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Nanoengineers mine tiny diamonds for drug delivery

EVANSTON, Ill. --- Northwestern University researchers have shown that nanodiamonds -- much like the carbon structure as that of a sparkling 14 karat diamond but on a much smaller scale -- are very effective at delivering chemotherapy drugs to cells without the negative effects associated with current drug delivery agents.

Their study, published online by the journal Nano Letters, is the first to demonstrate the use of nanodiamonds, a new class of nanomaterials, in biomedicine. In addition to delivering cancer drugs, the model could be used for other applications, such as fighting tuberculosis or viral infections, say the researchers.

Nanodiamonds promise to play a significant role in improving cancer treatment by limiting uncontrolled exposure of toxic drugs to the body. The research team reports that aggregated clusters of nanodiamonds were shown to be ideal for carrying a chemotherapy drug and shielding it from normal cells so as not to kill them, releasing the drug slowly only after it reached its cellular target.

Another advantage of the material, confirmed by a series of genetic studies also reported in the paper, is that nanodiamonds do not cause cell inflammation once the drug has been released and only bare diamonds are left. Materials currently used for drug delivery can cause inflammation, a serious complication that can predispose a patient to cancer, block the activity of cancer drugs and even promote tumor growth.

There are a lot of materials that can deliver drugs well, but we need to look at what happens after drug delivery,' said Dean Ho, assistant professor of biomedical engineering and mechanical engineering at Northwestern's McCormick School of Engineering and Applied Science, who led the research. How do cells react to an artificial material left in the body? Nanodiamonds are highly ordered structures, which cells like. If they didn't, cells would become inflamed. From a patient's perspective, this is very important. And that's why clinicians are interested in our work.

novel drug delivery systems, such as the one being developed by Dean and his team, hold great promise in cancer therapeutics,' said Steven Rosen, M.D., director of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University and Genevieve E. Teuton Professor of Medicine at Northwestern's Feinberg School of Medicine. We anticipate they will allow for more sophisticated means of targeting cancer cells while sparing healthy cells from a drug's toxicity.

To make the material effective, Ho and his colleagues manipulated single nanodiamonds, each only two nanometers in diameter, to form aggregated clusters of nanodiamonds, ranging from 50 to 100 nanometers in diameter. The drug, loaded onto the surface of the individual diamonds, is not active when the nanodiamonds are aggregated; it only becomes active when the cluster reaches its target, breaks apart and slowly releases the drug. (With a diameter of two to eight nanometers, hundreds of thousands of diamonds could fit onto the head of a pin.)

The nanodiamond cluster provides a powerful release in a localized place -- an effective but less toxic delivery method,' said co-author Eric Pierstorff, a molecular biologist and post-doctoral fellow in Ho's research group. Because of the large amount of available surface area, the clusters can carry a large amount of drug, nearly five times the amount of drug carried by conventional materials.

Liposomes and polymersomes, both spherical nanoparticles, currently are used for drug delivery. While effective, they are essentially hollow spheres loaded with an active drug ready to kill any cells, even healthy cells that are encountered as they travel to their target. Liposomes and polymersomes also are very large, about 100 times the size of nanodiamonds -- SUVs compared to the nimble nanodiamond clusters that can circulate throughout the body and penetrate cell membranes more easily.

Unlike many of the emerging nanoparticles, nanodiamonds are soluble in water, making them clinically important. Five years ago while working in Japan, I first encountered nanodiamonds and saw it was a very soluble material,' said materials scientist Houjin Huang, lead author of the paper and also a post-doctoral fellow in Ho's group. I thought nanodiamonds might be useful in electronics, but I didn't find any applications. Then I moved to Northwestern to join Dean and his team because they are capable of engineering a broad range of devices and materials that interface well with biological tissue. Here I e focused on using nanodiamonds for biomedical applications, where we're found success.

nanodiamonds are very special," said Huang. They are extremely stable, and you can do a lot of chemistry on the surface, to further functionalize them for targeting purposes. In addition to functionality, they also offer safety -- the first priority to consider for clinical purposes. It's very rare to have a nanomaterial that offers both.

It's about optimizing the advantages of a material,' said Ho, a member of the Lurie Cancer Center. Our team was the first to forge this area -- applying nanodiamonds to drug delivery. We're talked to a lot of clinicians and described nanodiamonds and what they can do. I ask, is that useful to you? They reply, Yes, by all means."

For their study, Ho and his team used living murine macrophage cells, human colorectal carcinoma cells and doxorubicin hydrochloride, a widely used chemotherapy drug. The drug was successfully loaded onto the nanodiamond clusters, which efficiently ferried the drug inside the cells. Once inside, the clusters broke up and slowly released the drug.

In the genetic studies, the researchers exposed cells to the bare nanodiamonds (no drug was present) and analyzed three genes associated with inflammation and one gene for apoptosis, or cell death, to see how the cells reacted to the foreign material. Looking into the circuitry of the cell, they found no toxicity or inflammation long term and a lack of cell death. In fact, the cells grew well in the presence of the nanodiamond material.

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In addition to Ho, Huang and Pierstorff, the other author of the paper, titled Active Nanodiamond Hydrogels for Chemotherapeutic Delivery, is Eiji Osawa, of the Nanocarbon Research Institute, Ltd., Chiba, Japan.