Project Title: Treatment of Traumatic Vision Loss in a New Mouse Model of Blast Injury
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Background: Traumatic blast injury can result in the loss of neurons, visual dysfunction, and blindness. There is no accurate animal model of primary blast injury to the eye. As a result, there is a lack in understanding the mechanisms of cell death resulting from blast injury, making it difficult to design effective treatments to preserve vision in injured war fighters.

Objective: The overall goal of this research project is to understand the genetic mechanisms that control blast injury responses in the eye and develop an effective treatment that can be delivered on the battlefield.

Specific Aims: 1) Optimize and calibrate a mouse model of blast injury to the eye; 2) Determine the mechanism of cell death caused by blast injury; and 3) Determine if systemic delivery of a novel therapeutic agent will rescue retinal neurons from cell death after blast injury to the eye.

Study Design: Scientists will use a modified blast cannon to exert over-pressure onto one eye of the mouse. Both eyes will be examined and the responses will be compared to control eyes from non-blast exposed mice. The force of the compressed air on the eye will be measured and used to establish a dose response curve of force measured versus cell death. Investigators will use multiple forces in the range that causes tissue damage in humans. Researchers will analyze the effects of an overpressure blast at different time-points to locate the peak of cell death and characterize the form of cell death and type of cells affected by this primary blast injury. Researchers will characterize the mechanism of cell death by evaluating hallmark changes in well-defined molecular pathways that lead to different modes of cell death—apoptosis, necrosis, and autophagy. Researchers will then determine if a modified form of erythropoietin (EPO) will rescue neurons from this blast injury. Dr. Rex’s laboratory works on the neuroprotective effects of EPO. It is a secreted cytokine that can cross the blood brain and blood retina barriers to prevent cell death of central nervous system neurons after systemic delivery. Scientists will systemically deliver a modified form of EPO to mice at different time points post-blast to determine the efficaciousness of this treatment and the therapeutic window after blast injury. The success of this therapy will be determined by analysis of retinal function and structure. Visual function will be measured by electroretinograms, visually evoked potentials, and a behavioral assay that can measure visual function in each eye independently. The integrity of retinal structure will be determined in vivo by high resolution optical coherence tomography and ex vivo by standard histological analysis.

Relevance: This project has the potential to lead to treatments for loss of vision due to primary blast injury to the eye in three ways. First, through the generation and characterization of a model of blast-induced vision loss. Second, by determining the type of neurons that die after blast injury and the mechanism of cell death. Third, by demonstrating rescue with a therapeutic that can quickly translate to the clinic and to the battlefield where a single systemic injection could provide rapid treatment. By developing an early intervention it may be possible to rescue dying neurons and prevent the accompanying functional losses.