Projects funded in the 100% Fund Competition

Since 2018, over half a million dollars has been provided in granting opportunities to researchers through the funding partners of the 100% Fund.

The purpose of The 100% Fund is to target directly pediatric cancers that are rare and hard to treat—cancers that have not responded to available therapies. Projects can range from discovery to clinical trials but must be targeted at delivering a treatment intervention. The goal is to fund research with the potential to deliver improved treatment and increased survival rates.

Outcome & Impact Statements of the past recipients of the grants are included.

Funding Partners for the 100% Fund 2018 – 2021:

FIGHT LIKE MASON FOUNDATION

Coast TO Coast AGAINST CANCER FOUNDATION

Research is the Answer
Fundraising is the Lock
Awareness is the Key
Team Naomi Get Well Now Foundation

Team Finn

Phoebe Rose Rocks FOUNDATION

Mélia's Memory

Childhood Cancer Canada

GREAT CYCLE CHALLENGE CANADA

100% Fund Grants – *Outcome & Impact*

$113,737 awarded July 2018, 2-year grant

Ted Gerstle (The Hospital for Sick Children): MRI-guided High Intensity Focused Ultrasound-controlled hyperthermia to activate thermosensitive liposomal doxorubicin to treat rhabdomyosarcoma (RMS) in a mouse model

Doxorubicin is used to treat rhabdomyosarcoma (RMS) tumours but has devasting side effects. RMS tumours were created in mice and treated with a novel variant of doxorubicin that is temperature sensitive (TS) and administered using magnetic resonance guided high intensity focused ultrasound (MRgHIFU). This combination could decrease tumour growth and minimize the drug's accumulation in the rest of the body by focusing its release at the tumour site using the targeted heating from MRgHIFU, thereby reducing potential toxic side effects. This pre-clinical project could lead to an increase in the survival of patients with RMS and reduce the associated side effects.

100% Fund Grants – *Outcome & Impact*

$92,535 awarded July 2018, 2-year grant

Sumit Gupta (The Hospital for Sick Children): The characterization of previously undetected MLL gene abnormalities in infant ALL.

Our goal was to determine whether infants with acute lymphoblastic leukemia who do not have the typical genetic finding of a rearrangement of the MLL gene (MLL-R) on standard testing actually do have abnormalities in this gene when you use more advanced testing techniques. We have now completed all our analyses. We found that infants without standard MLL-R do not have more difficult to find MLL abnormalities, and that their gene expression profile is not similar to that of infants with standard MLL-R. We did however also find some new findings about what genetic changes do exist in babies without the standard MLL. For example, we found babies with a subtype of leukemia call Ph-like which until now has only been described in older children, adolescents, and adults. These findings have implications for how we categorize and treat infants with leukemia in the future.

100% Fund Grants – *Outcome & Impact*

$120,000 awarded July 2019, 2-year grant | $45,000 awarded December 2021, 1-year grant

Jason Berman (Children's Hospital of Eastern Ontario Research Institute):

- Developing an MLL-rearranged infant leukemia model for the screening of novel therapeutics and investigating the role of KMT2C in the rapid onset of infant leukemia using zebrafish.
- Deciphering the functions of KMT2C in normal hematopoiesis and rapid onset infant leukemia using zebrafish

Infant leukemia is frequently caused by mutations in Mixed Lineage Leukemia 1 (MLL1; KMT2A) that result in the formation of MLL-fusion genes. To better understand how these mutations cause leukemia and to create a system for the efficient screening of new and targeted therapies, we created an animal model. We generated zebrafish that have mutations in the KMT2C genes, having an under-production of both red and white blood cells. We believe these defects in blood development lead to increased susceptibility to infection and we continue to assess the impact of this mutation on blood development.

For our second project we expanded our animal model. We also developed zebrafish lines that express the MLL fusion genes exclusively in blood cells to mimic the leukemia phenotype seen in human infants. We are currently studying how blood development is altered in these mutants. These novel zebrafish lines will serve as robust models for screening novel therapies for infant leukemia.

100% Fund Grants – *Outcome & Impact*

$120,000 awarded December 2019, 2-year grant | $45,000 awarded July 2021, 1-year grant

Rebecca Gladdy (Lunenfeld-Tanenbaum Research Institute, Toronto):

- Epigenetic chemical screens to identify novel therapeutic strategies for rhabdomyosarcoma.
- Hunting for therapeutic targets in Rhabdomyosarcoma: Comparative proteomics in cross-species model systems for precision diagnostics and rapid drug testing

Survival rates in high-risk Rhabdomyosarcoma (RMS) patients remain frustratingly unchanged over the last decade and more effective drugs are needed. In pediatric cancer, epigenetic changes that control the function of genes may be what is driving this cancer.

In project 1, nine epigenetic drugs (drugs that modify the packaging of DNA), were selected and we studied how these epigenetic drugs affect RMS tumors. This knowledge could potentially lead to RMS being treated with targeted therapy.
In project 2 we focused on combination therapy of epigenetic drugs and targeting important cancer proteins. The discovery of important cancer proteins that can be further studied for the development of new drugs will lead to better treatment options and improved survival for vulnerable RMS patients with hard-to-cure cancers across Canada and throughout the world.