

## HIV-1 Mutations in the Population

HIV-1 is notorious for eluding scientists and physicians with its rapidly evolving genome. Despite that Dr. Robert Gallo discovered the cause of AIDS in 1984, the HIV virus, we still have yet to synthesize a cure. The current go-to is combination antiretroviral therapy, but only helps us manage the virus. However, HIV's reverse transcriptase causes the enzyme to rapidly "evolve" by incorrectly substituting nucleotides when transcribing from RNA to DNA. The occasional mutation can create a more robust virus, making certain drugs ineffective. To better gauge HIV-1 mutations in the population, Rhee et al. analyzed the genomes of patients from Stanford University in addition to previously sequenced genomes. Their aim is to understand which mutations in the population are indicative of transmitted resistance.

In the study, Protease and Reverse Transcriptase mutations were characterized, as they are the main targets in antiretroviral therapy. It becomes exigent to characterize and track HIV-1 mutations, as many drug resistant mutations are "clinically relevant", i.e. people with the disease are currently in need of alternative medicines. Biochemical analysis has shown that this can result in spatial changes of inhibitor binding sites (L23I, Y181C) and in increasing the energy requirements for inhibitor binding (E34Q, T74S).

The patients chosen for the study have a well-characterized history of antiretroviral therapy. Out of 5867 people who has the protease gene isolated, 3178 had taken at least one protease inhibitor (PI) and 2689 people were PI naïve. Out of 6247 people that had reverse transcriptase isolated, 2551 patients had only taken NTRIs and 1573 patients had taken at least one NNTRI (the literature did not further specify).

# Mutations	PI	NTRI	NNTRI
Unique	73	47	37
Previously Known drug resistance?	53 (21 positions)	34 (18 positions)	19 (10 positions)
Nonpolymorphic? (i.e. rare)	60 (34 positions)	43 (24 positions)	26 (15 positions)

By controlling for these different treatments, the study isolated nonpolymorphic (prevalence <0.05), treatment associated genes that should be tracked in the future. The mutations can serve as sensitive markers in studying the transmittance of drug-resistant HIV.