Furthermore, information on critical evolutionary trajectories that could be responsible for resistance can be obtained using whole genome sequencing. In turn, proteins or biochemical pathways within those trajectories could also provide candidates for the discovery of agents that target mechanisms of resistance and prevent the development of resistance. For example, *Pseudomonas aeruginosa*, evolved to colistin resistance in a laboratory environment using quantitative evolution pipeline, exhibits accumulation of mutations specific to resistance in the pmrAB two-component system. This confirmed the previously established link to the colistin resistance (Mehta et al. 2017). Such invaluable information can be utilized in not only the development of new inhibitors in *P. aeruginosa*, but this approach can be utilized in the discovery of mutations responsible for resistance in other bacterial strains.

It is not always that new target biomolecules should be identified to overcome the bacterial resistance. DNA gyrase, an essential bacterial enzyme, is a well-established and primary target for fluoroquinolones. The mutations in bacterial DNA gyrase result in quinoline resistance (Gruger et al. 2004), thus requiring a novel mechanism to utilize this bacteria-specific target. The 3D structure of *S. aureus* DNA gyrase can be utilized for discovery of compounds that target both Gram-positive and Gram-negative bacteria. A thiophene-based inhibitor ([*N*-(2-amino-1-phenylethyl)-4-(1H,2H,3H-pyrrolo[2,3-β]pyridin-3-yl)thiophene-2-carboxamide]) was found to be active in both Gram-positive and Gram-negative resistant strains by binding to the protein at a site remote from the DNA cleavage site. This previously unexploited pocket in gyrase can be used for the design of drug candidates against fluoroquinolone-resistant bacteria (Chan et al. 2017).

One of the possible future target and underexplored targets is RecA, a bacterial multifunctional protein essential to genetic recombination, DNA repair, and regulation of SOS response. RecA is a recombinase protein implicated in the bacterial drug resistance, survival, and pathogenicity (Pavlopoulou 2018), where the activation of bacterial SOS response is responsible for the development of antibiotic intrinsic and/or acquired resistance (Bellio et al. 2017), and therefore could be a potential drug target (Nautiyal et al. 2014).

The above demonstrates that there are considerable efforts in the discovery of novel targets, druggability potential of known proteins, or identification of new sites on known target proteins. There are challenges in utilizing such information and obtaining drug candidates interacting with these new target sites, which may be overcome a greater integration of available of the experimentally obtained information and computational resources.