Temperature-Sensitive Nanoparticles Open New Avenues for Drug Delivery

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Many types of nanoparticles can cross the cell membrane and deliver their therapeutic payload into tumor cells. In some instances, however, nanoparticles can become trapped inside endosomes, distinct compartments within a cell in which enzymes can break down some anticancer agents. As a result, anticancer genes or drugs that must reach the nucleus in order to kill the cell may never reach their intended destination intact.

In an attempt to address this potential problem, researchers at the Korea Advanced Institute of Science and Technology in Daejeon, South Korea, have developed polymer nanoparticles that can expand rapidly in response to a temperature change. This expansion breaks endosomes apart, releasing their contents into the cellular cytoplasm. In a related paper, the same investigators demonstrate that they can stabilize these temperature-sensitive nanoparticles using gold nanoparticles.

Writing in the journal Biomacromolecules, Tae Gwan Park, Ph.D., and collaborators describe the formulation experiments they conducted with a series of polymers to develop nanoparticles whose size depends on temperature. These studies showed that a mixture of poly(ethylenimine) (PEI), a polymer used to deliver genes to cells, and a commercially available, complex polymer known as Pluronic F-127, will form nanoparticles whose volume increases more then 40-fold when the temperature drops from 33 ° C to 24 ° C. Pluronic F-127 is composed of alternating sections of two other polymers: poly(ethylene oxide) and poly(propylene oxide).

When added to tumor cells growing in culture at 37°C, dye-containing temperature-sensitive nanoparticles entered the cells and became sequestered in endosomes within 30 minutes. The researchers then dropped the temperature of the culture medium to 20°C for 15 minutes – electron microscope images showed clearly that the nanoparticles had swollen, disrupted the endosomes, and released their dye payload into the cytoplasm. In control experiments using temperature-stable polymer nanoparticles, the researchers did not detect dye in the cytoplasm following the abrupt temperature change. The researchers are now working to develop methods of producing localized "cold-shock" in tissues.

In a second paper, published in the journal Langmuir, Park and his colleagues reported on a second type of temperature-sensitive polymer nanoparticle that uses gold nanoparticles, rather than poly(ethylenimine), in combination with Pluronic F-127. These hybrid nanoparticles were more stable, and hence may be better able to withstand the turbulent physical conditions in the bloodstream, yet they also increased their size dramatically in response to a sharp temperature drop. The researchers note that because the gold particles form an outer shell surrounding a polymer core, it should be possible to use the outer gold shell as a site on which to attach tumor-targeting molecules using well-developed chemistry.

The work using temperature-sensitive nanoparticles to disrupt endosomes is detailed in a paper titled, "Temperature-sensitive pluronic/poly(ethylenimine) nanocapsules for thermally triggered disruption of intracellular endosomal compartment." This paper was published online in advance of print publication. An abstract of this paper is available through PubMed.

The work using gold nanoparticles to stabilize temperature-sensitive micelles is detailed in a paper titled, "Thermosensitive pluronic micelles

stabilized by shell cross-linking with gold nanoparticles." This paper was published online in advance of print publication. An abstract of this paper is available at the journal's website.

Source: National Cancer Institute