Targeted Nanoparticles Boost Arsenic's Anticancer Punch

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Arsenic trioxide has a long history as a potent human poison, but it also has proven valuable as one of the primary treatment options for acute promyelocytic leukemia. Efforts to use arsenic trioxide to treat other types of cancer are under way, but clinical trials are revealing that the extreme toxicity of this material is likely to limit its utility as a broad-spectrum anticancer agent.

A new report appearing in the journal *Molecular Cancer Therapeutics* suggests that targeted nanoparticles may be able to overcome the dose-limiting toxicities of arsenic trioxide while simultaneously boosting this chemical's anticancer activity. This work was led by Thomas O'Halloran, Ph.D., an investigator with the Nanomaterials for Cancer Diagnostics and Therapeutics Center for Cancer Nanotechnology Excellence based at Northwestern University.

Although several research teams have prepared nanoparticulate formulations of arsenic trioxide, these efforts have been plagued by the ability of arsenic trioxide to leak rapidly out of the nanoparticles. Dr. O'Halloran and his colleagues appear to have solved this problem by encapsulating arsenic trioxide along with nickel ions within a lipid-based nanoparticle coated with poly(ethylene glycol). The resulting nanoparticles retain their arsenic trioxide payload and are stable at refrigerator temperatures for more than 6 months. In addition, the composition of the nanoparticle makes them unstable when subjected to the slightly acidic conditions found inside tumor cells. As a result, the nanoparticles fall apart and release arsenic trioxide only after being

taken up by malignant cells.

To further improve the therapeutic characteristics of nanoparticle-encapsulated arsenic, the investigators added a small amount of folic acid to the nanoparticle's outer layer. Folic acid binds to a high-affinity folic acid receptor that is found on many types of tumors. Using several experimental methods, the researchers demonstrated that folate-targeted nanoparticles are efficiently taken up by tumor cells but are ignored by other types of cells. The researchers also showed that nanoparticle-encapsulated arsenic trioxide is far more toxic to tumor cells than is the drug by itself and that the coencapsulated nickel ions further increase the potency of nanoparticulate arsenic trioxide.

This work, which is detailed in the paper "Folate-mediated intracellular drug delivery increases the anticancer efficacy of nanoparticulate formulation of arsenic trioxide," was supported by the NCI Alliance for Nanotechnology in Cancer, a comprehensive initiative designed to accelerate the application of nanotechnology to the prevention, diagnosis, and treatment of cancer. Investigators from Purdue University also participated in this study. An abstract is available at the journal's Web site.

Source: National Cancer Institute (news : web)