New Imaging Techniques Based on Metallic Nanoclusters

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An interdisciplinary team of researchers from the Georgia Institute of Technology and Emory University has won a four-year $2.4 million grant from the National Institutes of Health (NIH) to develop novel in-vivo cellular imaging techniques based on quantum dots made of silver or gold atoms.

Image: Fluorescence is shown from solutions of small gold nanoclusters dissolved in water. These nanoclusters behave like multielectron artificial atoms, emitting at discrete wavelengths in the visible and infrared with the wavelength increasing with the size of the cluster. Shown from left to right are emission from solutions of Au_5, Au_8, and Au_{13} clusters.

The grant, from the National Institute of General Medical Sciences, is one of nine awarded nationally to launch exploratory centers for the development of new high resolution cellular imaging techniques. Part of the NIH "Roadmap for Medical Research" initiative, it is one of two such centers to be won by collaborative research teams from Georgia Tech and Emory University.

"We will be developing a toolbox of methods for high-resolution in-vivo intracellular imaging with the goal of producing dramatic improvements in sensitivity and signal-to-noise over what is available now," explained Robert Dickson, associate professor in the Georgia Tech School of Chemistry and Biochemistry and principal investigator for the new center. "These more sensitive imaging methods will allow researchers to follow the activity of a single protein molecule, providing a more detailed understanding of dynamic processes in living biological systems."

The work will build on the highly-fluorescent, water-soluble quantum dots developed since 2002 by Dickson's research team. Made up of small numbers of gold or silver atoms, the nanoclusters are strongly fluorescent and have narrow excitation and emission spectra. Less than a nanometer in diameter, they are also smaller than the semiconductor-based quantum dots now commonly used as cellular probes.

In the August 13, 2004 issue of the journal Physical Review Letters, Dickson's research team reported on strongly-fluorescing quantum dots made up of 5, 8, 13, 23 or 31 gold atoms. Each cluster size emits at a different wavelength, producing ultraviolet, blue, green, red and infrared fluorescence, with the smaller structures being more efficient emitters.

To these clusters, the Emory-Georgia Tech research team will create novel, modular dendrimer scaffolds enabling specific recognition and binding to biological molecules of interest within cells. They will also develop techniques for getting the probes into living cells.

Dickson believes the metallic quantum dots will complement existing probe technology based on semiconductor quantum dots and organic dyes. Beyond their small size and strong fluorescence, the narrow excitation spectrum of the metallic quantum dots should make them particularly useful for fluorescence resonance energy transfer (FRET) techniques used to measure the proximity of different molecules.

Because of their larger size and broad excitation range, semiconductor quantum dots cannot be effectively used in FRET studies.

Beyond the development of new probe technologies, the center will also focus on commercialization activities, working with companies to make the new probes available to the scientific community.

"Our goal is to increase the sensitivity of these probes such that we can follow the dynamics of an individual protein, potentially watch trafficking of individual proteins inside a cell. We hope to eventually watch protein-protein interactions, and with energy transfer from two different species, look at their association and potentially even follow signal transduction cascades inside living systems," Dickson said. "We have already received significant interest from companies wanting to tap this capability."

The metal cluster probes take advantage of the unique properties of nanometer-scale structures, Dickson notes.

"We are really taking the concepts of nanoscience and applying them to biology, creating applications in nanomedicine and nanobiotechnology," he said. "When you make them small enough, metal clusters fluoresce with outstanding optical properties. Taking those properties and making the clusters biocompatible will allow us to improve upon existing probe technologies."

Yih-Ling Tzeng, assistant professor in the Division of Infectious Diseases at Emory University's School of Medicine, said the new probes may find uses in her work with infectious diseases.

"This is an exciting collaboration and a great opportunity to broaden my research program by developing generally useful tools for high sensitivity biomedical imaging," she said. "In addition, the strong collaborative effort between Emory and Georgia Tech continues to be a model for successful interdisciplinary endeavors."

Charles Liotta, vice provost for research and graduate studies at Georgia

Tech, believes the two NIH roadmap grants received by Georgia Tech and Emory University researchers recognize a significant research strength at the two Atlanta institutions.

“Receipt of this new award demonstrates the strength of the collaboration between Emory University and Georgia Tech,” he said. “This interdisciplinary research at the intersection of nanotechnology and biology will lead to important advances in the field of cellular probes.”

Beyond Dickson and Tzeng, the research team includes Uwe Bunz, Donald Doyle, Christoph Fahrni, and Marcus Weck, all from Georgia Tech.

The other center, led by Shuming Nie – an associate professor in the Wallace Coulter Department of Biomedical Engineering operated jointly by Emory University and Georgia Tech – focuses on bioaffinity nanoparticle probes for molecular and cellular imaging. The technology uses on core-shell semiconductor quantum dots.

Source: Georgia Institute of Technology