New Nanotube Findings Give Boost to Potential Biomedical Applications

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Carbon nanotubes have shown real promise as highly accurate vehicles for delivering antitumor agents into malignant cells, but a dearth of data about what happens to the tubes after they discharge their medical payloads has been a major stumbling block to progress. Now, two studies at the Center for Cancer Nanotechnology Excellence Focused on Therapy Response have revealed some reassuring answers after months of tracking the tiny tubes inside mice.

Studies in mice had already shown that most nanomaterials tend to accumulate in organs such as the liver and spleen, which was a concern because no one knew how long they could linger there. But fears that the tiny tubes might be piling up in vital organs can now be put to rest, according to research study leader Hongjie Dai, Ph.D., and colleagues at Stanford University and the Center for Cancer Nanotechnology Excellence Focused on Therapy Response.

Dr. Dai and his group found that carbon nanotubes leave the body primarily through the feces, some by way of the urine. “That's nice to know,” Dai said. “This now proves that they do get out of the system.”

Even more important, the data from this study, which were published in the Proceedings of the National Academy of Sciences of the United States of America, should also allay worries that the nanotubes, by simply remaining in the organs for a long time, would prove toxic to the mouse. “None of the mice died or showed any anomaly in the blood chemistry or in the main organs,” said Dr. Dai. “They appear very

healthy, and they are gaining weight just like normal mice. There's no obvious toxicity observed."

The key to this study was the Stanford investigators' use of Raman spectroscopy to monitor the location and concentration of carbon nanotubes in the mouse body. Carbon nanotubes yield strong and characteristic Raman signals. Previous detection methods that relied on attaching fluorescent labels or spectroscopic tags to the nanotubes had yielded unreliable results, largely because the stability of the carbon nanotube-fluorescent tag construct was too short to reveal the ultimate fate of the nanotubes.

Using Raman spectroscopy also enabled the investigators to monitor how long the nanotubes remained in circulation, a key pharmacological property. These pharmacokinetic data showed that coating carbon nanotubes with polyethylene glycol (PEG) produced nanotubes with circulating lifetimes of about 10 hours, which is suitable for drug and imaging agent delivery purposes.

In a second study conducted by Jin Miyawaki, Ph.D., Kyushu University, and colleagues in Japan found that pure single-walled carbon nanohorns, which are similar to carbon nanotubes, are also nontoxic over a 3-month period, even at excessive doses. In a study published in the journal ACS Nano, the investigators presented data showing that instilling carbon nanohorns directly into the lungs of rats produced no toxicity; oral doses were not toxic except at levels exceeding 2 grams of nanohorn per kilogram of body weight, far higher than any exposure expected under reasonable circumstances. Mutagenesis assays suggested that carbon nanohorns are not carcinogenic, either.

Dr. Dai and colleagues' work is detailed in the paper "Circulation and long-term fate of functionalized, biocompatible single-walled carbon nanotubes in mice probed by Raman spectroscopy." This work was

supported by the National Cancer Institute's (NCI) Alliance for Nanotechnology in Cancer. An abstract of this paper is available through PubMed.

The work by Dr. Miyawaki and colleagues appears in the paper "Toxicity of single-walled carbon nanohorns." Investigators from NEC Corporation and Meijo University also participated in this study. An abstract is available at the journal's Web site.

Source: National Cancer Institute