MOI Project 2

Investigation of the antiphage properties of aminoglycoside antibiotics and impact of bacterial (self-)resistance mechanisms

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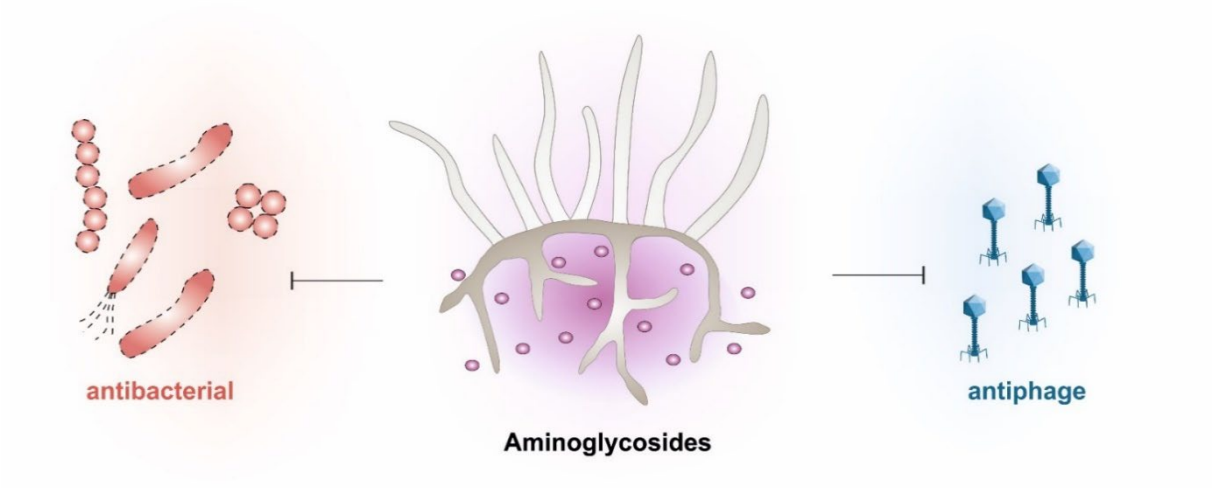
Bacteria of the actinobacterial genus *Streptomyces* produce a variety of bioactive molecules with antibacterial, fungicidal or immunosuppressive effects. However, the function of these molecules in the context of viral infections caused by bacteriophages (phages for short) has hardly been investigated to date. It has recently been shown that DNA-intercalating substances of the class of anthracyclines as well as various aminoglycoside antibiotics block infection by phages in a broad range of bacterial species at an early stage of infection (1, 2).

Due to the antibacterial properties of these substances, bacterial natural product producers have diverse mechanisms of intrinsic resistance. This includes aminoglycoside-modifying enzymes, 16S rRNA methyltransferases and efflux systems. The aim of this project is to investigate the influence of antiobiotic resistance in the context of the antiviral properties of aminoglycoside antibiotics and to further elucidate their mechanism of action.

These studies will offer crucial insights into the molecular mechanisms of action of antiviral secondary metabolites, contributing to a deeper understanding of their role as part of the bacterial immune system.

Methodology

Molecular Microbiology, Next-generation sequencing, Fluorescence microscopy & live cell imaging in microfluidic chips



References

(1) Kever L, Hardy A, Luthe T, Hünnefeld M, Gätgens C, Milke L, Wiechert J, Wittmann J, Moraru C, Marienhagen J, **Frunzke J** (2022) Aminoglycoside antibiotics inhibit phage infection by blocking an early step of the phage infection cycle. *mBio*, doi.org/10.1101/2021.05.02.442312.

(2) Luthe T, Kever L, Thormann K, and Frunzke J (2023) Bacterial multicellular behaviour in antiviral defense. *Current Opinion in Microbiology*, doi: 10.1016/j.mib.2023.102314.