Why so many antibodies fail to protect against HIV infection

November 18 2010

Researchers have been stymied for years over the fact that people infected with the AIDS virus do indeed produce antibodies in response to the pathogen – antibodies that turn out to be ineffective in blocking infection.

Now, scientists at Duke University Medical Center can explain why: Some of the earliest and most abundant antibodies available to fight HIV can't actually "see" the virus until after it's already invaded a healthy cell.

The scientists based their conclusion on the results of a series of crystallography and biochemical experiments that revealed the specific molecular structures different types of antibodies need to have in place in order for them to mount an effective defense.

Previous research had shown that two of the most robust antibodies against HIV –antibodies called 2F5 and 4E10 – target a specific part of the outer coating of the virus called the MPER region of gp41. The antibodies, which operate in a lock and key relationship, are able to latch on to the virus as it reveals this vulnerable part of its structure, referred to as an "Achilles heel" of the AIDS virus.

"What our studies revealed, however, is that the virus actually creates two versions of this 'Achilles heel,' says Barton Haynes, MD, director of the Duke Human Vaccine Institute (DHVI) and the senior author of the study appearing online in *Nature Structural & Molecular Biology*. "One version is for these rarer, broadly-neutralizing antibodies, and the other

is for the more abundant, first-responding antibodies that won't be able to do much good because the Achilles heel isn't detectable to them until the virus has already gained entry."

Nathan Nicely, PhD, the lead author of the study and a member of the DHVI, designed and conducted most of the crystallography studies. "This structure has been difficult to obtain, but now that we have it, it has been instrumental in our understanding why this non-neutralizing antibody interacts with the HIV-1 outer coat."

Haynes says the findings are important because they distinguish what parts of the virus an antibody needs to recognize from those parts that are decoys. "We are homing in on a better understanding of what the immune system needs to do in order to mount an effective defense against HIV."

Provided by Duke University Medical Center