Singapore-MIT Alliance for Research and Technology

SMART researchers discover unique lysin capable of killing deadly multidrug-resistant bacteria

Novel lysin Abp013 has shown promising antimicrobial ability against Acinetobacter baumannii and *Klebsiella pneumoniae*

- *Lysins, which are enzymes produced by bacteriophages, have shown promising potential as an alternative to antibiotics, especially against drug-resistant bacteria*
- *The discovery of Abp013 will help researchers engineer lysins with better antimicrobial potency, especially against multidrug-resistant bacteria*
- *As bacterial infections such as pneumonia and meningitis claim more lives each year due to growing resistance against antibiotics, it is crucial to develop novel alternative bacteria-killing agents*

Singapore, 17 February 2022 – Researchers from the Antimicrobial Resistance (AMR) Interdisciplinary Research Group (IRG) at Singapore-MIT Alliance for Research and Technology (SMART), MIT's research enterprise in Singapore, alongside collaborators at Nanyang Technological University, have identified a novel phage lysin – Abp013 – that could be used as an alternative antimicrobial agent against two of the most deadly bacteria: *Acinetobacter baumannii* and *Klebsiella pneumoniae*. The study is supported by the National Research Foundation (NRF) Singapore, under its Intra-CREATE Collaborative Seed Grant.

Lysins – enzymes produced by bacteriophages – have displayed great potential as a novel class of antimicrobials as their properties allow them to quickly and directly target key structural components of a bacteria's cell walls, and in doing so, reduce the bacteria's ability to develop resistance.

The inappropriate and extensive use of antibiotics over the past few decades have led to the emergence of antimicrobial resistance – a phenomenon in which bacterial strains develop mechanisms to resist medicines designed to kill them. In 2019 alone, it is estimated that 4.95 million people died from infections either associated with or attributable to antimicrobial resistance. This already pressing issue, compounded further by the widespread usage of antibiotics during the COVID-19 pandemic, highlights the urgent need for new therapeutic agents that are difficult for bacteria to develop resistance against.

"Antimicrobial resistance remains an ever-growing threat to humankind, and an increasing number of people die each year from superbug infections. The development of new bacteria-killing agents is crucial, and lysins have shown great promise in treating deadly chronic wound and lung infections against which no antibiotics are effective and limited treatment options are available," said Joash Chu, first author of the paper that documented the discovery, and former researcher at SMART at the time of the study.

Lysins have been highly effective in fighting Gram-positive bacteria – which do not have an outer lipid membrane and thus easily killed by lysins. Conversely, in Gram-negative bacteria, the presence of an outer membrane impedes many lysins from killing the bacteria efficiently. Hence, the discovery of novel lysin Abp013 is crucial in the advancement of treatment methods against multidrug-resistant Gram-negative pathogens.

In a paper titled *"Novel Phage Lysin Abp013 against Acinetobacter baumannii"* published in medical journal *Antibiotics*, the SMART AMR team reveals their findings on Abp013's ability to effectively access and kill various bacterial strains. The study showed that Abp013 displayed good permeability and killing activity against multiple *Acinetobacter baumannii* and *Klebsiella pneumoniae* strains, even when they are in a more complex environment in which typical lysins are ineffective.

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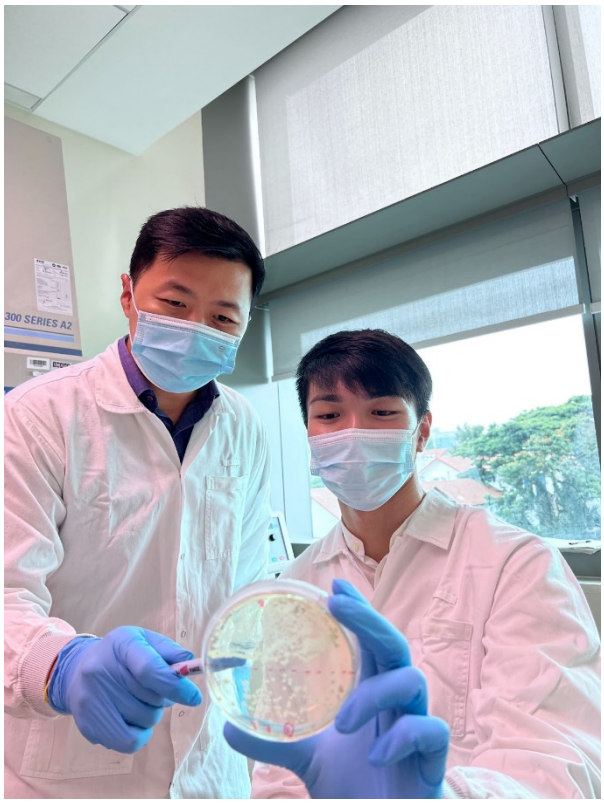

SMART AMR researchers Boon Chong Goh (left) and Joash Chu (right) evaluate the effectiveness of lysins against Acinetobacter baumannii. (Photo: Chia-ching Chan, SMART AMR)

Acinetobacter baumannii and *Klebsiella pneumoniae are* superbugs responsible for a multitude of potentially life-threatening infections, *such as* pneumonia *and* meningitis, especially among the ill and immunocompromised. Unfortunately, many strains of these bacteria are difficult to treat as they grow increasingly resistant to antibiotics. Typically, to treat *Acinetobacter* infections, healthcare providers have to send a specimen for laboratory testing to determine which antibiotics are effective in fighting the bacteria. Thus, the important discovery of Abp013 and its unique bacteria-targeting properties could advance the development of remedies for quicker and more effective targeting of these bacteria.

“Abp013 is the first Gram-negative lysin found to display host selectivity. Prior to the discovery of Abp013, no other lysins are capable of targeting *Acinetobacter baumannii* and *Klebsiella pneumoniae* but not *Pseudomonas aeruginosa*. Understanding the mechanism behind such selectivity will help guide the development of lysin variants customised to only target pathogenic bacteria, for more precise treatment of bacterial infections,” said Dr Goh Boon Chong, Principal Research Scientist at SMART AMR, and a co-corresponding author of the paper.

Moving forward, the researchers will further investigate the crystal structure of this novel lysin and understand its unique underlying mechanisms. These will open the possibility of swapping or merging the lysin’s components with other lysins or antimicrobial components to spur the engineering of Gram-negative lysins with superior potency, and lead to the development of alternative therapeutic agents that can resist the resistance.

SMART AMR has been developing methods for the customised targeting of bacteria using lysins, and these endeavours were nurtured by the early support of the SMART Innovation Centre. National Research Foundation (NRF) Singapore’s Intra-CREATE Collaborative Seed

Grant encourages and facilitates collaboration between CREATE's Partner Institutions co-located in Singapore, to achieve greater impact from collaborative research efforts.

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About Singapore-MIT Alliance for Research and Technology (SMART) [新加坡-麻省理工学院科研中心]

Singapore-MIT Alliance for Research and Technology (SMART) is MIT's Research Enterprise in Singapore, established by the Massachusetts Institute of Technology (MIT) in partnership with the National Research Foundation of Singapore (NRF) since 2007. SMART is the first entity in the Campus for Research Excellence and Technological Enterprise (CREATE) developed by NRF. SMART serves as an intellectual and innovation hub for research interactions between MIT and Singapore. Cutting-edge research projects in areas of interest to both Singapore and MIT are undertaken at SMART. SMART currently comprises an Innovation Centre and five Interdisciplinary Research Groups (IRGs): Antimicrobial Resistance (AMR), Critical Analytics for Manufacturing Personalized-Medicine (CAMP), Disruptive & Sustainable Technologies for Agricultural Precision (DiSTAP), Future Urban Mobility (FM) and Low Energy Electronic Systems (LEES).

SMART research is funded by the National Research Foundation Singapore under the CREATE programme.

For more information, please visit: http://smart.mit.edu

About Antimicrobial Resistance Interdisciplinary Research Group (AMR IRG)

The AMR IRG is a translational research and entrepreneurship program that tackles the growing threat of antimicrobial resistance. By leveraging talent and convergent technologies across Singapore and MIT, we aim to tackle AMR head-on by developing multiple innovative and disruptive approaches to identify, respond to, and treat drug-resistant microbial infections. Through strong scientific and clinical collaborations, our goal is to provide transformative, holistic solutions for Singapore and the world.

For more information, please log on to: http://amr.smart.mit.edu/#home

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