



ANNUAL REPORT

2016-17

SickKids[®]

THE HOSPITAL FOR
SICK CHILDREN

Department of
Paediatrics



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MESSAGE FROM OUR CHAIR

THE HEART AND SOUL OF CHANGE IS 'CREATIVITY AND INNOVATION'.



Striking the right balance to make a difference in the lives of our patients and families is a daunting task. All of us involved in the care for children have a deeply rooted connection to improve on this care and we take this challenge seriously. But how do we inspire change to happen?

Our approach is simple. "Each one of us can make a difference. Together we can make change happen."

The Department of Paediatrics 2016–17 Annual Report showcases how we are transforming care and making a difference through our unique collaborations, limitless boundaries of creativity, and immeasurable leaps of faith to bring innovation to reality.

It was tempting to share with you the hundreds of unbelievable stories, people, and impact that collectively fueled the power

to achieve a year of change. Instead, we chose a few stories from each of our 17 Clinical Divisions and Medical Education Programs. I will let the stories tell you how the intersection of 'creativity and innovation' are transforming paediatric health care and changing health outcomes for our patients and families. The future of our children is looking brighter!

Ronald D. Cohn, M.D. FACMG

Professor and Chair,
 Department of Paediatrics University of Toronto
 Paediatrician-in-Chief, The Hospital for Sick Children
 R.S. McLaughlin Foundation Chair in Paediatrics
 Senior Scientist, The Hospital for Sick Children
 Professor, Department of Molecular Genetics,
 University of Toronto



The Department of Paediatrics Executive Committee members contribute strategically to advise the Paediatrician-in-Chief through a shared leadership and consensus model in areas of paediatric Research, Clinical Care, and Medical Education. Successful decisions through this model are achieved in part by a strong commitment

to a systems focus and adherence to strategic and operational priorities.

Membership: Dr. Ronald Cohn, Dr. Meredith Irwin, Chris Carew, Dr. Rayfel Schneider, Dr. Jeremy Friedman, and Dr. Mark Palmert (expected appointment October 2017). Not shown in this photo Dr. Rulan Parekh and Marilyn Monk.



IMPROVING DIAGNOSIS THROUGH RESEARCH AND INNOVATION

SOLVING A MEDICAL MYSTERY

Daniel Nevins-Selvadurai was three years old when he was admitted to SickKids with constant bleeding when he went to the washroom. When Staff Gastroenterologist and Senior Scientist Dr. Aleixo Muise saw Daniel in clinic, he quickly recognized the signs of inflammatory bowel disease (IBD). When IBD appears in very young patients there is usually a hereditary cause. But when Daniel was tested, he came up negative for the gene mutations known to cause IBD.

Daniel's situation became more severe and puzzling as he got older. Unlike most IBD patients, he developed unusual rashes and inflammation in his legs, ankles, feet, and blood vessels (vasculitis). He also had blood abnormalities like high white cell and low platelet counts. These symptoms suggested problems in Daniel's immune system. Daniel was referred to a number of SickKids clinical teams in Haematology/Oncology, Rheumatology, Immunology, Gastroenterology, Dermatology, and other specialties. They all did their best to address his painful symptoms, but none were able to tell Daniel and his family what was causing them.

“This research demonstrates how observations made in the clinic and the laboratory can complement each other to help us understand patient problems, advance basic knowledge, and translate research into new opportunities for improving care.”

In late 2014, Dr. Muise with other SickKids collaborators launched a major project to explore the genetic basis of IBD and similar diseases using advanced DNA sequencing techniques. “As we sequence the genomes of these rare patients, it is always exciting because we are uncovering novel mutations and identifying diseases that have never been studied before,” says Dr. Muise the principal investigator of this study.

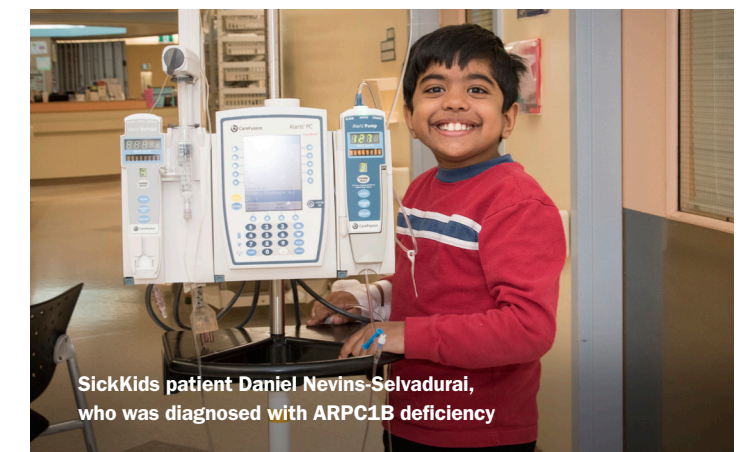
Daniel's unique symptoms made him an ideal candidate for this study, and after an extensive search, Dr. Muise and his team found a mutation in his DNA that no one had seen before. The result came as quite a surprise to the research team because the mutation was in ARPC1B. This gene produces a core protein of the Arp2/3 complex, which our cells need in order to change shape, move, divide, and perform other vital functions.

“At that time, most cell biologists would have told you that we cannot live without ARPC1B protein,” recalled the study's lead author Dr. Kahr, Staff Haematologist and Senior Scientist. “But when we examined Daniel's platelets we found that this protein was completely missing.”

The team subsequently discovered two other patients that were related to each other but not to Daniel, who had mutations that left them with very little ARPC1B protein. They had some of the same symptoms as Daniel, and like him they also had unusually small and oddly-shaped platelets. This abnormality had previously only been seen in patients with Wiskott-Aldrich syndrome, who often also have severe immune problems. When platelets from Wiskott-Aldrich syndrome patients are allowed to spread on a surface they form little discs, just like normal platelets. In contrast, Kahr's group observed that when platelets from the ARPC1B-deficient patients spread they sprouted bizarre spider-like tendrils.

“As a cell biologist and haematologist who treats children with platelet disorders, it was surprising to come up with these completely new insights into how platelets work,” says Dr. Kahr. “This research demonstrates how observations made in the clinic and the laboratory can complement each other to help us understand patient problems, advance basic knowledge, and translate research into new opportunities for improving care.”

Through this research which was subsequently published online in [Nature Communications](#) and international collaborations, a number of ARPC1B-deficient patients have been identified around the world. The SickKids team hopes their findings will lead to improved diagnosis and treatment for these patients. For example, the treatment of choice for children with Wiskott-Aldrich syndrome is a bone marrow transplant, and the SickKids team is working to determine if this might also be a suitable treatment for patients with ARPC1B deficiency.



SickKids patient Daniel Nevins-Selvadurai, who was diagnosed with ARPC1B deficiency

CITY'S DIVERSITY PROPELS DISCOVERY:

ETHNICITY MAY AFFECT THE HEALTH OF CHILDREN WITH KIDNEY DISEASE

From the city crowned to be the most diverse in the world, research on ethnic differences in children with nephrotic syndrome suggests that a child's ethnicity may influence not just the kidney disease's incidence, but ultimately its clinical outcomes.

The study, published in the [Clinical Journal of the American Society of Nephrology](#), found that children with South Asian roots are more frequently diagnosed with nephrotic syndrome than their European peers. With that, children of South Asian descent had significantly less complex clinical outcomes – including more complete remissions, fewer subsequent relapses, and a longer relapse-free period after initial steroid therapy. The study also found that East/Southeast Asian children were significantly less likely to be prescribed second-line agents such as cyclophosphamide compared with European children.

“Not only are we seeing more South Asian children with nephrotic syndrome than European children, but we found they respond differently to steroids with higher complete remission rates,” says the study's principal investigator, Dr. Rulan Parekh, Associate Chief of Clinical Research, Staff Physician in Nephrology and Senior Scientist. “Unravelling these ethnic differences is an important first step to determine if it's a common mechanism among all, or if there are unique traits between groups. Down the road, this knowledge may lead to the discovery of genetic or environmental factors that can account for these differences.”

Children with nephrotic syndrome experience edema, a type of swelling in the face, belly, hands, and other extremities after

an excessive amount of protein is filtered out of the blood and expelled through urine, due to the glomeruli's inability to filter waste products and fluids properly.

The longitudinal study identified and monitored a total cohort of 711 SickKids patients ranging in age from one to 18, who were diagnosed with and treated for nephrotic syndrome from 2001 to 2011. Analyses focused on the three largest ethnic groups – South Asians (33 per cent), Europeans (23 per cent), and East/Southeast Asians (10 per cent) – with the remaining accounting for other origins (33 per cent). All study participants were from the Census Metropolitan Area of Toronto.

Dr. Parekh notes that she decided to study ethnicity when she noticed a large incidence of nephrotic syndrome in Toronto children, something she never observed at other centres in the United States. Over a decade, the incidence changed from 1.99 to 4.71 per 100,000 children in Toronto, which she believes is because the general population's diversity has changed. The investigative group demonstrate that South Asian children have an incidence six times higher than those of European descent. Some of the key findings in the infographic below.

“Toronto offers the perfect snapshot to study ethnic differences in health. That is the uniqueness of studying diversity in such a multicultural hub,” says Dr. Parekh. “We could not do this research anywhere else.”

45% | 58%

South Asian and East/Southeast Asian children had 45 per cent and 58 per cent lower odds of developing frequent relapses of nephrotic syndrome compared to European children

26%

South Asian children were 26 per cent less likely to develop a first relapse compared to European children

35%

East/Southeast Asian children were 35 per cent less likely to develop a first relapse compared to European children

45% | 42% | 30%

The cumulative incidence at five years for use of cyclophosphamide among European, Southeast Asian and East/Southeast Asian children was 45 per cent, 42 per cent, and 30 per cent

50%

East/Southeast Asian children were 50 per cent less likely to be prescribed second-line agent cyclophosphamide compared to European children

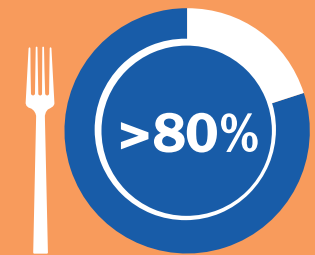


FOOD ALLERGIES AFFECT APPROXIMATELY 1 IN EVERY 20 CANADIAN CHILDREN



260

CHILDREN WITH SUSPECTED FOOD ALLERGIES UNDERGOING 'DE-LABELING'



OF CHILDREN CHALLENGED FOR FOOD OR DRUG ALLERGIES HAVE BEEN ABLE TO TOLERATE THE FOOD OR DRUG THEY PREVIOUSLY WERE LABELED AS ALLERGIC TO

'CHALLENGING' FOOD ALLERGIES

The Division of Immunology and Allergy has doubled the number of children with suspected food allergies undergoing 'de-labeling' to almost 260. Food allergies are an epidemic affecting approximately one in every 20 Canadian children. The constant fear from a potentially deadly reaction to food has a major impact on the quality of life of children and their families. However, it is now known that some children might 'outgrow' certain allergies to foods, while in other children the initial diagnosis may have been inaccurate. “In the past, we used to give kids an *Epipen* and advise them to avoid the food for the rest of their lives and that was it,” says Dr. Adelle Atkinson, Clinical Immunologist. “Our ultimate goal is to cure food allergies within the next 10 years, but on our way to achieving this goal, there are important milestones to recognize.”

One such milestone includes the results of the LEAP (Learning Early About Peanut Allergy) study in 2015 which challenged the earlier recommendations by which physicians previously advised the families of children at high risk of developing allergies. Previously, allergy prevention focused primarily on modifying maternal and lactation diets and avoiding potential allergenic foods in at-risk children. In fact, introducing certain foods in the first year of life has been shown to reduce the incidence of food allergies in certain situations. These findings are aligned with Clinical Practice Guidelines released in 2013 by the Canadian Society of Allergy and Clinical Immunology (CSACI) and US guidelines published by the National Institutes of Health and endorsed by CSACI.

Concurrently, while improving knowledge surrounding allergy prevention, the team continues to 'challenge' qualifying children

with the specific food that they are presumably allergic to. During these challenges, performed under close supervision in the Allergy Clinic, children eat increasing amounts of the food they were 'labeled' as allergic to. Results have shown that more than 80 per cent of children challenged in the clinic have been able to tolerate and eat the food they had avoided for many years, providing much needed relief to these children and their families.

This exercise is not only applicable to food allergies. A number of patients seen in the clinic are those with suspected allergies to antibiotics and biologics as well as other medications such as anesthetics and chemotherapy. These challenges have important implications on the type of treatment provided to patients both while at SickKids and within the community as misdiagnosis of an allergy to both essential and common treatments may lead to suboptimal patient outcomes. Moreover, antibiotic allergy de-labeling may improve antimicrobial stewardship measures as incorrect labeling is commonly associated with inappropriate antimicrobial prescribing and antimicrobial resistance. As such, the team has collaborated with the Antimicrobial Stewardship Committee to incorporate antibiotic allergy assessment into the ongoing stewardship work at SickKids.

As more and more families and colleagues learn of the success of de-labeling, an increasing number of children will be referred to the clinic and benefit from challenges. “Now there is hope that we can potentially cure/prevent allergies completely. It is a very exciting time in our field, because children and families have so many more options and so much to be hopeful about!”



**PROMOTING THE HIGHEST
QUALITY AND SAFEST
CARE FOR OUR PATIENTS**

SHIFT-CHANGE HANDOFF PROGRAM

RECOGNIZED FOR IMPROVING PATIENT SAFETY THROUGH STANDARDIZATION OF PROVIDER-TO-PROVIDER COMMUNICATION

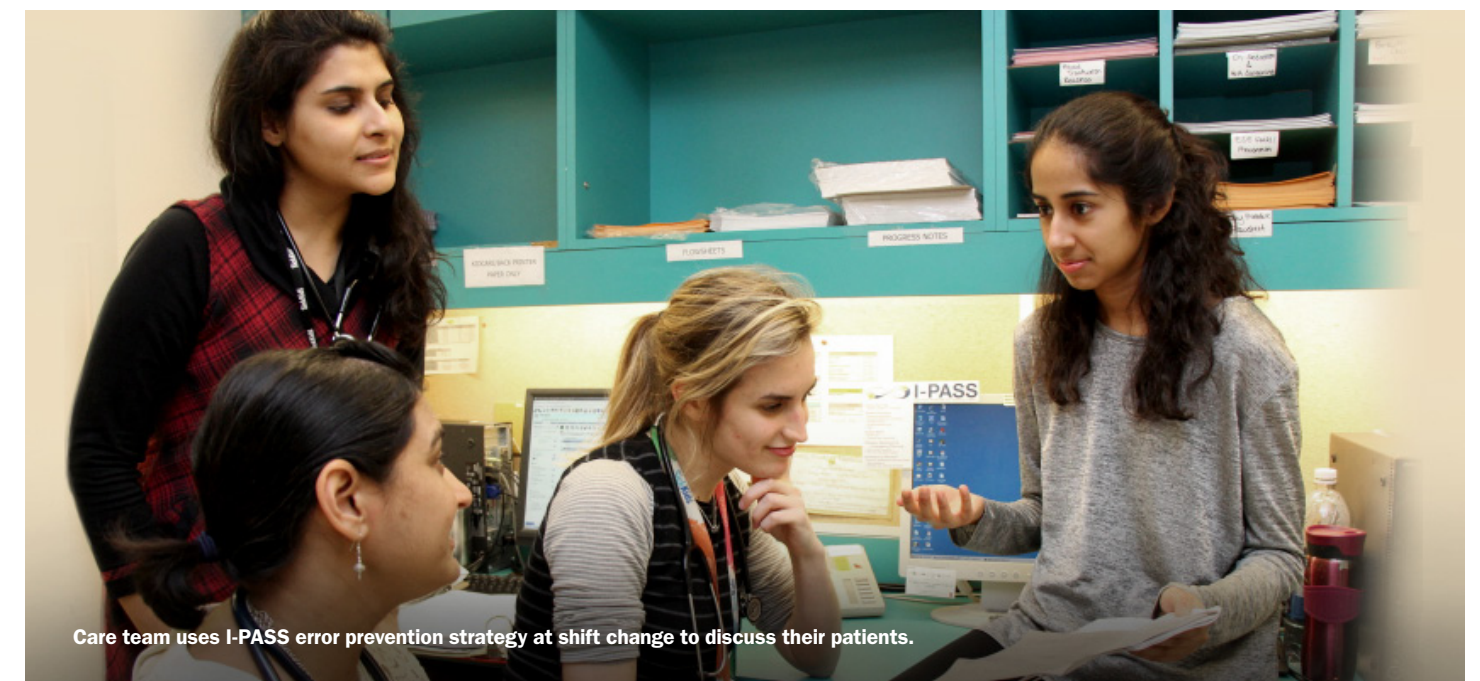
This year the I-PASS Study Group was recognized for excellence and leadership in patient safety with the John M. Eisenberg Patient Safety and Quality Award. The group was awarded in the category of “Innovation in Patient Safety and Quality at the National Level” and is being recognized for the international impact of this transformational communication program that brings standardized provider communication to handoffs of care. This award is the highest level of recognition from the National Quality Forum (NQF) and the Joint Commission in the United States and was presented at the NQF’s 2017 Annual Conference in spring 2017.

I-PASS (Illness severity, patient summary, action list, situational awareness and synthesis by receiver) is one part of a bundled intervention to promote reliable handover of a patient’s care from one health-care provider to another. SickKids was one of nine health care organizations who participated in the original study, which found harmful medical errors fell 30 per cent after implementation of the I-PASS handoff program. Since that study, I-PASS has been adapted and implemented in most units at SickKids, including surgical units, and at over 50 hospitals across the United States and Canada.

I-PASS handoff is one example of how clear, structured communication can significantly improve patient safety. While medical errors can occur as a result of several root causes,

miscommunication is a common theme in patient harm events in both at SickKids and in other hospitals. The expectation that all staff communicate in a clear and structured way is a core aspect of Caring Safely which represents SickKids’ commitment to eliminating preventable harm to patients and staff through all-staff education and a focus on improving SickKids’ safety culture.

Within the Division of Paediatric Medicine, a number of staff are closely involved with the ongoing work of the I-PASS Study Group. Dr. Trey Coffey, Staff Paediatrician and Medical Officer for Patient Safety, and Dr. Zia Bismilla, Staff Paediatrician, have assisted other hospitals with the implementation of I-PASS as mentors through the Society of Hospital Medicine Mentored Implementation Program. Kate Langrish, Clinical Director, Dr. Sanjay Mahant, Staff Paediatrician, and Dr. Carolyn Beck, Inpatient Medical Director, have also held formal roles. The team continues to champion the dissemination of the I-PASS handoff program across SickKids as well as contribute a number of related posters, manuscript submissions, studies, and publications. One recent study assessed the impact of structured family-centred communication during rounds on reported errors rates. The study, which resulted in an ancillary publication online in [JAMA Pediatrics](#), found that families provide unique information about hospital safety and the intervention had strong positive results on both safety reporting and the family experience.



Care team uses I-PASS error prevention strategy at shift change to discuss their patients.

OPTIMIZING THE CARE OF LONG-TERM VENTILATION PATIENTS

The Long-term Ventilation (LTV) Program, led by the Division of Respiratory Medicine, is dedicated to providing comprehensive consultation and ongoing management for children receiving long-term ventilation both at home, as well as those children who are at risk of requiring long-term ventilation in the future. The aim of the program is to optimize care of these children while at home and to support their families within the community.

The LTV Program was previously part of the Complex Respiratory Care Program at SickKids, but was established as its own program to provide more specialized and enhanced care to patients receiving or at risk of requiring long-term ventilation. The program has since expanded to a highly multidisciplinary team to provide care to and address the unique needs of this medically complex patient population.

Since its introduction, the program has both led and collaborated on several initiatives designed to enhance caregiver education, improve transition to home planning and care coordination with intensive care units including Holland Bloorview Kids Rehabilitation Hospital, and integrate care with community services including nursing at home and at school. Here's some of the ways how:

- Members of the LTV Program have worked in partnership with AboutKidsHealth to develop a [tracheostomy education manual](#) which was launched in 2017. The manual features a number of articles set to address the many questions families may have when learning that their child needs a tracheostomy tube. The manual also includes training materials which provide general knowledge to step-by-step guidance for areas such as

tracheostomy tube management, secretions and suctioning, stoma care, feeding, and emergency planning. The manual is accompanied by a map which outlines the major milestones families will face following the decision to proceed with long-term ventilation for their child to once the child is medically stable and resources are in place for home care.

- The LTV Program continues to facilitate the transition of patients to Holland Bloorview once medically stable and caregiver education sessions have started. As patients previously would have remained in the ICU during the eight-week caregiver training duration, this pathway has not only improved the transition and caregiver training experience for families but has also saved over 340 inpatient ICU days within the past three fiscal years since its introduction. The team also continues to work with West Park Healthcare Centre to transition patients from paediatric to adult care services. Both pathways are continuously improved through iterative feedback from patients and families.
- Led by the Learning Institute as well as the LTV and Complex Care Programs, Health Tech Junior was launched as a way to better standardize home care training within Ontario. Health Tech Junior runs workshops in caring for children using medical technology to teach and refresh community care nurses who care for patients using devices such as a tracheostomy, a ventilator, gastronomy tubes, and vascular access devices. The workshops, the first of their kind in Toronto were successfully piloted in October 2016. Leveraging the success of the current offerings, the team is working to apply the didactic and simulation-based training model to family caregiver training.



The LTV Program team from left to right: Dr. Aceel Alawadi, Joanna Polyviou NP, Dr. Jackie Chiang, Dr. Reshma Amin, Faiza Syed RRT, Tuyen Tran RRT, and Dr. Athari Almajed.



'WORK SMART' IN THE EMERGENCY DEPARTMENT

In Spring 2016, the Emergency Department formed a standing interdisciplinary working group in response to increasing patient visits. The aptly named 'Work Smart' Team was tasked

with developing and implementing a comprehensive strategy to ensure that safety and quality of care were not compromised by escalating volumes. Find out more below.



AN INTEGRATED NEWBORN CARE KIT TO SAVE NEWBORN LIVES IN PAKISTAN

Dr. Shaun Morris, Clinician-Scientist, Division of Infectious Diseases and Scientist, Centre for Global Child Health (C-GCH) along with C-GCH co-investigators including Drs. Lisa Pell, Diego Bassani, and Zulfiqar Bhutta and co-investigators at the Aga Khan University (AKU), Pakistan have recently completed a community-based, cluster randomized, controlled trial that enrolled over 5,000 pregnant women to assess the effectiveness of an integrated package of newborn interventions on newborn health outcomes in rural Punjab, Pakistan.

Worldwide, an estimated 2.7 million neonatal deaths occurred in 2015, accounting for nearly half of all under-five deaths. In Pakistan, more than 200,000 newborns die annually and neonatal mortality rates are higher than in any other South Asian country. The integrated newborn care kit (the iNCK) is low-tech, easy-to-use, and contains several evidence-based interventions that can fit into a single Ziploc bag—all for less than \$5 per kit. The iNCK components were selected based on evidence that they reduce or provide early identification of the most common causes of newborn death, including infection and complications related to premature birth and low birth weight, in some of the world's most at-risk and hard to reach populations. As the development of the growing brain can also be affected through the same insults that are major causes of mortality, reducing the number of these insults or detecting them sooner, may not only save lives but may also improve neurodevelopment. The iNCK was designed to be used primarily for home-based implementation by caregivers.

Contents of the iNCK include:

- A clean delivery kit to minimize infection at time of delivery.
- Chlorhexidine, which is applied to the umbilical stump and can reduce infections and mortality.
- An emollient to promote skin integrity, helping to reduce infection and prevent hypothermia.
- *ThermoSpot* to continuously monitor temperature and identify hypothermia and fever.
- A reflective infant blanket and reusable, instant heat pack to manage hypothermia.
- A handheld scale to identify low birth weight.

The iNCK was delivered to pregnant women by Lady Health Workers (LHW) who are local women trained to provide basic health education and interventions to their community. Compared to a control group who received the local standard of care, in the intervention group there was about a one-third reduction in infections of the umbilical cord (a predictor of newborn sepsis) and about a three-times greater identification of home born low birth weight babies by LHW. Overall there was not a significant difference in mortality between groups, however, in a post-hoc analysis, among iNCK recipients who were highly compliant (~30 per cent) in kit usage, there was about a 75 per cent reduction in mortality compared to a matched sub-group in the standard of care group. This study has demonstrated the potential to impact newborn mortality by delivering an intervention package directly to pregnant women through LHWs. Next steps include planning and implementing a Transition-to-Scale study in Pakistan and central Asia to better understand factors that optimize compliance.

IMPROVING HEALTH
OUTCOMES THROUGH
COLLABORATION



Dr. Shaun Morris provides education to pregnant women on the Integrated Newborn Care Kit in Rahim Yar Khan District, Punjab, Pakistan.



ASSESSING THE SAFETY AND EFFICACY OF IN-UTERO FETAL THERAPY

The Fetal Cardiac Program is one of the largest and most successful prenatal heart centres in the world. The program receives referrals from across Canada and is the only Canadian centre performing fetal cardiac interventions, in collaboration with maternal-fetal medicine specialists at Mount Sinai Hospital. Fetal cardiac interventions have been used to rescue fetuses with incipient heart failure and also to explore whether cardiac development and disease progression can be altered. Research is one of the foundations of the program and drives advances in medical care for babies with heart problems during pregnancy.

The CIHR-funded Fetal Atrial Flutter and Supraventricular Tachycardia (FAST) Therapy Trial is the first fetal-maternal prospective multi-centered randomized controlled trial (RCT) that addresses the knowledge gap of the efficacy and safety of specific transplacental drug regimens in suppressing fetal atrial flutter and supraventricular tachycardia (SVT). Although SVT, including fetal atrial flutter are the most common causes of in-utero fetal therapy, none of the medications used to date have been evaluated for their effects on the mother and baby in a RCT. As a result, in the absence of such evidence, there is no consensus for the optimal management of SVT. The study is led by Dr. Edgar Jaeggi, Staff Cardiologist and Fetal Cardiac Program Lead alongside collaborators from the trial's national coordinating centres in the US, UK, and the Netherlands.

The components of the FAST Therapy Trial include three prospective sub-studies to determine the efficacy and safety of commonly used transplacental drug regimens used for suppressing fetal atrial flutter with or without hydrops – the abnormal collection of fluid in fetal organ spaces. The study also includes the opportunity to enroll non-randomized subjects into a prospective observational cohort study ([FAST Registry](#)). This area of the FAST Therapy Trial aims to document the treatment and outcomes of the entire atrial flutter and SVT patient group, including those receiving alternate medication treatment or where the baby is delivered for postnatal cardioversion, in order to analyze and compare management options based on outcomes. The team anticipates that earlier and more effective cardioversion will be significantly associated with higher rates of normal term deliveries and less perinatal mortality, morbidity, and resource utilization due to shorter hospitalization.

The FAST Therapy Trial is the largest clinical trial led by a SickKids' investigator to date. The trial is currently active at SickKids and Mount Sinai Hospital in Ontario with 14 subjects randomized to date and is preparing to start at 30 other sites across Canada, the US, UK, the Netherlands, and Germany amounting to over 6,000 participants in total. Furthermore, more than 50 sites have signed up for participation in the FAST Registry.

CONGENITAL HEART DISEASE:

FROM SURVIVING TO THRIVING

The multidisciplinary teams in Neurology, Cardiology, Cardiac Intensive Care, Psychology, and Neonatal Follow-Up, have launched the new Cardiac Neurodevelopment (CND) Program. This SickKids initiative is based on the premise that promoting optimal developmental outcomes for children with congenital heart disease (CHD) requires attention from before the baby is born, throughout their hospital stay, and beyond.

Congenital heart disease is one of the most common birth defects affecting about one in 100 newborns each year. Thanks to medical advances within the last decade, the outcomes for neonates and children treated surgically for CHD has improved greatly with many of these individuals leading relatively healthy lives. These children, however, are more likely than other children to have brain injury and abnormal brain development causing cognitive, behavioral, or learning delays and challenges. Through the CND Program the focus is now to ensure that children with CHD thrive in their development.

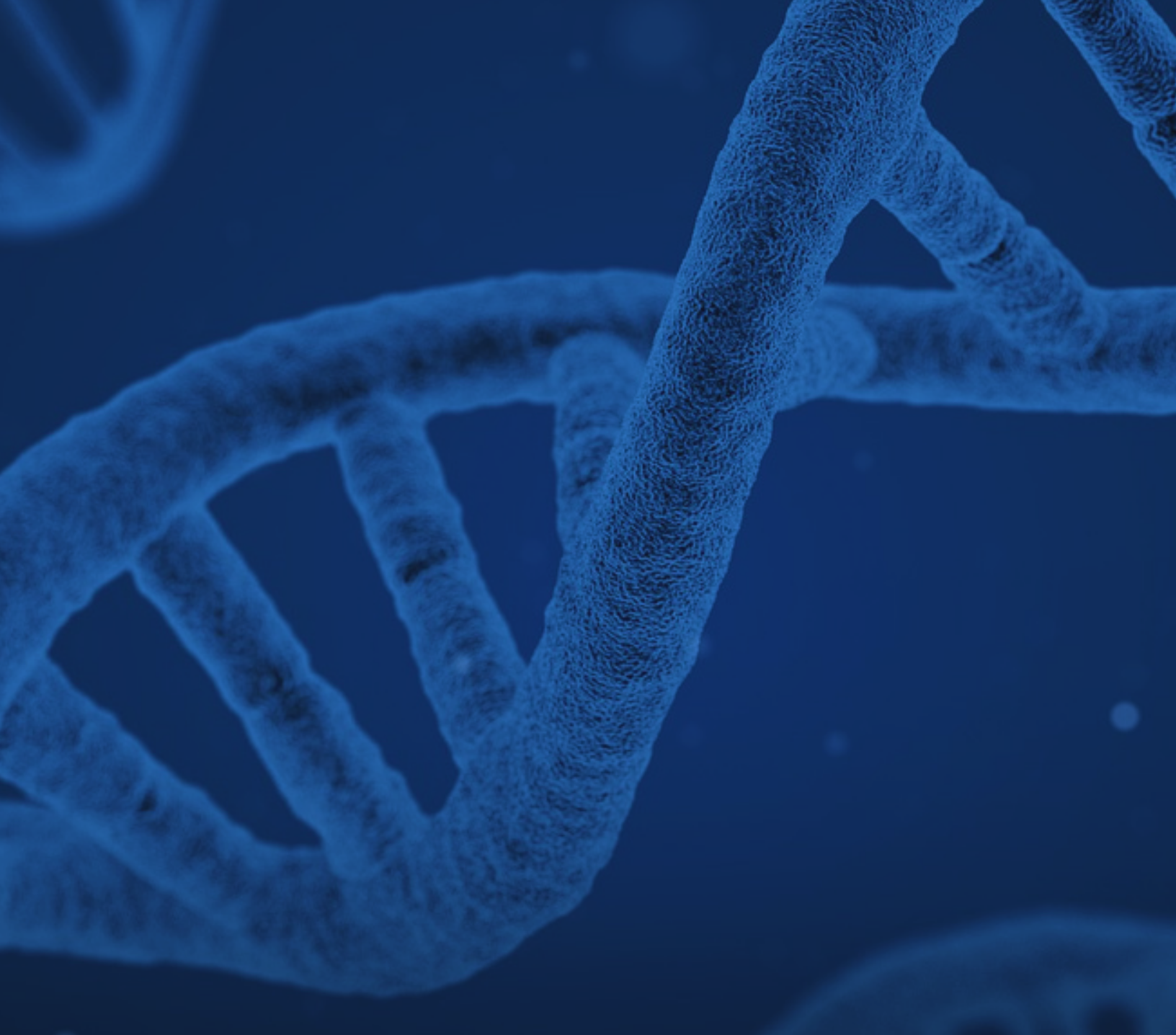
Research led by members of the CND Program has shown that cardiac surgery is not the only cause of brain injury in babies with CHD; heart disease itself is also the problem. As a result

of these findings, in a clinical initiative led by Dr. Vann Chau, Staff Neurologist, the program actively monitors this at-risk population - neonates born with CHD - through brain MRI scans and neurology assessments before and after surgery. In addition, these neonates are followed to 18 months of age through the Neonatal Follow-Up Program to assess motor-skills, social development, language, and learning ability to determine if the child is developing normally.

As the period before surgical repair is critical for brain development, the CND Program Leads, Drs. Mike Seed, Staff Cardiologist/Cardiac Radiologist and newly appointed Division Head, Cardiology and Steven Miller, Staff Neurologist and Division Head, Neurology are piloting a trial to put mothers of babies identified with high-risk CHD on supplementary inhaled oxygen during the third trimester to promote brain development for which adequate oxygen is key. As this intervention is a safe and feasible method of improving oxygenation of the fetal brain, the results of the trial will be used to evaluate whether supplementing mothers with oxygen helps brain development in fetuses with CHD. This trial is supported by the [CHILD-BRIGHT](#) Network; a \$25 million national patient-oriented research initiative co-led by Dr. Miller.



Members of the Cardiac Neurodevelopment Program.



TRANSFORMING CARE THROUGH PRECISION MEDICINE

NEW KICS CANCER SEQUENCING PROGRAM: COLLABORATION AND INNOVATION LEADING TO MORE TARGETED THERAPIES

The SickKids Cancer Sequencing Program (KiCS) is a collaboration between the Division of Haematology/Oncology and the Department of Paediatric Laboratory Medicine which is implementing clinical-grade genome sequencing for cancer patients at SickKids.

Led by Dr. David Malkin, Senior Oncologist and Director of the Cancer Genetics Program, Dr. Adam Shlien, Associate Director of Translational Genomics, and Dr. Gino Somers, Head of Pathology, this exciting three-year clinical research project brings together experts in haematology/oncology, pathology, bioinformatics, genetics, genomic research, and genetic counselling. The project, which launched in 2016, uses Next Generation Sequencing (NGS) to determine the genetic profiles of tumours, which will help clinicians identify the best individualized treatment options for children with cancer, including patients with the most challenging cancers at diagnosis and those who have experienced a relapse. Precise diagnosis and genetic stratification of these children's own tumours can inform decisions about their care, identify patients who are genetically predisposed to cancer, and identify potential avenues for innovative experimental therapies.

These same sequencing efforts will also advance cancer research by providing new knowledge about the molecular profile of cancers. With this information, researchers can study how better to manipulate and kill cancer cells or stop them from growing and spreading. These findings will have the potential to lead to even further improved health outcomes for children and the adults they will become.

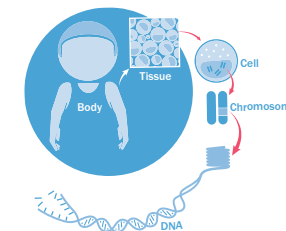
"In paediatric oncology, we are constantly looking to develop and bring better treatments to children with cancer and at the same time reduce toxicity and morbidity," says Dr. Malkin. "Tumour and paired normal tissue/blood sequencing has the potential to revolutionize how we care for our patients."

With support from the Garron Family Cancer Centre and the Great Cycle Challenge Canada, KiCS is now providing sequencing to patients across Ontario as well as nationally and internationally. In addition, clinically validated diagnostic assays using *NanoString* and *RainDance* droplet PCR technology are currently being developed and implemented to provide rapid diagnosis based on genetic alterations.

▶ [Click here for more information](#)

Cells and DNA

Our bodies are made up of cells, which contain our DNA. DNA (also known as the genome), packaged in structures called chromosomes, is like a large book that has all the instructions for how we grow and how our body functions. RNA, a messenger sequence made from the DNA, is used to carry out the instructions of the DNA. This information is coded in the form of genes. There are about 25,000 genes in each cell of our body. Genes define things like the colour of our hair and our eyes, but changes in our genes can cause health problems, including cancer. We do not always know why these changes occur; sometimes the change is passed down in a family and sometimes the gene change just happens by chance.



Cancer Genetics

Cancers develop when a number of new, harmful changes, or "variants" – also called mutations – occur in a cell's DNA and prevent important genes from working properly. These mutations allow cells to multiply and spread unchecked. A cancer's mutations can serve as a "fingerprint" to follow its progress, and can provide important information about how to specifically treat it. Researchers have learned that different tumours have different mutations, even if the cancer started in the same organ. There is also evidence that a recurrent cancer (a cancer that comes back after treatment) has different mutations than the original cancer.

Most of the time, mutations that lead to cancer development occur by chance. Sometimes, cancers develop in individuals who have an underlying "predisposition" for tumour development. This means that there may be a genetic variant that they were born with, or that they inherited, that makes them more susceptible to getting cancer.

What the KiCS study is about

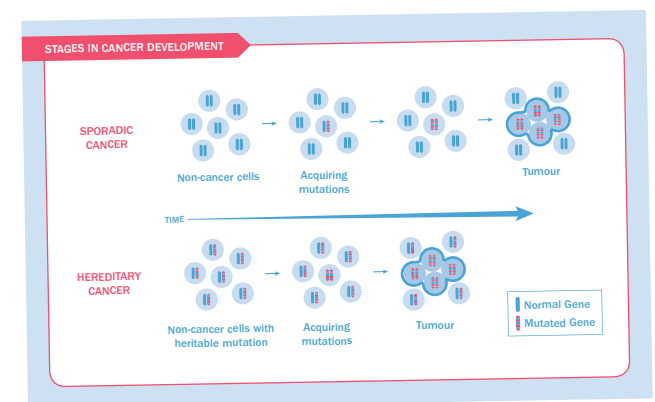
KiCS is a research study that is being done at SickKids. Current genetic testing typically involves examining one gene or a few genes at a time. A new kind of genetic test, called next generation sequencing (NGS), allows us to test thousands of genes at the same time. We want to know if this new test can help us:

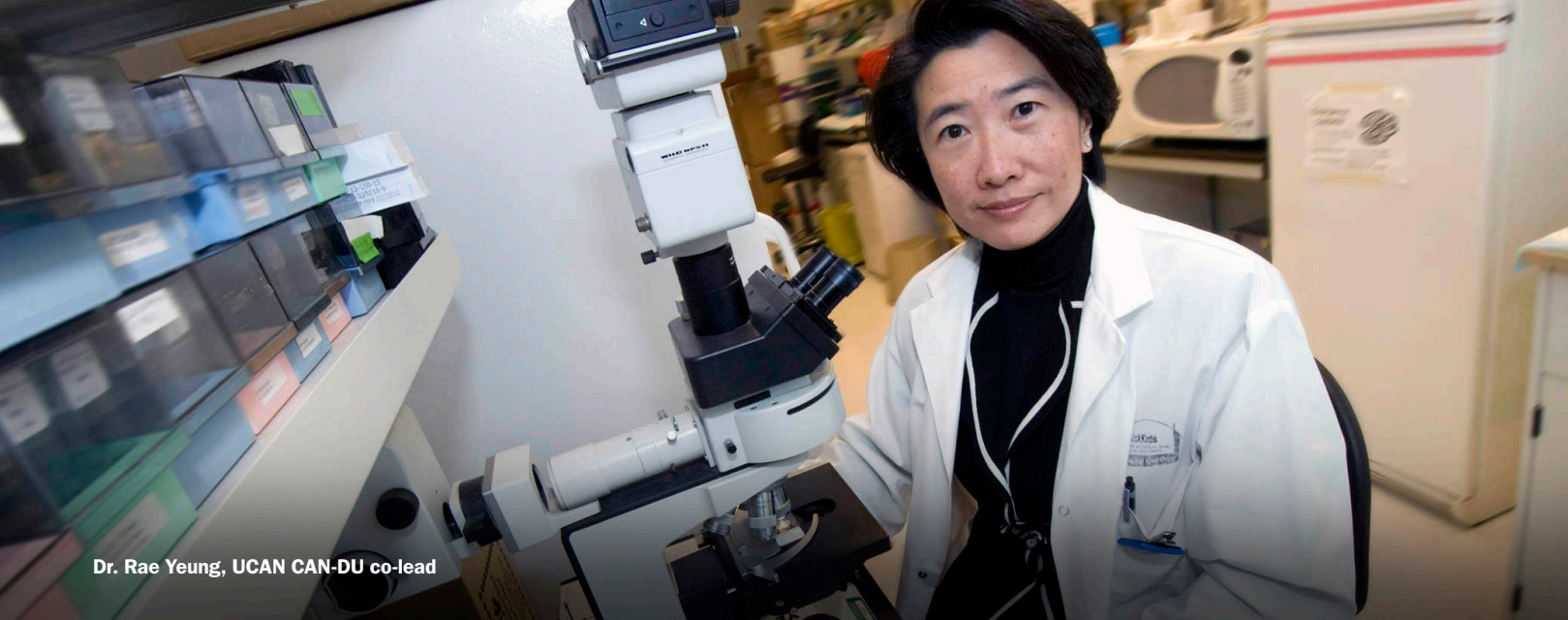
1. Better characterize your child's tumour and identify its unique "fingerprint"

2. Use this information to identify possible specific medications/treatment options for your child's tumour
3. Use this information to follow the tumour's response to treatment
4. Gain information about your child's prognosis
5. Understand the cause of your child's cancer

Samples

DNA will be isolated from both cancer cells and normal, healthy tissue sample from the same patient. The healthy cells give the scientists a reference DNA sequence to which they can compare genetic changes in the patient's tumour cells. The samples obtained for analysis will vary. We will collect blood and tumour (during biopsy or tumour removal) on every patient, and may collect saliva, skin, bone marrow, and/or spinal fluid on some patients.





Dr. Rae Yeung, UCAN CAN-DU co-lead

A ‘PRECISE’ APPROACH TO TREATING CHILDHOOD ARTHRITIS

An international research network aimed at personalizing medicine for children with arthritis received a multi-million dollar boost in 2017. Dr. Rae Yeung, Staff Rheumatologist and Senior Scientist and her co-lead Dr. Nico Wulffraat from University Medical Center Utrecht received \$8 million over six years from CIHR and ZonMw (the Netherlands Organisation for Health Research and Development) and Reumafonds (the Dutch Arthritis Foundation).

The initiative called UCAN CAN-DU is part of the Understanding Childhood Arthritis Network (UCAN) which was founded by Dr. Yeung in 2009 as a way to collaborate with researchers around the world studying basic research in paediatric rheumatology. Today, UCAN now has members from over 50 countries and over 300 sites. Through this network, Canada and the Netherlands combined will have more patients and biosamples than any other cohort in the world. UCAN CAN-DU includes all paediatric rheumatologists in Canada and the Netherlands and will use the investment to develop genomic tests and to determine individualized therapy for children living with arthritis in an attempt to treat children quicker, more efficiently, and with fewer side effects.

As described by Dr. Yeung, there is a very narrow window of opportunity to treat affected children before their joints are damaged by disease. The idea is, if caught early enough, there is potential to change the biology of disease and prevent damage. “With genomic testing we want to be able to tell which

child is at high risk or low risk for joint destruction,” explains Dr. Yeung. “For the high-risk children we want to be able to identify them early and give them strong medication right away. Similarly, we do not want to expose low-risk children to strong medications un-necessarily.”

To date, success has been achieved in addressing systemic arthritis; the most severe form of arthritis that not only causes inflammation of a child’s joints, but many parts of their body including the hearts and lungs. A molecule called IL-1Beta has been found to be responsible for this inflammation. “We have preliminary data from a genomic test that shows whether these children have active disease or not and will respond to blocking IL-1Beta or not. The medication to block IL-1Beta is often given by a needle and often for many years. From these genomic tests we can determine whether a child will respond to this medication and when they can stop this medication,” says Dr. Yeung.

Currently, there are about 10,000 children affected with arthritis in Canada. The systemic arthritis sub-group is only one of seven sub-groups and it represents only about 10 per cent of children living with arthritis. Next steps include identifying tests and drugs for the remaining 90 per cent of children who live with arthritis so that they have a better chance of receiving the appropriate treatment. This new funding provides the ability to generate the data required to inform treatment decisions at the bedside in order to make children better.

STUDY SHOWS HOW GENOME SEQUENCING MAY HELP PREVENT ADVERSE DRUG EVENTS

Today, in the era of precision medicine, genome sequencing has not only significantly improved doctors’ ability to diagnose inheritable diseases, but has also enabled scientists and clinicians alike to create new treatments and tailor clinical care to the specific child’s genetic information.

New research led by the Division of Clinical Pharmacology and Toxicology and published online in [npj Genomic Medicine](#) demonstrates yet another way genetic information can benefit clinical care and may even enhance patient safety and preventative medicine.

The study compared pharmacogenetics results from traditional testing with that of results generated by using genome sequencing. The researchers looked at 67 DNA variants in 19 genes with known effects on drug response and compared the results with patients’ genome sequencing data.

“As whole genome sequencing is being done more regularly to help find a diagnosis for patients with rare diseases, this information could also be used to identify DNA variants in children that affect medication safety and effectiveness: pharmacogenes. In order to use this information confidently, we need to ensure that these technologies reliably and accurately identify pharmacogenes,” says Iris Cohn, Clinical Research Pharmacogenetics Advisor and lead author of the study.

The research team found that sequencing was more than 99 per cent accurate for almost all of the pharmacologically important genes, except for one gene. Importantly, they also identified at least one medically actionable pharmacogenetic variant in 95 out of 98 paediatric patients who participated in the study.

“To find medically actionable variants in the vast majority of cases is astonishing,” says Cohn. She explains that the identification of genetic differences in our genes can be used to predict whether a medication will be effective for a particular person and can inform safe medication decisions, such as dosage as well as prevent adverse drug reactions.

Of those 95 patient participants, approximately 30 children had significant information which would influence how medication would be prescribed over the child’s lifetime, and could protect them from severe side effects if they had to be given this medication in the future.



Iris Cohn, lead author of the study

“Our study shows how pharmacogenetics can play a critical role in the shift toward predictive and preventative medicine. There are only so many drug-gene interactions that we are aware of, so it will not prevent all adverse reactions, but it adds another important medication safety layer. Even if it would help prevent three out of 100 adverse events, I would say this is very successful!”

SickKids currently offers pharmacogenetic tests in a pilot project to approximately 200 children and 100 adults to see how we might be able to incorporate pharmacogenetic testing into clinical practice. In the future, the researchers hope that pharmacogenetic information will help health-care providers make effective and safe treatment decisions in children and adults throughout their lifetime.



ENHANCING LEARNING OPPORTUNITIES AND CONTINUING EDUCATION

HOW TnECHO HELPS GIVE NEONATOLOGISTS THE FULL PICTURE

Targeted Neonatal Echocardiography (TnECHO) refers to the use of cardiac ultrasound by trained neonatologists to evaluate cardiovascular health in sick newborns. Enhanced physiologic assessment of cardiovascular health has the potential to ensure patients receive care appropriate for their diagnosis, reducing the delivery and costs of imprecise care, and promoting better allocation of resources.

The TnECHO Program, established as a collaborative initiative between the Divisions of Neonatology and Cardiology, is now recognized as a global leader in the delivery of clinical care, training of subspecialty neonatologists, innovation, and fostering research. The program, led by SickKids neonatologists Drs. Patrick McNamara and Regan Giesinger, as well as collaborators from Mount Sinai Hospital (Drs. Amish Jain and Poorva Deshpande) and Sunnybrook Health Sciences Centre (Dr. Dany Weisz) is internationally recognized for imaging research in neonates with perinatal hypoxia-ischemia, pulmonary

hypertension, and patent ductus arteriosus. The group has developed a highly coveted one-year fellowship program, which is offered annually to two trainees and has led the effort to solicit the Royal College of Physicians and Surgeons to recognize this training in TnECHO as an Area of Focused Competency. Innovations developed through the program include the TnECHO 'app' available for free from iTunes, a dedicated website (tnecho.com), and, more recently, Instagram-guided learning (@tnecho.to).

Nationally, the program has shepherded adoption of TnECHO guided practice in most neonatal intensive care units across Canada. Since its inception, leadership from the group continues to grow the foundation of the Canadian TnECHO collaborative which is now linked to the Canadian Paediatric Society. Internationally, through the Neonatal Hemodynamics Advisory, the group is playing a major advocacy role in guiding global education and fostering innovation and research.

The image shows a large ultrasound scan of a heart on the left. On the right, there is an overlay of an Instagram profile for 'tnecho.to'. The profile shows 26 posts, 96 followers, and 0 following. The bio includes the text: 'TnECHO.TO Please send unique cases, new and interesting science and opportunities to TnECHO.toronto@gmail.com. www.tnecho.com/'. Below the bio is a grid of various ultrasound images and text snippets. At the bottom of the overlay, there is a link: 'Click here for TnECHO Instagram'.

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SICKKIDS TEACHING SCHOLARS PROGRAM:

AN INTERPROFESSIONAL TEACH-THE-TEACHER COURSE

SickKids is the largest paediatric teaching center in Canada, with the largest faculty of medical, nursing, and allied-health teachers. As such, ensuring that our teachers are well trained, not only as care providers, but also as educators is a priority.

To help achieve this goal, a one-year interprofessional certificate course – The Teaching Scholars Program - was launched to develop the skills of teachers in paediatrics and nursing as well as allied-health professionals at SickKids. This highly regarded course focuses on the essentials of adult learning and teaching through sessions co-facilitated by award-winning and experienced teachers and mentors. The course offers mentorship in the development of educational initiatives and innovations as well as course work promoting best strategies in pedagogy and assessment. Through small group work, seminar discussions, role play, and simulation, program participants learn how to recognize and capitalize on learning opportunities to create and support a learning environment within the child health

context. The goal of the program is to provide participants with foundational principles and approaches to teaching and learning within a clinical setting that advances interprofessional education and/or care with graduates of the program better enabled to actively contribute to the culture of teaching and learning with the goal of improving care.

Upon its introduction, the course reached full capacity within days of opening registration. Program sessions received high satisfaction ratings by participants and the second year of the course that began in the fall of 2017 ‘sold out’ again within days of posting for applications.

The program is sponsored by both the Department of Paediatrics and the Learning Institute and is co-directed by Michele Durrant, Interprofessional Education Specialist and Dr. Mark Feldman, Director, Continuing Education.



PAEDIATRIC UPDATE REACHES NEW HEIGHTS

The Department of Paediatrics’ flagship departmental continuing education (CE) event, Paediatric Update is reaching new heights as the largest paediatric CE event led by a department of paediatrics in Canada. Learn more about Paediatric Update below.



PROGRAM	PROGRAM COMPONENTS	PROGRAM HIGHLIGHTS
<p>Program Format</p> <p>This program is designed to help care professionals. It focuses on how to recognize and capitalize on learning opportunities in the child health system. Participants with experience in teaching and learning are encouraged to apply.</p> <p>The session format is interactive involving small group work, seminar discussion, role play and simulation</p>	<p>This program will provide an opportunity for clinicians to interact with like-minded colleagues interested in education. The session format is interactive involving small group work, seminar discussion, role play and simulation. Each session will be co-facilitated by experts from different professional disciplines. These individuals are award winning, seasoned teachers and mentors.</p>	<ul style="list-style-type: none"> • Creating an effective learning climate • Teaching in the clinical setting • Developing your learning plan and principles of learner assessment • Supporting the learner in difficulty • Curriculum development and program evaluation • Interactive teaching • Interprofessional programming and facilitation • Appraisal of research in education and principles of quality improvement • Teaching and learning for change • Using Technology in Teaching • Project development and scholarly presentation

REDEFINING HEALTH SERVICE DELIVERY AND MODELS OF CARE

A NEW CLINIC FOR EHLERS-DANLOS SYNDROME OFFICIALLY OPENS

Patients with Ehlers-Danlos Syndrome (EDS) and other rare diseases now have improved access to coordinated care. Just in time for Rare Disease Day 2017, Dr. Eric Hoskins, Minister of Health and Long-Term Care and Michael Coteau, Minister of Children and Youth Services announced a \$991,000 investment to support the operation of an EDS clinic run jointly by SickKids and the University Health Network.

Ehlers-Danlos Syndrome is a group of disorders characterized by joint hypermobility, skin and tissue fragility, and variable degrees of systemic involvement that make them difficult to diagnose and manage. Through support from the Ministry of Health and Long-Term Care, the collaborative EDS Program supports patients and families living with EDS by providing timely diagnosis, education, and expertise in the treatment and management of EDS. “Previously, EDS patients would have a long diagnostic journey, bouncing from specialty to specialty to address the many symptoms of the disease” says Dr. Roberto Mendoza-Londono, Staff Geneticist and Interim Division Head, Clinical and Metabolic Genetics. “The introduction of the EDS Clinic allows us to educate patients, families, and treating physicians about the condition and offer a more coordinated approach to their care.”

Since the announcement, the program has engaged a highly multidisciplinary team which includes a geneticist, paediatrician,

nurse practitioner, advanced physiotherapist, a psychologist, and a social worker. The program has also established collaborative service models to promote care that is integrative and specific to the unique needs of the patients seen. For example, clinics, led by the Division of Paediatric Medicine, are facilitated in an interdisciplinary fashion with all team members in attendance to promote a ‘one-stop’ approach for patients. In addition, the program’s nurse practitioner will accompany patients to other clinic visits across the Hospital. The joint-clinic approach also improves the transition from paediatric to adult health care by providing a cohesive transition plan for adolescent patients whose care will be coordinated at Toronto General Hospital once they turn 18.

“This clinic is an example of how we can collaboratively streamline the care of rare diseases in multidisciplinary environments,” says Dr. Mendoza-Londono who leads the EDS Program as Medical Director.

The program is the first in Canada to provide care and lead research related to EDS. With similar challenges faced for other rare diseases, the program’s framework may, in the future, serve the needs of other patients with unique and complex disorders.



The SickKids EDS Clinic team from left to right: Dr. Roberto Mendoza-Londono, Dr. Kathryn Walker, Dr. Sarah Schwartz, Constance O'Connor NP, Brianne Burton PT, and Ramandeep Sran

TRANSLATING RESEARCH INTO PRACTICE:

DEVELOPING CARE PATHWAYS TO IMPROVE OUTCOMES FOR CHILDREN AND YOUTH WITH CEREBRAL PALSY

The Division of Developmental Paediatrics is providing active leadership in the development of clinical practice guidelines and care pathways for important health issues for children with disabilities.

A 'care pathway' is defined as a practical summary, including an algorithm, of evidence informed guidelines or the best evidence for an aspect of care/services for individuals with childhood-onset disabilities to inform clinical practice. Led by Dr. Darcy Fehlings, Clinician-Scientist and Division Head, Developmental Paediatrics, two pathways were developed for the American Academy of Cerebral Palsy and Developmental Medicine (AAPDM). These pathways - Dystonia Management in Individuals with Cerebral Palsy (CP) and Osteoporosis Management in CP - are designed to inform physicians, therapists, and nurses caring for children/youth with non-ambulatory CP. The pathways are featured online through the AAPDM and are partnered with a systematic review published in Developmental Medicine and Child Neurology in 2016.

Locally, a team at Holland Bloorview Kids Rehabilitation Hospital developed a pathway to meet the unique needs of children/youth seen with CP. There is international consensus, led by investigators in Australia and Europe, that children with CP have

a higher risk of hip subluxation and dislocation. After examining current practices for screening for hip subluxation at Holland Bloorview and reviewing the evidence for hip monitoring in CP, the interdisciplinary team which includes physician, nursing, physiotherapy, and Evidence to Care (EtC) representation developed the Hip Surveillance Care Pathway. The pathway is designed to inform caregivers, physicians, nurses, and physiotherapists when a hip x-ray is required to check for the hip sliding or being out of joint and when to refer to the Orthopaedic or Hypertonia Clinics.

Since its implementation in 2016, the team has interviewed practitioners and conducted chart audits to help determine both the pathway's impact and whether any modifications were required. Interview results demonstrated that, prior to the care pathway's implementation, only 33 per cent of Holland Bloorview clinicians followed evidence-informed guidelines for hip surveillance and 86 per cent of children with CP seen at Holland Bloorview had hip surveillance consistent with the care pathway. Today these numbers have increased to 100 per cent and 95 per cent, respectively. This care pathway is an example of impactful knowledge translation and was recognized by EtC with a Holland Bloorview Knowledge Translation Champion award.



CHAK and Paediatric Project ECHO teams participate in a mock TeleECHO Clinic

PROMOTING COORDINATED WEIGHT-MANAGEMENT CARE THROUGHOUT ONTARIO

The Ontario Paediatric Bariatric Network (OPBN) aims to identify priorities and recommend strategies for the achievement of coordinated surgical and medical care services for children and youth who are overweight or obese. Established in 2014, the network, for which Dr. Jill Hamilton, Endocrinologist is the co-lead, is comprised of members from 11 interdisciplinary paediatric obesity programs in Ontario along with representation from other health-care organizations, Local Health Integration Networks, the Provincial Council for Maternal and Child Health (PCMCH), and the Ministry of Health and Long-Term Care (MOHLTC).

The OPBN promotes consistency in standards of practice, resources, and outcome measures across Ontario hospital and community-based paediatric obesity programs to address the growing need for the care of patients within the general community as well as those with chronic disease or comorbidities including obesity as a result of medication or environmental changes. Following a shared-care model, the network allows for more patients to receive treatment closer to home thus reducing expenses and travel, as well as the overall burden on families. In 2017, the MOHLTC provided funding to the PCMCH to further the coordination of the OPBN, including the evaluation of clinical and health-system indicators. At SickKids, Dr. Hamilton and the Centre for Healthy Active Kids (CHAK) play a leadership role in the development of the OPBN.

To accelerate training in paediatric obesity management, the OPBN will be participating in the pediatric bariatric stream of Project ECHO. Funded by the MOHLTC, [Paediatric Project ECHO](#) aims to further build capacity in the community by connecting community-based health-care providers including physicians, nurses, and allied-health professionals with multidisciplinary specialists at SickKids through a cloud-based videoconferencing platform. The model 'moves knowledge, not people' by using multi-point interactive videoconferencing to conduct virtual clinics with health-care providers across geographic areas. Launching in 2018, Bariatric ECHO will feature TeleECHO Clinics held weekly as well as Core Competency training offered twice a year to build capacity for health-care providers in areas including motivational interviewing, obesity comorbidities, and obesity and mental health. Sessions will be introduced in two phases; first with clinics and curriculum tailored to address the unique needs of the multidisciplinary OPBN teams, followed by the needs of primary care providers in the community.

Through the OPBN and Paediatric Project ECHO, Dr. Hamilton and the CHAK team hope to better address the unique needs and challenges of weight management care and prevent the comorbidities of obesity, including cardiovascular disease and type II diabetes, before they happen.



► [Click here for more information](#)



Members of the YFP from left to right: Sharon Lorber MSW RSW, Gillian Liberman MSW RSW, Dr. Trisha Tulloch, Nicole Murphy RN, Gillian Thompson NP, Dr. Ashley Vandermorris

BY THE NUMBERS

389

POSTGRADUATE RESIDENTS AND FELLOWS

46

COUNTRIES REPRESENTED BY POSTGRADUATE RESIDENTS AND FELLOWS

TALKING ABOUT BABY TALK:

FACILITATING SPEECH AND LANGUAGE SERVICES FOR CHILDREN OF ADOLESCENT MOTHERS

The Young Families Program (YFP), part of the Division of Adolescent Medicine provides health services for adolescent mothers and their children. The program acts as the medical home for both the mother and the infant and will follow the family until the child reaches two or three years of age.

It has been shown that a relationship exists between early speech and language delays and low socioeconomic status (SES) which is typically seen in families of the YFP. Low SES children may experience a 30 million word gap by age three. This preschool speech and language delay may result in lack of school readiness and overall school success. Within the YFP, approximately 45 per cent of children demonstrate expressive speech delays with the majority of families failing to follow-up with speech and language pathology and audiology referrals required for assessment and intervention.

To address this gap, in partnership with Toronto Public Health, the YFP sought to identify barriers to and facilitators of engagement with speech and language services. With the goal of determining patient preferences for receiving speech and language services. A number of methods were used to collect feedback. All YFP parents were invited to complete a voluntary, self-administered survey which included open and closed-ended questions centred on three themes; home literacy environment, barriers to accessing speech and language services, and concerns regarding children's speech and language development. Parents within the YFP were also invited to participate in a speech

and language workshop and focus group to explore models for service delivery such as embedded sessions led by a speech pathologist, play-based interventions, or the use of apps.

It was ascertained that offering an embedded speech and language service led by a speech and language professional in a safe environment and with other adolescent mothers was the preferred delivery model. As SickKids is the medical home of these patients, the families have a relationship with the YFP care model and other families in the program which therefore can establish the desired safe space for participants. In addition, it is opportunistic to offer as many services as possible under one roof across the patient's continuum of care.

"Our ultimate goal is to create a literacy rich environment which stresses the importance of reading for this at-risk population," says Gillian Thompson, Nurse Practitioner, Adolescent Medicine. Thompson, as well as other staff members of the YFP have since attended staff workshops to incorporate elements of speech and language teaching into clinical encounters.

Toronto Public Health has committed to the partnership and the SickKids team is working to establish a critical mass of participants by partnering with the Family Centre and other programs within SickKids. Family Centre librarians through donations have also begun to provide age-appropriate reading materials to allow staff to run reading interventions as part of the model of care.

+\$120M

RECEIVED IN RESEARCH GRANTS AND AWARDS*

227

FULL-TIME FACULTY

73,262

EMERGENCY DEPARTMENT VISITS

134

PART-TIME FACULTY

120

ADMINISTRATIVE STAFF

A photograph of two young children standing on a balcony or walkway, looking out through a large, arched glass window. The child on the left is wearing a red hoodie and dark pants, while the child on the right is wearing a plaid shirt and dark pants. The window frames the view of a city street with buildings, including one with a 'DELTA CHELSEA' sign. The entire image has a teal color cast.

DELTA
CHELSEA

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THE HOSPITAL FOR
SICK CHILDREN

Department of
Paediatrics