multidrug-resistant *A. baumannii* strain revealed 31 differentially expressed proteins, including three proteins involved in biofilm suppression and the oxidative stress response (Karami-Zarandi et al. 2017). These authors hypothesized that it may be the result of adaptation of the hypermutator strain. Due to mutations, likely random mutations, one can imagine that the impact of this phenotype varies according to strains and situations.

9.2.11 Multidrug Efflux Pumps

Planktonic bacteria and bacteria in biofilm exhibit differences in cell permeability, including efflux pump activity, which could be related to the differences observed in the susceptibility to antibiotics (Berlanga et al. 2017). Overproduction of the resistance-nodulation-cell division (RND)-type efflux pumps AdeABC and AdeIJK was demonstrated to alter bacterial membrane composition, resulting in decreased biofilm formation but not motility (Yoon et al. 2015). Similar results were described by Vieira et al. (2017) for the CmeABC MDR pump in *Campylobacter jejuni* with *Acanthamoeba polyphaga* by using a modified gentamicin protection assay. Mutants of *tol*C, a gene encoding a part of the AcrAB-TolC system in *E. coli*, exhibit decreased adhesion and biofilm formation, but expression of AcrAB only protects *E. coli* from forming biofilm against low concentrations of ciprofloxacin (Soto 2013). Pamp et al. (2008) also showed that *P. aeruginosa* mutants defective in mexAB-oprM-mediated antimicrobial efflux are not able to develop a tolerant subpopulation in biofilms. Buffet-Bataillon et al. (2016) showed that quaternary ammonium compounds (QACs) are able to induce overexpression of efflux pumps, which could lead to a stress response, facilitating mutation in the quinolone resistance determining region and biofilm formation with an increased risk of the transfer of mobile genetic elements carrying fluoroquinolone or QAC resistance determinants. Wang et al. (2017) investigated the interactions of *S. mutans* with the quaternary ammonium monomer dimethylaminohexadecyl methacrylate and showed that it could induce persister formation in biofilms, but the authors did not describe the molecular mechanisms that explain these results.

Another explanation for the implication of efflux pumps in the formation of biofilm could be increased extrusion or intrusion of quorum-sensing molecules (Soto 2013).

9.3 Usual and Innovative Means to Overcome Biofilm Resistance in Biofilms

Faced with the difficulty of treating infections caused by bacteria in biofilms, many strategies have been attempted to tackle biofilms (Kostakioti et al. 2013; Lee et al. 2016; Ribeiro et al. 2016; Wood 2016, 2017; Taha et al. 2018).