News

RNA nanoparticles fight cancer

Successful in mice and lab-grown human cells

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RNA nanoparticles have been built that can deliver drugs to specific cells and have already shown promise against cancer in mice and human cell cultures.

The nanoparticles are assembled from three short pieces of ribonucleic acid and resemble miniature triangles.

They have the right size to gain entry into cells and the right structure to carry other therapeutic strands of RNA inside them.

"RNA has immense promise as a therapeutic agent against cancer, but until now we l an efficient system to bring multiple therapeutic agents directly into specific cancer c they can perform different tasks," says research team leader Peixuan Guo of Purdue "Physicians have hoped that nanotechnology might provide a solution to the problem possible that the application of these tiny triangles could lead to the solution."

Using their nanoparticles, Guo and colleagues have delivered three different therapeu into a cell at the same time, which is considered a major accomplishment that points particles' potential.

A news release describes the research:

> RNA molecules come in many variant forms, and the sort that the team mimic from the phi29 virus—called pRNA—also can be linked to other types of RNA t longer, hybrid strands with properties the researchers could assign.
>
> "We looked around for RNA strands that would behave in certain ways when t encounter a cancer cell because each of them needs to perform one step of th therapy," Guo explained. "An effective agent against cancer needs to accompl several tasks. It needs first to recognize the cancer cell and gain access to its interior, and then it needs to destroy it. But we'd also like the agent to leave a for us, to mark the path the molecule has taken somehow. That way, we can pinpoint the location of the cancer and trace the outcome after the treatment.

To accomplish these tasks, the team turned to other forms of RNA that can in with the goings-on inside cells. The team sorted through a variety of RNA forn have shown promise for disease treatment and found three that could perform of the desired tasks. One example is "small interfering RNA," or siRNA, which deactivates certain genes in cells. The others are RNA aptamers, which bind t cancer cell surface markers, and ribozymes, which can be designed to degrad specific RNA in cancer cells or viruses.

"We linked each of the three therapeutic strands with a piece of pRNA, formin hybrid strands," Guo said. "Then, using techniques we learned from our earlie we were able to combine all three into triangles that are between 25 and 40 nanometers wide. This is the Goldilocks size for any nanoparticle that is to be the body—not too big, not too small."

Particles larger than about 100 nanometers are generally too large to pass thr cell membranes into the cell's interior, Guo said, and the body has a hard time retaining particles smaller than 10 nanometers. But the tiny triangles fit, and worked well enough to interrupt the growth of human breast cancer cells and leukemia model lymphocytes in laboratory experiments.

"One characteristic of cancer cells is that they do not stop growing, which is o reason tumors develop," Guo said. "Once inside, the siRNA essentially instruct cells to 'stop not stopping.' The nanoparticles had done their work on the brea cancer cell cultures within a few days."

Additionally, the team found that the nanoparticles completely block cancer development in living mice. A group of mice that were in the process of develo cancer were tested with the nanoparticles, and they did not develop the disea second group that was tested with mutated inactive RNA all developed tumors

There are several hurdles to go before the findings can be applied in people, such as ways to protect the RNA from degradation by enzymes in the body.

The research is reported in two related papers in the journals *Nano Letters* and *Huma Therapy*.

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