NON-CONFIDENTIAL SUMMARY

INVENTOR(S): **FANG LIU**

CAMH TECHNOLOGY ID: 004-2006

BUSINESS OPPORTUNITY

The Centre for Addiction and Mental Health is seeking a partner to complete pre-clinical development and to launch clinical trials that would employ these peptides.

Novel Therapeutics for Stroke

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 2017, the number of acute ischemic stroke patients in 8 major markets was 17.9 million and is expected to grow to 22.8 million by 2028. Total healthcare costs, including hospital care for stroke survivors, lost productivity, and premature mortality was estimated at $34 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 2017, sales of stroke management products in the US were approximately $3.4 billion and are forecasted to reach $5.1 billion by 2027. 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 (GluA2) 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 GluA2/GAPDH complex, through coupling with Siah1, translocates to the nucleus and activates a p53-dependent cell death pathway. Coupling between GluA2 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-GluA2NT1-3-2) specifically disrupts the GluA2-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).

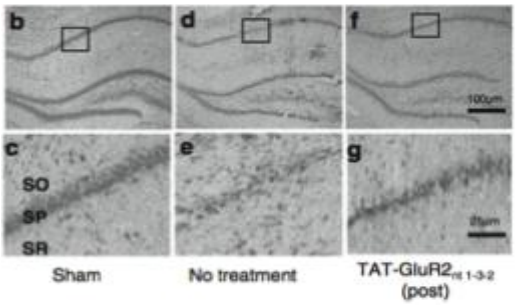

Figure 1: *Protective effects of the TAT-GluA2NT1-3-2 peptide in a preclinical model of ischemia. (b-c) sham control hippocampus. (d-e) Ischemia-induced significant neuron loss in the hippocampus. The interfering peptide significantly improves neuronal survival, 2 hours post administration (f-g). SO, stratum oriens; SP, stratum pyramidale; SR, stratum radiatum.*

Stage of Development

- Administration of an interfering peptide that is able to disrupt the GluA2-GAPDH interaction *in vivo* significantly protects against ischemia-induced cell death in preclinical models of global and focal ischemia.

Advantages

- Small peptide, CNS targeting, with a novel and highly specific mechanism of action.
- Our interference peptide can selectively inhibit the interaction between GluA2 and GAPDH.
    - Does not block ligand binding, and thus does not interfere with normal physiological functions associated with the GluA2 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)

Zhai et al (2013) Neurobiol. Dis. 54:392-403.

Intellectual Property

Patents issued in the US

FOR MORE INFORMATION CONTACT

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