Medical Xpress

Sexually transmitted HIV: Key mechanisms elucidated in men

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Having suggested in 2011 that the urethra is a novel entry site for HIV, a team from the Institut Cochin (CNRS/Inserm/Université Paris Descartes, with the support of Anrs), has now confirmed this hypothesis and identified the cells and mechanisms brought into play: the immune system cells macrophages, present in the epithelium of the urethra, allow the entry of HIV. This work, published online on the website of the journal Mucosal Immunology, could make it possible to test novel HIV/AIDS prevention strategies.

While the mechanisms of rectal or vaginal infection in women are quite well described, penile infection in men remains poorly understood. Clinical studies conducted in the 2000s showed that circumcision could reduce the risk of infection in men by 60% during sexual intercourse. Following this work, the Institut Cochin team demonstrated that the mucous membrane on the inner layer of the foreskin was one of the main entry sites for HIV. However, since circumcision does not provide complete protection, it remained to be determined what other mucous sites in the penis could facilitate HIV infection.

To localize these entry sites, the researchers used penis tissue taken from healthy adult males during transgender surgery. HIV can, a priori, penetrate via three areas of the penis: the glans, the end of the urethra known as the fossa navicularis and the part of the urethra located inside the penis.. By placing the mucous membranes covering these three areas in contact with the HIV virus, the researchers observed that the glans and the fossa navicularis resist infection. On the other hand, the virus

efficiently penetrates the penis through the urethra, which is also an entry site for many other sexually transmitted pathogens, such as gonococci or chlamydia (these results were presented in part at the international Conference on Retroviruses and Opportunistic Infections.

The researchers are now focusing on molecular and cellular infection mechanisms. They have demonstrated that, in the urethra, the immune system cells responsible for the phagocytosis of pathogenic agents, known as macrophages, are the first to be invaded by HIV. This had never been observed in this type of mucous membrane. At the same time, the cells of the epithelium stop secreting the signals retaining the macrophages. Consequently, the infected macrophages leave the epithelium, allowing HIV to propagate. The researchers thus observed that, in the mucous membrane of the urethra, the TCD4+ lymphocytes - the main target of the virus - are not infected because they are immature. They could be infected later, after migration of HIV to the ganglia. The researchers now seek to determine whether the macrophages of the urethra constitute reservoirs preventing the virus from being completely eliminated by tritherapy treatment. This work is important from a fundamental viewpoint and it makes it possible to shed light on how the urethra can be an entry site for HIV in men, whether they are circumcised or not. It could also lead to the development of new prevention strategies.

More information: Ganor, Y. et al. The adult penile urethra is a novel entry site for HIV-1 that preferentially targets resident urethral macrophages, *M Revol and M Bomsel*, received 14 June 2012; accepted 17 October 2012; advance online publication 28 November 2012. doi:10.1038/mi.2012.116

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