HIV Vaccine Candidate Gives Rise to Broadly Neutralizing Antibodies in Rabbits

These types of antibodies are able to neutralize a wide breadth of HIV strains.

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An experimental HIV vaccine elicited broadly neutralizing antibodies against the virus in an early test in rabbits.

Publishing their findings in the journal Immunity, researchers from Scripps Research Institute in La Jolla, California, and the nonprofit research organization IAVI designed a vaccine made from a protein that mimics the Env protein on HIV's surface.

HIV uses the Env protein to bind to the CD4 receptor on certain immune cells to begin the process of infecting the cell. The study authors engineered a version of the protein that alters its essential structures and is stable enough to use as a vaccine. To model how Env would appear on the surface of an actual HIV particle, the scientists employed fat-related molecules called liposomes and studded them densely with the synthetic Env proteins.

Normally, collections of sugar-related molecules called glycans help shield the site on Env that binds to the CD4 receptor from an attack by the immune system. With this in mind, in the initial "priming" immunization, the study authors created versions of Env that had that binding site partially exposed.

Then, in subsequent booster immunizations given to 12 rabbits over a 48-week period, the scientists included Env proteins with the glycan protection to the binding site restored. These shots also included Env proteins based on a variety of strains of HIV, in hopes of eliciting antibodies that target structures on Env common to multiple viral strains.

Another dozen rabbits served as a control group, receiving only a single shot of a version of Env with the CD4 binding site shielded by glycan.

The experimental strategy prompted a much stronger response. Five of the rabbits in the experimental group developed antibodies against HIV that could neutralize multiple isolates of the virus.

Looking at the antibodies of the rabbit that had the strongest response to the vaccine, the investigators found two different types of broadly neutralizing antibodies. One, E70, blocked the site on Env where the protein binds to the CD4 receptor by grabbing one of the shielding glycans.

The other antibody, 1C2, targeted another spot on Env, causing the protein to destabilize so that it could no longer drive the virus to enter immune cells. This antibody had a broad effect, neutralizing 87% of a panel of 208 different HIV isolates.

“It’s an initial proof of principle but an important one, and we’re now working to optimize this vaccine design,” the study’s senior author, Richard Wyatt, PhD, a professor in the department of immunology and microbiology at Scripps, said in a press release.

Wyatt and his colleagues will continue to work on the vaccine in small animals, with the goal of moving into nonhuman primate research and then into clinical trials in humans

To read a press release about the study, click here.

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