

Thursday, June 05, 2008

Testing the Toxicity of Nanomaterials

A fast screening method could help separate the good from the bad.

By Alexandra M. Goho

In light of mounting concerns regarding the potential toxicity of some nanomaterials, scientists have designed a rapid screening tool to help predict which ones are likely to be harmful. Hundreds of nanotechnology-based products are already on the market--in everything from sunscreens and cosmetics to paints and car bumpers--and many more are in the pipeline. However, studies assessing the safety of nanomaterials are limited. As a result, scientists and policy makers have been calling for more systematic reviews of the risks that these nanoscale materials might pose to human health.

Given the large diversity of engineered nanomaterials, which can vary in their chemical makeup, size, shape, and coating, assessing their toxicity has been a challenge. Studies in animals are expensive and time consuming, and although testing nanomaterials in cell cultures can yield useful information, different cell types can respond differently to the same nanomaterial.

"Nanomaterials are really complex, and if you just carry out one or two tests, you're going to miss something," says [Andrew Maynard \(http://www.wilsoncenter.org/index.cfm?topic_id=166192&fuseaction=topics.profile&person_id=166223\)](http://www.wilsoncenter.org/index.cfm?topic_id=166192&fuseaction=topics.profile&person_id=166223), chief science advisor to the Project on Emerging Nanotechnologies, at the Woodrow Wilson International Center for Scholars, in Washington, DC. What's more, results from experiments in cells often don't match those from animal studies.

To address these challenges, [Stanley Shaw \(http://csb.mgh.harvard.edu/about/shaw\)](http://csb.mgh.harvard.edu/about/shaw), a chemical biologist at Massachusetts General Hospital Center for Systems Biology, and his colleagues at the Broad Institute of Harvard and MIT designed a high-throughput screening method. Inspired by cancer studies in which scientists classify different types of cancer based on patterns of gene expression, Shaw and his colleagues sought to develop a tool that could screen large numbers of different nanomaterials and classify them based on their toxicity.

As a proof of concept, the researchers tested 50 different nanoparticles--mainly particles used for medical imaging. These included mostly iron-based particles, as well as several types of quantum dots. The particles also had various chemical coatings.

The researchers tested each of the nanoparticles in four different types of cells--immune cells from mice, two types of human blood-vessel cells, and human liver cells--and at four different dosages. To create the different combinations, a robotic system similar to that used for drug screening placed the nanoparticles inside tiny wells on a plate containing hundreds of separate wells. Each well contained one cell type. The screening system then detected changes in the cells' metabolism in response to the nanomaterial. Computer software analyzed the data, looking for relationships between the different particles.

"We're trying to get a sense of what these materials do in a broader variety of contexts," says Shaw. "It makes you less dependent on the idiosyncrasies of a particular cell type." By using multiple cell types in different contexts, the researchers were able to identify classes of particles that have similar effects on cells. The group then tested three of the nanoparticles in mice and showed that the effects that the particles produced in the animals matched the effects observed in the cells.

The new screening tool, described in the [Proceedings of the National Academy of Sciences \(http://www.pnas.org/\)](http://www.pnas.org/), could help narrow the list of nanomaterials that need to undergo animal testing. It could also help researchers who are developing different applications focus their efforts on nanomaterials that are less risky, says Shaw.

Although the researchers tested a small range of materials, there's no reason why this method could not be applied to other types of materials, says Maynard. "The real power of this technique will be shown if it can work for really diverse nanomaterials, including different types of carbon nanotubes and different structures of materials." Recent studies suggest that certain types of [carbon nanotubes behave like asbestos \(http://www.technologyreview.com/Nanotech/20815/\)](http://www.technologyreview.com/Nanotech/20815/). Therefore, it would be interesting to see whether other types of nanotubes are less hazardous, adds Shaw. And although his team used cells that imaging nanoparticles are likely to encounter when injected intravenously, other cell types could be used as well, he says. For instance, if the particle is something that is inhaled, then researchers could use different types of lung cells.

However, Maynard cautions that testing particles for their effect on lung cells could be tricky with this system. The imaging particles used in the study mix well with water and are designed to circulate in the body. Figuring out how to expose the cells to airborne particles might be difficult. Still, he says, the study offers a new paradigm for assessing the toxicity of nanomaterials.

"We need a lot more of these kinds of well-designed and carefully thought-through studies," says [John Balbus \(http://www.edf.org/page.cfm?tagID=894\)](http://www.edf.org/page.cfm?tagID=894), chief health scientist at the Environmental Defense Fund, based in New York. "I'm optimistic that once these [high-throughput] studies start accumulating, we will gain a real understanding of the biological effects of nanomaterials."

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Thursday, June 12, 2008

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