



## **Euro-ATAXIA Scientific Research Conference and AGM 2009**

**Euro-ATAXIA** is a federation of European ataxia charities of which Ataxia UK is a member and this year's Scientific Research Conference and AGM was hosted by the Spanish ataxia organisation, Federación de Ataxias de España (FEDAES). The event was held in Valladolid on the 25 and 26 September and was attended by representatives from the *euro-ATAXIA* member organisations as well as by scientific researchers. Representatives from Ataxia UK were Sue Millman, Chief Executive; Professor Barry Hunt, Trustee and Chair of the Scientific Advisory Committee, and Dr Alison Stevenson, Research Officer.

This is a summary of the dominant ataxia research and clinical research that was presented at the meeting, written by Alison Stevenson. (Detailed updates of Friedreich's ataxia research are not given here as they are included in the report of the FARA Therapeutics Symposium.)

### **SCA1**

An overview of research into SCA1 was given by Dr Antoni Matilla Duenas. Researchers are discovering more about what goes on at a molecular level in SCA1 and this should help with ideas about possible new treatments. Potential interventions may involve correcting the altered gene expression that is seen in SCA1 or using gene therapy to block the effects of the mutant SCA1 gene. Lithium is also a potential treatment. It promotes survival signals, reduces the toxic effects of mutant SCA1 protein and improves motor coordination in a mouse model of SCA1. It is currently undergoing clinical trials in SCA1.

### **SCA3**

SCA3 is caused by a mutation in the gene that encodes for a protein called ataxin-3. Dr Luis Pereira de Almeida has been investigating a gene therapy technique called RNA interference (RNAi) in rats to assess its suitability for the treatment for SCA3. The technique works by preventing the formation of a faulty protein from a mutated gene by interfering with the gene's message, the RNA. Dr Almeida has shown that RNAi can reduce the toxic effects of mutant ataxin-3 and decrease degeneration of nerve cells in a rat model of SCA3. Future studies will investigate the effects of the RNAi technique in different rodent model of SCA3 and look at safety, efficacy and delivery of the RNAi.

### **SCA8**

Dr Victor Volpini spoke about the mutation causing spinocerebellar ataxia type 8 (SCA8) and how it has been found to coexist with other mutations (SCA2, SCA3 and Friedreich's ataxia (FA) mutations) in individuals from some families.

## **SCA28**

Dr Franco Taroni gave an update on research into the molecular mechanisms that underlie SCA28, one of the most recently discovered SCAs. The gene that is mutated in SCA28 has been identified as AFG3L2, which codes for a protein that is enriched within the Purkinje cells of the brain. The AFG3L2 protein forms part of a larger protein complex that is involved in the quality control of proteins in the mitochondria, the energy producing parts of the cell. This is the first time that a mitochondrial protein has been linked with a SCA.

## **Very late onset ataxia**

Dr David Genis defined very late onset ataxia as having an age at onset of over 60 and described how it could be further sub-divided into two types of ataxia. One type occurs firstly in episodes, later being followed by a progressive, worsening ataxia whereas the other type is a more 'pure' cerebellar ataxia (not associated with other clinical features, eg eye problems) and is a much more slowly progressing condition. Both types are sporadic, that is they appear spontaneously or randomly and do not following a particular pattern of inheritance. These types of ataxia are the most common type of ataxia in older people and are the most prevalent type of ataxia after dominantly inherited forms of ataxia.

## **Deferiprone in FA**

The effects of deferiprone in 22 children and young people (aged 8 to 25) with FA, who were already taking idebenone, were investigated by Dr Mercedes Pineda and colleagues. They found improvements in mobility and heart function as well as reduced iron accumulation in the brain. However, two people developed neutropenia (low white blood cell numbers) and further investigation is required to establish who will benefit most from this type of treatment.

## **Pioglitazone in FA**

The rationale for testing pioglitazone in FA was presented by Dr Pierre Rustin. There are many reasons for looking at this drug: it promotes energy production and antioxidant pathways, it has shown benefits in one person with multiple sclerosis and in mouse models of neurodegenerative conditions, and there are limited side effects associated with it. A trial of pioglitazone in FA will recruit people aged 7-24 who are ambulatory. Although the trial will be taking place in France, it will also be open to people from other European countries from 2010. Please contact the Ataxia UK office for details.

## **Potential treatments for different types of ataxia**

Dr Arpa has tested a range of potential treatments in a series of small studies on his patients. His studies of idebenone in people with Friedreich's ataxia (FA) suggested that long-term treatment could prevent progression of cardiomyopathy in adults and children, but that stabilisation of neurological symptoms was only seen in children. Positive effects were also seen in FA with riboflavin, a vitamin with antioxidant properties which showed neurological and cardiac improvements. IGF-1 treatment



was studied in different spinocerebellar ataxias (SCAs) and showed the most improvements in people with SCA3, some improvements in people with SCA1 and no significant improvement in people with SCA7. Erythropoietin (EPO), a hormone that promotes red blood cell production in the body and deferiprone, a drug that mops up excess iron (an iron chelator), were also tried although problems with recruiting and maintaining study participants meant that few conclusions can be reached from these studies.

### **Coenzyme Q10 (CoQ10) in ataxia**

Dr Rafael Iriberry and his group have been studying Coenzyme Q10 (CoQ10) in ataxia. People with ataxia were assessed for CoQ10 deficiency by a muscle biopsy and blood test and given CoQ10 supplements for two years. (CoQ10 levels needed to be measured from fibroblasts, as plasma levels were not an accurate predictor of CoQ10 deficiency.) All people with a CoQ10 deficiency experienced significant improvements in their neurological symptoms, compared with only one of those who did not have an underlying deficiency.

**For more support or information please contact: Ataxia UK, Lincoln House, Kennington Park, 1 – 3 Brixton Road. London SW9 6DE**

**Website: [www.ataxia.org.uk](http://www.ataxia.org.uk).**

**Helpline: 0845 644 0606 Tel: +44 (0)20 7582 1444 Fax: +44 (0)20 7582 9444**

**Email: [helpline@ataxia.org.uk](mailto:helpline@ataxia.org.uk).**