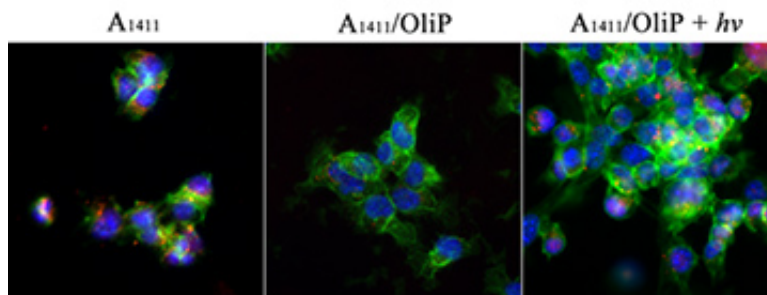


DNA paired with light could help guide drugs to their targets

December 8 2014, by Tom Ulrich



Left: Short snippets of DNA called aptamers (red) readily get into cancer cells (green and blue) on their own. Center: They can't penetrate cells when stuck to an oligonucleotide. Right: However, they regain the ability when the oligonucleotide's bonds are broken by UV light. Credit: Lele Li

You have a drug. You know what you want it to do and where in the body you need it to go. But when you inject it into a patient, how can you make sure your drug does what you want, where you want, when you want it to?

Daniel Kohane, Harvard Medical School professor of anesthesia at Boston Children's Hospital, has one potential solution.

In the *Proceedings of the National Academy of Sciences*, Kohane, who also runs the Laboratory of Biomaterials and Drug Delivery at Boston Children's; postdoctoral fellows LeLe Li and Rong Tong; and Robert

Langer, HMS senior lecturer on surgery at the Massachusetts Institute of Technology, describe a drug targeting system that's based on a combination of ultraviolet light and short, single strands of DNA called aptamers.

Aptamers hold appeal as [drug delivery](#) tools—or as drugs themselves—because they're small, penetrate tissues rapidly and resist enzymatic breakdown in the bloodstream. They're readily synthesized, can be tagged onto drugs or other therapeutic molecules and can be designed to stick to specific targets similar to how an antibody would.

Their downside, though, is that they spread easily through the body and tend to accumulate in normal tissues, such as liver and kidneys. Thus, it's hard to get enough aptamers to the site of the diseased tissue to have a therapeutic effect, and one can get off-target effects.

"DNA and RNA aptamers are very useful, and have been widely used for biomedical applications like sensing, targeted imaging and drug delivery," said Li. "But to use them for targeted tumor therapy, for instance, we need to improve their targeting efficiency."

The research team's solution was to use light. They engineered a complementary short DNA strand, called an [oligonucleotide](#), containing chemical bonds that break in UV light.

In the absence of UV, the oligonucleotide and the aptamer stick together, stopping the aptamer from binding to its target.

In the presence of UV, though, the oligonucleotide's light-sensitive bonds break, snapping it into even smaller DNA pieces that float away, giving the liberated aptamer a chance to bind to its target cells.

"In the rest of the body, the aptamer isn't activated," Kohane explained.

"You get the specific effect of the aptamer only where you shine the light. Which allows you great spatial and temporal control over where your therapeutic action takes place."

The research team tested the approach's utility in breast cancer cell lines and in a mouse model of breast cancer, using an aptamer targeted to the protein nucleolin, found on the surface of many kinds of cancer cells.

In both systems, the aptamer alone easily bound to nucleolin and penetrated cancerous cells. Adding the oligonucleotide kept the aptamer from binding to its target—until the researchers turned on a UV laser, breaking up the oligonucleotide and freeing the aptamer to bind to nucleolin again.

The mouse model demonstrated the approach's power in a live animal: The researchers found they could readily control accumulation of the oligonucleotide-bound aptamers in tumors simply by shining their UV light on the mice. They also noted that the method significantly reduced the amount of [aptamer](#) accumulating in the liver and kidneys relative to the tumors.

"There are very few demonstrations of something like this working in vivo," Kohane said. "It's the kind of work that brings together two different areas, aptamers and light activation, that don't ordinarily mix."

Kohane added that this method could potentially complement other light-activated drug technologies his lab has developed, like drug-loaded nanoparticles that squeeze out their payload when exposed to UV light, or gold nanoparticles that heat up in near-infrared light to cook diseased cells.

"You could tag aptamers to passive particles, ones that don't react to [light](#)," he said, "or to particles that are triggered by the same or different

wavelengths. Those are some of the kinds of approaches we're thinking about."

More information: "Aptamer photoregulation in vivo." *PNAS* 2014 111 (48) 17099-17103; published ahead of print November 17, 2014, DOI: [10.1073/pnas.1420105111](https://doi.org/10.1073/pnas.1420105111)

Provided by Harvard Medical School

Citation: DNA paired with light could help guide drugs to their targets (2014, December 8) retrieved 10 April 2024 from <https://medicalxpress.com/news/2014-12-dna-paired-drugs.html>

<p>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.</p>
--