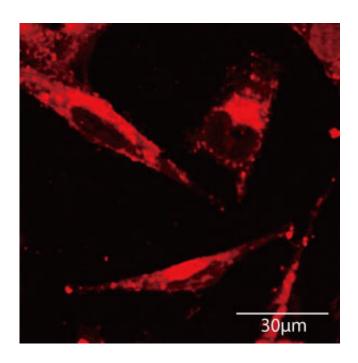


Multi stimuli-responsive nanocapsules selectively deliver drugs to exactly where they are needed

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Magnetic, pH-responsive nanoparticles deliver the antitumor drug doxorubicin (fluorescing red in this image) to cancer cells. Credit: American Chemical Society

A nanoparticle-based drug delivery system that can sense and respond to different conditions in the body, as well as to an externally applied magnetic field, could enhance doctors' ability to target drugs to specific sites of disease.



A*STAR researchers created the multifunctional nanocapsules by wrapping magnetic <u>iron oxide</u> nanoparticles inside a biocompatible polymer coat that could be tuned to respond to acidity or temperature. The team has already shown that the nanoparticles can selectively deliver the toxic antitumor drug doxorubicin to <u>cancer cells</u>.

Some previous nanoparticle <u>drug delivery</u> systems have incorporated <u>magnetic field</u> responsiveness, and others have shown pH- or temperature-responsiveness. The nanoparticles developed by Chaobin He, Zibiao Li and their colleagues at the A*STAR Institute of Materials Research and Engineering are unusual in that they combine multiple stimuli-responsive behaviors into a single nanoparticle.

The team made their nanoparticles by coating iron oxide particles with silica, then attaching the biocompatible poly(lactide) (PLA) polymer via a process known as stereocomplexation. The PLA polymer strands self-assemble themselves around the iron core, forming a flexible shell that can be loaded with drug molecules.

The iron oxide core allows doctors to physically target the encapsulated drug to specific sites in the body using an external magnetic field, explains Zibiao Li, a member of the team. "This characteristic of stimuli-responsive nanocarriers is especially important in cancer therapy to prevent the serious side effects of chemotherapy," he says. By selectively delivering chemotherapy drugs to a tumor, the drug's harmful effect on healthy cells can be minimized.

The researchers further enhanced the selective delivery of their nanocapsules by coating them with newly-designed PLA copolymers that can respond to changes in pH or temperature. A polymer named PLA-PDMAEMA, for example, swells up in acidic conditions, loosening its grip on its cargo of drugs as it expands. As tumor cells are typically more acidic environments than healthy cells, these nanoparticle should



selectively release their drugs within cancer cells.

When the researchers loaded their PLA-PDMAEMA coated nanoparticles with the anticancer drug doxorubicin, they showed that the drug was released significantly faster under acidic conditions. Initial tests with breast cancer cells confirmed the capsules' were taken up by the cells and able to release their cargo to kill the cells.

The next step will be to optimize the size of the nanocapsules size, before testing them in animal models. "Further exploration of using these nanoparticles for combined drug delivery and bioimaging are also in progress," Li says.

More information: Zibiao Li et al. Facile Layer-by-Layer Self-Assembly toward Enantiomeric Poly(lactide) Stereocomplex Coated Magnetite Nanocarrier for Highly Tunable Drug Deliveries, *ACS Applied Materials & Interfaces* (2016). DOI: 10.1021/acsami.5b09822

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