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La Jolla, CA

2018 The Part The Cloud to RESCUE Brain Cell Degeneration in Alzheimer's Disease -$1,000,000

A biomarker directed study to reduce inflammation in Alzheimer's Disease

This Phase 1b clinical trial will explore the safety and efficacy of a drug-XPRO1595 as a strategy to combat brain inflammation in individuals with Alzheimer's.

PI

- M.D., Washington University School of Medicine, 1982
- Chief Executive Officer of INmuneBio Inc.
- Past Chief Medical Officer (2010-11) of Adienne SRL, emerging biotech company in Bergamo, Italy
- Fellow of the American College of Surgery since 1991.

STUDY

- CADRO category: Translational Research & Clinical Interventions
- This is Dr. Tesi's first Association award

Background

The immune system consists of many different cell types whose interactions and functions govern the immune response in the body. Tumor Necrosis Factor (TNF) is an important immune signaling molecule that helps recruit immune cells to the sites of damage or infection in the body. However, excessive TNF could recruit too many cells to a specific area that causes abnormal inflammation and leads to damaged cells. People with Alzheimer's have elevated levels of TNF in their brains, which could contribute to nerve cell damage in the brain and cognitive impairment. Previous studies in animal models have shown TNF's involvement in the production and impaired removal of tau tangles – one of the main hallmarks of Alzheimer's. However, not all TNF is bad; TNF molecules signal to remove toxic debris in a healthy brain.

Despite the evidence, currently approved drugs that block TNF activity are not ideal candidates for Alzheimer's. The physical size of the drugs keeps them from effectively crossing from the bloodstream into the brain, and many drugs do not selectively block the TNF molecules, which disturb the delicate balance of TNF activity in the brain. Animal studies using XPRO1595- a compound that is designed to selectively block abnormal TNF activity in the brain while preserving the healthy TNF response- demonstrated improved cognition, enabled removal of toxic debris in brain cells, and stabilized the immune system thereby preventing inflammation.

Research Plan

Dr. Tesi plans to use a compound called XPRO1595 to treat TNF by selectively blocking its abnormal activity. Dr. Tesi will enroll people with moderate Alzheimer's that have confirmed levels of beta-amyloid as well as high levels of biomarker C-reactive protein (CRP) in their blood.

Elevated CRP levels in the blood suggest increased brain inflammation; CRP is known to increase the immune response. Therefore, people with elevated levels of this protein may be likely to respond better to drugs targeting TNF. By identifying

volunteers with increased CRP levels, Dr. Tesi and his team hope to see an increase in the benefit of XPRO1595 over 12 weeks.

Impact

This study is the first step towards a larger Phase 2 clinical trial, which could establish the effectiveness of the drug, XPRO1595 in Alzheimer's. This Phase1b study will provide key data to support the use of CRP as a biological marker in blood, for measuring brain inflammation as well as how CRP relates to Alzheimer's cognitive symptoms, and markers like amyloid and tau.