

Whole-Genome (33,000 genes) Affymetrix DNA Microarray Analysis of Gene Expression in Chronic Fatigue Syndrome

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Background:

Chronic fatigue syndrome (CFS) is a complex disorder characterised by persistent fatigue, musculoskeletal pain and post-exertional malaise. The mechanism of fatigue in CFS is not known and as no reliable diagnostic test is available, misdiagnosis is common and treatment regimes vary. As CFS symptoms are multi-systemic and are often preceded by infections, gene expression in peripheral blood mononuclear cells (PBMC) was examined. The study was carried out to determine if any characteristic changes in biochemical pathways could be identified. This would identify biomarkers and provide a rational basis for targeted pharmacotherapy.

Methods:

Whole human genome DNA microarray analysis was performed on RNA isolated from PBMC. Affymetrix HG-U133 (A+B) DNA chips which include probe sequences for the entire human genome, 33,000 genes, were used. Eight male patients with CFS (18-54 years, mean 36 years) and seven age-matched male healthy controls (22-58 years, mean 34 years) were included in the initial microarray study. An additional twenty patients with CFS and twenty age and sex matched controls were recruited for RT-PCR and western blot assays in order to verify the microarray data for a number of putative biomarkers.

Findings: Iterative group analysis of the differentially expressed genes indicate that in CFS:

- (a) there is a shift of immune response with preferential antigen presentation to MHC class II receptors, downregulation of the MHC class I system with a consequential suppression of Natural Killer cells and fN_T-cell receptors,
- (b) increased cell membrane prostaglandin-endoperoxide synthase activity with downstream changes in oxygen transport and
- (c) macrophage activation with phagocytosis of apoptotic neutrophils.

Interpretation:

A comprehensive map of gene expression has been generated by whole-genome DNA microarray assay for patients with CFS. Several biomarkers have been identified by the microarray assay and confirmed by RT-PCR and western blot analysis. Functional changes affected by altered gene regulation offer an explanation of the fatigue experienced by patients with CFS. Western blot/ELISA assays of key biomarker genes can be used to support the clinical diagnosis and identify candidates for treatment trials in CFS.

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