Press release
Evry, January 28th, 2020

Rare disease of the immune system

Gene therapy success in Chronic Septic Granulomatosis

American and British teams led by Drs Kohn (University of California, Los Angeles), Malech (NIH), Williams (Boston Children's) and Trasher (Great Ormond Street Institute of Child Health) published yesterday in *Nature Medicine* the conclusive results of a gene therapy trial conducted in the United States and Great Britain in 9 patients with X-linked Chronic Septic Granulomatosis (X-CGD), a rare and severe immune dysfunction. Six of them are free of treatment for complications generated by the disease. Genethon, which contributed to the research that led to these trials and sponsored initial clinical studies, is pleased with these results.

Chronic Septic Granulomatosis is a rare genetic disease due to a mutation on the X chromosome. Boys affected by this disease have a deficient immune system that predisposes them to serious infections. Indeed, from the first years of life, the patients suffer from repeated infections, sometimes deep abscesses, atypical pneumonia but also chronic inflammation including gum or digestive tract. Each infectious episode reduces the quality of life and life expectancy of patients. Until now, only bone marrow transplants could prolong the life of patients.

The gene therapy approach consists in restoring the activity of the defective NAPDH oxidase in the patient's phagocytic cells (neutrophilic polynuclear cells, monocytes/macrophages) by gene transfer using a lentiviral vector. This lentiviral vector - G1XCGD - was developed at Genethon by Dr. Anne Galy (Inserm/UMR951/Généthon, UEVE, Université Paris Saclay), in collaboration with Dr. Adrian Thrasher of London and Prof. Manuel Grez of Frankfurt. The clinical batches were produced by YposKesi, an industrial production platform for gene therapy medicinal products created by AFM-Telethon and BPIfrance. Genethon is the promoter of the first European trial, launched in 2013, which is still in progress, the first results of which were reported yesterday in *Nature Medicine*.

Nine patients (4 in Europe and 5 in the United States), aged 2 to 27 years, were treated in clinical trials conducted in the UK and the United States. Seven of them, followed for 12 to 36 months after treatment, did not contract any infection. Two patients died during the trial as a result of complications acquired prior to gene therapy treatment.

"We are very proud of these clinical results, which once again demonstrate the unique capacity of our laboratory to develop therapeutic projects, from concept development to clinical trials by integrating manufacturing. These results are also the result of a rich

collaboration with the best British and American clinical experts." said Frédéric Revah, Chief Executive Officer of Genethon.

"This is the first time that a sustainable treatment has been obtained by gene therapy in this disease, confirming the advantages of the lentiviral technology that has been used to treat hematopoietic stem cells," says Anne Galy, Director of the Blood and Immune System Diseases Program at Genethon.

This international effort has also been supported by the European Commission through funding by the 7th Framework Programme in Health of the European project **Net4CGD** of which Genethon is the coordinator.

These results led to a strategic alliance formed by Genethon with the British company Orchard, which has an exclusive license on G1XCGD allowing the clinical development of this gene therapy drug to continue.

About Genethon - www.genethon.fr

Created by the AFM-Telethon and located in Evry (France), Genethon is a non-profit research and development centre dedicated to the development of biotherapies for rare diseases, from research to clinical validation. Genethon specializes in the discovery and development of gene therapy drugs and has several ongoing clinical, preclinical and research programs for genetic diseases of muscle, blood, immune system and liver. A first product to which Genethon has contributed has obtained marketing authorization in the United States in 2019 and is currently undergoing approval in Europe for spinal muscular atrophy. 7 other products resulting from Genethon's R&D, alone or in collaboration, are currently in clinical trials, and several others are in the preparation phase for clinical trials in 2020 and 2021.

Accessing Genethon's pipeline

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