a series of protein-protein interactions that underlies glutamate (GluR2) containing α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA) receptor-mediated excitotoxicity as a novel target for treatment of stroke induced neuronal death and brain damage. The internalized GluR2/GAPDH complex, through coupling with Siah1, translocates to the nucleus and activates a p53-dependent cell death pathway. Coupling between GluR2 and GAPDH increases during and after stroke, in turn activating key signaling pathways that lead to neuronal cell death. Administration of the interfering peptide (TAT-GluR2NT1-3-2) specifically disrupts the GluR2-GAPDH protein-protein interaction in vivo, as demonstrated in a preclinical model of ischemic stroke. The interfering peptide protects cells against ischemic-induced stroke, increasing neuronal survival and total infarct volume for up to 6 hours post administration (Figure 1).

Stage of Development:
- Administration of an interfering peptide that is able to disrupt the GluR2-GAPDH interaction in vivo significantly protects against ischemia-induced cell death in preclinical models of global and focal ischemia.
- In parallel to the preclinical peptide research we are starting the identification of small molecules mimicking the functional effect of our peptides.

Advantages:
- Small peptide, CNS targeting, with a novel and highly specific mechanism of action.
- Our interference peptide can selectively inhibit the interaction of between GluR2 and GAPDH.
  - Does not block ligand binding, and thus does not interfere with normal physiological functions associated with the GluR2 receptor.
- Positive in vivo data – in preclinical models of focal and global ischemia.
- Agents that selectively inhibit neurotransmitter interaction are likely to be safer than receptor antagonists.

Notable Publication(s):

Intellectual Property:
Patent issued in the United States and patent applications filed in Europe.

Business Opportunity: The Centre for Addiction and Mental Health is leading the commercialization of this technology. We are seeking a partner to complete pre-clinical development and to launch clinical trials that would employ either peptides or small molecules approaches.