A decade of difference for Sanfilippo research

Evaluating our impact on driving research 2013-2023

Sanfilippo Children's Foundation

September 2023

A decade of difference for Sanfilippo research

For 10 years—with your help—the Sanfilippo Children's Foundation has driven research for a world without Sanfilippo syndrome.

The aim has always been to drive high quality research to halt disease progression, repair damage and improve quality of life, and to stimulate collaboration and capacity in the field of Sanfilippo research. By analysing internal data and surveying funded researchers, we have examined the extent and nature of our support for research against the intent of our research strategy.

Evaluation shows we have made an enormous contribution both in Australia and globally, but it is also clear collaboration is at the heart of everything we do in recognition that solving Sanfilippo needs the collective knowledge and efforts of the entire international Sanfilippo community. Today we have a vibrant, diverse and expanding research community, our pool of research tools and resources is growing, and there are many promising therapeutic candidates in development.

This significant shift in the research landscape has only been possible due to the incredible support from families, donors, partners, researchers and clinicians, and government. Thank you is simply not enough. The difference you have made—and continue to make—in realising the opportunity to solve Sanfilippo syndrome and change the story for thousands of families around the world fills us with hope our goal will be reached soon.

What is Sanfilippo syndrome?

Mucopolysaccharidosis III (MPS III), or Sanfilippo syndrome is a type of genetic childhood dementia affecting 1 in 70,000 births. Children are missing an enzyme that clears away cell waste, and as this waste builds up it turns toxic and progressively causes damage to the brain and other complications.

Without a current cure and with only a few treatments available, most children with Sanfilippo syndrome never make it to adulthood.

Fast facts

- One in 169 people are healthy carriers of the faulty gene that causes Sanfilippo syndrome.
- Every year around five children are born with Sanfilippo in Australia. About 2000 children are born worldwide.
- There are four subtypes of MPS III: A, B, C and D.

A message from Meg

It is bittersweet reflecting on the past decade.

It seems so long, yet feels like only yesterday my children Isla and Jude were diagnosed with Sanfilippo syndrome.

I can recall the very moment I had the epiphany that led to starting the Sanfilippo Children's Foundation in 2013. When I realised the only thing worse than losing both of my beautiful children to this dreadful, unthinkable disease would be if their short lives were lived in vain. I could not stand by and watch Sanfilippo take everything it was going to from us and do nothing to change this for other families facing this devastating diagnosis.

Over the last 10 years there has been so much heartbreak, yet so much hope. I reflect on the beautiful children we have lost, but also the deep and profound joy they brought to those who loved them and the progress they each inspired.

Challenges that once seemed insurmountable, now have solutions on the horizon.

Today, there is so much to celebrate and be proud of. The lasting impact Sanfilippo Children's Foundation has delivered. The unwavering drive and ambition we still push forward with. And most importantly, the clarity of vision for how we are going to get there from here. To that place now within our reach — a world without Sanfilippo.

Megan Maack, Founder

Front cover: Kyuss

Thank you!

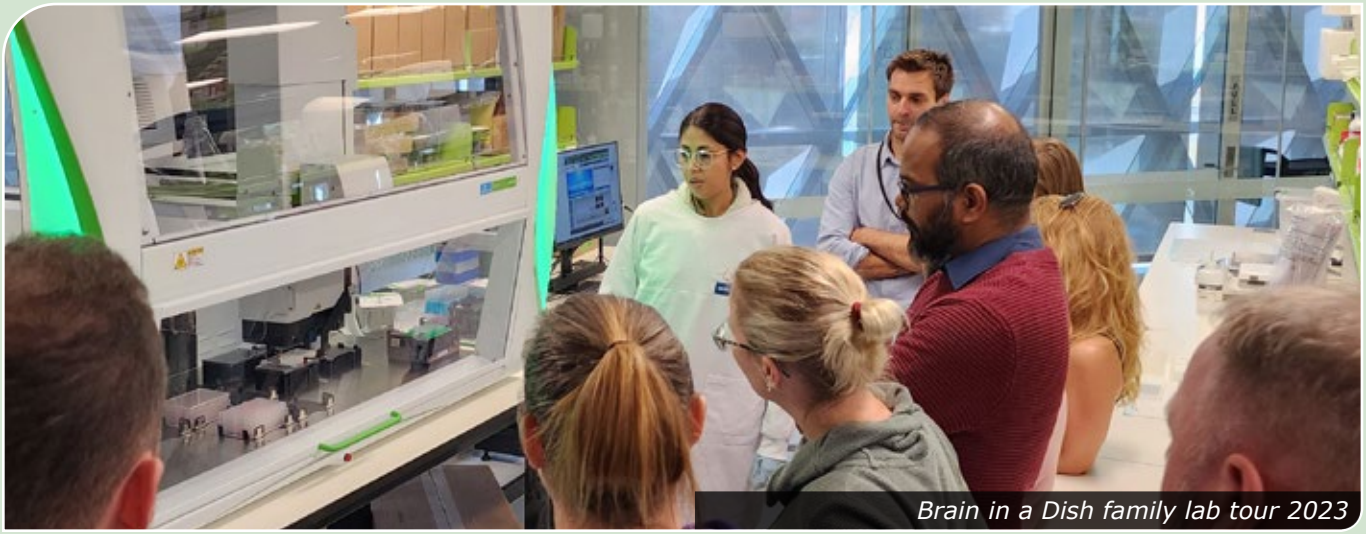
The scale of progress by the research community over the past decade has only been possible because of the amazing efforts of our families, supporters, fundraisers, sponsors, partners and donors.

The Sanfilippo community is beyond incredible and we are grateful to have your support. To everyone who has donated, run a fundraising event, helped raise awareness of Sanfilippo, volunteered time, contributed expertise, advocated on behalf of families, taken part in a challenge... we cannot thank you enough.

Driving research - our approach

Sanfilippo Children's Foundation aims to stop disease progression, repair damage and improve quality of life by:

- *funding the best research*
- *driving translational research*
- *encouraging innovation and collaboration*
- *building next-generation capability.*



Brain in a Dish family lab tour 2023

What do we fund?

Incubator grants: to help get ideas started and test novel concepts in the hope of generating results that may attract larger scale funding.

Translational research: projects showing potential to progress to treatments.

Scholarships: supporting postgraduate researchers.

Strategic projects: initiatives designed to speed up development of therapies and improve patient outcomes.

How do we select the right projects?

All research grant applications are assessed through a robust review process involving external peer reviewers, our Scientific Advisory Board and families affected by Sanfilippo.

This process validates that the proposed 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
- Relevant to families affected by Sanfilippo.

Scientific Advisory Board

Our volunteer Scientific Advisory Board, composed of expert clinicians and researchers, guide our research strategy and review all grant applications to the Foundation. We are also grateful to the wider network of external expert peer reviewers who provide critical feedback on grant applications.

Evaluating our impact

To understand the impact of our investment into research, we asked ourselves if we had funded the best research in line with our aims. Are we achieving what we set out to do?

We examined our internal data and research reports and surveyed funded researchers. Of 28 researchers surveyed (working on 32 projects), 61% gave their feedback (with survey results available for 59% of projects). This report outlines some of the major achievements from our investment in research over our first ten years.

Ten years of research impact

2015

Australia's first clinical trial for Sanfilippo is secured

2016

Our Scientific Advisory Board is established to oversee the foundation's first grant round

2017

Sanfilippo Children's Foundation is awarded Research Australia's Advocacy Award at the Annual Health & Medical Research Awards

2018

$2 million of Australian Government funding is secured for the '*Sanfilippo Brain in a Dish*' drug discovery project

2019

The Foundation provides seed funding to help establish the Childhood Dementia Initiative

2020

The inaugural annual Solving Sanfilippo Symposium is held in Adelaide

2022

The Global Roadmap for Sanfilippo Syndrome Therapies is launched

The first-ever global consensus clinical care guidelines for Sanfilippo syndrome are published

A further competitive MRFF grant is secured to continue the Brain in a Dish project

SCF collaborates on three successful MRFF grants to pursue treatments and newborn screening avenues for Sanfilippo syndrome

2023

The International Sanfilippo Syndrome Alliance is established

More than $7.5 million so far has been directed to research across 41 different projects and initiatives

Matilda

We've directed over $7.5 million to 41 research projects

Funding directed by the Sanfilippo Children's Foundation into research projects and initiatives.

	Number of projects	Total (AUD)*
Research grants	30	$4,207,102
Brain in a Dish project	1	$2,500,000
Abeona/Ultragenyx clinical trial	1	$449,330
Strategic projects and scholarships	9	$372,912
Total	**41**	**$7,529,344**

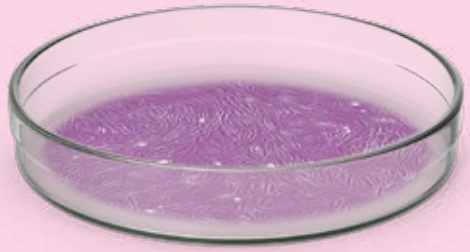
*Total includes committed and leveraged funds, which includes $1,596,768 from co-funders for research grants and $2,000,000 of Australian Government MRFF funding for the Brain in a Dish project.

We created the world-first flagship project: Sanfilippo 'Brain in a dish'

In 2018 Sanfilippo Children's Foundation secured a $2 million Medical Research Future Fund (MRFF) grant from the Australian Government to establish a drug-repurposing platform for Sanfilippo syndrome.

Australian researchers used donated skin cells from children with Sanfilippo and reverse engineered these into stem cells and then into neurons, creating a 'brain in a dish' – an individualised representation of a person's brain tissue.

This groundbreaking project has generated a wealth of detailed information about the biological impact of Sanfilippo syndrome on neurons to broadly benefit the field of Sanfilippo research. The drug screen is underway and will hopefully identify drugs already approved for other conditions, with potential benefit for treating Sanfilippo that can be fast-tracked into clinical trials. This project recently secured another $750,000 in competitive MRFF funding.



We brought a clinical trial to Australia

Sanfilippo Children's Foundation invested in one of the first gene therapy clinical trials for Sanfilippo syndrome type A.

Through our support an Australian trial site was established and Australian children with Sanfilippo type A were treated in 2017. A total of 22 children worldwide have now accessed this promising treatment.

Early safety and efficacy results are encouraging, and potentially life-changing results are being seen in children treated before the age of 3 years. Brain growth and development of cognitive skills are tracking close to the typical development seen in children without Sanfilippo.

This trial, initiated by Abeona Therapeutics and now continued by Ultragenyx, was only made possible through the collaboration of international patient groups, researchers, clinicians and industry. Follow-up of patients is continuing, with regulatory approval the ultimate goal.

Dr Nick Smith, Clinician Researcher

We collaborated to develop best practice clinical guidelines

For decades, clinicians and families have lacked clear guidance on best practice care for people with Sanfilippo.

To end this guesswork, Sanfilippo Children's Foundation and Cure Sanfilippo Foundation USA collaborated with international clinical experts to develop the Consensus Guidelines for Sanfilippo Syndrome Clinical Care.

The guidelines, published in 2022, provide clear recommendations on Sanfilippo syndrome-specific care management and monitoring of disease-related changes. The guidelines have been widely disseminated and shared with families who are using them successfully to advocate for the best clinical care and supportive therapies for their children.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Sanfilippo syndrome: consensus guidelines for clinical care

Nicole Muschol, Roberto Giugliani, Simon A. Jones, Joseph Muenzer, Nicholas J. C. Smith, Chester B. Whitley, Megan F. Drake, Kristina Elvidge, Lisa Melton, Cara O'Neill on behalf of MPS III Guideline Development Group

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Abstract

Sanfilippo syndrome is a group of rare, complex, and progressive neurodegenerative lysosomal storage diso characterized by childhood dementia. The clinical management of patients with progressive neurological de multisystem involvement requires a multidisciplinary team with experience in the management of neurodeg disorders. Best practice guidelines for the clinical management of patients with these types of rare disorders


Callum

We provided seed funding to help establish the Childhood Dementia Initiative

Childhood Dementia Initiative, headed by our founder Megan Maack, has been instrumental in raising awareness of and educating people on childhood dementia, its impact on children and their families, the need for systemic health system and policy reform and more investment in research. Sanfilippo syndrome is one of over 70 types of childhood dementia and collectively these conditions cause a similar number of deaths as childhood cancer. Sanfilippo Children's Foundation is a proud partner of Childhood Dementia Initiative.

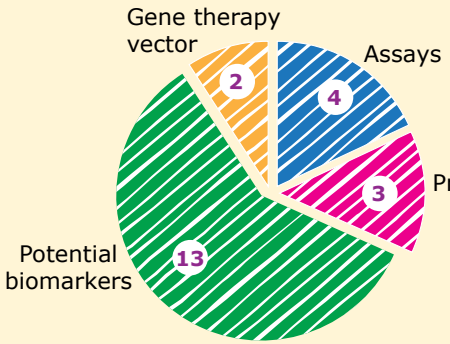
childhood dementia INITIATIVE

Research innovation and collaboration

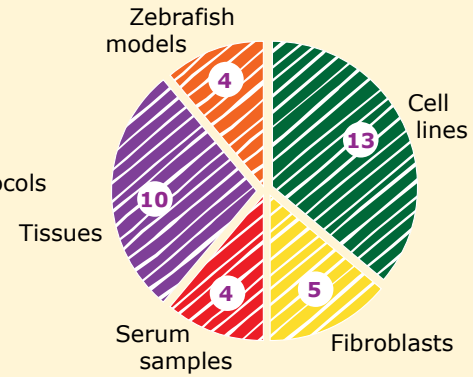
To date our funded research has generated 22 new research tools and 36 biological resources, helping out other Sanfilippo syndrome researchers

Assays, protocols and datasets developed as part of a research project are vital to enable the next stages of research. They can also be shared with other researchers to facilitate additional research projects. Biomarkers identified in research studies can help identify pathways and molecules that may lead to new treatments. Ultimately, they may be used in clinical studies to track disease severity or treatment response. Shareable biological resources include human blood and cell samples, animal tissues, and animal models such as mice, fruit fly and zebrafish models. These also enable further research projects and collaborations beyond the original project and are critical for testing new experimental therapies.

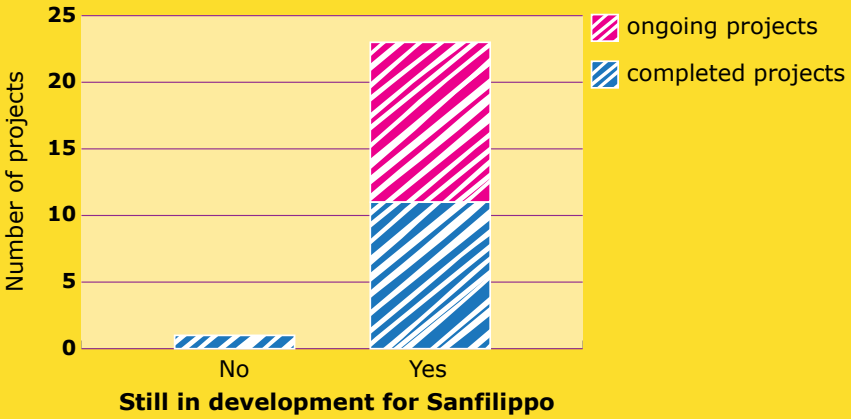
Types of non-biological tools created



Biological resources generated from all funded projects



Therapeutic candidate still undergoing development or testing



New treatment options have been explored

Researchers funded by Sanfilippo Children's Foundation have developed or investigated over 20 new therapeutic candidates. All but one continue to be explored in pre-clinical research studies. Greater funding and novel funding mechanisms and collaborations are urgently needed to drive the ongoing development of the most promising candidates into later stage pre-clinical research and clinical trials.

We co-funded research into two new gene therapy vectors for Sanfilippo types B and C

Sanfilippo Children's Foundation co-funded two projects aimed at optimising gene therapy vectors to deliver gene therapies for Sanfilippo more efficiently and effectively. Both projects were awarded Incubator grants in the 2016 grant round and were among the first projects to be co-funded with international Sanfilippo patient organisations. This helped foster strong and enduring international relationships.

Both projects also retained and trained a significant number of young researchers and led to productive new collaborations.

While these are examples of highly successful translational projects, both require further investment in order to reach a clinical trial. The research teams are continuing this work in active pre-clinical development and seeking commercial partners.

We've funded research across the globe and built a network of international researchers

Over the past decade researchers from 14 countries have applied to our grant funding rounds, reflecting the breadth and connectedness of the Sanfilippo research community.

Our funded projects and relationships with researchers have helped 17 researchers start new collaborations. Additionally, over half of our funded projects have involved at least two laboratories from the outset.

A huge thank you to our co-funding partners

- Cure Sanfilippo Foundation (USA)
- Fondation Sanfilippo Suisse (Switzerland)
- Sanfilippo Initiative (Germany)
- Sanfilippo Fundacja (Poland)
- Associação Sanfilippo Portugal
- Sanfilippo Fighters (Italy)
- L'association Sanfilippo Sud (France)
- Asociación Sanfilippo Barcelona (Spain)
- Associação Sanfilippo Brasil
- Jonah's Just Begun (USA)

Our funding generates further funding for Sanfilippo research - over $6 million and counting!

Researchers funded by Sanfilippo Children's Foundation have subsequently secured a further $3.8 million dollars from other granting organisations. We've also collaborated with our funded researchers on over 14 major government and non-government grant applications. This has yielded another $2.34 million for research into Sanfilippo syndrome and related diseases.

International patient groups generously helped co-fund many research projects we selected for funding, reflecting the incredible appetite for collaboration in the international Sanfilippo community.

We have attracted and retained researchers from different fields to focus on Sanfilippo

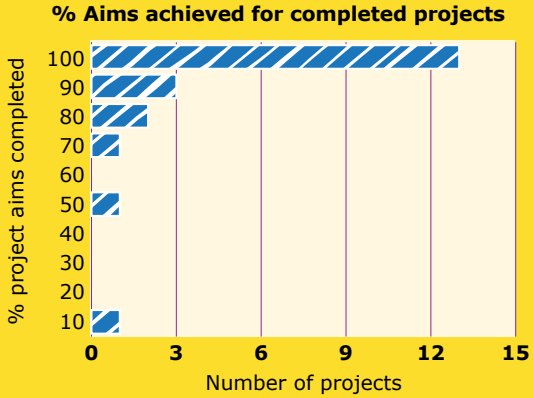
Seven funded researchers were working on completely different neurodegenerative diseases, mainly adult dementias, prior to securing a Sanfilippo Children's Foundation grant. We've also supported the early careers of six postgraduate researchers through our PhD top-up scholarships.

Oliver

Jessie Mei Mei

Most funded projects have achieved all their aims

Research is unpredictable, and even the most well designed projects do not always go according to plan. However, this high rate of meeting project aims suggests the rigour we take to select the most promising research has been successful, and projects are led by highly capable teams with the ability to see these through to completion. We actively work with researchers to monitor progress and solve issues as these arise, and this has been key to building stronger relationships and additional collaborations.

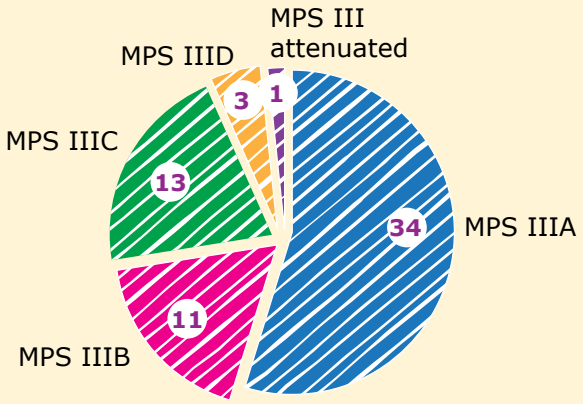


Research benefits all subtypes and other conditions

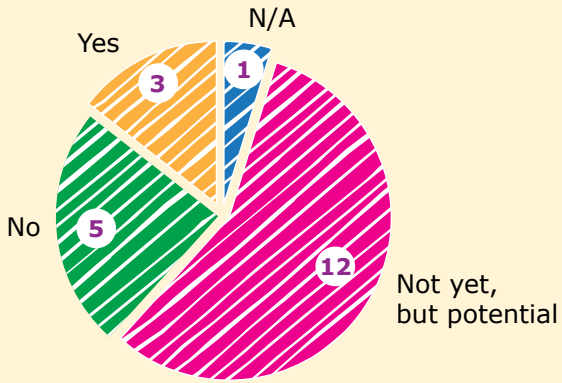
We have funded research into all Sanfilippo subtypes. Of 21 completed projects, 14% had already extended to other subtypes and nearly 60% have potential to be applied to more subtypes.

Six projects had findings that can be applied to other conditions, such as other neuronopathic mucopolysaccharidoses and lysosomal storage diseases

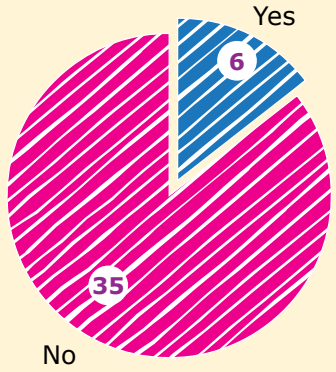
Number of projects studying each subtype



Findings applied to other subtypes
(completed projects only)



Project findings could be applied to other diseases



Looking ahead

Significant progress has been made in driving forward the field of Sanfilippo research both in Australia and globally. We have a vibrant, diverse and growing research community, we have a growing pool of research tools and resources and we have a large number of therapeutic candidates in development.

However, there is a great deal of work still to do.

The Global Roadmap for Sanfilippo Syndrome Therapies has been endorsed by the international Sanfilippo community and sets out the pathway to rapidly deliver solutions for all affected families. Implementation of this roadmap is the key to achieving our aim of a world without Sanfilippo syndrome. But this will take leadership and the collective efforts of the international Sanfilippo community — patient organisations, families, researchers, clinicians, governments and industry — to harness the incredible opportunities ahead.

The promise of new scientific discoveries, earlier diagnosis through screening, and the progress of therapies towards regulatory approval are in sight. At this pivotal point in our journey we must pursue our goal with unrelenting courage, determination and urgency to realise the benefits for children with Sanfilippo and their families as soon as possible.

WIth your support we will turn heartbreak into hope, and hope into solutions.


Skye

Sanfilippo
Children's Foundation

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