Adipose-Derived Stem Cells Alleviate Visual Deficits in Blast Injury

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**Institution Receiving Award:** TENNESSEE, UNIVERSITY OF, HEALTH SCIENCE CENTER  
**Program:** VRP  
**Proposal Number:** VR150072  
**Award Number:** W81XWH-16-1-0778  
**Funding Mechanism:** Technology/Therapeutic Development Award  
**Partnering Awards:**  
**Award Amount:** $1,499,996.00

View Technical Abstract
Objectives and Rationale: Ocular trauma is the fourth most common injury sustained in military combat today. More than 70 percent of ocular injuries in Afghanistan and Iraq are blast injuries from Improvised Explosive Devices (IEDs). IEDs cause a dramatic increase in air pressure, followed by a negative pressure phase, causing retinal detachment and optic nerve damage. Blast causing traumatic brain injury (TBI) frequently is also associated with progressing vision problems that can result in blindness. Most of what we know about mild TBI in humans is based on sports injuries and acceleration/deceleration injuries (e.g., motor vehicle accidents). Relatively less research has been performed on blast-induced brain injuries. The current methods of treatment for these visual deficits are, in any case, far from satisfactory and, in most cases do not address the underlying neurodegeneration.

Using a well-established mild TBI blast mouse model, we recently have identified that inflammation plays a major role in the observed neurodegeneration. As a consequence of increased inflammation, certain neuronal cell types in the back of the eye "flare up" resulting in visual deficits, giving us an impetus to use this as a target to treat TBI. One approach that has gained interest in the past few years for neurodegenerative patients is the delivery of biochemical compounds that help the neurons in the retina stay alive and regrow past the site of injury to re-establish sight. This approach, however, would require patients to undergo repeated injections into the eye for an undetermined amount of time, an undesirable outcome.

Alternatively, the concept has recently evolved of repairing terminally differentiated organs with cell-based therapy. Our laboratory pioneered the use of cells derived from the human adipose tissue (ADSC, adipose-derived stem/stromal cells) that are readily available and could potentially be useful as a therapeutic strategy in retinal diseases. ADSC are known to secrete a variety of proteins that have been shown by others and us to be neuroprotective. Therefore, in this study, we will test the hypothesis that ADSC and/or anti-inflammatory proteins released by ADSC rescue from blast-related retinal damage and improve visual function.

Our preliminary data from our mild TBI model is consistent with our hypothesis showing remarkable improvement in visual signals from live mice post-ADSC treatment. In addition, ADSC seem to home to the injured sites of the retina and protect leaky blood vessels, a surprising finding that we observed. The latter observation is in line with our previous work on diabetic animals, which also show leaky blood vessels, and ADSC seem to stop them from leaking, suggesting similar mechanisms may be operative in TBI. Using various biochemical, molecular, and histological tests, we will further confirm our hypothesis.

Potential Impact of the Research: Stem cell therapies will likely help to preserve the vision in Soldiers with blast injuries affecting the retina. We expect these studies to teach us how ADSC work as anti-inflammatory therapies. ADSC are derived by a minimally invasive procedure such as liposuction to harvest adipose tissue, followed by any processing required to obtain an appropriately defined and functionally consistent population of cells with the desired characteristics. An additional advantage of the use of ADSC is that their use will likely eliminate the need for repeated injections into the eye since ADSC survive and naturally secrete anti-inflammatory proteins directly into the retina over a long period of time. One of our collaborating partners developed these stem cells and the proteins derived from these cells in a "clean room" facility, and we expect these will advance our ability to rapidly take these studies into human clinical trials. If successful, treatment for TBI and other retinal diseases (like diabetic retinopathy) using ADSC could become clinical practice within 5-10 years.

Military Benefits: This proposal is of high interest to military Service members, Veterans, and their family members. Due to the nature of their work, military members are at an increased risk for TBI from explosive blast, ballistic, blunt, and penetrating trauma. Unfortunately, there is currently no effective treatment against TBI. The devastating lifelong effects of visual loss and blindness seen in this pathology severely affect the quality of life of the individuals and their family members and communities in general. Furthermore, the economic cost of vision impairment related to TBI without direct ocular injury is well in excess of $2 billion
annually for the military. The development of an effective treatment for TBI would greatly enhance the quality of life of military members following a traumatic event and would drastically reduce the healthcare costs associated with the care of individuals with severe visual loss for the rest of their lives.

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