Researchers develop natural protein cage for improved cancer drug delivery

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Washington State University researchers have developed a unique, tiny protein cage to deliver nasty chemotherapy chemicals directly to cancer cells. Direct delivery could improve treatment and lessen what can be horrendous side effects from toxic drugs.

In their study, published in the October issue of *Biomaterials Science*, the researchers built a drug delivery system using apoferritin, the same ball of natural proteins that carries iron around in blood without letting the iron leak out. Apoferritin is made of 24 pieces that can conveniently open and close, depending on surrounding acidity.

While some research has been done on using apoferritin for drug delivery, this is the first time it was used to target lung cancer cells.

Kills more than 70 percent of lung cancer cells

Led by Yuehe Lin, professor in the WSU Voiland College's School of Mechanical and Materials Engineering, the researchers inserted the anticancer drug daunomycin into the cage. They modified the cage's exterior with a ligand, a signal-triggering molecule, making the cage particularly attractive to a common cancer cell receptor.

With the addition of a small amount of acid, adjusting the pH to below neutral, the protein cage slightly opened and let the drug jump inside, where it stayed until it came to the cancer cell. When the ball of drugs

entered the acidic environment of the cancer cell, the cage opened and delivered the drug directly to its foe.

Testing the system with lung cancer cells, the researchers showed that the ligand-guided protein cages selectively penetrated and killed more than 70 percent of the cancer cells.

Normal cells remain healthy

Unlike with the typical methods for drug delivery used in chemotherapy, the system did not attack healthy lung cells.

The system was shown to work nearly as well as - or in some cases better than - when the drug was freely moving, the type of scenario that causes the commonly experienced cancer treatment side effects.

"Our efficiency in killing the cancer cell was very high with no toxicity to normal cells," said Lin. "At the cell level, we were able to demonstrate it was very effective."

Preliminary studies promising

Lin emphasized that the work is still preliminary and has a long way to go before it can be used on people. The researchers were studying the drug delivery system at the cellular level and hope to continue the research with future animal studies.

More information: Yanan Luo et al. Hyaluronic acid-conjugated apoferritin nanocages for lung cancer targeted drug delivery, *Biomater. Sci.* (2015). DOI: 10.1039/C5BM00067J

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