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EDITORIAL

Winners of the 2017 JA Ōmura Awards for excellence

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In recognition of and to commemorate Prof. Ōmura's Nobel Prize in Physiology or Medicine in 2015, the Editorial Board of *The Journal of Antibiotics* has changed the name and the design of the JA Medal to the JA Ōmura Award. The first JA Ōmura Award for an article will be given for the outstanding paper entitled "Application of bacterial cytological profiling to crude natural product extracts reveals the antibacterial arsenal of *Bacillus subtilis*" by Kit Pogliano and colleagues at University of California San Diego [1]. In this article, the authors report the general usefulness of bacterial cytological profiling (BCP) for not only understanding the mechanism of action (MOA) but also identification of bioactive substances in crude extracts, which allowed for the identification of two distinct antibacterial activities from the culture broth of *Bacillus subtilis*, translation inhibition and membrane permeabilization.

As a result of the extensive use of antibiotics in the clinic, pathogenic bacteria have evolved resistance to nearly all classes of antibiotics, which poses serious threats to human health. It is therefore clearly important to identify antibacterial molecules with unique MOA. However, elucidation of MOA at the molecular level is one of the most challenging tasks in drug discovery, which generally requires multiple assays and substantial amounts of time. The winners' group previously developed BCP, a rapid and powerful approach for identifying the cellular pathway affected by antibacterial molecules [2]. The cytological profiles of bacterial cells treated with each antibacterial drug, which are created by staining cells with multiple fluorescent dyes, successfully distinguished between inhibitors that affect different cellular pathways as well as different targets within the same pathway. In the award-winning paper, this technology was applied to identify multiple biological activities in crude natural product extracts, providing a new platform for screening for unique biological activity and guiding natural product extract fractionation. Furthermore, the authors offered an in situ version of BCP that works with strains grown on a solid medium plate. BCP is an exciting new technology for antibiotic research, and its application to the discovery of minor components possessing alternative MOAs in crude extracts, which are overlooked by traditional screening methods, is of high importance.

The 2017 winner of the JA Ōmura Award for reviews goes to a seminal and comprehensive overview on glycopeptide antibiotics, entitled "Glycopeptide antibiotics: Back to the future" authored by Matthew A. Cooper and coworkers at the University of Queensland [3]. A family of antibiotics with glycosylated tricyclic or tetracyclic heptapeptide cores are collectively called glycopeptide antibiotics (GPAs). Vancomycin, a founding member of GPAs, has been used as a 'drug of last resort' in the fight against many infections by Gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA). Vancomycin was discovered in the 1950s by Eli Lilly & Co and continues the integral role in frontline therapy it has had for over half a century, even today. To overcome the drawbacks associated with vancomycin including the emergence of resistance, several new GPAs including semisynthetic ones have been developed. This review article comprehensively covers this evergreen topic and is considered one of the masterpiece reviews on GPAs, in addition to the article awarded the JA Medal last year on GPA biosynthesis [4].

The review begins with a history of vancomycin from discovery to its approval as a 'certifiable antibiotic' by the United States Food and Drug Administration (FDA) in 1958. Surprisingly, its chemical structure was not fully elucidated until 1982 and confirmed by X-ray crystallography in 1996. There are clinical limitations of vancomycin including its relatively poor pharmacokinetic properties and side effects. However, a dramatic rise in

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drug resistance to β-lactams due to the constant and extensive use of β-lactam antibiotics has made vancomycin re-emerge as a key weapon in the fight against β-lactam-resistant bacteria. Meanwhile, MRSA strains with reduced vancomycin susceptibility such as heterogeneous vancomycin intermediate (hVISA), vancomycin intermediate (VISA), and vancomycin resistant (VRSA) that acquired the enterococcal *vanA* operon gene were found in clinical practice, an issue that threatens its continued effectiveness. In this review article, the authors report the current state of development of the second generation of GPAs with improved pharmacokinetic and safety profiles. Teicoplanin is another naturally occurring GPA which is better tolerated than vancomycin, and applicable to outpatient therapy. Furthermore, semisynthetic lipoglycopeptide derivatives with improved properties such as telavancin, dalbavancin, and oritavancin have been developed and recently approved by the FDA. This review provides profound insights into further development of more effective GPAs against drug-resistant pathogens, and as such, it is a worthy recipient of the 2017 JA Ōmura Award.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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ABOUT THE WINNERS

Dr. Poochit Nonejuie Poochit Nonejuie is a microbiologist specializing in the field of antibiotic mechanism of action and resistance. He received his B.Sc. in Biochemistry from Chulalongkorn University, Thailand and his Ph.D. from the University of California, San Diego (UCSD) in the Division of Biological Sciences under the supervision of Dr. Joe Pogliano. During his Ph.D. at UCSD, he developed a fluorescence microscopy-based technique, as called Bacterial Cytological Profiling (BCP), which rapidly identifies the antibiotic mechanism of action. After he graduated, he continued his postdoctoral research on BCP with Dr. Joe Pogliano but mainly focused on applying BCP into various aspects of antibiotic research including antibiotic resistant mechanism of pathogens, antibiotic synergy study, and screening of natural product-derived antibacterial molecules. He is now a principal investigator at the Institute of Molecular Biosciences, Mahidol University, Thailand and currently working on BCP-based antibiotic research involved in developing an *Acinetobacter baumannii*-specific antibiotic discovery platform, antimicrobial peptide resistance mechanism study, and natural product-derived antibiotic screening from untapped resources in Thailand.

Dr. Rachelle Trial Rachelle Trial is a scientist and industry recruiter with expertise in Molecular Biology, Microbiology, Cell Biology, and microscopy. She received her PhD in 2008 from the University of Utah. During her PhD, she studied circadian rhythms in cyanobacteria (*Synechococcus elongatus*) and focused on establishing the mechanism of circadian global gene regulation via chromosome compaction. She was the recipient of a NIH Genetics Training Grant in 2006. Dr. Trial joined Dr. Kit Pogliano's laboratory at the University of California, San Diego in 2008 as a Postdoctoral Fellow (her work was supported by a NIH NRSA Postdoctoral Fellowship). In Dr. Pogliano's lab, she investigated the outcomes of interactions between *Bacillus subtilis* and other bacterial strains that were newly isolated from soil samples by fine-tuning a side-by-side assay on different media types. Along with Dr. Poochit Nonejuie, she used bacterial cytological profiling (BCP), a method that utilizes fluorescence microscopy, to determine the mechanism of action of crude extracts and purified secondary metabolites from undomesticated *B. subtilis*. She also worked on a project to characterize the role of a membrane-anchored enzyme that is essential for engulfment and sporulation (SpoIID) in peptidoglycan degradation. After her postdoctoral work, Dr. Trial joined PharmaScouts as a Senior Executive Recruiter. PharmaScouts is an executive recruiting company

comprised of scientists who focus on recruiting scientific and executive management, particularly those with advanced scientific degrees, for life science companies. Dr. Trial uses her scientific knowledge and experience to build long-term relationships with candidates and clients to advance discovery and development in the biotech/pharmaceutical industry.

Prof. Mark Butler Associate Professor Mark Butler obtained his PhD from the University of Melbourne in marine natural products, under the supervision of Prof Robert Capon, in 1992. Following a postdoctoral position with Prof G. Robert Pettit at the Arizona State University, Mark joined the Queensland Pharmaceutical Research Institute (now part of GRIDD) in 1994, which was a new joint venture between Griffith University and AstraZeneca, working with Prof Ronald Quinn. In 1999 he moved to Singapore to lead the Natural Product Chemistry group at the Centre of Natural Product Research (CNPR), which worked predominantly with GlaxoSmithKline. In 2002, CNPR was privatized to become MerLion Pharmaceuticals. At MerLion, the Natural Product Chemistry group was involved with lead discovery, pre-clinical and clinical development with a focus on microbial-derived antibacterials. From 2009 to 2017 Mark worked with Prof Matthew Cooper at the Institute for Molecular Bioscience, at the University of Queensland (UQ), concentrating on anti-infective lead discovery, pre-clinical drug development and mode of action studies. He recently obtained his MBA (UQ, 2017) and is currently undertaking antibiotic research and business development with Prof David Paterson at the Centre for Clinical Research (UQCCR). Mark was a Clarivate Analytics highly cited author in Pharmacology and Toxicology in 2016 and 2017, and was a member of the WHO Advisory Group for the analysis of the antibiotic pipeline in 2017.