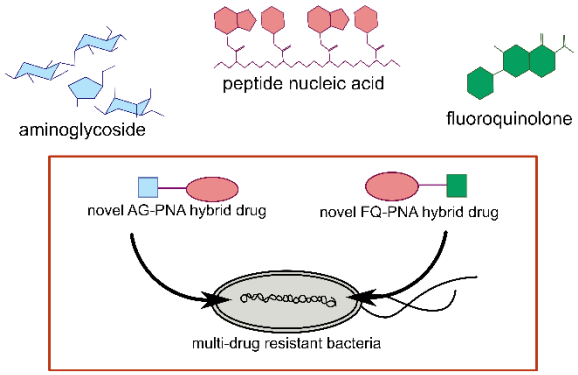
Conjugates of peptide nucleic acids with aminoglycosides and fluoroquinolones as a novel strategy to target multi-drug resistant bacteria



Antimicrobial resistance is a growing threat in global healthcare and medicine. This term refers to the ability of microorganisms to withstand the effects of drugs that are used to kill them or stop their growth. This means that infections caused by these microbes may become impossible to treat. The serious problem of multi-drug resistant bacteria requires action from healthcare providers, policymakers, and the scientific community. Due to this, extensive research to find new effective drugs with a novel mode of action is needed. Unfortunately, the process of developing new medicaments is very time-consuming and costly. A potential strategy to solve this problem may be applying already existing antibiotics but connecting them to another active agent to form one dual-acting drug.

One of the promising candidates for this approach is **peptide nucleic acid (PNA).** This modification of the naturally occurring DNA or RNA has many advantages like improved biostability, and what is most important – the ability to effectively bind to natural nucleic acids. Properly designed PNA sequences can bind to fragments of bacterial messenger RNA that encodes crucial proteins. This binding block their translation (and thus the production of an essential protein) and in consequence inhibit bacterial growth which leads to bacterial cell death.

The main objective of this project is the covalent conjugation of PNA with already known antibiotics – aminoglycosides (neomycin and amikacin) and fluoroquinolones (ciprofloxacin and levofloxacin) and testing their antimicrobial activity on different drug-resistant bacterial strains.

These antibiotic classes were previously successful, but the spreading antibiotic resistance decreased their efficiency. Therefore, PNA-based conjugates planned in this project may be a promising strategy to restore their activity and become an important tool in the fight against multi-drug resistant bacteria.