In-silico approaches to understand antibiotic resistance in clinically important bacterial pathogens

Sravan Kumar Miryala, Sudha Ramaiah and ***Anand Anbarasu****

Medical & Biological computing laboratory, School of Biosciences & Technology,Vellore Institute of Technology, Vellore-632014, India
Email: aanand@vit.ac.in

Abstract

The emerging drug resistance in the pathogenic bacteria renders the treatment option difficult and new therapeutic approaches need to be explored to combat against the infectious causing microbes. In our study, we have employed systems biology approach to understand the molecular basis of drug resistance strategies exerted by *E. coli, P. mirabilis* and *F. tularensis* strains using gene interaction network analysis. We have also studied the functional role of β-lactamase genes *penA* and *SHV-11* in drug resistance. Our results suggest that the *penA* gene play a crucial role in peptidoglycan biosynthesis, β-lactam resistance, amide ligasebiosynthesis and also in metabolism of glutathione. The β-lactamase gene *SHV-11* primarily aids bacteria in preserving genome integrity by surviving environmental stress through a DNA damage repair process. The genes *gyrA, parC, gyrB, parE, recA, dnaA, polB, dnaK, mutS,* and *dnaN* account for more than 41% of all interactions in the network and hence, these genes can be regarded hub nodes in the network and can be exploited as therapeutic targets in new drug discovery. In other study, we observed that the *E. coli* AMR genes contribute mainly to multidrug efflux systems such as mdtEF-toC tripartite efflux pump and macABtolC efflux pump. The *P. mirabilis* genes *rpoB, tufB, rpsl, fusA* and *rpoA* could be exploited as the potential drug targets as these genes are observed to have a critical role in regulating the vital functions within the bacterium. Furthermore, we have made an attempt to understand the molecular level interactions between the host cellular components and the *F. tularensis* genes. The *F. tularensis* genes *purL, katG, proS, rpoB* and *fusA* having more number of direct interactions with the host genes and are observed to have key role in adaptability to various stressors.