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HIV: Current Research

Commentary

Boosting Immune System Functioning through Enhanced Combined Antiretroviral Treatment

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DESCRIPTION

After over 30 years of tremendous work and advancement in the area, neither preventative nor therapeutic vaccinations against Human Immunodeficiency Virus (HIV) are now available. This study discusses about the vaccination techniques and vaccine candidates that have moved to efficacy trials in recent years, with generally disappointing outcomes. Based on biological and epidemiological facts, an innovative and rather contrarian strategy has led to select the HIV protein Tat for the creation of preventative and therapeutic HIV vaccines. Tat's involvement in the virus's life cycle, as well as experimental and epidemiological data supporting its importance in the natural history of HIV infection and comorbidities were examined.

The preclinical and clinical development of a Tat therapeutic vaccine is then discussed, which helps to establish key determinants for intensification of combination Antiretroviral Therapy (cART) and a functional cure by improving immune system functionality and homeostasis and reducing viral reservoir in virologically suppressed vaccines. Future advances and possible uses of the Tat therapeutic vaccine, as well as the justification for its usage in preventative efforts, are also highlighted.

This contribution will prompt a rethinking of current paradigms for the development of HIV/AIDS vaccines, with an emphasis on targeting viral proteins important in HIV pathogenesis. Thus far, neither HIV vaccine design based on structural proteins nor empirical vaccines have been effective, reaffirming the notion that a pathogenetic approach is required to discover critical virulence characteristics to target with a vaccine. A "pathogenesis-driven" strategy, in particular, should try to target key viral components important for virus transmission, activation, and maintenance of virus reservoirs. Tat vaccination is an example of a "pathogenic-driven" intervention that, because it is targeted at preventing viral transmission and dissemination, has the potential to be successful for both preventative and therapeutic measures.

The argument is based on data that HIV-1 Tat, which is required for HIV gene expression, replication, and cell-to-cell transmission, appears to be important in the early stages of viral acquisition. In a therapeutic environment, cART intensification with a Tat vaccine has been shown to improve CD4+ T cell recovery and immune system activities while decreasing viral reservoirs and immunological activation/dysregulation. These combined actions may mitigate the unfavorable impacts of noncompliance with medication on viral transmission and, as a result, global community VL, new infections, and drug resistance. As a result, an intervention that restores immune responses may allow for drug-free periods. The durability of the increase in CD4+ T cell count and the progressive decrease in HIV proviral DNA to undetectable levels observed in vaccinees over the 8-year follow-up is encouraging in this regard, as a lower proviral HIV-1 DNA load at study entry has been independently associated with a delayed and milder HIV-1 RNA rebound after Antiretroviral Therapy Interruption (ATI) and post-treatment control.

Similarly, after ATI, volunteers inoculated with Tat Oyi had a delayed and poorer HIV RNA comeback, while mounting significant immune responses against Tat. Notably, the 33-g dosage was the most immunogenic and effective of the three doses studied (11, 33, and 99 g), which is consistent with the findings from the ISS T-002 study, which found that the 30-g dose of recombinant Tat protein produced the greatest outcomes. The Tat vaccine should also be tested in poor immunological responders to see if it improves the response to cART at the start of treatment, with the goal of shortening the time to a virological and immunological response.

It is also critical to test the Tat vaccine in HIV-infected cART-treated adolescents and children, as they are on antiretroviral treatment for the longest time and thus require approaches that ensure virus control despite poor adherence, the adoption of therapy simplification regimens, or prolonged time off-therapy. Tat might also be used as a co-treatment to boost the efficacy of pre-exposure prophylaxis.

To identify the impact of vaccination on solid-tissue HIV reservoirs and residual illness, it will be critical to examine the effects of the Tat vaccine in these circumstances on HIV DNA in lymphoid tissues and other compartments, as cART does not

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address the latent HIV reservoir. In fact, the Tat vaccine is expected to reduce the rate of treatment failure and the prevalence of AIDS and non-AIDS comorbidities, as well as allow for periodic drug-free time, particularly in infants, children, and adolescents who face lifelong cART and its severe side effects, which can lead to low therapy adherence. Furthermore, increased reduction of cART-resistant latent HIV reservoirs as a result of Tat immunization promises to minimize HIV rebound due to insufficient adherence, which is one of the primary reasons of drug resistance and viral transmission.