Researchers design global HIV vaccine that shows promise in monkeys

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The considerable diversity of HIV worldwide represents a critical challenge for designing an effective HIV vaccine. Now, a scientific team led by Beth Israel Deaconess Medical Center (BIDMC) has shown that bioinformatically optimized HIV vaccine antigens known as "mosaic" antigens might be useful in the design of a global HIV vaccine. This study, which was conducted in monkeys, is published today in the journal *Cell*.

"A global HIV vaccine would offer major biomedical and practical advantages over most other HIV vaccine candidates, which are limited to certain regions of the world," says lead author Dan H. Barouch, MD, PhD, Director of the Center for Virology and Vaccine Research at BIDMC, Director of the Vaccine Program at the Ragon Institute of MGH, MIT and Harvard, and Professor of Medicine at Harvard Medical School. "To our knowledge, this study represents the first evaluation of the protective efficacy of a candidate global HIV antigen strategy in nonhuman primates."

In this new publication, the authors demonstrate for the first time that mosaic HIV vaccine antigens can afford partial protection in rhesus monkeys against challenges with a stringent simian-human immunodeficiency virus. These mosaic vaccine antigens have been developed for optimal immunologic coverage of global HIV diversity.

Barouch and his team studied the immunogenicity of HIV mosaic Env/Gag/Pol antigens administered to monkeys using viral vectors. Env, Gag, and Pol are three major HIV proteins. After immunization, the monkeys were repetitively exposed to multiple simian-human immunodeficiency virus challenges and the investigators evaluated the ability of the vaccines to block infection.

Although most animals immunized with the mosaic HIV vaccine became infected by the end of the study, the researchers observed an 87 to 90 percent reduction in monkeys' probability of becoming infected each time they were exposed to the virus. In contrast, monkeys that received sham vaccines became infected more quickly.

"These findings indicate that these optimized vaccine antigens can afford partial protection in a stringent animal model," says Barouch.

The investigators found that the immunized monkeys mounted antibody responses against diverse strains of HIV noting, "Protection was dependent on several different types of antibody responses, suggesting that the coordinated activity of multiple antibody functions may contribute to protection against difficult-to-neutralize viruses." The monkeys also mounted cellular immune responses to multiple regions of the virus.

The researchers note that most previous HIV vaccine candidates have typically only been testedin monkeys for protection against easy-to-neutralize viruses rather than against a difficult-to-neutralize virus like the one used in this study. Also, each viral challenge in the study was approximately 100-fold more infectious than typical sexual HIV exposures in humans.

"These data suggest a path forward for the development of a global HIV vaccine and give us hope that such a vaccine might indeed be possible," said Barouch. "We are planning to advance this HIV vaccine candidate into clinical trials next year," he adds.

Provided by Beth Israel Deaconess Medical Center