Purdue scientists treat cancer with RNA nanotechnology

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WEST LAFAYETTE, Ind. – Using strands of genetic material, Purdue University scientists have constructed tiny delivery vehicles that can carry anticancer therapeutic agen offering a potential wealth of new treatments for chronic diseases.

The vehicles look nothing like delivery trucks, though that is their function once inside the body. Inste nanoparticles, which are assembled from three short pieces of ribonucleic acid, resemble miniature tri particles possess both the right size to gain entry into cells and also the right structure to carry other inside with them, where they are able to halt viral growth or cancer's progress. The team has already successfully against cancer growth in mice and lab-grown human cells.

"RNA has immense promise as a therapeutic agent against cancer, but until now we have not had an multiple therapeutic agents directly into specific cancer cells where they can perform different tasks," Peixuan Guo, who is a professor of molecular virology at Purdue with joint appointments in Purdue's C School of Veterinary Medicine and Weldon School of Biomedical Engineering. "Physicians have hoped t provide a solution to the problem, and it's possible that the application of these tiny triangles could le

"With these devices, Dr. Guo was able to deliver three different therapeutic agents into a cell at the sa scientist at the National Institute of General Medical Sciences, which is part of the National Institutes incredible accomplishment that points to the versatility and potential medical value of these nanopart

The research appears in two related papers being published in the scientific journals Nano Letters and Members of Guo's research team are from Purdue, the University of Central Florida and the University including Songchuan Guo, Annette Khaled, Feng Li, Sulma Mohammed and Nuska Tschammer.

Guo's team created their nanoparticles by linking together different kinds of RNA, a task that their pre them ample opportunities to practice. Several years after building a tiny "motor" from several strands a bacteria-killing virus called phi29, the team learned how to manipulate these stringy molecules into rods, triangles and arrays.

"We speculated at that time that these shapes would be useful purely as physical scaffolding on which nanodevices could be constructed," Guo said. "But RNA, which carries genetic messages within cells, a functions. We realized that if we built different kinds of therapeutic RNA onto the RNA scaffolding and we might be able to respond to several challenges that have confronted the medical field."

RNA molecules come in many variant forms, and the sort that the team mimicked from the phi29 viru be linked to other types of RNA to form longer, hybrid strands with properties the researchers could a

"We looked around for RNA strands that would behave in certain ways when they encounter a cancer needs to perform one step of the therapy," Guo explained. "An effective agent against cancer needs t It needs first to recognize the cancer cell and gain access to its interior, and then it needs to destroy i agent to leave a trail for us, to mark the path the molecule has taken somehow. That way, we can pir cancer and trace the outcome after the treatment."

To accomplish these tasks, the team turned to other forms of RNA that can interfere with the goings- sorted through a variety of RNA forms that have shown promise for disease treatment and found thre the desired tasks. One example is "small interfering RNA," or siRNA, which deactivates certain genes aptamers, which bind to cancer cell surface markers, and ribozymes, which can be designed to degra cells or viruses.

"We linked each of the three therapeutic strands with a piece of pRNA, forming three hybrid strands," techniques we learned from our earlier work, we were able to combine all three into triangles that are nanometers wide. This is the Goldilocks size for any nanoparticle that is to be used in the body – not t

Particles larger than about 100 nanometers are generally too large to pass through cell membranes ir

said, and the body has a hard time retaining particles smaller than 10 nanometers. But the tiny triang well enough to interrupt the growth of human breast cancer cells and leukemia model lymphocytes in

"One characteristic of cancer cells is that they do not stop growing, which is one reason tumors devel the siRNA essentially instructs the cells to 'stop not stopping.' The nanoparticles had done their work cultures within a few days."

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

"The results are very promising, but we still have several hurdles to jump before we can test this ther "First and foremost, we must ensure that it is as safe as we think it is. Some RNA can be toxic to non though our nanoparticles appear to go straight to the cancer cells where we want them to go, we hav anywhere else before we can inject them into a living person."

Stability of the RNA also is a factor the team must consider. Although they previously published data nanoparticles are more stable than other RNA, Guo said the team still needs to find better ways to pr degradation by enzymes in the body.

Although the group still needs to prove the safety of their tiny creations, Guo said, they remain confid milestone for medical nanotechnology. The team has already obtained further results that could help nanoparticles.

"Many studies have shown that therapeutic forms of RNA, such as siRNA or ribozymes, could be put t the main obstacle has been finding the delivery method that can bring them to specific cells simultane "Nanotechnology is beginning to pay off here in that it may have provided us with a solution to the pr the work we have done so far and refine it for human trials."

The team's work is supported in part by grants from the National Institutes of Health and the Departm

Guo is affiliated with Purdue's Cancer Center and Birck Nanotechnology Center.

The Cancer Center, one of just eight National Cancer Institute-designated basic-research facilities in t to help cancer patients by identifying new molecular targets and designing future agents and drugs fo treating cancer.

The Birck Nanotechnology Center is located in Purdue's new Discovery Park, located on the southwest Programs include undergraduate teaching, graduate research and technology-transfer initiatives with in biology, chemistry, physics and several engineering disciplines participate in the research.

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