

## **Publication**

A systematic molecular epidemiology screen reveals numerous human immunodeficiency virus (HIV) type 1 superinfections in the Swiss HIV Cohort Study

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BACKGROUND: Studying HIV-1 superinfection is important to understand virus transmission, disease progression, and vaccine design. But detection remains challenging, with low sampling frequencies, and insufficient longitudinal samples. METHODS: Using the Swiss HIV Cohort Study(SHCS), we developed a molecular epidemiology screening for superinfections. A phylogeny built from 22,243 HIV-1 partial-polymerase sequences was used to identify potential superinfections among 4,575 SHCS participants with longitudinal sequences. A subset of potential superinfections was tested by near-full-length viral genome sequencing (NFVGS) of bio-banked plasma samples. RESULTS: Based on phylogenetic and distance criteria, 325 potential HIV-1 superinfections were identified and categorised by their likelihood of being detected as superinfection due to sample misidentification. NFVGS was performed for 128 potential superinfections: Of these, fifty-two were confirmed by NFVGS, 15 were not confirmed, and for 61 sampling did not allow for confirming or rejecting superinfection because the sequenced samples did not include the relevant time points causing the superinfection signal in the original screen. Thus, NFVGS could support 52/67 adequately sampled potential superinfections. CONCLUSIONS: This cohort-based molecular approach identified, to our knowledge, the largest population of confirmed superinfections, showing that, while rare with a prevalence of 1-7%, superinfections are not negligible events.

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