RV144 vaccine efficacy increased against certain HIV viruses

September 10 2012

Scientists used genetic sequencing to discover new evidence that the first vaccine shown to prevent HIV infection in people also affected the viruses in those who did become infected. Viruses with two genetic "footprints" were associated with greater vaccine efficacy. The results were published today in the online edition of the journal *Nature*.

"This is the first time that we have seen pressure on the virus at the genetic level due to an effective HIV vaccine," said Morgane Rolland, Ph.D., a scientist at the U.S. Military HIV Research Program and lead author of the study. The analysis revealed evidence of a vaccine-induced immune response on two sites of Env-V2 region located on HIV's outer coat. For viruses carrying these two particular signatures, the vaccine efficacy increased to 80 percent.

"These findings reinforce both the RV144 result and the previous study showing that antibodies directed at the V1V2 region reduce the risk of infection. Taken together the work suggests that the Env-V2 region could be a critical target for future HIV vaccines," noted Col. Jerome Kim, senior author on the study.

"Genetic sequencing is an important and independent assessment of the immune responses induced by the vaccine," said Paul Edlefsen, Ph.D., a biostatistitian at the Statistical Center for HIV/AIDS Research and Prevention (SCHARP) who co-led the study. Researchers examined HIV genome sequences from 110 volunteers who participated in the Thai HIV vaccine trial, RV144, and who subsequently became infected with

HIV. Results indicate that the HIV viruses infecting trial participants were different in persons who received vaccine compared to those who received placebo.

Researchers focused their analysis on the V2 portion of the HIV virus after a study published earlier in 2012 found that antibodies specific to the V1V2 region of the HIV genome correlated with lower risk of infection. This new genetic sequencing study showed that the viruses that broke through or escaped from these immune responses have genetic differences in the same V2 region, indicating that the vaccine exerted pressure in this region.

HIV viruses that escape from antibodies and manage to infect a person have genetic footprints, or mutations, that can prevent them from being recognized by the immune system. These changes can be seen in the genetic sequence of the virus. The research team sequenced more than a thousand full-length viruses to look very carefully at which changes corresponded to "escape" mutations.

"This study underscores the realistic optimism you see in the HIV vaccine research field today. We are making substantive progress in understanding what it will take to develop a more effective HIV vaccine which will ultimately help us end this pandemic." said Col. Nelson Michael, director of MHRP.

The study team included researchers with the U.S. Army's Military HIV Research Program (MHRP) at the Walter Reed Army Institute of Research, The Statistical Center for HIV/AIDS Research and Prevention (SCHARP) at the Fred Hutchinson Cancer Research Center and the University of Washington. The project was supported by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, and a cooperative agreement between the Henry M. Jackson Foundation for the Advancement of Military

Medicine, Inc., and the U.S. Department of Defense (DoD).

More information: S. Rerks-Ngarm et al., Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand. *NEJM* DOI: 10.1056/NEJMoa0908492 (2009).

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Provided by US Army Medical Research Institute of Infectious Diseases