TREAT-NMD Partner Newsletter No. 6 — 13th April 2007

Welcome to the 6th weekly newsletter for TREAT-NMD partners and supporters

Newsletter contents

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1. TREAT-NMD Website

This week activity leaders have been asked to provide content for the website relating to their activities and workpackages. All activity leaders should have received a proforma to fill in and return to Rachel Thompson. The website is an important public face for the TREAT-NMD project and as such we want it to provide useful information written in an interesting and straightforward style suitable for "public consumption". We hope you enjoy the challenge and look forward to receiving your contributions.

TREAT-NMD Website Proforma – deadline 25th April 2007

Information Systems and Services (ISS) from Newcastle University are responsible for developing the TREAT-NMD website, and over the coming months they will be working to produce a complete communications platform or "intranet" for the network.

This will provide the network with a collaboration environment to enable effective communication through such tools as

- mailing lists / discussion forums
- shared file upload spaces for managing meeting minutes, research papers and other electronic documentation
- collaborative documentation tools such as wikis (see http://en.wikipedia.org/wiki/wiki for details of what a wiki is)
- shared group calendars to manage network meetings and events

The use of advanced access management technologies will provide members of the network with secure, personalised access to all of the tools and facilities from anywhere in the world via the web – ensuring that collaboration and communication can continue in real time, and the partners can remain in close contact.

The tools are planned to grow along with the network, and underpin the continuing collaboration and excellence which already exists within the TREAT-NMD network. If there is a particular facility you would like to have available via the partner intranet, please contact arron.scott@newcastle.ac.uk with your suggestions.

To partners who have e-mailed work package updates: since you have provided us with interesting material that shows just how active the TREAT-NMD network already is, we would like to make use of your contributions on the website. If you would like to amend your submission, send additional information for inclusion or have any objections to us publishing your information in the public section of the website then please e-mail stephen.lynn@newcastle.ac.uk.

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2. Conference Reports

The ethics of human clinical gene transfer: a CliniGene/CONSERT think tank.
Geneva, April 2nd - 3rd 2007

Report by Simon Woods, University of Newcastle.

Following the TREAT-NMD "kick-off" meeting at Evry, Simon Woods (UNEW) was invited to attend and represent the work of TREAT-NMD at this think tank meeting in Geneva. CliniGene is a European Network for the Advancement of Clinical Gene Transfer; CONSERT is a European Network dealing with the Concerted Safety and Efficiency Evaluation of Retroviral Transgenesis for Therapy of Inherited Diseases. Both programmes involve gene transfer clinical trials and are aiming to reach safe and efficacious gene therapies for human diseases. This meeting brought together clinicians, scientists, regulators, ethicists and lawyers as well as representatives from industry and patient groups from 10 nations. The meeting addressed issues including the challenges of basic science, clinical trials, public perceptions and concerns, regulatory and ethical issues.
The meeting was organised into three themes "Why?", "When?" and "How?" The "Why" addressed the question of whether gene therapy is a good choice for a particular treatment, prevention in human disease and whether there are more risk-free alternative treatments. The "When" theme addressed the level and extent of preclinical testing including animal experimentation and safety testing prior to the first clinical use in humans. The "How" theme addressed the design and safety of a clinical trial. A special keynote addressed the prospects for improved technologies in this moving field and their expected impact on ethics and ethical perception.

Simon Woods addressed the "When" theme with a talk entitled: "When should Gene therapy be performed in the course of a disease? The case of DMD: Social and ethical considerations." Simon's talk began with an outline of the aims of TREAT-NMD and its key partners. Simon went on to use Duchenne Muscular Dystrophy (DMD) as an exemplar of the translational research the project is aiming to address. Using the example of Antisense Oligonucleotides (AONs) Simon described how this intervention may be effective in modifying DMD into a milder Becker-like form of the disease offering hope to the many affected children. In addition to describing a forthcoming clinical trial he also addressed the ethical issues which attend early phase non-therapeutic clinical trials in children. Issues include the complexities of parental informed consent and the child's assent, the challenges of researching within a population who are desperate to find solutions and the issue of selecting the most appropriate research population. The presentation led to several questions and wide discussion of the issues.

It was clear that there are common concerns and many overlapping issues between the three networks and this was an excellent opportunity to establish a mutual understanding of our respective aims and important contacts for future collaboration.

Brickless centre 2007 meeting.
Århus, Denmark. March 1st-3rd 2007

Report by Thomas Sejersen, Karolinska Institute

Since 1992 the Danish muscular dystrophy foundation (Muskelsvindfonden) has arranged multidisciplinary scientific meetings at 1-2 year intervals. The meetings, attracting around 150-200 participants from Denmark,

Norway, Sweden, and this year also Finland, function as a platform for information exchange between the Nordic countries. The theme for the 2007 Brickless meeting, held in Århus, Denmark, March 1-3, was hereditary polyneuropathies, fatigue in neuromuscular disorders, presentation of a Scandinavian reference document for standards of diagnosis and care for myotonic dystrophy type 1, and a revised document for standards of diagnosis and care for Duchenne muscular dystrophy, as well as presentation of the TREAT-NMD initiative and network. Invited speakers talking on hereditary neuropathies included Mary Reilly, giving an overview on the diagnostics, clinical features and treatment, Gustav Pfeiffer talking on quality of life measurements, and Mark Jensen discussing pain in HMSN. Laureen Krupp later talked on fatigue in neuromuscular disorders followed by presentations on the Scandinavian reference documents on myotonic dystrophy type 1 by Björn Lindvall and Duchenne muscular dystrophy by Thomas Sejersen. Thomas Sejersen also introduced the TREAT-NMD initiative to the Brickless meeting.

Swedish network meeting for NMD.
Uppsala, Sweden. March 15th-16th 2007

Report by Thomas Sejersen, Karolinska Institute

Multidisciplinary teams from the 7 Swedish regional centres for neuromuscular disorders in childhood meet yearly to discuss cases of special interest, research activities, and general matters on organization related to diagnosis and care for neuromuscular disorders. The 2007 meeting, held March 15-16 in Uppsala, Sweden, was arranged by Eva Kimber in association with Mar Tulinius. The theme for the 2007 meeting was respiratory care in SMA. The national centre for respiratory care presented its experience with assessments and care of respiration, including non-invasive and invasive ventilator support. This was followed by presentation of the experiences from each of the 7 regions, several times leading to discussions on ethical issues related to level of ventilatory support used in the most severe cases. The TREAT-NMD initiative, particularly the work on developing standards of diagnosis and care for SMA and DMD, were presented and discussed.

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3. 'Fact-finding Questionnaire' – deadline 27th April 2007

The fact finding questionnaire was e-mailed to key contacts within each partner organisation on Thursday 12th April 2007. Please decide amongst yourselves who is the best person to complete it and return one copy per organisation to emma.heslop@newcastle.ac.uk **before 27th April 2007**.

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4. Progress update on active work packages

Thank you to all the work package leaders who provided a progress update on their active work packages. We feel that this was a valuable section and would like to continue to provide updates to partners regarding the progress of active work packages. We would therefore encourage you to e-mail stephen.lynn@newcastle.ac.uk with further updates as and when they occur.

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5. Funding / Awards

Eppendorf Award for Young European Investigators

Prize Money: **€15,000**
Application Deadline: **June 30, 2007**

The Eppendorf Award for Young European Investigators is presented to young scientists for outstanding achievements in the field of biomedical research based on methods of molecular biology. This prize, which reflects the past and future of Eppendorf, in a manner befitting the wishes of the company's founders, Dr. Heinrich Netheler and Dr. Hans Hinz, is intended to symbolize the close links between the company and the

field of biomedicine. The award was first established in 1995 on the occasion of Eppendorf's 50th anniversary. Since 1998, the prize has been presented in association with the scientific journal Nature.

http://tinyurl.com/2ex76n

Eppendorf & Science Prize for Neurobiology

Prize Money: **US$25,000**
Application Deadline: **June 15, 2007**

The Eppendorf & *Science* Prize for Neurobiology acknowledges the increasing importance of this research in advancing our understanding of how the brain and nervous system function - a quest that seems destined for dramatic expansion in the coming decades. This international prize, established in 2002, is intended to encourage and support the work of promising young neurobiologists who are not older than 35 years. The prize is awarded annually to one young scientist for the most outstanding neurobiological research based on methods of molecular and cell biology conducted by him/her during the past three years, as described in a 1,000-word entrance essay.

http://tinyurl.com/yum3gc

The Wellcome Trust Translation Awards

Purpose
Translation Awards (TAs) are grants designed to respond to the funding gap in the **commercialisation of new technologies** in the biomedical area. The awards:

- aim to enhance the opportunities for research exploitation broadly and across the university sector
- provide support for projects that will be managed by principal investigators and technology transfer offices working together
- may also be used to support joint projects involving participants from more than one institution.

Who can apply?
Translation Awards are primarily aimed at **innovative scientists** in conjunction with their technology transfer office or its equivalent, and, if appropriate, small spin-out companies from the institution. Awards will be made jointly to the academic scientist(s), technology transfer office or, if appropriate, another entity.

What types of projects may be funded?
Projects covering any aspect of technology development that can be applied to the biomedical sciences, providing the project:

- addresses a defined need in healthcare
- is at an early stage (i.e. insufficiently developed to attract first-round professional financing), yet has the potential to achieve a commercial follow-on at the conclusion of the project (e.g. as a licensing deal or start-up company)
- typically may be designed to establish proof-of-principle or reduction-to-practice of a technology.

Progress against a project plan will be measured against specific milestones. A case as to how the technology will be marketed will also be needed. Awards will normally be for periods of **two to three years**.

How to apply
Technology Transfer staff at the Wellcome Trust will be happy to advise applicants during the preparation of a proposal. Please read the **TA application guidelines** (http://www.wellcome.ac.uk/assets/wtx022036.doc) and **Wellcome Trust Grant Conditions** (http://www.wellcome.ac.uk/doc_WTD004055.html). It is recommended an executive summary (http://www.wellcome.ac.uk/assets/wtx024473.doc) is completed and sent to Technology Transfer before completing the application form (http://www.wellcome.ac.uk/assets/wtx022041.doc)

Timing
There is an open call for proposals and **applications may be submitted at any time**.
The Wellcome Trust aims to achieve a submission to decision time of no more than three to four months. Incomplete applications or queries arising after submission may delay processing.

Contact
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Wellcome Trust
Gibbs Building
215 Euston Road
London NW1 2BE, UK
T +44 (0)20 7611 8202
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E techtransfer@wellcome.ac.uk
http://www.wellcome.ac.uk/node2620.html

Marie Curie individual fellowships

Marie Curie individual fellowships in FP7 are aimed at experienced researchers with more than four year's research experience or a PhD and cover all areas of research, including the socio-economic sciences and humanities. The researcher and the host institution jointly submit a proposal for a research project on a topic of their choice.

Nationals of EU Member States or Associated Countries can go to a European country other than their country of origin, or to a country outside Europe, for a period of 1-2 years (in the latter case, there is a mandatory return period in Europe of at least one year).

Third country nationals may come to a host institution in a Member State/Associated Country for 1-2 years and if they are nationals of a developing or emerging economy, there is an optional grant to aid return to their country of origin.

If you are thinking of applying for an individual fellowship (as detailed in Partner 2 Newsletter) please contact one of the TREAT-NMD Coordination Team for assistance. The deadline for applications for this year is 14th August 2007.

http://www.treat-nmd.eu/assets/documents/TREAT-NMD_partner_newsletter_No2.pdf

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6. Latest News / Research

The Basel Biozentrum Taps Phenyx as protein Identification Platform

Biozentrum of the University of Basel will integrate GeneBio's Phenyx software platform for MS data analysis into its multi-tiered proteomics cluster

http://www.tmcnet.com/usubmit/2007/03/29/2451969.htm

Female stem cells build more muscle

By ANITA SRIKAMESWARAN
Tuesday, April 10, 2007

Female stem cells are more able than male ones to do the heavy lifting of regenerating muscle. So say researchers at Children's Hospital and the University of Pittsburgh, School of Medicine, who have found that stem cells derived from female muscle tissue, make more muscle cells than those that come from males. The findings were published in this week's Journal of Cell Biology.

Not only could the information influence treatment approaches for Duchenne muscular dystrophy and shed light on why some therapies work better in women than in men, but also "this may explain in part why we have so many conflicting results in the (scientific) literature," said senior investigator Dr. Johnny Huard, director of Children's stem cell research centre.

Scientists who attempt to replicate other groups' findings might not know whether stem cells had been gathered from or injected into male or female subjects. The new research indicates that those factors could dramatically affect the outcome of experiments, Huard noted. "We don't pay attention to those variables," he said. "So not only is it good (to know) for basic biology ... but it may also open the eyes of a lot of investigators." The work was supported by the National Institutes of Health, the Muscular Dystrophy Association and other advocacy and academic sources.

Several years ago, Huard's team isolated stem cells from skeletal muscle that had the ability to both renew themselves and produce high numbers of specialized muscle fibres. They hoped the find could lead to a treatment for Duchenne muscular dystrophy.

In addition, the muscle-derived stem cells could generate other specialized cells, including bone, cardiac and cartilage cells. To further their research, the researchers transplanted stem cells from male animal tissue into female animals. The Y, or male, chromosome could then be tracked to provide assurance that any muscle regeneration was the result of the transplanted male cells, Huard explained. The experiments revealed that cells from female animals were better at generating muscle fibres than ones from males.

Four out of 10 populations of female cells that were injected into dystrophic mice had a regeneration index higher than 200. The index describes a ratio of dystrophin-positive muscle fibres per 100,000 donor cells. The researchers found that only one out of 10 male cells scored higher than 200 on the index. The average was 95, and six out of 10 female cell populations exceeded that number. Also, female cells built more muscle in female recipients than in male ones, but still did better than male stem cells did in either female or male animals. That suggests that sex hormones play a role, although they are not the sole factor, Huard said. Male and female cells also responded differently to environmental stress, such as oxygen depletion.

http://www.scrippsnews.com/node/21043

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7. Articles

The myopathic form of coenzymeQ10 deficiency is caused by mutations in the electro-transferring-flavoprotein dehydrogenase (ETFDH) gene

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Coenzyme Q10 (CoQ10) deficiency is an autosomal recessive disorder with heterogenous phenotypic manifestations and genetic background. We describe seven patients from five independent families with an isolated myopathic phenotype of CoQ10 deficiency. The clinical, histological and biochemical presentation of our patients was very homogenous. All patients presented with exercise intolerance, fatigue, proximal myopathy and high serum CK. Muscle histology showed lipid accumulation and subtle signs of mitochondrial myopathy. Biochemical measurement of muscle homogenates showed severely decreased activities of

respiratory chain complexes I and IIþIII, while complex IV (COX) was moderately decreased.CoQ10 was significantly decreased in the skeletal muscle of all patients. Tandem mass spectrometry detected multiple acyl-CoA deficiency, leading to the analysis of the electron-transferring-flavoprotein dehydrogenase (ETFDH) gene, previously shown to result in another metabolic disorder, glutaric aciduria type II (GAII). All of our patients carried autosomal recessive mutations in ETFDH, suggesting that ETFDH deficiency leads to a secondary CoQ10 deficiency. Our results indicate that the late-onset form of GAII and the myopathic form of CoQ10 deficiency are allelic diseases. Since this condition is treatable, correct diagnosis is of the utmost importance and should be considered both in children and in adults. We suggest to give patients both CoQ10 and riboflavin supplementation, especially for long-term treatment.

Brain Advance Access published April 5, 2007 page 1-8.
doi:10.1093/brain/awm054

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8. Upcoming Conferences, Meetings and Workshops

- **MD-Net Annual General Meeting**
  8th-10th June
  Würzburg

- **1st Canadian Conference on Rare Disorders and Orphan Products Policy**
  24th-25th April 2007
  Ottawa, Canada
  http://www.raredisorders.ca/

- **11th Congress of the European Federation of Neurological Societies (EFNS 2007)**
  25th-28th August 2007
  Brussels, Belgium.
  http://efns2007.efns.org/

- **7th Congress of the European Pediatric Neurology Society**
  26th-29th September 2007
  Kusadasi, Turkey.
  http://www.epns2007.org/

- **XVIII. Neuromuskulární sympozium (18th Neuromuscular Symposium)**
  Neuromuskulární sekce ČNS (Neuromuscular Section of the Czech Neurological Society)
  11th – 12th May 2007
  Hotel Santon, Brno, Czech Republic
  http://www.meritis.cz/neuromuskularni-sekce/

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9. About this newsletter and the mailing list

This newsletter is intended to be used as a tool to keep TREAT-NMD partners informed of network activities. If you have received this newsletter you have been subscribed to a mailing list called "treatnmd-partners" and are a partner of TREAT-NMD. If you ever want to write a message to reach all of the recipients of this newsletter, write to treatnmd-partners@newcastle.ac.uk and your message will automatically be distributed to contacts within partner organisations.

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10. Send us your news and views!

We encourage all partners to send their own news and updates, either directly to all partners by writing to this list at treatnmd-partners@newcastle.ac.uk or to emma.heslop@newcastle.ac.uk for inclusion in the next newsletter. What else would you like us to include in the newsletter? Write to emma.heslop@newcastle.ac.uk with your feedback.

Please e-mail us with any information you have on upcoming education and training opportunities including workshops, conferences, funding, exchange programmes, clinical placements, visiting professorships and lectureships.

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11. Publicising TREAT-NMD

As part of efforts to raise the awareness of and publicise TREAT-NMD at conferences, workshops and other meetings we have produced a general double-sided colour flyer introducing TREAT-NMD and detailing the TREAT-NMD partner organisations. The flyer is now available for download from the TREAT-NMD web site at http://www.treat-nmd.eu/assets/documents/TREAT-NMD_Flyer.pdf. We have also added an editable version in Microsoft Publisher format (higher resolution, better for those intending to print it), which you can download and have printed yourself at http://www.treat-nmd.eu/public_html/private/docs/TREAT-NMD_Flyer.pub. We have also had a limited quantity of flyers printed, so if you would like some to be posted to you for a specific event, please write to r.h.thompson@newcastle.ac.uk.

If you are planning to attend any workshops, conferences or meetings please let us know and please take our promotional material along to help promote TREAT-NMD. The TREAT-NMD logo is available to download from the partners' area of the website at http://www.treat-nmd.eu/private/. Please also ensure that you include it on any abstract, papers and posters you prepare in which you mention TREAT-NMD.

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12. TREAT-NMD link from your website

In an effort to increase the profile of TREAT-NMD we are asking partners to add a link to the TREAT-NMD website from their existing website. Many of the partners have already done this – thank you! For those of you who have not, we would be very grateful if you could arrange for a link to be created.

To download a web-friendly TREAT-NMD button for your website please click on the following link and copy the appropriate line of code to your website: http://www.treat-nmd.eu/link.htm
Alternatively the TREAT-NMD logo is available on the website at http://www.treat-nmd.eu/private/ for you to create your own hyperlink.
