et al. 2006; Linares et al. 2006; Yim et al. 2006; Martínez 2008; Aminov 2009; Bernier and Surette 2013; Andersson and Hughes 2014; LeRoux et al. 2015). These potential roles of antibiotics were studied mainly under laboratory conditions using low antibiotic concentrations and under the umbrella of hormesis hypothesis (Davies et al. 2006; Fajardo and Martínez 2008). In this concept, the effects of antibiotics are dose dependent: low-concentration antibiotics affect the regulation of specific sets of genes in target bacteria, while the increasingly higher concentrations provoke stress responses, with the even higher concentrations being lethal. It has been suggested that the main role of low-concentration antibiotics in nature is regulatory in contrast to the lethal effects of high-dose antibiotics used by humans for infectious disease treatment (Aminov 2009). Another relevant question is whether the drugs at different concentrations interact with the same cellular targets.

23.15 Low-Dose Antibiotics: Phenotypic Effects

Recently, the effects of low-dose antibiotics have been summarized by us in a research topic (Nosanchuk et al. 2014). Probably the best-studied model is opportunistic pathogen *P. aeruginosa*, infection with which is often fatal for cystic fibrosis patients. It has been shown during the early days of investigating the effects of low-dose antibiotics that the subinhibitory concentrations of a macrolide antibiotic, azithromycin, suppress its pathogenic properties such as alginate overproduction and biofilm formation *in vitro* (Ichimiya et al. 1996). The subinhibitory concentrations of other antibiotic classes such as ceftazidime (β-lactam) and ciprofloxacin (quinolone) also appeared to be effective in suppressing the quorum-sensing-regulated virulence factors of this bacterium (Skindersoe et al. 2008). According to the authors, the potential mechanism for this effect is the interaction of these two drugs with the cellular membrane, which affects its permeability and subsequently the flux of the quorum-sensing molecule *N*-3-oxo-dodecanoyl-L-homoserine lactone. It is important to note here that these two antibiotics at therapeutic concentrations have differential targets, the bacterial cell wall for ceftazidime and bacterial topoisomerases for ciprofloxacin.

Interestingly, however, the antibiotics of the same classes as described above, with the same model bacterium (Skindersoe et al. 2008), may demonstrate the opposite effects as well. Exposure of *P. aeruginosa* to the subinhibitory concentrations of another β-lactam, imipenem, for example, results in the elevated alginate production and in the increased volume of biofilm (Bagge et al. 2004). Another quinolone drug, norfloxacin, at subinhibitory concentrations induces the formation of biofilm by *P. aeruginosa* (Linares et al. 2006). These discrepancies suggest that the degree of freedom in interaction with cellular targets is higher at subtherapeutic concentration. Thus, the antibiotics of the same class,