'Smart' nanoprobes light up disease

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Quantum dots programmed to glow in presence of enzyme activity

Researchers from Rice University's Center for Biological and Environmental Nanotechnology (CBEN) have developed a "smart" beacon hundreds of times smaller than a human cell that is programmed to light up only when activated by specific proteases. Altered expression of particular proteases is a common hallmark of cancer, atherosclerosis, and many other diseases.

In the September issue of the journal *Biochemical and Biophysical Research Communications*, lead authors Jennifer West, the Isabel C. Cameron Professor of Bioengineering and director of CBEN's biological research program, and Rebekah Drezek, the Stanley C. Moore Assistant Professor of Bioengineering and assistant professor of electrical and computer engineering, describe development of a new nanoprobe for visualization of proteolytic activity in vivo.

"The idea is to develop a 'smart' nanostructure that is dark in its original state but lights up very brightly in the presence of enzymatic activity associated with a particular disease process," said West. "Other groups have used targeted nanostructures including quantum dots for molecular imaging, but they have never been able to adequately solve the problem of clearly distinguishing between the 'cancer is here' signal and the background light which arises from nanostructures not specifically bound to their molecular targets."

Rice's technology solves this longstanding problem by using emissive

nanoparticles called quantum dots that give off light in the near-infrared (NIR), a rare portion of the spectrum that has no background component in biomedical imaging. Near-infrared light also passes harmlessly through skin, muscle and cartilage, so the new probes could alert doctors to tumors and other diseases sites deep in the body without the need for a biopsy or invasive surgery.

The probe's design makes use of a technique called "quenching" that involves tethering a gold nanoparticle to the quantum dot to inhibit luminescence. The tether, a peptide sequence measuring only a few nanometers, or billionths of a meter, holds the gold close enough to prevent the quantum dot from giving off its light.

In their test system, the Rice team used a peptide tether that is cleaved by the enzyme collagenase. The researchers first showed that luminescence of the quantum dots was cut by more than 70 percent when they were attached to the gold particles. They remained dark until the nanostructures were exposed to collagenase after which the luminescence steadily returned.

Ultimately, the researchers hope to pair a series of quantum dots, each with a unique NIR optical signature, to an index of linker proteases.

"There is currently a critical need for methods to simultaneously image the activity of multiple proteases in vivo," said Drezek. "This is important not only for early detection of several diseases, but perhaps more significantly, in understanding and monitoring the efficacy of therapeutic interventions, including the growing class of drugs that act as protease inhibitors. What is particularly powerful about the protease imaging probes described in this study is the combination of the contrast enhancement achievable through an activateable probe with the imaging advantages provided by the brightness, photostability, and tunability of quantum dots."

Source: Rice University