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Genotypic characterization of multi-drug resistant coliform bacteria: Insights into their mechanisms of antibiotic resistance using Whole Genome Sequencing

Prajakta A. Hatekar[1], Sushrut Kulkarni[1], Priti P. Yewale[1], A. Mandal[2], N.N. Nawani[1*] and J. Jass[3]

[1]Microbial Diversity Research Center, Dr. D. Y. Patil Biotechnology and Bioinformatics Institute, Dr. D. Y. Patil Vidyapeeth, Pune, 411 033, INDIA

[2]Systems Biology Research Center, School of Biosciences, University of Skövde, SWEDEN

[3]The Life Science Center, School of Science and Technology, Örebro University, Örebro, SWEDEN

[*]Corresponding author: neelunawani@gmail.com

Abstract

Anthropogenically polluted water is a potential reservoir for pathogenic microorganisms and micro-contaminants like antibiotics. Due to the selective pressure of antibiotics, resident bacteria tend to acquire resistance mechanisms through mutations, genome rearrangements and horizontal gene transfer. (Darvinism: Survival of the fittest!). This study aimed to isolate and characterize multi-drug resistant coliform bacteria from natural water bodies of Pune city and to analyse whole genome sequences for identification of genomic alterations possibly responsible for multi-drug resistance (MDR). The isolates were identified by next generation sequencing. Sequence type of isolates was determined by Multilocus sequence typing (MLST). Genes responsible for antibiotic resistance were identified using Comprehensive Antibiotic Resistance Database (CARD). The isolates were found resistant to third and fourth generation cephalosporins and carbapenems which is very alarming as these are the antibiotics of last resort. The mechanisms of resistance developed by isolates were efflux pump mediated drug resistance and β- lactamase production. Mutation rate was found higher when set of genes responsible for efflux pump mediated drug resistance (*mdt A, mdt B, mdt C, mex J, mex K, opr N*) was analysed. Mutation leading to change in single amino acid (Arg-235 to Lys) was detected in *Pseudomonas aeruginosa* ST- 635 for the gene $bla_{\text{PDC-3}}$. *Escherichia coli* ST-410 and ST- 617 were found single amino acid variants for the gene $bla_{\text{CMY- 47}}$ (Pro-121 to Ser). Mutations observed in CMY-47 and PDC-3 are indicative of rapid evolution of AmpC β- lactamases. Indiscriminate use of antibiotics has resulted into emergence and dissemination of MDR leading to antibiotic- driven adaptive bacterial evolution.

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