

# Rebuilding the evolutionary history of HIV-1 unravels a complex loop

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An essential component of the human immunodeficiency virus (HIV-1) molecular machinery responsible for infecting cells consists of functionally-specialized layers, according to a study by investigators at the University of California San Diego (UCSD) Antiviral Research Center (AVRC), published November 23 in *PLoS Computational Biology*.

The unprecedented genetic diversity and adaptability of HIV-1 has so far foiled the best efforts to eradicate the global HIV/AIDS epidemic. The surface of the HIV-1 particle is studded with protein spikes that allow the virus to enter human cells. This study examined an important component of the protein spike called the third variable loop (labeled “V3”).

Protein components like V3 are problematic because they are so diverse; up to 35% of the amino acids can differ between strains of HIV-1. Exposed to human antibodies, V3 rapidly evolves to avoid the immune system. However, the V3 loop’s critical function as a docking mechanism for HIV-1 to infect cells must impose limits on these evolutionary contortions. By deciphering the hidden limits on HIV-1 evolution, scientists hope to facilitate the development of antiviral drugs and vaccines.

The investigators developed a new method combining techniques from molecular evolution and artificial intelligence. They reconstructed the evolutionary history underlying 1,145 genetic sequences encoding the V3

loop to discover groups of amino acids that were biologically dependent on each other. These “co-evolving” amino acids formed ties across the V3 loop like rungs on a ladder, corroborating models from structural studies of the same protein.

The investigators caution that this study was restricted to a small portion of the genome. Nevertheless, the study represents a significant advancement in our understanding of HIV-1 evolution and identifies important targets in the protein spike for future research.

Citation: Poon AFY, Lewis FI, Kosakovsky Pond SL, Frost SDW (2007) An evolutionary-network model reveals stratified interactions in the V3 loop of the HIV-1 envelope. PLoS Comput Biol 3(11): e231. doi:10.1371/journal.pcbi.0030231 [www.ploscompbiol.org](http://www.ploscompbiol.org)

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