

HIV-Specific Antibodies in HIV-Uninfected Women

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It is believed that a large percentage of unprotected sex acts with an HIV-infected partner never result in virus transmission that leads to systemic infection. However, repeated HIV exposure that does not result in persistent infection may still influence the immune system of the uninfected partner. For example, both HIV-specific T cells and neutralizing antibodies have been detected in vaginal secretions or the seminal fluid of HIV-negative individuals believed to have been repeatedly exposed to HIV via unprotected sex with HIV-infected partners. A recent study by researchers in the Vaccine and Infectious Disease Division and their collaborators detected IgA antibodies with HIV antigen specificity in vaginal secretions of HIV seronegative women who participated in a microbicide trial in Africa. Their results were published in *PLoS ONE*.

The first part of the study compared several sampling methods for obtaining vaginal secretions to detect IgG and IgA antibodies. From a cohort of five HIV-seropositive and five HIV-uninfected women in Seattle, the researchers determined that there was no statistical difference in antibody titers obtained from the three sampling devices tested. They also revealed that the IgG antibodies from the HIV-positive women reacted broadly across eight HIV-1 envelope antigens, but the IgA antibodies were only specific for the gp41 subunit.

Having validated the methods for sample collection and HIV-specificity determination in vaginal secretions, the researchers next looked at samples obtained from 57 HIV-seronegative women comprising the control arm of a microbicide efficacy trial in Southern Africa. Of the 57 women, nine were found to have HIV-specific IgA antibodies, but no HIV-specific IgG antibodies were detected in any of the women. Interestingly, the vaginal IgA antibodies were directed at HIV Env gp120/gp140 and gp41 in six and three women, respectively, which contrasted to the IgA antibodies detected in the HIV-positive women in Seattle, which were only specific for gp41.

This study confirmed previous observations of mucosal HIV-specific IgA antibodies in uninfected women with a higher risk of exposure to HIV. The fact that these samples came from participants of a microbicide trial, even if they were from the untreated control group, may have provoked study organizer Dr. Florian Hladik to contemplate several lines of inquiry for further investigation.

"An important question now is whether an efficacious microbicide, one that successfully inactivates HIV, would lead these disabled viruses to stimulate a mucosal immune response," said Dr. Hladik. "In such a scenario, we should find mucosal anti-HIV antibodies more frequently in women using the active product than in women using a placebo."

"The next question would then be whether these responses contribute to protection, so that HIV infection would be prevented by a two punch mechanism: direct antiviral activity of the microbicide plus emerging protective immunity stimulated by contact with inactivated viruses."

He admits that this hypothesis may sound far-fetched, but cites evidence from a recent study to support his case. It showed "that a new class of highly cross-neutralizing antibodies likely requires immune stimulation with entire native viral spikes rather than just parts (Huang, et al. 2014)." Dr. Hladik speculates that, "microbicide-inactivated natural whole virions could provide just that kind of stimulation."

This PLOS One study is part of a [PLOS journals collection highlighting recent advances in HIV mucosal immunology](#).

[Seaton KE, Ballweber L, Lan A, Donathan M, Hughes S, Vojtech L, Moody MA, Liao H-X, Haynes BF, Galloway CG, Richardson BA, Karim SA, Dezzutti CS, McElrath MJ, Tomaras GD, Hladik F.](#)

2014. HIV-1 Specific IgA Detected in Vaginal Secretions of HIV Uninfected Women Participating in a Microbicide Trial in Southern Africa Are Primarily Directed Toward gp120 and gp140 Specificities. *PLoS One* 9: e101863.

See also: [Huang J, Kang BH, Pancera M, Lee JH, Tong T, Feng Y, Georgiev IS, Chuang GY, Druz A, Doria-Rose NA, Laub L, Sliepen K, van Gils MJ, de la Peña AT, Derking R, Klasse PJ, Migueles SA, Bailer RT, Alam M, Pugach P, Haynes BF, Wyatt RT, Sanders RW, Binley JM, Ward AB, Mascola JR, Kwong PD, Connors M.](#) 2014. Broad and potent HIV-1 neutralization by a human antibody that binds the gp41-gp120 interface. *Nature* doi: 10.1038/nature13601. [Epub ahead of print]

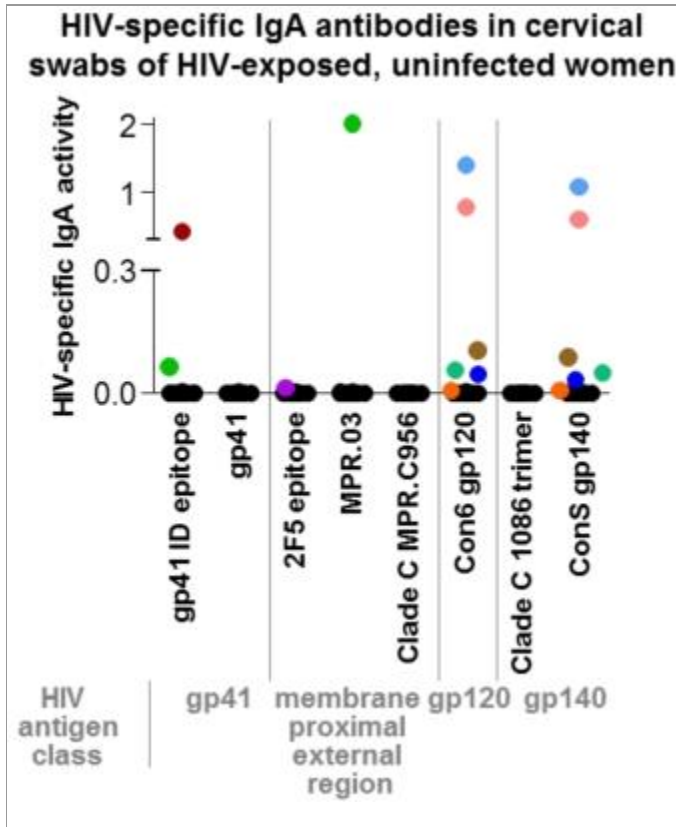


Image provided by Dr. Florian Hladik

Cervical swab samples from HIV-uninfected women revealed specificity to various HIV-1 Env antigens. For the 57 microbicide trial participating women, black symbols signify negative responses and colored symbols signify positive responses, with colors indicating specific women.