Impact for Children's Health 2023–2024

LUMINESCE Alliance

Innovation for Children's Health

Our Vision

is to be Australia's most ground-breaking, innovative and translational paediatric research hub that will change children's health around the world.

Our Mission

is to have a voice on a national and international platform so that our research is disseminated and implemented to directly improve the health of children.

Our Purpose

is to empower our partners to work together in changing the global landscape in paediatric research.

Our partners

Luminesce Alliance - Innovation for Children's Health is a not-for-profit cooperative joint venture established with the support of the NSW Government to coordinate and integrate paediatric research.

The Sydney children's Hospitals Network
care, advocacy, research, education

Children's Cancer Institute

CHILDREN'S MEDICAL RESEARCH INSTITUTE
Jeans for Genes®

THE UNIVERSITY OF SYDNEY

UNSW SYDNEY

Supported by the
NSW GOVERNMENT

Thank you to our Board Members for their constant support and wisdom. You can read more about our Board Members on our website.

Acknowledgment of Country

Luminesce Alliance acknowledges the Traditional Custodians of Country throughout Australia and their connections to land, sea and community. We pay our respect to their elders past and present and extend that respect to all Aboriginal and Torres Strait Islander peoples today.

Contents

Message from the Chair

Luminesce Alliance was established in 2016 to try to unify the significant paediatric research and translation capability in NSW.

With relatively small funding and in just eight years, this unique entity has brought together clinicians and researchers across five leading institutions who may not otherwise have had the opportunity to collaborate to this extent.

The benefits of working together are evident in this report. Our world-leading research has brought breakthrough treatments to the children of NSW and achieved significant benefits for our health system.

We've facilitated clinicians and researchers to jointly drive research agendas and translate that collaborative research into our hospitals. And, unlike conventional funding entities, we've turbocharged impact by providing access to cutting-edge infrastructure through our Enabling Platforms.

This kind of support is incredibly rare in paediatric research. It's attracted and retained some of the world's best and brightest to work in NSW.

Our support has also allowed our members to leverage our proof-of-concept funding into significant research funding, achieving greater return on investment than we could have imagined.

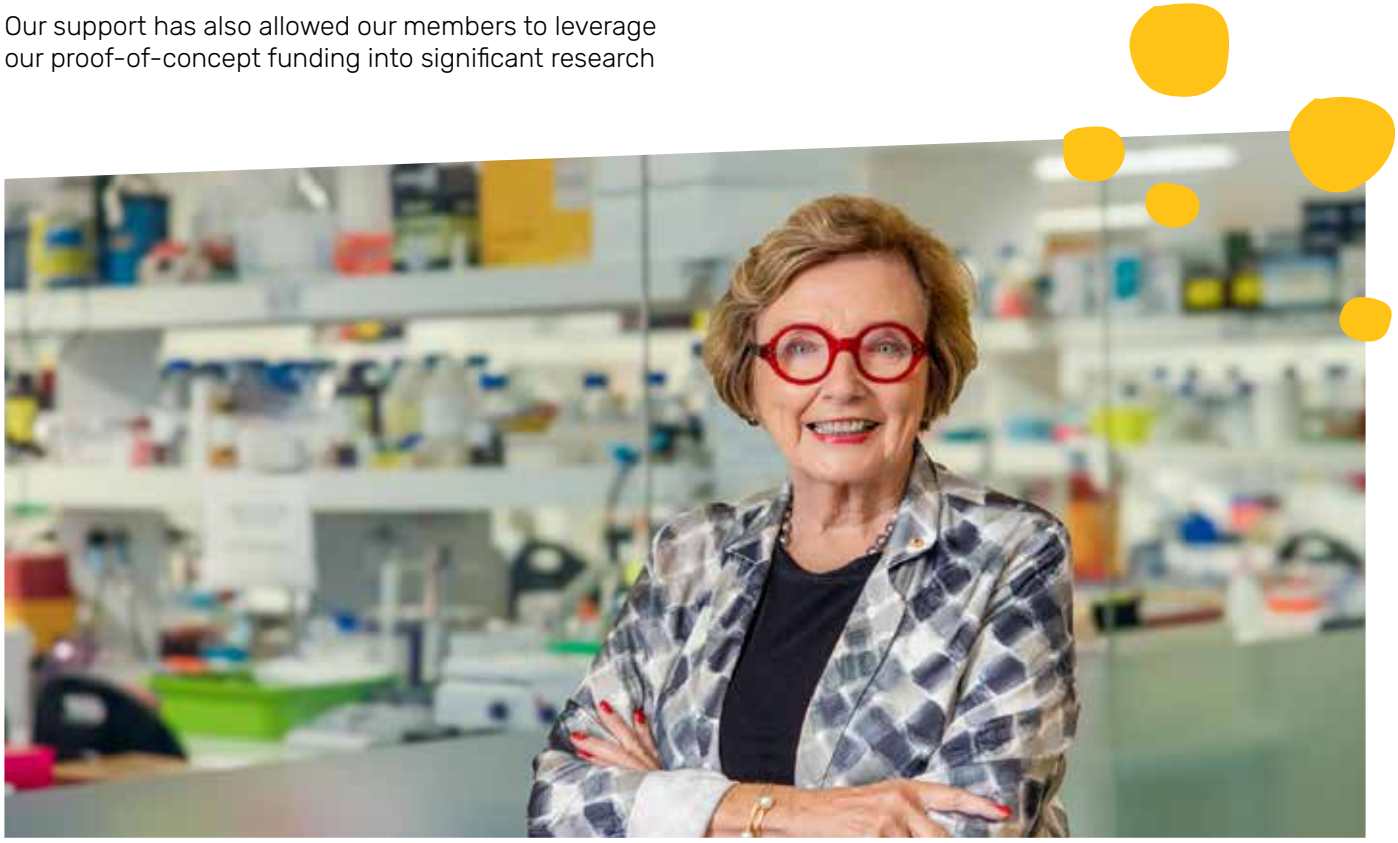
We've shown that this collaboration makes us bigger than the sum of our parts. Our Partners – all world-leading organisations in their own right – tell us time and again they can achieve more as part of Luminesce Alliance than would be possible individually.

But there's much more to do.

We would love to extend our reach north to John Hunter and south to the Illawarra. We want to collaborate with researchers and medical faculties at different universities and in different hospitals around Australia, and partner internationally to change children's health globally.

We're only just starting to scratch the surface, and we look forward to the possibilities ahead.

Kathryn Greiner AO
Chair
Luminesce Alliance



Message from the Executive Director

When families discover their child has a rare disease, neurodevelopmental disorder or cancer, they often tell us they feel very alone. One of the reasons is that so little research has been done internationally on rare paediatric conditions.

We're aiming to change that. Achieving better outcomes for families and children is our number one priority.

But it's not just a question of doing more medical research. We also need to make sure new findings are rapidly brought into the health system.

That's what we're aiming to do with our five Enabling Platforms. Funded in April 2023, these platforms are available to support researchers across all our member institutions.

They cover the entire research pipeline, from identifying and understanding disease-causing genes using functional genomics and big data, to delivering new drugs using precision therapy, developing world-leading best practice to support the psychosocial aspects of child disease, and health economics and implementation research to translate research discoveries into new models of care.

The Enabling Platforms have already supported research that would not have otherwise occurred. I'm excited to see where this leads.

The extraordinary achievements described in this report would not be possible without our Partners' commitment to the collaboration, the dedication and hard work of the researchers and clinicians, and the support of the NSW Department of Health.

I would like to thank everybody who has contributed to our outstanding impact this year. It's been an immense privilege to be part of this work.

Ms Anastasia Ioannou
Executive Director
Luminesce Alliance

Our Enabling Platforms

In 2023, with a $20 million funding commitment from the NSW Government to 2027, we developed infrastructure and collaborative networks known as Enabling Platforms.

The Luminesce Alliance Enabling Platforms are functional specialisations that cross disease areas and organisations to deliver collaborative, multidisciplinary and contemporary research and clinical health programs.

They create a precision medicine ecosystem transcending organisational boundaries, enhancing access to scientific resources for paediatric researchers and clinicians. They expedite discoveries, accelerate translation into the health system, and improve outcomes for children with rare genetic diseases, cancers and neurodevelopmental disorders.

Enabling Platforms add significant value by:

- **Fostering collaboration:** Enhancing partnerships across disciplines.
- **Encouraging innovation:** Promoting multidisciplinary approaches and creative thinking.
- **Integrating commercialisation:** Streamlining research translation into practical applications.
- **Supporting geographic strategies:** Strengthening connections within and across research precincts.
- **Accelerating efficiency:** Addressing gaps and speeding up translation processes.
- **Reinforcing competitiveness:** Enhancing strategic advantages in the field.

This year's Impact Report highlights the implementation of these five platforms, demonstrating how collaboration within Luminesce Alliance harnesses the diverse talent, knowledge and experience of our partners to drive their development.

These platforms deliver significant value to NSW by advancing cutting-edge research with real-world applications that improve children's lives and reinforce the state's leadership in translational paediatric research, yielding substantial health and economic benefits, including:

- Lives saved
- Lives improved
- Reduced prevalence of paediatric diseases
- Increased support for high-quality STEM jobs
- Attraction of private industry investment to NSW
- Enhanced opportunities for out-of-state grants and investment.

Functional Genomics
Making genetic knowledge count

Data
A new paediatric data ecosystem

Precision Therapy
Delivering innovative therapies for kids

Psychosocial
Wraparound care for patients & their carers

Health Systems Implementation and Economics
Making effective changes in the healthcare system

About us

Luminesce Alliance is comprised of five key partner organisations: the Children's Cancer Institute, the Children's Medical Research Institute, The Sydney Children's Hospitals Network, UNSW Sydney and The University of Sydney.

The organisations work together to galvanise and accelerate NSW-led paediatric research, delivering ground-breaking medical and research developments, far beyond their individual capabilities.

With the vital support of the NSW Government, Luminesce Alliance accomplished significant milestones through its flagship enabling platform, the Centre for Paediatric Precision Medicine, established in 2019.

This pioneering platform has been a catalyst for transformative clinical trials and gene discoveries. It enabled spinal muscular atrophy testing in NSW and ACT newborn screening, leading to national adoption and access to gene therapy Zolgensma® via the Pharmaceutical Benefits Scheme. It supported the ZERO Childhood Cancer Program and launched a world-first psychosocial initiative ensuring the psychological, social and educational wellbeing of patients, siblings and caregivers. Additionally, the platform has attracted and retained leading researchers in NSW, contributing to the global knowledge base for the prevention and cure of childhood diseases.

The platform's impact is evident with a 12-fold return on the NSW Government's $24 million investment, generating more than $300 million in additional research grants, supporting nearly 200 STEM jobs, fostering 500+ collaborations, and producing nearly 200 publications in five years.

Luminesce Alliance has continued to create a significant number of new STEM jobs, supported the facilitation of numerous pharma and investigator-led clinical trials, and collaborated with a wide range of national and international organisations. We have also contributed to findings on paediatric precision medicine through a collection of peer-reviewed publications and a series of presentations both in Australia and internationally.

Our history

2015

Luminesce Alliance established as Paediatrio

2016

NSW's first small-scale vector manufacturing facility established for gene and cell therapy clinical trials

2019

$24m funding for Paediatric Precision Medicine Program 2019–2023

Australia's first stem cell and organoid facility established

Paediatrio rebrands to become Luminesce Alliance

Australia's largest paediatric computational biology team established

2020

Children's brain cancer trial opens in Australia

Newborn spinal muscular atrophy (SMA) screening introduced in NSW and ACT after a successful pilot, paving the way for a national rollout to screen all Australian newborns and enabling early treatment with gene therapy

2021

Luminesce Alliance partners with the NSW Department of Education to promote the STEM workforce

Luminesce Alliance provides $1.35m in seed funding for eight innovative research projects

2022

Gene therapy and diagnosis breakthrough for retinal genetic eye diseases

Lab-grown mini-organs advance eye, brain and heart disease research

Standardised RNA testing procedures are developed to deliver patients with a precise molecular diagnosis

Luminesce Alliance takes the lead on finding biomarkers for Rett syndrome

Luminesce Alliance-funded PREDICT trial provides vital insights into underlying genetic abnormality that predisposes children to cancer

2023

$20m funding for Enabling Platforms Program 2023–2027

Luminesce Alliance contributed to more than 10 clinical trials of novel therapies in a variety of rare diseases, including gene therapy, and supported 30 patients participating in these trials

Launch of our revamped Illuminate newsletter

PEACH-E evaluation funded to focus on social determinants of health

Protocol paper of PREDICT cancer predisposition trial

Luminesce Alliance funds a study looking at speeding up and streamlining the discovery of new drugs to treat childhood cancers

Precision Medicine Program 2019–2023 successfully completed

Luminesce Alliance supports data linkage team to map the prevalence of juvenile arthritis, leading to additional funds for a national data surveillance system

2024

Luminesce Alliance supports world-first psychosocial research informing resources and support for children with cancer and their families

Luminesce Alliance supports the first Australian inherited retinal disease patient and family day

Luminesce Alliance and Child UnLimited partnership strengthens consumer engagement initiatives

The ZERO Program, led by the Children's Cancer Institute and Kids Cancer Centre at Sydney Children's Hospital, Randwick, and supported by Luminesce Alliance, shows that precision medicine outperforms standard therapy in clinical response and survival

Enabling Platforms become available for researchers

Highlights 2019–2024

Our team

Meet the people behind Luminesce Alliance.

Read more

195+ STEM jobs

373 research projects

32 clinical trials

20 facilitated R&D IPs and commercial collaborations

502 collaborations with national and international organisations

186+ peer-reviewed publications adding to precision medicine knowledge

250 presentations made locally, nationally and internationally

$309m in additional leveraged research funding

Paediatric Precision Medicine Program 2019–2023 – from a grant of $24m leveraged $294.4m – a 12 fold return on the initial investment

Enabling Platforms Program 2023-2027 – from a grant of $20m leveraged $14.6m within only 18 months

Enabling Platforms available for researchers

We funded access to infrastructure and capability support in the following areas:

- Psychosocial and equity-focused research support
- Functional genomic subsidised support services
- THINK Advanced Therapeutics Pipeline Program

For more information on our national and international collaborators refer to our website.

luminesce.org.au

#LuminesceAlliance2024

The Luminesce Alliance Conference, *Paediatric Precision Medicine: Advancing research and patient care,* shares research innovations and foster horizon-scanning discussions in the translation of precision medicine into our health systems.

Read more

Research Australia membership

Luminesce Alliance became a member of Research Australia, the national peak body for health and medical research. It is the only organisation to represent the entire health and medical research pipeline including universities; medical research institutes; the pharmaceutical, medical technology and biotechnology sectors; consumer groups; and health corporates. We are pleased to work with Research Australia to ensure Australians understand the connection between health and medical research and an improved health system.

We were shortlisted as finalists for Research Australia's Digital and Data Health Innovation Award for our Advanced Genome and Transcriptome Analytics Project (see page 19).

We've also had several articles published in Research Australia's magazine, INSPIRE.

- EPIC-CP Pilot to benefit all Australian children living with disabilities - Luminesce Alliance (October 2024)
- Luminesce Alliance researchers feature in Research Australia's latest report (September 2024)

Luminesce Alliance supported projects and investigators featured in Research Australia's INSPIRE (December 2023).

A new website

Launched in October 2024, our new website focuses on being user-friendly for our community.

luminesce.org.au

Functional Genomics Enabling Platform

Functional genomics is the study of how genes and parts of the human genome contribute to different biological processes. It looks at how genes and other parts of the biological system work together to cause disease. This understanding can lead to:

- improved diagnosis of childhood cancers, neurodevelopmental disorders and genetic diseases
- better treatments such as new therapies and medical technologies
- better access to first in-human clinical trials for children in NSW
- better genetic counselling.

Our functional genomics research pipeline brings together all the current clinical and research activity across Luminesce Alliance, including teams working in cancer, rare genetic diseases and neurodevelopmental disorders.

The pipeline focuses on building our knowledge base of genetic variants that are of uncertain significance, inadequately understood, or novel. We model disease using stem cells and organoids (mini-organs grown in the laboratory using stem cells) and use new functional genomics methodology to understand genomic abnormalities that cause the disease. We can then test new therapies for a range of conditions including:

- inherited retinal disorders and vision impairment
- neurodevelopmental disorders
- telomere disorders – haematological diseases and bone marrow failure
- paediatric cancer.

PATIENT STORY

Grace's story

Grace is a fun-loving, kind and inquisitive eight-year-old girl. She loves to play restaurants with her friends Eliana and Samantha, go to school, and pet her labradoodle Tully. Her smile lights up the room.

Grace lives with ADCY5-related movement disorder syndrome, an ultra-rare genetic condition caused by a mutation in the ADCY5 gene.

Fewer than one in every one million children has this condition. It causes Grace to have multiple episodes of abnormal movements called 'dystonic movement storms' that are triggered when she gets sick, tired, anxious, stressed or frustrated.

The episodes can be life threatening. If the abnormal movements can't be stopped, Grace could experience respiratory failure or cardiovascular collapse. During a dystonic storm, her body is in a hypermetabolic state that can lead to muscle breakdown.

Managing all this impacts the whole family. During the episodes, Grace needs to be physically managed by two people, she may need to be hospitalised, and she becomes exhausted mentally and physically.

The disorder also means Grace can't sit, stand or walk by herself, and it also significantly affects her speech. 'It's really challenging for her,' says her mother, Emma, a former nurse. 'She is so mad and sad with her body.'

The family first noticed something wasn't quite right when Grace was four months old. They eventually got a diagnosis when she was 3 ½.

'We were so relieved to finally have some answers and to find out our daughter had a normal life expectancy and intelligence, but because the condition is so rare, the treatment path is unclear,' says Emma.

This year the family – Dad Adam and older brothers William and Ollie – have raised $140,000 to fund a PhD student to join A/Prof Wendy Gold's team and work on ADCY5 full-time.

A/Prof Gold says having the Functional Genomics Enabling Platform to support discovery is really important.

'It's got every capability that we need – all the infrastructure that's required and the expertise with leading researchers who are able to actually deliver.'

Emma says the family wouldn't change Grace for the world because of the beautiful little girl she is, but it would be wonderful to improve her function and the disabling impact these movement episodes have on her body and functionality.

Grace's dream is to one day walk Tully, says Emma. 'No pressure, Wendy!'

Unpacking the complexity of rare disorders

Funding from Luminesce Alliance is driving world-first discoveries that could revolutionise treatment options for kids with rare genetic neurodevelopmental disorders.

A/Prof Wendy Gold and her team have made an exciting discovery of two promising new biomarkers for the rare genetic disorder Rett syndrome.

Biomarkers are essentially molecules such as genes or proteins in the body that can be measured to show whether someone has a disease, and whether treatment is working. It means doctors will one day be able to monitor Rett syndrome in children by taking blood samples, which is simpler and less invasive than current diagnostic methods.

This work has gained international attention. A/Prof Gold says it establishes NSW as having world-leading expertise and infrastructure in genetic research and is likely to attract more clinical trials to NSW.

She says there are more than 7,000 rare disorders and less than 5% of them have a drug approved by the US Food and Drug Administration (FDA) that can help.

'I want to create a pipeline where we can take patients' blood and look for biomarkers. That will mean the success of clinical trials will be that much higher because there's a primary endpoint,' A/Prof Gold says.

'We'll be able to show a certain molecule has changed after treatment, which will provide support evidence to the FDA that the drug works.'

The research involves analysing combined 'omic' data* to understand the complex interactions between genes, proteins and metabolites in the body, what these do to cells, and how they contribute to the disorder in children.

continued p13

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- **A/Prof Wendy Gold**
  Head, Molecular Neurobiology Research Group, Kids Research, The Children's Hospital at Westmead; The University of Sydney

* 'Omics' refers to studying the molecules and their processes within cells and tissues, such as through DNA and RNA sequencing

The approach opens the door for new ways of diagnosing disease using blood samples, for tracking how disease develops over time, and for assessing whether clinical trials have worked.

A/Prof Gold says the work would not be possible without Luminesce Alliance funding, which provides access to expertise and infrastructure across five Luminesce Alliance Enabling Platforms at a fraction of the normal price.

Initial funding from Luminesce Alliance was leveraged into a Medical Research Future Fund grant to look for biomarkers in brain organoids from Rett syndrome patients. The Luminesce Alliance Functional Genomics Enabling Platform has allowed the team to expand its work beyond Rett syndrome to include the neurodevelopmental condition STXBP1 and other rare diseases.

A/Prof Gold says it's extremely difficult to get funding to study rare genetic diseases in children.

'I wouldn't have been able to do a fraction of what I'm doing now without Luminesce Alliance support,' she says.

'Access to the Enabling Platforms is not just a resource, it's not just infrastructure, it's not just expertise. It's that broad professional network that's enabled us to be so much more productive and to be able to tap into resources that we didn't know we needed.'

> *I wouldn't have been able to do a fraction of what I'm doing now without Luminesce Alliance support.*
>
> - **A/Prof Wendy Gold**

Luminesce Alliance enables increase in rare disease research innovation and capacity

At the STXBP1 Summit conference in Philadelphia in July 2024, A/Prof Gold received interest from multiple organisations and researchers after highlighting her STXBP1 biomarker studies. This is the first time a multi-omic approach to identifying blood biomarkers has been used to address the rare disease STXBP1.

Biomarker studies use less invasive blood samples, which then supplement physical and genetic tests, to indicate the pathogenic processes and changes (functional genomics) that may occur as a result of therapeutic treatment.

A/Prof Gold says the research would not have happened without the Luminesce Alliance Functional Genomics Enabling Platform and the initial Luminesce Alliance-funded Rhett biomarker study.

'It's hard for families to fund research support for their rare disease. Because of the increased accessibility afforded to me by the Luminesce Alliance Functional Genomics Enabling Platform, it is so rewarding for me to now be able to say to families that yes, I can do this research for you,' she says.

Nurturing NSW's best and brightest students

> **This experience gave me valuable insights into how bioinformatics can contribute to understanding brain function and ultimately help people.**
>
> – **Sarah Alshammery**
> PhD student at the Kids Neuroscience Centre, The University of Sydney.

Sarah Alshammery first met A/Prof Wendy Gold on a placement in the third year of her Bachelor of Biomedical Science at the Australian Catholic University.

'I didn't really know what research was, or what opportunities existed,' says Sarah, who is doing a PhD with the Kids Neuroscience Centre at The University of Sydney.

Her PhD is on inflammation and epigenetics in neurodevelopmental and neuropsychiatric disorders.

Sarah says her early exposure to labs run by paediatric neurologist Prof Russell Dale and A/Prof Gold – and her inspiring mentorship – played a key role in shaping her academic trajectory.

In her Bachelor of Science (Honours) in Applied Medical Science at The University of Sydney, she pivoted during the pandemic to learn R language, a programming language for statistical computing that she used to analyse publicly available brain transcriptome data (data about the RNA molecules expressed from genes).

It meant a steep learning curve, but it became incredibly rewarding as she started to make sense of the data.

'This experience gave me valuable insights into how bioinformatics can contribute to understanding brain function and ultimately help people,' Sarah says.

She then went on to do her PhD with the Kids Neuroscience Centre, using big data to find differences in biological pathways in the brain cells of children with complex neurodevelopmental and neuropsychiatric disorders.

Sarah says: 'A better understanding of the underlying biology of these conditions brings us one step closer to developing treatments that target the disease mechanisms themselves, rather than simply managing symptoms.

'This could lead to more effective, personalised therapies that truly address the root causes of these disorders, offering better outcomes for these children.'

Sarah plans to carve out a research career where she can integrate bioinformatics, clinical research and molecular biology to tackle challenging questions and drive innovation.

'Part of the reason why this has been such a great place to do a PhD is that I've been part of a multidisciplinary team. It's given me the opportunity to develop a wide range of skills, from hands-on lab techniques to computational data analysis,' Sarah says.

'I feel like there's so much out there to be explored.'

Our incredible human mini-organs

‘Organoids’ grown in the lab are helping researchers test new drugs for genetic disease without the need for animals.

- **A/Prof Anai Gonzalez Cordero**
  Group Leader, Stem Cell Medicine and Head, Stem Cell & Organoid Facility, Children’s Medical Research Institute, Senior Lecturer, Faculty of Medicine and Health, The University of Sydney

Testing drugs to treat genetic disease is usually done on animals such as zebra fish, frogs or mice before eventually moving to clinical trials in humans.

But stem cell technology has opened the door to a revolutionary new way of accelerating drug discovery for genetic disease – by testing gene therapies on patients’ own organs, generated in a petri dish.

Human organoids are mini, simplified versions of organs grown in the laboratory that are generated from patients’ own stem cells. The stem cells are collected from a patient’s skin or blood then reprogrammed to grow into a tiny organ with the exact genetic features the researchers want to study.

That means new therapies can be tested directly on the organoids before they’re eventually brought to patients.

Group Leader A/Prof Anai Gonzalez Cordero says it’s a much more reliable, efficient and economical process because researchers have a good idea how a drug will work in a patient’s cells well before they start a clinical trial.

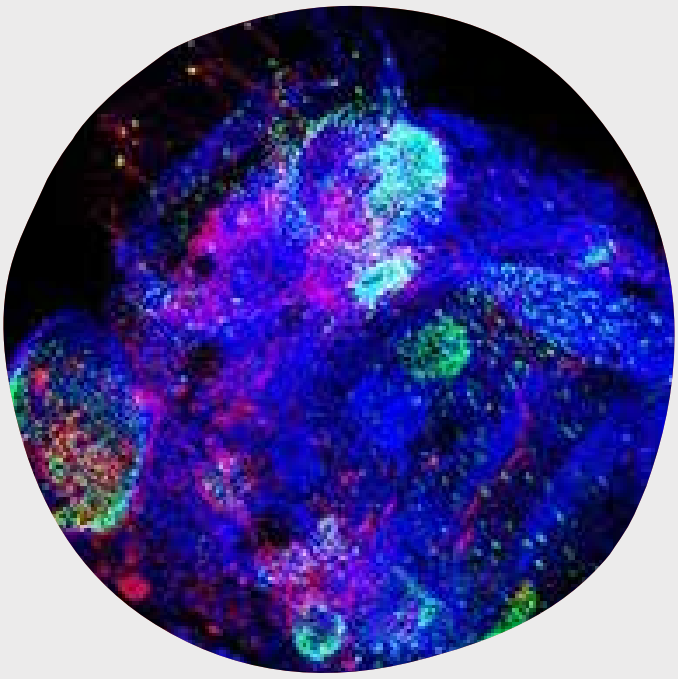
‘For example, if someone wants to study a neurodevelopmental disorder, we can just grow our cells into a brain organoid and characterise it in the way they need for their research,’ she says.

Funded in part by Luminesce Alliance, the Stem Cell and Organoid Facility at the Children’s Medical Research Institute has already developed 50 types of stem cells.

The organoids it can generate include kidney, liver, heart, lungs and retina – research that has led to new understanding of the genetic cause of a blinding eye disease in children and given access to a new therapy for patients in Australia.

The plan is to automate the production of the organoids so they’re more widely available to researchers across Australia.

More research is needed to develop more complex organoids that mimic the circulation and immune system in real organs.



Taking NSW into the CRISPR era

CRISPR (short for 'clustered regularly interspaced short palindromic repeats') is a technology adapted from the genome editing systems in bacteria. It uses genetic 'scissors' to snip strands of DNA or RNA, enabling scientists to precisely edit the genome of all living things.

The gene editor CRISPR-Cas9 won the Nobel Prize in Chemistry in 2020. The first therapy based on this technique, for sickle cell anaemia, was approved in the United States in 2024.

Postdoctoral Scientist Dr Carolyn Shembrey has been pushing the boundaries of how this technology could benefit sick children in NSW.

Her work as part of A/Prof Paul Ekert's team at the Children's Cancer Institute involves a newer CRISPR technology called CRISPR-Cas13, which edits RNA rather than DNA. Changes to RNA are temporary, whereas editing someone's DNA makes a permanent change.

Dr Shembrey says: 'You can essentially use this tool to target proteins that would otherwise be undruggable – because of the shape of the protein, there's no area on it that you can make a drug stick to.

'With CRISPR tools, we're able to target the process one step earlier and reprogram these molecular systems to cut up the mutation very specifically.'

Dr Shembrey met the Children's Cancer Institute's A/Prof Ekert when she was working at the Peter MacCallum Cancer Centre in Melbourne. She was attracted by CRISPR's potential to solve genetic variations identified through ZERO Childhood Cancer (ZERO), Australia's national precision medicine program, which is run in partnership by Children's Cancer Institute and the Kids Cancer Centre at Sydney Children's Hospital, Randwick.

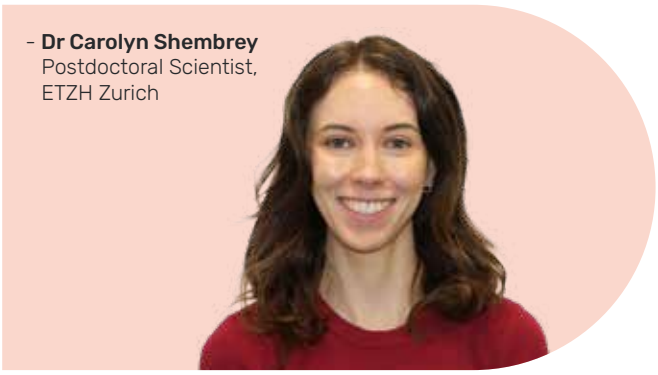
'In cancer research you might be researching one specific mutation, but with CRISPR it might be a mutation that comes up in lots of different cancers,' Dr Shembrey says.

'I like that about the research. It's kind of agnostic – you can develop one tool that could benefit patients with lung cancer or sarcoma or brain tumours.'

This year, Dr Shembrey started work at ETH Zürich, a science and technology university in Switzerland, learning from the best in the field about other types of CRISPR systems and how the technology can be used at scale to target thousands of mutations at once. She plans to incorporate what she has learned into ZERO when back in Australia.

'I really love the problem solving, I find the challenge of the science very stimulating,' she says.

'But beyond that, I think it's profoundly unfair that cancer happens to children just because of an anomaly in their genome.'



– **Dr Carolyn Shembrey**
Postdoctoral Scientist,
ETZH Zurich

Understanding how faulty genes influence children's cancers

World-first research funded by Luminesce Alliance is helping researchers to make critical discoveries about how faulty genes affect the biology of children's cancer.

- **A/Prof Paul Ekert**
Deputy Director, Research Themes; Translational Tumour Biology Group Leader, Children's Cancer Institute

The Translational Tumour Biology group is tapping into the huge potential for new scientific discoveries in all the genetic data that's being collected by the Zero Childhood Cancer Program (ZERO).

ZERO, Australia's national precision medicine program run in partnership by Children's Cancer Institute and the Kids Cancer Centre at Sydney Children's Hospital, Randwick, offers genetic sequencing of childhood cancers diagnosed in Australia to find the mutations, or spelling errors, that contribute to cancer.

This means treatment can be precisely targeted to the tumour's unique genetic profile. Every child diagnosed with cancer in Australia has access to the program.

'But what of all the hundreds or thousands of genetic mutations we haven't discovered yet?' says A/Prof Paul Ekert, Deputy Director, Research Themes; Translational Tumour Biology Group Leader, Children's Cancer Institute.

'Any one of them could be responsible for driving cancer – and understanding how they work means we might have a drug or can develop a new drug to fix them.'

A/Prof Ekert's group is studying these genetic mutations to understand what they mean – how they affect the way a cancer's cells function and, more importantly, whether treatments can prevent the cell from dividing and causing a tumour.

They're using a new technology called CRISPR-Cas13. It means they can manipulate strands of RNA in the laboratory to model tumour cells with a certain genetic change they're interested in. The researchers observe how that genetic change affects the way the cell works, and then identify new or use existing drugs fix the problem.

This year, the group has published a paper on their new techniques in the prestigious journal *Nature Structural & Molecular Biology*. They're one of the only groups in the world conducting this research in paediatric cancers.

One day, the new knowledge they're generating will lead to revolutionary new treatments for children with cancer.

This is made easier and quicker due to the group's collaborations with the other Enabling Platforms, which mean there's a seamless pipeline from collecting data from children's tumours, through to understanding the biology in the cells, and then on to developing new drugs.

Luminesce Alliance has provided funding for this invaluable basic research, which would otherwise be very difficult to get funded in Australia.

Data Enabling Platform

Data underpin all aspects of modern healthcare research and delivery and have become exponentially richer and more complex.

This requires new ways of standardising, storing, comparing, analysing and interpreting information.

Data are at the core of personalised medicine, which relies on producing, comparing and assessing data on a patient's unique genetics, environmental exposures, lifestyle and symptoms.

Luminesce Alliance is growing its capacity to translate rich and complex data into new treatments, new prevention strategies and clinical impact.

The Data Enabling Platform harnesses data for research and improved clinical care. By establishing a unified data strategy, the Platform is removing duplication and waste, connecting data capabilities, and leveraging expertise to enable precision medicine.

Whole genome sequencing in just six hours to find cures for kids

- **A/Prof Mark Cowley**
Deputy Director, Enabling Platforms and Collaboration; Computational Biology Group Leader, Children's Cancer Institute.

New computational tools developed by the Advanced Genome and Transcriptome Analytics program have made whole genome sequencing available to hundreds of sick children every year.

When a child is diagnosed with cancer in Australia, they're now offered a chance to be enrolled on the Zero Childhood Cancer Program, Australia's national precision medicine program.

A sample of the child's tumour is taken for whole genome sequencing, then the data are analysed to find its probable genetic cause. This information is interpreted and fed back to clinicians to inform treatment – an approach that has been shown to more than double the 18-month survival rate of children with high-risk cancers.

The engine room behind this process is the Advanced Genome and Transcriptome Analytics capacity. It analyses the whole genome sequencing data for every patient, identifies thousands of genetic changes, and uses tools built to match these genetic changes to the right diagnosis and evidence-based treatment options.

Originally funded by Luminesce Alliance in 2019, the program is now analysing over 850 whole genomes every year – an eight-fold increase since 2022.

The process is now well established in our hospitals, and, most importantly, it's trusted by clinicians, says A/Prof Mark Cowley, Deputy Director, Enabling Platforms and Collaboration; Computational Biology Group Leader, Children's Cancer Institute.

'With the help of Luminesce Alliance, we've built tools that have changed practice and generated the evidence that this type of analysis matters,' he says.

Working with its partners and funded by Luminesce Alliance, the team has developed tools that allow tumour genome sequencing in a fraction of the time and cost.

Analysing whole genome sequence data requires vast amounts of computing resources which used to cost big dollars. Since receiving the Luminesce Alliance support in 2019, the group has substantially reduced the cost of analysis to approximately $100, reduced the time it takes to analyse the data from 48 to 18 hours, and reduced the footprint of the raw data to quarter of its original size. All these innovations have enabled the team to scale up the analysis capacity to every child with cancer in Australia, while halving the overall time that it takes for a patient to receive a personalised molecular report.

Further efficiencies have been achieved by using cloud computing through the Equinix Data Centre. While it may only take 18 hours to analyse the data, in reality more than 5,000 hours of computing are performed in parallel by renting dozens of different cloud computers for short periods of time.

The team is also pushing the boundaries of data analytics by investigating the use of RNA sequencing and liquid biopsies in precision medicine.

A/Prof Cowley would like to refine the computational tools even further so they can be used on any cloud computing platform by anyone in the world.

This will ultimately result in swifter diagnosis, more targeted treatments, and cures for children with cancer and rare genetic diseases.

Cutting-edge research using liquid biopsies

> **With this funding, we will start to make sense of tumours at multiple points in time. We think this could transform the field by creating a non-invasive test.**

Tumour whole genome sequencing can provide invaluable information at a snapshot in time, but because it requires an invasive surgery to take a sample of tumour, it can't be used to measure progress of treatment over time.

Cancer is currently monitored by scans or changes in patients' symptoms. Cancer doctors told us they needed a better way of telling whether treatment is working.

With Luminesce Alliance funding, A/Prof Cowley and his team at the Children's Cancer Institute are investigating whether they can use a new method to gather the DNA they need for analysis, as often as they need it – through liquid biopsies.

Liquid biopsies look for cancer cells or small pieces of DNA shed into the patient's bodily fluids, such as blood or urine.

The team is working on a blood test that can measure the presence of tumour down to one in a million fragments of DNA.

That will mean it will be possible to quantitively track how treatment such as surgery, chemotherapy or radiation therapy changes a tumour's DNA, whether the cancer is spreading, and whether it's possible to predict these changes.

In other words, it will provide definitive proof whether the treatment is working.

A/Prof Cowley says researchers usually do a single biopsy of the tumour, study the genome, and try to work out the diagnosis and the best treatment plan. 'But we know some children relapse, even with what we think is the right therapy, and we want to understand why, and change treatments as soon as we know they aren't working, before waiting for the patient to get sick,' he says.

'With this funding, we will start to make sense of tumours at multiple points in time. We think this could transform the field by creating a non-invasive test.'

Using big data to shine a light on children's conditions

– **Prof Natasha Nassar**
Financial Markets Foundation for Children Chair in Translational Childhood Medicine, NHMRC Investigator Fellow at the Children's Hospital at Westmead Clinical School, The University of Sydney.

This platform has shown how data linkage can be a valuable way to understand more about rare childhood diseases and cancers.

When a child is diagnosed with a very rare disease or cancer, often little is known about their long-term outcomes and it's difficult for doctors to confidently explain to families what to expect.

Tracking the progression and outcomes of rare diseases is usually done through studying and observing patients, in hospital and clinical patient studies, or by setting up registries to collect patient information.

The Kids-Link Data Enabling Platform has shown that this can be achieved in a different way by using data that have already been collected and linking datasets on all children in NSW who have experienced a condition over the past 20 years.

Project Lead Prof Natasha Nassar, Chair in Translational Childhood Medicine at The University of Sydney, says data linkage can help to understand the number of patients affected by a specific condition, survival rates, the causes and the natural history of a disease.

'Rather than needing a registry, we've show we can actually use what's already collected to identify children with certain diseases and then look at the long-term impacts of their condition on their health, health service use or on education,' Prof Nassar says.

'Our work is helping clinicians understand the disease, but also helping them educate their patients on what they're up against.'

Data linkage de-identifies each patient then combines the data that are routinely collected on them throughout their lives.

For example, datasets might include hospital admissions, emergency department attendance, medication use, school outcomes such as NAPLAN scores, and death registration.

The insights add another dimension to medical research. They can be used to understand causes of disease and evaluate the impact of treatments in the long term. They provide invaluable information for clinicians and families and can support advocacy for rare disease.

The platform has already shown it can use linked data from the Ministry of Health to quantify congenital heart disease in NSW. It has leveraged the initial investment from Luminesce Alliance to receive funding from Cancer Australia and the Medical Research Future Fund to scale a study on children's cancer outcomes nationally.

The aim is to build capacity to look at many more rare diseases and cancers.

Our work is helping clinicians understand the disease, but also helping them educate their patients on what they're up against.

PATIENT STORY

Scout's story

Being part of the ZERO program has been a godsend for Scout and her family.

Scout was born into a family of four. Mum Edwina says that everything about her pregnancy was normal. Then some worrying signs began to appear.

'I was holding her and I noticed there were movements I hadn't seen before,' Edwina says. 'It wasn't newborn jitters; it was like she was having a seizure.'

Scout was moved into the newborn intensive care unit where an x-ray was done, and her parents were informed that there had been a bleed in her brain, indicating she'd had a stroke.

About a week later, Scout's Dad Sean came home from work and asked Edwina what was going on with Scout's head. 'It just looked different,' he says. 'It looked quite swollen.'

After a CT scan and an MRI, Edwina and Sean were told their baby had a tumour and needed surgery to relieve pressure on her brain. Pathology tests revealed that Scout had a type of brain cancer known as a high-grade glioma, for which the standard treatment is chemotherapy.

> **When your child is sick, you lose all hope. And it's this research, ZERO, that gives you that little bit of hope to hold onto.**

Meanwhile, Scout was enrolled on the ZERO Program. A sample of her tumour was sent off for analysis by the Computational Biology Research Group supported by Luminesce Alliance. This team, the largest of its kind in Australia, can process vast amounts of molecular data much faster, allowing informed treatment recommendations in real time for children with cancer such as Scout.

The ZERO results confirmed that Scout's cancer was a high-grade glioma with a gene mutation known as an ALK fusion. This meant that a targeted therapy called an ALK inhibitor could potentially be used to treat it.

The information proved a godsend, as scans revealed that seven months of standard chemotherapy had failed to stop Scout's tumour from growing.

When the ZERO team tested Scout's tumour in the lab, they found it was extremely sensitive to an ALK inhibitor called alectinib. Scout now had an exciting new treatment option.

She began receiving the new drug in November 2023. In January 2024, scans showed her tumour had shrunk by 30%. Then a second scan in March revealed it was stable.

Just two weeks into the new treatment, Scout's demeanour changed noticeably.

'It was like a switch,' Sean says. 'From stopping chemo to starting the trial, it was like she was a completely different child. She was more active, more vocal, everything changed. And that was because of this treatment.

'When your child is sick, you lose all hope. And it's this research, ZERO, that gives you that little bit of hope to hold onto. When you've got none, that little bit means a lot.'

Unlocking the power of clinical informatics to predict health outcomes

- **Prof Tom Snelling**
School of Public Health, The University of Sydney; Professor of Infectious Diseases; Clinical Lead, Learning Health Unit, Sydney Children's Hospitals Network

Luminesce Alliance is investing in clinical informatics, a fast-growing specialty around the world that analyses electronic medical records data to look for patterns, and then predict the best course of action.

There's huge potential in the wealth of medical information being collected by our hospitals every day in the form of electronic medical records.

The Luminesce Alliance Data Enabling Platform's Clinical Data Analytics team is working out how to tap that resource to improve care.

For example, if a child comes to hospital with a fever, clinical informatics could work out the probability that the child has a bacterial versus a viral infection, the benefit of additional testing, and recommend which antibiotics to prescribe before culture results are available. These decisions are all currently made based on clinicians' level of knowledge and experience.

But the power of clinical informatics is only as good as the quality of the data that's collected. Like in almost every hospital in the world, the data captured in Australia's electronic medical records can't be used in its current state.

The way the electronic medical records (eMR) are set up, clinicians don't always enter the data in a standardised way. For example, information about a patient's blood pressure might be entered in the middle of an unstructured slab of text rather than in a dedicated field; often the data of interest are missing, entered incorrectly, or are out of date.

Another problem is that hospitals use a range of different 'languages' for their eMRs, meaning one hospital's data system can't easily talk to another.

The Clinical Data Analytics team is researching how to organise electronic data in a way that will make it easier for clinicians and researchers to use it, make sense of it, and to learn from it.

Clinical Lead Learning Health Unit at Sydney Children's Hospitals Network, Prof Tom Snelling, says the data in the eMR are an enormous untapped resource for learning about how to improve the quality and the safety of care.

'Our work is really about improving the quality of the data that's being entered and then organising and assembling it in a way that makes it a useful available asset for clinicians and researchers,' he says.

The idea is to transform electronic data into a standardised structure, translating it into a common language that can be used to communicate with other hospitals across Australia and internationally.

Ultimately, the aim is that data will be collected routinely at every stage of the patient journey, analysed by advanced tools like AI, and fed back to clinicians in emergency and on the wards.

Precision Therapy Enabling Platform

Precision therapy has the potential to transform the lives of children suffering from rare genetic diseases, cancer and neurodevelopment diseases by offering potential cures.

NSW is the national leader in paediatric disease research and coordinated clinical trials networks. The Platform enhances these capabilities by bringing together a uniquely skilled workforce to create a pipeline platform that bridges the gap between disease biology and the development for new drug candidates for paediatric diseases.

The Platform initiates transformative phase I and phase II clinical trials to target diseases across cancer, rare diseases such as liver diseases, blinding eye diseases and neurodevelopmental disorders, and develop policies and procedures to enable clinical trials to be translated into clinical care.

Enabling the delivery of new advanced therapeutics for kids

- **Adjunct A/Prof Paula Bray**
Director of Research, Sydney Children's Hospitals Network

This program of work is helping to prepare the NSW Health hospital system for the upcoming avalanche of new advanced therapeutics for kids.

Advanced therapeutics such as gene and cell therapy hold immense hope for patients – but they're also highly complex and it's difficult to bring them to the paediatric patients who need them.

Even if we have the funding and expertise to run a clinical trial, we still need to navigate numerous regulatory and ethical approval processes. These are important, but they take time.

We also need to facilitate systems and culture in our hospitals so advanced therapeutics can be embedded in clinical care. Healthcare professionals, including medical, nursing, pharmacy and allied health, require education and training in this new therapeutic landscape. Also, families need support to make difficult decisions, often at times when they're already experiencing anxiety and grief about a serious diagnosis.

This crucial work is enabled and expedited by extensive resourcing that would not readily be available in a busy hospital system. The Kids Advanced Therapeutics (KAT) Enabling Platform is figuring out how to get the system ready to provide these treatments to kids.

Adjunct A/Prof Paula Bray, Director of Research at The Sydney Children's Hospitals Network, says advanced therapeutics offer an incredible opportunity for children and young people with irretractable conditions.

'But it's also quite a different way of managing how we care for and deliver treatments,' she says.

'We need to think about so many things, from getting the correct molecular diagnosis through to genetic counselling and then setting up the wards so we can be delivering these complex interventions.'

The KAT program supports scientists and clinicians from their work in the lab through to the hospital wards. It is a truly bench-to-bedside approach. It provides start-up services for clinical trials, offers regulatory support and patient advocacy, nurtures partnerships and collaboration, ensures health system readiness, identifies infrastructure needs, and provides clinician education and engagement.

The impact of this program is nationally and internationally recognised and has led to more complex clinical trials being offered in NSW.

One day, it's hoped NSW will have developed capabilities, systems and processes to deliver advanced therapeutics for a wide range of different conditions and diseases, and that this revolutionary medicine becomes business as usual in paediatric hospitals.

PATIENT STORY

Abby's story

In a major advancement for personalised medicine, The Children's Hospital at Westmead has launched a world-first clinical trial investigating the use of phage therapy to treat a chronic bacterial infection in children with cystic fibrosis (CF).

Twelve-year-old Abby, from Lightning Ridge in outback NSW, was the first patient to be enrolled in the trial, which will use bacteria-eliminating viral treatments called bacteriophages (phages) to treat *pseudomonas aeruginosa* infection.

Pseudomonas aeruginosa is a common bacteria that are found in places such as showers and swimming pools and ordinarily has no lasting impact for healthy people. However, those living with CF are at greater risk due to the predisposition of their lungs to infection.

Abby is among the one in four CF patients impacted, after contracting the infection in 2017.

'It feels like you can't really breathe as much as normal, and your lungs feel really tight,' Abby says.

Once established, *pseudomonas aeruginosa* develop a unique biofilm, which acts as a barrier against the immune system and antibiotics.

> **It feels like you can't really breathe as much as normal, and your lungs feel really tight.**

Currently, the only available treatment for the infection is prolonged and repeated courses of strong antibiotics, which can lead to hearing impairment and kidney disease, and is not always effective in treating the infection.

The new trial, funded by Cure4 Cystic Fibrosis (Cure4CF) in collaboration with the Sydney Children's Hospitals Foundation, will aim to use phage therapy to directly target the infection without these side effects. It is the first major step in demonstrating the suitability of phages as a routine treatment.

'Phages are specific and specialised viruses that can be exactly matched to eliminate bacteria without harming human cells,' says Dr Jagdev Singh, trial lead and Paediatric Respiratory and Sleep Consultant at The Children's Hospital at Westmead.

The phages will be manufactured locally at the Westmead Institute for Medical Research, part of the Westmead Health Precinct.

Dr Singh says that if the project is successful, it could open the door for further research and more advanced studies in phase two and three trials and could offer a potentially lifesaving treatment for children with CF, like Abby.

Phase one of the Cure4CF personalised phage treatment of *pseudomonas aeruginosa* for children with CF clinical trial will involve about 10 children. If successful, the trial will expand nationally and internationally, before furthering the treatment to target other bacteria that cause lung damage in patients with difficult to treat lung infections.

Luminesce Alliance supports the infrastructure that enables delivery of such clinical trials.

World-first trial for kids with Duchenne muscular dystrophy

Three boys in NSW became the first in the world to receive a new gene replacement therapy for Duchenne muscular dystrophy in a trial that had only 10 spots internationally.

The support of the Kids Advanced Therapeutics (KAT) Enabling Platform means NSW is a highly attractive site for complex clinical trials because we have clinical capacity, dedicated start-up support, and provide rapid evaluation.

Dr Michelle Lorentzos, Advanced Therapeutics Medical Lead at The Sydney Children's Hospitals Network, says the KAT Enabling Platform supports her to deliver innovative clinical trials to patients.

'Various sponsors or industry players often propose these clinical trials to us, but they're still quite high risk for the patients and they're quite resource intensive,' she says.

'At the moment, if a child accesses a gene therapy clinical trial and that trial turns out to be ineffective, then that child has no further opportunity to be on any other clinical trial in the future.'

Dr Lorentzos says she knew little about gene therapy when she finished her training as a neurologist.

'I was able to access the resources and expertise facilitated by the KAT program to safely and effectively deliver gene therapy trials to patients across NSW,' she says.

'Now I am working within the KAT program to support doctors across other areas of medicine deliver these complex trials to their patients. So, the program is also developing capacity and knowledge in the paediatric profession.'

As part of this, the KAT program developed a clinical trial evaluation flying squad that brings together everyone with the necessary expertise to look at governance, ethics and the medical data to decide whether a trial is suitable for a patient.

'It means we clinicians are able to use a peer-review process to select the best possible trials for our patients,' says Dr Lorentzos.

'The KAT program meets a need that I hear from families all the time in clinic – how can we make this happen?'

I was able to access the resources and expertise facilitated by the KAT program to safely and effectively deliver gene therapy trials to patients across NSW.

– **Dr Michelle Lorentzos**
Advanced Therapeutics Medical Lead,
Sydney Children's Hospitals Network

Australia's only drug discovery and development capability for kids

Working with colleagues across Luminesce Alliance, the THerapeutic INnovations for Kids (THINK) is discovering new treatments for paediatric cancer, rare diseases and neurodevelopmental disorders.

With little investment in paediatric pharmaceuticals, THerapeutic INnovations for Kids (THINK) is the only group in Australia focused on developing new drugs specially for children.

Based at the Children's Cancer Institute, THINK brings together a group of data analysts, computational experts, biologists, medicinal chemists and pharmacologists to mine genomic data for what's gone wrong in cancer, and then develop new molecules that might change that biological process.

Prof Ian Street, Director of THINK, Children's Cancer Institute, says there are lots of biological differences between childhood and adult cancers, but most medicines used for childhood cancers are first developed for adults.

'We want to turn that process on its head and find a drug for childhood cancers first, and then develop it to the point we can run a paediatric clinical trial.'

THINK provides an end-to-end drug discovery pipeline – from genomic sequencing to identifying possible drug targets using computational biology, understanding their biological function, testing them with hundreds of thousands of molecules to see if any will stop the process, and then developing successful compounds into pharmaceuticals to be tested on patients in clinical trials.

A/Prof Greg Arndt, THINK's Head of Drug Discovery Biology, says this involves a massive multidisciplinary team.

'We've set up quite an extensive computational system and then we have biologists, medicinal chemists and pharmacologists all built into the THINK program so we're in a position to actually design these new medicines,' says A/Prof Arndt, who is also Conjoint A/Prof, School of Clinical Medicine, UNSW Sydney.

The first projects are already passing through the pipeline with support from Luminesce Alliance, including a promising new treatment for the childhood cancer neuroblastoma.

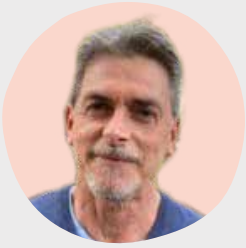
Children's Cancer Institute researchers have identified a possible treatment target for neuroblastoma – a protein called METTL5 that is linked strongly to poor survival in children with this cancer.

First, a key researcher at Children's Cancer Institute studied the protein to understand its role in the disease. A/Prof Tao Liu found that knocking down the METTL5 protein caused the cancer to stop growing.

The THINK team then inserted the METTL5 gene into bacteria so they could grow a large quantity of the protein for testing. They used this to screen more than 300,000 compounds to see if any of them would block the protein's biological activity.

They found several promising compounds. These were then given to medicinal chemists to develop into possible pharmaceuticals. It's hoped that this will lead to a clinical trial of a new drug in NSW.

- **A/Prof Greg Arndt**
  Head of Drug Discovery Biology, THerapeutic INnovations for Kids, Children's Cancer Institute; Conjoint A/Prof, School of Clinical Medicine, UNSW Sydney



- **Prof Ian Street**
  Director, THerapeutic INnovations for Kids, Children's Cancer Institute

Psychosocial Enabling Platform

The Psychosocial Enabling Platform supports precision medicine studies, with an equity focus on priority populations, ensuring all patients and families' needs are met and that all children and young people benefit from precision medicine.

Applying a psychosocial lens to paediatric precision medicine ensures that the psychological, social and educational wellbeing of patients, their siblings, and their caregivers is not left behind with rapid advances in 'omics' technology and treatment-focused clinical research.

The platform has an equity focus on priority populations including Aboriginal and Torres Strait Islander children, children from culturally and linguistically diverse communities, children with lived experience of disability, children from rural and regional areas and/or those affected by socioeconomic disadvantage.

It aims to provide psychosocial resources for families, support education and schooling for children having paediatric precision medicine and their siblings, and enhance mental health in children and families accessing paediatric precision medicine. It also supports and educates healthcare professionals in delivering precision medicine.

Focusing on the things that matter most to families

- **Dr Kate Hetherington**
Research Fellow and Clinical Psychologist, Behavioural Sciences Unit, School of Clinical Medicine, UNSW Sydney and Sydney Children's Hospital, Randwick

- **Prof Claire Wakefield**
School of Clinical Medicine, UNSW Sydney, Executive Director, Behavioural Sciences Unit, Sydney Children's Hospital, Randwick

The Psychosocial Enabling Platform is making sure that patient and family wellbeing, including equitable access to health care, is addressed as we roll out our precision medicine treatments.

Precision medicine is a medical approach to disease prevention and treatment that incorporates an individual's genetic, environmental and lifestyle factors.

For children, it is a new frontier offering much promise for disease prevention and cure in the areas of paediatric cancers, rare diseases and neurodevelopmental disorders.

However, participating in precision medicine can be complex for families. Beyond the medical treatment, there are usually so many other things to consider – how to navigate the system, how to afford the costs of supporting a sick child, and how to address practical problems like getting to hospital and taking time off work.

As medical science advances rapidly and new treatments become more readily available, the Psychosocial Enabling Platform is making sure the psychological, social and educational wellbeing of patients, their siblings and their caregivers is not left behind.

It's the only research group worldwide studying how to address these needs alongside precision medicine, offering researchers specialised psychosocial and equity-focused support.

Lead investigator Dr Kate Hetherington says that as well as offering precision-guided therapy, it's important to address other issues in a family-centred, holistic way.

'It's about more than just offering the fancy new treatment,' says Dr Hetherington, Research Fellow and Clinical Psychologist, Behavioural Sciences Unit, School of Clinical Medicine, UNSW Sydney and Sydney Children's Hospital, Randwick.

'It's about understanding the needs of the whole family, communication, and support – all those soft processes that run alongside the hard science but have a huge impact in terms of quality of life and wellbeing, and that can impact the outcome of the therapy.'

The Psychosocial Enabling Platform offers expertise and resources for clinicians and researchers across Luminesce Alliance. For example, it advises on how to engage consumers meaningfully, how to manage distress in a clinical trial, and how to best support patients' educational and mental health needs.

To ensure treatment is provided equitably to everyone who needs it, the platform is offering expertise to the Providing Enhanced Access to Health Services (PEACH) project, which is strengthening outcomes for children across priority populations in NSW, and is supporting the EPIC-CP trial to meet the needs of families with children who have cerebral palsy.

The platform's work is creating a stir internationally and has also attracted the interest of clinicians and scientists in NSW, says Prof Claire Wakefield, a medical psychologist with the School of Clinical Medicine at UNSW Sydney and Executive Director, Behavioural Sciences Unit, Sydney Children's Hospital, Randwick.

'This is a remarkable platform that is supporting the next generation of professionals who care about psychosocial factors to do the best possible research that will then help them to advocate for families,' she says.

Social prescribing for children with cerebral palsy

Through the Psychosocial Enabling Platform, Luminesce Alliance is supporting Equitable Pathways and Integrated Care in Cerebral Palsy (EPIC-CP), a pilot study into a world-first social prescribing intervention co-designed for and by people with cerebral palsy.

Social prescribing involves health staff linking patients to support services to address the other areas of their lives that affect health outcomes, such as education, employment, housing and transport. It's an approach that has been championed and used for decades by Aboriginal Community Controlled Health Organisations.

EPIC-CP aims to identify and address the unmet social needs of children with cerebral palsy who are also living with disadvantage. EPIC-CP will systematically and sensitively link families with a 'Community Linker' (a trained non-medical staff member) and/or a resource pack to help them access the health, social and education services, with the aim of providing holistic, family-centred care to improve their quality of life and wellbeing.

Prof Sue Woolfenden, Professor of Community Paediatrics at The University of Sydney, says children with cerebral palsy and other disabilities tend to have more severe outcomes if their families are socioeconomically disadvantaged.

'In my experience, families often have a lot going on. They might have issues with housing, they might not have access to a car, or they're experiencing food insecurity,' says Prof Woolfenden, who is also Director of Community Paediatrics at Sydney Local Health District.

'That all means they don't necessarily have the capacity to follow through with their NDIS application, do their early intervention, or meet their therapeutic goals.'

EPIC-CP is supported by Luminesce Alliance, the Sydney Children's Hospitals Foundation and the Cerebral Palsy Alliance Research Foundation. It is recruiting more than 120 families of children with cerebral palsy at the three Paediatric Rehabilitation Services of the NSW Children's Hospitals.

The trial was co-designed with more than 200 participants and overseen by research advisers with lived experience of cerebral palsy.

In my experience, families often have a lot going on. They might have issues with housing, they might not have access to a car, or they're experiencing food insecurity.

- **Prof Sue Woolfenden**
  Director, Community Paediatrics Sydney Local Health District;
  Professor of Community Paediatrics, The University of Sydney

PATIENT STORY

Will's story

Will Pierce was just four days old when he had his first complex, catastrophic seizure. Then he had another. And another.

His parents, Kris and David, spent most of that first year in and out of hospital managing Will's condition while caring for his twin sister, Ella. They also noticed that his development was not keeping pace with his twin's. By nine months, Will had deteriorated to the point that he was sent home for end-of-life care.

Then, one day, Kris saw him smile. It gave her hope.

Despite his debilitating seizures, Will grew into a teenager who continued to manage the impacts of his conditions. When he was 14, some of his DNA stored in the United States from a research study years earlier was finally sequenced, and he was diagnosed with the rare genetic disease SCN2A-related disorder.

Now 22, Will is one of the oldest people in the world diagnosed with SCN2A so his future is unknown. He loves highland cattle, transport and bird watching. It's been a long road to get him to this point, says Kris.

'Having a child with a rare, complex condition is very isolating,' she says. 'His twin sister has had to witness her brother being rushed off in an ambulance countless times, and of course that's had ongoing implications for her.

> **Not many people see the work his extensive support team have to do to enable Will to have the quality of life he now enjoys or the impact on the broader family.**

Kris gave up work for about 15 years to care for Will full-time but has now rekindled her career – consulting to research institutes, industry and community groups to ensure quality consumer engagement drives priorities and guides decisions in health care.

Kris is Director of Consumer Engagement at Child UnLimited, an Australian network of researchers, clinicians, advocates and families working to improve the clinical care and quality of life of children, adolescents and young adults living with a chronic illness or disability.

This year, Child Unlimited announced a strategic partnership with the Luminesce Alliance Psychosocial Enabling Platform to ensure that consumers are guiding its research around precision medicine.

Kris says precision medicine is providing hope to families, but the treatments are so new that there are insufficient support systems around them.
'We can invest millions of dollars into cures, but we also need to support families and healthcare professionals now through developing models of care and support systems, particularly psychosocial supports,' she says.

'That's what really interests me in working with the Psychosocial Enabling Platform. I think it's really important for families to be seen.'

Health Systems Implementation and Economics Enabling Platform

The Health Systems Implementation and Economics Enabling Platform incorporates implementation research and health economics evaluation.

Implementation research helps evidence to be translated into practice. It makes sure treatments are accessible to everyone, informed by evidence, and suitable for different patients and in different contexts.

Health economics is a branch of economics concerned with issues of healthcare efficiency, effectiveness, value and behaviour. Health economics is important to make the case for new treatments and to support funding and regulation.

The platform will begin by evaluating a program focused on reducing inequality in priority populations. It has the potential to lead to decreased risk of hospitalisation, reduced hospital stays, increased clinic attendance, improved child health outcomes and decreased health expenditure.

Implementation framework enables the delivery of equitable health access for kids

Evidence generated by evaluating a bold innovation in Sydney has led to the rollout of this valuable program for children throughout NSW.

- **Prof Karen Zwi**
Paediatrician and Head of Community Child Health and Clinical Program Director for Priority Populations at Sydney Children's Hospital, Randwick

- **Prof Raghu Lingam**
Paediatric Population and Health Services Research, UNSW Sydney; Consultant Paediatrician. Sydney Children's Hospitals Network

There are hundreds of great ideas for changing the health service and ensuring equitable health access and outcomes for children. However, most of these initiatives never achieve what they set out to do because either they are not rolled out (implemented) properly or they are not evaluated and therefore not sustained.

Luminesce Alliance's Health Systems Implementation and Economics (HSIE) Enabling Platform seeks to change this. By embedding experts in implementation research, health economics and health services evaluation from the start of projects, this platform aims to boost the chances of implementation success. The team then evaluates the projects to gather evidence to see if they've had an impact on child health and have provided value for money – meaning they are more likely to be funded into the future.

HSIE Enabling Platform Lead Investigator Prof Raghu Lingam says the platform enables researchers and clinicians to take what they have learned from people on the ground and come up with innovative ways to improve their healthcare experience.

'We can then translate innovation back into real life system change on the ground,' says Prof Lingam, Consultant Paediatrician at The Sydney Children's Hospitals Network and Professor in Paediatric Population and Health Services Research at UNSW Sydney.

As an exemplar of this approach, Luminesce Alliance has funded the evaluation of the Providing Enhanced Access to Health Services (PEACH) project.

This three-year program is improving equity in health services for children and young people from priority populations including Aboriginal and Torres Strait Islander, culturally and linguistically diverse, refugee and asylum seekers, individuals with disabilities, and children in out-of-home care, all of whom tend to experience poorer health outcomes.

The HSIE Enabling Platform's evaluation of PEACH (referred to as PEACH-E) is assessing impact on health outcomes within these priority populations, exploring ways to better support staff in its implementation, and evaluating the program's cost-effectiveness.

The evaluation work already done has helped make the case for more funding. With a new grant applied for this year, PEACH aims to expand across NSW – all with a framework to make sure it's implemented properly and will be sustainable into the future.

Conjoint Prof Karen Zwi, HSIE Enabling Platform Lead Investigator, says the evaluation support has been invaluable to the success of PEACH.

'They've helped us gauge whether or not the implementation is going according to plan, and we've constantly shifted and changed so that implementation is optimised throughout,' says Prof Zwi, who is also Paediatrician and Head of Community Child Health and Clinical Program Director for Priority Populations at Sydney Children's Hospital, Randwick.

'The evaluation framework has enabled us to collect all the impact data right from the beginning – not only the number of kids and how many times they've been seen, but actually whether their health improved. And that informs the sustainability of the program.'

How Seaneen is changing the system

Seaneen Wallace is a proud Gungarri and Bundjalung woman who is improving the way health services are delivered to patients from priority populations.

She's working on the evaluation of the Providing Enhanced Access to Health Services (PEACH-E) project, which is improving equity for patients from Aboriginal and Torres Strait Islander, refugee and asylum-seeking and culturally and linguistically diverse backgrounds, and those living with a disability or who have experienced out-of-home care.

Funded by the NSW Ministry of Health, PEACH focuses on actively identifying these patients and recording them in hospitals' systems. The program then provides recommendations for early access to health services and enhances the care they receive, such as making sure families are followed up and linked to support workers. It also supports health staff to ensure cultural safety and equity for patients.

'The ultimate goal is to improve their health access and outcomes, because we know that they have poorer outcomes for many reasons,' says Seaneen who is Priority Populations Care Navigator, PEACH-E Project Co-ordinator, Diversity Health, Sydney Children's Hospitals Network.

'PEACH is looking at how we can provide the tailored, personalised, patient-centred care that they require. And those needs might be slightly different, depending on their background.'

Consulting with patients and carers is a key element of PEACH-E. The team has met repeatedly with more than 50 consumers to ask them about their experiences in the health system and what could be done better.

Some of the issues they identified have already been fixed in the redevelopment of both children's hospitals – like better signage in different languages, and a better layout with toilet doors that aren't too heavy for children living with disability.

Seaneen and the team have also consulted widely with health staff to find out better ways of creating change on the ground.

They discovered that staff found it difficult to find time for cultural safety training, so the team hired a cultural capability officer to deliver bespoke training at more flexible times. They've also changed the medical record system so it's easy to identify whether a child is from one or more priority populations, with prompts to link families to appropriate support services.

Seaneen, who started her career as a dietitian before moving into public health, says this work has enabled her to make changes to the system that she found frustrating as a clinician. She now plans to move onto a PhD related to Aboriginal health access.

She says she has been inspired by working with people like Karen Zwi, the HSIE Enabling Platform Lead Investigator, who uses her research skills as a leader of a clinical team in an organisation.

'I just see that as so beneficial, and it's definitely something where there's so much opportunity to make a difference in Aboriginal health.'

PEACH is looking at how we can provide the tailored, personalised, patient-centred care that they require. And those needs might be slightly different, depending on their background.

- **Seaneen Wallace**
  Priority Populations Care Navigator, PEACH-E Project Co-ordinator, Diversity Health Sydney Children's Hospitals Network

Looking forward

Precision medicine holds huge promise for transforming the outcomes of kids with rare genetic diseases, neurodevelopmental disorders and cancer.

Luminesce Alliance has established NSW as a national and international leader in paediatric precision medicine, and has given the children of our state access to world-class research and translation into the clinic.

Now it's time to integrate precision medicine into the health system.

We'll be working closely with NSW Health, our partners and collaborators to prepare the health system for precision medicine, create the enabling infrastructure researchers and clinicians need to realise its benefits, and make our world-leading advances available for children everywhere.

You can find out more about our work on our website.

luminesce.org.au

LUMINESCE Alliance

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The Sydney children's Hospitals Network

care, advocacy, research, education

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