How nanotubes enter cells

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Scientists worldwide are teasing apart the precise mechanisms behind how tubes of carbon only nanometers or billionths of a meter wide enter cells, findings that researchers could employ to help these nanotubes deliver medicines or genes into the body, experts told UPI's Nano World.

Physical chemist Hongjie Dai's team at Stanford University in California are exploring carbon nanotubes as therapeutic agents. For instance, while biological tissue is transparent to near-infrared light, carbon nanotubes absorb it, and Dai and his colleagues in August reported that by tagging carbon nanotubes so that they would specifically latch onto cancer cells and shining near-infrared lasers on them, they could kill just cancer cells without harming normal tissue.

Dai's team also showed that carbon nanotubes could carry proteins and DNA into cells potentially to help deliver drugs or therapeutic genes. Compared with a solid spherical nanoparticle, a hollow nanotube has more surface area with which to carry molecules, explained biomolecular engineer Michael Strano at the University of Illinois at Urbana-Champaign.

Dai and his colleagues wanted to pinpoint how carbon nanotubes enter cells and where they end up inside. Compounds can enter either a cell using passive mechanisms that do not consume energy, where they just pass through the cell membrane, or via active mechanisms such as endocytosis, where cells engulf a target.

Knowing the route carbon nanotubes take and their final destinations could help determine what kinds of molecular bonds researchers should use to attach compounds with, organic chemist Alberto Bianco at the Institute of Molecular and Cellular Biology at Strasbourg in France explained. For instance, endocytosis places substances inside acidic cellular compartments known as lysosomes and endosomes. If scientists know nanotubes will end up there, they can attach drugs or genes using disulfide bonds, which get cleaved within lysosomes, "and thus we can release biological cargo from the nanotube transporters," Dai said. "Disulfide bonds are widely used for in vitro delivery and are among the most efficient."

Endocytosis requires either energy in the form of the molecule ATP or warmth. Dai and his colleagues found cooling cell cultures or dosing cells with an inhibitor that stopped ATP production meant they could no longer absorb carbon nanotubes, suggesting cells take up carbon nanotubes using endocytosis. Inhibitors against a tripod-shaped protein called clathrin specifically showed that cells apparently use a clathrin-dependent endocytosis pathway to absorb the tubes. Dai's team published its findings online Dec. 8 in the international scientific journal Angewandte Chemie.

Prior research from Bianco and organic chemist Maurizio Prato at the University of Trieste in Italy, chemical engineer Kostas Kostarelos at the University of London and their colleagues, who are also investigating carbon nanotubes as delivery vehicles for drugs or genes, suggested carbon nanotubes entered cells via a mechanism other than endocytosis. Strano pointed out this discrepancy is due to the different molecules each team attached to their carbon nanotubes. While Bianco and his colleagues used positively charged peptides, Dai's team used negatively charged DNA and proteins.

Strano added that Bianco and his colleagues found their carbon

nanotubes got carried into the nucleus, while Dai's team's tubes appeared to disperse more generally across the cell. "There is a lot of research to explore in both cases," Strano said. For instance, Bianco's teams tubes could be used more for gene delivery, while Dai's team's tubes might be used to heat the cell as a whole for anti-cancer strategies.

Ultimately, future research should test how effective carbon nanotubes are compared with competing nanotechnologies, Strano said. For instance, scientists have also been investigating other nanomaterials, such as hollow nanoparticles, for use in drug and gene delivery, and gold-silica nanoparticles known as nanoshells for a heat-based anti-cancer therapy similar to that Dai and colleagues proposed using carbon nanotubes.