# Diagnostics and Biomarkers

## Improved Biomarker to Guide Surgical Care of Combat-related Traumatic Brain Injury (TBI)

TBI has been a signature wound in recent conflicts. The use of improvised explosive devices (IEDs) resulting in high-energy blasts and subsequent multimodal creation of extreme injury patterns not seen in previous conflicts has created enormous challenges in the medical and surgical management of these wounded Service Members. Severe TBI is often accompanied by secondary injury due to anatomic and biochemical processes and is treated with hemicraniectomy and cerebrospinal fluid (CSF) drainage. Key decisions regarding diagnosis of vasospasm, antibiotic therapy, removal of CSF access, and bony reconstruction are made based upon examination, monitoring, lab and imaging studies, and clinical judgment. Understanding immunologic implications with a mechanistic focus directed towards clinically translatable therapeutic manipulation, and their consequences, calls for the development of accurate clinical decision support tools (CDST). Using patient-specific clinical variables combined with local and systemic biomarkers, CDST can be developed that can guide and optimize treatment in patients with severe TBI.

Researchers at the Surgical Critical Care Initiative (SC2i) at Uniformed Services University of the Health Sciences (USUHS) in collaboration with Emory University and funded by the Defense Health Program (DHP) are developing a predictive model capable of addressing key decision points for patients with severe TBI. These key decision points include: (1) onset of vasospasm; (2) timing of removal of ventriculostomy and decision to place permanent ventriculoperitoneal shunt; (3) onset of ventriculitis/encephalitis and antibiotic utilization; and (4) timing of craniofacial reconstruction. Major objectives are to develop a repository of CSF and serum and correlate data with clinical outcomes to develop predictive models. The key research accomplishments in fiscal year 2016 (FY16) include: (1) the reapproval by the Institutional Review Board (IRB) of the study protocol; (2) engagement with the Emory Emergency Medicine and Neuroscience Department staff to improve recruitment and sample collection; and (3) successful collection, validation, and transfer of samples collected from the first five patients added to the Bioinformatics Core Services aggregated clinical and assay data. In addition, patient enrollment in the study has increased to 1-2 patients per month resulting in a cumulative enrollment of 11 patients. Furthermore, vasospasm was detected in one of the study patients through the research-funded transcranial Doppler imaging; as a result, the patient was treated accordingly. This initial effort will serve as a roadmap for follow-on applications for biological discovery and development of next generation patient diagnostics and personalized treatments. The subsequent focus will be on detection and even prediction of deterioration before it becomes clinically apparent in TBI combat casualty patients. Leveraging both clinical and biomarker data, and using advanced machine learning techniques, this project is prospectively analyzing patient and injury-specific characteristics associated with the aforementioned complications and outcomes of interest in order to identify both significant predictors of specific outcomes as well as to identify potential general and biochemical/cellular targets for therapeutic intervention. Next generation patient diagnostics and personalized treatments that are developed for the outcomes of this study are expected to guide and optimize treatment in patients with severe TBI.