

Double-Duty Nanoparticles Overcome Drug Resistance in Tumors

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Cancer cells, like bacteria, can develop resistance to drug therapy. In fact, research suggests strongly that multidrug resistant cancer cells that remain alive after chemotherapy are responsible for the reappearance of tumors and the poor prognosis for patients whose cancer recurs. Indeed, multidrug resistance occurs in over 50% of patients whose ovarian cancer relapses, accounting in large part for the high mortality associated with ovarian cancer.

In an attempt to circumvent the mechanisms that cancer cells use to avoid cell death following chemotherapy, researchers at Northeastern University, led by Mansoor Amiji, Ph.D., have created a polymeric nanoparticle that delivers a one-two punch to multidrug resistant ovarian cancer cells.

The first blow comes from the drug ceramide, which overwhelms an enzyme that drug-resistant tumor cells use to avoid apoptosis, the programmed cell death that chemotherapy triggers.

The nanoparticle delivers its second blow in the form of paclitaxel, a potent anticancer agent used as a first-line therapy for ovarian cancer. Amiji, the principal investigator of one of the National Cancer Institute's Cancer Nanotechnology Platform Partnerships, and his colleagues published their results in the journal *Cancer Research*.

Using drug-resistant ovarian cancer cells growing in culture, the investigators showed that treatment with the multifunctional nanoparticle

produced 100% mortality among the cultured cells. Moreover, ceramide co-therapy sensitized the drug-resistant cells to such a degree that they became as sensitive to the cell-killing effects of paclitaxel as are non-drug-resistant ovarian tumor cells. The researchers note that followup experiments showed that nanoparticle-delivered ceramide, in fact, did restore the drug-resistant cells' ability to undergo apoptosis.

This work, which was supported by the National Cancer Institute's Alliance for Nanotechnology in Cancer, is detailed in the paper "Modulation of intracellular ceramide using polymeric nanoparticles to overcome multidrug resistance in cancer." Investigators from the Massachusetts General Hospital also participated in this study. An abstract of this paper is available through [PubMed](#).

Source: National Cancer Institute

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