Retrovirology

Poster presentation

Silencing of viral RNAs by small double-stranded siDNA

Karin Moelling*[1,2], Jochen Heinrich[1], Alexey Matskevich[1], Lina Wittmer-Elzaouk[1] and Terry Kwok[1]

Address: [1]University of Zurich, Switzerland, 8006 Zürich, Switzerland and [2]Institute of Advanced Studies, Germany, 14193 Berlin, Germany
* Corresponding author

from Frontiers of Retrovirology: Complex retroviruses, retroelements and their hosts
Montpellier, France. 21-23 September 2009

Published: 24 September 2009

Retrovirology 2009, **6**(Suppl 2):P58 doi:10.1186/1742-4690-6-S2-P58

This abstract is available from: http://www.retrovirology.com/content/6/S2/P58

Background

We are developing an alternative approach to siRNA, which may be designated as siDNA, small interfering DNA, by using hairpin-loop-structured DNA oligodeoxynucleotides (ODN), targeted to viral or cellular mRNAs. ODNs activate the viral RNase H in retroviral particles and cellular RNases H inside the cell. Also Ago2 may play a role. Other inhibitory mechanisms such as translational arrest may contribute.

We selected ODNs against various viral and mRNAs of HIV [1-3], HSV [4], Influenza [5], HCV, HBV, and telomerase RNA in malignant melanoma cells in mice [6]. The ODNs were applied with or without carriers. Furthermore their effects were directly compared to those of single-stranded antisense DNAs and siRNAs to allow comparison of the various efficiencies. The ODNs were most effective in HIV. We are able to induce HIV suicide [7], inactivate HIV virus particles to prevent infections, inactivate cell-free HIV in the blood from infected individuals [8], in the vagina of mice [9], and increase survival time of retroviral-infected mice [10]. Also influenza virus replication was reduced in the lungs of a mouse model. Furthermore we could reduce malignant melanoma-formation targeting the telomerase. The effects are sequence- and dose-dependent, but the optimal algorithm is not yet known. We are analyzing whether there is a preference for G tracts, which may form higher-ordered structures. The dsODNs are often superior to single-stranded antisense DNA and resemble the effects of siRNAs [11] but with different kinetics. The method may complement existing silencing approaches.

References

1. Jendis J, Strack B, Moelling K: **Inhibition of replication of drug-resistant HIV type 1 isolates by polypurine tract-specific oligodeoxynucleotideTFO A.** *AIDS Res Hum Retroviruses* 1998, **14:**999-1005.
2. Jendis J, Strack B, Volkmann S, Boni J, Moelling K: **Inhibition of replication of fresh HIV type 1 patient isolates by a polypurine tract-specific self-complementary oligodeoxy-nucleotide.** *AIDS Res Hum Retroviruses* 1996, **12:**1161-1168.
3. Moelling K, Abels S, Jendis J, Matskevich A, Heinrich J: **Silencing of HIV by hairpin-loop-structured DNA oligonucleotide.** *FEBS Lett* 2006, **580:**3545-3550.
4. Falkenhagen A, Heinrich J, Moelling K: **Short hairpin-loop-structured Oligodeoxynucleotides reduce HSV-1 Replication.** *Virol J* 2009, **6:**43.
5. Kwok T, Helfer H, Alam MI, Heinrich J, Pavlovic J, Moelling K: **Inhibition of influenza A virus replication by short double-stranded oligodeoxynucleotides.** *Arch Virol* 2009, **154:**109-114.
6. Noreen F, Heinrich J, Moelling K: **Antitumor activity of small double-stranded oligodeoxynucleotides targeting telomerase RNA in malignant melanoma cells.** *Oligonucleotides* 2009, **19:**169-178.
7. Matskevich AA, Ziogas A, Heinrich J, Quast S, Moelling K: **Short partially double-stranded oligodeoxynucleotide induces reverse transcriptase-mediated cleavage of HIV RNA and abrogates infectivity of virions.** *AIDS Res Hum Retroviruses* 2006, **22:**1220-1230.
8. Heinrich J, Mathur S, Matskevich AA, Moelling K: **Oligonucleotide-mediated retroviral RNase H activation leads to reduced HIV-1 titer in patient-derived plasma.** *AIDS* 2009, **23:**213-221.
9. Wittmer-Elzaouk L, Jung-Shiu J, Heinrich J, Moelling K: **Retroviral self-inactivation in the mouse vagina induced by short DNA.** *Antiviral Res* 2009, **82:**22-28.
10. Matzen K, Elzaouk L, Matskevich A, Nitzsche A, Heinrich J, Moelling K: **RNase H-induced suicide of a retrovirus by oligodeoxy-nucleotides in a mouse model.** *Nat Biotechnol* 2007, **25:**669-674.
11. Moelling K, Matskevich A, Jung JS: **Relationship between Retroviral Replication and RNA Interference Machineries.** *Cold Spring Harb Symp Quant Biol* 2006, **71:**365-368.