

# Researchers' new goal: Drug-free remission for HIV infection

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A group including leading academic and industry scientists has issued a challenge to researchers in the field of HIV/AIDS: find a way to effectively purge latent HIV infection and eliminate the need for chronic, suppressive therapy to control this disease. "The Challenge of a Cure for HIV Infection," to be published in the March 6 issue of *Science*, calls for a coordinated initiative involving academia, industry, patient advocates and government to accelerate the search for a cure.

Highly active antiretroviral therapy (HAART) for the chronic suppression of HIV replication has been the major accomplishment in HIV/AIDS medicine, a therapy now being used by more than four million people around the world to keep the latent HIV virus in check, according to lead author Douglas Richman, Professor of Pathology and Medicine at the University of California San Diego and the Florence Seeley Riford Chair in AIDS Research. He is Director of the Center for AIDS Research at UC San Diego and staff physician at the VA San Diego Healthcare System.

While HAART therapy has allowed many patients to assume a relatively healthy life, unencumbered by symptoms or side effects of the once-daily treatment, HAART is no panacea, according to the authors which include David M. Margolis of the University of North Carolina, Chapel Hill, Warner C. Greene of the Gladstone Institute of Virology and Immunology and UC San Francisco, Daria Hazuda of Merck and Co., Roger Pomerantz, of Tibotec Pharmaceuticals Inc. and Johnson & Johnson Corporation and the late Martin Delaney of "Project Inform."

The team states that combination therapy for HIV infection represents a triumph for modern medicine. However, they add that HAART's success is limited by its cost, the requirements of lifelong adherence required to contain persistent HIV infection - meaning that interruption of treatment can result in a rapid rebound of replicating HIV virus - and the unknown effects of such long-term treatment. There is already growing concern about increased rates of heart disease, diabetes, liver disease and many forms of cancer in aging HIV-infected patients on treatment, according to the paper.

"If we could purge the latent reservoir of HIV infection, we could withdraw chronic suppressive therapy - with great potential impact on cost, toxicity, convenience and transmission," Richman said, adding that the scientific challenges to achieving this goal are substantial but "considering the payoff, the effort is well worth it."

The goal of HIV therapeutics, they propose, should be a drug-free remission. Such a goal requires understanding of the persistence of HIV infection or low-level viremia - the presence of the virus in the bloodstream. Persistent infection is maintained in reservoirs like latently infected lymphocytes or macrophage cells of the immune system. There may be other, as yet unrecognized, reservoirs as well. As multiple mechanisms may contribute to maintenance of this viral latency, combination approaches would likely be required to eradicate infection. Such therapeutic approaches would also affect host cell function, says Richman, so global immune activation must be avoided.

The scientists agree that a major clinical and ethical challenge will be how to safely test future drug development in humans since current antiretroviral therapy is so effective and relatively safe. However, such studies would be required in order to cure HIV. The difficulty of developing a preventive vaccine or microbicide for HIV puts even great pressure on other methods in order to contain the ongoing pandemic of

HIV.

"Without a vaccine, we are left with the substantial financial burden of lifelong treatment for tens of millions of people," said Richman.

"Acknowledging and addressing the challenges outlined in this paper is the first step toward progress."

"Success - if achieved - will not occur quickly," Richman added. "But, bear in mind, the dramatic success of combination antiretroviral therapy which has transformed HIV/AIDS in the developed world and is beginning to impact the developing world required 15 years of substantial effort."

Source: University of California - San Diego

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