BC PROVINCIAL Pediatric Oncology Hematology Network

NEWSLETTER

BC Cancer Agency CARE & RESEARCH An agency of the Provincial Health Services Authority

BC CHILDREN'S HOSPITAL An agency of the Provincial Health Services Authority

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Childhood Cancer and Blood Research Group

Mission Statement

The Childhood Cancer and Blood Research (CCBR) Program conducts research that improves the lives of children and young adults with cancer, blood and related disorders.

Cancer Research

In the last 40 years the survival rate for children with cancer has risen from 10% to 80%. However, every day, 36 children are diagnosed with cancer. Approximately 1 out of 5 of these children will die. Children's cancer affects all ethnic, gender and socio-economic groups. Research, and thus advances in care, has driven these improvements but these statistics show that research is essential for progress and development of future therapies. Researchers at the CCBR are particularly interested in optimizing cure and care through discovery by concerting their efforts in three specific areas of research:

- developing a more thorough understanding of cancer biology and discovering targeted therapeutics in order to develop improved treatments with less devastating clinical effects
- developing a more detailed understanding of immune responses in patients undergoing transplant in a hope to circumvent Graft versus Host disease (GVHD)
- following patients in long term follow up care with the hope of gaining insight into ways of preventing late effects of current cancer treatments.

Research Group

The CCBR at the Child & Family Research Institute (CFRI), located on the BC Children's Hospital site, is noted for being the second largest pediatric cancer research group in Canada with over 186 peer reviewed publications in the last 5 years.

The CCBR has recently established a BioBank to enable the ethical collection and storage of pediatric biospecimens for research purposes. For more information about the CCBR BioBank and how you can participate please visit the BioBank web page http://www.cfri.ca/biobank/

Laboratory Research

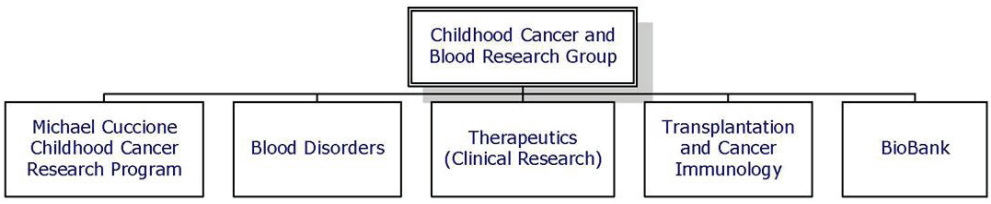
The scientists of the CCBR Program, under the leadership of clinician-scientist Dr. Kirk Schultz, are focused on understanding the complexities and treatments of childhood blood disorders and cancer.

Clinical Research

The CCBR is a national and international leader in cooperative clinical trials groups including:

- Children's Oncology Group (COG), http://www.childrensoncologygroup.org/
- Pediatric Blood Marrow Transplant Consortium (PBMTC), http://www.pbmtc.org/
- C17 developmental therapeutics group (C17 DVL), http://www.c17.ca
- Therapeutics Advances in Childhood Leukemia and Lymphoma (TACL), https://ipcr.chla.usc.edu/tacl/

Organisational Chart for the CCBR



The goal of clinical research in the CCBR cluster is to coordinate and provide leadership for the development of clinical phase I and phase II treatment protocols, utilizing agents identified by the basic/translational component of the research cluster.

To find out who the researchers are, please visit the CCBR section of CFRI website http://www.cfri.ca/childhood-cancer-research.asp and click on each of the Three Key Areas of Activity.

The CCBR group and the Clinical Research Program are the designated Tumour Group for Pediatrics at BC Children's Hospital, BC Cancer Agency and University of British Columbia. BC Children's Hospital and BC Cancer Agency are agencies of the Provincial Health Services Authority.

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Update...

New President Arrives at BCCA

An internationally-renowned oncologist, Dr. Max Coppes, with extensive experience treating children with cancer in Canada and the US, has been the president of the BC Cancer Agency since September 2012. Prior to joining the BC Cancer Agency, Dr. Coppes served as senior vice-president at the Children's National Medical Centre in Washington, DC, where he led the Center for Cancer and Blood Disorders. He will continue to teach and practice medicine at the University of British Columbia and BC Children's Hospital. We welcome Dr. Coppes to Vancouver and look forward to working with him.

Focus on Clinical Research

Believe it or not, the pediatric Oncology/Hematology/BMT clinical research program at the University of British Columbia had its humble beginnings in 1970 when the program adopted the protocols of the Children's Cancer Group (CCG) in order to contribute to the scientific advancement of children's cancer treatments. More than 40 years later, the program is part of a vastly active research network whose goals include maximizing the effectiveness of treatment, decreasing toxicities, improving quality of life and learning about the molecular mechanisms of disease to personalize treatment. Already, the cancer cure rate for children has evolved from <10% 40 years ago to nearly 80% today. Further scientific advancement continues to be pursued, and the BC Children's Hospital (BCCH) clinical research program has been expanding to accommodate growing research requirements.

Types of Oncology/Hematology/BMT Clinical Trials at BCCH include:
Interventional
Currently Open/Pending 42 trials
- Phase I, II, and III Treatment protocols
- Supportive Care protocols

Non-interventional
Currently Open/Pending 46 studies
- Biology studies
- Registries
- Quality of life studies
- Cancer control trials
- Retrospective reviews [not included below]

The majority of clinical research protocols are developed by the Children's Oncology Group (COG), a National Cancer Institute supported clinical trials group. It is the world's largest organization devoted exclusively to childhood and adolescent cancer research. The COG includes 200+ leading children's hospitals, universities, and cancer centers across North America, Australia, New Zealand, and Europe.

Other studies are developed by industry (pharmaceutical companies), investigator initiated, and group affiliations such as the C17 (Canadian Centres Battling Cancer and Blood Disorders in Children), NCIC (National Cancer Institute of Canada), TACL (Therapeutic Advances in Childhood Leukemia), Canadian Brain Tumor Consortium, Canadian Blood and Marrow Transplant Group, as well as many others.

In order to facilitate the program's clinical research trials, the research program infrastructure includes various research support staff: Clinical Research Manger, Clinical Research Associate (CRA) Manager, eight CRAs. Here is a snapshot of what they do:
- Ethics applications and various regulatory tasks
- Track new patients to evaluate eligibility for trials
- Recruit and/or enroll patients/families to studies
- Review protocols and coordinate study activities
- Send samples and imaging for central review
- Maintain accurate documentation of all study activities including adverse events/toxicities
- Monitor treatment and study evaluations closely to ensure data integrity
- Report accurate information to the main data center
- Order study drugs
- Develop strategies to increase study compliance by doctors, nurses and patients
- Participate in audits from multiple sources: COG, Health Canada, BCCH Monitors, Industry Monitors, CIBMTR, FACT

The clinical research trial program at BCCH is expanding to include more Phase I/II treatment studies that involve investigational new drugs as monotherapy or in addition to the standard of care. Some of these drugs have been tested in the adult population already, but may also be beneficial to the pediatric population. Phase I/II drugs provide more options for children who have relapsed, refractory, or progressive disease or for children with rare diagnoses. Currently, there are 10 Phase I/II oncology trials open, with 6 pending approval and 5 closed since 2011.

Within the program, 17 interventional and non-interventional studies are specifically hematology or BMT trials. These studies provide unique opportunities for not only developing/testing new treatments, but also exploring genetics of chronic diseases and the effects of long term treatment. BMT research also focuses on establishing a standard of care for the vast array of cases and complex protocols, factors and outcomes. Research in these areas is continually expanding.

Director of Research:
Dr. Kirk Schultz

COG Principal Investigator:
Dr. Caron Strahlendorf

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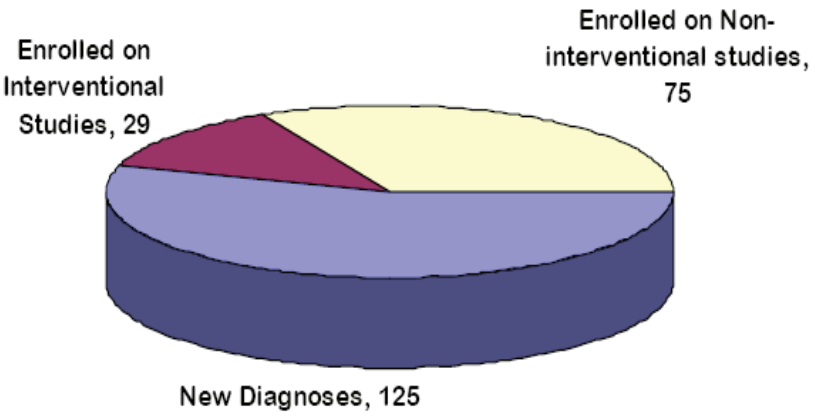
Annual Enrollments BCCH Onc/Hem/BMT Averages from 2003-2011



Targeting the Seeds of Cancer Relapse

Removing an overactive protein from some types of brain tumours actually stops the growth of cancer cells, researchers have found. Their discovery opens the door to developing a drug that targets the protein and improves survival. Brain tumours are one of the most common causes of childhood death from cancer.

The protein, YB-1, is known to play an important role in fetal brain development. In studying mice, the researchers found that YB-1 normally turns off after birth. However, when they examined cancer cells from seven patients who had an aggressive brain tumour called glioblastoma – one of the least curable types of brain tumours – the researchers saw that YB-1 was reactivated. In addition, the researchers discovered that YB-1 is present in the brain tumour's stem cells. These are normal brain stem cells – which usually give rise to specialized brain cells for functions such as learning and memory – that became cancerous through a genetic mutation. When the researchers removed YB-1 from cancer cells and cancer stem cells in the lab, both cell types stopped growing. "Our lab studies showed that brain tumour cells need YB-1 to grow," says Dr. Sandra Dunn, who led the research. "When we removed YB-1, the tumour stem cells not only stopped growing, they also regained the appearance of normal brain cells. This is a key observation as cancer stem cells are resistant to chemotherapy and radiation."

To confirm that YB-1 is associated with cancer stem cells, the researchers analyzed tumour samples from 342 U.K. patients. YB-1 was present in cells alongside two proteins known as markers for cancer stem cells. They also found that YB-1 was present in 67 per cent of the samples from patients whose cancer had relapsed. "Chemotherapy and radiation therapy are effective treatments for killing the bulk of tumour cells, but are not always effective at killing cancer stem cells," says Dr. Dunn. "We believe that cancer stem cells are the source of cancer relapse." The next step is to find targeted drugs that shut down YB-1. "If we can target YB-1, then we can target cancer stem cells and potentially prevent brain tumours from coming back," says Dr. Dunn. "Targeted therapies could improve survival rates, prevent relapse and reduce some of the life-long complications of cancer treatment for children and adults. For children with glioblastoma, it could mean a better chance to live a long, healthy life."

Dr. Abbas Fotovati former UBC post-doctoral fellow, CFRI, under Dr. Sandra Dunn's supervision
First author on this co-authored paper, published August 2011 in Cancer Research.

Dr. Sandra Dunn, CFRI Scientist
Associate Professor in the Divison of Hematology and Oncology, UBC Department of Pediatrics

Excerpt of article from Child & Family Research Institute 2011/12 Annual Report

One Disease Different Faces

A disease caused by bone marrow transplants has at least two distinctive molecular forms, each of which might need a different treatment approach, researchers at the Child & Family Research Institute (CFRI) have discovered. Donor blood and bone marrow transplantation is a key treatment for blood-related cancers, blood disorders and some autoimmune diseases. However, in a quarter of children who receive donated bone marrow, the donor immune cells attack the recipient's tissues, a debilitating disease called chronic graft-versus-host-disease (cGVHD). cGVHD is the number one cause of transplantation-related illness, and kills one-in-five children within 15 years of its onset. "We've found evidence that there may be different pathological mechanisms responsible for chronic GVHD depending on when the disease presents after bone marrow transplantation," says Dr. Jacob Rozmus, who led the study. Previous research at CFRI under Dr. Kirk Schultz, Dr. Rozmus' supervisor, has revealed that there are two distinct periods of cGVHD onset — within three to eight months of transplantation, and after nine months. It's also known that, after the use of immunosuppressants, a transplant patient's immune system reconstitutes itself in gradual steps. Dr. Rozmus' study explored whether it was possible to see the cGVHD differences over time reflected in small proteins called cytokines that play a critical role in cell communication. The researchers examined the cytokine profiles of 33 early onset and 11 late onset cGVHD patients, all of whom were part of the Children's Oncology Group phase III trial for cGVHD treatment. "Despite our small number of patients, we found significantly different cytokine patterns between the early and late onset cGVHD groups," says Dr. Rozmus. While he says the results require validation in a larger study, they reveal the potential power of cytokine profiles as an accurate molecular marker for treating children with cGVHD. "Cytokines could potentially be used to diagnose cGVHD and help clinicians choose the best course of therapy," says Dr. Schultz, in whose lab the current work was done.

"*Early and Late Extensive Chronic Graft-versus-Host Disease in Children Is Characterized by Different Th1/Th2 Cytokine Profiles: Findings of the Oncology Group Study ASCT0031*," published in the journal Biology of Blood and Marrow Transplantation, May 2011.

Dr. Jacob Rozmus,
UBC Post-Doctoral Fellow, CFRI
Pediatric Oncologist, BCCH

Dr. Kirk Schultz, Clinician Scientist
Head of CCBR Cluster, CFRI
Pediatric Oncologist, BCCH
Professor, Division of Hematology and Oncology, UBC Department of Pediatrics

Excerpt of article from Child & Family Research Institute 2011/12 Annual Report

Banking on the Future

Collecting Biospecimens from Cancer Patients to Advance Research

The BioBank at BC Children's is the first childhood cancer bank in the province, but the first biobanks were created about 15 years ago. Since then researchers around the world have benefited from sharing data and samples for multiple purposes.

"It is difficult for British Columbia to contribute to collaborative projects with childhood cancer researchers across Canada without its own BioBank," says Dr. Kirk Schultz. "This is a critical resource to further research across Canada to help cure more children and adolescents with cancer."

Dr. Suzanne Vercauteren, hematopathologist at BCCH and chair of the CCBR BioBank, says that patients at BCCH who choose to donate samples to the Biobank will benefit local research and facilitate larger national and international research projects. Patients at BCCH also have the option of donating their samples for local research only.

"The samples are extremely valuable for research in the field of cancer," says Dr. Vercauteren, who headed the launch of the program. Dr. Schultz, who played a significant role, says funding was provided by a private donation that will sustain the program for two years. Now that it's up and running, he hopes funding comes through to keep the program going. The survival rate for young cancer patients has shot up from 10% to almost 80% in the last 40 years due to advances in research, but the goal is to have no child or teenager die from their cancer.

To learn more about the BioBank, visit www.cfri.ca/BioBank.

Excerpt of article from the BC Children's Hospital Foundation Speaking of Children Summer 2012 magazine

Nanaimo Paediatric Oncology Services

In 2009, Child Health BC funded the opening of the Paediatric Ambulatory Health Clinic (PAHC) at Nanaimo Regional General Hospital. This new clinic was built with a mandate to provide outpatient services to the children living in central and northern communities of Vancouver Island and to bring subspecialty services closer to home. The clinic has a multidisciplinary team which includes nurses, diabetes educators, dietitian, child life specialist, psychologist, and paediatricians.

Even before it officially opened, the clinic provided supportive care to paediatric oncology patients as part of its medical daycare program. At that time, the adult Cancer Clinic at Nanaimo Regional General Hospital (NRGH) was able to provide some simple chemo service to the paediatric patients.

In 2011, the PAHC team, in collaboration with the Pediatric Oncology Hematology Network (POHN) and the NRGH Adult Cancer Clinic, developed a plan to address the needs of the paediatric population and to provide a safe environment for treatment within the PAHC in Nanaimo. The group decided to capitalize on past experience in paediatric oncology within the PAHC: Both Debbie Dymond (Pediatric Ambulatory Nurse Clinician) and Shauna Kazeil (then the Pediatric Nurse Educator and now the Pediatric Clinical Coordinator) had worked at BCCH in Oncology and had experience with paediatric oncology protocols and chemotherapy. Two of the local paediatricians, Drs. Peter MacDougall and Kelly Cox, also had experience and professional interest in the area and were willing to support the change and see these patients in close consultation with the oncologists at BCCH. The Adult Cancer Clinic was also willing to support the PAHC team with the preparation of the medications by their skilled pharmacists and also act as a "back-up" should there be any gaps in nursing coverage. The team in Nanaimo is completed by Rosanne Garcia and the other nurses who provide supportive care in the PAHC; Kelly Raymond, child life specialist; Dawn Redden who provides clerical support to the program; and a host of other professionals and support personnel that serve the children in so many ways. For more information about the clinic, please call 250-739-5852.

Return Undeliverable Canadian Addresses to:
BC Children's Hospital
Provincial Pediatric Oncology/Hematology Network
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Vancouver, BC V6H 3V4

The Provincial Pediatric Oncology/Hematology Network

The Network is an interdisciplinary organization whose goal is to ensure appropriate diagnosis, management, follow-up, and end-of-life care for pediatric patients with malignancies and blood disorders.

The Network supports community hospitals and practitioners, and develops partnerships with other health care facilities to enable seamless and integrated care for patients and families on treatment and off treatment.

It will further develop and enhance the research programs of basic, translational, and clinical research to better childhood cancer control and improve outcomes for these patients and their families.

For More Information

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