DEBCT: Genetically Corrected, Induced Pluripotent Cell-Derived Epithelial Sheets for Definitive Treatment of Dystrophic Epidermolysis Bullosa

Grant Award Details

DEBCT: Genetically Corrected, Induced Pluripotent Cell-Derived Epithelial Sheets for Definitive Treatment of Dystrophic Epidermolysis Bullosa

Grant Type: Therapeutic Translational Research Projects

Grant Number: TRAN1-10416

Project Objective: Pre-IND meeting for autologous COL7A-1 gene corrected iPSC-derived epithelial sheets, aka "DEBCT", to treat dystrophic epidermolysis bullosa.

Investigator:

Name:	Anthony Oro
Institution:	Stanford University
Type:	PI

Disease Focus: Epidermolysis Bullosa, Skin Disease

Human Stem Cell Use: iPS Cell

Cell Line Generation: iPS Cell

Award Value: $5,107,353

Status: Active

Grant Application Details

Application Title: DEBCT: Genetically Corrected, Induced Pluripotent Cell-Derived Epithelial Sheets for Definitive Treatment of Dystrophic Epidermolysis Bullosa

Public Abstract:

Translational Candidate

DEBCT is an autologous iPS-derived COL7A1-corrected keratinocyte graft indicated for the treatment of all chronic open wounds in patients with RDEB.

Area of Impact

RDEB patients lack type VII collagen and have chronic wounds that lack an abundance of keratinocyte stem cells. DEBCT skin grafts will close wounds.

Mechanism of Action

RDEB patient keratinocytes contain mutations in COL7A1, lack the adhesion protein type VII collagen, and suffer profound skin fragility, chronic open wounds, and stem cell depletion. DEBCT is a COL7A1-corrected autologous keratinocyte stem cell sheet, when grafted onto wounds, adhere tightly and provide long-term wound closure. Autologous, corrected iPS cells can be grown in large quantities and can be induced to produce keratinocyte stem cells, allowing clinical scaling and manufacturing.

Unmet Medical Need

Children with the debilitating inherited blistering disorder Recessive Dystrophic Epidermolysis Bullosa lack the COL7A1 gene and experience painful non-healing wounds over their body, and risk death from cancer later in life. Current therapy is palliation costing thousands of dollars per month.

Project Objective

Pre-IND meeting and DEBCT pivotal study plan

Major Proposed Activities

- Optimize cGMP-compatible one step reprogramming and correction to autologous IPS cells and develop cGMP-compatible nucleic acid reagents
- Optimize coupling efficiency of COL7A1-corrected iPS-derived graftable keratinocytes and develop cGMP-compatible CD49f cell separation protocol
- Perform rodent pilot efficacy and safety studies of DEBCT keratinocyte grafts prior to a Pre-IND FDA meeting

Statement of Benefit to California:

While Epidermolysis Bullosa is a rare orphan disease, many of the common alleles are found in people of Latin American descent, a significant population in California. Children with the debilitating inherited blistering disorder experience painful non-healing wounds over their body, with current palliative therapy costing thousands of dollars per month. Long-term wound closure with DEBCT, a therapy developed in California, would lead to lower overall health costs and improved quality of life.
