Cancer drug delivery research cuts time from days to hours

July 22 2008

Researchers at Case Western Reserve University have developed a technique that has the potential to deliver cancer-fighting drugs to diseased areas within hours, as opposed to the two days it currently takes for existing delivery systems.

Using laboratory mice, drug delivery time from injection to the cancer cells was reduced from two days to mere hours. Using this as a model for potential human use, cancer patients may someday soon receive the benefits of cancer-fighting drugs within hours of injection.

Findings are discussed in a paper, co-authored by Clemens Burda, associate professor of chemistry and director of the Center for Chemical Dynamics and Nanomaterials Research at Case Western Reserve University and graduate student Yu Cheng, appearing in the current edition of the Journal of the American Chemical Society.

The system uses gold nanoparticle vectors to deliver photodynamic therapy (PDT) drugs through the bloodstream to cancerous sites.

"Gold nanoparticles are usually not used for the PDT drug vector," said Cheng. "However, gold is chemically inert and nontoxic."

Photodynamic therapy utilizes light-sensitive drugs that, when exposed to light of a certain wavelength, will energize and burn away cancer cells.

Because exposure to light activates these drugs, PDT patients must keep

out of bright lights for days while the drugs make their way through the bloodstream to the cancer site. At that time, they are activated by a light focused on the specific area of the body.

"By shortening the waiting time from drug injection to activation, PDT patients are much less inconvenienced and tend to have a more normal lifestyle," said Burda.

Looks like a "Hairy Ball"

The drug delivery system uses a gold nanoparticle (Au NP) as its hub. Gold is non-toxic to the human body, and has a versatile surface chemistry, large surface-to-volume ratio and variable size and shape.

Each Au NP is coated with polyethylene glycol (PEG) ligands, giving it the appearance of a hairy ball, said Burda. These PEG molecules offer several advantages over other materials: they are soluble in fats and water, don't interact with proteins in the bloodstream and help protect the drug, keeping it safe and stable until delivery to the cancer site.

Between each PEG ligand, molecules of a photodynamic chemotherapy drug (Pc 4) are attached to the Au NP. The Pc 4 drug (a phthalocyanine compound) was developed at Case Western Reserve by Malcolm Kenney, professor of chemistry.

When the nanoparticle reaches the cancerous tissue the drug molecules are released and uploaded to the diseased area. Focused red light is used to energize the drug in the patient once it has been delivered to the tumor.

Burda says that a potential future research project would look at providing a time-release administration of the drug rather than a more all-at-once release. In the long term, Burda hopes to make the Au NP

delivery system applicable to a broad range of diseases.

The Au NP has a diameter of 5 nm. The addition of PEG ligands expands the total diameter to 32 nm, larger than some other nanoparticles currently in use, but still small enough to pass unencumbered through the bloodstream.

A single 1/4-mL injection holds approximately 100 million Au NPs, each carrying approximately 100 drug molecules.

Tail to Tumor in Two Minutes

In the laboratory of Baowei Fei, assistant professor of radiology and biomedical engineering at Case Western Reserve, these Au NPs have been used to treat mice with cancerous tumors. Once the Au NPs have been injected into the tail, the Pc 4 is uploading into the diseased area within minutes. The accelerated speed of drug administration in mice is due in part to the much more efficient dispersion of the NP delivered drug.

When tested on human cells called HeLa – a line of laboratory-grown human cells used in testing – most of the drug is uploaded within one hour.

Testing on human beings may not begin for some time. Commercialization will take even longer due to Food and Drug Administration (FDA) testing and approval. However, all of the components – Au Nps, PEG ligands and Pc 4 – have already received FDA approval.

What's Next

Burda says that as Au NP testing continues, short-term goals include minimizing the amount of material and drug load needed for effective interaction with cancer cells; optimizing potential targeting systems on the PEG ligands for faster, even more specific placement in diseased areas; and increasing the overall effectiveness of nanoparticle enhanced therapy.

"The system is very modular," says Burda. "We can change the size and shape of the Au core NPs and we can change the functionality of the PEG ligands. This should lead to optimization of the drug targeting and therapy. If our research is successful, other researchers might adapt this drug delivery system to other diseases and applications."

Source: Case Western Reserve University