Bacteriocin and quorum sensing: struggle for existence of lactic acid bacteria

Jiro Nakayama
Department of Bioscience and Biotechnology, Faculty of Agriculture, Kyushu University

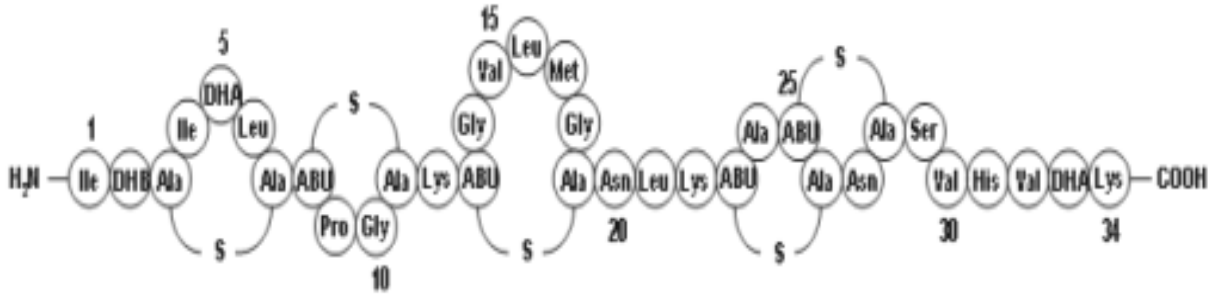
Lactic acid bacteria (LAB) produce lactate showing antimicrobial activity and spontaneously protect the fermented food from spoilage. This lactate productivity of LAB has been utilized well in bioindustry since long time ago. On the other hand, bacteriocins, that are also antimicrobial compounds produced by LAB, have recently shown promise in the application for food and pharmaceutical industries. Many bacteriocins show the antibacterial activity at sub-ppm levels while they are easily degraded into small oligopeptides and amino acids in nature and hardly induce the resistant bacteria. With these features, bacteriocins are expected as safe and ecological antimicrobials in the new century. The antagonism of bacteriocins can be easily realized by in vitro experiment, in which the growth inhibitory zone by bacteriocin is usually larger and clearer than that by lactate. This suggests that antibacterial activity of bacteriocins is much more superior to that of lactate. Moreover, bacteriocins are interesting as a means to achieve a competitive advantage in complex ecosystem consisting of a number of different micro-organisms.

Bacteriocins are proteinaceous compounds whose structures are diverse but classified into several classes with certain common structures. Bacteriocins produced by LAB show antibacterial activity against some other species or strains at nanomolar level. Their mode of action generally targets cytoplasmic membrane and forms pore resulting in efflux of ions and sometime also ATP. This kind of mode of action is common not only in bacteriocins but also other antimicrobial peptides of other organisms such as magainin of flog. It is also known that some bacteriocins bind to certain docking molecules, e.g., lipid II or mannose permease, at first and then inserted into phospholipids bilayer. This mode of action can explain the lower MIC of bacteriocins compared to other antimicrobial peptides directly targeting cytoplasmic membrane. It is also suspected that the concentration of docking molecule on the cell surface determines the susceptibility of the target cell.

In terms of microbial ecology, the difference in antimicrobial spectrum indicates that each bacteriocin targets different competitors and maybe had gained the antibacterial activity under the different niche. For example, lactococcin Q found in our laboratory shows quite narrow antimicrobial spectrum only against *Lactococcus lactis* and its closely-related species, whereas nisin shows broad antimicrobial spectrum even though both bacteriocins are produced by *L. lactis* (see figure below). Lactococcin Q can be considered to be encoded by the selfish gene because it targets same species as the host. Bacteriocin genes are generally encoded together with immunity gene. This means that the host cell harboring bacteriocin gene cluster can survive and grow.

It is also interesting to know how LAB control the expression of bacteriocin gene in nature. Quorum sensing is one of well-studied systems involved in bacteriocin gene control. Quorum sensing is a cell-density dependent regulatory system in which autoinducing signal molecule mediates cell-to-cell communication. By using this system, each bacterial cell senses the number of cells of same species or same strain and adjusts the timing of expression of certain genes. LAB often use quorum sensing for the control of bacteriocin expression in which LAB attack the competitor only when the concentration of the bacteriocin producers is high enough to suppress the growth of competitive strain. Some LAB strains produce more than one bacteriocin. We found that *Enterococcus faecium* NKR5-3 produces at least four different bacteriocins temporally named peptide A to D. Interestingly, expression of these four bacteriocins appears to be induced by peptide D, which is a sort of concerted regulation. This seems to be an efficient system to turn on the offensive phenotype.

Nisin Q produced by *Lactococcus lactis* 61-14 (Class I)



Zendo *et al.*, Biosci. Biotechnol. Biochem., 67,1616 (2003)

Lactococcin Q produced by *Lactococcus lactis* QU4 (Class IIb)

Lactococcin Qα : SIWGDIGQGVGKAAYWVGKAMGNMSDVNQASRINRKKKH

Lactococcin Qβ : KKWGWLAWVEPAGEFLKGFGKGAIKEGNKDKWKNI

Zendo *et al.*, Appl. Environ. Microbiol., 72, 3383 (2006)