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The Genetics of Breast Cancer

How Genetic Variations Might Contribute to Survival Disparities

Breast cancer will affect one in ten women every year and it is the second most fatal form of cancer in women following lung cancer. Despite having a lower incidence of breast cancer, African American women have a higher breast cancer mortality rate than white women, due in part to diagnosis of the disease at a more advanced and less curable stage (Ghafoor). Additionally, Black, Hispanic and American Indian women are more likely to be diagnosed for breast cancer at more advanced stages and thus have a poorer survival rate after diagnosis compared with White women (Li). Finally, in today's technologically inclined society where medical services such as genetic testing are now available to identify individuals at an increased risk for certain diseases including breast cancer, minorities and underserved individuals are less likely to benefit from these advances (Hall). The extent to which genetic differences impact the survival rates of breast cancer patients of different racial groups is currently being determined to find out if disparities in breast cancer survival are in fact due to biological differences.

An important aspect to consider for differential outcomes of breast cancer patients is within the variations of genetic sequences. While African American women are less likely to develop breast cancer, they are most likely to die from it in comparison to all other races. This paradox might have a biological basis behind it. Recently, scientists have identified a gene that becomes more active as breast cancer becomes more

aggressive and is found more frequently in African American women. Called BP1, the homeobox gene associated with ER-negative breast cancer is active in 89% of tumors in African-American women but in only 57% of tumors in white women, according to Patricia E. Berg, PhD, from George Washington University Medical Center (Macneil). Gene expression assay studies have also identified breast cancer subtypes that are biologically distinct. The high-grade, ER-negative cancers seen in African American women may represent the "basal-like subtype," which has a poor prognosis. Comparative analyses would be needed to evaluate whether the basal-like breast tumors are more common in African-American women than in women of other racial and ethnic groups (Chlebowski). A genetic predisposition to a more aggressive form of cancer that is particular to a certain race is able to contribute to disparities in survival regardless of socioeconomic status. If medical scientists use genetic research to discover the molecular basis of tumors and cancers found in minority patients, they can determine whether there is a link between the disparities in stage detection, treatment received and survival rates and genetic variations.

There are already some discoveries of differences at the molecular level of the cancer that researchers have observed. Olapade, an oncologist at the University of Chicago, found that many of the young black women in her clinic who did not inherit BRCA mutations seemed to develop a form of breast cancer that closely resembled those seen in BRCA1 carriers. The Estrogen-receptor negative tumors discussed earlier are tumors not fueled by estrogen and thus unresponsive to drugs such as tamoxifen and raloxifene that cut off their supply of the hormone. They also metastasize and spread more quickly than ER-positive tumors (Couzin). Furthermore, Olapade believes that the

prevalence of aggressive tumors in her black patients is the result of the interplay of genes and environment. She is currently using research from the Chicago Health-Disparity Center on the effects of rats that are socially isolated early in life and how it increases "stress and vigilance and prompts immune system changes leading them to develop breast tumors 40% earlier and four times more often" than rats who are not isolated. Now the center is recruiting hundreds of African-American women with breast cancer in Chicago to begin assessing whether social isolation and stress-hormone levels predispose to cancer (Couzin).

Studying the science behind disparities is controversial for many researchers who believe that results will suggest inferiority and superiority on a racial and genetic basis. Results could potentially mark one race least healthy and others most healthy, which would create numerous problems on the social interaction level. Additionally, results could lead to race based treatments and medicine, a future that many people are weary of because of problems that could arise with this including lower quality treatment going to one racial group and better quality going to others.

African-American women are four times more likely than white women to have a genetic mutation that makes their breast tumors much more aggressive, which means faster growing and more deadly. Germ line mutations in breast cancer-predisposing genes place affected individuals at increased risk for early onset, high-grade, hormone receptor-negative disease, and these are features that characterize African American breast cancer patients (Genetic Mutation Linked to More Aggressive Breast Tumors in African-American Women). Genetic testing can help determine risk for developing these

mutations but unfortunately genetic counseling programs have tended to be underused by African Americans because of high cost, limited access and knowledge of testing and counseling options and probably cultural beliefs and concerns as well.

Tumor suppressor genes such as the BRCA genes and p53 are normal genes in our DNA that can lead to tumor formation upon mutation or removal. Scientists at Yale University studied the tumors of 145 African-American women and 177 white women diagnosed between 1987 and 1989 and found that African-American women were four times more likely to show significant alterations in the tumor-suppressing p53 gene (Genetic Mutation Linked to More Aggressive Breast Tumors in African-American Women). This finding supports the notion that biological discrepancies between the two races are leading to disparities in breast cancer survival because African American women are at a higher risk of developing significant alterations or mutations in their p53 tumor suppressor gene. A higher rate of developing significant p53 mutations is likely connected to the increased chance of African American women developing aggressive and more fatal types of tumors.

An additional study supporting genetic variation as a source of breast cancer disparities was conducted at Emory University in which African American and White breast cancer patients were examined for triple-negative tumors. A triple negative tumor does not have estrogen, progesterone or HER2, which are all hormones doctors often target in hormonal therapy treatment. The results of this particular study were that for African American women, 47% of tumors were triple negative compared with 22% of

tumors in white women (Whitworth). Hence they found that the percentage of tumors that are difficult to treat is highest in African American breast cancer cases and has a negative impact on these women's survival rate.

It is the ultimate goal that through clinical research scientists can determine where in the genetic sequence might breast cancer mortality be affected differently based on race. One hindrance to overcome is the fact that minorities are less likely to undergo clinical trials and thus research data is limited. Minority breast cancer patients are currently experiencing dismal disparities in breast cancer survival but if the genetic component of this issue can be determined better treatment and prevention options can be accurately designed that address breast cancer at the genetic level.

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