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Thinking Big with the Very Small: Focus of New Cancer Nanotechnology Center at UCSD

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Rex Graham

In a new national effort to fight cancer with "nanoscale" devices that find and destroy tumor cells while leaving healthy tissue unharmed, the National Cancer Institute (NCI) today awarded the University of California, San Diego $3.9 million in the first year of a five-year $20 million initiative to establish a Center for Cancer Nanotechnology Excellence (CCNE). The UCSD center will use nanotechnology to develop anti-cancer therapies that directly target tumor cells; more accurate and faster diagnostics; and ways to track down cancer cells that survive therapy.

The NCI named a total of seven university centers to develop clinically useful nanotechnology "platforms" to treat, understand, and monitor cancer. The UCSD team includes engineers, chemists, and biologists who will collaborate with physicians at the Rebecca and John Moores UCSD Cancer Center, and colleagues at the Burnham Institute for Medical Research and University of California campuses at Irvine, Riverside, and Santa Barbara, to develop nanotechnology devices so small that they are measured on a molecular scale.

"This Center for Excellence will bring the best minds in engineering, basic and translational research, and clinical care together to apply the power of nanotechnology to the improved treatment of cancer, the second leading cause of death in our society today," said UCSD Chancellor Marye Anne Fox. "Such an effort represents the tremendous value of collaboration, not only across disciplines, but also among institutions, resulting in important innovations that benefit our society."

The focus of the UCSD team will be to develop "mother ships," smart nanoplatforms capable of homing in on tumors and delivering payloads of smaller particles to perform various tasks in the tumors. About the size of a red blood cell, these micron-sized nanoporous mother ships would move through the body, target specific tumor cells or the blood vessels that feed them. After arriving at their destinations, mother ships would release their payload nanoparticles, which could be designed to help image tumors, enter cells and perform measurements, and deliver therapies. Chemists at UCSD together with materials scientists at the University of California, Santa Barbara nanofabrication facility will synthesize nanoparticles that will be coated with "biolinkers," molecules developed at the Burnham Institute to make the particles attach to specific types of tumor cells.

"Nanotechnology allows us to much more specifically and accurately deliver an array of promising new treatments to the exact positions in the body where they are needed," said Sadik Esener, professor of electrical and computer engineering at the UCSD Jacobs School of Engineering and the principal investigator of the UCSD center. "Nanotechnology will also enable doctors to get more rapid noninvasive feedback on the effectiveness of treatment, and when biopsies are needed, these approaches will require much smaller tissue samples for analysis in the laboratory."

The UCSD Center for Excellence will focus on non-invasive treatments for leukemia and breast cancer to take advantage of the expertise in studying those diseases by scientists at the Moores UCSD Cancer Center. "Cancer nanotechnology is one of the most exciting and promising areas of cancer research today. This science of the very small may translate to very big changes for cancer patients," said Dr. Dennis Carson, director of the Moores UCSD Cancer Center. "We are developing powerful drugs and other chemotherapeutic agents that are

more and more effective when they reach their target. But we need engineers and materials scientists to build the nanodevices that can deliver these agents to the target. At the cancer center, we are embracing nanotechnology as part of our focus on translating scientific advances into new options for patients."

The UCSD-based center will focus on six projects, each to develop new technologies that when integrated together will create platforms for more powerful and selective cancer therapy. The technologies will be evaluated in animal models. In order to help identify inventions with commercial potential, representatives from General Electric Company, Honeywell, Irvine Sensors Corporation, Nanogen, and Enterprise Partners Venture Capital will serve on a committee to regularly evaluate the progress of the research at UCSD.

Roger Tsien, a UCSD professor of pharmacology and biochemistry, will lead a team that includes Fox in the development of very small nanoparticles that move unimpeded through the blood and healthy tissues and organs. However, when the nanoparticles encounter tumor cells, tumor-associated enzymes will trigger them to clump together, trapping the nanoparticles in the tumor but not in healthy tissue. Clumping is expected to enhance the ability of the nanoparticles to capture energy from external radiation to help produce images or kill the tumors selectively and noninvasively.

A team led by Erkki Ruoslahti, a distinguished professor at the Burnham Institute and an expert in directing nanoparticles to desired sites in the body, will design nanoparticles that can go inside a cancer cell, extract themselves, and report what they found.

Esener and Michael Sailor, a professor of chemistry and biochemistry at UCSD, will use the results of Tsien's and Ruoslahti's nanoparticle experiments to create porous "mother ships" that would home in on tumors and release their nanoparticle payloads. Rather than immediately dispatching tumors, the mother ships may be used to identify and image tumors, take measurements, and then kill the tumors by releasing anti-cancer drugs on cue.

A project led by Carson and Dr. Thomas Kipps, deputy director of the Moores UCSD Cancer Center, will study nanoparticles designed to monitor genetic changes occurring within cancer cells over time. The particles will be programmed to deliver nanodiagnostic tools at precisely defined points in time during tumor progression.

Recurring metastatic disease accounts for the majority of cancer deaths. David Cheresh, a pathology professor at the Moores UCSD Cancer Center, will focus on eradicating tumor cells that survive anti-cancer therapy with a "smart nanoplatform." Cheresh plans to experiment with programmable particles whose target-binding properties can be finely tuned to hunt and kill residual disease.

A team at UCSD consisting of Andrew Kummel, a professor of chemistry and biochemistry, Michael H. Heller, a professor of bioengineering, and Kim Prather, a professor of chemistry and biochemistry, will collaborate with Mihri Ozkan, a professor of electrical engineering at UC Riverside to develop near-real-time instruments enabled by nanotechnology to look for tell-tale single cancer cells and probe them to analyze their health conditions. The UCSD division of the California Institute for Telecommunications and Information Technology will supply some of the facilities and support for this project.

The other universities named today as Centers for Cancer Nanotechnology Excellence are: University of North Carolina; Emory University and Georgia Institute of Technology; Massachusetts Institute of Technology and Harvard University; Northwestern University; California Institute of Technology; and Washington University in St. Louis, MO. Each of the CCNE awardees includes an NCI-designated cancer center that is affiliated with schools of engineering and physical sciences, and partnered with not-for-profit organizations and/or private sector firms, with the specific intent of advancing the technologies being developed.

Founded in 1979, the Rebecca and John Moores UCSD Cancer Center is one of 39 centers in the United States to hold NCI designation as a Comprehensive Cancer Center. Part of the UCSD Medical Center, the Moores Cancer Center ranks among the top centers in the nation conducting basic and clinical cancer research, providing advanced patient care and serving the community through outreach and education programs.

Media Contacts: Denine Hagen, (858) 534-2920, mobile: (858) 245-8506 Leslie Franz, (619) 543-6163, mobile: (619) 994-5432 Rex Graham, (858) 822-3075, mobile: (858) 232-2706