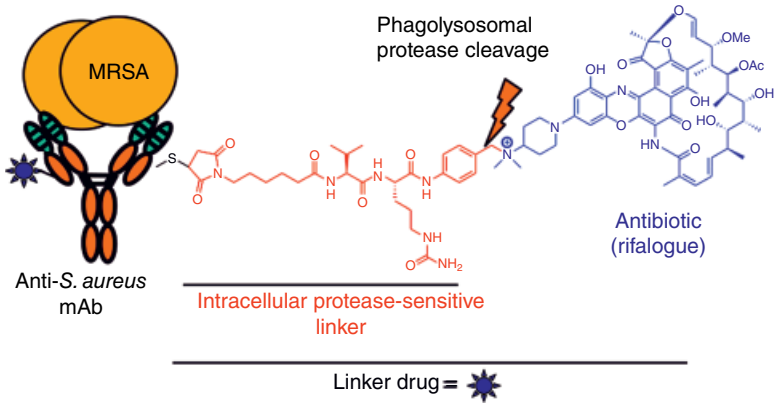

Scheme 16.8 Schematic illustration of the antibody–antibiotic conjugate. *Source:* Reproduced from Lehar et al. (2015) with permission. Copyright 2015 Nature Publishing Group.

had better pesticide effect and also had the potential to be used in curing invasive infections.

Because some drug-resistant bacteria had persisted bacterial cells, which reduced the cellular transport activity and neutralized effective antibiotics, a new antibiotic Pentobra (**23**) with bacterial cell-targeted moiety was designed and synthesized by Schmidt et al. (2014). By introducing a specific 12 amino acid sequence, the tobramycin was endowed with spontaneous permeability. All the relating biological results demonstrated that the modified molecule obtained higher antibacterial activity against both Gram-positive *S. aureus* and Gram-negative *Escherichia coli*, and it also remained noncytotoxic to eukaryotes as expected. As the mentioned resistant *S. aureus*, it has been proved that the precursor peptidoglycan terminus in vancomycin-resistant bacteria was remodeled from D-Ala-D-Ala to D-Ala-D-Lac via mutation (Perkins 1982). The single atom exchange from "NH" to "O" in the cell wall precursors of resistant bacteria resulted in the avoiding action of initial vancomycin. Based on these studies about the mutations sites of antibiotic interactions, Boger's group has done researches about antibiotic modifications for enhancing the binding activity. For countering this mutation, [Ψ[C(=NH)NH]Tpg^4] (**24**) with a complementary single atom exchange in the vancomycin core structure was synthesized and reported in 2011 (Xie et al. 2011). Although its binding ability to the natural D-Ala-D-Ala ligand is twofold less than vancomycin, while it represents a 600-fold increasing to the mutated D-Ala-D-Lac. Its MIC value against vancomycin-resistant bacteria *Enterococcus faecalis* is as low as 0.31 μg ml^{-1}. Furthermore, a range of durable antibiotics (**25**) and (**26**) were created, and they were described with the outstanding features that avoid many known antibiotic resistance mechanisms (Okano et al. 2017). Firstly, the binding