Understanding Potential Toxic Effects of Carbon-Based Nanomaterials

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Various types of carbon-based nanomaterials, such as buckyballs and nanotubes, have shown promise as drug delivery tools and imaging agents, but reports of toxicity associated with some of these materials have raised questions about their ultimate utility in clinical oncology. Three recent reports in the literature provide new insights into why certain carbon-based nanomaterials are toxic to cells and others are not.

Writing in the journal *Nano Letters*, a team of researchers based at the École Polytechnique Fédérale de Lausanne in Switzerland report their studies on how shape, size and surface properties affect cellular toxicity. This team, led by Arnaud Magrez, Ph.D., added increasing concentrations of multi-walled carbon nanotubes, carbon nanofibers, or carbon nanoparticles to three different types of cultured human lung tumor cells and measured changes in cell proliferation and overall cellular health. The researchers found evidence of toxicity as soon as 24 hours after dosing with all three materials and in each cell line, though multi-walled carbon nanotubes were the least toxic in all assays.

The investigators noted that they were surprised that carbon nanoparticles proved to be the most toxic of the three materials they studied, though they added that this finding suggests that “dangling bonds” could be responsible for the toxicity of carbon nanomaterials. Highly reactive dangling bonds – carbon atoms not bonded to three other carbon atoms and thus available to react with biomolecules – are more prevalent in the carbon nanoparticles tested than in either nanofibers or nanotubes.

A second paper in Nano Letters, this one written by collaborators at the Centre National de la Recherche Scientifique (CNRS) in Strasbourg, France, and the University of Trieste in Italy, presents data showing that functionalized nanotubes are not toxic at all to three major classes of immune system cells. In this study, the investigators prepared two types of nanotubes whose surfaces had been modified in order to attach various targeting or therapeutic molecules and to render them soluble in water. In this case, the modifications were used to attach fluorescent dye molecules to enable intracellular tracking.

Studies with both types of nanotubes showed that they were taken up readily by immune system cells. However, none of the immune cells showed any signs of toxicity. Additional experiments showed that the functionalized nanotubes did not affect the functional activity of these cells either. The researchers note that their results confirm the findings of other laboratories that water-soluble carbon nanotubes have limited or no toxicity when tested in a wide variety of cell types.

To better understand how cells process one type of carbon nanomaterial, a team of investigators at the University of Cambridge in the United Kingdom, used high-resolution three-dimensional electron microscopy to track where buckyballs, or C 60, travel to in cells. Using non-toxic doses of buckyballs, the investigators found that buckyballs concentrated in intracellular lysosomes, along the cell membrane, along the nuclear membrane, and within the nucleus. Finding significant numbers of the nanoparticles in these latter two locations was a surprise to the investigators. They noted that accumulation of buckyballs within the cell nucleus could lead to DNA damage.

The work examining the toxicities of multiple materials is detailed in a paper titled, “Cellular toxicity of carbon-based nanomaterials.” Investigators from the University of Lausanne, in Switzerland, and the University of Fribourg, in Switzerland, also participated in this study. An

abstract of this paper is available through PubMed.

The work on buckyball uptake is detailed in a paper titled, “Uptake of C(60) by human monocyte macrophages, its localization and implications for toxicity: studied by high resolution electron microscopy and electron tomography.” An abstract of this work is available through PubMed.

The work on carbon nanotubes is detailed in a paper titled, “Functionalized carbon nanotubes are non-cytotoxic and preserve the functionality of primary immune cells.” This paper was published online in advance of print publication. An abstract is available at the journal’s website.

Source: National Cancer Institute