

**Myology 2008**  
May, 26 - 30



# Press Kit

Myology 2008  
3<sup>rd</sup> international congress of myology  
26 – 30 May, Marseille

**For further information :**

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Evry, 13 May 2008

## **PRESS RELEASE**

3<sup>rd</sup> international congress of myology  
*Marseille – 26 to 30 May 2008*

### **Myology and neuromuscular diseases at the turning point towards treatment**

**Walking, reaching out, jumping, getting up, but also breathing, digesting and eating etc. All these acts demanded of our bodies in order that they function correctly are possible thanks to the some 500 muscles that make them up, and which represent 40% of our body weight. While fundamental knowledge about the muscle continues to grow, clinical research is also making great strides. It is in this context – as the turning point towards treatment is getting under way with about forty clinical trials ongoing or in preparation – that the AFM is organising its third international scientific congress devoted to myology from 26 to 30 May in Marseille.**

Myology is not only an emerging science, but – increasingly – a motor of innovation in the field of medicine. It concerns diseases affecting the two most inaccessible organs: the nervous system and the striated muscle. This obstacle has challenged researchers' capacities for innovation and led to the development of new therapeutic leads. Myology 2008, the international scientific congress organised by the AFM in Marseille from 26 to 30 May 2008, will bring together nearly 1000 researchers and muscle disease specialist physicians in order to share the considerable advances made in recent years in the development of these innovative therapeutic leads.

Since Myology 2005, the previous AFM congress in Nantes, decisive progress has been made. New therapeutic leads (gene, cell and pharmacological therapies) are being developed and trials are proliferating. But, as neuromuscular diseases are rare diseases, they present new challenges: patient cohorts are limited, therapeutic principles are increasingly based on a precise genetic mutation rather than on a disease, thus researchers and physicians need new preclinical and clinical tools of therapeutic evaluation.

Combining fundamental research and therapeutic strategies, the programme of this congress is structured around the main groups of neuromuscular disease and devotes two whole mornings to two transversal themes: the heart, a vital muscle particularly in neuromuscular diseases, and stem cells, whose therapeutic potential is increasingly being demonstrated.

On Friday 30 May a common day with the *International Rehabilitation Conference in Neuromuscular Diseases* will be held, also organised by the AFM. This congress – which brings together specialist physicians and paramedical personnel (mainly physiotherapists) – has been organised on alternate years in different European countries over the last ten years. For this fifth congress, and to accompany the turning point towards treatments, the AFM wished to organise it on the heels of Myology 2008. Thus it will contribute to reinforcing the dialogue between researchers and physicians, particularly concerning the effectiveness of emerging treatments with its underlying difficulty of making an accurate evaluation of the functioning and muscular performance of patients.

*Under the patronage of Valérie Pécresse, Minister of Higher Education and Research and Roselyne Bachelot-Narquin, Minister of Health, Sports and Youth. Myology 2008 is supported by the City of Marseille and the Treat-NMD network.*

### **President**

Thomas Voit (Institute of Myology, Paris)

### **Scientific organising committee**

Serge Braun (AFM, Evry)

Margaret Buckingham (CNRS, Pasteur Institute, Paris)

Nicolas Lévy (Inserm, La Timone University Hospital, Marseille)

Judith Melki (Hadassah University Hospital, Jerusalem)

Eugenio Mercuri (Catholic University, Rome)

Marc Peschanski (I-Stem, Evry)

Jean Pouget (AP-HM, La Timone University Hospital, Marseille)

Jean-Jacques Schott (Inserm, Nantes)

J. Andoni Urtizberea (AP-HP, Hôpital Marin, Hendaye)

### **Myology 2008 in figures:**

- Nearly 1000 participants expected, of whom about 1/3 from abroad
- 92 speakers of whom: 45 are French, 9 American, 6 Italian, 6 British, 4 German, 4 Swiss, 2 Japanese, 2 Canadian and 2 Australian.
- Approximately 500 scientific posters on display

### **Press Contacts**

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# All about Myology 2008

## 3<sup>rd</sup> international congress of myology

Myology 2008 is an international scientific congress organised in Marseille from 26 to 30 May by a patients' association, the AFM. It is presided by Thomas Voit, a neuropaediatrician, specialist in muscle diseases and Medical and Scientific Director of the Institute of Myology in Paris.

Three years after Myology 2005 in Nantes, this third congress will bring together nearly 1000 researchers and physicians specialist in the muscle and its diseases. It will continue the dynamic of the turning point towards treatments launched by the AFM. Therapeutic leads are increasing in number, and some of them are resulting in trials in humans. Thus Myology 2008 will seek to take stock of this medical and scientific revolution by encouraging exchange and comparing emerging therapeutic leads, but also by sharing the first clinical results.

### **Scientific programme of the congress: principal neuromuscular disease groups and thematic half-days**

- Structural myopathies
- Motoneuron diseases
- Laminopathies / Dystrophinopathies
- Stem cells (Tuesday morning)
- The heart (Wednesday morning)
- Gene-based therapies (Friday morning)
- Evaluation of the neuromuscular patient (Friday afternoon)

### **A forum entirely devoted to young researchers**

No rapidly-developing emerging scientific field can thrive unless it supports the young researchers who invest their talents in it. This support ensures its growth and the broadening of its knowledge base. Therefore, the AFM has chosen to devote a whole afternoon of its congress to the young researchers it supports. Ten of them will be presenting their work on the Tuesday afternoon.

### **Highlights of the congress**

Expert researchers of international renown in their fields will be present at Myology 2008. Among them are: two Japanese researchers **Shin'ichi Takeda** (therapeutic approaches to neuromuscular diseases) and **Ichizo Nishino** (fundamental mechanisms of the normal and pathological muscle), the Italians **Giulio Cossu** and **Yvan Torrente** (adult muscle stem cells), the French **Marc Peschanski** (stem cells), **Nicolas Lévy** (specialist of laminopathies and progeria) and **Luis Garcia** (gene therapy of myopathies), the Americans **Kenneth Chien** (gene and cell therapies of the heart) and **Lee Sweeney** (gene and pharmacological therapies of the muscle), the Australian and British researchers **Steve Wilton** and **George Dickson** (pioneers of exon skipping), and the Swiss **Daniel Schümperli** (gene surgery, splicing mechanisms).

Please note also two satellite symposia organised by two laboratories: **Genzyme** on Pompe disease ("New insights into Pompe disease", on Wednesday

at 19h) and **PTC Therapeutics** on its clinical trial concerning Duchenne myopathy (Friday at 12h15).

### **Myology 2008 – “à la carte” treatments**

Myology 2008 is privileged to bring together the pioneers of gene surgery:

- **Shin'ichi Takeda** (Japan): Tuesday 27 May at 9h15
- **Steve Wilton** (Australia): Wednesday 28 May at 17h30
- **George Dickson** (UK): Friday 30 May at 9h30
- **Daniel Schümperli** (Switzerland): Friday 30 May at 10h45

And the researchers who are at present developing these techniques for neuromuscular diseases:

- **Judith van Deutekom** (Netherlands): Friday 30 May at 10h45
- **Luis Garcia** (France): Friday 30 May at 10h45
- **Yvan Torrente** (Italy): Wednesday 28 May at 16h30

### **President: Thomas Voit**

Neuropaediatrician, specialist in muscle diseases  
Scientific and Medical Director of the Institute of Myology (Paris)

### **Scientific organising committee**

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### **Myology 2008 en chiffres :**

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# **What's new since Myology 2005 ?**

## **The turning point towards treatments**

### **Nearly 40 clinical trials under way or in preparation**

From the end of the 1980s the AFM traced out the stages along the path to drug development: the first human genome maps, identification of genes responsible for diseases, proof of concept for new therapies etc. The strategy paid off – with 40 clinical trials under way or in preparation, the AFM is entering into the era of treatments just 20 years after the first Téléthon. The question today is to transform these trials into real therapeutic successes – an ambitious and expensive challenge, as trials in humans cost several million euros and the development of a drug usually takes more than ten years.

In all, these trials concern nearly 30 diseases, both neuromuscular (around 50%) and non-neuromuscular:

- 15 neuromuscular diseases
- 4 neurological or neurodegenerative diseases: adrenoleukodystrophy, Huntington disease, Friedreich ataxia and Sanfilippo disease (2 different types)
- 3 blood diseases: drepanocytosis, beta-thalassemia and porphyria
- 3 immune deficiencies: DICS-X, ADA and WASP
- 1 skin disease: epidermolysis bullosa (2 different types)
- 1 eye disease: Leber amaurosis/pigmentary retinitis (one child and one adult type)
- 1 ageing disease: progeria
- coronary thrombosis

The breakdown of these trials is as follows:

- gene therapy (45%) to correct a genetic mutation and produce missing or deficient protein
- cell therapy to regenerate diseased tissue (15%)
- classic pharmacology (40%) either with molecules already used for other diseases but likely to be beneficial for neuromuscular diseases or new molecules likely to attack directly the cause or consequences of genetic damage

By supporting public research teams, engaging in industrial partnerships and developing tools of general interest, the AFM has only one objective – to speed up the development of therapies to cure as yet incurable diseases. From the first Téléthon in 1987 to today, scientific and medical research has made enormous progress. Thanks to the AFM's impetus, therapeutic leads and clinical trials are proliferating.

## **Cell therapy: the stem cell boom**

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Concerning cell therapy, recent years have been marked by stem cell and regenerative medicine. Whether adult or embryonic, stem cells seem to be able to cure or repair any deficient organ.

For myologists, the therapeutic potential of stem cells is daily becoming clearer – in particular for the cure or repair of the muscle whose degeneration is the cause of many patient deaths – the heart. Far exceeding the simple framework of neuromuscular diseases, the issue of cardiac cell therapy, particularly using adult or embryonic stem cells, will therefore take a prominent place in the Myology 2008 congress programme:

- special "stem cell" morning, Tuesday
- special "heart" morning, Wednesday
- contributions from key researchers in these two fields, such as: Kenneth Chien (USA), Shin'ichi Takeda (Japan), Marc Peschanski and Michel Pucéat (I-Stem, Evry), Patricia Lemarchand (Thorax Institute, Nantes), Robert Kelly (IBDML, Marseille), Bernard Fleischmann (Germany) or Christine Mummery (Netherlands).

## **Gene therapy: towards true gene surgery for "à la carte" treatments**

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Based on a simple concept (gene-drug transfer into the nucleus of a cell), gene therapy now proposes a multiplicity of therapeutic approaches with the same objective: that of predicating an ever-deepening understanding of the genetic dysfunctions that lead to a given disease in order to repair the defective parts of the gene. This gene surgery can intervene during the different stages leading from gene to protein. Besides gene transfer, there exist at present several tools with which "à la carte" treatments can be envisaged. Moreover, some of these treatments are the subject of trials in humans.

Gene surgery brings together several different techniques:

- **RNA surgery:** antisense oligonucleotides, exon skipping, exon reintroduction, readthrough Stop codons etc.
- **DNA surgery:** meganucleases, zinc finger proteins etc.

## **Exon skipping: intervention at the moment of splicing**

Exon skipping depends on "tools" with which our cells are naturally equipped – antisense RNAs. Schematically, these small molecules composed of bases "attach themselves" to specific places on the pre-RNA messenger and indicate to the cell machinery that a particular piece of pre-RNA messenger should be eliminated. By mimicking this natural phenomenon, researchers are capable of modifying the text of the RNA messenger. Thus, exon skipping can contribute to the production of a protein whose absence or deficiency is at the origin of a disease. It should be noted that this protein is functional, though slightly smaller than normal.

***Diseases potentially concerned:*** Duchenne myopathy, cystic fibrosis, haemophilia, thalassaemia, cancers, viral diseases such as AIDS and herpes etc.

### **Where are the researchers at?**

#### **➤ Phase I clinical trial on Duchenne myopathy terminated**

*The company Prosensa and the University of Leiden Medical Centre (Netherlands)*  
Exon skipping by antisense oligonucleotides (synthetic molecule) in 4 young boys affected with Duchenne myopathy (*New England Journal of Medicine*, 27 Dec 2007).  
Start-up between now and end-2008 of a phase I/II trial with general distribution of the treatment in the organism.

#### **➤ Phase I clinical trial begun on Duchenne myopathy**

*Hammersmith Hospital in London (UK), consortium between the British company MDEX and AVI Biopharma Inc (USA)*  
Exon skipping by morpholinos (another type of antisense oligonucleotide). 2 patients out of 9 included.

#### **➤ Preclinical work on Duchenne myopathy**

*Institute of Myology (Paris), Généthon (Evry)*  
Exon skipping using the U7 gene, normally present in cells, which codes for an antisense RNA transported by an AAV vector, with a view to a phase I clinical trial.

### **Top billing for exon skipping at Myology 2008!**

Most of the world-class researchers working on exon skipping will be at the Myology 2008 congress:

- **Shin'ichi Takeda** (Japan): Tuesday 27 May at 9h15
- **Yvan Torrente** (Italy): Wednesday 28 May at 16h30
- **Steve Wilton** (Australia): Wednesday 28 May at 17h30
- **George Dickson** (UK): Friday 30 May at 9h30
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## **Stop codon readthrough: intervention at the ribosome level**

With "stop codon readthrough" researchers intervene at the last stage of protein synthesis – the ribosome level. All healthy genes possess a Stop codon at their extremity. This indicates to the ribosome that it must cease its "translation" activity as the protein is full. However, certain mutations result in so-called "premature" Stop codons, as they are situated before the end of the messenger RNA. When the ribosome gets to their level, it stops translating – in other words, too early.

This is sometimes what happens to dystrophin, the protein whose absence or manufacturing deficiency is at the origin of Duchenne myopathy. "Stop codon readthrough" therefore consists of provoking the ribosome to disregard the premature stop signal and continue its translation until a complete and functional protein is obtained.

***Diseases potentially concerned:*** around 15% of genetic diseases, including Duchenne myopathy and cystic fibrosis.

### **Where are the researchers at?**

#### **➤ Tolerance (phase I) and increasing dose (phase I/II) studies for Duchenne myopathy and cystic fibrosis terminated**

*Lee Sweeney (University of Pennsylvanie, USA) and the company PTC Therapeutics (USA) New molecule: PTC124.*

38 young boys affected with Duchenne myopathy and carriers of genetic mutations at the origin of the appearance of premature Stop codons.

International large scale (165 patients) and long term (one year) phase II/III trial begun in May 2008 and involving 3 French clinical centres (Institute of Myology in Paris, Nantes University Hospital and La Timone University Hospital in Marseille).

### **Stop codon readthrough at Myology 2008:**

The international trial under way by PTC Therapeutics will be widely presented during the congress:

- **Lee Sweeney (USA)** : Friday 30 May at 8h45

*"Applications of stop codon readthrough on DMD and other neuromuscular diseases"*

- **PTC Therapeutics symposium** Friday 30 May at 12h15

## **Meganuclease recombination systems: intervention at DNA level**

"Meganuclease recombination systems" are molecules which combine two natural phenomena: meganucleases and DNA homologous recombination. Schematically, meganucleases are "DNA scissors," enzyme proteins which recognise then cut predetermined pieces of the DNA molecule. As for homologous recombination, it is a system of DNA repair with which cells are naturally equipped.

Therefore, meganuclease recombination systems are composed of 2 elements: scissors to cut the piece of DNA carrying the genetic mutation and a piece of "drug" DNA with at its extremities so-called "homologous" sequences allowing the piece of DNA to be naturally inserted in the right place in the cell genome, i.e. at the location of the cut. To summarise, using meganuclease recombination systems "cut and paste" operations can be undertaken in the genome.

**Diseases potentially concerned:** all recessive or dominant monogenic diseases, viral diseases due to DNA viruses (AIDS, herpes, hepatitis B, papillomavirus etc), different cancers, degeneration and lesions treated by cell therapy.

### **Where are the researchers at?**

Meganuclease recombination systems, which have already been used to modify genetically plant and animal models, are not yet at patients' bedsides. Nevertheless, they are beginning to prove their worth *in vitro* (on patient cells):

- **In vitro correction of the gene anomaly involved in the disease known as "moon children" disease (*Xeroderma pigmentosum*)**
- **In vitro correction of DICS-X (X-linked severe combined immune deficiency) – Alain Fischer, Necker-Sick Children's Hospital (Paris, AP-HP/Inserm)**
- **In vitro correction of the *Rag1* anomaly (concerning another severe combined immune deficiency) – Luigi Notarangelo, Children's Hospital Boston (USA)**

### **Meganucleases and other forms of gene surgery presented during Myology 2008:**

- **George Dickson** (UK): Friday 30 May at 9h30  
"Antisense and RNAi technologies: from natural phenomena to new therapeutics"
- **Jean-Pierre Cabaniols** (France): Friday 30 May at 10h45  
"Meganucleases for genome surgery of inherited diseases"
- **Jack Puymirat** (Canada): Friday 30 May at 10h45  
"Targeting of mutant DMPHK transcripts in mouse model of myotonic dystrophy type 1"