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**PRESS RELEASE**

## **Neuromuscular diseases**

### **Identification of two new genes responsible for a congenital myasthenic syndrome and Emery-Dreifuss muscular dystrophy**

Research teams at the *Institut de Myologie* (Myology Institute) in Paris have identified two new genes responsible for neuromuscular diseases: a congenital myasthenic syndrome and Emery-Dreifuss muscular dystrophy. A crucial milestone in terms of understanding these diseases and developing treatment strategies, in the immediate term, these discoveries will make it possible to more accurately diagnose diseases and offer genetic counselling to the families concerned.

#### **Congenital myasthenic syndrome**

The teams led by Daniel Hantaï (Inserm research manager, *Unité Mixte de Recherche en santé* (Joint health research unit) 975 Inserm/UPMC/*Institut de Myologie*) and Laurent Schaeffer (UMR 5239 ENS/CNRS/University of Lyon 1) have identified a gene in which mutations are responsible for a congenital myasthenic syndrome. This research, which was published on 14 August in *The American Journal of Human Genetics*, has been supported by AFM thanks to Telethon donations.

Congenital myasthenic syndromes (CMS) are a heterogeneous group of disorders affecting the neuromuscular junction, a zone of communication between the motor nerve, which commands, and the muscle, which reacts. They are characterised by localised or general muscle weakness, aggravated by exertion, droopy eyelids (ptosis), paralysis of the eye muscles (ophthalmoplegia) and swallowing difficulties. The severity of the symptoms is variable, ranging from sudden respiratory failure at birth to more moderate signs that only become apparent in adulthood. Around ten genes playing a key role at the neuromuscular junction have already been identified as causing CMS but there is still no precise molecular diagnosis for more than half of these patients.

The researchers studied the case of a patient suffering from CMS with no mutations in genes so far identified as causing CMS. They demonstrated that mutations in a new gene – the *AGRN* gene located on chromosome 1 – were responsible for the disease. *AGRN* encodes agrin, an extracellular matrix protein that appears to play a crucial role in maintenance of the neuromuscular junction. A mutation in this gene is thought to be responsible for the disorganisation of the neuromuscular junction observed by the scientists.

## **Emery-Dreifuss muscular dystrophy**

The team led by Gisèle Bonne (Inserm research manager, *Unité mixte de recherche en santé* (Joint health research unit) 974, Inserm, UPMC, CNRS UMR 7215-*Institut de Myologie*) has identified a new gene responsible for Emery-Dreifuss muscular dystrophy. This research, which was published on 27 August in *The American Journal of Human Genetics*, has been supported by AFM thanks to Telethon donations.

Emery-Dreifuss muscular dystrophy (EDMD) is characterised by muscle weakness and wasting, associated with early tendon contractures and cardiomyopathy. Its severity and progression are very variable from one family to another and within the same family. Its inheritance may be X-linked, autosomal dominant or recessive. The genetic origin of 35% of EDMD cases is known. In these cases, it is associated with mutations in two genes encoding ubiquitous nuclear envelope proteins: *EMD* encoding emerin for X-linked EDMD and *LMNA* encoding lamins A/C for autosomal EDMD.

However, more than 60% of patients do not carry mutations in either of these two genes, suggesting the involvement of other genes. By studying the genome of six informative families and one isolated case, the researchers demonstrated the existence of a new gene involved in X-linked forms: the *FHL1* gene located on the X chromosome and encoding a protein responsible for maintenance of cell structure, as well as regulation of signals within the cell, functions that are shared by emerin and lamins A/C. Clinically, this form of EDMD is thought to be characterised by specific cardiac involvement, combining conduction defects, arrhythmia and hypertrophic cardiomyopathy.

### ***The Institut de Myologie (Myology Institute) in brief:***

Created in 1996 by the *Association Française contre les Myopathies* (AFM – French Muscular Dystrophy Association), thanks to Telethon donations, the *Institut de Myologie* (IDM) is an international centre of expertise in the field of muscles and their diseases located within the Pitié-Salpêtrière hospital complex. Its main feature is that it brings together complementary activities at a single site, as part of a close partnership between AFM, Inserm (French National Institute of Health and Medical Research), AP-HP (Paris Public Hospitals), UPMC (Pierre et Marie Curie University) and CNRS (French National Centre for Scientific Research): treatment, fundamental, applied and clinical research, and teaching, in order to understand muscles, how they work, develop and age, their diseases, and also to offer better care to patients and develop treatments for them. It incorporates almost 250 research scientists, doctors, students and associated personnel, and boasts 5000 m<sup>2</sup> of laboratory space. Twenty-two clinical protocols are underway at the site. AFM's total support for IDM represented almost €7 million in 2008.

### **To find out more:**

Association Française contre les Myopathies

[www.afm-france.org](http://www.afm-france.org)

Contact number for families: 0 810 811 088 (cost of a local call)

Institut de Myologie

[www.institut-myologie.org](http://www.institut-myologie.org)

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