NON-CONFIDENTIAL SUMMARY

INVENTOR(S): **BRUCE POLLOCK, JOSE NOBREGA**

CAMH TECHNOLOGY ID: 014-2016

BUSINESS OPPORTUNITY

The Centre for Addiction and Mental Health is seeking partners to either license or co-develop this technology. CAMH is open to various forms of collaboration.

Novel Cell-Based Assay for Serum Assessing Anticholinergic Toxicity in Cognitive Impairment

Market Need

Drugs that block cholinergic receptor function in the brain are known to be associated with cognitive impairment, including confusion, decreased attention and memory deficits. A number of prescription medications, as well as common over-the-counter medications can increase anticholinergic load in the blood, and thus contribute to cognitive deficits. The elderly, who often take multiple medications for various different types of health issues, are particularly vulnerable in this respect. The effect of these medications on cholinergic receptors in the brain makes it difficult to differentiate cognitive deficits induced by aggregate anticholinergic burden from similar deficits resulting from pathological conditions, including mild cognitive impairment and dementia-type conditions. In combination, high anticholinergic burden and underlying dementia increases the risk of delirium and behavioral consequences. Due to the prevalence of various degrees of cognitive decline in the elderly, some 35.6 million people worldwide, at present and projected to be in excess of 115 million in 2050, it is imperative that a test be devised which accurately and objectively differentiates cognitive impairment due to anticholinergic loading and would permit rapid clinical intervention.

Technology Description

We have now developed a reliable laboratory assay for quantifying the anticholinergic burden in human serum, using cloned receptors expressed in stable cell lines. We have tested our novel serum anticholinergic activity (SAA) protocol in an open trial and have shown that a single administration of scopolamine, a known anticholinergic drug, induced significant increases in the anticholinergic burden of all subjects. Furthermore, scopolamine was shown to induce cognitive deficits after a single administration in older, cognitively intact subjects. In contrast to previous protocols, our assay overcomes two main limitations.

1. The new protocol targets cloned muscarinic M1 receptors stably expressed in cell lines (instead of tagging all five muscarinic receptor subtypes in rat brain tissue). The M1 receptor subtype is by far the most abundant muscarinic receptor in the brain and is also the one that has been most clearly implicated in cognitive functions.
2. The new protocol includes the removal of large proteins from serum prior to the assay.

Stage of Development

- Proof of concept studies are complete, further clinical validation is needed

Advantages

- Significantly increased validity, sensitivity and reliability of the assay.
- Validity is greatly increased by removing the confounding effect of large serum proteins and decreasing binding to internalized receptors.
- Specificity and sensitivity are significantly improved by using cell lines expressing only M1 receptors, and as such devoid of other potential binding sites for the radioligand.
- The original SSC method relied on dissection of rat cortical tissue, a major source of variability as well as a limitation given the need for expertise and access to rodents.

Notable Publication(s)

www.sciencedirect.com/science/article/pii/S1056871916301708

Intellectual Property

This invention is protected by a PCT patent application.

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