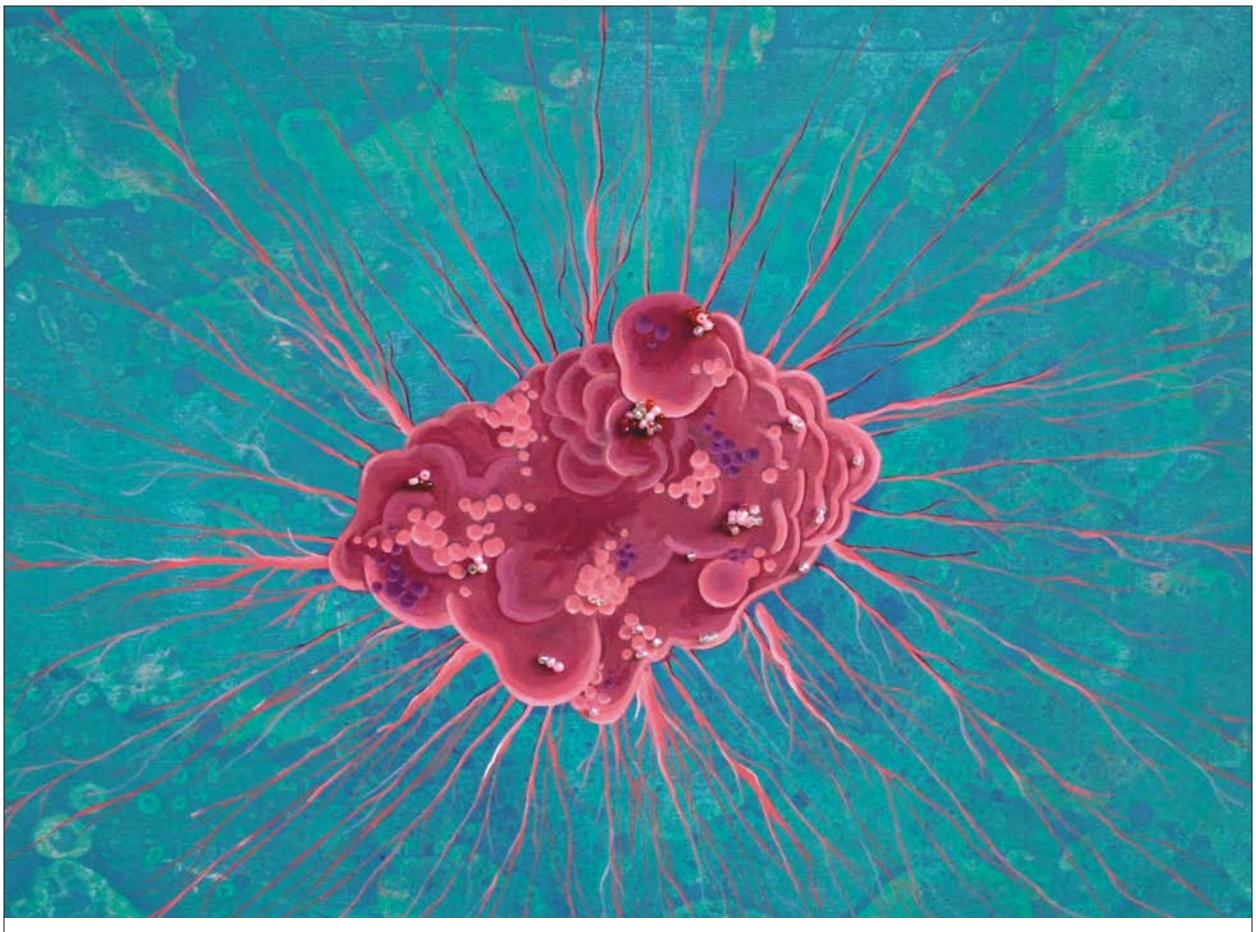

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Key Information About Breast Cancer Risk and Development Is Found in 'Junk' DNA

A new genetic biomarker that indicates an increased risk for developing breast cancer can be found in an individual's "junk" (non-coding) DNA, according to a new study featuring work from researchers at the Virginia Bioinformatics Institute (VBI) at Virginia Tech and their colleagues.

The multidisciplinary team found that longer DNA sequences of a repetitive microsatellite were much more likely to be present in breast cancer patients than healthy volunteers. The particular repeated DNA sequence in the control (promoter) region of the estrogen-related receptor gamma (ERR) gene -- AAAG -- contains between five and 21 copies and the team found that patients who have more than 13 copies of this repeat have a cancer susceptibility rate that is three times higher than those who do not. They also discovered that this repeat doesn't change the actual protein being reproduced, but likely changes the amount.

The researchers from VBI's Medical Informatics and Systems Division, the University of Texas Southwestern Medical Center and the University of Liverpool, United Kingdom, report their findings in an upcoming edition of the journal Breast Cancer Research and Treatment. The study is currently available online. The group sequenced a specific region of the ERR-ã gene in approximately 500 patient and volunteer samples. While the gene has previously been shown to play a role in breast cancer susceptibility, its mechanism was unknown.

"Creating robust biomarkers to detect disease in their early stages requires access to a large number of clinical samples for analysis. The success of this work hinged on collaborations with clinicians with available samples, as well as researchers with expertise in a variety of areas and access to the latest technology," explained Harold "Skip" Garner, VBI executive director who leads the institute's Medical Informatics and Systems Division. "We are now working to translate this biomarker into the clinical setting as a way to inform doctors and patients about breast cancer susceptibility, development, and progression. Akin to the major breast cancer biomarkers BRCA1 and BRCA2, this will be of particular benefit to those high-risk patients with a history of cancer in their family."

The majority of DNA is non-coding, meaning its not transcribed into protein. The largest amount of this type of DNA consists of these microsatellites -- specific repeated sequences of one to six nucleotides within the genome. There are over two million microsatellites in the human genome, yet only a small number of these repetitive sequences have previously been linked to disease, particularly neurological disorders and cancer.

"We've become increasingly aware that non-coded DNA has an important function related to human disease," said Michael Skinner, M.D., Professor of Pediatric Surgery at the University of Texas Southwestern Medical Center and collaborator on the project. "Replication of this study in another set of patients is needed, but the results indicate that that this particular gene is an important one in breast cancer and they reveal more details about the expression of the gene. This kind of work could eventually result in the creation of a drug that would specifically interact with this gene to return expression levels to a normal range."

"Ninety percent of all the breast cancer patients we see aren't considered high risk patients, which means there wasn't any indication that they would be susceptible to breast cancer," said Dr. James Mullet, a Radiologist at Carilion Clinic's Breast Care Center. "This compels us to screen everyone in some way. If we had a better test -- one that is more robust and sensitive, but also specific -- we could make sure the women with most risk are getting properly screened for breast cancer."

"One practical clinical application of this research is to have a test available that would allow us to tailor our screening better," Mullet said. "For example, we could lessen patients' time, expense, and worry if we could better determine which patients would need only a mammogram, as opposed to additional tests like ultrasound or screening breast MRI. This work may also give us genetic insight into the cause of the breast cancer that may develop in those 90 percent of patients who are not currently identified as high risk."

According to Garner, "There is a big gap between what is suspected and what is known about the genetics of cancer. While more work is needed to better understand how these changes play a role in cancer, these results can be used now as a new test for breast cancer susceptibility and, as our data suggests, for colon cancer susceptibility and possibly other types of cancer. We think this is just the beginning of what there is to be found in our junk DNA."

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