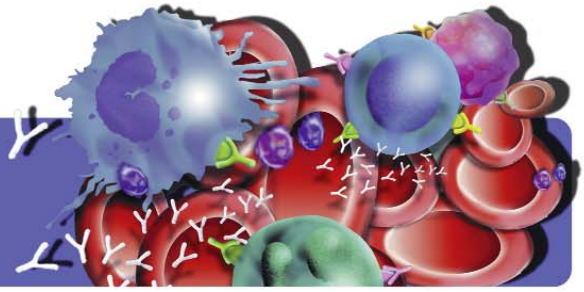
Microcosm-III

CIHR Institute of Infection and Immunity

Fall 2009



In this issue

Message from the Scientific Director

As I complete my term as founding Scientific Director of the Institute of Infection and Immunity, it is fitting to reflect on the outcomes and impacts of the Institute's activities over the past nine years. Together with the research community, our partners, and stakeholders, we have a lot to be proud of. Our joint activities have led to the improved health of Canadians and have made us ready to respond to new health opportunities and threats. Many of these achievements are documented in impact and outcome assessment reports that are discussed elsewhere in this newsletter. I would like to highlight areas in which III has excelled, acting as a catalyst, providing leadership, and fostering productive partnerships.

III has catalyzed research in infection and immunity by both identifying areas that require research attention and building capacity. For example, Autoimmune Diseases was a priority area identified in our 2002 Strategic Plan, and with good reason. These debilitating, chronic diseases affect nearly 5% of our population, and yet the mechanisms underlying their pathogenesis are largely unknown. In 2003, III held a workshop that brought together researchers and stakeholders to discuss commonalities among these diseases. This led to funding for multidisciplinary teams to address the underlying mechanisms of disease. Research began in 2007 and is ongoing.

Our Safe Food and Water Initiative brought together researchers from both federal government agencies and academia who had not previously worked together and fostered research linkages. This ultimately led to the establishment of PrioNet, a Network of Centres of Excellence in prion diseases, which would have been unlikely without our early efforts.

More recently, under our Vaccines of the 21st Century Strategic Initiative, we have consulted with the research community and key stakeholders to identify obstacles in vaccine research and development. One of the obstacles is the need for a better understanding of the human immune system. Our new initiatives in immunotherapy using a systems biology approach and innate immunity are fresh approaches to this research challenge. In January 2009, we hosted a meeting of vaccine funders in order to begin to develop public/private partnerships and other innovative funding strategies to support vaccine and immunization research in Canada. While there is still work to be done, we believe that we have laid a foundation that will support future research in this priority area.

In terms of leadership, we played a key role in responding to the SARS outbreak in 2003 in both funding research and in establishing the Canadian SARS Research Consortium. The research supported by the Consortium led to an understanding of SARS transmission during the outbreak and has subsequently had broad health, social and economic impacts as well as lessons learned for H1N1. In addition, we have continued to provide leadership with federal initiatives in responding to the global challenges of HIV/AIDS through the creation of the CIHR HIV/AIDS Research Advisory Committee (CHARAC), participation in the Canadian HIV Vaccine Initiative (CHVI) and continued support for clinical trials research through the internationally renowned CIHR Canadian HIV Trials Network (CTN).

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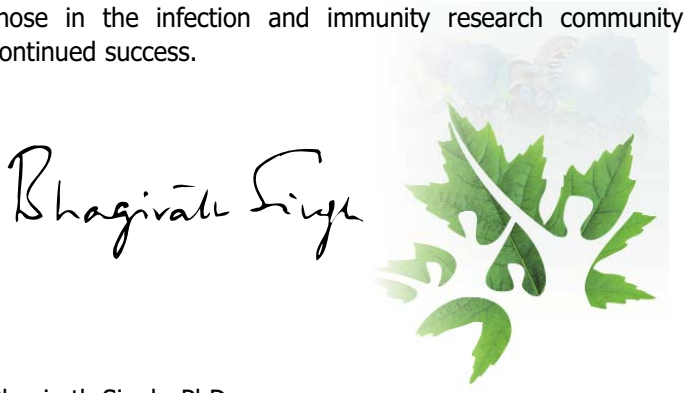
Our partnerships have allowed us to develop a research agenda that is more relevant to the real health problems of Canadians, to leverage funds to enhance research efforts, and to improve the uptake of research results. We worked closely with partners to support hepatitis C research in the country and we have taken a leadership role in bringing together partners such as the Public Health Agency of Canada, the Canadian Food Inspection Agency and others to develop the Pandemic Preparedness Strategic Research Initiative in 2006. This early preparation has built the necessary research capacity to respond to the current H1N1 influenza pandemic and has created linkages so that research results will be rapidly taken up by key stakeholders. Our support through training programs and the new investigator forums has provided significant opportunities and mentoring for the next generation of infection and immunity researchers that will allow them to be successful in their careers. In addition, our support of established investigators through bridge funding opportunities on a regular basis has sustained the current research capacity across the country.

Research in infection and immunity holds great promise as an area in which significant health impacts with potential for global impact can be achieved. The activities that we together have been involved in over the past nine years are helping to achieve the Institute's ultimate goal: to improve health and health care for all Canadians through the provision of the best evidence and scientific advice available.

I thank our Institute staff in London, Ontario and Ottawa and current and past members of our Institute Advisory Board and CIHR HIV/AIDS Research Advisory Committee for their support, dedication and commitment to make our combined efforts such a success. I also thank our partners and the research community for their guidance, advice and help with various initiatives that they helped us to launch. I wish all those in the infection and immunity research community continued success.



Bhagirath Singh, PhD
Scientific Director
CIHR Institute of Infection and Immunity

Funding Decisions

The following funding decisions have been announced over the previous months. Consult the CIHR website for full details (http://www.cihr-irsc.gc.ca/e/38649.html).

June 2009

- Operating Grant: Winter 2009 Priority Announcements:
  - o Institute of Infection and Immunity
  - o III Bridge Funding
  - o HIV/AIDS
  - o Canadian HIV Vaccine Initiative

July 2009

- Fellowship: Winter 2009 Priority Announcement (HIV/AIDS)

August 2009

- Catalyst Grant: Pandemic Preparedness
- Catalyst Grant: HIV/AIDS (Community-Based Research)
- Master's Award: HIV/AIDS (Community-Based Research)
- Meetings, Planning and Dissemination Grant: Infection and Immunity
- Operating Grant: HIV/AIDS (Community-Based Research)
- Other: Capacity Building Workshop in HIV/AIDS (Community-Based Research)
- Canada-UK Joint Health Research Program on Antibiotic Resistance
- Research Facilitators in HIV/AIDS (Community-Based Research)

September 2009

- Catalyst Grant: Vaccines of the 21st Century
- Pandemic Outbreak Response

November 2009

- Catalyst Grant: Pandemic Outbreak Research Response

Funding Opportunities

The CIHR Institute of Infection and Immunity is dedicated to supporting research and building research capacity in the areas of infection and immunity. For more information about the full list of current funding opportunities offered by CIHR-III, visit the III home page (www.cihr.gc.ca/iii.html) and click on the "III Funding Opportunities" link on the top right menu. Most opportunities are released in June and December of each year.

New III Advisory Board Members

The Institute is pleased to welcome five new members to our Institute advisory board:

Eric Brown, McMaster University
Roy Duncan, Dalhousie University
Anthony Jevnikar, University of Western Ontario
Mohammed Karmali, Public Health Agency of Canada
Brian Ward, McGill University

The Institute would like to thank board members, whose term has expired - Drs. Robert Clarke, Jim Lavery, Mark Loeb, Joaquin Madrenas, Marc Ouellette and David Speert - for their dedication and contributions. The full list of current Institute Advisory Board members is available on the III website: http://www.cihr.gc.ca/e/37572.html.

III: Changing the approach to infection and immunity research

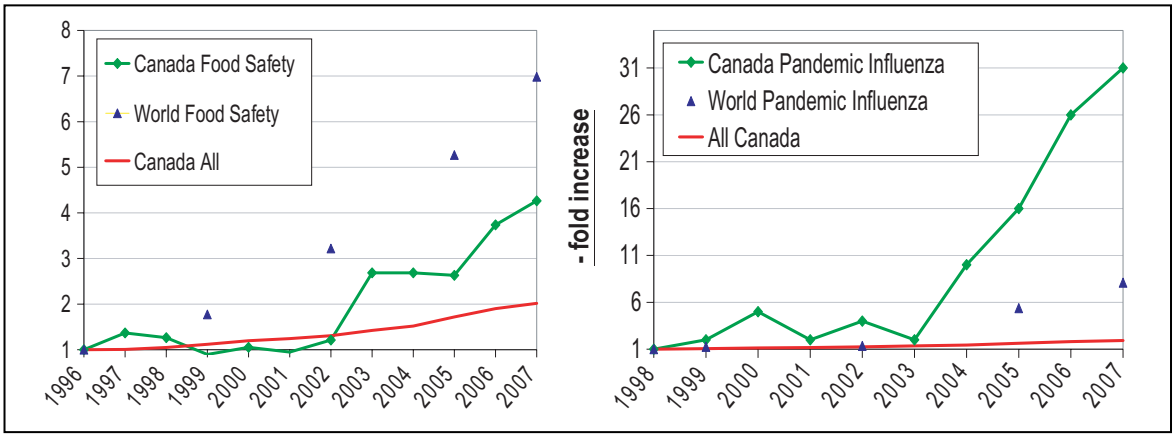
III is approaching a critical transition as its founding Scientific Director completes his term. At this time, it is appropriate to ask: What changes to infection and immunity research has the Institute brought about since its inception, and what have been the impacts? To answer these questions, III evaluated the outcomes and impacts of the Institute as a whole and also performed separate outcome and impact assessments of research supported in two strategic areas: SARS and HIV/AIDS.

Impacts of III

Dr. Mark Bisby and Ms. Michelle Campbell performed an assessment of the outcomes and impacts of the Institute by analysing information gathered from researcher, partner, and advisory board member interviews, in addition to gathering information from web sites and databases. Their full-length report can be found at: http://www.cihr-irsc.gc.ca/e/39364.html. Key findings and quotes from the report are summarized below.

Changes to the infection and immunity research agenda

III has targeted investments to both emerging and ongoing health threats that were under-researched or neglected by traditional research funding modes. A key feature has been III's rapid and nimble response to public health issues such as safe food and water, and also its proactive role in identifying and supporting critical areas such as pandemic preparedness. This strategic approach is working, and is evident, for example, in the spectacular growth in the number of Canadian publications in strategic areas such as food safety and pandemic influenza (see figure).



Relative growth in Canadian and World publications in Food Safety (left) and Pandemic Influenza (right) since 1996.

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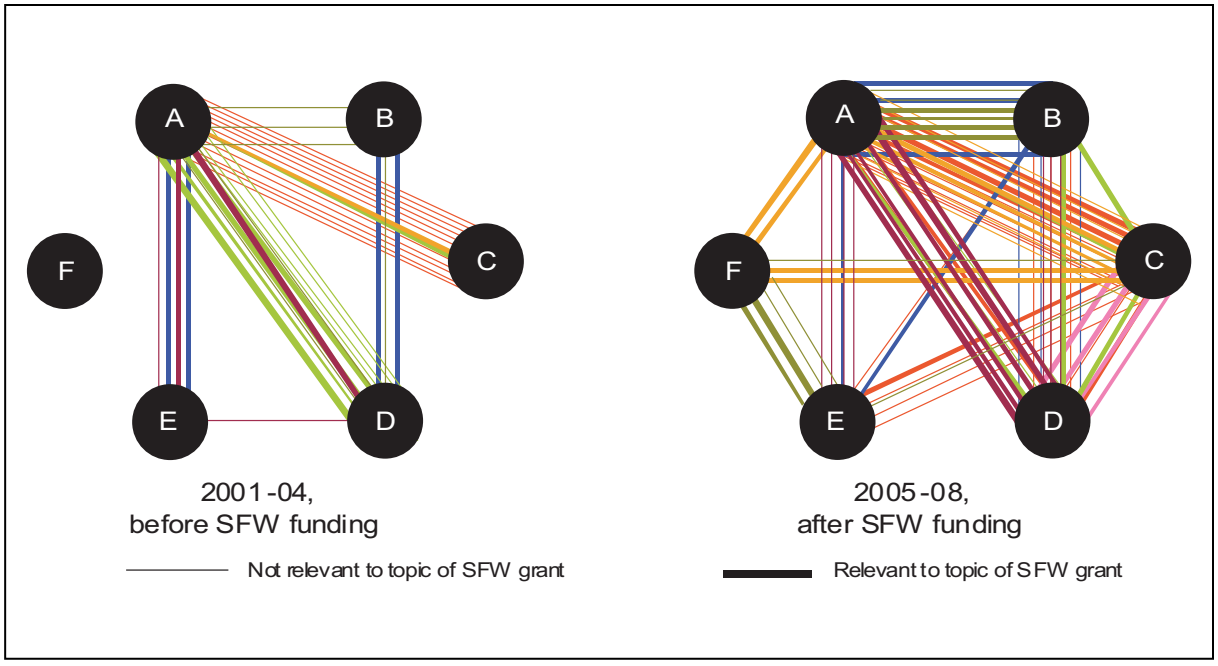
Changes in how research is done

The largest and most fundamental change associated with III is the dramatic growth of research teams. While it is still early days, these collaborations are real, sustained, and yield results. III has made strategic team research not just respectable, but truly innovative. The collaborative nature of the research that has been supported is evident by comparing the number of co-publications among researchers before and after team funding (see figure).

"Before CIHR, HIV research was in trouble; we were a decade behind most countries. We now have multiple world-class leaders, both in fundamental research and in health care delivery."



Co-publication among members of Safe Food and Water Initiative (SFWI) funded teams. Each line represents a co-publication; each colour a different team.

Changes in how infection and immunity research is being used

III has excelled at creating opportunities for linkage and exchange between researchers and research users, including health practitioners, policy makers and industry. For example, research supported by III has helped governments address very specific and immediate questions such as the value of Ontario's universal seasonal influenza immunization program and ways to address the recent increase in *C. difficile* infections. An example of linkages to industry is the Emerging Team Grants in the "Novel Alternative to Antibiotics" Research Initiative, which was launched in partnership with over 20 public and private sector organizations, including six industrial partners. These early linkages increase the probability of realizing commercial and economic impacts of the funded research.

"A major advantage of SFWI grants iscommunity building with people you wouldn't otherwise know or work with. We brought together 6 arms of government, provinces, academics, and industry together to discuss the problems and come up with a strategy."

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In summary, III is successfully demonstrating what can be achieved under CIHR's new mandate. As III transitions into its next phase, it will want to build new strategies upon core assets and strengths which have led to its success.

"One thing III has been able to do is strengthen connections between government departments and academia, such as with the pandemic task force, which mixes researchers and policy makers. It provides a meeting place for these groups."

Outcomes and Impacts of SARS research

In 2003, with SARS spreading in different parts of the world, research was urgently needed to reduce SARS transmission and to identify treatments. III rapidly coordinated research efforts and worked with partners to fund critical research. Given that six years has passed since the outbreak, the time was right for CIHR to assess the impact of the funded research. This section highlights some of the key findings from the report.

CIHR concluded that the investment in research has yielded health, social and economic dividends. The greatest impact was in advancing knowledge, but the results also led to improved health-care and health systems, informed policy decisions and generated economic benefits.

Advancing Knowledge
Breakthroughs were communicated in over 100 publications and through over 300 meeting presentations. The SARS-related articles were published in higher quality journals and were cited more frequently than the researcher's other publications. Drs. James Dennis and Eleanor Fish, for example, devised a new treatment protocol for SARS infection using the antiviral agent interferon-alpha that has been adopted by the WHO and Centers for Disease Control and Prevention. Dr. Fish used this knowledge to identify and patent novel interferon mimics that could be used to treat several types of viral disease.

Building Capacity
Over 80 trainees from undergraduates to post-doctoral fellows were supported by the funding, and of these nine individuals went on to secure their own funding in related areas. Both national and international collaborations were fostered. An outcome was the research network that Dr. Robert Anderson established centered in Canada, Taiwan and Thailand for the study of emerging viral respiratory disease.

Informing Decision-Making
The research results contributed to subsequent research, influenced public policies, health system services, and health practice and led to the development of new methods, practices and potential products. In one case, Dr. Ross Upshur identified ethical issues during the SARS outbreaks that he used to develop an ethical framework for pandemic influenza. The framework was adapted by the WHO and has been incorporated into pandemic plans in Canada, United States, New Zealand and Europe.

Health and Health Systems Impacts
SARS research led to advances in the prevention, diagnosis and treatment of SARS and other infectious diseases. During the SARS outbreak, the research conducted by Dr. Mark Loeb and collaborators led to improved methods to detect the SARS virus in patient samples, methods to predict which SARS patients would have poor outcomes, and to the conclusion that masks of any type significantly reduce the spread of SARS. This is just one example of contributions by SARS researchers.

Economic Impacts
Economic impacts include one spin-off company, three patent applications and the attraction of additional funding to create 30 jobs in Canada. A case in point was the high-throughput screening assay that Dr. François Jean developed and used to identify a novel anti-SARS viral agent. This assay has subsequently been adapted and used for discovery of novel protease inhibitors of the hepatitis C virus. The hepatitis C market is estimated to exceed $8 billion in 2012, and hepatitis C protease inhibitors will have applications in more than 20% of affected patients.

In addition to these and other impacts, SARS highlighted the need for CIHR to take a proactive role to prepare for future infectious disease outbreaks. In 2006, with the threat of a possible influenza pandemic, the Institute of Infection and Immunity established the Pandemic Preparedness Strategic Research Initiative to build and maintain capacity in pandemic preparedness and influenza research. The global spread of a new pandemic strain of influenza in 2009 illustrates the wisdom of this approach. Thus, these investments in research have had health, social and economic benefits and have ensured our readiness to face current and future health threats. Contact the Institute for a copy of the full report.

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Making a difference in HIV/AIDS

Research supported under the CIHR HIV/AIDS Research Initiative (CHARI) and by regular CIHR funding is leading to improved approaches to HIV/AIDS prevention, treatment and care. So say Dr. Mark Bisby and Michelle Campbell who recently assessed the impacts of CIHR-supported HIV/AIDS research. The assessment will provide critical information for the upcoming international ten-year review of CIHR as well as future evaluations of the Federal Initiative to Address HIV/AIDS in Canada. A brief summary of the impacts is provided below. Please contact Jennifer Gunning for the full impact assessment.

By several measures, research capacity and productivity in HIV/AIDS research in Canada has grown extensively since 2001. For example, the CIHR HIV/AIDS Research Initiative has supported 216 individual training and salary awards and an additional 259 individuals have received CIHR awards through other funding programs. The number of investigators receiving grants from the CIHR HIV/AIDS Research Initiative has grown each year and reached over 450 in 2008-09. Overall, results from Canadian HIV/AIDS research have been published in high quality journals and have been frequently cited. Canadian researchers are also making outstanding contributions to international HIV/AIDS efforts through leadership, research collaborations, and, for example, as part of the CIHR Canadian HIV Trials Network, which has made Canada a desirable and effective partner in internationalclinical trials.

In addition to advancing knowledge and building research capacity, the findings of the Canadian researchers are already improving health both nationally and internationally. For example, the clinical trial led by Stephen Moses showing that circumcision can prevent HIV transmission by 50% has contributed to UNAIDS and World Health Organization endorsement of male circumcision as an effective HIV prevention strategy, demonstrating the direct impact of research on the prevention of new infections. For those already infected, Canada's research leaders have been instrumental in slowing the progression of the disease and improving the quality of life of people living with HIV. Examples include Bernard Belleau's discovery of 3TC, and Mark Wainberg proving its effectiveness. Canadian researchers also demonstrated that the "triple cocktail" could reduce AIDS deaths by 90%. The supported research is also helping to reduce the social and economic impact of HIV/AIDS. Given that it can take several years for the impact of research to be fully realised, it is likely that research projects that have just been completed or are ongoing will yield novel prevention, treatment and public health strategies in the future.

By the numbers
Canadian HIV/AIDS researchers
Have doubled since 2001
Include 4 of the world's top 10 most productive HIV/Aids reasearchers
Are located at 66 institutions across Canada, up from 14 in 2001

Canadian HIV/AIDS papers
Represent 5% of all papers on HIV/AIDS worldwide
Are the second most frequently cited in the world
Make up 15% of the "Top 20" most cited papers
Often (45%) include international collaborators

H1N1 Update

H1N1 2009 Influenza Update

CIHR is working with the research community to mitigate the impact of the 2009 H1N1 influenza pandemic. As part of its Pandemic Preparedness Strategic Research Initiative (PPSRI), III has brought researchers and stakeholders together to enhance knowledge sharing and to set research priorities. The PPSRI has built research capacity, fostered collaborations and used innovative funding approaches, ensuring a rapid research response to H1N1.

Setting Priorities and Enhancing Collaboration

On April 27, 2009, immediately after reports that a novel strain of H1N1 influenza virus had spread to Canada, III convened an urgent meeting of the PPSRI Task Group to identify areas requiring research attention. The research areas were refined at a meeting entitled "Canadian Pandemic Preparedness Meeting: H1N1 Outbreak Research Response", that was held in Toronto on July 8, 2009. III organized and hosted the meeting, with support from Canadian Food Inspection Agency and the Rx&D Health Research Foundation. In addition to priority setting, the meeting provided an opportunity for the over 180 influenza and pandemic experts in attendance to share current research results, develop research strategies and collaborate with partners and end-users. The PPSRI Task Group continues to monitor the H1N1 pandemic and meets regularly to discuss new research opportunities.

H1N1 Research Priorities
Epidemiology and the natural history of infection
Biology of the virus and antivirals
Immune response and contributing factors of disease severity
Vaccine development and evaluation
Ethical and intellectual property issues
Health services and policy research

Supporting Pandemic Research

Vaccine Evaluation

Approval of funds for the PHAC/CIHR Influenza Research Network (PCIRN) was expedited to allow a national team of over 80 scientists from 30 research institutions across Canada to conduct a post-licensure evaluation the H1N1 pandemic vaccine. PCIRN will focus on rapid testing for safety and effectiveness of the vaccine in Aboriginal children and adults, adults with chronic illness, infants 6 to 35 months and adults diagnosed with HIV. The network will inform Canadian immunization procedures and policies both during the current pandemic and in preparing for annual seasonal influenza outbreaks.

Pandemic Teams in Antivirals and Mathematical Modelling

As part of the PPSRI, III developed an innovative approach to prepare in advance for outbreak research. In collaboration with the Public Health Agency of Canada, III created the "Catalyst Grant: Pandemic Outbreak Team Leader" program. Its goal was to provide development funds to team leaders who could bring together a national research team in the event of an influenza pandemic. With the advent of the H1N1 outbreak, research proposals prepared by the previously identified team leaders were rapidly peer reviewed and funded. Dr. Guy Boivin at Laval University is leading a team that is studying the genetic evolution of pandemic H1N1 2009 influenza virus and its susceptibility to antiviral drugs, while the team led by Dr. Babak Pourbohoul at the University of British Columbia is developing mathematical models to understand the transmission and spread of the virus.

Catalyst Grant: Pandemic Outbreak Research Response

III announced $1.2 million for the "Catalyst Grant: Pandemic Outbreak Research Response" funding opportunity in July 2009. Five successful research groups were funded in October 2009 following expedited application deadlines and peer review. Much of the research focuses on determining why certain individuals infected with the H1N1 influenza virus develop severe illness and on discovering both clinical and public health interventions that will reduce disease severity.

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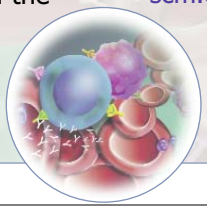
Grants funded under the " Catalyst Grant: Pandemic Outbreak Research Response " competition		
Principal Investigator	**Research Organization**	**Title**
Robert A Fowler	Sunnybrook Health Sciences Centre	Influenza-and H1N1-Related Critical Illness - Demand and Capacity in the Health Care System: the Canadian ICU Flu Study
Allison J McGeer	Mount Sinai Hospital (Toronto)	Outcomes of Pandemic Influenza in Pregnancy (OPIP)
John W Schrader	University of British Columbia	A novel Canadian platform to reduce the mortality of novel H1N1 influenza
Satyendra Sharma	University of Manitoba	The mechanism and immunological correlates of severe respiratory illness following 2009 H1N1 pandemic influenza virus infection
Cécile L Tremblay	Centre Hospitalier de l'Université de Montréal (CHUM)	Controlling the Influenza A H1N1 pandemic strain infection: dynamics and mechanisms of innate and adaptive immune responses in a system biology approach

Pandemic Preparedness

Without question, the PPSRI, which was established in 2006, readied the research response to the current H1N1 influenza pandemic. The PPSRI nurtured researchers who have the expertise, infrastructure and tools to carry out essential studies. It also created linkages between researchers and those who will use the research knowledge. For more information on the PPSRI and the need for pandemic preparedness see: French MB, Loeb MB, Richardson C and Singh (2009) Research preparedness paves the way to respond to pandemic H1N1 2009 influenza virus. Can J Infect Dis Med Microbiol 20(3):e63-e66

KT in Action - Germs Away!

Dr. Michael Mulvey, a CIHR-III funded researcher, and his team are developing educational tools to teach kids how to keep germs away. They have formed the Northern Antibiotic Resistance Partnership (NARP) comprised of community members, health care professionals, educators and research scientists working together to study antimicrobial resistant bacteria causing infections in northern communities. Their "Germs Away" teaching tool, aimed at grades 4-6 gives lessons on how germs spread and how to prevent it. Also available on the website are hand washing posters aimed at children, podcasts, training videos, radio spots and guidelines for physicians on the management of community associated methicillin resistant *Staphylococcus aureus* (CA-MRSA). The "Germs Away" program has been piloted in 19 Northern Saskatchewan schools and already Dr. Mulvey is reporting a decrease in the rates of CA-MRSA. For more information on the "Germs Away" program visit http://www.narp.ca/edu.htm



Meetings and Events

The following meetings and events will be of interest to the CIHR-III community:

- Canadian Society for Immunology (CSI) Spring 2010 Meeting, April 23-26, 2010, Sheraton on the Falls, Niagara Falls, ON, Canada (http://www.csi-sci.ca/scientificmeeting/meetingwelcome10.aspx)
- Association of Medical Microbiology and Infectious Disease (AMMI) 2009 Annual Conference, May 6-8, 2010, Edmonton, AB, Canada (http://www.ammi.ca/annual_conference/index.php)
- Canadian Association of HIV Research (CAHR) Annual Canadian Conference on HIV Research, May 13-16, 2010, Saskatoon, SK, Canada (http://www.cahr-acrv.ca/programs-services/cahr-conference/)
- Canadian Society of Microbiologists (CSM) Annual Conference, June 14-17, 2010, McMaster University, Hamilton, ON, Canada (http://www.csm-scm.org/english/announcements_details.asp?id=314)