

# Researchers clarify cellular uptake mechanisms for carbon nanotubes

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They look like the tiniest of needles and have the potential to channel pharmaceutical agents into targeted living cells: carbon nanotubes are long, thin, nanoscale tubes made of one (or more) layers of carbon atoms in a graphite-like arrangement. Drugs can be hooked on to their exteriors and can thus be carried into the cell along with the nanotube. But how?

Hongjie Dai and his team at Stanford University have systematically examined the cellular uptake mechanism for nanotubes with various biological cargos including DNA and proteins.

In order to develop tailored nano-transporters that duly deliver their cargo, it is important to know which route they take through the cell membrane. Molecules can get into the interior of a cell by various means. First, the researchers needed to determine if this is a case of active or passive transport. The passive transport mechanisms do not consume energy; molecules just pass the membrane.

Regarding active mechanisms, nanotubes might enter the cell by so-called endocytosis: Parts of the cell membrane include the molecules and migrate into the interior. This requires energy in the form of ATP and sufficiently high temperatures. Dai and his colleagues cooled some cell cultures and reacted others with an inhibitor that stops ATP production. In both cases the cells were no longer able to absorb nanotubes. “We conclude that this is an energy-dependent endocytosis mechanism,” says Dai. For the nanotubes, among the different types of endocytosis pathways the researchers thought two mechanisms in particular seemed

likely: caveolae-mediated and clathrin-dependent endocytosis.

Caveolae are little indentations made of lipids in the cell membrane. Molecules from the medium enter the indentation, which then closes itself off into a bubble that migrates into the cell interior. By means of inhibitors, the researchers disrupted the lipid distribution in the cell membrane, thus disrupting the caveolae—this did not prevent intake of the nanotubes. The clathrin-dependent mechanism involves the docking of molecules from the medium at special docking stations on the exterior of the membrane. Tripod-shaped protein molecules, clathrin, are bound to the docking site inside the membrane.

The clathrin molecules aggregate into a two-dimensional network that forms an arch that results in a cavity in the membrane. This again results in a bubble that closes itself off and wanders into the interior of the cell. Sugar-containing or potassium-free media destroy clathrin sheets. The cell cultures were thus placed under these conditions and were no longer able to absorb the nanotubes. Says Dai, “This clearly indicates clathrin-dependent endocytosis for carbon nanotubes used in our work.” This result contradicts the results of another group who propose a non-endocytotic mechanism. The reasons for the discrepancy have yet to be determined.

Source: Angewandte Chemie

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