TREAT-NMD Partner Newsletter No. 14 and Club of Interest Newsletter No. 8

8th June 2007

Welcome to the eighth newsletter for the TREAT-NMD Club of Interest. This week's edition features an information-packed report from the SMA meeting held in May and details of a number of FP7 calls that may be of particular interest to network members.

We hope you enjoy the newsletter and look forward to hearing your comments - write to info@treat-nmd.eu with anything you'd like to say. Feel free to forward this message to anybody you think might find it of interest, or invite them to sign up to receive the newsletter by visiting our website.

Best wishes,

Katie, Volker, Stephen, Emma, Arron and Rachel – the TREAT-NMD coordination team

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Newsletter contents

1. About this newsletter

This is a weekly newsletter sent to all members of TREAT-NMD's "Club of Interest" worldwide. We are receiving new subscriptions all the time, so if you've missed the earlier editions of the newsletter and would like to catch up, please visit our newsletter archive online at http://www.treat-nmd.eu/news/newsletter/ where you will find all back-issues. If you have received this letter from a friend or colleague and would like to subscribe directly, please visit our website at http://www.treat-nmd.eu/ where you will find a subscription form at the bottom of the homepage. You can also use the same form if you no longer wish to receive this newsletter – just select the unsubscribe button.

2. Working with us

TREAT-NMD aims to be an inclusive rather than an exclusive network, and you do not have to be based in Europe or be a partner to be involved. International collaboration with experts from all over the world is already taking place, and new links are being developed.

If you are involved in any of TREAT-NMD's areas of interest and have something you'd like to say or a suggestion of where we could work together, we encourage you to get in touch by writing to us at info@treat-nmd.eu

3. TREAT-NMD news and reports

TREAT-NMD workshop on Spinal Muscular Atrophy – outcome measures, databases and standards of care. Naarden 12-13th May 2007

A TREAT-NMD meeting on spinal muscular atrophy (SMA) was held to coincide with a European Neuromuscular Centre workshop on SMA which had assembled representatives of many of the European centres caring for patients with spinal muscular atrophy for discussion of possible clinical trials. Several members of the ICC group for SMA attended from the USA, and we are delighted that this collaboration is extremely fruitful. The discussion was also broadened to have a discussion on outcome measures in Duchenne muscular dystrophy as so many of the areas of interest overlap between ambulant SMA and DMD.

1. Outcome measures for SMA type 1, 2 and 3 and DMD
Work in the last couple of years has led to the development of several scales for functional assessment. Various scales are available for use now in different trial scenarios and the choice of outcome measures will depend on factors such as the length of a planned trial and the level of disability of the participants. There is also scope for further development of outcome measures, particularly when considering the current emphasis of the regulatory agencies on outcomes which are perceived to be "life altering".

Natural history studies are helping to inform the development of prognostic indicators especially in SMA 1. The definition of these areas will be crucial for the execution of successful clinical trials. Three studies have collected data on survival of SMA 1, but there may be scope to develop a further prospective dataset based on the newly adopted standards of care.

TREAT-NMD will be working in several areas to evaluate, improve and train centres in the use of specific outcome measures:
1. Development of registry and systematic reviews of outcome measures (for further information contact Michael Rose at m.r.rose@kcl.ac.uk).
2. Evaluation of myometry in extended range of muscle groups in SMA (discussion forum to be set up – proposed moderator Marion Main).

3. The assessment of activity monitoring as an outcome measure in SMA (discussion forum to be set up and moderated by Sonia Messina – interested parties should contact Sonia at messinasonia@libero.it). A meeting to address experience in activity monitoring will be held in Paris on July 11, organised by Thomas Voit.
4. Develop an active working group to interact with the ICC outcome measures group (Eugenio Mercuri to convene).
5. Explore plans to get European translations of neuromuscular module of PedsQoL.
6. Discussion of whether further data collection in SMA 1 is indicated (discussion forum to be set up – proposed moderator Sabine Rudnik-Schoeneborn).
7. Initiate a debate of the patient and parent view on the impact of different outcomes to clinical trials.
8. Via the education and training network in conjunction with the outcomes measures group provide resources for teaching materials and exchange visits for evaluators.

Those interested in taking part in any of the above discussions should contact Rachel Thompson at the TREAT-NMD coordination office (rachel.thompson@treat-nmd.eu).

2. Registries for SMA
The establishment of a harmonised database / registry for SMA patients is a major aim of the network, led by Hanns Lochmüller and Christophe Beroud. Work is moving forward alongside the plans for registry development in DMD:

1. Plans are in place for a UMD based registry with harmonisation where possible with existing registries
2. Content definition is ongoing – contributions / comments welcome via the TREAT-NMD website at http://www.treat-nmd.eu/biobanks/
3. Database curators meeting is to take place on 11 June
4. National plans to be assembled
5. Patient groups are involved in interface

3. Standards of care
TREAT-NMD has an activity to develop and disseminate standards of care in SMA and DMD. This workshop concentrated on SMA where a very representative international working group within the ICC has already used literature review and expert consensus via the Delphi technique to generate care standards. The workshop participants were able to share this document ahead of publication, and there was general agreement that this is an excellent and very thorough starting point for the development of care standards to be adopted and disseminated via the network, though some areas require further work which will be carried out with the original members of the ICC working group. TREAT-NMD activity in this area will move forward in the following areas:
1. Develop a précis of the ICC document for clinical use and circulate via website
2. Set up working groups to develop document further in specific areas
3. Involve patient groups in dissemination of standards (Ria Broekgaarden to liaise and co-ordinate)
4. Involve national networks on dissemination of standards (partners to take forward)
5. Use registries as a tool to disseminate standards of care (long-term goal)
6. Use registries as a tool to monitor standards of care / natural history

General areas for development
The TREAT-NMD group is committed to seeking opportunities to move forward with clinical trials in SMA in collaboration with other similar efforts, such as those based in the USA. Specific examples where there is already activity include the collaborations with the ICC on outcome measures and standards of care, and cross talk with the Indianapolis Registry. Other areas to be developed include sharing of data from previous and ongoing trials to allow cross validation of control data and the systematic testing of new target molecules.

For international trials (likely to be necessary given the small patient numbers) there will be the need for collaborations of funding groups, which TREAT-NMD will explore. Contact with industrial groups interested in bringing drugs to trial will also be encouraged, as the TREAT-NMD network would be a good portal for the delivery of trials of promising compounds. Prioritisation of such potential drug targets will be addressed.

Ongoing active discussion lists include:

- Registries and biobanks,
- Standardised assessment of animal models,
- Outcome measures for clinical trials (especially patient's perspective),
- Standards of diagnosis and care in DMD and SMA.

If you would like to be involved in any of these discussions or if you know someone who would like to contribute, please let the TREAT-NMD office know (by writing to rachel.thompson@treat-nmd.eu).

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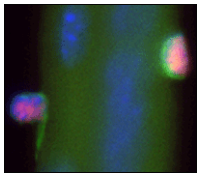
4. Pick of the articles



Newfound Stem Cells May Lead to Regenerative Therapies for Damaged Muscles

The discovery of versatile stem cells in muscle tissue could help combat the progression of muscular dystrophy.
By Nikhil Swaminathan

DIVISION IN PROGRESS: A satellite stem cell (the bump on the left hand side of the muscle fiber) gives rise to a muscle stem cell by an asymmetric cell division. Image: courtesy of Michael Rudnicki

Canadian researchers have identified a previously unknown type of stem cell in muscles that may one day be targeted to treat muscular dystrophy, a debilitating degenerative disease that affects some 250,000 Americans.

"It basically is the discovery of a new type of stem cell—a satellite stem cell," says Michael Rudnicki, director of the Sprott Center for Stem Cell Research at the Ottawa Health Research Institute (OHRI). So-called satellite cells were previously believed to be involved exclusively in helping injured muscles repair themselves.

But Rudnicki and colleagues found that mouse muscles actually contain two different types of satellite cells—90 percent of which are preprogrammed to become muscle tissue and another 10 percent that are uncommitted and could conceivably become bone, fat or some yet to be determined cell type.

The researchers report in *Cell* that they tagged muscle stem cells in mice in an attempt to track the activation of the gene *Myf5*. The gene codes for a protein, which functions, according to Rudnicki, as the "first genetic entry point into the muscle lineage."

They found that the gene was active in the stem cells predestined to become muscle, but switched off in the other version. When the cells operating sans active *Myf5* divided, one of the daughter cells contained an activated gene and the other had no *Myf5* function. When *Myf5*-positive genes were inserted, they just went on to become muscle cells. On the other hand, cells with the inactive genes divided into both types of stem cells, helping to replenish the entire satellite cell reserve.

The new discovery could lead to new therapies for degenerative diseases like muscular dystrophy, which is characterized by progressive weakening of skeletal muscle tissue. "I think where the promise lies is in understanding the molecular control and pathways of the cells," Rudnicki says.

He notes that in Duchenne muscular dystrophy, the most prevalent form of the disorder, preliminary evidence suggests that the satellite stem cells are largely depleted over time, allowing muscle damage to spread instead of being mended as stem cells are used up without being replenished. He says that muscle damage could potentially be slowed or halted in patients if they were treated with biological entities that could target and turn *Myf5* off in some muscle stem cells, creating in turn more satellite stem cells to repopulate the dwindling cell reservoir.

http://www.sciam.com/article.cfm?articleID=E3DA1666-E7F2-99DF-3D596D3DE6D0976A&chanID=sa007

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5. Calls for proposals

FP7 HEALTH Work Programme (Call FP7-HEALTH-2007-B)

The Health Work Programme is aimed at improving the health of European citizens and increasing the competitiveness and boosting the innovative capacity of European health-related industries and businesses, while addressing global health issues including emerging epidemics. Emphasis will be put on translational research (translation of basic discoveries into clinical applications including scientific validation of experimental results), the development and validation of new therapies, methods for health promotion and prevention including promotion of child health, healthy ageing, diagnostic tools and medical technologies, as well as sustainable and efficient health care systems. **TREAT-NMD partners who are interested in these call topics should contact ACIES or UNEW for assistance.**

Deadline: 18 September 2007, at 17.00, Brussels local time[1]
Indicative budget: to be announced

[1]At the time of the publication of the call, the Director-General responsible may delay this deadline by up to two months.

NOTE: The call is still provisional because it requires approval of the 2008 budget.

The full text of the 2007 Health call document is available via CORDIS at ftp://ftp.cordis.europa.eu/pub/fp7/docs/a_wp_200701_en.pdf. The following calls have been extracted as being potentially most interesting to TREAT-NMD partners and Club of Interest members.

HEALTH-2007-1.1-4: SME-driven collaborative research projects for developing tools and technologies for high-throughput research. The focus should be on developing and improving tools and technologies for: cell based assays, sequencing; gene expression, proteomics, genotyping and phenotyping; structural genomics; bioinformatics and systems biology; metabolomics, other "omics". These SME-driven projects should be specifically designed to encourage industry, preferably SME efforts towards research and innovation. The expected project results should clearly be of interest and potential benefit to SME(s). All consortia should have at least 40 % of the requested EC contribution budget going to SMEs.
Funding scheme: Collaborative projects (Small or medium-scale focused research projects targeted to SMEs).

HEALTH-2007-1.2-5: Standardisation and improvement of pre-analytical procedures for in vitro diagnostics. Provide pan-European quality assurance schemes and guidelines for pre-analytical procedures such as sample collection, handling, transportation, processing and storing of clinical samples. Tissue samples, blood samples and perhaps other specimens should be considered. The project should focus both on the standardisation of existing pre-analytical procedures and on the identification of critical steps in the pre-analytical procedure which need further development and improvement. It should also include training aspects. Involvement of industry is highly recommended.
Funding scheme: Collaborative project (Large-scale integrating project).

HEALTH-2007-1.2-6: High throughput molecular diagnostics in individual patients for genetic diseases with heterogeneous clinical presentation. The project should lead to the development of new diagnostic tools exploiting the knowledge of the human genome in combination with advanced read-out technology. Deliverables must be the development of a high throughput, sensitive, reliable and especially cost effective diagnostic test per disease category, which displays clear advantages over currently available diagnostic strategies. Special attention should be given to disease categories with heterogeneous clinical presentation, and/or locus heterogeneity, such as primary immunodeficiencies, muscle disorders, growth deficiencies, hearing or vision impairments and hemoglobinopathies. The project must address quality assurance issues and validation aspects, and should offer opportunities for industrial exploitation, preferably through SMEs.
Funding scheme: Collaborative projects (Small or medium-scale focused research projects).

HEALTH-2007-1.4-4: Development of emerging gene therapy tools and technologies for clinical application. This project should aim to exploit emerging gene therapy tools and technologies, such as use of genome editing and repair (RNAi, site specific recombination, etc.) to correct genetic defects, or new gene transfer techniques (novel virus vectors, targeted nanoparticles, bacterial DNA-based vector, bactofection,

etc.), which overcome the limitations of existing tools and for which preclinical proof of concept has already been established. The project should address biological activity, pharmacokinetics and toxicology of the gene therapy vector, establish biomarkers and assays for the evaluation of clinical trials, and take a translational approach towards early clinical research for therapeutic intervention. It should mobilise industrial and academic partners and address ethical and regulatory issues.
Funding scheme: Collaborative project (Large-scale integrating project).

HEALTH-2007-3.1-4: Improving clinical decision making. Development and validation of a methodology to measure the quality of clinical decisions. The methodology should be applied to explain variations of care in seemingly similar populations resulting from the clinical decision making process in different health care settings to allow comparative analyses of quality of care. This research should strengthen the clinical governance process for measurable improvements in clinical decision making. **Funding scheme:** Collaborative projects (Small or medium-scale focused research projects).

HEALTH-2007-3.1-6: Continuity of clinical care. Analysis of clinical care at the primary care/hospital interface and its effect on quality in terms of health outcome and costs in different settings. Identify and validate factors determining the outcome of integration in different settings for a provision of a continuum of quality clinical care at the primary care/hospital interface.
Funding scheme: Collaborative projects (Small or medium-scale focused research projects).

HEALTH-2007-3.2-3: Mobility of health professionals. Analyse mobility of different cadres of health professionals to, from, and within the European Union (extent; factors reducing or facilitating mobility; effects on remaining staff, health care services, and health outcomes; economic costs). Evaluate the effectiveness of existing financial and non-financial incentive schemes and policy responses addressing mobility trends. Develop recommendations for strengthening human resource policies in European and targeted third countries. The participation of organisations from the targeted third countries and regions is considered an asset to reinforce the impact of the action.
Funding scheme: Collaborative projects (Small or medium-scale focused research projects).

HEALTH-2007-3.4-1: Disease networks of centres of reference. Scoping study on the feasibility of developing guidelines, criteria and areas to develop European networks of centres for diseases requiring a particular concentration of resources or expertise, which would also be focal points for research, information dissemination and evaluation and medical training.
Funding scheme: Coordination and Support Action (Support action).

HEALTH-2007-4.1-4: Identifying patients' needs in the clinical trials context. The goal of this topic is to identify the needs of patients as related to clinical outcome: How can patients be better mobilised and empowered in the clinical trials landscape, which are the clinical outcomes that really matter to patients, and how can they be integrated into clinical trials. These questions should be addressed involving patients, clinicians, regulators, and researchers (industrial and academic) on a broad basis in order to cover a broad spectrum of diseases.
Funding scheme: Coordination and Support Action (Coordination or Support action).

HEALTH-2007-4.2-1: Adapting off-patent medicines to the specific needs of paediatric populations. Support will be given to studies dedicated to provide evidence for specific paediatric use of off-patent medicinal products currently used off-label. Studies include the assessment of pharmacokinetics (as well as data analysis and extrapolation by means of *in silico* models), efficacy and safety, and/or the development of appropriate formulations. Project proposals must take account of the priority list of Off-Patent Medicinal Products of the Paediatric Working Party of the European Medicines Agency (EMEA), and of the Regulation of the European Parliament and of the Council on medicinal products for paediatric use and amending Regulation (EEC) N° 1768/92, Directive 2001/83/EC and Regulation (EC) N° 726/2004, Brussels, 29.9.2004, COM (2004 599 final, 2004/0217 (COD). The priority list is available at the following address: http://www.emea.europa.eu/pdfs/human/peg/49677706en.pdf.
Funding scheme: Collaborative projects (Small or medium-scale focused research projects with a maximum EC contribution of € 6,000,000/project).

6. Partner-specific items

TREAT-NMD 6 month activity report

The 6 month activity report is due on the 15th June 2007.

1. The Activity Leader should ask each **Work Package Leader** from her/his Activity to complete the information on her/his WP (i.e. Work Package objectives, Progress towards objectives, Ethics, Deviations from project work program, deliverable and milestones and dissemination of knowledge). WP leaders can do this by updating their 3 month report and sending it to their Activity Leader **as soon as possible**.
2. The Activity Leader **consolidates** information from the Work Packages of her/his Activity, and provides an overview of actions undertaken.
3. The Activity Leader **sends** the consolidated report to ACIES (eu-new@acies.fr) no later than the **Friday 15th June**

Cost-Effort forms

The first overview on costs and resources spent during these 6 first months of TREAT-NMD is required before the Governing Board meeting at the end of June. Therefore, could you please send ACIES your cost and efforts follow-up sheets before the **15th June**? These sheets, designed for each partner, are **downloadable** from the private part of the website (http://www.treat-nmd.eu/private/ under "Cost forms").

Posters and presentations for Governing Board meeting

Partners have been asked by Stephen Lynn to prepare and present posters and/or presentations for the Governing Board meeting. Templates are available to download from the private section of the website http://www.treat-nmd.eu/private/.

As a general guide, can we please request that all posters should be printed A1 size (594x841 mm or 23.4x33.1 inches). The poster template page setup is set at A1 size. The posters will be on display from the evening of Sunday 1st July until the close of the meeting on Tuesday 3rd July. The UNEW team are very happy to help you in preparing the content for these posters, so please feel free to contact us.

You will also find on this web page a template for producing PowerPoint presentations related to the network. Please use this template when designing presentations that you intend to give on your activities within the network. We hope you find these templates useful.

Reimbursement guidelines

As the number of TREAT-NMD activities are increasing across the network reimbursement guidelines have been drawn up to help simplify your planning and implementation of TREAT-NMD related meetings and workshops. These guidelines have been posted on the private section of the web site and will be incorporated into the next version of the TREAT-NMD Project Management Manual. Please print-out and read these guidelines – they will help you to correctly identify the source for reimbursement when attending workshops and meetings.

Discussion forums / lists

Would you like us to set up a discussion forum for you on the TREAT-NMD website?
If so, please e-mail rachel.thompson@treat-nmd.eu.

Calls for proposals / funding opportunities

Please forward to us at the Coordination Office any calls for proposals and funding opportunities you receive within your institution. We will then advertise these in the newsletter and on the website.

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7. Send us your news and views!

We encourage all partners and supporters to send their own news and updates and we will be happy to include them in future editions of the newsletter. Please send your contributions to emma.heslop@treat-nmd.eu

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