

A new antibiotic kills pathogens without detectable resistance

Ling and Schneider et al, 2015
Nature doi:10.1038/nature14098

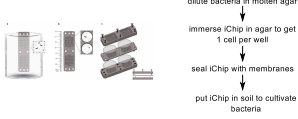
"Teixobactin is the first new class of antibiotic announced in decades."
-forbes.com

uncultivated bacteria could be a source of novel compounds and antibiotics

99% of bacteria cannot be isolated from single cells on petri dishes.

If an initial colony can be grown, 50% of bacterial can then be cultured on petri dishes.

in situ cultivation of bacteria with iChip

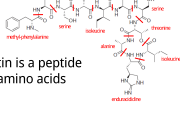


screened 10,000 isolates for ability to inhibit *S. aureus* growth in petri dishes

16S tree of novel isolate, *Eleftheria terrae*



isolated active compound and determined its structure



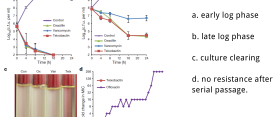
teixobactin is a peptide of 11 amino acids

teixobactin encoded by 2 non-ribosomal peptide synthase genes



proteins synthesize a peptide independent of ribosome domains in synthases are same order as amino acids in teixobactin

Teixobactin lyses *S. aureus* cultures

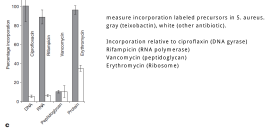


Teixobactin kills gram positive, but not gram negative bacteria

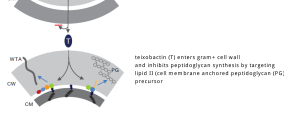
Organism and genotype	Teixobactin MIC (μg/ml)
<i>S. aureus</i> (M554)	0.25
<i>S. aureus</i> + 3 DMS	0.25
<i>S. aureus</i> (M554)	0.25
<i>Enterococcus faecalis</i> (IRE)	0.5
<i>Enterococcus faecium</i> (IRE)	0.5
<i>Streptococcus pneumoniae</i> (penicillin ^r)	0.03
<i>Streptococcus pyogenes</i>	0.06
<i>Streptococcus agalactiae</i>	0.12
<i>Vibrio group streptococci</i>	0.12
<i>S. anthracis</i>	0.06
<i>Clostridium difficile</i>	0.005
<i>Propionibacterium acnes</i>	0.06
<i>M. tuberculosis</i> H37Rv	0.125
<i>Pseudomonas aeruginosa</i>	4
<i>Neisseria meningitidis</i>	2
<i>Escherichia coli</i>	2.5
<i>Escherichia coli</i> (GmES)	2.5
<i>Pseudomonas aeruginosa</i>	>32
<i>Klebsiella pneumoniae</i>	>32

MIC=minimum inhibitory concentration

Teixobactin inhibits peptidoglycan synthesis similar to vancomycin



Model of teixobactin action



Mice infected with *S. aureus* survive if given teixobactin

