## Retrovirology



Poster presentation

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# Inhibition of HIV-I expression and replication by SOFA-HDV ribozymes against Tat and Rev mRNA sequences

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**Background**RNA-based compounds are promising methods to inactivate viruses. New specific hepatitis delta virus (HDV)-derived ribozymes are natural molecules that can be engineered to specifically target a viral RNA. We have designed specific on-off adapted (SOFA) HDV-ribozymes targeting the regions of the HIV-1 RNA in the Tat and Rev sequences.

### Results

We show that these SOFA-HDV ribozymes cleave their Tat RNA target in vitro. They inhibit the Tat-mediated transactivation of HIV-1 long terminal repeat by up to 62 and 86% in luciferase and beta-galactosidase assays, respectively. Inactivation of transfected HIV pNL4-3 molecular clone reached a fourfold inhibition by reverse transcriptase assay of the supernatant and an almost undetectable Gag protein synthesis. *In vivo* RNA cleavage reached 66 and 86% for two of the tested ribozymes showing that the decrease in HIV production is due to the direct decline in spliced and unspliced viral RNA. These SOFA-HDV-ribozymes were able to target four HIV-1 strains, showing an extended potential to act on multiple HIV variants. When transfected before HIV-1 infection, they prevented incoming virus to be expressed.

## Conclusion

Our results show that SOFA-HDV-ribozymes show a great potential to target HIV and to be used as therapeutic agents in gene therapy.