



Research finding solutions to *HIV/AIDS*



Research finding solutions to *HIV/AIDS*



Canadian Institutes of Health Research
160 Elgin Street, Rm 97 • Address Locator: 4809A
Ottawa, Ontario K1A 0W9 • www.cihr-irsc.gc.ca/iii.html

HIV/AIDS Research:



Dr. Bhagirath Singh, Scientific Director, CIHR Institute of Infection and Immunity

More than 20 years after the first case of HIV/AIDS was diagnosed, the disease remains a significant global health threat. Since that initial diagnosis, an estimated 25 million people of all ages, races, genders and economic status have died of AIDS. Around the world, almost 40 million people are living with HIV. The statistics are discouraging, but those infected, their families and their communities continue to live in hope - hope for better ways to prevent the disease, hope for better and more affordable treatments and hope for a world that does not discriminate against those living with HIV/AIDS. Most of all, they hope, one day, to eradicate this devastating disease.

Their hope is shared by the health research community in Canada. Dedicated researchers are exploring the possibilities that will help make headway in protecting people at risk, improving the quality of life of those living with HIV/AIDS and reducing the impact of the disease on individuals and communities. Eradication remains the ultimate goal on which we are all focused.

The Canadian Institutes of Health Research (CIHR), as a key partner in the Government of Canada's Federal Initiative to Address HIV/AIDS in Canada (FI-HIV/AIDS), is providing leadership in the area of research. Supported by funds from both the FI-HIV/AIDS and CIHR, HIV/AIDS research is in a unique position within the health research sector in Canada, with federal investments that will continue to grow over the next 3

Transforming hope to reality

years. CIHR and the research community are committed to contributing significantly to the improved health of Canadians, particularly people living with HIV/AIDS, and to preventing its spread.

With leadership from the CIHR HIV/AIDS Research Advisory Committee (CHARAC) and input from other stakeholders, we are able to set priorities for HIV/AIDS research, so that we can capitalize on the greatest opportunities and respond to the greatest needs. Our new HIV/AIDS Community-Based Research (CBR) Program brings the voices of those affected most by HIV/AIDS to the table and fosters research and partnerships that meet the needs of affected communities.

Research has helped to transform HIV from a certain death sentence to a manageable chronic disease. With help from stakeholders and researchers, CIHR anticipates the day when research on treatments and prevention will transform our hopes of eradicating HIV/AIDS into a tangible reality.



Bhagirath Singh

Dr. Bhagirath Singh

Scientific Director

CIHR Institute of Infection and Immunity

CIHR at a glance

Founded in 2000, the Canadian Institutes of Health Research (CIHR) is Canada's response to the global revolution in health research. CIHR's mandate is to create new knowledge - and translate that knowledge into improved health, a strengthened health care system and new health products and services for Canadians.

CIHR takes a problem-based, multidisciplinary approach to the health challenges facing Canadians. Its inclusive approach brings together researchers from all disciplines, from the social sciences to biomedical sciences, informatics and engineering.

By building partnerships, national and international, CIHR brings new perspectives to health and ensures that research findings are applied where they are needed.

The majority of CIHR funding goes toward supporting investigator-initiated research. A portion, however, goes toward health issues of strategic importance, including HIV/AIDS. CIHR, in addition to devoting a proportion of its own funding to HIV/AIDS research, also administers the research portion of the Federal Initiative to Address HIV/AIDS in Canada. The CIHR Institute of Infection and Immunity leads CIHR's work in this area.



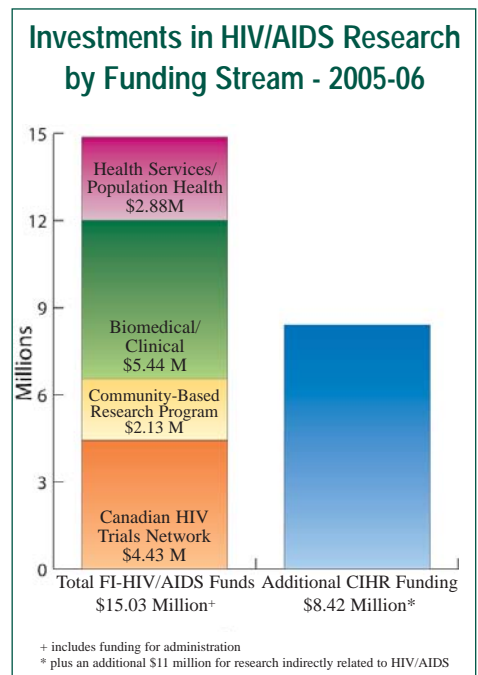
CIHR IRSC
Canadian Institutes of Health Research Instituts de recherche en santé du Canada

CIHR HIV/AIDS Research Initiative

Over the past 20 years, the Government of Canada has made significant commitments to the fight against HIV/AIDS in Canada and globally. The Federal Initiative to Address HIV/AIDS in Canada (FI-HIV/AIDS) is a renewed federal response to HIV/AIDS that encompasses a wide range of programs, from prevention, to care and treatment, to research. Funding for FI-HIV/AIDS is increasing substantially, from \$42.2 million in 2003-04, to \$84.4 million by 2008-09.

About a quarter of FI-HIV/AIDS funding is committed to research, with this funding administered by CIHR. This funding is increasing significantly, from \$10.3 million in 2003-04 to \$22.6 million in 2008-09. This funding is permitting Canadian researchers to continue to build on their strong track record of achievement, including developing one of the first antiretroviral drugs, AZT; leading the search for a vaccine based on natural resistance among some populations; and taking a population health approach to preventing HIV infections, particularly among marginalized populations such as Aboriginal peoples.

Funding from the FI-HIV/AIDS, together with the funding CIHR continues to commit out of its own budget to research in this area, resulted, in 2005-06, in the largest annual investments in HIV/AIDS research to date by CIHR and 259 grants and awards being supported.



Setting Directions for Research:

The CIHR HIV/AIDS Research Advisory Committee



*Dr. Chris Power,
Chair of CHARAC*

The CIHR HIV/AIDS Research Advisory Committee (CHARAC) is composed of researchers from across the full spectrum of health research, as well as representatives from five CIHR Institutes, community organizations, the Public Health Agency of Canada and the Ministerial Council on HIV/AIDS. The Committee, established in 2003, advises CIHR on HIV/AIDS research priorities and the development of strategic programs to meet these priorities.

The CIHR HIV/AIDS Research Initiative has sustained and built upon existing Canadian strengths in HIV/AIDS research. At the same time, it has focused efforts on building capacity for such research in areas where research capacity needed to be built, in particular, the areas of health services and population health, as evidenced by the launch of three strategic requests for applications targeting these areas of research.



*2005 CIHR HIV/AIDS Research Advisory
Committee*

(Top Row) From Left to Right: Anita Rachlis, Liviana Calzavara, Catherine Hankins, Sean Hosein, Donald Weaver, Nina Arron

(Bottom Row) From Left to Right: Robb Travers, Aslam Anis, Chris Power, Bhagirath Singh, Jonathan Angel

Missing: Earl Nowgesic, Martin Schechter, Mark Wainberg

To guide future investments, CHARAC, in consultation with HIV/AIDS stakeholders and researchers, has identified seven key areas to be addressed through strategic means such as targeted requests for applications. They are:



Recent funding opportunities have encouraged the development or enhancement of teams of researchers who take unique approaches to addressing research issues in these priority areas. To help further develop the research agenda in priority areas, CIHR and CHARAC have established working groups that ensure a wide range of partners and expertise are involved in this process.

A unique Canadian contribution: The Canadian HIV Trials Network

Clinical trials are a vital step in "putting our ideas to work" in preventing and treating HIV/AIDS and improving the quality of life of those infected with the virus. Setting up scientifically sound and ethical clinical trials, however, can be a challenge. Established in 1990 as a cornerstone of the federal AIDS strategy (the precursor to FI-HIV/AIDS), the Canadian HIV Trials Network (CTN) is an innovative partnership of clinical investigators, physicians, nurses, people living with HIV/AIDS, pharmaceutical manufacturers and others that facilitates important clinical trials of the highest scientific and ethical standards. This flexible and responsive network fosters trial development and provides an established infrastructure for quick implementation of trials. The network also has access to a wide pool of patients to aid recruitment into studies. Its existence makes Canada an ideal place to conduct pivotal trials.

As of April 2005, the CTN had:

- Reviewed 208 trial protocols
- Implemented 89 clinical trials involving 8,448 volunteers at sites across Canada
- Contributed to advances in HIV clinical care
- Enrolled another 11,000 Canadians in CTN expanded (compassionate) access trials.

Reaching out globally

HIV/AIDS has become overwhelmingly a disease of the developing world. In 2004, more than 95% of new HIV infections were in developing countries and more than half of the newly infected were children. In some cases, solutions developed in rich countries can be adapted to lower and middle income countries (LMIC). In other cases, the unique situations that exist in these countries require research leading to new solutions.



Canadian researchers have a history of conducting pivotal HIV/AIDS research in LMIC countries that have been hit hard by the epidemic. Carrying out research projects specifically designed for these countries enables a deeper understanding of the epidemic and permits the more rapid translation of the benefits of HIV/AIDS research to people in these highly affected countries.



The creation of the Global Health Research Initiative (GHRI), a partnership between CIHR, the Canadian International Development Agency (CIDA), the International Development Research Centre (IDRC) and Health Canada, has strengthened Canada's involvement and investment in global health research.

Since its inception, the GHRI, in partnership with the HIV/AIDS Research Initiative, has funded 13 health research projects intended to build partnerships among Canadian-LMIC health research teams to address global health issues.

The research is helping to develop local solutions to local problems while building research capacity in these countries to continue the fight against HIV/AIDS. Examples of funded projects include:

<i>An HIV/AIDS prevention program for young women in Southern India</i>	
<i>Caring for people with HIV/AIDS in Latin America in the age of antiretro-viral drug therapy</i>	
	<i>Transforming violent gender relations to reduce the risk of HIV/AIDS among South African women and girls</i>
	<i>Behavioural approaches to preventing HIV/AIDS in Sub-Saharan Africa</i>

The GHRI will continue to build global research partnerships and support research and its effective use that will improve the health of communities around the world through the Teasdale-Corti Global Health Research Partnership Program, a collaborative initiative of the four founding partners of the GHRI that aims to foster partnerships and collaboration, build research capacity and encourage interactions among researchers and research users. Eight of the 32 research teams invited to submit full proposals to the Teasdale-Corti Program have projects focused on HIV/AIDS.



Community-based research: Where HIV/AIDS hits home


Community involvement has been a hallmark of health research and action on HIV/AIDS from the beginning of the epidemic. Communities continue to play a central role in HIV/AIDS research, creating a model for communities taking action on other diseases and conditions.

The HIV/AIDS Community-Based Research (CBR) Program was created to assist community-based organizations, non-governmental organizations and institutions in developing the knowledge necessary to carry out their HIV/AIDS work in the most effective manner and to help create the expertise within these communities to conduct their own research. The program is offered in two streams - Aboriginal and General. Through the HIV/AIDS CBR Program, CIHR is supporting research that engages communities in all stages of research, from the definition of the research question to ensure relevance to the community, to capacity building and integration of community members in conducting research, to promoting its active participation in the development and implementation of the dissemination strategy.



The CIHR HIV/AIDS Community-Based Research Program currently supports 24 research and capacity-building projects and 10 trainees.



Projects in the Aboriginal stream have focused on:

<i>Aboriginal cultural competence for HIV/AIDS health care providers</i>		
<i>Obstacles to access antiretroviral therapy for Aboriginal people living in urban areas</i>		
<i>Sexual violence, HIV/AIDS and Aboriginal women</i>		
<i>Analysing the implementation of the Chiyikiyaa program for the prevention of HIV and sexual health promotion of students in the Terres-Cris-de-la-Baie-James (Eeyou Istchee) communities</i>		
<i>Two-Spirit Women's experience of homophobia in the context of HIV/AIDS provision</i>		

In the General stream, projects have focused on:

<i>Developing rural HIV/AIDS information networks</i>	
<i>The impact of housing support and homelessness on the health outcomes of people living with HIV/AIDS in Ontario</i>	
<i>HIV prevention, intervention and care among sex workers and their partners</i>	
<i>Engaging people from HIV endemic countries (Nigeria, Sudan and South Africa)</i>	
	<i>Who are the black men who have sex with other men in Toronto?</i>
	<i>The impact of complementary and alternative medicine in the quality of life and rehabilitation of persons living with HIV/AIDS</i>
	<i>Understanding the role of basic needs and addiction treatment readiness on HIV prevention among needle exchange clients</i>

Building research capacity in communities: Research Technical Assistants

Involving community-based organizations in HIV/AIDS research is one of the central goals of the HIV/AIDS CBR Program. The challenge is that many community-based organizations, already stretched by trying to deliver their primary mandate with limited resources, may not have the capacity to participate in research.

CIHR, through the HIV/AIDS CBR Program, provides funding for Research Technical Assistants (RTAs) to help develop and enhance the HIV/AIDS community-based research capacity among community organizations. RTAs work collaboratively with organizations within defined geographic areas to identify, plan and deliver a wide range of capacity-building initiatives. Grants to support RTAs are offered both within the Aboriginal and general streams.

RTAs can take on a wide range of activities that can include, but are not limited to, assisting AIDS Service Organizations to build research skills, develop research proposals and protocols, establish linkages with academic research partners and develop individualized work plans.

CIHR Investments in HIV/AIDS Research are Paying Off:

Since its creation in 2000, CIHR has spearheaded Canada's national research efforts to fight HIV/AIDS. CIHR-funded researchers have made important advances in a wide variety of areas.

Biomedical Research

- The emergence of drug-resistant variants of HIV has limited the options available for successfully treating AIDS. McGill University's Dr. Mark Wainberg and his team have made important contributions to the study of antiviral drug development and HIV drug resistance. In 1989, Dr. Wainberg, in collaboration with BioChem Pharma Inc. made the initial identification of 3TC as an anti-viral drug. He continues to work in the area of drug resistance and the identification of novel targets in the viral life cycle for drug development, while also focusing on the development of microbicides and preventive vaccines.



Dr. Michel Tremblay,
Université Laval

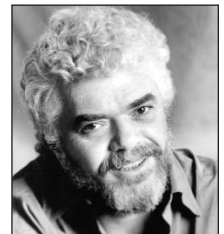
- Dr. Michel Tremblay of *Université Laval* is also focusing on resistance to antiretroviral drugs and new ways to circumvent this resistance. He has found evidence that treatment with statins, cholesterol-lowering drugs, can decrease HIV replication and attachment to target cells. The ability of statins to limit the initial steps in virus replication provides a new approach for treating HIV-1 infection.

Six years of research advances against HIV/AIDS

- Researchers at Toronto's Hospital for Sick Children, University of Toronto, led by Dr. Clifford Lingwood, have found a novel molecule that prevents many types of HIV from infecting different kinds of cells by binding to the virus and preventing it from fusing with the host cell. Therapies using this molecule would employ a different mechanism than most current anti-HIV treatments and even drug-resistant strains of HIV are susceptible. The molecule is soluble, making it particularly promising for use in a topical microbicide that women can apply before intercourse to prevent transmission of the virus.
- CIHR-funded researchers, Dr. Louis de Repentigny from the *Université de Montréal* and Dr. Paul Jolicoeur from the *Institut de recherches cliniques de Montréal*, have identified defects in immune cells that give rise to a fungal infection commonly found in HIV patients called candidiasis. The infection can limit food consumption, leading to weight loss, which threatens patients general health and well being. The infection is often resistant to conventional anti-fungal treatments. The new knowledge will help in the development of more powerful and effective treatments for the fungal infection.

Vaccine Development

- Vaccine development is the ultimate and challenging goal of much HIV/AIDS research. Dr. Francis Plummer and his team at the National Microbiology Laboratory are helping to move a step closer to achieving this goal with their work on people who are resistant to HIV infection. They have discovered that cytotoxic T cells (CTL) that are reactive to HIV are present in both the blood



**Dr. Francis
Plummer,**
*National Microbiology
Laboratory*

Vaccine Development (cont'd...)

and genital mucosa of resistant women, supporting the belief that a mucosal-based vaccine is the best hope. They have also discovered that CTL can be elicited by single or infrequent exposures to HIV, suggesting that a single — or low-dose vaccine that elicits CTL responses may be possible. In 2005, Dr. Plummer received a grant from the Bill and Melinda Gates Foundation Grand Challenges in Global Health Initiative, co-funded by CIHR, to continue his work on natural resistance to HIV.

- Working with the same group of HIV-resistant female commercial sex workers in Nairobi, Dr. Keith Fowke of the University of Manitoba was part of a team that has found that women who are resistant to HIV respond differently to a peptide called p24, which could result in their CD4 T cells living longer and functioning differently than in HIV-positive women. The immune environment and the p24-specific immune responses of HIV-resistant women should be considered in the design and development of an effective HIV vaccine.
- Dr. Mario Ostrowski at the University of Toronto is using state-of-the-art techniques in immunology and virology to design a new, improved version of an HIV vaccine made from the canarypox virus. While the current vaccine has been shown to be safe in humans, it does not create strong immune responses. If the new vaccine developed by Dr. Ostrowski is shown to be more effective in mice and monkeys, it will move on to clinical testing in humans.
- A team led by Dr. Jonathan Angel of the Ottawa Health Research Institute is conducting the first Canadian-led controlled trial of a therapeutic HIV vaccine, that is, a vaccine which is intended to treat those already infected. The trial combines two products, both of which have been shown



Dr. Jonathan Angel and his team
Ottawa Health Research Institute

in separate tests to induce different aspects of the immune response. The trial is seeking to determine whether the two work effectively together and at what dosages.

Clinical Research

- A study led by Drs. Sharon Walmsley of the University Health Network and Sylvie Trottier of *Université Laval* has found that both nelfinavir and zidovudine as part of highly active antiretroviral therapy (HAART) result in a substantial decline in disease progression. However, nelfinavir is better tolerated than zidovudine.
- AIDS-related dementia affects 20 per cent of people with AIDS and usually begins seven-to-ten years into the disease — meaning that, as survival rates increase, more and more patients will experience the dementia. A drug being tested for use in cancer is showing promise for halting AIDS-related dementia, according to a study by Dr. Chris Power of the University of Alberta.
- A strong sense of self-efficacy and a positive attitude toward taking medication were the most significant predictors of adherence to antiretroviral therapy, according to a study out of *Université Laval*. Led by Dr. Gaston Godin of the Research Group on Behaviours in the Field of Health, the study also found that not living alone and being a male were other predictors of success, but suggested that interventions aimed at improving adherence to the therapy focus on the first two predictors.



Dr. Gaston Godin,
Université Laval

Health Systems and Services

- A team at the University of Toronto, led by Drs. Peter Newman and Charmaine Williams, is studying ways to ensure Black women are explicitly included in strategies to disseminate HIV vaccines that may become available in the next decade. This research aims to change the trend of Black women being left out of research that could help decrease their vulnerability to infection and disease, and being one of the last groups to benefit from health care innovations.



***Dr. Josie Geller and
her team***

*BC Centre for Excellence in
HIV/AIDS*

- Dr. Josie Geller and her team at the BC Centre for Excellence in HIV/AIDS have developed a tool to measure patients' readiness to adhere to Highly Active Antiretroviral Therapy (HAART). The Antiretroviral Readiness and Motivation Scale (ARMS) could allow physicians and other caregivers to better predict which patients will adjust quickly to HAART and take steps to help those who will face more challenges in adhering to the regimen.

Population and Prevention

- The Polaris HIV Seroconversion Study, led by Dr. Liviana Calzavara of the University of Toronto, has found that people at risk of HIV become less worried about it the longer they test negative, believing the high-risk behaviour they engage in is safe. The results underscore the need for enhanced counselling for those who repeatedly test negative for the virus and continue to engage in high-risk behaviour.

- Aboriginal injection drug users in Vancouver are becoming infected with HIV at twice the rate of non-Aboriginal injection drug users, according to research by Dr. Patricia Spittal of the BC Centre for Excellence in HIV/AIDS. Her team's findings emphasize the importance of a public health strategy planned and implemented in partnership with the Aboriginal community to reduce the harms of injection drug use among its members.



Dr. Patricia Spittal,
*BC Centre for
Excellence in
HIV/AIDS*

- A study involving adolescents in juvenile rehabilitation centres, conducted by Dr. Gaston Godin of *Université Laval*, increased the intention of adolescents to use condoms with a new partner and their ability to surmount obstacles to their use, including lack of availability, consumption of alcohol or drugs, shyness, and the partner refusing to use the condoms. Adolescents in juvenile rehabilitation centres appear to be more vulnerable to STD and HIV transmission than other teenagers. The study focused on an intervention that included explicit information about unsafe and safer sexual practices, as well as communication and negotiation skills developed through activities such as role playing and improvisation.

International

- New HIV infections in the worst-hit regions of India have declined by a third, according to a partnership between University of Toronto researcher Dr. Prabhat Jha and Indian researchers funded, in part, by CIHR. The research indicates that condom use and awareness programs can have a significant impact. The study tracked HIV prevalence among young women attending pregnancy or antenatal clinics in India's southern and northern states. Disease transmission in India is mostly due to male use of female sex workers, which puts their wives in a vulnerable position.
- *Université Laval's* Dr. Michel G. Bergeron and his team have developed a microbicide called the Invisible Condom® (IC) that could prevent STDs and HIV/AIDS. In a Phase I clinical trial involving 47 women and 23 men in Québec, the IC was shown to be well tolerated. With current support from CIHR, they are now testing its safety and acceptability in a Phase I/II clinical trial involving 452 healthy African women in Cameroon. A final Phase III effectiveness trial is being planned, involving nearly 5,000 women at high risk of acquiring HIV infection. If the IC is proven effective, it has the potential to empower women and help them control their own sexual destiny while preventing millions of cases of HIV/AIDS and other STDs.



*Dr. Michel
Bergeron,
Université Laval*