

## **Gene expression in peripheral blood mononuclear cells from patients with chronic fatigue syndrome**

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N Kaushik [1], D Fear [2], S C M Richards [3], C R McDermott [3], E F Nuwaysir [4], P Kellam [5], T J Harrison [6], R J Wilkinson [7], D A J Tyrrell [8], S T Holgate [9] and J R Kerr [1]

### Affiliations:

[1] Department of Paediatric Infectious Diseases, St Mary's Campus, Imperial College, 2nd Floor, Medical School Building, Norfolk Place, London W2 1PG, UK

[2] The Randall Centre, New Hunt's House, King's College London, Guy's Campus, London SE1 1UL, UK

[3] Dorset CFS Service, Wareham, Dorset, UK

[4] Nimblegen Systems Inc, 1 Science Court, Madison, WI 53711, USA

[5] Department of Infection, Windeyer Institute of Medical Sciences, Royal Free and University College School of Medicine, London W1T 4JF, UK

[6] Department of Medicine, Windeyer Institute of Medical Sciences

[7] Wellcome Trust Centre for Research in Clinical Tropical Medicine, Faculty of Medicine, Imperial College London, London W2 1PG, UK

[8] CFS Research Foundation, 2 The Briars, Rickmansworth, Hertfordshire WD3 6AU, UK

[9] MRC Department of Immunopharmacology, University of Southampton, Southampton SO16 6YD, UK

**Background:** Chronic fatigue syndrome (CFS) is a multisystem disease, the pathogenesis of which remains undetermined.

**Aims:** To test the hypothesis that there are reproducible abnormalities of gene expression in patients with CFS compared with normal healthy persons.

**Methods:** To gain further insight into the pathogenesis of this disease, gene expression was analysed in peripheral blood mononuclear cells from 25 patients with CFS diagnosed according to the Centers for Disease Control criteria and 25 normal blood donors matched for age, sex, and geographical location, using a single colour microarray representing 9522 human genes. After normalisation, average difference values for each gene were compared between test and control groups using a cutoff fold difference of expression  $\geq 1.5$  and a p value of 0.001. Genes showing differential expression were further analysed using Taqman real time polymerase chain reaction (PCR) in fresh samples.

**Results:** Analysis of microarray data revealed differential expression of 35

genes. Real time PCR confirmed differential expression in the same direction as array results for 16 of these genes, 15 of which were upregulated (ABCD4, PRKCL1, MRPL23, CD2BP2, GSN, NTE, POLR2G, PEX16, EIF2B4, EIF4G1, ANAPC11, PDCD2, KHSRP, BRMS1, and GABARAPL1) and one of which was downregulated (IL-10RA). This profile suggests T cell activation and perturbation of neuronal and mitochondrial function. Upregulation of neuropathy target esterase and eukaryotic translation initiation factor 4G1 may suggest links with organophosphate exposure and virus infection, respectively.

Conclusion: These results suggest that patients with CFS have reproducible alterations in gene regulation.

Abbreviations: CFS, chronic fatigue syndrome; NBS, National Blood Service; PBMC, peripheral blood mononuclear cells; PCR, polymerase chain reaction

Keywords: chronic fatigue syndrome; pathogenesis; gene expression; T cell activation; mitochondrion; neurone; organophosphate; virus infection; interleukin 10 receptor

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