Retrovirology

BioMed Central

Oral presentation

Self-inactivation of HIV by its own RT/RNase H

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from 2006 International Meeting of The Institute of Human Virology
Baltimore, USA. 17–21 November, 2006

Published: 21 December 2006

Retrovirology 2006, **3**(Suppl 1):S57 doi:10.1186/1742-4690-3-S1-S57

HIV can be induced to self-inactivation by its own RT/RNase H by a double-stranded oligodeoxynucleotide (ODN) targeted to the highly conserved polypurine tract PPT. Treatment of HIV-infected cells inhibit HIV infection, including HIV isolates from patients and drug-resistant strains [1,2]. The ODN is highly sequence-specific and destroys HIV RNA efficiently inside the cell, while BaL RNA, containing 3 mismatches in the PPT, is only weakly affected [3]. Furthermore, treatment of HIV particles in vitro abrogates their infectivity [4]. Intravenous treatment of mice infected with Spleen Focus Forming Virus (SFFV) reduces the virus titer transiently and long-lasting, depending on the regimen of therapy, by 10 to 20 fold (man. in prep.). The antiviral effect depends on the complementarity of the RNA-DNA hybrid and to some extent on the sequence of the second arm [3,4]. The hybrid activates the viral RT/RNase H, which irreversibly destroys the viral RNA before a DNA copy is made [3,4]. The ODN may be designated as "siDNA", since it resembles siRNA in respect to length and sequence specificity, and both involve enzymes related by evolution in structure and function, PIWI and RNase H [5]. We describe a novel HIV suicide mechanism mediated by the viral RT/RNase H, which destroys the viral RNA in particles and in newly infected cells, where other cellular enzymes may enhance the effect.

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