Pack 'Em In -- Gold Nanoparticles Improve Gene Regulation

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Investigators at Northwestern University have found that packing small interfering RNA (siRNA) molecules onto the surface of a gold nanoparticle can protect siRNAs from degradation and increase their ability to regulate genes involved in cancer. As a result of this discovery, cancer researchers have at their disposal a relatively straightforward method of delivering these potent gene-regulating agents into targeted cells.

Chad Mirkin, Ph.D., principal investigator of the Nanomaterials for Cancer Diagnostics and Therapeutics Northwestern University Center for Cancer Nanotechnology Excellence, led the research team that developed the methods needed to create these densely packed siRNA-nanoparticle conjugates. The investigators published their results in the *Journal of the American Chemical Society*.

One of the difficulties in working with potentially therapeutic siRNA molecules is that they are highly unstable, particularly in the presence of even trace levels of enzymes called nucleases that break down nucleic acids. To ensure that the surface of the gold nanoparticles was devoid of any nucleases, the investigators developed a harsh stripping method. To the researchers' surprise, this treatment had no effect on the optical or physical properties of the nanoparticles. The researchers also found that without this pretreatment, they were unable to add any RNA molecules to nanoparticles. With the pretreatment, the resulting 13-nanometer gold nanoparticles held an average of 34 siRNA molecules each.

Using confocal microscopy, the investigators were able to watch the nanoparticles enter cultured tumor cells. More importantly, the researchers also showed that once inside the cell, the siRNA was able to escape from the nanoparticle surface and inactivate its gene target. The amount of gene silencing achieved with the siRNA-nanoparticle construct was double that observed when cells were treated with siRNA alone. The investigators note that other experiments suggest that this boost in therapeutic efficacy arises because of improved siRNA stability when associated with gold nanoparticles.

This work, which was detailed in the paper “Gene regulation with polyvalent siRNA-nanoparticle conjugates,” was supported in part by the NCI Alliance for Nanotechnology in Cancer, a comprehensive initiative designed to accelerate the application of nanotechnology to the prevention, diagnosis, and treatment of cancer. An abstract is available at the journal’s Web site.

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