Canadian Center for Vaccinology
Annual Report
2012–13

improving health through vaccine research

By Brandon Martin, age 11, Mount Carmel Elementary School, New Waterford, NS
CCfV is made possible by a continuing collaboration of Dalhousie University, the IWK Health Centre, and Capital Health. The CCfV’s 20,000 sq ft facility in the IWK Health Centre includes laboratories for microbiological and molecular research, ambulatory and inpatient clinical trial facilities, data analysis, training and conference space. It was founded in 2007 with financial assistance from the Canada Foundation for Innovation, the Nova Scotia Research and Innovation Trust, and the Government of Nova Scotia’s Department of Economic Development, among others. The Clinical Research/Vaccine Challenge Unit, which opened in 2009, was made possible by additional funding from Sanofi Pasteur.
As you will read in the following pages, CCfV investigators and support personnel continue to conduct and publish a variety of vaccine-related research. The curiosity, expertise and determination of CCfV investigators continue to contribute to the health of all Canadians, from laboratory research, to evaluation of new and established vaccines, to examination of programs and policies. Much of this research expands beyond our borders and engages CCfV members in vaccine safety and program issues in many countries throughout the world.

Research conducted here in Halifax contributes to Canadian and worldwide health networks. The longest standing network anchored at CCfV, now in its 22nd year, is the Canadian Immunization Monitoring Program, Active (IMPACT), which connects 12 pediatric hospitals in Canada to report the more serious hospitalized cases and selected outpatient visits for adverse events and vaccine-preventable diseases. IMPACT feeds its important data into the Canadian Adverse Event Following Immunization Surveillance System (CAEFISS) of the Public Health Agency of Canada. CAEFISS, in turn, forwards its data to the World Health Organization which monitors global vaccine safety and effectiveness.

Another large network centered at CCfV, the Public Health Agency of Canada – Canadian Institutes of Health Research Influenza Research Network (PCIRN), has been renewed for another three years to solidify the connections among Canadian researchers. This network has made an enormous contribution to our knowledge of influenza, its impact on population health, the effectiveness of the vaccines and our ability to quickly implement programs in the event of a pandemic. PCIRN has also been very effective in leveraging its core support and expanding its capabilities through collaborative research agreements with the corporate sector.

Clinical trials to test vaccine safety and effectiveness continue to provide the bulk of research activity at CCfV, despite a worldwide decline in funding for clinical research. Some exciting new trials will be initiated this coming year by the Pan Provinicial Vaccine Enterprise (PREVENT), of which CCfV is a founding member. In addition to clinical trials, CCfV personnel conduct surveys and educational programs to increase public understanding of vaccines. It is anticipated that our capacity for research will increase in 2013 with the addition of new faculty, successful grant applications, and the continuation of large projects such as PCIRN.

Educational efforts at CCfV include a rotation of trainees from undergraduate to post-graduate studies, bi-weekly seminars and journal clubs, and an annual symposium combined with Infectious Diseases Research Day organized by the Dalhousie Divisions of Infectious Diseases of the Departments of Pediatrics and Medicine together with Dalhousie Infectious Diseases Research Alliance. While investigators, trainees and support personnel often present their research at Halifax-based events, all go further afield to regional, national and international forums, bringing recognition to Halifax-based research and the collaborators who make it possible.
Vision

CCfV is an integrated collaborative multidisciplinary vaccine research team committed to excellent research. CCfV unites the biomedical and clinical sciences with the social sciences and humanities to effectively span the research continuum from basic discovery to translation into useful vaccines to prevent disease in humans and to change population and public health outcomes.

Organization

Activity within CCfV is organized into three groups:

- Vaccine Discovery Group
- Vaccine Evaluation Group
- Health Policy & Translation Group

An Advisory Committee of CCfV investigators and external advisors provides counsel on the strategic direction and objectives of CCfV research.

PCIRN** Research 2012–13

- CIHR* Funded $1,156,798
- Industry Funded $3,781,719

CIHR* and Other Granting Agencies Funded $291,769
Industry Funded $751,986
PCIRN** CIHR Funded $889,580
PCIRN** Industry Funded $339,598
Discovery Group researchers are making great strides towards the development of novel vaccines, with an emphasis on new antigens, delivery systems, adjuvants, and mucosal immunity.

Comprised of researchers from the fields of bacteriology, molecular biology, virology, and immunology, the Group creates an environment in which close collaboration rapidly enhances research and development and provides excellent training opportunities. Members of the Discovery Group interact with other members of the Center’s Vaccine Evaluation and Health Policy & Translation Groups as well as industry leaders and researchers from other universities.

**Highlights**

- Genetically engineered oral commensal *S. gordonii* to express heterologous antigens in order to produce an oral pertussis vaccine (S. Lee & S. Halperin)
- Vaccine development and immunological studies on RSV, dengue and other infectious disease pathogens (R. Anderson)
- Fusogenic liposomes as a mechanism to deliver vaccines directly into cells (R. Duncan)
- Development of viral vector-based recombinant gene delivery system to stimulate mucosal immunity; understanding the role of Th1/Th17 balance in anti-*Chlamydia* immunity and development of clinical immunoassays and parameters for evaluation of vaccine candidates against *Chlamydia* (Jun Wang)
- Application of measles, hepatitis B, and hepatitis C viruses to developing new vaccines, antiviral agents, and gene therapy (C. Richardson)
- Novel adjuvants in mouse model of influenza, and PCIRN’s reference laboratories for influenza antibody testing (T. Hatchette)
- Surveillance of immune responses to *Clostridium difficile* (J. LeBlanc)
- Novel adjuvant vaccine formulations (M. Mansour, M. Stafford)
- Immunoepidemiological studies for anti-*Haemophilus influenzae* type a vaccine development (M. Ulanova)
The Clinical Trials Research Centre (CTRC) is the centre of vaccine evaluation at CCfV.

Investigators and staff provide expertise in the development and implementation of studies ranging from first-in-human phase 1 to post licensure phase 4 trials. The CTRC team includes expertise in clinical infectious diseases, epidemiology, statistics, and data management and analysis. Both the safety and immunogenicity of candidate vaccines are studies, as well as the field effectiveness of vaccines and their effects on disease burden, vaccine compliance, and public acceptance.

Evaluative research in 2012 focused on human papillomavirus vaccines in adolescent girls and women, vaccines in pregnancy (pertussis and group B streptococcus), enhanced influenza vaccines for older persons, severe outcomes with influenza infection leading to hospitalization, quadrivalent influenza vaccines in children, rotavirus vaccine, zoster (shingles) vaccine in older persons, and meningococcal infection in children and vaccines for immune compromised persons with cancer.

In 2012 there were 1584 participants in 25 different studies requiring 5079 visits and 1061 follow up phone calls. In addition, more than 1500 completed surveys were analyzed.

Companies sponsoring studies in 2012 included:

- AstraZeneca
- GlaxoSmithKline
- Merck
- Novartis Vaccine
- Pfizer
- Sanofi Pasteur

Public-sector organizations funding clinical research through grants or contracts have included the following:

- Canadian Institutes of Health Research
- Public Health Agency of Canada
- The Michael Smith Foundation
Research Highlights

Health Policy & Translation Group

The Health Policy and Translation Group is a multidisciplinary collection of researchers, public health officials, clinicians, and trainees. Members of the Group are engaged in research projects across Canada and the U.S. as well as in Central and South America, Africa, Asia and Europe. The Group meets monthly to update each other on current and future research, and to discuss issues that affect the translation of this research into policy and programs.

Highlights

- Studying challenges surrounding immunization in specific populations (e.g. pregnant women, health care workers and students, marginalized groups, communities in Canada’s North)
- Investigating vaccine safety standards in developing countries, and the capacity for these countries to implement immunization programs
- Examining and addressing vaccine hesitancy
- Promoting strategies to reduce immunization pain
- Improving curriculum in health workers’ formal education programs
- Developing immunization education materials for school-aged children
- Increasing public access to vaccine research data
- Assessing the effects of interpretations of privacy legislation on vaccine research
- Analysing knowledge, attitudes and behaviours as social determinants of vaccine acceptance and hesitancy
- Utilizing computer-based e-health information systems to more accurately measure and improve vaccine uptake
Trainees’ Highlights

Since CCfV investigators work in a variety of disciplines, so do the trainees they supervise. Some of the 2012 trainees in vaccinology-related studies are listed below.

Undergraduate Summer

- **Health Law Institute**: Amanda Whitehead
- **Microbiology & Immunology**: John deRosenroll, Christopher Lee, Sheren Anwar Siani

Undergraduate Honours

- **Microbiology & Immunology**: Patrick Lakner, Kathleen Logie, Cara MacRae, Diandra Miller, Adam Rocker

Master’s

- **Applied Health Services Research**: Sanela Gajic
- **Community Health & Epidemiology**: Jill Carter, Venessa Ryan, Michael Young
- **Mathematics and Statistics**: Christina Wang
- **Microbiology & Immunology**: Raidan Al-Yazidi, Bassel Dawod, Maram Hulbah, Farhan Khan

PhD

- **Biochemistry**: Supavadee Polyiam
- **Interdisciplinary**: Sharon Batt, Robyn MacQuarrie

Postdoctoral Fellows

- **Microbiology & Immunology**: Elizabeth Acosta-Ramirez, Sebastien Delpeut, Yan Huang, Sarah McAlpine, Amanda Lang, Ryan Noyce (Banting postdoctoral fellow), Muzaddid Sarker, Ricky Siu
- **Sociology and Social Anthropology**: Conor O’Dea

Undergraduate Medical

- **Obstetrics & Gynecology**: Alex Legge

Postgraduate Residents

- **Pediatrics**: Cora Constantinesc, Heba Ghandoura, Jennifer Smith
- **Surgery**: Mathew Brace
The CCfV Laboratory supports clinical trials and epidemiological research, and is also a referral laboratory for industry, government or collaborative research.

CCfV provides Good Laboratory Practice (GLP) compliant assays for measuring antibodies against pertussis antigens, diphtheria and tetanus toxoids and influenza (hemagglutination inhibition assays). The CCfV Laboratory also processes cells for assays measuring cell-mediated immunity. CCfV is the home of one of the PHAC/CIHR Influenza Research Network (PCIRN) laboratories which anchors the Serious Outcomes Surveillance Network (SOS). CCfV’s PCIRN laboratory provides testing for the diagnosis of both influenza and pneumococcal infection including polymerase chain reaction (PCR), and molecular typing of pneumococcal serotypes. CCfV’s PCIRN laboratory is actively testing all of the specimens submitted to the SOS network from across Canada to better determine the effectiveness of the influenza vaccine and develop a more comprehensive picture of the epidemiology of other respiratory pathogens in patients admitted to hospital during the influenza season. CCfV’s PCIRN laboratory is led by Todd Hatchette and Jason LeBlanc while the pertussis laboratory is overseen by Scott Halperin.

The Biosafety Level 3 laboratory is capable of handling risk level 3 emerging and ono-indigenous animal pathogens. In 2012, this laboratory was used for research on canine distemper virus recombinants and lentivirus recombinants. Goatpox and PPRV (peste des petits ruminants virus) will soon be added.

To test serum antibody titres to Influenza, 6773 Hemagglutination Inhibition (HAI) assays and 2244 MicroNeutralization (MNeut) assays were conducted in CCfV laboratories in 2012. 102 PBMC (peripheral blood mononuclear cell) tests were performed to measure immune response to antigens.
CCfV Researcher Profiles

The multidisciplinary membership of CCfV results in a wide variety of vaccine-related research activity. On the following pages some of this research is highlighted but it is not an all inclusive summary of all research conducted by CCfV members.

Robert Bortolussi MD

Bob Bortolussi is a pediatric infectious disease clinician and a Professor of Pediatrics and Microbiology and Immunology at Dalhousie University. Bob has published over 100 original articles and book chapters on bacterial infection, newborn host defence and training of clinician scientists. The later topic is now his major academic interest. Bob developed the interdisciplinary problem-based curriculum for the CIHR training program, the Canadian Child Health Clinician Scientists Program (CCHCSP) and adapted to be used by PCIRN vaccine researchers and by clinicians in Africa. The curriculum and his book "Handbook for Clinician Scientists" are now used in 17 Universities in Canada and by clinician scientist groups in Europe, and Africa. Bob directs the Pediatric Infectious Diseases training Program and the Clinical Investigator program (CIP) for the Faculty of Medicine at Dalhousie University and is co-founder of "MicroResearch", a clinician scientist capacity building program in the developing world.

Todd Hatchette MD

Todd Hatchette is Medical Microbiologist who is the one of the Directors of the Virology and Immunology section and Chief of Service of the Division of Microbiology, QEII Health Science Center. As the Province's only medical virologist, Dr. Hatchette has expertise in the clinical and laboratory diagnosis of viral infections. Dr. Hatchette's research interests include:

- molecular aspects of influenza infection and host restriction;
- use of influenza as a model to test new vaccine delivery systems;
- development and evaluation of new diagnostic methods;
- seroepidemiology of infectious diseases in Nova Scotia and Canada.

Matthew Herder LLM, JSM

Matthew Herder is an Assistant Professor in the Faculties of Medicine and Law at Dalhousie. His research focuses on university-industry relationships, intellectual property rights, and the impact of commercial interests on academic researchers and governmental institutions. He is the Principal Investigator on a three-year CIHR funded operating grant entitled “Emerging Health Researchers and the Commercialization of Academic Science.” Current works in progress related to vaccinology include an article examining, from legal and ethical perspectives, influenza virus sharing within an international surveillance network, and a paper calling for open access to laboratory assays used in connection with several widely licensed vaccines.
**Song Lee PhD**

Song Lee's laboratory is investigating the use of *Streptococcus gordonii* as a live oral vaccine vehicle. The goal is to achieve a protective immune response through oral colonization, investigating the use of the recombinant *S. gordonii* to generate a live oral vaccine against childhood diseases. Novel platforms for the development of single-dose vaccines for neonates are also being investigated, as well as host-*S. gordonii* interactions and factors regulating antigen production in *S. gordonii*, to understand the recognition of *S. gordonii* by the host cells and the “bottle-neck” of foreign protein production to provide means to generate an efficient vaccine vehicle.

**Noni MacDonald MD**

Noni MacDonald is Professor of Pediatrics and Computer Science, with a clinical appointment in Paediatric Infectious Diseases at the IWK Health Centre. As a founding member of CCfV she launched the coordinated initiatives of the Health Policy and Translation Group, particularly looking at vaccine safety and programs. She has published over 300 papers, is the Editor in Chief of Paediatrics and Child Health, and a former Editor in Chief of CMAJ. She was a founding member of the WHO Global Advisory Committee on Vaccine Safety and now is a WHO advisor on strengthening vaccine safety programs in developing countries. She was recently named Distinguished Lecturer at the Canadian Immunization Conference.

**Kathryn Slayter Pharm D**

Kathryn Slayter is currently Assistant Professor, Faculties of Medicine and Health Professions and Clinical Pharmacy Specialist with the Division of Infectious Diseases, Department of Medicine and Chair of the Antimicrobial Agents Subcommittee at Capital Health. She is the author for Canadian Routine Immunizations for the Compendium of Pharmaceuticals and Specialties (CPS). Her recent research includes: primary investigator of a national study of pneumococcal conjugate vaccine in HIV infected individuals; assessing disposition of antivirals for influenza in obesity; vaccination in splenectomised individuals which has influenced local and provincial immunization practices. Dr. Slayter is a member of the Pharmacists as Immunizers (PAI) research team, which will explore the role of pharmacists as immunizers and their impact on immunization rates and disease prevention in the Maritimes.
Bruce Smith PhD

Bruce Smith is a Professor in the Department of Mathematics and Statistics at Dalhousie University. His interests centre on the role of dependence in statistical analysis, including temporal dependence and dependence induced by pedigree structure. Bruce works with a group of three other statisticians at CCfV. In addition to providing basic statistical and data management support for clinical trials, the group is involved in statistical research on methods for accommodating and correcting for the seasonality observed in many infectious diseases, and in the development of novel methods for the analysis of serial dilution data.

Karina Top MD

Karina Top is a pediatric infectious disease specialist and Assistant Professor in the Department of Pediatrics, Dalhousie University. Her research focuses on vaccine safety. She is studying the quality reporting of seizures after immunization through Canada’s post-licensure surveillance system, in collaboration with the Public Health Agency of Canada and Canadian Immunization Monitoring Program Active. She is also working to establish a Special Immunization Clinic in Halifax as part of a national PCIRN network to standardize the assessment and follow-up of patients who have experienced adverse events following immunization or have potential contraindications to immunization.

Jun Wang PhD

Jun Wang is assistant Professor in the departments of Microbiology & Immunology and Pediatrics at Dalhousie Medical School. Her research focuses on developing a recombinant adenovirus-based mucosal vaccine against respiratory and genital chlamydial infection, which has also lead to investigation of the interleukin-17 (IL-17) pathway, a mechanism that protects us from bacteria like Chlamydia and also plays a role in the development of cancer. Dr. Wang is also working on translating basic knowledge into the discovery of human-compatible immune adjuvants and the development of robust immunoassays for evaluating new vaccines in animal models and eventually in human clinical trials.
Examples of Refereed Publications of Vaccine-Related Research by CCfV Members 2012


**Huzair F.** Commentary: The influenza vaccine innovation system and lessons for PDPs. Human Vaccines & Immunotherapeutics 8:3, 1–4; March 2012


MacDonald NE, Rosenfield D, Flegel K, Stanbrook MB. Waging war against rotavirus at home and abroad. CMAJ 2012;184(9): 1011


Meir-Stephenson V, Slayter K. Reducing the Risk of Infection in a patient who will undergo splenectomy. CMAJ. Published ahead of print August 13, 2012 cmaj.ca/content/184/9/1053.full/reply#cmaj_el_712652.


Scholastic A, Kyomuhangi T, Santorino D, MacDonald N, LeBlanc J. Healthy Child Uganda survey of knowledge , attitudes and behaviours of village health team members toward their health care responsibilities in southwest Uganda. Paediatr Child Health 2012;17: e89


Full & Associate CCfV Members

- Acosta Remirez, Elizabeth
- Adongo, Louise
- Allen, Victoria
- Anderson, Robert
- Andrew, Melissa
- Baylis, Francoise
- Bentley, James
- Bortolussi, Bob
- Butler, Gillian
- Coombs, Ann
- de Antueno, Roberto
- Dodds, Linda
- Doroshenko, Alexander
- Downie, Jocelyn
- Dummer, Trevor
- Duncan, Roy
- Graham, Janice
- Haase, David
- Halperin, Beth
- Halperin, Scott
- Hatchette, Todd
- Herder, Matthew
- Holmes, Elaine
- Huang, Yan Yan
- Isenor, Jennifer
- Kaposy, Chris
- Khaperskyy, Denys
- Langley, Joanne
- LeBlanc, Jason
- Lee, Song
- MacDonald, Noni
- MacDougall, Donna
- MacQuarrie, Robyn
- Mailman, Tim
- Mansour, Marc
- McAlpine, Sarah
- McCormick, Craig
- McGill, Kim
- McGrath, Pat
- McNeil, Shelly
- Melnychuk, Ryan
- Mombourquette, Dee
- O’Keefe, Cathy
- Oliver, Gertrude
- Richardson, Chris
- Sanou, Aboubakary
- Sarwal, Shelly
- Scott, Jeff
- Skedgel, Chris
- Slaunwhite, Jason
- Slayter, Kathryn
- Smith, Bruce
- Smith, Jennifer
- Smith, Steven
- Sommers, Ryan
- Stanford, Marianne
- Steenbeek, Audrey
- Strang, Robert
- Sweet, Lamont
- Top, Karina
- Ulanova, Marina
- Wang, Jun
- Ward, Courtney
- Watson-Creed, Gaynor
- Whelan, Noella
- Wisner, Amanda
- Wranik, Dominka
- Zhang, Qingli
The Clinical Research Unit (CRU) is a 5,400-square-foot, state-of-the-art inpatient and outpatient research facility.

The Clinical Research Unit (CRU) is CCfV’s 5,400 sq. ft., state-of-the-art inpatient and outpatient facility for research. Located in the IWK Health Centre in Halifax, the 10-bed unit can host any study that requires a secure, comfortable, well-equipped facility where research participants can stay for hours, days, or weeks. It adds significant capability to research efforts in the Atlantic Region.

Clinical Research / Vaccine Challenge Unit

Facility Features

- 10 single isolation rooms, each with: monitoring and diagnostic equipment, HEPA-filtered exhaust air, negative pressure to contain pathogens, TV, wireless Internet, telephone, mini fridge
- central monitoring at nurses’ station
- procedure/examination room
- meeting room
- controlled access to the unit
- secure lockers
- outside deck for ambulatory patients