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Characterisation of peptides designed against the omega loop of class A β-lactamases to reverse antimicrobial resistance in bacteria

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Abstract

Mycobacterial infections result in huge damage to public health and economy each year because of the alarming emergence of extensively drug-resistant strains of *Mycobacterium tuberculosis* (WHO, 2019). Mycobacteria have long known to be intrinsically resistant to β-lactam antibiotics. B-lactamases are enzymes those protect bacterial cells by hydrolyzing β-lactam ring of antibiotics making them ineffective. Class-A β-lactamases have a conserved structural domain called omega loop (RLDRWETELNEAIPGDARD) participating in catalytic activity being a part of the drug-binding pocket of the enzyme. In this work we have attempted to design and characterize some peptides against the omega-loop of class A β-lactamases to reverse antimicrobial resistance in bacteria. Primarily, about 100 peptides were designed against the conserved sequence of omega-loop of class A β-lactamases. The peptides sequences were subjected to different bioinformatics tool and finally, 10 peptides were synthesized by Fmoc Solid-Phase Synthesis Peptide (SPPS) strategy (J.M. Palomo, 2014). Whole-cell phenotypic evaluations were done to ascertain the hydrolytic potential of pbad-blatem1 (class A β-lactamases) against different β-lactam antibiotics in presence of all the synthesized peptides in different bacteria (*E. Coli* CS109, *Mycobacterium smegmatis* and *Mycobacterium tuberculosis* H37Rv) and we observed a significant decreased level of hydrolytic activity of blatem1 in the presence of peptides. Thus, the study may explore the role of peptides in masking of omega-loop facilitating β-lactams to kill the bacteria.

Biography:

Sarmistha Biswal is an ASEM-DUO (UK-India) Exchange Fellow between Indian Institute of Technology (IIT), Kharagpur, India and the Institute of Structural and Molecular Biology, Birkbeck, University of London. She is a young woman investigator whose current research interest is in tackling antibiotic resistance in infectious bacterial diseases. She has published peer-reviewed research articles and presented her research in international meetings.

Speaker Publications:

1. "Glutamic acid at position 152 and serine at position 191 are key residues required for the metallo-β-lactamase activity of NDM-7"; Kumar G, Issa B, Biswal S, Jain D, Bhattacharjee A, Ghosh AS; International Journal of Antimicrobial Agents/ 2020 Jan;55(1):105824.
2. "Glutamate residues at positions 162 and 164 influence the beta-lactamase activity of SHV-14 obtained from *Klebsiella pneumoniae*"; Kumar G, Biswal S, Nathan S, Ghosh AS; FEMS Microbiol Lett/ 2018 Feb 1;365(2).
3. "A putative low-molecular-mass penicillin-binding protein (PBP) of *Mycobacterium smegmatis* exhibits prominent physiological characteristics of DD-carboxypeptidase and beta-lactamase"; Bansal A, Kar D, Murugan RA, Mallick S, Dutta M, Pandey SD, Chowdhury C, Ghosh AS; Microbiology/ 2015 May;161(Pt 5):1081-1091.
4. "A single amino acid substitution in the Ω-like loop of *E. coli* PBP5 disrupts its ability to maintain cell shape and intrinsic beta-lactam resistance"; Dutta M, Kar D, Bansal A, Chakraborty S, Ghosh AS; Microbiology/ 2015 Apr;161(Pt 4):895-902.
5. "PBP5, PBP6 and DacD play different roles in intrinsic β-lactam resistance of *Escherichia coli*"; Sarkar SK, Dutta M, Chowdhury C, Kumar A, Ghosh AS; Microbiology/ 2011 Sep;157(Pt 9):2702-2707.
6. "Loss of O-antigen increases cell shape abnormalities in penicillin-binding protein mutants of Escherichia coli"; Ghosh AS, Melquist AL, Young KD; FEMS Microbiol Lett/ 2006 Oct;263(2):252-7.

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