NON-CONFIDENTIAL SUMMARY

INVENTOR(S): **FANG LIU**

CAMH TECHNOLOGY ID: 002-2009

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 either peptides or small molecule approaches.

Schizophrenia – Novel Antipsychotic

Market Need

Schizophrenia is a severe mental illness with disturbances in thinking, perception, emotions, social behavior, coupled with hallucinations and delusions. The global lifetime prevalence of schizophrenia is estimated at 4 per 1000. Direct and indirect healthcare costs in the US alone for patients with schizophrenia were estimated at $94 to $102 billion in a study conducted in 2016. Indirect healthcare costs contributed 50-85% of these estimates. The global schizophrenia therapeutics market was valued at $6.4 billion in 2015, and is expected to reach $7.3 billion by 2025. Current therapeutics, such as Zyprexa, Risperdal, and Seroquel are used to treat schizophrenia, but have a host of undesirable side effects, such as weight gain, altered glucose and lipid metabolism, sedation, confusion, and social withdrawal. In fact, 74% of patients discontinue use within 18 months of therapy due to either poor tolerability or incomplete efficacy. Therefore, there is an unmet need for more effective therapeutics.

Technology Description

Our researchers have shown that two key proteins, the dopamine D2 receptor (D2R) and the protein "disrupted in schizophrenia 1" (DISC1), form a protein-protein interaction complex (Figure 1). D2R-DISC1 complex formation has been shown to contribute to the pathophysiology of schizophrenia. The D2R-DISC1 complex is significantly enhanced in preclinical models of schizophrenia and in human postmortem brains of patients suffering from schizophrenia. Through the characterization of the protein-protein interaction, we have developed a peptide that specifically interferes with this coupling; leading to the development of a breakthrough therapy capable of delivering enhanced affinity, efficacy, and a superior side effect profile.

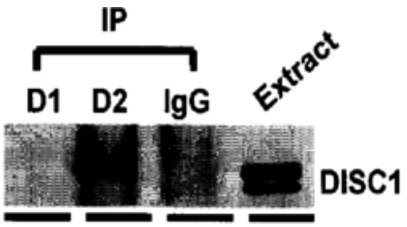

Figure 1: *Co-immunoprecipitation of D2R with DISC1 in preclinical subjects brain striatal tissue. As a control, the D1 receptor did not immunoprecipitate the DISC1 protein.*

Stage of Development

- Administration of an interfering peptide that disrupts the D2R-DISC1 complex significantly reduced schizophrenic symptoms in both drug induced schizophrenic preclinical models, and in a genetic mutant preclinical model.
  - Importantly, administration of this interfering peptide did not induce catalepsy, a severe side effect of the typical antipsychotics.
- 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.
- Positive preclinical data using both genetic mutant and drug induced schizophrenia models.
- Does not induce catalepsy, a strong predictor of acute extrapyramidal side effects of antipsychotic medications.
- Our interference peptide selectively inhibits the aberrant interaction between D2R-DISC1.
  - Does not interfere with normal physiological functions associated with the D2 receptor.
- Safety & Toxicity – Agents that selectively inhibit interaction are likely to be safer than receptor antagonists.

Notable Publication(s)

Su et al. 2014 Neuron 84 (6): 1302-16.

Intellectual Property

Patent issued in the US

FOR MORE INFORMATION CONTACT

Dr. Klara Vichnevetski
Director, Industry Partnerships & Technology Transfer
klara.vichnevetski@camh.ca
416 595-6056

Centre for Addiction and Mental Health
33 Russell Street, Suite 4039
Toronto, Ontario, Canada M5A 2S1
www.camh.ca