



FINGERPRINT

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Dr John Mitchell

John joined us in September of last year from The Institute of Molecular Medicine in Oxford, where he worked on inherited blood disorders. John completed his PhD in the Biophysics Department of Portsmouth University, working on DNA structure, and in Oxford was involved in the physical mapping of the genes. Mapping can take place once a gene has been located in a specific chromosome region. Our study at Charing Cross is still at the 'gene hunt' stage; but John has been hard at work ever since his arrival and we now have a clearer idea of the chromosome regions in which the elusive MND gene is not to be found!

SCIENCE IN ACTION MEETING in November 1997 was deemed to be successful and informative by those who attended. Jackie de Belleruche started the afternoon with a brief overview of the work going on here. The participants then split into informal groups to be shown round the various laboratories, where each scientist explained his/her particular area of research and the techniques used. One visitor reports...

"As usual during the long haul from Euston to Fulham, I heartily wished the hospital back on its original site in Charing Cross! The welcoming cup of tea on arrival restored my spirits, however; and after Professor Jackie de Belleruche's introductory summary, we all trooped out of the Glenister rooms and into the rain. Jackie very decently apologised for the weather and we very decently forgave her as we scurried across to the labs in the main building to meet... The Scientists: the men and women in white coats, who were going to shine light on our darkness and explain everything. Well, they did; and what I could understand of it (genetics being a very complicated subject) was both fascinating and encouraging. Then it was back to the seminar room for another cuppa, after which Dr Richard Orrell discussed new treatments 'in the pipeline'--and gladdened our hearts with his belief that gene therapy would be available within the next ten years. Yippee!! Then Juliet brought us up to date with the Helpline and information service, and after that it was time to say 'See you next year!' and dash back to wherever we'd all come from. It had been an interesting afternoon and was, I'm sure, much appreciated by everyone -- most especially those of us who live under the shadow of Familial MND."

LOOKING FOR THE SOD 1 MUTATION- A PERSONAL ACCOUNT

"Having lost my grandmother, mother and two aunts to MND by the time I had reached the age of 30, I was overjoyed to learn that at last there was a 'test' available. I asked my GP to refer me to the nearest Genetic Clinic. It may sound weird, but for 12 years, since the loss of my mother, I'd lived with the belief that eventually I would have MND and the prospect of a 'test' was an amazing relief. At the genetic clinic, however, I was told I'd have to undergo at least three counselling sessions, about two months apart, before they would even do the 'test' and then it would be another six weeks before the result was received from a London hospital that was doing research into Familial MND. I was devastated! I understand the reasons for careful counselling; but felt strongly that each case should be treated individually. With my family history I was only too familiar with the disease -- **and hadn't I been through enough already? Did they not realise the knowledge that I had gained over the years?**

I eventually had the blood test done in July 1996, thinking I would know the result in around six weeks and would then be able to sort things out that needed to be done if it turned out that I was at serious risk of developing MND. But the six weeks stretched into three months and then to six months before I was finally informed: 'We'll contact you when we have the results!' I do feel bitter about that long delay. This was *my life* they were talking about! They didn't seem to realise the traumatic effect it was having on me - normally one of the strongest, most level-headed and practical people you could wish to meet.

In March 1997, **STILL** awaiting the 'test' results, I developed soreness around my knee. I eventually went to my G.P.'s surgery, where one of the partners diagnosed a torn ligament, even when the soreness developed into a slight limp. I had my own suspicions, but, determined not to let my imagination run away with me, I decided to take a weeks holiday for some fun and sun (knowing what I would have to face if the symptoms persisted).

On my return, having stumbled numerous times while on holiday, I knew I had to go back to my G.P. To say she was 'gob-smacked' is

an understatement: she told me MND is a disease you learn about at Medical School but may never see unless a patient happens to present with it. I knew then that I had MND. And yet that *couldn't* be right -- as it was twenty years too soon!

I made an appointment to see a consultant neurologist, coincidentally, the one who had treated two other members of my family who'd had MND, and in the interim phoned the Genetic Clinic to let them know that I was having unmistakable symptoms even before diagnosis. A few days later found out that my neurologist had sent them a letter asking why I was still waiting, and 'Hey Presto!' they suddenly appeared. (No coincidence, I'm sure...) What gives anybody the right to decide that they should keep results from someone who has probably taken a long time plucking up courage to have the test in the first place?

As expected the results confirmed that I had the same faulty gene as my mother and aunts had. Unfortunately I'd been right after all. I felt strangely relieved to know one way or the other and understand what was happening. During the following week I saw the neurologist, and he, after a thorough examination and a little persuasion, confirmed that he didn't think it could be anything else. Although it was very unusual, considering I was only 31 years old; *I didn't think it could be anything else*. MND normally affects you between the ages of 50-70 years.

- CAROLINE ROGERS.

Why Does A Result Take So Long?

The first thing to remember is that the only test available is for the SOD-1 mutation, which is found in only 20% of families affected by Familial MND. (The remaining 80% have an as yet undetermined mutation - see FINGERPRINT No.6). Having a mutation in the SOD-1 gene does not inevitably mean that you will get MND - approximately one in five of those with the mutation will die before the age of 80 years without developing the disease; they may, for instance, die of another disease or by accident.

The test itself, for anyone at risk of inheriting the faulty SOD-1 gene, could hardly be simpler: a small blood sample is taken. But the problems with testing may be numerous. First you must be referred by your GP to your local Genetics Clinic; and since consultant geneticists cover a large region and are rarely based at a single hospital, it could be several months before you receive an appointment.

Each Genetics Clinic maintains strict guidelines to ensure that its clients are fully prepared for and aware of the full consequences of their genetic test before giving written consent to the procedure. There are normally at least three counselling sessions over several months. Because the SOD-1 mutation test is not a routine NHS service, the geneticist (or in some cases the consultant neurologist) must contact a research team that carries out this procedure. And because NHS funds are rarely available for this test, the search for an individual SOD-1 mutation may have to be fitted in between the research team's regular funded work. They will probably have to cover the cost out of their own limited budget- which may mean that your blood sample can't be processed until enough other samples have arrived to make the procedure economic. A thorough test requires an initial screen, when the gene is analysed in five parts (each a separate procedure), followed by duplicate or triplicate sequence reaction tests; which costs several hundred pounds. (Some centres charge this for the preliminary screen alone.)

The scientists, all too aware of the implications of a positive result, naturally want to check and recheck their research findings, to

ensure that a result is absolutely correct before being passed on to the clinic. (Not a delaying tactic!) These checks are vital for both scientist and client. Since the technique for locating the SOD-1 mutation is at the forefront of modern scientific research, discrepancies do occasionally occur which can mean that the checking process will take much longer than anticipated or that the result is not as uniform as we would hope. This can lead to the checks going on for even longer. The client, meanwhile, continues to wait...

WHAT'S IN A NAME?

It's complicated, but we thought you'd like to know - so here it goes. . . the Charing Cross & Westminster Medical School has merged with Imperial College of Science, Technology and Medicine. The old Biochemistry Department (of which we used to be a part) has moved to Imperial College site in South Kensington; but the Molecular Neurobiology group led by Prof. de Belleruche, is still based at the Charing Cross Hospital site and is now part of the Department of Neuromuscular Diseases. (This new department is part of the Division of Neuroscience and Psychological Medicine, which includes Psychiatry, Neurogenetics and Neuroendocrinology.)



COLLABORATIONS

We constantly refer to the work going on within the research group at Charing Cross, and are sure that you do not need reminding that we are not the only ones working on MND in this country. You may not be aware, however, that there are similar groups working all over the Europe. From time to time we collaborate with other research groups and so pool not only our brain-power but ideas and research developments.

Among the most successful collaborations to date have been those with..... Norway, Sweden, Holland, Poland, Czech Republic, Italy, Spain, Portugal and Ireland.



Contact us and tell us what you think

Should we institute a regular Correspondence page? Please tell us what YOU want to see in FINGERPRINT. For instance, is there anything that you feel we should explain more clearly? Anything that you specially want to tell us? See your comment, question,

joke - whatever - immortalised in FINGERPRINT No.10! Write
E-mail or fax your contribution to:

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