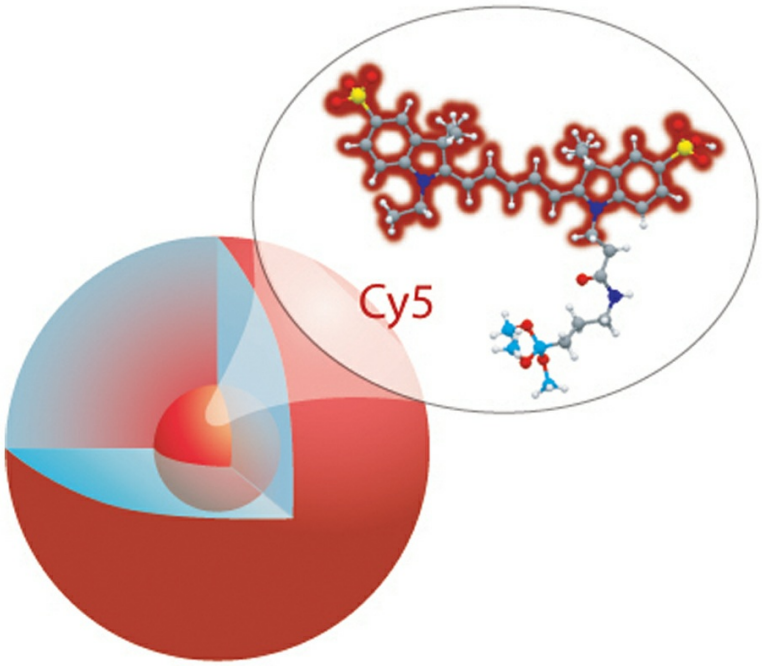
What if a tumor could be lit up by a fluorescent imaging agent, or probe, that is safe, biologically stable, and bright enough for a physician to detect it noninvasively, maybe even with a handheld optical device?

According to Michelle S. Bradbury , an Memorial Sloan Kettering Cancer Center clinician-scientist who specializes in molecular imaging and neuroradiology, such fluorescent probes would have wide applications in detecting and treating cancer. For instance, they might help surgeons to define tumor margins during surgery or detect cancer spread. “It sounds simple conceptually,” she said, “but no optical probes that meet all the necessary requirements for use in the clinic are yet available.” Currently quantum dots, a type of nanoparticle, are used extensively as probes in the laboratory, but their toxicity makes them unsuitable for medical purposes.

Recent studies in mice led by Dr. Bradbury showed that a new generation of nanoparticles called “C dots” might be used for imaging tumors in patients. About one-thousandth the size of a red blood cell, C dots are small enough to be transported in the blood across the body’s tissues and excreted efficiently through the urine. “C dots have been developed and optimized for biomedical applications in the laboratory of my collaborator, Uli Wiesner [a professor of materials science and engineering at Cornell University],” explained Dr. Bradbury. “Their unique properties and safety afford us the opportunity to reach a new level of tumor diagnosis and treatment.” The findings were published in the January issue of *Nano Letters*. [PubMed Abstract]

Each C dot is a shell of silica encapsulating molecules that emit long-wavelength light, which easily penetrates tissues. The shell enhances the brightness and stability of these molecules, and is also what makes the C dot biologically safe. “Silica is found in some of the oldest single-cell organisms on this planet,” said Dr. Wiesner. “Had silica not been a biocompatible, nontoxic material, evolution would have eliminated it a long time ago.” To further optimize C dots for medical applications, his team coated them with a polymer that prevents them from clumping or being recognized by the body as a foreign substance.



Graphic representation of a C dot, a nanoparticle made of silica with fluorescent molecules (Cy5) at its core. C dots could offer a safe way to light up tumors and will be explored for medical imaging applications at Memorial Sloan Kettering.

"To the immune system, the particles look like tiny water droplets, so they are free to circulate in the blood until they reach their destination," explained Oula Penate-Medina, a nanochemist at Memorial Sloan Kettering. A co-author of the study, he labeled the C-dot surface with radioactive molecules. The C dots could then be tracked using two different imaging technologies as they traveled through a mouse's body: by observing their fluorescence emission using an optical scanner, and by detecting their radioactive signal through positron emission tomography (PET) imaging. "The dual imaging modality allows us to validate what we are observing using fluorescence imaging," Dr. Bradbury explained.

To test if C dots could be used for tumor targeting, the researchers have tagged them with a protein fragment called RGD, which binds to a protein abundant on cells lining tumor blood vessels. When this probe is injected into a mouse model of human melanoma , it binds to tumors within an hour and can be retained there for several days. In the future, C dots could be tailored to bind specifically to certain tumor types, or even to an individual patient's tumor. They could then be used to deliver drugs or radioactive molecules to tumors.

"This project has launched a multidisciplinary effort here at Memorial Sloan Kettering. We are grateful to Hedvig Hricak [Chair of the Department of Radiology] for promoting initiatives in applied nanotechnology research and to Steven Larson [Chief of Memorial Sloan Kettering's Nuclear Medicine Service] for his expertise in developing radiolabeled probes for use in patients," said Dr. Bradbury. "We are also working with Snehal Patel , a head and neck surgeon, and Ricardo Toledo-Crow, manager of our Research Engineering Laboratory, to bring C dots into the clinic and to build optical instrumentation."

"Our ultimate goal is to develop C dots for a range of oncology applications, such as minimally invasive surgical procedures or image-guided patient assessments," Dr. Bradbury added. "Memorial Sloan Kettering is an ideal place for this effort. Not only do we have all the resources and knowledge it takes to bring a discovery from the laboratory into the clinic, we also have the in-house competence for developing new instrumentation. With all these assets, we are likely to see a new generation of medical imaging tools in our clinics within the next five years."

Other investigators involved in the study were Andrew A. Burns and Erik Herz of Cornell University; Miriam Benezra and Jelena Vider of Memorial Sloan Kettering; and researchers at Hybrid Silica Technologies, Inc.

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