Promise of nanodiamonds for safer gene therapy

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Gene therapy holds promise in the treatment of a myriad of diseases, including cancer, heart disease and diabetes, among many others. However, developing a scalable system for delivering genes to cells both efficiently and safely has been challenging.

Now a team of Northwestern University researchers has introduced the power of nanodiamonds as a novel gene delivery technology that combines key properties in one approach: enhanced delivery efficiency along with outstanding biocompatibility.

"Finding a more efficient and biocompatible method for gene delivery than is currently available is a major challenge in medicine," said Dean Ho, who led the research. "By harnessing the innate advantages of nanodiamonds we now have demonstrated their promise for gene therapy."

Ho is an assistant professor of biomedical engineering and mechanical engineering in the McCormick School of Engineering and Applied Science and a member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

Ho and his research team engineered surface-modified nanodiamond particles that successfully and efficiently delivered DNA into mammalian cells. The delivery efficiency was 70 times greater than that of a conventional standard for gene delivery. The new hybrid material could impact many facets of nanomedicine.

The results are published online by the journal *ACS Nano*.

"A low molecular weight polymer called polyethyleneimine-800 (PEI800) currently is a commercial approach for DNA delivery," said Xue-Qing Zhang, a postdoctoral researcher in Ho's group and the paper's first author. "It has good biocompatibility but unfortunately is not very efficient at delivery. Forms of high molecular weight PEI have desirable high DNA delivery efficiencies, but they are very toxic to cells."

Multiple barriers confront conventional approaches, making it difficult to integrate both high-efficiency delivery and biocompatibility into one gene delivery system. But the Northwestern researchers were able to do just that by functionalizing the nanodiamond surface with PEI800.

The combination of PEI800 and nanodiamonds produced a 70 times enhancement in delivery efficiency over PEI800 alone, and the biocompatibility of PEI800 was preserved. The process is highly scalable, which holds promise for translational capability.

The researchers used a human cervical cancer cell line called HeLa to test the efficiency of gene delivery using the functionalized nanodiamonds. Glowing green cells confirmed the delivery and insertion into the cells of a "Green Fluorecent Protein (GFP)"-encoding DNA sequence. This served as a demonstrative model of how specific disease-fighting DNA strands could be delivered to cells. As a platform, the nanodiamond system can carry a broad array of DNA strands.

Regarding toxicity measurements, cellular viability assays showed that low doses of the toxic high-molecular PEI resulted in significant cell death, while doses of nanodiamond-PEI800 that were three times higher than that of the high-molecular weight PEI revealed a highly biocompatible complex.

Ho and his research team originally demonstrated the application of nanodiamonds for chemotherapeutic delivery and subsequently discovered that the nanodiamonds also are extremely effective at delivering therapeutic proteins. Their work further has shown that nanodiamonds can sustain delivery while enhancing their specificity as well.

Having demonstrated the safety of nanodiamonds and their applicability toward a variety of biological uses, Ho's team is pursuing aggressively the steps necessary to push them towards clinical relevance. Current studies are boosting the targeting capabilities of the nanodiamonds while also evaluating their pre-clinical efficiency.

"There's a long road ahead before the technology is ready for clinical use," Ho said, "but we are very pleased with the exciting properties and potential of the nanodiamond platform."

More information: The title of the *ACS Nano* paper is "Polymer-Functionalized Nanodiamond Platforms as Vehicles for Gene Delivery." In addition to Ho (senior author) and Zhang, other authors of the paper are Mark Chen, Robert Lam and Xiaoyang Xu, all from Northwestern, and Eiji Osawa, from the NanoCarbon Research Institute at Shinshu University, Nagano, Japan.

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