Novel Functions of Human Immunodeficiency Virus Protein Vif

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2013

HIV encodes viral protein Virion Infectivity Factor (Vif) and it is essential for viral invasion of host innate immunity. In the absence of Vif, the viral replication is restricted by host anti-HIV factor APOBEC3G, which is a cytidine deaminase that induces modification of cytosines to uracils in newly synthesized viral DNA, resulting in non-functional viruses. Previous studies revealed that Vif hijacks host E3 ubiquitin ligase complex to induce degradation of APOBEC3G and counteracts host innate defense to allow continuous viral replication. Recently, two independent studies (Lager et al, Zhang et al, Nature 2012) discovered that Vif also interacts with host factor CBFß, which is crucial for degradation of APOBEC3G. Besides its role in Vif-mediated APOBEC3G degradation, CBFß is also a constitutive binding partner for RUNX proteins. RUNX proteins are key transcription factors for lineage-specific gene expression in several major developmental pathways. Runx1 and Runx3 play key roles in hematopoiesis and multiple stages of T cell differentiation. Both Runx1 and Runx3 are expressed at high level in HIV target cells, including CD4+ T cells and macrophages. Our preliminary data indicate that instead of inducing degradation of Runx proteins, Vif associates with Runx/CBFß complex and is translocated into the nucleus with the transcription complex. Moreover, our experiments suggest Vif modifies Runx/CBFß regulation on its target genes, including IL-2 and IFNg. However, global effects of Vif on Runx target genes, how Vif affects Runx/CBFß transcriptional activity and T cell differentiation is unknown. The proposed study will reveal novel functions of Vif in association with Runx/CBFß complex and provide new insights on viral-host interaction during HIV infection.