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Bitter pill:
Painkillers' safety called into question


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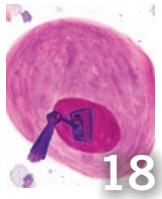
Green fingers:
Eric Green lays out his vision for genomics research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Tag team:
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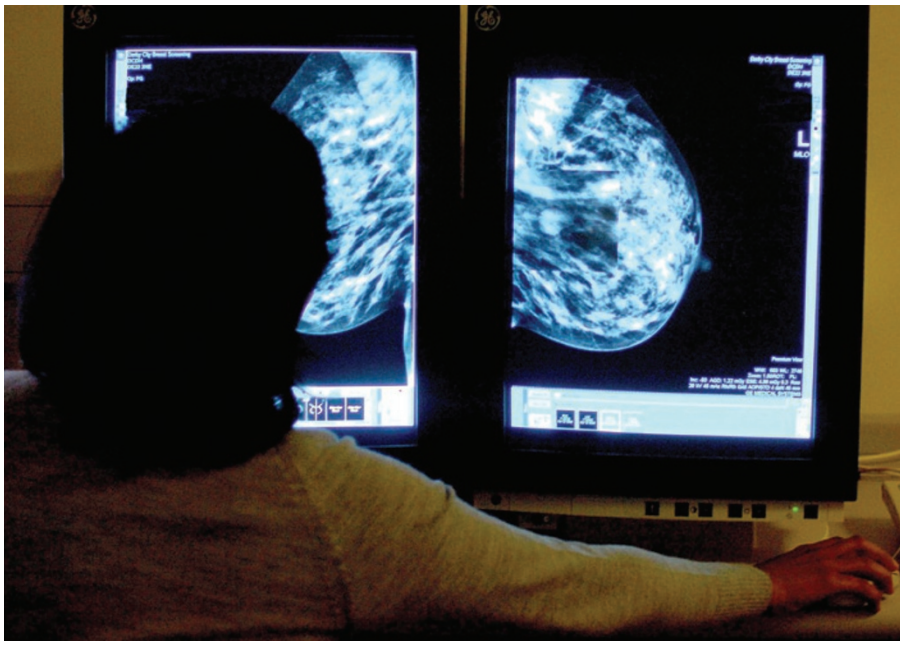
Biomarkers still off the mark for detecting breast cancer

Fifty years ago, the radiologist Robert Egan developed the first easily reproducible mammogram. Yet the anniversary is hardly golden. Prominent opinion articles and a US government task force have recently questioned when and how often to use the screening technique, which has led some cancer biologists to wonder: could biomarkers find breast cancer sooner? So far, the answer remains "not yet," but some scientists see signs of success ahead.

Many researchers are searching for breast cancer–specific biomarkers everywhere from urine to nipple fluid. One contender that is moving ahead in clinical research is a urine test to detect molecular complexes that form between estrogen and DNA. These can detach from the chromosome, causing mutations that might trigger tumors. Last year, a team led by Ercole Cavalieri, of the University of Nebraska Medical Center in Omaha, found elevated levels of the carcinogenic complexes in women at a high risk of developing breast cancer and women with newly diagnosed breast cancer, but not in healthy controls (*Breast Cancer Basic Clin. Res.* **3**, 1–8; 2009). Cavalieri says that these biomarkers turn up well before a mammogram would find a cancerous lump, "but we don't know yet exactly how many years before the cancer you can see the risk."

Breast cancer tests that use blood-based biomarkers are the most advanced, says Aparna Jotwani, an oncologist at the Fred Hutchinson Cancer Research Center in Seattle. Although none of these tests are ready for the clinic, dozens of them are in the experimental pipeline, Jotwani adds. Some of these detect proteins associated with the insulin-like growth factor pathway, for example, whereas others flag microRNAs linked to breast tumors.

Some experts, however, are less confident in the potential of these early biological indicators. "We haven't seen anything that looks remotely convincing with respect to early detection from circulating biomarkers or samples of local fluids," says Jeffrey Marks of the US National Cancer Institute's Early Detection Research Network. He points out that mammography is safe and highly effective. Consequently, "the properties of a biomarker test would have to be through the roof to be adopted," he says.



Associated Press

Seeing double: Mammograms sometimes produce equivocal results

Many still believe that biomarkers could one day provide such a high-powered test. But, rather than focusing on any single signpost, investigators will need to combine collections of biomarkers, says James Basilion, a molecular imaging scientist at Case Western Reserve University in Cleveland. "Genomics suggests that multiple markers can better assess the disease," he says.

In fact, current genomic and proteomic technologies can produce plenty of candidate biomarkers for breast cancer panels. The real bottleneck, notes Amanda Paulovich, a proteomics expert at the Hutchinson Center, comes in testing them. For example, developing even a research-grade antibody-specific assay for a single protein biomarker can take more than a year and upward of $100,000, thereby prohibiting large numbers of markers from being tested at the same time.

To develop a technology capable of analyzing large batches of potential biomarkers in a cost-effective manner, Paulovich, together with Steven Carr, a biochemist at the Broad Institute in Cambridge, Massachusetts, plan to use a targeted form of mass spectrometry to simultaneously generate around 400 assays for 200 proteins. Backed by a recent $4.8 million stimulus grant from the National Cancer Institute, they will then validate those tests in a panel of breast cancer cell lines. "To meet the challenge of population screening, we need more personalized, likely multivariate, approaches to detection," Paulovich says.

Others agree that biomarkers will ultimately be used in combination with other technologies. Jotwani, for one, does not see biomarkers taking the place of mammography, but rather complementing it. "The more we know, the better we can treat patients," she says.

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