



Targeting gram-negative 'Superbugs': Polymyxin SAR

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As described in the 'Bad Bugs, No Drugs' paper published by the Infectious Diseases Society of America (IDSA), the world is facing an enormous and growing threat from the emergence of Gram-negative bacteria that are resistant to almost all available antibiotics, including the last-line therapy polymyxins. In recent years, virtually no novel drugs targeting multidrug-resistant (MDR) Gram-negative bacteria, in particular *Pseudomonas aeruginosa*, have been developed. Therefore, there is an urgent need for new antibiotics, particularly those active against Gram-negative 'superbugs' *P. aeruginosa*, *Acinetobacter baumannii* and *Klebsiella pneumoniae*. This presentation reviews the current understanding of the mechanisms of microbiological activity and bacterial resistance of polymyxins, followed by a comprehensive treatise on the SAR of the polymyxins and the various analogs that have been investigated. The SAR data suggest that the unique three dimensional architecture of polymyxins is required for both lipopolysaccharide binding and antibacterial activity. The collective SAR knowledge in the literature provides valuable information for the design of lead peptides that display significant antimicrobial activity against Gram-negative 'superbugs' resistant to all currently available antibiotics including the last-line polymyxins.

Biography

Associate Professor Jian Li received his PhD in 2002 from the University of South Australia (Adelaide, Australia). He is the Group Head of Antibiotic Research at Monash University. He has an internationally recognised track record in polymyxin pharmacology. Dr Li has 72 publications in peer-reviewed journals with 1,217 citations, one PCT application, two provisional patents, one book chapter and 57 scientific presentations. He is an Associate Editor of BMC Microbiology, and a member of editorial boards of three other international journals. Since 2004, Dr Li has attracted >\$10M funding from American National Institutes of Health, Australian government and pharmaceutical companies.