Evaluation of GALNT16 polymorphisms to breast cancer risk in Chinese population

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Abstract
Background: Polypeptide N-acetylgalactosaminyltransferase 16 (GALNT16) is an N-acetylgalactosaminyltransferase gene that alters protein O-glycosylation, which plays a role in tumor development. This study aims to explore the association of eight GALNT16 polymorphisms with susceptibility to breast cancer (BC).

Methods: This case–control study included 563 BC patients and 552 age-matched healthy controls from the Chinese Han population. The genotypes of GALNT16 polymorphisms were detected using the Agena MassARRAY. The relationship between GALNT16 polymorphisms and BC risk was evaluated using a chi-squared test with an odds ratio (OR) and 95% confidence intervals (CI) under five genetic models.

Results: We observed that rs2105269 and rs72625676 were associated with higher BC risk in younger patients with age ≤51 (rs2105269, codominant: \( p = .006 \); recessive: \( p = .005 \); additive: \( p = .018 \); and allele: \( p = .012 \); rs72625676, codominant: \( p = .038 \); recessive: \( p = .037 \)). For rs1275678 polymorphism, there was a significantly decreased risk of BC among elder patients (codominant: \( p = .017 \); dominant: \( p = .019 \); additive: \( p = .030 \); and allele: \( p = .029 \)). Further analysis by clinical characteristics showed rs2105269 was associated with tumor size and lymph node metastasis.

Conclusion: Our study suggests that GALNT16 polymorphisms are associated with BC susceptibility in Chinese population.

KEYWORDS
breast cancer, GALNT16, polymorphism, susceptibility

1 | INTRODUCTION

Breast cancer (BC) is the most common cancer and the second leading cause of cancer-related death in women worldwide (Coleman et al., 2011; Jemal et al., 2011). According to data released by the World Health Organization (WHO), the newly diagnosed cancer cases showed in 2012 accounted for 25.2% of all female primary cancer. In China, the number of new cases of BC was recently reported as 187,000, ranking first in the incidence rate of female cancers and posing...
a serious threat to the health and quality of life of Chinese women (Fitzmaurice et al., 2017). It is widely known that multiple factors, especially genetic factors, contribute to BC susceptibility (Liu et al., 2017). Recent studies showed, critical genetic and epigenetic alterations in genes encoding glycosyltransferases can cause pathologic changes in several disease states, including cancer (Palamar, Shearston, Dawson, Mateu-Gelabet, & Ompad, 2016).

Polypeptide N-acetylgalactosaminyl transferases (GALNTs) are a large family of enzymes, which initiate the transfer of N-acetylgalactosamine (GalNAc) from UDP-GalNAc to the hydroxyl group of a serine or threonine residue have been associated with epithelial diseases (Chasman et al., 2008; Hussain, Nasir, & Al-Aama, 2013; Tian et al., 2015). The unusually large number of GALNTs is unique to O-glycosylation and the multiplicity of conserved isoforms in metazoan evolution suggests a need for cell- or tissue-specific isoforms (Bennett et al., 2012). To date, 20 GALNT family members have been identified in humans, and these isozymes have been shown to exhibit differential but overlapping substrate specificities and cell type-dependent expression patterns (Pratt et al., 2004; Wandall et al., 1997). Hence, the GALNT can be grouped into subfamilies. In subfamily Ib (T2/T14/T16), GALNT2 is the only well-characterized isoform in the literature, but preliminary studies of these three enzymes show related functions (Bennett et al., 2012). And, it has been reported that downregulation of GALNT2 promoted cell proliferation, migration, invasion, and tumor metastasis (Liu et al., 2016; Song et al., 2016; Yao-Ming et al., 2011). GALNT14 promotes lung-specific BC metastasis by modulating self-renewal and interaction with the lung microenvironment (Song et al., 2016). Although, it has been identified that GALNT16 significantly enriched for specific biological functions related to protein and lipid metabolism, insulin/IGF pathway-protein kinase B signaling cascade, prolactin signaling pathway, and AMPK signaling pathways, the functional roles of GALNT16 on BC progression are poorly understood (Gao et al., 2017).

Thus, in order to assess the effect of single-nucleotide polymorphisms (SNPs) in GALNT16 on BC risk, we conducted a case–control study to explore the association between eight SNPs of GALNT16 and BC risk in Chinese Han population.

### METHODS

#### 2.1 Study subjects

A case–control study was performed with 563 BC patients randomly recruited from Shaanxi Provincial Cancer Hospital. All patients, who were Han Chinese, had confirmed by histopathological analysis. The exclusion criteria included...
patients who were diagnosed with other types of cancers and/or underwent radiotherapy or chemotherapy. And the control group was comprised of 552 unrelated and age-matched healthy individuals (without any underlying illnesses) from the same hospital. The methods were carried out in accordance with the World Medical Association Declaration of Helsinki, and the study was approved by the ethics committee of Shaanxi Provincial Cancer Hospital. After obtaining written informed consent, the data on clinical characteristics of patients, including tumor site, tumor size, lymph node metastasis, disease stage, Ki67 status, estrogen receptor (ER) status and progesterone receptor (PR) status, and human epidermal growth factor receptor (HER2) status, were collected from medical records.

2.2 Genotyping assay

Peripheral blood of all subjects were collected in tubes containing EDTA and stored at −80°C. Then DNA was extracted using the GoldMag whole blood genomic DNA purification kit (GoldMag Co. Ltd., Xi’an, China) according to the manufacturer’s protocol, and the quantity of DNA was measured by spectrometry (NanoDrop 2000 spectrophotometer, Thermo Scientific, Waltham, MA). Eight SNPs in GALNT16 with a minor allele frequency (MAF) > 5% of the 1,000 Genomes Project data were selected in the present study. Agena MassARRAY Assay Design Software (version 3.0, Agena Bioscience, San Diego, CA) was used to design multiplexed SNP MassEXTEND assay. And Agena MassARRAY RS1000 was used to detect SNP genotyping (Fei et al., 2014; Xia et al., 2014, 2015). Primers of the eight SNPs are listed in Table 1. Data were analyzed with Agena Typer Software (version 4.0, Agena Bioscience, San Diego, CA).

2.3 Statistical analysis

SPSS software (version 18.0, Chicago, IL) was used for statistical analyses of data. The Student t test or chi-squared test was used to examine the differences of basic parameters between two groups. Hardy–Weinberg equilibrium as well as the differences in allele frequencies between cases and controls were examined by chi-squared test for each SNP. The BC risk associated with genotypes was estimated by odds ratios (OR) with 95% confidence intervals (CI) for five different genetic models. We further performed haplotype analysis and linkage disequilibrium. For all test, a two-tailed p-value <.05 was considered statistically significant. HaploReg v4.1 (https://pubs.broad institute.org/mammals/haploreg/haploreg.php) was conducted to predict the potential functions of the SNPs. And Gene Expression Profiling Interactive Analysis public database (GEPIA) (http://gepia.cancer-pku.cn/) was used to analyze GALNT16 expression of BC and normal samples. Furthermore, we evaluated the relationship between prognostic significance of BC and the expression of GALNT16 using Kaplan–Meier plotter (http://kmplot.com/analysis/).
TABLE 3  Basic information of candidate single-nucleotide polymorphism (SNPs) in the study

| Gene  | SNP         | Role | Position | Case (563) MA | Control (552) MA | p-HWE | HaploReg                                  |
|-------|-------------|------|----------|---------------|------------------|-------|------------------------------------------|
|       |             |      |          | MA            |                  |       |                                          |
|       | GALNT16     |      |          | 69280517 A    | 69328592 C       | .3917 | Selected eQTL hits                       |
| rs2105269 | intronic    |      |          | 69289592 C    | 69293300 A       | .2504 | Enhancer histone marks, DNAse            |
| rs61466740 | intronic     |      |          | 69307268 T    | 69312014 C       | .2709 | Motifs changed                           |
| rs72625676 | intronic     |      |          | 69319346 G    | 69335147 A       | .0897 | DNAse, Motifs changed                    |
| rs1275678 | intronic     |      |          | 69345012 A    | 69345012 A       | .2651 | Enhancer histone marks, DNAase           |
| rs11623483 | intronic     |      |          |                |                  |       |                                          |

Abbreviations: HWE, Hardy-Weinberg equilibrium; MA, minor allele; MAF, minor allele frequency; SNPs, single-nucleotide polymorphism.

3 | RESULTS

3.1 | Characteristics of the study subjects

Our study included 563 patients with BC and 552 healthy controls. The clinical and demographic characteristic of BC patients and controls are shown in Table 2. The cases and controls were matched by age (Student t test, p = .767). About 315 patients had a tumor size ≥2 cm and 275 patients had lymph node metastasis. Besides, patients with more than 10 percent of Ki67 are 365. The percentage of patients with PR-, ER-, and HER2-positive status was 60.57%, 67.14%, and 48.49%, respectively.

3.2 | Basic information and potential functions of the selected GALNT16 SNPs

The detailed information of eight SNPs in GALNT16 was listed in Table 3. For all SNPs, the MAFs were greater than 5% and the observed genotype frequencies complied with HWE in the control group. In addition, we annotate the functional elements of these selected SNPs using HaploRegv4.1. The results revealed that the SNPs in GALNT16 were involved in the regulations related to selected eQTL hits, enhancer histones, DNAse, and motifs changed.

3.3 | Association of GALNT16 SNPs with breast cancer susceptibility

The genotypic and allelic frequencies of GALNT16 rs2105269, rs61466740, rs72722128, rs72625676, rs745781, rs1026385, rs1275678, and rs11623483 in cases and controls are shown in Table 4. We evaluated their associations with risk of BC by chi-squared test and OR and five genetic models (codominant, dominant, recessive, additive, and allele) were applied to assess the potential association by logistic regression adjusted for age (Zhou et al., 2014). However, we did not observe any significant association between the GALNT16 polymorphisms and BC risk in all genetic models.

3.4 | Stratified analysis of GALNT16 polymorphisms and BC risk

Then we performed a subgroup analysis regarding the effect of GALNT16 polymorphisms, and rs2105269, rs72625676, and rs1275678 polymorphisms on BC according to age are displayed in Table 5. The results indicated that rs2105269 was associated with increased BC risk in the women with age ≤51 (codominant model: OR = 2.16, 95% CI = 1.25–3.17, p = .006; recessive model: OR = 2.08, 95% CI = 1.24–3.49, p = .005; additive model: OR = 1.35, 95% CI = 1.05–1.73, p = .018; and allele model: OR = 1.38, 95% CI = 1.07–1.79,
| Polymorphism  | Genotype | Case          | Control        | OR (95% CI) | p-value |
|--------------|----------|---------------|----------------|-------------|---------|
| rs2105269    | CODOMINANT | AA            | 89 (15.8%)     | 1.25 (0.87–1.79) | .237    |
|              |          | AG            | 263 (46.71%)   | 1.02 (0.79–1.32) | .875    |
|              |          | GG            | 211 (37.48%)   | 1           |         |
|              | DOMINANT  | AA-AG         | 352 (62.52%)   | 1.07 (0.84–1.36) | .586    |
|              |          | GG            | 211 (37.48%)   | 1           |         |
|              | RECESSIVE | AA            | 89 (15.80%)    | 1.23 (0.88–1.72) | .223    |
|              |          | AG-GG         | 474 (84.19%)   | 1           |         |
|              | Allele   | A             | 441 (39.17%)   | 1.10 (0.92–1.30) | .298    |
|              |          | G             | 685 (60.83%)   | 1           |         |
|              | additive |               |               | 1.09 (0.92–1.30) | .312    |
| rs61466740   | CODOMINANT | CC            | 35 (6.22%)     | 1.29 (0.77–2.17) | .337    |
|              |          | CT            | 212 (37.66%)   | 1.12 (0.87–1.43) | .379    |
|              |          | TT            | 316 (56.13%)   | 1           |         |
|              | DOMINANT  | CC-CT         | 247 (43.87%)   | 1.14 (0.90–1.45) | .284    |
|              |          | TT            | 316 (56.13%)   | 1           |         |
|              | RECESSIVE | CC            | 35 (6.21%)     | 1.23 (0.74–2.06) | .419    |
|              |          | CT-TT         | 528 (93.78%)   | 1           |         |
|              | Allele   | C             | 282 (25.04%)   | 1.12 (0.93–1.37) | .238    |
|              |          | T             | 844 (74.96%)   | 1           |         |
|              | additive |               |               | 1.13 (0.93–1.37) | .234    |
| rs72722128   | CODOMINANT | AA            | 11 (1.95%)     | 0.81 (0.36–1.83) | .612    |
|              |          | AG            | 138 (24.51%)   | 0.94 (0.72–1.23) | .654    |
|              |          | GG            | 414 (73.53%)   | 1           |         |
|              | DOMINANT  | AA-AG         | 149 (26.47%)   | 0.93 (0.71–1.21) | .583    |
|              |          | GG            | 414 (73.53%)   | 1           |         |
|              | RECESSIVE | AA            | 11 (1.95%)     | 0.93 (0.73–1.17) | .533    |
|              |          | AG-GG         | 552 (98.05%)   | 1           |         |
|              | Allele   | A             | 160 (14.21%)   | 0.93 (0.74–1.18) | .568    |
|              |          | G             | 966 (85.79%)   | 1           |         |
|              | additive |               |               | 0.82 (0.37–1.85) | .639    |
| rs72625676   | CODOMINANT | TT            | 38 (6.75%)     | 1.04 (0.64–1.67) | .887    |
|              |          | TC            | 229 (40.67%)   | 1.07 (0.84–1.37) | .569    |
|              |          | CC            | 296 (52.58%)   | 1           |         |
|              | DOMINANT  | TT-TC         | 267 (47.42%)   | 1.07 (0.84–1.35) | .581    |
|              |          | CC            | 296 (52.58%)   | 1           |         |
|              | RECESSIVE | TT            | 38 (6.75%)     | 1.00 (0.63–1.61) | .986    |
|              |          | TC-CC         | 525 (93.25%)   | 1           |         |
|              | Allele   | T             | 305 (27.09%)   | 1.04 (0.86–1.26) | .664    |
|              |          | C             | 821 (72.91%)   | 1           |         |
|              | additive |               |               | 1.05 (0.86–1.26) | .652    |
| Polymorphism  | Genotype | Case          | Control         | OR (95% CI) | p-value |
|---------------|----------|---------------|-----------------|-------------|---------|
| rs745781      |          |               |                 |             |         |
| Codominant    | CC       | 25 (4.44%)    | 27 (4.90%)      | 0.91 (0.52–1.59) | .734    |
|               | CG       | 186 (33.04%)  | 179 (32.55%)    | 1.01 (0.78–1.30) | .930    |
|               | GG       | 352 (62.52%)  | 345 (62.73%)    | 1           |         |
| Dominant      | CC-CG    | 211 (37.48%)  | 206 (37.39%)    | 1.00 (0.78–1.27) | .985    |
|               | GG       | 352 (62.52%)  | 345 (62.61%)    | 1           |         |
| Recessive     | CC       | 25 (4.44%)    | 27 (4.90%)      | 0.90 (0.52–1.58) | .720    |
|               | CG-GG    | 538 (95.56%)  | 524 (95.10%)    | 1           |         |
| Allele        | C        | 236 (20.96%)  | 233 (21.14%)    | 0.99 (0.81–1.21) | .915    |
|               | G        | 890 (79.04%)  | 869 (78.86%)    | 1           |         |
| Additive      |          |               |                 | 0.99 (0.80–1.21) | .884    |
| rs1026385     |          |               |                 |             |         |
| Codominant    | GG       | 4 (0.71%)     | 5 (0.91%)       | 0.80 (0.21–3.02) | .746    |
|               | GA       | 93 (16.52%)   | 82 (14.86%)     | 1.14 (0.82–1.57) | .442    |
|               | AA       | 466 (82.77%)  | 465 (84.24%)    | 1           |         |
| Dominant      | GG-GA    | 97 (17.23%)   | 87 (15.76%)     | 1.12 (0.81–1.53) | .496    |
|               | AA       | 466 (82.77%)  | 465 (84.24%)    | 1           |         |
| Recessive     | GG       | 4 (0.71%)     | 5 (0.91%)       | 0.79 (0.21–2.95) | .724    |
|               | GA-AA    | 559 (99.29%)  | 547 (99.09%)    | 1           |         |
| Allele        | G        | 101 (8.97%)   | 92 (8.33%)      | 1.08 (0.81–1.46) | .593    |
|               | A        | 1,025 (91.03%)| 1,012 (91.67%)  | 1           |         |
| Additive      |          |               |                 | 1.01 (0.81–1.46) | .579    |
| rs1275678     |          |               |                 |             |         |
| Codominant    | AA       | 5 (0.89%)     | 9 (1.63%)       | 0.53 (0.17–1.58) | .253    |
|               | AC       | 104 (18.47%)  | 115 (20.83%)    | 0.85 (0.64–1.15) | .296    |
|               | CC       | 454 (80.64%)  | 428 (77.54%)    | 1           |         |
| Dominant      | AA-AC    | 109 (19.36%)  | 124 (22.46%)    | 0.54 (0.18–1.63) | .277    |
|               | CC       | 454 (80.64%)  | 428 (77.54%)    | 1           |         |
| Recessive     | AA       | 5 (0.89%)     | 9 (1.63%)       | 0.82 (0.63–1.08) | .150    |
|               | AC-CC    | 558 (99.11%)  | 543 (98.37%)    | 1           |         |
| Allele        | A        | 114 (10.12%)  | 133 (12.05%)    | 0.82 (0.63–1.07) | .148    |
|               | C        | 1,012 (89.88%)| 971 (87.95%)    | 1           |         |
| Additive      |          |               |                 | 0.82 (0.63–1.08) | .153    |
| rs11623483    |          |               |                 |             |         |
| Codominant    | AA       | 41 (7.30%)    | 45 (8.17%)      | 0.85 (0.54–1.33) | .475    |
|               | AG       | 216 (38.43%)  | 223 (40.47%)    | 0.89 (0.70–1.15) | .384    |
|               | GG       | 305 (54.27%)  | 283 (51.36%)    | 1           |         |
| Dominant      | AA-AG    | 257 (45.73%)  | 268 (48.64%)    | 0.89 (0.70–1.12) | .323    |
|               | GG       | 305 (54.27%)  | 283 (51.36%)    | 1           |         |
| Recessive     | AA       | 41 (7.30%)    | 45 (8.17%)      | 0.89 (0.57–1.38) | .600    |
|               | AG-GG    | 521 (92.70%)  | 506 (91.83%)    | 1           |         |
| Allele        | A        | 298 (26.51%)  | 313 (28.40%)    | 0.91 (0.75–1.10) | .317    |
|               | G        | 826 (73.49%)  | 789 (71.60%)    | 1           |         |
| Additive      |          |               |                 | 0.91 (0.76–1.01) | .318    |

Note: All results are adjusted for age.
Abbreviations: BC, breast cancer; CI, confidence interval; OR, odds ratio.
Furthermore, compared with the wild genotype of rs72625676, we found a significantly increased risk of BC associated with the variant genotypes in two models (codominant model: OR = 2.30, 95% CI = 1.05–5.03, \( p = .038 \); recessive model: OR = 2.27, 95% CI = 1.05–4.89, \( p = .037 \)) for the women whose ages are no more than 51. Nevertheless, rs1275678 had relationship with significantly decreasing the risk of BC in the subgroups of age >51 for genetic models (codominant model: OR = 0.60, 95% CI = 0.40–0.91, \( p = .017 \); dominant model: OR = 0.62, 95% CI = 0.41–0.92, \( p = .019 \); additive model: OR = 0.66, 95% CI = 0.46–0.96, \( p = .030 \); and allele model: OR = 0.66, 95% CI = 0.45–0.96, \( p = .029 \)).

### 3.5 Haplotype analysis of GALNT16 polymorphisms and BC risk

As shown in Table S1, we did not find significant association between GALNT16 haplotype and BC risk. We observed three blocks, they are block 1 (rs61466740 and rs72722128), block 2 (rs72625676, rs745781, and rs1026385), and block 3 (rs1275678 and rs11623483) (Figure 1). We further conducted haplotype analysis in age subgroups. In the subgroup of age >51, we found two blocks (block 1: rs61466740 and rs72722128, block 2: rs72625676 and rs745781) (Table S2 and Figure S1). For the individuals younger than 51 years...
old, C rs72625676 Grs745781Ars1026385 haplotype increased BC risk (p = .046) (Table S3). As shown in Figure S2, we observed two blocks (block 1: rs72625676, rs745781, and rs1026385; block 2: rs1275678 and rs1162345). The numbers inside the diamonds indicate the D' for pairwise analyses.

3.6 | Relationship between GALNT16 SNPs and clinical features of BC patients

In order to identify the effect of GALNT16 SNPs on different clinical characteristics of BC patients, we then analyzed the relationships between GALNT16 polymorphisms and a series of clinicopathological parameters, such as tumor size/size, lymph node metastasis, and hormonal receptor status. As shown in Table 6, we found that the mutational genotype frequency of rs2105269 was significantly higher in patients with tumor size greater than 2cm (homozygote model: OR = 2.01, 95% CI = 1.00–4.03; heterozygote model: OR = 1.66, 95% CI = 1.03–2.69; dominant model: OR = 1.74, 95% CI = 1.11–2.73; additive model: OR = 1.48, 95% CI = 1.07–2.06; and allele model: OR = 1.47, 95% CI = 1.06–2.03) and lymph node metastasis (heterozygote model: OR = 1.59, 95% CI = 1.10–2.32). However, no significant association was detected in other clinical parameters of BC patients.

3.7 | Bioinformatics analysis of GALNT16 expression and prognosis

Based on GEPIA dataset, GALNT16 presented higher expression in BC tissues than in normal tissues (Figure S3). Then, the significantly association between GALNT16 expression and BC prognosis was found according to Kaplan–Meier plotter (hazard ratio = 0.64; 95% CI = 0.55–0.75; p = 1.7e-08; Figure S4).

4 | DISCUSSION

Glycosylation is a posttranslational modification and is associated with various physiologic events. The aberrant expression of glycosyltransferase and the immature glycan structure of proteins and lipids are observed in the development and progression of cancers (Brockhausen, 1999; Fuster & Esko, 2005; Park, Katagiri, Chung, Kijima, & Nakamura, 2011; Park et al., 2010; Potapenko et al., 2010). Abnormalities of the glycan structure of glycoproteins are frequently observed in BC cells (Fuster & Esko, 2005; Park et al., 2011, 2010). In particular, the oncogenic roles of some cancer-specific glycosyltransferases had been identified and characterized previously. To further investigate the oncogenic role of aberrant glycosyltransferase expression, we attempted to identify the association of GALNT16 polymorphisms and BC risk. In this case–control study, we successfully genotyped eight SNPs in the GALNT16 and found that GALNT16 polymorphisms are associated with BC susceptibility in the Chinese and may be involved in tumor progression.

GALNT16 (Polypeptide N-acetylgalactosaminyltransferase 16) is a protein coding gene, which catalyzes the initial reaction in O-linked oligosaccharide biosynthesis and transfers an N-acetyl-D-galactosamine residue to a serine or threonine residue on the protein receptor. An important paralog of this gene is GALNT2. Recent studies reported that GALNT2 genetic polymorphisms were associated several cancers, including gastric adenocarcinoma, neuroblastoma, ovarian cancer, and BC (Gill et al., 2013; Liu et al., 2016; Terry et al., 2010; Wan-Ling et al., 2014). Although the overexpression of GALNT2 involved in the cell growth of BC, only few researches are done on this field (Taisuke et al., 2014). Likewise, the overexpression of GALNT14 plays a critical role in cell migration, invasion, and proliferation of BC by stimulating the epithelial mesenchymal transition of BC cells (Huanna et al., 2015). As Ib subfamily, GALNT16 shares the same intron numbers (with minor variations in introns positions) with GALNT2 and GALNT14. The currently available data on the enzymatic functions of GALNTs support the proposed subfamily classification. Moreover, due to the high sequence similarity of Ib subfamily, similar biological functions can be postulated.

Our study focused on the relationship of GALNT16 and BC risk in Chinese Han populations and found that rs2105269 and rs72625676 polymorphisms were associated
with an increased BC risk in the women with age ≤51, and a relationship was found between the rs1275678 and BC subjects with age >51, which may predict rs1275678 is a protective factor. Furthermore, the A allele of rs2105269 was related with a larger size of tumor (≥2cm). It was also correlated with lymph node metastasis, indicating that patients with A allele of rs2105269 are more likely to have a worse prognosis. Our results update the previous studies, suggesting the critical to some SNPs could affect the susceptibility of \textit{GALNT16}.

Some limitations could not be ignored in the study. First, choosing bias inevitably exists as this is a hospital-based, single-center study. Second, we did not analyze the impact of other risk factors such as lifestyle, family history, and menopausal status because of a lack of such data from both patients and controls. As our case–control study is the first research to elucidate on the association of \textit{GALNT16} polymorphisms with BC risk, large sample size and further confirmation in other ethnic populations are needed.

### TABLE 6

| Variables          | OR(95% CI) | Homozygote | Heterozygote | Dominant | Recessive | Additive | Allele |
|--------------------|------------|------------|--------------|----------|-----------|----------|--------|
| Tumor site         |            |            |              |          |           |          |        |
| Left               | 1.53 (0.96–2.43) | 1.07 (0.76–1.51) | 1.17 (0.85–1.62) | 1.47 (0.96–2.24) | 1.20 (0.96–1.51) | 1.19 (0.95–1.49) |        |
| Right              | 1.04 (0.64–1.71) | 1.00 (0.71–1.4)   | 1.01 (0.73–1.39) | 1.04 (0.66–1.65) | 1.01 (0.80–1.28) | 1.02 (0.81–1.28) |        |
| Tumor size         |            |            |              |          |           |          |        |
| <2 cm              | 1.00       |            |              |          |           |          |        |
| ≥2 cm              | 2.01 (1.00–4.03) | 1.66 (1.03–2.69) | 1.74 (1.11–2.73) | 1.53 (0.80–2.92) | 1.48 (1.07–2.06) | 1.47 (1.06–2.03) |        |
| LN metastasis      |            |            |              |          |           |          |        |
| Negative           | 1.00       |            |              |          |           |          |        |
| Positive           | 0.86 (0.51–1.45) | 1.59 (1.10–2.32) | 1.3730.96–1.95) | 0.66 (0.41–1.08) | 1.05 (0.82–1.34) | 1.05 (0.82–1.34) |        |
| Stage              |            |            |              |          |           |          |        |
| I–II               | 1.00       |            |              |          |           |          |        |
| III–IV             | 1.03 (0.59–1.81) | 1.06 (0.70–1.59) | 1.05 (0.71–1.55) | 1.00 (0.60–1.67) | 1.02 (0.78–1.34) | 1.03 (0.79–1.34) |        |
| PR                 |            |            |              |          |           |          |        |
| Negative           | 1.00       |            |              |          |           |          |        |
| Positive           | 0.96 (0.57–1.62) | 0.86 (0.59–1.25) | 0.88 (0.62–1.26) | 1.05 (0.65–1.69) | 0.95 (0.74–1.22) | 0.95 (0.74–1.22) |        |
| ER                 |            |            |              |          |           |          |        |
| Negative           | 1.00       |            |              |          |           |          |        |
| Positive           | 1.14 (0.64–2.01) | 1.04 (0.69–1.55) | 1.06 (0.72–1.55) | 1.12 (0.66–1.88) | 1.06 (0.81–1.38) | 1.06 (0.81–1.38) |        |
| HER2 status        |            |            |              |          |           |          |        |
| Negative           | 1.00       |            |              |          |           |          |        |
| Positive           | 0.94 (0.45–1.97) | 1.01 (0.60–1.70) | 0.99 (0.61–1.62) | 0.93 (0.47–1.85) | 0.98 (0.69–1.39) | 0.98 (0.69–1.38) |        |
| Ki67               |            |            |              |          |           |          |        |
| <10%               | 1.00       |            |              |          |           |          |        |
| ≥10%               | 0.93 (0.51–1.68) | 1.05 (0.68–1.64) | 1.02 (0.67–1.54) | 0.90 (0.52–1.55) | 0.98 (0.74–1.31) | 0.99 (0.74–1.32) |        |

Note: OR of significant association is presented in bold.

Abbreviations: BC, breast cancer; CI, confidence interval; ER, estrogen receptor; LN, lymph node; OR, odds ratio; PR, progesterone receptor.

### 5 CONCLUSION

In summary, this case–control study indicates that the \textit{GALNT16} polymorphisms are associated with BC susceptibility in the Chinese population and may be involved in tumor progression. Further functional studies and large population-based prospective studies are required to provide accurate evidence about the influence of \textit{GALNT16} variants on BC.

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### CONFLICT OF INTEREST

All authors declare that they have no conflict of interests.
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**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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