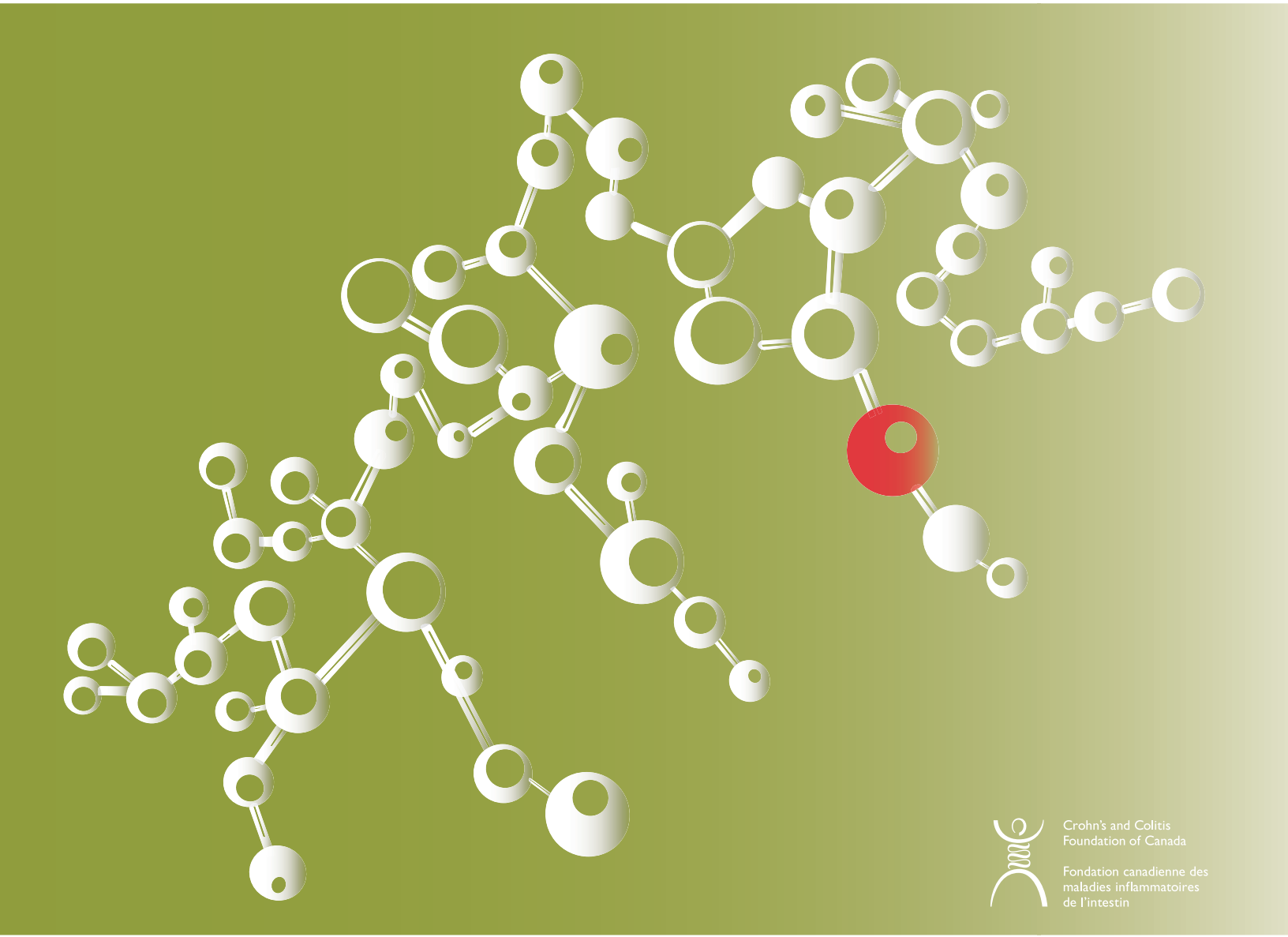
2012 RESEARCH REPORT



Crohn's and Colitis Foundation of Canada

Fondation canadienne des maladies inflammatoires de l'intestin

MESSAGE FROM THE CHAIR OF THE SCIENTIFIC & MEDICAL ADVISORY COUNCIL

Dr. John Wallace, Chair, Scientific & Medical Advisory Council

AND THE CHIEF SCIENCE & EDUCATION OFFICER

Aida Fernandes, Chief, Science & Education Officer

The Crohn's and Colitis Foundation of Canada's (CCFC) commitment to finding a cure for Inflammatory Bowel Disease (IBD) and improving the lives of those with IBD is stronger than ever. Canada is the home to many of the world's top IBD scientists. Thanks to the intensive world-class research funded by the CCFC, our researchers are making important progress on every front – from understanding the basic mechanisms, epidemiology, and genetics to developing new treatments for individuals living with Crohn's disease (CD) and ulcerative colitis (UC).

In fiscal year 2011/12, the CCFC invested more than $5.4 million in top-calibre IBD research. The grants cover a wide variety of research initiatives including triggers of inflammation, genetics, and microbe interactions. The CCFC also supports some of the most progressive and innovative projects that bring together the finest scientific minds in the field to find new approaches and treatments for IBD.

Through partnerships with the Canadian Institutes of Health Research (CIHR), Canadian Association of Gastroenterology (CAG) and provincial granting agencies, the CCFC has leveraged its investments to train 31 future IBD researchers, encouraging them to pursue careers in IBD research, and support additional IBD-related research.

The CCFC is pushing the dial on translating research into outcomes through a new research partnership with biotech company, Vertex Phamaceuticals, in conjunction with the Universities of Sherbrooke, Toronto and McMaster. This cutting-edge collaboration represents a unique business model which will improve access to many of the most exciting emerging technologies in the world and help accelerate our understanding of disease, and subsequently, the discovery, development and commercialization of new medicines for IBD.

We hope you enjoy learning about our research progress in this edition of the Research Report and we thank you for your ongoing support and encouragement. Together, we will continue to make significant progress in research and care and make IBD a thing of the past.

Warmest wishes,

John Wallace, PhD
Chair, Scientific & Medical Advisory Council

Aida Fernandes, MBA
Chief Science & Education Officer

$1,530,911
number of additional dollars leveraged from government and industry to match CCFC's investment of $507,641 in support of IBD research

41
number of research grants supported by the CCFC through our Grants-in-Aid, Innovations in IBD and partnership programs

17
number of major hospitals and universities across Canada supported by CCFC research grants and awards

2170
number of subjects recruited to participate in CCFC's GEM study

BUILDING CAPACITY IN THE IBD RESEARCH COMMUNITY

The CCFC supports IBD researchers throughout their careers, from undergraduate students working in research labs through to established senior scientists. By co-funding salary awards, fellowships, and student scholarships we are building research capacity, ensuring that significant research effort remains focused on IBD.

TRAINING AWARDS ensure a reliable supply of highly-qualified personnel develop the knowledge and skills required to become a researcher. They are awarded to top-ranked undergraduate, graduate and post-doctoral trainees who have demonstrated potential for a career in IBD-related research.

Fellowships

CCFC/Canadian Institutes of Health Research/ Canadian Association of Gastroenterology

FELLOW	INSTITUTION	INVESTMENT IN 2011/12
Frann Antignano	Hospital for Sick Children	$15,000
Ramzi Fattouh	Hospital for Sick Children	$15,000
Salim Saad	University of Alberta	$15,000
Martin Stahl	BC Children's Hospital	$22,500
David Prescott	University of Toronto	$22,500
David Reed	McMaster University	$37,500

CCFC/Alberta Innovates

FELLOW	INSTITUTION	INVESTMENT IN 2011/12
Brian Gulbranson	University of Calgary	$19,000
Christina Hirota	University of Calgary	$12,000
Weiwei Wang	University of Alberta	$5,000

Studentships, Prizes and Book Awards

Alberta Innovates

STUDENT	INSTITUTION	INVESTMENT IN 2011/12
James Cotton	University of Calgary	$3,900

Michael Smith Research Foundation

STUDENT	INSTITUTION	INVESTMENT IN 2011/12
Marta Wlodarska	University of British Columbia	$4,146
Megan Himmel	University of British Columbia	$1,750
Yanet Valdez	University of British Columbia	$3,500

CCFC/Fonds de recherche du Québec Santé (FRQS)

STUDENT	INSTITUTION	INVESTMENT IN 2011/12
Kim Beauregard	University of Sherbrooke	$10,000
Joannie Allaire	University of Sherbrooke	$10,000
Valérie Gagné	Laval University	$ 10,000

CCFC/Manitoba Health Research Council

STUDENT	INSTITUTION	INVESTMENT IN 2011/12
Carolyn Weiss	Manitoba Institute of Child Health	$8,925

CCFC/Canadian Association of Gastroenterology

STUDENT	INSTITUTION	INVESTMENT IN 2011/12
Bonnie Cheung	University of British Columbia	$7,000
Tessa Van Tol	University of British Columbia	$7,000
Stephanie Mah	University of Alberta	$7,000
Jordan Iannuzzi	University of Calgary	$7,000
Lucas Mastropaolo	Hospital for Sick Children	$7,000
Matthew Bernstein	University of Manitoba	$7,000
Jane Natividad	McMaster University	$750
Janice Kim	McMaster University	$750
James Beaton	University of British Columbia	$750
Gelareh Noureddin	University of British Columbia	$750

SALARY AWARDS provide salary support to young investigators showing outstanding promise of developing an independent research career in IBD.

CCFC/Canadian Institutes of Health Research/ Canadian Association of Gastroenterology

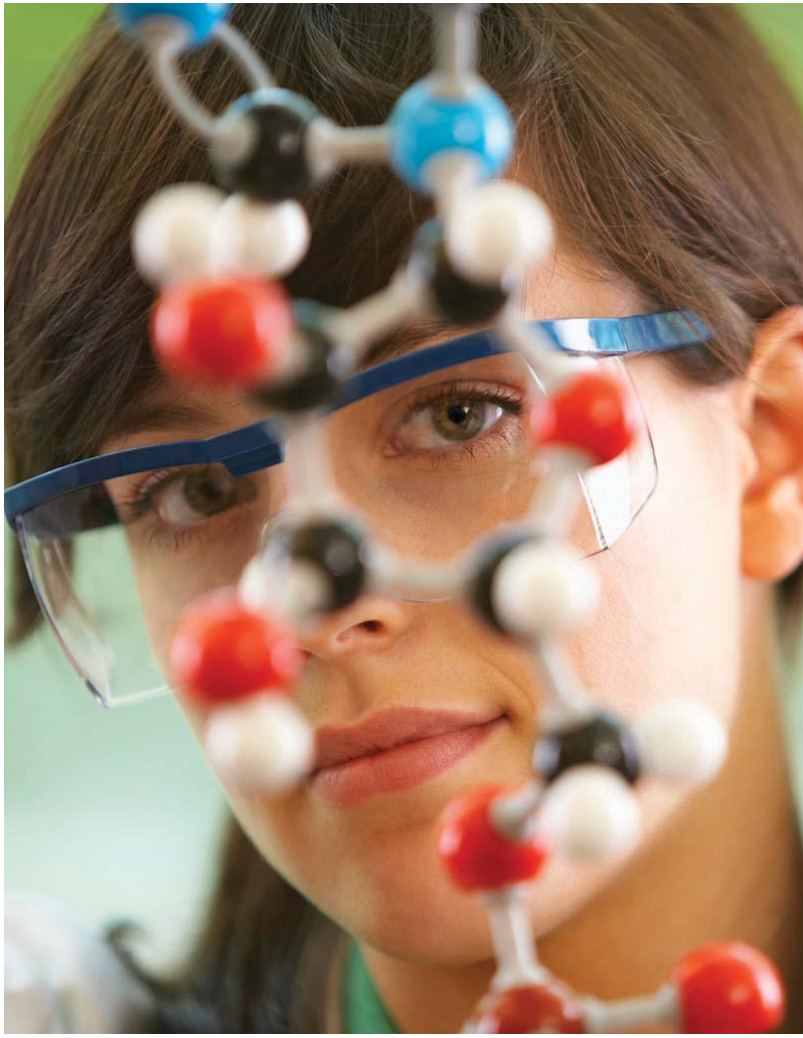
INVESTIGATOR	INSTITUTION	INVESTMENT IN 2011/12
Dr. Sly	University of British Columbia	$57,500
Dr. Nguyen	University of Toronto	$12,500

Facilitated by the CCFC, the **Endowed Chair** at the Farncombe Family Digestive Health Research Institute at McMaster University will support an established investigator in the field of IBD research, with a specific emphasis on ulcerative colitis. The successful applicant will have an international reputation for basic, applied, and/or clinical research. The Chair will join a multidisciplinary group of basic and clinical researchers with access to a high-tech facility, a microbiome research centre, and a regional centre for IBD patients.

CCFC Chair in Ulcerative Colitis

INVESTIGATOR	INSTITUTION	INVESTMENT IN 2011/12
TBD*	McMaster University	$500,000

** At print time, the inaugural Chair was being recruited*



GENERATING NEW IDEAS TO BETTER TREAT OR CURE IBD

In order to generate new ideas to better treat or cure IBD, the CCFC supports a number of different research programs (Innovation Grants, Government Partnerships, Industry Partnerships, GEM Projects, and Grants-in-Aid). Our continued investment in these programs ensures a diversified research portfolio which encourages innovation and builds on the scientific breakthroughs achieved to date.

Innovations in IBD Research grants provide seed funding for investigators to explore novel, high-risk, breakthrough research ideas or strategies that have the potential to cure or more effectively control IBD.

Innovations in IBD Research grants

INVESTIGATOR	INSTITUTION	INVESTMENT IN 2011/12
Dr. Sly	University of British Columbia	$50,000
Dr. Levings	University of British Columbia	$25,000
Dr. Waterhouse	University of Calgary	$50,000

In collaboration with the **Canadian Institutes of Health Research (CIHR)'s Institute of Genetics and Institute of Infection and Immunity**, CCFC has leveraged its funds to support cutting-edge team grants related to critical IBD issues.

CCFC/CIHR Team Grants

INVESTIGATOR	INSTITUTION	INVESTMENT IN 2011/12
Dr. Rioux	University of Montreal	$25,000
Dr. Croitoru	Mount Sinai Hospital	$25,000
Dr. Stadnyk*	IWK Health Centre	$31,150

**In partnership with CIHR & Nova Scotia Health Research Foundation*

The **CCFC-Vertex Sponsored Research Program** will be investigating the role of bacteria in IBD and the body's response to an imbalance of these bacteria. This research is intended to help us better understand the underlying biology of IBD and identify potential targets for future IBD medicines.

CCFC/Vertex Sponsored Research Program

INVESTIGATOR	INSTITUTION	INVESTMENT IN 2011/12
Dr. Gray-Owen	University of Toronto	$50,000
Dr. Coombes	McMaster University	$25,000
Dr. Boudreau	University of Sherbrooke	$48,270

The **Genetic, Environmental and Microbial (GEM) Project** is a major, multi-centre clinical research study investigating the causes of Crohn's disease funded by the CCFC to the tune of $5.5 million over the past five years. With over 2,000 study participants from 32 sites located across Canada, United States and Israel, this landmark, one-of-a-kind study will have broad-reaching benefits to the international IBD community. The GEM data and research platform has led to several ancillary studies which have secured an additional $2.5M from Canadian government to support these spin-off research projects.

Genetic, Environmental and Microbial (GEM) Project

INVESTIGATOR	INSTITUTION	INVESTMENT IN 2011/12
Dr. Croitoru	Mount Sinai Hospital	$207,000

Grants-in-Aid (GIA) of Research grants support high-quality research projects that will enhance our understanding of IBD and have the potential to cure or more effectively control the disease. GIAs build on the achievements and strengths of the world-class IBD research community in Canada by supporting the pipeline for discovery of new IBD therapies and keeping cutting-edge researchers in Canada. The research projects funded by the Foundation are devoted to finding the causes of IBD (bacterial and genetic triggers), developing new treatments that block the inflammatory process, and treating the complications related to IBD.

FINDING THE CAUSES AND UNDERSTANDING THE TRIGGERS OF IBD

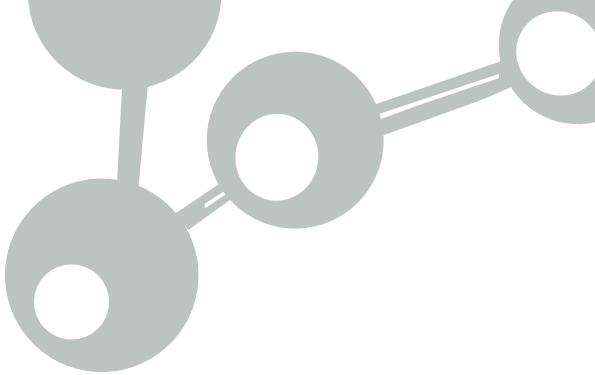
Microbial Triggers

Bacteria in the intestines play a pivotal role in Crohn's disease and ulcerative colitis. People with IBD respond differently to the normal bacteria that live in the gut. Research in this area is trying to understand how bacteria may contribute to or potentially even prevent the development of disease. This work may provide new insights into the causes of IBD and help identify new strategies to either prevent the disease or stop the inflammation.

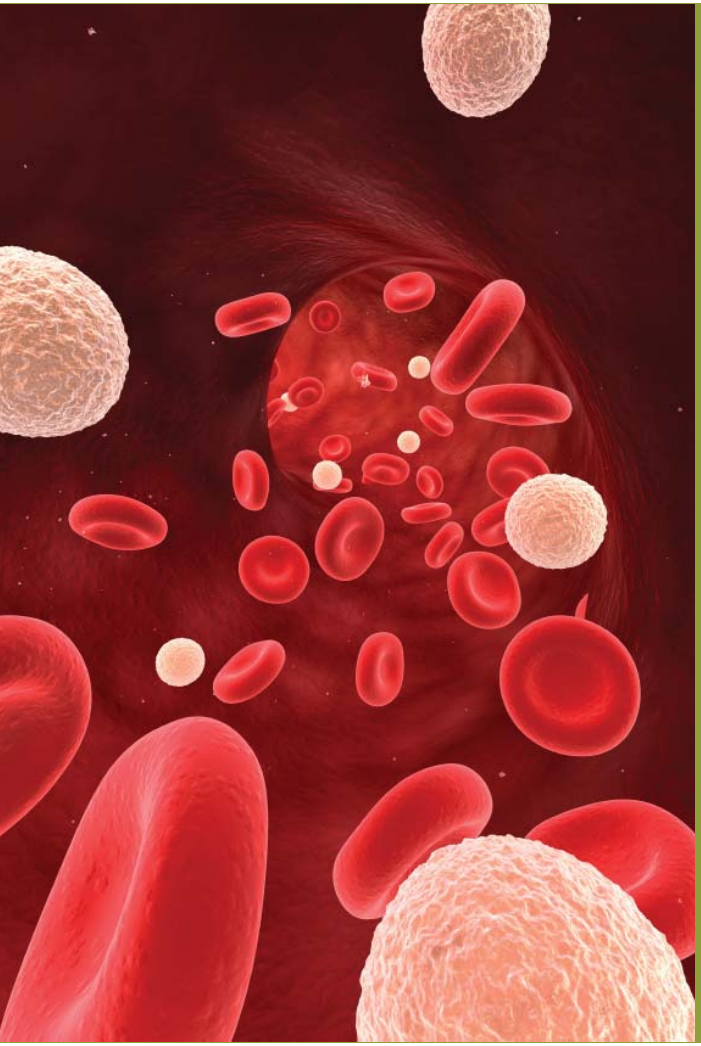
Dr. Verdu McMaster University Investment in 2011/12: $123,322	Dr. Verdu is investigating whether inflammation can be affected by bacteria or by adding a specific probiotic. This work will determine the potential value of probiotics to reduce or prevent IBD. Also, Dr. Verdu is using germ-free mice to investigate how bacteria from patients with IBD impact inflammation in high-risk individuals.
Dr. Giradin University of Toronto Investment in 2011/12: $124,910	The gene that was first identified to be associated with IBD is Nod2, which senses bacteria. Dr. Giradin is studying how Nod proteins affect the body's response to bacteria in the gut. His goal is to identify the bacterial triggers in order to find what causes the uncontrolled autoimmune response that ultimately leads to disease progression.
Dr. Buret University of Calgary Investment in 2011/12: $122,296	Acute infection with *Camplylobacter jejuni* can start or worsen gut inflammation in IBD patients. Dr. Buret is studying how Campylobacter jejuni may disrupt the gut microbiome and trigger the IBD disease process in motion. This work may shed new light on the mechanisms responsible for intestinal inflammation in IBD.
Dr. Gray-Owen University of Toronto Investment in 2011/12: $125,000	Dr. Gray-Owen is investigating whether a bug called "adherent and invasive *E. coli* (AIEC) sticks to and penetrates the lining of the gut, and potentially contributes to the chronic inflammation in IBD. This study will provide new insights into the cause of IBD and may lead to new ways to either prevent or stop the inflammatory process.
Dr. Petrof Queen's University Investment in 2011/12: $125,000	Dr. Petrof is investigating whether a common gut bacterium which is also a probiotic, has anti-inflammatory benefits. Research into this area may lead to safer IBD treatments that would reduce the negative inflammatory response, while maintaining the body's critical host defenses.

Genetic Markers and Personalized Medicine

There are many genes associated with an increased risk of IBD. Research in this area is looking to identify which genetic markers are predictors of disease onset or severity so that healthcare professionals are better able to screen and personalize treatments. Genetic research is also trying to understand the role of certain genes in turning on inflammation or decreasing the body's ability to kill some bacteria.



Dr. Silverberg Mount Sinai Hospital Investment in 2011/12: $125,000	Dr. Silverberg is evaluating the genes and microbes that are associated with the onset and recurrence of inflammation following surgery. This may help healthcare professionals predict which CD patients are likely to develop recurrent inflammation after surgery.
Dr. Beck University of Calgary Investment in 2011/12: $125,000	Many of the genes associated with an increased risk of IBD are involved in immune response. Dr. Beck is studying how mutations in a particular gene decrease our ability to kill some bacteria and induce hyper-inflammation.
Dr. Asselin University of Sherbrooke Investment in 2011/12: $125,000	Dr. Asselin is studying the role of proteins, which control genetic and epigenetic information in gut cells, during inflammation. In the long term, this research program may lead to better treatments for IBD.
Dr. Silverberg Mount Sinai Hospital Investment in 2011/12: $62,500	Dr. Silverberg is trying to find genetic markers that will, with a simple blood test, enable health care professionals screen individuals with CD most likely to develop severe or mild disease. This will enable more personalized therapies that will benefit patients' quality of life and reduce complications.
Dr. Jones Hospital for Sick Children Investment in 2011/12: $62,500	Two gene mutations associated with CD are Nod2 (which senses bacteria within the cell) and ATG16L1 (which is needed for digesting and recycling material inside the cell). Dr. Jones is studying how these two genes might be involved in causing disease in order to develop better therapies to treat and prevent IBD.



DEVELOPING NEW TREATMENTS THAT BLOCK INFLAMMATION

The immune response in persons living with IBD does not work properly. New treatments are needed that "turn off" the exaggerated response seen in IBD. Research in this area is studying how immune cells respond and control inflammation. This work may lead to new therapies that can treat IBD or take advantage of the body's natural "anti-inflammatory" features to promote healing.

Dr. Lomax Queen's University Investment in 2011/12: $72,535	Dr. Lomax is studying how a particular branch of the nervous system can regulate the immune system and change the severity of inflammation. This work will determine whether targeting the nervous system is a viable treatment option for IBD.
Dr. Madsen University of Alberta Investment in 2011/12: $69,406	Dr. Madsen is examining how patients with IBD respond to different types of bacterial DNA, in order to understand how and why gut cells of patients with IBD do not respond the same way that healthy individuals do. This work may lead to new bacterial DNA therapies that treat active inflammation.
Dr. Gendron University of Sherbrooke Investment in 2011/12: $74,970	Dr. Gendron is investigating a receptor that plays an important role in inflammation and influences the outcomes of IBD. Dr. Gendron is developing new molecules which regulate this receptor by reducing inflammation and by stimulating wound healing and IBD remission. This work could lead to new drug candidates to treat IBD.
Dr. McKay University of Calgary Investment in 2011/12: $71,006	Dr. McKay is seeking to enhance one's own natural immune defenses to block disease rather than intervene with drugs. Dr. McKay is investigating whether alternatively activated macrophages (AAM) could stop inflammation in the intestine and be developed as a novel therapy for IBD.
Dr. Croitoru University of Toronto Investment in 2011/12: $74,896	Dr. Croitoru is studying how the immune cells of the gut interact with bacteria and defining how bacteria may trigger or prevent colitis. Understanding how these molecules control regulatory T cells may lead to new treatments that change the inflammation permanently.
Dr. Kubes University of Calgary Investment in 2011/12: $125,000	The gut uses specific proteins to sense bacteria, including molecules called Toll-like receptors (or TLRs). Dr. Kubes is focusing on how bacterial signals trigger IBD in order to design new therapies that take advantage of our natural anti-inflammatory powers to promote intestinal healing in IBD patients.
Dr. Philpott University of Toronto Investment in 2011/12: $125,000	People with CD, who have mutations in a bacterial-sensing protein, called Nod2, have a hyper-reactive immune response. Dr. Philpott is investigating how Nod proteins control inflammation in order to discover new treatments for IBD.
Dr. Sarfati Centre du Recherche Investment in 2011/12: $18,286	Dendritic cells (DCs) recognize harmful and harmless external threats. When not regulated properly, DCs may misinterpret a harmless encounter and start an immune response, leading to chronic intestinal inflammation. Dr. Sarfati is studying DCs in human intestinal tissue of CD and healthy patients. This may lead to new therapies for IBD patients.

Dr. Rivard University of Sherbrooke Investment in 2011/12: $125,000	The cells lining the gut are called intestinal epithelial cells (IECs). IECs cause our immune system to respond when the barrier to the external environment fails and coordinate with leukocytes (a type of white blood cells) present in the gut. Dr. Rivard is studying a signaling molecule, which may be involved in the immune response in order to prevent gut inflammation.
Dr. Boudreau University of Sherbrooke Investment in 2011/12: $124,192	Dr. Boudreau is studying how two inflammatory regulators play a role in reducing inflammation. By identifying the specific signaling pathways and targeting the genes affected by these regulators may lead to the new therapies for IBD.
Dr. Chadee University of Calgary Investment in 2011/12: $125,000	The large intestine is covered with thick mucus that forms a protective barrier against bad bacteria and substances. In IBD, the mucus layer is very thin and the inflamed gut becomes susceptible to bacterial invasion. Dr. Chadee is studying the role of mucin in maintaining a healthy protective barrier as a treatment option for IBD.
Dr. Khan McMaster University Investment in 2011/12: $124,883	Dr. Khan is examining what role a hormone called serotonin plays in regulating an immune response. This may lead to improved therapeutic strategies to combat gut inflammatory disorders, including IBD.
Dr. Jacobson BC Children's Hospital Investment in 2011/12: $124,781	The cells lining the gut form a physical barrier between the contents of the digestive tract and the underlying immune and nervous systems. This is achieved by tight junction proteins that bind neighbouring cells together. In IBD, this physical barrier is impaired. Dr. Jacobson is investigating ways to prevent disruption, and strengthen the barrier as a new therapy for IBD.
Dr. Wallace McMaster University Investment in 2011/12: $125,000	Dr. Wallace is studying how inflammation is turned off and how the processes might be malfunctioning in IBD. Dr. Wallace is testing experimental drugs in different types of intestinal inflammation in order to find the best doses and the best routes of administering the drugs.
Dr. Sigalet University of Calgary Investment in 2011/12: $67,075	Dr. Sigalet is investigating the effects of a hormone made by the intestine. Dr. Sigalet has shown that this hormone actually increases the number of anti-inflammatory nerves to dramatically reduce gut inflammation. This work will may lead to a new therapy that reduces inflammation by stimulating the natural anti-inflammatory powers of the gut.

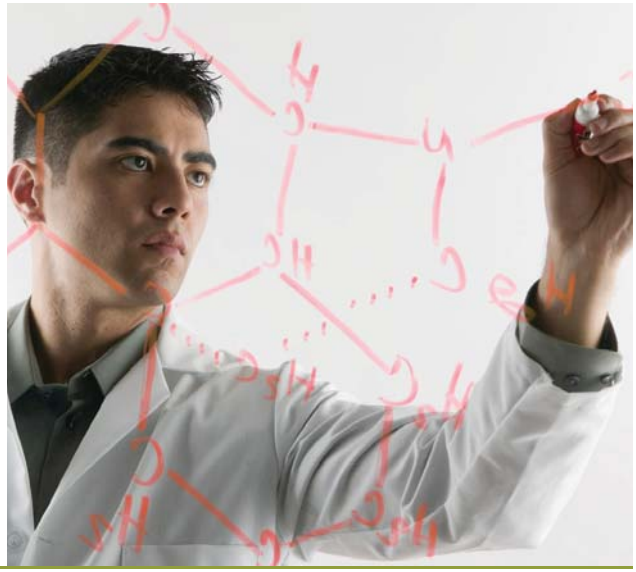
TREATING COMPLICATIONS

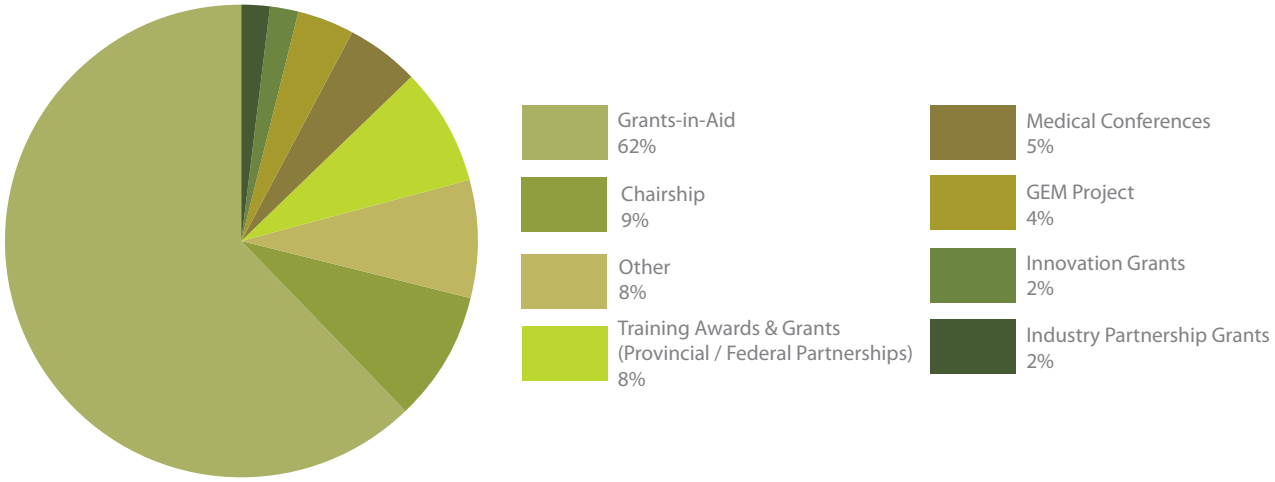
Despite the use of drugs that can help control intestinal inflammation in IBD patients, there are still important complications that need to be addressed. A number of research projects are currently investigating certain complications associated with IBD including cancer, pain, scarring and depression.

Dr. MacNaughton University of Calgary Investment in 2011/12: $125,000	Proteases break down proteins. Some proteases can trigger colonic inflammation but how this happens is not known. Dr. MacNaughton is studying protease-induced inflammation in order to identify new drugs to treat IBD. This work may also help to better understand inflammation-associated colorectal cancer, which occurs in some UC patients.
Dr. Allen-Vercoe University of Guelph Investment in 2011/12: $54,702	Chronic inflammation could be an initiating factor in colorectal cancer, which explains why IBD patients are more at risk for developing colorectal cancer. Dr. Allen-Vercoe is investigating whether a bug associated with periodontitis (an inflammatory condition in the mouth) can be used as a biomarker for colorectal cancer in order to develop an early, non-invasive screening test.
Dr. Vanner Queen's University Investment in 2011/12: $187,500	Dr. Vanner aims to understand the factors that control pain in IBD in order to develop new treatments. Dr. Vanner is developing a detection system in humans to monitor the levels of cysteine proteases in order to guide therapy. Alternatively, understanding how to increase the levels of naturally-released opioids that reduce pain could be another avenue for treating pain.
Dr. Vallance University of British Columbia Investment in 2011/12: $125,000	Repeated inflammation in the gut can cause "fibrosis" resulting in scar tissue. Ultimately this can block normal gut function, causing illness and even death. Dr. Vallance is studying whether bacteria in the gut, and the specific parts of the immune system that recognize those bacteria, are responsible for stricture formation. This work may lead to new clinical interventions to treat or prevent strictures.
Dr. Blennerhassett Queen's University Investment in 2011/12: $124,971	Dr. Blennerhassett is studying how nerve cells present throughout the GI tract are damaged and how this may lead to stricture formation. Overall, this will improve our understanding of neuron damage and repair in order to prevent stricture formation in IBD.
Dr. Bercik McMaster University Investment in 2011/12: $140,796	Anxiety and depression are common in patients with IBD but it is not known whether they are the consequence of, or precede this chronic illness. Dr. Bercik is investigating whether depression and/or anxiety in mice is associated with abnormal gut microbiome, which would predispose mice to increased inflammation. This may lead to a new approach for treating IBD patients with anti-depressants and improve patients' quality of life.

RESEARCH INVESTMENTS IN 2011/12

Grants-in-Aid	$3,325,525
Chairship	$500,000
Training Awards & Grants (through Provincial & Federal Partnerships)	$410,371
GEM Project	$207,000
Medical Conferences	$292,020
Innovation Grants	$125,000
Industry Partnership Grants	$123,270
Other (Impact of IBD Report & allocated research program costs)	$425,860
Grand Total	**$ 5,409,046**





NEED FOR FUNDING

36
Research proposals reviewed

21
Research proposals eligible for funding

7
New research projects CCFC can afford to fund

14
Research projects that remain unfunded

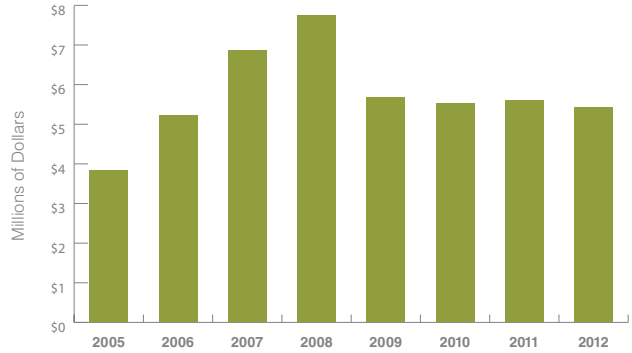
$5.3M
Cost of unfunded research

PROMOTING KNOWLEDGE EXCHANGE

In November 2011, the CCFC hosted its first national **Future Directions in IBD Medical Conference** for researchers, gastroenterologists and other allied healthcare professionals in Canada. Leading medical experts and researchers discussed the latest ideas and advances in medical research and clinical care.

Conference Grants and Meeting Awards help facilitate researchers and trainees with an opportunity to informally present their original research findings to the scientific community and build collaborations for future research endeavors.

RESEARCH INVESTMENTS (2005-2012)



WHAT LIES AHEAD
GRANTS-IN-AID OF RESEARCH 2012-2015

Dr. McKay University of Calgary $358,336	Alternatively activated macrophages as a therapy for ulcerative colitis
Dr. Lomax Queen's University $358,336	Sympathetic neuroimmune interactions during IBD
Dr. Gibson University of British Columbia $358,336	IBD risk through intestinal microbes and dietary fats
Dr. Mallevaey University of Toronto $358,336	iNKT cells in IBD
Drs. Surette, Moayyedi, Lee McMaster University $331,740	Fecal biotherapy clinical trial in ulcerative colitis
Dr. Jirik University of Calgary $356,550	Prion protein regulation of IBD in mice
Drs. Amre, Mack, Deslandres, Janchou, Marcil University of Montreal/ CHU Ste-Justine $299,350	Pre-clinical utility of epigenetic markers in Crohn's disease in children

CONCLUSION

The Crohn's and Colitis Foundation of Canada appreciates the generosity and ongoing support of our donors, partners, sponsors and volunteers, who are making this progress in IBD research possible. Moreover, the CCFC is honoured to have the guidance of our Scientific & Medical Advisory Council and the expertise of our Grant Review Committee to identify the most promising research that is inspiring hope for a cure and helping people with IBD cope with their disease.

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lift the veil of silence and raise money to fund
Inflammatory Bowel Disease research and education

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to join us in our mission to find the cure.

Crohn's and Colitis
Foundation of Canada

Fondation canadienne des
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Our registered charity number is 11883 1486 RR 0001