

HIV-1 protease and RT mutations according to subtype and antiretroviral therapy: A watch list for epidemiologic studies using a web-based application

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Background: The effect of HIV-1 subtype and drug therapy on genotypic resistance evolution is not well defined. Tracking drug resistance as global drug access and therapy increase requires an accessible application to monitor the drug resistance evolution and to interpret genotypic resistance in non-B subtypes.

Methods: Protease and RT sequences obtained from the international non-B workgroup and the published literature were used to create an updatable online application cataloging the frequency of each amino acid at each position according to subtype and therapy. The application contains a set of user-defined parameters that color-codes mutations based on their frequency in naïve persons with a particular subtype (default =0.5%) and on these frequencies ratios in treated and naive persons (default =10-fold).

Results: Protease non-B sequences were obtained from 2054 naive persons (13% subtype A,28% C,10% D,7% F,7% G,15% CRF01_AE,21% CRF02_AG) and 1519 PI-treated persons (8% subtype A,32% C,9% D,11% F,22% G,9% CRF01_AE, 9%,CRF02_AG), and from 1789 naive and 2585 treated B-infected persons. RT non-B sequences were obtained from 593 naïve persons (8% subtype A,36% C,6% D,6% F,7% G,21% CRF01_AE,16% CRF02_AG) and 1083 NRTI and/or NNRTI-treated persons (12% subtype A,32% C,11% D,6% F,17%

G,15% CRF01_AE,6% CRF02_AG), and from 1083 naive and 3579 treated B-infected persons. The default mutations watch list (=0.5% in naïve persons and =10-fold in treated persons) included 55 amino acid mutations which occurred in at least 1 subtype at 36 protease positions, and 80 amino acid mutations which occurred in at least 1 subtype at 61 RT positions.

Conclusions: Striking differences in inter-subtype mutations can be monitored using a web-based application that highlights mutations according to their relative frequency in treated and naive persons. This allows rapid identification of new potential resistance mutations and provides access to data collected by multiple researchers in the field to update a watch list for epidemiologic studies.