

synthesis, such as IL-10, and repressing pro-inflammatory cytokine levels of IL-12 and TNF- α .

Treatment with the peptide protected rats against other lethal infections caused by both Gram-negative and Gram-positive antibiotic-resistant strains. Clavanin-MO showed antimicrobial activity by killing bacteria and further helped to resolve infections through its immunomodulatory properties. Therefore, the combination of antimicrobials and immunomodulatory properties represent a new approach to treat infections from antibiotic-resistant strains.

19.3.4 Antibodies plus Reltecimod

In spite of all advantages, a few immunomodulators for use against infections have advanced to clinical stage development. A good example is Reltecimod (AB103), an immunomodulator used to treat soft tissue necrotizing infections. AB103 binds to co-stimulatory receptor CD-28, which modulates immune response. It significantly diminishes the acute inflammatory response leading to tissue and organ damage. This drug is not yet released for use and is currently in clinical development phase 3.

19.4 Potentiators of Antibiotic Activity

Resistance to antibiotics can be classified as intrinsic and acquired resistance. Intrinsic resistance is caused by the lack of target in the bacterial cell, causing some bacteria naturally not to respond to an antibiotic. However acquired resistance refers to the ability of the bacteria to acquire antibiotic resistance through mutations or acquisition of foreign DNA encoding for resistance determinants. The main mechanisms of resistance to antibiotics are (i) production of enzyme that inactivates the antibiotic by hydrolysis or transfer of a chemical group, causing steroid; (ii) overexpression of efflux pumps, which eliminate a wide variety of compounds out of the cell; (iii) reduction or elimination of cellular permeability through changes in the outer membrane permeability, which decreased the effective entry of the antibiotic; (iv) modification of the microbial target by genetic mutation or posttranslational modification of the target; and (v) biofilm formation.

These potentiators of antibiotic activity can be applied either by reversing resistance mechanisms or by sensitizing intrinsic resistant strains. The approaches used to combat MDR include antibiotic–antibiotic combinations (synergistic antimicrobial combinations – potentiators of antibiotic activity) and pairing of antibiotics with nonantibiotics (adjuvants are active molecules that in combination with antibiotics enhance the antimicrobial activity of nonantibiotics).