Artificial Nanoscale Cholesterol Carrier Targets Brain Tumors

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Low-density lipoprotein, better known as LDL, is one of the chief villains involved in the development of coronary artery disease. But new research results suggest that for cancer patients with glioblastoma multiforme (GBM), the most common malignant brain tumor in adults, synthetic LDL-like nanoparticles could prove to be the vehicle of choice for delivering potent anticancer drugs to tumor cells while sparing healthy neighboring cells.

Writing in the International Journal of Pharmaceutics, a team of investigators led by Trudy Forte, Ph.D., at the Children's Hospital of Oakland Research Institute, describes its development of a multicomponent nanoparticle that targets a cell-surface LDL receptor that is overproduced by glioblastoma cells, as well as by other tumor cells. Healthy brain cells, in contrast, have relatively low levels of the LDL receptor in their cell membranes.

To construct their nanoparticles, the investigators started with a mix of lipids, cholesterol, and a small, synthetic protein that contains two functional regions. One region acts as an LDL receptor binding region and the other as a lipid binding region that helps hold the nanoparticle together. Initial experiments confirmed that the resulting 10-nanometer diameter particles bound efficiently to the surface of GBM cells growing in culture and that they could prevent this binding using a compound known to inhibit the interaction of natural LDL particles with their receptor.

Using a fluorescent dye as a model drug, the researchers then showed that glioblastoma cells took up the synthetic nanoparticles. The investigators note that the small size of these synthetic nanoparticles make them suitable for delivery into the brain using a technique known as convection enhanced delivery. Natural LDL particles do not cross the blood-brain barrier.

This work is detailed in a paper titled, “Synthetic nano-low density lipoprotein as targeted drug delivery vehicle for glioblastoma multiforme.” Investigators from the Lawrence Berkeley National Laboratory and the University of California, Berkeley, also participated in this study. This paper was published online in advance of print publication. An abstract of this paper is available at the journal’s website.

Source: National Cancer Institute