Microcosm-III

CIHR Institute of Infection and Immunity

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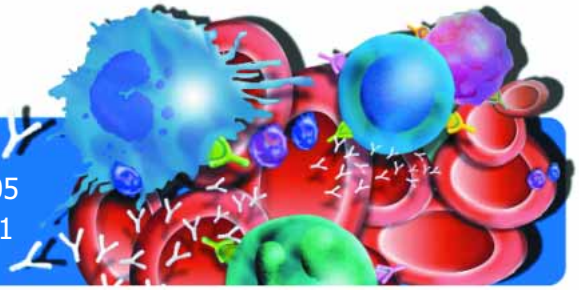

In this issue

Message from the Scientific Director

Establishing and supporting research initiatives

The unique role of a CIHR Scientific Director is to work with other CIHR Institutes, individuals on our Institute Advisory Board, the larger research community, health charities and other stakeholders to set research priorities and support strategic research initiatives. At this stage of Institute development it is critical to assess the outcome of this effort to know if we are making a difference. This issue of the newsletter includes evidence of this process at various stages of completion. A diverse set of new strategic initiatives developed by the Institute, including novel technology applications in health research, social and behavioural research in HIV/AIDS and hepatitis C, and research on microbial contamination of food and water, have received funding this year. The Institute's role in supporting excellence in research has allowed us, from time to time, to bridge fund peer reviewed grants that have received very high scores but were not approved due to lack of funds. The role of the Institute is not always to fund research in our strategic initiatives but to enhance and champion research in areas of the Institute's mandate that can make an impact, for example the mad cow or bovine spongiform encephalopathy (BSE) issue.

The prion disease, BSE, is once again in the news with reports of new cases in Canadian cattle. The Institute recognized the need to define a Canadian agenda for prion disease research when it brought together leading prion experts and health-policy decision makers in Edmonton in September 2003. The recommendations made by conference participants helped to prompt the federal government to establish a new Network of Centres of Excellence (NCE) on BSE and other transmissible spongiform encephalopathies which will begin operation in the fall of 2005.

The outbreak of Severe Acute Respiratory Syndrome (SARS) in 2003 illustrated the need for a network of experts and organizations to rapidly set research priorities and provide immediate funds to appropriate investigators. At the time of the outbreak, the Institute played a key role in coordinating the Canadian research response to SARS by creating the Canadian SARS Research Consortium (CSRC). Results of some of the research supported by the Institute and other Consortium members are reported in this issue of the newsletter. The effectiveness of the CSRC is being formally evaluated by the Institute, and lessons learned from that evaluation will help shape research responses to future infectious disease outbreaks.

III will continue to develop strategic research agendas around the main strategic themes of the Institute and other emerging research issues as there is always the need to build research capacity and support underdeveloped research areas. We will also continue to develop partnerships with stakeholders to foster stronger links with the Institute.

Dr. Bhagirath Singh, Ph.D.
Scientific Director
CIHR Institute of Infection and Immunity (III)

III Events

III New Investigator Forum 2005

The Institute of Infection and Immunity is very pleased to host the Institute's first New Investigator Forum. The Forum will be held April 15-17, 2005 and aims to strengthen infection and immunity research by facilitating peer networks of new investigators and by providing opportunities for both formal and informal interactions with renowned senior scientists working within the mandate of the Institute. The program will include informative workshops, presentations of cutting-edge science and information on tools and mechanisms which support research in Canada.

For further information about the Forum please visit the website at http://www.nif-fnc.ca

Canadian Society for Immunology Annual Meeting 2005

From April 7-10, 2005 the Institute of Infection and Immunity will participate as an exhibitor at the Canadian Society for Immunology Annual Meeting in Whistler, BC. In addition the Institute will sponsor a graduate student travel award and a postdoctoral fellow travel award to attend the meeting.

For more information about the meeting please visit the Canadian Society for Immunology website at http://www.csi.ucalgary.ca/CSI2005.nsf/2005/

Novel Alternatives to Antibiotics Workshop

Recognizing the problems associated with increasing antibiotic resistance and the reduction in antimicrobial pharmaceutical research, the Institute of Infection and Immunity and partners are taking a proactive approach in identifying critical areas of research that might lead to the development of alternatives to existing antibiotic drugs or changes in current antibiotic prescribing practices. On March 10/11, 2005, the Institute and partners will host an invitational workshop in Vancouver that will bring together experts from across Canada to discuss alternative methods to combat antibiotic resistance. It is anticipated that the recommendations from this workshop will provide the foundation for the launch of a future strategic initiative.

III Publications

Meeting the Challenge of Prion Diseases: Conference Proceedings and International Research Planning Workshop Report

The report is available on our website at http://www.cihr-irsc.gc.ca/e/17711.html

Research Symposium on Integrating Discovery Platforms in Autoimmune Diseases

The report is available on our website at http://www.cihr-irsc.gc.ca/e/19225.html

Innovation and Challenges in Funding Rapid Research Responses to Emerging Infectious Diseases: Lessons Learned from the Outbreak of Severe Acute Respiratory Syndrome

Published in the Canadian Journal of Infectious Diseases & Medical Microbiology, http://www.pulsus.com/Infdis/15_03/sing_ed.htm

Health Research: The Key to HIV/AIDS Solutions

is available on our website at http://www.cihr-irsc.gc.ca/e/25832.html

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SARS RESEARCHERS PRODUCE RESULTS

Severe acute respiratory syndrome (SARS) emerged as a new respiratory disease in China at the end of 2002 and quickly spread to several countries, including Canada. SARS was determined to be caused by a new type of coronavirus (SARS-CoV). Other types of human coronaviruses produce only mild cold-like symptoms, whereas 5 to 10% of individuals who contracted SARS died.

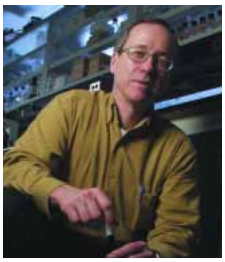
In April 2003, in response to the SARS crisis, the CIHR Institute of Infection and Immunity (III) launched a request for proposals (RFP) in partnership with the Ontario Research and Development Challenge Fund, the Canadian Network for Vaccines and Immunotherapeutics, Le Fonds de la recherche en santé du Québec, and Health Canada for research into the causes and consequences of SARS. Within a month, four research groups had their research proposals approved.

Dr. Michel Bergeron's team developed assays for the detection of SARS-CoV and other human coronaviruses. The team also successfully developed a very rapid and simple sample preparation procedure for extracting SARS-CoV RNA from respiratory specimens. Ongoing work includes improvements to protocols for the rapid extraction of viral RNA from other types of clinical specimens.

Dr. Mark Loeb assembled a large number of co-investigators from hospitals, research institutes and universities to form the Canadian SARS Research Network. Investigators developed several RNA extraction protocols and assays to detect SARS-CoV. A study comparing the best extraction and assays on a large panel of clinical specimens from cases and controls is ongoing.

The Canadian SARS Research Network was engaged in numerous epidemiological and clinical research projects, two of which are summarized here. One project led by Dr. Loeb and Dr. Allison McGeer examined the risk factors involved in the transmission of SARS from patients to health care workers. The investigators found that increased time in a patient's room, closeness to the patient's airway, and lack of masks increased the risk of transmission. Another study, led by Dr. Marie Louie, showed that most patients recover well from SARS. Lung function returned to normal three months after SARS, but fatigue and muscle weakness caused mild disability. By six months, the majority of patients had returned to work.

A major accomplishment of the research team assembled by **Dr. James Dennis**, was a clinical study, led by co-investigator Dr. Eleanor Fish, of interferon alfacon-1, an interferon α possessing high antiviral activity. SARS patients treated with interferon and corticosteriods had increased blood oxygen levels and faster resolution of lung abnormalities compared to patients treated with corticosteroids alone. The group is working with the Global Influenza Programme Group to design interferon treatment protocols that could be used in a future outbreak of SARS or influenza.



Another avenue of investigation of the Dennis group was the use of microarray methods to track changes in the nucleotide sequence of SARS-CoV RNA in an effort to monitor how quickly the virus changes with time. Viral RNA from 100 patient samples was sequenced, and the sequences are currently being analyzed. The procedures are being extended to viruses such as influenza and West Nile. Changes in viral nucleotide sequences occur frequently and a comprehensive knowledge of these changes is useful for vaccine designers and epidemiologists.

Dr. Danuta Skowronski's multi-disciplinary, multi-site research team sought to develop a human vaccine and succeeded in creating several vaccine preparations, including inactivated whole and adenovirus vector vaccines. Vaccine trials in ferrets and mice have been completed and a report is pending.

In other work, the team developed and validated diagnostic tests including PCR and serologic neutralization assays that have been shared with other agencies and used in animal model vaccine evaluation. The neutralization assay was used in a sero-survey of health care workers in British Columbia who cared for patients with SARS to examine the possibility of further spread; no evidence for unrecognized spread was

Continued on page 4

SARS RESEARCHERS PRODUCE RESULTS (*continued*)

found among more than 400 workers tested. Mathematical models based on contact network theory have been developed by this team to predict the spread of SARS through communities and for quantitatively comparing the impact of public health interventions. The team is also embarking on in vitro evaluation of the immunologic correlates of disease and its severity among persons with SARS and matched controls in the Toronto area.

In July 2003, human-to-human transmission of SARS was halted through a massive public health effort. Although it is impossible to predict, there are reasons to be concerned about the possible return of SARS. An animal, and possibly a human, reservoir may now exist and numerous laboratories with SARS-CoV represent a potential source of future re-emergence. Maintaining interest in vaccine development given the uncertainty of its return becomes an ongoing challenge. What is certain is that the lessons learned from SARS have enhanced our understanding and our ability to respond to this and future emerging pathogens.

LAUNCH OF THE NEW HIV/AIDS COMMUNITY-BASED RESEARCH PROGRAM

On November 1, 2004, the CIHR Institute of Infection and Immunity, in partnership with the CIHR Institute of Aboriginal Peoples' Health, announced the first round of Requests for Applications (RFA) under the new HIV/AIDS Community-Based Research (CBR) Program. The Program supports applications that engage communities in health research on HIV/AIDS, empowering communities to take control of health promotion and practices to reduce the risk and incidence of HIV/AIDS infection in all settings.

The HIV/AIDS CBR Program was established with the creation of the Canadian Strategy on HIV/AIDS (CSHA) in 1998. Initially administered by Health Canada, the CBR Program was transferred to CIHR in April 2004. This Program is intended to support the goals of the CSHA and to assist community-based groups, non-governmental organizations and institutions in developing the knowledge necessary to carry out their HIV/AIDS work in the most effective manner. The specific objectives of the program are:

- To promote the conduct of community-based research that addresses needs in Aboriginal and non-Aboriginal communities engaged in the response to HIV/AIDS
- To provide opportunities for effective research partnerships between affected communities and researchers
- To promote the rapid dissemination and translation of knowledge created through community-based research
- To further develop the capacity of Aboriginal and non-Aboriginal communities to conduct community-based research

The Program invites applications in two CBR streams: the Aboriginal Stream and the General (non-Aboriginal) Stream. Each stream will be made up of two components: Research and Capacity Building.

The first round of RFA included six categories of grants and awards: Operating Grants, Development Grants, Research Technical Assistant Grants, Capacity Building Workshops, Doctoral Research Awards and Masters Research Awards.

Detailed information on the program can be found at
http://www.cihr-irsc.gc.ca/e/25182.html

III Welcomes New Advisory Board Members

Dr. James Lavery
St. Michael's Hospital/University of Toronto

Dr. Joaquin Madrenas
Robarts Research Institute/The University of Western Ontario

Ms. Mary Catharine McDonnell
South Shore Health, Lunenburg, NS

Dr. Allison McGeer
Mount Sinai Hospital/University of Toronto

Dr. Chris Power
University of Calgary

The Institute would like to thank those members who have recently retired from the Board,

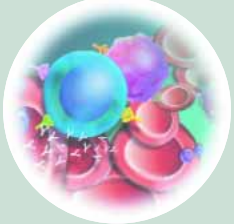
Dr. Abdullah Daar,

Dr. Jack Gauldie,

Dr. Kevin Glasgow and

Ms. Helaine Shiff

for their dedication and contributions.



III Strategic Funding Decisions

Novel Technology Applications in Health Research

The Novel Technology Applications in Health Research program will stimulate both the development of new techniques and methodologies of value in biomedical research and clinical practice and also the application, in health research, of technologies that already exist in science-based research disciplines not traditionally associated with the life sciences. Six innovative projects in the areas of infection and immunity were funded.

Novel Technology Applications in Health Research

Principal Investigator	Title
Dr. Jan J. Dubowski Université de Sherbrooke	Quantum dot template for fast and simultaneous detection of different infectious agents
Dr. Damian Labuda Hôpital Sainte-Justine (Montréal)	Developing diagnostic tools through in vitro molecular evolution
Dr. Peter S. Pennefather University of Toronto	Development of simplified and portable serology technology for monitoring progression of infectious disease with microliter blood samples
Dr. Andrew D. Rutenberg Dalhousie University	Micromanipulation of bacterial division
Dr. Pere Santamaria University of Calgary	New tools to characterize, manipulate and analyze the phenotypic contribution of extended regions of mammalian genomes, beginning with the human MHC
Dr. Brian J. Ward The Res. Inst. of the McGill University Health Ctr.	SELDI-ToF MS in blood-borne protozoan infections: novel diagnostic approach and new insights into host-parasite interactions

Social and Behavioural Research Issues in HIV/AIDS and Hepatitis C Interdisciplinary Capacity Enhancement Team Grants Program

These Interdisciplinary Capacity Enhancement Team Grants are intended to provide support for new or existing groups conducting multidisciplinary research in the area of social and behavioural issues in HIV/AIDS and hepatitis C. The grants will enable teams to build capacity and add expertise to their core capabilities and to develop strategies for knowledge translation.

Social and Behavioural Research Issues in HIV/AIDS and Hepatitis C Interdisciplinary Capacity Enhancement Teams Grant Program

Partners: The CIHR/Health Canada HIV/AIDS Research Program and the Health Canada/CIHR Research Initiative on Hepatitis C

Principal Investigator	Title
Dr. Louise Balfour Ottawa Health Research Institute	Improving health care knowledge, treatment preparedness, treatment adherence, and quality of life among HIV and hepatitis C patients
Dr. Benedikt Fischer The Centre for Addiction and Mental Health (Toronto)	Investigating socio-behavioural risk, prevention and treatment factors for HCV in special populations
Dr. Gaston Godin Université Laval	Prévention du VIH/sida et de l'hépatite C: Recherche sociale et comportementale
Dr. Susan A. Kirkland Dalhousie University	Atlantic Interdisciplinary Research Network: Social and behavioural issues in hepatitis C and HIV/AIDS

III Emerging Infectious Diseases Priority Announcement

III invited applications to the regular operating grants competition that focused on research involving, but not limited to, vaccine development, host immune responses and clinical sequelae to SARS and West Nile Virus. In addition, III welcomed applications relating to any other newly identified and previously unknown pathogen or infectious disease and six diverse projects received funding.

Emerging Infectious Diseases Priority Announcement

Principal Investigator	Title
Dr. Guy Boivin Université Laval	Role of hemagglutinin changes on antigenic properties, virulence and drug resistance of influenza A viruses
Dr. Tom Hobman University of Alberta	Role of the West Nile virus core protein in virus replication and host cell death
Dr. William W. Jia University of British Columbia	Application of peptide array for SARS diagnosis and treatment
Dr. James W. Kronstad University of British Columbia	Morphogenesis of fungal pathogens
Dr. Mark Loeb McMaster University	Long term impacts of severe West Nile virus infection: A cohort study
Dr. Carl Lowenberger Simon Fraser University	Characterization of the innate immune response of mosquitoes to parasites and pathogens

Safe Food and Water Initiative: Microbial Contamination of Food and Water and Antimicrobial Resistance in the Food Chain - Phase II - Establishing a Framework

The program was designed to lay a framework for the coordination of Canadian research on the microbial contamination of food and water and antimicrobial resistance in the food chain. The goal of the Request for Applications was to promote the formation of new research teams, or the expansion of existing teams, in which academic and federal government funded researchers combine their skills and resources in order to more efficiently and effectively address specific research questions. Seven multi-disciplinary teams were funded in this competition.

Safe Food and Water Initiative: Microbial Contamination of Food and Water and Antimicrobial Resistance in the Food Chain - Phase II - Establishing a Framework

Partners: Institute of Population and Public Health, Health Canada, Environment Canada, Agriculture and Agri-food Canada, the Canadian Food Inspection Agency and the National Research Council

Principal Investigator	Title
Dr. Neil Cashman University of Toronto	The Canadian Prion Disease Network: Meeting the challenge
Dr. Judith Isaac-Renton University of British Columbia	Safe drinking water through source surveillance: Assessing impacts of environmental factors and microbial contamination of watersheds on community health
Dr. Mohammed Karmali University of Guelph	Comparative pathogenesis and public health significance of verocytotoxin-producing Escherichia coli serotypes
Dr. Marie Louie Sunnybrook and Women's College Health Sciences Centre	Prospective multi-province surveillance for antimicrobial-resistant Escherichia coli in drinking and recreational source waters: Impact on humans and the environment
Dr. Asit Mazumder University of Victoria	Source tracking and environmental determinants of coliform bacteria in source water under various land-use in British Columbia
Dr. Subash Sad University of Ottawa	Modulation of immunity and development of therapeutics against Salmonella
Dr. Diane Taylor University of Alberta	Pathogenesis and antibiotic resistance in Campylobacter

Kidney Transplantation Fellowship Awards

A partnership between the Institute of Infection and Immunity, The Kidney Foundation of Canada and the Canadian Society of Transplantation, the Kidney Transplantation Fellowship is designed to provide up to 3 years of support for full-time, postdoctoral research training in the kidney transplantation field in Canada or abroad. The objective of this program is to promote and enhance the development of clinician scientists in Canada involved in basic and clinical kidney transplantation research in order to build research capacity and improve the prestige and appeal of careers in this discipline. Congratulations to **Dr. Sang Kim** from the University of Toronto on receiving the first award under this program.

Pilot Project Grants for New Investigators

The program was designed to support innovative, pilot or feasibility research in the area of infection and immunity by new investigators who are within their first five years of an academic appointment. Grants will enable new investigators with novel ideas and observations to conduct pilot studies and/or gather evidence necessary to determine the viability of new research directions. There was a high level of interest in this RFA and the Institute was pleased to be able to fund 25 excellent proposals.

Pilot Project Grants for New Investigators

Principal Investigator	Title
Dr. Ali Ashkar McMaster University	Study of human leukocyte function in alymphoid RAG-2/gamma chain null mice in response to human viral infections and cancer
Dr. James Booth Sunnybrook and Women's Health Sciences Centre	Cell biology of toll-like receptors
Dr. Lori Burrows Hospital for Sick Children	Peptidoglycan synthesis and bacterial biofilm formation
Dr. Deborah Burshtyn University of Alberta	Vaccinia virus modulation of natural killer cells
Dr. Benoit Cousineau McGill University	Development of a new generation of live vaccines using Lactococcus lactis
Dr. Keith Fowler University of Manitoba	The role of immune activation and CD4 gene polymorphisms in an HIV seroconversion cohort from Kisumu, Kenya
Dr. Michael Glogauer University of Toronto	Non-invasive oral rinse assay (NORA) to monitor neutrophil tissue delivery: monitoring susceptibility to infection in neutropenia, neutrophil related disorders and patients recovering from bone marrow transplantation
Dr. David Granville University of British Columbia	Protease inhibitor-9/serine protease inhibitor-6: role in heart transplant rejection
Dr. Eyal Grunebaum Hospital for Sick Children	Correcting purine nucleoside phosphorylase (PNP) deficiency in mice by intracellular delivery of human PNP combined with the HIV-TAT protein transduction domain
Dr. David Guttman University of Toronto	Functional screen for Pseudomonas aeruginosa type III secreted effector proteins
Dr. David Heinrichs The University of Western Ontario	Methodologies to investigate Gram-positive bacterial pathogenesis
Dr. Brent Johnston Dalhousie University	Role of the chemokine receptor CXCR6 in inflammatory autoimmune disease
Dr. Nathalie Labrecque Hôpital Maisonneuve-Rosemont	Regulation of hematopoiesis and memory T cell generation by interleukin-21
Dr. Megan Levings **Dr. Michael Grigg** University of British Columbia	T regulatory cells in Toxoplasma pathogenesis
Dr. Chen Liang Sir Mortimer B. Davis Jewish General Hospital- Montreal	Understanding of the interactions between viral vif protein and a cellular factor APOBEC3G: implications for future HIV/AIDS therapies

Pilot Project Grants for New Investigators (continued)

Principal Investigator	Title
Dr. Paul Macpherson Ottawa Health Research Institute	Down regulation of the interleukin-7 receptor on circulating CD8 T-cells during HIV infection
Dr. Aaron Marshall University of Manitoba	Role of novel signal transduction molecules in regulating the activation and production of allergic mediators by mast cells
Dr. Alice Mui University of British Columbia	Immunotolerance therapy for transplantation
Dr. Norman Neumann University of Calgary	Development of advanced multiplexed diagnostic tools for the detection and molecular characterization of waterborne pathogens
Dr. Patrick Provost Université Laval	Significance of the interaction between Dicer and 5-lipoxygenase
Dr. William Stanford University of Toronto	Sca-1 signalling in hematopoietic stem cells
Dr. Natalie Vergnolle University of Calgary	Cleavage of proteinase-activated receptor-2 by proteinases from intestinal pathogens of the Escherichia coli family modulates the host inflammatory response
Dr. Peter Von Dadelszden University of British Columbia	The role of Chlamydophila pneumoniae and cytomegalovirus in pre-eclampsia: a link between pre-eclampsia and later atherosclerosis?
Dr. Yonghong Wan McMaster University	Development of safe and effective genetically engineered dendritic cell-based tuberculosis vaccines
Dr. Minna Woo St. Michael's Hospital (Toronto)	Caspase8 and autoimmune islet destruction

Institute Advisory Board Members 2004-2005