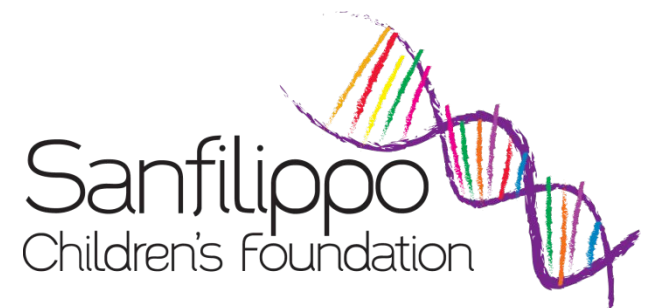


Research Strategy

Sanfilippo Children's Foundation



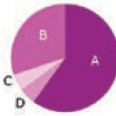
January 2022

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What is Sanfilippo Syndrome (MPS III)?


A Rare, Life-Limiting Disease That Is Part Of A Wider Group Of Disorders

LSD	Lysosomal Storage Disorders 50 main diseases 1 in 5,000 births	The lysosome is a very small unit in the cell and contains enzymes responsible for recycling cellular materials. A LSD is a disease where those materials don't get recycled correctly and accumulate in the cell, causing dysfunctions.
MPS	MucoPolySaccharidosis 7 main diseases 1 in 25,000 births	MPS are complex sugar molecules also called GAGs (GlycoAminoGlycans) naturally produced by the body and used in the building of bones, cartilage, skin, and tissues. The body continuously produces GAGs which need to be recycled.
MPSIII	MPSIII or Sanfilippo 4 disease types 1 in 70,000 births	Children with MPSIII lack an enzyme required to recycle the heparan sulfate, one of the many complex sugar molecules (GAGs) the body needs, resulting in extra storage of these molecules in the cells.
	MPSIII Type A, B, C, D A & B most common, C & D rarer	Each Sanfilippo type corresponds to a particular enzyme that is deficient. There is considerable variation in severity and life expectancy within each type.

A Progressive & Fatal Disease


Children at birth appear healthy; the first symptoms are often mild developmental delays. The disease progresses very differently from one child to the next, making it very difficult to predict.

Early Years (2-6)




Stage 1
Mild developmental delays

Teenage Years



Stage 2
Extreme activity and difficult behaviour

Stage 3



Stage 3
Gradual decline with shortened lifespan

Symptoms spectrum

- Brain, sense & nerves
- Nose, throat, chest & ear
- Mouth & teeth
- Heart
- Bowel
- Bones & joints
- Hands & feet
- Skin & hair

The disease does not yet have a cure and only limited palliative treatment currently exist; average life expectancy is 15-20 years. However medical research has recently achieved promising break-throughs with real hopes for the future.

An Autosomal Recessive Genetic Condition

Genetic

Recessive

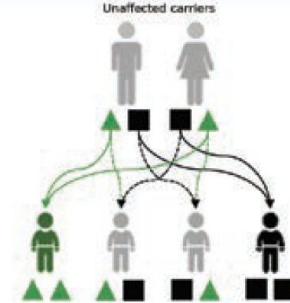
Autosomal

It is inherited: children get one defective gene from both their parents. With both parents carriers, there is 1 chance out of 4 for each child to inherit the disease.

Each individual has two copies of each gene. In recessive disorders, affected individuals have two defective genes. Individuals who have one defective gene and one healthy copy are called carriers and are unaffected.

The defective gene is on a chromosome that is not a sex chromosome. Both males and females can be affected in autosomal disorders and either males or females can be a carrier for the disease.

Unaffected carriers




Affected 25% Unaffected Carrier 50% Non-carrier 25%

▲ Defective gene ■ Healthy gene

A Metabolic Form Of Childhood Dementia


Metabolic

Metabolism is the set of life-sustaining chemical transformations within the cells. These transformations are done through the actions of **enzymes** which act as catalysts; the missing enzyme in Sanfilippo results in a metabolic disorder.



Dementia

The disorder affects primarily the cells in the brain and is considered a childhood dementia. Children experience hyperactivity, sleeplessness, loss of speech and cognitive skills, mental retardation, cardiac issues, seizures, loss of mobility and finally death.



About Sanfilippo Children's Foundation

Sanfilippo Children's Foundation's purpose is to drive research for a world without Sanfilippo Syndrome.

- Founded in September 2013 by a parent of two children with Sanfilippo Syndrome
- We are working to achieve our purpose by:
 - **Funding research** globally
 - Enabling access to **emerging treatments** and clinical trials
 - Raising **awareness** amongst the community
 - Providing diagnosed families with clear, up-to-date **information**
 - **Fundraising** to achieve the above aims
- Governance includes a Board of Directors and Scientific Advisory Board.

About Sanfilippo Children's Foundation

- Implemented a competitive research funding program in 2016 which funds 4 to 5 projects per year
- Our established program funds only the best research after rigorous review following the framework of the NHMRC
- In addition to our competitive grant round, a range of strategic projects have been implemented
- Our projects are aimed at halting progression of the condition, reversing damage and improving quality of life
- Key achievements of the Foundation include:
 - Enabled an Australian arm of global gene therapy clinical trial at Adelaide Women's & Children's Hospital
 - Won the 2017 Advocacy Award in the Research Australia annual Health & Medical Research Awards
 - Secured a \$2million grant from the Federal Government's Medical Research Future Fund (MRFF) with a further \$500,000 from the SCF for a collaborative 'Brain in a Dish' project
 - Funding of basic research has resulted in several promising therapies moving forward in the drug development pipeline towards clinical trial
 - Brought a glimmer of hope to families of children battling Sanfilippo Syndrome.

Scientific Advisory Board



Prof Ian Alexander



Assoc Prof Kim Hemsley



Dr Nicholas Smith



Prof Sarah Spencer



Dr Michel Tchan



Assoc Prof Karin Borges



Dr Jana Vukovic

Board of Directors



Megan Donnell



Angeline Veeneman



Mark Arnold



Alison Butt

Research Strategy Overview

As a rare condition, Sanfilippo Syndrome struggles to attract research funding from larger funding bodies. With our funding we aim to ensure that this devastating condition receives the research attention it requires.

Our research strategy:

- Aims to maximise the impact of the funds we invest, we identify the research areas that promise to make the greatest scientific advances and have the most relevance for our families.
- Defines three focus areas – halt disease progression, repair damage and improve quality of life. We believe that investment in these areas is essential to bring desperately needed treatments to the market.
- Offers research grants with applications assessed via a robust review process to ensure we fund the most promising research.

Investment is planned for research grants that fall into four categories:

1. Translational research grants
2. Incubator grants
3. Scholarships
4. Strategic projects

Research Focus Areas

Our research strategy focuses on 3 priority areas and our funding program considers projects that address these.

Halt disease progression

- Projects with potential to halt disease progression early to optimise brain development
- Effective treatments for all disease subtypes
- Strategies to enhance the effectiveness of emerging therapies

Repair Damage

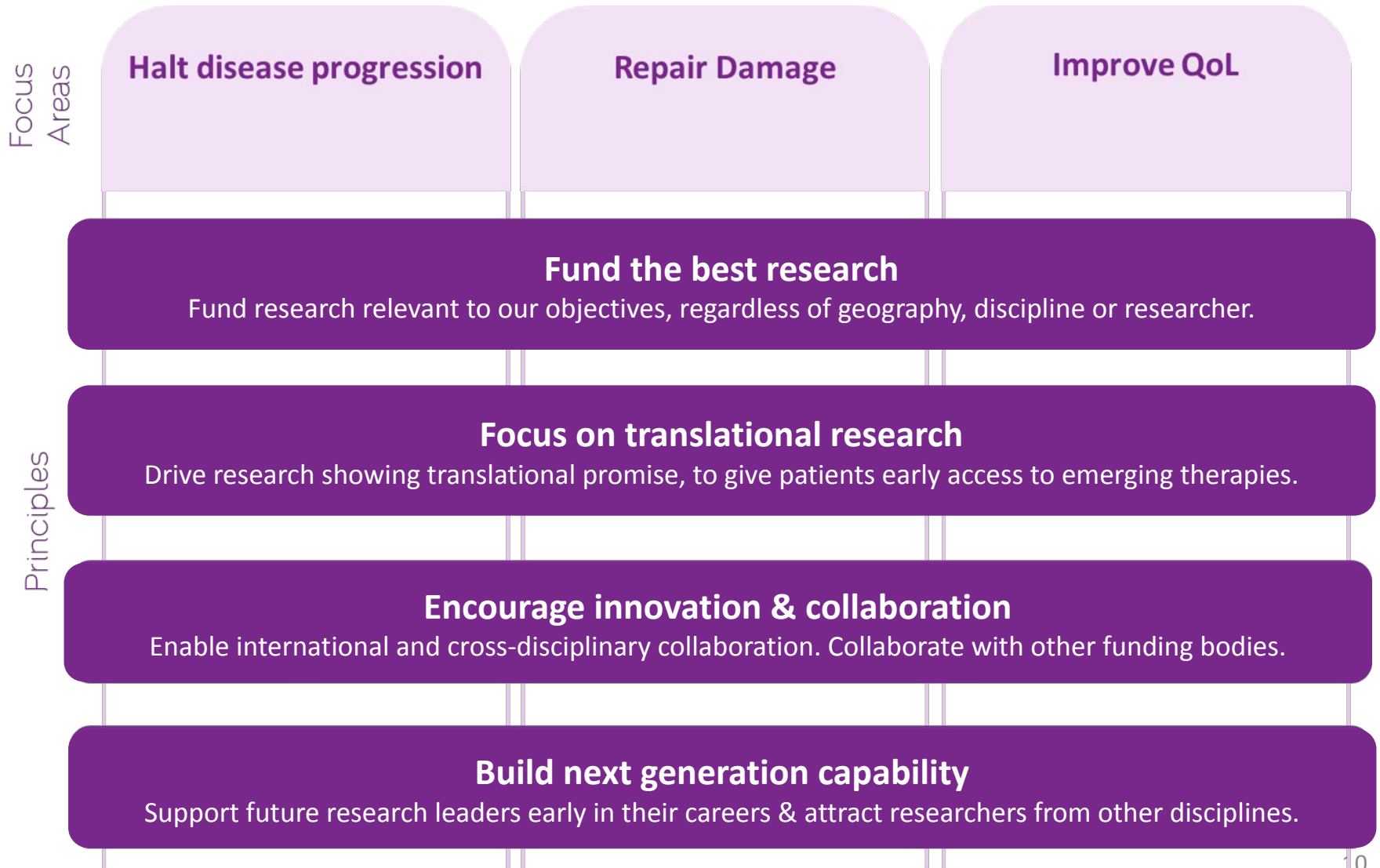
- Repair and reverse cell damage caused by Sanfilippo
- Broad application of neuro-regenerative treatments, for example repurposing approved drugs
- Opportunity to collaborate with researchers working on other neurodegenerative diseases

Improve QoL

- Improve quality of life of children/adults with Sanfilippo
- Palliative care and symptom management specific to Sanfilippo

Future funding areas may include: Prevention (including pre-conception), diagnosis and prognostic markers.

Research Principles



Funding Program

Translational Research Grant

Fund projects with significant proof of concept data available to demonstrate potential to move through the translational pipeline towards treatment. This includes pre-clinical and clinical research.

Larger grants may be considered for co-funding with partner funding bodies.

Typically in the range of \$150k to \$300k per year for up to three years

Incubator Grants

Focus on small scale projects that involve:

- Novel, innovative ideas and approaches; or
- Development of new insights that improve disease understanding with potential to inform future research projects; or
- Potential to generate results that may attract larger scale funding

Typically in the range of \$50 to \$100k over 1 year

Scholarships & Fellowships

- Co-funded Postgraduate scholarships offering premium top-ups & travel allowances (partnering with NHMRC or Universities)
- Postdoctoral and Clinical Research fellowships to be considered for future funding

Co-funded \$5k/year over 3 years

Postdoc/clinical research TBA

Strategic Projects

- Targeted funding of research and infrastructure identified as capable of speeding up the development of therapies, for example:
 - new disease models
 - clinical guidelines
 - collaboration tools.

As required

How we fund research

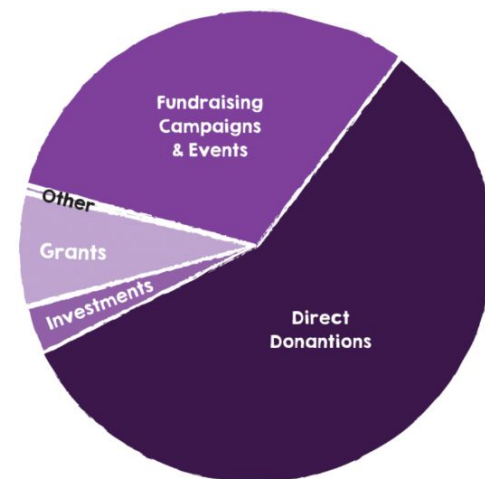
Our funds are raised primarily through fundraising campaigns and events initiated by the Foundation, our supporters and families of children with Sanfilippo. We have a duty to ensure that this money is used to fund research that has the greatest chance of having an impact on the lives of children affected by Sanfilippo.

Whenever possible, we will invest funds with the potential for not only a scientific return but also a commercial return for reinvestment in Sanfilippo research. This allows us to optimise our limited resources.

Sanfilippo Children's Foundation has a competitive research funding application program. All applications are assessed through a robust peer review process involving our scientific advisory board and external reviewers.

Using peer review ensures that the research is:

- scientifically valid, relevant and significant
- timely and achievable
- not duplicating other work
- using appropriate methodologies
- carried out by researchers with the right skills and facilities
- providing value for money.



FY 18 / 19

Projects Funded to Date

Details of projects funded to date can be found on our website:

<https://www.sanfilippo.org.au/research/funded-projects>

