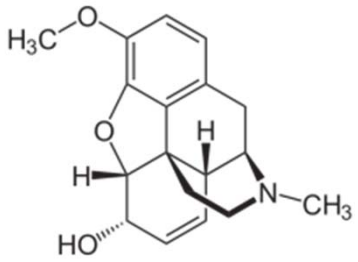
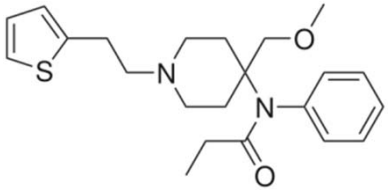
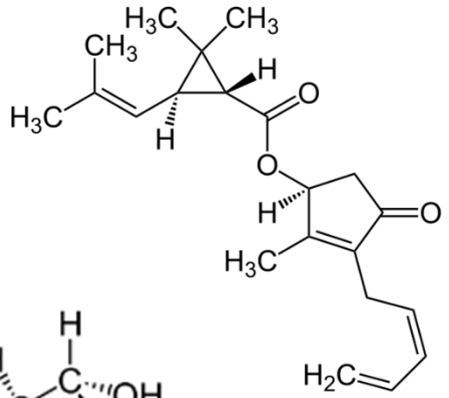
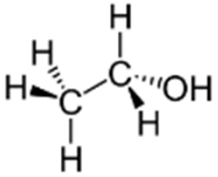
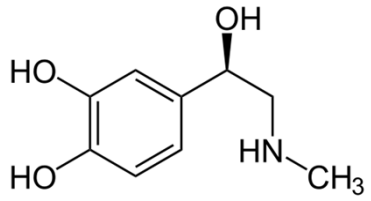
Metaboliten und kleine Moleküle

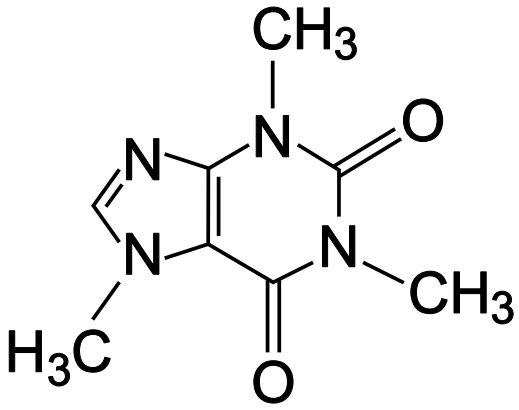


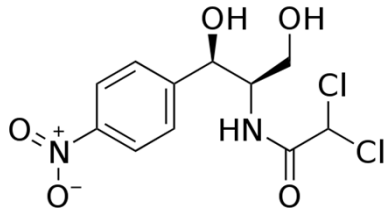


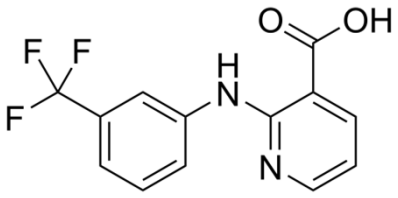


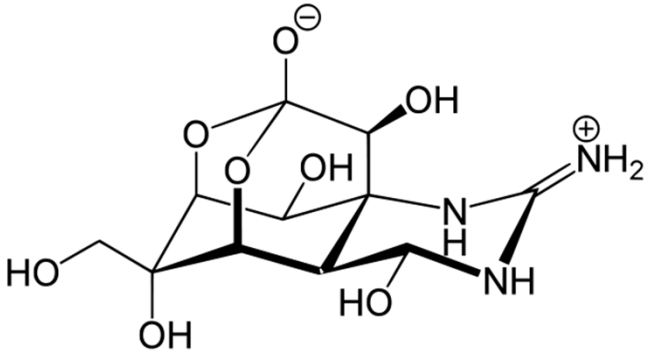


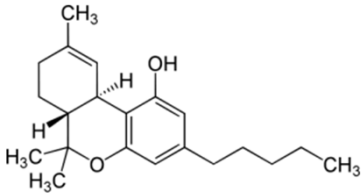








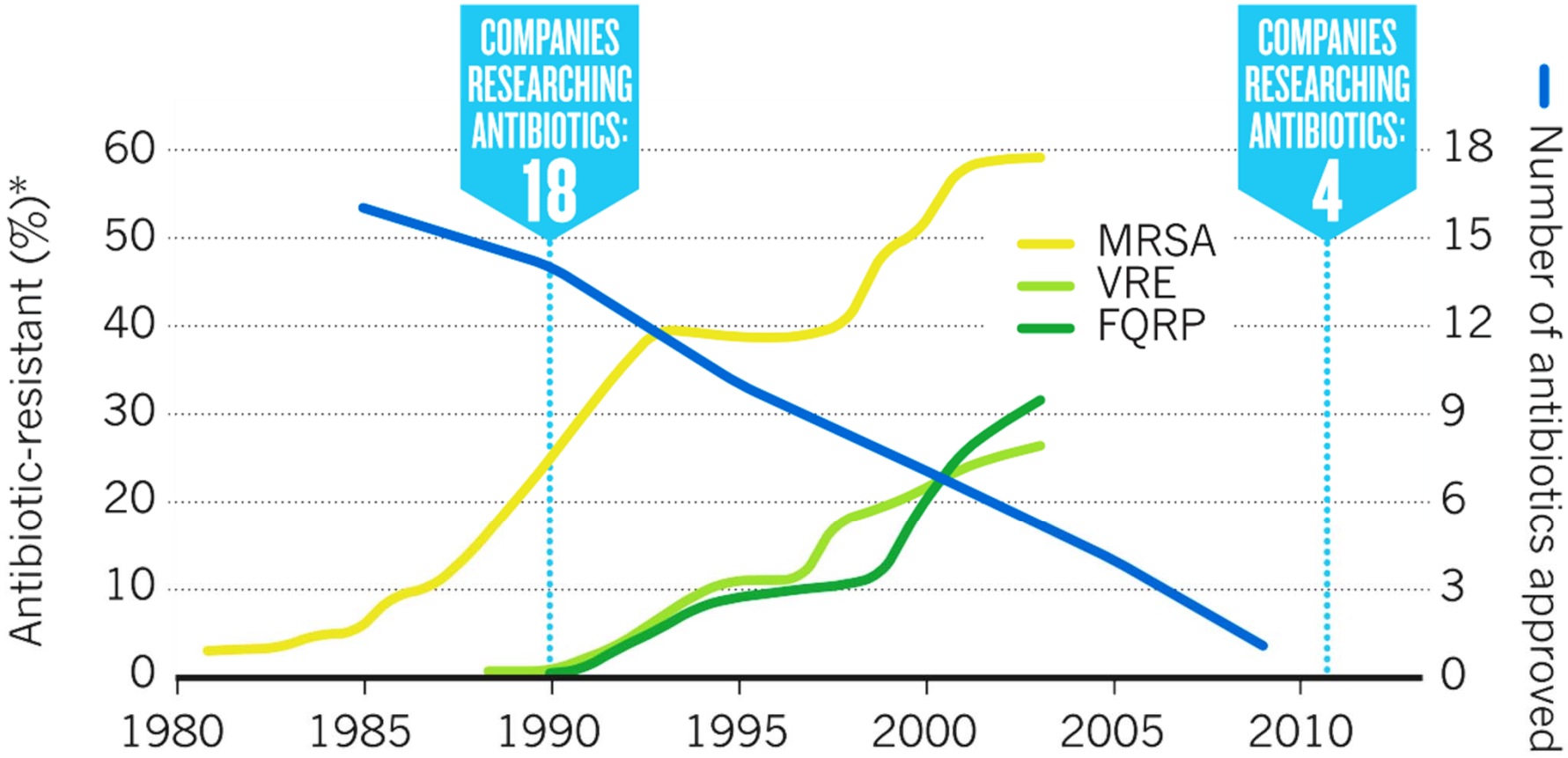




[Cooper and Shlaes, *Nature* 2011]

A PERFECT STORM

As bacterial infections grow more resistant to antibiotics, companies are pulling out of antibiotics research and fewer new antibiotics are being approved.



*Proportion of clinical isolates that are resistant to antibiotic. MRSA, methicillin-resistant *Staphylococcus aureus*. VRE, vancomycin-resistant *Enterococcus*. FQRP, fluoroquinolone-resistant *Pseudomonas aeruginosa*.

ARTICLE

Nature, 2015

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A new antibiotic kills pathogens without detectable resistance

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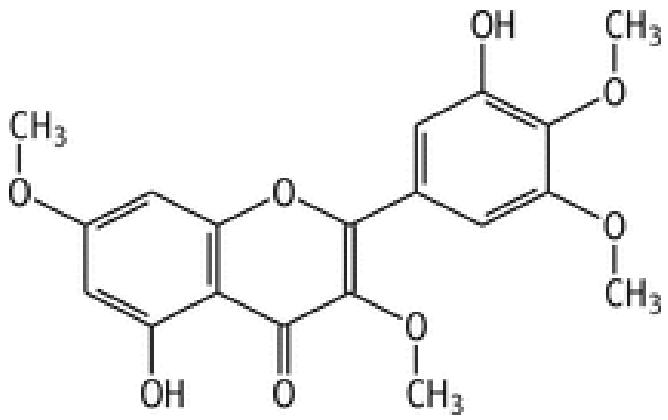
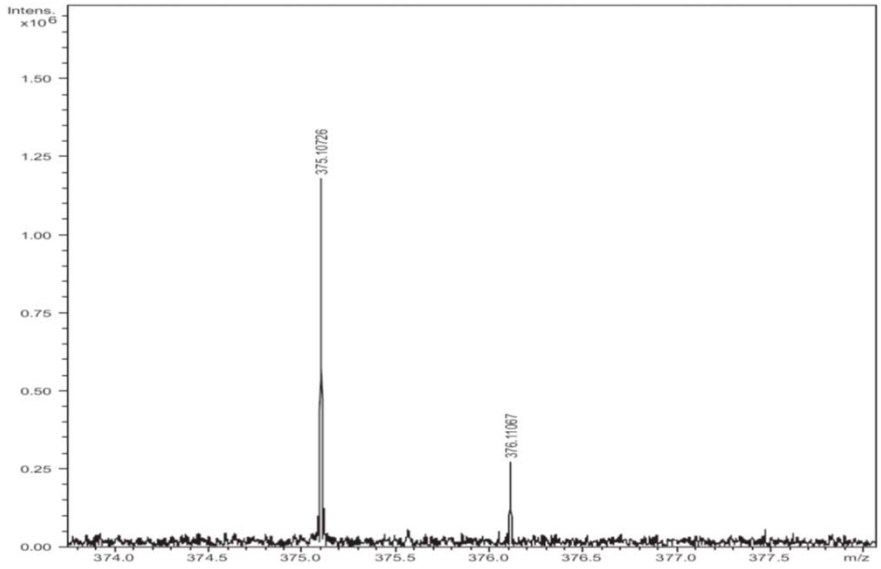
Antibiotic resistance is spreading faster than the introduction of new compounds into clinical practice, causing a public health crisis. Most antibiotics were produced by screening soil microorganisms, but this limited resource of cultivable bacteria was overmined by the 1960s. Synthetic approaches to produce antibiotics have been unable to replace this platform. Uncultured bacteria make up approximately 99% of all species in external environments, and are an untapped source of new antibiotics. We developed several methods to grow uncultured organisms by cultivation *in situ* or by using specific growth factors. Here we report a new antibiotic that we term teixobactin, discovered in a screen of uncultured bacteria. Teixobactin inhibits cell wall synthesis by binding to a highly conserved motif of lipid II (precursor of peptidoglycan) and lipid III (precursor of cell wall teichoic acid). We did not obtain any mutants of *Staphylococcus aureus* or *Mycobacterium tuberculosis* resistant to teixobactin. The properties of this compound suggest a path towards developing antibiotics that are likely to avoid development of resistance.

Widespread introduction of antibiotics in the 1940s, beginning with penicillin[1,2] and streptomycin[3], transformed medicine, providing effective cures for the most prevalent diseases of the time. Resistance development limits the useful lifespan of antibiotics and results in the requirement for a constant introduction of new compounds[4,5]. However, antimicrobial factors through the chambers enables growth of uncultured bacteria in their natural environment. The growth recovery by this method approaches 50%, as compared to 1% of cells from soil that will grow on a nutrient Petri dish[10]. Once a colony is produced, a substantial number of uncultured isolates are able to grow *in vitro*[14]. Extracts from 10,000

Fourier Transform Ion Cyclotron Resonance MS



$C_{19}H_{18}O_8$



Isotopenverteilung

element (symbol)	isotope	mass	abundance	av. mass
hydrogen (H)	^{1}H	1.007825	99.985 %	
	^{2}H	2.014102	0.015 %	1.007975
carbon (C)	^{12}C	12.0	98.890 %	
	^{13}C	13.003355	1.110 %	12.011137
nitrogen (N)	^{14}N	14.003074	99.634 %	
	^{15}N	15.000109	0.366 %	14.006727
oxygen (O)	^{16}O	15.994915	99.762 %	
	^{17}O	16.999132	0.038 %	
	^{18}O	17.999161	0.200 %	15.999305
phosphor (P)	^{31}P	30.973762	100 %	30.973762
sulfur (S)	^{32}S	31.972071	95.020 %	
	^{33}S	32.971459	0.750 %	
	^{34}S	33.967867	4.210 %	
	^{36}S	35.967081	0.020 %	32.064388

proton (p^+, $^{1}H^+$) 1.00728 Da, neutron (n) 1.008665 Da, electron (e^-) 0.00054 Da

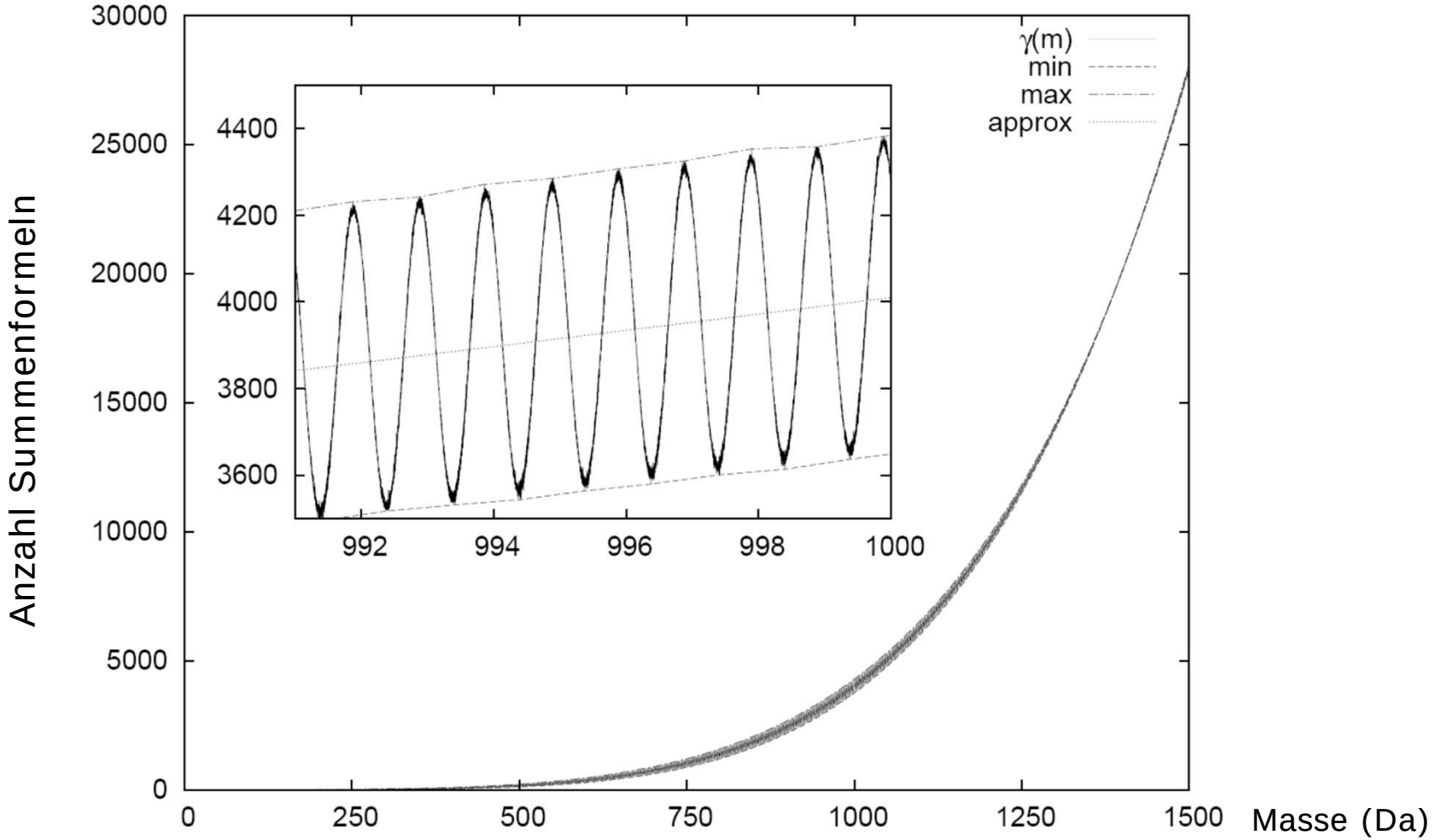
Isotopologe

^{12}C	^{13}C	^{1}H	^{2}H	^{16}O	^{17}O	^{18}O	nom. mass	mass (Da)	abundance %
12	0	22	0	11	0	0	342	342.116215	84.9204
11	1	22	0	11	0	0	343	343.119570	11.4384
12	0	22	0	10	1	0	343	343.120431	0.3558
12	0	21	1	11	0	0	343	343.122492	0.2803
12	0	22	0	10	0	1	344	344.120460	1.8727
10	2	22	0	11	0	0	344	344.122925	0.7062
11	1	22	0	10	1	0	344	344.123786	0.0479
11	1	21	1	11	0	0	344	344.124647	0.0007
12	0	22	0	9	2	0	344	344.125847	0.0378
12	0	21	1	10	1	0	344	344.126708	0.0012
12	0	20	2	11	0	0	344	344.128769	0.0004

…und so weiter und so fort bis zur maximalen Nominalmasse 398

Isotopologe von Haushaltszucker (Sucrose) $\mathbf{C_{12}H_{22}O_{11}}$

Anzahl Summenformeln



- Elemente CHNOPS, #Zerlegungen pro Bin der Breite 0.001 Da
- bei 1000 Da (±0.002 Da) schon 10000 Möglichkeiten!

Ablaufplan der Identifikation