Early Intervention Stem Cell-Based Therapy (EISCBT) for Corneal Burns and Trauma

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Institution Receiving Award: PITTSBURGH, UNIVERSITY OF  
Program: VRP  
Proposal Number: MR130197  
Award Number: W81XWH-14-1-0465  
Funding Mechanism: Vision Research Program - Translational Research Award  
Partnering Awards:  
Award Amount: $992,782.00

PUBLIC ABSTRACT

Corneal trauma and chemical burns lead to corneal scarring, producing a long-term reduction in vision, sometimes blindness. Corneal scarring and decompensation are the second-most common causes of poor vision among ocular injuries in combat, commonly caused by explosions with fragmentary munitions and by chemical and thermal exposure. Although corneal transplantation is effective at restoring vision, it is not an ideal solution for the warrior. The eye must stabilize for weeks or months before surgery, and afterward, corneal strength is compromised and the recipient usually requires long-term ophthalmological care. The half-life of uncomplicated corneal transplants is 10-15 years, after which a new transplant is required. There is a high failure rate in corneal re-grafts leading to complex medical solutions, sometimes with unsatisfactory outcomes. Corneal scarring and subsequent transplantation, therefore, compromise the effectiveness of military personnel and represent a considerable human and financial cost to the system.

Our work has led to the discovery of stem cells in the transparent connective tissue of the cornea. These corneal stromal stem cells (CSSC) can be greatly expanded in culture in the laboratory and can restore transparency to mice with congenically cloudy corneas. In this application, we present data showing that if applied to the surface of the cornea immediately after an injury, CSSC completely block formation of the scar tissue. The process appears to result from suppression of the inflammation process that leads to scarring. Stem cells are obtained from donated eyes from tissue banks and thus come from individuals of different ages and backgrounds. Although we can control for disease (like HIV) in these tissues, we have no means yet of determining the quality of the stem cells. The first aim of this project will discover genes in the CSSC that correlate with their ability to block scarring. We will develop a rapid, simple test that can serve as a quality control for each CSSC cell line to assure it will work to block scarring. In the second phase of the project, we will devise a thin collagen sheet in which CSSC cells will be embedded to act as a regenerative corneal bandage (ReCoBand). These bandages can be held in place on the cornea by a soft contact lens. We will optimize means of storing them frozen so they will be available to doctors in field hospitals. In the third phase of the project, we will investigate the timing for the start of therapy to determine how soon the bandage needs to be put in place after an injury. We will also ask how well the bandages work on more serious chemical burns to the cornea.

At the end of this 3-year project, we will have defined the components required to create a novel treatment system that prevents corneal scarring. If used before scars form, it may alleviate the need for some corneal transplants. The research from this project will allow us to move directly into an application to the Food and Drug Administration for a new "biologic device." Because the stem cells in this device do not actually enter the body, this device will be considered safer than procedures involving transplantation of stem cell and thus may move to clinical trials in a timely manner.

When it becomes available, the ReCoBand will be essential as an emergency device in the field to treat burns and trauma that are
generated in battlefield situations. The device should also be valuable in civilian situations of trauma and may also find application in other instances where inflammation causes a threat to corneal transparency. If successful, the ReCoBand may save vision of many and reduce the need for corneal transplantation.