Researchers determine how antibody recognizes key sugars on HIV surface

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HIV is coated in sugars that usually hide the virus from the immune system. Newly published research reveals how one broadly neutralizing HIV antibody actually uses part of the sugary cloak to help bind to the virus. The antibody binding site, called the V1/V2 region, represents a suitable HIV vaccine target, according to the scientists who conducted the study. In addition, their research reveals the detailed structure of the V1/V2 region, the last part of the virus surface to be visualized at the atomic level.

The study was led by Peter D. Kwong, Ph.D., chief of the Structural Biology Section of the Vaccine Research Center at the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health.

Some people who have been infected with HIV for several years begin to make antibodies that can neutralize a wide range of virus strains. These broadly neutralizing antibodies bind to one of four sites on the virus. One site involves a sugar at a spot called amino acid residue 160. (Amino acids are the building blocks of proteins.) The sugar is located on the protein-based spikes that jut out of the surface of HIV.

The new study demonstrates how a broadly neutralizing HIV antibody called PG9 disarms the virus by grabbing hold of the sugar at residue 160, along with part of a second sugar and a short string of amino acid residues in the V1/V2 region of an HIV spike.

Similarly, a separate, recently published report* from the IAVI Neutralizing Antibody Center at The Scripps Research Institute showed how a different broadly neutralizing HIV antibody also binds to the virus via two sugars and a string of amino acid residues. Taken together, these two studies indicate that in some cases, the combination of viral sugars and amino acids can form the binding site for broadly neutralizing HIV antibodies.

The new study may also help scientists who are examining data from the clinical trial of the first HIV vaccine to demonstrate effectiveness in people (http://www.physorg.com/news172992753.html). Recent analyses of blood samples from that trial showed that study participants who were vaccinated and then developed antibodies to the V1/V2 region were less likely to become infected. Although the role of those antibodies in protection against HIV is unknown, this finding underscores how understanding antibody-V1/V2 binding could aid the design of a more effective HIV vaccine.

More information: JS McLellan et al., Structure of HIV-1 gp120 V1V2 domain with broadly neutralizing antibody PG9. *Nature* DOI: 10.1038/nature10696 (2011).

*R Pejchal et al., A potent and broad neutralizing antibody recognizes and penetrates the HIV glycan shield. *Science* DOI: 10.1126/science.1213256 (2011).

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