subfamilies (Hvorup et al. 2003). Family 1 primarily harbors MATE drug efflux systems inherent in bacterial microorganisms (Hvorup et al. 2003). Family 2 members are composed of MATE transporter systems found mainly in eukaryotic organisms (Hvorup et al. 2003). Members of MATE family 3 are found chiefly in the eubacteria (bacteria) and the archaebacteria (archaea), which are all prokaryotic organisms (Hvorup et al. 2003). In general, the MATE transporters are energized by ion motive forces and work via an antiport system in an ion–substrate exchange manner (Huda et al. 2003b; Otsuka et al. 2005; Steed et al. 2013; Song et al. 2014). The primary amino acid sequences of the MATE transporters vary in length between 400 and 1000 residues (Chen et al. 2002; Huda et al. 2003a). The secondary structures consist of 12 transmembrane α-helices that traverse the membrane in a zigzag manner (He et al. 2010; Zhang et al. 2012).

The tertiary structures for several key bacterial MATE transporters have been elucidated (Lu et al. 2013a, b; Tanaka et al. 2013; Symersky et al. 2015). The first of these MATE transporter crystal structures to be elucidated is NorM from the bacterium *V. cholerae*, also denoted as NorM-VC (He et al. 2010). The NorM structure was found to devoid of bound substrate and in an open configuration facing the periplasmic side of the cytoplasmic membrane (He et al. 2010). Shortly after the elucidation of the NorM-VC structure, other MATE transporter structures were reported, for NorM-NG from *N. gonorrhoeae* (Lu 2016), DinF from *Bacillus halodurans* (Lu et al. 2013a), and PfMATE from *Pyrococcus furiosus* (Tanaka et al. 2013). These MATE transporters shared similarities in structures with a pseudo-twofold axis of symmetry involving two helical bundles composed of helices 1 through 6 and helices 1 through 12 (Lu 2016). Studies of highly conserved amino acid residues within the MATE transporters have served as a basis for the development of a mechanistic model involving an ion-driven solute transport system across in the membrane through the transporters (Kuroda and Tsuchiya 2009; Nies et al. 2016). Future work will be interesting to determine to what extent other related MATE transporters, or even non-MATE transporters, harbor the current ion-coupled substrate transport models, as well. In any case, members of the MATE transporter superfamily will also certainly constitute clinically appropriate bacterial and cancer targets for putative modulation.

8.1.2.4 SMR Superfamily of Drug Efflux Pumps

The SMR family of antimicrobial transporters belongs to the overall larger drug/metabolite transporter (DMT) superfamily (Paulsen et al. 1996; Jack et al. 2001). As a whole, members of the SMR family confer bacterial resistance to antibiotic and antiseptic agents, especially those agents that fall under the quaternary ammonium compound (QAC) class of antimicrobial agents (Paulsen et al. 1996). The SMR pumps are also secondary active transporters, being driven by ion motive forces, such as that provided by protons (Schuldiner 2009; Dastvan et al. 2016). Additionally, transporters belonging