# The evolution of drug resistance within a HIV population

January 23 2014

Drug resistance mutations in HIV reduce the genetic diversity in the rest of the virus genome when they spread within an infected patient, but they do so to a different extent in different patients. A new study published in *PLOS Genetics*, by Dr Pleuni Pennings and colleagues, found that in some patients a resistance mutation to a particular drug appeared in a single virus particle, which then rapidly proliferated until the entire viral population within the patient consisted of its progeny and was also resistant to the drug. In other patients the same resistance mutation occurred in multiple viral particles within a short window of time, which led to a more heterogeneous, but still drug-resistant, viral population.

One of the big questions that has concerned biologists working on HIV for two decades now is that of the "effective population size" of the virus within a patient. The effective population size is a mathematical quantity that determines, among other things, how quickly drug resistance may evolve. Estimates of this quantity for HIV based on different methods range widely, from 1,000 to 100,000,000, leaving researchers puzzled. Dr Pennings and colleagues observed that drug resistance in HIV evolves by means of so called hard and soft selective sweeps. In a hard sweep, the entire resistant population consists of progeny of a single virus particle; in a soft sweep, it consists of progeny of different virus particles. These two types of sweeps leave distinct signatures in the viral genome: hard sweeps wipe out genetic diversity, while soft sweeps do not. Pennings and colleagues realized that they could use the fraction of soft and hard sweeps for a particular drug-

resistance mutation called K103N to estimate the effective population size of HIV within a patient. They estimate this quantity to be around 150,000.

For the current study, Dr Pennings and colleagues re-analyzed an old dataset from a clinical trial in the late 1990s. The data were very rich, with multiple sequences at multiple time points for more than one hundred patients. The authors focused on a subset of patients where the evolution of resistance could be best observed. In this subset of patients, the current study shows convincingly that soft sweeps and hard sweeps occur in HIV.

In the future, Dr Pennings plans to study patients treated with other drugs to understand how these drugs affect the HIV effective population size. This research may help understand which drugs are more effective in preventing evolution of resistance.

Provided by Public Library of Science