conferenceseries.com SciTechnol
15th International Congress on
VISION SCIENCE AND EYE
August 10-11, 2017 | London, UK

Rajamani Lakshminarayanan et al., Int J Ophthalmic Pathol 2017, 6:4
DOI: 10.4172/2324-8599-C1-002

Rational design of Cell-selective Antimicrobial Peptides

Rajamani Lakshminarayanan[1,2] and **Roger W Beuerman**[1,2]
[1]Singapore Eye Research Institute, The Academia, Discovery Tower Level 6, Singapore
[2]Ophthalmology and Visual Sciences Academic Clinical Program, Duke-NUS Graduate Medical School, Singapore

The evolution of antibiotic-resistant pathogens pose significant threat to human health and healthcare systems and account for considerable economic burden world-wide. In particular, the Gram-negative bacteria adapted sophisticated machineries that can overcome all the available pathways targeted by current antibiotics. Agents that target cytoplasmic membranes of prokaryotes are attractive alternatives for combating antimicrobial resistance owing. Cationic antimicrobial host defense peptides have been shown to elicit rapid bactericidal action by targeting cytoplasmic membrane of the bacteria, but their cytotoxicity for mammalian cells limited their therapeutic potential. Our preliminary investigations that the cationic polymer ε-polylysine has superior cell-selectivity than isomeric α-polylysine. Based on this preliminary data, we replaced α-lysine residues in prolific pore forming peptide, melittin from bee venom, with ε-lysine residues and determined their cell selectivity. Melittin elicited toxic effect on both microbial as well as mammalian cells confirming its poor cell selectivity. However, substitution of N-terminal α-lysine with ε-lysine residues increased the cell selectivity while C-terminal substitution did not alter the properties. Multiple substitution of ε-lysyl residues enhanced the cell selectivity significantly. Two such peptides displayed excellent antimicrobial activities against MRSA, vancomycin-resistant enterococci, antibiotic-resistant *P. aeruginosa*, carbapenem-resistant enterobacteriacae and azole-resistant *Candida* spp strains. The modified melittin peptides display rapid bactericial properties and slightly weaker pore-forming properties than melittin while non-cytotoxic for mammalian cells. We further confirmed the enhanced cell selectivity upon α-lysylation in mastoparan B, the antimicrobial peptide present in harnet's venom. Together, these results establish the rational modification of multifunctional host-defense peptides by α-lysylation with improved cell selectivity.

Biography

Dr. R. Lakshminarayanan obtained his PhD from the Department of Chemistry at the National University of Singapore. He was a recipient of the Singapore Millennium Foundation Postdoctoral Fellow and then obtained further postdoctoral training at the University of Southern California. Since 2009, he has been working as a Principal Investigator II at the Singapore Eye Research Institute. His major interests include antimicrobial polymers and peptides, antimicrobial coatings for medical devices, new crosslinking methods for electrospinning of hydrogel polymers and protein aggregation diseases. He has published more than 80 papers in reputed journals, 3 book chapters and 6 invention disclosures.

lakshminarayanan.rajamani@seri.com.sg

Notes: