

**Abstract:**

The discovery of penicillin by Fleming in 1928 was an historical milestone in the fight against infectious disease. Over the following fifty years, pharmaceutical companies discovered and developed over 100 antibiotics effective against a wide range of human pathogens. More recently, the dramatic rise in antibiotic-resistant pathogens has stimulated renewed efforts to identify, develop or redesign antibiotics active against these multi-resistant bacteria. This review focuses on such efforts directed at one large and highly diverse family of toxins, the bacteriocins, which hold great promise as the next generation of antimicrobials. The majority of bacteriocins differ from traditional antibiotics in one critical way: they have a relatively narrow killing spectrum and are, therefore, toxic only to bacteria closely related to the producing strain. Accordingly, they can be considered “designer drugs” that target specific bacterial pathogens. In this review we focus on recent attempts to generate custom designed bacteriocins using genetic engineering techniques. These efforts illustrate the potential of genetically-modified bacteriocins to solve some of the most challenging problems in disease control.