Breast Cancer Stamp Funds New NCI Program

By Liz Savage

For the last 9 years, the U.S. Postal Service’s breast cancer stamp has come to the rescue of breast cancer researchers in need of funding. Now a new program introduced by the National Cancer Institute narrows the focus of the research funded by the stamp but asks bigger questions.

The proceeds from the stamp are now funneled into the breast cancer premalignancy program, which funds research on premalignant lesions, cancer prevention techniques, and methods for detecting breast cancer or precancers earlier.

Since Congress first enacted the stamp program in 1997, NCI has received more than $35 million from stamp sales, which funded more than 50 grants and one clinical trial. These grants covered the breadth of breast cancer research, from high-risk investigations to more well-established research, but the program lacked cohesion, according to NCI Director John Niederhuber, M.D.

“I didn’t really feel at the time that we were using this resource optimally. It seemed that we should have a goal of what we’d like to accomplish,” he said.

In the fall of 2005, Niederhuber and NCI’s Executive Committee proposed that the program be revamped to focus on one theme, and the premalignancy program was born. The program’s steering committee, which consists of NCI investigators who were selected for their interest in precursor research, chose six projects around the theme of premalignancy—projects that would require interdisciplinary, multi-institutional collaboration. The aim of the program was to pool the NCI’s resources—both dollars and brainpower—to explore an area of research that the cancer community considered underresearched and underfunded. The program intends to fund projects both inside and outside NCI.

“The question of why some premalignant lesions remain benign while others become malignant has important implications, both for clinical management and fundamental understanding of the biology of cancer,” Dinah Singer, Ph.D., director of the division of cancer biology at NCI and cochair of the program’s steering committee, said in an e-mail. “If we could clearly distinguish between those lesions, treatments could be appropriately tailored, minimizing unnecessarily aggressive treatment for those lesions that will remain benign and devising appropriate treatment strategies for those that will convert to a malignant phenotype.”

The extra money from the stamp provides an opportunity to do the kind of high-risk research that would not otherwise get funded, given the NCI’s tight budget, said Cheryl Marks, Ph.D., associate director of the division of cancer biology. “With this funding climate, where there isn’t much money, having someone come forward with an application that is really rather a fishing expedition, meaning you really don’t know what you’re looking for … this type of science doesn’t usually peer review very well.”

The six projects, which are all in the early stages or have yet to begin, ask intentionally broad questions in the hope of seeding new areas of research and generating testable hypotheses that will be easier to fund in the future.

Marks is currently recruiting research teams for a project to identify the differences among premalignant lesions. While she and her colleagues are still waiting for grant applications from researchers, they hope that this research will ultimately lead to new diagnostic tests, therapies, and imaging techniques.

“We want to catalog differences among lesions that have been described by pathology, and maybe then we can come up with some better definitions. Right now the definitions are very flabby, very broad,” Marks said. With the current methods, physicians have a limited arsenal for predicting which early lesions are harmless and which will turn deadly.

Early detection also describes the projects overseen by Mark Sherman, M.D., a senior research fellow in NCI’s division of cancer epidemiology and genetics who, along with researchers at University of Vermont and the University of California, San Francisco, is trying to tease out the differences between high-density and low-density breast tissue to better understand the relationship between breast density and breast cancer risk. Studies have shown that high breast density is a risk factor for breast cancer in women, and Sherman and his group suspect that the microenvironment of dense breasts is a key factor in determining whether epithelial cells will give rise to cancer. They are just beginning to enroll patients in the study, which will analyze the molecular structure of breast tissue from women undergoing biopsies.
Sherman’s group is particularly interested in the role that hormones and inflammation play in influencing breast density and, ultimately, breast cancer. “Not all dense areas are created equal. Some dense areas literally contain the cancer of interest or concern, and other dense areas are entirely innocuous,” Sherman said. Establishing which dense areas lead to tumors would allow physicians to more accurately determine a woman’s breast cancer risk.

Another important method of early detection, mammography, has its obstacles to overcome as well. Stephen Taplin, M.D., program director of the mammography interpretation project, is working with Breast Cancer Surveillance Consortium investigators to improve how radiologists read mammograms. Staying alert and reading accurately are perhaps the greatest challenges for any radiologist, who is often finding just four to six cancers in every 1,000 mammograms. Because finding cancers is so rare, two key questions that the investigators will address are how to measure radiologists’ accuracy in interpreting mammograms and whether reading more of them will improve their ability to accurately spot cancers. With that information, they will try to identify a minimum number of images that radiologists should be required to read each year. During this 3-year project, the research team plans to develop an educational program that they hope will improve mammography interpretation.

“What the stamp money has done has allowed us to go beyond just measurement and ask if you can change it,” said Taplin, a senior scientist in the applied research program of NCI’s division of cancer control and population sciences. “With a little bit of money you can understand the problem better, and so we’re getting better and better at understanding the problem, but you still can’t fix the problem. It’s much better to be able to understand and change within the same research group. But it does require more money and a multidisciplinary team.”

The remaining premalignancy projects are no exception. One, with the goal of improving recruitment, will examine the decision-making process of women who enroll in chemoprevention trials. (When this study will begin is unclear since it is nested in a chemoprevention trial called the P-4 Study to Evaluate Letrozole and Raloxifene, STELLAR, which has been put on hold.) Another project seeks to identify new biomarkers that will provide better...
definitions for breast stem cells and breast cancer stem cells. “If we could find a signature of surface markers on those cells, we can image the potentially transformed stem cell in the otherwise normal breast and find precancer much earlier. And then it can be targeted with smarter molecular targeting,” said Barbara Vonderhaar, Ph.D., head of the stem cell project and cochair of the breast and gynecologic malignancies faculty in the NCI’s center for cancer research.

The final project does not specifically investigate premalignancy, though it could lead to new methods for imaging and targeting early lesions. The research group is trying to show the effectiveness of injecting iron oxide–filled nanotubes at the cancer site to improve breast cancer imaging that uses MRI.

The collaborative nature of the projects is one of the premalignancy program’s best assets, according to Dwight Randle, Ph.D., a senior scientific advisor at the Susan G. Komen Breast Cancer Foundation. Not only are researchers teaming up across institutions and disciplines, but the public can join in as well. “This is a great way for the public to show that they are involved in the fight against breast cancer, and every time they use a [breast cancer] stamp they can remind others to get involved as well,” he said.

However, the fate of the premalignancy program is uncertain at the moment. The breast cancer stamp has been reauthorized three times since Congress first passed the Stamp Out Breast Cancer Act in 1997. The current reauthorization will expire at the end of this year, but senators Diane Feinstein, D-Calif., a cosponsor of the original bill, and Kay Bailey Hutchison, R-Texas, have proposed legislation to extend the sale of the stamp for another 2 years. However, Niederhuber says there is little fear that the program could end this year.

“There is every likelihood that it will continue. There is a lot of public support for it.”