Probing the promise and perils of nanoparticles

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For all its promise, the prospect of using nanoparticles in biomedical applications and consumer products has raised concerns about possible harmful effects of the miniscule materials. Scientists at the University of Michigan are addressing those concerns by investigating how certain kinds of nanoparticles damage cell membranes—enough to cause cell death in some cases—and how the damage can be prevented.

"If you're inventing these sorts of materials, you need to be concerned about their impact," said Mark Banaszak Holl, a U-M professor of chemistry and of macromolecular science and engineering. "We're trying to do both: make important new materials and be excited about what can be done with them, but at the same time, understand what their potential downsides might be." Banaszak Holl and graduate students Pascale Leroueil and Seungpyo Hong will discuss their research at the 229th national meeting of the American Chemical Society in San Diego March 13-17.

In collaboration with other researchers at U-M's Center for Biologic Nanotechnology, Banaszak Holl's lab has been studying nanoparticles known as dendrimers, tiny spheres whose width is ten thousands times smaller than the thickness of a human hair. Dendrimers have shown promise for precisely delivering drugs to their targets inside the body, but high concentrations of these nanoparticles can be toxic. In earlier work, U-M researchers discovered that dendrimers punch nanoscale holes in cell membranes, making the membranes more permeable. At high enough concentrations, they can completely destroy the membranes,

killing cells in the process. But the damage can be prevented by engineering dendrimers in particular ways, such as modifying their surfaces to make them neutral instead of charged, the scientists found. And, added Banaszak Holl, "not only does engineering make them less harmful, but it also makes them better at what we want them to do. You don't lose anything; it's all a gain."

More recently, Leroueil studied other types of charged nanoparticles called polycationic polymers—already being used to deliver drugs and genes—to see if they behaved like dendrimers. "It turns out that they cause the same permeability and, in general, they cause membrane destruction as well," said Banaszak Holl. Neutral polymers, however, did not damage membranes.

Both Leroueil's work and the earlier research used model membranes to probe the effects of nanoparticles. Now, the research group is exploring their interactions with living cells.

"Just because we see hole formation in the model system doesn't mean that it really happens in the cell," said Banaszak Holl. But early results of experiments with living cells suggest that the same types of nanoparticles that punch holes in model membranes also damage membranes in living cells and make the membranes more permeable. Hong is now trying to learn more about the biological mechanisms involved. The usual explanation for how polycationic polymers and similar nanoparticles get into cells involves a process called polycation-mediated endocytosis. But Hong's experiments suggest that nanoscale hole formation may be at least as important in allowing materials to travel through membranes.

The work that Banaszak Holl, Hong and Leroueil will discuss is one of several major research programs under way in the U-M Center for Biologic Nanotechnology—a multi-disciplinary group includes researchers from the Medical School, the College of Engineering, and

the College of Literature, Science, and the Arts, and focuses on biomedical applications of nanomaterials. Collaborators on this work include James R. Baker, Jr., the Ruth Dow Doan Professor of Biologic Nanotechnology; Bradford Orr, professor of physics and director of the Applied Physics Program; research associate Jennifer Peters and research investigators Anna Bielinska and Istvan Majoros.

Source: University of Michigan