Carbon nanostructures -- elixir or poison?

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A Los Alamos National Laboratory toxicologist and a multidisciplinary team of researchers have documented potential cellular damage from "fullerenes" -- soccer-ball-shaped, cage-like molecules composed of 60 carbon atoms. The team also noted that this particular type of damage might hold hope for treatment of Parkinson's disease, Alzheimer's disease, or even cancer.

The research recently appeared in *Toxicology and Applied Pharmacology* and represents the first-ever observation of this kind for spherical fullerenes, also known as buckyballs, which take their names from the late Buckminster Fuller because they resemble the geodesic dome concept that he popularized.

Engineered carbon nanoparticles, which include fullerenes, are increasing in use worldwide. Each buckyball is a skeletal cage of carbon about the size of a virus. They show potential for creating stronger, lighter structures or acting as tiny delivery mechanisms for designer drugs or antibiotics, among other uses. About four to five tons of carbon nanoparticles are manufactured annually.

"Nanomaterials are the 21st century revolution," said Los Alamos toxicologist Rashi Iyer, the principal research lead and coauthor of the paper. "We are going to have to live with them and deal with them, and the question becomes, 'How are we going to maximize our use of these materials and minimize their impact on us and the environment?'"

Iyer and lead author Jun Gao, also a Los Alamos toxicologist, exposed cultured human skin cells to several distinct types of buckyballs. The differences in the buckyballs lay in the spatial arrangement of short branches of molecules coming off of the main buckyball structure. One buckyball variation, called the "tris" configuration, had three molecular branches off the main structure on one hemisphere; another variation, called the "hexa" configuration, had six branches off the main structure in a roughly symmetrical arrangement; the last type was a plain buckyball.

The researchers found that cells exposed to the tris configuration underwent premature senescence—what might be described as a state of suspended animation. In other words, the cells did not die as cells normally should, nor did they divide or grow. This arrest of the natural cellular life cycle after exposure to the tris-configured buckyballs may compromise normal organ development, leading to disease within a living organism. In short, the tris buckyballs were toxic to human skin cells.

Moreover, the cells exposed to the tris arrangement caused unique molecular level responses suggesting that tris-fullerenes may potentially interfere with normal immune responses induced by viruses. The team is now pursuing research to determine if cells exposed to this form of fullerenes may be more susceptible to viral infections.

Ironically, the discovery could also lead to a novel treatment strategy for combating several debilitating diseases. In diseases like Parkinson's or Alzheimer's, nerve cells die or degenerate to a nonfunctional state. A mechanism to induce senescence in specific nerve cells could delay or eliminate onset of the diseases. Similarly, a disease like cancer, which spreads and thrives through unregulated replication of cancer cells, might be fought through induced senescence. This strategy could stop the cells from dividing and provide doctors with more time to kill the abnormal cells.

Because of the minute size of nanomaterials, the primary hazard associated with them has been potential inhalation—similar to the concern over asbestos exposure.

"Already, from a toxicological point of view, this research is useful because it shows that if you have the choice to use a tris- or a hexa-arrangement for an application involving buckyballs, the hexa-arrangement is probably the better choice," said Iyer. "These studies may provide guidance for new nanomaterial design and development."

These results were offshoots from a study (Shreve, Wang, and Iyer) funded to understand the interactions between buckyballs and biological membranes. Los Alamos National Laboratory has taken a proactive role by initiating a nanomaterial bioassessmnet program with the intention of keeping its nanomaterial workers safe while facilitating the discovery of high-function, low-bioimpact nanomaterials with the potential to benefit national security missions. In addition to Gao and Iyer, the LANL program includes Jennifer Hollingsworth, Yi Jiang, Jian Song, Paul

Welch, Hsing Lin Wang, Srinivas Iyer, and Gabriel Montaño.

Los Alamos National Laboratory researchers will continue to attempt to understand the potential effects of exposure to nanomaterials in much the same way that Los Alamos was a worldwide leader in understanding the effects of radiation during the Lab's early history. Los Alamos workers using nanomaterials will continue to follow protocols that provide the highest degree of protection from potential exposure.

Meantime, Los Alamos research into nanomaterials provides a cautionary tale for nanomaterial use, as well as early foundations for worker protection. Right now, there are no federal regulations for the use of nanomaterials. Disclosure of use by companies or individuals is voluntary. As nanomaterial use increases, understanding of their potential hazards should also increase.

Provided by Los Alamos National Laboratory