

When they looked at DNA test results, however, they found that the spectrum of mutations was very different for families of African as opposed to European ancestry.

"These mutations are inherited, so they tend to reflect a person's racial and ethnic ancestry," Olopade said. The Ashkenazi Jewish mutations are the most common and consistent, but there are distinctive "founder" mutations in BRCA1 and BRCA2 associated with other European ethnic groups, such as the Germans, Dutch, or Scots.

As expected, damaging mutations in BRCA1 or BRCA2 were most common in Ashkenazi Jewish families.

Sixty-nine percent of high-risk women tested (20 out of 29) had a mutation, and 85 percent of those mutations were one of three well-documented variants associated with this ethnic group.

Deleterious mutations were also common in non-Jewish, non-Hispanic whites. In this group, 46 percent of women tested (36 out of 78) had a mutation known to be deleterious. Many of these could be traced to "founder" mutations from ethnic backgrounds.

Documented mutations already known to be harmful, however, were less frequent among African-American women. In this group, despite having a strong family history of breast cancer, only 27 percent of those tested (13 out of 43) had a mutation known to increase cancer risk.

African-American women, however, were almost four times as likely as non-Jewish, non-Hispanic whites (44.2 percent versus 11.5 percent) to have other variations in these genes, mutations that have not yet been characterized or linked to disease.

"Some of these variants are probably benign," said Olopade. "And some of them probably contribute to susceptibility."

The common, well-known "protein-truncating" mutations, such as those that afflict Ashkenazi Jewish women, produce a nonfunctional protein with large segments missing. The African-American variants appear to cause smaller changes that may impair, but not shut down, protein function.

The average age of diagnosis for all families in the study was 46. For African-American women with mutations known to be harmful, it was 43.6. For those with "variants of undetermined significance," it was 50.5. For those with no identifiable mutation, it was 42--the youngest of all.

The finding that women without mutations in either BRCA1 or BRCA2 get the disease so early suggests that African-American families with multiple early breast cancers have harmful mutations in another, as yet unidentified, breast cancer susceptibility gene.

"We still have a lot to learn about the ties between genetics and breast cancer in African-Americans as well as many other minority groups," Olopade said. "But we already know enough about the risk factors and the disease to help those most at risk by designing protocols for prevention and early detection."

The take home message, she added, is that women with a family history of breast and/or ovarian cancer should meet with a genetic counselor to have their risk assessed, consider genetic testing, and take appropriate precautions.

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Source: University of Chicago Hospitals

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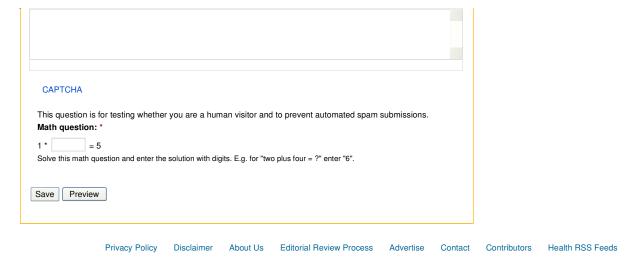
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