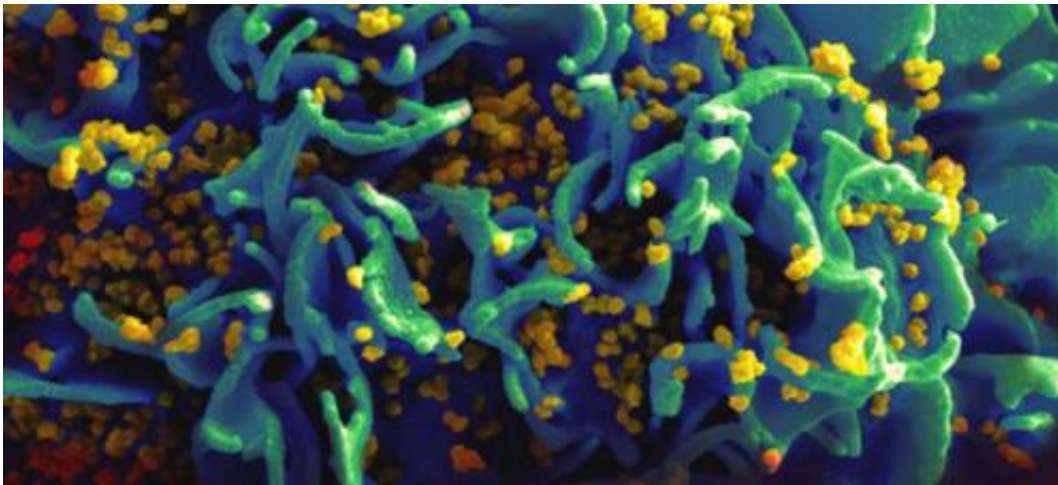


Bacterial communities of female genital tract have impact on inflammation, HIV risk

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An HIV-infected cell. Credit: NIAID

A team led by researchers from Massachusetts General Hospital (MGH) and the Ragon Institute of MGH, MIT and Harvard has found that the most common bacterial community in the genital tract among healthy South Africa women not only is significantly different from that of women in developed countries but also leads to elevated levels of inflammatory proteins. In a paper in the May 19 issue of *Immunity*, the investigators describe finding potential mechanisms by which particular bacterial species induce inflammation and show that the presence of those species and of elevated levels of inflammatory proteins could increase the risk of HIV infection.

"Ours is the first study to identify a specific bacterial community in the genital tract of healthy [women](#) that is highly pro-inflammatory, and we show this community is common in the women we studied in South Africa," says Douglas Kwon, MD, PhD, of the Ragon Institute and the MGH division of Infectious Diseases, senior author of the report. "We also identified specific mechanisms by which the [immune system](#) senses these [bacterial species](#) and potential mechanisms linking that response to increased HIV susceptibility."

The authors note that, although inflammatory reactions in the female genital tract can prevent or eliminate many [sexually transmitted infections](#), activation of the immune system paradoxically increases the risk that exposure to HIV will lead to infection. In the past, the bacterial population of the female tract was believed to be very simple and - based on what was seen in white, premenopausal women - dominated by a single *Lactobacillus* species. Since mild vaginal infections that alter the dominant microbial community can increase the risk of acquiring HIV and other sexually transmitted diseases, the researchers designed the current study to investigate whether differences in the genital microbial communities of healthy women might affect overall susceptibility to infection.

Analysis of genital samples from a group of 94 young black South African women - who were HIV negative and had no disease symptoms - revealed that only a minority had the sort of *Lactobacillus*-dominant bacterial communities commonly seen in U.S. women. The researchers grouped the samples they studied into four community types - what they called cervicotypes - based on the dominant bacterial species. The most common cervicotype among the study participants was very diverse, with low levels of *Lactobacillus* and no single dominant bacterial group.

To assess levels of immune activation in the study participants, the researchers measured levels of the immune system signaling molecules

called cytokines in vaginal fluid samples and found significant individual differences - as much as 1,000-fold in some cases. Elevated cytokines were not associated with active sexually transmitted infections or with factors such as sexual frequency or the use of condoms or hormonal contraceptives. Comparing cytokine levels among the cervicotypes revealed that the low-Lactobacillus, high-diversity communities were more than four times as likely to have elevated genital inflammatory cytokines. In fact, the presence of community was a better predictor of inflammation than was the presence of [sexually transmitted diseases](#) or other vaginal infections.

The researchers found that women with the highest levels of genital inflammation also had elevated levels of CCR5+ CD4+ T cells, the cells that are infected by HIV, in their genital tracts. "It has been shown that having a higher frequency of these HIV target cells at the site of exposure increases the risk of infection," says study lead author Melis Anahtar, an MD/PhD candidate in the Harvard/MIT Division of Health Sciences and Technology. "It's possible that treatments targeting specific genital bacteria could improve the effectiveness of measures - such as antiretroviral vaginal gels - designed to prevent HIV infection. In addition, finding that women with elevated genital inflammation may be three times more likely to become HIV-infected suggests that generally targeting the genital microbial population may further reduce risk."

An assistant professor of Medicine at Harvard Medical School, Kwon adds, "Understanding the impact of differences in the genital microbial population could also have implications for pregnant women and their infants. Some of the pro-inflammatory species that we found in our study were originally found in infected amniotic fluid and may contribute to the risk for premature birth and other complications of pregnancy." The research team is now investigating the specific mechanisms by which the immune system senses the presence of specific bacterial species in the female [genital tract](#) as well as examining

the potential role of the broader microbial population, including viruses and fungi.

Provided by Massachusetts General Hospital

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