

DISTINCT DOMAINS WITHIN APOBEC3G AND APOBEC3F INTERACT WITH SEPARATE REGIONS OF HIV-1 Vif

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Human APOBEC3G (A3G) and APOBEC3F (A3F) inhibit the replication of Vif-deficient human immunodeficiency virus type 1 (HIV-1). HIV-1 Vif overcomes these host restriction factors by binding to them and inducing their degradation. Thus, the Vif-A3G and Vif-A3F interactions are attractive targets for antiviral drug development, as inhibiting these interactions could allow the host defense mechanism to control HIV-1 replication.

Recently, it has been reported that amino acids 105 to 156 of A3G are involved in the interaction with Vif; however, to date the region of A3F involved in Vif binding has not been identified. Using our previously reported Vif mutants that are capable of binding to only A3G (3G-binder) or only A3F (3F-binder), in conjunction with a series of A3G-A3F chimeras, we have now mapped the APOBEC3-Vif interaction domains. We found that the A3G Vif-interaction domain is located between amino acids 126 to 132 of A3G, which is consistent with the conclusions of previous studies. The Vif-A3F interaction did not occur in the homologous domain, but instead was located between amino acids 283 to 300 of A3F.

These studies are the first to identify the A3F Vif-interaction domain and show that distinct domains of A3G and A3F interact with different Vif regions. Pharmacological inhibition of either or both of these Vif-A3 interactions should prevent the degradation of the APOBEC3 proteins and could be used as therapy against HIV-1.