Scientists explain binding action of 2 key HIV antibodies; could lead to new vaccine design

November 9 2009

A very close and detailed study of how the most robust antibodies work to block the HIV virus as it seeks entry into healthy cells has revealed a new direction for researchers hoping to design an effective vaccine.

"Our study clearly showed that we've been overlooking a very important component of antibody function," says S. Munir Alam, Ph.D., an associate professor of medicine at Duke University Medical Center and lead author of the paper appearing in the Proceedings of the National Academy of Sciences.

Alam, a member of the Duke Human Vaccine Institute and study senior author Bing Chen, Ph.D., assistant professor of pediatrics, Harvard Medical School and Children's Hospital Boston, studied two potentially powerful antibodies against HIV, 2F5 and 4E10. Both of these are rare, broadly neutralizing antibodies, meaning that they can block a number of different strains of the HIV virus. They accomplish that by binding to the "Achilles heel" of the virus - the so-called outer coat membrane proximal region - a part of the outer protein coating next to the viral membrane that opens up and is exposed to the antibodies for just a few minutes during the process of cell fusion and infection.

But the problem for infection control is that such powerful antibodies are rare in HIV infection, and current experimental vaccines have been unable to generate such antibodies. In addition, the window of

opportunity for such antibodies to act is very narrow.

"The target region on the virus is only open for a few minutes - maybe 15 minutes or less," says Alam. "Unless the antibody is very close by and ready to home in on it, it won't work. That means our goal has to be the creation of a vaccine that can induce a whole lot more of these antibodies and have them ready to go at the earliest moment of infection."

"Fortunately, our study gave us new information that will help us accomplish this goal," says Chen.

The 2F5 and 4E10 antibodies have unusually long, loopy protein segments that are hydrophobic, meaning that they are attracted to lipids. The researchers found that successful docking of the antibody to the HIV outer coat membrane region required antibody attachment to HIV's membrane, which contains lipid.

"This two-step mechanism, not previously appreciated, might extend to antibodies that protect against other viruses," says co-author Stephen Harrison, Ph.D., of Harvard Medical School, Children's Hospital Boston, and the Howard Hughes Medical Institute.

The research team is already working on designing a vaccine that incorporates a lipid component. "The demonstration of the role of virion lipid reactivity in the overall function of these neutralizing antibodies has provided key insights into what the immune system may need to see to make such antibodies", says co-author and Vaccine Institute Director Barton Haynes. "New vaccine designs trials based on these observations are now ongoing in animals."

Source: Duke University Medical Center (news : web)