

## Most detailed mapping of virus "sugar shield"

December 1, 2020

Researchers in Los Alamos National Laboratory's Theoretical Division along with their partners from Scripps Research Institute developed a novel imaging method that led to the most detailed glycan (or sugar molecule) mapping of HIV. These sugar molecules shield the virus from the immune system, and therefore, gaps where sugar is lacking are ideal for vaccine targeting.

Sugar shields, which are extremely dynamic and flexible, have been notoriously difficult to image; however, they are incredibly important for HIV, influenza, and coronavirus treatment. The density of this protective barrier can vary over the viral spike proteins, essentially determining where antibodies can and cannot bind.

The researchers used an integrated approach to imaging that included cryo-electron microscopy, computational modeling, and site-specific mass spectrometry. This novel method delivered the first-ever detailed mapping of sugars on the HIV spike protein, known as Env.

Along with sugar location, the researchers gained an understanding about the dynamic nature of the molecules. They found that the individual sugars don't just move around randomly on the spike protein's surface, rather the sugars clump together in tufts and thickets, interacting with each other.

Likewise, when the researchers began removing the sugars from Env, they found the functionality, shape, and stability of Env began to fall apart. This elucidated a new role of which the researchers were unaware the sugars were playing.

"Being able to visualize and quantify the glycan shield in such extraordinary detail gives us an edge in the ongoing battle against viruses," said lead author Srirupa Chakraborty, a postdoctoral researcher in Theoretical Biology and Biophysics and the Center for Nonlinear Studies.

This new sugar-shield mapping approach is poised to aid vaccine design and development for many glycogen-shielded viruses, including HIV.

**Funding:** The researchers acknowledge the LANL High Performance Computing Division for providing computational facilities. The work was supported by the National Institute of Allergy and Infectious Diseases (CHAVD), the Bill and Melinda Gates Foundation, and the IAVI Neutralizing Antibody Center.

References: Z. T. Berndsen *et al.* "Visualization of the HIV-1 Env glycan shield across scales," *Proceedings of the National Academy of Sciences* (2020). DOI: 10.1073/pnas.2000260117

S. Chakraborty *et al.* "Quantification of the Resilience and Vulnerability of HIV-1 Native Glycan Shield at Atomistic Detail," *Cell iScience*. In Press. <a href="https://doi.org/10.1101/846071">https://doi.org/10.1101/846071</a>

Los Alamos National Laboratory www.lanl.gov (505) 667-7000 Los Alamos, NM

Managed by Triad National Security, LLC for the U.S Department of Energy's NNSA

