

Institute of Infection and Immunity Overview of Achievements 2000-2005

Introduction

Infectious diseases such as influenza and HIV/AIDS can have devastating impacts on human health and the global economy. Finding ways to protect people from infection through immunity research and the development of vaccines are issues of vital importance to countries throughout the world. These health threats and challenges make the work of the Institute of Infection and Immunity—one of the 13 institutes of the Canadian Institutes of Health Research (CIHR)—increasingly important.

The creation of the Institute changed the Canadian research landscape in the areas of infection and immunity. As a direct result of the Institute's leadership and through its close collaboration with many partners and stakeholders, a national research agenda for infection and immunity has been developed. The coordinated approach taken by the Institute and its partners is contributing to the long-term health and quality of life of Canadians and strengthening our health care system.

The Institute supports the development of leading-edge, evidence-based and cost-effective infection and immunity research. Its programs and activities target health issues of everyday concern, including autoimmunity, influenza, tissue transplantation, hepatitis C, asthma, safe food and water and emerging infectious diseases. Throughout its first five years, the Inside

Profile of the Institute

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Summary

Institute has proactively approached the challenges of infection and immunity research by setting priorities for research and putting in place programs to address these priorities, while ensuring the long-term vitality of the infection and immunity research community with support for training and career development. Although remaining focused on its priorities, the Institute has also responded in a timely and effective manner to emerging challenges, such as SARS, prion disease and influenza and it has taken every opportunity to expand its reach by working with partners such as the Bill and Melinda Gates Foundation.

This overview describes the Institute's impact and demonstrates how the Institute, with valuable contributions from its partners and stakeholders, is achieving its strategic objectives.

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Profile of the Institute of Infection and Immunity

The Institute of Infection and Immunity was created in 2000 with a mandate to develop and coordinate research in infection and immunity and to ensure the results from research are translated and applied to help improve the health and quality of life of Canadians. The Institute is headed by a Scientific Director, supported by a small staff and an Institute Advisory Board (IAB) composed of 16 internationally renowned infection and immunity experts.

The Institute undertakes a variety of activities in support of its mandate. It provides funding for infection and immunity research, establishes and nurtures partnerships and fosters networking, knowledge creation and communications. Since its inception, the Institute has supported CIHR's strategic initiatives, including innovative interdisciplinary training programs. Fourteen strategic training programs in health research are directly related to the Institute and collectively these programs address most of its identified research priorities. When combined with programs to enhance the establishment of new researchers (an example is a well-subscribed program to fund pilot projects for new investigators), these initiatives will ensure the development of a vibrant research culture. More recently, the Institute has become an active proponent of the Clinical Research Initiative, which is aimed at strengthening Canada's capacity for clinical research by training and sustaining the next generation of clinician-researchers.

In the past five years, the Institute has provided more than \$17 million in funding and supported approximately 110 research projects in diverse areas, including:

- New technologies and health services in antimicrobial resistance;
- Rapid research responses to SARS and other infectious disease outbreaks in Canada;
- Social and behavioural research in HIV/AIDS and hepatitis C;
- Research on the microbial contamination of food and water and the disinfection of Canada's drinking water;
- Pandemic and inter-pandemic influenza prevention and control strategies;
- Predisposing risk factors, treatment and prevention strategies for asthma, and the impacts of asthma on Canada's health services and systems;
- Use of stem cell technologies to treat autoimmune diseases such as diabetes;
- New approaches to host susceptibility and resistance to pathogens;
- · Innovative approaches in regenerative medicine; and
- Recruitment of the next generation of infection and immunity researchers in Canada.





The Institute works with a wide range of partners relating to infection and immunity. Through its partnerships the Institute is developing and coordinating research and ensuring research results get used for the benefit of Canadians. Examples of the Institute's partners include Fonds de la recherche en santé du Québec, the Michael Smith Foundation for Health Research, the Canadian Patient Safety Institute, the Canadian Network for Vaccines and Immunotherapeutics, Health Canada, the Bill and Melinda Gates Foundation and the Public Health Agency of Canada (PHAC). The Institute could not have realized its achievements to date without the valuable contributions made by these and other partners. It fully expects that its partnerships will continue to play an important role in the future.

One of the early activities of the Institute was extensive consultations with all partners and stakeholders. As a result of these consultations, the Institute identified two strategic research priorities—infectious diseases and host response—with several related themes grouped under each (see the table below).



These research priorities are contained in the Institute's strategic plan, released in 2002. Through a continuous process of discussion and consultation with both the research community and the Institute's Advisory Board, the Institute reaffirms the relevance of these research areas to the Institute's mandate and to the larger infection and immunity community. Several of these research themes also align with larger CIHR initiatives in global health and regenerative medicine.





Progress on Strategic Research Priorities

PRIORITY AREA: INFECTIOUS DISEASES

Antimicrobial Resistance

From a public health perspective, resistance caused by increased and/or inappropriate antimicrobial drug use is a growing health and environmental threat. The extensive use of antibiotics is contributing to the creation of drug-resistant disease-causing microbes.

The Institute has done considerable work in this area, including leading and sponsoring a national policy conference as well as supporting research agenda-setting workshops on antimicrobial resistance. These meetings involved input from the Institute's stakeholders and partners, scientists, epidemiologists, clinicians, government and relevant health organizations.

These activities have resulted in the creation of research programs focusing on surveillance, basic research and new technology and health services in antimicrobial resistance. Examples of antimicrobial resistance research projects supported by the Institute include:

- Examination of antimicrobial resistance in acute care of seniors (Dr. Mark Loeb, McMaster University); and
- A study of patterns of antimicrobial resistance in Canada's northern communities (Dr. Michael Mulvey, National Microbiology Laboratory, PHAC).

Emerging Infectious Diseases

The threats of biological terrorism and emerging infectious diseases require collaborative research efforts with CIHR institutes, government agencies, voluntary health organizations and private sector partners.

The Institute is playing a key role in leading Canada's research efforts in infectious disease research. It has held research agenda-setting conferences on bioterrorism and *Clostridium difficile (C. difficile)*. Examples of emerging infectious diseases research projects supported by the Institute include:



- Evaluating the clinical benefits and safety of the anti-viral drug Infergen in SARS treatment (Dr. James Dennis, University Health Network, Toronto); and
- Several projects examining emerging pathogens in influenza, West Nile virus and the SARS coronavirus (Drs. Guy Boivin, Université Laval; Tom Hobman, University of Alberta;
 and Mark Loeb, McMaster University).





The Institute was the lead organization in developing Canada's call for a research plan of action in response to the SARS outbreak. In record time, the Institute mobilized the infectious disease research community and stakeholders to collaborate on planning, coordinating and funding SARS research. This enabled Canada to pull together 18 research project applications within two weeks, which were subsequently peer reviewed in an unparalleled time of just three weeks; four major projects were approved for funding.

The Institute spearheaded the creation of the Canadian SARS Research Consortium (CSRC), engaging national and provincial governments, the private sector and health associations to coordinate, promote and support SARS research focusing on diagnostics, vaccine development, therapeutics, epidemiology, databases, public health and community impact. It was instrumental in creating a national SARS research program and providing information and advice to public health bodies and the media. It helped create a distribution system for SARS samples that will be a model for patient sample collections in future outbreaks. In addition, the Institute established the Canadian Rapid Research Response Team (C3RT), a virtual network of Canadian stakeholders and international partners charged with working together to develop rapid research responses to future infectious disease outbreaks in Canada. Together with the Public Health Agency of Canada, the Institute recently organized a workshop

to establish research priorities for a potential pandemic influenza epidemic, and is working with federal government departments to implement a Canadian preparedness plan.

Ongoing support from the Institute has also enabled several prominent Canadian researchers to develop their research programs to the point where they have achieved success in receiving funding from the Bill and Melinda Gates Foundation's Grand Challenges in Global Health initiative. These researchers are:

- Developing a single-shot vaccine (Dr. Lorne Babiuk, University of Saskatchewan);
- Conducting research on factors associated with HIV resistance among women and their families (Dr. Frank Plummer, University of Manitoba); and
- Studying new ways to boost the body's ability to fight infectious diseases found in the developing world, such as malaria, typhoid fever, E. coli and tuberculosis (Dr. Brett Finlay, University of British Columbia).











HIV/AIDS

HIV/AIDS is a global health problem with serious social and economic impacts. A new research strategy is needed to improve the quality and duration of life of HIV-infected individuals, reduce disease transmission and progression, improve treatment and reduce drug toxicity.

CIHR is one of four federal partners in the Federal Initiative to Address HIV/AIDS in Canada and the Institute of Infection and Immunity is the lead CIHR Institute for identifying and developing HIV/AIDS research initiatives in Canada. The CIHR HIV/AIDS Research Advisory Committee (CHARAC) was established by the Institute to advise on strategic priorities; with this advice, the Institute is playing an integral part in Canada's response to the HIV/AIDS pandemic by:



- Supporting biomedical, clinical, health services and population health research programs in HIV/AIDS;
- Supporting clinical trials in Canada through the Canadian HIV Trials Network;
- Administering the HIV/AIDS Community-based Research Program, which fully integrates affected communities in HIV/AIDS research; and
- Partnering with the CIHR Institute of Aboriginal Peoples' Health on a research program to address the epidemic in Aboriginal populations.

The Institute has also been working closely with Health Canada and the Bill and Melinda Gates Foundation to support Canada's research contribution to the Global HIV/AIDS Vaccine Enterprise.

Examples of HIV/AIDS research projects supported by the Institute include:

- A study to explore the impact of housing support and homelessness on the health outcomes of people living with HIV/AIDS in Ontario (Ruthann Tucker, Fife House and Dr. Saara Greene, York University); and
- An examination of the connection between HIV infection, maternal immunity and regimens of antiviral medication on mother-to-child transmission of HIV (Dr. Hugo Soudeyns, Hôpital Sainte-Justine).



Hepatitis C

Building researcher capacity in the area of blood-borne infections is an urgent priority. Liver disease due to the hepatitis C virus is, in particular, a major and growing health problem.

The Institute has been an active player in Canada's research effort to combat hepatitis C. It has been working collaboratively with he federal government in a variety of activities and initiatives, such as identifying liver disease due to the

hepatitis C virus and increasing the number of hepatitis researchers in Canada in areas such as pathogenesis, modes of transmission, treatment, access to care and prevention through interventions in risk behaviours. An example is the hepatitis C research project that establishes a government and community-based Atlantic Network to improve the identification, treatment and prevention of hepatitis C for people in Atlantic Canada (Dr. Susan Kirkland, Dalhousie University). Another example is the research project on psycho-educational intervention in HIV/AIDS and hepatitis C patients (Dr. Louise Balfour, Ottawa Health Research Institute).

The Institute was instrumental in helping to assess research needs and gaps in social and behavioural research issues in HIV/AIDS and hepatitis C and in launching a research priority program to look at these issues. The Institute is also working with other federal agencies and departments to stimulate hepatitis C research.

Microbiologically Safe Food and Water

Public concern about the microbiological safety of food and drinking water and its impact on our social, psychological and economic well-being requires interventions informed by systematic research initiatives and effective knowledge translation.

The Institute has played a key leadership role in helping the Canadian research effort to address how to best protect our food and water supplies. It has developed multiple partnerships with both governments and the private sector in the area of safe food and water and it has taken many steps in this area, including:

- Creating and managing Canada's first Canadian Research Coalition for Safe Food and Water, an 18-member body that coordinates a national Research agenda in safe food and water;
- Leading and sponsoring a major international conference on the challenges of prion diseases, in partnership with the CIHR Institute of Population and Public Health; this initiative resulted in important recommendations used to create a Network of Centres of Excellence (NCE) on prion diseases;
- Supporting a traveling museum exhibit that provides advice to communities on food safety and links between diet, exercise and susceptibility to chronic diseases such as diabetes, heart disease and cancer; and
- Funding a research project in partnership with the Canadian Water Network focusing on the disinfection of Canada's drinking water.









Examples of microbiologically safe food and water research projects supported by the Institute include:

- Tracking environmental determinants of coliform bacteria in source water in British Columbia (Dr. Asit Mazumder, University of British Columbia); and
- Examining antimicrobial-resistant E. coli in drinking and recreational source waters (Dr. Marie Louie, Sunnybrook and Women's College Health Sciences Centre).

Novel Vaccine Development



Vaccines are safer and more cost-effective than other therapeutic interventions for infectious diseases. Research in vaccine development and delivery platforms, coupled with mechanisms for rapid knowledge translation, is crucial.

The Institute has made significant progress in supporting new vaccine research in human health by establishing a specific research priority program area in innovative vaccine development. Examples of novel vaccine development research projects supported by the Institute include:

- Examining the side effects experienced following the re-vaccination of individuals with a previous history of oculorespiratory syndrome (Dr. Danuta Skowronski, University of British Columbia); and
- Looking at innovative vaccine development and delivery methods, with an emphasis on vaccines for infectious diseases of particular importance to human health, such as hepatitis C and HIV/AIDS (Dr. Lorne Babiuk, University of Saskatchewan).

The Institute is also partnering with PHAC on a number of initiatives, including:

- Establishing a strategic plan for a Canadian Vaccine Initiative;
- Working on an Influenza Immunization Program Evaluation Task Group to fund research comparing universal influenza immunization programs with programs that target high risk populations; and
- Determining national research priorities to enhance pandemic and inter-pandemic influenza prevention and control strategies.





Progress on Strategic Research Priorities

PRIORITY AREA: HOST RESPONSE

Asthma and Allergy

Asthma and allergy are health problems with major economic impacts. Research in this area is needed to understand the interactions among genes, allergens, environmental factors and the host immune system.



The Institute is supporting and funding asthma and allergy research projects that will make significant progress in these areas. The projects are examining the underlying mechanisms that cause asthma, predisposing risk factors, treatment and prevention strategies and impacts on health services and systems. The Institute is supporting a program to train new researchers in these areas with a multidisciplinary approach covering diverse fields such as population health, cellular and molecular immunology, smooth muscle physiology and clinical medicine (Dr. Kent Hayglass, University of Manitoba). The Institute has also been funding research projects focusing on increasing Canada's competitiveness internationally in asthma and allergy research with the goal of attracting new research talent to ensure excellence in the next generation of Canadian researchers.

The Institute is collaborating with AllerGen NCE Inc., and the Canadian Cystic Fibrosis Foundation to enhance research in asthma and allergy. To this end, a major program investigating mucosal immunity in the lung and upper respiratory tract will be funded in 2006. In addition, the Institute, is working closely with other Institute stakeholders to support research on environmental factors that may be involved in asthma.

Autoimmune Diseases

Autoimmune diseases cause major suffering and morbidity. Research efforts that integrate new knowledge of genetics, immunology and molecular biology are needed to understand, prevent and manage autoimmune diseases and their complications. Research is also needed to elucidate the basic mechanisms and the genetic and environmental factors that may cause autoimmune diseases.

The Institute has made major efforts to support initiatives that create and integrate new knowledge to understand, prevent and treat autoimmune disease. Its work in this area has included organizing a research symposium to develop a framework for a Canadian health research agenda in autoimmune diseases and funding new research projects studying Type 1 diabetes. These projects were supported by the



Institute in partnership with the Juvenile Diabetes Research Foundation International and the CIHR Institute of Nutrition, Metabolism and Diabetes.





In addition, the Institute was influential in establishing a partnership with the Stem Cell Network - another of Canada's Networks of Centres of Excellence - and the Juvenile Diabetes Research Foundation International to support a research consensus conference looking at the use of stem cell technologies to treat diabetes. The Institute organized and sponsored a research agenda-setting symposium that looked at the basic mechanisms leading to autoimmune diseases and investigating the commonalities among them. These conferences and dialogues with numerous interested partners, including the National Institute of Allergy and Infectious Disease, culminated in the release of a large scale clinical autoimmunity research team initiative in late 2005.

An example of an autoimmune disease research project supported by the Institute is:

• Pancreatic islet generation from human stem cells (led by Dr. David Hill, Lawson Health Research Institute, University of Western Ontario).

Innate Immunity



Innate or natural immunity plays a large part in resistance to all infectious diseases, in susceptibility to autoimmune diseases, in the development of asthma and allergy and also in organ transplantation and tissue regeneration. Research is needed to determine the interactions among predisposing genes, allergens, environmental factors and the host immune system in order to better understand how strengthening innate immunity can help in efforts to prevent and treat these conditions.

The Institute is supporting a number of proactive initiatives in innate immunity research. These initiatives include creating a research priority program to fund research projects focusing on host susceptibility and resistance to pathogens and identifying new approaches to immune modulation for initiatives addressing novel alternatives to antibiotics.

Examples of innate immunity research projects supported by the Institute include:

- Investigating host susceptibility to HIV 1 infection (Dr. Michel Tremblay, Centre hospitalier de l'Université Laval); and
- Identifying novel pathways in host response to infection (Dr. Silvia Vidal, University of Ottawa).





Organ Transplantation and Regeneration

Tissue regeneration and replacement are likely to become important therapeutic modalities for many diseases resulting in end-stage organ failure. Research in transplantation and stem cell biology offers both great opportunities and significant challenges, especially with regard to ethical and legal considerations.

The Institute is currently engaged in a number of key research initiatives in organ transplantation and regeneration research. These include a research program area addressing the current inadequate supply of donated organs and aimed at improving, through transplantation, the quality of life for those with end-stage organ failure, as well as a research program aimed at understanding how to develop functional cardiovascular tissues in chronic degenerative circulatory diseases.



The Institute partnered with the Heart and Stroke Foundation of Canada and the Michael Smith Foundation for Health Research to fund the training of future Canadian

health researchers in transplantation and regenerative medicine. In partnership with six other CIHR Institutes and nine external health organizations, the Institute has been involved in the CIHR strategic initiative in regenerative medicine and nanomedicine. In conjunction with the Juvenile Diabetes Foundation International, the Institute will fund two teams investigating the regeneration of pancreatic endocrine tissues, a strategy for the treatment of diabetes. Another example of an organ transplantation and regeneration project supported by the Institute is the Transnet network, in which scientists from across Canada contribute data from transplant patients in order to develop genetic biomarkers for transplant rejection and tolerence (Dr. David Kelvin, University Health Network, Toronto).

The Institute has also worked in partnership with the Kidney Foundation of Canada and the Canadian Society of Transplantation on a program to enhance clinical research capacity through clinical research fellowships in the area of transplantation.

Summary

Issues that are addressed by the Institute of Infection and Immunity are of global concern. This overview demonstrates that, since its inception, the Institute has made, and continuously strives to make, an impact in infection and immunity research in Canada. Together with its affiliated researchers, stakeholders and partners, the Institute has created a strategic research agenda with clearly defined priorities and improved coordination to help solve some of the most important infection and immunity problems currently facing Canada and the world.

