Charting genetic differences in breast can improve care for underserved populations

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A study comparing DNA and RNA data from Nigerian breast cancer patients to patients in a United States database found that certain aggressive molecular features were far more prevalent in tumors from Nigerian women than in black or white American women.

In the Oct. 9, 2018 issue of *Nature Communications*, the study's authors say those differences in multiple molecular features could potentially explain disparities in breast cancer mortality for women from Nigeria, and perhaps other West African nations.

"We think our data provide insights that could make a significant difference," said study author Olufunmilayo Olopade, MD, the Walter L. Palmer Distinguished Service Professor of Medicine and Human Genetics, associate dean for Global Health and director of the Center for Clinical Cancer Genetics at the University of Chicago Medicine.

"Understanding the molecular mechanisms that trigger these lethal breast cancers," she added, "is a crucial first step toward intervention."

The study, "Characterization of Nigerian breast cancer reveals prevalent homologous recombination deficiency and aggressive molecular features," compares genomic data from 1,037 U.S. patients, provided by The Cancer Genome Atlas (TCGA), to genomic data from 194 Nigerian women with breast cancer. The researchers found multiple, often unexpected, genetic differences between the racial and ethnic groups.

Although the Nigerian patients in the study were on average, much younger, they had more advanced disease at diagnosis and higher mortality rates than women from the TCGA group, most of whom were of European heritage.

The researchers identified 25 different genes from Nigerian patients that were significantly mutated. Aggressive features found in these women include the inability to repair damaged DNA—a mutational process known as homologous recombination deficiency (HRD).

One of the most frequently mutated genes was the tumor-suppressor gene TP53. Sixty-two percent of the African women in the study had TP53 alterations, compared to 46 percent of African-Americans with breast cancer and 29 percent of the TCGA group, primarily U.S. women of European ancestry.

Overall, younger Nigerian patients had more mutations in TP53, and in GATA3, which is associated with estrogen receptors, than black patients from the TCGA. White TCGA patients had fewer mutations than black TCGA patients.

They also found significant cancer-related mutations in three genes that had not been previously associated with breast cancer: PLK2, KDM6A and B2M. (A fourth gene was identified after the current study was under review.) PLK2 is a presumed tumor suppressor. KDM6A is frequently mutated in other cancers, and B2M inactivation has been associated with lung cancer.

Tumors from Nigerian women were frequently characterized by "molecular features of aggressive disease," said co-senior author Jordi Barretina, Ph.D., formerly at the Novartis Institutes for Biomedical Research in Massachusetts, now the Director of the Girona Biomedical Research Institute in Spain. "The most prominent was the prevalence of

homologous recombination deficiency."

The study, according to the authors, "lays the foundation for a more concerted effort to reduce disparities in cancer outcomes by first closing the knowledge gaps. Nigerian women," they add, "could benefit from increased access to genomically-tailored treatments."

In a related commentary, published Oct. 8, in *Cancer Cell*, Olopade, Jason Pitt (now at the National University of Singapore), and Yonglan Zheng from the University of Chicago add that "it is now time to develop interventions that promote health equity. Broad access to genomic analysis coupled with improved availability of effective evidence-based treatment and innovative clinical trials have the potential to close widespread mortality gaps."

More information: Jason J. Pitt et al, Characterization of Nigerian breast cancer reveals prevalent homologous recombination deficiency and aggressive molecular features, *Nature Communications* (2018). DOI: 10.1038/s41467-018-06616-0

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