Stop AMR Global Media Monitor

14 – 20 December 2019

From cancer medication to antibiotic

Antibiotic development from scratch is a costly and long-term process. As such, looking for alternative pathways to new antimicrobials is of interest. One such path was taken by a team of researchers at the University of Munich that modified existing approved drugs into antibiotics. The drug they modified was originally developed for cancer and after their work was able to effectively target and kill methicillin-resistant Staphylococcus aureus (MRSA). The latter is a key target of new antimicrobial research as it is frequent and numerous strains have evolved multiple resistance.

The drug studied had sorafenib as an active ingredient, and it already had the ability to affect MRSA. After modification into a molecule they called PK150, a kinase, the effect was 10 times stronger. The modification enabled the kinase to stop targeting human cells and become more specific against bacterial targets. It targets unconventional structures of MRSA and two of these targets were further investigated by the team: inhibition of a key metabolism protein; the cell wall. Regarding the latter, instead of targeting the cell wall formation directly, like penicillin or methicillin, PK150 impacts the production volume and as a result, the bacteria produces too many proteins, which control the thickness of the cell wall, outside of the membrane and the cell therefore breaks open.

No development of resistance was observed by the team. Furthermore, PK150 also showed effectiveness against both biofilms and persisters. "MRSA infections are very often chronic, as the bacteria can become dormant. PK150 even kills these, as well as germs protected in biofilms," says Prof. Dietmar Pieper, head of the HZI research group "Microbial Interactions and Processes".

Source: EurekAlert! 16 December 2019

BARDA to fund development of antibiotics for resistant gram-negatives

The Biomedical Advanced Research and Development Authority (BARDA) has just allocated a second round of funding to Qpex Biopharma in order to continue the development of a portfolio of antibiotics that specifically target gram-negative bacteria with antibiotic resistance. The amount received is $20 million and three products will be put through clinical studies:

• "ORAvanceTM: an orally-administered, beta-lactamase inhibitor (BLI) based product to treat infections that occur in the outpatient and community setting caused by drug-resistant gram- negative bacteria, including extended-spectrum beta-lactamase (ESBL)- and carbapenemase- producing Enterobacteriaceae"

• "OMNIvanceTM: an IV-administered BLI-based product with best-in-class coverage of key pathogens, including carbapenem-resistant Acinetobacter, Enterobacteriaceae and Pseudomonas"

• "QPX9003: a next-generation IV-administered polymyxin with an enhanced therapeutic profile designed to address highly drug-resistant infections caused by Pseudomonas and Acinetobacter."

"We are grateful for our successful and longstanding partnership with BARDA, whose commitment to address the global and growing threat of antimicrobial resistance has been unparalleled," Qpex Biopharma President and CEO Michael Dudley, PharmD, said in a company press release. "Our team has made rapid progress since forming the company just over a year ago, and the continued support from BARDA puts us in a strong position as we transition to a clinical-stage company."

Source: CIDRAP, 16 December 2019

FDA clears disposable duodenoscope

Resistance to antibiotics often evolves in hospitals where antibiotics are frequently used, and bacteria can easily spread between patients and medical staff by direct contact or through colonizing objects. One such object, is the duodenoscope, which is a tube with a camera that, when threaded through a patient's mouth and into the small intestine, can allow visualization of the upper gastrointestinal tract. It is made of many different parts and as such is difficult to clean, which makes it a perfect place for bacteria to develop and grow and these could potentially be multi-resistant and infect the next patient. As such, disposable duodenoscope could prove useful and the first one, called the EXALT Model D single-use duodenoscope, has just been approved by the US Food and Drug Administration (FDA).

Jeff Shuren, MD, JD, Director of the FDA Center for Devices and Radiological Health, stated that "The availability of a fully disposable duodenoscope represents another major step forward for improving the safety of these devices, which are used in more than 500,000 procedures in the U.S. each year."

Source: CIDRAP, 16 December 2019

New animal model shows effective treatment for latent tuberculosis

Tuberculosis is not only dangerous as one of the most fatal infectious diseases globally but also through its ability to lay dormant. Indeed, the bacteria is able to enter a latent form that does not produce symptoms. "People with latent tuberculosis infection remain a source of disease because they can potentially reactivate at any point in time," Dr. Kaushal, Director of the Southwest National Primate Research Center, said. This latent state can be reversed through external factors such as poor immunity (e.g. HIV, ageing, another infection, etc.). This is problematic as current treatments for this pathogen are long and patients often stop them once symptoms have subsided. This leaves open the door for these dormant cells to survive.

In a 10-month study, Dr. Kaushal and Jyothi Rengarajan, PhD, Associate Professor of Medicine at Emory University and the Yerkes National Primate Research Center developed a model to study this latent state of Tuberculosis and were then able to successfully treat it. Rhesus macaques were used as the model organism and they were infected through an aerosolization chamber with a low-dose of the pathogen, thereby introducing a latent infection. A combination of two antibiotics, isoniazid and rifapentine, were used for three weeks on half of the primates, with the rest serving as controls. TO trigger the awakening of the pathogen into its active form, the macaques were subsequently infected with the Simian immunodeficiency virus (SIV), the counterpart of HIV. 70% of the monkeys that had not undertaken the antibiotic course developed TB whilst none of the treated did. This effectively suggests the treatment managed to get rid of the latent pathogen cells.

"The antibiotic treatment we used for this study is a new, shorter regimen the CDC recommends for treating humans with latent tuberculosis, but we did not have direct evidence for whether it completely clears latent infection" says Dr. Rengarajan. "Our experimental study in macaques showing almost complete sterilization of bacteria after treatment suggests this three-month regimen sterilizes humans as well."

Source: EurekAlert! 17 December 2019

Compound in green tea plant shows potential for fighting TB, finds NTU-led research team

Tuberculosis is one of the deadliest infectious diseases globally and strains have increasingly been developing resistance to traditional antibiotics. It is therefore important to look for alternatives. One such alternative has been discovered in the green tea plant by researchers from the Nanyang Technological University, Singapore. It is an antioxidant, epigallocatechin gallate (EGCG), which was found to inhibit the growth of the pathogen. Its mode of action is based on diminishing the energy the pathogen cell can produce by inhibiting the ATP synthase enzyme.

This was discovered by altering the DNA sequence of the ATP synthase gene in two bacteria belonging to the same family as M. tuberculosis, Mycobacterium smegmatis and Mycobacterium bovis, and observing a slowing of cell growth and altered colony shape due to a decrease in energy storage molecule production. The next step was to find a compound that could inhibit ATP synthase to reproduce the same effect. EGCG was the only compound tested that significantly reproduced these effects.

The team is now looking at improving the EGCG molecule to increase its potency as an antibiotic.

Source: EurekAlert! 17 December 2019

A self-cleaning surface that repels even the deadliest superbugs

Healthcare acquired infection (HAIs) are one of the key drivers of AMR and often lead hospitalised patients to contract more severe illnesses during their stays. Healthcare practices are perfect breeding ground from multiple-resistant bacteria with patients and doctors constantly contaminating surfaces they come into contact with. As such, the discovery made by researchers at McMaster University has the potential to be ground-breaking. They have developed a 'self-cleaning surface' where bacteria are not able to latch onto. This could be used on door knobs and other appliances and objects to ensure bacteria do no spread as fast.

A conventional transparent wrap was modified through Nano-scale engineering and chemistry and drew inspiration from water-repellent lotus leaves. Microscopic wrinkles were introduced to the material's surface that simply exclude any particle from sticking, whether it is blood or microbial cells for example.

"We can see this technology being used in all kinds of institutional and domestic settings," Didar says. "As the world confronts the crisis of anti-microbial resistance, we hope it will become an important part of the anti-bacterial toolbox."

Source: EurekAlert! 13 December 2019

Extensively drug-resistant Shigella identified in Australia

Shigellosis, a highly contagious diarrheal disease, which is spread through the faecal-oral route, is caused by four different Shigella species, including Shigella sonnei. Strains of the latter were observed to be extensively drug-resistant in Australia. 184 isolates of the strain were identified (172 male and 17 female patients) all very closely related to each other and forming a distinct clonal lineage. This suggests the bacteria mainly spread through men having sex with men (MSM). The lead author of the study, Prof. Deborah Williamson from the University of Melbourne, stated "In this study, we used whole genome sequencing to show that all of the cases from the past year and a half are highly related to each other, which strongly suggests person-to-person transmission within specific sexual networks."

In most cases, antibiotics are not needed to treat this disease, however when required, the use of oral ciprofloxacin is recommended with the alternative being azithromycin.

The authors of the study stated that "The emergence and spread of extensively drug-resistant Shigella among MSM has clinical and public health implications […] Given the propensity of MSM-associated Shigella to spread around the globe, our findings have relevance to other countries, and clinicians should be aware of the emerging potential for clinical failure of empirical oral antimicrobial agents."

Source: CIDRAP, 19 December 2019