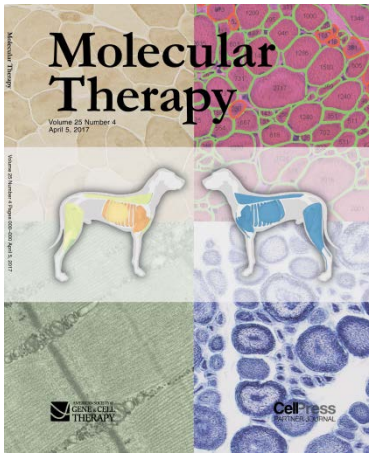
New step towards the treatment of myotubular myopathy: gene therapy restores strength and prolongs lives in affected dogs



Evry (France), 5 April, 2017. A team of researchers in France, led by Dr. Ana Buj-Bello (Genethon/Inserm) and teams at the University of Washington and Harvard Medical School in the United States, achieved a new step towards the treatment of myotubular myopathy by gene therapy. The researchers demonstrated the efficacy of administration of a therapeutic vector by a single intravenous injection and identified the dose that restores long-term muscular strength in a large animal model of the disease.
This work, published today in *Molecular Therapy*, has been achieved thanks to donations from the French Telethon and the support of the Myotubular Trust.

Myotubular myopathy is an X-linked genetic disease affecting 1 in 50,000 newborn boys. It is caused by mutations in the MTM1 gene encoding myotubularin, a protein involved in the functioning of muscle cells. The severe form of the disease leads to hypotonia, generalized muscle weakness and death in early infancy due to breathing difficulties. Dogs naturally affected by this myopathy also have a reduced life expectancy. To date, there is no effective treatment for this rare disease.

In the present study, Genethon's team developed and manufactured an adeno-associated virus (AAV) vector able to deliver a normal copy of the MTM1 gene in the entire musculature. The AAV product was administrated by a simple intravenous injection in ten week-old dogs manifesting the first symptoms of the disease – instead of the locoregional route of administration used in previous studies (*Science Translational Medicine, January 2014*).

The treatment restored whole-body muscle strength and function, and prolonged the life of affected dogs. Treated dogs were indistinguishable from normal animals 9 months after product injection.

Dr. Ana Buj-Bello, Genethon/Inserm said: « ***We report a dose-finding study and show the therapeutic benefit of the vector by a single intravenous injection. It is a clinically-relevant route of administration and represents a step towards a clinical trial in patients***".

Myotubular myopathy : From the mouse experimence to the human clinical trial

Publication: ***Systemic AAV8-mediated gene therapy drives whole-body correction of myotubular myopathy in dogs.*** David L Mack[1,2], Karine Poulard[3,4], Melissa A Goddard[2], Virginie Latournerie[3,4], Jessica M Snyder[5], Robert W Grange[6], Matthew R Elverman[2], Jérôme Denard[3], Philippe Veron[3,4], Laurine Buscara[3,4], Christine Le Bec[3], Jean-Yves Hogrel[7], Annie G Brezovec[6], Hui Meng[8], Lin Yang[9], Fujun Liu[9], Michael O'Callaghan[10], Nikhil Gopal[11], Valerie E. Kelly[1], Barbara K Smith[12], Jennifer L. Strande[13-15], Fulvio Mavilio[3,4], Alan H Beggs[16], Federico Mingozzi[3,4,17], Michael W Lawlor[8], Ana Buj-Bello[3,4#], and Martin K Childers[1,2#]

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About Genethon - www.genethon.fr

Genethon, located in Evry, France, is a non-profit R&D organisation dedicated to the development of biotherapies for orphan genetic diseases, from the research to clinical validation. Genethon is specialized in the discovery and development of gene therapy drugs and has multiple ongoing programs at clinical, preclinical and research stage for neuromuscular, blood, immune system, liver and eye diseases.

About AFM-Téléthon - www.afm-telethon.fr

The French Muscular Dystrophy Association (AFM) federates patients with neuromuscular diseases and their parents. Thanks mostly to donations from France's annual Telethon (€92.7 million in 2016), the AFM-Telethon has become a major player in biomedical research for rare diseases in France and worldwide. It currently supports 34 clinical trials for genetic diseases affecting the eye, blood, brain, immune system and neuromuscular system. Thanks to its Genethon research lab, the AFM-Telethon stands out through its unique ability to produce and test its own gene-based medicines.

About Inserm

Founded in 1964, the French National Institute of Health and Medical research (Inserm) is a public science and technology institute, jointly supervised by the French Ministry of National Education, Higher Education and Research and the Ministry of Social Affairs. Inserm is the only French public research institute to focus entirely on human health with nearly 15000 researchers, engineers, technicians, post-doctoral students and more than 300 laboratories. The mission of its scientists is to study all diseases, from the most common to the rarest.
Inserm is a member of Aviesan*, the French National Alliance for Life Sciences and Health founded in 2009.
** Other founding members of Aviesan : CEA, CNRS, CHRU, CPU, INRA, INRIA, Inserm, Institut Pasteur, IRD*
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About Myotubular Trust - www.myotubulartrust.org

Anne Lennox and Wendy Hughes, two parents of children affected by myotubular myopathy, set up the Myotubular Trust in February 2006. It was very clear that as a rare condition, research into myotubular myopathy could lag substantially behind the scientific developments in other fields of muscle disease, due to lack of dedicated funds, and the difficulty of "competing" with other more common diseases. The Founding Patron is the renowned Professor Victor Dubowitz, Emeritus Professor of Paediatrics at University of London and President of the World Muscle Society. Professor Francesco Muntoni, Professor of Pediatric Neurology and Head of The Dubowitz Neuromuscular Centre at the Institute of Child Health/Great Ormond Street Hospital for Children, London, serves as scientific advisor and Chair of the Scientific Advisory Board, which supervises research grant awards. In 2010 the Trust became incorporated as a company limited by guarantee (07260229) registered in England and Wales.

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