Scientists freeze virus fragment in shape recognized by immune system

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One strategy for designing an HIV vaccine involves identifying the key viral surface structures, snipping them off and developing a method to present these fragments to the immune system. When some parts of the surface of HIV are removed, they change shape such that antibodies no longer recognize and bind to them. A research team led by investigators at the Vaccine Research Center at NIAID has developed a strategy to overcome this.

One approach to an HIV vaccine is to teach the immune system to recognize certain protein structures on the viral surface and produce antibodies that bind to those structures and neutralize HIV. A strategy for designing such a vaccine involves identifying the key viral surface structures, snipping them off and developing a method to present these fragments to the immune system. When some parts of the surface of HIV are removed, however, they change shape such that antibodies no longer recognize and bind to them. A research team led by investigators at the Vaccine Research Center of the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, has developed a strategy to overcome this problem. The strategy has implications for scientists designing vaccines for HIV/AIDS as well as for other viral diseases.

The team has fashioned a technique for extracting an antibody-recognizable portion of the surface of a virus and placing this surface fragment, known as an epitope, into a computer-designed protein scaffold. The scaffold locks the epitope in the shape recognized by the

immune system. In theory, when a fixed epitope is introduced into an animal model (or, eventually, a person), the immune system recognizes the epitope and makes antibodies against it. These antibodies could serve as an army ready to bind to the invading virus and prevent it from causing infection.

To demonstrate this scaffolding technique, the scientists applied it to a shape-changing epitope on the surface of HIV that is recognized by an HIV-neutralizing antibody known as 2F5. The epitope adopts a helical or spiral shape when removed from the surface of HIV, but the 2F5 antibody-recognizable version of this epitope has an irregular, kinked shape. The scientists placed copies of the kinked epitope into scaffolds that locked it in that form. Then the researchers injected these scaffold-bound epitopes into guinea pigs. In response, the animals' immune systems made antibodies very similar to 2F5 that bound tightly to the epitope.

This study demonstrates that the engineering of protein scaffolds can be a potentially useful approach in vaccine design. The NIAID researchers are continuing to refine this technique and apply it to the design of vaccines for HIV/AIDS as well as other infectious diseases.

More information: G Ofek et al. Elicitation of structure-specific antibodies by epitope scaffolds. *Proceedings of the National Academy of Sciences* DOI:10.1073/pnas.1004728107 (2010)

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