



US DEPARTMENT OF DEFENSE

BLAST INJURY RESEARCH PROGRAM COORDINATING OFFICE

Injury Models

Tissue Non-Specific Alkaline Phosphatase (TNAP) in the Etiology and Diagnosis of Tauopathy After Blast Exposure

CTE, a tau protein-linked neurodegenerative disorder observed in athletes with multiple concussions, shares clinical symptoms and neuropathological characteristics with those seen in victims of blast exposure. Prevention of tau phosphorylation and facilitation of the dephosphorylation of phospho-tau are critical to prevent tauopathy and preserve/restore neuronal microtubule assembly. TNAP serves this major role in the brain by dephosphorylating phospho-tau. Researchers at WRAIR have shown that the activity and expression of TNAP in the rat brain significantly decreased after blast exposure and was associated with increased phosphorylation of tau, revealing the potential role of TNAP in the development of tauopathy and CTE after blast exposure. The decreased activity/expression of TNAP in the brain was associated with a decreased TNAP activity in the plasma, pointing to the potential use of TNAP activity/level in the plasma or cerebrospinal fluid as a diagnostic marker of blast-induced tauopathy/CTE. A manuscript describing these results is in press (Neuroscience Letters) and a full patent application has been filed to claim that TNAP level/activity in the plasma can be used as a biomarker for the diagnosis and prognosis of tauopathy/CTE and intranasal delivery of TNAP can provide an effective treatment strategy against tauopathy/CTE phosphorylation of tau protein occurs preferentially at serine 396 in a severity-dependent, regionally selective manner.