

Helping bladder cells to clear urinary infections

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Researchers at EPFL have identified how an established treatment for recurrent urinary tract infections strengthens the bladder's own defenses while helping antibiotics reach bacteria hidden inside its cells.

Image: Image of bladder epithelial cells infected with *E. coli* (magenta), untreated-control (left) or treated with Uro-Vaxom® (OM-89, right). Treatment strongly increases LAMP1-positive lysosomes (cyan). 2026 EPFL- Kathrin Tomasek- CC-BY-SA 4.0

Urinary tract infections, or UTIs, are among the most common bacterial infections, caused mostly by the uropathogenic bacterium *Escherichia coli*. But even after antibiotic treatment, a large number of patients experience another UTI.

One reason is that the bacterium can enter the cells of the bladder's lining (its "epithelium") and hide there, sheltered from both antibiotics and the patient's immune system. Surviving like this, these bacteria can later multiply again and cause recurrent UTIs, which become a bigger problem since repeated antibiotic treatment risks generating antibiotic resistance.

Researchers led by Kathrin Tomasek and John McKinney at the Laboratory of Microbiology and Microtechnology at EPFL, with Christian Pasquali and Mario Romani from OM Pharma, have now identified a way to strengthen the bladder cells' own ability to eliminate these hidden bacteria. Their study, published in *PLOS Pathogens*, shows that the drug OM-89, marketed as Uro-Vaxom®, activates cellular degradation pathways in bladder epithelial cells while also increasing the amount of antibiotic that enters them.

OM-89 has been used for several decades to help prevent recurrent UTIs. It is mainly known for stimulating the immune system, but the new in vitro study reveals a second mechanism of action: a direct effect on the cells lining the bladder.

The lysosome connection

The researchers studied mouse and human bladder epithelial cells using organoid models and differentiated cell cultures. They exposed the cells to OM-89, infected them with different strains of uropathogenic *E. coli* and treated them with antibiotics. They then tracked bacterial survival, antibiotic uptake and changes in cellular pathways involved in destroying intracellular material.

The results pointed to lysosomes, the acidic compartments inside cells that break down unwanted material. OM-89 increased lysosomal acidification as well as the activity of lysosomal enzymes.

When the researchers blocked lysosomal acidification, OM-89's protective effect was lost. This showed that lysosomal activity is directly involved in reducing bacterial regrowth in recurrent UTIs.

Helping antibiotics reach persistent bacteria

At the same time, OM-89 increased the accumulation of antibiotics inside bladder epithelial cells. When OM-89 and antibiotics were co-administered in the experimental models, bacterial killing increased and bacterial regrowth after antibiotic removal decreased.

This effect extended across different antibiotic classes and several bacterial strains, including clinical samples from patients.

The researchers were also able to reproduce key effects in both mouse and human bladder epithelial models, while analysis of independent human bladder datasets linked lysosomal activity with immune and antibacterial pathways.

“We found that OM-89 doesn't just stimulate the innate immune system as previously assumed,” says Tomasek. “It acts directly on bladder cells, strengthening their degradation pathways so they can destroy hidden bacteria more effectively while also helping antibiotics reach those bacteria—together reducing regrowth of the bacteria after treatment ends.”

The findings point toward a host-directed approach to recurrent infection: rather than targeting bacteria alone, treatment could also reinforce the antimicrobial machinery of the infected tissue itself.

More broadly, the study identifies lysosomal pathways in the bladder epithelium as a potential target for future treatment combinations designed to improve antibiotic outcomes.

Christian Pasquali, Senior Scientific Liaison Director at OM Pharma and former Head of Preclinical Research says: “While the results come from preclinical models and do not change the approved indication or use of Uro-Vaxom®, they deepen our understanding of how OM-89 may help strengthen the bladder's natural defenses against recurrent infection and reinforce the scientific foundation supporting its use.”

Other contributors

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