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The next generation of antibiotics might be right under our feet

Andrew Beattie

The discovery of a new antibiotic called teixobactin was announced by international team of researchers, in January this year. It is the most significant new antibiotic to be discovered in more than 30 years, and it may help combat the growing number of drug-resistant bacteria.

However, there are two reasons why the discovery of this “game-changing” antibiotic is far more significant than the media has generally portrayed.

The first is because it was isolated from a bacterium that was previously unculturable. Bacterial chemistry and metabolism is so diverse, flexible and complex that their vital growth factors are often totally unknown. So, until now, it has been impossible to grow colonies of most of them in the lab for experimentation.

The startling situation is that microbiologists tell us that most bacteria – an estimated 99% – are currently regarded as unculturable. Thus this discovery opens the door, even if only a chink, to a vast new untapped resource for medicine, especially new antibiotics.

If one previously unknown bacterial species has yielded a new and spectacular hope in the fight against disease, then what awaits discovery among the many millions of the others?

Hot chip

Let's backtrack and briefly explore the technological breakthrough involved. The first is the astonishing fact that the resource was one gram of dirt from a grassy field in the state of Maine in the United States. The geography is probably irrelevant, though, as any handful of soil contains thousands of different kinds of bacteria and billions of individual bacterial cells.

The novel technology involved is known as the iChip, and it is simple in concept. Since we do not know what chemicals to add to our laboratory substrates in order to culture most bacteria, why not somehow keep them in their native soil and grow them there?

This is enabled by the iChip, which is a small grid of tiny compartments, each sheathed with permeable membrane and each occupied by a single bacterial cell.

These cells have been diluted out from a soil sample and manoeuvred so that there is one per compartment. The iChip is then placed back into the soil where the sample originated and where their unknown growth factors are evidently present. The cells multiply into cultures of a size sufficient to obtain their secretions, including any antibiotics.

The surprise was not only that the researchers were able to obtain useful antibiotic secretions – in this case from a new species called Eleftheria terrae – but many of the new bacteria had uncertain relationships to any others.

Lab trials showed the new antibiotic killed 100% of highly resistant golden staph strains. It did this by destroying two different structural targets in the bacterial cell wall, a detail likely to make it very hard to evolve resistance. Teixobactin is now in preclinical trials.

Gold in the ground

Now we should backtrack even further. Antibiotics were largely developed by culturing soil microbes and extracting natural products from them. This approach came to be regarded as old-fashioned following massive investment into new synthetic methods by the pharmaceutical companies.

Unfortunately, though greatly hyped, synthetic methods have disappointed. The industry is now once again looking for natural products. A critical reason for this change in direction is that bacterial pathogens are evolving resistance not just to single antibiotics but to groups of them that are sufficiently similar in structure that resistance to one leads to resistance to many, a phenomenon called "cross-resistance".

The industry seeks novelty. This, it turns out, is already a feature of natural products. This is not to say that synthetic methods are dead. In fact, they are more likely these days to use a natural product as the starting point for further research.

Thus the second real significance of the discovery is the return to natural products as a basic resource for industrial innovation. Perhaps surprisingly, this places the academic discipline of evolutionary ecology at its cutting edge.

A better worked example illustrates this. When molecular biologists were looking for enzymes that remained stable when heated, they asked the evolutionary question: have these enzymes already evolved naturally?

Logic led them to the bacteria of hot springs, where they found an enzyme that revolutionised medicine and the biological industries, Taq polymerase in the bacterium Thermus aquaticus.

The bacteria have been on this planet for billions of years. While we do not know how long Eleftheria terrae has been around, its product, teixobactin, has evolved over untold generations. Its various precursors have been tried and tested by the rigours of natural selection. All free of charge.

The teixobactin discovery, together with the exploding levels of research into the bacteria of the human body and the soil, mean that at long last we are waking up to the true potential of microbial biodiversity, which is the greatest part of all biodiversity.

Thus, despite all the doom and gloom surrounding superbugs and the dearth of new antibiotics, there is now more cause for optimism. This can even be seen in the pages of the world's top science journals as microbiologists urge a return to microbial biodiversity as a primary resource for new medicines and in Rockefeller University's citizen science project, Drugs from Dirt, which aims to source soil samples from across the world for drug discovery.

Thanks to soil bacteria, we might have a way to fight back after all.

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