49: Genetic ancestry-dependent Differences in Breast Cancer-induced Field Defects in the Tumor-adjacent Normal Breast

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Scientists know that genetic ancestry affects how cancer develops. For example, women of African American ancestry suffer higher mortality from triple-negative breast cancer than women of European ancestry. Breast cancer in Hispanic and Native American women is less prevalent, and these women have better outcomes when they do develop breast cancer. What is it about ancestry that is responsible for these differences?

Researchers already have looked at properties of breast cancer tumors among these populations. For this study, they wanted to examine the properties of the tissues near tumors to see what happens to give rise to formation of cancer. They then compared this "normal-adjacent tissue" to the tissue of women who had never had breast cancer. They hope that understanding these cellular changes based on genetic ancestry may lead to the development of another tool for detecting breast cancer at its earliest stages.

Methods:

Scientists used 100 age-matched tissue samples from healthy women who had donated to the Komen Tissue Bank and tumor normal-adjacent tissue from 100 women with breast cancer. They matched the samples for age, body mass index, ancestry and other factors so that they could compare "true" normal tissue to normal-adjacent tissue from similar women.

Findings:

The researchers found several differences among genetic ancestry in the "true" normal tissue and in the nearby-adjacent tissues.

For example, ZEB1 cells, important molecules in the regulation of DNA damage, were higher in the normal breast tissues in women of African American ancestry than other groups. Elevated ZEB1 cells in European American women were found only in breast cancer tissue.

Another factor, FOXA1, associated with a better outcome in primary tumors, was found to be lower in the nearby-adjacent tissues of women of African American ancestry. GATA3 levels, perhaps responsible for changes in the nearby-adjacent tissue, were lower in that tissues of women of European American ancestry but not in women of African American ancestry, compared to "true" normal tissue of both groups.

Why this study is important:

The researchers said that for future cancer biomarker studies, looking at normal-adjacent tissue is not enough, as it is molecularly abnormal. Instead, "true" normal tissue should be used because gene expression in this tissue is unique and influenced by genetic ancestry. This means future screening or detection methods may consider genetic ancestry to be better able to predict breast cancer risk.