Phylogenetic Method of Identifying HIV-1 Transmission Foci in British Columbia

Angela McLaughlin¹,², P. Richard Harrigan³, Jean Shoveller¹,², Jeffrey Joy¹,³

¹ British Columbia Centre for Excellence in HIV/AIDS, St. Paul's Hospital, ² School of Population and Public Health, University of British Columbia, ³ Department of Medicine, University of British Columbia

**Background**

- Identifying areas that are at a high risk for ongoing HIV transmission is critical for prioritization of limited public health resources to support people living with HIV and prevent new cases.
- Despite advancements in testing and treating, foci of high transmission remain, even in developed countries.
- Since transmission of HIV to a new host is equivalent to the formation of a new lineage, diversification rates inferred from viral phylogenetic trees can serve as estimates for transmission rates.
- By combining patients' diversification rates, viral load measurements, and geographic data, we built a predictive model to identify areas with high HIV-1 incidence that are expected to experience ongoing transmission.

**Methods**

We applied this method to 1,685 HIV-1 sequences from 1,188 anonymized patients living in British Columbia, Canada between 2008 and 2013. The data were split into three 2-year time intervals in order to build three approximate maximum likelihood phylogenetic trees using FastTree2.1 from which the diversification rates were calculated (Figure 2). The diversification rate (DR) for each tip is the reciprocal sum of its branch lengths from root to tip, weighted by the distance of the branch from the root. To maintain patient confidentiality, census tracts were merged with proximate census tracts until no fewer than five patients resided in that polygon in any time interval for a final 57 merged census tract polygons. Longitudinal summary statistics were generated for merged census tracts of patient residence. HIV incidence in each merged census tract was estimated using the date of patients' first detectable viral load measurement. Mean age, proportion male, and other risk factors were also estimated for each merged census tract. A predictive multiple linear regression model was trained using data from the 2008-2009 time interval. The model was then tested on the subsequent time intervals (2010-2011, 2012-2013) by comparing each merged census tract's predicted HIV incidence rank with its observed HIV incidence rank. Ethical approval for this study was granted by the Providence Health Care/University of British Columbia Research Ethics Board.

**Results**

Figure 3. A predictive spatial regression model was fit using log10(diversification rate), and log10(viral load) to predict cumulative HIV incidence. The 2008-2009 time interval was used to train the model and then the data was tested on the subsequent time intervals (2010-2011, 2012-2013). The predicted rank, where 1 is the highest incidence in the time interval, was compared to the observed rank for each merged census tract's cumulative incidence. The predictive fit was evaluated for each time interval separately: R² = 0.64 for 2008-2009, R²=0.62 for 2008-2009, and R²=0.80 for 2012-2013.

**Conclusions**

- Areas that are home to people living with HIV who have simultaneously high viral load and HIV transmission rates, as measured by phylogenetic diversification rate, have high cumulative HIV incidence.
- By aggregating data by patients' census tract of residence, studies of the temporal and spatial distribution of phylogenetic and clinical traits of HIV can identify areas at risk of ongoing transmission.
- Phylogenetic data can complement traditional epidemiological data by providing insight into temporally-informed between-host evolution.
- Foci of high HIV-1 transmission remain active in developed countries that approach the 90-90-90 target.

**Acknowledgments and Financial Disclosure**

Thank you to the BC Centre for Excellence in HIV/AIDS at St. Paul's Hospital for coordinating the Drug Treatment Program and to the participants in the program for participating in HIV research in British Columbia. Angela McLaughlin has received funding through the BC Centre for Excellence in HIV/AIDS, Canadian Health (CIHR), and the University of British Columbia Faculty of Medicine. The authors have no conflicts of interest to disclose.