Nanotechnology

Defining nanomaterial interactions using biological systems

Stacey Harper

See-through fish embryos help to demonstrate the advantages of an integrated approach in testing how small particles can alter living organisms.

23 January 2009, SPIE Newsroom. DOI: 10.1117/2.1200901.1427

Materials between 1 and 100nm in size behave differently than larger materials of the same composition. They exhibit intriguing new properties that have the potential to radically improve human health through targeted drug delivery, bionic and prosthetic development, improved imaging and diagnostics systems, and novel therapeutics and regenerative medicines. According to the Project on Emerging Nanotechnologies,[1] 803 consumer products already exploit nanoscale materials in merchandise ranging from cosmetics to children's plush toys. But amid the excitement surrounding the revolutionary potential of nanotechnology, such as electronics integrated into organisms featured in the 1970s television show ‘The Six Million Dollar Man,’ how do we ensure these new materials do not inadvertently harm or even destroy parts of our world?

Several major challenges must be overcome to ensure the safety of new nanomaterials. First, studies on how and why nanoparticles interact with the environment and organisms are lacking. It is impossible to assess potential exposure risks without this information. Second, we do not currently have the tools to measure all nanomaterial characteristics that may be important. Moreover, we may not fully comprehend what we need to measure. Finally, with every element in the periodic table as fair game—and the countless ways in which materials can be mixed and matched—the sheer diversity of potential nanomaterials is mind-boggling.

At the Oregon Nanoscience and Microtechnologies Institute (ONAMI), a collaborative group of scientists are confronting concerns through the Safer Nanomaterials and Nanomanufacturing Initiative.[2] As part of an international research community, we are building well-characterized nanomaterial libraries, contributing to standards development, and establishing precise methods for measuring the potential toxic impacts of these new substances. Evaluation of nanomaterial-biological interactions will supply much needed data, improve public trust of nanotechnology, and provide industry with information to better direct the development of safer nanoproducts.[3–6]

Figure 1. Light micrographs of zebrafish development 8 (bottom right), 24 (bottom left), and 120h (top) after fertilization.

At Oregon State University, we have also developed new testing procedures that allow us to study integrated system responses in whole animals using small amounts of nanomaterial solutions.[4] We use a small aquarium fish, the zebrafish (*Danio rerio*), to rapidly test the biological response to many different types of nanomaterials. By testing libraries of nanomaterials that differ in only one aspect, size for example, we hope to identify features common to these substances that can cause adverse effects and, consequentially, identify material modifications that can minimize hazard.

Nanomaterials that interact with molecular signaling pathways, intercellular interactions, or normal cellular processes can be identified by evaluating the reaction of actively developing organisms to nanomaterial exposure. Zebrafish embryos develop externally and are optically transparent, so body malformations, behavioral abnormalities, and any other developmental disruptions, including death, can be seen without the need for invasive techniques. In our assay, zebrafish are exposed to nanomaterials 8h after they are fertilized when they are still just a ball of cells (see Figure 1). Within 24h, proper signaling between the cells ensures that the zebrafish have all of their body organs and start to resemble fish. After 120h, biological response to nanomaterial exposure can be measured at the molecular,[7] cellular,[8] and whole-animal level.[9]

After testing numerous types of nanomaterials, we report that extraordinarily small changes in the size, charge, and chemical makeup of nanomaterials can lead them to behave radically differently when they interact with living systems.[9] In carbon fullerenes and gold nanoparticles, for example, the biological response was more related to the electrical charge of the nanomaterial than to the size. On the other hand, the toxic potential of metal oxides was more dependent on chemical composition and shape than size or charge.

The method of entry into the animal system also changed how some materials behaved. Fluorescent nanomaterials made of polystyrene or cadmium selenide were distributed to different organs in zebrafish depending on how they were administered and the surface chemicals of the nanomaterials. In contrast, metal oxides that were injected into embryonic zebrafish showed similar responses to those absorbed through the skin.

Studies to date have demonstrated the utility of using the embryonic zebrafish model for investigating the biological activity and toxic potential of nanomaterials.[4,7–10] We have generated a wealth of information from screening-level assays and detailed investigations into nanomaterial-induced cellular death, inflammation, and oxidative stress, including the location of such stress in whole embryos.[7,8,11] We have also identified some key attributes that determine nanomaterial disposition in whole animals, such as core composition and surface chemistry, as well as the route of exposure.[9,10]

Data from our studies has been organized in a functional informatics system, the Nanomaterial-Biological Interactions Knowledgebase,[12] which will allow cross-species and cross-platform analysis in a metadata format. Furthermore, we have established collaborations across the nanobioinformatics community to facilitate the translation of data into knowledge and to broadly disseminate that information through a federated network in the future.

Understanding how and why certain nanomaterials interact with biology is critical for both the development of novel applications and to mitigate the undesirable impacts of nanotechnology. This information is required urgently so that industry can be seen to develop in an informed and secure manner. The good news from ONAMI researchers is that the vast majority of materials we have tested—over 160 nanomaterials to date—appear to be relatively safe. Our future research will investigate why some substances are less safe by taking advantage of rapid biological tests and libraries of nanomaterials to define design rules for acceptable use through iterative testing and redesign.

Our research efforts are partially supported by the Oregon State University Research Office, the Safer Nanomaterials and Nanomanufacturing Initiative of the ONAMI grant FA8650-05-1-5041, Environmental Protection Agency STAR grant RD-833320, and National Institute of Environmental Health Sciences grants ES03850 and ES07060.

Stacey Harper

Safer Nanomaterials and Nanomanufacturing Initiative
ONAMI
Corvallis, OR
http://www.onami.us/NanoNet/researchers.php?id=26

Stacey Harper, an active member of ONAMI, is an assistant professor of nanotoxicology in the Department of Environmental and Molecular Toxicology and the School of Chemical, Biological, and Environmental Engineering at Oregon State University.

References:

1. http://www.nanotechproject.org Project on Emerging Nanotechnologies. Accessed 6 January 2009.
2. http://www.greennano.org Safer Nanomaterials and Nanomanufacturing Initiative. Accessed 6 January 2009.
3. K. A. D. Guzman, M. R. Taylor, J. F. Banfield, Environmental risks of nanotechnology: national nanotechnology initiative funding, 2000–2004, *Env. Sci. Technol*. 40, no. 5, pp. 1401-1407, 2006. doi:10.1021/es0515708
4. S. L. Harper, J. A. Dahl, B. L. S. Maddux, R. L. Tanguay, J. E. Hutchison, Proactively designing nanomaterials to enhance performance and minimize hazard, *Int'l J. Nanotechnol*. 5, no. 1, pp. 124-142, 2008. doi:10.1504/IJNT.2008.016552
5. P. H. Hoet, I. Bruske-Hohlfeld, O. V. Salata, Nanoparticles: known and unknown health risks, *J. Nanobiotechnol*. 2, no. 1, pp. 12, 2004.
6. R. H. Hurt, M. Monthioux, A. Kane, Toxicology of carbon nanomaterials: status, trends, and perspectives on the special issue, *Carbon* 44, no. 6, pp. 1028-1033, 2006. doi:10.1016/j.carbon.2005.12.023
7. C. Y. Usenko, S. L. Harper, R. L. Tanguay, Exposure to fullerene C60 elicits an oxidative stress response in embryonic zebrafish, *Toxicol. Appl. Pharmacol.* 229, no. 1, pp. 44-55, 2008. doi:10.1016/j.taap.2007.12.030
8. C. Y. Usenko, S. L. Harper, R. L. Tanguay, In vivo evaluation of carbon fullerene toxicity using embryonic zebrafish, *Carbon* 45, no. 9, pp. 1891-1898, 2007. doi:10.1016/j.carbon.2007.04.021
9. S. L. Harper, C. Y. Usenko, J. Hutchison, B. L. S. Maddux, R. L. Tanguay, In vivo biodistribution and toxicity depends on nanomaterial composition, size, surface functionalization, and route of exposure, *J. Exp. Nanotechnol*. 3, no. 3, pp. 195-206, 2008. doi:10.1080/17458080802378953
10. S. L. Harper, B. L. S. Maddux, J. Hutchison, R. L. Tanguay, Biodistribution and toxicity of nanomaterials in vivo: effects of composition, size, surface functionalization, and route of exposure, *Nanotech* 2007, no. 2, pp. 666-669, 2007.
11. K. P. Vercruysse, S. L. Harper, D. M. Ivory, M. M. Whalen, K. S. Saili, R. L. Tanguay, Potential anti-inflammatory properties of biologically synthesized nanoparticles of gold or silver, *Nanotech* 2008, no. 2, pp. 501-504, 2008.
12. http://oregonstate.edu/nbi Nanomaterial-Biological Interactions Knowledgebase. Accessed 6 January 2009.

Comments:

Submit a comment (requires sign-on).