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Media Contact:

Lisa Reilly, 301-500-3633, lreilly@hivresearch.org

New sequencing study provides insight into HIV vaccine protection

RNA-sequencing reveals B cell gene signature associated with protective efficacy of SIV and HIV vaccine regimens

In a new study, scientists led by the U.S. Military HIV Research Program (MHRP) at the Walter Reed Army Institute of Research identified a transcriptional signature in B cells associated with protection from SIV or HIV infection in five independent trials of HIV-1 vaccine candidates. The gene expression signature was found to correlate with protection in the only human HIV vaccine trial that previously showed modest efficacy, RV144. Results from the study were published today in *Science Translational Medicine*.

This signature and specific genes were previously shown to be induced in response to influenza and yellow fever vaccination in humans. "We think this B cell signature is a broad indicator of effective responses after vaccination and could potentially be used to help design effective vaccines against HIV and other pathogens," said Dr. Rasmi Thomas, MHRP's Chief of Host Genomics and senior author of the publication. More broadly, Thomas said the RNA-Sequencing (RNA-Seq) methods used in this study could prove to be a valuable tool to discover protective correlates in other clinical and preclinical trials.

The study examined RNA-Seq data from preclinical HIV-1 vaccine candidate trials. Researchers hypothesized that partial efficacy observed in those studies could be due to variations in host gene expression elicited by the investigational vaccines. Using for the first time in HIV trials a next-generation sequencing method called RNA-Seq, they observed a common protective gene signature in the non-human primates.

Next, researchers investigated whether or not this B-cell signature was associated with protection from HIV infection in the only clinical human HIV vaccine study to show modest efficacy: the RV144 trial conducted by MHRP and its partners in Thailand. RV144 used a completely different vaccine Pox-protein regimen than what was used in the non-human primate studies.

The B cell signature that correlated with protection in the preclinical studies also correlated with protection in the RV144 human vaccine efficacy trial, and in 2 additional Pox-protein

vaccines in NHP. This B cell signature also associated with higher levels of a functional antiviral antibody response called antibody-dependent cellular phagocytosis, or ADCP that could shed some light on why the vaccine was protective.

"We're excited because the identified gene signature associates with protective efficacy for the two vaccine regimens that are currently being tested in human efficacy trials in Africa, the Imbokodo study and HVTN702," said Thomas of the findings. "This new correlate of protection provides a clue as to why the vaccines were partially protective previously and may help to understand the mechanisms of efficacy in these new studies."

About MHRP

MHRP, centered at the Walter Reed Army Institute of Research (WRAIR), aims to protect the U.S. Military from HIV and improve global health by conducting research to develop an HIV vaccine, reduce new infections and advance strategies to induce long-term HIV remission. Long-term, researchers plan to combine the heroin vaccine with an HIV vaccine candidate. For more information, visit www.hivresearch.org.