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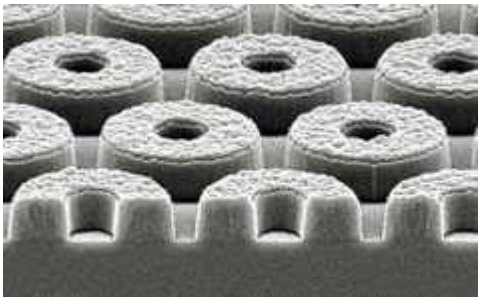
Scientists: Shape is key in nanomedicine



Nanoparticles are designed to prevent clumping, given an aerodynamic shape for use in inhalers, and engineered to align. Nanoparticles can be as large as a few dozen nanometers, and a nanometer is about one-five-hundred-thousandth the length of the period at the end of this sentence.

ZOE ELIZABETH BUCK, Staff Writer
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The emerging science of nanomedicine has researchers rushing to make smaller and smaller particles in an effort to infiltrate the microscopic world of cells, strands and proteins that keeps our body functioning.

But a team of researchers from the UNC-Chapel Hill Medical Center says that making the particles tiny is not all that's necessary. Instead, the key to interacting effectively with our bodies' microscopic systems is molding the drugs into the right shape, UNC-CH scientists reported this week in the online edition of the Proceedings of the National Academy of Science.

"Shape matters a lot in biology; we've known that for years," said Joseph DeSimone, a chemistry professor at UNC-CH who led the research team.

Nature figured out how to infiltrate our bodies ages ago. Rod-shaped bacteria evolved to sneak past our defenses and invade the nuclei of cells. So by imitating the shape of these bacteria, DeSimone's team figured, scientists could launch cancer-fighting therapies into the nuclei of cells.

"It's a very exciting possibility," DeSimone said, noting that the idea is intriguing to big pharmaceutical companies as well. DeSimone's company, Liquidia, which is based in Research Triangle Park, is working to bring the UNC-CH technology into manufacturing as soon as possible. He said Liquidia is already working with pharmaceutical companies to develop medical applications, and they hope to move into clinical trials within two years.

Vaccine development is at the top of DeSimone's list of potential applications.

Vaccines -- such as the new shot Gardasil, which protects against human papillomavirus -- often need to be administered multiple times to be effective because the body will typically clear out the drug before the proper immune response has time to develop. But the right-shaped vaccine nanoparticles could fool the body into letting the vaccine circulate in the bloodstream for longer, reducing the number of required doses.

In the Third World, where getting a shot could mean miles of travel on foot, condensing immunization regimens into a single dose could save lives.

Another promising application for custom-shape nanoparticles is chemotherapy, which can be devastating to a patient's body.

"There are a lot of chemotherapy drugs that are really toxic to the heart or the kidney," DeSimone said. "By controlling the size and shape, we should be able to de-target these organs."

To create the synthetic particles, DeSimone's team developed what are essentially a series of microscopic muffin pans made of clear plastic. DeSimone held up a sheet and pointed a laser beam at it. The pattern of light refracted on the tabletop revealed the tiny rod-shape molds of various lengths imprinted in the plastic -- synthetic versions of the rod-shape bacteria.

The UNC-CH team also manufactures molds that create worm shapes, red blood cell shapes, and doughnut shapes, among others.

DeSimone said additional applications of this technology are extensive.

Dangerous pollutants could be shaped in such a way that our bodies would be unable to absorb them. Patients could be transfused with synthetic red blood cells matching their specific blood type. Cargo particles could sneak RNA into cell nuclei to stop the production of proteins associated with cancer.

"This is important for environmental scientists, drug designers, oncologists, dermatologists, inhalation -- any number of fields," DeSimone said. "Nobody else is doing this. It's a huge unmet need."

Concerns

The ability to control how particles interact with our bodies comes at a critical point in the development of commercial nanotechnology. Critics fear that we don't know enough about the nanoparticles now being used in consumer products, including cosmetics, sunscreens and textiles, and that they could have adverse biological effects.

Terry Davies, a senior adviser for the Projects for Emerging Nanotechnologies in Washington, said the very promise of the tiny particles is also a danger.

"Their small size means that they can get to places that other things can't," said Davies. "Particles taken in a dietary supplement could end up in the brain or the placenta. We just don't know."

The small size could also change the properties of familiar materials, he added.

"Aluminum in ordinary amounts is something we use every day, but nano-sized aluminum is highly explosive," he said.

Davies' worries are supported by a study published in the May edition of Nature Nanotechnology. The study found that carbon nanotubes could have the same devastating effects on the lungs as asbestos.

"We've never had a broad technology that did not have some adverse consequences," Davies said. "Right now we just don't know enough to say what the consequences could be."

DeSimone said he recognizes the importance of understanding the consequences of letting nanoparticles loose in the human body, and has made it the focus of his research. By designing the nanoparticles carefully and precisely, he said, the UNC-CH team can understand and control what they interact with, and how.

"When you have the ability to precisely control both the size and shape of the particles, you can lay out the ground rules to understand exactly what roles they play," DeSimone said.

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