

Gene silencing of viruses (HIV) by short double-stranded DNA

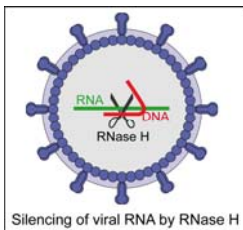
Prof. Dr. Karin Moelling
Universität Zurich, MPI für Molekulare Genetik Berlin

Challenge

Gene silencing is a mechanism to control gene expression by small sequence-specific nucleic acids, such as antisense or siRNA. We developed a novel approach by using a hairpin loop DNA for targeting RNA, which could be called siDNA. With this approach we are inactivating viral and cellular genes involved in cancer. We are inducing HIV to commit suicide by a short DNA. This happens before or early during infection and prevents viral replication. Applications envisaged are prevention of sexual transmission, of mother-to-child transmission, the main two routes of viral spread, and therapy of resistant viruses.

Technology

We are using short, partially double-stranded DNA for induction of HIV suicide before infection. The DNA enters the virus particle and the cell and prevents viral replication. The activated enzyme is the RNase H, one of the 4 enzymes of HIV, the only one not yet targeted by therapy, which I discovered several years ago. We have shown that the viral load in the blood is reduced in a few hours and disease progression reduced or completely prevented in a mouse retrovirus model (See Ref.). HIV from 30 infected individuals from Zurich and Africa was treated once ex vivo and showed in primary material a reduction of the viral RNA



levels, which was more than 1000fold in 33% of the cases. Also a retrovirus treatment in the mouse vagina showed a significant reduction of virus load. The approach is under investigation for other viruses and cancer. Since we are mimicking a natural step of the virus prematurely, there is no selective pressure for mutations.

Developmental Status

For HIV no more animal studies required. Preclinical studies are sufficient to proceed with clinical trials. Toxicology studies, GMP material are required. Platform technology with other applications under investigation.

Commercial Opportunity

In-licensing or collaboration partnership for development into a therapy.

Patent Situation

One patent issued in the USA, others pending

Further Reading

Matzen et al. and Moelling, Nature Biotech 25,669 and 643 (2007)

Der Spiegel ,June 4th (2007)

University of Zurich and
MPI f.MolGen,, Berlin

moelling@immv.uzh.ch

moelling_priv@gmx.net

Tel 0049-1723274306

0041-79 8008337