**Project Title:** Platform for Rapid Delivery of Biologics and Drugs to Ocular Cells and Tissues following Trauma  
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**Background:** Multiple cell death pathways are triggered in neurons following exposure to blast waves. A large group of biologics are currently available that can block cell death. None of these biologics are currently used in the combat theater. Following blast pressure wave associated trauma, there is a limited window of opportunity within which to intervene before cell death programs such as apoptosis are irreversible. The barrier to the rapid delivery of biologics into neurons is the cell membrane. The research team has developed a small peptide called peptide for ocular delivery (POD) that can enter neurons without toxicity. POD can be conjugated to cargo and rapidly ferry the cargo into the cell. They envisage that in the combat theater, members of the Armed Forces will be equipped with lyophilized POD conjugated to anti-apoptotic proteins in the medical kit and this therapeutic will be suspended and applied directly to the eye or injected into the vitreous subsequent to exposure to blast.

**Objective:** The overall goal of this proposal is to test anti-apoptotic proteins fused to a peptide for ocular delivery (POD), which reportedly enters neurons without toxicity, to reduce the damage to neurons following exposure to blast waves in combat.

**Hypothesis:** POD may enable delivery of functional anti-apoptotic proteins across the plasma membrane of cells/neurons in the retina and cornea and may attenuate apoptosis and loss of cells.

**Specific Aims:** In Aim 1, anti-apoptotic proteins fused with POD will be synthesized, the ability of these proteins to cross the plasma membrane of cells in culture and inhibit ultraviolet (UV)-induced apoptosis will be measured, and the kinetics of uptake of these proteins in vivo by topical application on the cornea or by intravitreal injection or subretinal injection in mice will be characterized. In Aim 2, the most efficient POD fusion protein from Aim 1 will be delivered to the retinas of mice by intravitreal or subretinal injection, the retina will subsequently be challenged with UV radiation, and the efficacy of the proteins administered post-injury will be measured.

**Study Design:** To design and synthesize several anti-apoptotic proteins fused to POD and measure the ability of these proteins to cross the plasma membrane and inhibit ultraviolet radiation induced apoptosis in vitro and in vivo.

**Relevance:** These studies will move us significantly closer to the generation of a practical therapeutic that can be added to the medical kit of members of the Armed Forces to reduce damage to neurons following exposure to blast waves while in the combat theater.