

Investigators find window of vulnerability for STIs to infect female reproductive tract

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Charles R. Wira, PhD, and colleagues at Dartmouth's Geisel School of Medicine have presented a comprehensive review of the role of sex hormones in the geography of the female reproductive tract and evidence supporting a "window of vulnerability" to HIV and other sexually transmitted infections (STIs). Published in *Nature Reviews in Immunology*, Wira's team presents a body of work that National Institutes of Health evaluators called, "a sea change" for research in the female reproductive tract (FRT).

"The FRT is tremendously complex and the normal changes that occur to hormones during the [menstrual cycle](#) are set up to optimize conditions for implantation and pregnancy. To facilitate implantation during the second half of the menstrual cycle, the hormones suppress normally protective activities to allow pregnancy to progress, which would otherwise be prevented," explained Wira. "Our overall goal is to understand the underlying molecular mechanisms through which hormonal changes affect implantation."

The benefits of these findings, said author Marta Rodriguez-Garcia, PhD, are directly applicable to other reproductive challenges including gynecological cancers such as cervical cancer, which is a product of [human papilloma virus](#) (HPV), infection, infertility, and the epidemic spread of STIs.

"We were drawn to the conclusion that the 'window of vulnerability' created to ensure pregnancy also provides an opportunity for a potential

pathogenic bugs like HIV or HPV to enter and infect the FRT," Wira said. He noted that all aspects of the immune system are precisely regulated by the [sex hormones](#) estradiol and progesterone, which are secreted during the menstrual cycle. They affect epithelial cells, fibroblasts, and immune cells in the FRT to modify their functions and, hence, the individual's susceptibility to STIs in ways that are unique to specific sites in the FRT.

In the future, the "window of vulnerability" will lead to concept changes at several levels. At the biological level, determining where and when infections occur could lead to development of new delivery systems for microbicides that are menstrual-cycle dependent. The studies could lead to new concepts for therapeutics that confer protection by enhancing intracellular anti-viral activity. And, at the behavioral level, it could lead to changes in sexual activity, such as the identification of a safer time in the cycle to have sex. In the arena of drug development, there is escalating interest in microbicides, vaccines, and contraceptives, and the Wira studies involving chemical contraceptives will be critical in determining whether certain formulations enhance FRT HIV immune protection without increasing the risk of infection of HIV target cells.

More information: "The Role of Sex Hormones in Immune Protection of the Female Reproductive Tract" *Nature Reviews in Immunology*, [www.nature.com/nri/journal/vao ... nt/full/nri3819.html](http://www.nature.com/nri/journal/vao...nt/full/nri3819.html)

Provided by The Geisel School of Medicine at Dartmouth

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