Emphasizing the Provocative

NCI awards grants through program designed to "stimulate ideas and inspire progress"

The question first came to Ramsey Badawi, PhD, more than a decade ago: If one built a positron emission tomography (PET) scanner significantly longer than today's standard 15-cm models, how useful would it be? Such a device, he thought, would not only be more sensitive but also would allow physicians and researchers to assess the physiologic function of a much larger portion of the body at a single point in time.

Convinced of the potential value of such a device, especially in light of the need to spot smaller and smaller cancers, Badawi's lab began to simulate a 2-m PET scanner, which would be long enough to scan a person from head to toe all at once, using computer software. However, Badawi lacked funding to develop the technologies to build the actual device—until recently.

In August, Badawi, the director of nuclear medicine research at the University of California, Davis, received a 3-year grant from the National Cancer Institute (NCI) to get started. The grant was funded through the agency's Provocative Questions project, an initiative that supports research addressing one of 24 questions (see http://provocativequestions/nci.nih.gov/rfa) related to cancer risk, prevention, development, detection, diagnosis, or treatment. The questions were compiled based on website submissions and discussions with dozens of investigators at NCI workshops held in 2010 and 2011.

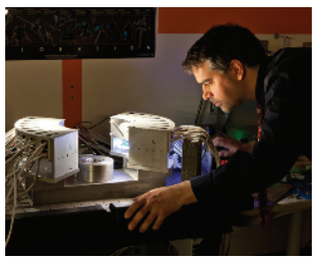
NCI received more than 700 applications for Provocative Questions funding, a number that was "even more than I expected," says NCI Deputy Director Douglas Lowy, MD. Only 57 grants, with commitments totaling $22 million in fiscal year 2012, were awarded. The funded research projects relate to 20 of the 24 questions.

The response to the project was so positive, Lowy adds, that NCI plans to issue more questions in fiscal year 2013.

VARIED PROJECTS BREAK BARRIERS

Badawi's project tackles Question 13, which asks whether tumors can be detected when they are 2 to 3 orders of magnitude smaller than those currently detected. To be picked up with current imaging tools, tumors generally need to measure about 1 cm; Badawi says his new PET scanner will have the ability to spot smaller clusters of cells, aiding in diagnosis and treatment. In addition, the longer scanner could help researchers better understand how dissemination correlates with disease progression, thus potentially improving treatment with targeted therapies and reducing radiation exposure.

The scanner could also record a high-definition "movie" of how drugs move through the body, letting researchers see whether a drug reaches its target. "This will allow us to rule out drugs that won't work without having to go through expensive clinical trials," Badawi explains.



UC Regents

Ramsey Badawi, PhD, received an NCI Provocative Questions program grant to develop the technologies necessary to build a giant PET scanner that would allow physicians to spot much smaller cancers than they currently can.

Another grant recipient, Johns Hopkins' Cynthia Sears, MD, will delve into Question 12—which seeks to answer what novel infectious agents cause cancer and what mechanisms induce the tumors—by examining how certain microbes lead to colon cancer. Sears had previously linked enterotoxigenic *Bacteroides fragilis*, bacteria that cause diarrhea and live only in the colon, to colon cancers in mice. However, her explorations in the field had slowed somewhat due to a lack of research dollars.

"When the Provocative Questions possibility came up, we realized that we might broaden that project to understand better how bacteria contribute to colon cancer in people," says Sears. "It was a unique opportunity."

Using more than 100 human tumor samples banked at Johns Hopkins, Sears and her colleagues will study how bacteria engage with epithelial cells and how their relationship varies in different parts of the colon—information that can then be correlated with patient outcomes. In addition, they aim to identify microbial, immunologic, and—with researchers at Scripps Institute in La Jolla, CA—metabolic biomarkers associated with colorectal cancer, which could lead to improved disease detection and treatment, says Sears.

Question 5, which asks how some drugs used for nonmalignant conditions can protect against or be used for treatment of cancer, was perfect for Stephen Byers, PhD, a molecular oncologist at Georgetown Lombardi Cancer Center in Washington, DC. For years, he has studied cadherin-11, an adhesion molecule overexpressed by some aggressive breast and brain tumors—and that seems to play a role in rheumatoid arthritis (RA).

To block cadherin-11, Byers and his team made a drug they dubbed sd133. Coincidentally, a Georgetown colleague discovered that the COX-2 inhibitor celecoxib (Celebrex; Pfizer) fits with the cadherin-11 binding site, making it a potential treatment for these cancers, too. Michael Brenner, MD, at Boston's Brigham and Women's Hospital, had produced cadherin-11 antibodies and was testing them against RA in mice. The researchers joined forces for the Provocative Questions project to see if their agents might halt both cancer and RA and, if so, how.

"We need to figure out how cadherin-11 transmits a signal—and what that signal is—that allows cancer cells to grow and causes the symptoms of RA," Byers says.

Badawi notes that the Provocative Questions program breaks through the "culture of conservatism" that surrounds most scientific funding, especially during tight economic times. "I don't mean that as a criticism—that's just the nature of the beast," he says. "The message from the NCI with the Provocative Questions program is, 'We don't want you to always be conservative.' That's allowed us to break through the funding barrier." —*Suzanne Rose* ■

For more news on cancer research, visit *Cancer Discovery* online at http://CDnews.aacrjournals.org.