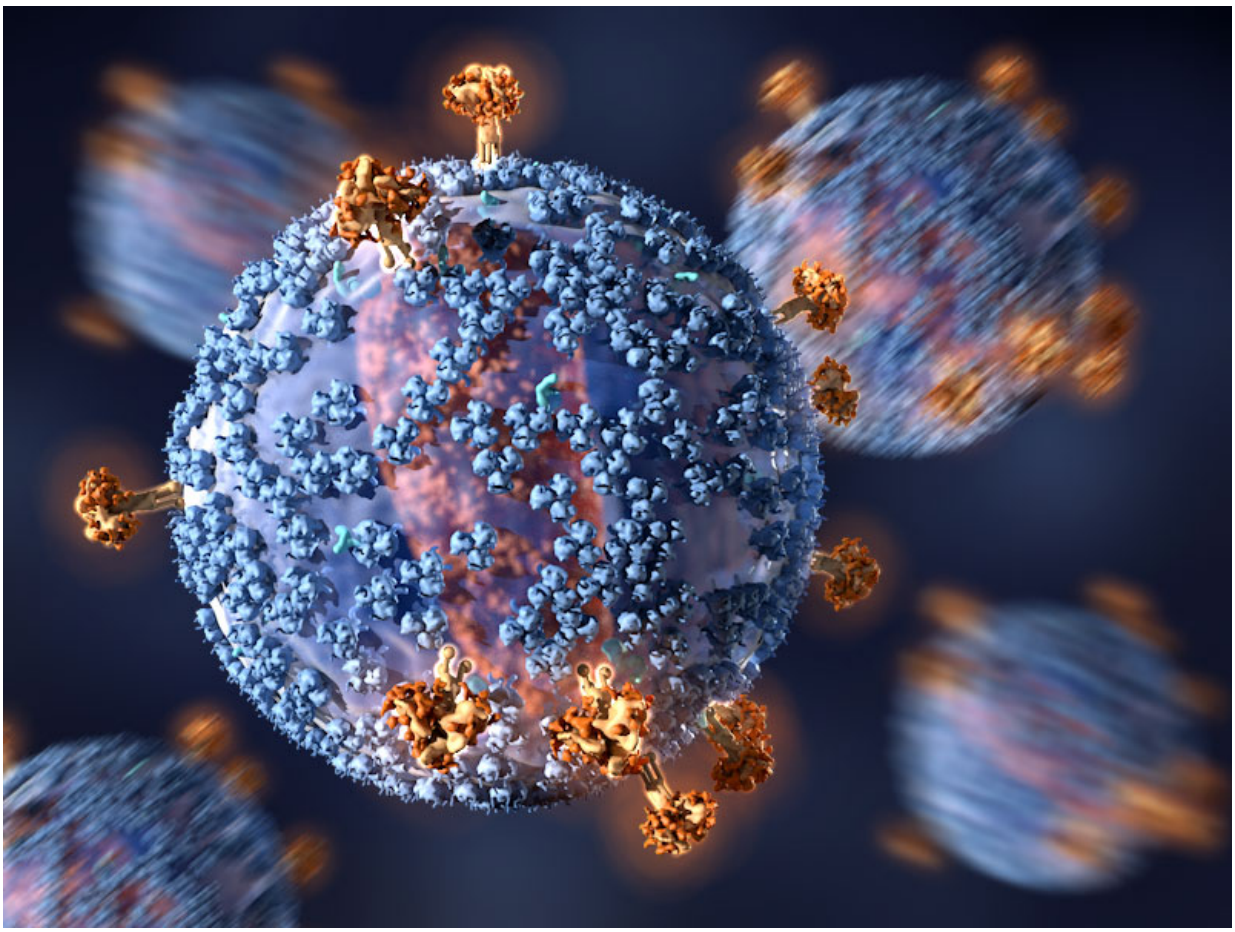
Patient with unique antibodies helps researchers develop strongest HIV-attacking antibody to date

January 30 2017, by Bob Yirka



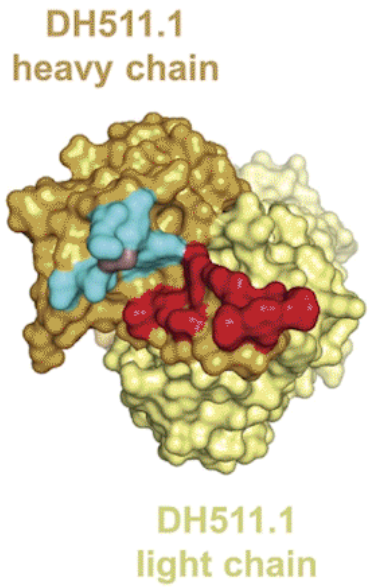
The human immunodeficiency virus (HIV). Credit: Chris Bickel / AAAS

(Medical Xpress)—A large international team of researchers has created what they are describing as the most powerful HIV-attacking antibody ever made. In their paper published in the journal *Science Immunology*, the team describes how they were able to use naturally occurring antibodies with unique HIV fighting abilities to create the new antibodies and what it means for the development of a vaccine.

HIV, has of course, proven to be a difficult virus to stop. Not only is it diverse, but it has a tendency to mutate, which has made developing a vaccine for it nearly impossible. In this new effort, the researchers report on a new development in the never-ending struggle to find a way to beat the virus for good.

The research began with the discovery of a patient who was found to make an antibody that neutralized a wide range of HIVs. This was a significant find because of the way that research into creating a vaccine works. It is not enough simply to find such an antibody in a person; researchers have go back in history and find out how it arose in a particular individual—a sequence of events that would require years of effort by the host immune system to take advantage of the ways B cells mutate.

Meanwhile, the team also looked at blood plasma from the same patient and identified another useful antibody, one related to another they had found—both of them, the researchers note, are variants of an antibody known as DH511.



Broadly neutralizing antibodies come in all sorts of shapes and conformations, each with different approaches to fighting HIV-1. DH511.2_K3 is an engineered hybrid antibody that can disarm 99% of various HIV-1 strains, exceeding the neutralizing capabilities of 10E8, one of the most wide-acting and potent antibodies known. Credit: Williams et al., *Sci. Immunol*. 2, eaal2200 (2017)

Next, the team pulled parts from each of the two antibodies they had obtained and constructed new antibodies out of them until they found what they believed was the most powerful combination possible. Testing confirmed they were on to something, as the antibodies proved to be capable of neutralizing 206 out of 209 strains of HIV found around the world. The antibody is so effective, the researchers note, because of its unique binding properties—it does so very close to the virus' plasma membrane, which allows it to block important aspects of the viral life cycle.

The progress made by the team represents another small step forward in the development of a vaccine against HIV infection—one among many that will over the next decade, the researchers believe, lead finally to a product that can be put to use.

More information: LaTonya D. Williams et al. Potent and broad HIV-neutralizing antibodies in memory B cells and plasma, *Science Immunology* (2017). DOI: 10.1126/sciimmunol.aal2200

Abstract

Induction of broadly neutralizing antibodies (bnAbs) is a goal of HIV-1 vaccine development. Antibody 10E8, reactive with the distal portion of the membrane-proximal external region (MPER) of HIV-1 gp41, is broadly neutralizing. However, the ontogeny of distal MPER antibodies and the relationship of memory B cell to plasma bnAbs are poorly understood. HIV-1–specific memory B cell flow sorting and proteomic identification of anti-MPER plasma antibodies from an HIV-1–infected individual were used to isolate broadly neutralizing distal MPER bnAbs of the same B cell clonal lineage. Structural analysis demonstrated that antibodies from memory B cells and plasma recognized the envelope gp41 bnAb epitope in a distinct orientation compared with other distal MPER bnAbs. The unmutated common ancestor of this distal MPER bnAb was autoreactive, suggesting lineage immune tolerance control. Construction of chimeric antibodies of memory B cell and plasma antibodies yielded a bnAb that potently neutralized most HIV-1 strains.