ES-Derived Cells for the Treatment of Alzheimer's Disease

Grant Award Details

ES-Derived Cells for the Treatment of Alzheimer's Disease

Grant Type: New Faculty I

Grant Number: RN1-00538-A

Project Objective: used stem cell technology to invent a novel method to identify antigen-specific T cells from almost anyone's blood. The major goal of this grant was to isolate and characterize T cells that respond to an important player in
Alzheimer's disease pathology, Amyloid-beta (Aβ), though it can be adapted to other conditions and disease that require the isolation of antigen-specific CD4+ T cells.

Investigator:

Name:	Douglas Ethell
Institution:	University of California, Riverside
Type:	PI

Disease Focus: Aging, Alzheimer's Disease, Neurological Disorders

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $621,639

Status: Closed

Progress Reports

Reporting Period: Year 2, UCR

View Report

Grant Application Details

Application Title: ES-Derived Cells for the Treatment of Alzheimer's Disease

Public Abstract: Alzheimer's disease is the most common cause of dementia in the elderly, affecting over 5 million people in the US alone. Boosting immune responses to beta-Amyloid (Aβ) has proven beneficial in mouse models and Alzheimer's disease (AD) patients. Vaccinating Alzheimer's mice with Aβ improves cognitive performance and lessens pathological features within the brain, such as Aβ plaque loads. However, human trials with direct Aβ vaccination had to be halted to brain inflammation in some patients. We have demonstrated that T cell immunotherapy also provides cognitive benefits in a mouse model for Alzheimer's disease, and without any detectable brain inflammation. Translating this approach into a clinical setting requires that we first develop a method to stimulate the proliferation of Aβ-specific T cells without triggering generalized inflammatory response, as happens with vaccinations. Adaptive immune responses are provided by T cells and B cells, which are regulated by the innate immune system through antigen presenting cells, such as mature dendritic cells. We propose to leverage the power of embryonic stem (ES) cells by engineering dendritic cells that express a recombinant transgene that will specifically activate Aβ-specific T cells. We will test the effectiveness of this targeted stimulation strategy using real human T cells. If successful, this approach could provide a direct method to activate beneficial immune responses that may improve cognitive decline in Alzheimer's disease.

Statement of Benefit to California: Alzheimer's disease is the most common cause of dementia in the elderly, affecting more than 5 million people in the US. In addition to being home to more than 1 in 8 Americans, California is a retirement destination so a proportionately higher percentage of our residents are afflicted with Alzheimer's disease. It has been estimated that the number of Alzheimer's patients in the US will grow to 13 million by 2050, so Alzheimer's disease is a pending health care crisis. Greater still is the emotional toll that Alzheimer's disease takes on it's patients, their families and loved one. Currently, there is no effective treatment or cure for Alzheimer's disease. The research proposed here builds on more than 7 years of work showing that the body's own immune responses keep Alzheimer's in check in young and unaffected individuals, but deficiencies in T cell responses to beta-amyloid peptide facilitate disease progression. We have shown that boosting a very specific T cell immune response can provide cognitive and other benefits in mouse models for Alzheimer's disease. Here we propose to use stem cell research to propel these findings into the clinical domain. This research may provide an effective therapeutic approach to treating and/or preventing Alzheimer's disease, which will alleviate some of the financial burden caused by this disease and free those health care dollars to be spent for the well-being of all Californians.

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