Review

Cancer Epidemiology, Biomarkers & Prevention

Breast Cancer in Latinas: A Focus on Intrinsic Subtypes Distribution

Silvia J. Serrano-Gómez[1], Laura Fejerman[2], and Jovanny Zabaleta[3,4]

Abstract

Breast cancer is the most frequent cancer in women worldwide. It is classified into intrinsic subtypes characterized by different molecular profiles and prognosis. The prevalence of the different intrinsic subtypes varies between population groups. IHC surrogates based on the expression of the estrogen receptor, progesterone receptor, and HER2 have been widely used to study the distribution of intrinsic subtypes in non-Hispanic whites and African Americans, but data are limited for Hispanic/Latina women. Similarly, most studies analyzing gene expression profiles only include women of European descent. This review focuses on studies that describe the distribution of breast cancer subtypes in Hispanic/Latina women and highlights the need for more research in this population. *Cancer Epidemiol Biomarkers Prev; 27(1); 3–10. ©2017 AACR.*

Introduction

Breast cancer is the most common cancer in women worldwide (1–3). In the United States, it accounts for 29% of all cancer cases diagnosed and 15% of all cancer-related deaths reported annually (1, 3, 4).

There are notable differences in breast cancer incidence and mortality between populations in the United States. Data from the Surveillance, Epidemiology and End Results Program (SEER) showed that the age-adjusted incidence for non-Hispanic white (NHW) women was 128.0, 125.2 for African Americans (AAs), 92.4 for Hispanic/Latinas, 97.3 for Asian/Pacific Islanders (APIs), and 81.2 for Native Americans/Alaskan Natives (5). Despite the relatively low incidence of breast cancer in Hispanic/Latinas, their risk of mortality is higher than in NHWs [HR = 1.4; 95% confidence interval (CI), 1.3–1.5], even after adjustment for tumor characteristics and treatment (HR = 1.1; 95% CI, 1.0–1.2; refs. 1, 6–8).

The reason for the differences in the mortality rates between population groups is still not fully understood. Some researchers propose that differences in socioeconomic and cultural factors limit health care and treatment access, contributing to increased mortality rates in Hispanic/Latinas and AA women (9). However, other studies reported that the observed differences remained significant after adjustment for access to health care, treatment, and other sociodemographic factors (10–13). A better understanding of the similarities and differences in the biological characteristics of breast tumors between racial/ethnic groups, with consideration of variation in ancestral genetic ancestry contributions, could provide important insights into observed differences in outcome. We provide a description of published studies on the distribution of breast cancer intrinsic subtypes and molecular profiles in Hispanic/Latina women and highlight the need for more research in this population.

Materials and Methods

Eligible studies

All studies originally published in English and confirmed as focused on tumor subtype characterization in Hispanics/Latinas were included in this review.

Publication search

We searched the published literature using PubMed (NIH, Bethesda, MD). To identify studies we queried medical subject headings (MeSH): "breast cancer subtypes" and "Latinas" that retrieved 29 publications, from which 8 were included in this paper. We also searched for "breast cancer intrinsic subtypes" and "Hispanic," and this search retrieved 62 papers, from which 19 were eligible for this review; 8 of them were already included from the last search. Finally, we used "breast cancer subtypes distribution" and "Hispanic," and we found 59 publications, from which 4 were included in this paper. The last search was on July 11, 2017. All resulted studies were retrieved, and cited publications were checked for related publications. We limited our electronic search to original English-language publications and published since 2007 to include only studies from the last 10 years.

Definition of breast cancer intrinsic subtypes

In 2000, Perou and colleagues (14) published the first article classifying breast cancer into intrinsic subtypes based on gene expression profiles. Using a cDNA microarray of 65 surgical specimens from 42 different individuals, Perou and colleagues defined a list of "intrinsic" genes that have consistent expression in tumors from the same patient (i.e., primary and metastasis) but differ between tumors from different patients. This analysis revealed 4 main molecular subtypes: luminal, HER2-enriched,

[1]Grupo de investigación en Biología del Cáncer, Instituto Nacional de Cancerología, Bogotá, D.C., Colombia. [2]Department of Medicine, University of California San Francisco, San Francisco, California. [3]Stanley S. Scott Cancer Center, LSUHSC, New Orleans, Louisiana. [4]Department of Pediatrics, LSUHSC, New Orleans, Louisiana.

Note: L. Fejerman and J. Zabaleta contributed equally to this work.

Corresponding Author: Silvia J. Serrano-Gómez, Instituto Nacional de Cancerología, Calle 1a #9-45, Bogotá, D.C. 11001000, Colombia. Phone: 5730-1271-0656; Fax: 571-432-0160; E-mail: silviajserrano@gmail.com

doi: 10.1158/1055-9965.EPI-17-0420

basal-like, and normal-like. ER^+ tumors, identified as luminal, are characterized by increased expression of genes from luminal cells, such as *GATA, X-box binding protein 1*, *trefoil factor 3*, and *hepatocyte nuclear factor* (15). The luminal group is, in turn, divided into luminal A and B subtypes, with the luminal B expressing higher levels of proliferation-related genes and often expressing *HER1*, *HER2*, and/or *cyclin E1*, whereas luminal A subtype have a higher expression of genes such as the *estrogen receptor gene (ESR1)* and *GATA3* (16–19). The estrogen receptor-negative (ER^-) group is divided into basal-like, HER2-enriched, and normal-like. The basal-like subgroup is characterized by expression of basement membrane cytokeratins such as *CK5/6* and *CK17*; and lacks the expression of *ESR1* and its coexpressed genes. Patients with *BRCA1* mutations have been associated with the development of basal-like tumors (20–22). The HER2-enriched subtype is associated with high expression of *ERBB2* and genes in the 17q22.24 locus including *GRB7* and *MIEN1* (23–26). The normal-like subtype is still a matter of debate as some researchers have considered it as an artifact due to contamination with normal tissue adjacent to the tumor (27). Its molecular profile is characterized by the expression of genes typical of basal epithelial cells and adipose cells and low expression of genes from luminal epithelial cells (14, 28, 29).

The clinical implication of this new classification became apparent 1 year later when the same group, using a larger set of tumors, demonstrated that each of the intrinsic subtypes was associated with different prognoses (14, 29, 30). The HER2-enriched and basal-like subtypes have the poorest prognosis when compared to the luminal subtypes. Among luminal tumors, the luminal B has worst prognosis compared with luminal A, which is expected given its high expression of cell proliferation genes (31–36).

Breast cancer in Hispanic/Latina women

The terms "Hispanic" or "Latino" are generally used to refer to people from Mexico, Cuba, Puerto Rico, Central or South America. Latinos constitute the largest, youngest, and fastest-growing minority group in the United States (37). An estimated 55 million people living in the United States self-identified as Hispanic or Latino (38), representing 17% of the total population in United States in 2014, and predicted to increase to 35% by the year 2050 (39). Hispanic/Latinos is a heterogeneous group that originated from the admixture of Native American, European, and African ancestries. Hispanic/Latinos can self-identify as any race defined by the 2000 United States Census (37, 38, 40, 41).

Fejerman and colleagues (42) showed the first evidence of association between genetic ancestry and breast cancer risk in Hispanic/Latinas from the San Francisco Bay area. They found an increased risk of breast cancer for every 25% increase in European ancestry (OR = 1.79; 95% CI, 1.28–2.79) that remained significant after adjusting for known risk factors for the disease (OR = 1.39; 95% CI, 1.06–2.11). Two years later they retested the association in women from Mexico to explore the possibility that the original finding was due to environmental factors. In this population, they replicated the original association finding that for every 25% increase in European ancestry (modeled as a continuous variable), there was a 20% increase in breast cancer risk (95% CI, 1.03–1.41; ref. 43). Fejerman and colleagues (41) also showed that genetic ancestry was associated with breast cancer-specific survival in a sample of Hispanic/Latinas from California. Women with more than 50% Native American ancestry had a mortality hazard that almost doubled that of Hispanic/Latinas with 50% or less of Native American ancestry.

Recently, a population-based study using SEER registries found an increase in the risk of breast cancer mortality in Hispanic/Latina women (44, 45). Ooi and colleagues (8), also based on SEER data, found that Hispanic/Latina women have 1.1-fold greater risk of breast cancer-specific mortality compared to NHW women after adjusting for disease characteristics, treatments, and some socioeconomics characteristics such as poverty and education (8).

Differences in mortality among population groups might be explained by a combination of differences in socioeconomic and biological factors (46). For example, Hispanic/Latinas are usually diagnosed at more advanced stages of the disease, possibly as a consequence of poor access to mammography screening and delayed follow-up of an abnormal mammography (44, 45). Additionally, some studies have suggested that differences in language spoken, cultural beliefs, and other factors contribute to inconsistencies in the screening and follow up of an abnormal mammogram even in populations with similar access to screening (47–49). Regarding biological factors, population-based studies in the United States have reported that Hispanic/Latina women are more likely to have ER^- tumors, compared with NHW women (50, 51), similar to what has been reported for AA women (44).

Distribution of intrinsic subtypes of breast cancer in Hispanic/Latina women

Different available surrogates for molecular classification of breast cancer into intrinsic subtypes have been proposed (Table 1). The basic and most used classification includes the evaluation of hormone receptors (HR) ER and progesterone receptor (PR) and the evaluation of HER2 by IHC. The St. Gallen surrogates included Ki67 to better stratify luminal tumors.

The prevalence of breast cancer intrinsic subtypes varies according to race/ethnicity (Table 2). There have been multiple studies evaluating the distribution of IHC-based tumor subtypes in Hispanic/Latinas using population-based registries from SEER (52, 53). These studies report a higher prevalence of triple negative tumors in Hispanic/Latinas compared to NHW women, with percentages in Hispanic/Latinas ranging between 14% and 15% depending on the study. Using polytomous logistic regression modeling, the $HR^+/HER2^-$ as the reference subtype, and NHW as the reference explanatory variable (52), they have also

Table 1. Available surrogates for molecular classification of breast cancer

	Definitions		
Intrinsic subtype	**HR and HER2**	**St. Gallen 2011**	**St. Gallen 2013**
Luminal A	ER^+ and/or PR^+, $HER2^-$	ER^+, $HER2^-$, Ki67 <14%	ER^+, PR>20%, $HER2^-$, Ki67<20%
Luminal B	ER^+ and/or PR^+, $HER2^+$	ER^+, $HER2^+$, Ki67>14%	ER^+, $HER2^-$ and/or PR < 20% or Ki67 > 20% ER^+, $HER2^+$
HER2-enriched	ER^-, PR^-, $HER2^+$	ER^-, PR^-, $HER2^+$	ER^-, PR^-, $HER2^+$
Triple negative	ER^-, PR^-, $HER2^-$	ER^-, PR^-, $HER2^-$	ER^-, PR^-, $HER2^-$

Table 2. Prevalence of breast cancer intrinsic subtypes in different populations

				Prevalence of breast cancer intrinsic subtypes			
Race/ethnicity	**Reference**	**Source**	**Subtypes definition**	**Luminal A**	**Luminal B**	**HER2-enriched**	**Triple negative**
NHW	Plasilova (58)	The National Cancer Database (NCDB)	HR and HER2	74.80%	9.70%	4.10%	11.40%
AA				59.60%	11%	5.60%	23.70%
API				70.10%	11.70%	6.90%	11.20%
US Latinas				67.40%	11.90%	5.80%	14.80%
Other/Unknown				71.80%	11.00%	5.10%	12.10%
NHW	Sineshaw (59)	The National Cancer Database (NCDB)	HR and HER2	66.80%	8.90%	3.80%	10.20%
AA				51.70%	10.00%	5.00%	21.10%
API				63.50%	10.60%	6.10%	10.10%
US Latinas				58.20%	10.60%	5.20%	13.10%
Other/Unknown				57.30%	10.40%	4.90%	11.00%
NHW	Kurian (55)	California Cancer Registry	HR and HER2	71.60%		16.90%	11.50%
AA				53.00%		22.40%	24.60%
API				62.80%		27.20%	10.00%
US Latinas				59.30%		24.00%	16.70%
NHW	Howlader (52)	SEER registries	HR and HER2	75.50%	9.80%	4.00%	10.70%
AA				60.20%	11.40%	6.00%	22.50%
API				71.10%	12.30%	6.90%	9.70%
US Latinas				68.20%	11.40%	5.70%	14.70%
NHW	Chen (53)	SEER registries	HR and HER2	76%	9.40%	3.90%	10.70%
AA				60.70%	10.90%	5.70%	22.60%
API				71.80%	11.90%	6.60%	9.70%
American Indian/ Alaska Native				71.40%	12.10%	4.70%	11.90%
US Latinas				68.70%	11.60%	5.70%	14%
US Latinas	Banegas (51)	California Cancer Registry	HR and HER2	62.60%	13.80%	8.10%	15.60%
NHW	Clarke (56)	California Cancer Registry	HR and HER2	62%	9%	4%	9%
AA				47%	11%	6%	20%
API				55%	12%	8%	9%
US Latinas				52%	11%	7%	13%
NHW	Singh (64)	Hospital-based	HR and HER2	76,50%	8,80%	4,90%	9,80%
AA				58,90%	11,40%	6,80%	22,80%
US Latinas				59,00%	11,80%	9,50%	19,70%
Chinese				65,60%	9,60%	10,50%	14,30%
Indian				50,10%	12,20%	14,30%	23,30%
NHW	Hines (60, 85)	4-Corners Breast Cancer Study	HR and HER2	70.60%	8.40%	5.90%	15.10%
US Latinas				50.70%	17.30%	14.50%	17.40%
NHW	Kwan (63)	The Life After Cancer Epidemiology (LACE) study	HR and HER2	75.30%	11.10%	3.10%	10.50%
AA				59.40%	9.00%	3.20%	28.40%
API				71.40%	15.90%	6.40%	6.30%
US Latinas				68.50%	14.20%	6.60%	10.70%
Other				68.50%	13.00%	5.50%	13.00%
NHW	Kroenke (61)	The Life After Cancer Epidemiology (LACE) study and Pathway study	HR and HER2	52.00%	32.90%	3.90%	11.00%
AA				31.40%	34.40%	4.50%	29.70%
API				47.70%	36.80%	6.60%	8.90%
US Latinas				45.50%	35.80%	4.70%	14.00%
Other				39.30%	39.70%	4.00%	17.10%
NHW	Sweeney (62)	The Life After Cancer Epidemiology (LACE) study and Pathway study	PAM50	55.20%	20.90%	12.50%	8.20%
AA				43.20%	8.70%	11.60%	30.40%
API				55.20%	21.50%	12.40%	5.00%
US Latinas				44.20%	24.00%	15.60%	11.60%
Latinas from Mexico	Lara-medina (65)	National Cancer Institute in Mexico	HR and HER2		76,90%		23,10%
Latinas from Costa Rica	Srur-Rivero (67)	Hospital-based Costa Rica	HR and HER2	62.30%	9,00%	9.50%	17.10%
Latinas from Brazil	de Macêdo Andrade (68)	Hospital-based Brazil	St Gallen 2011	23.79%	44.61%	14.50%	17.10%
Latinas from Puerto Rico	Ortiz (70)	Hospital-based Puerto Rico	HR and HER2	61.80%	13.30%	7.50%	17.30%
Latinas from Colombia	Serrano-Gómez (71)	National Cancer Institute in Colombia	HR and HER2	52.49%	15.95%	10.30%	20.60%
			St Gallen 2011	36.21%	30.23%	8.64%	20.60%
			St Gallen 2013	26.25%	37.21%	8.64%	20.60%
Latinas from Colombia	Gómez (74)	Hospital-based Colombia	St Gallen 2011	22.30%	56.40%	9.10%	12.20%
Latinas from Mexico	Martinez (66)	Clinical-based	HR and HER2	59.80%		23.60%	16.60%
Latinas from Peru	Vallejos (75)	Hospital-based Peru	HR and HER2	49.3%	13.20%	16.2%	21.3%

Abbreviations: NHW: Non-Hispanic white; AA: African American; API: Asian-Pacific Islander.

reported a higher risk of developing triple negative tumors and $HR^-/HER2^+$ tumors among Hispanic/Latinas (OR = 1.3; 95% CI, 1.2–1.5 and OR = 1.4; 95% CI, 1.2–1.6, respectively).

Similar results have been observed in studies that used data from the California Cancer Registry (CCR; refs. 51, 54–56). The prevalence of triple negative subtype in these studies ranged between 13% and 17%. Concordant with previous reports, some of these studies also observed that Hispanic/Latina women were more likely to be diagnosed with triple negative disease (OR = 1.23; 95% CI, 1.14–1.34) when compared to NHW (54). Banegas and colleagues (51) used data from the CCR and analyzed the association between breast cancer subtype and patients attributes and found that foreign-born Hispanic/Latina women were significantly more likely than U.S.-born Hispanic/Latina women to be diagnosed with $HR^-/HER2^+$ subtype (OR = 1.17; 95% CI, 1.02–1.35). Moreover, lower socioeconomic status (SES) was also associated with a higher risk for triple negative and $HR^-/HER2^+$ subtypes. Even though this study included a large number of Hispanic/Latina women, they were all residents of California and therefore mostly of Mexican descent (51, 57). This result cannot be generalized to all Hispano/Latino subpopulations.

Plasilova and colleagues (58) used The National Cancer Database (NCDB) to analyze the characteristics of 38,813 breast tumors defined by the expression of HR and HER2 in women diagnosed between 2010 and 2011. They observed that among Hispanic/Latina women, the luminal A subtype was the most prevalent (67.4%) followed by triple negative (14.8%), luminal B (11.9%), and HER2-enriched (5.8%). Sineshaw and colleagues (59) also used the NCDB data. They analyzed 260,174 breast cancer cases from that database and found that the prevalence of triple negative subtype in Hispanic/Latina was 13.8%. This latter analysis showed that Hispanic/Latina women had 1.26 times greater odds of being diagnosed with HER2-enriched subtype (OR = 1.26; 95% CI, 1.16–1.37) and 1.17 times greater odds of being diagnosed with triple negative subtype (OR = 1.17; 95% CI, 1.11–1.24) using NHWs as reference population and the luminal A subtype as reference subtype.

Population-based studies such as The Life After Cancer Epidemiology (LACE) study and the 4-Corners Breast Cancer Study are valuable sources to explore ethnic differences in the distribution of breast cancer subtypes. Hines and colleagues (60) reviewed pathology reports and established tissue microarrays in a sample of 188 women (69 Hispanic/Latina women and 119 NHW women) who were Colorado participants in the 4-Corners Breast Cancer Study. Five immunohistochemically markers (ER, PR, HER2, EGFR, and CK5/6) were evaluated using standard IHC staining methods. They also found that Hispanic/Latina women had a higher prevalence of ER^- tumors ($ER^-/PR^+/HER2^+$, $ER^-/PR^+/HER2^-$, ER^-, $PR^-/HER2^+$, $ER^-/PR^-/HER2^-$) compared to NHW women (36.2% vs. 22.7%). Specifically, Hispanic/Latina women were reported to have a higher proportion of triple negative subtype compared to NHW (17.4% and 15.1%, respectively), but this difference was not statistically significant. Kroenke and colleagues (61) analyzed 1,635 breast cancer patients from the Pathways and LACE study and found a higher prevalence of triple-negative subtype (14%) when compared with the prevalence of this subtype in NHW (11.0%).

The study by Sweeney and colleagues (62) is the largest study to date describing the distribution of intrinsic subtypes based on PAM50 classification (27). This study included 1,319 women and observed an increased prevalence of the most aggressive intrinsic subtypes such as HER2-enriched (15.6%) and luminal B (24.0%) in Hispanic/Latina women when compared to women from other races/ethnicities.

Hispanic/Latina women have also been reported to have a relatively high proportion of $HER2^+$ tumors ($ER^+/PR^+/HER2^+$, $ER^+/PR^-/HER2^+$, $ER^-/PR^+/HER2^+$, $ER^-/PR^-/HER2^+$), even after adjustment for tumor characteristics such as grade, stage, ER status, and risk factors such as number of children and alcohol consumption (38). Hines and colleagues (60) observed that Hispanic/Latina women had a significantly higher prevalence of $HER2^+$ tumors ($HR^+/HER2^+$ and $HR^-/HER2^+$) compared with NHWs (31.95% vs. 14.3%, respectively, $P < 0.01$). Specifically they observed a higher prevalence of the HER2-enriched subtype in Hispanic/Latina compared with NHWs (14.5% vs. 5.9%). These results are concordant with those in Kwan and colleagues (63), which included 2,280 women from the LACE study. These women were diagnosed with invasive breast cancer between 1997 and 2000. Breast cancer subtypes were defined by the expression of HR and HER2. They reported that HER2-enriched subtype tumors ($HR^-/HER2^+$) were more common in Hispanic/Latinas (OR = 2.19; 95% CI, 1.16–4.13) and Asians (OR = 2.02; 95% CI, 1.05–3.88) than NHWs. Howlader and colleagues (52) also observed a high prevalence of HER2-enriched tumors but in an early-onset group (11.4%) compared with an older group (6.47%). Banegas and colleagues (51) found that foreign-born Hispanic women were significantly more likely to be diagnosed with $HR^-/HER2^+$ than $HR^+/HER2^-$ breast cancer (OR = 1.17; 95% CI, 1.02–1.35) compared with U.S.-born Hispanic women.

We found one hospital-based study from United States. Singh and colleagues (64) analyzed the distribution of intrinsic subtypes of breast cancer in a sample of 2,120 patients from five major racial/ethnic groups: NHW, AA, and Hispanics/Latinos from the United States, Chinese (Jilin, China), and Indian (Delhi, India), and according to age (early-onset $\leq$40 years and older group $\geq$50 years and older). This study included patient race data from the Memorial Sloan Kettering Cancer Center for AA patients, New York University School of Medicine for NHW patients, The University of Texas MD Anderson Cancer Center for Hispanic/Latino patients, The First Hospital of Jilin University (China) for native Chinese patients, and Rajiv Gandhi Cancer Institute & Research Centre (Delhi, India) for native Indian patients. The IHC data on HR and HER2 was retrieved from each participating study to classify breast cancer into intrinsic subtypes. They found that the prevalence of triple negative breast cancer was higher in Indians (23.3%) followed by AA (22.8%), Hispanic/Latina (19.7%), Chinese (14.3%), and NHW (9.8%). Similar percentages were observed for triple-negative disease in the early onset group (31.57%, 23.15%, 22.77%, 12.2%, and 16.66% respectively, for the same population groups). In the older onset group, the prevalence of triple-negative subtype was higher in AA (22.52%), followed by Indians (21.55) and Hispanic/Latina (14.7%).

Studies in Hispanic/Latina women from Latin American countries

All studies described above had been conducted in individuals born or residing in the United States. However, similar results

have been reported for Hispanic/Latina women in Latin America. All of the studies described below are hospital-based.

Lara-Medina and colleagues (65) analyzed the expression of HR and HER2 by IHC in 2,074 Hispanic/Latino breast cancer patients from the National Cancer Institute in Mexico City and were diagnosed between 1998 and 2008. They reported a high prevalence of triple-negative subtype (23.1%). This percentage is similar to the prevalence reported in AA women (23%–30%), and higher than that in NHW women (10%–13%). This study included 20.4% of patients with a family history of breast cancer and therefore the presence of *BRCA1* mutations could be a contributing factor to the high prevalence of triple-negative tumors reported.

Martinez and colleagues (66) assessed tumor subtype prevalence in 1,041 women of Mexican descent enrolled in a binational breast cancer study. They recruited patients in two hospitals in the United States (The Arizona cancer center and the M.D Anderson Cancer Center); and three in Mexico (the Universidad de Sonora, the Instituto Tecnológico de Sonora and the Universidad de Guadalajara). The prevalence of triple negative subtype was 16.7% overall but a higher proportion of ER^- ($HR^-/HER2^+$ and $HR^-/HER2^-$) tumors was observed for women in Mexico compared with those in the United States.

Srur-Rivero and colleagues (67) analyzed 199 breast cancer patients from the San Juan de Dios Hospital in Costa Rica diagnosed between 2009 and 2010. This hospital is a reference cancer treatment center for Costa Rica's South Central Region. Breast cancer subtypes were defined by the expression of HR and HER2. The median age at diagnosis was 53 years. The prevalence of the triple-negative subtype was 17.4%.

In Brazil, de Macedo Andrade and colleagues (68) evaluated the expression of HR, HER2, and Ki67 following the recommendations of St. Gallen panel from 2011 (69) to assign breast tumors from 633 women into intrinsic subtypes. Data from pathology reports were obtained from the "Fundação de Assistência da Paraíba" (FAP) public hospital of Campina Grande, Paraíba, Brazil. They reported luminal B as the most prevalent subtype (44.61%), followed by luminal A (23.79%), triple negative (17.10%), and HER2-enriched (14.5%). Even though triple-negative intrinsic subtype was found as the third most prevalent, the percentage reported in this study is similar to what has been reported previously in Hispanic/Latina women (51, 60, 65, 67).

Ortiz and colleagues (70) found that the two most prevalent subtypes were luminal A (61.8%) and triple negative (17.3%) in a sample of 663 patients diagnosed with invasive breast cancer between 2002 and 2005 at the I. Gonzalez Martinez Oncologic Hospital and the Auxilio Mutuo Hospital in Puerto Rico.

Several studies have been conducted in Colombia. Our group analyzed the distribution of breast cancer–intrinsic subtypes in 301 patients from the National Cancer Institute in Colombia (INC) diagnosed between 2008 and 2012 (71). The INC has a double role in cancer control in Colombia: (i) It advices the Ministry of Health on all national cancer-related issues (policies, strategies, surveillance for cancer control and prevention); and (ii) it is the National Comprehensive Reference Center for cancer treatment. The mean age at diagnosis was 56.6 years. Using the different surrogates proposed by the St. Gallen panel of experts in 2011 (69) and in 2013 (72), we found that following the recommendations of the St. Gallen 2013 surrogates, the luminal B subtype was the most prevalent (37.2%). Although using the 2011 St. Gallen surrogates the most prevalent subtype was luminal A (36.21%), an enrichment of luminal B was noticed when compared with the basic classification that included the evaluation of HR and HER2 (30.23% vs. 15.95%, respectively). The high prevalence of luminal B subtype is concordant with the findings reported by Macedo Andrade and colleagues (68). We also observed high proportion of triple-negative tumors (20.6%). We found a higher proportion of African ancestry in patients with triple-negative tumors, which is consistent with the literature (11, 19, 46, 73). Gomez and colleagues (74) analyzed the distribution of breast cancer intrinsic subtypes in 328 clinic-based patients from Medellin, Colombia, diagnosed between January 2009 and December 2010. The mean age at diagnosis for this study was 52.9 years. They followed St. Gallen 2011 surrogates (69) and found that the luminal B represented more than 50% of the intrinsic subtypes identified.

In Peru, Vallejos and colleagues (75) analyzed 1,198 breast cancer patients diagnosed between January 1, 2000, and December 21, 2002, in the Instituto Nacional de Enfermedades Neoplásicas in Lima and retrieved the expression of HR and HER2. They observed a high prevalence of more aggressive intrinsic subtypes, such as triple negative (21.3%) and HER2-enriched (16.2%).

Despite the hererogeneity in the reported prevalence of different molecular subtypes among Hispanic/Latina women, most studies suggest a high prevalence of the more aggressive subtypes (i.e., ER^- and luminal B; Table 2). This heterogeneity may be related in part to the differences in the classification methods used, biases associated with clinic/hospital-based studies (as opposed to registry-based studies), and to differences in the genetic ancestry from the Hispanic/Latina women analyzed (76, 77).

Discussion

Hispanic/Latinas represent a heterogeneous population group with variation in European, Indigenous American, and African ancestry proportions (39) as well as lifestyle and environmental exposures.

There are multiple risk factors that have been associated with differences in the distribution of breast cancer–intrinsic subtypes between population groups, including lifestyles and reproductive factors (78–83). Hispanic/Latina women and AA share some of these risk factors, for example, these two population groups tend to have children at an earlier age, have a higher body mass index and have low physical activity, all characteristics previously associated with the risk of developing triple-negative tumors.

The prevalence of breast cancer intrinsic subtypes change according to the age of the patients included in the studies. Different studies have reported that the age at diagnosis of breast cancer in AA is earlier which is also associated with the development of triple-negative tumors. A similar pattern is observed in Hispanic/Latina women, who are diagnosed at a younger age, compared with NHW (50 years vs. 61 years, respectively; refs. 6, 45, 56). Some of the previously mentioned studies analyzed the age at diagnosis in women from different races/ethnicities (52, 53, 56, 60, 64) and found that Hispanic/Latina women were usually diagnosed at younger ages when compared with NHW. When the

prevalence of intrinsic subtypes were analyzed according to age groups and ethnicity, some authors did not find statistical significant difference in the distribution of intrinsic subtypes according to age groups (56, 64). These results suggest that the high prevalence of triple-negative subtype in Hispanic/Latinas is not fully explained by differences in the age groups analyzed in the different studies.

It is important to emphasize that the studies included in this review are based on different sources of information. Some studies are based on data from population registries (51–53, 55, 56, 58–63) and, others are hospital/clinic based (64, 65–68, 70, 71, 74, 75). The population-based studies tend to report lower prevalence of the more aggressive tumors (ranging between 12% and 17%) compared with hospital/clinic-based studies (ranging between 12% and 23%; Table 2), which is to be expected when the hospitals included in the studies are reference centers and therefore tend to receive patients that could not be adequately served by local hospitals/clinics. However, population-based studies show that Hispanic/Latinas have higher prevalence of more aggressive subtypes such as triple-negative and HER2-enriched tumors compared with NHWs (51, 55, 60, 61; Table 2) and, therefore, further research should be conducted to unveil possible behavioral/environmental or genetic factors that might be contributing to this observation.

Increasing evidence has demonstrated differences in gene expression profiles between AA patients compared with non-AA patients (84–87). In fact, gene expression profiles might change according to the ancestral genetic architecture of the individual's genome (88). However, there is a lack of information regarding gene expression profiles in Hispanic/Latinas of different national and ancestral backgrounds. More studies of gene expression including Hispanic/Latino patients are needed to assess possible biological heterogeneity that might be relevant in terms of treatment efficacy and outcome.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: S.J. Serrano-Gómez, L. Fejerman, J. Zabaleta
Development of methodology: J. Zabaleta
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): L. Fejerman
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): S.J. Serrano-Gómez, L. Fejerman, J. Zabaleta
Writing, review, and/or revision of the manuscript: S.J. Serrano-Gómez, L. Fejerman, J. Zabaleta
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): S.J. Serrano-Gómez
Study supervision: L. Fejerman

Received May 18, 2017; revised July 27, 2017; accepted October 16, 2017; published OnlineFirst October 20, 2017.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin 2015;65:5–29.
2. Globocan 2012: Estimated cancer incidence mapwi. Estimated incidence, mortality and 5-year prevalence: women [cited 2015 Feb 19]. Available from: http://globocan.iarc.fr/Pages/fact_sheets_population.aspx.
3. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin 2016;66:7–30.
4. Toriola AT, Colditz GA. Trends in breast cancer incidence and mortality in the United States: implications for prevention. Breast Cancer Res Treat 2013;138:665–73.
5. Surveillance Epidemiology and End Results. 2016 Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database. Available from: http://seer.cancer.gov/statfacts/html/breast.html. Access date May 2017.
6. DeSantis CE, Fedewa SA, Goding Sauer A, Kramer JL, Smith RA, Jemal A. Breast cancer statistics, 2015: convergence of incidence rates between black and white women. CA: Cancer J Clin 2016;66:31–42.
7. Jemal A, Center MM, DeSantis C, Ward EM. Global patterns of cancer incidence and mortality rates and trends. Cancer Epidemiol Biomarkers Prev 2010;19:1893–907.
8. Ooi SL, Martinez ME, Li CI. Disparities in breast cancer characteristics and outcomes by race/ethnicity. Breast Cancer Res Treat 2011;127:729–38.
9. Gerend MA, Pai M. Social determinants of Black-White disparities in breast cancer mortality: a review. Cancer Epidemiol Biomarkers Prev 2008;17:2913–23.
10. Chavez-Macgregor M, Liu S, De Melo-Gagliato D, Chen H, Do KA, Pusztai L, et al. Differences in gene and protein expression and the effects of race/ethnicity on breast cancer subtypes. Cancer Epidemiol Biomarkers Prev 2014;23:316–23.
11. Amend K, Hicks D, Ambrosone CB. Breast cancer in African-American women: differences in tumor biology from European-American women. Cancer Res 2006;66:8327–30.
12. Parise CA, Caggiano V. Disparities in race/ethnicity and socioeconomic status: risk of mortality of breast cancer patients in the California Cancer Registry, 2000–2010. BMC Cancer 2013;13:449–459.
13. Newman LA, Griffith KA, Jatoi I, Simon MS, Crowe JP, Colditz GA. Meta-analysis of survival in African American and white American patients with breast cancer: ethnicity compared with socioeconomic status. J Clin Oncol 2006;24:1342–9.
14. Perou CM, Sorlie T, Eisen MB, van de Rijn M, Jeffrey SS, Rees CA, et al. Molecular portraits of human breast tumours. Nature 2000;406:747–52.
15. Cancer Genome Atlas Network. Comprehensive molecular portraits of human breast tumours. Nature 2012;490:61–70.
16. Creighton CJ. The molecular profile of luminal B breast cancer. Biologics 2012;6:289–97.
17. Cheang MC, Chia SK, Voduc D, Gao D, Leung S, Snider J, et al. Ki67 index, HER2 status, and prognosis of patients with luminal B breast cancer. J Natl Cancer Inst 2009;101:736–50.
18. Tran B, Bedard PL. Luminal-B breast cancer and novel therapeutic targets. Breast Cancer Res 2011;13:221.
19. Carey LA, Perou CM, Livasy CA, Dressler LG, Cowan D, Conway K, et al. Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. JAMA 2006;295:2492–502.
20. Mavaddat N, Barrowdale D, Andrulis IL, Domchek SM, Eccles D, Nevanlinna H, et al. Pathology of breast and ovarian cancers among BRCA1 and BRCA2 mutation carriers: results from the Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA). Cancer Epidemiol Biomarkers Prev 2012;21:134–47.
21. Foulkes WD, Stefansson IM, Chappuis PO, Begin LR, Goffin JR, Wong N, et al. Germline BRCA1 mutations and a basal epithelial phenotype in breast cancer. J Natl Cancer Inst 2003;95:1482–5.
22. Turner NC, Reis-Filho JS. Basal-like breast cancer and the BRCA1 phenotype. Oncogene 2006;25:5846–53.
23. Nadler Y, Gonzalez AM, Camp RL, Rimm DL, Kluger HM, Kluger Y. Growth factor receptor-bound protein-7 (Grb7) as a prognostic marker and therapeutic target in breast cancer. Ann Oncol 2010;21:466–73.
24. Pradip D, Bouzyk M, Dey N, Leyland-Jones B. Dissecting GRB7-mediated signals for proliferation and migration in HER2 overexpressing breast tumor cells: GTP-ase rules. Am J Cancer Res 2013;3:173–95.

25. Vinatzer U, Dampier B, Streubel B, Pacher M, Seewald MJ, Stratowa C, et al. Expression of HER2 and the co-amplified genes GRB7 and MLN64 in human breast cancer: quantitative real-time reverse transcription-PCR as a diagnostic alternative to immunohistochemistry and fluorescence in situ hybridization. Clin Cancer Res 2005;11:8348–57.
26. Kpetemey M, Dasgupta S, Rajendiran S, Das S, Gibbs LD, Shetty P, et al. MIEN1, a novel interactor of Annexin A2, promotes tumor cell migration by enhancing AnxA2 cell surface expression. Mol Cancer 2015;14:156.
27. Parker JS, Mullins M, Cheang MC, Leung S, Voduc D, Vickery T, et al. Supervised risk predictor of breast cancer based on intrinsic subtypes. J Clin Oncol 2009;27:1160–7.
28. Cadoo KA, Traina TA, King TA. Advances in molecular and clinical subtyping of breast cancer and their implications for therapy. Surg Oncol Clin N Am 2013;22:823–40.
29. Sorlie T, Perou CM, Tibshirani R, Aas T, Geisler S, Johnsen H, et al. Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. Proc Natl Acad Sci USA 2001;98:10869–74.
30. Eroles P, Bosch A, Perez-Fidalgo JA, Lluch A. Molecular biology in breast cancer: intrinsic subtypes and signaling pathways. Cancer Treat Rev 2012; 38:698–707.
31. Hu Z, Fan C, Oh DS, Marron JS, He X, Qaqish BF, et al. The molecular portraits of breast tumors are conserved across microarray platforms. BMC Genomics 2006;7:96.
32. Sotiriou C, Neo SY, McShane LM, Korn EL, Long PM, Jazaeri A, et al. Breast cancer classification and prognosis based on gene expression profiles from a population-based study. Proc Natl Acad Sci USA 2003; 100:10393–8.
33. Yu K, Lee CH, Tan PH, Tan P. Conservation of breast cancer molecular subtypes and transcriptional patterns of tumor progression across distinct ethnic population. Clin Cancer Res 2004;10:5508–17.
34. Banerji S, Cibulskis K, Rangel-Escareno C, Brown KK, Carter SL, Frederick AM, et al. Sequence analysis of mutations and translocations across breast cancer subtypes. Nature 2012;486:405–9.
35. Cheang MC, Voduc D, Bajdik C, Leung S, McKinney S, Chia SK, et al. Basal-like breast cancer defined by five biomarkers has superior prognostic value than triple-negative phenotype. Clin Cancer Res 2008;14:1368–76.
36. Prat A, Perou CM. Deconstructing the molecular portraits of breast cancer. Mol Oncol 2011;5:5–23.
37. González Burchard E, Borrell LN, Choudhry S, Naqvi M, Tsai HJ, Rodriguez-Santana JR, et al. Latino populations: a unique opportunity for the study of race, genetics, and social environment in epidemiological research. Am J Public Health 2005;95:2161–8.
38. Lynce F, Graves KD, Jandorf L, Ricker C, Castro E, Moreno L, et al. Genomic disparities in breast cancer among Latinas. Cancer Control 2016;23:359–72.
39. Stern MC, Fejerman L, Das R, Setiawan VW, Cruz-Correa MR, Perez-Stable EJ, et al. Variability in cancer risk and outcomes within US Latinos by national origin and genetic ancestry. Curr Epidemiol Rep 2016;3:181–90.
40. Siegel R, Naishadham D, Jemal A. Cancer statistics for Hispanics/Latinos, 2012. CA Cancer J Clin 2012;62:283–98.
41. Fejerman L, Hu D, Huntsman S, John EM, Stern MC, Haiman CA, et al. Genetic ancestry and risk of mortality among U.S. Latinas with breast cancer. Cancer Res 2013;73:7243–53.
42. Fejerman L, John EM, Huntsman S, Beckman K, Choudhry S, Perez-Stable E, et al. Genetic ancestry and risk of breast cancer among U.S. Latinas. Cancer Res 2008;68:9723–8.
43. Fejerman L, Romieu I, John EM, Lazcano-Ponce E, Huntsman S, Beckman KB, et al. European ancestry is positively associated with breast cancer risk in Mexican women. Cancer Epidemiol Biomarkers Prev 2010;19:1074–82.
44. Iqbal J, Ginsburg O, Rochon PA, Sun P, Narod SA. Differences in breast cancer stage at diagnosis and cancer-specific survival by race and ethnicity in the United States. JAMA 2015;313:165–73.
45. Siegel RL, Fedewa SA, Miller KD, Goding-Sauer A, Pinheiro PS, Martinez-Tyson D, et al. Cancer statistics for Hispanics/Latinos, 2015. CA Cancer J Clin 2015;65:457–80.
46. Danforth DN Jr. Disparities in breast cancer outcomes between Caucasian and African American women: a model for describing the relationship of biological and nonbiological factors. Breast Cancer Res 2013;15:208.
47. Fejerman L, Ziv E. Population differences in breast cancer severity. Pharmacogenomics 2008;9:323–33.
48. Karliner LS, Napoles-Springer A, Kerlikowske K, Haas JS, Gregorich SE, Kaplan CP. Missed opportunities: family history and behavioral risk factors in breast cancer risk assessment among a multiethnic group of women. J Gen Intern Med 2007;22:308–14.
49. Kaplan CP, Haas JS, Perez-Stable EJ, Gregorich SE, Somkin C, Des Jarlais G, et al. Breast cancer risk reduction options: awareness, discussion, and use among women from four ethnic groups. Cancer Epidemiol Biomarkers Prev 2006;15:162–6.
50. Patel TA, Colon-Otero G, Bueno Hume C, Copland JA III, Perez EA. Breast cancer in Latinas: gene expression, differential response to treatments, and differential toxicities in Latinas compared with other population groups. Oncologist 2010;15:466–75.
51. Banegas MP, Tao L, Altekruse S, Anderson WF, John EM, Clarke CA, et al. Heterogeneity of breast cancer subtypes and survival among Hispanic women with invasive breast cancer in California. Breast Cancer Res Treat 2014;144:625–34.
52. Howlader N, Altekruse SF, Li CI, Chen VW, Clarke CA, Ries LA, et al. US incidence of breast cancer subtypes defined by joint hormone receptor and HER2 status. J Natl Cancer Inst 2014;106. pii: dju055.
53. Chen L, Li CI. Racial disparities in breast cancer diagnosis and treatment by hormone receptor and HER2 status. Cancer Epidemiol Biomarkers Prev 2015;24:1666–72.
54. Bauer KR, Brown M, Cress RD, Parise CA, Caggiano V. Descriptive analysis of estrogen receptor (ER)-negative, progesterone receptor (PR)-negative, and HER2-negative invasive breast cancer, the so-called triple-negative phenotype: a population-based study from the California Cancer Registry. Cancer 2007;109:1721–8.
55. Kurian AW, Fish K, Shema SJ, Clarke CA. Lifetime risks of specific breast cancer subtypes among women in four racial/ethnic groups. Breast Cancer Res 2010;12:R99.
56. Clarke CA, Keegan TH, Yang J, Press DJ, Kurian AW, Patel AH, et al. Age-specific incidence of breast cancer subtypes: understanding the black-white crossover. J Natl Cancer Inst 2012;104:1094–101.
57. Ennis S, Rios-Vargas M, Albert N. The Hispanic population: 2010; 2011. https://www.census.gov/prod/cen2010/briefs/c2010br-04.pdf
58. Plasilova ML, Hayse B, Killelea BK, Horowitz NR, Chagpar AB, Lannin DR. Features of triple-negative breast cancer: analysis of 38,813 cases from the national cancer database. Medicine 2016;95:e4614.
59. Sineshaw HM, Gaudet M, Ward EM, Flanders WD, Desantis C, Lin CC, et al. Association of race/ethnicity, socioeconomic status, and breast cancer subtypes in the National Cancer Data Base (2010–2011). Breast Cancer Res Treat 2014;145:753–63.
60. Hines LM, Risendal B, Byers T, Mengshol S, Lowery J, Singh M. Ethnic disparities in breast tumor phenotypic subtypes in Hispanic and non-Hispanic white women. J Women's Health 2011;20:1543–50.
61. Kroenke CH, Sweeney C, Kwan ML, Quesenberry CP, Weltzien EK, Habel LA, et al. Race and breast cancer survival by intrinsic subtype based on PAM50 gene expression. Breast Cancer Res Treat 2014;144: 689–99.
62. Sweeney C, Bernard PS, Factor RE, Kwan ML, Habel LA, Quesenberry CP Jr, et al. Intrinsic subtypes from PAM50 gene expression assay in a population-based breast cancer cohort: differences by age, race, and tumor characteristics. Cancer Epidemiol Biomarkers Prev 2014;23:714–24.
63. Kwan ML, Kushi LH, Weltzien E, Maring B, Kutner SE, Fulton RS, et al. Epidemiology of breast cancer subtypes in two prospective cohort studies of breast cancer survivors. Breast Cancer Res 2009;11:R31.
64. Singh M, Ding Y, Zhang LY, Song D, Gong Y, Adams S, et al. Distinct breast cancer subtypes in women with early-onset disease across races. Am J Cancer Res 2014;4:337–52.
65. Lara-Medina F, Perez-Sanchez V, Saavedra-Perez D, Blake-Cerda M, Arce C, Motola-Kuba D, et al. Triple-negative breast cancer in Hispanic patients: high prevalence, poor prognosis, and association with menopausal status, body mass index, and parity. Cancer 2011;117:3658–69.
66. Martinez ME, Wertheim BC, Natarajan L, Schwab R, Bondy M, Daneri-Navarro A, et al. Reproductive factors, heterogeneity, and breast tumor subtypes in women of Mexican descent. Cancer Epidemiol Biomarkers Prev 2013;22:1853–61.
67. Srur-Rivero N, Cartin-Brenes M. Breast cancer characteristics and survival in a Hispanic population of costa rica. Breast Cancer 2014;8:103–8.
68. de Macedo Andrade AC, Ferreira Junior CA, Dantas Guimaraes B, Pessoa Barros AW, Sarmento de Almeida G, Weller M. Molecular breast cancer

subtypes and therapies in a public hospital of Northeastern Brazil. BMC Women's Health 2014;14:110.
69. Goldhirsch A, Wood WC, Coates AS, Gelber RD, Thurlimann B, Senn HJ, et al. Strategies for subtypes–dealing with the diversity of breast cancer: highlights of the St. Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2011. Ann Oncol 2011;22:1736–47.
70. Ortiz AP, Frías O, Pérez J, Cabanillas F, Martínez L, Sánchez C, et al. Breast cancer molecular subtypes and survival in a hospital-based sample in Puerto Rico. Cancer Med 2013;2:343–50.
71. Serrano-Gomez SJ, Sanabria-Salas MC, Hernandez-Suarez G, Garcia O, Silva C, Romero A, et al. High prevalence of luminal B breast cancer intrinsic subtype in Colombian women. Carcinogenesis 2016.
72. Goldhirsch A, Winer EP, Coates AS, Gelber RD, Piccart-Gebhart M, Thurlimann B, et al. Personalizing the treatment of women with early breast cancer: highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2013. Ann Oncol 2013;24:2206–23.
73. Millikan RC, Newman B, Tse CK, Moorman PG, Conway K, Dressler LG, et al. Epidemiology of basal-like breast cancer. Breast Cancer Res Treat 2008;109:123–39.
74. Gomez R, Ossa CA, Montoya ME, Echeverri C, Angel G, Ascuntar J, et al. Impact of immunohistochemistry-based molecular subtype on chemosensitivity and survival in Hispanic breast cancer patients following neoadjuvant chemotherapy. eCancer Medical Science 2015;9:562.
75. Vallejos CS, Gomez HL, Cruz WR, Pinto JA, Dyer RR, Velarde R, et al. Breast cancer classification according to immunohistochemistry markers: subtypes and association with clinicopathologic variables in a peruvian hospital database. Clin Breast Cancer 2010;10:294–300.
76. Ruiz-Linares A, Adhikari K, Acuna-Alonzo V, Quinto-Sanchez M, Jaramillo C, Arias W, et al. Admixture in latin america: geographic structure, phenotypic diversity and self-perception of ancestry based on 7,342 individuals. PLoS Genet 2014;10:e1004572.
77. Sans M. Admixture studies in Latin America: from the 20th to the 21st century. Hum Biol 2000;72:155–77.
78. Jung S, Spiegelman D, Baglietto L, Bernstein L, Boggs DA, van den Brandt PA, et al. Fruit and vegetable intake and risk of breast cancer by hormone receptor status. J Natl Cancer Inst 2013;105:219–36.
79. Wu Y, Zhang D, Kang S. Physical activity and risk of breast cancer: a meta-analysis of prospective studies. Breast Cancer Res Treat 2013;137:869–82.
80. Vona-Davis L, Rose DP, Hazard H, Howard-McNatt M, Adkins F, Partin J, et al. Triple-negative breast cancer and obesity in a rural Appalachian population. Cancer Epidemiol Biomarkers Prev 2008;17:3319–24.
81. Chlebowski RT, Chen Z, Anderson GL, Rohan T, Aragaki A, Lane D, et al. Ethnicity and breast cancer: factors influencing differences in incidence and outcome. J Natl Cancer Inst 2005;97:439–48.
82. Phipps AI, Chlebowski RT, Prentice R, McTiernan A, Wactawski-Wende J, Kuller LH, et al. Reproductive history and oral contraceptive use in relation to risk of triple-negative breast cancer. J Natl Cancer Inst 2011;103:470–7.
83. Li CI, Beaber EF, Tang MT, Porter PL, Daling JR, Malone KE. Reproductive factors and risk of estrogen receptor positive, triple-negative, and HER2-neu overexpressing breast cancer among women 20–44 years of age. Breast Cancer Res Treat 2013;137:579–87.
84. Martin DN, Boersma BJ, Yi M, Reimers M, Howe TM, Yfantis HG, et al. Differences in the tumor microenvironment between African-American and European-American breast cancer patients. PLoS One 2009;4:e4531.
85. Grunda JM, Steg AD, He Q, Steciuk MR, Byan-Parker S, Johnson MR, et al. Differential expression of breast cancer-associated genes between stage- and age-matched tumor specimens from African- and Caucasian-American women diagnosed with breast cancer. BMC Res Notes 2012;5:248.
86. Stewart PA, Luks J, Roycik MD, Sang QX, Zhang J. Differentially expressed transcripts and dysregulated signaling pathways and networks in African American breast cancer. PLoS One 2013;8:e82460.
87. Field LA, Love B, Deyarmin B, Hooke JA, Shriver CD, Ellsworth RE. Identification of differentially expressed genes in breast tumors from African American compared with Caucasian women. Cancer 2012;118:1334–44.
88. Huo D, Hu H, Rhie SK, Gamazon ER, Cherniack AD, Liu J, et al. Comparison of breast cancer molecular features and survival by African and European Ancestry in The Cancer Genome Atlas. JAMA Oncol 2017.