Evaluating Genome-Wide Association Study-Identified Breast Cancer Risk Variants in African-American Women

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Abstract

Genome-wide association studies (GWAS), conducted mostly in European or Asian descendants, have identified approximately 67 genetic susceptibility loci for breast cancer. Given the large differences in genetic architecture between the African-ancestry genome and genomes of Asians and Europeans, it is important to investigate these loci in African-ancestry populations. We evaluated index SNPs in all 67 breast cancer susceptibility loci identified to date in our study including up to 3,300 African-American women (1,231 cases and 2,069 controls), recruited in the Southern Community Cohort Study (SCCS) and the Nashville Breast Health Study (NBHS). Seven SNPs were statistically significant (P≤0.05) with the risk of overall breast cancer in the same direction as previously reported: rs10069690 (5p15/TERT), rs9999737 (14q24/RAD51L1), rs13387042 (2q35/TNP1), rs1219648 (10q26/FGF2), rs8170 (19p13/BABAM1), rs17817449 (16q12/FTO), and rs13329835 (16q23/DYLY2). A marginally significant association (P<0.10) was found for three additional SNPs: rs1045485 (2q33/CASPB8), rs4849887 (2q14/INHBB), and rs4808801 (19p13/ELL). Three additional SNPs, including rs1011970 (9p21/CDKN2A/2B), rs941764 (14q32/CDC80C), and rs17529111 (6q14/FAM46A), showed a significant association in analyses conducted by breast subtype. The risk of breast cancer was elevated with an increasing number of risk variants, as measured by quintiles of the genetic risk score, from 1.00 (reference), to 1.75 (1.30–2.37), 1.56 (1.15–2.11), 2.02 (1.50–2.74) and 2.63 (1.96–3.52), respectively. (P=7.8×10−16). Results from this study highlight the need for large genetic studies in AAs to identify risk variants impacting this population.

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Introduction

Breast cancer is one of the most common malignancies diagnosed among women worldwide, including women of African descendant. African American (AA) women experience a disproportionate burden of breast cancer. Age-adjusted mortality rate of this cancer is more than 40% higher in AAs than in European-ancestry populations. AA women tend to be diagnosed with breast cancer at a younger age and with more aggressive types of the disease, such as ER- (estrogen receptor negative) and ER−/PR+ (HER2 negative) breast cancer. Within AAs, women having a higher African ancestry level, estimated by ancestry informative markers (AIMs), have been shown to have an increased likelihood of ER−/PR+ versus ER+/PR+ breast cancers [1]. However, such association was not observed in the Women’s Contraceptive and Reproductive Experiences (CARE) study [2].

To date, four high-penetrance genes (BRCA1, BRCA2, TP53, and PTEN) and four moderate-penetrance genes (CHEK2, ATM, BRIP1, and PALB2) have been discovered for breast cancer [3]. Candidate gene studies have largely failed to identify low-penetrance loci which can be robustly replicated in other studies [3]. Genome-wide association studies (GWAS) have emerged as the most widely used approach to identify genetic variants for complex diseases [4]. Since 2007, 67 common genetic susceptibility loci have been discovered, including 25 from several earlier GWAS [5–21] and 42 from a recent international Collaborative Oncological Gene-Environment Study (COGS) [22]. However, except the 5p15/TERT locus which was discovered among AA women [20], all other risk variants initially were identified in studies conducted in European or Asian descendants. Given the considerable differences in genetic architecture, including allele frequencies, linkage disequilibrium (LD) structure, and genetic diversity between the African-ancestry genome and genomes of Asian- and European-ancestry populations [23], it is important to investigate whether GWAS-identified variants are associated with breast cancer risk in African-ancestry populations. This investiga-
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Table 1. Characteristics of study participants.

| Characteristic | Cases (N=1,231) | Controls (N=2,069) | P value |
|----------------|-----------------|-------------------|---------|
| Sample sources |                 |                   |         |
| NBHSa           | 488             | 272               |         |
| SCCSb           | 743             | 1,797             |         |
| Age (year, mean ± sd) | 54.83±9.74     | 55.14±9.64        | 0.37    |
| Age at menarche (year, mean ± sd) | 12.60±1.87      | 12.83±2.04        | 0.002   |
| Postmenopausal (%) | 78.69           | 73.49             |         |
| Number of live births (median, range) | 3 (1, 16)       | 3 (1, 18)         | 0.027   |
| Age at first live birth (year, mean ± sd)^c | 20.95±5.09      | 20.42±4.77        |         |
| Breast cancer family history (%) | 20.69           | 10.36             |         |
| BMI (kg/m^2, mean ± sd) | 31.95±7.34       | 31.49±8.07        |         |
| BMI in postmenopausal women | 32.16±7.21       | 31.45±7.97        | 0.03    |

aThe Nashville Breast Health Study.
bThe Southern Community Cohort Study.
cAmong parous women.

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African Ancestry Level and Breast Cancer

We did not find any statistically significant association between African ancestry level and breast cancer risk. On average, cases had 83.22% African ancestry, and controls had 83.36%. No significant association was observed between African ancestry level with breast cancer subtype, either. The African ancestry proportion was 82.50%, 82.74%, and 82.25% for ER+/PR+, ER−/PR−, ER−/PR−/HER2− cases, respectively (Table S1). However, difference was observed between the two study cohorts with a higher African ancestry level in the SCCS than in the NBHS. On average, the African ancestry level is 85.23% and 80.14% in controls, and 84.50% and 81.22% in cases from the SCCS and NBHS, respectively.

Evaluation of SNPs in 25 Previously Reported Loci

Two SNPs have been discovered in the 10q21/ZNF365 locus: rs10995190 in Europeans [21] and rs10822013 in East Asians [17]. These two SNPs are not in LD based on data from HapMap Africans (r^2 = 0.001), and both of them were included in the present study. Similarly, in the locus 16q12/TOX3, SNPs rs4784227 and rs3803662 were discovered in Asians [14] and Europeans [7], respectively. SNP rs4784227 was not included in the COGS SNP array. SNP rs17271951, which was in strong LD with rs4784227 based on HapMap Africans (r^2 = 1.0), was used as a substitute. SNPs rs17271951 and rs3803662 are not in LD in HapMap Africans (r^2 = 0.03), and both of them were included in the final analyses. In the 10q26/FGFR2 locus, both rs1219648 and rs2981582 were discovered in Europeans but were in moderate LD in HapMap Africans (r^2 = 0.25). For the 6q25/TAB2 locus, rs4853570 was used to replace the originally reported SNP rs4853572 [28] which was not included in the COGS SNP array (r^2 = 1.0 in HapMap Africans). For the other 21 loci, one index SNP (reported in previous GWAS) per locus was selected. Therefore, in total, 28 SNPs in previously reported 25 loci were investigated in the present study. Five of them were deviated from Hardy-Weinberg test with P<0.05, including rs1045485, rs10995190, rs13281615, rs889312, and rs999737.

Of the 28 SNPs, 19 SNPs had an OR of breast cancer risk in the same direction as initial reports. This is higher than expected under the null hypothesis (P = 0.04, binomial sign test). Five SNPs were nominally statistically significant (P≤0.05) in the same direction as previously reported (Table 2 and Table S2). SNP rs10069690 in the 5p15/TERT locus, previously discovered in African-ancestry population, showed a moderate-strong association in the present study with OR (95% CI) 1.19 (1.05–1.36) and P-value 0.007. Notably, the MAF is very low (0.047 in controls) for SNP rs999737 at 14q24/RAD51L, however, a strong association was observed for this SNP, with OR (95% CI) 1.59 (1.15–2.19) and P-value 0.005. Alleric OR (95% CI) for the other 3 SNPs are 1.17 (1.04–1.33) for rs13387042 (P = 0.011), 1.17 (1.04–1.33) for rs1219648 (P = 0.011), and 1.25 (1.07–1.47) for rs8170 (P = 0.006). The CASP8 SNP (rs1045485) identified previously through a candidate gene approach has a low frequency (MAF = 0.065) in AAs. A marginally significant association was found for this SNP with OR (95% CI) of 1.25 (0.96–1.62) and P-value 0.096. Significant association was observed for SNP rs4973768 at 3p24/SLCAAT in this study, however, in the opposite direction as previously reported. No association was observed with the other 21 SNPs. Among them, the minor allele in rs10771399 at 12p11/PTHLH is very rare in AAs with MAF=0.034 in controls.

Evaluation of SNPs in 42 Newly Identified Loci

Of the 42 SNPs, one for each of the 42 loci recently discovered in European-ancestry populations [22] were included in the present study. Among them, SNPs rs11780156, rs13329835, rs13536907, rs616488, and rs6762644 were deviated from HWE test with P<0.05. Among the 42 investigated SNPs, 27 had an OR of breast cancer risk in the same direction in Europeans (Table 2 and Table S2). However, only two of them showed a nominally statistically significant association (P≤0.05). The OR (95% CI) was 1.21 (1.06–1.37) for rs17817449 at 16q12/PR, 1.16 (1.01–1.32) for rs13329835 at 16q23/TAB2, and 1.25 (1.07–1.47) for rs8170 (P = 0.006). The CASP8 SNP (rs1045485) identified previously through a candidate gene approach has a low frequency (MAF = 0.065) in AAs. A marginally significant association was found for this SNP with OR (95% CI) of 1.25 (0.96–1.62) and P-value 0.096. Significant association was observed for SNP rs4973768 at 3p24/SLCAAT in this study, however, in the opposite direction as previously reported. No association was observed with the other 21 SNPs. Among them, the minor allele in rs10771399 at 12p11/PTHLH is very rare in AAs with MAF=0.034 in controls.
Table 2. Associations of breast cancer risk with 10 SNPs located in reported breast-cancer susceptibility loci in African Americans with P<0.1.

| SNP       | Chr./gene | Allele | RAF (cases/ controls) | N (cases/ controls) | OR (95% CI) | P_trend | Power (%) |
|-----------|-----------|--------|------------------------|---------------------|-------------|---------|-----------|
| rs1045485 | 2q33/CASP8 | G/C    | 0.946/0.935            | 1,113/930           | 1.99 (0.57–6.93) | 2.38 (0.70–8.04) | 0.096  | 54        |
| rs13387042| 2q35/TNP1  | A/G    | 0.762/0.739            | 1,230/2,059         | 1.14 (0.82–1.59) | 1.35 (0.98–1.87) | 0.011  | 86        |
| rs10069690| 5p15/TERT  | T/C    | 0.629/0.592            | 1,112/930           | 1.39 (1.07–1.81) | 1.50 (1.15–1.97) | 0.007  | 86        |
| rs1219648 | 10q26/GFR2 | G/A    | 0.456/0.416            | 826/1,769           | 1.12 (0.92–1.37) | 1.39 (0.99–1.79) | 0.011  | 83        |
| rs999737  | 14q24/RAD51L1 | C/T | 0.966/0.953            | 1,113/930           | 2.08 (0.39–11.20) | 3.24 (0.62–16.98) | 0.005  | 97        |
| rs8170    | 19p13/BABAM1 | A/G | 0.212/0.177           | 1,112/930           | 1.19 (0.98–1.44) | 1.90 (1.15–3.12) | 0.006  | 88        |
| rs4849887 | 2q14/NHBB  | C/T    | 0.725/0.697            | 1,113/930           | 1.15 (0.83–1.60) | 1.30 (0.94–1.80) | 0.075  | 52        |
| rs17817449| 16q12/DYL2  | T/G    | 0.636/0.597            | 1,113/930           | 1.02 (0.79–1.34) | 1.37 (1.04–1.80) | 0.004  | 92        |
| rs13329835| 16q23/DYL2  | G/A    | 0.677/0.655            | 1,113/930           | 0.88 (0.65–1.20) | 1.16 (0.86–1.58) | 0.037  | 71        |
| rs4808801 | 19p13/ELL  | A/G    | 0.305/0.279            | 1,112/929           | 1.09 (0.90–1.31) | 1.34 (0.96–1.85) | 0.091  | 50        |

- The closest gene.
- Risk/reference alleles based on NCBI Human Genome Build 36 forward strand.
- Risk allele frequency of cases and controls.
- Adjusted with age, study (NBHS and SCCS), and the first ten principal components.
- Power to identify an association at an alpha level of 0.05 under additive model.

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Evaluation of Associations by Breast Cancer Subtypes

Association results between SNPs with risk of breast cancer by subtypes, including ER+, ER-, and ER−/PR−/HER2−, are presented in Table 3. Only SNPs that showed significant (P<0.05) or marginally significant (P≤0.1) association with any of these three subtypes of breast cancer are presented. Three SNPs that were not associated with overall breast cancer showed nominally statistical significance (P≤0.05) in analysis by subtypes in the same direction as previously reported. SNPs rs1011970 at 9p21/CDKN2A/2B and rs941764 at 14q32/RAD51C were associated with ER+ breast cancer with ORs (95% CI) 1.27 (1.05–1.54) (P=0.014) and 1.26 (1.02–1.56) (P=0.032), respectively. SNP rs17529111 at 6q14/FAM156 was associated with ER−/PR−/HER2− tumor with OR (95% CI) of 1.97 (1.02–3.82) (P=0.043). Differences in the strength of the association were also observed for three other SNPs across breast cancer subtypes. SNP rs17817449 at 16q12/FTO showed an association with ER+ tumor with OR (95% CI) of 1.32 (1.09–1.60) but not with ER− or ER−/PR−/HER2− tumors. Both rs10069690 at 5p15/TERT and rs999737 at 14q24/RAD51L1 showed the strongest association for ER−/PR−/HER2− breast cancer though associations were also observed for ER+ and ER− cancers.

Genetic Risk Score (GRS) Analyses for Overall Breast Cancer

Significant associations were observed between GRS and risk of breast cancer (Table 4). ORs (95% CIs) for overall breast cancer risk across increasing quintiles of GRS were 1.00 (reference), 1.75 (1.30–2.37), 1.56 (1.13–2.11), 2.02 (1.50–2.74) and 2.63 (1.96–3.52) (P=7.8 x 10^-10). Such associations were also observed for all three subtypes of breast cancer.

Discussion

In the present study, we investigated associations of 70 index SNPs in 67 breast cancer susceptibility loci identified to date in up to 1,231 cases and 2,069 controls of AA women. We found that seven SNPs were significantly associated (P<0.05) and three SNPs were marginally significantly associated (P<0.10) with overall breast cancer risk in the same association direction as previously reported. Three additional SNPs showed a significant association (P<0.05) when stratified by breast cancer subtype. GRS analyses showed significant associations with the risk of overall or subtype of breast cancer.

In the present study population, on average, approximate 83% of genetic ancestry is African origin, which is similar to the estimate in other studies [1,2,29,30]. Women in the SCCS have a higher African ancestry level than those in the NBHS. In the NBHS, most women were recruited in Tennessee, while SCCS women were recruited in 12 southern states including Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Tennessee, Mississippi, South Carolina, North Carolina, Virginia, and West Virginia. We did not find a significant difference in African ancestry level between breast cancer cases and controls or across breast cancer subtypes. These results are consistent with the recent finding in the CARE Study [2]. However, in another study, significant association was observed between genetic ancestry with ER+, PR+, or localized breast tumors [1]. In the present study, data for ER, PR and HER2 were available for only a portion of the subjects. Therefore, statistical power in regard to subtype of breast cancer analyses may be limited.

Among the ten SNPs that showed significant or marginally significant association with overall breast cancer risk in the present study, six have been investigated in previous studies of African-ancestry populations [20,25,31–36]. SNP rs10069690 (5p15/TERT) was originally discovered in a GWAS of AAs [20], so it is expected that this SNP should be replicated in the present study. For SNP rs1219648 at 10q26/GFR2, association was observed in our previous study [23], the Carolina Breast Cancer Study (CBCS) [32], and the Women’s Health Initiative (WHI) study [35], but not...
in the Women’s Insights and Shared Experiences study [36]. SNP rs13387042 was replicated in our previous study [25] and in a consortium study of 3,016 cases and 2,743 controls [33], but not in the WHI study [35], the CBCS [32], nor another pooled study [34]. SNP rs8170 at 19p13/FTO was only investigated in a pooled study from Africans and AAAs and no association was observed [34]. Both CASP8 SNP (rs1045485) and RAD51L SNP (rs999737) have MAF <5% in African-ancestry populations. Therefore, it is not surprising that these two SNPs were not replicated in all previous studies of African-ancestry populations [32–34]. The other four SNPs that showed associations with overall breast cancer in the present study, rs4898887, rs17817449, rs13329835 and rs4808801, were recently discovered [22] and have not been evaluated in previous studies of African-ancestry populations.

We did not replicate associations for the other 60 reported SNPs with the risk of overall breast cancer. Inconsistent results were reported for some of them in previous studies of African-ancestry populations. For example, SNP rs3803662 at 16q12/TOX3 was replicated in the WHI [35], but not in the Black Women’s Health Study (BWHS) [37], the CBCS [32] and others [25,34]. In addition, a significant association has been found for this SNP with association in the opposite direction as previously reported [9]. SNP rs2981582 (10q26/FGFR2) was significantly associated

### Table 3. Association of breast cancer risk with selected GWAS-identified SNPs located in reported breast-cancer susceptibility loci in African Americans, by breast cancer subtypes.

| SNP           | Chr./Gene | ER+ (N = 369) OR (95% CI) | ER- (N = 195) OR (95% CI) | ER+/PR-/HER2- (N = 68) OR (95% CI) | Heterogeneity P |
|---------------|-----------|---------------------------|---------------------------|---------------------------------|----------------|
| rs13387042    | 2q35/TNP1 | 1.20 (0.99–1.47)          | 1.10 (0.86–1.42)          | 1.00 (0.67–1.51)               | 0.985          |
| rs10069690    | 5p15/TERT | 1.18 (0.98–1.42)          | 0.075                     | 1.36 (1.07–1.72)               | 0.011          |
| rs9485370     | 6q25/TAB2 | 1.21 (0.97–1.52)          | 0.093                     | 0.85 (0.65–1.10)               | 0.209          |
| rs1011970     | 9p21/CDC2N2A2B | 1.27 (1.05–1.54) | 0.014*                      | 0.96 (0.75–1.22)               | 0.733          |
| rs999737      | 14q24/RAD51L | 1.39 (0.88–2.18) | 0.156                      | 2.20 (1.11–4.36)               | 0.024          |
| rs17271951    | 16q2/TOX3  | 1.14 (0.79–1.66)          | 0.485                     | 1.00 (0.62–1.62)               | 0.994          |
| rs8170        | 19p13/BBAM1 | 1.30 (1.04–1.64) | 0.023                      | 1.36 (1.03–1.81)               | 0.033          |
| rs4898887     | 2q14/INHBB | 1.23 (1.00–1.50)          | 0.045                     | 1.25 (0.96–1.61)               | 0.093          |
| rs6762644     | 3p26/ITPR1  | 1.18 (0.99–1.41)          | 0.067                     | 1.09 (0.87–1.36)               | 0.440          |
| rs9790517     | 4q24/TET2  | 0.95 (0.64–1.40)          | 0.790                     | 1.52 (0.98–2.35)               | 0.064          |
| rs17529111    | 6q14/FAM46A | 0.97 (0.67–1.42) | 0.893                      | 1.32 (0.84–2.07)               | 0.229          |
| rs9693444     | 8p21/RPL17P3 | 0.96 (0.80–1.16) | 0.675                      | 1.21 (0.96–1.52)               | 0.099          |
| rs11199914    | 10q26/FGFR2 | 1.00 (0.83–1.19) | 0.965                      | 1.09 (0.87–1.37)               | 0.444          |
| rs941764      | 14q32/CCDC88C | 1.26 (1.02–1.56) | 0.032                      | 0.92 (0.72–1.19)               | 0.536          |
| rs17817449    | 16q2/TOX3  | 1.32 (1.09–1.60)          | 0.004*                    | 1.15 (0.91–1.46)               | 0.235          |
| rs1436904     | 18q11/CHST9 | 1.02 (0.83–1.27) | 0.822                      | 1.09 (0.83–1.44)               | 0.528          |
| rs4808801     | 19p13/EML  | 0.95 (0.78–1.17)          | 0.644                     | 1.24 (0.97–1.59)               | 0.083          |

*Only SNPs that showed significant (P<0.05) or marginally significant (P<0.1) association with any of these three subtypes of breast cancer are presented.

The closest gene.

Adjusted with age, study (NBHS and SCCS), and the first ten principal components.

Results from P<0.05 were bolded.

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### Table 4. Association of genetic risk score (GRS) with breast cancer risk in African Americans.

| GRS quintile | Controls N = 929 | All cases N = 1,110 | ER+ cases N = 337 | ER- cases N = 188 | ER+/PR-/HER2- cases N = 67 |
|--------------|-----------------|---------------------|-------------------|-------------------|-----------------------------|

| GRS quintile | Controls N = 929 | All cases N = 1,110 | ER+ cases N = 337 | ER- cases N = 188 | ER+/PR-/HER2- cases N = 67 |
|--------------|-----------------|---------------------|-------------------|-------------------|-----------------------------|
| Q1           | 185             | 133                 | 1.00 (reference) | 38                 | 1.00 (reference)            |
| Q2           | 185             | 221                 | 1.75 (1.30–2.37) | 66                 | 1.91 (1.20–3.02)            |
| Q3           | 194             | 202                 | 1.56 (1.15–2.11) | 68                 | 1.90 (1.20–2.99)            |
| Q4           | 176             | 236                 | 2.02 (1.50–2.74) | 73                 | 2.39 (1.51–3.77)            |
| Q5           | 189             | 318                 | 2.63 (1.96–3.52) | 92                 | 2.85 (1.83–4.45)            |

| Phet trend   | 7.8 × 10^-10   | 5.2 × 10^-4         | 4.3 × 10^-4        | 4.5 × 10^-4        |

GRS was constructed based on 8 SNPs, including rs1045485, rs10069690, rs999737, rs8170, rs4898887, rs17817449, rs13329835 and rs4808801.

Adjusted for age, study, and the first ten principal components.

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Note: Table 3 and Table 4 are from the paper titled "Breast Cancer Genetic Loci in African Americans."
with breast cancer risk in two studies [32,33], but not in the other studies [25,33,36,39]. The WHI study reported a significant association for rs10941679 at 5p12/16RIP39 [35], and one study showed association for rs863686 at 9q31/KLF4 [33], however, other studies did not replicate these two SNPs [25,34,39]. In general, results that approximately 90% of index SNPs were not replicated in AAs are consistent with results from previous studies in African-ancestry populations [25,32-39]. Rebbeck et al. [36] did not find any association for three investigated SNPs. Huo et al. [34] evaluated 19 genetic loci and none of them were replicated. Five of the seven investigated SNPs in the CBCS [32], 21 of the 22 investigated SNPs in the WHI [35], and 14 of 19 SNPs in a consortium study [33] were not replicated.

Because of the large difference in genetic architecture between African-ancestry and European/African ancestry populations, failure to replicate most of the reported SNPs in AAs is not surprising. Most, if not all, index SNPs identified in GWAS are associated with breast cancer risk through their strong LD with causal variants. African-ancestry populations have shorter LD and more genetic variations than European/Asians. The vast majority of SNPs were originally discovered in the 2q35/3p21, 5q11/MAP3K1, 10q26/FGFR2, and 19p13/BABAM1 loci [33]. Second, allele frequencies for the index SNPs differ considerably across ethnic groups. Many index SNPs have lower MAF in AAs than in Europeans/Asians. Even if the effect size of the index SNP is the same across populations, larger sample size is required to detect association in AAs due to the lower MAF. Third, the vast majority of SNPs were originally discovered among European populations, who have a much higher proportion of ER+ than ER- breast cancer. Because of this, most of the reported risk variants are, in general, more strongly associated with ER+ than ER- cancer [22]. African-ancestry women have a higher proportion of ER- breast cancer than European-ancestry women; this may be another reason for the non-replication in AAs.

To our knowledge, this is the first study in AAs that has evaluated index SNPs in all breast cancer susceptibility loci identified to date. However, the sample size in our study is relatively small, especially when stratified by breast cancer subtype. Some of the null associations observed in this study could be due to inadequate statistical power. Meta-analysis by pooling together all existing data in the AA populations will increase the statistical power to evaluate the effects of these variants in AAs. The other limitation of this study is that we only investigated index SNP in each locus. Large-scale fine mapping studies are needed to identify genetic risk variants at these loci in African-ancestry populations. Such work will be very helpful to identify causal variants for breast cancer.

In summary, in this African-ancestry population study, we replicated approximately 10% of index SNPs in 67 breast-cancer susceptibility loci. Heterogeneity was observed across the breast cancer subtype. These results show the complexity in applying GWAS findings to African-ancestry populations. Large-scale studies in AAs are needed to discover genetic risk variants which impact this population.

Supporting Information

Table S1 African genetic ancestry proportion of study participants estimated by AIMs.

Table S2 Association of breast cancer risk with 60 SNPs located in reported breast-cancer susceptibility loci in African Americans with P>0.1.

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Author Contributions

Conceived and designed the experiments: JL, WZ. Performed the experiments: QC. Analyzed the data: JL. Contributed reagents/materials/analysis tools: JL, WZ. Drafted the manuscript: JL. Wrote the paper: JL.

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