Georgia State Researchers Discover Novel Way to Treat IBD with Lipid Nanoparticles

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Oral delivery of lipid nanoparticles that target the colon with nucleic acids is a novel therapeutic strategy for treating ulcerative colitis, according to a new study by researchers in the Institute for Biomedical Sciences at Georgia State University.

The researchers investigated whether orally delivering interleukin-22 (IL-22) mRNA-loaded lipid nanoparticles to the colon could be a new, effective treatment for ulcerative colitis. IL-22 expression in the colon is known to have strong anti-inflammatory effects against ulcerative colitis.

Their findings, published in the journal Biomaterials, report that mice with acute ulcerative colitis that orally received the novel lipid nanoparticles with IL-22 mRNA targeting their colon experienced accelerated healing. This demonstrates the new lipid nanoparticle-based delivery system may provide a powerful gene therapy strategy for treating ulcerative colitis.

Inflammatory bowel disease (IBD), an umbrella term for Crohn's disease and ulcerative colitis, is a relapsing and chronic inflammatory disorder of the gastrointestinal tract that affects more than 3 million adults in the United States. The cause of disease is unknown, so it's challenging to develop effective diagnostics and therapeutics for IBD. Most current treatments are delivered directly into the bloodstream and cause severe short- or long-term side effects, such as affecting gut bacterial or fungal function and promoting cancer development.

IL-22, a protein that regulates the stability of cells that line body surfaces and promotes wound healing during intestinal inflammation, plays a protective role against pro-inflammatory mediators and is strongly associated with genes susceptible to IBD.

Previous studies have found that injection of a lipid and IL-22 complementary DNA complex is a potentially powerful strategy for treating colitis in animals, but this requires surgery and specific injection skills. Oral delivery offers a more accessible treatment strategy and developing an oral nucleic acid delivery method for IBD treatment appears to be more valuable in improving human health.

In this study, the researchers engineered new lipid nanoparticles with three major lipids identified in ginger-derived nanoparticles used in previous studies: phosphatidic acid (PA), monogalactosyldiacylglycerol (MGDG) and digalactosyldiacylglycerol (DGDG). IL-22-mRNA was encapsulated within the new lipid nanoparticles.

“Oral delivery of IL-22 lipid nanoparticles elevated the protein expression level of IL-22 in the colonic tissue of mice,” said Dr. Didier Merlin, a Regents’ Professor in the Institute for Biomedical Sciences at GeorgiaState and a senior research career scientist at Atlanta Veterans Affairs Medical Center. “Mice with acute colitis that were fed IL-22 lipid nanoparticles experienced an accelerated healing process, as indicated by the recovery of more body weight and colon length.”

In addition, the mice had reduced histological index, colonic myeloperoxidase activity, fecal lipocalin concentration and mRNA expression levels of pro-inflammatory cytokines.

“Our results suggest that our reversely engineered lipid nanoparticles are an excellent mRNA delivery platform for treating ulcerative colitis,” Merlin said.

Read the original article on GeorgiaState University.