HIV-1 Superinfection in the Swiss HIV Cohort Study: a Large Scale Screen

(Abstract Number: 947)

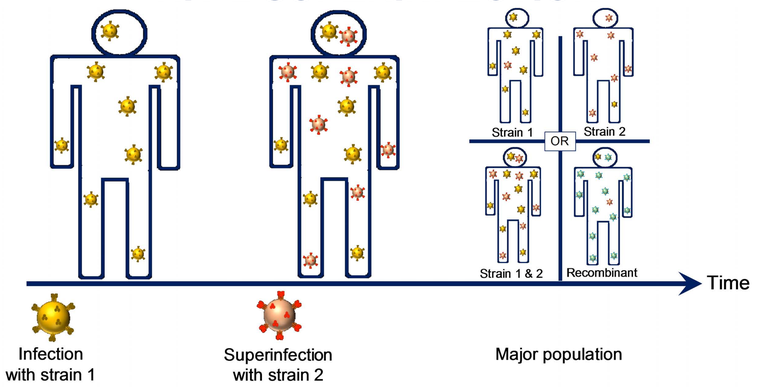
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TAKE HOME MESSAGES

We estimated a minimum rate of superinfection in our cohort of 2%.
Our molecular epidemiology approach is the largest screening to identify HIV-1 superinfection using longitudinal samples to date.
This work sets the basis to validate and characterize HIV-1 superinfection using next generation sequencing in our cohort.

HIV-1 SUPERINFECTION



CHALLENGES

1. The superinfecting strain may outcompete or be outcompeted by the first strain

2. Superinfection is difficult to discern from co-infection

3. Intra-subtype superinfection is difficult to prove, especially if caused by viruses from similar transmission clusters

4. The sampling frequencies are too low and the systematic screenings of large populations to date are missing due to lack of needed longitudinal samples in untreated patients

OBJECTIVE

Determine the incidence of HIV-1 superinfection in the Swiss HIV Cohort Study (SHCS)

WORKFLOW

The Swiss HIV Cohort Study (SHCS)

Longitudinal study

>20,000 HIV-Infected individuals in Switzerland

Follow up approximatively every 3 months with detailed questionnaire every 6 months

Biobank and separate clinical and epidemiological data

Aims to provide optimal care, reduce transmission and study HIV

The Zurich Primary HIV Infection Cohort Study

>360 patients with documented PHI

95% of the patients are in the SHCS

Sequences from the genotypic resistance tests of HIV pol region including the protease and the reverse transcriptase

25,378 sequences

1

1st Filtering step

Patients information matching
Remove non-cohort patients

21,872 sequences ⇔ 11,738 patients
(include 332 ZPHI patients – 538 sequences)

2

Pairwise alignment

Muscle program using
HXB2 reference gene: pol 2,253-3,870

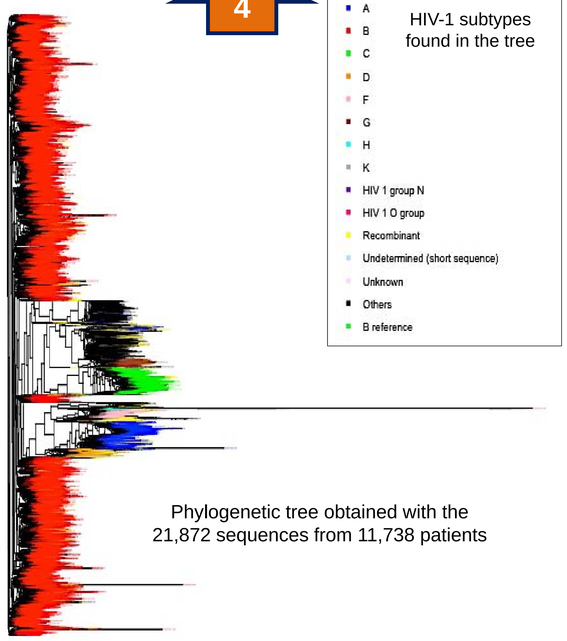
Remove alignment gaps

MIT MEME package

Tree construction

FastTree software

3



Phylogenetic tree obtained with the 21,872 sequences from 11,738 patients

4

Patients with at least 2 sequences in the SHCS
14,692 sequences ⇔ **4,558 patients**
(include 357 ZPHI sequences ⇔ 151 patients)

Patients with at least 4 sequences in the SHCS
7,063 sequences <=> **1,224 patients**
(include 27 ZPHI sequences – 6 patients)

2nd Filtering step

Remove patients with only one sequence available

5

1st Selection criteria

Remove monophyletic clusters with the condition that ≥20 patients must be included in the smallest cluster that includes all of the focal patient's sequences

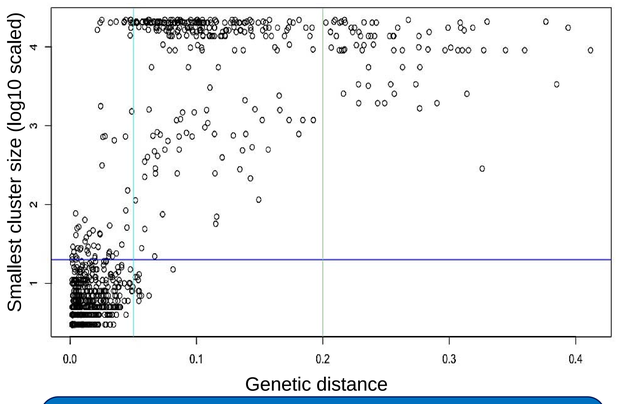
4,558 patients - 3,627 patients in monophyletic clusters = **931 patients**

6

2nd Selection criteria

The genetic distance between the focal patient's sequences ≥5%

Genetic distance > 5% ➔ 341 patients



330 potential superinfection cases when applying selection criteria 1 and 2 simultaneously.
(include 7 candidates in the ZPHI)

7

Hypothetical mislabelling categories

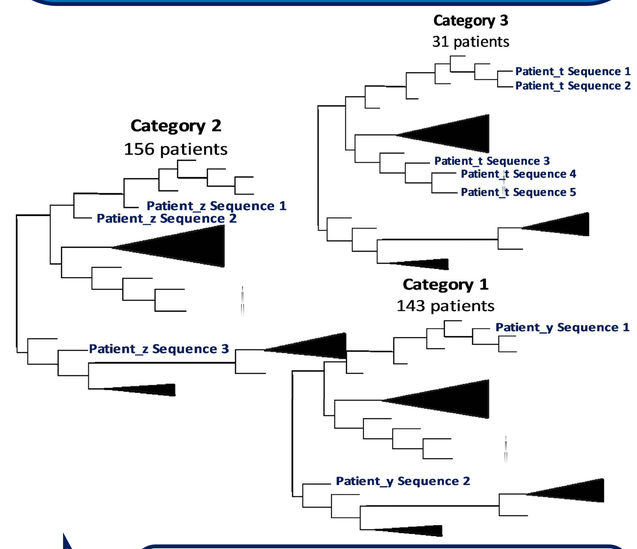
Categories based on the number of longitudinal sequences per patient and the spatial positioning of these sequences in the phylogeny.

RESULTS

Category 3 patients are the superinfection candidates that cannot be explained by mislabelling of one sequence.
25 out of 31 patients with ≥ 4 sequences (1 ZPHI patient)

With these 25 patients out of the 1,224 individuals with ≥ 4 longitudinal sequences, we estimated a minimum rate of superinfection in our cohort of 2%.

Longitudinal plasma samples from patients in these categories will undergo full-length HIV-1 sequencing using next generation sequencing for further analysis



A special thanks to the patients for their participation, the study nurses and the physicians of the Swiss HIV Cohort Study and the Zürich Primary HIV Infection Cohort Study