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.

Novel Therapeutic for the Treatment of Multiple Sclerosis

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. By characterizing the protein-protein (GluA2-GAPDH complex) interaction, we have created a novel series of peptides and small molecules that interfere with this coupling, and could lead to the development of a therapy capable of an enhanced affinity, efficacy, and a superior side effect profile.

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 interfering peptide TAT-G-G pep to EAE preclinical models significantly improves neurological outcome.
    - 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.
- A series of small molecules have been developed that interfere with GluA2-GAPDH coupling. These are currently being further optimized for late stage pre-clinical development.

Advantages

- Novel and highly specific mechanism of action.
- *In vitro* data - our interference peptide can selectively inhibit the interaction of two functionally distinct neurotransmitter receptors.
- Positive *in vivo* data in the EAE model of MS.
- The interference peptide selectively inhibits the aberrant interaction between GluA2 and GAPDH.
- 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: Provisional patent application filed March 2019

FOR MORE INFORMATION CONTACT

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