other protein homologs from diversified hosts have been shown to control infectious diseases with the cooperation of the host complement lytic action, with many evidences proved in murine models. Fewer studies have also shown that they could also be used to degrade EPS and compose new anti-biofilm agents. Overall, depolymerases proved their potential as alternatives to antibiotics to control multidrug-resistant bacterial pathogens. Moreover, due to their high specificity and ability to discriminate the bacterial polysaccharides, they are also expected not to interfere with the normal flora.

15.3 Peptidoglycan-Degrading Enzymes

During their replication cycle, the genome and the progeny particles of tailed phages need to cross the bacterial cell. The first needs to get in (Figure 15.1b) and the second has to get out (Figure 15.1i). In both cases, phages need to degrade the peptidoglycan (a polymer also known as murein), the major component of the bacteria cell wall and the responsible for the structural integrity and shape of the cell. To accomplish that, they use different enzymes that are specialized for each case (Figure 15.2) (Oliveira et al. 2018). In the first case, to facilitate injection of their genome, phages use VALs, enzymes anchored to the phage particle that promote a local degradation of the peptidoglycan. This peptidoglycan digestion must not be harsh to prevent premature death of the host cells. In the second case, phages use endolysins, late proteins synthesized as soluble molecules that degrade the peptidoglycan to a large extent from within the cells, causing lysis of the cells, allowing the release of the phage progeny (Schmelcher et al. 2012).

Besides degrading the same polymer, VALs and endolysins face a diverse and changeable composition of the peptidoglycan. Peptidoglycan is composed of several chains of alternating residues of *N*-acetylmuramic acid (MurNAc) and *N*-acetylglucosamine (GlcNAc), connected by β-1,4 glycosidic bonds, linked to a short stem tetrapeptide. Whereas the carbohydrate backbone is conserved in all bacteria, the peptide moiety made of L- and D-amino acids is only conserved in Gram-negative organisms (Silhavy et al. 2010). In Gram-positive bacteria, it is considerably more diverse in terms of length and composition. As a response to this variability, VALs and endolysins have evolved to recognize and degrade all peptidoglycan types found in phage hosts. Their diversity, enzymatic activity, and biotechnological applications are discussed in the next sections.

Different enzymatic catalytic domains (ECDs) can cleave different peptidoglycan bonds and, depending on the bond that they cleave, they have different classifications (Figure 15.4) (Oliveira et al. 2013). Glycosidases cleave the glycan component at the reducing end of GlcNAc as the *N*-acetyl-β-D-glucosaminidases, or at the reducing end of MurNAc as the *N*-acetyl-β-D-muramidases (often called lysozymes or muramidases) and the lytic transglycosidases. The