

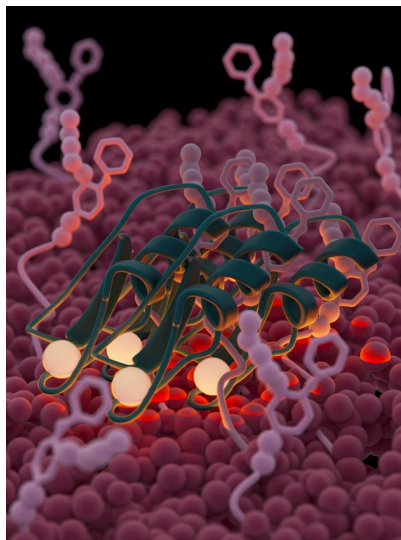
## Cracking Nature's Recipes to Design Lipid-Targeting Antibiotics

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Antimicrobial resistance is a global health threat, calling for new antibiotics. Good candidates could be peptide-based compounds that target special lipids that only exist in bacterial, but not in human cell membranes. These drugs kill pathogens without detectable resistance, which has generated considerable interest.

Here, using an integrative structural biology approach, we show that drugs that target special lipids in bacterial membranes use sophisticated supramolecular killing mechanisms<sup>1-3</sup>.



1. Shukla, R. et al. *Teixobactin kills bacteria by a two-pronged attack on the cell envelope*. *Nature* 608, 390-396, doi:10.1038/s41586-022-05019-y (2022).
2. Shukla, R. et al. *An antibiotic from an uncultured bacterium binds to an immutable target*. *Cell* 186, 4059-4073.e4027, doi:10.1016/j.cell.2023.07.038 (2023).
3. Jekhmane, S. et al. *Host defence peptide plectasin targets bacterial cell wall precursor lipid II by a calcium-sensitive supramolecular mechanism*. *Nature Microbiology* 9, 1778-1791, doi:10.1038/s41564-024-01696-9 (2024).