



## TREAT-NMD Partner Newsletter No. 5

5<sup>th</sup> April 2007

Welcome to the 5<sup>th</sup> weekly newsletter for TREAT-NMD partners and supporters

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### 1. 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](mailto:treatnmd-partners@newcastle.ac.uk) and your message will automatically be distributed to contacts within partner organisations.

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### 2. 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](mailto:treatnmd-partners@newcastle.ac.uk) or to [emma.heslop@newcastle.ac.uk](mailto: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](mailto: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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### 3. 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](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](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](mailto: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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#### **4. Resources**

The coming weeks will see a number of changes to the website as we update the existing pages and create new content sections. If there is anything in particular you would like to see on the website, please email your suggestions to [arron.scott@newcastle.ac.uk](mailto:arron.scott@newcastle.ac.uk).

After the Easter break all partners will be receiving forms to fill in to provide content for the website relating to their activities and workpackages. 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”.

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](mailto:stephen.lynn@newcastle.ac.uk).

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#### **5. 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 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.

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#### **6. 3 Monthly Report – deadline 9<sup>th</sup> April**

Bénédicte Charrin from ACIES recently e-mailed all Activity Leaders asking them to complete and submit a 3 monthly report. We would like to remind you that it is the Activity Leaders responsibility to ensure that the Work Package Leaders (for the activity that they are responsible for) submit their reports to the AL and that the AL completes the form and returns it to Bénédicte Charrin ([eu-new@acies.fr](mailto:eu-new@acies.fr)) before 9<sup>th</sup> April 2007.

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#### **7. 'Fact finding Questionnaire'**

We will be issuing the questionnaire to all partners next week. The deadline for the completed questionnaire to be returned to the TREAT-NMD coordination team will be 27<sup>th</sup> April 2007.

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## 8. Progress update – Cochrane

### WP10.2 Systematic reviews of interventions for NMD

For many areas of management in NMD, systematic reviews of the evidence base are lacking. Such reviews are crucial for establishing standards of care and for planning future trials. Through the editorial base for the Cochrane Neuromuscular Disease Group at King's College London, this workpackage will provide the systematic reviews of interventions relevant to the TREAT-NMD programme. We have identified and commissioned key reviews. Some have been completed and others are in progress.

#### **A selection of Cochrane Systematic Reviews published:**

**Rehabilitation interventions for footdrop in neuromuscular disease** Sackley C, Disler PB, Turner-Stokes L, Wade DT

<http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD003908/frame.html>

**Surgery for scoliosis in Duchenne muscular dystrophy** Cheuk DKL, Wong V, Wraige E, Baxter P, Cole A, N'Diaye T, Mayowe V.

<http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD005375/frame.html>

**Glucocorticoid corticosteroids for Duchenne muscular dystrophy** Manzur AY, Kuntzer T, Pike M, Swan A

<http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD003725/frame.html>

**Treatment for mitochondrial disorders** Chinnery P, Majamaa K, Turnbull D, Thorburn D

<http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD004426/frame.html>

#### **Reviews in progress:**

**Treatment for Charcot-Marie-Tooth disease**

<http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD006052/frame.html>

**Treatment for spinal muscular atrophy type I**

<http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD006281/frame.html>

**Treatment for spinal muscular atrophy type II and III**

<http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD006282/frame.html>

Preparing and keeping up to date systematic reviews of all interventions for neuromuscular disease is a major task and its accomplishment will require the whole-hearted collaboration of many members of the TREAT-NMD programme.

Please let us know of any intervention which you think would benefit from a Cochrane Systematic Review at [cochranenmd@kcl.ac.uk](mailto:cochranenmd@kcl.ac.uk). If you would like to know more visit our website [www.kcl.ac.uk/cochranenmd](http://www.kcl.ac.uk/cochranenmd) or contact us.

If you would like to author a new review, we would be very pleased to hear from you. We do provide training and support in systematic reviewing. This includes literature searching, detailed methodological advice and instruction in meta-analysis. We support reviews through the editorial process until they are acceptable for publication in the Cochrane Database of Systematic Reviews, part of The Cochrane Library, an electronic information resource containing systematic reviews of effectiveness of interventions. This resource is widely available in academic and health institutions and disseminated internationally.

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## 9. 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](mailto:stephen.lynn@newcastle.ac.uk) with further updates as and when they occur.

As mentioned above, we would like to make use of this information on the public section of the website. If those partners who have already submitted their updates have any objections to this could you please email [stephen.lynn@newcastle.ac.uk](mailto:stephen.lynn@newcastle.ac.uk). If you would like to re-write or add additional information to your section for the website please let us know.

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## 10. Funding

### EuroBioForum 2007 – Expressions of interest

The European Science Foundation invites expressions of interest for the EuroBioForum 2007. Expressions of interest are invited from researchers for pan-European large-scale research programmes addressing future challenges in life sciences research and demanding a coordinated funding policy at the European level to reach the necessary critical mass of expertise and funding resources. Applications can be submitted by a single proposer but it must be emphasised that the programme proposal should be supported by a network of scientists. EuroBioForum will take place between 5 and 7 December 2007 in Lisbon, Portugal.

Deadline: 5pm, 28 May 2007

<http://www.researchresearch.com/getPage.cfm?pagename=fundingOpRecord&lang=EN&type=default&id=180767>

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## 11. Latest News / Research

- **Drug Discovery Collaboration for Spinal Muscular Atrophy Expanded**

Families of Spinal Muscular Atrophy (FSMA) and Paratek Pharmaceuticals, Inc. announced they have extended their joint R&D collaboration to develop a drug candidate for the treatment of Spinal Muscular Atrophy (SMA), the leading genetically inherited cause of death of children under the age of two years.

Further information

<http://www.emaxhealth.com/24/10732.html>

- **Sequencing benefits of dystrophin in the Duchenne but not in the Becker muscular dystrophy**

The Duchenne and Becker muscular dystrophies are due to alterations in the gene encoding dystrophin. The large size of this gene and the number of mutations associated with the illness are an obstacle to the use of genetic tests. [Akber et al.](#) tested the utility of associating amplification of the dystrophin gene and direct sequencing of the coding regions and intron-exon boundaries. This combination has enabled them to detect the causal mutations in 98% of the individuals presenting with DMD but only 60% of patients diagnosed with BMD. In addition, the identified mutations in BMD are all deletions or duplications. It would therefore not seem necessary to carry out a dystrophin gene sequencing for the molecular diagnosis of this latter disease.

Click the following title to read more about "[Muscular dystrophy, Duchenne and Becker types](#)"

Genet Test; 10(4):229-43; Winter 2006

- **New therapeutic insight into Duchenne muscular dystrophy**

In the April 1st issue of *Genes & Development*, Dr. Bruce Spiegelman (Dana Farber Cancer Institute) and colleagues identify a key genetic component of and possible therapeutic target for Duchenne muscular dystrophy.

Duchenne muscular dystrophy (DMD) is the most common form of muscular dystrophy, affecting about 1 in 3000 males each year.

Dr. Spiegelman and colleagues found that a protein called PGC-1 alpha regulates the point of connection between the end of a motor neuron and a muscle fibre in the neuromuscular junction. Previous research has shown that PGC-1 alpha expression is induced by physical exercise and motor neuron activity, and mediates the anti-atrophic effects of nerve activity on muscle mass.

Dr. Spiegelman and colleagues analyzed the function of PGC-1 alpha in a mouse model of DMD. They found that PGC-1 alpha activates the expression of several genes that are aberrantly inactivated in DMD. In fact, by inducing PGC-1 alpha expression in these transgenic mice, the scientists were able to improve DMD symptoms.

"These data clearly show that experimental elevation of PGC-1 alpha has therapeutic promise in an animal model of Duchene's muscular dystrophy. We hope this will lead eventually to therapeutics for a terrible disease for which there is no effective treatment at the present time," explains Dr. Spiegelman.

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## 12. Calls for Papers, Posters and Proposals

### ESF Exploratory Workshops- Call for Proposals 2007

Deadline- 27th April 2007

#### Details

These small, interactive group sessions are aimed at opening up new directions in research to explore new fields with a potential impact on developments in science. The workshops, which usually last 1-3 days, have a wide participation from across Europe and involve young, independent researchers and scholars with leadership potential. The relatively small scale (in terms of people involved) provides an ideal platform for focus on the topic and for all participants to contribute to discussions and plan follow-up collaborative work. Interdisciplinary topics are greatly encouraged

Further Information: <http://www.esf.org/workshops/>

### British Council Researcher Exchange Programme - New Call for Applications

Deadline- 2nd June 2007

#### Details

The British Council is announcing a call for proposals under its initiative aimed at supporting new links between early stage researchers in the UK and in other countries. The Researcher Exchange Programme (RXP) is a £250,000 initiative that provides individual researchers with awards covering travel and subsistence costs, and some consumables costs, needed to develop new scientific collaborations and contacts through exchange visits of between one week and three months' duration.

The research link can be in any area of science, engineering and technology, including social sciences and humanities. The maximum award that can be applied for is £5,000.

Further Information: [www.britishcouncil.org/science-rxp](http://www.britishcouncil.org/science-rxp)

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## 13. Articles

### Neuromuscular Disorder

<http://journals.elsevierhealth.com/periodicals/NMD>

### The mitochondrial pathogenesis of Ullrich Congenital Muscular Dystrophy may open therapeutic perspectives.

Ullrich congenital muscular dystrophy (UCMD) is a severe, genetically and clinically heterogeneous muscle disorder linked to collagen VI deficiency. Following earlier studies suggesting that mitochondrial dysfunction could be responsible for the myopathy of a mouse model of collagen VI diseases (Mitochondrial dysfunction and apoptosis in myopathic mice with collagen VI deficiency. Irwin WA, et al., Nat Genet. 2003; 35(4):367-71), a recent manuscript indicates that mitochondrial dysfunction could be the basis of UCMD as well (Mitochondrial

dysfunction in the pathogenesis of Ullrich congenital muscular dystrophy. Angelin et al. *PNAS*. 2007; 104: 991-996). The study is based on a detailed characterization of cell cultures from five patients that are representative of the spectrum of severity of UCMD and bear different genetic mutations of collagen VI genes. In all cases mitochondria displayed an abnormal phenotype that could be traced to inappropriate opening of the permeability transition pore (PTP), an inner membrane channel that causes mitochondrial dysfunction and cell death. Inhibition of the PTP by cyclosporin A was able to rescue mitochondrial function and cell viability, suggesting the possibility that cyclosporin A can be used to cure the disease in patients.

**Mitochondrial dysfunction in the pathogenesis of Ullrich congenital muscular dystrophy and prospective therapy with cyclosporins.** Alessia Angelin, Tania Tiepolo, Patrizia Sabatelli, Paolo Grumati, Natascha Bergamin, Cristina Golfieri, Elisabetta Mattioli, Francesca Gualandi, Alessandra Ferlini, Luciano Merlini, Nadir M. Maraldi, Paolo Bonaldo, and Paolo Bernardi. *PNAS*. January 16, 2007. vol. 104 no. 3. p 991-99 <http://www.pnas.org/cgi/content/full/104/3/991>

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## SMA Foundation

### NIH/NINDS Director Highlights Remarkable Scientific Advances in SMA Research in Congressional Hearing

**Washington, D.C. – March 29, 2007** – In Senate Subcommittee on Labor-HHS-Education Appropriations hearings this week, National Institute of Neurological Disorders and Stroke Director, Story C. Landis Ph.D., testified on the remarkable scientific advances that have been made in spinal muscular atrophy research over the past decade. This is an excerpt from her remarks:

A decade ago, spinal muscular atrophy (SMA) was one of hundreds of poorly understood inherited disorders that affect the nervous system, and the outlook for developing treatments was bleak. The discovery of the gene defect that causes SMA revealed a rational strategy for developing drug therapy. In just a few years, the NINDS SMA Project developed a detailed drug development plan and tested hundreds of new compounds in laboratory tests. Most recently, some of these potential drugs increased the amount of the critical missing protein to normal levels in cultured cells from patients who have SMA. The SMA Project is testing the effectiveness of these compounds in animals with SMA and assessing their safety to bring these potential drugs to clinical trials, offering significant promise for helping people who have SMA.

Research on SMA illustrates the path from gene to understanding to treatment. Researchers have now characterized well over 200 mutations that cause neurological disorders. For inherited ataxias, Batten disease, Down syndrome, Huntington's disease, muscular dystrophy, Rett Syndrome, neurofibromatosis, and many other previously baffling disorders, researchers have genetically engineered animals that mimic the human disorder and then replaced genes, turned harmful genes off, turned up compensatory genes, or counteracted gene defects with drugs that target the affected cellular functions. In the future, application of these strategies to patients could preempt or even reverse the damage caused by gene defects. NINDS is aggressively pursuing opportunities to translate science advances such as these to treatments.

Full text of Dr. Landis's testimony is available [here](#).

### Enrico Bertini's attributed comments:

It is remarkable that the therapeutical paradigm on SMA, which hopefully is starting to be common for many inherited neurological disorders, was recently brought to the attention of the Senate Subcommittee on Labor-HHS-Education Appropriations in USA by the Director of the National Institute of Neurological Disorders and Stroke (NINDS), Story C. Landis PhD. This means that there is a strong commitment by the NINDS to focus on potential drugs for Clinical Trials. NINDS will surely participate actively at the SMA "Summit on Drug Development" organized by the International Coordination Committee on Clinical Trials in SMA which will be held on September 28<sup>th</sup> and 29<sup>th</sup> 2007 at the Hyatt Bethesda, Maryland, USA.

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## Neurology

Cross–Europe Initiative for Treatment of Neuromuscular Disease: A Unique Opportunity for Collaboration.  
International Newsletter  
Hanns Lochmüller

### Neurology 2007;68;1089-1090

<http://www.neurology.org/cgi/content/full/68/14/1089>

If your institution does not subscribe to Neurology you may download the article from the private section of the TREAT-NMD website: [http://www.treat-nmd.eu/private/docs/INL\\_April\\_Neurology.pdf](http://www.treat-nmd.eu/private/docs/INL_April_Neurology.pdf)

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## 14. Upcoming Conferences, Meetings and Workshops

- **Update in Neuromuscular disorders – Hammersmith Muscle Course**  
Date: Wednesday - Friday, 13 - 15 June 2007  
Venue: The National Heart & Lung Institute, London  
More details: [www.symposia.org.uk](http://www.symposia.org.uk)
- **European Human Genetics Conference 2007**  
Date: 16-19 June 2007  
Venue: Nice, France  
[More details](#)
- **12th International Congress of the World Muscle Society**  
Date : 17-20 October 2007  
Venue: Giardini Naxos, Taormina Mare (Messina), Sicily, Italy  
[More details](#)
- **4th European Conference on Rare Diseases (ECRD 2007)**  
Date: 27-28 November 2007  
Venue: Lisbon, Portugal  
[More details](#)
- **FightSMA Annual Conference: The Good Fight 2007**  
Date : April 22-27, 2007,  
Venue: Washington, D.C.
- **American Academy of Neurology (AAN) 59th Annual Meeting**  
Date: April 28-May 5, 2007,  
Venue: Boston, Massachusetts  
<http://am.aan.com/>  
The ICC is holding an affiliate meeting on Tuesday May 1st from 6:00PM – 7:30PM  
SMA Advocacy groups will sponsor a booth with information about SMA
- **Ukrainian Institute of Clinical Genetics (UICG), Families of SMA (FSMA, Ukraine) SMA Symposium**  
Date: May 22-24, 2007  
Venue: Kharkiv, Ukraine  
<http://www.uicg.org.ua/index-e.html>
- **Families of SMA (FSMA) 11th Annual International SMA Research Group Meeting**  
Date: June 21-23, 2007  
Venue: Schaumburg, Illinois  
<http://www.fsma.org/researcher-news.shtml>
- **SMA Summit on Drug Development**  
Date: September 28-29, 2007  
Venue: Hyatt Bethesda, Maryland