

Bacterium carrying a cloned Bt-gene could help millions infected with roundworms

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Intestinal nematodes and roundworms infect more than one billion people worldwide. These parasites lead to malnutrition and developmental problems, especially in children. Unfortunately, resistance to the existing drug treatment is increasing. Now a team of researchers has successfully inserted the gene for a naturally-occurring, insecticidal protein called Bt into a harmless bacterium. This could then be incorporated into dairy products, or used as a probiotic to deliver the protein to the intestines of people afflicted with roundworms. The research is published in *Applied and Environmental Microbiology*, a journal of the American Society for Microbiology.

The Bt crystal protein is used in organic insecticidal sprays and has been produced in genetically modified plants as a safe pesticide to kill insects that eat those plants. Bt can also kill some nematodes. In the study, the investigators used the gene for one type of the insecticidal protein, which is naturally produced by the soil bacterium, Bacillus thuringiensis.

The investigators spliced the gene into a plasmid, a short, circular piece of DNA which can replicate independently of the genome in most bacteria. The investigators then inserted the plasmid into *Lactococcus lactis*, a bacterium that ferments milk to produce yogurt, cheese, and buttermilk. *L. lactis* was also the first genetically modified organism to be used to treat human disease.

An important property of this bacterium has to do with an odd discovery these researchers made nearly 15 years ago. Normally, molecules of



substantial size can only escape from a cell either if cellular machinery in the cell membrane actively exports them, or if the microbe breaks open in a process called lysis. "We observed that large proteins could be released from this particular bacterium without cell lysis or an active export system", said Todd Klaenhammer, PhD, Distinguished University Professor in the Department of Food, Bioprocessing and Nutrition Sciences, at North Carolina State University, Raleigh. He said the mechanism for this "leaky *Lactococcus* phenomenon" is not completely understood. Importantly, the leaky behavior did not interfere with normal bacterial cell growth or viability, he said.

In the next step, the investigators found that this <u>genetically modified</u> microbe could inhibit the common laboratory roundworm, C. elegans, via the cloned and expressed Bt protein.

This method of treating roundworm infections orally with food grade bacteria could be very inexpensive, said Klaenhammer. This would be a huge advantage, because roundworms infect millions of people in impoverished nations.

"What if someday children who are infected with parasitic round worms could simply eat a dish of locally made fermented milk or yogurt and be cured," said lead author Evelyn Durmaz, MS, a research associate at North Carolina State University. Klaenhammer also noted that "Our laboratories are currently investigating the possibilities of using probiotic bacteria and food safe bacteria to orally deliver vaccines and other biotherapeutics directly to the GI tract."

Provided by American Society for Microbiology

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