

Progenitor Cells Secreting GDNF for the Treatment of ALS

Grant Award Details

Progenitor Cells Secreting GDNF for the Treatment of ALS

Grant Type: Disease Team Therapy Development - Research

Grant Number: DR2A-05320

Project Objective: Objective is to complete pre-clinical studies with a neural progenitor cell line transfected with GDNF, file an IND and complete a Phase 1 clinical trial in ALS patients.

Investigator:

Name:	Clive Svendsen
Institution:	Cedars-Sinai Medical Center
Type:	PI

Disease Focus: Amyotrophic Lateral Sclerosis, Neurological Disorders

Human Stem Cell Use: Adult Stem Cell

Award Value: \$16,168,464

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 3

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Reporting Period: Year 4

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Grant Application Details

Application Title: Progenitor Cells Secreting GDNF for the Treatment of ALS

Public Abstract: This project aims to use a powerful combined neural progenitor cell and growth factor approach to treat patients with amyotrophic lateral sclerosis (ALS or Lou Gehrig's Disease). ALS is a devastating disease for which there is no treatment or cure. Progression from early muscle twitches to complete paralysis and death usually happens within 4 years. Every 90 minutes someone is diagnosed with ALS in the USA, and every 90 minutes someone dies from ALS. In California the death rate is one person every one and a half days. Human neural progenitor cells found early in brain development can be isolated and expanded in culture to large banks of billions of cell. When transplanted into animal models of ALS they have been shown to mature into support cells for dying motor neurons called astrocytes. In other studies, growth factors such as glial cell line-derived growth factor (or GDNF) have been shown to protect motor neurons from damage in a number of different animal models including ALS. However, delivering GDNF to the spinal cord has been almost impossible as it does not cross from the blood to the tissue of the spinal cord. The idea behind the current proposal is to modify human neural progenitor cells to produce GDNF and then transplant these cells into patients. There they act as "Trojan horses", arriving at sick motor neurons and delivering the drug exactly where it is needed. A number of advances in human neural progenitor cell biology along with new surgical approaches have allowed us to create this disease team approach.

The focus of the proposal will be to perform essential preclinical studies in relevant preclinical animal models that will establish optimal doses and safe procedures for translating this progenitor cell and growth factor therapy into human patients. The Phase 1/2a clinical study will inject the cells into one side of the lumbar spinal cord (that supplies the legs with neural impulses) of 12 ALS patients from the state of California. The progression in the treated leg vs. the non treated leg will be compared to see if the cells slow down progression of the disease. This is the first time a combined progenitor cell and growth factor treatment has been explored for patients with ALS.

Statement of Benefit to California: ALS is a devastating disease, and also puts a large burden on state resources through the need of full time care givers and hospital equipment. It is estimated that the cost of caring for an ALS patient in the late stage of disease while on a respiration is \$200,000-300,000 per year. While primarily a humanitarian effort to avoid suffering, this project will also ease the cost of caring for ALS patients in California if ultimately successful. As the first trial in the world to combine progenitor cell and gene transfer of a growth factor, it will make California a center of excellence for these types of studies. This in turn will attract scientists, clinicians, and companies interested in this area of medicine to the state of California thus increasing state revenue and state prestige in the rapidly growing field of Regenerative Medicine.

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