

BRAIN GENE EXPRESSION SIGNATURES FROM CEREBROSPINAL FLUID EXOSOME RNA PROFILING

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While the Visual Impairment and Intracranial Pressure (VIIP) syndrome observations have focused on ocular symptoms, spaceflight has been also associated with a number of other performance and neurologic signs, such as headaches, cognitive changes, vertigo, nausea, sleep/circadian disruption and mood alterations, which, albeit likely multifactorial, can also result from elevation of intracranial pressure (ICP). We therefore hypothesize that these various symptoms are caused by disturbances in the neurophysiology of the brain structures and are correlated with molecular markers in the cerebrospinal fluid (CSF) as indicators of neurophysiological changes.

Exosomes are 30-200 nm microvesicles shed into all biofluids, including blood, urine, and CSF, carrying a highly rich source of intact protein and RNA cargo. Exosomes have been identified in human CSF, and their proteome and RNA pool is a potential new reservoir for biomarker discovery in neurological disorders.

The purpose of this study is to investigate changes in brain gene expression via exosome analysis in patients suffering from ICP elevation of varied severity (idiopathic intracranial hypertension -IIH), a condition which shares some of the neuroophthalmological features of VIIP, as a first step toward obtaining evidence suggesting that cognitive function and ICP levels can be correlated with biomarkers in the CSF.

Our preliminary work, reported last year, validated the exosomal technology applicable to CSF analysis and demonstrated that it was possible to obtain gene expression evidence of inflammation processes in traumatic brain injury patients. We are now recruiting patients with suspected IIH requiring lumbar puncture at Baylor College of Medicine. Both CSF (5 ml) and human plasma (10 ml) are being collected in order to compare the pattern of differentially expressed genes observed in CSF and in blood. Since blood is much more accessible than CSF, we would like to determine whether plasma biomarkers for elevated ICP can be identified. This may eventually lead to a blood test to diagnose intracranial hypertension.