GENOME WATCH

Milk and two oligosaccharides

Alan Walker

This month's Genome Watch reviews three recent papers that describe bifidobacterial genomes.

Bifidobacteria comprise a phylogenetically distinct group of approximately 30 species of Gram-positive, anaerobic rods belonging to the Actinobacteria phylum and are common inhabitants of the gastrointestinal tract of humans and other mammals. Infants are born sterile but bacterial colonization of the gut occurs rapidly after birth. In breast-fed infants, bifidobacteria frequently predominate in the gastrointestinal tract and consequently might have a role in the development and maturation of the healthy gut. After weaning, however, the population of bifidobacteria declines, and these species are less abundant members of the gut microbiota in adults. *Bifidobacterium* species have therefore gained attention as potential probiotics, with several postulated therapeutic benefits.

Sela *et al.*[1] recently reported the complete genome sequence of *Bifidobacterium longum* subsp. *infantis*, a subspecies that commonly inhabits the infant gastrointestinal tract. *B. longum* subsp. *infantis* has the largest bifidobacterial genome reported to date, comprising a 2.83 Mb chromosome that is estimated to contain 2,423 protein coding sequences. Genomic analysis revealed intriguing insights into the intimate connection between this bacterium and its infant host. The genome contains complete pathways for the synthesis of the vitamins riboflavin, thiamine and folate, which could benefit the infant. In addition, a novel 43 kb cluster of genes dedicated to the import and use of human milk oligosaccharides (HMOs) that infants cannot digest was identified. Sequence analysis confirmed the presence of this cluster in other *B. longum* subsp. *infantis* strains, suggesting that there is a conserved

mechanism for HMO utilization in this subspecies. From a human evolutionary point of view, supplying milk oligosaccharides that have no nutritional value for the infant would seem to be an inefficient use of the mother's resources. The authors postulate that instead, these oligosaccharides might be involved in the selective enrichment of commensal species such as *B. longum* subsp. *infantis*.

Genome sequences from three strains of *Bifidobacterium animalis* subsp. *lactis* have also recently been reported[2,3]. *B. animalis* subsp. *lactis* naturally inhabits the gastrointestinal tract but is also the most common *Bifidobacterium* species to be used as a probiotic in North America and Europe. At around 1.9 Mb in size, these three genomes are smaller than those found in other bifidobacteria. However, a comparison of these strains with previously sequenced genomes of *B. longum* subsp. *longum* and *Bifidobacterium adolescentis* indicated that a reasonable proportion of genes are conserved among all bifidobacteria. Notably, however, many of the genes involved in HMO catabolism in the *B. longum* subsp. *infantis* genome were not present in *B. animalis* subsp. *lactis*, indicating that there are niche-specific adaptations between these two groups. Genome analysis did, however, indicate the presence of a range of other factors that are important for colonization and persistence in the gastrointestinal tract, such as the ability to degrade a range of milk galactosides and plant-derived oligosaccharides, and a bile salt hydrolase that mediates tolerance to bile. Insight into the probiotic function of *B. animalis* subsp. *lactis* was provided by the identification of the *fos* gene cluster. This cluster is involved in processing fructooligosaccharides, which are common prebiotics and known bifidogenic factors.

There are now several complete and ongoing bifidobacterial genome sequencing projects. The results promise to increase our understanding of the co-evolution between mammalian hosts and their commensal inhabitants, niche adaptation by gut microorganisms and the genetic basis for colonization and persistence in the human gut, which could prove useful for the development of new probiotics.

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1. Sela, D. A. *et al.* The genome sequence of *Bifidobacterium longum* subsp. *infantis* reveals adaptations for milk utilization within the infant microbiome. *Proc. Natl Acad. Sci. USA* **105**, 18964–18969 (2008).
2. Kim, J. F. *et al.* Genome sequence of the probiotic bacterium *Bifidobacterium animalis* subsp. *lactis* AD011. *J. Bacteriol.* **191**, 678–679 (2009).
3. Barrangou, R. *et al.* Comparison of the complete genome sequences of *Bifidobacterium animalis* subsp. *lactis* DSM 10140 and BI-04. *J. Bacteriol.* 17 Apr 2009 (doi:10.1128/JB.00155–09).

DATABASES
Entrez Genome Project:
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=genomeprj
Bifidobacterium adolescentis | *Bifidobacterium animalis* subsp. *lactis* | *Bifidobacterium longum* subsp. *infantis*

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