

Manufacturing Practice) guidelines. Unable to use the previous T-cell bank, Crawford and Haque collaborated with colleagues at the Scottish National Blood Transfusion Services Centre in Aberdeen, where a clinical GMP-grade EBV-specific T-cell bank has been established. The bank is now operational, Haque said.

“Anyone from any country can apply to the bank for cells.”

Such a T-cell immunotherapy approach also can be used to treat EBV-related disorders that are not transplant related, Haque said, who recalled a young girl who developed an EBV lymphoma in her brain. She was treated with

EBV-specific CTLs from the bank while she waited for a matched bone marrow donor. “An off-the-shelf drug would be great.”

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Study Finds Black Women Have Denser Breast Tissue Than White Women

By Sue Rochman

A study using a new tool to measure mammographic density found that black women have denser breast tissue than white women. The findings add to the research on breast density, cancer disparities, and risk-based screening.

Breast density refers to the amount of fibroglandular tissue in the breast when observed on a mammogram. Dense breast tissue shows up white on a mammogram, as do cancer cells, making it difficult for the radiologist to spot a tumor. About half of all women who have screening mammography are found to have dense breast tissue. About 40% of these women have heterogeneously dense breast tissue and about 10% have extremely dense breast tissue.

Breast density also serves as an independent predictor of breast cancer risk. Women with heterogeneously dense breast tissue have about a 1.2 times greater risk of developing breast cancer than that of women with average breast density. Women with extremely dense breast tissue have about twice the risk.

Studies comparing breast density between black women and white women have had mixed results. For the new study, researchers quantified breast density on mammography images from 1,589 black women and 1,256 white women by using a validated, publicly available, automated software algorithm called LIBRA (Laboratory for Individualized Breast Radiodensity Measurement) developed at the University of Pennsylvania. (<http://www.cbica.upenn.edu/sbia/software/LIBRA/>) The analysis controlled for other known breast cancer risk factors, including body mass index, prior biopsy, age at menarche, menopause status, family

history, age at first birth, and use of menopausal hormone therapy.

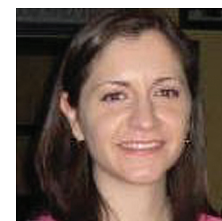
Black women had statistically significantly higher absolute breast area density (40.1cm²) than white women

“We hope that it will inform more research exploring to what extent breast density mediates breast cancer risk and breast cancer outcomes. If we do find there are racial differences in density and that these differences are associated with differences in risk or outcome, then there are implications for who needs supplemental screening.”

(33.1cm²). Black women also had statistically significantly higher volumetric density (263.1cm³) than white women (181.6cm³). The findings were presented in April in a poster session at the 2015 annual meeting of the American Association for Cancer Research in Philadelphia.

“We know that it’s harder to see a tumor on mammography in women with dense breasts, but we don’t know

the underlying biology that causes women with high density to be at higher risk for breast cancer,” said Anne Marie McCarthy, Ph.D., research fellow at



Anne Marie McCarthy, Ph.D.

Massachusetts General Hospital in Boston, who presented the study. “We want to get a better sense of the underlying biology of density and how we can

perhaps use a better measurement for breast density to predict breast cancer risk.”

Lisa Newman, M.D., surgical oncologist and director of the Breast Care Center at the University of Michigan Comprehensive Cancer Center in Ann Arbor, studies breast cancer in black women in the United States and in Ghana, Africa. Newman called the findings thought-provoking, noting the paucity of data on mammographic patterns in large cohorts of black and white U.S. women. Newman also said that additional studies would need to replicate the findings in other patient populations before the results could be generalized to black women in this country and internationally.

The American Cancer Society estimates that 231,840 women will be diagnosed with—and 40,290 will die of—breast cancer this year. Studies have found that in women older than 45 years, black women have a lower incidence of breast cancer but a higher mortality. The overall 5-year relative survival rate for breast cancer diagnosed between 2002 and 2008 was

90% for white women and 78% for black women. In women younger than 45 years, both incidence and mortality from breast cancer are higher in black women than in white women. Black women also are more likely to be diagnosed with an advanced-stage tumor, a factor in their lower overall survival. However, stage for stage, survival is lower for black women than white women.

Researchers are studying how social and economic factors contribute to these disparities. Those factors include access to mammographic screening and quality health care, as well as reproductive patterns, such as age at menarche, age at first birth, and breastfeeding. They also are looking at how reproductive, environmental, and genetic factors may contribute to biological variations in breast tumors found in black women and white women. Black women are more likely than white women to be diagnosed with tumors that have a higher grade and are not hormone sensitive. Black women also are at higher risk than white women of being diagnosed with a triple-negative or basal-like

breast tumor, subtypes that tend to be more aggressive.

Determining the basis for these disparities is not easy. Racial identities are not discrete categories but rather social constructs. In cancer research, Newman said, “race often acts as a surrogate for characteristics that are more prevalent among minority populations, such as poverty and suboptimal nutrition or dietary habits. Because these characteristics are linked to cancer risk, they can also be confounders in studies of cancer disparities.” Newman said genotyping studies now under way “that can quantify extent of geographically defined ancestral background” could yield more insights into race, hereditary risk, and cancer risk.

Breast density research is being fueled, in part, by laws—passed in 22 states to date—requiring doctors to inform women who have mammography screening whether they have dense breast tissue and should consider supplemental screening. However, no evidence-based guidelines exist on what, if any, supplemental screening women with dense breast tissue should have.

“There is an effort to develop risk-based screening guidelines and an attempt to identify the women who may benefit from supplemental or earlier screening,” said Carol Lee, M.D., a diagnostic radiologist at Memorial Sloan-Kettering Cancer Center in New York. “Density is a very complicated issue. Asian women tend to have denser breasts than white women, but they have a lower breast incidence—so regardless of density there are a lot of different factors to what constitutes risk that we still know very little about.”

The software algorithm the researchers used “is validated only for research, so there are no direct clinical applications at this time,” McCarthy said. “We hope that it will inform more research exploring to what extent breast density mediates breast cancer risk and breast cancer outcomes. If we do find there are racial differences in density and that these differences are associated with differences in risk or outcome, then there are implications for who needs supplemental screening.”

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P **PDQ (Physician Data Query)** is the National Cancer Institute’s source of comprehensive cancer information. It contains peer-reviewed, evidence-based cancer information summaries on treatment, supportive care, screening, prevention, genetics, and complementary and alternative medicine. The summaries are regularly updated by six editorial boards. The following PDQ summaries were recently updated:

Couch FJ, Hart SN, Sharma P, et al. Inherited Mutations in 17 Breast Cancer Susceptibility Genes Among a Large Triple-Negative Breast Cancer Cohort Unselected for Family History of Breast Cancer. *J Clin Oncol* 33(4): 304–11, 2015. PMID: 25452441

The **PDQ Genetics of Breast and Gynecologic Cancers** summary was recently updated to include the results of a large study of 1,824 patients with triple-negative breast cancer unselected for family history in which 14.6% of patients were found to have a mutation in an inherited cancer susceptibility gene. BRCA1 mutations accounted for the largest proportion (8.5%), followed by BRCA2 (2.7%); PALB2 (1.2%); and BARD1,

RAD51D, RAD51C and BRIP1 (0.3%–0.5% for each gene). In this study, those with mutations in BRCA1/BRCA2 or other inherited cancer susceptibility genes were diagnosed at an earlier age and had higher grade tumors than those without mutations.

To review the summary, please use the following link:

http://www.cancer.gov/types/breast/hp/breast-ovarian-genetics-pdq/#link/_2448

Kote-Jarai Z, Mikropoulos C, Leongamornlert DA, et al. Prevalence of the HOXB13 G84E germline mutation in British men and correlation with prostate cancer risk, tumour characteristics and clinical outcomes. *Ann Oncol* 26(4):756–61, 2015. PMID: 25595936

The **PDQ Genetics of Prostate Cancer** summary was recently updated to include the results of a case-control study that included 8,652 cases and 5,252 controls and further validated the association of the HOXB13 G84E variant with prostate cancer (OR, 2.93; 95% CI, 1.94–4.59; $P = 6.27 \times 10^{-8}$). The risk was higher among men with a family history and in those with early-onset prostate cancer (diagnosed at age 55 years or younger). No association was found between carrier

status and Gleason score, cancer stage, overall survival, or cancer-specific survival. To review the summary, please use the following link:

http://www.cancer.gov/types/prostate/hp/prostate-genetics-pdq/#link/_1207

Beadles CA, Rianne Wu R, Himmel T, et al.: Providing patient education: impact on quantity and quality of family health history collection. *Fam Cancer* 13(2): 325–32, 2014. PMID: 24515581

The **PDQ Cancer Genetics Risk Assessment and Counseling** summary was recently updated to include a study that demonstrated that patient education improved the completeness of family history collection, which may lead to more-accurate risk stratification, referrals for genetic counseling, and changes to management recommendations.

To review the summary, please use the following link:

http://www.cancer.gov/about-cancer/causes-prevention/genetics/risk-assessment-pdq/#link/_188_toc

The **PDQ Supportive and Palliative Care Editorial Board** recently completed a major update of the Nausea and Vomiting