

Nanoparticles Overcome Anticancer Drug Resistance

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Too often, chemotherapy fails to cure cancer because some tumor cells develop resistance to multiple anticancer drugs. In most cases, resistance develops when cancer cells begin expressing a protein, known as p-glycoprotein, that is capable of pumping anticancer drugs out of a cell as quickly as they cross through the cell's outer membrane. New research from the University of Kentucky shows that nanoparticles may be able to get anticancer drugs into cells without triggering the p-glycoprotein pump.

Writing in the *Journal of Controlled Release*, a team led by Russell Mumper, Ph.D., describes its work using untargeted nanoparticles made of cetyl alcohol and polysorbate, which the investigators have named E78 nanoparticles, as a delivery vehicle for the potent anticancer drug paclitaxel. Biodistribution studies with the formulation and with free paclitaxel revealed few significant differences in which the active drug ends up in the body.

Next, the investigators injected the nanoparticle-entrapped paclitaxel, empty nanoparticles, free paclitaxel, or saline directly into paclitaxel-resistant human colon tumors growing in mice. Nineteen days after injection, tumors in the animals treated with nanoparticle-entrapped paclitaxel were 47 percent smaller than those treated with free paclitaxel and 70 percent smaller than those in animals treated with plain nanoparticles or saline.

One surprising finding from this study was the fact that free paclitaxel had any effect at all on tumors known to be resistant to the drug. Further investigation showed that this effect was likely a result of paclitaxel's ability to inhibit angiogenesis. The researchers concluded that nanoparticulate-entrapped paclitaxel was able to suppress tumor growth by killing tumor cells directly and through inhibition of angiogenesis.

This work is detailed in a paper titled, "In-vivo efficacy of novel paclitaxel nanoparticles in

paclitaxel-resistant human colorectal tumors."

Based in part on these results, the NCI is now funding further work with a tumor-targeted version of this nanoparticle to determine if it can be used to overcome drug resistance in breast cancer patients. An abstract of this paper is available [through PubMed](#).

Source: National Cancer Institute

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