Multigene testing replacing BRCA tests for breast cancer risk, researcher says

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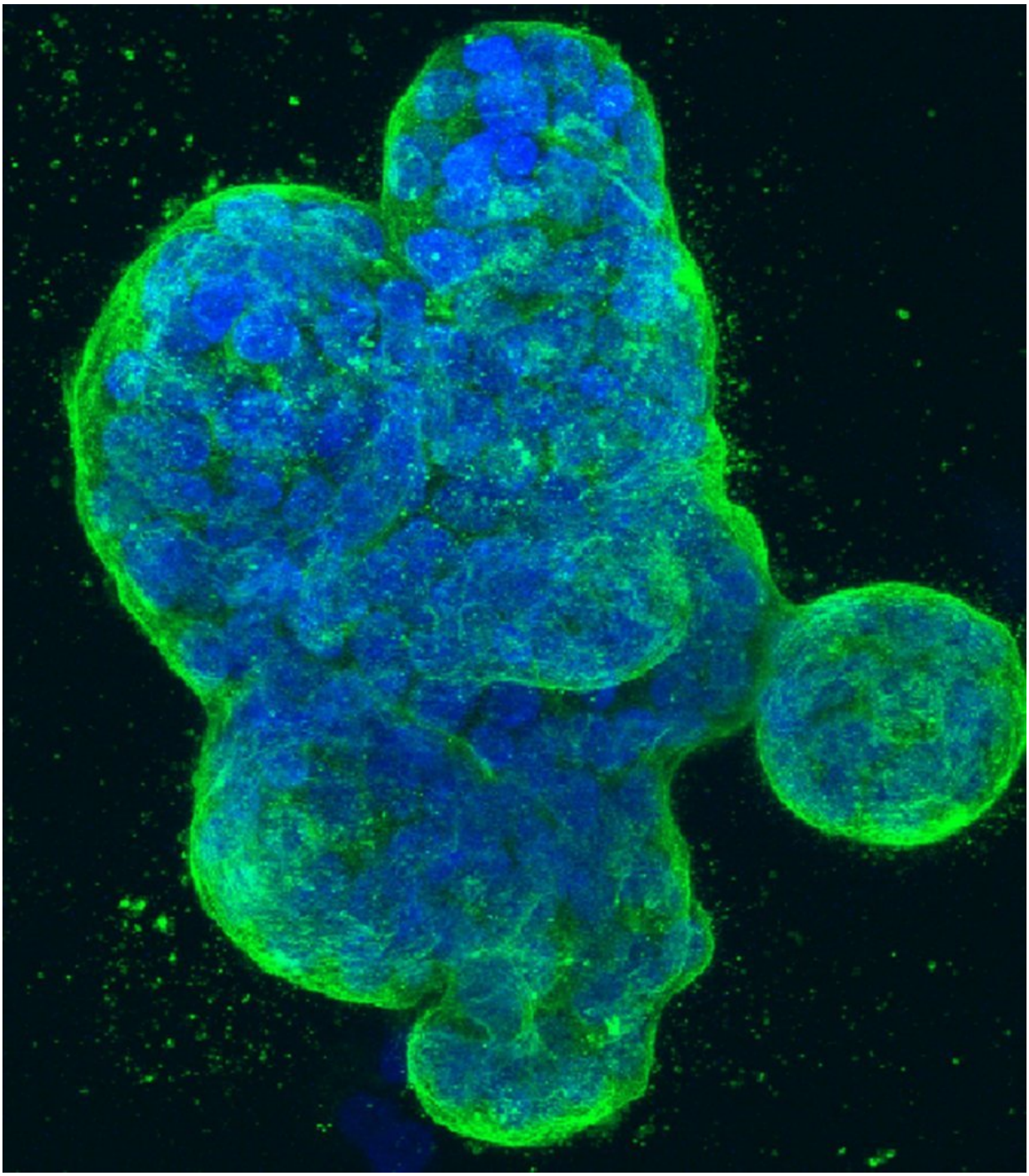

Three-dimensional culture of human breast cancer cells, with DNA stained blue and a protein in the cell surface membrane stained green. Image created in 2014 by Tom Misteli, Ph.D., and Karen Meaburn, Ph.D. at the NIH IRP.

The use of genetic tests aimed at detecting the presence of mutations in the BRCA1 and BRCA2 genes in women with breast cancer is rapidly declining in favor of tests that can detect multiple cancer-associated mutations, according to researchers at the Stanford University School of Medicine and five other U.S. medical centers.

Some researchers had wondered whether multigene testing, which may identify genetic mutations of uncertain clinical significance, would lead more women to consider prophylactic mastectomies—a surgery in which both breasts are removed to prevent future cancers—out of an abundance of caution. However, the current study did not show an increase in mastectomies associated with testing more genes.

The shift reflects a growing acknowledgement by clinicians that multigene panel tests can yield more clinically useful information for patients and their unaffected relatives, the researchers said.

Overall, multigene panels were about twice as likely as the tests for BRCA1 and BRCA2 to identify disease-associated genetic variants, the study found. However, multigene testing was more likely than the BRCA-only testing to be delayed until after surgery to remove the tumor. This time lag may limit a patient's treatment options, the researchers said.

'Becoming the norm'

"In general, multigene panel tests yield more clinically useful results and are rapidly becoming the norm," said Allison Kurian, MD, associate professor of medicine and of health research and policy at Stanford. "Newly diagnosed women should ask their doctors whether they may be appropriate candidates for genetic testing. They should also advocate for the opportunity to discuss genetic testing and its implications with an experienced clinician, such as a genetic counselor, in a timely manner."

A paper describing the research will be published May 10 in *JAMA Oncology*. Kurian is the lead author. Steven Katz, MD, MPH, professor of medicine and of health management and policy at the University of Michigan, is the senior author.

Multigene panel tests are more likely than BRCA-only tests to yield information about both a patient and her family members, who may be unwitting carriers of disease-associated mutations. "This is very important because it offers the opportunity for genetically targeted, primary cancer prevention in unaffected relatives," Kurian said. "Some prior research has shown that this 'cascade testing' of unaffected relatives is cost-effective, and there are currently several initiatives underway to improve upon the delivery and success rates of cascade testing."

The researchers surveyed over 5,000 women who had been diagnosed with stage-0 to stage-2 breast cancer between 2013 and 2015. They asked the women if they'd had genetic testing, and, if so, who ordered it, when it was performed and what type of tests they underwent. A novel feature of this study was that genetic results came directly from the testing laboratories and were linked to population-based cancer registry data. This data linkage provided substantially greater depth and accuracy of genetic information than in previous studies.

They found that only about one-quarter of the women had received any genetic testing. This number stayed relatively constant throughout the two-year period. However, of those who were tested, the proportion who received multigene panel testing increased steadily over time, from about 26 percent of those tested in early 2013 to about 66 percent in mid-2015. Conversely, the proportion of women who received BRCA-only testing during the same time period decreased from about 74 percent to about 34 percent.

Multigene panel testing was about twice as likely as BRCA-only testing to identify disease-associated mutations. But it was also more likely to reveal mutations of uncertain clinical significance, particularly in racial or ethnic minorities. This disparity is likely due to the fact that most genes were sequenced first in white patients, and the causative effect of variations in other minorities is not clear. This finding emphasizes the need for research in diverse populations to clarify genetic uncertainty and reduce racial disparities in the clarity of genetic test results, the researchers say.

Timing of tests varied

The timing of the tests also varied, the study found. Although the majority of the women tested got their results prior to surgery to remove the tumor, many did not. About 33 percent of women receiving multigene panel testing were tested after surgery, versus about 20 percent of women receiving BRCA-only testing—perhaps due to a recognition by clinicians that interpreting the results of a multigene panel can be complex and requires the expertise of genetic counselors, who are not always rapidly available.

"Furthermore, patients and their clinicians may view genetic testing as a lower priority than tumor biology and pathology testing which most directly inform the treatment options," said Katz.

"As genetic testing has become more comprehensive and less expensive, we have begun to see a significant problem in terms of the genetic-counselor workforce," Kurian said. "More genetic counselors are needed, and they should be integrated into routine cancer care. There is also a need for new care-delivery models that effectively triage appropriate patients to timely genetic counseling."

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