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2020 Part the Cloud: Translational Research Funding for Alzheimer's Disease (PTC) - $750,000

SEMA4D Blockade Safety and Brain Metabolic Activity in Alzheimer's Disease

This Phase 1 clinical trial will evaluate an experimental drug that may reduce inflammation in the brain.

PI

- Ph.D., Massachusetts Institute of Technology,1972
- President and CEO of Vaccinex, Inc.
- Former faculty at University of Rochester and Columbia University

STUDY

- CADRO category: Translational Research & Clinical Interventions

Background

Astrocytes commonly referred to as "helper cells" are the most numerous cell type in the brain. They help support brain cell health and a number of other important brain functions. Studies show that brain inflammation during brain diseases including Alzheimer's, may limit the ability of astrocytes to perform these important functions. Researchers have shown that in brain diseases including Alzheimer's disease, astrocytes may migrate to areas of nerve damage, and facilitate the removal of potential toxins and initiate repair mechanisms. However, the demands of this damage response may limit the astrocytes' ability to perform other important functions.

Dr. Maurice Zauderer's team has previously observed in mouse models of Huntington's disease that damaged nerve cells turn on a protein called SEMA4D. SEMA4D appears to impact the ability of astrocytes to perform key functions, such as transporting energy molecules (glucose) throughout the brain. The brain uses glucose for its metabolism (which is the efficient use of sugar and oxygen as fuel for cell activity). The researchers have found that blocking SEMA4D using an antibody improves glucose transport in people with Huntington's disease. Dr. Zauderer and his team have also observed abnormal metabolism in Alzheimer's, and have seen an association of changes in this biology with loss of cognitive function. As a result, they believe that blocking SEMA4D may also benefit individuals with Alzheimer's as a possible therapeutic approach

Research Plan

Dr. Zauderer and colleagues will lead a phase I clinical trial to evaluate the safety and tolerability of an experimental antibody that targets and blocks SEMA4D activity in 40 individuals with Alzheimer's. Participants will receive the experimental antibody every four weeks for 24 weeks, and the research team will evaluate its overall safety. Dr. Zauderer's team will also measure glucose levels in participants using specialized brain scans called positron emission tomography, or PET scans. Dr. Zauderer believes that using this specific type of PET scan to detect changes in glucose levels across

different brain regions will provide important insights into how the antibody might impact brain metabolism and in turn may impact cognitive function.

Impact

This clinical trial represents an important step to determine if an experimental antibody might benefit people with Alzheimer's. If successful, the results of this work could lead to future large-scale clinical trials that test the ability of the experimental antibody to delay, or slow brain changes associated with Alzheimer's.

Made possible through the generous funding from the Part the Cloud, benefiting the Alzheimer's Association.