

P007 Synthetic PNA-peptide conjugates as inhibitors of HIV-1 Tat-dependent *trans*-activation in cells

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The *trans*-activation response element (TAR) of Human Immunodeficiency Virus is an RNA stem loop that controls viral gene transcription through a complex mechanism that involves the HIV protein Tat. Inhibition of Tat-dependent *trans*-activation provides opportunities for the development of novel anti-HIV agents. We have shown previously that oligonucleotide analogues complementary to TAR, when delivered by cationic lipids, block *trans*-activation sequence-dependently and dose-dependently in a HeLa cell assay involving stable luciferase reporters and also block syncytia formation caused by cell surface expression of viral proteins in HeLa T4 LTR β -gal cells infected with HIV-1. We now show that peptide nucleic acids (PNA) complementary to TAR, when disulfide-conjugated to certain cell-penetrating peptides and incubated with reporter HeLa cells for 24 h in the absence of a delivery agent can block Tat-dependent *trans*-activation. Such activity may be enhanced by co-administration of the lysosomotropic agent chloroquine. Antiviral studies of such PNA-peptides are in progress.