bacteria reduce their metabolism, resulting in slower growth and creating what has been called persister cells, which will be described in more detail in the next section (Fux et al. 2005; Lewis 2008). These cells are less sensitive to most antibiotics, as antibiotics tend to target metabolic processes in the bacterial cells (Fux et al. 2005; Li and Zhang 2007). To target resistance in biofilms, a few different strategies have been pursued. The most explored avenue is to interfere with inter-bacterial communication or so-called quorum sensing (QS) involving three separate systems of molecules: acylhomoserine lactone (AHL) QS system restricted to Gram-negative bacteria, the autoinducing peptide (AIP) system in Gram-positive bacteria, and the autoinducer-2 (AI-2) system present in both types of bacteria (Waters and Bassler 2005; Brackman et al. 2012; Brackman and Coenye 2015; Singh et al. 2017). Four strategies have been investigated to inhibit QS and thus block biofilm formation.

The first is to target signal synthesis (Hentzer and Givskov 2003). This has been successfully done for AHL production and resulted in clearance of bacterial infections, including *P. aeruginosa* lung infection *in vivo* (Parsek et al. 1999; Hoffmann et al. 2007). It has also been done for AI-2 *in vitro* although no evaluation of biofilms has been performed so far (Shen et al. 2006; Han and Lu 2009).

The second strategy, quorum quenching (QQ), is a broad term for disrupting QS signaling based on degradation or inactivation of the signaling molecules. This has been accomplished by enzymatic degradation of AHL (Reimmann et al. 2002; Chun et al. 2004; Yang et al. 2005), but as far as we are aware, no specific quenchers have been described for AIP or AI-2.

A third strategy, which sometimes is included in the concept QQ, is inhibition of signaling based on signal analogues. Both synthetic and natural molecules have been found for each of the three systems that affect biofilm formation and show increased clearance of infection *in vivo*. For more specific information see Rasmussen et al. (2005), Ren et al. (2005), Ishida et al. (2007), Morohoshi et al. (2007), Brackman et al. (2011), Jakobsen et al. (2012), Cirioni et al. (2013), Roy et al. (2013, 2018), Aggarwal et al. (2015), and Kuo et al. (2015).

Finally, the fourth strategy of QQ is to block signal transduction. One group of molecules that show big promise is furanones (originally from cinnamon) that in various studies have blocked signal transduction and affected biofilm formation *in vitro* as well as in a variety of animal models of infection with *P. aeruginosa*, *E. coli*, *Bacillus subtilis*, *Streptococcus* spp., and other organisms to increase the sensitivity to antibiotics (Hentzer and Givskov 2003; Ren et al. 2004; Christensen et al. 2012; He et al. 2012; Starkey et al. 2014). Although promising results have been shown with these compounds, toxicity is currently limiting their use. As QS is involved in several types of bacterial group behavior, not only biofilm formation, this means that similar strategies may be used to inhibit virulence, competence, and conjugation that are involved in pathogenesis and spread of antibiotic resistance.