New study of the molecular roots of recurrent bladder infections could lead to a vaccine

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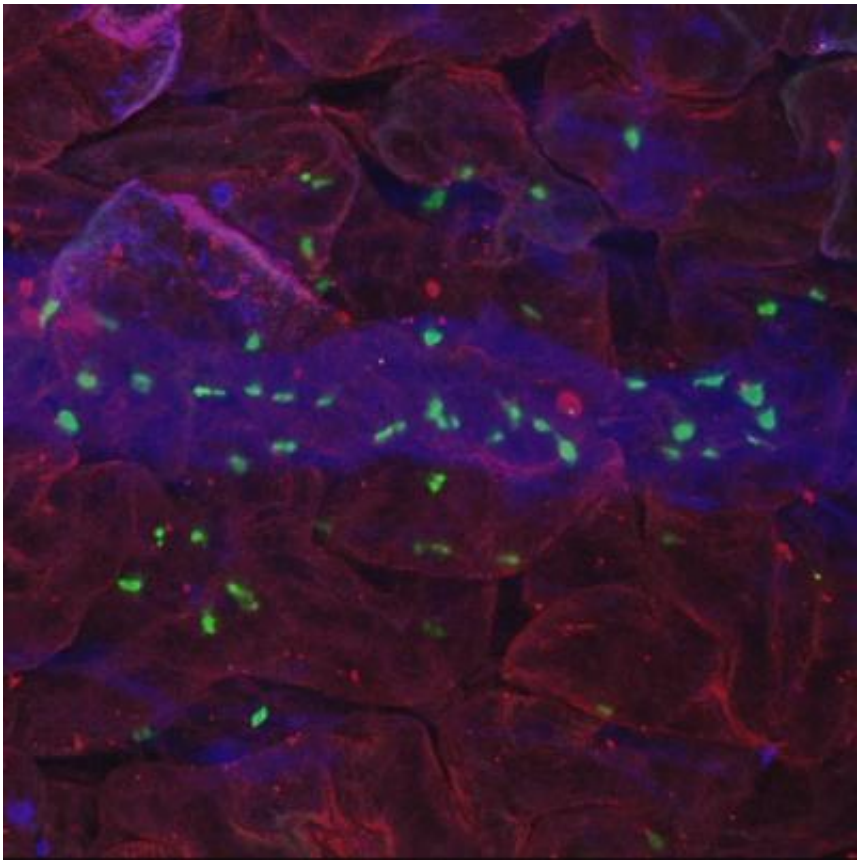
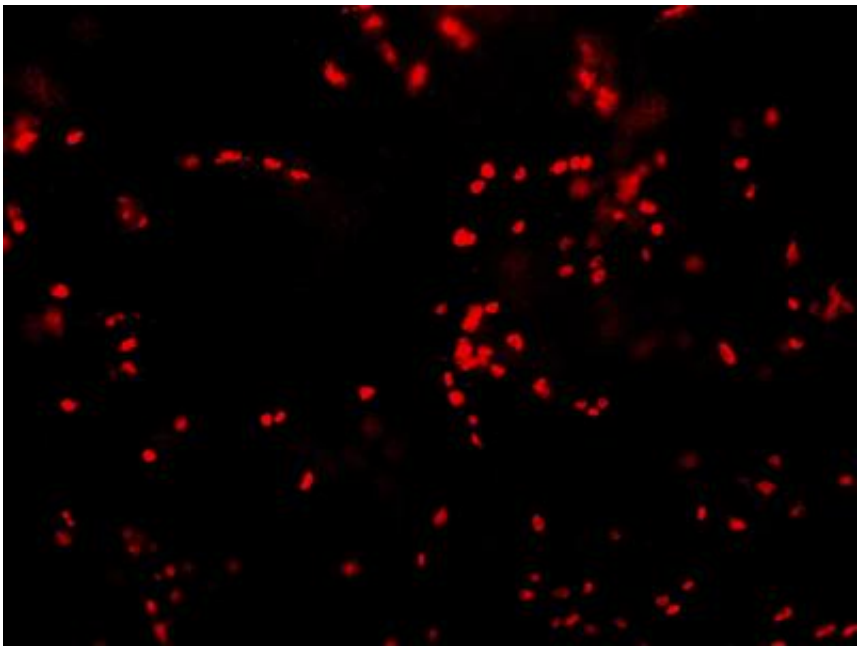


This is an array of mast cells in a whole mount image of the mouse bladder. Credit: *Immunity*, Chan et al.

Urinary-tract infections are the second most common bacterial infection in humans, and many of them are recurrent. A study published by Cell Press on February 14th in the journal *Immunity* reveals the cellular and

molecular basis of recurrent bladder infections and suggests possible treatment strategies, such as vaccines, to prevent this common problem.

"Our study shows for the first time that the bladder is unable to mount an effective immune response to bacteria, which could explain the high frequency of recurrent infections," says senior study author Soman Abraham of Duke University Medical Center. "These observations give us a new understanding of how immune responses are regulated in the bladder and may have implications for the treatment of recurrent infections."

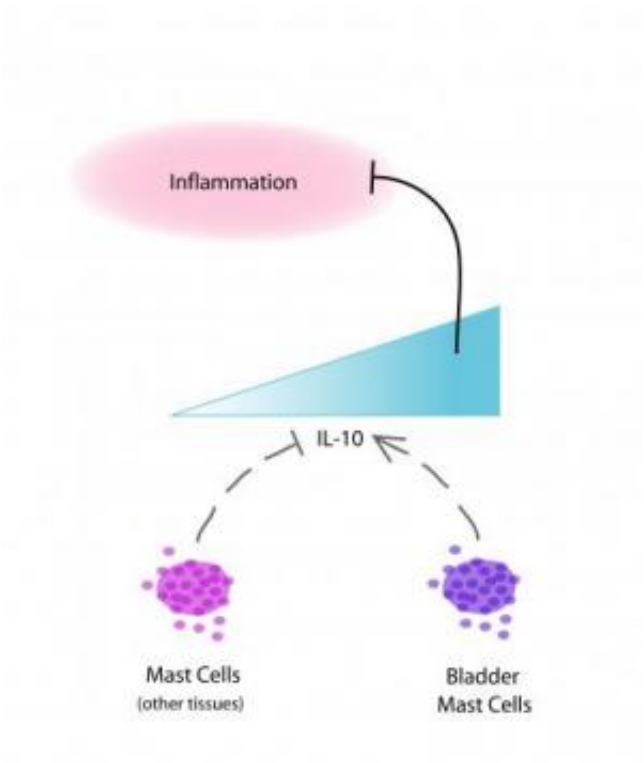


This is a cluster of mast cells found underneath superficial bladder epithelium. Credit: *Immunity*, Chan et al.

Urinary-tract infections are caused by *Escherichia coli* (*E. coli*), and the bladder in particular is prone to recurrent infections, but it is not known why. Some organs, such as the gut, that store waste products are considered "immune-privileged sites," which need to tolerate the

presence of microbes. As a result, the immune system does not activate as readily. Similarly, the bladder might require subdued immune responses to tolerate its contents (e.g., proteins in urine), prevent autoimmunity, and minimize tissue damage. If the bladder were an immune-privileged site, it might explain why it is prone to recurrent infections. But until now, the bladder has not been considered an immune-privileged site, so it has not been clear how this organ balances host defense with microbe tolerance.

In the new study, Abraham and his team found that *E. coli* persists in the bladders of mice for weeks after initial infection. These mice failed to produce antibodies against *E. coli* in response to initial infection or recurrent infection, suggesting that immune memory was impaired. The persistence of bacteria and suppressed immune responses in the bladder were mediated by the production of the molecule interleukin-10 by mast cells, which previously were known for their role in mounting immune responses against bacteria during the early stages of bladder infection. The results reveal that mast cells play a complex and key role in balancing host defense and tolerance in the bladder and in maintaining this organ as an immune-privileged site.



This is a cartoon showing how bladder mast cells are uniquely able to reduce inflammation by producing IL-10. Credit: Chan et al., *Immunity*

"The study suggests that provoking a strong immune response in the bladder through vaccination may be a possible strategy to prevent recurrent infections," Abraham says. "Moreover, the findings could influence our understanding of additional conditions involving the bladder, such as bladder cancers."

More information: doi: 10.1016/j.immuni.2012.10.019

Provided by Cell Press