Researchers develop magnetic molecular machines to deliver drugs to unhealthy cells

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Scientists from UCLA's California NanoSystems Institute and Korea's Yonsei University have developed an innovative method that enables nanomachines to release drugs inside living cancer cells when activated remotely by an oscillating magnetic field.

The new system — the first to utilize a class of porous nanomaterials driven by a magnetic core — has the potential to improve both targeted drug-delivery and magnetic resonance imaging in the treatment of cancer and other diseases.

The research appears in the July issue of the *Journal of the American Chemical Society*.

In recent years, cancer research has increasingly focused on developing therapies that, unlike chemotherapy, target only cancer cells while leaving healthy cells unharmed. To that end, scientists have created nanomachines that can trap and release drug molecules from pores directly into individual cancer cells in response to a stimulus.

While many methods have been created for controlling how and when pores load and unload their cargos, for therapeutic applications, an external and noninvasive method of activation is preferable for the most effective results.

The new method, developed by the research groups of Jeffrey Zink, a UCLA professor of chemistry and biochemistry, and Jinwoo Cheon, a

professor of chemistry at Korea's Yonsei University, uses a material that combines a framework of mesoporous silica nanoparticles with magnetic zinc-doped iron oxide nanocrystals, along with attached nanovalves that help hold drug molecules in the pores. When a magnetic-field stimulus is applied, the valves open and release the drug molecules from the pores into the target cells.

"The hydrophobic nature of the interior of the pores, as well as the ability to functionalize the silica surface with hydrophilic functionalities, makes these particles attractive for anti-cancer drug delivery," Zink said. "Adding a magnetic core to the silica-based nanoparticles is of interest for its potential applications in magnetic resonance imaging, as addition of the magnetic core may make it useful as a contrast agent."

For this study, nanoparticles carrying the anti-cancer drug doxorubicin were introduced to and endocytosed by breast cancer cells. When the cancer cells containing the nanoparticles were then exposed to an oscillating magnetic field, cell death occurred.

"The novel magnetic-core silica nanoparticles are effective in activating nanovalves which release anti-cancer drugs when they are exposed to an oscillating magnetic field," Zink said.

The magnetic-field oscillation causes the zinc-doped iron oxide nanocrystals to heat. This increased heat causes the molecular machines to activate, and the doxorubicin in the pores is delivered into the cells.

"Magnetic nanocrystals are important in biomedical applications because they can be used for both therapeutics and imaging," said Cheon, director of the National Creative Research Initiative Center for Evolutionary Nanoparticles and the H.G. Underwood Professor of Chemistry and division head of the Nano-Medical National Core Research Center at Yonsei University.

"The ability to deliver anti-cancer drugs only to the cancer cells without affecting healthy cells is of key importance," added Cheon who is also a visiting professor at UCLA's CNSI.

Experiments for the research project were performed by UCLA graduate students Courtney Thomas and Daniel Ferris and Yonsei University graduate students Je-Hyun Lee and Eunsook Kim, who are part of the research group of professor Jeon-Soo Shin. The research team also involved Fraser Stoddard, a professor of chemistry at Northwestern University who began his collaboration with Zink while he was a professor of chemistry at UCLA. During his UCLA tenure, Stoddart served as Fred Kavli Chair of Nanosystems Sciences and director of the CNSI, positions now held by distinguished professor of chemistry Paul S. Weiss.

The next step in the research will be to examine the effects in vivo and to determine if we can use this to offer precise control over location of delivered drugs. The ultimate goal would be to develop this system to have applicability in treatment of cancer patients.

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