Scientists develop nanogels that enable controlled delivery of carbohydrate drugs

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Carnegie Mellon University scientists have developed tiny, spherical nanogels that uniformly release encapsulated carbohydrate-based drugs. The scientists created the nanogels using atom transfer radical polymerization (ATRP), which will ultimately enable the nanogels to deliver more drug directly to the target and to dispense the drug in a time-release manner.

The nanogels — only 200 nanometers in diameter — possess many unique properties that make them ideal drug-delivery tools, according to Daniel Siegwart, a graduate student in University Professor Krzysztof Matyjaszewski's laboratory at Carnegie Mellon. Siegwart will present his research Monday, Aug. 20 at the 234th national meeting of the American Chemical Society in Boston.

ATRP, a controlled living radical polymerization process, allows chemists to precisely regulate the composition and architecture of the polymers they are creating. Siegwart and colleagues used ATRP in inverse miniemulsion to make nanogels with a uniform network of cross-linked polymer chains within a spherical nanoparticle.

"A uniform mesh size within the nanogels should improve the controlled release of the encapsulated drugs," said Siegwart. "The major advance of this system is that ATRP allows one to prepare nanogels that are uniform in diameter. The size of the particles can be tuned, and we are currently investigating how nanogels of different sizes enter cells. The results may allow us to better understand the mechanism of endocytosis and to target

specific tissues, such as cancer cells that have a more permeable membrane."

In their most recent advance, the Carnegie Mellon team incorporated the model carbohydrate drug rhodamine isothiocyanate-labeled dextran into the nanogel's uniform mesh core. When the nanogels degraded, the model carbohydrate drug was released over time. The experiments were carried out with Jung Kwon Oh, a former postdoctoral associate in the Matyjaszewski lab who developed ATRP in inverse miniemulsion.

The new nanogels, which are nontoxic and biodegradable, can also accommodate molecules on their surfaces. During nanogel synthesis, the ATRP process allows scientists to incorporate "targeting groups" on the nanogel surface that can interact with specific receptors, such as those on the surface of a cancer cell. In addition, the nanogels can escape the notice of the body's immune system, thus prolonging circulation time within the bloodstream.

"The basic composition of the nanogels is based on an analogue of poly(ethylene oxide), a well-established biocompatible polymer that can enhance blood circulation time and prevent clearance by the reticuloendothelial system, the part of the immune system that engulfs and removes foreign objects from the body," said Siegwart.

In a recent article published in the *Journal of the American Chemical Society*, the Carnegie Mellon team demonstrated that its novel nanogels could be used to encapsulate doxorubicin, an anticancer drug. When the scientists mixed the doxorubicin-loaded nanogels with HeLa cancer cells in the laboratory, the doxorubicin was released, penetrating the cancer cells and significantly inhibiting their growth. They carried out this work in collaboration with Jeffrey Hollinger, professor of biomedical engineering and biological sciences and director of the Bone Tissue Engineering Center at Carnegie Mellon.

Source: Carnegie Mellon University