



Committed to Defeating Motor Neurone Disease through Innovative Fundamental Research

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The Euan MacDonald Centre has flourished in 2011. In terms of the research, there have been high-impact publications in scientific journals, success with grant applications and many innovative new ideas and collaborations. We even impressed the First Minister during his recent visit.

There has been some consolidation of infrastructure — such as the move of some of the stem cell research work to the new Scottish Centre for Regenerative Medicine (SCRM) — a concrete start to some long-term and ambitious projects such as the Voice Banking initiative, and the commencement of building work, both material and electronic, for the Anne Rowling Regenerative Neurology Clinic and its website.

The Supporters too have been energetic and imaginative: walking, dancing and golfing to fundraise and even donating wedding gifts. I would like to express my heartfelt thanks on behalf of everyone at the EMC for these tremendous efforts.

It is my hope that over the next few years, and working with our local, national and international collaborators, we will make discoveries, and deliver clinical trials in the Anne Rowling Clinic, which will begin to change the outlook for patients with MND and other neurodegenerative diseases.

*Prof Siddharthan Chandran
Director, Euan MacDonald Centre*

VIP visit

Following on from the visit by HRH The Princess Royal in the Spring, the EMC members enjoyed a visit from the First Minister, Alex Salmond, in October.

The First Minister was welcomed by Prof Siddharthan Chandran and Prof Sir Timothy O'Shea (Principal of the University) and met Euan MacDonald and members of his family. He then took a tour of the labs, meeting many researchers and discussing their work.

It was by all accounts a very successful visit; Mr Salmond remarked that he was very impressed by all the work going on in the Centre, and took a special interest in the voice banking initiative.



left: Andrea Serio describes his research work to the First Minister; above: The First Minister meets Euan and Liz MacDonald



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VIP visit



Anne Rowling Regenerative Neurology Clinic



Research and Supporters' news

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All charitable activities for the Centre are administered by The University Development Trust, registered charity no. SC004307.



Building work begins on Anne Rowling Regenerative Neurology Clinic

The Clinic is no longer merely a concept, but real bricks and mortar – or at least a ceremonial spade with a red ribbon.

JK Rowling buried a time capsule at a Groundbreaking Ceremony in November to mark the £10M donation that she made in memory of her mother, who died of multiple sclerosis age 45.



JK Rowling buries the time capsule, watched by Prof Sir Timothy O'Shea, Principal of the University

The buried capsule contains written accounts from patients living with multiple sclerosis and other neurodegenerative diseases, as well as contributions from clinicians, commenting on current treatments and their hopes for the future.

The Clinic will be the Edinburgh hub for Regenerative Neurology and will target multiple sclerosis and MND. All aspects of the Clinic are gathering momentum, and it is due to open next year. Watch the temporary website at <http://www.annerowlingclinic.com/> for the latest news.



Architect's impression of the new building, outside the Chancellor's Building at Little France

A day in the life of MND Nurse Specialist, Judith Newton



*Judith Newton, MND Nurse Specialist
photo: Ian Freck for MND Scotland*

The impact of being told that you have or are related to someone with Motor Neurone Disease is devastating. Every week, I meet families who are living and coping with MND.

To me, MND is all about "Time". In a busy world where we are being told nobody has any, when caring for MND families, the key is to give Time.

Nurses and doctors are portrayed as always rushing. We are developing the MND clinics around the south-east of Scotland to be different. We allow for Time. As MND health professionals, we need to attend to the present and plan for the future.

Accurate information allows people and families to be aware of treatment choices so that they can "cherry pick" what is right for them. This ultimately allows the person with MND to remain in control. Only by listening and communicating can we get this right.

With all the advances in MND research, we are now more able to understand the complexities of this condition. I strive to take this research and translate it into how we can improve patient care and ultimately, their quality of life.



Voice Banking Success

We hope that most of you are aware of our initiative to “bank” the voices of volunteers to enable the generation of synthesised, individual and natural-sounding voices for MND patients who have speech difficulties.

We were thrilled with the response to our call in September for donor voices and since then have built up a donor recording bank of 200 voices. We have a fairly good demographic spread but only Edinburgh is really well represented and we need more Scottish accents! There is also a dearth of over-40s, particularly males, so if there are any men who fit this category and would like to participate, please email Shuna on info@smart-mnd.org for details.

In the New Year, we will start recording patient voices and “repairing” damaged patient voices using the donor recordings. This is the first step in road-testing our ability to give the patient a synthesised voice as near to their own as possible for use in a communication aid should they require it.

We would like to take this opportunity to thank you all for participating in this exciting project, and on behalf of the patients who will benefit from the voice repair facility - thank you.



The state-of-the-art anechoic recording studio at the Informatics Forum on Crichton Street, where voice recording takes place

Below are a few of the highlights among the many papers published recently by EMC Principal Investigators.



Human embryonic stem cell derived astrocytes mediate non-cell-autonomous neuroprotection through endogenous and drug-induced mechanisms. Gupta K, Patani R, Baxter P, Serio A, Story D, Tsujita T, Hayes JD, Pedersen RA, Hardingham GE, Chandran S. *Cell Death Differ.* 2011 Nov 18. doi: 10.1038/cdd.2011.154.

Siddharthan Chandran and Giles Hardingham are studying the role of astrocytes in protecting neurons against injury. Astrocytes are a type of glial cell; the glial environment

Research Highlights

plays an important role in supporting neuronal function. Kunal Gupta and colleagues derived functional astrocytes in a dish from human embryonic stem cells using a series of chemical signals.

They found that these astrocytes could protect stem cell-derived neurons from oxidative injury by hydrogen peroxide, and that this protection was greatly enhanced by treatment of the astrocytes (but not neurons) with the chemical CDDO(TFEA). The enhancement was effected by increased production of glutamate-cysteine ligase and glutathione, by CDDO(TFEA)-mediated activation of the transcription factor Nrf2. This work demonstrates that astrocytes could be a therapeutic target for human disorders associated with neuronal oxidative stress, including MND.

Reversible molecular pathology of skeletal muscle in spinal muscular atrophy. Mutsaers CA, Wishart TM, Lamont DJ, Riessland M, Schreml J,

Comley LH, Murray LM, Parson SH, Lochmüller H, Wirth B, Talbot K, Gillingwater TH. *Hum Mol Genet.* 2011 Nov 15;20(22):4334-44. Epub 2011 Aug 12.

Tom Gillingwater, Simon Parson and colleagues investigated the role of muscle in the motor neurone disease, spinal muscular atrophy (SMA). Although motor neurons undoubtedly contribute directly to the development of SMA, the role of muscle is less clear. Using mouse models of SMA and human patient muscle biopsies, the authors demonstrated significant disruption to the molecular composition of muscle, even without detectable nerve degeneration. Interestingly, the muscle pathology was improved when the mice were treated with an FDA-approved histone deacetylase inhibitor drug. It is therefore possible that some of the muscle injury in SMA is reversible.



Plasticity of tyrosine hydroxylase and serotonergic systems in the regenerating spinal cord of adult zebrafish. Kuscha V, Barreiro-Iglesias A, Becker CG, Becker T. *J Comp Neurol.* 2011 Aug 9.

Catherina Becker is studying the molecular mechanisms of neuro-regeneration in the zebrafish, a useful, transparent model organism that can regenerate its nerves and spinal cord after injury.

In this study, Catherina and colleagues examined chemical signals in the regenerated zebrafish spinal cord. Swimming behaviour recovered about 6 weeks after injury to the spinal cord, and this correlated with an increase in terminal varicosities in the spinal cord above the lesion site. Brain-derived dopaminergic and serotonergic signalling in the spinal cord was abolished below the site of injury.

The recovery in swimming behaviour despite these massive changes indicates the significant plasticity of the adult spinal network during regeneration.

Evidence of social understanding impairment in patients with amyotrophic lateral sclerosis. Cavallo M, Adenzato M, Macpherson SE, Karwig G, Enrici I, Abrahams S. *PLoS One.* 2011;6(10):e25948. Epub 2011 Oct 5.

Theory of Mind is defined as the ability to attribute mental states such as intentions and beliefs to others, in order to understand and predict their behaviour and behave accordingly.

Based on neuroimaging evidence, Sharon Abrahams and colleagues hypothesised that Theory of Mind deficits could be found among the 50% of amyotrophic lateral sclerosis (MND) patients who demonstrate abnormalities of the prefrontal cortex. They tested 15 ALS patients with an experimental protocol that distinguished between private (non-social) intentions and social intentions. As they predicted, the ALS patients were impaired on social intention tasks only. The results support the existence of specific cognitive defects in some ALS patients, which parallel those found in fronto-temporal dementia.

Featured Researcher

Prof Richard Ribchester



Richard is Professor of Cellular Neuroscience

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I am interested in all aspects of the biology of neuromuscular junctions (NMJ's). These are the connections made by motor neurones with muscles. Very early signs of MND can be observed at these tiny, cellular 'spot welds' that join nerve fibres (axons) to muscles.

We are presently developing a 'live-imaging' technique, using slender optical-fibre probes to observe directly when disease has triggered the breakdown of NMJ's. The results so far are encouraging but there are many technical hurdles still to overcome. Eventually, this method might be used to measure the effectiveness of new treatments for MND that prevent the degeneration of NMJ's.

Differential protection of neuromuscular sensory and motor axons and their endings in Wld(S) mutant mice. Oyebode OR, Hartley R, Singhota J, Thomson D, Ribchester RR. *Neuroscience.* 2011 Oct 20.

The fragmentation of axons and their nerve endings that occurs after a nerve is cut is called Wallerian degeneration, and normally occurs within 1 or 2 days of nerve injury in mice.

Richard Ribchester and colleagues are interested in a gene mutation, Wld(S), which extends the survival of functioning axons and their endings for up to 3 weeks after nerve section. Here, Oyinlola Oyebode and others studied the pattern and rate of degeneration of sensory axons and their neuromuscular junctions in mice carrying the Wld(S) mutation, and compared them with motor axons and their terminals. To enable their observation, the neurons were labelled with the fluorescent proteins YFP or CFP.

Surprisingly, sensory endings were preserved for up to 20 days, at least twice as long as the most resilient motor nerve terminals. This may be most simply explained by differences in the expression level of Wld(S) protein between neurones. Mimicking Wld(S)-induced protection may have application in the treatment of neurotoxicity or peripheral neuropathies.



Supporters' News

Robyn Ruane and Elizabeth Mackintosh-Walker (pictured below) organised an awareness- and fundraising event at Geddes House in Nairn.

Over seventy people enjoyed an evening of fine food and excellent entertainment, whilst raising over £2500 for the EMC. Siannie Moodie entertained the guests with her clarsach playing, and poets Richard Medlington and Elspeth Murray presented their Festival Fringe poetry. The delicious food was provided by Nairn-based companies Wester Ross Fisheries, Connage Dairy and The Really Garlicky Company.

Many of those who attended the event have lost loved ones to MND, and Shuna Colville, MND Research Nurse at the EMC, spoke movingly of the work that she and colleagues are doing to help patients in Scotland fight this very cruel illness.



David Calder completed the Three Peaks Challenge in May, raising £2500.

David writes of his experiences "The three peaks certainly was a challenge; with rain, hail, wind, thunder and lightning. Combined with less than one hour sleep and 450 miles in a cramped mini bus full of 11 sets of wet clothing and muddy boots. There were times when you had to dig deep mainly due to general fatigue, harsh weather and lack of sleep.



It was a great experience and I am very grateful for everyone's support and generous sponsorship."



GOOD TO KNOW...

Almost 300 people receive e-updates from the EMC.

Over 250 people are following the EMC on Facebook

MND patient and beneficiary of Rab's Fund, Robert Paulley (pictured below, left, with Siddharthan Chandran), visited the EMC in June with Rab's Fund trustees Neil Riddell and Ryan McKenna.

Rab's Fund (www.rabsfund.com) later donated over £1000 to the EMC.



The sun shone on The Ballater Chiels' Texas Scramble Golf Day and it raised an amazing £20,000 for the EMC. Next year will be the Chiels' 10th year of fundraising for the local community and generously contributing to the EMC.



Not just an average sponsored walk

Jean Reynolds, with her daughter Mairi and her dog Molly, were sponsored to walk the 64-mile Northumbrian Coastal Path north from Cresswell, near Newbiggin by the Sea, to Berwick upon Tweed.

WE WOULD LIKE TO SAY A HUGE THANK YOU TO ALL THOSE WHO HAVE ORGANISED AND SUPPORTED FUNDRAISING EVENTS THIS YEAR.

For information on how to organise your own event please contact Kerry.Mackay@ed.ac.uk / 0131 650 9221.