Nanovectors combine cancer imaging and therapy

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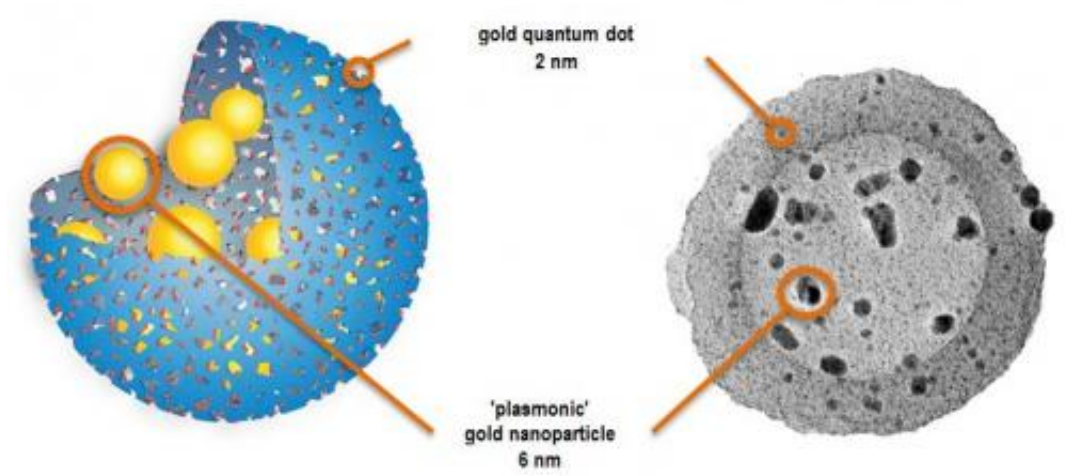

Diagram and electronic microscopy image of a “quantum rattle”: a porous silica shell (in blue in the diagram) is filled with gold dots, all on a nanometric scale. Gold is present in two forms: particles smaller than 2 nm (dots) in the pores of the shell, and larger particles (7 nm) in the central cavity. Credit: Mathew Hembury, Ciro Chiappini Glenna L. Drisko et al, with the authorization of *PNAS* These images are available at the CNRS photo library, phototheque@cnrs.fr

Researchers at Imperial College London and the Laboratoire de chimie de la matière condensée de Paris (CNRS/Collège de France/UPMC) have designed and developed hybrid gold-silica nanoparticles, which are turning out to be genuine therapeutic "Swiss Army knives". Tested in mice and on cultured human cells, they make it possible to combine two forms of tumor treatment and three imaging techniques. They notably

have a greater drug loading and delivery capacity than carriers currently on the market, which opens interesting perspectives for cancer research. The results were published in *PNAS* on February 4, 2015.

Developing a tool coupling three complementary imaging techniques (MRI, near-infrared fluorescence and a type of ultrasound imaging called "photoacoustic") with two forms of therapy (chemotherapy and photothermal therapy), all within a sphere measuring 150 nanometers in diameter, is the feat recently accomplished by an international team of chemists and biomedical engineering specialists. To achieve this, the researchers synthesized hybrid objects consisting of a mesoporous silica shell containing gold quantum dots.

Gold quantum dots are small nanoparticles (less than 2 nanometers) with unique properties (fluorescence, heat production, magnetism) that are very different from those of solid gold, or even larger gold nanoparticles. However, their lack of stability in aqueous solvents (they tend to aggregate to form larger particles) had prevented their use in biology and medicine until now. By "infusing" porous silica shells with gold precursors, researchers succeeded in creating gold quantum dots in the pores of the shell (which stabilizes them), as well as larger gold nanoparticles in the central cavity. Stable in aqueous solutions, this "quantum rattle" structure can penetrate into the center of cells without toxicity. It also preserves the optical and magnetic properties of gold quantum dots, while maximizing their drug storage capacity.

The incorporation of hydrophobic gold in the silica sphere helped to very significantly increase its storage capacity for doxorubicin, an anticancer agent often difficult to stabilize in this type of porous matrix. The scientists believe that the proportion of molecules that would reach their target would rocket from 5 to 95%, in comparison to (liposomal-type) drug carriers currently on the market. In addition to this capacity to carry drugs, they have potential in photothermic therapy. In fact, when

they are excited by an infrared laser, the particles containing the gold quantum dots emit infrared fluorescence, but also enough heat—up to 51°C—to kill cancerous cells. This made it possible to reduce tumor mass in mice by 55% after a single treatment.

The production of heat can also be used for imaging purposes, as it causes a temporary dilation of gold quantum dots, which produces ultrasound waves that can be detected, as in ultrasound imaging. Moreover, the fluorescence emitted by the laser-excited particles travels through tissue (which does not absorb infrared in this wavelength), and can therefore be measured in a non-invasive manner. Finally, for sizes smaller than 2 nanometers, gold becomes magnetic. It is hence possible to use quantum rattles as a contrast agent for magnetic resonance imaging (MRI). These three imaging methods (near-infrared fluorescence, photoacoustic imaging and MRI) make it possible to observe the tumor in complementary ways, with very high spatial and temporal resolution.

The researchers are now exploring how to optimize these nanovectors. They would like to "functionalize" their surface with markers so that they can identify and specifically target cancerous cells. Finally, they hope to be able to reduce the size of the gold particles in the central cavity, in order to make the carrier entirely biodegradable.

More information: "Gold-Silica Quantum Rattles for Multimodal Imaging and Therapy," Mathew Hembury, Ciro Chiappini, Sergio Bertazzo, Tammy Kalbere, Glenna L. Drisko, Olumide Ogunlade, Simon Walker-Samuel, Katla Sai Krishna, Coline Jumeaux, Paul Beard, Challa S.S.R. Kumar, Alexandra Porter, Mark F. Lythgoee, Cédric Boissière, Clément Sanchez & Molly M. Stevens. *PNAS*, February 4, 2015. DOI: 10.1073/pnas.1419622112

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