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Researchers find new strategy to combat bacterial infections

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Increasing numbers of bacteria are developing antibiotic resistance. This forms a significant challenge in the battle against bacterial infections. Alvin Lo and Han Remaut (VIB/Vrije Universiteit Brussel) have identified a chemical substance with the potential of acting as a new drug to treat bacterial infections, particularly urinary tract infections. In contrast to the most popular antibiotics, this candidate drug does not destroy pathogenic bacteria, but rather disarms them. The benefit of this new strategy is that other (useful) bacteria are unharmed and there is a lower risk of the development and spread of resistance by bacteria.

Han Remaut (VIB/Vrije Universiteit Brussel): "It gives great satisfaction to see that years of fundamental research can result in a new strategy for the treatment of bacterial infections. Instead of killing the pathogenic bacteria, we have disarmed them; an approach with possible benefits compared to the current antibiotics."

Attachment of bacteria: a necessary evil in the pathogenic process

Many pathogenic bacteria attach to a cell before they can infect it, usually in a very similar manner. The research group led by Han Remaut has focused on a new approach in combating infections, which has succeeded in inhibiting this crucial step and thereby disarming the bacteria. In this case, they took aim at the bacterium that causes almost 80 % of urinary tract infections: the uropathogenic E. coli.

In order to prevent themselves being flushed out in the urine, E.coli bacteria attach themselves with the aid of hair-like structures: 'type 1 pili'. In 2011, Han Remaut and colleagues were the first to describe the pilus formation mechanism. Further research was necessary to translate these important structural insights into possible new drugs.

Structural insights used in the search for new drugs

Alvin Lo and colleagues from Remaut's group started screening databases of chemical components in search of chemical molecules that could inhibit pilus formation. This yielded an inhibitor that interferes with an essential step in the assembly process of the pili. As a test, they exposed E.coli bacteria to this component, resulting in the bacteria no longer being able to produce pili. These "naked" bacteria were no longer able to attach to their host.

Alvin Lo (VIB/Vrije Universiteit Brussel): "E.coli is not the only pathogenic bacterium that uses this mechanism for attachment. If further research reveals that our molecule does indeed efficiently combat urinary tract infections, then we can also use this strategy in the fight against other infectious diseases such as food poisoning or traveler's diarrhea."

More information: "Suppression of type 1 pilus assembly in uropathogenic Escherichia coli by chemical inhibition of subunit polymerization." Alvin W. H. Lo, Karen Van de Water, Paul J. Gane, A.W. Edith Chan, David Steadman, Kiri Stevens, David L. Selwood, Gabriel Waksman4, Han Remaut. *J. Antimicrob. Chemother*. (2013) First published online: December 8, 2013. DOI: 10.1093/jac/dkt467

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