

## **Degenerative ataxias and the potential for stem cell neuroprotection**

**Principal researchers: Dr Wilkins and Professor Scolding, Institute of Clinical Neurosciences, University of Bristol.**

### **Scientific summary**

Despite marked genetic heterogeneity, the spinocerebellar ataxias and other degenerative ataxias share many clinical and pathological features, suggesting a 'final common pathway' of disease pathogenesis. However, the precise mechanisms underlying neuronal loss within the cerebellum and brainstem in these conditions are unknown. Toxic 'gain-of-function' caused by mutant protein aggregates may cause death by a number of mechanisms including excitotoxicity, defects in energy metabolism, free radical generation or disruption in axonal transport mechanisms. Regardless of the precise mechanism of cell death, stem cells offer the potential of neuroprotection through their pleiotropic modes of action. In this study we propose to assess the influence of human bone marrow-derived stem cells on cerebellar neuronal survival *in vitro*. Cultured rodent cerebellar neurons will be exposed to a variety of insults, including exposure to free radicals and trophic factor withdrawal. Stem cells and factors secreted by stem cells will be added to cultures and the effect on neuronal survival determined. This project will provide important information concerning the neuroprotective properties of stem cells and is a necessary step in designing stem cell-based therapies for the treatment of degenerative ataxias.

### **Lay summary**

There has been much emphasis in the last few years on the potential for using stem cells to treat many different medical conditions, and this has been reflected in many advances in our understanding of the behaviour of stem cells. There are now human trials ongoing testing the use of stem cells in cardiac disease, and recently there have also been advances in neurology. A number of cell-based trials are, for example, ongoing in conditions such as Parkinson's disease (see Freed *et al.* 2001) and Huntington's disease (NEST-HD trials, Universities of Cardiff and Cambridge; Rosser and Dunnett, 2006), which offer promise for treatments of other neurological conditions such as the ataxias. To date there has been limited research in this field relating to the ataxias. This project will involve studying the potential for using adult-derived human bone marrow stem cells as future treatments for the ataxias. It represents the first step in this long-term strategy, the aim of which is to bring stem cell-based therapies eventually to clinical trials for the ataxias.

One of the advantages of using bone marrow stem cells is that bone marrow transplants have been used for many years for the treatment of leukaemia and there



is therefore much information available on the safety of their use in humans. This project involves using cerebellar cells taken from rodents and grown in culture. These nerve cells will be subjected to toxins which cause damage (trying to replicate damage seen in the ataxias) and the effect of stem cells on survival of the nerve cells will be tested. If this avenue of research appears useful, it will subsequently lead to testing the effect of stem cells in more complicated models (such as in whole animals which have been modified to be ataxic) and then eventually it may lead to human trials.

References:

Freed CR et al. Transplantation of embryonic dopamine neurons for severe Parkinson's disease. *N Engl J Med* 2001; 344:710-9.

Rosser A, Dunnett S. (2006) Cell transplantation for Huntington's disease. *The Lancet Neurology* 2006; 5 (4): 284-5.

**For more support or information please contact: Ataxia UK, Winchester House, Kennington Park, Cranmer Road. London SW9 6EJ**

**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).**