Mechanisms of HIV-1 subtype C resistance to GRFT, CV-N and SVN

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Abstract

We examined the ability of HIV-1 subtype C to develop resistance to the inhibitory lectins, griffithsin (GRFT), cyanovirin-N (CV-N) and scytovirin (SVN), which bind multiple mannose-rich glycans on gp120. Four primary HIV-1 strains cultured under escalating concentrations of these lectins became increasingly resistant tolerating 2 to 12 times their 50% inhibitory concentrations. Sequence analysis of gp120 showed that most had deletions of 1 to 5 mannose-rich glycans. Glycosylation sites at positions 230, 234, 241, 289 located in the C2 region and 339, 392 and 448 in the C3-C4 region were affected. Furthermore, deletions and insertions of up to 5 amino acids in the V4 region were observed in 3 of the 4 isolates. These data suggest that loss of glycosylation sites on gp120 as well as rearrangement of glycans in V4 are mechanisms involved in HIV-1 subtype C escape from GRFT, CV-N and SVN.