Introduction

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Bacteriocins constitute a large and functionally diverse family of toxins found in all major lineages of Bacteria and Archaea (Riley and Wertz, 2002). Recent studies reveal that bacteriocins play a critical role in mediating microbial interactions and may even play a more fundamental role in maintaining microbial diversity (Kerr *et al.*, 2002; Kirkup and Riley, 2004). Regardless of their precise function in nature, their importance in mediating microbial interactions is clear, based solely on their overwhelming abundance and diversity (Riley, 1998; Gordon and Riley, 1999; Riley and Gordon, 1999). Not only have bacteriocins been identified in most microbial species, but the diversity of bacteriocins is extraordinary, with tens of bacteriocin types found in a single species. According to Klaenhammer (1988), 99% of all bacteria may make at least one bacteriocin and the only reason more have not been isolated is that very few researchers have looked for them.

While bacteriocins are ubiquitous in nature and clearly serve some critical role, they also possess qualities that can be tapped for a myriad of applied uses. In recent years, bacteriocins have been targeted for use in human health, veterinary medicine, and food preservation (Cleveland *et al.*, 2001; Bower *et al.*, 2002; Gillor *et al.*, 2004, 2005). They are an attractive focus for drug development because they are active against every known human, animal, and plant pathogen existing in nature, they are remarkably stable proteins, and they are not toxic to human cells. In addition, many of them display a narrow range of activity enabling the creation of pathogen-specific designer drugs. The use of the bacteriocin nisin in food production (Breukink and de Kruijff, 1999) and colicins E and B in reducing the level of enteric pathogens in livestock (Gillor *et al.*, 2005) lends credence to their perceived promise in human and veterinary therapy.

The first bacteriocin was originally identified in 1925 by Gratia as an antimicrobial protein produced by *Escherichia coli* (Gratia, 1925) and was named "colicin" based on the producing species in which it was identified. Since then, bacteriocins have been the most extensively studied microbial defense system. There are two main features that distinguish the majority of bacteriocins from classical antibiotics: (i) bacteriocins are ribosomally synthesized and (ii) bacteriocins have a relatively narrow killing spectrum (Riley and Wertz, 2002). Bacteriocin genes are either chromosomally or plasmid encoded. The resulting toxin proteins employ a variety of killing mechanisms, including cytoplasmic membrane pore formation, cell wall interference, and nuclease activity (Braun *et al.*, 1994; Smarda and Smajs, 1998).

The bacteriocin family exhibits a diversity of proteins in terms of size, microbial target, mode of action, release, and immunity mechanisms. In an attempt to sort this diverse family, bacteriocins are roughly classified into two main groups, the toxins produced by Gram-negative bacteria and those produced by Gram-positive bacteria.

The bacteriocins produced by Gram-positive bacteria resemble many of the antimicrobial peptides produced by eukaryotes, such as defensins (Papagianni, 2003); they are generally cationic, amphiphilic, membrane-permeabilizing peptides, approximately 2–6 kDa in size (van Kraaij *et al.*,, 1999; McAuliffe *et al.*, 2001). Typically, the biosynthesis of bacteriocins of Gram-positive bacteria is self-regulated with dedicated transport mechanisms facilitating its release (van der Wal *et al.*,, 1995). To date, bacteriocins produced by lactic acid bacteria (LAB), fermenting bacteria long used in the preservation of meat and milk, are the best characterized (Klaenhammer, 1988; Nes *et al.*, 1996). Although many bacteriocins produced by lactic acid bacteria have been shown to be effective against pathogens and spoilage bacteria (see Chapters 9 and 10), only nisin is currently licensed for food use in a partially purified form (see Chapter 10). Significant advances have recently been made in our understanding of the genetic determinants encoding bacteriocin production, their organization, and the molecular mechanisms through which they mediate antibiosis (see Chapter 2). As a result, research is currently under way to improve the efficacy of bacteriocins by genetic manipulation to enable their production in non-native hosts (see Chapters 3, 4, and 6).

Bacteriocins produced by Gram-negative differ from those of Gram-positive bacteria in two fundamental ways: (i) they are usually released through cell lysis and (ii) they are often dependent on host regulatory pathways (Braun *et al.*, 1994; Smarda and Smajs, 1998). For the most part, applied research on bacteriocins has focused on bacteriocins produced by LAB. Nevertheless, one main drawback is that the LAB toxins only inhibits the growth of Gram-positive bacteria. Gram-negative infectious agents responsible for either human, animal or plant diseases, such as *Aeromonas*, *Escherichia*, *Xanthomonas*, *Erwinia*, and *Pseudomonas*, are only rarely sensitive to LAB bacteriocins, unless they are coupled with chelating agents. Consequently, the potential of bacteriocins to contain or kill these pathogens is now being extensively investigated (see Chapters 4 and 8).

Bacteriocin application

The dramatic rise in antibiotic-resistant bacterial pathogens has resulted in renewed efforts to identify, develop, and redesign antibiotics. Several chapters discuss the increasing number of studies exploring the potential of bacteriocins in veterinary medicine (see Chapter 7), crop management (see Chapter 8), food preservation (see Chapters 9 and 10) and human health (see Chapters 4 and 6). In addition, some bacteriocins have been shown to exhibit cytotoxic activity against animal cells (see Chapter 5).

Bacteriocins have long served to mediate naturally occurring microbial population and community dynamics. Their universal presence and surprising abundance argues that these toxins are very successful in whatever precise roles they serve in nature. As we continue to identify and characterize this outstanding diversity of protein toxins, we find an ever-increasing role list of potential applications for bacteriocins in human health and agriculture. The bacteria have done the hard work, evolving a sophisticated set of defense systems, all

we require is the knowledge and creativity to apply them to meet some of our more pressing environmental and health challenges.

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