

## POSTER 15

### STRUCTURAL CHARACTERIZATION OF THE INTERACTION OF THE RT RNASE H INHIBITOR

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Reverse transcriptase (RT) in human immunodeficiency virus-1 (HIV-1) is a bi-functional enzyme, having two activities, (i) a DNA polymerase that converts HIV genomic RNA into DNA and (ii) an RNase H that selectively degrades the RNA. Currently, although 13 nucleoside inhibitors and 4 nonnucleoside inhibitors that target the polymerase site are clinically available, no effective RNase H inhibitor with a nano-molar dissociation constant exists. To optimize RNase H inhibitors for affinity and specificity, structural based information about the inhibitor-RNase H interaction is critical. A previous structural study of RT in the presence of an acylhydrazone inhibitor demonstrated that the inhibitor bound only to the RT proximal site, not to the RNase H site, despite the ability of the inhibitor to hinder both RT and RNase H activity. Here, we present solution state NMR experiments to identify the binding sites of RNase H inhibitors to the RNase H fragment.