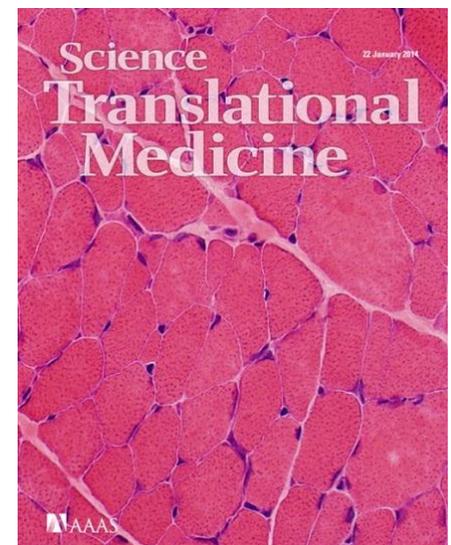


PRESS RELEASE

**EMBARGOED: Not for release until 14:00 Eastern Standard Time
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Efficacy of gene therapy demonstrated in canine and murine models of myotubular myopathy

Evry (France), 22 January, 2014. A team of French researchers, led by Dr. Anna Buj-Bello (Genethon/Inserm) and teams at the University of Washington and Harvard Medical School in the United States, have demonstrated the efficacy of gene therapy in models of myotubular myopathy, an extremely severe neuromuscular disease in children. Transfer of the **MTM1** gene, which is deficient in the disease, corrected the affected muscles in mice and dogs and prolonged the survival of treated animals. This work, published today in **Science Translational Medicine**, has been achieved thanks to donations from the French Telethon and the support of the Myotubular Trust.



[**► Discover the images of treated dogs**](#)

(to get those images, contact us at +33 1 69 47 28 59 or presse@afm.genethon.fr)

Myotubular myopathy is an X-linked genetic disease affecting 1 in every 50,000 newborn boys. It is caused by mutations in the gene **MTM1** encoding myotubularin, a protein involved in the functioning of muscle cells. In its most serious form, it causes hypotonia, generalized muscle weakness and death in the first years of life. There is currently no effective treatment for this severe rare disease.

The study by the French team at Genethon, and the U.S. team at the University of Washington, aimed at evaluating the efficacy of a single intravenous injection of an adeno-associated virus (AAV) expressing myotubularin in the muscles of mice and dogs which carry an **MTM1** mutation.

In 2009, the group directed by Dr. Anna Buj-Bello performed the first study of gene therapy on mice with this disease at Genethon. Their success led to the development of a study in dogs which naturally carry this genetic abnormality, in collaboration with U.S. teams from Boston and Seattle. The vectors used for gene therapy have been developed and manufactured at Genethon.

Exceptional results: normalization of muscle strength and respiratory function and prolonged survival

The results of the study indicate an increase in muscle strength and improved respiratory function as well as improved mobility, and prolonged survival.

This normalization is the first demonstration of persistent correction by a single injection of AAV intravenously in a large animal model of neuromuscular disease. A single dose of drug-vector permitted the long-term expression of myotubularin in muscles.

For Dr. Anna Buj Bello, principal investigator at Genethon: *"These results are the culmination of four years of research and show how gene therapy is effective for this genetic muscle disease. We finally can envision a clinical trial in patients. These are very promising results."*

For Dr. Martin Childers from University of Washington: *« The implications of the pre-clinical findings are extraordinary for inherited muscular diseases. Two of our dogs treated with AAV-mediated gene therapy appear almost normal with little, if any, evidence, even microscopically, of disease caused by XLMTM. »*

For Dr. Alan Beggs, director of the Manton Center for Orphan Disease Research at Boston Children's Hospital: *"Demonstrating that gene therapy is effective in prolonging the lives of these dogs is extremely exciting, providing us with the necessary information to start planning clinical trials in humans."*

Fulvio Mavilio, Chief Scientific Officer Genethon and co-author of the study: *"These results have a significant impact on the prospect of developing treatments neuromuscular diseases. They are indeed very promising."*

Frédéric Revah, CEO Genethon: *"For the first time, researchers have obtained a systemic therapeutic effect on neuromuscular disease in dogs with a single intravenous injection: the treatment does not act locally but throughout the body. Genethon is proud to have worked with the best teams in the world and our next goal is working on the implementation of a clinical trial in humans."*

Laurence Tiennot-Herment, President of the AFM-Téléthon and Genethon : *"This result achieved by our laboratory Genethon, in association with the best American teams, is a major step forward for families who constantly fight the disease. Our determination to defeat the disease is stronger than ever and, thanks to the support of donors from Téléthon, we move step by step toward new victories."*

The AFM-Telethon in France, Muscular Dystrophy Association in the United States, Myotubular Trust in Britain, Anderson Family Foundation and Joshua Frase Foundation participated in the financing of this study.

Publication : Gene Therapy Prolongs Survival and Restores Function in Murine and Canine Models of Myotubular Myopathy. Martin K Childers^{1,2}, Romain Joubert³, Karine Poulard³, Christelle Moal³, Robert W Grange⁴, Jonathan A Doering⁴, Michael W Lawlor^{5,6}, Branden E. Rider⁵, Thibaud Jamet³, Nathalie Danièle³, Samia Martin³, Christel Rivière³, Thomas Soker⁶, Caroline Hammer³, Laetitia Van Wittenberghe³, Mandy Lockard⁷, Xuan Guan⁷, Melissa Goddard⁷, Erin Mitchell⁷, Jane Barber⁷, J. Koudy Williams⁷, David L Mack¹, Mark E Furth⁸, Alban Vignaud³, Carole Masurier³, Fulvio Mavilio³, Philippe Moullier^{3,9,10}, Alan H Beggs⁵, Anna Buj-Bello³

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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. To support clinical development of gene therapy drugs Genethon has built one of the largest facilities worldwide for the production of clinical-grade gene-therapy vectors.

About Inserm - www.inserm.fr

Created in 1964, the Institut national de la santé et de la recherche médicale (Inserm) is a public establishment, which operates under the joint authority of the French Ministry of Health and French Ministry of Research. Its researchers are dedicated to the study of all diseases, from the most common to the most rare. Inserm supports approximately 300 laboratories spread throughout France. All the teams together amount to approximately 13,000 researchers, engineers, technicians and managers. Inserm is a member of the National Alliance for the Life and Health Sciences, founded in April 2009. Inserm celebrated its 50th anniversary in 2014.

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

The French Muscular Dystrophy Association (AFM) federates patients with neuromuscular diseases (genetic diseases that causing progressive irreversible muscle atrophy lead to death) and their parents. Thanks in great part to donations from France's annual Telethon (€88,1 million in 2012), the AFM-Telethon has become a major player in biomedical research for rare diseases in France and worldwide. It currently funds 34 clinical trials for about different genetic diseases affecting the eye, the blood, the brain, the immune system, and muscles... 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 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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