Retrovirology



Poster presentation



# Novel Second Generation Anti-HIV shRNA Expressing vif and Decoy TAR Arrest the Virus-breakthrough Phenomenon Associated With siRNA-escape Variants

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We describe a novel chimera RNA expressing vif short-hairpin RNA (shRNA) and decoy *trans*-activation response region (TAR) RNA from a human U6 Pol II promoter, which enhanced the inhibition of human immunodeficiency virus (HIV) vif small-interfering RNA (siRNA) and arrested virus breakthrough by siRNA-generated escape variants in long-term culture assays. Our strategy was based on a second-generation anti-HIV-1 shRNA vector system, in which HIV-1 vif shRNA was fused to a decoy TAR RNA by a linker UU cleavage site to generate vif shRNA-decoy TAR RNA. Upon expression, the RNA molecule was cleaved and separated into vif siRNA and decoy TAR RNA. The synergistic effect of these molecules enhanced the inhibition of HIV-1 replication in a long-term culture assay and prevented virus breakthrough associated with siRNA-mediated escape variants. Combining shRNA with decoy TAR RNA as second-generation anti-HIV shRNA may provide practical basis for applying siRNA-based gene therapy to the treatment of HIV/AIDS.