

introduction of a new antibiotic and with the regulatory constraints to their use, requires the development of effective alternatives, a research that is still in the early stages (WHO 2014; Ruer et al. 2015).

During the last decades, bacteriophages (phages) gained attention in the West as alternatives to antibiotics. Phages are viruses that infect bacteria. Compared to antibiotic therapy, the use of phages has become very appealing: (i) they show great specificity and efficiency in lysing the host bacteria, without affecting the natural flora of the patient; (ii) phages are effective against antibiotic-resistant bacteria (Loc-Carrillo and Abedon 2011); (iii) as viruses of bacteria they are harmless for humans and animals; (iv) they replicate only when the host bacterium is present, allowing to increase their concentration where they are needed; (v) the costs of production and development are far lower than that of antibiotics (Loc-Carrillo and Abedon 2011); (vi) they are the most abundant entities on earth rendering easy to find a phage infecting a particular host. However, many regulatory hurdles still exist as regards the use of phages due to their viral nature, and still, bacteria can also acquire resistance to phages (Labrie et al. 2010).

Current advances in sequencing technologies and DNA manipulation introduce more insights on phage-derived proteins used for bacterial control in food, agriculture, and health (Santos et al. 2018). Though some applications involving phage-encoded proteins can be performed by the phage itself, the use of their proteins has advantages considering the regulatory issues and public acceptance. Phages have evolved for billions of years to recognize, multiply, and kill their hosts in a very competent and efficient manner. To understand the role of phage proteins and their potential as antimicrobials, it is important to depict the phage replication cycle (Figure 15.1).

The phage life cycle starts with the encounter of the phage and its host. Phages interact with bacterial cell surface through adsorption. In this process, phage proteins specifically recognize receptor structures on the bacterial cell. At this time point, phages may need the action of phage enzymes, such as depolymerases that degrade host capsular structures, to gain access to their receptors (Figure 15.1a) (Pires et al. 2016).

After meeting and recognizing the host, phages eject their DNA into the host cell in a process facilitated by phage enzymes, namely, VALs, which are part of the phage structure. These enzymes produce pores in the bacterial peptidoglycan, allowing the passage of the phage genetic material (Figure 15.1b) (Kutter and Sulakvelidze 2005). When the nucleic acid is inside the host cell, a decision has to be made depending on the phage nature: lysogenic or lytic pathway (Figure 15.1c). In the case of a temperate phage, the lysogenic pathway may be chosen leading to the integration of the phage nucleic acid into the bacterial chromosome as a prophage (Figure 15.1d). The phage will replicate along with the bacterial genetic material passing to the bacterial daughters (Figure 15.1e) until a specific stimulus triggers the lytic pathway. When this happens, or after