Nanoparticles Effective in Killing Cancer with One-Two Punch of Chemotherapeutics

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Research studies, based at the University of Pennsylvania, demonstrate that biodegradable nano-particles containing two potent cancer-fighting drugs are effective in killing human breast tumors.

The unique properties of the hollow shell nano-particles, known as polymersomes, allow them to deliver two distinct drugs, paclitaxel, the leading cancer drug known by brand names such as Taxol, and doxorubicin directly to tumors implanted in mice. Their findings, presented online in the journal *Molecular Pharamaceutics*, illustrate the broad clinical potential of polymersomes.

"The system provides a number of advantages over other Trojan horse-style drug delivery system, and should prove a useful tool in fighting a number of diseases," said Dennis Discher, a professor in Penn's School of Engineering and Applied Science and a member of Penn newly established Institute for Translational Medicine and Therapeutics. "Here we show that drug-delivering polymersomes will break down in the acidic environment of the cancer cells, allowing us to target these drugs within tumor cells."

One key feature of molecular mechanism involves putting pores in the cancer cell membranes and has been simulated with supercomputers by Michael F. Klein and Goundla Srinivas of Penn's Department of Chemistry. While cell membranes and liposomes (vesicles often used for drug-delivery) are created from a double layer of fatty molecules called phospholipids, a polymersome is comprised of two layers of synthetic

polymers. The individual polymers are degradable and considerably larger than individual phospholipids but have many of the same chemical features. This results in a structure that looks like a very small cell or virus.

Discher and his colleagues take advantage of the polymersome properties to ferry their drug combination to the tumor. The large polymers making up the shell allow paclitaxel, which is water-insoluble, to embed within the shell. Doxorubicin, which is water-soluble, stays within the interior of the polymersome until it degrades. According to the researchers, the polymersome and drug combination is self-assembling the structure spontaneously forms when all of the components are suitably mixed together.

"Recent studies have shown that cocktails of paclitaxel and doxorubicin lead to better tumor regression than either drug alone, but there hasn't been any carrier system that can carry both drugs as efficiently to a tumor," said Fariyal Ahmed, the lead author, former doctoral student in bioengineering,and now a fellow at Harvard Medical School. "Polymersomes get around those limitations

Discher developed polymersomes with Penn bioengineer Daniel Hammer in the 1990s. The Discher lab is further studying the drug- and gene-delivery capabilities of polymersomes, tailoring their shapes, sizes, loading and degradability to each application. Discher theorizes that polymersomes could be made capable of traveling to places in the body that are difficult for most drug-carrier systems to access.

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Co-authors on these findings include Aaron Brannan and Frank Bates of

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Source: University of Pennsylvania