Expanding the arsenal

Understanding how antibiotics work would help outwit resistant bacteria

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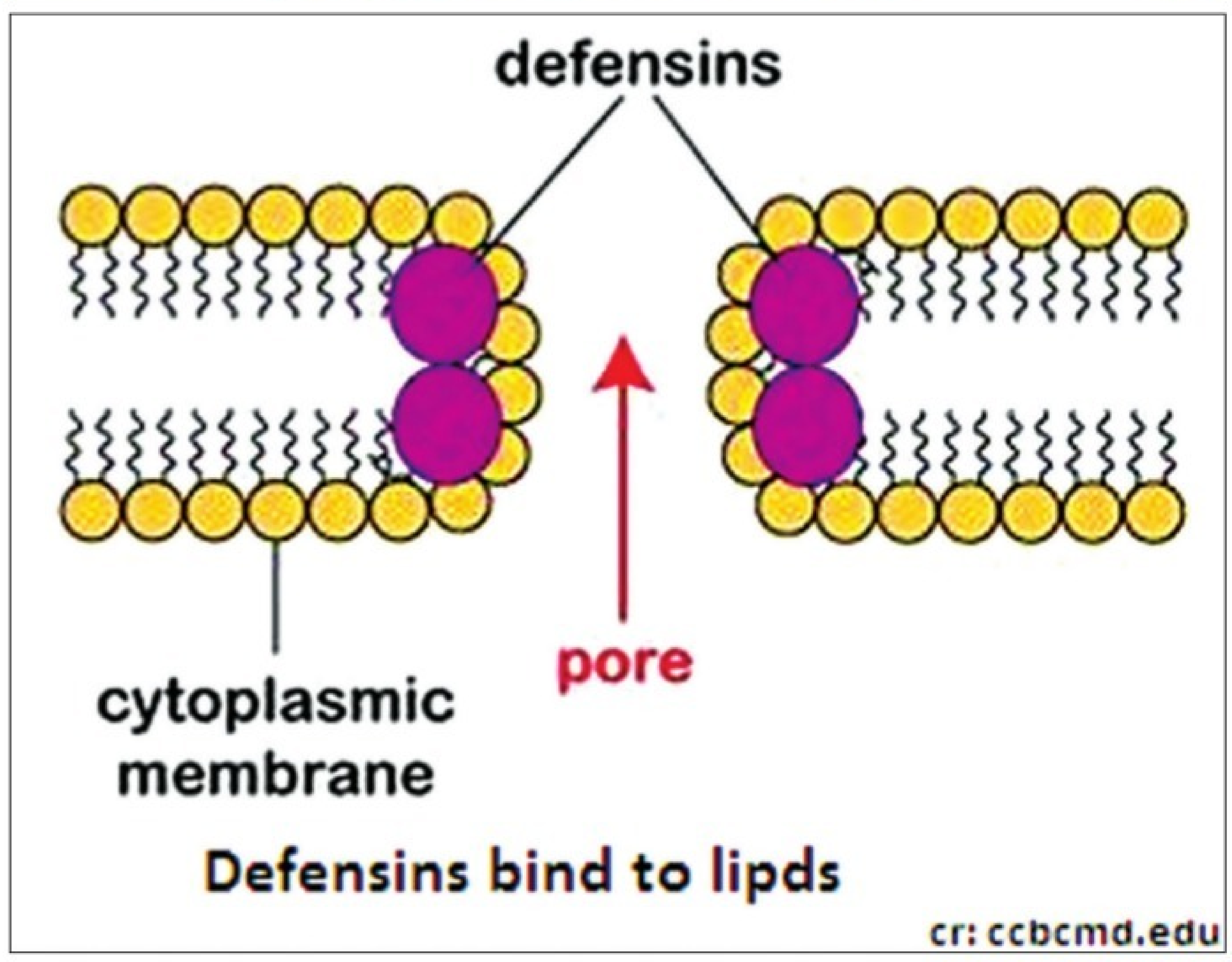

When antibiotics were discovered, they promised freedom from many kinds of disease. What we did not allow for was that bacteria would find ways of avoiding the new threat. Now, we have wide-spread misuse of antibiotics, which is not helping to contain the danger, and an alarm has been sounded of antibiotics being passed by and a "return to the dark ages of medicine"!

Michael Järvå, Fung T Lay, Thanh Kha Phan, Cassandra Humble, Ivan KH Poon, Mark R Bleackley, Marilyn A Anderson, Mark D Hulett and Marc Kvansakul, a team from La Trobe Institute of Molecular Science, Melbourne, Australia, report in the journal, *Nature Communications*, the mechanism of anti-fungal substances in a variety of the tobacco plant, which are effective against a leading antibiotic-resistant microorganism. The advance may lead to new ways for fighting bacterial infection.

That some fungi and plants are effective against bacteria was known since ancient times. In 1928, Alexander Fleming discovered that a molecule, penicillin was the active agent in many molds. While Fleming proposed that the molecule could be used in medicine, reasonably pure penicillin was extracted by chemists only in 1942. Penicillin and some other similar molecules, now known as antibiotics, played a great role in saving lives of allied soldiers during World War II. Since then, there has been rapid development of natural and synthetic antibiotics for dealing with specific as well as "broad spectrum" bacterial infections.

Antibiotics are small molecules that affect parts of bacterial cells, parts that are not there in body cells or in different forms. One of the ways antibiotics act is by breaking down the bacterial cell wall. Another is by blocking vital processes, like DNA multiplication or the production of some proteins. Body cells do not have cell walls and have different internal processes. Antibiotics hence destroy or immobilise bacteria, but leave body cells comparatively unaffected.

Viruses, which act mainly by taking over a host cell's resources, have negligible internal processes and no cell wall. This is why antibiotics are not useful to treat viral infections.

But antibiotics do affect bacteria -- and this is with the help of shape features of the antibiotic molecule that fit complementary features on or inside the bacteria. It is because of these shape features that antibiotics affect only specific bacteria. But some antibiotics affect many bacteria. These often affect body cells too and certainly affect the useful bacteria, such as those found in the intestines. The shape specificity, however, gives the bacterium an opportunity to change its vulnerable shape feature and escape the antibiotic's attention.

If we take low doses of antibiotics or antibiotics when we do not need to, vulnerable bacteria do get killed, but occasional individuals, with chance features that do not match the antibiotics' shape features, manage to escape. The result is that these infrequent but resistant bacteria begin to dominate, and in time, they grow in numbers as a new, resistant strain.

We then have an outbreak of a disease which used to be managed, but is now out of control, as the antibiotic of choice does not work. Scientists are hence constantly at work to discover or develop new antibiotics that are effective against new strains of disease-causing bacteria. The work, however, is largely trial and error and hit or miss, as we do not have a deep understanding of the mechanics of the different ways that antibiotics work.

Apart from antibiotics that are isolated or synthesised in this way, however, animals and plants generate their own anti-microbial substances, "as a first line of defence against pathogens". "Essentially all plant and animal species produce substances called "defensins", which exhibit broad antimicrobial activity, as an important component of their innate immune systems," the team at La Trobe Institute at Melbourne say in the paper.

"Defensins have multiple mechanisms of action, including modulation of immune responses, triggering the production of reactive oxygen species, cell cycle interference, inhibition of enzymes and ion channel activity, as well as the disruption of membranes. Plant defensins can also play roles in root development and plant reproduction, underscoring the diversity of biological functions that can be meditated by this family of molecules," the authors of the paper says. Extracts from different animals or plants have hence become important sources for dealing with antibiotic-resistant pathogens.

One of the key strategies that defensins employ to immobilise bacteria, the paper says, is to disrupt the membranes of the cell wall. The team refers to their earlier work where they had found that the action of defensins was by connecting with specific molecular portions, called phospholipids, associated with bacteria, and forming chains or nets that immobilised bacteria or made the cell walls porous. The paper says that there are some tentative ideas about how the defensins go about disrupting the cell wall, particularly the nature of the complex that the defensins form with the bacteria lipids.

The team has now taken up the case of defensins found in the plant, Nicotiana alata, an ornamental tobacco species, which is also known as jasmine tobacco, sweet tobacco or winged tobacco. One of the defensins, the defensin 1 of Nicotiana alata, or NaD1, is known to attack Candida albicans, a kind of yeast that is toxic to some humans. To investigate the mechanism of the action, the team used transmission electron microscopy to study the crystal structure of the complex formed by NaD1 with the lipid, phosphatidic acid. The complex revealed by the study was found to confirm one of the proposed forms and also to reveal the nature of pairing or combining of defensins with lipids. The action of NaD1 on Candida albicans was also studied using variations of forms of NaD1 and it was found that the forms where specific portions of NaD1 were modified lost the ability to suppress Candida.

The molecular pathway followed by defensins to deal with bacteria is different from the way usual antibiotics go about the task. Defensins could hence become an important new instrument to control bacteria that have found ways to evade antibiotics. The work of the Melbourne team has confirmed an important conjecture of the form of the defensin-lipid complex and then identified some detail of the structure of the defensin molecule that plays a pivotal role in suppressing bacteria.

"It's an exciting discovery that could be harnessed to develop a new class of life-saving antimicrobial therapy to treat a range of infectious diseases, including multi-drug-resistant golden staph, and viral infections such as HIV, Zika virus, Dengue and Murray River Encephalitis," Mark Hulett, one of the researchers said.

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PLUS POINTS

Ancient high

The growth of wild cannabis was rife in Europe during the Stone Age, but the plant disappeared from the continent before the first farmers had a chance to cultivate it, according to new research.

Scientists have previously struggled to determine where the plant grew, as its similarity to the related common hop meant usual methods of studying pollen fossils had proved difficult. However, a group of researchers from the University of Vermont led by John McPartland now believe they may have solved the mystery, by examining what else was growing in the area.

In a study published in *Vegetation History and Archaeobotany*, the team concluded that if other ancient pollen collected from a location were from plants common on grassy steppes, the sample is likely to be cannabis. If other fossils suggest the area was woodland, it can be assumed the plant was a hop, the research states.

The new theory led the team to re-examine samples of Stone Age fossil pollen from more than 470 sites across Europe, concluding cannabis was present on dry tundra landscapes during the period.

However, when the first farmers set foot on the continent from West Asia around 9,000 years ago, the plant was already beginning to disappear as the continent warmed. McPartland said there was little evidence that these new farmers cultivated the plant. "If it wasn't there they couldn't domesticate it," he told the *New Scientist*.

However, cannabis did return to Europe around 4,500 years ago during the Bronze Age, when pastoralists from the Eurasian steppe moved into the continent, bringing the plant with them.

Best known in the modern world for its psychoactive properties; it was likely reintroduced onto the continent to be made into textiles. However, McPartland said that he believed it was possible that early European farmers did use cannabis as a drug, in societies where alcohol would not yet have been commonplace.

"Even muted psycho-activity would have been appreciated by people who did not yet have alcohol," he said.

The Independent

Distant stars

After detecting a whiff of oxygen, astronomers have determined that stars in a faraway galaxy formed 250 million years after the Big Bang — a rather short time in cosmic terms — in a finding that sheds light on conditions in the early universe.

Their research, published last week, provides insight into star formation in perhaps the most distant galaxy ever observed. The scientists viewed the galaxy, called MACS1149-JD1, as it existed roughly 550 million years after the Big Bang, which gave rise to the universe about 13.8 billion years ago.

Light emitted by MACS1149-JD1 travelled 13.28 billion light years before reaching Earth. Looking across such distances lets scientists peer back in time. A light year is the distance light travels in a year or 5.9 trillion miles (9.5 trillion km).

The detection of oxygen in MACS1149-JD1 was particularly instructive. The universe initially was devoid of elements such as oxygen, carbon and nitrogen, which were first created in the fusion furnaces of the earliest stars and then spewed into interstellar space when these stars reached their explosive deaths.

The researchers confirmed the distance of the galaxy with observations from ground-based telescopes in Chile and reconstructed the earlier history of MACS1149-JD1 using infrared data from orbiting telescopes. The research was published in the journal, *Nature*.

The Jakarta Post/ANN

All in the signs

Collaborative robots will work closely with humans in manufacturing workplaces of the future

JONATHAN AITKEN

Robots are steadily becoming more commonplace in manufacturing. Traditionally these are large robot manipulators that look daunting but are highly efficient at their task, and capable of repeating operations with extremely accurate precision. Due to their high weight capacity, it is not safe to have humans near them so we have to partition the environment. We operate them safely by keeping people away.

Typically manufacturing robots exist within a safety cage, obvious through a steel barrier, or using a light barrier, which halts movement if a safety zone is entered. At present we are seeing a new generation of robots being developed called collaborative robots or cobots. This robot is designed to operate around humans working with them and sharing the same space.

The introduction of cobots will be especially important in the manufacturing sector, which is set to be transformed by the deployment of collaborative robots in support of traditional manual roles. This will provide significant opportunities for increases in efficiency as workers can delegate simple, repetitive, or load-bearing tasks to their cobot and focus on higher-level elements.

For example, the cobot may hold a piece whilst they work on it, turning it as appropriate for the process element freeing the need to clamp and re-clamp. Alternatively the cobot may undertake a dangerous element of the process, such as welding or working in an environment, which may be challenging for the worker.

Whilst it can make the environment more pleasant for the worker it is natural that, being human, they will have expectations about their interaction, and the nature and characteristics of the cobot. Should the experience of working with a cobot be primarily negative, the clear benefits will not be turned towards increases in industry efficiency.

This is especially true for understanding how unskilled workers with little experience with robots will be affected by their introduction, and how to facilitate their transition from manual to semi-automated work processes. The attitude of the workforce towards the interaction will play a significant role in the uptake of the technology.

In the first study of its kind, we have investigated how static graphical signage can improve performance and reduce anxiety in participants physically collaborating with a semi-autonomous robot. This study involved 90 participants who were split among three groups -- an experimental group were presented with graphical signage related to the task; an active control group were presented with irrelevant signage; and a control group were presented with no signage whatsoever.

Participants were instructed that they would be co-working with the KUKA iiwa robotic arm on a Human Robot Interaction task in a manufacturing-type scenario. The KUKA arm was stationed at a "workbench", along with 18 narrow vertical tubes, six of which contained bolts. Participants were instructed that the bolts needed to be extracted from the tubes and placed in storage behind them.

The bolts were inaccessible to the human (due to the depth and diameter of the tubes), and while the robotic arm could access each of the tubes, it needed to be directed to each of the bolts by the participant to the tubes containing bolts. The task could be completed only by participants collaborating with the robotic arm. Participants were not provided with further instructions on how to operate the robot.

Participants in both the experimental and active control groups showed higher emotional valence, compared to the control group, indicting the mere appearance of signs was sufficient to positively impact user feelings. However, only in the experimental group were participants significantly more productive, showing that improved robot usability can be attributed to relevant instructional signage. Furthermore, only in the experimental group did the anxiety of participants correspond to their success rate (with greater task success leading to lower anxiety), suggesting a positive feedback loop between signage and successful actions leads to increased confidence.

At a time when workers are concerned about the threat posed by robots to jobs, and with advances in technology requiring upskilling of the workforce, it is important to provide intuitive and supportive information to users. Whilst increasingly sophisticated technical solutions are being sought to improve communication and confidence in human-robot co-working, our findings demonstrate how simple signage can still be used as an effective tool to reduce user anxiety and increase task performance.

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