Past HIV vaccine trials reveal new path to success

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A multi-national research team led by Duke Medicine scientists has identified a subclass of antibodies associated with an effective immune response to an HIV vaccine.

The finding, reported in the March 19, 2014, issue of the journal *Science Translational Medicine*, helps explain why a combination of two vaccines was able to show some effect, when one vaccine alone did not. The study also provides key insights that could aid development of new vaccines.

"More is not always better with an antibody response," said senior author Georgia D. Tomaras, Ph.D., director of the Laboratory of Immune Responses and Virology at Duke Human Vaccine Institute. "Instead, it's the underlying quality of the immune response. Going forward with other vaccine trials, it will be important to know the subclass, specificity and antiviral functions of antibodies that are induced."

Tomaras and colleagues examined two HIV vaccine trials previously conducted in Thailand. The first trial they revisited, called VAX003, was completed in 2003 and studied an investigational vaccine among intravenous drug users. The vaccine was found to be ineffective.

The second trial, known as RV144, concluded in 2009 and involved more than 16,000 adults. It used two vaccines in combination – one as the prime vaccine and the second as a boost. The boost was the same investigational vaccine used in the earlier VAX003 trial. In the RV144 study, the combination vaccine was 31.2 percent effective at preventing

HIV infection – a success rate that was unprecedented, but considered too low to advance the vaccine to common use.

In both trials, the vaccines induced the production of antibodies that targeted the same region of the HIV virus. In fact, the vaccine used in the VAX003 trial actually elicited higher levels of most of the antibodies than the prime/boost combination of the more successful RV144 trial.

But there was one exception. Tomaras and colleagues found that participants in the RV144 vaccine trial were more likely to have HIV-specific IgG3 antibodies, compared to individuals in the VAX003 trial. The HIV-specific IgG3 response correlated with decreased infection risk, but the effect waned over time, similar to the declining efficacy observed in the RV144 trial.

"HIV-1 specific IgG3 is one biomarker that can be evaluated in further vaccine candidates. It provides a specific way to benchmark HIV-1 vaccine candidates against the one partially efficacious vaccine to date." Tomaras said.

More information: "Vaccine-Induced Env V1-V2 IgG3 Correlates with Lower HIV-1 Infection Risk and Declines Soon After Vaccination," by N.L. Yates, *Science Translational Medicine*, 2014.

Provided by Duke University Medical Center

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