

Created in 1990 and funded by AFM-TELETHON,

Genethon, a pioneer in deciphering the human genome and identifying the genes associated with genetic diseases is today fully dedicated to the design, development and production of **gene therapy treatments for rare diseases.**

At Genethon more than 230 scientists, clinicians and engineers specialized in gene therapy drug development, from research to the clinic, have joined forces in order **to provide these innovative treatments to patients affected with rare disorders. These treatments also pave the way for new therapeutic approaches for frequent disorders.**

In 2012 Genethon received the Prix Galien France for pharmaceutical research into “Medicines destined for rare diseases – cell therapy and gene therapy.”

In 2013 Genethon’s production facility, Genethon BioProd obtained certification as a pharmaceutical manufacturer from the French National Medical Safety Agency (ANSM).

Therapeutic projects

A defective gene causes a genetic disease by disturbing the normal production or activity of a protein necessary for cell function. Gene therapy consists of introducing a normal gene into the affected cells in order to restore the production or the function of the missing or deficient protein. The therapeutic gene is brought to the cells via "carriers," called vectors, which generally are derived from viruses that have been rendered harmless.

Genethon is conducting several clinical trials of gene therapy in France and abroad, and has several projects at various stages of preclinical development.

These projects, which are developed internally or within the framework of partnerships, concern neuromuscular pathologies, diseases of the eyes, the liver, the immune system and the central nervous system.

CURRENT CLINICAL TRIALS

Phase I/II international clinical trial for Wiskott-Aldrich Syndrome (WAS)

Wiskott-Aldrich syndrome is an immune deficiency. The prognosis for children affected by this disease is very poor. Gene therapy, which has already been used to treat other hereditary immune deficits, represents a major hope for these young patients. The clinical trial in progress is a result of research at Genethon by Dr. Ann Galy's group (Genethon/INSERM).

This trial, for which Genethon is the promoter in Europe, is being performed:

- In France, at the Hôpital Necker-Enfants malades, Paris ;
- In the UK at the Great Ormond Street Hospital, London ;
- In the US at the Boston Children's Hospital.

Phase I/II multicentric international trial for Chronic Granulomatous Disease (CGD)

Chronic Granulomatous Disease (CGD) is a hereditary disease caused by an alteration in the activity of phagocytes, rendering them incapable of destroying the micro-organisms (bacteria, fungus, etc.) which invade the body. This disorder is characterized by the occurrence, very early in life, of severe, recurrent and profound infections that are resistant to treatment, and by hyper-inflammation causing the formation of granulomas and leading to tissue complications.

This trial, for which Genethon is the promoter, is being performed in parallel in

- France, at the Hôpital Necker-Enfants malades, Paris ;
- The UK, at the Great Ormond Street Hospital, London ;
- Germany at the Frankfurt University Hospital ;
- Switzerland at the University Children's Hospital, Zurich.

Phase I/II trial for the Leber's Hereditary Optic Neuropathy (LHON)

Leber's Hereditary Optic Neuropathy (LHON) is a rare genetic disease of vision, due to a defect in a mitochondrial gene. It involves sudden loss of central vision which is usually asymmetric, with onset usually between 15 and 30 years of age. There is no effective treatment for this disease at the moment.

This project is the result of original research by Dr Marisol Corral-Debrinski and Pr José-Alain Sahel (Institut de la Vision, Paris). The preclinical stages were carried out in the framework of a collaboration between Genethon and the Gensight company, which is conducting the clinical development in partnership with Genethon and the Institut de la Vision.

The clinical study is in progress.



UPCOMING TRIALS

Phase I/II trial for Duchenne muscular dystrophy

Genethon has played a pioneering role in demonstrating the usefulness of exon skipping as a strategy for the treatment of Duchenne muscular dystrophy. This muscular dystrophy is the most serious of the diseases caused by a deficit in dystrophin, the protein which gives muscles the property of resistance to effort: without it, the muscle fibers degenerate. There are 150 to 200 new cases in young boys each year in France. With the Institut de Myologie (Paris) and Atlantic Gene Therapy in Nantes, Genethon is piloting a large-scale preclinical study. Its result will be a determining factor in human trials.

Phase I/II Trial for Fanconi's anemia

Fanconi's anemia is a rare genetic disease that affects the stem cells of blood and which leads to bone marrow failure, congenital abnormalities and a predisposition to cancer. This project is being carried out in collaboration with J. Bueren's group (CIEMAT, Madrid) and Pr. Juan Sevilla's group (Hopital Jesus del Nino, Madrid), in the framework of the Eurofancon European consortium.



Cure through Innovation

Genethon is also conducting research which should lead to clinical trials in the coming years, notably:

- For neuromuscular diseases

As a complement to the exon skipping therapy project, Genethon is developing a treatment for *Duchenne muscular dystrophy* by transfer of the microdystrophin gene, in collaboration with the Institut de Myologie (Paris) and Royal Holloway University (London).

In collaboration with American groups from the University of Washington in Seattle and Harvard Medical School in Boston, Genethon has demonstrated the efficacy of gene therapy in a canine model of *myotubular myopathy*. The treatment has corrected the symptoms of the disease and prolonged survival of the treated animals. Based on these results, Genethon is collaborating with Audentes Therapeutics, a biotechnology company specialized in the development of treatments for rare muscle diseases, in order to set up a clinical trial. This rare and severe genetic disease of skeletal muscle affects boys who exhibit hypotonia and generalized muscle weakness from birth.

In collaboration with the Institut de Myologie (Paris), Genethon is undertaking a development project for *severe infantile spinal muscular atrophy*, a rare genetic disease characterized by a loss of motor neurons of the spinal cord which leads to atrophy of the limbs and the trunk. It affects both boys and girls from birth.

Finally, several research projects on *limb-girdle muscular dystrophies and calpainopathies* are being conducted.

- For diseases of the liver and other metabolic diseases: *Crigler-Najjar syndrome* is a disease due to deficiency of a liver enzyme which prevents elimination of bilirubin, which is a neurotoxic substance. A product is being developed, and this approach may be applicable to other liver diseases.

- For immune deficits and blood diseases

- For diseases of the central nervous system: In collaboration with AP-HP and the CEA (Atomic Energy Commissariat), Genethon is participating in the development of a gene therapy treatment for *Huntington's disease*, a hereditary neurodegenerative disease characterized by involuntary movements (chorea), behavioral problems, psychiatric problems and dementia.

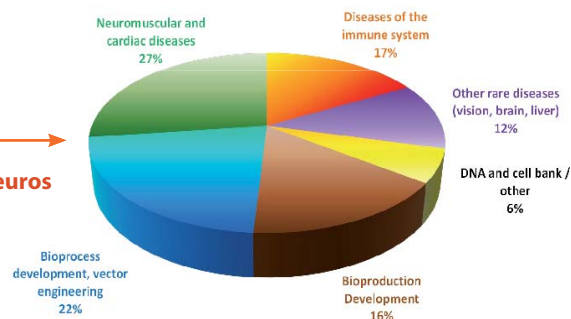


With its **Genethon BioProd*** production center, which is the culmination of 20 years of research excellence, Genethon has an ability which is unique in the world for the bioproduction of gene therapy products for rare diseases.

**Built with the financial support of Ile-de-France Regional Council, Essonne Departmental Council and Genopole®.*

KEY FIGURES

Global budget for Genethon 2013: 31,4 million euros



230 collaborators, specialists in development of biotherapy products:

Scientists, engineers, pharmacists, physicians, specialists in clinical development, etc.

- 10 000 m² of laboratories ;
- 21 new patent applications since 2010 ;
- More than 1000 scientific publications since 1991 ;
- 5000 m² for bioproduction and quality control, including 2500 m² of classified and restricted-access laboratories ;
- 4 suites for vector production, for a production capacity of more than 20 clinical batches per year at full capacity.



Genethon, member of the Biotherapies Institute for Rare Diseases, is at the heart of national and international networks

To accelerate research and produce the medicines of tomorrow, Genethon is following a policy of international collaborations with numerous laboratories in Europe, the USA and Japan.

Genethon also coordinates or participates in national and international networks, enabling it to ensure the highest standards of preclinical and clinical development for each disease.



www.pgt-consortium.fr

PreIndustrial Gene Therapy vector Consortium (PGT)

The PGT Consortium was awarded a grant from the 'Avenir Investment' Program in the first Call for Proposals for pre-industrial demonstrators in biotechnology.

The consortium is composed of four first-class actors in the domain of gene therapy and bioproduction in France: **Genethon** and **GenoSafe** which are located in Evry, and **Atlantic BIO GMP** (ABG-EFS) and a **University Hospital Center**, both located in Nantes.

The ambition of PGT is to play a central role in the international arena in the production of gene therapy vectors which are essential for the large number of clinical trials currently taking place in the domain of biotherapies.

PGT has a double objective: to accelerate the development of methods for vector production and quality control based on pharmaceutical norms and to respond to the growing demand for therapeutic vectors for clinical trials for rare diseases, which are becoming more and more frequent world-wide.



www.net4cgd.eu

The Net4CGD network for immune deficits

Net4CGD is a European project of the FP7 program of the European Commission. Net4CGD is concentrating on the clinical development of a new orphan drug for gene therapy which could rapidly become a new therapeutic option for patients affected by the X-linked form of chronic granulomatous disease (CGD). The Net4CGD consortium is composed of 11 European partner institutions and is coordinated by Genethon.

Ocular diseases gene therapy network

Co-led by **Genethon**, Prof. José-Alain Sahel (**Institut de la vision**) and Dr. Fabienne Rolling (**Inserm**), this network aims to accelerate clinical development for therapeutic projects targeting rare ocular diseases by providing access to a first-tier development infrastructure and technology platform. This network includes the top eye-disease and gene therapy specialists in France and in Switzerland.



ADNA program (Diagnostic Advances for New Therapeutic Approaches)

Supported by Bpifrance, the ADNA program is coordinated by **Institut Mérieux** and aims at contributing to the development of personalized medicine in the fields of genetic disease, cancers, and infectious disorders by providing health professionals with innovative and novel tools for bio-diagnosis and therapy. Within this program, Genethon leads **projects for the development of gene therapy drugs for neuromuscular pathologies and technological projects for bioprocess development and biomarkers.**

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