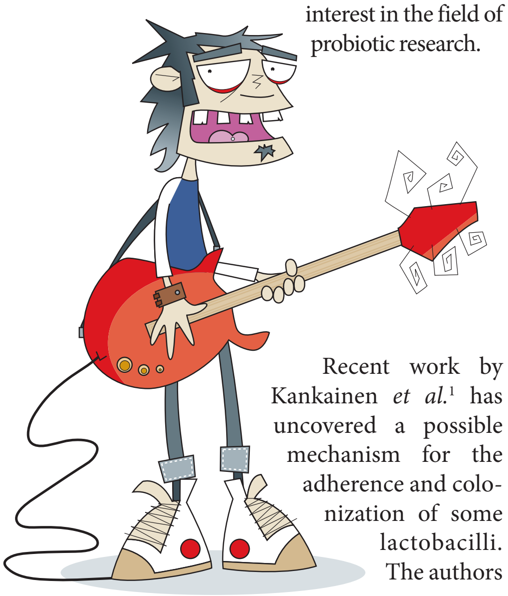
GENOME WATCH

Probiotics stick it to the man

Alan Walker

This month's Genome Watch highlights the part that genomics can play in generating new insights into the interactions of probiotic *Lactobacillus* strains with the human gut.

Lactobacilli are Gram-positive, facultatively anaerobic or microaerophilic bacteria that inhabit a range of ecological niches. They are common inhabitants of the gastrointestinal and vaginal tracts and are also important for the production and preservation of a range of fermented food products. However, they are perhaps most widely known as probiotic organisms, which are consumed as live dietary supplements and have been postulated to have a number of health-promoting benefits. It seems that long-term colonization of the gut does not occur, however, and after the consumption of supplements has ceased the probiotic strains gradually disappear from the colon. Therefore, strains that can adhere to intestinal tissue or mucus are likely to have an extended interaction with the host and are of noteworthy interest in the field of probiotic research.



Recent work by Kankainen *et al.*[1] has uncovered a possible mechanism for the adherence and colonization of some lactobacilli. The authors sequenced and compared the genomes of *Lactobacillus rhamnosus* GG, a commonly used probiotic bacterium, and *L. rhamnosus* Lc 705, an industrial strain that is used as an adjunct starter culture in dairy products. At around 3 Mb in size, the genomes of both strains are larger than those of most other lactobacilli sequenced to date. There is a high degree of synteny between the two genomes, and most predicted proteins have greater than 98% average amino acid identity. However, each genome is marked by the presence of distinct genomic islands, which the authors speculate are likely to have been acquired by horizontal gene transfer. Of note, one of the islands that was detected only in *L. rhamnosus* GG seems to contain a set of genes (*spaCBA*) encoding three pilin proteins and another gene encoding a pilin-dedicated sortase that is required for the assembly of pilus structures. Pili are protrusions of the cell surface and have previously been shown to be important for colonization and host interaction in other Gram-positive bacteria. *L. rhamnosus* GG has previously been shown to adhere to mucus and epithelial cell lines around 10 times as efficiently as *L. rhamnosus* Lc 705, and human intervention trials showed that *L. rhamnosus* GG persists in the intestinal tracts of healthy volunteers for 7 days longer than *L. rhamnosus* Lc 705. This led the authors to investigate whether the presence of the SpaCBA pili is crucial to the enhanced colonization ability of *L. rhamnosus* GG.

Firstly, they demonstrated that SpaC pilin is expressed in *L. rhamnosus* GG (but not in *L. rhamnosus* Lc 705) cell wall protein extracts using immunoblotting with SpaC-specific antibodies. Next, they verified the presence of SpaCBA pili on the surface of *L. rhamnosus* GG cells by immunogold electron microscopy. The crucial role of SpaC in enhancing *L. rhamnosus* GG colonization was then convincingly shown by the finding that both wild-type *L. rhamnosus* GG treated with SpaC antiserum and *spaC*-inactivated mutants exhibited attenuated adherence to human intestinal mucus. The authors therefore concluded that the greater persistence in the human gut of *L. rhamnosus* GG compared to *L. rhamnosus* Lc 705 is probably due to the mucus-binding capacity of the SpaCBA pili. This is the first reported observation of mucus-binding pili in probiotic lactic-acid bacteria and gives the first indication that pili are crucial to the colonization capabilities of the probiotic *L. rhamnosus* GG.

Coincidentally, Morita *et al.*[2] recently completed the genome sequencing of *L. rhamnosus* ATCC 53103, which is another probiotic strain and is derived from *L. rhamnosus* GG. Genomic analysis of this strain revealed a very high degree of global synteny with the genome of *L. rhamnosus* GG, except for the fact that the genome of *L. rhamnosus* ATCC 53103 is around 5 kb shorter and contains an 8.9 kb inverted region. Further work to determine whether the *L. rhamnosus* ATCC 53103 genome encodes functional SpaCBA pili will shed more light on the importance of adhesion to mucus during colonization of the human gut by these probiotic *Lactobacillus* strains.

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1. Kankainen, M. *et al.* Comparative genomic analysis of *Lactobacillus rhamnosus* GG reveals pili containing a human-mucus binding protein. *Proc. Natl Acad. Sci. USA* **106**, 17193–17198 (2009).
2. Morita, H. *et al.* Complete genome sequence of probiotic *Lactobacillus rhamnosus* ATCC 53103. *J. Bacteriol.* 9 Oct 2009 (doi:10.1128/JB.01287–09).

DATABASES

Entrez Genome project: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=genomeprj
Lactobacillus rhamnosus GG | *L. rhamnosus* GG str. ATCC 53103 | *L. rhamnosus* Lc 705

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