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Volunteer Information Sheet for Jones *et al*., Phylogenetic approach to recover integration dates of latent HIV sequences within-host. *PNAS.* September 2018

Volunteer donation of blood, generously provided by anonymous volunteers, allowed us to examine ways to better treat and possibly cure HIV. These study results were published in the journal of *PNAS* in September of 2018.

The HIV reservoir is primarily comprised of infected CD4+ T-cells that harbor a "dormant" copy of HIV within them. These latently HIV-infected cells can persist in this dormant state for years, but can be activated at any time to produce infectious HIV. Current treatments for HIV effectively block viral replication but do not target the latent HIV reservoir, and it is for this reason that current HIV treatment needs to be maintained for life. Here, we report a new method to study the dynamics and genetic composition of latent HIV sequences. This method uses information regarding the evolution of HIV within the individual study participant, from before they went on treatment. The paper describes the development and validation of this method using computer- simulated and previously published HIV sequence data, and then describes its application to HIV sequence datasets from two participants who agreed to participate in this study.

1) What was the goal of our study?

The goal of this study was to develop a method that uses information on the evolution of HIV within an individual as a tool to better understand the dynamics of the latent reservoir.

2) How is this study related to a cure for HIV?

A major obstacle to an HIV cure is that the virus integrates itself into the human genome, where it can persist latently for decades before producing infectious HIV. It is unclear whether latent HIV sequences accumulate continuously in the body and whether these persist indefinitely. If so, an individual's HIV reservoir should consist of HIV sequences that integrated at different time points throughout their course of infection, even after many years on suppressive therapy. Our method was designed to answer this and other fundamental questions regarding the genetic composition of the latent HIV reservoir. We envision that the results of using our methodology may be useful in developing HIV cure strategies.

3) Why are participant samples important to this research?

Without participant samples, we would have been restricted to computer simulation (which may not reflect reality) and published datasets (which are limited in number). These insights into the composition of the latent HIV reservoir would not have been possible without the generosity of study participants.

4) What was learned? What next?

We applied our methodology to two participants who had initiated treatment more than 5 years following their HIV diagnosis, and who subsequently had maintained viral suppression on therapy for approximately a decade. In both participants we found that the HIV sequences within their latent reservoirs had been seeded throughout the course of the infection and had persisted to the present day. In one participant, we isolated latent virus strains more than 20 years old. Our next steps include using this method to compare the composition of the latent reservoir in larger numbers of participants with different clinical histories. We also hope to compare latent HIV sequences in different types of immune cells and/or locations in the body, as well as to investigate whether the specific site of HIV integration into the human genome influences a given latent HIV sequence's longevity. We also intend to expand our methodology to use deep sequencing data.

For more information about this study, please contact Dr. Zabrina Brumme (zbrumme@sfu.ca).