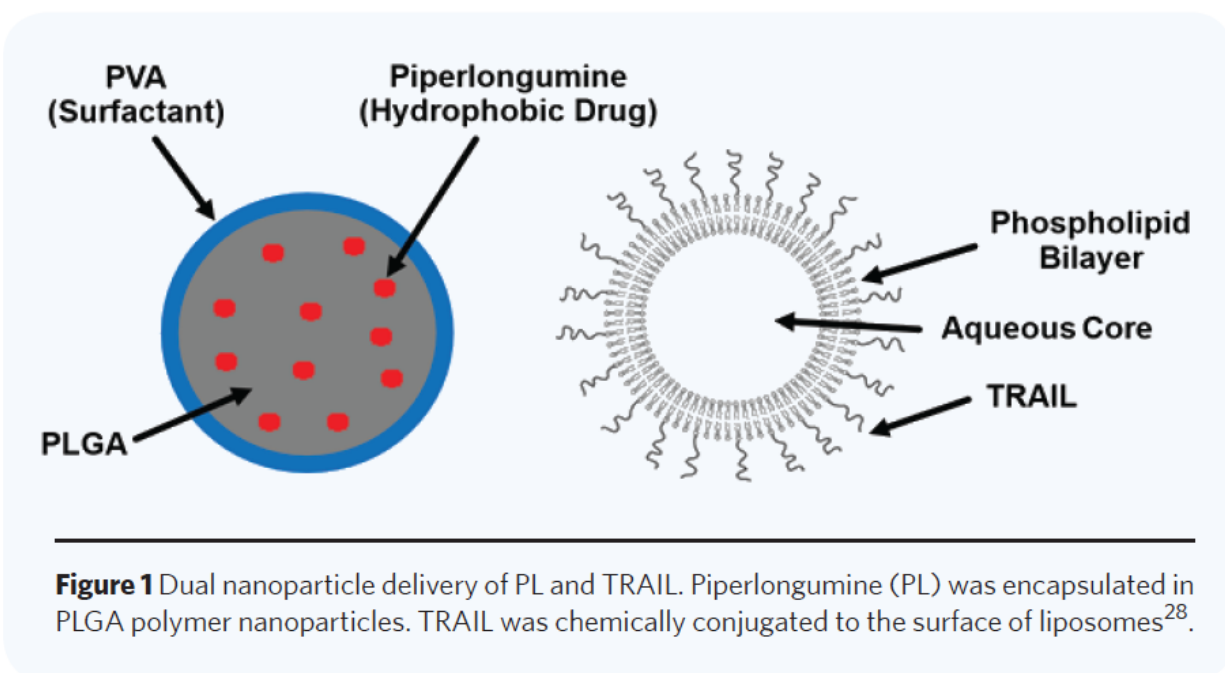


Two-stage nanoparticle delivery of piperlongumine and TRAIL anti-cancer therapy

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Piperlongumine (PL) was encapsulated in PLGA polymer nanoparticles. TRAIL was chemically conjugated to the surface of liposomes. Credit: World Scientific Publishing

A team of researchers from Cornell University in Ithaca, New York demonstrated a drug delivery mechanism that utilizes two independent vehicles, allowing for delivery of chemically and physically dis-tinct

agents.

The mechanism was utilized to deliver a new anti-cancer combination therapy consisting of piperlongumine (PL) and TRAIL to treat PC3 prostate cancer and HCT116 colon [cancer cells](#). PL, a small-molecule hydrophobic drug, was encapsulated in poly (lactic-co-glycolic acid) (PLGA) nanoparticles. TRAIL was chemically conjugated to the surface of nanoscale liposomes. PL was first administered to sensitize cancer [cells](#) to the effects of TRAIL. PC3 and HCT116 cells had lower survival rates in vitro after receiving the dual nanoparticle therapy compared to each agent individually. In vivo testing involved a subcutaneous mouse xenograft model using NOD-SCID gamma mice and HCT116 cells. Two treatment cycles were administered over 48 hours. Higher apoptotic rates were observed for HCT116 [tumor cells](#) that received the dual nanoparticle therapy compared to individual stages of the nanoparticle therapy alone. The report appears in the latest issue of the journal *Technology*.

"We have found that liposomal TRAIL shows great promise for the destruction of tumor cells in the bloodstream, lymphatic system, and also in solid tumors," says Daljit S. and Elaine Sarkaria Professor Michael R. King, Ph.D., of Cornell University and senior author of the study.

In the paper, the Cornell researchers describe a nanoparticle-based drug delivery mechanism developed for a combination cancer therapy. Nanoparticle delivery platforms have been previously pursued for a variety of cancer therapies. A number of studies have focused on complex particle structures and designs aimed at improving delivery. The Cornell group's system utilizes a different approach through the use of a dual nanoparticle delivery mechanism. Therapeutic components were administered through separate particles as opposed to delivering the agents in a single particle. Given the hydrophobic nature of the TRAIL sensitizer, the drug was encapsulated in polymer-based

nanoparticles.

In the study, researchers observed of a higher number of apoptotic cells in mouse trials, consistent with their observed laboratory results that demonstrated an increased therapeutic efficacy when utilizing the two-stage nanoparticle therapy compared to each individual nanoparticle stage alone. The dual nanoparticle delivery system provided a level of flexibility when administering the two stages of the therapy, allowing for an opportunity for sensitization of the tumor cells prior to administering the second component of the therapy.

The team from Cornell is working now to develop a new therapeutic approach to target cancer cells in the bloodstream for the prevention of prostate cancer metastasis, that utilizes circulating leukocytes as a carrier for the apoptosis ligand TRAIL. Once introduced into the bloodstream, E-selectin/TRAIL liposomes attach to the surface of peripheral blood leukocytes, to render these "unnatural killer cells" cytotoxic to circulating cancer cells without affecting blood cell or endothelial cell viability. They previously showed that viable cancer cells can be rapidly cleared from the bloodstream, using liposome-bound TRAIL concentrations that are two orders of magnitude lower than the dosages used in prior human clinical trials of soluble TRAIL protein. More recently, they have found that E-selectin/TRAIL liposomes can completely block metastasis and also shrink primary prostate cancer tumors in mice.

More information: Charles C. Sharkey et al. Two-stage nanoparticle delivery of piperlongumine and tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) anti-cancer therapy, *TECHNOLOGY* (2016). [DOI: 10.1142/S2339547816500011](https://doi.org/10.1142/S2339547816500011)

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