Nanoparticle created as diagnostic, therapeutic agent; brain tumors targeted

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Researchers working with a man-made, metal-filled nanoparticle are developing the material for use as a diagnostic and therapeutic agent that may boost the sensitivity of MRI techniques and improve the diagnosis and treatment of brain tumors.

Panos Fatouros, Ph.D., a professor in the Department of Radiology at Virginia Commonwealth University, has been awarded a five-year, $3.7 million grant from the National Institutes of Health's National Cancer Institute to lead a team of scientists from VCU and Virginia Tech. In a cooperative effort, they will work to further develop, produce and test nanoparticles that can identify brain tumor cells and selectively target them for radiation therapy.

Harry Dorn, Ph.D., and Harry Gibson, Ph.D., both chemistry professors at Virginia Tech, along with other colleagues created a nanoparticle called a functional metallofullerene (fMF), also known as a "buckyball," that will serve as the basis for the proposed research. It is envisioned that this research will generate a multi-functional platform that will integrate diagnostic and therapeutic functions.

"The metal-filled nanoparticles developed by our colleagues at Virginia Tech, and the advances in imaging, molecular biology and drug delivery at VCU, have opened the possibility for combined targeted diagnosis and therapy of tumors and their infiltrative aspects," said Fatouros. In effect, one can look at these nanoparticles as targeted drug delivery vehicles.

Tumor cells that extend beyond the well-defined tumor margins are often impossible to visualize with current imaging techniques. According to Fatouros, this research may one day benefit patients with advanced brain tumors by enabling treatment of tumor cells that have spread beyond the visible margins of the tumor on CT and MRI scans. Fatouros said that these tumor cells are most likely to result in recurrence of the brain tumor and that improved methods of attacking these cells offer the possibility of delaying or preventing brain tumor relapse.

Fullerenes represent another pure form of carbon; the others are graphite and diamond. Fullerenes are hollow carbon cage-like molecules that were discovered in the 1970s. For decades, scientists attempted to put atoms with useful properties inside these cages. In 1999, Dorn and his colleagues succeeded and were able to encapsulate rare earth metals in the hollow interior of these nanoparticles that can easily be recognized by MRI techniques. They created useful quantities of these metal-filled fullerenes and changed their shape, creating an entire family of metallofullerenes.

The filled fullerenes became functional in 2002, when Dorn's Ph.D. student, Erick Iezzi discovered how to add organic reagents to the exterior of the carbon cage and make the molecule water soluble. Gibson has since created a multitude of ways to attach guest molecules to the fullerene host, so the fMFs can attach to disease sites in a variety of ways, perhaps as photodynamic therapy agents.

Preliminary experiments conducted in the VCU labs of Fatouros and William Broaddus, M.D., Ph.D., a neurosurgeon at VCU, using rat models and the buckyballs created by Dorn has shown some promise. These researchers have used the nanoparticles in novel imaging and drug delivery methods to detect tumors implanted in a rat's brain. They found that the nanoparticles highlighted the tumors more effectively than existing imaging agents. The fMF material provides improved brain tissue differentiation and a dark outline of the tumor margin, making surgical removal more precise. These preliminary results will be published in the scientific journal, Radiology.

In addition the VCU-Virginia Tech team also has demonstrated that when using the fMF as a contrast agent for MRI examinations, the material is at least 40 times more effective than current commercial agents.

The Virginia Tech researchers plan to load the fMFs with a metal that can be neutron activated to produce useful radioisotopes and fluorescent materials. Some of this work will be conducted at the Oak Ridge National Lab. “We will make the fMFs radioactive so they can be used in treatment and make the fmFs fluoresce so the doctors can track it and watch the tumor shrink,” Dorn said. These particles will be further modified by the VCU-Virginia Tech teams to target cancer cells.

Source: Virginia Commonwealth University

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