Buckyballs could deliver multi-drug therapy to tumors

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In the ongoing search for better ways to target anticancer drugs to kill tumors without making people sick, researchers find that nanoparticles called buckyballs might be used to significantly boost the payload of drugs carried by tumor-targeting antibodies.

In research due to appear in an upcoming issue of the journal *Chemical Communications*, scientists at Rice University and The University of Texas M. D. Anderson Cancer Center describe a method for creating a new class of anti-cancer compounds that contain both tumor-targeting antibodies and nanoparticles called buckyballs. Buckyballs are soccer ball-shaped molecules of pure carbon that can each be loaded with several molecules of anticancer drugs like Taxol®.

In the new research, the scientists found they could load as many as 40 buckyballs into a single skin-cancer antibody called ZME-018. Antibodies are large proteins created by the immune system to target and attack diseased or invading cells.

Previous work at M. D. Anderson has shown that ZME-018 can be used to deliver drugs directly into melanoma tumors, and work at Rice has shown that Taxol can be chemically attached to a buckyball.

"The idea that we can potentially carry more than one Taxol per buckyball is exciting, but the real advantage of fullerene immunotherapy over other targeted therapeutic agents is likely to be the buckyball's potential to carry multiple drug payloads, such as Taxol plus other

chemotherapeutic drugs," said Rice's Lon Wilson, professor of chemistry. "Cancer cells can become drug resistant, and we hope to cut down on the possibility of their escaping treatment by attacking them with more than one kind of drug at a time."

Researchers have long dreamed of using antibodies like ZME-018 to better target chemotherapy drugs like Taxol, and M. D. Anderson's Michael G. Rosenblum, Ph.D., professor in the Department of Experimental Therapeutics and Chief of the Immunopharmacology and Targeted Therapy Laboratory, has conducted some of the pioneering work in this field.

"This is an exciting opportunity to apply novel materials such as fullerenes to generate targeted therapeutics with unique properties," Rosenblum said. "If successful, this could usher in a new class of agents for therapy not only for cancer, but for other diseases as well."

While it's possible to attach drug molecules directly to antibodies, Wilson said scientists haven't been able to attach more than a handful of drug molecules to an antibody without significantly changing its targeting ability. That happens, in large part, because the chemical bonds that are used to attach the drugs -- strong, covalent bonds -- tend to block the targeting centers on the antibody's surface. If an antibody is modified with too many covalent bonds, the chemical changes will destroy its ability to recognize the cancer it was intended to attack.

Wilson said the team from Rice and M. D. Anderson had planned to overcome this limitation by attaching multiple molecules of Taxol to each buckyball, which would then be covalently connected to the antibodies. To the team's surprise, many more buckyballs than expected attached themselves to the antibody. Moreover, no covalent bonds were required, so the increased payload did not significantly change the targeting ability of the antibody.

Wilson said certain binding sites on the antibody are hydrophobic (water repelling), and the team believes that these hydrophobic sites attract the hydrophobic buckyballs in large numbers so multiple drugs can be loaded into a single antibody in a spontaneous manner to give the antibody-drug agent more "bang for the buck."

"The use of these nanomaterials solves some intractable problems in targeted therapy and additionally demonstrates the increasing value of the team science approach bridging different disciplines to uniquely address existing problems," Rosenblum said.

Source: Rice University