Sanfilippo Syndrome is a mucopolysaccharidosis (MPS)

MPSs are genetic diseases caused by the absence or malfunctioning of certain enzymes that lead to the accumulation of complex molecules called glycosaminoglycans (GAGs) inside cells.

Sanfilippo syndrome is characterized by the accumulation of a GAG called Heparan Sulfate (HS). Four enzymes participate specifically in the breakdown of HS and, depending on which enzyme is absent or deficient, Sanfilippo syndrome is classified into 4 subtypes (A, B, C, and D).

In Sanfilippo syndrome Type A, the gene encoding sulfamidase is affected, resulting in absent or deficient expression of the sulfamidase enzyme.

Despite being a multisystem disease, it mainly affects the central nervous system with:

- Behavioral alterations
- Psychomotor retardation
- Language deterioration
- Severe dementia

Other affected organs:
- Respiratory system
- Musculoskeletal system
- Bowel, liver and spleen

What is a rare disease?

In Europe, a rare disease is defined as that affecting fewer than 5 in 10,000 people.

- 30% of affected people will die before reaching the age of five
- 80% of rare diseases are of genetic origin
- 50% of rare diseases affect children

Nearly 3 million people are affected in Spain.

Many rare diseases appear in infancy, such as the Sanfilippo Syndrome Type A or mucopolysaccharidosis IIIA (MPS)

The Sanfilippo Syndrome Type A affects 10 in one million people
Symptoms of Sanfilippo syndrome Type A

**0-2 YEARS**
- No symptoms

**3-9 YEARS**
- Behavioral alterations
- Severe temper tantrums
- Sleep disturbances
- Progressive impairment of mental functions, especially language
- Progressive impairment of motor skills

**10-15 YEARS**
- Severe dementia
- Loss of verbal communication
- Epilepsy
- Loss of the ability to walk

**SYMPTOMS WITH ONSET AT VARIABLE AGE**
- Facial dysmorphisms and mild macrocephaly
- Hearing impairment and visual alterations
- Ear, nose, throat and chest infections
- Visceromegaly (enlarged liver and spleen)
- Diarrhea/constipation
- Mild skeletal alterations
- Progressive impairment of mental functions, especially language
- Progressive impairment of motor skills
- Development of the investigational phase

**PHASE 1-2 PHASE 3**
- Clinical trials
- Administration
- Safety
- 1st evidence of efficacy
- Efficacy and safety in patients
- Confirmation of efficacy and safety
- Studies on the natural history of the disease as clinical trials control

**TREATMENT APPROVAL, MARKETING AND ADMINISTRATION**

Currently, there is no curative treatment for this syndrome. Only palliative care is available, which relieves the symptoms and alleviates the suffering of patients and their families. Much progress has been made in the development of a gene therapy that could be highly beneficial for treating patients with this disease.

**What is gene therapy?**

It is an alternative treatment with huge potential, because it offers hope for correcting the genetic disorder.

**RESEARCH**

- Selection of the normal functional gene: human sulfamidase
- Introduction of the therapeutic gene in a non-pathogenic Adeno-Associated Virus Vector (AAV)
- Vector administration in the cerebrospinal fluid (CSF) and entry into the nucleus of brain cells. Beginning of production of the enzyme sulfamidase and distribution in the Central Nervous System
- Diffusion of the gene therapy product from CSF into the bloodstream, reaching the liver. Hepatocytes produce and secrete the enzyme, which is spread throughout the body
- Generalized restoration of enzyme activity, disappearance of glycosaminoglycan accumulation, and correction of pathological alterations

**SANFILIPPO SYNDROME TYPE A CAN BE OVERCOME THANKS TO THE COMMITMENT OF ALL**

- CBATEG. Universitat Autònoma de Barcelona, Septiembre 2011 “Gene Therapy, a new tool to cure human diseases”
- The Lysosomal Storage Research Group at The Hospital for Sick Children Toronto, Canada. Febrero 2011. “What in the world is a lysosome”
- Whole body correction of mucopolysaccharidosis IIIA by intracerebrospinal fluid gene therapy. J Clin Invest. 2013 Aug 1; 123(8): 3254-3271
- http://www.orpha.net/inheritance/3516.php