

Surface Plasmon Resonance Imaging-Based Epigenetic Assay for Blood DNA Post-Traumatic Stress Disorder Biomarkers

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Abstract : Post-Traumatic Stress Disorder (PTSD) is a mental health problem that people may develop after experiencing traumatic events such as combat, natural disasters, and major emotional challenges. Tragically, the number of military personnel with PTSD correlates directly with the number of veterans who attempt suicide, with the highest rate in the Army. Research has shown epigenetic risks in those who are prone to several psychiatric dysfunctions, particularly PTSD. Once initiated in response to trauma, epigenetic alterations in particular, the DNA methylation in the form of 5-methylcytosine (5mC) alters chromatin structure and represses gene expression. Current methods to detect DNA methylation, such as bisulfite-based genomic sequencing techniques, are laborious and have massive analysis workflow while still having high error rates. A faster and simpler detection method of high sensitivity and precision would be useful in a clinical setting to confirm potential PTSD etiologies, prevent other psychiatric disorders, and improve military health. A nano-enhanced Surface Plasmon Resonance imaging (SPRi)-based assay that simultaneously detects site-specific 5mC base (termed as PTSD base) in methylated genes related to PTSD is being developed. The arrays on a sensing chip were first constructed for parallel detection of PTSD bases using synthetic and genomic DNA (gDNA) samples. For the gDNA sample extracted from the whole blood of a PTSD patient, the sample was first digested using specific restriction enzymes, and fragments were denatured to obtain single-stranded methylated target genes (ssDNA). The resulting mixture of ssDNA was then injected into the assay platform, where targets were captured by specific DNA aptamer probes previously immobilized on the surface of a sensing chip. The PTSD bases in targets were detected by anti-5-methylcytosine antibody (anti-5mC), and the resulting signals were then enhanced by the universal nanoenhancer. Preliminary results showed successful detection of a PTSD base in a gDNA sample. Brighter spot images and higher delta values (control-subtracted reflectivity signal) relative to those of the control were observed. We also implemented the in-house surface activation system for detection and developed SPRi disposable chips. Multiplexed PTSD base detection of target methylated genes in blood DNA from PTSD patients of severity conditions (asymptomatic and severe) was conducted. This diagnostic capability being developed is a platform technology, and upon successful implementation for PTSD, it could be reconfigured for the study of a wide variety of neurological disorders such as traumatic brain injury, Alzheimer's disease, schizophrenia, and Huntington's disease and can be extended to the analyses of other sample matrices such as urine and saliva.

Keywords : epigenetic assay, DNA methylation, PTSD, whole blood, multiplexing

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