New insights into HIV virus shed light on how it evades immune surveillance

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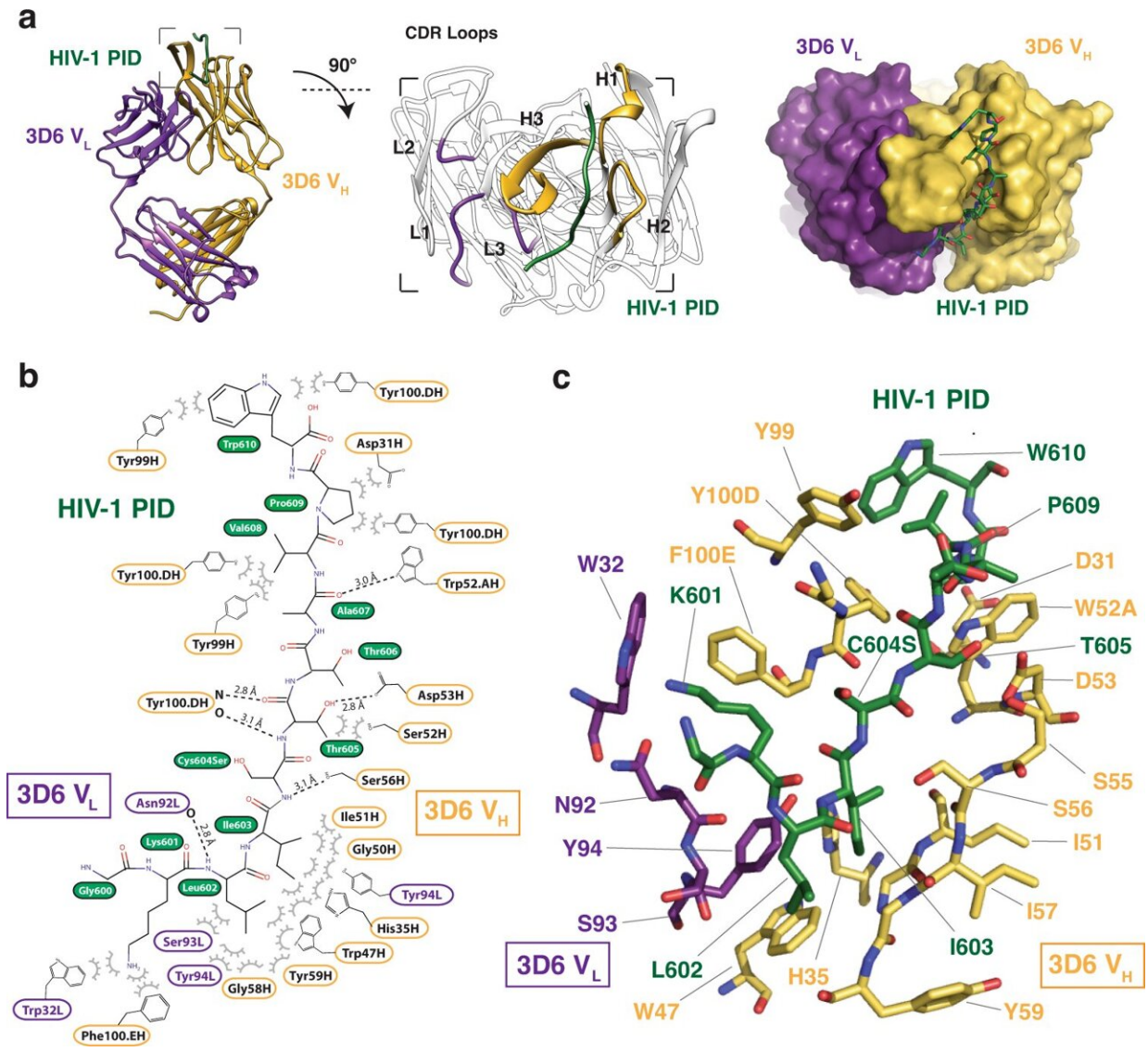

Overall structure of Fab 3D6 complexed to HIV-1 gp41 PID. a. The crystal structure of the Fab 3D6-PID complex shows the PID region in an extended

conformation coordinated mainly by the VH subunit. Fab 3D6 CDR-H3 forms a pseudo-β-sheet with the HIV-1 PID. b. Interaction map of Fab 3D6 and the PID peptide. Interactions were determined by PISA analysis80 and manual inspection. Hydrogen bonds are shown by dashed lines. HIV-1 PID residue S598 (wild-type Cys598) was not visualized in this structure. HIV-1 residue S604 (labeled Cys604Ser) is coordinated by a hydrogen bond with Fab 3D6 residue S56H. c. Stick representation of the antigen-binding site in which the HIV-1 PID peptide is colored in the dark green, heavy chain in yellow, and light chain in purple. Credit: Jonathan D. Cook et al, *Communications Biology* (2022). DOI: 10.1038/s42003-022-03235-w

About 36 million people have died from AIDS-related illnesses and approximately 38 million people globally are living with HIV.

Dr. Jonathan Cook, a resident physician specializing in medical microbiology at the University of Toronto, is investigating key proteins on the HIV virus that are crucial to developing an effective vaccine.

"These proteins are so interesting because they are necessary for a virus to infect a human," said Cook. "By blocking their function, we can avert the kinds of infections that you see routinely."

He and Adree Khondker in the lab of Prof. Jeffrey E. Lee from the Temerty Faculty of Medicine have published a paper in *Communications Biology* that reveals new information on how the HIV virus interacts with immune systems.

Using the CMFC beamline at the Canadian Light Source at the University of Saskatchewan, the research team analyzed the outer proteins on the HIV virus. They discovered that an area of one protein acts as a decoy—diverting the immune system's response towards a false target.

This tactic allows the virus to successfully infect human cells and to cause disease.

"The immune system recognizes this sequence on the virus, which is usually a good thing. But, in this situation, the antibodies that the immune system makes don't protect you from infection," Cook said.

With the help of the CLS, the researchers confirmed that this decoy area on the HIV protein shapeshifts to entice an ineffective immune response.

Cook and his colleagues hope that their research will provide a strategy for future vaccine design that will avoid this region—allowing for a better immune response and a more effective vaccine.

Cook has been using the CLS for over a decade and said the facility has benefited his work.

"We've been able to get research material on Monday, ship it to the CLS on Wednesday, and get our data set on Friday," Cook said. "It's really revolutionized the way we screened our research materials and has expedited our research."

More information: Jonathan D. Cook et al, Conformational plasticity of the HIV-1 gp41 immunodominant region is recognized by multiple non-neutralizing antibodies, *Communications Biology* (2022). DOI: 10.1038/s42003-022-03235-w

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