The Method to Give Bacteria Probiotic Features by Genetic Engineering

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OVERVIEW

Genetic mutations in adherent-invasive Escherichia Coli (AIEC) inhibit gut inflammation

- Defines the role of host immune factors in the regulation of bacteria involved in colitis
- Provides a strategy for the research and treatment of inflammatory bowel disease

BACKGROUND

Inflammatory bowel disease (IBD) is caused by genetic and environmental factors that alter intestinal homeostasis in susceptible individuals. The propensity to develop colitis is associated with abnormal changes in microbial populations of the gut in individuals with impaired immune systems. Microbes on the surface of intestinal cells express various conserved molecules, structures, and antigens that can be recognized by the host immune system for microbe killing and eradication. Many IBD-associated loci are known to regulate the recognition and killing of bacteria as well as the function of immune cells. The formation of IBD is commonly associated with an increased abundance of adherent-invasive Escherichia coli (AIEC), though the mechanism for this relationship remains unclear. A need exists to better understand the biologic role of AIEC in promoting IBD with the goal of producing novel treatments for colitis.

INNOVATION

Researchers have discovered that AIEC with mutations of genes that regulate surface polysaccharides can inhibit gut inflammation in a mouse model of colitis. Biochemical and functional studies show that mutation of the gene required for the production of certain surface polysaccharides rendered AIEC more sensitive to the immune system while retaining their ability to outcompete related bacteria in vitro. The specific AIEC mutation in Wzy, a gene that encodes the enzyme responsible for biosynthesis of the surface polysaccharide layer, permits the bacteria to colonize the intestine under while also protecting mice from colitis. The

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protective function of surface polysaccharide synthesized by Wzy is primarily observed under inflamed conditions, suggesting a role for host immune factors in the regulation of wzy-dependent bacterial fitness. This discovery provides new insights into the mechanisms by which gut microbes control colitis via the complement system and provides a possible strategy for the generation of probiotic strains resistant to host elimination.