Diagnostics and Biomarkers

A Panel of Serum Micro Ribonucleic Acid (MiRNA) Biomarkers for the Diagnosis of Severe to Mild Traumatic Brain Injury (mTBI) in Humans

Department of Pathology at the Uniformed Services University of the Health Sciences (USUHS) is active in TBI research and was awarded a grant in 2010 from the Defense Medical Research and Development Program (DMRDP) managed by the Congressionally Directed Medical Research Program (CDMRP) to establish a miRNA based biomarker for TBI. TBI is a problem with epidemic magnitude involving Service Members, civilians, and professional athletes. MTBI, more commonly referred to as a concussion, accounts for more than 75 percent of the total reported TBI cases in the US Armed Forces. These mild injuries are often difficult to diagnose because of the absence of clear clinical symptoms and lack of sensitive diagnostic methods. Studies conducted within the Department of Pathology laboratory at USUHS have identified novel miRNA based biomarkers to diagnose mTBI. MiRNAs are small non-coding ribonucleic acids (RNAs) present inside a living cell which play key roles in the regulation of gene expression. In a recently published article in Scientific Reports, the collaborative research team identified a panel of miRNAs which show promise in detecting mild to severe TBI.[1] The research team investigated the presence of miRNAs in the blood samples from patients who suffered from an acute mild to severe TBI and compared these results with blood from healthy volunteers. A panel of 10 miRNAs was identified that were present only in the serum of mild to severe TBI groups and absent in healthy individuals and the trauma control patients. Four out the 10 miRNAs were found to be present at higher concentration in the cerebrospinal fluid (CSF) in TBI patients in comparison to the controls. A patent application (Application no: PCT/US2015/036925) has been filed for this discovery. Another article accepted for publication in the journal Brain Injury describes the kinetics of miRNA expression changes in the brain after TBI and their potential molecular targets.[2] Previous work from the same laboratory identified a miRNA biomarker, let-7i, for blast induced mTBI.[3,4] MiR-let-7i, reported in this study has been included in a recently initiated (2016) clinical trial at the University of Vienna, Austria (https://clinicaltrials.gov/ct2/show/NCT02639923), to assess its potential to diagnose acute mTBI. These studies lay the foundation for the development of novel miRNA based blood diagnostic testing for TBI. These findings have the potential to improve the diagnosis of mild to severe TBI using a non-invasive biomarker to determine the extent of injury. The ability to more accurately diagnose TBI may critically impact the medical care and safe return to duty (RTD) status of future Service Members with the goal of decreasing the long-term impact and complications of TBI.

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2 Chandran, R., Sharma, A., Bhomia, M., Balakathiresan, N. S., Knollmann-Ritschel, B. E., & Maheshwari, R. K. (2016). Differential expression of microRNAs in the brains of mice subjected to increasing grade of mild traumatic brain injury. Brain Injury, 1–14. https://doi.org/10.1080/02699052.2016.1213420

3 Balakathiresan, N., Bhomia, M., Chandran, R., Chavko, M., McCarron, R. M., & Maheshwari, R. K. (2012). MicroRNA let-7i is a promising serum biomarker for blast-induced traumatic brain injury. Journal of Neurotrauma, 29(7), 1379–1387. https://doi.org/10.1089/neu.2011.2146

4 Sharma, A., Chandran, R., Barry, E. S., Bhomia, M., Hutchison, M. A., Balakathiresan, N. S., … Maheshwari, R. K. (2014). Identification of serum microRNA signatures for diagnosis of mild traumatic brain injury in a closed head injury model. PloS One, 9(11), e112019. https://doi.org/10.1371/journal.pone.0112019