Unique individual demonstrates desired immune response to HIV virus

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One person's unique ability to fight HIV has provided key insights into an immune response that researchers now hope to trigger with a vaccine, according to findings reported by a team that includes Duke Medicine scientists.

The person had a rare combination of both lupus and HIV. Lupus, specifically systemic lupus erythematosus, or SLE, is a disease in which the immune system attacks the body's cells and tissue.

In an analysis published March 10, 2014, in the *Journal of Clinical Investigation*, the Duke-led research team detailed how the individual's immune system made a desired type of neutralizing antibodies that is considered essential to an effective vaccine response.

"Over the years we have searched for and now have found one person with SLE who was also chronically infected with HIV to determine if this person could make broad neutralizing antibodies," said Barton F. Haynes, M.D., director of the Duke Human Vaccine Institute and senior author of the study. "We found that the patient did indeed make these important antibodies, and by determining how this immune response occurred, we have enhanced our understanding of the process involved."

Haynes said a huge barrier to creating an effective HIV vaccine has been the difficulty in eliciting the broad neutralizing antibody response. These antibodies arise in a few people infected with HIV, but it takes at least two years.

In 2005, Haynes found that some broad neutralizing antibodies to HIV cross-reacted with the body's tissues in a process termed autoreactivity. Autoreactive antibodies are kept in check by the body's immune tolerance controls, which sense antibodies that react with the body and prevent them from being made.

Haynes's hypothesis has been that these autoreactive broad neutralizing antibodies are not routinely made because the immune system targets them as harmful and keeps them in check. In essence, the virus has found a unique escape mechanism from neutralizing antibodies by adapting itself to look like the body's tissues.

In an autoimmune disease such as lupus, the immune tolerance controls are defective, so the broad neutralizing antibodies should be produced, the Duke team reasoned.

Haynes and colleagues, including lead author Mattia Bonsignori, M.D., assistant professor of medicine at Duke, identified an individual with both lupus and HIV and found that, after several years, the person made the desired broad neutralizing antibodies.

Remarkably, the broad neutralizing antibody found in the lupus individual was autoreactive, and reacted with similar molecules in the body called double stranded DNA, or dsDNA, that are made in individuals with lupus who do not have HIV.

"The cross-reactivity of the broad neutralizing antibody with dsDNA was very surprising and provided support for the hypothesis that broad neutralizing antibodies are similar to the autoantibodies that arise in lupus patients who are not infected with HIV," Bonsignori said.

The findings in no way suggest that individuals with lupus are immune to HIV, and they, like all individuals, should protect themselves from

contracting the virus. Rather, it suggests that when individuals with lupus do become infected with HIV, they can eventually make broad neutralizing antibodies, although unfortunately too late to help them fight off the infection.

"Our study of this person with SLE and HIV has been critically instrumental in our understanding of the unusual biology of the remarkable host control of antibody responses to the conserved broad neutralizing sites of the HIV envelope," Bonsignori said. "We are hopeful that these insights in lupus will aid in our implementation of strategies for designing experimental vaccines capable of overcoming the host tolerance control of broad neutralizing antibodies."

Provided by Duke University Medical Center