Gonorrhea manipulates an anti-infection mechanism in the female reproductive tract

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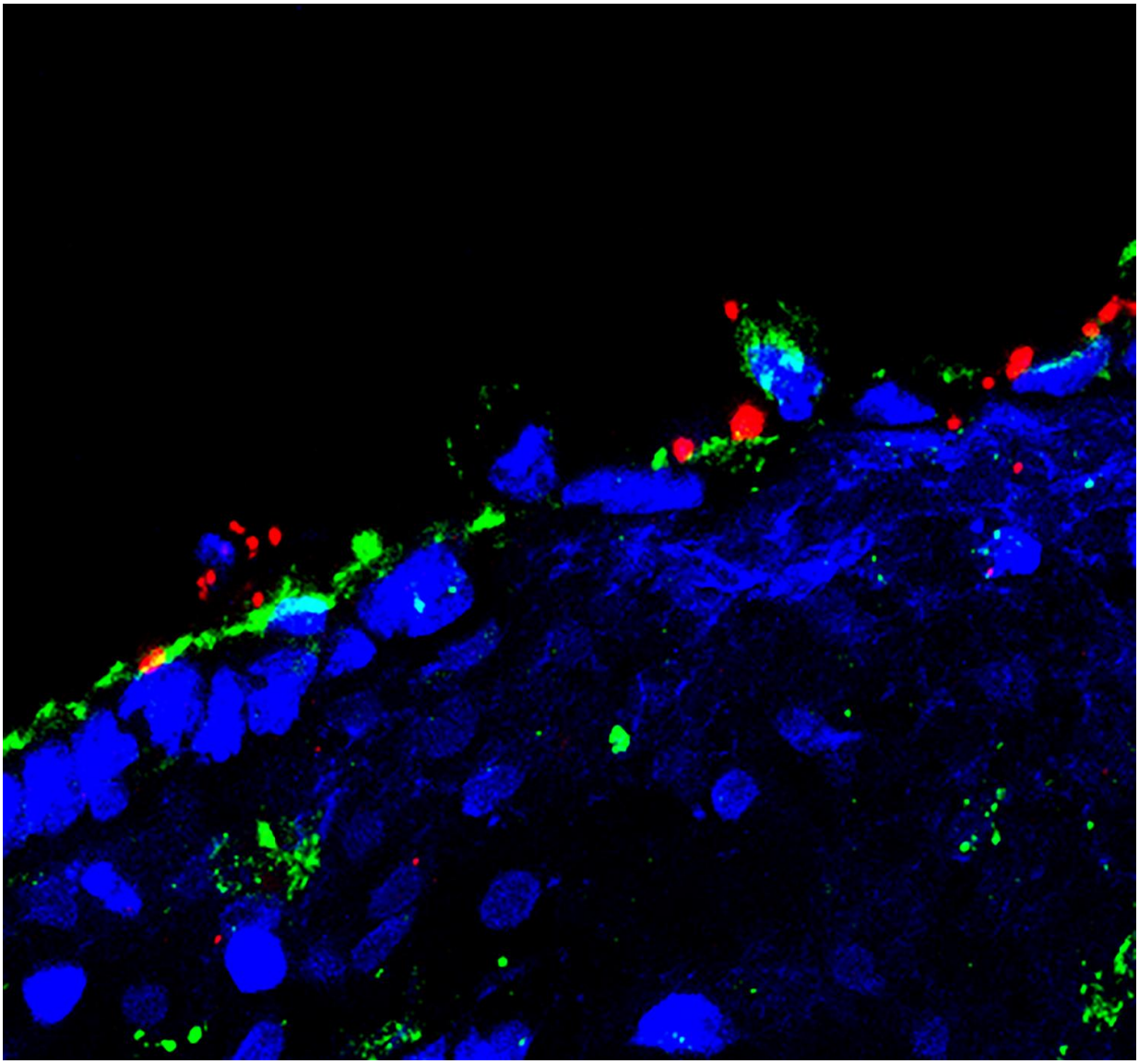

Neisseria gonorrhoeae infection in the human endocervical tissue is visualized by

immunofluorescence microscopy. Bacterial (red) colonization causes columnar endocervical epithelial cells to shed and lose the barrier function, which allows bacteria to enter the endocervical tissue. Frozen tissue sections were stained for immunofluorescence with specific antibodies to the apical junctional protein ZO1 (green) and *N. gonorrhoeae* (red) and the nuclear dye DAPI (blue). Credit: Liang-Chun Wang, Department of Cell biology and Molecular Genetics, University of Maryland, United States of America

The bacterium that causes gonorrhea infects the female reproductive tract by breaking connections between cells in the tract's protective lining, according to new research published in *PLOS Pathogens*.

Gonorrhea is a widespread sexually transmitted disease caused when *Neisseria gonorrhoeae* bacteria infect the normally protective inner lining of human genital tissues. In women, the opening of the uterus, known as the endocervix, serves as a primary infection site for *N. gonorrhoeae*. However, the strategy used by *N. gonorrhoeae* to penetrate the lining of the endocervix has been unclear.

To investigate this mechanism, Liang-Chun Wang of the University of Maryland, College Park, and colleagues needed to develop an alternative to the mouse models normally used to study gonorrhea, since they have been inadequate for this purpose. The team developed a new model using tissue samples obtained from the human endocervix.

The researchers infected the endocervix tissue, as well as lab-grown cells of the same type as those that line the endocervix, with *N. gonorrhoeae*. They then employed a variety of molecular and imaging techniques to examine the infection mechanism.

The results demonstrate that *N. gonorrhoeae* penetrates the endocervix lining by interfering with a normally protective process. Usually,

infected cells in the lining can be shed and disposed of without breaking the tight connections between cells that keep the lining uncompromised. *N. gonorrhoeae* appears to be able to break these connections and induce cell shedding, opening paths for penetration without reducing its ability to adhere to and invade the cells of the lining.

The scientists showed that *N. gonorrhoeae* causes disruption of cellular connections and cell shedding by promoting activation and accumulation of a human protein known as non-muscle myosin II. Depending on the particular genes being expressed by *N. gonorrhoeae* at any given time, the team found, it can either promote or inhibit this penetration mechanism.

This study represents the first laboratory demonstration of the penetration of *N. gonorrhoeae* into the human endocervix and provides new insights into gonorrhea infection.

More information: Wang L-C, Yu Q, Edwards V, Lin B, Qiu J, Turner JR, et al. (2017) Neisseria gonorrhoeae infects the human endocervix by activating non-muscle myosin II-mediated epithelial exfoliation. *PLoS Pathog* 13(4): e1006269. DOI: 10.1371/journal.ppat.1006269

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