O4. Genome-wide population genomics of intrapatient HIV-1 evolution

Jan Albert[1,2] Fabio Zanini[3], Johanna Brodin[1], Lina Thebo[1], Christa Lanz[3], Göran Bratt[4], Richard A Neher[3]
jan.albert@ki.se

Affiliates: [1]Department of Microbiology, Tumor and Cell Biology, Karolinska Institute, Stockholm, Sweden [2]Department of Clinical Microbiology, Karolinska University Hospital, Stockholm, Sweden [3]Evolutionary Dynamics and Biophysics, Max Planck Institute for Developmental Biology, Tübingen, Germany [4]Department of Clinical Science and Education, Venhälsan, Stockholm South General Hospital, Stockholm, Sweden

Background
Within an infected host HIV-1 rapidly accumulates mutations, in part to evade immune recognition.

Methods
To characterize this evolutionary process, we performed whole genome deep sequencing of HIV populations in 9 untreated patients with 6-12 longitudinal samples spanning 5-8 years of infection. Next-generation sequencing using the Illumina platform resulted in more than 100 Million sequence reads. Quality control experiments showed that mutations as rare as 0.3% could be tracked and linkage information was retained over the length of the reads (approximately 500bp). We provide access to the data set via a web application that allows interactive exploration of the evolutionary dynamics.

Results
Minor genetic variation within patients mirrors global HIV-1 diversity, suggesting that universal fitness costs control the level of diversity at individual nucleotide positions. Almost one third of mutations that evolve following transmission are reversions towards the ancestral HIV-1 sequence represented by an alignment of all subtypes within HIV-1 group M. Reversions are observed throughout infection and their rate increase with conservation of the nucleotide position. Frequent recombination limits linkage disequilibrium to about 100 base pairs. However, hitch-hiking due to remaining short range linkage causes levels of synonymous diversity to be inversely related to the speed of evolution.

Conclusions
We report one of the most complete portraits of intrapatient evolution HIV-1 available to date. By analysing divergence, diversity, linkage and recombination, we show that within the infected individual, HIV-1 is an extensively recombining population in a constant struggle between immune evasion and maintenance of virus function.