Retrovirology

BioMed Central

Invited speaker presentation

Novel vaccine and gene therapy approaches against HIV-AIDS

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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):I24 doi:10.1186/1742-4690-6-S2-I24

This abstract is available from: http://www.retrovirology.com/content/6/S2/I24

The design of novel anti-HIV vaccination and gene therapy strategies will be presented, including pilot experiments in animal models. Our gene therapy approach uses the RNA interference (RNAi) machinery to make human cells resistant to HIV-1. The problem of viral escape and the control of viral escape by means of a combination-RNAi therapy will be discussed. A humanized mouse model has been set up as pre-clinical test system to address the safety and efficacy of lentiviral vector-delivered RNAi cassettes. Our vaccination approach deals with the novel concept of a conditional-live virus that can be turned on and off at will. Live-attenuated virus confers the most potent protection against wild-type virus challenge in the SIV/macaque vaccination model. However, such a vaccine is not pursued because of safety reasons as the vaccine virus persists and may evolve into a pathogenic variant. We therefore designed an SIVmac239Δnef variant that is dependent on doxycycline for replication by replacing the natural Tat/TAR transcription mechanism by the Tet-system for inducible gene expression. Replication of this virus can be switched off after vaccination, which will prevent evolution. The first rhesus macaque test yielded a marked vaccine effect. This new conditional-live virus will be a useful tool to identify the correlates of protection by this vaccine strategy.