Injury Models

Multi-omics Analysis of Nutritional Countermeasures Used against Traumatic Brain Injury (TBI) and Traumatic Stress in Rodent Models

Researchers at the Integrative Systems Biology Program (US Army Center for Environmental Health Research (USACEHR)) are working with collaborators from the Military Nutrition Division (US Army Research Institute of Environmental Medicine (USARIEM)) and the Blast-Induced Neurotrauma Branch at the Walter Reed Army Institute of Research (WRAIR) to evaluate injury-induced changes in rat models of TBI using multi-omics assays. The focus of this research is to study closed head TBI in the context of a single concussion and adding external stressors (e.g. immobilization), adding nutritional interventions, and defining the cell biology, neurology (motor, memory, and emotional damage), and return to duty (RTD) (recovery) questions. USARIEM researchers hypothesized that the ingestion of an anti-inflammatory dietary mix as post-injury treatment agents will decrease cognitive deficits and the extent of closed-head neurohistological traumatic injury in these rats. WRAIR researchers hypothesized that the unfavorable brain polyunsaturated fatty acids (PUFA) composition frequently seen in the typical Western diet (resulting from n-3 PUFA deficiency associated with the n-3/n-6 dietary imbalance) increases vulnerability to TBI-related disorders. Together the researchers predict that diets supplemented with n-3 PUFA will reduce this vulnerability when given prophylactically prior to the TBI and will enhance recovery when continued post-TBI or stress. Using laboratory rats maintained on specially formulated diets, WRAIR has explored this possibility employing established models of blast TBI and traumatic stress to ascertain whether vulnerability to TBI or stress is exacerbated by the n-3 PUFA-deficient diet. Researchers at USACEHR have been assaying the samples using several -omics platforms including messenger ribonucleic acid (mRNA) complimentary deoxyribonucleic acid (cDNA) array, micro ribonucleic acid (miRNA) sequencing, liquid chromatography–mass spectrometry based metabolomic assays, and targeted proteomics to identify and validate potential surrogate markers from blood and neuronal tissues. USACEHR is also performing metagenomic assays to observe changes in microbiome and metabolite content in response to stressor exposure using these rodent models. The aim is to identify model-specific and cross-model conserved putative biomarkers after integrating multi-omics readouts. Preliminary data from USARIEM using rats exposed to mild or moderate TBI showed that exposure to acute immobilization stress significantly affected bacterial populations in the large intestines of rats exposed to mild TBI (mTBI) (Figure 1). Current studies are assessing the pathophysiological responses associated with moderate TBI that are ameliorated by an anti-inflammatory diet, using this systems biology approach. Researchers at WRAIR are conducting parallel rodent experiments in which the influences of different n 3/6 ratio diets on responses to TBI and stress are being assessed. The researchers anticipate that as the evaluations of samples from this study progress, the molecular characteristics of these cohorts may provide insights into the interplay of nutritional status and trauma along with revealing potential benefits of dietary supplementation and providing additional opportunities for dietary supplementation in Service Members exposed to TBI.

FIGURE 1: Gut Microbiome Changes at Phyla level-TBI in a Rat Model