Cellular nanoscale drug delivery from the inside out

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Delivering a dose of chemotherapy drugs to specific cancer cells without the risk of side affects to healthy cells may one day be possible thanks to a nanoscale drug delivery system being explored by researchers at the U.S. Department of Energy's Ames Laboratory. Using tiny silica particles call mesoporous nanospheres to carry drugs inside living cells, Ames Laboratory chemist Victor Lin is studying different methods to control whether or not the particle delivers its pharmaceutical payload.

"First, the nanospheres are only about 200 nanometers in diameter, roughly the size of a virus, so they won't trigger an immune response in the body," Lin said. "They're also biocompatible so they can be readily absorbed by the cells."

But it's the structure of the nanospheres that makes drug delivery possible. The spheres have thousands of parallel channels running completely through them. Through capillary action, the spheres can soak up molecules of the drug to be delivered. When the channels are filled, the ends of channels are "capped" to safely seal the drug inside. Once the caps are in place, the nanospheres are "washed" to remove the drug from the outer surface.

The type of material used for the end caps, how they're held in place, and how they're released is the focus of Lin's work. The caps can be dendrimers, biodegradable polymers, genes, proteins, metallic nanoparticles, or semiconductor nanocrystals – also known as quantum dots – and are held in place by chemical bonds. Once the nanospheres

are inside the target cells, a trigger is used to pop the caps off and release the drug.

"We're looking at two levels of control," Lin said of the trigger mechanism. "One level is to have the cell control the release and the other would be to control the release externally."

Lin explained that the chemical bond holding the cap in place can be engineered to be unphased by chemicals present in normal cells. However, in cancer cells these chemicals, such as antioxidants, appear in much higher concentrations and would break the bonds on the caps and release the drugs. In this way, only cancer cells could be targeted with powerful chemotherapy drugs such as Taxol or doxorubicin, while the nanospheres inside the normal cells would remain capped and therefore not cause unwanted side affects by damaging healthy cells.

To achieve external control, Lin is using iron-oxide nanoparticle caps which can be manipulated by a magnetic field. In a simple demonstration of the principle, Lin holds a refrigerator magnet up to a liquid-filled glass vial containing human cervical cancer cells grown in vitro that contain nanospheres capped with iron-oxide particles. The cells slowly migrate and cluster to the side of the vial next to the magnet.

"By using a powerful magnet, we can first concentrate the nanospheres at a particular point, such as a tumor site, and then use the magnetic field to remove the caps and release the drug," Lin said. "The advantage of using a magnetic trigger as opposed to a ultraviolet light trigger is that there's no limit to the depth of tissue we are able to probe … think of an MRI."

Beyond the possibilities for intercellular drug delivery, the nanospheres may provide the key to studying what takes place within a cell. Currently, scientists have difficulty introducing chemicals or genes into

cells without either damaging the cell or causing a chain-reaction of events that can't be tracked.

"With current gene therapy, it's possible to switch genes on and off, but you don't really know if you are affecting other parts and processes of the cell as well," Lin said. "You may be able to get a plant cell to produce a certain desired product, but the yield may drop significantly."

By using externally controlled nanospheres, Lin explains that it may be possible to sequentially release genes, chemical markers and other materials within cells in order to track what happens and what specific changes take place. This phase of Lin's research ties into a larger plant metabolomics project at Ames Laboratory.

Source: Ames Laboratory