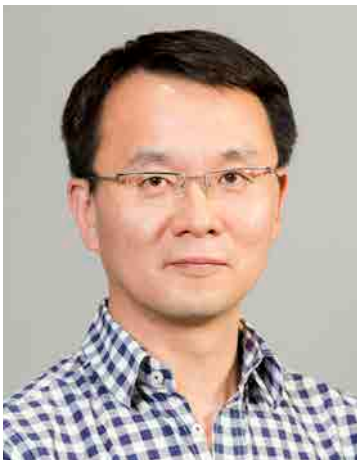

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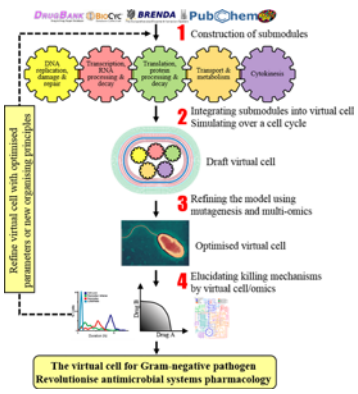
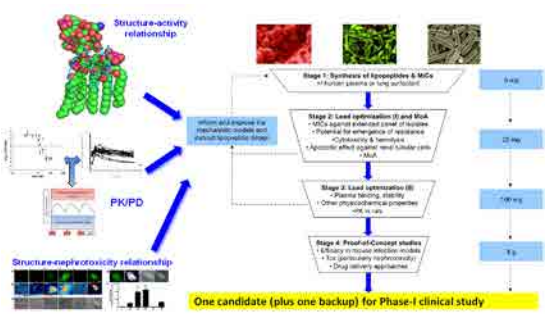
The World Health Organisation (WHO) has identified antimicrobial resistance as one of the three greatest threats to human health globally. With a marked decline in the discovery of novel antibiotics, the world is now facing an enormous and growing threat from the emergence of bacteria that are resistant to all available antibiotics. In particular, no new antibiotics will be available for many years to come against Gram-negative 'superbugs' *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Klebsiella pneumoniae*; and polymyxins have been increasingly used as the last-line therapy. We employ systems pharmacology and computational biology approaches to investigate the mechanisms of polymyxin activity, resistance and nephrotoxicity; and optimise their clinical use. Furthermore, the pharmacological information obtained underpins the discovery of novel safer polymyxins. Our research is mainly funded by the National Institutes of Health (USA) and NHMRC, and targets an urgent global medical challenge due to antibiotic resistance.

Research Projects

1. **Bacterial virtual cells**
2. **Mechanisms of polymyxin activity, resistance and nephrotoxicity using genomics, transcriptomics, proteomics, metabolomics and molecular imaging approaches**
3. **Discovery of novel and safer polymyxins against Gram-negative 'superbugs'**



Virtual cell modelling for bacteria.



Discovery of novel safer polymyxins.

Selected significant publications:

1. Mahamad Maifiah MH, Cheah SE, Johnson MD, Han ML, Boyce JD, Thamlikitkul V, Forrest A, Kaye KS, Hertzog P, Purcell AW, Song J, Velkov T, Creek DJ and **Li J**. 2016. Global metabolic analyses identify key differences in metabolite levels between polymyxin-susceptible and polymyxin-resistant *Acinetobacter baumannii*. *Sci Rep*. 6, 22287.
2. Henry R, Crane B, Powell D, Deveson Lucas D, Li Z, Aranda J, Harrison P, Nation RL, Adler B, Harper M, Boyce JD and **Li J**. 2015. The transcriptomic response of *Acinetobacter baumannii* to colistin and doripenem alone and in combination in an in vitro pharmacokinetics/pharmacodynamics model. *J Antimicrob Chemother* 70:1303-1313.
3. Azad MA, Roberts KD, Yu HH, Liu B, Schofield AV, James SA, Howard DL, Nation RL, Rogers K, de Jonge MD, Thompson PE, Fu J, Velkov T and **Li J**. 2015. Significant accumulation of polymyxin in single renal tubular cells: a medicinal chemistry and triple correlative microscopy approach. *Anal Chem* 87, 1590-1595.
4. Velkov T, Roberts KD, Nation RL, Wang J, Thompson PE and **Li J**. 2014. Teaching 'old' polymyxins new tricks: New-generation lipopeptides targeting Gram-negative 'superbugs'. ACS *Chem Biol* 9(5):1172-1177.
5. Sandri AM, Landersdorfer CB, Jacob J, Boniatti MM, Dalarosa MG, Falci DR, Behle TF, Bordinhao RC, Wang J, Forrest A, Nation RL, **Li J** and Zavascki AP. 2013. Population pharmacokinetics of intravenous polymyxin B in critically ill patients: implications for selection of dosage regimens. *Clin Infect Dis* 57, 524-531.