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Scientists find mechanism that helps HIV evade antibodies, stabilize key proteins

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NIH scientists have discovered a mechanism involved in stabilizing key HIV proteins and thereby concealing sites where some of the most powerful HIV neutralizing antibodies bind, findings with potential implications for HIV vaccine research.

Numerous spikes jut out of the surface of HIV, each containing a set of three identical, bulb-shaped proteins called gp120 that can be closed together or spread apart like the petals of a flower. Some of the most important sites targeted by HIV neutralizing antibodies are hidden when the three gp120s, or the trimer, are closed, and the gp120 trimer remains closed until the virus binds to a cell.

The researchers discovered that certain amino acids located on the gp120 protein undergo a process that stabilizes the trimer in its closed position. In this process, called sulfation, the amino acids acquire a sulfur atom surrounded by four oxygen atoms. By either blocking or increasing sulfation of these amino acids, the researchers changed the sensitivity of the virus to different neutralizing antibodies, indicating that the trimer was being either opened or closed.

The scientists suggest that if the synthesized gp120 widely used in HIV research were fully sulfated during manufacture, the resulting product would adopt a more true-to-life structure and more closely mirror the way the immune system sees unbound HIV. This might help generate a more effective HIV vaccine. The researchers add that full sulfation of gp120 may enable scientists to crystallize the molecule more readily,

which also could advance HIV vaccine design.

More information: R Cimbro et al. Tyrosine sulfation in the second variable loop (V2) of HIV-1 gp120 stabilizes V2-V3 interaction and modulates neutralization sensitivity. *Proceedings of the National Academy of Sciences* DOI: 10.1073/pnas.1314718111 (2014).

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