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Virus used to create experimental HIV vaccines directly impairs the immune response

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Leading efforts to create an HIV vaccine have hinged on the use of viruses as carriers for selected elements of the HIV virus. Recently, however, evidence has emerged that some of these so-called viral vector systems may undermine the immune system and should not be used for vaccine development. Now, a new study from scientists at The Wistar Institute provides strong support for the idea that some viral-vector vaccines may cause more harm than good.

The findings show that an HIV vaccine construct incorporating one of these viruses, called adeno-associated virus, or AAV, directly interferes with the immune response to the HIV virus. Specifically, while it induces HIV-specific T cells, as intended, those cells are functionally impaired in important ways. At least one major HIV vaccine development project currently uses an AAV vector, so the findings are of immediate significance. A report on the study will be published online November 15 in the *Journal of Clinical Investigation*.

“What do these results mean?” asks Hildegund C.J. Ertl, M.D., director of the Wistar Institute Vaccine Center and senior author on the new study. “Put simply, they mean that AAV vaccines against HIV may potentially cause harm and that, without additional pre-clinical studies, they should not be used in humans.”

In the experiments, conducted in mice, the researchers used a typical

vaccine regimen, priming the immune system with an experimental AAV vaccine against HIV and following it with a booster immunization using an HIV vaccine construct incorporating another viral vector called adenovirus, or Ad. Other viral vectors in addition to Ad were also tried as boosters.

Follow-up assays of the immune response showed that, in all cases, HIV-specific T cells induced by the AAV-vector only poorly protected from infection in a challenge model, failed to secrete adequate levels of important immune-system activating chemicals called cytokines, and most importantly were severely impaired in their ability to proliferate upon re-encounter with their antigen.

Taken together, the data partly outline a condition known as T-cell exhaustion, seen in a number of chronic infections, including HIV, hepatitis B, and hepatitis C, as well as in some cancers, such as melanoma.

“Why would you want to inject people with a vaccine that’s going to have a detrimental effect?” Ertl asks. “AAV vaccines against HIV may do more harm than good by robbing people of their natural immune response to HIV.”

Source: The Wistar Institute