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Paper 1.

Transcriptomic Profiling of Medial Temporal Lobe Epilepsy

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Abstract

Epilepsy is one of the most prevalent neurological disorders affecting ~1% of the population. Medial temporal lobe epilepsy (MTLE) is the most frequent type of epilepsy observed in adults who do not respond to pharmacological treatment. The reason for intractability in these patients has not been systematically studied. Further, no markers are available that can predict the subset of patients who will not respond to pharmacotherapy. To identify potential biomarkers of epileptogenicity, we compared the mRNA profiles of surgically resected tissue from seizure zones with non-seizure zones from cases of intractable MTLE. We identified 413 genes that exhibited ≥2-fold changes that were statistically significant across these two groups. Many of these differentially expressed genes had not been described in the context of MTLE including claudin 11 (CLDN11) and bone morphogenetic protein receptor, type IB (BMPRIB). In addition, we found significant downregulation of a subset of GABA associated genes. We also identified molecules such as BACH2 and ADAMTS15, which are already known to be associated with epilepsy. We validated one upregulated molecule, serine/threonine kinase 31 (STK31), and one downregulated molecule, SMARCA4, by immunohistochemical labeling of tissue sections. These molecules need to be further validated in large scale studies to determine their potential use as diagnostic as well as prognostic markers in intractable MTLE.

Journal: Journal of proteomics and bioinformatics
Paper: 2

Gene Expression Profiling of Tuberculous Meningitis


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Abstract

Tuberculous meningitis (TBM) is a form of extra pulmonary tuberculosis that is associated with severe neurological deficits and a high mortality. Early diagnosis of TBM is a major challenge despite the availability of several diagnostic methods. Existing diagnostic methods and markers are inadequate for early diagnosis of TBM owing to poor specificity and sensitivity. DNA microarray technology permits high-throughput identification of differentially expressed genes. In order to identify molecules as candidate biomarkers for early diagnosis
or as therapeutic targets in TBM, we carried out transcriptomic analysis of brain
tissue using whole human genome oligonucleotide arrays. From this gene
expression analysis, we identified 2,434 genes that were differentially expressed
at least two-fold in TBM cases as compared to controls. The large majority of the
differentially expressed genes encoded proteins that are involved in
metabolism, cell growth, transport, immune response, cell communication and
signal transduction. We confirmed the upregulation of two molecules, serpin
peptidase inhibitor, clade A member 3 (SERPINA3) and glial fibrillary acidic
protein (GFAP), at the protein level by immunohistochemical analysis. The
findings from our study should help us understand the molecular mechanisms
underlying TBM and to develop better diagnostic and therapeutic strategies
against this deadly disease.

Paper 3
Journal: Journal of proteomics and bioinformatics

iTRAQ-based quantitative proteomic approach for identification of
potential biomarkers for Rabies

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ABSTRACT

Rabies is a fatal acute viral disease of the central nervous system (CNS) and is an important public health problem in Asian and African countries. In the critical stage of rabies the disease manifest with the signs of encephalitic (furious) or paralytic (numb) rabies. Early diagnosis of this disease is particularly important as rabies is often fatal if not treated with prophylactic measures immediately after the infection and the molecular biomarkers associated with rabies is poorly understood. In this study, we investigated the quantitative proteomic profiles of human brain tissues with clinical conditions of encephalitic rabies and paralytic rabies in comparison with normal human brain tissues using iTRAQ approach. We identified 451 proteins, which included a set of proteins expressed differentially between encephalitic and paralytic rabies. We have identified several novel differentially expressed proteins which could be employed as novel potential biomarkers for rabies diagnosis. We observed a subset of proteins such
as karyopherin alpha 4 (KPNA4) were overexpressed only in paralytic rabies but proteins like glutamate ammonia ligase, (GLUL) were overexpressed in paralytic as well as encephalitic rabies. We have validated two upregulated molecules, glutamate ammonia ligase and calcium calmodulin dependant kinase 2 alpha (CAMK2A) by immunohistochemical labeling of tissue sections as well as by dot blot assay. These molecules need to be further validated in large scale studies to determine their potential use as diagnostic biomarkers in rabies. This is the first study to systematically profile clinical subtypes of human rabies using a quantitative proteomics methodology. Our results have shown an expression signature which defines different clinical manifestations of rabies which strengthens the confidence in the expression based classification of diseases.

Journal: Journal of proteome Research