Nanomedicine system engineered to enhance therapeutic effects of injectable drugs

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In an article featured on the cover of the March issue of *Nature Nanotechnology,* Mauro Ferrari, Ph.D., of The University of Texas Health Science Center at Houston presented a proof-of-concept study on a new multistage delivery system (MDS) for imaging and therapeutic applications. This discovery could go a long way toward making injectable drugs more effective.

“This is next generation nanomedicine,” said Ferrari, the senior author. “Now, we’re engineering sophisticated nanostructures to elude the body’s natural defenses, locate tumors and other diseased cells, and release a payload of therapeutics, contrasting agents, or both over a controlled period. It’s the difference between riding a bicycle and a motorcycle.”

The study - “Mesoporous silicon particles as a multistage delivery system for imaging and therapeutic applications” - was conducted with researchers from The University of Texas M. D. Anderson Cancer Center and Rice University.

Nanotechnology offers new and powerful tools to design and to engineer novel drug delivery systems and to predict how they will work once inside the body. “The field of therapeutic nanoparticles began with tiny drug-encapsulated fat bubbles called liposomes, now commonly used in cancer clinics worldwide. Targeting molecules were later added to liposomes and other nanovectors to assist in directing them to diseased cells,” Ferrari said.

Getting intravenous agents to their intended targets is no easy task. It's estimated that approximately one of every 100,000 molecules of agent reaches its desired destination. Physicians are faced with the quandary of increasing the dosage, which can lead to side effects or reducing the dosage, which can limit the therapeutic benefits.

The multistage approach, according to Ferrari, is needed to circumvent the body's natural defenses or biobarriers, which act as obstacles to foreign objects injected in the blood stream. "To overcome this problem, we hypothesized and developed a multifunctional MDS comprising stage 1 mesoporous particles loaded with one or more types of stage 2 nanoparticles, which can in turn carry either active agents or higher-stage particles. We have demonstrated the loading, controlled release and simultaneous in vitro delivery of quantum-dots and carbon nanotubes to human vascular cells," the authors write.

In addition to circumventing biobarriers, Ferrari's team is working on the biochemical modifications required to efficiently deliver the MDS to a specific cancer lesion. "We have preliminary data that show that we can localize a payload of diagnostic agents, therapeutic agents or combination of both to target cells. Once on site, the molecules can be released in a controlled way and then the MDS will degrade in 24 to 48 hours, be transformed into orthosilicic acid and leave no trace in the body," Ferrari said.

Lead author Ennio Tasciotti, Ph.D., senior postdoctoral fellow in the NanoMedicine Research Center at the UT Health Science Center at Houston, said the proof-of-concept study would have not been possible without a multidisciplinary effort including contributions from mathematicians, physicists, engineers, chemists and biologists.

"We are dealing with objects that are in the billionth of a meter size range and to study such objects we used cutting edge technologies,"

Tasciotti said. “The characterization of the particles was performed using scanning electron and atomic force microscopy, dynamic light scattering, fluorimetry and flow cytometry. The interaction of particles with cells was studied using fluorescence and confocal microscopy as well as a series of assays intended to determine cell viability and internalization rate of the nanoparticles.”

The study is included in the March 2 Advance Online Publication on *Nature Nanotechnology’s* Web site.

Source: University of Texas