



December 11, 2020

Mrs. Jenny Doull  
Phoebe Rose Rocks Foundation  
44 Laval Street, Ottawa, ON K1L 7Z8

Dear Jenny,

Since the start of the COVID-19 pandemic we have witnessed massive changes to our daily lives, our work and the choices that we make for ourselves and our families. Things we have always cherished have become even more precious, and while this time has been one of uncertainty, it has also been one of heightened focus on what truly matters and the feeling of immense gratitude.

Jenny, we are grateful for the opportunity to get to know you, Jon and other members of your board personally and professionally over the last number of years. In a year full of unknowns, your pledge to support PROFYLE at CHEO is one of few things we could count on. To say “thank you” doesn’t seem to go far enough, but please know that it is said with sincerity and profound gratitude.

We are thankful to witness the incredible legacy you and Jon have created in memory and in honour of Phoebe. Each year you make a meaningful impact, but this year this is especially true, in more ways than one. We continue to be inspired by your kindness and we feel honoured that you have put your trust in us to ensure CHEO’s Research and Oncology teams have what they need to navigate research and care through this pandemic.

As you can imagine, COVID-19 is having a major impact on the way CHEO serves kids and families. Alex Munter said it best, “COVID-19 is disrupting kids’ lives, but we can’t have COVID-19 destroy their futures.” Jenny, by supporting research at CHEO and the tireless work of Dr. Sawyer, Dr. Berman, and the rest of the CHEO PROFYLE team, you are ensuring we keep kids diagnosed with cancer a priority.

We are pleased to present your Donor Impact Report highlighting the impact your incredible gift of \$75,000 had this past year. We realize fundraising is hard work, especially this year, and we greatly appreciate all your efforts. Thank you for continuing to believe in us; your trust as shown by your generosity makes the vital work at CHEO possible. As a donor, you are essential to our success as a children’s hospital and research institute. We hope that when you, Jon and your board read this report you see yourself in the progress of the team’s research and work.

On behalf of everyone at CHEO and the CHEO Research Institute, thank you for your unwavering support.

With sincere gratitude,

Kevin Keohane  
President and CEO  
CHEO Foundation

Pat Zareba  
Annual Giving Officer  
CHEO Foundation



**Dear Phoebe Rose Rocks Foundation Board Members,**

On behalf of Dr. Raveena Ramphal, Dr. Donna Johnston, and Dr. Lesleigh Abbott, and myself, I wish to express our sincere gratitude for the support that Jenny Doull and the Phoebe Rose Rocks Foundation have provided to us over the past year. In many ways it has been a difficult year due to the COVID pandemic, but the work you are supporting was deemed critical in March, and therefore was granted special permission to continue, despite the closure of many other hospital and research programs. We have enrolled 14 patients with rare or unusual tumours, difficult to diagnose tumours and relapsed patients with no further curative treatment options at CHEO from August 2019 to August 2020. These are patients that had exhausted first line treatments and needed the hope that the PROFYLE project would provide to identify alternative therapies.

We are also happy to share the exciting news that we have expanded the enrolment locally and are now able to include young adults in the Terry Fox PROFYLE research program, which was part of the original intent and a large focus of the PROFYLE team nationally over the past year. Ottawa was among the first 5 centres nationally to accomplish this. We succeeded in getting this project through the Research Ethics Board at the Ottawa Hospital, and can now accept patients up to the age of 29y with rare and difficult to treat tumours for PROFYLE. In addition, we realized that some of our patients did not have fresh frozen tumour samples available for sequencing, which is a requirement for PROFYLE, so we have submitted a proposal to the CHEO research ethics board for the Kids Cancer Sequencing project (KiCS), which is similar to PROFYLE but accepts paraffin embedded tumour samples, which will allow more children at CHEO with rare tumours to have the benefit of tumour sequencing.

The funding from the Phoebe Rose Rocks Foundation has allowed us to continue our research, in collaboration with the PROFYLE project, to identify inherited cancer predisposition syndromes, novel drug possibilities, and clinical trials which CHEO patients may be eligible for based on the genomic changes identified. The importance of this research project for immediate clinical care was underscored in March, when most research programs were shut down, yet PROFYLE was rapidly granted permission to continue. Our patients and their families continue to have access to a program that provides ongoing hope.

We realize fundraising is hard work, and especially so this year as so many fundraisers, such as your annual golf tournament, could not run. We continue to ensure that every dollar we receive in funding is spent wisely to help patients who stand to benefit the most from this cancer sequencing project. Thank you from the bottom of our hearts.

Yours sincerely,

**Dr. Sarah Sawyer PhD., MD, FRCPC, FCCMG**

Medical Geneticist, CHEO

Associate Professor, University of Ottawa, Department of Pediatrics



## OVERVIEW OF THE PROGRAM

For the first time in Canadian history, more than 30 pediatric cancer research and funding organizations have joined forces through Terry Fox PROFYLE. This pan-Canadian project gives children, adolescents and young adults who are out of conventional treatment options another chance to beat their cancer – by molecularly profiling the tumours of these patients, no matter where they live in Canada.

CHEO officially partnered with the Terry Fox PROFYLE Program in the spring of 2019. **This is a national program and means that each patient from CHEO has access to national expertise in sequencing, genomic and clinical interpretation of the data, and alternative treatment options and clinical trials information. This is truly a world class project that you are supporting.**

Along with the treating oncologist, Dr. Sawyer determines which CHEO patients are likely to benefit from sequencing, and then sees these families in her Pediatric Cancer Clinic to consent them for the PROFYLE study. She then follows up with the families for a discussion on the results of the germline sequencing results. Drs. Raveena Ramphal, Donna Johnston, and Lesleigh Abbott are Oncologists who are active in identifying patients with cancer who would benefit from research participation in PROFYLE, and who meet with the families to review the tumour changes identified by the PROFYLE project and decide upon treatment strategies or alternatives that are presented by the molecular tumour board.

As a complement to the sequencing work, Dr. Jason Berman co-leads the Model Systems Node where his lab has pioneered the transplantation of human pediatric cancer cells into zebrafish larvae to pre-clinically evaluate responses to targeted drugs, specifically inhibition of cancer cell growth and spread. The hope is to impact therapeutic decisions for a patient, thereby personalizing their cancer treatment. Responses to targeted drugs, specifically inhibition of cancer cell growth and spread, can be assessed within days, simply by adding the drugs to the water in which the larvae are bathed. This is a short enough timeframe to impact therapeutic decisions for a patient, thereby personalizing their cancer treatment.

**By supporting the PROFYLE program locally at CHEO, the Phoebe Rose Rocks Foundation is directly benefitting several families who otherwise would not have answers to their questions or tailored treatment protocols.** This year this was especially important, as your support ensured patients with a difficult to diagnose, refractory, or metastatic cancer continued to have access to this upfront sequencing and drug screen methods to help guide their treatment plan during the Covid-19 pandemic.

## YOUR IMPACT – Genomic Sequencing Approach

The work that you are supporting was deemed critical and granted special permission to continue in March 2020, despite the closure of many other hospital and research programs mandated by the government as a result of the COVID pandemic. Your donation on behalf of the Phoebe Rose Rocks Foundation allowed the research to continue, within a national framework, to identify novel drug possibilities and clinical trials which CHEO patients may be eligible for based on the genomic changes identified in their tumours.



**From August 2019 to August 2020 14 patients were enrolled from CHEO into PROFYLE.** These were patients who had relapsed disease, metastatic disease, or difficult to treat primary tumours for whom first line treatments were known to have minimal effectiveness. Of these 14 patients, 12 had solid tumours and 2 were patients with Leukemia. Of these 14, three patients were diagnosed with an inherited cancer predisposition syndrome that had increased their risk of cancer and caused their pediatric cancer. **This knowledge allowed oncologists to personalize the management of 2 of these patients. This information then allowed the team to identify which other members of the family are also at increased risk of cancer, and they now have personalized cancer screening and surveillance programs put in place.** Also importantly, they were able to identify which siblings and family members were **not** an increased risk of cancer, and did not need to have intensive cancer surveillance since they did not carry the same risk factor as the child with cancer did.

**Sequencing also identified 3 adult-onset cancer predisposition syndromes in pediatric patients.** Although there currently isn't evidence that mutations in these genes increased the childhood risk, this is an active area of study. This information however does allow for testing the parents and putting in place personalized screening and cancer programs for them now, and eventually when the patient is older this knowledge will alter their long-term cancer surveillance as well.

**There were 4 patients in whom clinically actionable findings were identified in the tumour.** For one of these patients this mutation suggested an alternate course of follow up and monitoring, and for two it provided a potential drug target and alternative therapy to complement existing therapies, or to be investigated if the current therapy failed. For the fourth patient the information unfortunately came too late for the patient to benefit, however the team is actively pursuing research studies in tumour tissue that has been donated by the family through Dr. Jason Berman's model systems node.

## YOUR IMPACT – The Model Systems Node

**The model systems node has now completed the research ethics board (REB) application and has been approved to obtain liquid or solid tumor samples from CHEO PROFYLE patients.** When PROFYLE patients present at CHEO, they will now be asked if they would like to consent to the model systems aspect of this program. Either a solid (sarcoma, neuroblastoma) or a liquid (leukemia) tumour sample can be donated to the Berman lab for transplantation into larval zebrafish to assess rapid drug response data. **These data will ultimately be reported to the PROFYLE Molecular Tumor Board and the attending physician to potentially impact treatment decisions for that patient.**

**The team has also embarked upon a collaboration with the Zero Childhood Cancer (ZCC) program in Australia, which is that country's version of PROFYLE.** The ZCC program has already transplanted hard-to-treat cancers from children into mice and compared the response to different drug combinations between patients and their mouse avatars. However, these mouse models take many months to generate and, as such, cannot be used in real time to help prioritize therapy for these patients. There are no zebrafish researchers as part of the ZCC project, so the Berman lab was approached to determine if the more rapid responses we can test in zebrafish accurately predicts the responses seen in their mouse models and their patients. **This is a tremendous opportunity to retrospectively evaluate the efficacy of our zebrafish platform compared to current gold standard mouse transplant models. Evidence of a high**



**level of predictive accuracy will go a long way to establishing the credibility of applying therapeutic response data in the zebrafish to inform treatment decisions in patients as part of the PROFYLE project.**

The material transfer agreement (MTA) between the University of Sydney that houses the ZCC Program and CHEO and other Canadian institutions has been back and forth as part of legal review over the last 6 months (delayed because of COVID) and should be finalized in the next two weeks. While awaiting these samples, the team has completed a host of single drug and drug combination toxicity assays in zebrafish using the drugs that were used in the first 3 patients and their respective mouse models that were selected with ZCC investigators as part of a pilot project. These toxicity assays establish the doses to be used and as such the Berman lab is poised to receive samples from the ZCC, transplant the samples into larval zebrafish and test the above-mentioned therapeutics for data comparison between the murine xenotransplantation model and individual patient data. **Furthermore, frozen pediatric tumour samples from the British Columbia Children's Hospital have been approved to be expanded in mice at the University of Calgary and then sent to CHEO for transplantation into zebrafish. This will be a proof-of-principle study to coordinate efforts between the PROFYLE model systems nodes across the country.** After expansion, this sample will also be sent to other nodes for other proteomic and genetic analyses. There has also been extensive progress in the RedCap PROFYLE model system database generated by Dr. Jennifer Chan at the University of Calgary. This database is accessible to all PROFYLE model system members to coordinate and track all samples collected and models that have been generated.

**It is important to note that while PROFYLE was deemed essential research and continued during the first wave of the COVID-19 pandemic, access to the Berman lab (located at the University of Ottawa) was restricted from mid-March to mid-June.** Unfortunately, no model organism research was able to take place during this time. Since mid-June the team has been able to return to the lab, albeit at only 60% capacity with members of the research team rotating through the lab to allow for proper social distancing. **Having said that, bench work related to PROFYLE was resumed, as mentioned above in the context of the drug optimization studies for the ZCC collaboration, and the team is now able to begin zebrafish xenotransplantation assays for CHEO PROFYLE patients who consent to model organism studies.**

*"We have also applied to a number of funding opportunities to complement the support provided by the Phoebe Rose Rocks Foundation for the model organism activities at CHEO. Unfortunately, we were unsuccessful with our application to the Can-GARD: Advanced Therapies for Rare Diseases 2020 Spring Accelerator Grant Competition. As you are aware, we have recently submitted an application to the Children's Hospital Academic Medical Organization (CHAMO) Innovation Competition and that application is currently under review, but we hope to hear back before the end of the calendar year. Thank you for providing a letter of support for this grant submission. These additional funds will enable us to scale up our modeling activities and include studying samples from patients enrolled in PROFYLE at SickKids and the IWK Health Centre in Halifax."- Dr. Jason Berman*

**THANK YOU!**

