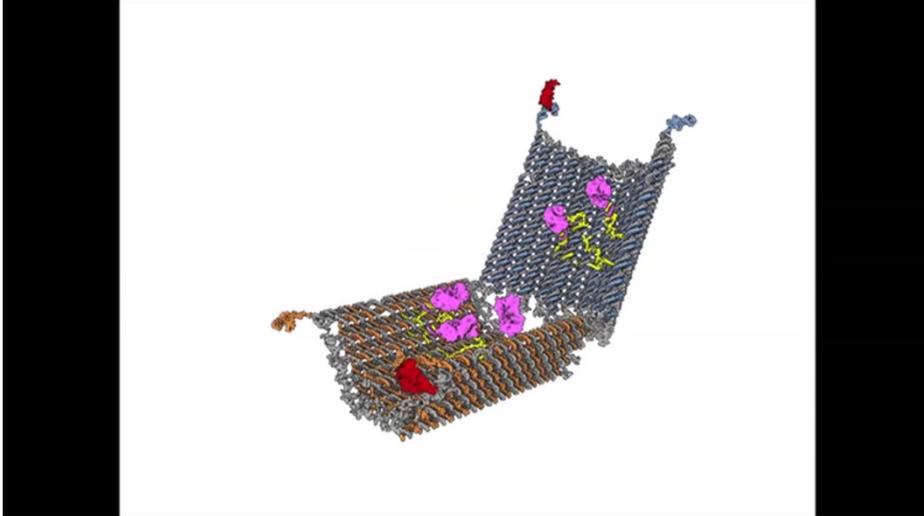


DNA robot could kill cancer cells

Device identifies target then releases deadly payload.

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16 February 2012



DNA nanorobot from Wyss Institute on Vimeo.

DNA origami, a technique for making structures from DNA, may be more than just a cool design concept. It can also be used to build devices that can seek out and destroy living cells.

The nanorobots, as the researchers call them, use a similar system to cells in the immune system to engage with receptors on the outside of cells.

“We call it a nanorobot because it is capable of some robotic tasks,” says Ido Bachelet, a postdoctoral fellow at Harvard Medical School in Boston, Massachusetts, and one of the authors of the study, which is published in this week’s issue of *Science*¹. Once the device recognizes a cell, he explains, it automatically changes its shape and delivers its cargo.

The researchers designed the structure of the nanorobots using open-source software, called Cadnano, developed by one of the authors — Shawn Douglas, a biophysicist at Harvard’s Wyss Institute for Biologically Inspired Engineering. They then built the bots using DNA origami. The barrel-shaped devices, each about 35 nanometres in diameter, contain 12 sites on the inside for attaching payload molecules and two positions on the outside for attaching aptamers, short nucleotide strands with special sequences for recognizing molecules on the target cell. The aptamers act as clasps: once both have found their target, they spring open the device to release the payload.

“You can think about it as a sort of combination lock,” says Bachelet. “Only when both markers are in place, can the entire robot open.”

The researchers tested six combinations of aptamer locks, each of which were designed to target different types of cancer cells in culture. Those designed to hit a leukaemia cell could pick that cell out of a mixture of cell types then release their payload — in this case, an antibody — to stop the cells from growing. They also tested payloads that could activate the immune system.

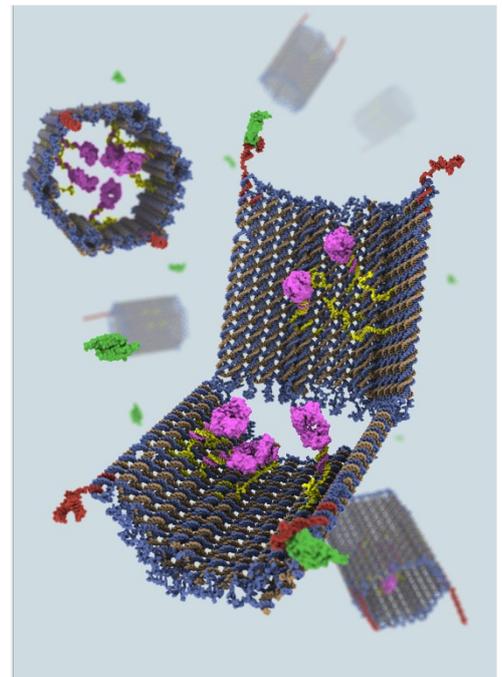


Image created by Campbell Strong, Shawn Douglas, & Gaël McGill using Molecular Maya & cadnano

DNA nanorobots can target cancer cells and deliver an antibody payload (purple).

The work “takes us one more step along the path from the smartest drugs of today to the kind of medical nanobots we might imagine”, says Paul Rothemund, a computational bioengineer at the California Institute of Technology in Pasadena, and inventor of DNA origami².

Right on target

Because the nanorobots can be programmed to release their payload only when the target cell is in the correct disease state, they achieve a specificity that other drug-delivery methods lack, says Hao Yan, a chemist and nanotechnologist at Arizona State University in Tempe. “This really takes advantage of the programmability of DNA nanotechnology.”

Whether or not these structures will work in a living organism remains to be seen. For one thing, they are designed to communicate with molecules on a cell's surface. “If your therapeutic target is inside the cell, it's going to be tricky,” says Bachelet.

What's more, the nanorobots are quickly cleared by the liver or destroyed by nucleases, enzymes chew up stray bits of DNA. It might be possible to coat them with a substance such as polyethylene glycol, widely used to boost the length of time a drug can remain in the body, says Douglas, or “maybe to borrow inspiration from other biomolecules or cells” — such as red blood cells — “that can circulate in the blood for a long time”. He and his colleagues are just beginning to think about testing the nanobots in mice, he says.

“If these sorts of problems can be solved, then the nanorobots have a chance at becoming real therapeutics,” Rothemund says.

Nature | doi:10.1038/nature.2012.10047

References

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2. Rothemund, P. W. K. *Nature* **440**, 297–302 (2006).