**Public Abstract**

Objectives/Rationale: The incidence of ocular trauma in the battlefield is rapidly rising as a percentage of overall injury, with estimates of ocular injury as high as 11% of all battlefield injuries in recent Mideast wars. In conventional warfare settings, ocular trauma may be caused by shrapnel or heat from blasts, but in unconventional warfare ocular trauma may result from chemical exposure from agents like mustard gas, as used in the Iran-Iraq war. Thousands of Iranian soldiers lost either their eyesight, or their eyes, as a result of exposure to chemical weapons deployed by Saddam Hussein. There are no effective treatments for severe chemical injury to the eye, and permanent vision loss or loss of the eye or eyes is common after such exposure. Ocular damage is caused acutely by chemical toxicity, and also by the patient's own inflammation in reaction to the injury. The combination of chemical toxicity and inflammation lead to inability of the eye to heal properly. If inflammation could be better controlled, then damage to the eye might be lessened, thus increasing the chance the eye would heal properly, with restoration of vision and function. Our research indicates that a protein, TSG-6, naturally produced by stem cells in the body, can reduce the inflammation caused by chemical injuries to the eye, and when tested in rodents, allowed for complete healing after injury of the eye with an alcohol solution. We believe that based on these results, TSG-6 will prove helpful in the treatment of more severe injuries that might occur on the battlefield, like those caused by mustard gas, acids, or lye.

Applicability and Impact: If TSG-6 is proven effective in a model of severe chemical ocular injury in rodents caused by lye, then it would likely be effective for other types of chemical injury such as those caused by mustard gas, acid, phosphorus, or other agents. Since the action of TSG-6 occurs by a unique, natural, and effective method of controlling inflammation, it would likely prove beneficial in many other types of ocular trauma that increase damage through secondary inflammation such as blast or heat injury, shrapnel, severe burns, or blunt force trauma with minimal risk. Patients injured by chemical exposure to the eye might be expected to exhibit improved healing, thus restoring vision or preserving the eye. Furthermore, for eyes in which treatment was delayed, TSG-6 could prove helpful in the regeneration of normal tissue, thus allowing for reconstructive surgery such as with corneal transplantation, which would otherwise be unsuccessful. Injuries sustained by Iranian soldiers with mustard gas in the Iran-Iraq war have led to loss of vision, blindness, and inflammation for decades, and inability to repair with transplant surgery. The use of TSG-6 in the acute setting might have prevented such outcomes, and the use in later settings could allow for future restoration with corneal transplant surgery. Outcomes of chemical ocular injury are dismal and consist of multiple surgeries, which usually fail. TSG-6 could shorten by years the duration of treatment and could reduce the need for, or eliminate altogether, the surgeries required for these injuries. TSG-6 could revolutionize the treatment of chemical ocular injuries and would restore patients to their normal job or functions without disability.

Benefits for Service Members and Veterans: Patients who have suffered acute or past chemical ocular injury could benefit from TSG-6 through preservation of visual function, or restoring the eye with proper healing or effective surgery. If proven effective, TSG-6 could be
extended to other types of ocular injury such as from burns, blasts, or shrapnel. Return to active duty or independent function without disability might be anticipated.