



MICHAEL CUCCIONE FOUNDATION

2021 REPORT ON GIVING



Michael Cuccione Foundation
CHILDHOOD CANCER RESEARCH

BC 
**Children's
Hospital**[™]
Foundation



Lilith, age 2



Dear Michael Cuccione Foundation,

It is a privilege to so often hear about people who benefit from the Michael Cuccione Foundation (MCF) and the Michael Cuccione Childhood Cancer Research Program (MCCCRP). Whether it's hearing from a new research fellow about their ground-breaking work, talking with lab leaders about their inspiring ambitions for the future, or reading stories of a child and family who have found new hope through a cancer treatment developed here, it is humbling and inspiring to see how profoundly the success and support of the Michael Cuccione Foundation is felt across BC Children's Hospital.

Not only is this effect felt at BC Children's, but also throughout Canada and the world. Michael once said, 'one can only do so much, but together, we can make a difference,' and the success of the MCCCRP through the collaboration of its team is proof of how true this statement is. Through its publications, external grants and collaborations, the MCCCRP is a leader in the international community of researchers dedicated to making childhood cancers a thing of the past, and this is all because of your visionary leadership, unwavering determination, and steadfast advocacy.

With Dr. Chris Maxwell's leadership, and with your continued commitment, the MCCCRP is in excellent hands to continue making significant steps towards our shared dream, which is a world where no family experiences the loss of a child to cancer.

With gratitude,

Malcolm Berry
*President & CEO,
BC Children's Hospital Foundation*



Angus, age 2

A MESSAGE FROM

DR. CHRIS MAXWELL

It's important to take an opportunity to reflect on the incredible success of the Michael Cuccione Foundation and its namesake Michael Cuccione Childhood Cancer Research Program at BC Children's. Since its inception in 2007, the MCCCCRP has recruited and nurtured world-leading researchers in childhood cancers and blood research.

Our program has grown steadily to include world-class principal investigators who are now leading national and international efforts to find new cancer treatments and improve the long-term health and well-being of children with cancer. Dr. Rebecca Deyell is leading Canadian teams that are working to bring new, more precise therapies to kids with difficult-to-treat cancers. Dr. Philipp Lange is establishing new ways to profile tumours in exquisite detail, which may identify new bullseyes to target in cancer cells or better ways to classify cancers and choose the most appropriate treatments. Dr. Amanda Li is heading an initiative that is bringing life-saving, experimental chimeric antigen receptor (CAR) T-cell therapy to kids at BC Children's and more hope to their families. Dr. James Lim has developed a first-in-Canada experimental model, using chicken egg embryos, to grow tumour cells outside the bodies of childhood cancer patients and examine the growth of these cells to evaluate new treatments. My own lab is discovering how primitive stem cells grow to better understand how this process is changed, and how we may correct it, in hereditary cancers that affect young people. Dr. Gregor Reid now

heads the collaborative BRAvE Initiative at BC Children's, which aims to uncover new precision therapies and understand the biology of childhood cancer, and his lab is also uncovering the ways in which the young child's immune system interacts with and fights leukemia cells.

Today's treatments can be highly effective at achieving remission but also highly damaging to the long-term health of the child. Dr. Rod Rassekh is leading teams that are developing new protocols to protect kids from the harsh side effects of cancer treatments. Dr. Jacob Rozmus is discovering the small inherited changes that affect the development of the immune system and contribute to the development of health disorders. Dr. Kirk Schultz continues to make major, first-in-world strides towards state-of-the-art approaches that make life-saving hematopoietic stem cell transplants safe, and continues to work on the next phase of CAR T-cell therapy research. Finally, Dr. Poul Sorensen is using innovative technologies to discover new targets in cancer cells and understand the many ways that cancer cells grow and resist today's treatments.

So many exceptional people contribute to the great successes of the MCCRCP and the research and innovation produced is immeasurably improved by the continued generosity and support of the Michael Cuccione Foundation. We are privileged and grateful for your long-standing dedication, advocacy and support.

Sincerely,



Chris Maxwell, PhD

*Interim Director, Michael Cuccione Childhood Cancer Research Program,
Interim Head, Oncology Research Program, Associate Professor of Pediatrics,
UBC & BC Children's Hospital Research Institute*

2021 BC CHILDREN'S HOSPITAL ONCOLOGY STATISTICS

139 NEW DIAGNOSES

28 TRANSPLANTS **26** RELAPSES

807 VIRTUAL APPOINTMENTS **40** OUTREACH CLINIC VISITS *PRE-PANDEMIC*

MCCCRP STATISTICS

10 LEAD INVESTIGATORS

32 FELLOWS/STUDENTS/TRAINEES

303 PUBLICATIONS IN THE LAST 5 YEARS INCLUDING **59** PUBLICATIONS IN 2020

129 PATIENTS IN TRIALS OR IN STUDIES



Amelie, age 14



NURTURING NEW TALENT

The MCCCCRP continues to attract and develop leading talent in childhood cancer research. We know that every treatment provided to oncology patients receiving care at BC Children's Hospital is the result of years of research and the ongoing work of brilliant and determined investigators, fellows, and students. Conquering childhood cancers depends on inspiring and nurturing new talent, and investing in new fields and projects in childhood cancer research. We're happy to share with you updates on PhD candidates and postdoctoral fellows who have benefited from your generosity.

Q&A WITH DR. NINA ROLF



WHAT ARE YOU CURRENTLY RESEARCHING?

In my work, I am most passionate about asking why relapse happens, and how to identify and treat relapse before it even occurs. We know that cancer cells are able to hide in the body and can evade the immune system or chemotherapy, so my aim is to understand how to identify and target these cancer cells. I am heavily involved in the Better Responses through Avatomics Evidence (BRAvE) initiative, which is our precision medicine platform. I am a physician scientist, meaning I have a background in both the clinical and research side of pediatric cancer treatment. Part of my role in BRAvE is to put on my clinical hat and develop modelling systems that can make it more straightforward to apply what we have learned to the clinic. This way, our research is far better able to help kids living with cancer today.

One important focus I have is minimal residual disease (MRD), which is when a small number of leukemic cancer cells survive in the body after chemotherapy. We know that children with these remaining cells have a higher risk of relapsing, so it is critical that we understand more about them. The trouble is there are so few of

these cells to study. Some of the work I do with Dr. Reid is to implant these cells into immunosuppressed models—a method called patient-derived xenografting—so we can multiply them and begin to study them in various ways.

I also work on other ‘omic’ methods, such as genomics and proteomics, to understand what makes these remaining cells different. Within BRAvE, we are approaching problems from many different directions. We are all in collaboration together, exchanging ideas and approaching the same problem from entirely different angles. I really value this approach and it’s what I think is needed to tackle the big questions in cancer research.

“I really believe we need to tackle the problems of this world together.”

WHAT ATTRACTED YOU TO PEDIATRIC CANCER RESEARCH?

I began to realize the obstacles in predicting and treating relapsed leukemia during my pediatric hematology and oncology fellowships first in Germany and then at BC Children’s Hospital. The real-life consequences of these barriers are heart-wrenching, and this really motivated me to pursue this five-year postdoctoral research fellowship in experimental and therapeutic approaches for childhood leukemia in Dr. Gregor Reid’s lab. I am still profoundly grateful for having received my initial Canadian funding from the Cucciones through the Cuccione Fellowship Award, where I started to carve out my research niche here at BC Children’s, initially with Dr. Kirk Schultz’ supervision. I therefore have a deep appreciation for the constant support of the Cuccione family that enabled the many research projects I have been involved in over the years.

WHAT HAS BEEN A HIGHLIGHT SO FAR?

It is always a highlight to share my research through publication, and being part of the international research community. For example, a recent publication of mine is about how we examined whether xenograft models accurately reflect how a patient's leukemia changes through time and through chemotherapy. For this we used a flow cytometer, which is a machine that can conduct large-scale sample analyses, looking at millions of cells per second.

Because I have been here for several years, another significant highlight has been seeing how much we have built, both in implementing important infrastructure and developing precision medicine approaches. Considering the time, effort, passion, and patience it takes to build something that lasts and does so much good, it's inspiring to see what we have achieved, not just within BRAvE, but across the different research labs. I'm very proud to be an integral part of that.

“To have such passionate people supporting us is an incredible thing and something I always associate with the Michael Cuccione Foundation. To build something and be able to dive into complex questions you need time, and constancy, so I am so grateful to have the continual support of the MCF. We really couldn't have made what we have without you.”

WHAT DO YOU DO IN YOUR SPARE TIME?

A lot of my time is caught up “supervising” two very young and curious prospective “PhD” students, aged seven and nine, our sons. Like so many kids, their endless enthusiasm and love for exploring, understanding and experimenting with everything around them is so inspiring, and certainly keeps me on my toes. They also remind me to be grateful, for being able to do this, for being healthy and to continue to work hard so that many more children can lead a healthy, joyful life. That’s what really drew me to pediatrics. Kids are very capable, very strong, joyfully resilient and remain so kind and caring despite immense hardships, which makes it so meaningful to walk alongside them while providing cancer treatment. Working towards developing innovative treatment approaches that hopefully one day will prevent relapse from ever occurring so that even more children can be cured—that’s worth all the effort and research headaches.

Q&A WITH AMANDA LORENTZIAN



WHAT ARE YOU CURRENTLY RESEARCHING?

I focus on identifying certain genetic mutations that can cause cancer cells to grow. If we can find these mutations and are able to target them with medication, we can treat the cancer without harming healthy cells. Most current therapies for cancers are very aggressive for young kids, especially since they are still growing, and this can lead to many long-term side effects. Over the last decade there have been many efforts to find alternative therapies that are not so aggressive, and the best way to do this is to have treatments that directly target only the cancer cells. This is what my work with Dr. Lange and Dr. Maxwell is all about—finding more targeted therapies that will be safer for kids.

A specific gene mutation may alter what we call a pathway, which is a series of chemical reactions that regulate processes in the cell. I focus on a pathway that is common for leukemia, the CDK 46 pathway, which causes cells to proliferate. There are medications out there to stop CDK 46 for breast cancers, and we're working on how to do the same for leukemia.

WHAT ATTRACTED YOU TO THE MCCRCP?

I had a bit of a different trajectory than many graduate students. After my undergraduate degree, I worked for a few years at a genetic sequencing company. When the company started exploring oncology, I was immediately pulled into cancer research. As a biotech company, we were only contributing one piece of the puzzle, but I wanted to play a bigger role in the research. So, I decided to go back to school. I reached out to Dr. Maxwell, and at the time, the MCCRCP was beginning the BRAvE initiative. This sounded like the perfect fit for me. Who wouldn't want to be a part of that?

WHAT HAS BEEN A HIGHLIGHT SO FAR?

The personal relationships I have made here have been a major highlight. I think we have a unique experience here at the MCCRCP, where these five completely different labs collaborate with each other so well. I think this just makes research so much better. Then of course there are the successes of having your research published, which are amazing highs. For example, I've recently submitted a paper with my team on how proteome analysis, or the analysis of proteins in a cell, can be used to better understand potential therapeutic targets, especially in the context of relapse.

WHAT DO YOU DO IN YOUR SPARE TIME?

I like to be outdoors. Obviously, in Vancouver there's lots to do; a lot of hiking and camping and skiing. I'm not from Vancouver, I'm from California, so it still feels like a new city to me. I really enjoy simply exploring the city and the area as much as I can while I'm here.

"I want to express my extreme gratitude and admiration for your support and all you do for us here. As you know, the research we do is so crucial, and to have all these resources available to us is important for us and for generations of families to come."

Q&A WITH TARIQ BHAT



WHAT ARE YOU CURRENTLY RESEARCHING?

I'm working with Dr. Lim on using chorioallantoic membranes (CAM) models to grow and study cancer cells. A chorioallantoic membrane surrounds the embryo of a chick inside an egg, and contains a network of blood vessels. We can use this membrane to implant and grow tumour cells from patients, so we can begin to test the effectiveness of particular cancer medications. CAM models have been used in medical research for a long time, but I'm working on new ways of using these models to examine tumour cells.

It's exciting because the process of growing and testing a tumour in a CAM is much faster than if we were to use a traditional model, for example. For a CAM it can take only a week to know whether a particular medication has affected the growth of a tumour. For other models it can take four to five months. This is important because the information from a CAM can be used almost immediately to help patients right here at BC Children's. For example, we can receive a sample from a patient and help suggest particular medications to the clinician based on the CAM model we have here. That close connection between this research and the oncology clinic is something very special and exciting.

WHAT ATTRACTED YOU TO THE FIELD OF PEDIATRIC CANCER RESEARCH?

Before becoming a PhD student here at MCCCRC, I was working for a pharmaceutical company that developed medications for a range of adult cancers. It was my role to screen the medications to see how effective they were and whether there was any sign of toxicity, or signs of how the medications may have harmful side effects. These are the final steps of developing a medication, and I wanted to know more about the very beginning, the research that begins the whole process of making an entirely new cancer medication that could make such an impact on people's lives.

WHAT HAS BEEN A HIGHLIGHT SO FAR?

The big highlight for me was when we successfully completed our CAM facility here, which is only a few years old. It was a great feeling to get our first samples from BC Children's BioBank, and start exploring the capabilities of the models in cancer research. A biobank is a collection of anonymous samples that we can use to help our research. Those first few times we began to use the CAM model, after all our preparation and planning, were very exciting.

WHAT DO YOU DO IN YOUR SPARE TIME?

I'm blessed with two kids, so most of my spare time is spent with them. We all like to play soccer, or try out other sports. We're a pretty sporty family. We might also like to go out hiking or do something in nature, making the most of where we are.

"I want to thank you for all your support, not just for this research but for the kids and families who will benefit from the new medications and treatments this research will lead to."

Q&A WITH DR. GEORGINA BARNABAS



WHAT ARE YOU CURRENTLY RESEARCHING?

I'm working on diverse projects, as you tend to do as a postdoctoral researcher, and I enjoy all of them. My first is focusing on a child who has a very rare type of thyroid tumour. Because it's so rare, the range of medications are limited, so I'm hoping to provide information that can contribute towards new therapies. I'm doing this by measuring the changes in protein levels that are specific to this particular cancer, so these can be used to target the tumour with medication without affecting healthy cells. This is a very collaborative project, as I'm working closely with Dr. Lim and Tariq Bhat, using their CAM model to grow versions of the tumour and seeing how it responds to different medications.

I am also applying a similar technique to a form of leukemia aggression that affects the brain and central nervous system (CNS), and can develop during a child's treatment or relapse later. Leukemia in the CNS can also be presented in the initial diagnosis but currently it is very challenging to know who will develop this condition. To address this, I am collaborating with Dr. Amanda Li at BC Children's to identify proteins in the cerebrospinal fluid that are specific to this cancer, in the hope that in the future we can find biomarkers that can be targeted by new treatments.

Finally, I'm exploring neuroblastomas, which are solid cancer growths that occur in the nervous system. Often these tumours are made up of not only cancer cells but also healthy cells, creating what is called a tumour microenvironment. These healthy cells can promote the cancer to be more aggressive, so I am using a special kind of microscope to separate and analyze the cancer from the healthy cells to learn more about how these different cells interact and how this might affect the disease progression or result in resistance to treatment.

WHAT ATTRACTED YOU TO THE MCCRCP?

I obtained my bachelors and masters in India and then my PhD in Israel, where I was working mostly on adult cancers, identifying the genes involved in breast and ovarian cancers. It was during my PhD studies that I knew I wanted to focus on how cancers developed, why the disease occurs again and again, and what treatments are possible. When I began studying childhood cancers, it amazed me how different pediatric cancers are from adult cancers, but it was also so sad to remember that the kids described in the research articles were someone's children, and how it affected people's lives. It moved my heart and made me want to apply to the MCCRCP. I reached out to Dr. Lange, and we got on well straight away. The rest is history.

WHAT HAS BEEN A HIGHLIGHT SO FAR?

One of the things I love about the MCCRCP is how closely everyone works together. I don't just share my results with Dr. Lange, but with every postdoctoral researcher and every PhD student across all the labs. I really like the way I'm growing here. The BioBank is right opposite my building so it's so easy to talk with pathologists there, and benefit from their clinical insight. I've never experienced working in such close collaboration with pathologists and clinicians, which is such a benefit as without their clinical knowledge, it can be impossible to interpret what I'm seeing. This collaboration is such an asset and has been a great highlight.

WHAT DO YOU DO IN YOUR SPARE TIME?

As I'm still new to Vancouver, I've been taking the opportunity to travel a lot, camping, hiking, trying as many outdoor activities as I can. I took a break over winter—as my first experience of a winter in this part of the world; it was a shock! I am really enjoying everything to do with outdoors here, though.

“I want to express my deepest gratitude to the Michael Cuccione Foundation. Being here at the MCCRCP is helping me grow as an independent researcher, learn and feel more confident in my work. I'm so grateful that I'm able to focus on rarer cancers to help children that do not so often benefit from research.”

CAR T-CELL THERAPY

Thank you, Michael Cuccione Foundation, for continuing to advocate for and support innovative CAR T-cell research. From 2019, BC Children's was able to begin enrolling eligible young patients for CAR T-cell therapy. Having overcome the unexpected obstacles of a global pandemic, clinical trials are in full swing, with Dr. Amanda Li having now treated six patients with pediatric leukemia at BC Children's Hospital over the past two years. The MCF's unwavering support has been instrumental in providing CAR T-cell therapy to BC kids with leukemia, lymphoma and other blood cancers. The success and promise of these clinical trials are being felt across the division of oncology at BC Children's.

CAR T-cell therapy is a form of cellular immune therapy where scientists can isolate a patient's own immune cells and modify them in the lab to teach them to perform specific tasks, such as killing cancer cells.

"Thank you for enabling us to continue developing cell therapy treatments that will drastically improve the quality of life of children across British Columbia."

***— Dr. Amanda Li, pediatric hematologist,
MCCCRP Investigator, BC Children's Hospital***

THE NEXT PHASE IN CAR T-CELL RESEARCH— A MESSAGE FROM DR. KIRK SCHULTZ

The continuing support and game-changing \$10.5 million commitment from the Michael Cuccione Foundation will make it possible for experts at the MCCRCP to begin the next phase in life-saving CAR T-cell research. A central part of this next phase is to follow the science, which means taking what we already know about CAR T cells and their interactions with pediatric cancers to develop CAR T-cell therapy for solid tumours, which affect approximately 60 per cent of children with cancer, and for acute myelogenous leukemia (AML). A key focus for this CAR T-cell research is sarcomas—cancers arising in connective tissue and bone, and some of the hardest to treat cancers that children face. Around a third of all relapsed solid cancers in children are sarcomas. The current CAR T-cell technology is not effective at treating sarcomas and other solid tumours, but with this new level of research at the MCCRCP and the unwavering support of the Michael Cuccione Foundation, we believe this challenge can be conquered.

Your generosity will also allow BC Children's to develop CAR T-cells locally, reducing the limitations inherent in relying on other centres for these cells. The long-term goal is to develop clinical trials for CAR T-cell therapy on solid tumours and AML right here at BC Children's. With your philanthropic leadership and support, my colleagues and I are excited to propel this ground-breaking phase of research forward.



Dr. Kirk Schultz

Investigator, Michael Cuccione Childhood Cancer Research Program at BC Children's Hospital, Pediatric Oncologist/Hematologist, and Co-Lead and Investigator, Childhood Cancer & Blood Research Group, BC Children's Hospital



CHECKING IN ON MARCEL

Last year we introduced you to Marcel from Fort St. James, BC, who in 2013 was diagnosed with leukemia. After years of treatment, and multiple relapses, doctors provided a new ground-breaking treatment option for Marcel, who became the first patient to receive CAR T-cell therapy right here at BC Children's.

Now, more than three years after his treatment, Marcel is thriving. "He enjoys riding his bike, helps me with the recycling, and cooks at home." Says his grandmother, Edna, who was happy to share with us his life as a teenager. "He watches wrestling twice a week and orders his usual pepperoni pizza."

With a life free from cancer before them, Edna and Marcel are so grateful for the new opportunity for hope the CAR T-cell therapy at BC Children's offered them. Thank you for making this possible for Marcel and his family.





THE RESEARCH DRIVING NEW TREATMENTS

Every new approach or therapy is the result of years of dedicated study and the coordination of talented and devoted research teams. Researchers at the MCCRCP are striving every day to better understand childhood cancers, find more effective treatments, and bring families renewed hope. We are excited to share with you the most recent updates and ambitions of the MCCRCP's initiatives.

BETTER RESPONSES THROUGH AVATOMICS EVIDENCE (BRAVE) INITIATIVE

Relapse is a word that can devastate families. When a child suffers a relapse, they are much less likely to survive their cancer. Important research at the MCCRCP focuses on how to prevent relapse, or be ready with an effective, tested treatment if it occurs. The BRAVE initiative has become nation-leading in precision medicine in oncology. The remaining cancer cells in a relapsed patient are often the most resistant to current treatments, so researchers within BRAVE examine their genetic makeup, identify mutations, and directly target those cells with improved therapies.

The researchers work by growing patient tumour cells in the lab so that clinicians can test new drugs and new therapies against them before those drugs are used to help treat kids. Donor support is driving this crucial research in personalized cancer treatment.

In partnership with the hematology team at BC Children's, researchers PhD candidate Amanda Lorentzian, and Drs. Chris Maxwell and Philipp Lange are soon to publish work on developing better ways to detect potentially resistant cancer cells. Using a technique called flow cytometry, researchers are working to detect small markers that are unique to drug and radiation-resistant tumour cells, in the hopes of highlighting risks of relapse before it happens.

"I want to say how important your support is to the ongoing research at BC Children's Hospital. It's a fight to improve treatments, and one that cannot be successful without the support donors are providing researchers every day. Thank you."

– Dr. Chris Maxwell

PRECISION ONCOLOGY FOR YOUNG PEOPLE (PROFYLE)

Investigators in the MCCCCRP at BC Children's are conducting ground-breaking studies with the purpose of understanding and ultimately developing life-saving clinical therapies for childhood cancers. World-class researchers at BC Children's, including Drs. Rebecca Deyell and Rod Rassekh, are working hard to develop innovative approaches that bring us closer to making pediatric cancer a thing of the past. An exciting example is PROFYLE, a national program which gives patients access to new drug options, contributes to research, and gives new hope to children and families.

When a child's tumour does not respond to standard therapies, doctors have to look to other treatments. The PROFYLE initiative works to find new, targeted therapies for hard-to-treat cancers. The initiative works by sequencing the genome (the complete set of a person's DNA) of a child, in order to find new therapies. While some other studies focus on small sections of a person's DNA, PROFYLE tries to look at all the whole of the unique genetic makeup of the child. To date, 60 children in BC have been enrolled in PROFYLE, and the number continues to grow. BC PROFYLE is anticipated to enroll 100 children with cancer in its first four years. Thanks to the MCF and other donors, this important initiative is being brought to kids across the province.

“PROFYLE relies on the help and support of donors. We want to offer this to every child coming through the door with hard-to-treat cancers. Hopefully one day this work will become standard for all kids, and this will have been possible with donor help. Thank you for supporting the infrastructure to allow for ground-breaking research such as this.”

– Dr. Rod Rassekh, pediatric oncologist & investigator, Michael Cuccione Childhood Cancer Research Program at BC Children's Hospital Research Institute

“We are in an amazing time where we have the opportunity to really work towards better and more effective treatments that work well for kids, have fewer side effects, and ultimately improve quality of life. Thank you so much for supporting these developments in oncology research.”

– Dr. Rebecca Deyell, pediatric oncologist & investigator, Michael Cuccione Childhood Cancer Research Program at BC Children's Hospital Research Institute

EARLY-PHASE CLINICAL TRIALS

Clinical trials offer patients and families the opportunity to access new treatment options, which would be otherwise unavailable, while also helping to advance knowledge of childhood cancers. The generosity of donors is enabling BC Children's to fast track access to clinical trials that provide targeted therapies for kids who require effective treatment quickly.

This past year has seen some incredible successes at BC Children's, including the launch of the first trial where genetically-edited stem cells are being used to treat hereditary disease. Researchers are also currently publishing work that shares how studying the genomes and proteins of a tumour of a child with acute myeloid leukemia can provide information about the relapse that may occur months or years later. Researchers are also working on a new trial that focuses on diffuse midline pontine gliomas (central nervous system tumours), which are extremely difficult to treat and have a very poor prognosis for children.

BC Children's has also served as the site for selected trials for Western Canada to open two Pediatric Cancer Immunotherapy Trial Network (PEDS-CITN) studies using new antibody approaches to treat relapsed or treatment-resistant cancer. Early-phase trial teams are also supporting remote access to clinical trials for children and families who are unable to access these studies locally.

Looking ahead, researchers from PROFYLE plan to launch a first-in-Canada platform study called 'Optimize' next year, in collaboration with pediatric oncology colleagues in Australia. This study will offer a range of targeted therapies to children with hard-to-treat cancers. Dr. Deyell is also excited about the planned opening of the PedAL, or pediatric acute leukemia, screening study, and targeted treatment sub-trials, in collaboration with the Leukemia Lymphoma Society and the Children's Oncology Group for children with relapsed or treatment-resistant acute leukemia. These remarkable achievements and future aims could not have been possible without the support of the Michael Cuccione Foundation.

A WORLD LEADER IN PEDIATRIC ONCOLOGY RESEARCH

“Because of the rare nature of childhood cancers, it is essential that researchers collaborate, across Canada and the world, and share resources and information as we all work towards a future where every child with cancer survives and thrives.”

– Dr. Chris Maxwell

Support from the Michael Cuccione Foundation has made it possible for researchers at the MCCRCP to publish widely in internationally acclaimed, peer-reviewed journals. Over the last five years, 303 articles have been published by scientists from the MCCRCP, including 59 last year. This collection of work not only continues to demonstrate the program’s position as a leader in childhood cancer research, but also helps illustrate how well researchers at BC Children’s understand that it is only with an international and collaborative mindset that childhood cancers can be conquered. Below is a list of selected publications that reflect the range and collaborative nature of research at the MCCRCP over the last year.

TITLE **PDX Models Reflect the Proteome Landscape of Pediatric Acute Lymphoblastic Leukemia but Divert in Select Pathways**

MCCCRP AUTHORS Lim CJ, Maxwell CA, Reid GSD, Lange PF

DATE March 2021

PUBLICATION *Journal of Experimental and Clinical Cancer Research*

This research evaluates the accuracy of patient-derived xenograft (PDX) models. This is done by comparing the proteins between the model and the patient. The article concludes that while there are differences in the protein processes, PDX models are a generally accurate model to help study and test treatments for leukemia in children.

TITLE **Crizotinib Response in a Neuroblastoma Patient with a Constitutional Mosaic Anaplastic Lymphoma Kinase I1170N-Activating Mutation**

MCCCRP AUTHOR Deyell RJ

DATE June 2021

PUBLICATION *Pediatric Blood and Cancer*

This article describes the response of a three-month-old child with neuroblastoma to a particular medication called crizotinib after genetic testing showed the child to have a certain variant of a gene mutation called I1170N. The study is the first to describe how crizotinib affects patients with this mutation.

TITLE **A Cross-Standardized Flow Cytometry Platform to Assess Phenotypic Stability in Precursor B-Cell Acute Lymphoblastic Leukemia (B-ALL) Xenografts**

MCCCRP AUTHORS Rolf N, Lange PF, Lim CJ, Maxwell CA, Reid GSD

DATE June 2021

PUBLICATION *Cytometry Part A*

This article describes how researchers examined whether PDX models for leukemia accurately reflect how a patient's immune system changes through time and through chemotherapy.

TITLE **Metabolomic Identification of A-Ketoglutaric Acid Elevation in Pediatric Chronic Graft-Versus-Host Disease**

MCCCRP AUTHORS Rozmus J, Schultz KR

DATE January 2022

PUBLICATION *Blood*

This article reports the results of a longitudinal evaluation of particular biochemicals in patients suffering from chronic graft-versus-host disease (cGvHD). This disease occurs after a child receives a bone marrow transplant, and the new donor immune system attacks tissues in the recipient. The study highlights particular metabolic patterns that may be used to classify cGvHD, opening up possibilities for new treatments to the disease.

TITLE **Proteomic Screens for Suppressors of Anoikis Identify IL1RAP as a Promising Surface Target in Ewing Sarcoma**

MCCCRP AUTHORS Li A, Sorensen PH

DATE November 2021

PUBLICATION *Cancer Discovery*

This article identifies a protein found on the surface of a cancer cell called IL1RAP, which is a key driver of the spread of Ewing sarcoma, a highly aggressive childhood cancer that grows in the bone or soft tissue around the bone. Because IL1RAP is minimally found in healthy tissues, this protein is a promising target for immunotherapy.

AMPLIFYING YOUR IMPACT

Support from the MCF is immeasurably valuable in its power to help secure external grants from traditional research funding sources such as the Canadian Institutes of Health Research (CIHR) and National Institutes of Health (NIH).

In response to the efforts of patients and their advocates, the federal government announced its commitment to provide \$22 million over the next two years to support the establishment of a national Pediatric Cancer Consortium with the ultimate goal of improving patient access to effective treatment. The current plan builds upon the collaborative success of three major national networks—PROFYLE, C17 Council (an organization composed of pediatric hematology, oncology, and stem cell transplant programs across Canada), and Cell Therapy Transplant Canada (CTTC). Importantly, MCCRCP researchers are leading and contributing to each of these networks. We are happy to share further examples of external funding with you.

SELECT EXTERNAL GRANTS

RESEARCHER **Dr. James Lim**

GRANT CIHR PROJECT GRANT

TOTAL FUNDING \$1,028,925/total (2021–2026)

PROJECT **Targeting CD47 in pediatric acute lymphoblastic leukemia**

RESEARCHER **Dr. Gregor Reid**

BCCHR
CO-INVESTIGATORS Philipp Lange, Chris Maxwell, Chinten James Lim

GRANT MITACS Accelerate

TOTAL FUNDING \$282,500/total (2022–2025)

PROJECT **Prospective characterization of relapse-driving blasts in acute lymphoblastic leukemia**

RESEARCHER **Dr. Gregor Reid**

GRANT CANCER RESEARCH SOCIETY OPERATING GRANT

TOTAL FUNDING \$126,000/total (2021–2023)

PROJECT **Prospective characterization of relapse-driving blasts in acute lymphoblastic leukemia**

RESEARCHER **Dr. Christopher Maxwell**

GRANT UBC STRATEGIC INVESTMENT FUND

TOTAL FUNDING \$100,000/total (2021–2022)

PROJECT **Canadian pediatric hematology and oncology network for preclinical studies**



Bishop, age 3

RECOGNIZING YOUR COMMITMENT

BC Children's Hospital Foundation is always proud to share the achievements of the MCCCCRP and celebrate and leverage the commitment of the Michael Cuccione Foundation to achieve further support for pediatric cancer research. Our Humans of Oncology video series shared your inspiring story and commitment with donors, as did the *Changing the Conversations* video presented at the 2021 Crystal Ball. Your words and generosity inspire others to realize what is possible, and this inspiration is best demonstrated during Childhood Cancer Awareness Month, where we partnered with the Michael Cuccione Foundation in a large-scale public campaign. By showing your commitment to match donations for up to \$500,000 you moved the public to donate more than \$465,000 over September towards CAR T-cell research.

2021 also saw the success of the Michael Cuccione Foundation's online *Kick for a Cure* and *Golf for a Cure* events, and a fundraising dinner at La Piazza Dario with one hundred guests, all of which worked to bring people together over the common cause of raising funds for childhood cancer research. Finally, the collaborative work of the MCCCCRP was shared in the Fall 2021 issue of SHINE, acknowledging the remarkable achievements research has made over the past decades, made possible through your support.

SOCIAL MEDIA ENGAGEMENT



| FINANCIALS | | Michael Cuccone Childhood Cancer Research Program | |
|--|--|--|---------------------|
| MCCCRP Revenues | | 2020/21 | 2021/22 |
| Michael Cuccone Foundation Annual Contribution | | \$ 250,000 | \$ 500,000 |
| Other fundraising on behalf of Michael Cuccone Foundation | | \$ 2,380 | \$ 109,106 |
| Michael Cuccone Fellowship endowment interest | | \$ 91,184 | \$ 88,614 |
| Other funding (including Annual Grant, General Oncology Research Fund, Johal Endowed Chair) | | \$ 1,332,789 | \$ 1,319,938 |
| Other funding held by MCCCRP program researchers | | \$ 852,833 | \$ 3,936,487 |
| Total Revenues | | \$ 2,529,186 | \$ 5,954,145 |
| MCCCRP Expenditures | | 2020/21 | 2021/22 |
| Salaries | | \$ 2,105,197 | \$ 3,016,662 |
| Michael Cuccone Fellowships | | \$ 35,000 | \$ 80,914 |
| Operating Expenses | | \$ 833,658 | \$ 1,731,697 |
| Total Expenditures * | | \$ 2,973,855 | \$ 4,829,273 |
| *MCF contributed \$1,355,000 in 2019/20, \$695,000 in 2020/21 and \$1,055,956 in 2021/22 towards program expenditures. | | | |
| Leveraging for Researchers | | | |
| External grants received by MCCCRP researchers (10) | | \$ 1,231,367 | \$ 1,563,571 |
| Facilitating Affiliated Researchers in CCBR | | | |
| External grants received by other researchers in the CCBR group (27) | | \$ 3,037,632 | \$ 4,438,391 |
| Total Leveraging for Researchers | | \$ 4,268,999 | \$ 6,001,962 |



Caitlin, age 3



THE MCCCRP TEAM



DR. CHRIS MAXWELL

Interim Director, Michael Cuccione Childhood Cancer Research Program

Interim Head, Oncology Research Program, BC Children's Hospital Research Institute

Associate Professor of Pediatrics, UBC & BC Children's Hospital Research Institute

Dr. Maxwell's research team studies how stem cells respond to cues that encourage their growth, and what goes awry when their division occurs without a key protein. By understanding how stem cells grow, Dr. Maxwell's team hopes to discover how to maintain healthy stem cells during cancer treatment.

THE MCCCRP TEAM



DR. REBECCA DEYELL

*Investigator, Michael Cuccione
Childhood Cancer Research Program
at BC Children's Hospital*

*Pediatric Oncologist/Hematologist,
BC Children's Hospital*

*Clinical Associate Professor, Division of
Oncology, Hematology & BMT, Department
of Pediatrics, Faculty of Medicine,
University of British Columbia*

Dr. Deyell is interested in developing early-phase clinical trials in pediatric oncology to expedite the transition of new, targeted drug therapies from the lab to the patient. She is a co-leader of the BC Pediatric Precision Oncogenomics (PedsPOG) study and of the Clinical Node for the national Precision Oncology For Young People (PROFYLE) program, which focus on finding individualized approaches to targeted therapies for patients with hard-to-treat cancers.



DR. PHILIPP LANGE

*Investigator, Michael Cuccione
Childhood Cancer Research Program
at BC Children's Hospital*

*Assistant Professor, Department of
Pathology and Laboratory Medicine,
Faculty of Medicine, University of
British Columbia*

*Canada Research Chair in
Translational Proteomics of
Pediatric Malignancies*

Dr. Lange's research focuses on proteins, the structural and functional building blocks of a cell. He and his team are working to identify proteins that are specific to certain cancers so they can be potentially targeted by precision therapies.



DR. AMANDA LI

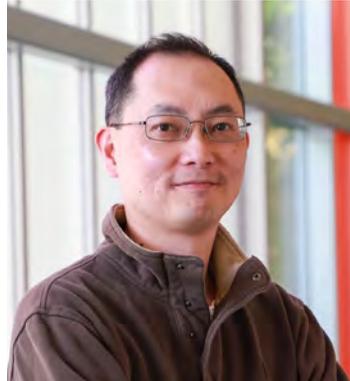
*Investigator, Michael Cuccione
Childhood Cancer Research Program
at BC Children's Hospital*

*Pediatric Oncologist/Hematologist,
BC Children's Hospital*

*Clinical Assistant Professor,
Division of Oncology, Hematology
& BMT, Department of Pediatrics,
Faculty of Medicine, University of
British Columbia*

Dr. Li leads the clinical trial component of chimeric antigen receptor (CAR) T-cell therapies program, which uses a patient's own immune system to target and eliminate certain hard-to-treat cancers.

THE MCCCRP TEAM



DR. JAMES LIM

*Investigator, Michael Cuccione
Childhood Cancer Research Program
at BC Children's Hospital*

*Associate Professor, Department
of Pediatrics, University of
British Columbia*

Dr. Lim and his research team are studying the interactions between leukemic cells and the microenvironment—the collection of cells and structures that support blood cell production—in the bone marrow. This work is providing insight into how these interactions can alter the response of tumour cells to treatments such as chemotherapy.



DR. ROD RASSEKH

*Investigator, Michael Cuccione
Childhood Cancer Research Program
at BC Children's Hospital*

*Pediatric Oncologist/Hematologist,
BC Children's Hospital*

*Clinical Associate Professor,
Division of Oncology, Hematology
& BMT, Department of Pediatrics,
Faculty of Medicine, University of
British Columbia*

The focus of Dr. Rassekh's research is to examine the long-term outcomes of children who have received chemotherapy to treat cancer. He hopes to better understand the genetic reasons some children experience more harmful side effects than others, and how these side effects can be reduced through protective strategies or more targeted therapies.



DR. GREGOR REID

*Investigator, Michael Cuccione
Childhood Cancer Research Program
at BC Children's Hospital*

*Assistant Professor, Division of
Hematology, Oncology and BMT,
Department of Pediatrics,
Faculty of Medicine, University
of British Columbia*

Dr. Reid explores the relationship between early-life infections and the risk of developing leukemia. His team seeks to understand the influence of the immune system as cancer progresses and to use this knowledge to develop approaches to stimulate cancer-fighting immune activity.

THE MCCCRP TEAM



DR. JACOB ROZMUS

*Investigator, Michael Cuccione
Childhood Cancer Research Program
at BC Children's Hospital*

*BMT Director, Pediatric Oncologist/
Hematologist, BC Children's Hospital*

*Assistant Professor, Division of
Oncology, Hematology & BMT,
Department of Pediatrics,
Faculty of Medicine, University
of British Columbia*

Dr. Rozmus' research focuses on the diagnosis and treatment of genetic problems in children's blood cells that often present as immune defects or cancer. This work will provide novel insights into the normal function of blood cells and help to better understand what's wrong with cancer cells, leading eventually to new therapies.



DR. KIRK SCHULTZ

*Investigator, Michael Cuccione
Childhood Cancer Research Program
at BC Children's Hospital*

*Pediatric Oncologist/Hematologist,
BC Children's Hospital*

*Co-Lead and Investigator, Childhood
Cancer & Blood Research Group,
BC Children's Hospital*

*Professor, Division of Hematology and
Oncology, Department of Pediatrics,
University of British Columbia*

Dr. Schultz's research group focuses on controlling the immune responses to blood and marrow transplantation (BMT) to improve immune therapy for childhood leukemia and provide safer tissue transplants. As well, the team is focused on developing approaches to using blood-derived stem cells to regenerate damaged tissues and establish a healthy immune environment.



DR. POUL SORENSEN

*Investigator, Michael Cuccione
Childhood Cancer Research Program
at BC Children's Hospital*

*Professor, Department of Pathology,
University of British Columbia*

Dr. Sorensen's laboratory uses a combination of approaches to understand how tumour cells respond to chemical signals from outside or within the cell that tell it to whether or not to divide. His research explores the how genetic mutations in malignant tumours have changed the response to these signals. The ultimate goal is to identify new therapeutic targets in childhood cancers.



Ella, age 2



THANK YOU FOR HELPING US FIGHT CHILDHOOD CANCERS

Thank you for your advocacy and steadfast support of childhood cancer research. Your ongoing support for the pursuit of innovative treatments—including CAR T-cell therapy—is instrumental in changing the future of childhood cancer care. What has and will be accomplished in the area of childhood cancer research at BC Children's would not be possible without the leadership, dedication and generosity of the Michael Cuccione Foundation. Thank you for standing together with us in our quest to one day reach a future where every child diagnosed with cancer survives and lives a long and healthy life.



Foundation

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