

Extensive host immune adaptation in a concentrated North American HIV epidemic

The BC-CfE Laboratory Program advances our understanding of HIV and how it can best be treated. The cutting-edge facility, housed at St. Paul's Hospital, acts as hub for genome research, receiving blood samples from across BC, Canada (not including Quebec) and countries around the world. The BC-CfE Laboratory has provided HIV drug resistance genotyping for virtually all Canadian provinces and territories since 1998, as well as for many countries worldwide. The lab also provides clinical services, including in the critical area of HIV drug resistance testing, to ensure patients are receiving the most effective treatments. By analyzing anonymized genome sequences of the HIV virus, researchers can gain a better understanding of how HIV is being spread and identify HIV strains of particular public health concern (e.g. drug-resistant strains). The BC-CfE Lab is accredited by the College of American Pathologists, the Diagnostic Accreditation Program of the College of Physicians and Surgeons of British Columbia and the World Health Organization.

FACT BOX

This study—by the BC Centre for Excellence in HIV/AIDS (BC-CfE), Simon Fraser University (SFU) and the Public Health Agency of Canada (PHAC), as well as Saskatchewan physician-researchers—represents the first molecular epidemiologic analysis of HIV in the province of Saskatchewan. The study compared anonymized HIV sequences from Saskatchewan to those found elsewhere in the United States and Canada.

Background

- HIV incidence rates in the Canadian province of Saskatchewan are among the highest on the continent, with rates in some regions more than tenfold higher than the Canadian national average.
- Since 2003, a concentrated HIV epidemic has been expanding in the province. Injection drug use is considered a primary risk factor.
- Saskatchewan health care providers and physicians have been reporting accelerated HIV progression to AIDS-defining illnesses.
- The 2016 Saskatchewan *HIV Prevention and Control Report*, produced by the Government of Saskatchewan, estimated that fewer than 50% of persons diagnosed with HIV since 2007 remained alive in 2016.

What are the key study findings?

- HIV is adapting to commonly expressed HLA (human leukocyte antigen) alleles in Saskatchewan. HLA are markers that exist on the genes of chromosome 6 in humans and are involved in the body's immune system response.
- The mutations seen in HIV sequences in Saskatchewan are particularly suited to the HLA allele profiles of populations currently seeing the most HIV prevalence in Saskatchewan. Eighty per cent of persons living with HIV in the province have Indigenous ancestry.



- The HIV strains that are more adapted to host immune responses are being transmitted at increasing frequency. More than 98% of the HIV sequences collected in Saskatchewan most recently (between 2015 and 2016) harboured at least one major immune resistance mutation.
- A Saskatchewan resident with B*51 HLA expression, for example, has a more than 75% chance of being infected with an HIV strain that is likely to be inherently capable of evading their cellular immune responses to some extent.
- HIV sequences in Saskatchewan are highly clustered, indicating that certain HIV strains are being widely and frequently transmitted in the population: 77.6% of HIV sequences from Saskatchewan resided within 26 clusters, where the three largest comprised 40.6% of the data. In contrast, only about 15% of the sequences collected from other sites across Canada and the United States resided within clusters.
- The HIV sequences belonging to these large clusters harboured the highest levels of immune resistance mutations.

What do these findings mean?

- Just as the transmission of drug-resistant HIV compromises therapy efficacy, transmission of HIV strains harbouring a certain mutation can compromise host antiviral immunity.
- HIV sequences harbouring major HLA-adapted mutations are being transmitted in Saskatchewan more widely and more frequently than those not harbouring such mutations.
- It should be emphasized that HIV antiretroviral therapy remains fully effective against HIV with immune resistance mutations.
- HIV treatment should be accessed immediately for individuals living with HIV in order to curb rapid disease progression and prevent onward transmission. HIV treatment taken consistently and effectively can increase quality of life and longevity, with a person living with HIV on treatment having a life expectancy close to that of the general population.

Methods:

1,144 unique, anonymized HIV sequences were analyzed. These were collected between 2000 and 2016 and comprised about 65% of cumulative provincial HIV cases in Saskatchewan. These sequences were compared with those from elsewhere in Canada and the US.



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