

Peripheral Blood Transcriptome Biomarkers for the Identification of Pree-Epileptic Patients

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Our goal is to identify prognostic peripheral biomarkers of epilepsy to develop an effective prognostic tool that would reliably predict whether chronic epilepsy would indeed develop in patients after initial precipitating event such as brain injury. To identify such biomarkers we applied a microarray-based approach for the analysis of gene expression in the peripheral blood. Experiments were performed in two well established rat models of chronic epilepsy: 1) systemic pilocarpine injection and 2) intrahippocampal kainic acid injection.

Samples of peripheral blood were collected before status epilepticus to establish a baseline and one, three, seven and thirty days after status epilepticus (SE). Isolated RNA was used for global transcriptome analysis using Agilent Rat Whole Genome microarrays. After SE, animals were continuously monitored using both EEG and video for the occurrence, frequency and severity of spontaneous recurrent limbic seizures for a period of six weeks. Seizure syndrome was retrospectively correlated with the changes in blood transcriptome profile. Identified gene expression changes were confirmed using semi quantitative RT-PCR.

Results showed that about 100 genes in each model were associated with later occurring epilepsy. Approximately 20% of identified genes were regulated in a similar fashion, independent of the model. This group of genes may mark processes specific for latent period of epileptogenesis and therefore may provide efficient tool for epilepsy prediction. The effectiveness of the identified biomarkers was blind-tested using a custom designed prognostic microarray and a separate group of animals.

Our data demonstrated that the molecular signature preceding the development of epilepsy is present in the peripheral blood transcriptome after an initial brain injury. This approach can be used both to screen and diagnose potential epilepsy patients, and to prospectively evaluate the effectiveness of antiepileptogenic therapies during the latent period of epileptogenesis.