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

(Abstract Number: 947)

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**Objective**

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

**Workflow**

1. **First 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

3. **Tree construction**
   - FastTree software

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

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 Filtering step**
   - Remove patients with only one sequence available
   - 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)

7. **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)

**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.

**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.

**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

**HIV-1 Superinfection**

Infection with strain 1

Superinfection with strain 2

Major population

Time

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.