



Novel HIV Vaccine Approaches

Although study results to date have been promising, they are early steps in a long process before vaccines can be tested in large clinical trials.

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Traditional vaccine approaches have not been able to prevent HIV, but researchers are exploring more sophisticated strategies. One novel approach, known as germline targeting, trains the immune system to produce broadly neutralizing antibodies (bnAbs) that target parts of the virus that don't change much as it evolves. Only about 15% of people with HIV produce these bnAbs naturally, but most have rare immature B cells that have the capacity to do so. To overcome HIV's ability to hide, scientists build immunogens, artificial constructs of viral proteins designed to provoke a robust immune response. A series of different primer and booster immunogens are used in a stepwise manner to encourage maturing B cells to produce bnAbs.

Scientists at the Scripps Research Institute created an immunogen dubbed eOD-GT8 60mer, designed to spur production of bnAbs similar to VRC01. The IAVI G001 trial demonstrated that most people who received an eOD-GT8 60mer primer vaccine developed specialized precursor B cells. Two follow-up studies showed that an mRNA version of the eOD-GT8 60mer vaccine (which Moderna calls mRNA-1644) primed immature B cells in mice, and boosters encouraged them to produce bnAbs that neutralize an HIV-like "pseudovirus."

Two other studies evaluated a different immunogen called N332-GT5, designed to elicit production of a bnAb known as BG18. Researchers showed that an N332-GT5 primer vaccine activated rare precursor B cells in monkeys. Two booster immunogens drove further maturation of these cells in mice, leading to production of bnAbs with increased affinity for HIV.

Meanwhile, researchers at the Duke Human Vaccine Institute tested another vaccine candidate that targets MPER, a hidden part of HIV's envelope that is briefly exposed as the virus prepares to enter a cell. Most of the 20 participants in the HVTN 133 trial developed antibody responses against MPER peptides after just two doses, and the most potent bnAbs neutralized various strains of HIV in the lab.

"To get a broadly neutralizing antibody, a series of events needs to happen, and it typically takes

several years postinfection,” says Duke’s Wilton Williams, PhD. “With this vaccine molecule, we could actually get neutralizing antibodies to emerge within weeks.”

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