Science News

RNA Nanoparticles Constructed to Safely Deliver Long-Lasting Therapy to Cells

ScienceDaily (Apr. 20, 2011) — Nanotechnology researchers have known for years that RNA, the cousin of DNA, is a promising tool for nanotherapy, in which therapeutic agents can be delivered inside the body via nanoparticles. But the difficulties of producing long-lasting, therapeutic RNA that remains stable and non-toxic while entering targeted cells have posed challenges for their progress.

See Also:

Health & Medicine
- Genes
- Prostate Cancer
- Human Biology

Matter & Energy
- Nanotechnology
- Organic Chemistry
- Biochemistry

Reference
- Human parainfluenza viruses
- RNA
- Nanomedicine
- Antiviral drug

In two new publications in the journal Molecular Therapy, University of Cincinnati (UC) biomedical engineering professor Peixuan Guo, PhD, details successful methods of producing large RNA nanoparticles and testing their safety in the delivery of therapeutics to targeted cells.

The articles, in advance online publication, represent "two very important milestones in RNA nanotherapy," says Guo.

"One problem in RNA therapy is the requirement for the generation of relatively large quantities of RNA," he says. "In this research, we focused on solving the most challenging problem of industry-scale production of large RNA molecules by a bipartite approach, finding that pRNA can be assembled from two pieces of smaller RNA modules."

Guo, Dane and Mary Louise Miller Endowed Chair of biomedical engineering, serves as director of the National Cancer Institute (NCI) Alliance for Nanotechnology in Cancer Platform Partnership Program at UC. He has focused his research on RNA for decades, pioneering its use as a versatile building block for nanotechnology, or for the engineering of functional systems at the molecular scale. In 1987, he discovered a packaging RNA (pRNA) in the bacteriophage phi29 virus which can gear a motor to package DNA into the viral protein shell. In 1998, his lab discovered that pRNA can self-assemble or be engineered into nanoparticles to gear the motor.

In his most recent research, Guo and colleagues detail multiple approaches for the construction of a functional 117-base pRNA molecule containing small interfering RNA (siRNA). siRNA has already been shown to be an efficient tool for silencing genes in cells, but previous attempts have produced chemically modified siRNA lasting only 15-45 minutes in the body and often inducing undesired immune responses.

"The pRNA particles we constructed to harbor siRNA have a half life of between five and 10 hours in animal models, are non-toxic and produce no immune response," says Guo. "The tenfold increase of circulation time in the body is important in drug development and paves the way towards clinical trials of RNA nanoparticles as therapeutic drugs."

Guo says the size of the constructed pRNA molecule is crucial for the effective delivery of therapeutics to diseased tissues.

"RNA nanoparticles must be within the range of 15 to 50 nanometers," he says, "large enough to be retained by the body and not enter cells randomly, causing toxicity, but small enough to enter the targeted cells with the aid of cell surface receptions.

In the paper, "Assembly of Therapeutic pRNA-siRNA Nanoparticles Using Bipartite Approach," Guo and his colleagues used two synthetic RNA fragments to create the 117-base pRNA, which was able to further assemble with other pRNA molecules and function in the bacteriophage phi29 viral motor to package DNA.

"The two-piece approach in pRNA synthesis overcame challenges of size limitations in chemical synthesis of RNA nanoparticles," Guo wrote. "The resulting nanoparticles were competent in delivering and releasing therapeutics to cells and

Peixuan Guo, PhD, Dane and Mary Louise Miller Endowed Chair in biomedical engineering with students in his lab at the Vontz Center for Molecular Studies. (Credit: Image courtesy of University of Cincinnati Academic Health Center)

Related Stories

Targeted Nanoparticles Incorporating SiRNA Offer Promise For Cancer Treatment (May 21, 2007) — The use of targeted nanoparticles offers promising techniques for cancer treatment. Researchers have been using small interfering RNA (siRNA), sometimes known as silencing RNA, to "silence" specific ... > *read more*

Gold Nanoparticles Could Improve Antisense Cancer Drugs (May 19, 2006) — In the fight against cancer, antisense drugs, which prevent genes from producing harmful proteins such as those that cause cancer, have the promise to be more effective than conventional drugs, but ... > *read more*

Advance Could Speed Use of Genetic Material RNA in Nanotechnology (Jan. 19, 2011) — Scientists are reporting an advance in overcoming a major barrier to the use of the genetic material RNA in nanotechnology -- the field that involves building machines thousands of times smaller than ... > *read more*

Researchers Developing Molecular Delivery Vehicles For Genetic Therapies (Dec. 10, 2006) — Researchers at New York University are working to develop molecular delivery vehicles that can be used to transport nucleic acids into diverse cell types, which may lead to eventual applications in ... > *read more*

Researchers Discover RNA Repair System In Bacteria (Oct. 22, 2009) — Researchers have discovered the first RNA repair system to be discovered in bacteria. The novelty of the newly discovered bacterial RNA repair system is that,

Just In:
Light Can Repair New Material When Scratched

Science Video News

Nanotechnology - Cleaning Up Our Water
Chemical engineers created nanoparticles out of gold and palladium to break down pollutants in groundwater. Adding the particles to groundwater. ... > *full story*

Biomedical Engineers' 'Body-on-a-Chip' Could Reduce Cost of Developing New Drugs

Hematologists Boost Immune Response in Bone-Marrow Transplant Patients

Engineers Create Exhibits on Achievements, Promise

more science videos

Breaking News

... from NewsDaily.com

REUTERS

- Scientists manipulate mosquitoes in malaria fight
- U.S. hi-tech energy unit extends life in budget deal
- Scientists take steps to making "bionic" leg
- NASA clears shuttle Endeavour for April 29 launch

more science news

In Other News ...

- "Restrepo" director killed in Libya: doctors
- Sarkozy tells Libyan rebels: "We will help you"
- Gold breaks $1,500 as investors seek security
- U.S. recommends death penalty in USS Cole attack
- Special Report: From Hannibal Lecter to Bernie Madoff
- Lobbying push targets lawmakers on debt vote
- True Finns see Portugal bailout opposition growing

silencing the genes within them. The ability to chemically synthesize these nanoparticles allows for further chemical modification of RNA for stability and specific targeting."

The second publication, "Pharmacological Characterization of Chemically Synthesized Monomeric phi29 pRNA Nanoparticles for Systemic Delivery," builds on that research, demonstrating that modified three-dimensional pRNA nanoparticles were readily manufactured through the two-piece approach. The modified nanoparticles were resistant to common enzymes that can attack and degrade RNA and remained chemically and metabolically stable.

Furthermore, when delivered to target cells in an animal model, the nanoparticles were non-toxic and did not induce an immune response, enabling the nanoparticles to bind to cancer cells in vivo.

Previous studies have encased therapeutic siRNA in a polymer coating or liposome for delivery to cells.

"To our knowledge, this is the first naked RNA nanoparticles to have been comprehensively examined pharmacologically in vivo and demonstrated to be safe, as well as deliver itself to tumor tissues by a specific targeting mechanism," he says. "It suggests that the pRNA nanoparticles without coating have all the preferred pharmacological features to serve as an efficient nanodelivery platform for broad medical applications."

Co-authors of "Assembly of Therapeutic pRNA-siRNA Nanoparticles Using Bipartite Approach" include Yi Shu, Mathieu Cinier, Sejal Fox and Nira Ben-Johnathan of the University of Cincinnati.

Co-authors of "Pharmacological Characterization of Chemically Synthesized Monomeric phi29 pRNA Nanoparticles for Systemic Delivery" include Sherine Abdelmawla and Songchuan Guo of Kylin Therapeutics and Purdue University, Limin Zhang, Sai M Pulukuri, Prithviraj Patankar, Patrick Conley, Joseph Trebley and Qi-Xiang Li of Kylin Therapeutics.

This study was funded by National Cancer Institute, National Institute of Biomedical Imaging and Bioengineering, National Institute of General Medical Sciences and Kylin Therapeutics Inc. Guo is co-founder of Kylin Therapuetics.

Email or share this story: | More

Story Source:

The above story is reprinted (with editorial adaptations by Science*Daily* staff) from materials provided by **University of Cincinnati Academic Health Center**.

Need to cite this story in your essay, paper, or report? Use one of the following formats:

APA University of Cincinnati Academic Health Center (2011, April 20). RNA nanoparticles constructed to safely deliver long-lasting therapy to cells. *ScienceDaily*. Retrieved April 21, 2011, from http://www.sciencedaily.com /releases/2011/04/110421091125.htm?utm_source=feedburner&utm_medium=feed&utm_campaign=Feed:%20sciencedaily%20(ScienceDaily:%20Latest%20Science%20News)

MLA

Note: If no author is given, the source is cited instead.

***Disclaimer**: This article is not intended to provide medical advice, diagnosis or treatment. Views expressed here do not necessarily reflect those of ScienceDaily or its staff.*

before the damaged RNA is sealed, a ... > *read more*

Attacking Cancer Cells With Hydrogel Nanoparticles (Feb. 17, 2010) — Researchers are using hydrogels -- less than 100 nanometers in size -- to sneak a particular type of small interfering RNA into cancer cells. Once in the cell the siRNA turns on the programmed cell ... > *read more*

New Drug Delivery Technique: Nanoblasts from Laser-Activated Nanoparticles Move Molecules, Proteins and DNA Into Cells (July 28, 2010) — Using chemical "nanoblasts" that punch tiny holes in the protective membranes of cells, researchers have demonstrated a new technique for getting therapeutic small molecules, proteins and DNA ... > *read more*

'Quiet Revolution' May Herald New RNA Therapeutics (Jan. 22, 2007) — Scientists at the University of Oxford have identified a surprising way of switching off a gene involved in cell division. The mechanism involves a form of RNA, a chemical found in cell nuclei, whose ... > *read more*

At Facebook headquarters, Obama seeks 2008 magic

more top news

Free Subscriptions *... from ScienceDaily*

Get the latest science news with our free email newsletters, updated daily and weekly. Or view hourly updated newsfeeds in your RSS reader:

Email Newsletters

RSS Newsfeeds

Feedback *... we want to hear from you!*

Tell us what you think of ScienceDaily -- we welcome both positive and negative comments. Have any problems using the site? Questions?

Your Name:

Your Email:

Comments:

Click button to submit feedback: Send It

Search ScienceDaily

Number of stories in archives: 101,537

Find with keyword(s): Search

Enter a keyword or phrase to search ScienceDaily's archives for related news topics, the latest news stories, reference articles, science videos, images, and books.