

Targeted Protein Degradation in Bacteria Contributes to Antibiotic Efficacy

The solution is a method to develop new antibiotic proteolysis targeting chimeras (PROTACs) that target proteins of interest for degradation in bacteria to counteract antibiotic resistance.

What is the Problem?

Proteolysis targeting chimeras (PROTACs) are heterobifunctional chemicals that simultaneously engage two proteins, a target protein of interest and an E3 ubiquitin ligase. PROTACs are highly effective at degrading proteins of interest and have the potential to overcome resistance to therapeutic treatments. However, PROTACs are largely untested in prokaryotic systems because bacteria lack the mammalian ubiquitin system required of PROTAC design. To address the continuing threat of antimicrobial resistance, there is a need to develop new antibiotic chemistries to actively counteract microbial resistance.

What is the Solution?

The solution is a method to develop new antibiotic PROTACs (AnTACs) that target proteins of interest for degradation in bacteria to counteract antibiotic resistance. AnTACs are composed of a classic target engagement strategy (antibiotic), chemical protease degrons, and variable linker chemistries. The antibiotic component of the AnTAC will kill bacterial cells and proteins of interest will simultaneously be targeted for degradation. Proteins responsible for antibiotic resistance, such as beta-lactamases, will also be targeted for degradation by AnTACs. Finally, AnTACs are highly likely to interfere with bacterial protein homeostasis, a possible new route of antibiotic activity.

What is the Competitive Advantage?

The competitive advantage of this technology lies in its ability to simultaneously kill bacterial cells and target proteins responsible for antibiotic resistance for chemical degradation. AnTACs are completely new means to addressing the issue of antibiotic resistance and have clinical potential to treat bacterial infections. They also present an exciting set of potential tool compounds for research use. As the global antibiotics market is valued at \$50.9 billion in 2023 with an expected CAGR of 4.2%, there is a significant opportunity for this technology to advance the field of antibiotic therapies for infectious diseases.

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Category

Therapeutics/Infection
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