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Breakthrough in cracking TB's defences

Lab tests show that use of peptides and drugs can slow down the bacteria's drug resistance

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Imagine troops armed with giant corkscrews, ripping through the walls of a fortress and taking it over.

This is what teams of scientists from around the world are attempting to do, on a molecular level, in the fight against superbugs – bacteria that have become resistant to antibiotics.

Associate Professor Rachel Ee's laboratory is a staging ground for the battle against tuberculosis, an infectious disease that killed 1.8 million people worldwide in 2015 and whose defences have strengthened against drugs meant to destroy it.

After two years of research, the National University of Singapore (NUS) scientist and her team have found a potential bullet – synthetic antimicrobial peptides.

Peptides designed by the team are corkscrew-shaped molecules which can drill into the TB bacteria's cell membranes, creating a passage for drugs to enter and kill the bacteria.

In the laboratory tests, this combined usage of the peptides and drugs was found to slow down the development of drug resistance by the bacteria.

"We tested them on drug resistant bacteria taken from patient samples and the bacteria did not show any signs of resistance against these peptides," said Prof Ee.

"Tests on human blood also found that the red blood cells were not damaged, even when the dosage was increased twentyfold or thirtyfold."

A paper on the study, done in collaboration with the Agency for Science, Technology and Research's Institute of Bioengineering and Nanotechnology as well as Imperial College London, was published in the Journal Of Antimicrobial Chemotherapy last August.

The researchers are among a growing number of scientists worldwide who are using corkscrew peptides to kill antibiotic resistant bacteria, including strains of E. coli which are a common cause of diarrhoea and can also spark illnesses like pneumonia.

The team also secured a second round of funding from the National Medical Research Council last month to continue its research, and hopes to move on to animal studies in the years ahead.

TB is caused by bacteria that usually attack the lungs. It is spread through droplets in the air when someone with an active infection coughs. Symptoms include a persistent cough, weight loss and coughing up blood.

The team said its research could shorten the length of treatment.

Compliance with the treatment regime is an issue as patients have to take several drugs for six to nine months.

Patients with drug resistant TB have to take drugs for up to two years.

The researchers said the peptides enhanced the effectiveness of the drugs, which could cut the dosage of the medication.

While it might still be early days for the use of peptides as the development of new treatments can take 10 to 15 years, Prof Ee said it is a much needed step forward in the fight against multi-drug resistant TB. "It will open up new approaches and avenues for tackling the drug resistance problem."

Of the 10.4 million people in the world who came down with TB in 2015, around 3 per cent contracted a multi-drug resistant strain.

There were 2,000 new TB cases here among Singapore residents and long-staying foreigners in 2015. The outbreak in Ang Mo Kio last June – when six individuals were diagnosed over four years with the same multi-drug resistant strain – is a reminder that the Republic is just as vulnerable.

A major challenge with peptide drugs is that they do not last as long as normal chemical drugs as they can be degraded by enzymes in the bloodstream, said Prof Ee.

The team added artificial amino acids to make the drugs stay intact in the body longer.

Associate Professor Tan Thuan Tong, head of the infectious diseases department at the Singapore General Hospital, said the NUS research is promising.

"Besides repurposed drugs and a few new ones undergoing clinical trials, there isn't much on the horizon so anything that works in the lab potentially can see success."

But he noted that more research has to be done and clinical applications will take time.

"Our immune system is such that it breaks down foreign proteins and peptides, which is why the team used artificial sequences and so on.

"Those are helpful but whether it will work in human beings or have adverse side effects still requires more study."

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Scientists Rachel Ee and Jasmeet Singh Khara are part of an NUS research team that has been developing corkscrew peptides to fight multi-drug resistant TB bacteria. ST PHOTO: JONATHAN CHOO

WELCOME ADDITION TO THE FIGHT AGAINST TB

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ASSOCIATE PROFESSOR TAN THUAN TONG, head of the infectious diseases department at SGH, on the NUS research.