



Press release  
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## **New gene therapy success in a rare disease of the immune system: Wiskott-Aldrich syndrome**

**French teams from CIC Biothérapie (AP-HP/Inserm), from pediatric hematology department of Necker Hospital for Children (AP-HP), led by Marina Cavazzana, Salima Hacein Bey Albina and Alain Fischer and from Genethon led by Anne Galy (Genethon/Inserm UMR-S951), and English teams from UCL Institute of Child Health and Great Ormond Street Hospital in London led by Adrian Thrasher and Bobby Gaspar demonstrated the efficacy of gene therapy treatment for Wiskott-Aldrich Syndrome (WAS). Six children that were treated and followed for at least 9 months had their immune system restored and clinical condition improved. This work, which was published today in the Journal of the American Medical Association (JAMA), was carried out with support from the AFM-Telethon.**

Wiskott-Aldrich syndrome is a rare congenital immune and platelet deficiency which is X-linked and has an estimated prevalence of 1/250 000. It is caused by mutations in the gene encoding the WAS protein (WASp) expressed in hematopoietic cells. This disease, which primarily affects boys, causes bleeding, severe and recurrent infections, severe eczema and in some patients autoimmune reactions and the development of cancer. The only treatment available today is bone marrow transplantation, which requires a compatible donor and can itself cause serious complications.

The Phase I / II study, with Genethon as the promoter, was launched in December 2010 and conducted in Paris and London to treat severely ill patients without a compatible donor. This study, which is ongoing, assesses the feasibility and efficacy of gene therapy in this indication. The article published in JAMA reports the results for the first six patients, aged 8 months to 16 years, where the monitoring period allowed assessment of the initial effects of the treatment.

The treatment involves collected blood stem cells carrying the genetic anomaly of patients and corrected them in the laboratory by introducing a healthy WAS gene using a lentiviral vector developed and produced by Genethon. The corrected cells were reinjected into patients who in parallel were treated with chemotherapy to suppress their defective stem cells and autoimmune cells to make room for new corrected cells. After reinjection, these cells were then differentiated into the various cell lines that make up the blood (red and white cells, platelets).

**To date treated patients showed significant clinical improvement.** Severe eczema and severe infection disappeared in all cases. Arthritis was eliminated in one patient and another saw major improvement in vasculitis of the lower limbs and was able to return to normal physical activity without a wheelchair. However, the rate of corrected platelets varies from one patient to another.

**Fulvio Mavilio, Chief Scientific Officer Genethon:** *"We are all very happy and encouraged by the results of this study. It is the first time that a gene therapy based on genetically modified stem cells is tested in a multicenter, international clinical trial that shows a reproducible and robust therapeutic effect in different centers and different countries. For very rare diseases such as WAS, multicenter clinical trials are the only effective way of proving the safety and efficacy of gene therapy and having it rapidly approved and made available to all patients. We are following the same approach for other rare and less rare blood diseases."*

**Frédéric Revah, CEO of Genethon,** the laboratory of the AFM-Telethon and the trial sponsor, said *"These first results of our clinical trial for the treatment of Wiskott Aldrich syndrome are very encouraging. They illustrate not only the ability of Genethon to carry out the upstream research to develop treatments for these rare and complex diseases, but also to construct and conduct international clinical trials, to produce these advanced therapy products, to work with international teams and to manage the regulatory aspects of the trials in France and abroad. These are skills that we implement for other international trials of gene therapy for rare genetic diseases of the immune system, blood, muscle, vision or liver... We will continue the current study with the objective of providing treatment for patients."*

**Marina Cavazzana:** *"The results obtained in this multicenter clinical trial constitute an important therapeutic advance (overhang) because they concern a complex pathology which affects almost all of blood cells with dramatic clinical consequences. After transfer of gene, the patients showed a significant clinical improvement due to the reexpression of the protein WASp in the cells of the immune system. The efficiency of the treatment of such a deficit for which a high level of correction of hematopoietic stem cells is required, indicates that it is from now on justifiable to hope to treat other complex genetic diseases as those affecting red blood cells."*

**Professor Thrasher** says: *"This is a very powerful example of how gene therapy can offer highly effective treatment for patients with complex and serious genetic disease. It also excitingly demonstrates the potential for treatment of a large number of other diseases for which existing therapies are either unsatisfactory or unavailable."*

**Publication: Outcome following Gene Therapy in Patients with Severe Wiskott-Aldrich Syndrome**

Salima Hacein-Bey Abina, PharmD, PhD<sup>1,2,3,4</sup>, H. Bobby Gaspar, MRCP, PhD<sup>5,6</sup>, Johanna Blondeau, MS<sup>1,2</sup>, Laure Caccavelli, PhD<sup>1,2</sup>, Sabine Charrier, PhD<sup>7,8</sup>, Karen Buckland, PhD<sup>5,6</sup>, Capucine Picard, MD, PhD<sup>9,10,11</sup>, Emmanuelle Six, PhD<sup>10,12</sup>, Nourredine Himoudi, PhD<sup>5,6</sup>, Kimberly Gilmour, PhD<sup>5,6</sup>, Anne-Marie McNicol, PhD<sup>5,6</sup>, Havinder Hara MS<sup>5,6</sup>, Jinhua Xu-Bayford, DipHE<sup>6</sup>, Christine Rivat, PhD<sup>5,6</sup>, Fabien Touzot, MD, PhD<sup>1,2,10,11</sup>, Fulvio Mavilio, PhD<sup>8</sup>, Annick Lim, MS<sup>13</sup>, Jean-Marc Treluyer, MD, PhD<sup>14</sup>, Sébastien Héritier, MD<sup>10,11</sup>, Francois Lefrere, MD<sup>1</sup>, Jeremy Magalon, PharmD <sup>1,2</sup>, Isabelle Pengue-Koyi, PharmD, PhD <sup>1,2,10</sup>, Géraldine Honnet, MD<sup>8</sup>, Stéphane Blanche, MD<sup>10,11</sup>, Eric A. Sherman, BA<sup>15</sup>, Frances Male, BA<sup>15</sup>, Charles Berry, PhD<sup>15</sup>, Nirav Malani, MS<sup>15</sup>, Frederic D. Bushman, PhD<sup>15</sup>, Alain Fischer, MD, PhD<sup>10,11, 12,16</sup>, †, Adrian J. Thrasher, MB, BS, PhD<sup>5,6,†</sup>, Anne Galy, PhD<sup>7,8</sup>, † and Marina Cavazzana, MD, PhD<sup>\*1,2,10, 12,†</sup>

**Affiliations:**

1 Biotherapy Department, Necker Children's Hospital, Assistance Publique-Hôpitaux de Paris, Paris, France.

2 Biotherapy Clinical Investigation Center, Groupe Hospitalier Universitaire Ouest, Assistance Publique-Hôpitaux de Paris, INSERM, Paris, France.

3 UTCBS CNRS 8258- INSERM U1022, Faculté des Sciences Pharmaceutiques et Biologiques, Université Paris Descartes, Paris, France.

4 Immunology Laboratory, Groupe Hospitalier Universitaire Paris-Sud, AP-HP, 78, rue du Général-Leclerc, 94270 Le-Kremlin-Bicêtre, France.

5 Section of Molecular and Cellular Immunology, University College London Institute of Child Health, London, UK.

6 Dept of Clinical Immunology, Great Ormond Street Hospital NHS Trust, London, UK.

7 INSERM, U951; University of Evry, UMR\_S951; Molecular Immunology and Innovative Biotherapies, Genethon, Evry, F-91002 France.

8 Genethon, Evry, F-91002 France.

9 Centre d'Étude des Déficits Immunitaires, Hôpital Necker-Enfants Malades, AP-HP, Paris, France.

10 Paris Descartes – Sorbonne Paris Cité University, Imagine Institute, Paris, France.

11 Immunology and Pediatric Hematology Department, Assistance Publique-Hôpitaux de Paris, Paris, France.

12 INSERM UMR 1163, Laboratory of human lymphohematopoiesis, Paris, France.

13 Groupe Immunoscope, Immunology Department, Institut Pasteur, Paris, France.

14 Clinical research Center Necker-Enfants Malades and Cochin Hospital Assistance Publique, Hôpitaux de Paris, Paris Descartes University.

15 Department of Microbiology, University of Pennsylvania School of Medicine, Philadelphia, PA, USA.

16 Collège de France, Paris, France.

### **About AFM-Téléthon - [www.afm-telethon.fr](http://www.afm-telethon.fr)**

The French Muscular Dystrophy Association (AFM) federates patients with neuromuscular diseases and their parents. Thanks in great part to donations from France's annual Telethon (€89,3 million in 2013), the AFM-Telethon has become a major player in biomedical research for rare diseases in France and worldwide. It currently funds about 30 clinical trials in different genetic diseases affecting the eye, blood, brain, 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 Généthon - [www.genethon.fr](http://www.genethon.fr)**

Created by the AFM-Telethon, Généthon's mission is to make available to patients innovative gene therapy treatments. Having played a pioneering role in deciphering the human genome, Généthon is today, with more than 200 scientists, physicians, engineers and regulatory affairs specialists, an international research and development center for preclinical and clinical gene therapy treatments for rare diseases. Généthon has the largest site in the world for GMP production of gene therapy products, Généthon Bioprod. In 2012, Généthon was the first associative laboratory to receive the 2012 Prix Galien for Pharmaceutical Research (France). As part of a therapeutic program on genetic diseases of the blood and immune system, Genethon working for over 10 years on gene therapy of Wiskott-Aldrich syndrome. The laboratory is currently conducting clinical trials for this disease in Europe, Paris and London, and the United States with the Children's Hospital Boston.

### **About Inserm - <http://presse-inserm.fr/en/>**

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 education, higher Education and Research and the ministry of social affairs, health and women's rights. The mission of its scientists is to study all diseases, from the most common to the most rare, through their work in biological, medical and public health research.

### **About Great Ormond Street Hospital for Children - [www.gosh.nhs.uk](http://www.gosh.nhs.uk)**

Great Ormond Street Hospital for Children NHS Foundation Trust is the UK's leading centre for treating sick children, with the widest range of specialists under one roof.

With the UCL Institute of Child Health, we are the largest centre for paediatric research outside the US and play a key role in training children's health specialists for the future.

### **About AP-HP - [www.aphp.fr](http://www.aphp.fr)**

AP-HP is a university hospital with European dimension all over the world recognized. Her 38 hospitals welcome every year 7 million sick people: in consultation, as a matter of urgency, during programmed hospitalizations or in home medical care. She assures a public service of health for all, 24 hours a day, and it is for her at the same time a duty and a pride. AP-HP is the first employer of Ile-de-France: 95 000 people - doctors, researchers, paramedical, administrative and labor personnels - work on it.

**Press contacts :**

**AFM – Généthon**

Stéphanie Bardon, Gaëlle Monfort - 01 69 47 28 28 - [presse@afm.genethon.fr](mailto:presse@afm.genethon.fr)

**Inserm**

Priscille Rivière - 01 44 23 60 97 - [presse@inserm.fr](mailto:presse@inserm.fr)

**AP-HP**

Olivier Bordy, Anne-Cécile Bard, Clémence Rémy – 01 40 27 37 22 -  
[service.presse@sap.aphp.fr](mailto:service.presse@sap.aphp.fr)

**Great Ormond Street Hospital NHS Trust and UCL Institute of Child Health**

Rachel Twinn - +44 20 7239 3029

[Rachel.twinn@gosh.org](mailto:Rachel.twinn@gosh.org)