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Two new studies show promise in tackling antibiotic resistance

Two new studies done in Singapore could solve the problem of antibiotic resistance, which is projected to kill 10 million people worldwide annually by 2050 if left unchecked, according to a 2019 report by the United Nations' Interagency Coordination Group on Antimicrobial Resistance.

In the first study, researchers from the Institute for Functional Intelligent Materials (I-FIM) at the National University of Singapore (NUS) have created a compound which can potentially treat non-tuberculous mycobacterial infections.

The bacteria which cause such infections are resistant to conventional medication because of their thick and impermeable cell envelope.

However, conjugated oligoelectrolytes – a class of synthetic antimicrobials – can prevent and circumvent antimicrobial resistance and can be engineered into a variety of therapeutic agents to fight a broad range of infections.

I-FIM principal investigator Guillermo Bazan, a corresponding author of the study, said: "Their unique structure, which facilitates the spontaneous interaction with lipid bilayers, allows them to breach the bacterial defences that so often thwart existing drugs."

COE-PNH2, the molecule designed by the I-FIM researchers, has shown high efficacy against *Mycobacterium abscessus,* one of the most prevalent mycobacterial species.

The compound attacks both replicating and dormant forms of the mycobacteria, eradicating them and reducing the likelihood of resistance or relapse.

"COE-PNH2 exhibited a low frequency of resistance in our study, which suggests that it may remain effective longer than existing treatments, providing patients with a more durable solution," said Professor Bazan.

Combined with conventional antibiotics, the use of COE-PNH2 may eventually reduce the treatment period for non-tuberculous mycobacterial infections to two to three months from the current 12 to 18 months, said Associate Professor Kevin Pethe of the Nanyang Technological University's (NTU) Lee Kong Chian School of Medicine (LKCMedicine).

"As COE is a relatively new antibiotic platform, the subsequent phase of this study requires us to understand the mechanism of action of the drug in greater detail," added Prof Pethe, the study's other corresponding author.

The study, which was funded in part by the NUS Yong Loo Lin School of Medicine's Kickstart Initiative, was published in scientific journal Science Translational Medicine on Feb 21.

In another study, researchers from NTU and the University of Toulouse in France have discovered how bacteria and their toxins trigger an immune response in humans, leading to inflammation.

Inflammation – where inflammatory cells travel to the site of an injury or infection in the body – plays an important role in fighting infections, but can also contribute to adverse side effects for people with chronic diseases, such as heart disease, or trigger autoimmune disorders such as lupus.

Over three years, the researchers found that when potassium ions in cells fall below a certain level, such as when tissue is damaged by an infection, they trigger an immune response where strong pro-inflammatory molecules are released.

While previous research showed that a gene known as NLRP3 is essential in controlling this process, the NTU and University of Toulouse study shows that the process is controlled by a pair of genes – NLRP1 and ZAKa – in organs such as the skin and lungs.

The findings were published in the peer-reviewed scientific journal Proceedings of the National Academy of Sciences in January.

Over the next five to 10 years, the research team will use the results of their study to develop drugs for skin conditions such as psoriasis and atopic dermatitis.

LKCMedicine's Assistant Professor Franklin Zhong said the findings show how the immune system has evolved various ways to sense disruptions in cellular ion balance – which can lead to diseases such as neurological disorders and heart failure – and how cells defend themselves when this balance is disrupted, such as when germs attack the body.

"Our findings present a new piece in the puzzle of how our immune system functions, and it could open doors to better treatments for diseases such as severe bacterial or viral infections," said Prof Zhong, who is the study's lead author.

The findings also have implications for the treatment of infections caused by antibiotic-resistant bacteria, he added.

Identifying alternative ways to manage immune responses, such as by targeting NLRP1 and NLRP3, could pave the way for innovative approaches to tackle infections, said Prof Zhong.

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