HIV vaccine research must consider various immune responses

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Last year, the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, held a scientific meeting to examine why certain investigational HIV vaccines may have increased susceptibility to HIV infection. In a new perspectives article appearing in the journal *Science*, HIV research leaders from NIAID (Anthony S. Fauci, M.D., and Carl W. Dieffenbach, Ph.D.) and its grantees at Emory University (Eric Hunter, Ph.D.) and the University of California, San Francisco (Susan Buchbinder, M.D.), summarize the findings and considerations for future HIV vaccine research.

Between 2005 and 2013, investigational HIV vaccines based on recombinant adenovirus type 5 (rAd5), a weakened type of cold virus designed to deliver genetic material, were tested in three clinical trials. Two of those studies, known as Step and Phambili, involved the same experimental vaccine. Both studies showed no efficacy against acquisition of HIV infection; however, they suggested an increased risk of HIV acquisition among vaccinated male study participants. Based on subsequent analyses, the authors hypothesize that the rAd5-based vaccines tested may have heightened susceptibility to HIV infection by activating for sustained periods CD4+ T-cells, the key target for HIV, while producing ineffective or limited protective effects against HIV.

Given the lack of efficacy demonstrated by rAd-5 based HIV candidates and the potential increased risk for HIV acquisition, further development of HIV vaccines using rAd-5 vectors are inappropriate, the authors write. Researchers who want to pursue HIV vaccines using different

adenoviruses or other vaccine delivery systems should perform a risk-benefit analysis that weighs the balance between the potential anti-HIV vaccine responses and protective benefit of the vaccine against the vaccine-induced risk of increased HIV acquisition due to heightened CD4+ T-cell activation.

Moving forward, the HIV vaccine research field would benefit by clarifying the role vaccine vectors play in overall HIV vaccine effectiveness, identifying biomarkers in nonhuman primates that indicate increased risk for HIV acquisition, and developing a better understanding of mucosal immune system responses to HIV vaccination, according to the authors.

More information: AS Fauci et al. Immune Activation with HIV Vaccines. *Science*. DOI: 10.1126/science.1250672

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