

The Scientist: NewsBlog:

Structure hints at Ebola's cunning

Posted by [Megan Scudellari](#)

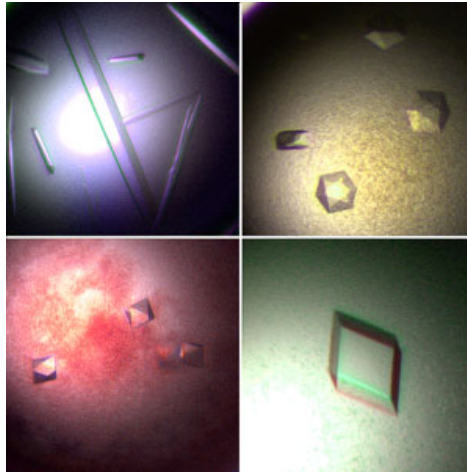
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Researchers have determined the crystal structure of the Ebola virus surface protein that binds host cells, they report online today in [Nature](#). The findings open the door to solving the long-standing mystery of the virus's mechanism of infection and designing drugs to combat the deadly hemorrhagic fever caused by [Ebola](#).

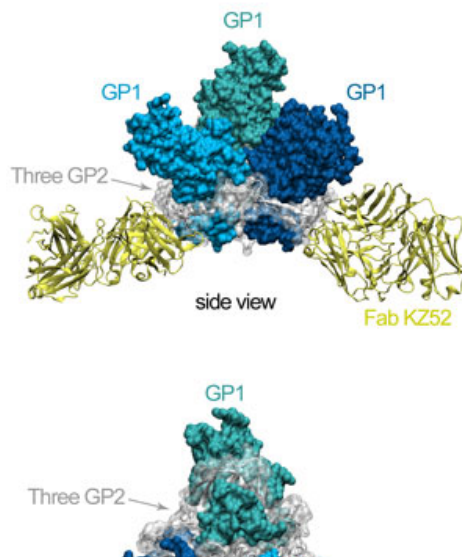
The paper is a "breakthrough," said [Lijun Rong](#), an associate professor at the University of Illinois at Chicago who was not involved in the study. People in the field have been looking for this structure for a long time, he emphasized, and the advance is "really exciting for us."

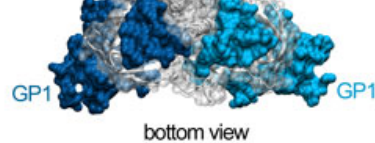
Ebola virus is a "clever little thing," said Erica Ollmann Saphire, an immunologist at the Scripps Research Institute and main author of the paper. "It's a tiny stripped-down machine of just seven genes, yet it's able to utterly defeat most defenses we can come up with against it." [Ollmann Saphire](#) became intrigued by the virus because of its "weird gymnastics" to make what it needs; for example, the virus can synthesize two distinct forms of glycoprotein (GP) from one gene. The rarer of these two proteins, the sole GP on the surface of the Ebola virus, binds and fuses the virion with human cells.

The team deciphered the structure of that GP using [X-ray crystallography](#). To map the structure, they needed to coax the proteins to condense and crystallize in solution - a challenge, because the protein is covered in sugar, a substance regularly used to prevent products from crystallizing. So the team made 140 different versions of the protein, bound to each of seven antibodies, and grew a total of 50,000 crystals, finally identifying one version that crystallized correctly.



Resulting images of the GP show the receptor binding site buried in the center of a chalice and protected by a canopy of other proteins. Ollmann Saphire hypothesizes that these cloaking molecules are shed in layers when the virus approaches a cell. The structure also revealed that within the protein - a trimer made up of GP1 and GP2 molecules - the GP1 subunits are loosely tied together by GP2 subunits like thread around a spool, Ollmann Saphire said. This formation could allow the GP1 subunits to spring away and expose the binding site upon fusion, she noted.





The newly-defined structure confirms mutagenesis work done [last year](#) by Wendy Maury at the University of Iowa and colleagues, which narrowed down a small region of the GP1 terminus as the probable receptor binding site. In the new paper, said [Maury](#), who was not involved in the study, Ollmann Saphire "takes that data and really nicely puts it in the context of their structure." Understanding the structure of GP "can't but help lead to better, more informed studies about how to generate [antivirals](#)," said Maury.

The most important next step and an ongoing effort in the field, Maury and Rong agree, is locating the receptor for Ebola on human cells. One has yet to be discovered, but not for lack of trying, said Rong, and knowledge of the structure will help that endeavor.

Image captions and credits:

First: Crystals of the Ebola virus glycoprotein in complex with an antibody from a human survivor. Photo: Jeffrey Lee and Erica Ollmann Saphire, TSRI

Second: The GP1 subunits (blue) are tied together by the GP2 subunits (white). A rare human antibody from an outbreak survivor (yellow) bridges the two subunits together. Image: Christina Corbaci and Erica Ollmann Saphire, TSRI

The crystal structure of the Ebola virus GP with the putative receptor binding site in pink, sequestered in the bowl of the GP chalice in white. Movie: Erica Ollmann Saphire, TSRI