



HIV drug resistance & Phylogeny

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Natural selection

- High turnover
- Mutation: 1 error/70 nt
- Recombination
- Viral reservoir



Drug resistance

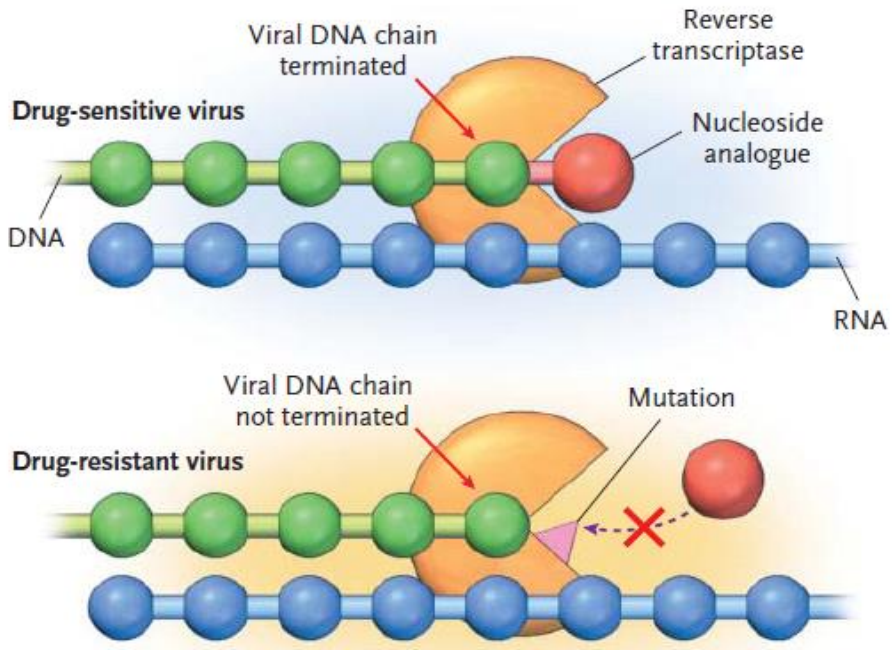
- HIV drug resistance refers to the ability of HIV to replicate in the presence of drugs
- Factors contributing to the selection of HIV drug resistance:
 - Regimen and drug-specific
 - Virus-related factors
 - Patient-specific factors
 - Programmatic factors



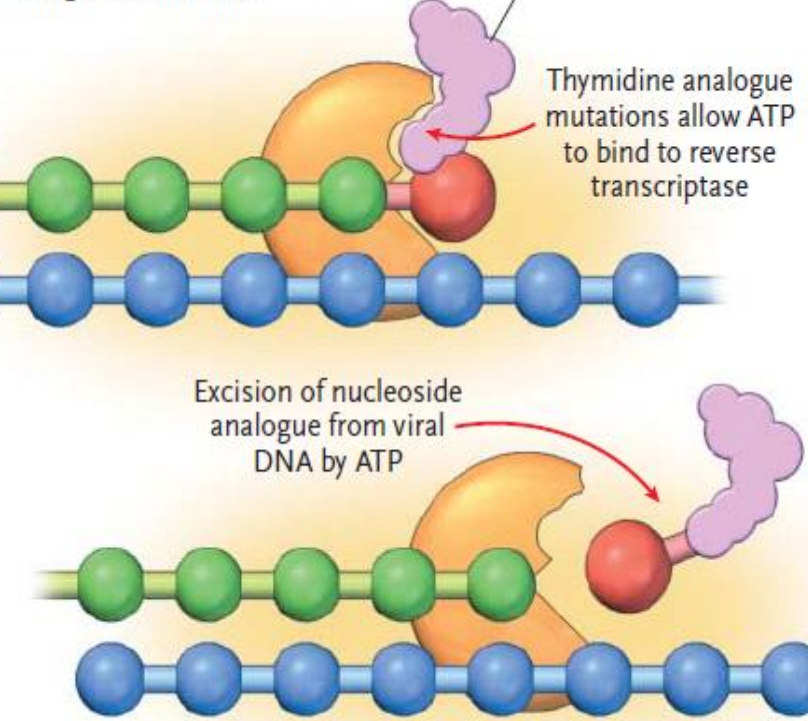
NRTIs

- 1- Sterical-inhibition: K65R, L74V, Q151M, M184V
- 2- Pyrophosphorylysis: M41L, D67N, K70R

A
Resistance by Interference with the Incorporation of a Nucleoside Analogue



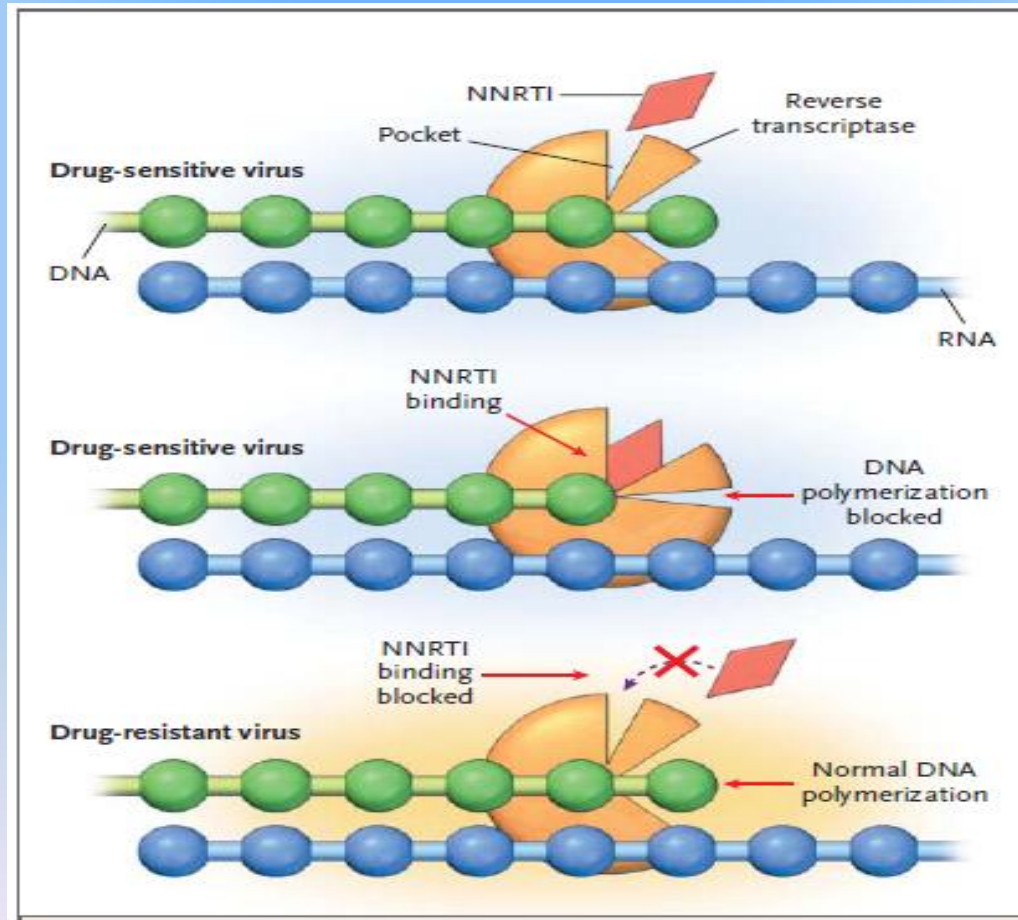
Drug-resistant virus





NNRTIs

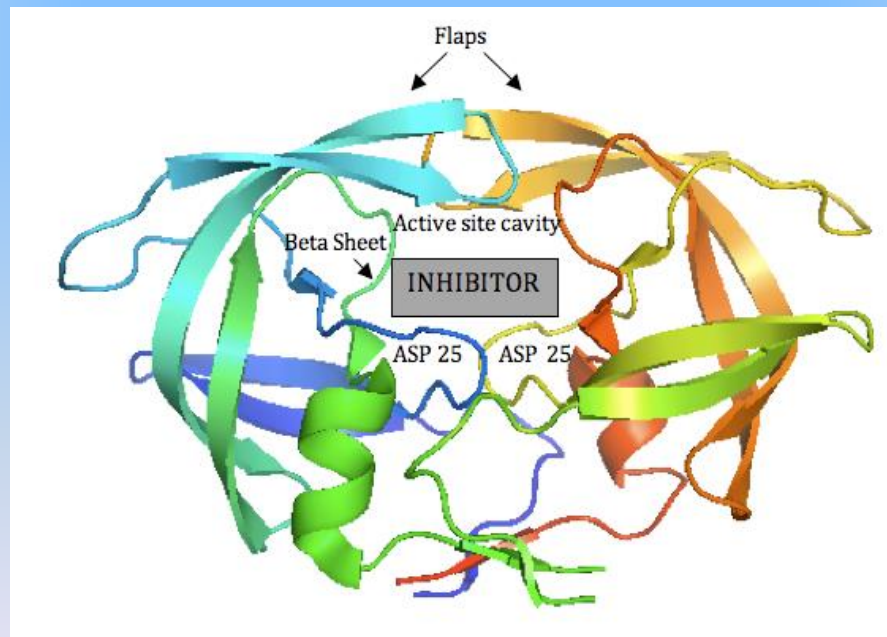
L100I, K103N, Y181C





PIs

- Early & secondary mutations: M46I ,I50V , V82A ,L90M





Why is drug resistance important?

- Drug resistance is the major obstacle for effective treatment (ADR & TDR)
- Monitoring HIV drug resistance is critical for optimal program management:
 - **Transmitted drug resistance (TDR)**
 - Selecting first-line treatment regimens
 - Identifying the most effective second-line
 - Selecting optimal approaches for preventing mother-to-child transmission



Drug resistance

- Minimizing drug resistance to HAART is important
- Entry into care
- ART initiation or switch
- Treatment failure
- In patients HIV RNA levels >1000 copies/mL
- Women entering pregnancy with detectable HIV RNA levels while on therapy
- within 4 weeks after discontinuing therapy



Mutation – treatment correlation

➤ AZT

- TAMs (M41L, D67N/E/G, L210W, T215F/Y K219E/Q/N/R)
- T69I
- M184V

➤ 3TC

- M184V
- TAMs (M41L, D67N/E/G, L210W, T215F/Y K219E/Q/N/R)



Drug resistance in Iran

Researcher	Journal	Year	NRTIs	NNRTIs	PIs
Hamkar, et al	AIDS	2010	76%	74%	45%
Mousavi, et al	Archives of virology	2010	2.5%		2.5%
Baesi, et al	Iranian journal of biotechnology	2012	66%	32%	
Baesi, et al	Modares Journal of Medical Sciences	2012			40%
Jahanbakhsh, et al	Plos one	2013	4.3%		
Baesi, et al	Journal of medical virology	2014	51%	61%	40%
Memarnejadian	Plos one	2015	10%	5%	

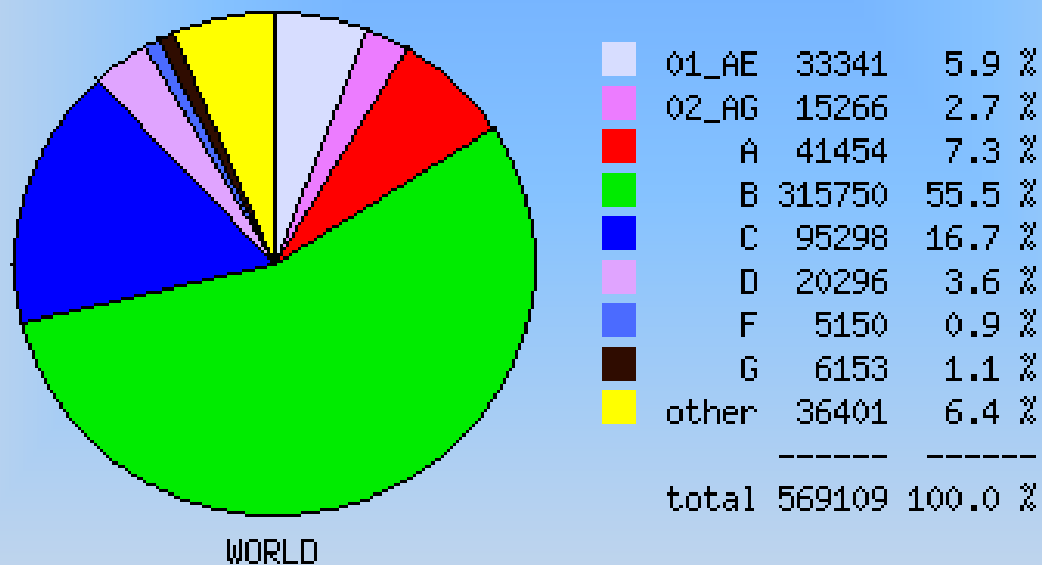


HIV Phylogeny

- **HIV-1 Major (M):** A-D, F-H, J and K (90%)
- **CRFs:** 72 CRFs (AE, AG, BC, ...)
- **URFs:** more than 1000 URF
- **HIV-1 Outlier (O)**
- **HIV-1 Not M_Not O(N)**
- **HIV-1 P group**
- **HIV-2**
- **SIV**

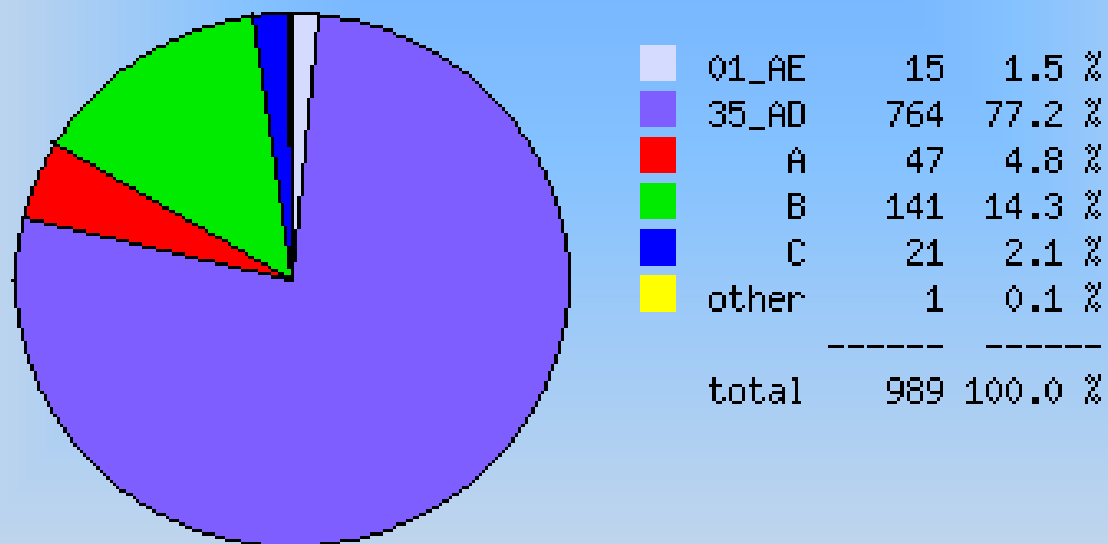


HIV-1 phylogeny





HIV phylogeny in Iran



IRAN, ISLAMIC REPUBLIC OF

Thanks

سال‌ها ره‌می‌رویم و در آخر
هم‌چنان در منزل اول اسیر