GARRON FAMILY CANCER CENTRE

2022 PROGRESS REPORT

Elliana,
SickKids leukemia patient

MAKING WAVES

Madeline Hayes studies better cancer drugs for patients—in zebrafish.

Madeline Hayes,
Molecular Genetics Scientists in Developmental and Stem Cell Biology at SickKids

OVER THE PAST decade, advances in genetic sequencing have led to breakthrough findings in cancer research. But how do we translate these discoveries into tangible, targeted treatments for patients? That's what drives SickKids developmental and stem cell biologist, Madeline Hayes. "Treating patients who have unique tumours with the same series of therapy isn't always effective. But there is a lot of biology that needs to be understood to develop safe targeted therapeutic approaches that will be an improvement over the current standard of care," says Hayes.

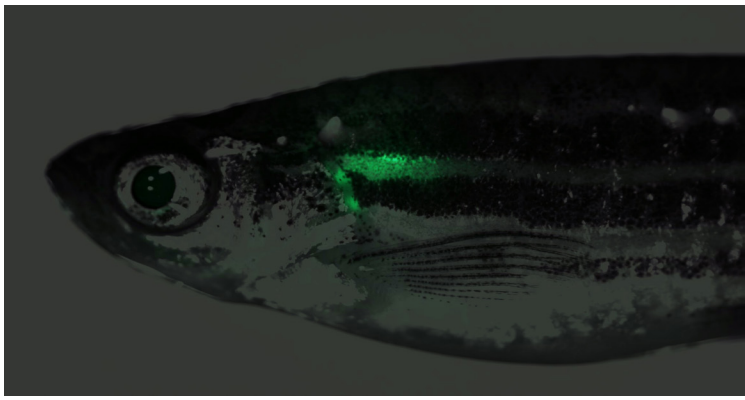
Hayes is working with the KiCS (SickKids Cancer Sequencing) Program at the GFCC and alongside brilliant colleagues to uncover the mysteries of how cancer develops and metastasizes on a cellular level. To do this, they'll use zebrafish, a small freshwater minnow popular in home aquariums —and science labs. Zebrafish are ideal to model human disease because their skin is translucent, they reproduce prolifically, and they can develop most types of tumours humans can, often through the same gene pathways.

Hayes and her team will take tissue from malignant tumour biopsies in humans and transplant it into zebrafish. This allows them to create individualized models of newly identified genetic abnormalities that lead to tumour formation, growth and metastases in high-risk metastatic neuroblastoma and other paediatric cancers.

"OUR WORK COULD BE THE CATALYST FOR KIDS BEING SCREENED FOR CANCER AND RECEIVING PERSONALIZED THERAPY FOR THEIR DISEASE."

"The abnormalities we're looking at are also associated with breast and ovarian cancers in adults but not well understood in paediatric cancers," Hayes explains. "Our work could be the catalyst for kids being screened for cancers and receiving personalized therapy for their disease."

Once they model the tumour, Hayes can also test treatments on zebrafish and collect reliable evidence for what is working and what isn't before considering new drug combinations for patients. This foundational research will serve as the preclinical data necessary to translate discoveries into new hope-inspiring treatments that our patients so desperately need.



HELPING INFANTS GET BETTER CARE

Rare brain cancer in babies has a new set of treatment guidelines.

For years there's been little hope for kids diagnosed with rare brain tumours like ETMR (Embryonal Tumour with Multi-layered Rosettes). Usually diagnosed in children ages 4 and under, ETMR tumours are aggressive, fast-growing and often found in areas of the brain responsible for intellectual and physical development. Of the 20 to 40 per cent of patients who survive ETMR tumours, most will experience a lifetime of side effects and disabilities from toxic treatments. While ETMR tumours are estimated to be one of the most common type of brain cancers in infants and young children, they are still poorly studied and understood. For Dr. Annie Huang, Senior Scientist in Cell Biology and Neurooncologist at SickKids, the status quo was unacceptable. She says, "We have to do better. Everyone deserves an answer. And if we don't know the answer, we have to find it."

Dr. Annie Huang,
Senior Scientist in Cell Biology and Neurooncologist at SickKids

In 2013, Dr. Annie Huang led a study proposing a new model for how ETMR tumours develop and suggested possible targets to investigate for novel therapies. These findings, published in Nature Genetics, shed light on the complex process of early brain development and showcased the need for better standard treatment protocols.

In September 2021, SickKids published the first ETMR clinical management guidelines based on a study of the world's largest cohort of patients. Together with 140 international collaborators, SickKids researchers analyzed tumour samples and clinical information from more than 200 ETMR patients through the Rare Brain Tumor Consortium (RBTC)—a global, clinical registry and repository for rare paediatric brain tumours founded by Dr. Huang, who is also the lead investigator on the study, Researchers discovered that although ETMR tumours typically develop in the cerebrum, the largest part of the brain, nearly half of the samples were found in other parts of the brain where they can mimic more common tumours, leading to misdiagnosis and failed treatment.

Through a systematic review of past therapy, the team found that many patients could benefit from a personalized treatment regimen. "Our study offers, for the first time, detailed insights into disease patterns in ETMR patients as well as optimal medical management using molecular diagnoses and treatment approaches currently available and used in other paediatric brain tumours," said Dr. Huang, who is also a Canada Research Chair in Rare Childhood Brain Cancers. "These guidelines offer a critical patient management framework previously unavailable to clinicians."

Support for breakthrough work like this has immediate and tangible implications for rare brain tumour patients worldwide. The data could also help support the development of clinical trials and more targeted therapies for other rare and deadly cancers.

MEET ELLIANA

IN JANUARY 2021 Elliana (Ellie), age 3, was fighting an intermittent fever. In the wee hours of one terrifying morning, things took a turn. She was on the floor of her room, pale and screaming, "My legs are breaking!" Ellie was in excruciating pain. Her parents rushed her to SickKids immediately, and after a few hours of diagnostic tests, the family received the shocking news: Ellie had acute lymphoblastic leukemia (ALL).

She was admitted to SickKids and immediately began chemotherapy which she received in the hospital and then at home through a port every ten days. The treatment is rough on her little body—and mind. And although the road has been long and fraught with challenges, Ellie is now in remission and on her fourth cycle of long-term maintenance therapy. "She takes medicine like a champ. It used to take more than 20 minutes to give her one medicine, but now she'll administer the syringes to herself and does it fast too," says her mom, Amy.

Ellie is finally easing back into her favourite activities like swimming and even attended summer camp. Still, the lasting physical and mental toll of the cancer and therapy is tremendous.

"We're hoping that one day treatment can be less invasive and much shorter in duration for kids like Ellie. Gifts to cancer research help to move this along," Amy shares, with gratitude.

SHE WAS ON THE FLOOR OF HER ROOM, PALE AND SCREAMING, "MY LEGS ARE BREAKING!"

ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) IS A CANCER OF THE WHITE BLOOD CELLS THAT ORIGINATES IN THE BONE MARROW, THE SPONGY TISSUE INSIDE THE BONES.

TWO-FOR-ONE TESTING

A livIng drug with better odds.

MOST CHILDREN with acute lymphoblastic leukemia (ALL) respond well to the traditional standard treatment protocol of chemotherapy. But the odds of survival are low for kids who don't respond to treatment or whose cancer comes back multiple times. For those patients, there's hope in the evolving field of immunotherapy. Specifically, CAR T-cell therapy offered at SickKids.

CAR-T therapy can be thought of as a living drug. It works by extracting a patient's T cells (blood cells that help to protect from infection and disease) from the blood, genetically modifying them to find and fight cancer cells by targeting a protein called CD19, and then putting the T-cells back into the blood to find and kill the disease.

CAR T-cell therapy has helped to significantly improve the outcome of patients who previously had very limited treatment options available. Still, about half of the patients treated relapse in the first year after treatment. One reason is that tumour cells mutate quickly and shed the target molecule and the CAR T-cells can't "see" the cancer anymore.

Recently, the SickKids CAR T-cell team at the GFCC was invited as the only Canadian institution to participate in an international study to test the next generation of CAR T-cells for ALL. "It's a dual-targeting CAR-T cell. In addition to targeting CD19, it targets another antigen called CD22. It's like a two for one," says Dr. Joerg Kruger, a physician in the Blood and Marrow Transplant and Cellular Therapy Section at the GFCC who will oversee the trial. "I'm grateful for opportunities like this to investigate new ways to treat very sick kids," Dr, Kruger says.

Innovative therapies are how we change the future of care for cancer patients. Your generosity is what makes it possible.

CELLULAR THERAPIES FACILITY UPDATE

Life-saving treatment depends on expert leadership.

Harnessing the immune system's power to perform bone marrow transplants and cellular therapies to treat and cure cancer and other illnesses — also known as immunotherapy — is one of the most transformative scientific discoveries in history. To keep pace, SickKids built a Cellular Therapies Facility. It's the first of its kind in Canada—a 1,690 square foot, state-of-the-art manufacturing suite and physical hub for discovery and clinical application.

Recently, a Facility Manager was hired to support the validation, training and application of the facility's advanced processing equipment, environmental controls and testing laboratory. The manager will ensure that every life-saving treatment and research activity is carried out safely, swiftly and with the most optimal use of high-quality resources in the name of best-in-class cancer care for our patients.

THANK YOU.

Every day, SickKids is working towards improving the lives of children with cancer and blood disorders, and our success depends on the support of donors like you. Thank you for your remarkable generosity.

For more information, please contact:

SickKids Foundation
525 University Avenue, 8th Floor
Toronto, Ontario M5G 2L3

PHONE 416.813.6166 **FAX** 416.813.5024

sickkidsfoundation.com

SickKids VS®

fundthefight.ca