CANCER GRAND CHALLENGES | Team: SAMBAI

Mutational Landscape of Triple-Negative Breast Cancer in African American Women

PATIENT-FRIENDLY TRANSLATION

Original Article*: https://doi.org/10.1038/s41588-025-02322-y*

This research study looks at the genetics of **Triple-Negative Breast Cancer (TNBC)** specifically in African American women. TNBC is an aggressive form of breast cancer that is more common in Black women than in any other racial group. Black women are nearly 3 times as likely to be diagnosed with TNBC as white women. TNBC has high mortality rates and is the only breast cancer sub-type that does not have a therapy to prevent recurrence.

1. The Main Finding: Biology is Somewhat Similar Across Races According to this Study

The most important takeaway is that the "instruction manual" (DNA) of TNBC tumors in Black women is very similar to the tumors found in White or Asian women. Think of DNA as a master blueprint or a permanent "instruction manual" for your body. DNA contains all the genetic information needed to build and operate you—determining everything from your eye color to how your organs function. It is a permanent record that you inherit from your parents and pass on to your children. A DNA mutation is a permanent change in the master blueprint of a cell. Because DNA is the permanent record stored in your cells, a mutation here is like a permanent error in an instruction manual.

- **Ancestry vs. Environment:** The study found that a person's African genetic ancestry did not change the way the cancer mutated. This suggests that the higher death rates seen in Black women may be driven more by social factors (like access to healthcare) rather than a unique "Black cancer biology."

2. Key Genetic "Drivers"

While the cancers are mostly similar, researchers found a few specific patterns in the tumors of Black women:

- **The TP53 Gene:** Almost every tumor (95%) had a mutation in a gene called *TP53*. This gene normally acts like a "brake" to stop cancer from growing; when it's broken, the cancer grows quickly.

- **The PIK3CA Gene:** Mutations in this specific gene were much **less common** in Black women compared to White or Asian women. This is important because there are specific drugs designed to target this gene.

3. Subtypes and Survival

The researchers identified different "signatures" or patterns in the DNA that can help predict how the cancer will behave:

- **The "HRD" Signature:** About half of the women had tumors with a "scar" in their DNA called Homologous Recombination Deficiency (HRD). Patients with this signature actually had **better survival rates**, likely because these tumors are more sensitive to chemotherapy.
- **The "Aging" Signature:** Patients whose tumors showed patterns related to aging and high BMI (body mass index) tended to have a more difficult prognosis.

4. Treatment Opportunities

The study found that many tumors in Black women actually have "weak spots" that could be treated with existing therapies:

- **Chemotherapy:** About **70%** of the tumors showed signs (like the HRD signature) that they would respond well to standard chemotherapy.
- **Targeted Therapy:** Over **50%** of the patients had a specific genetic "mistake" that could potentially be treated with modern targeted drugs or included in clinical trials.

Why Does This Matter to You?

This study proves that Black women have been left out of genetic research for too long. By mapping these tumors, doctors can better understand which treatments—like chemotherapy or newer "targeted" drugs—will work best for Black patients. It also reinforces that the disparities we see in cancer outcomes are likely not caused by "different" genes, but by the need for better access to the high-quality care that these genetic findings support. Ask for genetic testing and the opportunity to participate in clinical trials.