Symbiotic Relationship between Human and Bifidobacteria

Kenji Yamamoto
Graduate School of Biostudies, Kyoto University, Kyoto,
606-8502 JAPAN

Bifidobacteria are gram-positive anaerobes naturally present in the dominant colonic microbiota. They have been considered to be key commensals that promote a healthy intestinal tract because of their many beneficial effects on the host, such as regulation of the state of the intestine, reduction of harmful bacteria, immuno modulation, and anticarcinogenic activity. Bifidobacteria colonize the lower intestinal tract, an environment poor in saccharides since sugars are preferentially consumed by the host and microbes present in the upper intestinal tract. Therefore, in order to survive in the lower intestinal tract, they produce various kinds of exo- and endoglycosidases, by which they can utilize diverse carbohydrates.

Recently, we found that 1,2-a-L-fucosidase and endo-a-*N*-acetylgalactosaminidase are widely distributed in the genus Bifidobacteria. They act on sugar chains of mucin glycoproteins that abundantly present in intestine, and should be the key enzymes to better understand the symbiotic relationship between human and Bifidobacteria.

We found that *Bifidobacterium bifidum* produce a specific 1,2-a-L-fucosidase, and its gene has been cloned (1). The recombinant 1,2-a-L-fucosidase consists of 1,959 amino acid residues, and the recombinant catalytic domain specifically hydrolyzes the terminal a-(1→2)-fucosidic linkages of various oligosaccharides and sugar chains of glycoproteins. The primary structure of the catalytic domain exhibited no similarity to those of any glycoside hydrolases, and it was revealed that this enzyme constitutes a novel glycoside hydrolase family (GH family 95). To elucidate the structure of the enzyme, we solved the crystal structure of its catalytic domain (2). Overall structure consists of four regions: an N-terminal b-region, a helical linker, a helical barrel domain and a C-terminal b-region.

The intestinal tract is covered by secretion of mucin glycoproteins including blood group substances. These substances are abundant in a-1,2-fucosyl residues. Then, we suppose that adhesion of Bifidobacteria to intestinal tract may occur through Bifidobacterial 1,2-a-L-fucosidase.

Many Bifidobacteria were found to produce a specific endo-a-*N*-acetylgalactosaminidase, which is the endoglycosidase liberating the *O*-glycosidically linked galactosyl b1→3 *N*-acetylgalactosamine disaccharide from mucin glycoprotein. The structure of *O*-glycan of disaccharide is one of the most abundant core structure in mucin glycoproteins. The molecular cloning of the enzyme was carried out on *Bifidobacterium longum* based on the information in the database (3). The gene was found to code 1,966 amino acids and the enzyme constitutes a novel GH family 101. This enzyme is believed to be involved in the catabolism of oligosaccharide in intestinal mucin glycoproteins.

It has been widely accepted that oligosaccharides in human milk other than lactose play a key role in the growth of bacteria because an intestinal flora of breastfed infants is predominant with Bifidobacteria, whereas bottle-fed infants do not show such a rapid colonization. We found that *Bifidobacterium bifidum* produce a novel lacto-*N*-biosidase acting on human milk oligosaccharides. Human milk is reported to contain more than 100 oligosaccharides, and their building blocks are three basic core disaccharides, lactose, lacto-*N*-biose (galactosyl b1→3 *N*-acetylglucosamine), and *N*-acetyllactosamine (galactosyl b1→4 *N*-acetylglucosamine). The lacto-*N*-biosidase can release lacto-*N*-biose from various oligosaccharides in human milk. We cloned its gene and showed that the expressed protein consists 1,112 amino acids residues. We supposed that this enzyme is crucially involved in the degradation of human milk oligosaccharides.

References

1) Katayama, T., *et al. J.Bacteriol*., **186**, 4885-4893 (2004). 2) Ngae, M., *et al*. *J.Biol.Chem.,* **282**, 18497-18509 (2007). 3) Fujita, K. *et al. J.Biol.Chem.,* **280**, 37415-37422 (2005).