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A Growing Identity for Adolescent & Young Adult Oncology

BY ANNA R.K. FRANKLIN, MD

Erikson's theory of psychosocial development frames each stage by a crisis that is addressed. The crisis of adolescence is "identity versus role confusion" and is preceded by the childhood struggle of "industry versus inferiority." The field of adolescent and young adult (AYA) oncology has demonstrated competence and is in the midst of creating its own identity.

In 2005-2006, a Progress Review Group (PRG) on AYA oncology was co-sponsored by NCI and LIVESTRONG, which many consider the solidification of the field of AYA oncology. When Karen Albritton, MD, and Michael Caligiuri, MD, (co-chairs of the PRG) presented the PRG findings to the NCI leadership, repeatedly they were asked "Where is the data?" Ten years in, experts in the field of AYA oncology have demonstrated competence through the industrious review

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Shortcomings of Self-Reported Ethnicity in Breast Cancer

CME Article

BY KURT SAMSON

Asking women about their race and ethnicity to better gauge their risk of developing triple negative breast cancer (TNBC) may yield inaccurate results, according to a comparison of patient responses against their mitochondrial DNA (mtDNA).

Researchers at the UT Southwestern Medical Center, Dallas, screened 92 African-American, Caucasian, and Hispanic women and found that 13 percent had different heritage than they self-reported. Moreover, many women were unaware this could influence their risk of TNBC (*Cancer* 2016; DOI:10.1002/cncr.30267).

The study is believed to be the first to use mtDNA screening to evaluate the accuracy of self-reported ancestry in TNBC.

A total of 31 self-described African-American, 31 Caucasian, and 30 Hispanic

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Novel Mechanism In Drug Combination Shows Potential for Treating Leukemia

Researchers have discovered a novel mechanism in a combination drug therapy that shows potential as a new approach for treating acute myeloid leukemia (AML) and many other cancers. When combined, these agents cause interactions that significantly disrupt cancer cells' ability to survive DNA damage, according to a preclinical study published in *Cancer Cell* (DOI: http://dx.doi.org/10.1016/j.ccell.2016.09.002).

The study looked at a combination of two drugs, both of which significantly reduce some cancer cells' ability to survive and propagate. One was a DNA methyltransferase (DNMT) inhibitor, while the other was a poly(ADP-ribose) polymerase (PARP) inhibitor, talazoparib. PARP inhibitors target and block proteins, which cancer cells depend on to repair DNA for their survival. DMNT inhibitors, such as 5-azacytidine and decitabine, boost the interactions of PARP inhibitors to block these proteins even further, causing cancer cell death, the researchers found.

"Our preclinical data suggest that combining low doses of these inhibitors will enhance the clinical effects of both drugs as a potential treatment for patients with AML," said the senior author, Feyruz V. Rassool, PhD, Associate Professor of Radiation Oncology at the University of Maryland School of Medicine (UM SOM) and a researcher at the University of Maryland Marlene and Stewart Greenebaum Comprehensive Cancer Center (UMGCCC).

"Moreover, our initial data suggest that subtypes of AML with a poor prognosis are likely to be sensitive to this new therapeutic approach," she

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TNBC patients submitted mtDNA for analysis using a standard cheek swab. Among Hispanic women, 22 had no family history of breast cancer.

The greatest discordance (26%) was among self-described Hispanic patients. Three of these had Nigerian ancestry and one individual was of Ashkenazi Jewish descent. Hispanic patients were younger and had the largest tumor sizes, at 41 years and 4.5 cm, respectively.

That Hispanic patients were younger is troubling, the authors said, because breast cancer screening guidelines generally do not advise testing before age 50. Moreover, Hispanic women were also less likely to have a family history of breast cancer.

Haplogroups A, U, H, or B were the most common patterns associated with TNBC overall. Among Caucasian women, the H, U, and K haplogroups represented 65 percent of cases.

Eight patients were BRCA carriers, including five Hispanic women, two African-Americans, and one Caucasian. No between-group differences were observed in surgery, lymph node metastases, or survival.

Among African-American subjects in the study, 71 percent were of Nigerian, Cameroon, or Sierra Leone ancestry.

Self-described ethnicity did not correlate with oncologic outcome. Among 11 patients who died from breast cancer or were alive but had metastases at the time of last follow-up, 27 percent had Nigerian ancestry. This suggests they may have a more aggressive clinical course of TNBC with this mtDNA pattern, according to the researchers.

Larger Studies Needed

TNBC is characterized by tumors that do not express receptors for estrogen, progesterone, or HER2-neu and accounts for 15-20 percent of all breast cancers. TNBC is very aggressive and challenging to treat, and patients have a higher incidence of metastatic disease and an overall higher rate of death compared to women with other types of breast cancer.

Research has shown ethnicity may be related to response to neoadjuvant chemotherapy, as well as risk for toxicity from different chemotherapy regimens, in patients with TNBC. These individuals tend to be younger and more likely to be African-American or Hispanic. They also are less likely to be identified through traditional mammography screenings, which tend to target women 50 and older.

Ancestry from specific African countries may predispose women toward an increased risk of TNBC that does not respond to standard breast cancer therapies, such as tamoxifen, aromatase inhibitors, or trastuzumab, according to lead author Roshni Rao, MD, Associate Professor of Surgery and Director of the Harold C. Simmons Comprehensive Cancer Center.

"This type of assessment has the potential to be informative for other cancers where we see ethnic differences in frequency without understanding the cause," She said.

An estimated 10-30 percent of Americans may not be aware of their mixed ancestry, according to Rao.

"Because the cost of mtDNA screening is falling, it might be possible in the future to use such testing to better identify and stratify at-risk women. I think at some point the price of mtDNA testing will become more reasonable. Not long ago such tests cost around $1,000, but it has come down significantly in recent years. The price is certainly going in that direction, and I think at some point testing could become part of the standard workup for women."

This will be most beneficial for Hispanic women, where there was the most discordance between self-reported and actual ethnic origin, according to Rao.

"If you know your ancestry, then you could be included in the group that gets screened at a younger age," she said. "These results suggest further genetic testing can potentially become an important step in identifying those at risk."

An unexpected finding was that TNBC was strongly linked to Nigerian, Cameroon, and Sierra Leone ancestry, which might indicate that specific African countries may predispose women toward increased risk.

Rao said additional research to identify and validate the impact of mtDNA variation and its association with TNBC might help to more personalize risk assessment and allow for specific clinical recommendations for such women. It could also potentially help in developing ethnically tailored therapeutic interventions.

Additional studies identifying and validating variation in mtDNA in TNBC might help personalize risk assessment and allow development of specific clinical recommendations, as well as help develop ethnically tailored interventions to improve outcomes, according to the report.

"I expected some rate of discordance, perhaps in the 3-5 percent range, but what we found was surprising, especially among Hispanic women," Rao said.

"We are hopeful similar studies will be conducted in other locations. We have had a lot of interest from other institutions, especially those in areas with high minority populations such as New York and California. This is very important to either prove or disprove our findings about the rate of discordance."

African Studies

Rao noted that a large population sample of blood from African women, being conducted by other groups, should also help shed light on mtDNA in women from different parts of the continent to compare with TNBC incidence there and among African-American women.

Ruth O'Regan, MD, Division Head for Hematology and Oncology at the University of Wisconsin School of Medicine and Public Health in Madison, said that while there is interest in doing large TNBC studies in Africa, in two studies that have been conducted to date, one showed an increased risk of TNBC and the other did not.

The new findings help demonstrate the inherent shortcomings in self-reporting, and while the results show mtDNA screening has the potential to more accurately identify ethnicity, it may be some time before it becomes used as a screening tool, O'Regan told *Oncology Times*.

"This was a small series, but it is the first to compare mtDNA with self-reported ethnicity," she said. "I think we are eventually going to see more early screening of women from high-risk ethnic populations, but the cost of mtDNA testing may not be justified at this stage. I don't think that we'll be doing it within the next few years, but perhaps in the future."

Even with multiple different risk factors, it still comes down ancestry, O'Regan added.

"This research potentially breaks down barriers in multiethnicity in triple negative breast cancer, but if you have African-American or Hispanic ancestry, there is still a question of exactly how much higher is your risk of TNBC given other factors." OT

Kurt Samson is a contributing writer.

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Learning Objective for This Month's CME Activity: After participating in this CME activity, readers should be better able to identify the inherent shortcomings of self-reported ethnicity in triple negative breast cancer screening.