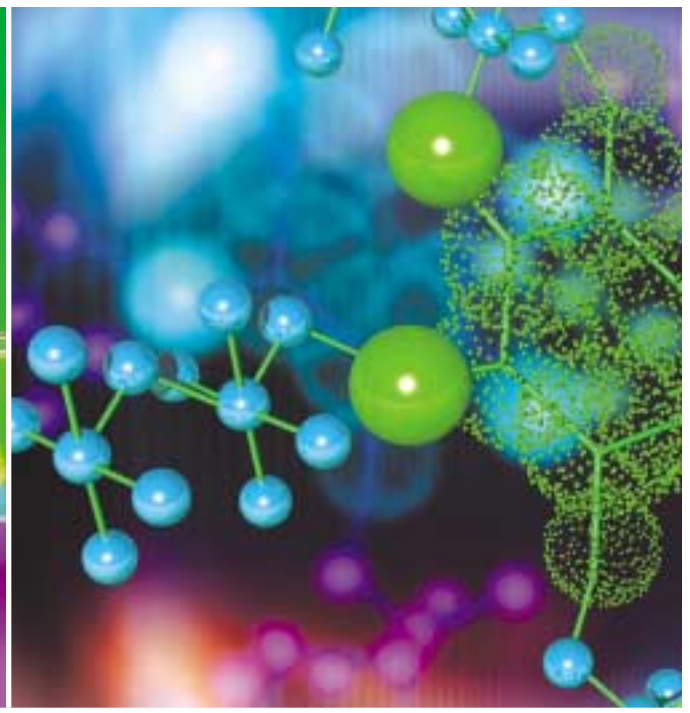


Science Making Miracles



Some Day Our Kids Will Ask Us About Accountability

CFRI researchers tackle the complex issues surrounding pharmaceutical drug safety and costs.

Most folks haven't heard of toxic epidermal necrolysis (TEN), but anyone could be susceptible to it. It is usually caused by an adverse reaction to pharmaceuticals, including non-steroidal anti-inflammatories and antibiotics.

TEN causes blisters that cover large portions of the body. Extensive skin peeling follows, and the raw, exposed skin looks like it's been scalded. Many people who get TEN die; survivors are often disabled.

Stories of adverse drug reactions (ADRs) can incite panic in pretty much anyone; about 35 million prescriptions are written each year in Canada. Yet, pharmaceuticals save lives, and reduce the need for invasive surgeries or other medical interventions. And so, balance is required.

"All activities have risks," says Dr. Bruce Carleton, a Senior Clinician Scientist with the CFRI Centre for Healthcare Innovation & Improvement. "But it's fair that providers of any products carrying risk inform consumers about the risks, as well as the potential therapeutic benefits."

Dr. Carleton is Director of the Pharmaceutical Outcomes and Policy Innovation (POPI) research unit, which brings together researchers from CFRI and other organizations and operates with funding from the Michael Smith Foundation for Health Research. He says drug reaction monitoring is key. One of POPI's main goals is to improve surveillance methods and disseminate ADR information to clinicians, patients and drug regulators. Since 2004 Dr. Carleton has been working with the

Canadian Pediatric Surveillance Program to capture information on serious and life-threatening adverse drug reactions from over 2,300 Canadian pediatricians. Dr. Carleton says 95% of ADRs aren't usually reported, so experts don't yet know how many are preventable.

Other ways to prevent adverse drug reactions may include predictive testing. Dr. Carleton is also co-principal investigator, along with Dr. Michael Hayden of the institute's Centre for Molecular Medicine and Therapeutics, on a project called the Genotype-Specific Approaches to Therapy in Childhood (GATC). The \$8.4 million project, funded by Genome Canada and others, aims to prevent adverse drug reactions by identifying predictive biomarkers for specific ADRs. These markers can then be used to predict - and prevent - ADRs in children, through dosing recommendations for commonly used drugs based on an individual's genetic make-up. Nine major Canadian pediatric health centres report children's adverse reactions and collect DNA samples.

In addition, POPI researchers are studying other complex issues, including drug effectiveness and cost management. For the last 15 years, drug costs have increased by \$300,000 a day in British Columbia alone. "It's the fastest sector of cost growth in health care. Drug safety is not the only question on people's minds. Effectiveness is also important. If we understood the incremental benefits of new drug therapies over existing alternatives then everyone would be better served."

"We need a variety of interlinked solutions, with academics, clinicians, health authorities, and pharmaceutical companies involved. Science needs to be there," says Dr. Carleton. "This is not a time for complacency. Some day our kids will ask us about accountability." ✎

Dr. Bruce Carleton in his office. Photo by C&W Media Production.

Discovery

The focus of the CFRI **Centre for Healthcare Innovation & Improvement (CHII)** is the effective translation of biomedical, clinical and population research into policies and practices that improve health care. Research concerns include evidence-based medicine, knowledge transfer through national information networks, disease mapping, and drug safety.

CHII scientists like Dr. Bruce Carleton collaborate with investigators from other CFRI research programs, such as the **Centre for Molecular Medicine and Therapeutics (CMMT)**. CMMT is dedicated to understanding the molecular and cellular basis of disease and to transferring research into effective clinical and therapeutic strategies. The centre brings

together scientists studying neurodegeneration, the genetics of behaviour, the genetics of cancer, bioinformatics, the development of animal models of human disease, intracellular trafficking, and predictive genomic markers for adverse drug reactions.

Knowing What to Look For is Half the Battle

Scientists at CFRI are conducting novel research that may allow them to predict, and ultimately prevent, diabetes.



Dr. Rusung Tan and Dina Panagiotopoulos in the lab. Photo by C&W Media Production.

When his family noticed Jason Dhami had lost weight, they had a suspicion. Jason's cousin has type 1 diabetes. "So we tested Jason's blood sugar. It didn't even register," says his mother, Nin Dhami. "We brought him to emergency, and he was diagnosed that night."

Over the next three days Jason visited the hospital to learn about the disease, and how to manage it with diet and insulin injections. Six weeks later, at Jason's first regular check-up, he and his family were approached by Dr. Dina Panagiotopoulos, an endocrinologist at BC Children's Hospital and diabetes researcher with the Child & Family Research Institute, and were asked to participate in a research study.

At the time, Dr. Panagiotopoulos was collaborating with Drs. Rusung Tan and Bruce Verchere to identify beta cell specific HLA Class I restricted epitopes in type 1 diabetes. In type 1 diabetes, an autoimmune disease, pancreatic beta cells are destroyed by cells of the immune system, cytotoxic T lymphocytes (CTL or killer T cells). CTL recognize peptide epitopes (short amino acid sequences) presented by human leukocyte antigen (HLA) class I molecules. In diabetes, CD8+ CTLs bind to peptides on the surface of beta cells and kill these insulin-producing cells.

In early 2005, Drs. Tan and Panagiotopoulos were awarded a \$557,000US grant from the National Institutes of Health to expand on their previous work. For their two-year study they're recruiting approximately 400 patients with new onset type 1 diabetes from BC Children's Hospital, as well as from the Barbara Davis Center for Childhood Diabetes in Denver, and about 250 of their first-degree relatives. Recruits' blood is drawn and then tested with novel peptides made by Drs. Tan and Panagiotopoulos. They hope to confirm the candidate HLA class I epitopes they identified through their previous research, and to identify new ones.

Dr. Panagiotopoulos says that blood samples have to be tested for the candidate epitopes within six months of diagnosis, because once the autoreactive CTL have completed their beta cell killing, they retreat back into the lymph nodes and decrease in numbers. "In mice, we've found that the highest frequency of CTL are actually in the blood right before diabetes develops," she says.

Once they know what epitopes to look for, the researchers hope to develop techniques to predict diabetes prior to onset. Dr. Tan, a renowned expert in CTL and autoimmunity, will develop peptide analogs to detect, with greater sensitivity, even lower frequencies of beta cell specific CTL. The researchers believe these peptide analogs may eventually also be used in vaccines, so diabetes can ultimately be prevented. ✎



Jason Dhami at BC Children's Hospital. Photo by C&W Media Production.

Thirteen-year-old Jason Dhami, an upbeat, confident student, is excited about starting high school. His favourite class is P.E. and he's happy he can continue playing trombone, though he doesn't necessarily want to be a professional musician – or, for that matter, a basketball player or a lawyer. "There are so many choices and opportunities. For now I'm going to keep my options open," he says.

Jason doesn't let type 1 diabetes limit him.

"Most people wouldn't realize he has diabetes," says his mother, Nin Dhami. "He's in good physical condition, and very active." She adds that he knows what to do. "He has quick sugar with him at all times, and a cell phone."

Since being diagnosed three years ago, Jason has learned to eat better and he knows how to identify sugar highs and lows. He began using an insulin pump two years ago and says, "It's way better, way easier."

Jason and Nin are both happy that diabetes research is being done at CFRI. "There are lots of bright people here," says Nin. "Diabetes research should be funded more than it is. What's more valuable than a human life?"

Discovery

Scientists with the CFRI Diabetes research program are on the cutting-edge of research seeking to cure, predict, and prevent types 1 and 2 diabetes. Areas of focus include islet cell biology, autoimmunity, genetics of diabetes, viral causes of the diseases, and emerging areas such as beta cell regeneration.

Immunology is one of CFRI's crosscutting research themes. Researchers such as Dr. Rusung Tan are working to better understand the immunophysiology and immunopathology of pediatric illnesses, and develop new diagnostic and treatment interventions.



Architect's rendering shows the new CFRI entrance. By Smith Carter Architects & Musson Cattell Mackey.

Painstaking Detective Work Unlocks Secrets of the Immune System

Sometimes things don't make sense – they seem backwards, with no rhyme or reason. Like when a child gets sick. Or when a child dies.

Maureen and Russel Baker lost their first son, Angus, to meningitis in 1998, when he was six years old. When their fourth son, Forrester, became seriously ill at nine months of age, they knew something was terribly wrong.

Forrester's neck began swelling as the family was planning their annual vacation to northern BC. While they drove north, Forrester's neck grew larger. "We didn't like it. We took Forrester to the hospital in Prince George," says Russel. Their son was put on antibiotics, but the situation worsened. Surgery cleared the infection, but then the swelling started again.

After two more surgeries in Victoria, one to remove five infected lymph nodes, Forrester was referred to BC Children's Hospital. Dr. David Speert, a pediatrician at BC Children's and program head of the CFRI's Infectious & Inflammatory Diseases research program, was brought in. "We did all the diagnostic studies," says Dr. Speert. "But what was happening didn't fit any known pattern of childhood immunodeficiency."

Because of research being conducted in Dr. Speert's lab, they were able to do tests on Forrester's Toll-like receptors, key components of the innate immune system. The innate immune system is ancestrally very old, and is shared with fruit flies and other animals, so it was once considered primitive, says Dr. Speert, who has been studying innate immunity with funding from CIHR for almost two decades. The adaptive, or acquired, immune system had been considered more sophisticated because it "learns" through experience with infections or immunizations. But, says Dr. Speert, the innate immune system's significance has only been recognized since the discovery of Toll receptors in fruit flies and Toll-like receptors in mammals (including humans), which have the unique capacity to recognize specific markers to pathogens. In other words, they are masters at pattern recognition.

Dr. David Speert, an expert in innate immunity, has made a discovery that could save Forrester Baker's life.

"Usually, well-regulated mechanisms would come into play after infectious challenges, but in this case it wasn't happening," says Dr. Speert. "Forrester had three serious infections with the same type of bacteria without any apparent gain of immunity." He and his team identified that Forrester had a mutation that affects IRAK 4, a key enzyme critical to the functioning of all nine known human Toll-like receptors. So, while Forrester's immune system recognizes that organisms are invading, it is not able to mount an immune response to certain types of bacteria. Dr. Speert says one would expect Forrester to be affected by other bacteria and viruses, but he is specifically susceptible to staph and pneumococcal bacteria.

Other members of the Baker family were also tested, and there is evidence that their first son had the same mutation. Dr. Speert and his colleagues have used DNA sequencing, and found that Forrester has only one base pair switched. He is the first child in North America identified with this condition. So far three others have been reported in Europe, but many more children may have the same type of mutation, making them much more vulnerable to life-threatening infections.

Dr. Speert put Forrester on low dose antibiotics, which he has taken every day for the last four years. "We immediately saw the results," says Maureen. "Dr. Speert has been thorough. He's explained everything, making sure we're aware of what's going on with Forrest."

"Dr. Speert does strong research," says Russel. "And he has a big heart. He's very supportive. We feel very safe having him as a backup. We're lucky to have him." 🙏



Forrester Baker with his mother Maureen. Photo by Forrester's father Russel Baker.

Forrester Baker, who has a genetic mutation that makes him susceptible to bacterial infections, is "holding his own, faring well," says his mother Maureen. "He is maturing and growing, playing with friends, being more adventurous. He loves it."

Forrester, soon to be six years old, is starting grade one. He and his brothers, Clint and Sam, are home schooled. "At first, the boys were going to school, but Forrester started getting sick," says their father, Russel. Forrester spent six weeks in hospital last year when he came down with pneumonia.

"When it's a bad flu season, we just don't go out," says Maureen. "People may think we're overcautious, but it's because of what we've been through."

The Victoria-based family is currently looking at relocating, and they hope to buy acreage, "a place where boys can be boys, have horses, all the fun stuff they miss in the city." Adds Maureen, "We want our boys to enjoy life and have a good time."

Discovery

Dr. David Speert is Head of the CFRI **Infectious & Inflammatory Diseases** research program. Investigators with this program focus on increasing knowledge about the causes, therapies and prevention of infectious diseases, and on discovering the cellular and molecular interactions that underlie the normal and abnormal responses of the immune system.

Most of our researchers are clinically-based at one of the three leading health care facilities that make up the Children's & Women's Health Centre of British Columbia, an agency of the Provincial Health Services Authority. In addition to conducting clinical research, investigators associated with our **Clinical Investigation** crosscutting theme oversee clinical trials and assist in pre-clinical evaluation and validation of new technologies, diagnostics and therapeutic interventions.



Dr. David Speert outside CFRI. Photo by C&W Media Production.



Rendering shows the new CFRI lobby. By Smith Carter Architects & Mission Creative/Mackey.



CFRI building exterior. Photo by T. Jager.

Message from the Board

2004/2005 has been a pivotal year for this research institute. As plans evolved for our \$38.9 million expansion, a parallel process to articulate our desired future unfolded. We examined the current reality, our hopes for the future, our relationships with key partners and internal stakeholders, our profile in the research community, and our internal processes.

We have been energized by the undertaking. We can now clearly visualize our new facility with the help of architectural models and renderings. We have a new name – The Child & Family Research Institute (CFRI) – and a new visual identity. Our mission and vision statements are renewed, and we have confirmed the values that will guide our work.

A process is currently underway to formalize types of membership in CFRI, from Senior Scientist and Clinician Scientist to Consultant. This will facilitate provision of appropriate levels of support for investigators, whose numbers are expected to climb significantly when the new research complex opens. Recruitment is underway in several key program areas and we are encouraged by the interest shown by many investigators in joining our research community.

Our relationships with our closest partners, the BC Children's Hospital Foundation, Children's & Women's Health Centre of British Columbia, an agency of the Provincial Health Services Authority, and the University of British Columbia, have been strengthened through ongoing dialogue, mutual support and joint ventures. And we are in the process of forging new linkages through discussions with other post secondary institutions. In addition, we are playing a critical role in several population-based research networks, including those supported by the Michael Smith Foundation for Health Research.

This work on building internal support systems, strengthening external relationships and recruiting leading scientists will continue in concert with the construction of new facilities, all of which will enable us to reach our potential as one of the most successful research institutes in the world.

On behalf of the Board of Directors, I would like to extend my gratitude and thanks to our Executive Director Dr. Stuart MacLeod and our Scientific Director Dr. Geoff Hammond for their inspired leadership, and to our committed administrative staff for their superb efforts this past year. And to those whom we are proud to serve – our investigators and their research teams – thank you for your dedication, capacity and perseverance. Our vision of "Science making miracles" is realized through your efforts. ✎



Maurice Mourton
Board Chair



Dr. Stuart MacLeod
Executive Director

Message from the Executive

Two recurring themes highlight the past decade at the Child & Family Research Institute (CFRI): remarkable success and steady growth. We have more than doubled our space; our external research funding has quadrupled; and our investigator membership has increased 35 per cent.

These phenomena create synergy. As we prepare for another doubling of our research space in the coming two years, recruitment opportunities for investigators and trainees have never been better and with additional space and topnotch research teams, funding opportunities abound.

2004/2005 was a year for broadening our external relationships and establishing internal processes to facilitate this growth. We initiated a process for formalizing membership in CFRI and developed terms of reference for Investigatorship Awards. We strengthened our communications, initiating a monthly on-line newsletter and open forums for information sharing. We upgraded and renovated existing space to accommodate work in population health, genetics, nutrition, reproductive health, and molecular medicine and therapeutics. New space was added off-site to accommodate our growing involvement with provincial, regional and national research networks.

CFRI continues to post better than average success rates in external grant and award competitions. The resulting funding enables us to take a leadership role in initiatives such as the Centre for Disease Modeling, the Canada Northwest FASD (Fetal Alcohol Spectrum Disorder) Research Network, the Canadian Molecular Cytogenetics Platform, Pediatric Palliative Care, Genotype-Specific Approaches to Therapy in Childhood, and the Centre for Research in Childhood Diabetes, to name a few.

During the year we made substantial progress towards a restructuring of the research landscape at Children's & Women's Health Centre of British Columbia, an agency of the Provincial Health Services Authority. We are committed to development of an environment where basic science, clinical science and population health sciences are seamlessly blended. Above all we want to compete successfully for new funds to be made available from CFI and CIHR for clinical research infrastructure in 2006/2007. In addition, we are actively pursuing academic relationships with the University of Victoria, Simon Fraser University, Royal Roads University, the University of Northern British Columbia, and the BC Institute of Technology.

Rendering shows the new CFRI lobby. By Smith Carter Architects & Musson Cattell Mackey.



2004/2005 BOARD & COMMITTEE MEMBERS

Board Members

Mr. Maurice Mourton (Chair)
Ms. Helen Low (Vice Chair)
Mr. Dennis Bettiol (to 01/05)
Dr. Don Brooks
Dr. Diane Finegood
Ms. Carol Gibson
Ms. Patricia Hanbury (from 06/05)
Dr. David Hardwick
Ms. Lynne Kent
Mr. Michael Marchbank (Alternates:
Ms. Sharon Toohey/Dr. Liz Whynot)
Mr. David Podmore
Dr. Gavin Stuart (Alternate: *Dr. Alison Buchan*)
Dr. Ron Woznow
Dr. Stuart MacLeod (ex officio)
Ms. Sue Carruthers (by invitation)

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Ms. Helen Low (Vice Chair)
Mr. Michael Marchbank (Alternates:
Ms. Sharon Toohey/Dr. Liz Whynot)
Dr. Stuart MacLeod (ex officio)

Finance and Audit Committee

Mr. Maurice Mourton (ex officio and Acting Chair)
Ms. Patricia Hanbury
Ms. Lynne Kent
Dr. Ron Woznow
Ms. Helen Low (ex officio)
Ms. Anita Chiu (non-voting member)
Dr. Stuart MacLeod (ex officio)
Mr. Thomas Chan (by invitation)

Our Mission

The Child & Family Research Institute conducts discovery research to benefit the health of children and families.

Our Vision – Science making miracles

We passionately pursue discovery, knowing our achievements have the capacity to transform lives.

Our Values

We work in an environment that values:

- Integrity
- Excellence
- Transformation
- Interaction
- Openness

OUR PARTNERS:

BC Children's Hospital Foundation

Since 1982, BC Children's Hospital Foundation has raised money to support the work of BC Children's Hospital, the province's only pediatric acute care hospital. The Foundation is united with its donors by a single, simple passion – to improve the health and the lives of the young people who enter BC Children's Hospital every day.

The foundation exists to provide financial support to BC Children's Hospital, Sunny Hill Health Centre for Children and the Child & Family Research Institute through accountability of contributions, stewardship of donors and advocacy to better accommodate sick and injured children and their families who live in all parts of the province.

Children's & Women's Health Centre of British Columbia

Children's & Women's is comprised of BC Children's Hospital and Sunny Hill Health Centre for Children, and BC Women's Hospital & Health Centre, agencies of the Provincial Health Services Authority. The wide spectrum of programs and services and close collaboration between these agencies makes Children's & Women's one of the



Dr. Geoffrey Hammond
Scientific Director

In the midst of these developments, we had many opportunities to celebrate the continuing success of our investigators. In November 2004 Prime Minister Paul Martin visited the institute to announce \$193 million for new Canada Research Chairs (CRC). He was accompanied by Hon. David Emerson, Minister of Industry and Minister responsible for the CRC Program and Dr. Eliot Phillipson, President of the Canada Foundation for Innovation. We currently have six CRCs among our faculty.

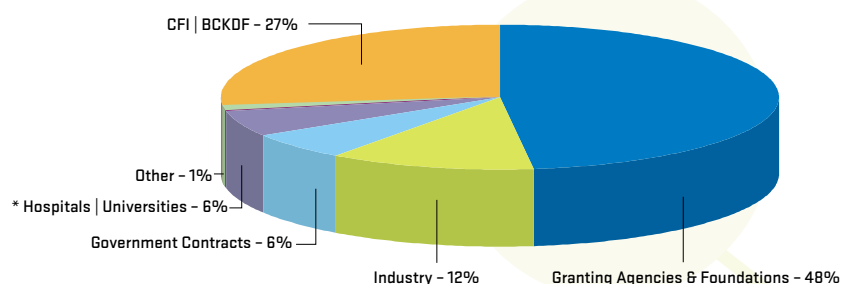
In March, Dr. David Scheifele was appointed CIHR/Wyeth Clinical Research Chair in Vaccines and in April Dr. Sheila Innis was honoured with the 2004 Bristol-Myers Squibb Foundation Freedom to Discover Award in Nutrition. Also in April, Minister of Health Ujjal Dosanjh spoke at the Canadian Therapeutics Congress, held in Vancouver, to update Health Canada's policies on pediatric therapeutics and drug safety.

We are fortunate to have strong and supportive partners. The BC Children's Hospital Foundation is renowned for its own success and has been a generous and committed supporter of our research institute for many years. Our efforts are also enriched by close ties to our principal academic partner, the University of British Columbia; our clinical partner, Children's & Women's; and the Provincial Health Services Authority, which provides the means for province-wide application of our research findings.

It has been, as the saying goes, a very good year, and we look to the future with optimism and anticipation. ✎

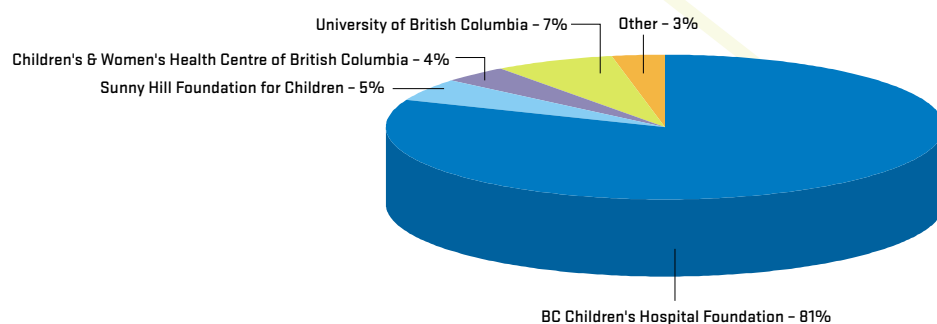
Financials

2004-2005 External Revenue – \$40.4 million



* Exclusive of academic salaries

2004-2005 Internal Revenue – \$9.0 million



Our Research Funding

The Child & Family Research Institute's 2004/05 revenue was approximately \$49.4 million, of which \$40.4 million was external funding, including grants, contracts and agreements. Approximately \$9 million in internal funding was received from BC Children's Hospital Foundation, University of British Columbia, Sunny Hill Foundation for Children and Children's & Women's Health Centre of British Columbia, an agency of the Provincial Health Services Authority. External funding in 2004/05 was received from more than 100 agencies, recognized here.

GRANTING AGENCIES AND FOUNDATIONS

Alzheimer Society of Canada
American Heart Association
Arthritis Society
BC Ataxia Society
BC Children's Hospital Foundation
BC Lung Association
BC Medical Services Foundation
Bong Pang Yee Endowment Fund
Canada Foundation for Innovation
Canadian Anesthesiologists' Society
Canadian Cystic Fibrosis Foundation
Canadian Diabetes Association
Canadian Liver Foundation
Canadian Foundation for AIDS Research
Canadian Foundation for Dietetic Research
Canadian Foundation for Women's Health
Canadian Gene Cure Foundation
Canadian Institute for Advanced Research
Canadian Institutes of Health Research
Canadian League Against Epilepsy
Canadian Society for Mucopolysaccharide & Related Diseases
Crohn's and Colitis Foundation of Canada
Cystic Fibrosis Foundation Therapeutics, Inc.
Cystic Fibrosis Foundation (USA)
Doris Duke Charitable Foundation
Garrod Association of Canada
Genome British Columbia
Heart and Stroke Foundation of BC & Yukon
Heart and Stroke Foundation of Canada
Hereditary Disease Foundation
High Q Foundation
Hospital for Sick Children Foundation
Huntington Society of Canada
Huntington's Disease Society of America
Institute of Molecular and Cell Biology
Juvenile Diabetes Foundation International
Lloyd Jones Collins Awards Foundation
Lotte & John Hecht Memorial Foundation
Michael Smith Foundation for Health Research
Molly Towell Perinatal Research Foundation
Multiple Sclerosis Scientific Research Foundation
National Alliance for Autism Research
National Alopecia Areata Foundation (USA)
National Cancer Institute of Canada
National Children's Cancer Fund (USA)
National Council on Bioethics in Human Research
National Institutes of Health
National Organization for Rare Disorders, Inc.
National Ovarian Cancer Association
National Science Engineering Research Council
Networks of Centres of Excellence
Ontario Mental Health Foundation
Prader-Willi Syndrome Association of USA
Rethink Breast Cancer
Rick Hansen Neurotrauma Initiative – BC
Social Sciences and Humanities Research Council
The Canadian Paediatric Society
The Jack and Doris Brown Foundation
Tzu Chi Foundation (Taiwan)
United Way of the Lower Mainland

GOVERNMENT

BC Cancer Agency
BC Ministry of Advanced Education, Training & Technology
BC Ministry of Children and Family Development
BC Ministry of Health
BC Ministry of Small Business & Economic Development
British Columbia Knowledge Development Fund
Centers for Disease Control and Prevention (USA)
Health Canada
Healthy Child Manitoba
Interior Health Authority
Provincial Health Services Authority
Vancouver Coastal Health Authority
Western Economic Diversification Canada

HOSPITALS | UNIVERSITIES

Auburn University
BC Children's Hospital
Children's Hospital of Eastern Ontario
Hospital for Sick Children's Research Institute
Medical College of Wisconsin
Ottawa Health Research Institute
Regina General Hospital
Sunnybrook and Women's College Health Sciences Centre
University of British Columbia

INDUSTRY

Abbott Laboratories
Amarin Neuroscience Ltd.
Amersham Biosciences
Applied Biosystems Canada
AstraZeneca Canada Inc
Biacore, Inc.
Bio-Rad Laboratories (Canada) Ltd.
Boehringer Ingelheim (Canada) Ltd.
Bristol-Myers Squibb, US (Princeton, NJ)
Cardiome Pharma Corp.
Centocor Inc.
Chiron Corporation
Corus Pharma
Dakocytomation Inc.
Eli Lilly Canada Inc.
ESBE Scientific
Fei Systems Canada Inc.
Fisher Scientific
Genzyme Corporation
GlaxoSmithKline Inc.
Hoffmann-La Roche Ltd (Canada)
IBM Canada
Immune Corporation
Infectio Diagnostic (IDI) Inc.
Janssen-Ortho Inc.
Lorenz Surgical – Biomet
Lundbeck Canada Inc.
Martek Biosciences Corporation
Mead Johnson Nutritional Group
Med Associates Inc.
MedImmune, Inc.
Merck & Co., Inc.
Merck Frosst Canada Ltd.
Merck Frosst Canada Inc.
Noldus Information Technology Inc.
Novartis Pharmaceuticals Canada Inc
Novo Nordisk
Ortho-Clinical Diagnostics
PerkinElmer Las Canada Inc.
PerkinElmer Life and Analytical Sciences, Inc.
Pfizer Canada Inc.
Purdue Pharma
QLT Inc.
Rinat Neuroscience Corporation
Sanofi Pasteur Limited
Serono Canada Inc
Shire Pharmaceutical Development Inc
SmithKline Beecham Pharmaceuticals (Canada)
Upjohn Company
VWR International Ltd.
Waters Corporation
WebMed Technology Inc.
Wyeth Pharmaceuticals
Wyeth-Ayerst Canada Inc.
Xenon Genetics, Inc.

OTHER

Russian Federation State Committee for Higher Education

most comprehensive clinical centres in North America, with approximately 300 beds and more than 4,200 staff. As a teaching hospital and major provincial health care resource, Children's & Women's participates in research to advance health care for women, youth, children and newborns in BC and beyond; CFRI supports this research and shares the 46-acre campus in Vancouver.

University of British Columbia

The University of British Columbia, one of Canada's largest and most prestigious public research and teaching institutions, is now ranked 35th among the world's 500 top universities, according to a study published by the European Commission. It offers a range of innovative undergraduate, graduate and professional programs in the

arts, sciences, medicine, law, commerce and other faculties. UBC ranks in the top 10 of North American universities in creation of spin-off companies, has particular strengths in biotechnology, and its research generates more U.S. Patent applications than any other Canadian institution.

Are We What Our Mothers Ate?

First-of-its-kind research demonstrates that maternal diet can influence a child's intestinal function.

A healthy diet is important in the management of inflammatory bowel disease (IBD), the name given a group of disorders that affect the intestinal system and includes Crohn's disease and ulcerative colitis. The exact causes of IBD are not yet known, but recent studies by Dr. Kevan Jacobson and collaborator Dr. Sheila Innis, both with the CFRI Nutrition research program, suggests that one important factor may be maternal diet.

Drs. Jacobson and Innis have been awarded a 2005 Discovery Award through the Natural Sciences and Engineering Council (NSERC) for their project "Dietary effects on intestinal epithelial barrier function." Recent published research by the two points to increasing evidence that fetal and neonatal nutrition impacts later health.


As a pediatric gastroenterologist who also does clinical research, Dr. Jacobson is also looking at the epidemiology of IBD in British Columbia. "We have unique circumstances here, in that all pediatric gastroenterologists in the province work at BC Children's Hospital, providing us with the opportunity to see most of the children under the age of 16 with gastrointestinal diseases." The hospital's clinic currently follows about 350 children with IBD.

While looking at provincial IBD incidence, Dr. Jacobson has been able to study its incidence in subpopulations. For instance, an estimated 6.5 children per 100,000 of the total BC population are diagnosed with IBD, while the IndoCanadian population has an incidence of 14.5 per 100,000.

Interestingly, says Dr. Jacobson, about half of the IndoCanadians in BC diagnosed with IBD have Crohn's disease. While the incidence of Crohn's disease in this population remains lower than that observed in the Caucasian population, the incidence is significantly higher compared to the worldwide population of Indians, who more typically have ulcerative colitis.

Dr. Jacobson is asking: if the population's genetic makeup is changing, what are these individuals being exposed to that is causing the change? He sees diet as a potentially major factor, especially with diet changing for each generation. As diets become more 'Westernized,' individuals increase their intake of Omega 6 fatty acids. "Lipids seem to be very important in the development of IBD," says Dr. Jacobson. For example, the dietary changes in Japan, with increased intake of Omega 6 fatty acids, have been associated with an increased incidence of Crohn's disease. By contrast, says Dr. Jacobson, the Inuit population, who consume very little Omega 6 fatty acids (but have a diet high in Omega 3 fatty acids), does not develop IBD.

"What effects does maternal lipid intake have on children's developing intestinal function? When is diet important? Before conception, during pregnancy, during lactation, or post-weaning?"

The novel and innovative studies that Drs. Jacobson and Innis are now doing on the effects of maternal diet on intestinal function promise possible means to treat and prevent IBD. Says Dr. Jacobson, "We're looking for ways to alter the natural history of the disease." 

Discovery

Nutrition and other factors in the environment can significantly impact the developing child, even before birth. CFRI **Nutrition** researchers work to develop innovative nutritional strategies for preventing and managing disease, and supporting children in reaching their maximum potential for physiological and neurological development and health throughout life. Nutrition-related health problems are addressed from the molecular and cellular level to that of clinical practice and population health.

The institute's **Reproductive Health** program focuses on basic science and clinical research into the health of women over the life span, especially in relation to their role as mothers. Investigations are targeted at understanding infertility, early pregnancy loss, congenital anomalies, pregnancy complications, preterm birth, pre- and post-partum depression, and reproductive cancers.



Dr. Kevan Jacobson in the hospital's ambulatory care building. Photo by C&W Media Production.

Discovery

Other CFRI research programs and crosscutting themes include our **Oncology** research program. Investigators are carrying out cutting-edge research on new and improved strategies for treating cancer in children and women. In particular, investigators are working to identify and target the genetic and molecular alterations that disrupt signal transduction pathways and give rise to cancers.

Our **Informatics** crosscutting theme includes bioinformatics and health and medical informatics researchers. Bioinformatics (also known as computational biology) links biological themes with the help of computer tools and databases. Health informatics brings together a broad range of complementary expertise, including electronic clinical information systems, data and signal acquisition

and processing, decision support and error detection and reduction, and health systems evaluation.

Another crosscutting theme is **Neurobiology & Mental Health**. A number of researchers at CFRI specialize in areas such as adolescent and child psychiatry, developmental pediatrics, rehabilitation medicine, neuropathology, and neuro-imaging.



Laura Arbour and Barbara Iyiraq, from Igloodik, Nunavut. Photo by her 8 year-old sister, Crystal Iyiraq.

"My studies are not about culture," says Dr. Arbour. "I can't speak about culture. But it is important to respect culture and community, and ensure that research is done in a culturally respectful way. We may be able to gain valuable scientific understanding about genetics, but everything being done is important for members of the community themselves."

This Research Belongs to the Community

Dr. Laura Arbour is working with Canadian Aboriginal communities to study the factors that may contribute to their increased burden of disease.

Medical geneticist Dr. Laura Arbour was first "taken by the North and the people there" during a required residency on Baffin Island. Then her postdoctoral fellowship project confirmed that those living in Canada's north had a higher rate of congenital heart defects than their southern counterparts.

Dr. Arbour has since worked with a number of Aboriginal communities, and she is a key contributor to developing guidelines to conducting research with native populations. She stresses the importance of ongoing consultation and involvement, given that Aboriginal communities were often exploited in the past.

"Research must reflect the needs of the community, and the community must be involved in all stages," says Dr. Arbour. During her studies Dr. Arbour works directly with communities, and keeps all participants up to date with research progress. "Also, it's really important that the community benefit, and that results be returned to it for its own use," she says. In the case of genetic testing, the DNA is considered "on loan" to the researchers.

In attempting to understand the factors that may contribute to the increased burden of disease faced by Aboriginal peoples, Dr. Arbour bridges community research with clinical and basic research. In a current project being conducted with six communities on Baffin Island, she's interviewed Inuit mothers of children with congenital heart defects about diet, pregnancy, and family history. She's also doing a chart review of births from the years 1999 to 2003. Her postdoctoral project found that in the 2,500 Inuit births from 1989 to 1993 there were twice the rate of birth defects overall, and four times the rate of septal heart defects compared to southern populations.

For the same project she's also studying the mothers' blood for levels of nutrients such as folate, vitamins A and B12. In addition, she and her co-investigators are testing whether there are genetic polymorphisms in the popula-

tion that may alter the ability to process some essential nutrients. For example, a variation in one gene that controls the absorption of folate through the intestine seems to be more common in study cases and their mothers compared to controls. This suggests that a lack of folate in the diet, and the interaction of a slightly altered gene may increase the risk for heart defects. Lack of folate and other vitamins has been linked to birth defects, including spina bifida and heart defects.

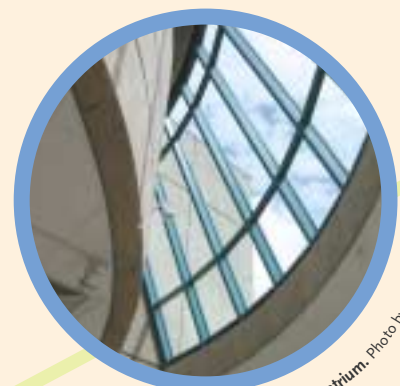
Large-scale public health efforts can help. In 1998 the United States and Canada mandated that all flours and cereals be fortified with folic acid, specifically to reduce defects such as spina bifida. In a northern diet, where there may be little folate overall, the question was whether folic acid added into flour is enough to prevent birth defects. Dr. Arbour says that since fortification there have been no children born with spina bifida in the Cree, who live on the Eastern coast of James Bay in Quebec - whereas the incidence used to be 1 in 260. In the Inuit, she has found that "cellular levels are good. The red blood cell folate is higher than expected. The current chart review will determine whether the rate of birth defects are reduced since fortification."

Dr. Arbour says communities can also take steps to improve their health once they know what factors may be involved. "The research should bring benefits, even if that's only increased awareness and an understanding of why the condition occurs, to start. They want information they can use to develop their own strategies to improve health." ✎

Discovery

Genetics is one of the crosscutting research themes at CFRI. From discoveries of the molecular basis of disease to the design of new and improved methods of diagnosis and therapy, advances in molecular genetics are positively affecting almost every aspect of health care research and delivery. The ability to screen patients' entire genomes for genetic variations promises to revolutionize our understanding of complex diseases such as diabetes and cancer. Further benefits will be gained as health researchers combine these advances with population-based studies and link molecular genetic data with well-defined clinical databases.

Another of the institute's research programs is **Community Child Health**. Investigators work to improve the health and well being of children and their families by understanding the biological, behavioural and social determinants of health and applying this knowledge to community-focused prevention, intervention and health promotion. A focus is on translation of research findings to everyday applications. The program brings together investigators whose expertise ranges from population-based epidemiology and health promotion to biobehavioural mechanisms underlying development.



Inside CFRI's atrium. Photo by T. Jager.



Outside the atrium. Photo by T. Jager.



Rendering of the new building. By Smith Carter Architects & Musson Cattell Mackey.

Our People

The outstanding success of the Child & Family Research Institute is possible because of its community of committed investigators, trainees, support staff and administration. Every effort has been made to be accurate; please accept our apologies for any errors or omissions.

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