

these signaling compounds. The antibiotic discovery programs have been confined, almost solely, to soil ecosystems, and the “dialects” we are mostly familiar with are those of the soil streptomycetes (Aminov 2017). But if antibiotics are used as a language of communication, then it must be “spoken” by a much broader diversity of microbiota by generating structurally similar compounds. The inclusion of other members of microbial communities and methods of testing for antibiotic production may uncover the genuine magnitude of the environmental antibiome language. For example, now we know that the β -lactams represent an abundant group of antibiotics and they are produced by a wide range of microorganisms (Aminov 2017), not confined to the representatives of the originally discovered *Penicillium* (Fleming 1929). Similarly, aminoglycosides and thiopeptides are produced by taxonomically divergent actinomycetes and *Bacillus* spp. (Flatt and Mahmud 2007; Brown et al. 2009; Liao et al. 2009) and cephalosporins – by fungi, actinomycetes, and Gammaproteobacteria (Liras et al. 2008; Liras and Martin 2006). Because of space limitations, only the carbapenem group of β -lactams, one of the most therapeutically important β -lactam antibiotics currently in use (Nicolau 2008), will be discussed in the context of how this signaling molecule has evolved in several lineages by convergent evolution to serve as a signaling regulatory molecule in a variety of microbiota.

23.19 Carbapenems: Convergent Evolution and Regulation in Different Bacteria

Initially, the biosynthesis of carbapenem was discovered in *Streptomyces cattleya* (Kahan et al. 1972). Later, the synthesis of structurally similar compounds was found to be performed by other *Streptomyces* species as well as by Gram-negative bacteria belonging to *Serratia* and *Erwinia* (Parker et al. 1982). Carbapenem compounds are also produced by a luminescent entomopathogenic bacterium *Photorhabdus luminescens* (Derzelle et al. 2002). Compared with the classical β -lactam biosynthesis pathway for penicillins, cephamycins, and cephalosporins, carbapenems are synthesized via a different pathway (Williamson et al. 1985). The genes involved in the synthesis of carbapenems are organized into clusters (McGowan et al. 1997; Cox et al. 1998; Derzelle et al. 2002; Núñez et al. 2003), and while the enzymes of the biosynthetic pathways share some similarities among the Gram-positive and Gram-negative producers, they are noticeably divergent (Coulthurst et al. 2005). These enzymes probably evolved from the primary metabolic enzymes in corresponding antibiotic producers and represent an example of convergent evolution.

These examples of convergent evolution can be seen from a different perspective, that is, as a convergence to kill (Fischbach 2009). Once again, we must emphasize here that achieving killing concentrations of antibiotics