Quantum Dots Reach Clinical Lab

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Bioconjugated quantum dots – luminescent nanoparticles linked to biological molecules – have shown great promise as tools for disease diagnosis and treatment, but their medical use has been limited by the lack of specific instructions for clinicians. Now, new clinical protocols detailing how to prepare, process and quantify these tiny particles will arm laboratory physicians with the information they need to track biomarkers in cells and tissues.

The new research guidelines and results were published in the May 3 issue of Nature Protocols. Using prostate cancer specimens, researchers at Emory University and the Georgia Institute of Technology have confirmed that bioconjugated quantum dots are effective in simultaneously identifying multiple molecular biomarkers in cancer tissue. The technology is a variation of immunohistochemistry, the laboratory staining process commonly used by pathologists to identify proteins in a tissue section from a cancer patient.

The scientists developed detailed protocols for using the technology, including antibody conjugation, preparation of tissue specimens, multicolor quantum staining, image processing and biomarker quantification. They also have developed bioinformatics and software tools for automated feature extraction and biomarker quantification.

The Emory-Georgia Tech team was led by Shuming Nie, a distinguished professor in the Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University, and by May Dongmei Wang, assistant professor in the Coulter Department and

Georgia Cancer Coalition Distinguished Scholar. Key faculty investigators at Emory also include Leland Chung, professor of urology, Ruth O'Regan, MD, associate professor of hematology and oncology and Georgia Cancer Coalition Distinguished Scholar, John Petros, MD, professor of urology and Jonathan Simons, MD, professor of biomedical engineering, hematology and oncology.

"I would like to thank all our investigators for their contributions to this tour de force project, which took more than two years to complete involving 12 investigators in five academic departments," says Nie.

"We have now resolved a major bottleneck in the use of multicolor quantum dot probes for cancer immunohistostaining," says Nie. "Quantum dot probes used in tissue diagnosis are considered to be one of the most important and clinically relevant applications for cancer technology in the near term. We believe that this technology will be ultimately useful in correlating a panel of biomarkers with disease progression and therapeutic response."

"Personalized medicine is poised to transform healthcare over the next several decades," says Wang, director of the bioinformatics and biocomputing core in the Emory-Georgia Tech Nanotechnology Center (CCNE). "New diagnostic and prognostic tools will increase our ability to predict the likely outcomes of drug therapy. Essential to this endeavor is the use of bioinformatics and systems biology to link each individual's molecule profile with disease diagnosis and treatment decisions."

Nanoparticles, which can be as tiny as 100,000 times smaller than the width of a human hair, have special "quantum" properties, including changes in color according to minute differences in size. Bioconjugated quantum dots are collections of different sized nanoparticles embedded in tiny beads made of polymer material. In a process called "multiplexing," they can be finely tuned to a myriad of lumninescent colors that can tag a multitude of different protein biomarkers or genetic sequences in cells or tissues.

Because the quantum dots have a cadmium core, scientists have been concerned about their potential toxicity if infused into the bloodstream of patients. Using the dots in the laboratory to detect biomarkers in cells and tissues outside the human body eliminates this concern. Quantum dots also have advantages over traditional dyes and stains often used in imaging. They are more brightly fluorescent, they resist photo bleaching and they can emit a broad range of colors simultaneously.

These properties make bioconjugated quantum dots highly promising for improving the sensitivity of disease diagnosis in the laboratory, and they are particularly important for detecting and analyzing cancer biomarkers that are present at low concentrations or in small numbers of cells. Biomarkers include altered or mutant genes, RNA, proteins, lipids, carbohydrates and small metabolite molecules.

"Aggressive cancer behaviors also could be better understood and rapidly predicted using these kinds of biomarkers," says Nie. "By defining the interrelationships between biomarkers, it could be possible to diagnose and determine cancer prognosis based on a patient's molecular profile, leading to personalized and predictive medicine."

The Emory and Georgia Tech scientists also believe the bioconjugated quantum dots will be useful in detection of bioterrorism agents such as anthrax, plague, botulism and viral hemorrhagic fevers.

Wang's group in the Wallace H. Coulter Department of Biomedical Engineering and the School of Electrical and Computer Engineering at Georgia Tech has developed a number of software tools for cancer nanotechnology, leading a major effort in "bio-nano-info" integration for personalized medicine.

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