Rod-shaped nanoparticles, rather than spherical, appear more effective at adhering to cells

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Conventional treatments for diseases such as cancer can carry harmful side effects—and the primary reason is that such treatments are not targeted specifically to the cells of the body where they're needed. What if drugs for cancer, cardiovascular disease, and other diseases can be targeted specifically and only to cells that need the medicine, and leave normal tissues untouched?

A new study involving Sanford-Burnham Medical Research Institute's Erkki Ruoslahti, M.D., Ph.D., contributing to work by Samir Mitragotri, Ph.D., at the University of California, Santa Barbara, found that the shape of nanoparticles can enhance drug targeting. The study, published in *Proceedings of the National Academy of Sciences*, found that rod-shaped nanoparticles—or nanorods—as opposed to spherical nanoparticles, appear to adhere more effectively to the surface of endothelial cells that line the inside of blood vessels.

"While nanoparticle shape has been shown to impact cellular uptake, the latest study shows that specific tissues can be targeted by controlling the shape of nanoparticles. Keeping the material, volume, and the targeting antibody the same, a simple change in the shape of the nanoparticle enhances its ability to target specific tissues," said Mitragotri.

"The elongated particles are more effective," added Ruoslahti. "Presumably the reason is that if you have a spherical particle and it has

binding sites on it, the curvature of the sphere allows only so many of those binding sites to interact with membrane receptors on the surface of a cell."

In contrast, the elongated nanorods have a larger surface area that is in contact with the surface of the endothelial cells. More of the antibodies that coat the nanorod can therefore bind receptors on the surface of endothelial cells, and that leads to more effective cell adhesion and more effective drug delivery.

Testing targeted nanoparticles

Mitragotri's lab tested the efficacy of rod-shaped nanoparticles in synthesized networks of channels called "synthetic microvascular networks," or SMNs, that mimic conditions inside blood vessels. The nanoparticles were also tested in vivo in animal models, and separately in mathematical models.

The researchers also found that nanorods targeted to lung tissue in mice accumulated at a rate that was two-fold over nanospheres engineered with the same targeting antibody. Also, enhanced targeting of nanorods was seen in endothelial cells in the brain, which has historically been a challenging organ to target with drugs.

Nanoparticles already used in some cancer drugs

Nanoparticles have been studied as vessels to carry drugs through the body. Once they are engineered with antibodies that bind to specific receptors on the surface of targeted cells, these nanoparticles also can, in principle, become highly specific to the disease they are designed to treat.

Ruoslahti, a pioneer in the field of cell adhesion—how cells bind to their surroundings—has developed small chain molecules called peptides that can be used to target drugs to tumors and atherosclerotic plaques.

Promising results

"Greater specific attachment exhibited by rod-shaped particles offers several advantages in the field of drug delivery, particularly in the delivery of drugs such as chemotherapeutics, which are highly toxic and necessitate the use of targeted approaches," the authors wrote in their paper.

The studies demonstrate that nanorods with a high aspect ratio attach more effectively to targeted cells compared with spherical nanoparticles. The findings hold promise for the development of novel targeted therapies with fewer harmful side effects.

More information: Using shape effects to target antibody-coated nanoparticles to lung and brain endothelium, www.pnas.org/cgi/doi/10.1073/pnas.1308345110

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