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Prospects of comparative genomics of β-lactamase genes in rapid antimicrobial resistance (AMR) detection and newer β-lactamase inhibitors

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Abstract

Beta-lactam antibiotics have been a prime choice for treating a number of infectious diseases. However, their widespread & indiscriminate use has resulted in microbial resistance towards this important class of antibiotics. Bacteria hydrolyze these antibiotics using their intrinsic/acquired antibiotic modifying enzymes, the β-lactamases. Studies from our laboratory using comparative genomics of β-lactamase genes and their promoters in a large number of *Y.enterocolitica* and *E.coli* strains revealed that, though the promoters were conserved, point mutations were present in different β-lactamase genes. Similar observations were also made while compiling a database of β-lactamase genes. Identification of consensus sequences among the β-lactamase genes of different bacteria could be useful for developing rapid and simple methods for detection of pathogens harbouring these genes. Our studies also revealed that mutations at sites other than active site of the enzyme may create diverse local changes in the 3D structure of the enzyme which might affect its binding affinity with β-lactam antibiotics as well as β-lactamase inhibitors. These findings might be useful for designing better β-lactamase inhibitors with improved efficiencies in future. Currently, we are working on developing a rapid and simple Loop Mediated Isothermal Amplification (LAMP) test using β-lactamase genes for detection of *Y.enterocolitica*. We are also working to identify novel sequences in β-lactamase genes which can be used as ideal targets for designing newer β-lactamase inhibitors. These studies would surely help us make assessments of the true potential of β-lactamase genes to serve as markers for rapid detection of AMR and salvaging several β-lactam antibiotics by designing novel β-lactamase inhibitors.

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