

19th International Symposium on ALS/MND

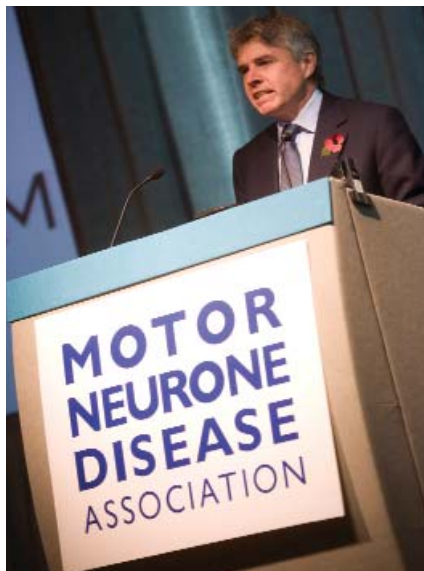
Conference details: 3-5 November, 2008, Birmingham, UK. **Reviewed by:** Belinda Cupid, Research Manager, Motor Neurone Disease Association, UK.

"These are tremendously promising times for scientists working in MND," commented Lord Drayson, Science and Innovation Minister, during his opening speech. Organised by the MND Association, UK, the meeting is a careful balance of presentations discussing biomedical research, clinical research and the clinical management of the disease, mostly organised in parallel sessions.

One of the biggest advances in the field of MND research in the last year has been the causal link between TDP43 and MND. In February 2008, mutations in the TAR DNA binding protein gene were found in two families affected by familial ALS. This new knowledge followed the discovery of aggregates of the encoded protein in the more common sporadic cases of MND, cases of MND with frontotemporal dementia and those with frontotemporal dementia alone. Presentations at the symposium gave delegates an update on the focus of research since February. These included confirming the link between TDP43 and the pathogenesis of the disease, establishing the function of wildtype protein and the interaction of TDP43 with other processes within the motor neurone.

As the knowledge and availability of non invasive ventilation (NIV) to help people with MND with respiratory symptoms improves, compliance continues to be a concern. A novel way to improve this was presented by Anabela Pinto from Lisbon. She explained that a lack of compliance is associated with the presence of abnormal breathing patterns. Half of the participants in her study used specially adapted ventilators, where parameters around their use were recorded. Recorded data were transferred via the internet to a central monitoring room on a weekly basis. Using these data, health professionals were able to adjust the ventilator settings remotely to better suit the patient. The group with the adapted ventilators achieved a high rate of compliance compared to those whose ventilator use was monitored during clinic appointments. Dr Pinto also found that they adapted more quickly to NIV.

Depressingly, the results of earlier drug clinical trials presented at the meeting were negative. The results of the latest insulin-like growth factor trial and that of co-enzyme Q10 showed no beneficial effects for people with MND. We must hope that that 'Trophos' study and others in the pipeline will bring happier news. Reasons for the poor track record of ALS clinical trials could be attributed to a number of factors in preclinical studies. Discussions at the International Symposium ranged from the entertaining (if you were not falling foul of his



Lord Drayson, Science and Innovation Minister, opening the 19th International Symposium on MND/ALS.

rules) presentation from Professor Chris Liplinski, to a number of sessions discussing disease models for MND/ALS. Prof Lipinski is a medicinal chemist. His 'rule of five' physico-chemical properties that potential drugs should meet go a long way to determining the likelihood of success of these drugs in the clinic.

Perhaps the most well known of disease models of ALS/MND is the (mutant Cu,Zn-superoxide dismutase 1) SOD1 transgenic mouse and more recently transgenic rat. The first transgenic mouse was created in 1996. Since then, literally hundreds of compounds have been tested in these mice for a beneficial effect. However, only one of these, riluzole, has made it to the clinic, leading to doubts on the validity of this model. The use of the SOD1 mouse in understanding the disease and developing treatments for it was discussed in a session encompassing a series of short pre-

sentations and a Panel question and answer discussion. Choice of SOD1 mutant, copy number, mouse genetic background and study design (drug administration pre- or post- symptom onset and robustness of phenotypic characterisation) were considered. In summing up the Chair concluded that we should not, as one of the speakers put it 'throw the baby out with the bath water', but that robust guidelines should be developed and implemented for their use. These would provide clarity for the biomedical researchers conducting these studies and also for their clinical colleagues seeking to interpret the results when considering whether to initiate clinical trials.

Transgenic rodents were not the only models of ALS/MND that were under discussion, one of the highlights was a talk from Joan Coates, presenting her data on the first sporadic ALS animal model – in dogs. Using a whole genome scan approach Prof Coates discovered that Canine degenerative myelopathy-affecting Pembroke Welsh corgis has a missense mutation in the SOD1 gene. Further investigation found this mutation, and spinal cord pathology similar to human ALS, in four other dog breeds. This research was published in PNAS in February 2009 (Awano et al DOI: 10.1073/pnas.0812297106).

It was encouraging to hear researchers talk about feasible applications for stem cells that may translate into the clinic. Nick Maragakis from Johns Hopkins University showed that transplantation of glial precursor cells into the cervical spinal cord of SOD1 rats resulted in the maintenance of respiratory function, longer survival and slower decline in forelimb (but not hindlimb) muscle strength. Over 85% of the glial precursor cells injected differentiated into astrocytes. These were unaffected by MND – their function was maintained and they did not contain protein aggregates. He concluded that this approach may have future application for preservation of respiratory function in the clinic.

In the closing session of the Symposium, Prof Clive Svendsen talked about a different approach for a cell based therapy. He has manipulated human mesenchymal stem cells to deliver an ex vivo gene therapy of GDNF into the muscles of a SOD1 rats. These injections slowed the progression of the disease and extended survival.

As over 800 delegates packed their bags to go home, I hope that it proved to be a thought provoking and memorable few days – memorable not just because this was the week that Lewis Hamilton became F1 world champion and the US voted for a new prostem cell president! ♦

There were over 800 people talking about MND research for three days, from 7 in the morning until 10 at night – the buzz was fantastic