Phylogenetic and Geographic Separation in HIV Infected People in British Columbia

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Introduction

Disease surveillance has traditionally employed space-time clustering methods to detect outbreaks. Genetic clustering is a comparatively new approach that has an unknown overlap with these surveillance methods.

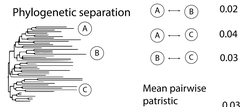
Here, we examine the relationship between genetic and geographic separation of people with HIV in British Columbia, Canada. Specifically, we examined:

1) The geographic separation among people in phylogeneticaly defined clusters.
2) How phylogenetic and geographic separation changes within phylogenetic clusters over time.
3) The relationship between geographic and phylogenetic separation among newly diagnosed individuals.

Methods

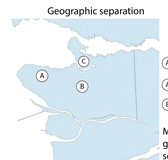
The BC phylogenetic monitoring program uses anonymized genotypes from the BC drug treatment program. At the time of this study, sequences from 9091 individuals, representing ~2/3 of the British Columbia incidence, were included.

Phylogenetic clusters are assembled from groups of 5 or more individuals based on pairwise tip-to-tip distances between sequences in a phylogenetic tree. We used a cut-off tip-to-tip distance of 0.02 expected nucleotide substituions per site.



A ⟷ B	0.02
A ⟷ C	0.04
B ⟷ C	0.03
Mean pairwise patristic separation	0.03

Geographic location of individuals was assigned to the Forward Sortation Area (FSA) of the treating physician. Genetic (above) and geographic (below) dispersion of a cluster was estimated by calculating the mean pairwise separation of each unique pair of individuals within a cluster.

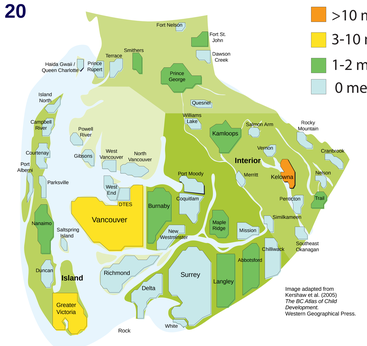


A ⟷ B	5 km
A ⟷ C	15 km
B ⟷ C	10 km
Mean pairwise geographic separation	10 km

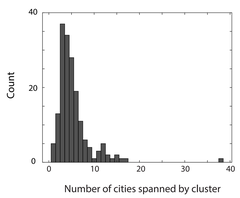
Genetic clusters can be geographically dispersed

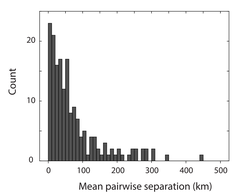
Phylogenetic clusters include members in regions throughout British Columbia. The geographic distribution of one cluster is shown on the cartoon map below.

Cluster 20



Clusters span from 1 to 38 cities (median 4, IQR 3-6) (histogram, below left) and have mean pairwise geographic distances between members ranging from 1 to 442 km (median 48 km, IQR 20-89 km) (histogram, below right).





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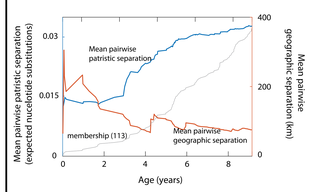
Genetic and geographic dispersion in clusters are independent

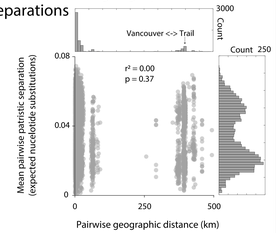
We compared the distributions of phylogenetic and geographic distances in the three most rapidly growing clusters. Plots below, left column, show the mean pairwise genetic and geographic separation within clusters over time. Plots below, right column, show scatter plots of current pairwise geographic and genetic distances separating cluster members.

Cluster 7

Expands genetically while contracting geographically

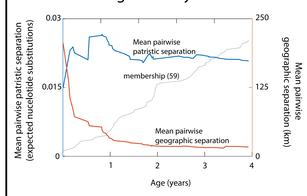


No correlation between geographic and genetic separations

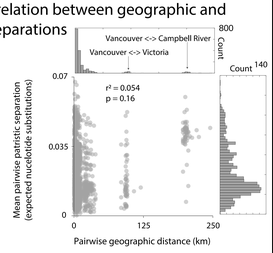


Cluster 55

Contracts geographically while stable genetically

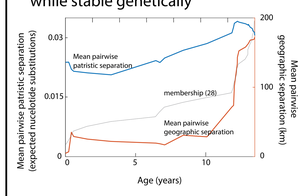


Weak correlation between geographic and genetic separations

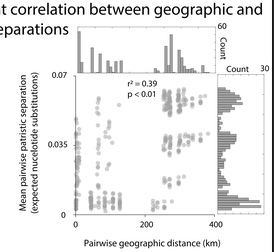


Cluster 155/203

Expands geographically while stable genetically



Significant correlation between geographic and genetic separations



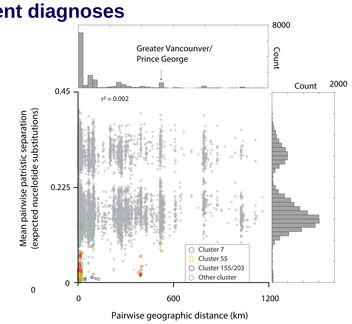
No correlation between geographic and genetic separation

To test whether genetic separation is independent of geographic separation, we compared the relationship between pairwise pastristic and geographic separation in the 200 most recently diagnosed individuals with HIV.

There was no significant relationship between these measures, confirming that genetic proximity provides information about related infections that is not found in geographic proximity.

Pairs within a single cluster are highlighted in color. Note that clusters are defined as having a minimum of 5 members. These related infections would not have been detected by examining geographic proximity alone.

All recent diagnoses



Conclusions

Phylogenetic clustering of people with HIV detects related infections that would not be found based on geographic proximity alone. Specifically:

1) Phylogenetic clusters of people with HIV in BC are geographically dispersed in many municipalities and across large distances.

2) In rapidly growing clusters, there is no consistent relationship between geographic and phylogenetic separation. Geographic dispersion can increase while genetic dispersion remains stable or declines.

3) There is no significant association between geographic and phylogenetic distances among unclustered individuals with HIV. Many individuals who are clustered geographically do not have related infections, and some with related infections are geographiclly far apart.