



Health Minister Dr. Margaret MacDiarmid poses with Dr. Julio Montaner, director of the BC Centre for Excellence in HIV/AIDS, at the B.C. government's announcement to expand the STOP HIV/AIDS pilot program across the province to help B.C. come closer to achieving an AIDS-free generation.

## B.C. government announces provincial expansion of landmark STOP HIV/AIDS pilot program

Health Minister Margaret MacDiarmid committed annual funding of 19.9 million to health authorities to help fulfill the Province's vision for an AIDS-free generation

On the eve of World AIDS Day and almost 25 years after being diagnosed with HIV, B.C. resident Walter Hiebert attended the announcement to express his gratitude for receiving timely treatment that saved his life.

Since 2009, Seek and Treat for Optimal Prevention of HIV/AIDS (STOP HIV/AIDS) has been implemented in Vancouver and Prince George, and has been successful in dramatically reducing HIV transmission by ensuring HIV-positive individuals have access to the best possible care and treatment.

At a news conference on November 30 at St. Paul's Hospital, Health Minister Margaret MacDiarmid and Minister of State for Seniors Ralph Sultan joined BC Centre for Excellence in HIV/AIDS' (BC-CfE) director Dr. Julio Montaner to announce the expansion of the pilot program across B.C.

"An AIDS-free generation is now in our sights," said Minister MacDiarmid. "I am pleased to announce the provincial expansion of the STOP HIV/AIDS program. By reaching and engaging more British Columbians at-risk for or living with HIV/AIDS, not only will better care be provided, the treatment will also significantly reduce the spread of the virus."

Beginning April 1, 2013, the STOP HIV/AIDS program will allow health professionals and community partners to better engage the broader community

and specific at-risk groups in HIV testing, reach more people with HIV/AIDS, and enable more British Columbians to be treated.

Expansion will be carried out by the province's health authorities with support and leadership from the BC-CfE, which pioneered the concept of Treatment as Prevention under Dr. Montaner's guidance. The BC-CfE will also continue to monitor and evaluate the progress of the program.

Dr. Montaner thanked the B.C. government for their ongoing support of this program to eliminate HIV/AIDS in the province. "B.C. is years ahead of the rest of the world in treating HIV/AIDS," said Dr. Montaner at the news conference. "We have a revolutionary new development in health care, right here. The results we have achieved are quite compelling, and the world is beginning to move [towards our approach]. The times are right."

B.C. is leading the way in its efforts to combat the epidemic. BC-CfE researchers recently published a new study, which found that B.C. is the only province in Canada showing a consistent decline in

new HIV diagnoses, in part due to the widespread availability of free antiretroviral treatment in the province. The study found that new HIV diagnoses in B.C. have dropped from 900 new cases each year in the mid-1990s, to 289 new cases in 2011.

B.C. resident Walter Hiebert can attest to the benefits of treatment. He was diagnosed in 1988 – a time when an HIV diagnosis amounted to a death sentence. In the mid-1990s he was put on highly active antiretroviral therapy (HAART) by Dr. Montaner. He spoke in support of the government's announcement at the news conference. "I watched a lot of friends die. If it wasn't for Dr. Montaner, I wouldn't be alive today. We live in a province that believes in evidence-based science," an emotional Hiebert told the audience.

The initial four-year, \$48-million STOP HIV/AIDS pilot has allowed health professionals in the pilot areas to identify more people who have HIV/AIDS and enabled more people to be treated with HAART. In contrast, in non-pilot health authorities, there has been an overall decline in the number of people being diagnosed with HIV and the number of people accessing treatment.



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– Walter Hiebert, a B.C. resident who was diagnosed with HIV in 1988 and spoke in support of the funding announcement at the news conference

» See full story above



# Next-generation sequencing provides new insights into HIV

Researchers at the BC Centre for Excellence in HIV/AIDS (BC-CfE) are developing innovative applications of next-generation sequencing technology to obtain new insights into HIV that could have implications for how patients are treated and protected from the virus.

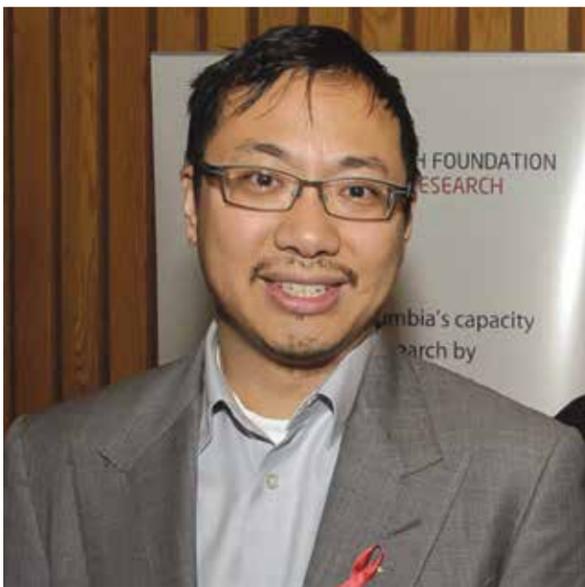
Next-generation sequencing works by using state-of-the-art instruments that automatically carry out millions of sequencing reactions for individual strands of DNA, producing massive amounts of genome data in an incredibly short period of time. This emerging technology is becoming an essential tool in the study of rapidly evolving populations of viruses and cancerous cells.

In a study published last month in the journal *PLOS Computational Biology*, researchers from the Laboratory Program at the BC-CfE, including lead author Art Poon, in collaboration with investigators at the University of Amsterdam, applied next-generation sequencing technology to reconstruct how HIV evolves within a single patient.

Specifically, the researchers looked at a key event in HIV disease progression known as the HIV co-receptor switch. In most HIV infections, the virus initially tends to bind to a co-receptor known as CCR5 in order to enter a cell. In many cases, the virus will spontaneously switch to binding another co-receptor known as CXCR4. This event is associated with a greater rate of disease progression.

In order to gain an understanding of the causes of this HIV co-receptor switch, the evolutionary histories of HIV within eight patients known to have undergone an HIV co-receptor switch were reconstructed using new computational techniques. Each history was recreated from samples of HIV genetic sequences that were derived from repeated blood samples by next-generation sequencing. With samples from different points in time, models of evolution were used to extrapolate back in time to ancestral viruses of each infection. This analysis revealed patient-specific dynamics in HIV evolution that shed new light on the determinants of the co-receptor switch.

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as the BC-CfE-pioneered Treatment as Prevention model," said Dr. Poon.

Applications of next-generation sequencing to dating the age of HIV infections were first put into practice by BC-CfE researchers in a study described last year in the journal *AIDS*. They developed a new technique which reconstructs the evolutionary "family tree" (called a phylogeny) relating hundreds of HIV sequences that were extracted from that patient's blood samples. The collection dates of these blood samples were then used to estimate the date of the earliest ancestral virus or "root" of the phylogeny. As a result, researchers were able to accurately estimate dates of HIV infection for patients by using genetic sequences of the virus.

The most recent applications of next-generation sequencing technology build upon these findings by providing HIV researchers with an unprecedented look at what the transmitted virus that established the infection looked like and how its descendants evolved within the patient.

## CMAJ editorial calls for routine HIV testing for all sexually-active Canadians

In a recent editorial in the *Canadian Medical Association Journal (CMAJ)*, Dr. Julio Montaner, director of the BC Centre for Excellence in HIV/AIDS (BC-CfE), and his co-authors said routine HIV testing should be offered to the general population, rather than only to high-risk individuals, to save lives and prevent new infections.

"It is now evident that HIV testing, based only on perceived risk, misses multiple opportunities for earlier diagnosis," wrote the authors in the editorial. "Routine HIV testing, on the other hand, has been shown to be acceptable and highly cost-effective. It is therefore imperative to implement and evaluate routine HIV testing across Canada."

Since 1996, the gold standard treatment for HIV, highly active antiretroviral therapy (HAART), has been available and has expanded the lifespan of people with HIV to near normal, and also reduced HIV transmission by more than 95 per cent.

Although HAART is extremely effective and widely available in Canada, we are not making the most of its benefits. The authors point out that too many of those infected are diagnosed late, sometimes very late. The Public Health Agency of Canada estimates that at least 25 per cent of people with HIV are unaware of their infection. And more than 50 per cent receive the diagnosis after immunodeficiency has been established (which means the person is more sick and less likely to benefit from treatment).

The U.S. recommends routine screening in all health care settings for patients aged 13 to 64 years. Canada currently



Dr. Reka Gustafson

has no recommendation for routine testing outside of prenatal screening and screening of the blood supply.

The authors recommend that Canada offer routine testing to everyone who is sexually active, to reduce the substantial portion of the cases currently being missed. In Vancouver, several hospitals offer HIV testing upon hospital or emergency room admission. Research shows routine screening picks up six new positives for every 1,000 HIV tests; anything above one HIV-positive test per 1,000 is considered cost effective.

The CMAJ editorial was co-authored by Dr. Reka Gustafson, a medical health officer and medical director of communicable disease control at Vancouver Coastal Health and Barbara Sibbald, a CMAJ deputy editor.

## Adherence to HIV treatment guidelines critical for patient health and survival

When HIV-positive individuals strictly adhere to highly active antiretroviral therapy (HAART) guidelines during their first year on treatment, they have a significantly higher survival rate, as compared to those with suboptimal compliance to HAART, according to researchers at the BC Centre for Excellence in HIV/AIDS (BC-CfE).

The study, published recently in the peer-reviewed journal *PLOS ONE*, investigated 3,543 HIV-infected individuals who were more than 19 years old and had never previously been on HAART when they started treatment between January 1, 2000 and August 31, 2009. Participants were followed until their death due to any cause, or if alive, until the last contact date or August 31, 2010, whichever came first. At the end of the follow-up period from 2000 to 2010, 499 (14 per cent) participants died.

BC-CfE researchers developed a simple and highly predictive metric, the Programmatic Compliance Score (PCS), to predict survival among HIV-positive individuals starting HAART for the first time. The PCS was based on the BC-CfE therapeutic guidelines in effect at the time, which were generally consistent with the International AIDS Society-USA (IAS-USA) antiretroviral therapy management guidelines.

The PCS is composed of six non-performance indicators:

- Having fewer than three CD4 cell count (immunity affected by HIV) determinations in the first year of HAART
- Having fewer than three plasma viral load (viral replication) tests in the first year of starting HAART
- Not having drug resistance testing prior to starting treatment
- Starting on a non-recommended HAART regimen
- Starting therapy with a CD4 count less than 200 cells/mm<sup>3</sup>
- Not achieving HIV viral load suppression within six months of starting HAART

The sum of these six indicators was used to develop the PCS score, with zero indicating full compliance with guidelines and six indicating non-compliance. The study found that individuals with a PCS score of four or higher (i.e. poor compliance with treatment guidelines) were 22 times more likely to die than those with a PCS score of zero.

Researchers believe that the study results independently validate the IAS-USA HIV therapeutic guidelines and highlight the importance of adhering to treatment guidelines to optimally decrease morbidity and mortality and reduce new HIV infections (as a result of increased likelihood of viral load suppression in infected individuals).

"Our results indicate that we have a unique opportunity in B.C. to offer the best treatment to all HIV-positive individuals, since we have a fully subsidized medical system where HAART, medical, and laboratory monitoring are free of charge to all these individuals," wrote Dr. Viviane Lima, lead author of the study and senior statistician at the BC-CfE, in her blog article for the *BC Medical Journal*.

## BC Centre for Excellence in HIV/AIDS

- > Improve the health of British Columbians with HIV through comprehensive research and treatment programs;
- > Develop cost-effective research and therapeutic protocols;
- > Provide educational support programs to health-care professionals;
- > Monitor the impact of HIV/AIDS on B.C. and conduct analyses of the effectiveness of HIV-related programs.

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