Researchers have developed a new generation of microscopic particles for molecular imaging, constituting one of the first promising nanoparticle platforms that may be readily adapted for tumor targeting and treatment in the clinic.

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> Study's Senior Author Michelle Bradbury, MD, PhD

According to the investigators at Memorial Sloan Kettering Cancer Center (MSKCC) and Cornell University, these particles are biologically safe, stable, and small enough to be easily transported across the body’s structures and efficiently excreted through the urine. It is the first time that all of these properties have been successfully engineered on a single-particle platform, called “C dots,” in order to optimize the

biological behavior and imaging properties of nanoparticles for use in a wide array of biomedical and life science applications. The work will be published in the January 2009 issue of *Nano Letters.*

“Highly sensitive and specific probes and molecular imaging strategies are critical to ensure the earliest possible detection of a tumor and timely response to treatment,” said the study’s senior author, Michelle Bradbury , MD/PhD, a physician-scientist specializing in molecular imaging and neuroradiology at MSKCC. “Our findings may now be translated to the investigation of tumor targeting and treatment in the clinic, with the goal of ultimately helping physicians to better tailor treatment to a patient’s individual tumor.”

Imaging experiments in mice conducted at MSKCC showed that this new particle platform, or “probe,” can be molecularly customized to target surface receptors or other molecules that are expressed on tumor surfaces or even within tumors, and then imaged to evaluate various biological properties of the tumor, including the extent of a tumor’s blood vessels, cell death, treatment response, and invasive or metastatic spread to lymph nodes and distant organs.

“Importantly, the ability to define patients that express certain types of molecules on their tumor surfaces will serve as an initial step towards improving treatment management and individualizing medical care,” said Dr. Bradbury.

Many of the contrast agents or probes currently used in medical imaging (such as GdDTPA for magnetic resonance imaging) are not specific to any particular tumor type. According to the study’s authors, the information gained from imaging tumors targeted with C dots may ultimately assist physicians in defining tumor borders for surgery, determining the extent of a tumor’s spread, mapping lymph node disease, and improving real-time visualization of small vascular beds, anatomic channels, and neural structures during surgery.

Created at Cornell University and modified at MSKCC, C dots have been optimized for use in optical and PET imaging and can be tailored to any particle size without adversely impacting its fluorescent properties. For the first time, researchers were able to make them small enough (in the 5 nanometer range) to remain in the bloodstream for a reasonable amount of time and be efficiently excreted by the kidneys. Researchers were also able to increase their brightness by 300 percent, enabling cancer cells to be tracked for longer periods of time in the body.

Their inner “core” is encapsulated in a shell of silica, a nontoxic element naturally found in fruits, grains, and vegetables, and contains optical dyes that emit light at longer wavelengths, resulting in an overall improvement in image quality compared to dyes that are commercially available.

Investigators also found that adding another type of molecular coating, called pegylation, protected C dots from being recognized by the body as foreign substances, thereby effectively extending the circulation time

to improve tumor-targeting capabilities.

By comparison, first generation nanoparticles, called quantum dots (Q dots), offer excellent brightness and provide good contrast during imaging, but their clinical potential is limited by their large size and risk of toxicity.

The authors conclude that while the next generation of nanoparticles holds much clinical promise, more work needs to be done before C dots are approved for use in humans.

The following investigators contributed to this collaborative work, which was supported by a grant from the Clinical and Translation Science Center at Weill Cornell Medical College and the Cornell Nanobiotechnology Center: Andrew A. Burns (lead author), Erik Herz and Ulrich Wiesner of Cornell University; Jelena Vider, Oula Penate-Medina, and Steven M. Larson of MSKCC; and Hooisweng Ow and Martin Baumgart of Hybrid Silica Technologies.