NON-CONFIDENTIAL SUMMARY

INVENTOR(S): **FANG LIU**

CAMH TECHNOLOGY ID: 001-2012

BUSINESS OPPORTUNITY

The Centre for Addiction and Mental Health is seeking a partner to complete pre-clinical development and to launch clinical trials using this approach.

Neuroprotective Small Molecule Therapeutic – MS & Optic Neuritis

Market Need

Multiple sclerosis (MS) is an autoimmune disease affecting the protective myelination of the central nervous system (CNS). The age of onset is between the ages 20 and 40. The disease results in debilitating impairments in motor control, speech and thought. Canada has one of the highest rates of MS in the world, followed by the United States. The market for MS is forecasted to reach $25.6 billion USD by 2026, with a CAGR of 3%, in the top 7 major markets. Current therapies rely on anti-inflammatory and immunosuppressant agents such as interferon-β, glatiramer acetate, and natalizumab. These medications reduce the rate of relapse during the initial disease stages, and do not prevent disease progression. As these medications are immunosuppressants they induce side effects including flu-like symptoms, dermal reactions, and susceptibility to CNS infections. Furthermore, they do not reduce long-term neurodegeneration. To date, there is no cure for MS, and despite treatment progression; the disease remains a significant therapeutic challenge.

Technology Description

Our scientists have identified a protein-protein coupling between the glutamate A2 (GluA2) - α-amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA) receptor and the extracellular protein glyceraldehyde-3-phosphate dehydrogenase (GAPDH) as a novel target for the treatment of MS, optic neuritis and related indications. By characterizing the protein-protein (GluA2-GAPDH complex) interaction, we have created a novel series of small molecules that interfere with this coupling, and demonstrate neuroprotective effects through the inhibition of glutamate-mediated excitotoxicity. This novel approach could lead to a therapy capable of enhanced affinity, efficacy and a superior side effect profile in comparison to traditional MS treatment strategies. Optic neuritis is a condition strongly associated with MS and an indication with well-defined endpoints that may serve to accelerate our path through clinical trials.

Stage of Development

- Our researchers have observed an enhanced GluA2-GAPDH interaction in samples from MS patients and the autoimmune encephalomyelitis (EAE) preclinical model, a widely accepted preclinical model for studying the clinical and pathological features of MS.
- Systemic delivery of our lead compounds to EAE preclinical models significantly improves neurological and locomotor outcomes.
  - Mitigates neuronal death and increases oligodendrocyte (cells that produce protective myelin) survival in the spinal cord.
  - Reduces axonal damage in the spinal cord of EAE preclinical models.
- **We have an optimized lead molecule that interferes with GluA2-GAPDH coupling, ready for late stage pre-clinical development.**

Advantages

- Novel neuroprotective and highly specific mechanism of action.
- Our lead compounds inhibit the aberrant interaction between GluA2 and GAPDH.
- Positive *in vivo* data in the EAE model of MS.
- *In vivo* evidence of increased neuronal and oligodendrocyte survival after treatment with lead small molecules.
- Does not interfere with normal physiological functions associated with the GluA2 receptor.
- Agents that selectively inhibit highly specific interactions are likely to be safer than receptor antagonists.

Notable Publication(s)

Zhai et al (2015) Ann Clin Transl Neurol 2 (4): 388 – 400

Intellectual Property

Peptide technology: Patent issued in the US

Small molecule: National stage applications filed in US, CA, AU, EP, CN

FOR MORE INFORMATION CONTACT

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