

Blood Genomics of Stroke

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Introduction:

All types of brain injury induce an inflammatory response involving elements of the bloodstream supplying the CNS. Characteristics of this response may be reflected in the genomic expression of inflammatory mediators found in peripheral blood. The hypothesis for our study is that the genomic expression pattern observed in whole blood can act as "genomic fingerprint" identifying the injury that precipitated it. Using microarray technology we investigated genomic expression of rat whole blood following hypoxia, ischemia, seizure, and hypoglycemia compared to untouched and sham-surgery controls. We also examined whole blood expression in healthy controls and human patients following ischemic stroke and transient ischemic attack (TIA).

Methods:

Adult rats were subjected to insult 24 hours prior to sacrifice, when brain and whole blood are harvested. Brain tissue was assayed for extent of neuronal injury and RNA was isolated from whole blood or leukocytes and applied to Affymetrix U34A microarrays. For the human study, patients were recruited from University Hospital and, if inclusion and exclusion criteria were met, a 20ml blood sample was drawn by peripheral venipuncture. Total RNA was isolated and applied to Affymetrix human U-133 Genechips. Data from both animal and human studies are processed for significance using Affymetrix Genechip software, Genespring software, and Significance Analysis for Microarray (SAM)

Results:

Different genomic expression patterns were observed in rat whole blood following the different modes of insult, with expression of batteries of genes either increasing or decreasing in each case compared to each other, untouched rats, and sham-surgery rats. Furthermore, a unique expression profile was correlated with the presence of neuronal injury. Individual genes in this profile, such as VMAT-2, demonstrated a form of dose-response, with greater expression correlated with more severe injury. Results from the human study are still being processed.

Conclusions:

These data indicate that various modes of neurological insult produce differing inflammatory responses (depending on severity of neuronal injury amongst other factors), mediated and traceable by changes in expression pattern in circulating blood cells. Individual genes in this profile may be useful in predicting the presence and extent of neuronal death following an insult. This is of great clinical significance as it suggests a cheap, simple, non-invasive method for diagnosing the type and severity of neurological insult in a human patient.