

# Elevating the hunt for environmental link to breast cancer

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Mammograms showing a normal breast (left) and a breast with cancer (right).  
Credit: Public Domain

Imagine that you are a molecular biologist who has spent the last 20 years in your lab, doggedly trying to figure out how chemicals in the environment cause human cells to become cancerous. One day a benefactor asks you what it would take to make real progress toward that goal. You say, "Maybe about \$5 million over a three-year period." And your benefactor says, "Done!"

That's pretty much the way it happened for David Sherr, professor of environmental health at Boston University and director of the school's Superfund Research Program. His fairy godmother was a little-known local group called Art beCAUSE Breast Cancer Foundation, which last fall announced a \$5 million grant to Sherr and four other researchers to identify the environmental causes of breast cancer and methods of preventing the disease.

Ellie Anbinder, founder and executive director of the foundation, said money for that kind of research has to come from the private sector because "the vast majority of government research monies go to treatment and cure." But she believes chemicals in the environment play a significant, if not dominant, role in breast and other cancers. Identifying them and putting pressure on policymakers to minimize exposure to them could be the first step in preventing the disease.

Epidemiologists have been trying for decades to demonstrate links between cancer and the environment. In 2011 the Institute of Medicine, an arm of the National Academy of Sciences, convened a blue-ribbon panel that found no solid evidence, with the "possible" exception of a few workplace chemicals such as benzene.

"It's a radioactive topic," said an official of the National Cancer Institute who asked not to be identified. "Many people feel strongly that chemicals in the environment are causing breast cancer. But we couldn't find any patterns."

Art beCAUSE (so named because the co-founder owned an art gallery, and one of the first projects saw artists donating a percentage of sales to research) has only \$350,000 of the promised \$5 million. "We'll give it to them as we raise it," said board chairman Bill Diercks.

Sherr said the first installment is enough for each of the five labs to hire

a dedicated researcher for a year. "It's a start," he said. "The critical element was to get everyone working together, which gives you a synergistic effect. We can share technology and resources and refine our ideas."

Sherr is working on a protein known as the aryl hydrocarbon receptor, which binds to environmental carcinogens and begins the aberrant signaling that causes cells to divide out of control. Two other members of the consortium - Dr. David Seldin, chief of hematology/oncology at Boston University, and Gail Sonenshein, professor of biochemistry at Tufts University School of Medicine in Boston - also are cell-signal researchers. The remaining members of the consortium are Charlotte Kuperwasser, an expert on the biology of [cancer stem cells](#) at Tufts, and Stefano Monti, a computational biologist at B.U.

Monti's project is to develop a high-tech genomic platform that can screen large numbers of chemicals quickly and economically for their ability to affect cancer-related signaling pathways in [human cells](#). The consortium believes high-throughput screening may be the only practical way to find out whether the more than 80,000 untested chemicals on the market today cause cancer.

The gold-standard test of carcinogenicity, the two-year rodent bioassay, uses 800 animals and costs \$2 million to \$4 million per compound. No wonder only about 1,500 chemicals have been tested so far. But most epidemiological studies have failed to identify environmental culprits, which Sherr says is not surprising.

"The critical exposures that result in breast cancer may have happened 10 or 20 years before diagnosis ..., in utero, or even a generation or two generations ago," Sherr said. "There is no realistic way for an epidemiologist to quantify exposure to any one [chemical](#) over that time frame, let alone the tens of thousands of chemicals and combinations

thereof. It's simply impossible with current technologies."

Most studies also fail to take account of genetic predisposition, or gene-environment interactions. "Let's assume that 1,000 chemicals of the 80,000 in the environment are carcinogens," Sherr said, "but each for a small subset of women with a particular genetic makeup. The overall effect of all those chemicals would be significant. But demonstrating that any one is a carcinogen by epidemiology would be a daunting if not impossible task."

The upshot is that even though environmental chemicals are probably at least partly responsible for some portion of breast cancer cases, proof is elusive.

"We assume that all these chemicals are innocent until proven guilty," Sherr said, "and I think it's too dangerous to do that. Do you want to grant those chemicals constitutional rights and bet your life ... ? Or do you want to do the science and find out which suspects we really need to look more closely at?"

The National Institutes of Health are doing some of that science. But Diercks said the institutes are "pretty careful about which projects they're funding. They want to fund things with more proven science and quicker returns."

Both funders and grantees are aware of the symbiosis of their efforts. Raising money helps the scientists do their work. At the same time, the scientific work helps the funders raise more money.

"If we can generate some preliminary results," Monti said, "it will increase visibility and make it more likely they will succeed" in raising the rest of the \$5 million.

Of course, even \$5 million isn't likely to prevent [breast cancer](#). "But in the research funding world," Diercks said, "there's a very definite leveraging effect of about 10 to 1. Once they publish results that get the attention of the NIH, the hope is that our \$5 million will get them \$50 million."

Kuperwasser is just thankful for the chance to do the science. "This work would never be funded by traditional funding mechanisms," she said, "because it's too outside the box. ... You can't propose large-scale fishing projects, because you can't predict the outcome before you do the work. But that's how important discoveries are made. You don't go out saying, 'I know there's going to be America across the water.' (Art beCAUSE) said, 'We're going to provide you the boat and money to explore what's out there.'

"It may or may not be enough" to get to the next level of funding, she said. "But we'll get as far as we can and report our findings. As explorers, you don't wait until you have enough money to complete the voyage. You put the boat in the water and start paddling."

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