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Commentary

HIV Analysis, Investigation and Research

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DESCRIPTION

Since Sinoussi et al. and Gallo et al. first identified HIV as the primary cause of AIDS in 1983, more than thirty years had passed. More than 35 million people are now living with HIV, and 25 million people have died from it. Every day in 2013 there are more than 5700 new HIV infections. Although viral replication can be managed with the help of the current Highly Active Antiretroviral Therapy (HAART), HIV-1 has not been eradicated. There was a latent reservoir, which could be identified by latently infected resting memory CD4+ T-cells. Therefore, until this reservoir is cleared, an HIV cure is not feasible. Additionally, 90 percent of those who are infected live in developing nations, where antiretroviral medications are typically unavailable.

More than 250 clinical trials, the majority of which were early-phase trials (phase I or II), had been carried out since the first phase I human trial of the AIDS vaccine in 1986 in Zaire (now the Democratic Republic of the Congo) by Zagury et al. For vaccine-induced immunity against infectious illnesses like HIV-1 and yellow fever, neutralizing antibodies were typically the first choice. So many studies in the first 10 years concentrated on humoral anti-HIV immunity. Based on this idea, researchers employed monomeric HIV-1 Env gp120 protein to stimulate humoral immune reactions specific to Env. Although gp120 immunogens could elicit type-specific binding antibodies to the immunogens themselves in early-phase clinical trials, they were unable to produce broadly Neutralizing Antibodies (bNAbs).

The failure of the antibody-inducing HIV vaccines to protect against HIV-1 infection in people in 1994 prompted a reevaluation of the global vaccine effort and introduced researchers to the concept of cellular immune response. Early vaccine investigations in rhesus monkeys by Hirsch et al. and Shiver et al. provided evidence for cellular immune protection. They found no evidence of sterility protection in their investigation, but they did find that rhesus monkeys survived longer after being challenged with homologous SIV, and this looked to be associated with a lower viral set point. The focus of research moved to T-cell immunity as virus-specific T lymphocyte responses appeared to be crucial in regulating SIV replication. HIV Vaccine is the most well-known HIV-1 vaccine that focuses on T-cell immunity.

The HIV-1 clade B Gag, Pol, and Nef-expressing rAd5 vectors used to create the vaccine candidate were mixed in a trivalent fashion. After challenging rhesus monkeys with the chimeric Simian-Human Immunodeficiency Virus (SHIV-) 89.6P, preclinical and phase I trial results demonstrated this vaccine's strong immunogenicity and ability to lower viral loads. However, the STEP trial was abruptly ended on September 18, 2007. Compared to placebo receivers, those who received the vaccine were unable to reduce early plasma viral levels or prevent infection. Additionally, a totally unexpected finding from the STEP experiment showed that more vaccine recipients contracted the infection.

CONCLUSION

Surprisingly, the RV144 Thai study showed a 31.2 percent efficacy in preventing HIV-1 infection two years after the STEP trial's failure, making it the first vaccine to show even a minor level of protection. Sanofi Pasteur's vCP1521 canarypox vectored vaccine and AIDSVAX B/E gp120 subunit vaccine, both of which have previously undergone testing in the VAX003 and VAX004 trial, were combined in the trial as a "prime-boost" regimen. High levels of IgA antibodies specific for the Env may have counteracted the effects of protective antibodies, according to the immunological correlates analysis of this study, which suggested that V1V2 antibodies may have contributed to the protection against HIV-1 infection.

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