

# Biologically targeted nanoparticles may boost radiation therapy effects

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(PhysOrg.com) -- Making a tumor more sensitive to radiotherapy is a primary goal of combining chemo and radiation therapy to treat many types of cancer, but with the chemotherapy drugs come unwanted side effects.

UNC scientists report what they believe is the first pre-clinical demonstration of the potential of molecularly targeted nanoparticles as a promising new class of agents that can improve chemoradiotherapy treatment. The nanoparticles target [tumor cells](#), thus sparing normal tissue and avoiding the systemic side effects often associated with [chemotherapy drugs](#). They reported their finding in the October 19, 2011 Epub issue of the American Chemical Society publication *ACS Nano*.

The team used the drug docetaxel, used to treat head and neck cancers. Andrew Wang, MD, assistant professor of [radiation oncology](#) and senior study author explains, "Docetaxel is a proven drug used in chemoradiotherapy, but it leads to many unwanted side effects on normal organs. Nanoparticle formulation of docetaxel, on the other hand, concentrates in tumors, which in turn leads to improved efficacy and fewer side effects."

"We developed a biodegradable nanoparticle formulation of docetaxel that targets the folate receptor, overexpressed in head and neck and other tumors. Folate is a water-soluble form of Vitamin B9. We found that the folate-targeted nanoparticle was more effective than the docetaxel or

non-targeted nanoparticle formulation of docetaxel. We also learned that timing of the radiation following administration of the nanoparticle formulation is critical.

"This information will be very helpful in the clinical translation of nanoparticle drugs in chemoradiation. Our group is currently evaluating two commercial formulations of nanoparticle taxane drugs in preparation for early phase clinical trials in the near future."

**More information:** Folate-targeted Polymeric Nanoparticle Formulation of Docetaxel is an Effective Molecularly Targeted Radiosensitizer with Efficacy Dependent on the Timing of Radiotherapy, *ACS Nano*, Just Accepted Manuscript. [DOI: 10.1021/nm203165z](https://doi.org/10.1021/nm203165z)

### **Abstract**

Nanoparticle (NP) chemotherapeutics hold great potential as radiosensitizers. Their unique properties, such as preferential accumulation in tumors and their ability to target tumors through molecular targeting ligands, are ideally suited for radiosensitization. We aimed to develop a molecularly targeted nanoparticle formulation of docetaxel (Dtxl) and evaluate its property as a radiosensitizer. Using a biodegradable and biocompatible lipid-polymer NP platform and folate as a molecular targeting ligand, we engineered a folate-targeted nanoparticle (FT-NP) formulation of Dtxl. These NPs have sizes of  $72\pm 4$  nm and surface charges of  $-42\pm 8$  mV. Using folate receptor over-expressing KB cells and folate receptor low HTB-43 cells, we showed folate-mediated intracellular uptake of NPs. In vitro radiosensitization studies initially showed FT-NP is less effective than Dtxl as a radiosensitizer. However, the radiosensitization efficacy is dependent on the timing of radiotherapy. In vitro radiosensitization conducted with irradiation given at the optimal time (24 hours) showed FT-NP Dtxl is as effective as Dtxl. When FT-NP Dtxl is compared to Dtxl and non-

targeted nanoparticle (NT-NP) Dtxl in vivo, FT-NP was found to be significantly more effective than Dtxl or NT-NP Dtxl as a radiosensitizer. We also confirmed that radiosensitization is dependent on timing of irradiation in vivo. In summary, FT-NP Dtxl is an effective radiosensitizer in folate-receptor over-expressing tumor cells. Time of irradiation is critical in achieving maximal efficacy with this nanoparticle platform. To the best of our knowledge, our report is the first to demonstrate the potential of molecularly targeted NPs as a promising new class of radiosensitizers.

Provided by University of North Carolina at Chapel Hill School of Medicine

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