

P004 Combinatorial selection, delivery and anti-viral activity of backbone modified Oligonucleotide aptamers against HIV-1 RT

V. Thiviyathan, A. Somasunderam, M. Ferguson, D. Rojo, W. O'Brien, & D. Gorenstein.

*University of Texas Medical Branch, Galveston, Texas
77555, USA*

Oligonucleotide based agents are emerging as potential therapeutic agents that can be attractive alternatives for the small molecule chemical drugs. Using combinatorial methods, we have selected a monothiophosphate backbone modified DNA molecule (aptamer) that specifically and tightly binds to the RNase H domain of the HIV reverse transcriptase (RT), a key enzyme in the viral life-cycle. The selected aptamer inhibited RNase H activity in *in-vitro* studies. In cell cultures, transfected aptamer markedly reduced HIV production in a dose-dependant manner. Gel electrophoresis mobility shift assays and NMR spectroscopy showed that the selected oligonucleotide aptamer binds to the isolated RNase H domain, but did not bind to a structurally similar RNase H from *E.coli*. The aptamer binds to the HIV-RT with an equilibrium binding constant of 70 nM. Viral inhibition was observed across a wide range of virus inoculum in a dose-dependant manner with the maximal inhibition of 83%. Suppression of virus was comparable to that seen with AZT at m.o.i. ≤ 0.005 . Using various liposome delivery agents, the DNA aptamer was transfected into HIV-infected astrocytoma adherent cells with greater than 70% efficiency.