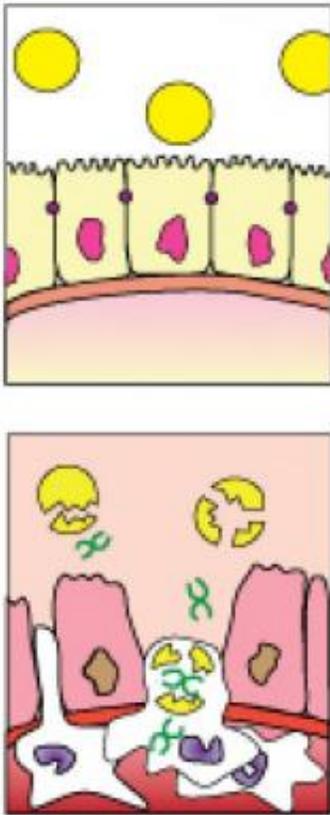


Thioketal nanoparticles: Researchers develop oral delivery system to treat inflammatory bowel diseases

October 10 2010



When delivered orally, thioketal nanoparticles remain stable in the harsh environment of the gastrointestinal tract, protecting siRNA and preventing its release to non-inflamed tissues (top). However, at sites of intestinal inflammation where unusually high levels of reactive oxygen species are present, the thioketal nanoparticles degrade and release siRNA to the site of inflammation (bottom). Credit: Scott Wilson

(PhysOrg.com) -- Researchers at the Georgia Institute of Technology and Emory University have developed a novel approach for delivering small bits of genetic material into the body to improve the treatment of inflammatory bowel diseases. Delivering short strands of RNA into cells has become a popular research area because of its potential therapeutic applications, but how to deliver them into targeted cells in a living organism has been an obstacle.

In the Oct. 10 advance online edition of the journal [Nature Materials](#), researchers describe how they encapsulated short pieces of RNA into engineered particles called thioketal nanoparticles and orally delivered the genetic material directly to the inflamed intestines of animals. The research was sponsored by the National Science Foundation and National Institutes of Health.

"The thioketal nanoparticles we designed are stable in both acids and bases and only break open to release the pieces of RNA in the presence of reactive oxygen species, which are found in and around inflamed tissue in the gastrointestinal tract of individuals with inflammatory bowel diseases," said Niren Murthy, an associate professor in the Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University.

This work was done in collaboration with Emory University Division of Digestive Diseases professor Shanthi Sitaraman, associate professor Didier Merlin and postdoctoral fellow Guillaume Dalmaso.

The thioketal nanoparticles protect the small interfering RNAs (siRNAs) from the harsh environment of the gastrointestinal tract and target them directly to the inflamed intestinal tissues. This localized approach is necessary because siRNAs can cause major side-effects if injected systemically.

In the paper, the thioketal nanoparticles were formulated from a new polymer -- poly-(1,4-phenyleneacetone dimethylene thioketal) (PPADT) -- and engineered to have a diameter of approximately 600 nanometers for optimal oral delivery.

For their experiments, the researchers used a mouse model of ulcerative colitis -- a debilitating [inflammatory bowel disease](#) in which the digestive tract becomes inflamed, causing severe diarrhea and abdominal pain that can lead to life-threatening complications.

The researchers orally administered thioketal nanoparticles loaded with siRNA that inhibits an inflammation-promoting cytokine called tumor necrosis factor - alpha (TNF- α). The nanoparticles traveled directly to the mouse colons where reactive oxygen species were being produced in excess and decreased the cytokine production levels there.



Colon tissue samples of (top) healthy tissue; (middle) ulcerative colitis treated with siRNA delivered by thioketal nanoparticles; (bottom) untreated ulcerative colitis. The tissue treated with siRNA-loaded thioketal nanoparticles exhibits intact epitheliums, well-defined fingerlike "crypt" structures and lower levels of inflammation like those seen in healthy tissue. Credit: Scott Wilson

Tissue samples from the colons treated with siRNA delivered by these thioketal nanoparticles exhibited intact epitheliums, well-defined fingerlike "crypt" structures and lower levels of inflammation -- signs that the colon was protected against ulcerative colitis.

"Since ulcerative colitis is restricted to the colon, these results confirm that the siRNA-loaded thioketal nanoparticles remain stable in non-inflamed regions of the [gastrointestinal tract](#) while targeting siRNA to inflamed intestinal tissues," explained the paper's lead author Scott Wilson, a graduate student in the Georgia Tech School of Chemical & Biomolecular Engineering.

The paper showed that thioketal nanoparticles have the chemical and physical properties needed to overcome the obstacles of gastrointestinal fluids, intestinal mucosa and cellular barriers to provide therapy to inflamed intestinal tissues, he added.

The researchers are currently working on increasing the degradation rate of the nanoparticles and enhancing their reactivity with [reactive oxygen species](#). The team also plans to conduct a biodistribution study to detail how the nanoparticles travel through the body.

"Polymer toxicity is something we'll have to investigate further, but during this study we discovered that thioketal nanoparticles loaded with siRNA have a cell toxicity profile similar to nanoparticles formulated

from the FDA-approved material poly(lactic-co-glycolic acid) (PLGA)," added Murthy.

In the future, thioketal [nanoparticles](#) may become a significant player in the treatment of numerous gastrointestinal diseases linked to intestinal inflammation, including gastrointestinal cancers, inflammatory bowel diseases and viral infections, according to Murthy.

More information: [dx.doi.org/10.1038/nmat2859](https://doi.org/10.1038/nmat2859)

Provided by Georgia Institute of Technology

Citation: Thioketal nanoparticles: Researchers develop oral delivery system to treat inflammatory bowel diseases (2010, October 10) retrieved 21 September 2024 from <https://phys.org/news/2010-10-thioketal-nanoparticles-oral-delivery-inflammatory.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.