Treatment Strategies

Anti-Lysophosphatidic Acid (LPA) Antibody Treatment for Protection against Blast-induced Neurotrauma and Ocular Injuries

Blast overpressure (BOP) exposure leads to severity-dependent brain injury. LPA is a bioactive lysophospholipid released from activated platelets, astrocytes, choroidal plexus cells, and microglia and is reported to play major roles in promoting inflammatory processes through signaling events mediated through specific G-protein coupled LPA receptors (LPARs). In particular, LPA is reported to be involved in blood brain barrier (BBB) disruption, Tau protein phosphorylation, and neuroinflammation leading to neurite retraction. Recent reports have noted elevated LPA and up-regulation of LPARs in both mice and humans following brain injury, and the neuroprotective efficacy of LPA antibodies (Lpathomab) in the rodent models. Researchers at Walter Reed Army Institute of Research (WRAIR), in collaboration with Lpath, Inc. (the developer of Lpathomab), are evaluating the role of LPA in ameliorating the deleterious effects of blast-induced neurotrauma and ocular injuries. Rats were exposed to single BOP using an Advanced Blast Simulator (ABS) and given one intraperitoneal injection of anti-LPA antibody (25 milligrams per kilogram body weight) at one hour post-blast. Researchers determined retinal pathology on days one and 15 post-blast using Hematoxylin and Eosin (H&E) staining and ocular function on days two and six post-blast using a visual acuity test. Findings to date reveal that anti-LPA antibody treatment significantly reduced retinal neuropathological changes and improved visual acuity in rats after blast exposure, reinforcing previous indications that therapies targeting LPA may provide effective countermeasures to blast injury. By revealing the neurobiological mechanisms that underlie BOP-induced ocular injury and vision impairments, these experiments will provide valuable insights into mitigation strategies and therapeutic countermeasures for affected Service Members.