



US DEPARTMENT OF DEFENSE

# BLAST INJURY RESEARCH PROGRAM COORDINATING OFFICE

## Mechanisms of Injury

### Military Personnel with Chronic Symptoms Following Blast TBI Have Differential Expression of Neuronal Recovery and Epidermal Growth Factor Receptor Genes

Researchers from WRNMMC and Madigan Army Medical Center, in conjunction with NIH, DVBIC, the Institutes of Nursing Research, USUHS CNRM, and the West Virginia University Health Sciences Center, investigated the mechanisms of persistent blast-related symptoms in a project sponsored by USUHS CNRM. Researchers examined the expression profiles of RNA transcripts across the genome to determine the role of gene activity in chronic symptoms following blast-TBI. Active duty military personnel with a medical history of blast TBI ( $n = 19$ ) that occurred during deployment were compared to control participants without TBI ( $n = 17$ ). Controls were matched to cases on demographic factors including age, gender, and race, and also in diagnoses of sleep disturbance, and symptoms of PTSD and depression. Using expression profiles of transcripts in microarray platforms of peripheral samples of whole blood, lists of significantly differentially expressed genes were generated. There were 34 transcripts in 29 genes that were differentially regulated in blast TBI participants compared to controls. Upregulated genes included epithelial cell transforming sequence and zinc finger proteins, which are necessary for astrocyte differentiation following injury. Tensin-1, which has been implicated in neuronal recovery in preclinical TBI models, was downregulated in blast-TBI participants. Protein ubiquitination genes, such as epidermal growth factor receptor, were also downregulated and identified as the central regulators in the gene network determined by interaction pathway analysis. This study identified a gene-expression pathway of delayed neuronal recovery in military personnel who experienced blast-TBI and/or chronic symptoms. Therapeutic agents that regulate these pathways may provide novel treatments for chronic blast-TBI-related symptoms.