**Life-Course Studies to Bolster Research on Environmental Effects**

“A tremendous amount of money has been spent in the past 20 years, and it has not unveiled the environmental factors for breast cancer risk in the way that we had hoped,” says Irv Hertz-Picciotto, PhD, professor and chief of the division of environmental and occupational health at the University of California, Davis. “But the science has now advanced so that we can make greater progress.”

Key to that research progress is to “focus on the influence of exposure to a variety of environmental factors during potential windows of susceptibility over the full life course, from the pre-natal experience through adult life,” declares a U.S. Institute of Medicine (IOM) report on breast cancer and the environment.

Hertz-Picciotto chaired the committee that put together the report, which broadly covers factors that are not directly inherited through DNA. It was released in December at the Cancer Therapy & Research Center (CTRC) and American Association for Cancer Research (AACR) San Antonio Breast Cancer Symposium (SABCS).

It’s not practical to attempt to understand lifelong effects of environmental factors on cancer initiation and progression by following large cohorts of women from womb to tomb, notes Robert Hiatt, MD, PhD, another committee member and professor and chair of the department of epidemiology and biostatistics at the University of California, San Francisco.

Instead, Hiatt says, the strategy will be to “link study cohorts across life stages and to create better links between animal models and humans.” Part of that effort, he adds, will be to develop and validate intermediate outcomes of cancer initiation and progression.

Additionally, Hertz-Picciotto suggests that in general, large clinical trials should gather data on environmental factors potentially affecting women’s risks of breast cancer, such as diet, weight gain, physical activity, exposure to ionizing radiation or chemicals, and the use of hormone therapy or oral contraceptives.

Although the IOM report found clear evidence of increased breast cancer risk for some factors, including ionizing radiation and obesity, “for many other factors, we found that the evidence was limited, in some cases contradictory, and in some cases absent,” says Hertz-Picciotto.

The report calls for heightened research on factors that show “provocative, but as yet inconclusive” evidence of risk. These factors include shift work; endocrine activity; interactions between man-made chemicals in the environment and other factors; epigenetic modifications, including those driven by man-made chemicals; and mutagenic chemicals such as benzene.

At SABCS, the report was criticized by patient advocates and some oncologists for what they see as overly cautious descriptions for some of these risks.

**Sequencing Pilot Matches Actual Patients with Trials**

Clinicians and researchers at the University of Michigan have developed a pilot system to enable the use of high-throughput sequencing in the cancer clinic. They have shown that they can perform a broad, deep genomic analysis of patients with drug-resistant cancer, and based on that data, potentially match patients with clinical trials, all within 3 to 4 weeks.

As the price of sequencing drops, researchers see the potential for whole-genome analysis, rather than tissue type or small numbers of biomarkers, to guide treatment. But how to integrate the huge amount of data generated by whole-genome analysis into the clinic in a practical way is still an open question, says Sameek Roychowdhury, MD, PhD, a pathologist at the University of Michigan.

Roychowdhury and his colleagues performed whole-exome sequencing of tumor and normal tissue, and whole-genome and transcriptome sequencing of the tumor, in one patient with metastatic colorectal cancer and a second patient with malignant melanoma. They then convened a Sequencing Tumor Board (composed of clinicians, geneticists, bioinformatics experts, ethicists,
CANCER DISCOVERY

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Updated version
Access the most recent version of this article at:
doi:10.1158/2159-8290.CD-ND121511OL-13

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