

## New strategy to combat cystitis

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One in three women will be faced at least once in her life with cystitis, for some the start of a constantly recurring infection. Cystitis is caused by *Escherichia coli* bacteria which fasten on to the wall of the bladder by means of thread-like structures (pili). Han Remaut of the VIB Department for Structural Biology Brussels, Vrije Universiteit Brussel reveals for the first time the complex interactions which lead to the formation of these pili. This knowledge can be used to develop new antibiotics to treat infections of the urinary tract.

### Cystitis

Around 80% of infections of the urinary tract are caused by the *Escherichia coli* bacteria, gram-negative rod-like bacteria. Although these bacteria form part of normal intestinal flora, virulent types can penetrate the bladder via the urethra and lead to urinary tract infections. These infections occur more often in women than in men and account for a large number of hospital-acquired infections, especially in the case of catheterized patients. Treatment consists of using existing antibiotics. However, the current generation of antibiotics is losing its power to fight these bacteria. Especially problematic are recurrent infections. There is an urgent need for new antibiotics.

### Bacteria adhere to the cells of the urinary bladder

Bacteria can adhere to a surface due to their hair-like structures, known as pili or fimbriae. In the case of uropathogenic *E. coli*, type 1 pili occur which consist of four different sub-entities. The biosynthesis (formation)



of these pili takes place through a conserved mechanism (the <u>chaperone</u> /usher biosynthesis route). As type 1 pili are responsible for the uropathogenic *E. coli* adhering to the host cells, these are promising targets for new antibacterials.

## Structural biological techniques to investigate pili formation

Han Remaut, together with colleagues working for the Institute of Structural and Molecular Biology, University of London, is investigating the mechanism responsible for the biosynthesis of these pili. For this purpose, they are using X-ray diffraction - the standard technique for determining the structure of proteins. Detailed knowledge about the structure of proteins is necessary to gain an insight into how they function.

Han Remaut and colleagues were the first to successfully image the assembly complex leading to pili biosynthesis. Furthermore, this is also the first snapshot of a protein transporter in action.

# New antibiotics for the treatment of infections of the urinary tract

This detailed knowledge about the biosynthesis of type 1 pili from *E. coli* can form the basis for the development of medicines which block the formation of the pili. If bacteria can no longer cling to the epithelial cells of the bladder, they will no longer be able to cause an <u>infection</u>. The mechanism responsible for E.coli attaching to the bladder is also used by other <u>bacteria</u>. As a result, this research can also contribute to the fight against other infectious diseases such as food poisoning or traveler's diarrhea.



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