



# CFS RESEARCH FOUNDATION

## Chronic Fatigue Syndrome Research Foundation

supporting high quality research aimed at understanding the basis of CFS/ME and its treatment

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# NEWSLETTER

No 10

**Before reading this Newsletter you may find the following explanations of two much used definitions helpful.**

### Gene Expression

Gene expression describes the behaviour of genes when attacked by an infection or other disturbance. Some genes become very active while others shut down. The overactive genes produce chemicals which cause the symptoms of the illness.

### Microarrays

Microarrays are revolutionising medical research. They allow rapid analysis of tens of thousands of genes at a time. One experiment can provide information about the activity of all 30,000 human genes.

Microarrays are made using a glass slide about 1" square onto which thousands of DNA molecules are attached each representing a single gene. After various processes the microarray is scanned to study the behaviour of the genes.

The team carrying out the gene expression study is able, using microarrays, to compare the activity of the genes in CFS/ME patients with the genes of normal healthy people.

**"It is clear that in these patients the gene function has changed and these changes can be detected and measured."**

This Newsletter is being written with a feeling of profound thankfulness. After decades of research looking at different aspects of CFS/ME we are now seeking its root causes and our research is already revealing these causes. We now realise we can get answers to the big questions we have been asking for so long.

When this study entitled **Investigation of gene expression in the peripheral blood lymphocytes of patients with Chronic Fatigue Syndrome (CFS)** started two years ago we were confident that it would provide some of the answers we were seeking and we hoped that it might give us some indication as to how the genes of people with CFS/ME were behaving compared with the genes in normal healthy people. The results, when they came, were greeted with a mixture of relief and tremendous excitement.

Trustees: The Rt Hon The Lord Bingham of Cornhill (Chairman). Andrew Gairdner FCA (Hon Treasurer).  
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It had needed courage to undertake this project. While studies in gene expression are not new, it is usual in other diseases to study samples from lesions, but there are no lesions in CFS/ME so we were using blood. We were also using microarrays for analysis and this is a new scientific technique. We all felt relief when we learned that the scientists had proved that it was possible to study genes from blood using microarrays. We also had a sense of triumph. Most important of all they proved that several genes in the patient group were behaving differently from those in the control group. Now we had some definite and provable facts which showed that this disease was real and could be demonstrated as such.

Now research into this disease has moved into a new dimension. We all recognise that this is a complicated illness which is why it has baffled scientists for so long and it is only because of new scientific technology that we are able to carry out this basic research. We can all take great pride in knowing that we are leading the way in seeking the causes, therapies and ultimately a cure for this illness. We are a very small organisation but the commitment of scientists, Trustees, members of the Research Committee, the office staff, our voluntary helpers and above all the donors, whether it be the grant-making trusts or our generous supporters, has made this possible. Thousands now suffering the appalling consequences of CFS/ME will have cause to be thankful for all this effort. However, we are still only on the way to therapies and a cure but they are now in our sights. The Foundation is extending its work fairly dramatically to bring forward the day when we will win this battle.

## **The Story So Far**

Those of you who have been our supporters for some time will already know the details of the early part of this project. For those of you who have joined us recently it might be helpful to read a very brief outline of this study. Dr Jonathan Kerr who is heading up this research obtained blood samples from 25 patients in Poole, Dorset who were either attending a CFS clinic run by Dr Selwyn Richards or who were bed-bound but in his care. The National Blood Transfusion Service provided samples from 25 healthy patients matched by age, sex and geographical location. These samples were studied using 3 laboratories in British medical schools and an American laboratory based in Iceland.

The scientists analysed 9,522 genes using a new scientific technique known as microarrays. This showed that 15 genes became more active and one less active in the patient group, but remained normal in the control group. While these results were exciting the Research Committee, realising their importance, felt that because this technique was so new the results might be disputed. So they decided that the work should be repeated using a different laboratory method called Taqman. The earlier results were confirmed. Dr David Tyrrell, Chairman of the Research Committee made this very important pronouncement "It is clear that in these patients the gene function has changed and these changes can be detected and measured."

It will be no surprise at all to people with CFS/ME that it was found that these genes showed problems in various systems including the immune system, in neurological function and mitochondrial metabolism (mitochondria are the powerhouse of the cell).

## The Next Chapter

These results were examined and discussed by the team who had been overseeing the work and it was decided that, as the problem seemed to involve so many different systems, it was imperative that the next stage should be undertaken by a multi-disciplinary team so that all the different facets of the illness could be addressed.

The team has members who are expert in fields such as rheumatology, psychology, psychiatry, infectious diseases and molecular virology. Each member of the group has a track record of academic achievement in CFS/ME or in areas which interconnect with the disease. It was ensured that there was a good balance between the clinical and academic aspects.

Dr Jonathan Kerr of St Mary's Campus, Imperial College London will continue to lead the study. Dr Selwyn Richards, Consultant Rheumatologist, Poole Hospital NHS Trust, will provide CFS/ME patients as well as people from groups with other diseases to act as controls. Normal controls will be supplied by the National Blood Transfusion Service. Dr Tim Harrison of the Windeyer Institute, UCL, will assist in some of the microbiological work and with the co-ordination of clinical centres. Professor Stephen Holgate, MRC Professor of Immunopharmacology at the University of Southampton, and Dr Paul Kellam, Senior Lecturer in Virology at the Royal Free and University College School of Medicine, London, will be involved in the review of data analysis. Professor David Nutt, Professor of Psychopharmacology, University of Bristol, will provide CFS/ME patients and cases of endogenous depression from primary care centres.

The next stage of the project is already underway. Blood samples are being taken from 50 patients in Dorset and from 50 normal healthy people to examine all genes in the human genome. It is possible that some genes which were not examined in the initial study may show even more marked activity in CFS/ME and these could be very important.

The team will go on to compare the genes of CFS/ME patients with those of people with other diseases to prove that the groups of genes already found to become overactive are peculiar to CFS/ME. The other diseases which are acting as controls are endogenous depression, rheumatoid arthritis, osteoarthritis, MS and prolonged fatigue of one to six months and normal persons with a degree of fatigue on the day of sampling. It is expected that the researchers will find some genes which are affected in CFS/ME patients are also affected in other diseases. This study will identify changes in gene expression that are found only in CFS/ME patients. They will then aim to develop diagnostic tests and to identify therapeutic targets. These targets will fall into two categories; firstly, those for which licensed drugs are already available and, secondly, targets for which new therapeutic drugs will have to be developed.

It is important that we find whether there is any variation in gene expression in patients in different parts of the country. So samples are to be taken from patients and controls in clinics in Dorset, London, Birmingham, Cardiff, Edinburgh and Sunderland.

The researchers will also examine the genes of patients with CFS/ME following documented acute infection with a specific infectious illness. The illnesses that have been chosen are parvovirus B19, Q-Fever and enteroviruses. Another part of the study is to examine in a smaller group the relationship between variation in expression of particular genes with variation in particular symptoms in CFS/ME patients.

The blood of ten patients with well defined and characterised CFS/ME will be sampled at monthly intervals over nine months and their genes will be examined and detailed records will be taken of the clinical symptoms present at each time of sampling. The possible relationships between the activity of particular genes and particular symptoms will be studied. It is likely that, as this research progresses, further mini studies will be necessary and the Research Committee of the Foundation would welcome this.

This team is by no means working in isolation. It has collaborative links with Dr John Chia of UCLA Medical Center, Torrance, USA, who is supplying samples from patients with enterovirus-associated CFS/ME. Professor Michael Levin, who is head of Dr Kerr's department, has a special interest in CFS/ME in children. Dr Tim Harrison and Dr Paul Kellam are members of the MRC UCL Centre for Virology.

Such a big and wide ranging study is expensive. We shall need hundreds of patients, extra resources for contacting and documenting patients clinically, and resources to do hundreds of laboratory tests. We shall also need to recruit skilled and energetic laboratory workers and provide them with the necessary equipment. The total cost of this is just over £1 million. We have funded the first two years, which are complete, and we have funds for a further year. This leaves us with £668,500 still to be raised.

The MRC has shown an interest in our work and we were invited to a meeting with them. They suggested that we should submit a grant application for part of the study which is in line with their policy of joint funding. We shall not know if our application has been successful until the summer of next year, so it is imperative that we go ahead with a vigorous fundraising campaign. We have an inspirational research programme ahead of us and a team of distinguished scientists to carry out the work. It is up to all of us to ensure that the scientists can go ahead with speed to conquer this disease which has been devastating the lives of thousands for so long.



I am pleased to send this donation in support of research into CFS/ME.

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