

# EVOLUTION OF DRUG-RESISTANT HIV-1 STRAINS AFTER TRANSMISSION

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Dutch Data Within Ongoing Cascade Study.

## Background

Infection with drug-resistant HIV-1 may affect the success of antiretroviral therapy, and persistence of such strains can result in further transmission.

## Methods

- Recent HIV-1 infections prospectively identified within the Amsterdam Cohort Studies.
- Population-based nucleotide sequence analysis of the HIV-1 *pol* gene at the first HIV-1 RNA sample available.
- Major drug resistant mutations identified based on the IAS-USA resistance table.
- Longitudinal samples sequenced for seven seroconverters [A-G] infected with strain conferring mutations resistant to NRTIs.

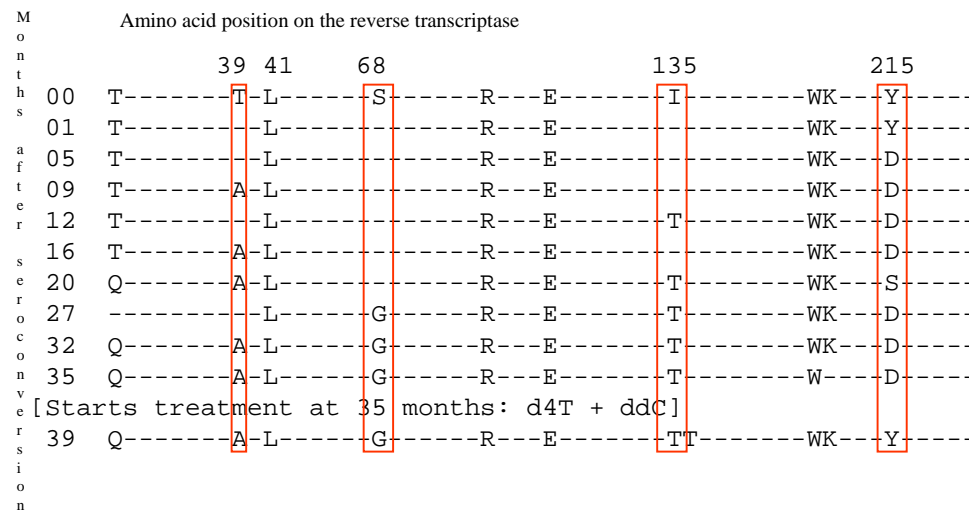
## Results

Years after seroconversion →

	0	½	1	1½	2	2½	3	4	5	7½
A	41L 215Y	41L 215Y/N	41L 215Y/N	41L 215N	41L 215N/D	41L 215N/D	41L 215N/D			41L 215D
B	67N 70R 215F 219Q	67N/D 70R 215F/S/L 219Q	therapy							
C	67N 70R 219Q	67N 70R 219Q	therapy							
D	68S 215Y	68S/N 215Y/S	68S/N 215S	therapy						
E	41L 68S 210W 215Y	41L 68S 210W 215D	41L 68S/G 210W 215D/S	41L 68S/G 210W 215D/S	41L 68S/G 210W 215D/S	41L 68G 210W 215D/S	therapy See right.			
F	215S							215S		
G	41L 215Y	41L 215Y/N	41L 215N/D	therapy	therapy	therapy	therapy	therapy	41L 215D	

## Interesting evolutionary pathway of HIV-1 in patient E failing therapy: *De novo* evolution instead of outgrowth of archived resistance.

- After 4 months of therapy 215D was replaced by 215Y.
- Last sequence before treatment identical to strain during treatment: except at amino acid position 215.
- Amino acid Y at position 215 evolved from amino acid D.
- After 8 years on range of therapies resistant mutations accumulated in RT and PR.



## Conclusions

Resistant HIV-1 strains formed new transmissible HIV-1 variants. Novel pathways on the fitness landscape are explored, when failing on therapy high plasma viral load will be retained and resistance to more drug-classes evolves.

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