

NEWS RELEASE

Media Contacts: Dr. Todd Klaenhammer, 919/515-2972 or
klaenhammer@ncsu.edu
Rodolphe Barrangou, 919/539-1313 or rbarraa@unity.ncsu.edu
Mick Kulikowski, News Services, 919/515-3470 or
mick_kulikowski@ncsu.edu

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Good GI Tract Bacteria Have Genetic Advantage Over Bad Bacteria

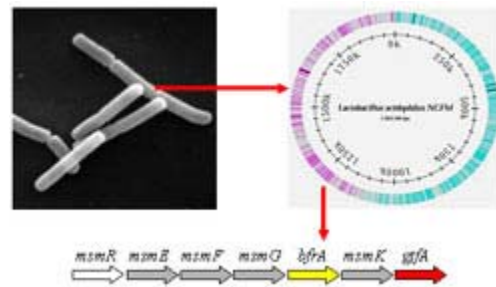
FOR IMMEDIATE RELEASE

North Carolina State University food microbiologists have discovered that, in the struggle for the undigested food inside your gastrointestinal tract, some “good” bacteria have a genetic advantage that allow them to capture and digest certain sugars for energy before “bad” bacteria can take a crack at eating those sugars.

The research is described in a paper published during the week of July 7 in the online edition of *Proceedings of the National Academy of Sciences*.

The good bacteria – *Lactobacillus acidophilus*, a member of the lactic acid bacteria – can be found in dairy products like milk, cheese and yogurt. They are used in food processing both as fermenting agents and as probiotics – beneficial organisms that reside naturally in the small intestine where they are believed to contribute to general health and well-being. The organism is now used extensively in products worldwide, including many yogurts and “Sweet Acidophilus” milk.

The NC State scientists – Dr. Todd Klaenhammer, Distinguished University Professor and William Neal Reynolds Professor of food science, microbiology and genetics; Rodolphe Barrangou, a Ph.D. candidate in functional genomics; and Eric Altermann, post-doctoral researcher in food science – discovered that turning on a group of genes, or operon, inside *L. acidophilus* allows this good bacterium to transport and internalize a complex sugar made up of repeating individual saccharides.



(Top left) *Lactobacillus acidophilus* NCFM; (top right) a schematic of the genome map of *Lactobacillus acidophilus* NCFM; (bottom) the operon, or set of genes, in *Lactobacillus acidophilus* NCFM that transports and utilizes fructo-oligosaccharide (FOS).

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Once inside the bacterium, this complex, called fructo-oligosaccharide, or FOS, is digested by cutting the individual fructose molecules off the end of the long oligosaccharide chain and these are then metabolized to provide energy to the organism. FOS is not digestible by humans and many other intestinal bacteria, some of which are unsavory and undesirable in large numbers. Therefore, feeding FOS can result in an increase in the number of desirable organisms already present in the human GI tract, or promote the growth of a probiotic culture being consumed from a product such as yogurt.

“FOS is a prebiotic, a special lunch that fuels the growth of beneficial probiotic bacteria in the GI tract,” says Klaenhammer, who is also the director of the Southeast Dairy Foods Research Center. “This research explains the connection between prebiotics like FOS and the increase of certain types of probiotic organisms in the GI tract.” Because *L. acidophilus* uniquely transports and internalizes FOS before utilizing it, other competing bacteria cannot metabolize FOS, or its component sugars, giving the probiotic bacteria a potential advantage for survival and retention in the intestine.

“*L. acidophilus* has better potential to compete for FOS because it is transporting FOS into itself,” Barrangou, the paper’s lead author, says. “When we knocked out the genes in the operon, the bacteria could no longer utilize FOS.” The majority of genomic investigations to date predict gene functions based on computer bioinformatic predictions. The involvement of the suspected genes for FOS utilization and metabolism were confirmed in this study by a functional genomic approach of disrupting the genes and correlating a loss of function – in this case, the inability to utilize FOS.

Klaenhammer says probiotic bacteria may help maintain normal and healthy microflora, or bacterial life, in humans; modulate the immune system; and possibly protect us from infection by intestinal pathogens. He says the number of bacterial cells found on our bodies actually outnumbers the human cells in our body tenfold, so having a healthy microflora is quite important for good health and resistance to disease.

Barrangou and Klaenhammer say that sequencing of the *L. acidophilus* genome was the key to discovering its relationship with FOS.

“We knew a great deal about *L. acidophilus*, but now that we have the genome sequence, we can look at its contents and predict what the organism can or cannot do,” Barrangou says. The research group is now studying other genes believed to be important to surviving gastric passage, attaching to the intestinal mucosa, and producing antimicrobial compounds that may promote the competitive ability of probiotic cultures.

“We’re seeking a mechanistic basis of probiotic functionality through genetics,” Klaenhammer says. “That means understanding exactly how the good guys do good things for human health and well-being, and discovering ways to do it better.”

The research is funded by Rhodia Inc., Dairy Management Inc., The Southeast Dairy Foods Research Center, the N.C. Dairy Foundation and the Environmental Biotechnology Institute.

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Note to editors: An abstract of the paper follows.

“Functional and comparative genomic analyses of an operon involved in fructo-oligosaccharide utilization by *Lactobacillus acidophilus*”

Authors: Rodolphe Barrangou, Eric Altermann, and Todd Klaenhammer, North Carolina State University; Robert Hutkins, University of Nebraska-Lincoln; and Raul Cano, California Polytechnic State University

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Abstract: *Lactobacillus acidophilus* NCFM is a probiotic organism that displays the ability to utilize prebiotic compounds, such as fructo-oligosaccharides (FOS), which stimulate the growth of beneficial commensals in the gastrointestinal tract. However, little is known about the mechanisms and genes involved in FOS utilization by *Lactobacillus* species. Analysis of the *L. acidophilus* NCFM genome revealed an *msm* locus composed of a transcriptional regulator of the LacI family, a four component ABC transport system, a fructosidase and a sucrose phosphorylase. Transcriptional analysis of this operon demonstrated that gene expression was induced by sucrose and FOS, but not by glucose or fructose, suggesting some specificity for non-readily fermentable sugars. Additionally, expression was repressed by glucose, but not by fructose, suggesting catabolite repression, via two *cre*-like sequences identified in the promoter-operator region. Insertional inactivation of the genes encoding the ABC transporter substrate binding protein and the fructosidase reduced the ability of the mutants to grow on FOS. Comparative analysis of gene architecture within this cluster revealed a high degree of synteny with operons in *Streptococcus mutans* and *Streptococcus pneumoniae*. However, the association between a fructosidase and an ABC transporter is unusual, and may be specific to *L. acidophilus*. This is the first description of a gene locus involved in transport and catabolism of FOS compounds, which can promote competition of beneficial microorganism in the human gastrointestinal tract.