RETROVIROLOGY

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Treatments for persistent HIV infection: the road ahead

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From 16th International Symposium on HIV and Emerging Infectious Diseases
Marseille, France. 24-26 March 2010

Effective antiretroviral therapy (ART) suppresses viremia and allows immunological recovery, but the intrinsic features of retroviral biology allow HIV infection to persist despite ART. Persistent infection is primarily characterized by the twin phenomenon of latent infection of long-lived cells of the immune system, and continued virus release from undefined cellular sources.

Of late has there been a reawakening of interest in strategies to purge these latent reservoirs of HIV with the goals of a drug-free remission of viremia and, ultimately, virus eradication. To achieve this, therapeutics that target host restrictions to proviral expression that exemplify latent infection, such as epigenetic modifications of chromatin about the HIV promoter, or deficiencies of key host transcription factors within resting CD4 T cells, have been explored in laboratory models of latency, and emerging humanized mouse and non-human primate model systems.

Most clinical studies of ART intensification have thus far shown little effect on persistent infection or persistent viremia, but plans for further human studies are underway. However, as multiple molecular mechanisms appear to underlie the establishment and maintenance of persistent, latent HIV infection, combined approaches may ultimately be necessary to effectively purge residual HIV genomes.

Beyond these near-term efforts, renewed translational efforts seek to re-examine the possibility of transplanting HIV-infected patients with cells resistant to virus infection, alongside expanding laboratory studies to directly excise, damage, or silence proviral genomes. It is clear that to control the HIV pandemic, the scientific, medical, and pharmaceutical communities must marshal new technological and logistical approaches to sustain innovative efforts to prevent and treat HIV, and to work towards a cure for HIV infection.

Published: 11 May 2010

doi:10.1186/1742-4690-7-S1-I17
Cite this article as: Margolis: Treatments for persistent HIV infection: the road ahead. *Retrovirology* 2010 **7**(Suppl 1):I17.

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