PICTURED ABOVE – Helena was diagnosed with acute lymphoblastic leukemia (ALL) at age three in 2009. After 841 days of chemotherapy, her treatment ended in July 2011 and Helena is now considered cancer-free. Helena is passionate about raising awareness about childhood cancer and was named the 2016/2017 Children’s Miracle Network Champion Child presented by Walmart.

COVER PHOTO – Victoria was diagnosed with neuroblastoma at SickKids when her parents Michelle and Phillip brought her to SickKids to investigate a strange mass in her abdomen. SickKids’ neuroblastoma team quickly developed a treatment plan for Victoria, which included a four-cycle regimen of intensive chemotherapy that she has now completed. Victoria remains under close supervision at SickKids, and the whole team is hopeful for a long and healthy life for her and her family.
The Garron Family Cancer Centre (GFCC) at the Hospital for Sick Children is pleased to present this annual report for 2015-2016, which provides an overview of the clinical, educational and research activities of the Centre during the last year.

Notable highlights of the Centre’s accomplishments in 2015-2016 include: SickKids continues to be a leader in translational childhood cancer research, enhancing our understanding of the root causes of cancer and providing the basis for new therapeutic approaches to treat patients. The identification of a new inherited genetic mechanism by SickKids researchers Adam Shlien and Uri Tabori, which predisposes children to difficult-to-treat cancers, has led to the development of novel treatment strategies using immunotherapies such as checkpoint inhibitors. An international clinical trial that will further evaluate this new treatment approach for children with malignancies associated with biallelic mismatch repair deficiency is being developed by SickKids investigators.

Significant progress has been made in our precision medicine program at SickKids for children with high-risk cancers. The GFCC has partnered with the Department of Pathology and Laboratory Medicine (DPLM) to launch the SickKids Cancer Sequencing (KiCS) program, which applies clinical-grade Next Generation Sequencing (NGS) technology for the enhanced analysis of childhood cancer genomics. A weekly Molecular Tumor Board is now underway to facilitate the translation of these complex datasets into clinically actionable information. These new capabilities provide the foundation for a growing portfolio of molecularly targeted drugs, which are already showing success in children with selected high-risk or recurrent cancers. SickKids is poised to be an international leader in the development and application of precision medicine to treat childhood cancers.

On January 19th, 2016, the GFCC held its inaugural Cancer Research Day in the PGCRL. Over 100 attendees heard an inspiring keynote address from GFCC Executive Council member Dr. Meredith Irwin and outstanding presentations from trainees selected based on the excellence of their research projects. Graduate Students, Postdoctoral and Clinical Research Fellows also participated in a busy poster session, with 35 presenters. The symposium showcased the outstanding cancer research being conducted at SickKids.

SickKids is profoundly grateful for a generous gift from the Women’s Auxiliary, which will help us address the important issue of pain control for children receiving cancer care. Clinical initiatives already implemented include the purchase of automated dispensing cabinets (ADCs) for safe and timely delivery of in-patient pain and other medications, and Continuous Ambulatory Delivery Device (CADD) pumps for better home management of severe pain. A research grant competition led to funding of four projects aimed at reducing the pain associated with cancer. Educational initiatives supported by this gift include a hypnosis workshop for frontline staff focused on cancer pain in children, a seminar on mindfulness for childhood cancer pain, and support for the participation of oncology nurses in an international paediatric pain conference held at SickKids.

We are grateful to the many patients and families from across Ontario and Canada whom our Centre is privileged to serve; to our devoted team of clinicians, educators and researchers who are dedicated to our vision, Healthier Children, A Better World. Thank you to our generous donors, and to our many members and supporters who are making the aspirations and achievements of the GFCC a reality.

Sincerely,

James A. Whitlock, MD
Director, Garron Family Cancer Centre
Division Head, Haematology/Oncology/BMT
Women’s Auxiliary Millennium Chair in Haematology/Oncology/BMT
Senior Associate Scientist, Child Health Evaluative Sciences
Professor of Pediatrics, University of Toronto
VISION
Better outcomes for children with cancer through multi-disciplinary collaboration, discovery and innovation.

MISSION
The mission of the Garron Family Cancer Centre (GFCC) is to facilitate and catalyze innovation in multi-disciplinary research, clinical care and education. Discovery and translation of new knowledge will transform clinical practice and improve clinical outcomes and quality of life for children and their families affected by cancer.

PRIORITIES
The GFCC leadership has identified three strategic priorities that align with and leverage existing institutional and programmatic strengths. These priorities provide a framework for the Centre’s activities and investments arising out of our strategic plan.

The three strategic priorities are:
• Innovative Cancer Therapies
• Personalized Cancer Care
• Cancer Stem Cell Biology

GOALS
The three broad goals of the GFCC are:

• to facilitate and promote innovation in multi-disciplinary cancer research
• to facilitate and promote innovation in multi-disciplinary evidence-based cancer care
• to facilitate and promote innovation in multi-disciplinary cross program cancer education.

The GFCC fosters innovative, novel and collaborative research that will transform our understanding of how cancer arises and progresses, and how we diagnose, treat and care for children with cancer.
EXECUTIVE COUNCIL

Chair
James Whitlock, MD
Director, Garron Family Cancer Centre
Division Head,
Haematology/Oncology/BMT
Women’s Auxiliary Millennium Chair
in Haematology/Oncology/BMT
Senior Associate Scientist,
Child Life Evaluative Services

Brent Derry, PhD
Senior Scientist,
Developmental and Stem Cell Biology Program,
Research Institute

Meredith Irwin, MD
Clinician-Scientist,
Division of Haematology/Oncology/BMT,
and Senior Scientist,
Cell Biology Program,
Research Institute

David Kaplan, PhD
Senior Scientist,
Neuroscience and Mental Health Program,
Research Institute

David Malkin, MD
Clinician-Scientist,
Division of Haematology/Oncology/BMT,
Senior Scientist, Genetics & Genome Biology Program,
Research Institute

Michael Taylor, MD, PhD
Neurosurgeon,
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Senior Scientist,
Developmental and Stem Cell Biology Program,
Research Institute

Judy Van Clieaf, RN, BScN, MN
VP Clinical

Sue Zupanec, NP, MN
Nurse Practitioner,
Division of Hematology/Oncology/BMT

Ex officio:
Colin Hennigar,
Director, Major Gifts,
SickKids Foundation
Karen Fung, Social Worker and Sears Patient Navigator

SEARS CANADA PATIENT NAVIGATOR PROFILE

Karen Fung is a Social Worker in the Division of Haematology/Oncology who spends half of her time as the Sears Canada Patient Navigator at SickKids. Combining patient navigation with social work is a natural fit as it advances many of the core social work functions including empowering individuals to access needed services, and communities and institutions to enhance service delivery to patients and families. As the Sears Canada Patient Navigator in the New Agent and Innovative Therapies (NAIT) Program at SickKids, Karen is able to assist patients and their families to navigate the logistical challenges and the complexities associated with accessing clinical trials. With the generous support of Sears Canada, it is the hope that this role will enhance collaboration with other Canadian centres, helping Canadian children with recurrent/refractory cancers and their families to more easily access new innovative treatment options closer to home.
An anonymous gift from the Women’s Auxiliary was donated to the GFCC to support research, clinical and educational initiatives to address cancer pain. SickKids leaders from the GFCC, Pain Centre and Paediatric Advanced Care Team (PACT) came together to formulate recommendations for optimal use of these funds to achieve the greatest impact among patients, families and healthcare providers. Among the initiatives to address the pain associated with cancer and its treatment was the procurement and implementation of automated dispensing cabinets (ADCs) and Continuous Ambulatory Delivery Device (CADD) pumps. ADCs are computerized drug cabinets used on the hospital unit that store medications and support the timely and safe delivery of narcotics and other drugs, thus reducing wait times for inpatient pain medications. CADD pumps facilitate home administration of intravenous pain medications, allowing patients and caregivers to better manage severe pain and promote comfort in children with cancer outside the hospital.

Diagnosed at SickKids with an advanced form of neuroblastoma that had spread to his liver, Bronson was five days old when he began his first round of chemotherapy. After weeks of aggressive treatment, his cancer went into remission. Following treatment, Bronson’s liver began to fail and he required a transplant. Fortunately his aunt was a match and could donate part of her liver. At less than three months, Bronson was a cancer survivor and a liver transplant recipient.
A common side effect of intensive cancer therapy is the loss of fertility. The SickKids Fertility Preservation Program (SKFPP), led by Dr. Abha Gupta, Dr. Armando Lornezo and Nurse Practitioner, Anne-Marie Maloney, aims to inform all patients diagnosed with cancer about their fertility risk and provide access to fertility preservation interventions when necessary. Since its inception in 2014, over 200 patients have been consulted through the program. SKFPP is committed to educating health care providers about Fertility Preservation, through publications and presentations at national and international conferences. All new nurses and fellows in the SickKids Division of Haematology/Oncology are educated by the SKFPP team during orientation. Multiple research and quality improvement studies to evaluate the SKFPP have helped refine the program and this year the SKFPP was recognized by Accreditation Canada as a Leading Practice.
A team of top Canadian scientists led by Dr. Peter Dirks, Garron Family Chair in Childhood Cancer Research, Senior Scientist and Neurosurgeon at SickKids, and Dr. Samuel Weiss, Director of the Hotchkiss Brain Institute, was awarded $11.7M from Stand Up To Cancer Canada (SU2C) to lead a major research initiative focused on glioblastoma, a highly malignant brain tumour. Previous research at SickKids has shown that a distinct population of stem cells, which can continually divide and avoid differentiation, are fundamental to the growth of these tumours. Dr. Dirks and colleagues will use multiple approaches to investigate the stem cells and devise new strategies to target them to eliminate disease recurrence in both adults and children. Detailed biological, genetic and epigenetic analysis of brain tumour stem cells from 70 glioblastomas and ependymomas will be performed. A library of chemicals will be screened in the hopes of discovering new drugs or drug combinations which may be effective in killing these resilient cells. This major funding announcement was made at SickKids in February, 2016.

Dr. Peter Dirks focuses on stem cell link in brain tumours

Dr. James Till, Dr. Peter Dirks and Dr. Samuel Weiss at the Stand Up To Cancer Canada cancer research funding announcement. The announcement took place at the Peter Gilgan Centre for Research at Learning at SickKids on World Cancer Day, February 4, 2016.

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Targeting glioblastoma cancer stem cells

Glioblastoma (GBM) is a very aggressive, fast growing type of brain tumour, which affects approximately 150 children in Canada every year. Research led by Dr. Peter Dirks, Garron Family Chair in Childhood Cancer Research, Senior Scientist and Neurosurgeon at SickKids, is focused on studying and inhibiting the growth of the cancer stem cells that are responsible for GBM recurrence and treatment resistance. Dr. Dirks is corresponding author on two very important studies published in Cancer Cell this past year. In the first, with co-investigator Dr. Mathieu Lupien of Princess Margaret Cancer Centre, they identified a protein that causes GBM stem cells to have irregular DNA structure, and is linked to the promotion of tumour growth and rapid proliferation of these cells. They also demonstrated that two known drugs, which control DNA structure, can be used to reduce growth of the cancer stem cells. In the second study, Dr. Dirks and colleagues tested the effects of 680 neurochemical compounds on the growth and survival of patient-derived GBM stem cells. These neurochemicals mediate the communication between mature brain cells and have recently been shown to control some aspects of neuron growth. The team found that compounds that modulate many of the neurochemical signaling pathways also had effects on GBM stem cells, in particular those that act through the dopamine receptor D4 (DRD4). Applying DRD4 antagonists to GBM stem cells selectively inhibited their growth. These two studies identify promising new weapons in the treatment of GBM.
Unique genetic features of a tumour, or within a patient’s constitutional DNA, can help determine the best therapeutic approach for the individual. SickKids is a leader in developing these precise diagnostic strategies for paediatric cancer patients, with the latest development being the implementation of cutting edge Nanostring technology. This is used to identify medulloblastoma subtypes and genetic alterations, called fusion transcripts, in leukemias, lymphomas, sarcomas and low grade gliomas. With start up support from the GFCC, Dr. Cynthia Hawkins and her team in the Department of Paediatric Laboratory Medicine are using Nanostring technology to develop clinically validated tests here at SickKids, which offer several advantages over conventional testing methods: Nanostring requires a very small amount of tumour tissue, allows multiple tests to be performed simultaneously, and provides rapid diagnosis for patients at SickKids and across Canada.

Dr. Sylvain Baruchel is a member of the Solid Tumour Section in the Division of Haematology/Oncology, and the Director of the New Agent and Innovative Therapy (NAIT) Program. Since March 2015, Dr. Baruchel has been leading the Phase 1 TOPAZ clinical trial, a multi-centre study of 8 sites across Canada, with additional centres showing interest in participating for Part 2 of the study. This study aims to determine the best dose combinations of Topotecan and Pazopanib in paediatric patients with recurrent or refractory solid tumours, including rhabdomyosarcoma, neuroblastoma and those of the central nervous system. As the first site to activate in March 2015, SickKids enrolled four patients in 2015 and to date, a total of 16 patients have been enrolled across all sites.

Dr. Cynthia Hawkins
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TERRY FOX FOUNDATION GRANTS $2.2 MILLION TO SICKKIDS RESEARCH TEAM

TERRTFOXY FOIX FOUNTAION GRANTS $2.2 MILLION TO SICKKIDS RESEARCH TEAM

The ultimate goals of the multidisciplinary team will be achieved using sequencing and computational models, genetic changes in the blood and innovative cancer imaging. Through these efforts they hope to develop a blood test that detects cancer earlier and identify treatments to prevent cancer from developing in patients who are at risk.

by the Terry Fox Foundation to study this syndrome. The Terry Fox New Frontiers Program Project Grant provides funding annually to groups conducting innovative research in cancer prevention, diagnosis and treatment. Drs. Adam Shlien and Anna Goldenberg of SickKids will use genomic sequencing and computational models to determine the genetic causes of LFS, while Dr. Malkin’s research group will focus on translating basic research findings into early detection and clinical surveillance strategies. Dr. Andrea Doria, a member of the SickKids diagnostic imaging team, is developing innovative cancer imaging strategies to improve early cancer detection and at Dalhousie, Dr. Jason Berman will use zebra fish as a LFS model to screen for new drug targets. This collaborative team approach to funding allows this research group to work towards improving outcomes for patients with this challenging syndrome.
A recent study by SickKids researcher Dr. Brent Derry, Senior Scientist Developmental & Stem Cell Biology, has uncovered an ancestral function of the p53 family of proteins in meiotic fidelity. Many studies have suggested a role for p53 in meiosis, but its function in the process has remained poorly understood. Using the nematode, *C. elegans*, as a model organism, Graduate Student Abigail Mateo, Dr. Derry and colleagues demonstrated that CEP-1 (the *C. elegans* p53-like protein) cooperates with the meiotic protein HIM-5, to maintain genomic stability. They found that CEP-1 is a critical factor in a cell’s choice of DNA repair pathway and when mutated, an error-prone method of DNA repair leads to the build-up of mutations, a hallmark of cancer. Dr. Derry and colleagues have begun collaboration with Dr. Meredith Irwin, Senior Scientist, Cell Biology, to investigate the conservation of this mechanism, which could shed light on how p53 promotes genome stability in human cells. Dr. Derry will also work with Dr. David Malkin, Senior Scientist Genetics & Genome Biology to determine the significance of these findings in patients with Li Fraumeni Syndrome, a cancer predisposition disorder, which is due to inherited p53 mutations. This research, supported by a GFCC Pitblado Discovery Grant, was recently published in Current Biology.
Compared to humans, the nematode worm, *C. elegans*, is tiny – only about 1 mm in length! While this simple organism only lives a few weeks, it has many similarities to humans, making it an excellent model for scientists to study. In fact, many discoveries in worms have made a significant impact on human biology, and provided scientists with enormous insight into human diseases.

Despite their simplicity, the structures of cells and tissues in worms are remarkably similar to humans at the microscopic scale.

**Cells** are very similar in worms and humans. They are comprised of the same organelles that allow them to carry out numerous biological functions needed to keep them alive. For this reason, the cells of a worm serve as a powerful model to understand how human cells work.

**Chromosomes** are made up of DNA and serve as the blueprints for the cell. As seen under a powerful microscope chromosomes are abnormal in cancer cells. When p53 is mutated the chromosomes in both human cancer cells and worm cells become fragmented and not very compact, compared with chromosomes in cells with intact p53.
Dr. Paul Nathan leads a CIHR-funded team to investigate cardiotoxicity caused by anthracycline chemotherapy in survivors of paediatric and adolescent cancers. Since 2012, the study has completed recruitment of over 1100 newly diagnosed cancer patients (Acute cohort) and survivors of childhood cancer (Survivor cohort) from across six study sites. To date, the focus has been on patient recruitment and follow-up as well as acquiring cardiac images and biological samples. To identify genes that may contribute to anthracycline-induced cardiotoxicity, genomic samples have been sequenced from patients who are either anthracycline-resistant or anthracycline-sensitive as suggested by their echocardiogram results. Certain biomarkers in the blood are also being investigated as indicators of the acute and long-term cardiac responses to anthracyclines. A sub-study was recently initiated at SickKids to explore whether cardiac magnetic resonance imaging could quantify the degree of fibrosis in children following anthracycline therapy and whether these findings can be correlated with echocardiographic parameters of cardiac dysfunction. Study findings are expected to inform long-term follow-up guidelines for childhood cancer survivors and will create scientific and clinical resources that will serve as a platform for future research into the cardiac outcomes of childhood cancer.

CARDIOTOXICITY IN PAEDIATRIC CANCER SURVIVORS

NOVEL APPROACHES TO THE PREDICTION, DIAGNOSIS AND TREATMENT OF CARDIAC LATE EFFECTS IN SURVIVORS OF CHILDHOOD CANCER

Jadyn was diagnosed with a type of brain tumour called anaplastic ependymoma at age five in 2008. Despite all the obstacles, including years of treatment and several relapses, Jadyn is a feisty and cheerful teenager and has been involved in many fundraisers for SickKids and other cancer charities.
Glioblastoma multiforme (GBM) is a highly malignant brain tumor and the most common cause of death among children with central nervous system neoplasms. Most GBMs recur despite treatment, resulting in a poor prognosis of less than 6 months median survival. Compared to adults, many paediatric GBMs are associated with predisposition syndromes and genetic mutations. One such syndrome is biallelic mismatch repair deficiency syndrome [bMMRD], which is unique in both the molecular events that lead to GBM formation and opportunities for innovative management of these tumors to improve survival.

The international biallelic mismatch repair consortium, led by SickKids staff Dr. Eric Bouffet, Dr. David Malkin and Dr. Uri Tabori, among others, completed a genetic sequencing study and delivered treatment to two siblings for immune checkpoint inhibition, targeting molecules on certain immune cells that need to be activated to start an immune response. Published in the Journal of Clinical Oncology in 2016, this work has resulted in the first ever response of patients with recurrent GBM to immune checkpoint inhibitors and is a novel immunotherapy approach. Based on this promising data, Dr. Eric Bouffet will be leading a clinical trial to further test the effectiveness of this treatment methods on more patients.

Emily is a feisty and affectionate six-year old who was diagnosed with leukemia at age three in 2013. After over two years of treatments, which included intensive chemotherapy, steroids, hospital stays, and the start of junior kindergarten, Emily now comes to SickKids for follow up and monitoring.
Population-based cancer registries collect data that can be used for disease surveillance, research, and control strategies by deriving estimates of incidence, prevalence, and outcomes in the population. In adults, the Union for Cancer Control’s TNM staging system provides a common language for standardizing data collection in adult populations. However, paediatric cancer staging criteria is more challenging for data management because of their relatively low incidence and broad range of disease variability.

To establish a consistent set of staging data collection criteria for the paediatric population, Dr. Sumit Gupta, Staff Oncologist and Clinician Investigator in the Division of Haematology/Oncology, assembled a panel of international experts and stakeholders of oncologists, cancer registrars and epidemiologists to build consensus. Through a modified Delphi approach the panel developed a series of guiding principles relevant to the collection of paediatric cancer stage in population-based registries. The staging recommendations, called the Toronto Paediatric Cancer Stage guidelines, were published in 2016 in Lancet Oncology. Global implementation of these guidelines in paediatric registries will ease international comparative incidence and outcome studies and improve population-based estimates of cancer data in children to better inform management, research and policy.
SICKKIDS NURSES FACILITATE ENROLLMENT IN CHILDREN’S ONCOLOGY GROUP TRIALS

Survival rates for children with cancer are better than ever, with an expected 80% of patients surviving at least 5 years after their diagnosis, due in part to clinical trials run through cooperative groups like the Children’s Oncology Group (COG). While much work needs to be done to bring the survival rate to 100%, clinician researchers are also increasing their focus on studies aimed at decreasing the toxicities of cancer treatment and improving patient quality of life. These types of studies, classified as cancer control (CCL) research within COG, are focused on priority areas such as infection control, neurological complications, palliative and supportive care to improve the lives of paediatric patients during and after treatment. Integral to the success of clinical trials is adequate enrollment of patients, and failure to do so can lead to early study closures and lost opportunities to implement evidence-based improvements to clinical practice. At SickKids, Nurse Practitioners are taking the lead in these important clinical trials and act as key facilitators for patients and families, informing them of relevant studies, discussing consent, and acting as a liaison to clinical research staff. Together with Clinical Research Assistants (CRAs), physicians, psychologists and pharmacists, these nurse-led efforts have resulted in SickKids becoming the centre with the second highest accrual rates for COG CCL trials. A review of the nurse-led accrual programs at SickKids and other paediatric centres was recently published in The Journal of Paediatric Oncology Nursing.

Multidisciplinary team efforts are needed to facilitate the enrolment of SickKids patients in Quality of Life - focused clinical trials
The majority of basic and translational research on medulloblastoma, the most common type of malignant paediatric brain tumour, is done using tumour samples or models of medulloblastoma that have not been exposed to prior treatment. Promising new agents and therapeutic approaches identified in such research, are then applied in the clinic, particularly when tumours have recurred after surgery and conventional chemotherapy and radiotherapy. The success of such approaches is dependent on the assumption that the primary tumour is adequately similar to the tumour post-treatment. In a recent study in Nature, a team led by Dr. Michael Taylor, Senior Scientist, Developmental & Stem Cell Biology, Neurosurgeon and Garron Family Chair in Childhood Cancer Research, developed and validated a ‘humanized’ mouse model of recurrent medulloblastoma and performed a direct genetic comparison between primary and recurrent tumours. Dr. Taylor’s team found that recurrent tumours have undergone drastic genetic changes due to clonal selection, hence many potential therapeutic targets identified in the primary tumour are unlikely to be present in tumours that recur. This important study suggests that for medulloblastoma, it should be mandatory to include re-biopsy to demonstrate maintenance of the target recurrent tumour.

NEW STRATEGIES FOR TREATMENT OF RECURRENT MEDULLOBLASTOMA

Dr. Michael Taylor
**WOMEN’S AUXILIARY CANCER PAIN RESEARCH GRANT COMPETITION**

In 2015 a $1 million gift was donated from the Women’s Auxiliary to the GFCC to support initiatives for Cancer Pain. Over the past year the GFCC and Pain Centre have developed a strategic plan to utilize this generous gift. To support cancer pain research, a research grant competition led to funding for the following four projects aimed at reducing the pain associated with cancer:

**Dr. David Kaplan – Novel therapeutics for paediatric chemotherapy-induced neuropathy**
Chemotherapy-induced neuropathies are an increasingly common side effect of cancer treatment of children. Symptoms include burning sensations in limbs, pain, numbness, drowsiness, loss of energy and appetite, fatigue, sleep disturbances, nausea and vomiting. While symptoms are often transient and reversible, the toxic effects of chemotherapy limit the amount of drugs that can be used to treat patients, and can be extremely debilitating and last a lifetime. The goal of Dr. Kaplan’s study is to identify new effective treatments for childhood chemotherapy-induced neuropathy, for which there is no current treatment. They have identified a drug used for other conditions in humans, that protect nerves from damage from chemotherapeutic agents and will determine whether the drug also protects mice that have chemotherapy-induced neuropathy. If the drug is proven effective in these mouse studies, it would provide support for its use in patients with chemotherapy-induced neuropathy.

**Dr. Lee Dupuis – Clinical Practice Guidelines for Pain Management for Healthcare Providers, Families and Children**
Cancer-related or cancer treatment-related pain is an important and common symptom. Clinical practice guidelines (CPG) are tools that help health care providers apply the latest medical evidence in the care they provide. Since there are currently no guidelines that focus on this topic, Dr. Dupuis and colleagues in collaboration with the Dutch Children’s Oncology Group, will develop a CPG specifically focused on pain management in children with cancer for use by healthcare providers. Using this new CPG, a team made up of paediatric oncology healthcare providers, children with cancer and their parents, health literacy experts, and graphic artists, will develop two documents of recommendations on pain management: one for children with cancer and one for their parents. Formatted to meet the needs of children with cancer, which will be assessed from direct user group feedback,

Laboratory-based projects funded through this generous gift will help uncover the biological mechanisms of pain related to cancer and will focus on the discovery of new therapeutic agents.
this work will facilitate the evidence-based management of pain in hospital and at home and will reduce the suffering of children with cancer.

Dr. Steve Prescott – Deciphering chemotherapy-induced excitability changes in sensory neurons induced from fibroblasts
Chemotherapy has dramatically improved cancer survival rates. However, life-saving chemotherapeutics can have permanent side effects. Nerve cells, or neurons, are particularly sensitive and can develop abnormal excitability, producing too few or too many action potentials - the electrical impulses responsible for neural coding. Spontaneously occurring action potentials in certain sensory neurons are perceived as burning pain in the hands and feet, a common feature of chemotherapy-induced peripheral neuropathy (CIPN). A major clinical problem among children treated for leukemia, 35% will develop this form of neuropathy. Researchers believe that certain individuals are genetically predisposed to CIPN and the differences between individuals could help decipher the underlying mechanisms: what chemotherapy-induced changes occur in the neurons of pain-susceptible patients that do not occur in the neurons of pain-resistant patients?

Dr. Prescott’s research seeks to pinpoint the molecular changes responsible for chemotherapy-induced pain, using stem cell technologies to compare neuronal excitability in cancer survivors who develop pain with those who do not. In a pilot project to first validate the use of stem cell-derived neurons, they will use mice to test whether neurons induced from fibroblasts recapitulate key properties of true sensory neurons, including chemotherapy-induced excitability changes. Results from this pilot project will provide a solid foundation for future studies using induced human neurons. This research seeks to ultimately yield new treatments to prevent or reverse the neuropathic pain suffered by increasing numbers of cancer survivors.

Dr. Jennifer Stinson – User-Centered refinement of the Pain Squad+ Pain Management App for Adolescents with Cancer – A Usability Study
It is estimated that 49-96% of adolescents with cancer (AWC) experience pain over the course of their cancer treatment, which negatively impacts their quality of life, impedes recovery, causes distress, and is associated with long-term morbidity. As the most common reason adult cancer patients utilize emergency health services, cancer pain also represents a significant cost burden to the healthcare system and to families. Pain Squad+, a smartphone-based pain management app that uses a game-like detective theme to encourage adherence, represents a unique way to manage cancer related pain for AWC in the home, school, and hospital. Prompting AWC to complete valid pain questionnaires on their phones, the Pain Squad+ app instantly provides algorithm-based real-time pain management advice, guiding AWC care decisions and preventing time delays between pain occurrence and treatment.

Early testing of Pain Squad+ with AWC by Dr. Stinson’s team indicates that AWC find the app is easy to use, satisfying, and an important component of their cancer care, while raising a number of needed modifications. The specific aim of this project is to use an iterative user-centered approach to refine the Pain Squad+ app, ensuring that it is easy to use and understand, not prone to errors, efficient, and satisfying to complete for AWC. Novel and effective methods are needed to address the problem of cancer pain in adolescents and Pain Squad+ may improve pain treatment and ultimately health-related quality of life for AWC.
The Garron Family Cancer Centre provides financial and administrative support for cancer workshops, conferences and symposia. The following events, held in the Peter Gilgan Centre for Research and Learning, were among those supported by the GFCC this year:

**9th International Paediatric Renal Tumour Biology Conference**

The 9th International Paediatric Renal Tumour Biology Conference (April 1 - 3), led by Dr. Ron Grant, attracted the top scientific experts in renal tumour biology, genetics and development from around the world. Keynote speakers Dr. Steve Potter, Dr. Charles Roberts, Dr. William Foulkes, Dr. Peter Houghton and Dr. Annie Huang, led sessions on the molecular mechanisms of renal tumour development, rhabdoid and other high risk tumours, renal tumour genetics/epigenetics and the translation of scientific findings to the clinic. The conference included a family session, which provided the opportunity for parents to learn about the latest research and advances in paediatric renal tumour treatment.

**Childhood Cancer Therapy Update**

The 8th Annual SickKids Childhood Cancer Therapy Update (CCTU) was held on Wednesday, February 3rd. With a goal of advancing paediatric oncology practice, this one-day interprofessional symposium brought together national and international experts to share leading practices and applied science. This included four visiting speakers: Dr. Catherine Bollard, Children’s National Medical Centre/George Washington University; Dr. Adam Fleming, McMaster Children’s Hospital; TJ Bains, Children’s Hospital of Eastern Ontario; and Mary Jo Decourcy, London Health Sciences Centre. The event had record attendance with more than 160 multi-disciplinary attendees (physicians, trainees, allied health, pharmacists and administrators), both in person and via webcast from multiple locations across Canada as well as various institutions and organizations across the Caribbean through the SickKids-Caribbean Initiative. Through a combination of plenary and workshop sessions, CCTU was a thought-provoking, relevant and scientific meeting to advance paediatric oncology care locally, nationally and internationally as evidenced by the overwhelmingly positive feedback collected from evaluations of the day.
Developmental & Stem Cell Biology Cancer Symposium
The Developmental & Stem Cell Biology Program held a full day cancer symposium which brought together leaders in a broad range of cancer research fields including cancer signaling, cancer stem cell biology, genomics, lineage analysis and tumour evolution. Eight internationally renowned speakers presented their work including Dr. Thomas Look, Dr. William Weiss, Dr. Kimberly Stegmaier, Dr. Jurgen Knoblich, Dr. Joseph Costello, Dr. Jeremy Rich, Dr. Ben Simons and Dr. Charles Swanton. SickKids researchers, clinicians, clinical fellows, postdoctoral fellows and graduate students were among the 300 registered attendees.

TACL/ITCC Meeting
The GFCC hosted an educational meeting of Therapeutic Advances in Childhood Leukemia & Lymphoma (TACL) and the Innovative Therapies for Children with Cancer (ITCC) consortia in October 2015. Over fifty investigators attended, representing forty-one academic research institutions, from nine different countries. The meeting provided an opportunity for SickKids researchers and clinicians to interact and collaborate with national and international childhood leukemia experts, with an emphasis on identifying new agents to treat high-risk disease.

GFCC Cancer Research Day
The inaugural GFCC Cancer Research Day was held on January 19th, with a focus on highlighting the research conducted SickKids’ trainees. Over 100 attendees heard presentations and visited posters from clinical and postdoctoral research fellows and graduate students. Dr. Meredith Irwin, Solid Tumour Haematology/Oncology Section Head, Senior Scientist, Cell Biology Program delivered the Keynote Address entitled “Bringing clinical and basic research discoveries to neuroblastoma care: Lessons learned on the road to a translational research career”. The symposium provided an opportunity to showcase the breadth of cancer research being conducted at SickKids and awards of excellence were presented to trainees in the following categories:

Best Oral Presentation - Graduate Student:
Alex Seong, Supervisor Dr. Meredith Irwin

Best Oral Presentation - Postdoctoral Research Fellow:
Kamila Szulc, Supervisor Dr. Don Mabbott

Best Oral Presentation - Clinical Fellow:
Ana Guerreiro Stucklin, Supervisor Dr. Michael Taylor

Best Poster presented - Graduate Student:
Patrick Sin-Chan, Supervisor Dr. Annie Huang

Best Poster presented - Postdoctoral Research Fellow:
Ellen van der Plas, Supervisor Dr. Brian Neiman

Best Poster presented - Clinical Fellow:
Natasha Alexander, Supervisor Dr. Meredith Irwin
On Saturday April 2nd 2016, the 5th Annual “It’s All About Me” Sibling Appreciation & Education Day was held to recognize the special role of siblings in the care of SickKids patients. Hosted at SickKids by the psychosocial staff in the Haematology/Oncology Program, the goal of this annual event is to enhance the quality of life of siblings, by providing age appropriate education to increase knowledge and creative, fun activities that promote the expression of feelings and enhance self-esteem. Siblings of both outpatients and inpatients took part in this education day. In total, 28 siblings attended the event that was open to all families in the Haematology/Oncology and Bone Marrow Transplant Programs. Some of the activities included learning about the hospital experience at the Teddy Bear Clinic, for younger participants, and tweens and teens making “All about me shields” and hope jars. At the end of the day, each participant received a medal to recognize their experience in their family’s cancer journey. The evaluation feedback was very positive, with siblings feeling empowered by the support they received, which in turn enhances their overall quality of life.

The annual Sibling Appreciation Day is an opportunity to acknowledge the impact childhood cancer has on the siblings of patients receiving cancer treatment. These siblings often have to make sacrifices like missing out on activities they would have done before the diagnosis in their family, and this event recognizes what they have had to go through while showcasing the important role they play in their families.
CHILDHOOD CANCER AND SICKLE CELL DISEASE AWARENESS EVENT

On September 13, 2016 the Garron Family Cancer Centre hosted the 9th Annual Childhood Cancer and Sickle Cell Disease Awareness Month event in the Garden Patio and Garden Terrace at SickKids. Patients and families were invited to take part in a Rockstars-themed event, in collaboration with 13 external partners, such as Gilda’s Club, Leukemia Lymphoma Society of Canada, Camp Ooch, Ronald McDonald House and Paediatric Oncology Group of Ontario. Each partner brought a rockstar-themed activity for patients to take part in such as making disco balls, rockstar sunglasses and Hollywood stars. Manulife Kids Science provided an engaging science experiment in which participants extracted DNA from strawberries. More than 30 patients and families attended this year’s event.

Marlow was two and a half years old when she was diagnosed with Stage 4 rhabdomyosarcoma in December 2011 and started treatment at SickKids in 2013. Marlow initially underwent an intensive 18 month treatment regime to eradicate her cancer. Following a relapse, Marlow is now back in remission which has enabled her to have a stem cell transplant in July 2016.
GARRON FAMILY CANCER CENTRE RESEARCH FELLOWS

The GFCC fellowships support clinicians, scientists and graduate students on an annual basis who are looking to advance their knowledge of cancer care and research. Through a competitive selection process the following fellowships were awarded for the 2015/16 academic year:

Dr. Ana Guerreiro Stucklin
Scotiabank Clinician Scientist Fellowship
Supervisor: Dr. Michael Taylor, Neurosurgeon, Division of Neurology, Garron Family Chair in Childhood Cancer Research, Senior Scientist, Development & Stem Cell Biology
Identification of mediators of chemo resistance in recurrent paediatric medulloblastoma using functional genomics

Medulloblastoma is an aggressive brain tumour that affects young children and teenagers. Tumour spread within the central nervous system is common and a remarkable challenge for paediatric oncologists. Conventional treatment consists of a combination of surgery, chemotherapy and radiation therapy, which often successfully shrinks the primary tumour but is less effective at controlling metastases. Understanding why medulloblastoma sometimes fails to respond to chemotherapy is key to developing novel and meaningful therapies. Dr. Stucklin and colleagues will conduct studies to address this neglected area of neuro-oncology by searching for genes that render tumour cells and metastases resistant to chemotherapy. This work will unveil mechanisms of chemoresistance and contribute to the development of better treatments and improve the outcome of children with medulloblastoma.

Dr. Deepak Chellapandian
Northbridge Fellowship in Cancer Research
Supervisor: Dr. Lillian Sung, Staff Physician, Division of Haematology/Oncology, Scientist, Child Life & Evaluative Sciences
Organ toxicities and infectious complications among childhood acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) in Ontario: A population-based cohort study.

The survival rates for childhood leukemia have improved significantly in the last two decades mainly as a result of improvements in cancer treatment, risk stratification and supportive care. Unfortunately, treatment related toxicities and mortality have also been trending up and are expected to be responsible for an increasing proportion of deaths. It is extremely important to understand the epidemiology of treatment-related toxicities that occurs from the point of diagnosis to late following completion of therapy. Clinically, the organs most likely affected by toxicity include heart, lungs, brain, liver, kidneys and toxicity related to infections. The aim of Dr. Chellapandian’s research is to determine the incidence of organ toxicities in children diagnosed...
with ALL and AML that occurs on and off treatment. This work will be important in evaluating the magnitude of each problem and identifying the risk factors associated with these toxicities related to therapy. This work will identify the most promising avenues for future research along the lines of preventable options for these toxicities and improving overall survival rates.

Dr. Emilie Ernoult
Christopher Brundage Leukemia Research
Supervisor: Dr. Jane McGlade, Associate Chief of Research, SickKids Research Institute, Principal Investigator, The Arthur and Sonia Labatt Brain Tumour Research Centre, Senior Scientist, Cell Biology

Role of GADS adaptor protein in acute lymphoblastic leukemia

BCR-ABL is a cancer causing gene which is a key factor in chronic myelogenous leukemia (CML) and a significant proportion of paediatric and adult B-cell acute lymphoblastic leukemia (B-ALL). The important role of the BCR-ABL oncogene in CML has led to the development specific drug therapies which target this faulty gene. These drugs are now part of the standard treatment regimen for CML, and can induce complete remission. However, drug resistance has become a major clinical issue in the treatment of CML. In addition these drugs have proven less effective in CML patients in the later phase of disease as well as patients with BCR-ABL positive B-ALL. Thus, there is a critical need to understand the signaling pathways that drive BCR-ABL positive myeloid and lymphoid leukemia and identify alternative drug targets. Dr. Ernoult and colleagues will use a technology called mass spectrometry to identify signaling proteins unique to BCR-ABL B-cell acute lymphoblastic leukemia, with the hopes that this will lead to new and complementary strategies to target the disease.

Dr. Jack Brzezinski
Supervisor: Dr. Rosanna Weksberg, Senior Scientist and Staff Geneticist, Department of Clinical and Metabolic Genetics, SickKids Research Institute and Associate Professor, Department of Paediatrics, University of Toronto

Combining Genetic and Epigenetic Data to Define a Biologically and Clinically Relevant Stratification of Wilms Tumors

Wilms tumour is the most common kidney cancer in children with approximately 50 new cases each year in Canada. Although many children can be cured with a combination of surgery, chemotherapy, and radiotherapy, the long-term side effects of these therapies can be significant and include kidney failure and second cancers. With a more precise system of predicting which children are more likely to have a relapse or second tumour, clinicians could tailor therapy to minimize the risk of these late side effects and also intensify therapy for those more likely to relapse. Dr. Brzezinski’s research is focused on discovering the genetic and epigenetic determinants of outcomes in Wilms tumours. These factors can then be used to identify biomarkers that will improve our ability to choose the best therapy for each child.

Dr. Michal Zapotocky
Supervisor: Dr. Uri Tabori, Staff Haematologist/Oncologist, Division of Haematology/Oncology, Senior Scientist, Research Institute and The Arthur and Sonia Labatt Brain Tumour Research Centre

Liquid biopsy as a tool to precision medicine in childhood cancer

Brain tumors are the most frequent cancer in childhood. There is increasing evidence that proportion of brain
tumors are driven by mutations in one of oncogenes. Tumor biopsy can be very challenging and associated with significant risk of morbidity and mortality. On top of that, no biopsy is performed in centrally located gliomas and these are diagnosed based on MRI findings. As such, no molecular diagnostic can be done from tumor tissue and these patients are disqualified from possible use of targeted therapies. Liquid biopsy is a method of detection of tumor cell-free DNA in patient’s plasma. This method is being tested in various adult cancers and allows to monitor response to therapy or to detect targetable mutations (e.g., RAS, BRAF, etc.).

Dr. Zapotocky and colleagues aim to establish tool for detection tumor specific alterations in plasma in paediatric population. Such a tool will serve for diagnosis of tumor specific mutations from patient’s blood. Moreover it will be used for monitoring of response to anticancer therapy and eventually early prediction of emerging relapse.

Dr. Natasha Alexander
UA Local 46 Childhood Cancer Fellowship
Supervisors: Dr. Sylvain Baruchel, Staff Physician, Division of Hematology/Oncology, Senior Associate Scientist, Physiology & Experimental Medicine; Dr. Meredith Irwin, Clinician-Scientist, Division of Haematology/Oncology, Senior Scientist, Cell Biology Program; Dr. Angela Punnett, Staff Physician, Division of Hematology/Oncology

New Agents and Innovative therapies (NAIT) and Neuroblastoma

Despite the improved outcomes for high-risk neuroblastoma (NB) with intensive multimodal therapy, 20% of patients have relapsed and refractory disease requiring further treatment. 131I-Metaiodobenzylguanidine (131I-MIBG) is a radiolabelled therapy used in upfront and relapsed NB, but as only a third of patients will respond, alternative imaging and treatment modalities are needed. Dr. Alexander and colleagues will investigate a new radiolabelled targeted agent called DOTATATE, which works on receptors for somatostatin that can be found in NB cells. 68Ga-DOTATATE PET/CT can be used to diagnose neuroblastoma and detect metastatic disease and 177Lu-DOTATATE is a potential treatment for relapsed neuroblastoma. This work will further investigate the relationship between somatostatin receptors and NB to better understand which patients would benefit most from DOTATATE imaging and therapy. They will also be working on clinical trials that will investigate use of 68Ga-DOTATATE PET/CT and 177Lu-DOTATATE in NB. Children and adolescents with cancer that has not responded to first or relapsed therapy may be offered therapy on early phase clinical trials within the New Agents and Innovative therapies (NAIT) programme at SickKids Hospital. Dr. Alexander is also working on NAIT educational projects to enhance the current training and experience for Paediatric Hematology/Oncology fellows, including using simulation and scenario-based teaching and assessment, in order to improve patient care and clinical expertise for future staff oncologists in this expanding area for children with cancer.

Dr. Nicolas Waespe
Sears Childhood Cancer Fellowship
Supervisor: Dr. Yigal Dror, Staff Physician, Division of Haematology/Oncology, Director, Marrow Failure and Myelodysplasia Program, Senior Scientist, Genetics & Genome Biology

The Impact of Genetic Mutations on the Phenotype of Patients with Inherited Bone Marrow Failure and Aplastic Anemia

Inherited Bone Marrow Failure Syndromes are associated with mutations in more than 70 different genes and lead
not only to severely low blood counts but also complications in many other organ systems. Some gene mutations harbor a very high risk of developing preleukemia (Myelodysplastic Syndrome), leukemia and other cancers. Standard testing methods identify these mutations in only some patients. Dr. Waespe and colleagues simultaneously analyzed 72 genes in more than 200 patients using Next Generation Sequencing. They study the effect of different gene mutations on the risk for development of complications including cancers. Dr. Waespe and colleagues were able to show that very large mutations, which are not routinely analyzed in these patients, are associated with a more extensive spectrum of affected organ systems (manuscript in preparation). Furthermore, they were able to show that a novel treatment for children with preleukemia leads to an improved event-free survival (manuscript published in Haematologica, Aug 2016). It is the expectation that further clarifying details on the genetic cause in patients with inherited and acquired Bone Marrow Failure will lead to improved cancer risk assessment and better treatment options for children with these diseases.

**FELLOWSHIPS FUNDED THROUGH THE SICKKIDS RESEARCH TRAINING CENTRE**

The GFCC provides funding to support Graduate Students and Postdoctoral Fellows through the SickKids Research Training Centre’s RESTRACOMP program.

In the past year, the GFCC has co-funded the following research students and fellows:

- Mushriq Al-Jazrawe “Investigating the roles of PDGF and Wnt signalling in aggressive fibromatosis” (mentor: Dr. Benjamin Alman)
- Orion Buske “Analysis of Li-Fraumeni mutation data” (mentor: Dr. Michael Brudno)
- Samantha Gauvreau “Investigation of the impact of radiation therapy on neurophysiological network connectivity and impact on brain tumour survivors” (mentor: Dr. Donald Mabbott)
- Brian Golbourn “Role of SNF5 in Atypical Teratoid Rhabdoid Tumours” (mentor: Dr. James Rutka) co-funded by the BTRC
- Julia Plakhotnik “Integrin-linked kinase regulation by alpha and beta parvin in cardiac stress and repair in response to chemotherapy” (mentor: Dr. Jason Maynes)
- Ivette Valencia Sama “Identification of novel therapies for metastatic neuroblastoma” (mentor: Dr. Meredith Irwin) co-funded by the James Fund
- Anh Tran “microRNAs Suppress apoptosis in Caenorhabditis elegans germline by antagonizing translation of BH3-only pro-apoptotic protein EGL1” (mentor: Dr. Brent Derry)
- Man Yu “Comparative Proteomic and RNA Sequencing of DIPGs” (mentor: Dr. Cynthia Hawkins)
- Wen Zhang “Identifying prognostic proteome signatures in human lung cancers” (mentor: Dr. Michael Moran)
- Yangjing Zhang “Role of Numb alternate splicing in tumorigenesis” (mentor: Dr. Jane McGlade)
- Caragh Miller “Incidence of cardiac late events in long-term childhood cancer survivors” (mentor: Dr. Paul Nathan)
AWARDS & MILESTONES

• Dr. Sean Egan, Senior Scientist, Developmental & Stem Cell Biology Program, was awarded the 2015 Breast Cancer Research Program Breakthrough Award from the U.S. Department of Defense through its Congressionally Directed Medical Research Programs

• Dr. David Malkin, Senior Scientist in the Genetics & Genome Biology Program, and Staff Physician in Haematology/Oncology, received the 2015 Henry Friesen Award and Lecture from the Canadian Society for Clinical Investigation for his leadership in the field of cancer genetics and his pioneering discoveries of the molecular basis of Li-Fraumeni syndrome

• Dr. Alvaro Lassaletta was the recipient of the James B. Nachman Junior Faculty Award in Paediatrics from the American Society of Clinical Oncology, supported by the James B. Nachman Paediatric Oncology Fund

• Dr. Avram Denburg, Staff Physician in the Division of Haem/Onc at SickKids, Staff Paediatrician at North York General Hospital, and a CIHR Doctoral Fellow in Health Policy at the Centre for Health Economics and Policy Analysis, McMaster University, received the 2015 Pierre Elliott Trudeau Foundation Scholarship

• Dr. Eric Bouffet, Professor of Paediatrics in the University of Toronto, GFCC Chair in Childhood Cancer Research and Head of the Neuro-oncology Section in the Division of Haem/Onc at SickKids, was elected President of the International Society of Paediatric Oncology (SIOP)

• Dr. Uri Tabori, Senior Scientist, Staff Physician in the Division of Haem/Onc at SickKids, and Associate Professor of Paediatrics and Institute of Medical Sciences at the University of Toronto, was the 2016 recipient of the Bernard and Francine Dorval Prize from the Canadian Cancer Society

• Dr. Michael Taylor, Paediatric Neurosurgeon at SickKids, Senior Scientist in the Research Institute and Associate Professor Departments of Surgery and Laboratory Medicine and Pathobiology at the University of Toronto, was awarded the 2016 K.J. Zülch Prize by the Gertrud Reemtsma Foundation

• Dr. Lillian Sung, Paediatric Oncologist and Clinician Scientist at SickKids, received the Woman of Action Award from the Israel Cancer Research Fund
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