

Active substance identified for the prevention of chlamydial infections

Pentamidine as potential prophylaxis against bacterial sexually transmitted diseases

Despite the significant increase in sexually transmitted diseases in recent years, there is currently no vaccine available against common bacterial pathogens such as chlamydia. In the search for ways to prevent infection, a research team from MedUni Vienna and CeMM has identified the active substance pentamidine as a promising candidate for the prophylaxis of chlamydial infections and possibly other bacterial sexually transmitted diseases. The study was recently published in the scientific journal *Cell Reports Medicine* (DOI: [10.1016/j.xcrm.2024.1016439](https://doi.org/10.1016/j.xcrm.2024.1016439))

In order to find previously unknown substances for the treatment of chlamydial infections, the scientific team led by Georg Stary (Professor of Dermatology at MedUni Vienna and Adjunct PI at CeMM) screened a comprehensive compilation of 2,200 active substances. While 28 of these significantly reduced the growth of chlamydia, one of the substances was even able to prevent infection: "In the mouse model, pentamidine was the only substance we tested that proved to be effective against chlamydia even at very low concentrations, both when applied systemically and locally in the genital area," reports principal investigator Georg Stary on the results.

Further investigations in the cell model revealed that chlamydia require the metabolism of the host cells for their own growth, which can be used as a new target against chlamydia. "The substance we identified suppresses the growth of the intracellular bacteria by inhibiting the metabolism of the host cells," says Georg Stary, explaining the mode of action of pentamidine, an antiprotozoal agent that is already widely used to treat certain infectious diseases. In addition to chlamydia, tests have shown that pentamidine also blocks the growth of *Neisseria gonorrhoeae*, the pathogen that causes gonorrhoea. "Lactobacilli as representatives of the vaginal flora, on the other hand, were still able to multiply at a comparable pentamidine concentration, which indicates good tolerance," emphasises first author Katja Knapp (PhD Student at the Department of Dermatology at MedUni Vienna and CeMM).

For years, there has been a significant increase in sexually transmitted infections, which can lead to massive problems for those affected due to antibiotic resistance or late complications. There are still no authorised vaccines against common bacterial pathogens such as chlamydia or *Neisseria*

gonorrhoeae. Several studies have investigated the antibiotic doxycycline for use after sexual contact (post-exposure prophylaxis) to prevent bacterial sexually transmitted diseases in high-risk groups. However, as there is a risk that both the pathogens and strains of the healthy microbiome can develop resistance to doxycycline over time, the newly identified active ingredient pentamidine represents a promising alternative. "Local application as a prophylaxis for chlamydial infections and possibly also other sexually transmitted infections could be recommended, especially for people with risk behaviour for infection with sexually transmitted pathogens," says Georg Stary in the run-up to further studies with pentamidine as a template for developing structurally similar substances that specifically target genital pathogens and are suitable for clinical application. In the meantime, the current findings are being pursued by MedUni Vienna for possible patenting.

Pictures attached

Photo: First author Katja Knapp and last author Georg Stary © Wolfgang Däuble / CeMM
Image: HeLa cells treated with Pentamidine (right) and controls with Chlamydia growth (in green, left) © Katja Knapp

The Study "Combination of compound screening with an animal model identifies pentamidine to prevent Chlamydia trachomatis infection" was published in *Cell Reports Medicine* on July 9, 2024. DOI: 10.1016/j.xcrm.2024.101643

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Funding: This study was supported by the Austrian Science Fund (FWF) and the Medical Scientific Fund of the Mayor of the City of Vienna.

The **CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences** is an international, independent and interdisciplinary research institution for molecular medicine under the scientific direction of Giulio Superti-Furga. CeMM is oriented towards medical needs and integrates basic research and clinical expertise to develop innovative diagnostic and therapeutic approaches for precision medicine. Research focuses on cancer, inflammation, metabolic and immune disorders, and rare diseases. The Institute's research building is located on the campus of the Medical University and the Vienna General Hospital.

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The Medical University of Vienna (MedUni Vienna) is one of the longest-established medical education and research facilities in Europe. With almost 8,000 students, it is currently the largest medical training centre in the German-speaking countries. With more than 6,000 employees, 30 departments and two clinical institutes, twelve medical theory centres and numerous highly specialised laboratories, it is one of Europe's leading research establishments in the biomedical sector. MedUni Vienna also has a medical history museum, the Josephinum.

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