Proceedings of the ASME 2008 Summer Bioengineering Conference (SBC2008)
June 25-29, Marriott Resort, Marco Island, Florida, USA

SBC2008-192418

SHAPE EFFECTS OF FILAMENTS VERSUS SPHERICAL PARTICLES IN FLOW AND DRUG DELIVERY

Dennis E. Discher

University of Pennsylvania

Interaction of spherical particles with cells and within animals has been studied extensively, but the effects of shape have received little attention. Here we use highly stable, block copolymer micelle assemblies known as filomicelles to compare the transport and trafficking of flexible filaments with spheres of similar chemistry.

The highly flexible worm-like micelles can be sonicated to generate kinetically stable spherical micelles composed of the same copolymer. The fission process exploits the finding that the cores of polycaprolactone are fluid, rather than glassy or crystalline, and core-loading of the hydrophobic anticancer drug delivery, paclitaxel (TAX) shows that the worm-like micelles load and solubilize twice as much drug as spherical micelles. In cytotoxicity tests that compare to the clinically prevalent solubilizer, Cremophor-EL, both micellar carriers are far less toxic, and both types of TAX-loaded micelles also show 5-fold greater anticancer activity on A549 human lung cancer cells. Based therefore on in vitro tests, PEO-PCL based worm-like filomicelles appear to be promising pharmaceutical nanocarriers with improved solubilization efficiency and comparable stability to spherical micelles, as well as better safety and efficacy in vitro compared to the prevalent Cremophor-EL TAX formulation.

In vivo tests prove even more interesting. In rodents, filomicelles persisted in the circulation up to one week after intravenous injection. This is at least ten times longer than spherical counterparts and is more persistent than any known synthetic nanoparticle. Under fluid flow conditions, spheres and short filomicelles are taken up by cells more readily than longer filaments because the latter are extended and pulled upon by the flow. Preliminary results further demonstrate that filomicelles can effectively deliver the anticancer drug paclitaxel and shrink human-derived tumours in mice. Although these findings show that long-circulating vehicles need not be nanospheres, they also lend insight into possible shape effects of natural filamentous viruses.