

**POSTER 33****APOBEC3F BLOCKS HIV-1 INTEGRATION BY INHIBITING VIRAL 3' END PROCESSING**

Wei Bu<sup>1,2</sup>, Jean L. Mbisa<sup>1</sup>, and Vinay K. Pathak<sup>1</sup>

<sup>1</sup>Viral Mutation Section, HIV Drug Resistance Program, National Cancer Institute-Frederick, and <sup>2</sup>Basic Research Program, SAIC-Frederick, Frederick, MD 21702

APOBEC3F (A3F) and APOBEC3G (A3G) are both host restriction factors that can potently inhibit human immunodeficiency virus type 1 (HIV-1) replication. Their antiviral activities are at least partially mediated by cytidine deamination which causes lethal mutations of the viral genome. We recently showed that A3G blocks viral plus-strand DNA transfer and inhibits provirus establishment in the host genome. Here, we investigated whether A3F similarly interferes with HIV-1 provirus formation. We observed that both A3F and A3G proteins inhibit viral DNA synthesis and integration, but A3F is more potent than A3G in preventing viral DNA integration. We further investigated the mechanisms by which A3F and A3G block viral DNA integration by analyzing their effects on viral cDNA processing using Southern blotting analysis. In contrast to A3G which generates a 6-bp extension at the viral U5 end of 3'-LTR, which is not a good substrate for integration, we found that A3F inhibits viral DNA integration by reducing 3' processing of viral DNA at both the U5 and U3 ends. Furthermore, we demonstrated that a functional C-terminal catalytic domain is more critical for A3G than A3F function in blocking HIV-1 provirus formation. Finally, we showed that A3F has a greater binding affinity for a viral 3'-LTR dsDNA oligonucleotide template than A3G. Taken together, we demonstrated that mechanisms utilized by A3F to prevent HIV-1 viral DNA integration were different from A3G, and that their target specificities and/or their affinities for dsDNA may contribute to their distinct mechanisms.

Funded by NCI Contract HHSN261200800001E