with P128 formulated as a hydrogel, a placebo gel, or a mupirocin nasal (30 mg per dose, 2% mupirocin ointment, GlaxoSmithKline). The median bacterial counts recovered in the P128 hydrogel-treated group was found to present a reduction of more than 2 log units than that of the control groups. Safety use and efficacy of P128 is now studied by GangaGen as a topical treatment in volunteers and patients who are nasal carriers of *S. aureus*, on a combined Phase I and Phase II clinical trials (ClinicalTrials.gov Identifier NCT01746654), respectively. Ply187AN-KSH3b was used to study for the first time a mouse model of *S. aureus* endophthalmitis, an infection of the intraocular cavities, which occur after ocular surgery or trauma (Singh et al. 2014). Eyes treated with Ply187AN-KSH3b with an intravitreal injection (1 μg per eye of mouse) 6 or 12 hours postinfection significantly reduced bacterial burden and the endophthalmitis outcome in mice. Furthermore, protein treatment maintained the normal retinal function and reduced inflammatory cytokines and neutrophil infiltration in the eyes. ClyH was tested in a *S. aureus*-induced bacteremia (Yang et al. 2014). Treatments with ClyH injected intraperitoneally three hours postinfection rescued more than 66.7% of mice from a deadly infection. Furthermore, daily injections of ClyH did not cause harmful effects. Finally, ClyF chemolysin was tested in a bacteremia and burned wound mice models (Yang et al. 2017). In the bacteremia model, ClyF intraperitoneal injected rescued up to 100% of mice from an otherwise deadly infection. No mice died when exposed to higher or repeated doses for five continuous days, which attest for its nontoxicity. In the mice burn wound infection model, topically applied ClyF in a single or double dose or double could reduce the skin bioburden by approximately 1.5 and 3.3 log units of *S. aureus* colonization. The histological analysis showed that ClyF-treated mice exhibited less *S. aureus* colonization below the epidermis of the skin compared to the mocked treated groups.

15.3.1.3 Remarks on VALs

The demonstration of peptidoglycan-degrading activity was first spotted with VALs by the "lysis from without" phenomenon observed in 1940, i.e. when an infection is aborted by a high number of phages that are puncturing the sane cell wall through enzymatic degradation, leading to premature cell death. These peptidoglycan-degrading enzymes have sparked the interested of many researchers to find novel antibacterial agents. Since their discovery, VALs have demonstrated to have better thermostatibility properties when compared to endolysins and differentiate from antibiotics by having (i) distinct mechanism of action, (ii) high specificity and activity against multidrug-resistant pathogens, and (iii) low probability of resistance development. Especially, the engineered VALs represent a new class of enzybiotics that could be custom designed to solve or improve antibacterial traits against emerging antimicrobial resistance.