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ANTIBIOTICS RESISTANCE

Concept article.

Teixobactin an antibiotic from soil bacteria for fighting Multiple Antibiotic Resistance phenomena.

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Abstract

The emergence of antibiotic-resistant bacteria is a growing threat to public health, and there is an urgent need for new antibiotics with novel mechanisms of action. Teixobactin is a promising relatively new antibiotic that was discovered in 2015 with a unique mechanism of action that makes it effective against multiple antibiotic-resistant bacteria. The antibiotic is produced by *Eleftheria terrae*, a Gram-negative bacterium, and is structurally distinct from other antibiotics, containing nonstandard amino acid residues. Teixobactin has shown potential in killing highly pathogenic and multidrug-resistant gram-positive bacteria, such as Methicillin-resistant Staphylococcus aureus (MRSA), Oxacillin-resistant Staphylococcus aureus (ORSA), and Mycobacterium tuberculosis (MTB). This article provides an overview of the discovery and potential uses of Teixobactin in the context of combating antibiotic resistance.

Key words: Teixobactin, Antibiotics, Soil bacteria, Antibiotic-resistance, MRSA, ORSA, MTB, Drugs, Diseases

Introduction

Antibiotic-resistant bacteria pose a significant threat to public health worldwide, as they are responsible for an increasing number of infections that are difficult to treat due to bacteria evolving mechanisms to evade the effects of commonly used antibiotics. The overuse and misuse of antibiotics have contributed to this problem, leading to the emergence of multidrug-resistant bacteria. In response to this problem, scientists have been searching for new antibiotics with novel mechanisms of action that can effectively kill antibiotic-resistant bacteria. To illustrate the gravity of the situation, it's perhaps important to mention the large preclinical development projects, as of 1 May 2019, 407 antibacterial projects from 314 institutions organized in pipeline discovery tool, Figure 1. The pipeline's focus is on Gram-negative pathogens, particularly bacteria on the WHO priority bacteria list. Teixobactin is one such antibiotic, which was discovered in 2015, harvested from soil bacteria, has shown potent activity against a range of gram-positive bacteria that are resistant to multiple antibiotics.

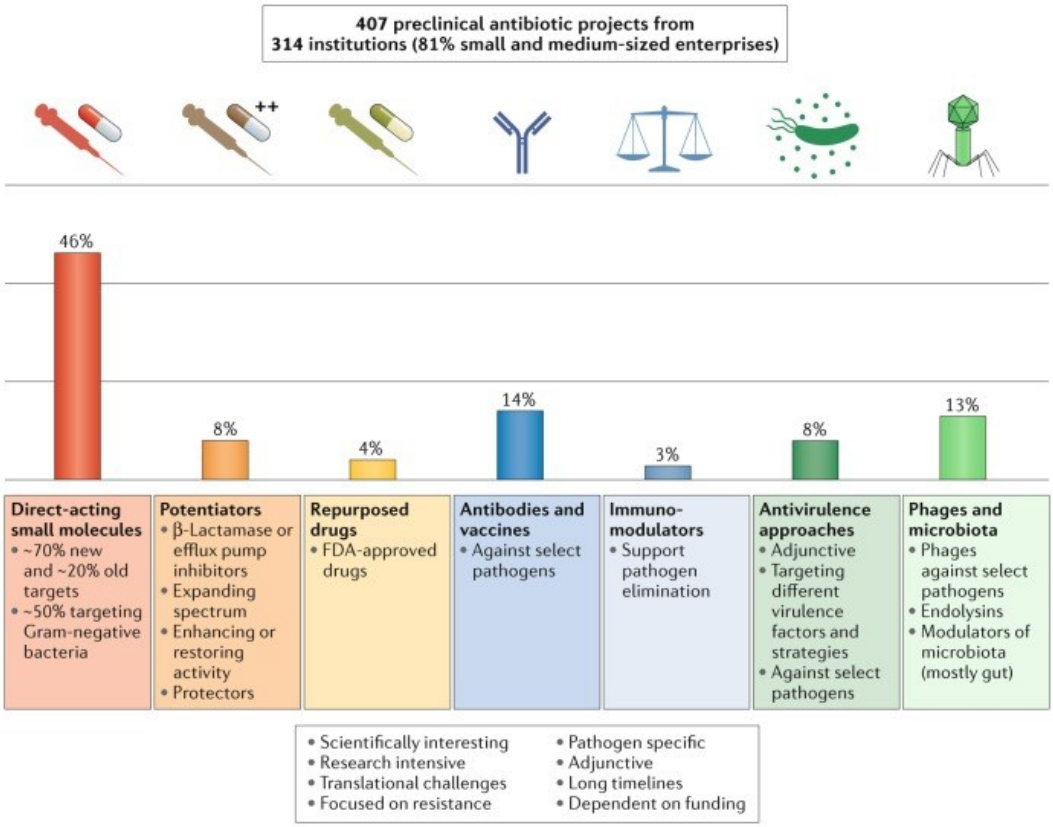

Figure 1. Overview of the preclinical antibacterial pipeline.
Source: The global preclinical antibacterial pipeline
https://www.nature.com/articles/s41579-019-0288-0

Discovery of Teixobactin

Teixobactin was discovered in 2015 by researchers from Northeastern University and NovoBiotic Pharmaceuticals, Ling et al., who developed a novel technique to isolate bacteria from soil samples, Figure 2. The bacterium that produces Teixobactin was named *Eleftheria terrae* and it is a gram-negative bacterium that had not been grown before in laboratory conditions, Figure 3. Teixobactin is a 'peptide-like' secondary metabolite produced by the bacterium, and it has a unique structure that includes several nonstandard amino acids.

Teixobactin has a unique mechanism of action, targeting cell wall biosynthesis and lipid II, a precursor for the peptidoglycan layer in bacterial cell walls. The antibiotic has shown potent activity against a range of highly pathogenic and multidrug-resistant gram-positive bacteria, including MRSA, ORSA, and MTB, without detectable resistance development.

Figure 2. Isolation of bacteria from soil samples using special
Source: Promising antibiotic discovered in microbial 'dark matter'
https://www.nature.com/articles/nature.2015.16675

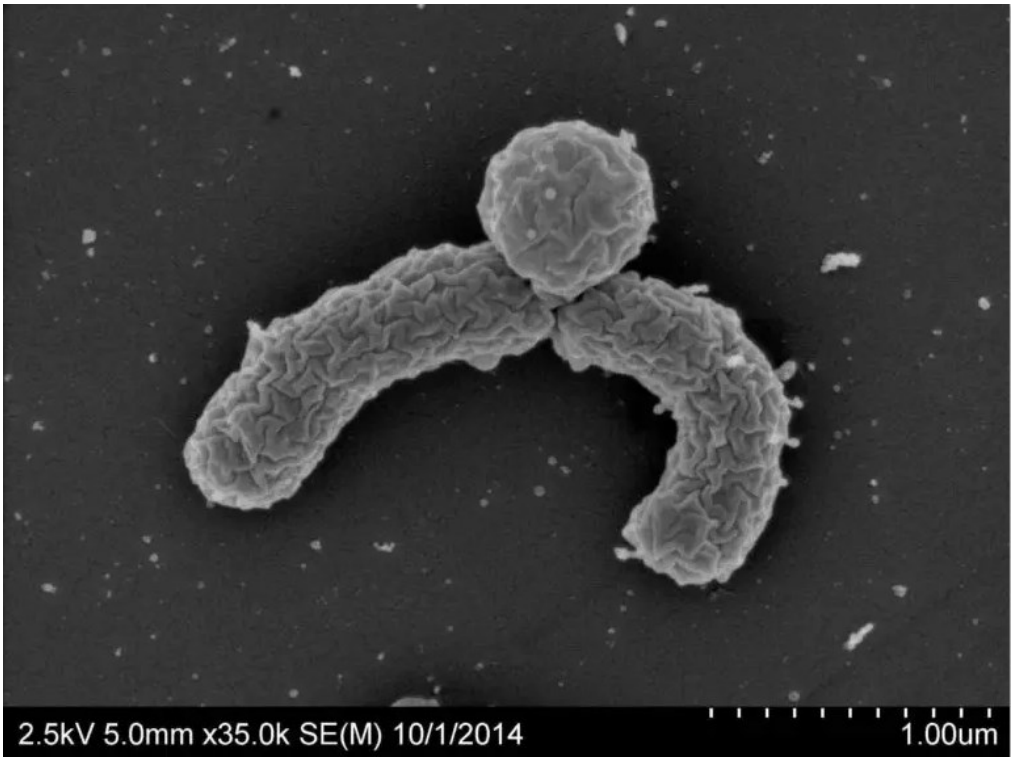

Figure 3. The soil bacteria *Eleftheria terrae*
Source : Teixobactina: un nuovo antibiotico contro i superbatteri ?
https://www.microbiologiaitalia.it/batteriologia/teixobactina-un-antibiotico-superbatteri/

Teixobactin Structure

The structural features of Teixobactin are quite interesting. It contains nonstandard amino acid residues, including three d-amino acids and l-allo-enduracididine, which makes it unique from other antibiotics, Figure 4. The distinctive pharmacological profile of Teixobactin is thought to contribute to its high activity against many known multi-antibiotic-resistant bacteria, as it adopts a different binding mode than most antibiotics, making it harder for the bacteria being attacked to develop resistance.

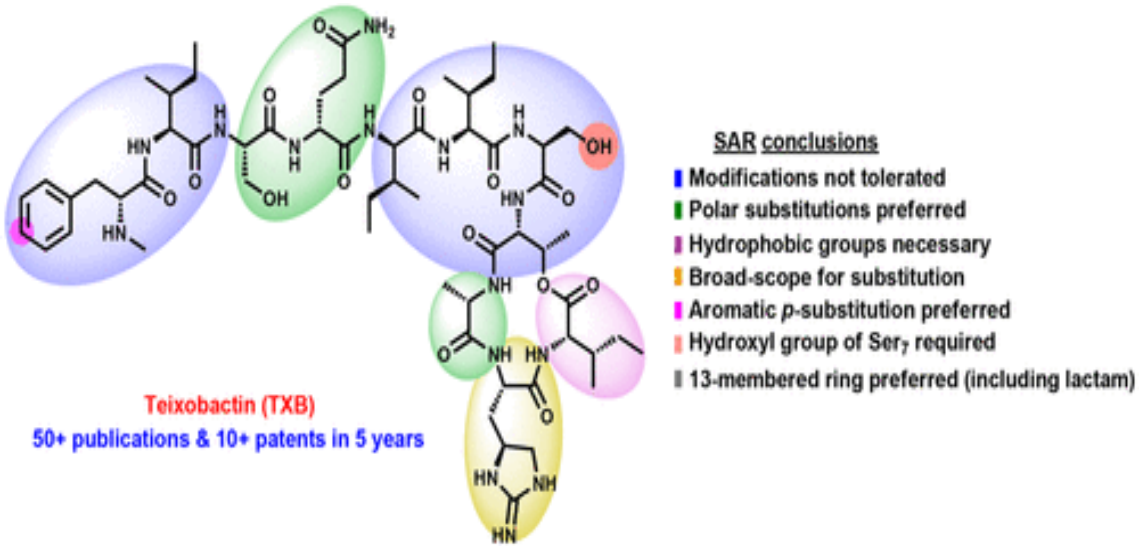

Figure 4. The structure of the antibiotic Teixobactin.
Source: Teixobactin: A Paving Stone toward a New Class of Antibiotics? https://pubs.acs.org/doi/10.1021/acs.jmedchem.0c00173

Mechanism of action

Teixobactin targets the cell wall of bacteria, preventing them from growing and replicating. This is in contrast to most antibiotics, which target specific proteins or enzymes in bacteria. Targeting the cell wall makes it much harder for bacteria to develop resistance, as the cell wall is a critical component of their survival.

Upon binding of lipid II, Teixobactin first forms small β-sheets then elongates into fibrils that eventually associate into lateral fibrillar sheets, obstructing biosynthesis of peptidoglycan and causing membrane defects, Figure 5. Teixobactin has been shown to be active against a range of gram-positive bacteria, including MRSA, ORSA, and MTB.

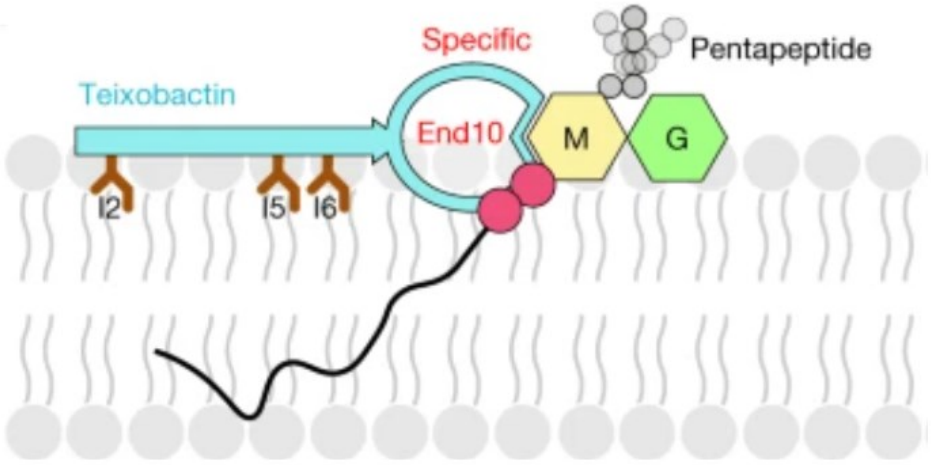

Figure 5. Illustration of the differential binding modes of natural Teixobactin.
Source: refer to Fig.3f at Model of the mode of action of teixobactin, https://www.nature.com/articles/s41586-022-05019-y

Pharmacology and potential for clinical use

Teixobactin has shown promise as a new antibiotic for the treatment of antibiotic-resistant infections. It has been shown to be active against a range of gram-positive bacteria, including those that are resistant to multiple antibiotics. Its unique mechanism of action and unusual structure make it difficult for bacteria to develop resistance, which is a major advantage over existing antibiotics. However, Teixobactin is still in the early stages of development, and further studies are needed to fully characterize its pharmacology and potential for clinical use.

The unique action mechanism of Teixobactin and its potency against multidrug-resistant bacteria make it a promising candidate for clinical use. Research is ongoing towards further exploring the potential uses of Teixobactin including its efficacy against other bacterial strains and its potential as a treatment for infections in humans.

Conclusion

Teixobactin is a promising new antibiotic that has the potential to revolutionize the way we combat antibiotic-resistant infections. Its unique mechanism of action and unusual structure make it a powerful tool in the fight against antibiotic-resistant bacteria. However, more research is needed to fully understand its pharmacology and potential for clinical use. With continued research and development, Teixobactin could eventually become an important new treatment option for patients with hard-to-treat infections.

The discovery of Teixobactin offers hope for the development of new antibiotics with novel mechanisms of action that can effectively combat antibiotic-resistant bacteria. Further research is needed to fully understand the potential uses of Teixobactin and to develop it into a clinically effective treatment.

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