Market Need: Attention Deficit Hyperactivity Disorder (ADHD) is diagnosed predominantly as a childhood onset behavioral disorder, and is characterized by a persistent pattern of abnormally high levels of activity, impulsivity, and/or inattention. These symptoms are associated with poor academic performance, and in adulthood, loss of productivity. In 2011, approximately 9% of children between the ages of 3-17 were diagnosed with ADHD in the United States (U.S.). The prevalence of adult ADHD is 5.2%, a major cause of work related loss of productivity.

Current therapeutics alleviate ADHD symptoms by blocking the dopamine transporter (DAT), which results in increased levels of synaptic dopamine. Unfortunately, these medications are non-specific, leading to unwanted side effects. Thus, there is an unmet need for the development of novel therapeutics for ADHD which have a higher degree of affinity and efficacy.

Technology Description: Our scientists have identified an interaction between DAT and the presynaptic dopamine type 2 receptor (D2) that results in increased levels of DAT cell surface expression, and the subsequent upregulation of its activity. The ability of the D2 receptor to physically couple to DAT and subsequently upregulate DAT activity by increasing DAT localization at the plasma membrane provides a novel method by which D2 receptors may facilitate the recruitment of DAT to synaptic regions. This mechanism may also underpin the cause of ADHD symptoms.

Through the characterization of this interaction our scientists have developed a peptide (TAT-DAT-NT1-1) that interferes with this coupling. Systemic administration of the interfering peptide (TAT-DAT-NT1-1) in a preclinical model decreases DA uptake providing a novel method for increasing levels of synaptic dopamine. As a result, this interfering peptide could lead to the development of a breakthrough therapy capable of delivering enhanced affinity, efficacy, and a superior side effect profile.

Stage of Development:
- In a preclinical model involving peptides that disrupt D2-DAT interaction exhibit decreased synaptosomal DA uptake and significantly increased locomotor activity, reminiscent of DAT knockout preclinical models.
- Our scientists are starting the identification of small molecules mimicking the functional effects of our peptides.

Advantages:
- Small peptide, CNS targeting, with a novel and highly specific mechanism of action.
- TAT-DAT-NT1-1 can selectively inhibit the interaction of two functionally distinct neurotransmitter receptors.
- Does not block ligand binding; thus it does not interfere with normal physiological functions associated with the D2 receptors or DAT transporter.
- Agents that selectively inhibit D2-DAT interaction are likely to be safer than receptor antagonists

Notable Publication(s):

Intellectual Property:
Patent issued in the United States

Business Opportunity: CAMH is seeking a partner to complete pre-clinical development and to launch clinical trials that would employ either peptides or small molecule approaches. We are also interested in testing propriety compounds provided by pharmaceutical companies.

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