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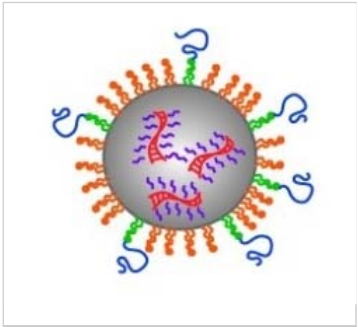
Fatty Bundles Sneak siRNA Into Cells

Nanotechnology: Lipid nanoparticles offer a new way to deliver therapeutic nucleic acids

By Erika Gebel

Department: Science & Technology
Keywords: solid lipid nanoparticles, siRNA, sustained release, drug delivery, gene therapy



Signed, Sealed, Delivered
A nanoparticle decorated with lipids (orange) and other molecules carries siRNA (red) in complex with a positively charged lipid (purple).
Credit: ACS Nano

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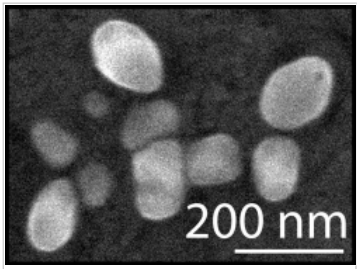

Small Packages
A scanning electron microscope shows the solid lipid nanoparticles that deliver therapeutic molecules.
Credit: ACS Nano

Inside a cell, small interfering RNAs (siRNAs) can silence genes responsible for disease, making them ideal molecules for gene therapy. But siRNAs have trouble getting there. Now researchers report that they can **smuggle the nucleic acids into cells** by wrapping them in lipid nanoparticles (*ACS Nano*, DOI: **10.1021/nn203745n**).

Like all nucleic acids, siRNAs are packed with negative charges, so they don't easily penetrate cells' hydrophobic membranes. To solve this problem, **Richard Zare** of **Stanford University** and his colleagues decided to encapsulate siRNAs in small greasy spheres called solid lipid nanoparticles. But because of the same negative charges, loading siRNAs into lipid nanoparticles is also difficult, says Zare. So the researchers mixed siRNA with a positively charged lipid called 1,2-dioleoyl-3-trimethylammonium-propane (DOTAP), which masked the nucleic acid's negative charge and provided a hydrophobic hook to draw the complex into the belly of the nanoparticle.

To test their delivery system, the researchers injected nanoparticles charged with a fluorescently labeled siRNA and DOTAP into the left hind feet of mice and injected the labeled siRNA alone into the right feet. They found that the left feet containing nanoparticles glowed for 11 days, while the right feet without the particles glowed for two. This difference, says Zare, suggests that the nanoparticles protect the siRNA from quick degradation and release the nucleic acids slowly over time—two desirable properties for delivery of gene therapies. Using fluorescence microscopy, the scientists spotted the fluorescent dye inside skin cells from the left feet, confirming the nanoparticles' ability to sneak siRNA into cells.

Zare's lab is now working on using their siRNA-carrying nanoparticles to shut down disease-causing genes in mice.

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Comments

Henk M. Buck Prof. Emeritus (11/27/2011 at 8:11 AM)

Dear Professor Erika Gebel,

In the past I and my former group in Eindhoven have been prepared phosphatemethylated DNA and RNA. These compounds show a number of interesting (bio)organic properties. Unfortunately,we published, too early, in Science april 1990 a study on the inhibition of certain RNA loops of hiv with site-selected phosphatemethylated DNA.These experiments were retracted because the long fragments were not methylated. However, they showed under the experimental conditions inhibition. I think that the reason was an anion - cation binding, as in your investigation, via the presence of trialkylammonium salts as part of the various steps during the synthesis. Recently, I published an article in Nucleosides Nucleotides Nucleic Acids (7 nov) about the role of the B-Z transition in DNA as a model for epigenetics.In that article I go in more detail with reference to the Science article, among others, on the important aspect phosphate shielding.
Please can you send me your article. With my best regards. Henk M. Buck, prof emeritus
» **Reply**

Lila Guterman **(11/28/2011 at 10:39 AM)**
Dear Prof. Buck,
Thank you for the comment! I am one of Erika Gebel's editors at C&EN.
Just to clarify: She is not one of the researchers who did the work -- she is the science writer who wrote this article about their work. If you would like the original paper, you can access it at the link to ACS Nano in Erika's article, or you may contact Prof. Zare to discuss it further.
Thank you again for the comment.
» **Reply**

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