Summary of journal article, Kaushik, N.; Kerr, J.R., *et al.,*"Gene Expression in peripheral blood mononuclear cells from patients with chronic fatigue syndrome,"
Journal of Clinical Pathology
Aug 58(8) (2005): 826-32.

The aim of the research was "to test the hypothesis that there are reproducible abnormalities of gene expression in patients with CFS compared to normal healthy persons."

Gene expression in peripheral blood mononuclear cells was compared between a group of 25 CFS patients and a group of 25 healthy controls. The groups were matched for age, sex, and geographical location. Patients in the CFS group were selected according to the 1994 CDC diagnostic criteria. However, the reliability of the data was (in our view) enhanced by the fact that the most of the CFS subjects were severely ill and required bed rest for much of the day.

Analysis of the cells for both groups was conducted using a single color microarray representing 9522 genes. Average difference values for each gene were compared between the two groups. For a gene to qualify as differentially expressed between the two groups, a standard of p value of 0.001 was used. *(This means that a difference in expression according to chance would occur only once in a thousand times. So a high standard of reliability was used.)*
When a gene showed differential expression, a second test with greater specificity was used—the Taqman real-time polymerase chain reaction (PCR).

Results:

35 genes were differentiated between the groups by the microarray analysis.

The PCR further limited the differential to 16 genes—"15 of which were upregulated… and one of which was downregulated…"

"This profile suggests T-cell activation and perturbation of neuronal and mitochondrial function."

Discussion:

"The expression of the 16 genes was significantly different…" between the patient and control groups. Most of the remaining portion of the article catalogs the potential effects of the upregulation and downregulation of the particular genes in the pathophysiology of CFIDS, according to the following system and metabolic process dysfunctions:

Immune response:

T-cell activation hypothesized by the upregulation of one gene and the down regulation of a second.

Neuronal component:

Six genes may be implicated in neuronal and other disturbances in CFIDS patients. One of these genes is involved in the mitochondrial process and "mutations have been shown to be associated with central nervous system hypomyelination [breakdown of nerve sheathing] and encephalopathy [brain pathology]."

The article speculates this could account for the findings of changes in the brain's white matter in CFIDS as well as the cognitive dysfunctions.

Other *mitochondrial involvement* may be caused by the upregulation of 3 other genes.

The *cell cycle* in CFIDS patients may be disrupted by the upregulation of two genes, which assist in controlling cell division.

"The upregulation of [gene] EIF4G1 identified in our present study may represent a common host response to persistent infection with several viruses."

Upregulation of two genes may be involved in *transcriptional perturbation*. Two other upregulated genes may be responsible for an increased defense to *oxidative stress*

seen in CFS.

An important aspect of this article is the citing of similar research findings by gene, either for CFS or other illnesses of possible similar origins or pathophysiology. The recent gene expression research by the CDC (Whistler *et al*.) is cited: "…which is interesting in light of our finding of upregulation of EIF4G1 transcript 5…Whistler and his colleagues have also reported this finding in patients with CFS who have rapid onset ('triggered' by virus infection) as compared with insidious onset…Various viruses have developed strategies to divert EIF4G1 from utilization by the cellular machinery…The best characterized example is that of poliovirus…" as well as a number of other viruses.

Further Update as of Sept. 2005:

Attention US-based CFS patients

Dr. Derek Enlander, of NYC, is collaborating in the research led by Dr. Jonathan Kerr, St George's Hospital, London on an exciting RNA genetic study of CFS. Dr. Kerr's team believes that it has discovered biological markers for CFS. They have found differences in gene expression in white blood cells, which could explain how viruses trigger ME/CFS. There is a genetic abnormality in the protein production in the mitochondria.

So far the work has been carried out on 25 patients and 25 healthy controls, and the results will be published in the *Journal of Clinical Pathology***.**

Now Dr. Kerr 's team is going to be testing 1000 patients. Not only do they hope to find this a diagnostic marker for ME/CFS but also they believe that this will lead to a treatment.

Dr. Enlander will be taking samples from ME/CFS patients who can get to NYC, the samples will then be sent to Dr. Kerr.

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