

POSTER 30**MUTATIONAL ANALYSIS OF THE DETERMINANTS FOR CYTOPLASMIC LOCALIZATION AND ANTI-RETROVIRAL ACTIVITY OF APOBEC3B**

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Human APOBEC3B (A3B) has been described as a potent inhibitor of retroviral infection and retrotransposition. However, we found that the predominantly nuclear A3B did not restrict infection by HIV or HIV Δ vif, while significantly inhibiting LINE-1 retrotransposition. A chimeric mutant A3G/B, in which the first 60 amino acids of A3B were replaced with those of A3G, was able to restrict HIV, HIV Δ vif, and HTLV-1 infection, as well as LINE-1 retrotransposition. In contrast to the exclusively cytoplasmic A3G, which is inactive against LINE-1 retrotransposition, A3G/B protein, while mainly localized to the cytoplasm, is also present in the nucleus. Further mutagenesis analyses revealed that residues 18, 19, 22, and 24 in A3B are the major determinants for nuclear vs cytoplasmic localization and anti-retroviral activity. Surprisingly, HIV Δ vif packages A3G, A3B, and A3G/B with close to equal efficiency into particles. Similarly unexpected, A3G/B with a mutation at position 127 (W127R), which has also been shown to be important for packaging of A3G, was incorporated at the wild-type level into particles while being inactive in retroviral restriction. As previously reported, the corresponding A3G mutant was inactive and no longer packaged. As in A3B, mutations E68Q and E255Q in the active centers of A3G/B resulted in loss of the inhibitory activity against HIV Δ vif and LINE-1. In summary, these observations suggest that the nuclear localization of A3B targets it to inhibit transposition of LINE-1 and LINE-1-dependent retroelements, and that redirecting A3B to the cytoplasm enables it to restrict retroviruses.