Molecular scissors technique to prevent the spread of antibiotic resistance genes in bacterial communities

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The decreased efficacy of antibiotics is a global problem and hinders the therapeutic outcome of previously treatable bacterial infections. In Europe, an estimated 33,000 people die due to antibiotic resistant

bacterial infections annually. Furthermore, these bacteria cause notable financial losses, for example, in animal husbandry. Due to the largely diminished pipeline for the development of new antibiotics, alternative treatments are urgently needed against antibiotic-resistant bacterial infections. In her doctoral dissertation at University of Jyvaskyla, Pilvi Ruotsalainen developed molecular gene scissors that target and destroy antibiotic resistance genes and prevent their spread in bacterial communities.

These mobile gene scissors can spread from one bacterium to another in bacterial communities and destroy antibiotic resistance genes by cutting DNA. As a result, the bacterium's sensitivity to antibiotics is restored and it is unable to spread the resistance gene to new bacteria.

Besides developing new treatment options, it is essential to understand how antibiotic resistance spreads in bacterial communities to prevent dispersal, says Pilvi Ruotsalainen. In her thesis, Ruotsalainen examined the spread of antibiotic resistance genes and the effect of different variables in their spread to sensitive bacteria.

Antibiotic resistance genes often reside in circular DNA molecules called plasmids, which can spread from one bacteria to another by conjugation. The results indicate that plasmids can rescue antibiotic sensitive bacteria, even in lethal drug concentrations. Therefore, these sensitive bacteria can potentially acquire antibiotic resistance "on the fly," even during otherwise effective antibiotic treatment.

"The spread of resistance plasmids into bacteria targeted with antibiotics would nullify the treatment outcome. Thus, it is essential to eliminate the antibiotic resistance genes, for example, from the symbiotic and harmless bacteria of gut microflora, as well. Perhaps in the future, we could use our mobile gene scissors for this," Ruotsalainen says.

Phages for treating bacterial infections

Bacterial viruses known as bacteriophages could also be used as a new treatment option to supplement antibiotics. Phages were first used to treat bacterial infections at the beginning of 20th century in the West. However, the discovery of antibiotics replaced phages as antimicrobials.

"The antibiotic crisis has raised new interest in phages. They are natural enemies of bacteria and can effectively eliminate antibiotic resistant bacteria. Our results showed that, if required, new phages can be readily isolated from environmental reservoirs for *Enterobacteriaceae* such as *Escherichia coli* and *Klebsiella pneumoniae*," Ruotsalainen says.

M.Sc. Pilvi Ruotsalainen defends her doctoral dissertation in Cell and Molecular Biology "Extended-spectrum β-lactamase-producing Enterobacteriaceae: risks during antibiotic treatment and potential solutions to cure carriage" on Friday 6th of September at 12 o'clock at Ambiotica (YAA303) at Department of Biological and Environmental Science (Survontie 9, Ylistönrinne). Opponent is Professor Mikael Skurnik from University of Helsinki and Custos is Docent Matti Jalasvuori from University of Jyvaskyla. The doctoral dissertation is held in Finnish.

More information: Enterobacteriaceae: risks during antibiotic treatment and potential solutions to cure carriage. urn.fi/URN:ISBN:978-951-39-7819-8

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