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Nano-syringe delivers combination, targeted brain cancer therapy

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Nanomedicine researchers at the Methodist Neurological Institute and Rice University have developed a way to selectively kill brain cancer cells by using a tiny syringe to deliver a combination of chemotherapy drugs directly into the cells. These findings will be published in the April 24 issue of the American Chemical Society journal *ACS Nano*.

Patients with glioblastoma multiforme (GBM), the most common and aggressive malignant primary brain tumor, typically have a prognosis of 14-month median survival time despite medical interventions, which currently include surgery, chemotherapy and radiation.

The Rice-Methodist group developed the hydrophilic carbon cluster (HCC) antibody drug enhancement system (HADES), named after the Greek god of the underworld. Through a 20-nanometer syringe, which is 2 million times smaller than a coffee mug, this nanovector successfully delivered a combination of three chemotherapy drugs into GBM cells in vivo, resulting in a high kill rate.

"Without our nano-delivery system, we know that current drug delivery would be highly toxic to patients if we tried to deliver all three of these drugs at once," said David Baskin, M.D., neurosurgeon at the Methodist Neurological Institute, who began his nanomedicine research in 2004 with the late Nobel laureate and Rice chemist Richard Smalley. "But delivered in combination using these nano-syringes, our research demonstrated extreme lethality, with at least a three-fold increase in the number of dead cancer cells following treatment. The nano-syringes

selectively deliver these drugs only to cancer cells, and appear not to be toxic to normal neurons and other non-cancerous brain cells."

HCCs are nanovectors with protective antioxidant properties, capable of transporting and delivering drugs and bioactive molecules. In order to bring the drug carriers close enough to the cancer cells and successfully deliver the chemotherapy combination, three different antibodies were combined with the HCC to allow the nanoparticle to stick to the cell membrane. The drugs stayed inside the HCC until it attached to the cell membrane. Once binding occurred, the drugs were released into the fatty (lipid) environment in the membrane. The chemical properties of the chemotherapy drugs inside the HCC are such that they prefer to accumulate in areas with high concentrations of lipids and avoid areas with high water content, such as the extracellular space.

"A new and exciting advance is that now we have a carrier with protective properties, unlike previous nanotubes which were shown to be toxic," said Martyn Sharpe, the paper's lead author and a scientist with the Methodist NI's department of neurosurgery. "Some of the chemotherapy agents used in this research traditionally perform poorly with GBMs. Now that we've shown a successful kill rate of these cells in vivo, we're looking at treating human tumors that will be grown in immune-compromised mice models."

As personalized medicine continues to evolve, Baskin says this research could also be significant for other forms of cancer, including breast and head and neck cancers.

The paper represents an important collaboration between the laboratories of Baskin at Methodist, and James Tour, Ph.D. with Rice University's Smalley Institute for Nanoscale Science. Further work developing this system and expanding its utility is under way with continued collaboration between these two research groups.

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