Project Title: Novel Drug Prevents Retinal Inflammatory Mediators and Apoptosis  
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Background: Ocular trauma constitutes one of the most common causes of unilateral morbidity and blindness in the world today. Due to improvements in body protective gear, the rates of combat-based morbidity and mortality have decreased; however, the number of ocular injuries has increased (from 0.57% during the Civil War to 13% in Desert Storm). Ocular damage occurring in more recent wars is often caused by explosions with fragmentary munitions and represents the 4th most common injury in Operation Iraqi Freedom. Despite improvements in eye protective wear, soldiers report injuries even while wearing eye protection in 24% of cases; in most instances use of eyewear is undocumented. Thus, despite advances in military protective wear, the blast produced by many improvised explosive device (IEDs) pose a significant threat of closed and open globe injuries through the fragmentary munitions.  
Objective: With a goal of improving treatment for these types of injuries, the researchers propose studies using a rodent eye-blast model designed to 1) identify the molecular/cellular pathways within ocular tissue that are activated in response to injury and 2) test the efficacy of a new drug which holds promise as a mitigator of these damage-triggered responses.  
Hypothesis: 1) To test the hypothesis that principle retinal changes produced in this model include an activation of inflammatory pathways (associated with increased levels of inflammatory markers, specifically TNFα and IL-1β) and apoptotic pathways (linked to increased apoptotic markers, specifically Bax, Bcl-xL, cytochrome C, Fas, and Fas ligand). 2) To test the hypothesis that treatment with a novel anti-apoptotic and anti-inflammatory agent, Compound 49b, within 1 day of blast injury will protect against retinal damage.  
Specific Aims: 1) Principle retinal changes produced in this model include an activation of inflammatory and apoptotic pathways; and 2) Treatment with a novel anti-apoptotic and anti-inflammatory agent, Compound 49b within one day of blast injury will protect against retinal damage.  
Study Design: This study will test whether ocular blast injury is associated with the activation of inflammatory and apoptotic pathways and whether the anti-inflammatory and anti-apoptotic Compound 49b will protect against retinal damage by topical treatment. Additionally, the study will examine whether the mechanism of retinal protection by Compound 49b involves insulin-like growth factor binding protein-3 (IGFBP-3).  
Relevance: As blast injury is reportedly associated with retinal damage (including reactive gliosis, inflammation, and cell apoptosis), pharmacological alleviation of these events may have a substantial impact on the treatment of pertinent cases in active duty troops and civilians alike.