Juliet,
SickKids patient

SICKKIDS CANCER SEQUENCING (KiCS) PROGRAM

2023 Progress Report

SickKids VS®

SEQUENCING SUCCESS

New study allows scientists to translate research into action.


Nori, SickKids cancer patient

The SickKids Cancer Sequencing (KiCS) Program analyzes the genetic material for kids with rare, relapsed, metastatic or treatment-resistant cancers. For them, survival rates are low, with few, if any, effective therapies. In a first for Canadian precision oncology, the KiCS research team led the most extensive genome sequencing study for Canadian paediatric cancer patients, transforming how we diagnose and treat the disease.

The team analyzed more than 860 genes linked to cancer in a group of 300 patients. According to the results published in Nature Cancer last year, the sequencing revealed at least one actionable genetic variation in 56 percent of patients, and 54 percent had variations that could be targeted for treatment.

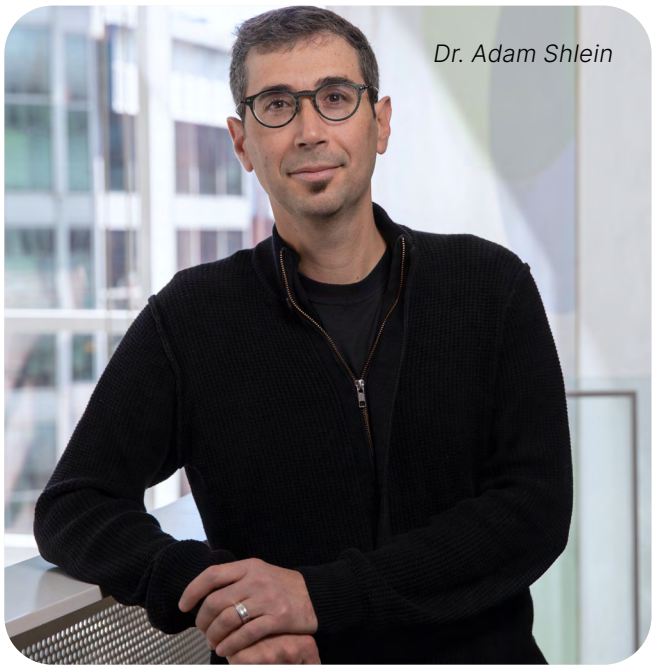
"The more data we have about these tumours, the more we are able to provide the most effective and individualized care possible for children with cancer, whether that means clarifying a diagnosis and starting a child on the correct care pathway, providing more treatment options for children with relapsed cancers, or identifying a predisposition which may inform care for their family."

–DR. ANITA VILLANI

Six percent of the identified variations led to changes or improvements in the diagnosis, influencing how patients were treated. "Knowledge really is power," says Dr. Anita Villani, oncologist, lead author, and co-director of KiCS and the Cancer Genetics Program at SickKids. "The more data we have about these tumours, the more we are able to provide the most effective and individualized care possible for children with cancer, whether that means clarifying a diagnosis and starting a child on the correct care pathway, providing more treatment options for children with relapsed cancers, or identifying a predisposition which may inform care for their family," she says. This project was also developed and led by KiCS co-directors Dr. Adam Shlein, a senior scientist in Genetics & Genome Biology and Garron Family Chair in Childhood Cancer Research, and Dr. David Malkin, the CIBC Children's Foundation Chair Child Health Research, SickKids Precision Child Health Initiative Co-lead, and Cancer Genetics Program Director.

The study exemplifies our SickKids vision for Precision Child Health, a movement centred on individualized care for every patient. “Until now, the cancer care pipeline has been relatively siloed, but Precision Child Health is changing how we practice medicine,” says Dr. Malkin. Researchers took snapshots of the tumours over time, showing how changes may inform diagnosis, the frequency of care and support new interventions. “Tumour sequencing is usually done once during a patient’s cancer diagnosis, if at all,” says Dr. Shlien. “But we saw tumour genomes changing substantially over the course of the disease. Further sequencing can help us support the provision of treatment that is not only unique to each tumour type but to each patient’s stage in the cancer journey.” Eventually, the team hopes to make conducting biopsies over time a standard part of care.

Learnings from the study also had implications for family members. For the 17 percent of patients who had previously undiagnosed variants in cancer predisposition genes, the sequencing allowed physicians to take the necessary steps to inform relatives and implement any tumour surveillance measures. The study continues to have ripple effects for subsequent studies, too. SickKids researchers used the newly published KiCS data as a launchpad to incorporate a machine-learning algorithm that classifies every known major type of childhood cancer and can refine or match a given cancer diagnosis for 85 percent of paediatric cancer patients. As well as pinpointing notable distinctions among cancer types, the data amassed by the research team, coupled with the platform’s capabilities, led to the identification of 455 cancer subtypes. The huge diversity in subtypes bolsters the notion that many childhood cancers stem from a common ancestry before branching into distinct tumour subtypes. For the first time, researchers can see subtle differences within cancer subtypes. This gives them a radically new way to look at and potentially identify the prognosis of cancers. For example, in cases of neuroblastoma, the most common extra-cranial solid tumour in children, the subtypes identified by this tool were important in predicting how severe the tumour is and the chances of survival. Also, the tool helped explain why sarcomas, tumours in the bones and soft tissues, don’t always respond well to immunotherapy. It found an imbalance in immune cells, which could guide us in finding new treatments. Dr. Shlien says, “As we add more samples to this growing atlas and validate it with even larger data sets and sample types, our classifier has the potential to become a universal test for diagnosing paediatric cancer.” What Dr. Shlein calls potential is now an imminent and real possibility.



Dr. Adam Shlein

MEET JULIET

A simple test could have helped doctors diagnose her cancer sooner.

Juliet received a leukemia diagnosis at the age of 14. It was devastating, but not entirely unexpected. Juliet's mother, Luana, has Li-Fraumeni syndrome (LFS), an inherited genetic condition linked to an almost 100 percent lifetime risk of cancer. She's already faced five different cancer diagnoses. So soon after her birth, Juliet underwent testing that confirmed she had LFS, too. For Juliet and other children with LFS, annual brain and whole-body MRIs and frequent blood draws, ultrasounds and physical exams are essential for early cancer detection .

KiCS researchers were part of a team that found a new way to detect cancer even earlier in people with LFS before a tumour becomes visible or symptoms start. They're using a technique known as a "liquid biopsy," which looks for DNA fragments left by cancerous cells in blood samples. Based on data form a recently published KiCS analysis of 170 blood samples from 82 individuals with LFS collected over several years, including from Juliet, SickKids researchers prove that early signs of Juliet's leukemia were present months before her diagnosis. It's a simple blood test to identify when and sometimes where cancer occurs. That is precision.

"Regular scans and check-ups are routine when you have LFS, but the ability to predict when and where cancers develop rather than react when one has already developed is life changing," says Luana.

100%

lifetime risk of getting cancer for individuals with LFS, like Juliet.

Juliet,
SickKids patient

THANK YOU

Your support helps us diagnose faster, treat smarter, and predict better. Together, we're healing the future for kids with cancer.

FOR MORE INFORMATION, PLEASE CONTACT:

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