

## New approach sees breakthrough in antibiotics research

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Scanning electron micrograph of S. aureus; false color added. Credit: CDC

Scientists using a revolutionary approach have devised an antibiotic that may offset the mounting problem of drug resistance for decades, they said on Wednesday.



Tested on lab mice—it could take five or six years to be authorised for humans—the drug could open a new front in the war on bacterial disease, the team reported in the journal *Nature*.

Called teixobactin, it hails from a new tool to screen for <u>soil bacteria</u> that exude natural antibiotic compounds.

In lab dish experiments, teixobactin killed resistant strains of tuberculosis and Staphylococcus—a source of skin, blood and lung infection—as well as anthrax and Clostridium difficile, a cause of diarrhoea.

It also cured mice infected with high doses of a superbug strain of Staphylococcus aureus.

Teixobactin performed as well as vancomycin, a powerful antibiotic generally used as a last resort against bacteria that can't be treated with first-line drugs but which has itself also started encountering resistance.

The mice showed no side effects, the authors said.

If all goes well, the new medicine "will be in clinical trials two years from now," said Kim Lewis of Northeastern University in Boston, Massachusetts, who is also a consultant for a pharma company, Novobiotic, which funded the research.

The drug works by binding to fatty molecules that are the building blocks for <u>bacterial cell walls</u>.

The binding point is "highly conserved," meaning it is less prone to mutation—the evolutionary process that drives <u>drug resistance</u>.

"It took 30 years for vancomycin to become resistant," Lewis told



journalists in a telebriefing.

Development of resistance for teixobactin "will take more than 30 years," he hoped.

## **Growing problem**

Experts have sounded ever-louder warnings about the toll of <u>antibiotic</u> <u>resistance</u> in lives and health costs as tougher bugs become harder to defeat.

Decades-long misuse of licenced drugs gave rise to the <u>resistant strains</u>, and big pharma spending on antibiotics discovery has failed to keep apace.

The most successful antibiotics, such as penicillin and streptomycin, were discovered during a "golden age" of research from the 1940s to the 1960s, derived from microbes which live in soil.

But it has become harder—and thus more expensive—to isolate new antibiotics from this source, and attempts to create synthetic alternatives have borne little fruit.

The new approach uses a screen called iChip, a palette with tiny wells each seeded with a single, different bacterial cell.

Taken from the soil for tests as before, the bacteria are no longer cultivated in a lab dish, but placed in the iChip back in the soil for a week or two to reproduce in their natural environment.

They grow more easily this way, and each iChip yields several types of bacteria at once—each of which are then tested to see if they kill S. aureus.



Teixobactin came from a study of 10,000 germs which yielded a shortlist of 25 bacteria of interest.

This tally was finally narrowed to one—a new species of so-called betapoteobacterium called Eleftheria terrae, whose active compound was then isolated.

If <u>clinical trials</u> find it is safe and effective, teixobactin will be the first of a brand-new pharmaceutical category called lipid II binding antibiotics.

Independent commentators hailed the announcement.

"We desperately need <u>new antibiotics</u> to tackle bacterial infections. This is a very promising development," Nigel Brown, head of Britain's Society for General Microbiology, told the Science Media Centre in London.

Teixobactin attacks so-called Gram-positive bacteria but not the Gramnegative class that includes the intestinal bug Escherichia coli, where resistance is also a big problem.

The iChip opens a way for finding more new drugs.

"It is likely that additional natural compounds with similarly low susceptibility to <u>resistance</u> are present in nature and waiting to be discovered," the paper said.

The screening tool "could be a game changer," Laura Piddock, a microbiologist at Britain's University of Birmingham, said in a separate reaction.

"It allows compounds to be isolated from soil, producing micro-



organisms that do not grow under normal laboratory conditions."

**More information:** A new antibiotic kills pathogens without detectable resistance, *Nature*, <u>dx.doi.org/10.1038/nature14098</u>

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