

First live targeting of tumors with RNA-based technology

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(PhysOrg.com) -- Finding and treating a tumor without disturbing normal tissue presents challenges - sometimes the most effective therapies can be invasive and harsh.

Researchers at Duke University Medical Center have devised a way they might deliver the right therapy directly to tumors using special molecules, called aptamers, which specifically bind to living [tumor](#) tissue.

They screened a large pool of aptamers in a rodent with [liver cancer](#) until they found the best molecule to bind to a tumor protein.

"We are already exploring attaching chemicals to the aptamers, so the aptamer molecules could deliver tumor-killing agents where they are needed, which is the next phase of our research," said senior author Bryan Clary, M.D., chief of the Division of Hepatopancreatobiliary and Oncologic Surgery.

The study was published in [Nature Chemical Biology](#) online on Nov. 29.

Aptamers are small pieces of RNA that bind to a specific [target molecule](#), usually a protein. They offer ease of use because they can be easily regenerated and modified and therefore have increased stability over some other agents, such as protein-based antibodies. Notably, they have a very low chance of immune-system interference, making them great candidates for tumor diagnosis and therapy.

"Most importantly, it's not necessary to have detailed knowledge of protein changes in the disease before the selection process," said lead author Jing Mi, M.D., Ph.D., assistant professor in the Duke Department of Surgery. "This greatly simplifies the process of molecular probe development. The selected aptamers can be used to discover proteins not previously linked with the disease in question, which could speed up the search for effective therapies."

The researchers used a large pool of RNA strands and applied them to a rodent with a liver tumor, the type of metastatic tumor that often results from a [colon cancer](#) tumor.

"We hypothesized that the [RNA molecules](#) that bind to normal cellular elements would be filtered out, and this happened," said Clary, who treats colon cancer patients. "In this way, we found the RNA molecules that went specifically to the tumor."

The researchers removed the tumor, extracted the specific RNA in the tumor, amplified these pieces of RNA to create a greater amount, and reinjected the molecules to learn which bound most tightly to the tumor. They repeated this process 14 times to find a good candidate.

The team found a tumor-targeting RNA aptamer that specifically bound to RNA helicase p68, a nuclear protein produced in colorectal tumors.

"This aptamer not only binds to p68 protein in cell culture, but also preferentially binds to cancer deposits in a living animal," Mi said. "The nice thing about this aptamer approach is that it could be used to discover the molecular signatures of many other diseases."

Clary said the process could be repeated with different types of tumors. For example, a scientist might take a breast cancer line and grow it in the lung as a metastasis model and then perform in vivo selection to identify

RNAs specifically binding to the lung tumor.

"This would work, theoretically," Clary said. "The idea of selecting molecules targeting a tumor growing in a body that results in a useful reagent for biologic exploration and therapy delivery in tumors is exciting."

In fact, based on earlier research done with proteins called peptides, the researchers expected that the aptamer process would find proteins in the blood vessels feeding the liver tumor, but instead they found the p68 target inside of tumor cells. "We think this is a valuable target because delivering to the sites inside of cells may make it easier to treat an entire tumor with drugs that are 'escorted' by the aptamer," Clary said.

He said that repeating the selection and amplification process with the same liver tumor could lead to development of other aptamers that bind well to proteins in tumor tissue besides p68. The team focused its initial efforts on developing an escort for p68 because this protein was known to be overexpressed in colon cancer.

Source: Duke University Medical Center ([news](#) : [web](#))

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