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The *POLR2E* rs3787016 polymorphism is strongly associated with the risk of female breast and cervical cancer

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ABSTRACT

The rs3787016 polymorphism, in polymerase II polypeptide E (POLR2E), was previously identified as being associated with the risk for prostate cancer, esophageal cancer, breast cancer, papillary thyroid carcinoma and liver cancer, suggesting that rs3787016 may server as a common genetic factor to affect individual susceptibility to cancer. To prove the hypothesis, we here performed a case-control study to explore the association between rs3787016 and cervical cancer risk, and to confirm the association between rs3787016 and breast cancer in a central Chinese population, which was followed by a meta-analysis to precisely estimate the association between rs3787016 and risk of female breast and cervical cancer. The genotyping was performed by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) and confirmed by sequencing. Our results indicated that rs3787016 was associated with the risk of both breast cancer and cervical cancer, and stratified analysis indicated that the association remained particularly for ≤60 years old females who smoke and drink. Moreover, after grouping breast cancer and cervical cancer together, our meta-analysis demonstrated that rs3787016 was associated with overall cancer risk and breast cancer risk. Collectively, the POLR2E rs3787016 polymorphism may be a valuable biomarker for female breast and cervical cancer predisposition.

1. Introduction

Breast cancer (BC) and Cervical cancer (CC) are two types of the most common malignant female cancers, and have been the leading cause of death related to female cancers around the world, especially in China [1,2]. Currently, surgical resection have been applied to BC and CC treatments, with satisfactory results achieved [3]. However, most BC and CC patients are diagnosed at a later stage, during which period the tumor invasion and metastasis are more likely to occur, resulting in limited treatment and prognosis. Therefore, early and effective diagnostic methods will be particularly necessary. Since single nucleotide polymorphism (SNP) is an important genetic marker for gene mapping of complex diseases such as human cancer [3,4], identification of certain SNPs associated with susceptibility to BC and CC would be of great help in the early diagnosis and treatment of BC and CC.

Long non-coding RNAs (LncRNAs), whose length ranges from 200 bp to 100 kb, are a new type of regulatory non-coding RNAs. Although lncRNAs have no open reading frame and the capacity of potential protein translation, they have been found to play important roles in diverse cellular processes and further be involved in tumorigenesis and tumor progression [5,6]. On the other side, SNP rs3787016 is a newly identified risk locus for prostate cancer in genome-wide association studies involving Caucasian population. The rs3787016 polymorphism is located in the fourth intron of RNA polymerase II polypeptide E (*POLR2E*) gene, which encodes a RNA polymerase II subunit and is responsible for synthesizing messenger RNA [7].

Interestingly, several followed-up studies have showed that the *POLR2E* rs3787016 polymorphism was significant associated with the susceptibility to prostate cancer [8], esophageal cancer [9], breast cancer [10], papillary thyroid carcinoma [11], and liver cancer [12], suggesting that rs3787016 may servers as a common genetic factor to affect individual susceptibility to cancer. To prove the hypothesis, we here examined the association between rs3787016 and cervical cancer risk. Moreover, we also conducted a replication study to assess the

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Table 1
Characteristics of BC patients, CC patients, and healthy female.

Variable		I. BC patients ($n = 480$)	II. CC patients ($n = 384$)	III. healthy females ($n = 500$)	*p-Value*[2]	
					I *vs.* II	I *vs.* III
Age	≤60 years	274 (57.1%)	204 (53.1%)	292 (58.4%)	0.677	0.117
	> 60 years	206 (42.9%)	180 (46.9%)	208 (41.6%)		
Smoking Status	Ever	137 (28.5%)	112 (29.2%)	137 (27.4%)	0.691	0.563
	Never	343 (71.5%)	272 (70.8%)	363 (72.6%)		
Drinking Status	Ever	143 (29.8%)	116 (30.2%)	141 (28.2%)	0.583	0.515
	Never	337 (70.2%)	268 (69.8%)	359 (71.8%)		

BC, Breast cancer; CC, Cervical cancer.
[1] Numbers in parentheses, percentage.
[2] Age, smoking status, and drinking status distributions of BC patients, CC patients, and normal controls were compared using a two-sided χ^2 test.

association between rs3787016 and breast cancer risk in a central Chinese population, which was different from the involved Chinese population in study of Xu et al. [10]. On the other side, we further performed a meta-analysis to provide a precise estimation of the association between rs3787016 and the risk of female breast and cervical cancer.

2. Material and methods

2.1. Participants

A total of 480 breast cancer patients, 384 cervical cancer patients and 500 healthy females were recruited in this study. All participants were biologically unrelated Han Chinese female living in central China (Hubei province). All the cancer patients were confirmed histopathologically and recruited from Hubei Cancer Hospital and Wuhan Xinzhou District People's Hospital between January 2015 and December 2016. The healthy females were selected from cancer-free individuals who visited Wuhan Xinzhou District People's Hospital for regular physical examinations between September 2014 and December 2016 or who volunteered to participate in the epidemiology survey during the same period. This study was approved by the Ethical Committees of Wuhan University of Technology (Approval No: WUT02720170925), and informed consent for participation in this study was obtained from all subjects.

2.2. The genotyping of POLR2E rs3787016 polymorphism

After collecting the peripheral blood samples (5 ml per participant) from all participants, the genomic DNA was then extracted using the TIANamp Blood DNA Kit (DP348; TianGen Biotech, Beijing, China), and stored at −20 °C before use. Next, the polymerase chain reaction-restriction fragment length polymorphism (PCR- RFLP) technique was performed to genotype the *POLR2E* rs3787016 polymorphism. The PCR primers were 5'-CATCAACATCACGCAGCACG-3' (forward) and 5'-CCC TGTCCTCCAAGCAC

TCAT-3'(reverse), which resulted in a 147 bp DNA fragment. The restrict enzyme used in this study was *NLaIII* (Takara Biotechnology Co. Ltd, Dalian, China). After overnight digestion and gel electrophoresis, rs3787016 C allele would produce two bands (127 bp and 20 bp), while rs3787016 T allele would produce one band (147 bp). For quality control, the PCR-RFLP assay was repeated twice for all subjects, and the results were 100% concordant. Moreover, 20% randomly selected PCR-amplified DNA samples were examined by DNA sequencing, the results were also 100% concordant.

2.3. Statistical analysis

The Statistical Program for Social Sciences (SPSS, version 15.0, Chicago, IL, USA) was employed to perform all the statistical analyses. Two-sided $\chi 2$ test was used to compare the differences in age, smoking status and alcohol status between cancer patients and healthy females. The frequencies of rs3787016 genotypes in healthy females was examined for deviation from HWE (Hardy-Weinberg equilibrium). Logistic regression analysis under six genetic models, including T *vs.* C (allele model), TT *vs.* CT (carrier model: T carrier *vs.* C carrier), TT *vs.* CC (homozygote model), CT *vs.* CC (heterozygote model), TT *vs.* CT + CC (recessive model) and TT + CT *vs.* CC (dominant model), was used to estimate the association between rs3787016 and cancer susceptibility. The STATA 14.0 software (Stata Corp, College Station, TX) was used to perform all statistical analyses in the following meta-analysis, whose method was previously described by Zhang et al. and Fu et al [13,14]. The *P* values less than 0.05 were considered statistically significant, and the Bonferroni correction for multiple testing was applied [15].

3. Result

Table 1 showed us the characteristics of BC patients, CC patients and healthy females. There were no significant differences for the distributions of age, smoking states and alcohol status between BC patients and healthy females, as well as between CC patients and healthy females, indicating that the cases and controls in this study were well matched.

In Table 2, it was found the genotypic frequencies of rs3787016 in healthy females were in agreement with HWE in normal controls ($P = 0.287$), suggesting the enrolled control participants were representative. After Bonferroni correction ($P < 0.0084$, 0.05/6), logistic regression analysis identified that rs3787016 was strongly associated with the risk of both BC and CC. Of note, allele T was a significant predisposition allele of BC (T *vs.* C, $P = 0.006$, OR = 1.29, 95%CI = 1.07–1.55) and individuals with genotype TT had a higher risk for BC compared with CC (TT *vs.* CC, $P = 0.007$, OR = 1.70, 95%CI = 1.16–2.50). Similarly, T allele had a higher risk for CC than those carrying the C allele (T *vs.* C, P = 0.001, OR = 1.38, 95%CI = 1.13–1.67) and TT genotype conferred higher risk for CC relative to CC and CC + TC genotypes (TT *vs.* CC, $P = 0.003$, OR = 1.88, 95%CI = 1.24–2.84; TT *vs.* TC + CC, $P = 0.007$, OR = 1.45, 95%CI = 1.21–1.91).

To identify the stratified effect of rs3787016 on risk of BC and CC, subgroup analysis based on the age, smoking status and drinking status was performed. Bonferroni correction ($P < 0.0084$, 0.05/6) was also applied. In Table 3, the results showed that these factors would affect the association between rs3787016 and risk of BC and CC. Specifically, rs3787016 exhibited significant association with BC risk in ≤60 years subgroup (T *vs.* C, $P = 0.008$, OR = 1.39, 95%CI = 1.09–1.76; TT *vs.* CC, $P = 0.007$, OR = 1.97, 95%CI = 1.20–3.24), smoking subgroup (T *vs.* C, $P = 0.002$, OR = 1.73, 95%CI = 1.23–2.45; TT *vs.* CC, $P = 0.003$, OR = 3.00, 95%CI = 1.47–6.12) and drinking subgroup (T *vs.* C, $P = 0.008$, OR = 1.60, 95%CI = 1.13–2.26; TT *vs.* CC, $P = 0.006$,

Table 2
Genotype and allele distributions of *POLR2E* rs3787016 polymorphism and its association with risk of BC and CC.

rs3787016	I. BC patients (*n* = *480*)	II. CC patients (*n* = *384*)	III. Healthy females (*n* = *500*)	HWE[b]	Logistic regression [*p*, OR(95% CI)][c]		
					Genetic Model	I *vs.* III	II *vs.* III
T	622 (64.8%)[a]	509 (66.3%)	588 (58.8%)		T vs. C	0.006, 1.29(1.07–1.55)	0.001, 1.38(1.13–1.67)
C	338 (35.2%)	259 (33.7%)	412 (41.2%)				
TT	202 (42.1%)	171 (44.5%)	178 (35.6%)	0.287	TT *vs.* TC	0.176, 1.21(0.92–1.59)	0.050, 1.33(1.00–1.78)
TC	218 (45.4%)	167 (43.5%)	232 (46.4%)		TT *vs.* CC	0.007, 1.70(1.16–2.50)	0.003, 1.88(1.24–2.84)
CC	60 (12.5%)	46 (12.0%)	90 (18.0%)		TC *vs.* CC	0.073, 1.41(0.97–2.05)	0.100, 1.41(0.94–2.12)
					TT *vs.* TC + CC	0.037, 1.31(1.02-1.70)	0.007, 1.45(1.11–1.91)
					TT + TC *vs.* CC	0.017, 1.54(1.08–2.19)	0.015, 1.61(1.10–2.37)

BC, Breast cancer; CC, Cervical cancer; HWE, Hardy-Weinberg equilibrium; OR, odds ratio; CI, confidence interval.
[a] Numbers in parentheses, percentage.
[b] Genotypic frequency of rs3787016 in healthy females was tested for departure from HWE using the χ^2 test.
[c] The *p* value was calculated using a two-sided χ^2 test, OR (95% CI) was estimated by logistic regression analysis.

OR = 2.85, 95%CI = 1.35–6.00), while not in > 60 years subgroup, non-smoking subgroup or non-drinking subgroup. Similarly, rs3787016 also significantly associated with CC risk in ≤ 60 years subgroup (T *vs.* C, *P* = 0.002, OR = 1.50, 95%CI = 1.16–1.95; TT *vs.* CC, *P* = 0.004, OR = 2.28, 95%CI = 1.31–3.95), smoking subgroup (T *vs.* C, *P* = 0.004, OR = 1.71, 95%CI = 1.19–2.46; TT *vs.* CC, *P* = 0.007, OR = 2.81, 95%CI = 1.33–5.93) and drinking subgroup (TT *vs.* CC, *P* = 0.007, OR = 3.36, 95%CI = 1.40–8.03; CT *vs.* CC, *P* = 0.003, OR = 3.63, 95%CI = 1.53–8.59; TT+CT *vs.* CC, *P* = 0.003, OR = 3.50, 95%CI = 1.53–8.00), while not in > 60 years subgroup, non-smoking subgroup or non-drinking subgroup. Moreover, all the frequencies of rs3787016 genotypes were in agreement with the HWE among normal controls in each subgroup (*P* > 0.05).

After comprehensively searching the relevant literatures, we only retrieved one publication that performed by Xu et al. to explore the association between rs3787016 and female breast cancer risk [10]. The characteristics of included studies for this meta-analysis were presented in Table 4. All studies were consistent with HWE in normal controls (*P* > 0.05). Similarly, an adjusted P value (< 0.0084, 0.05/6) after Bonferroni correction was applied. As shown in Table 5, we found that the T allele and T variant genotypes of rs3787016 were associated with a significantly higher overall cancer risk under five models (T *vs.* C, *P* < 0.001, OR = 1.29, 95%CI = 1.16–1.44; TT *vs.* TC, *P* = 0.001, OR = 1.33, 95%CI = 1.12–1.58; TT *vs.* CC, *P* < 0.001, OR = 1.71, 95%CI = 1.36–2.15; TT *vs.* CC + CT, *P* < 0.001, OR = 1.42, 95%CI = 1.20–1.67; TT + CT *vs.* CC, *P* = 0.002, OR = 1.35, 95%CI =

Table 3
Stratification analyses of *POLR2E* rs3787016 genotype and allele according to age, smoking status and drinking status.

Groups		Allele		Genotype				Logistic Regression [*P* value, OR(95% CI)][b]					
		T	C	TT	CT	CC	HWE[a]	T *vs.* C	TT *vs.* TC	TT *vs.* CC	TC *vs.* CC	TT *vs.* TC + CC	TT + TC *vs.* CC
≤60 years	BC patients	354	194	115	124	35		0.008, 1.39 (1.09-1.76)	0.275, 1.22 (0.85-1.76)	0.007, 1.97 (1.20-3.24)	0.053, 1.61 (0.99-2.61)	0.059, 1.39 (0.99-1.95)	0.014, 1.77 (1.12-2.78)
	CC patients	271	137	91	89	24		0.002, 1.50 (1.16-1.95)	0.133, 1.35 (0.91-2.00)	0.004, 2.28 (1.31-3.95)	0.060, 1.69 (0.98-2.91)	0.020, 1.55 (1.07-2.23)	0.011, 1.94 (1.16-3.24)
	Healthy females	332	252	100	132	60	0.406						
> 60 years	BC patients	268	144	87	94	25		0.295, 1.16 (0.88-1.54)	0.187, 1.33 (0.87-2.02)	0.351, 1.34 (0.73-2.47)	0.694,1.13 (0.62-2.06)	0.326, 1.22 (0.82-1.81)	0.493, 1.22 (0.69-2.16)
	CC patients	238	122	80	78	22		0.187, 1.22 (0.91-1.64)	0.212, 1.32 (0.86-2.02)	0.298, 1.40 (0.74-2.63)	0.847,1.06 (0.57-1.99)	0.165, 1.33 (0.89-2.00)	0.526, 1.21 (0.67-2.18)
	Healthy females	256	160	78	100	30	0.821						
Ever-smoking	BC patients	182	92	61	60	16		0.002, 1.73 (1.23-2.45)	0.133, 1.50 (0.88-2.55)	0.003, 3.00 (1.47-6.12)	0.051, 2.00 (1.00-4.00)	0.018, 1.82 (1.11-2.98)	0.009, 2.40 (1.25-4.61)
	CC patients	148	76	50	48	14		0.004, 1.71 (1.19-2.46)	0.130, 1.54 (0.88-2.68)	0.007, 2.81 (1.33-5.93)	0.106, 1.83 (0.88-3.79)	0.024, 1.82 (1.08-3.07)	0.022, 2.22 (1.12-4.40)
	Healthy females	146	128	42	62	33	0.567						
Never-smoking	BC patients	440	246	141	158	44		0.206, 1.15 (0.93-1.43)	0.503, 1.12 (0.81-1.54)	0.207, 1.34 (0.85-2.12)	0.418, 1.20 (0.77-1.89)	0.322, 1.17 (0.86-1.58)	0.276, 1.27 (0.83-1.94)
	CC patients	361	183	121	119	32		0.045, 1.27 (1.01-1.60)	0.166, 1.27 (0.91-1.78)	0.070, 1.59 (0.96-2.61)	0.380, 1.25 (0.76-2.04)	0.075, 1.34 (0.97-1.84)	0.159, 1.40 (0.88-2.22)
	Healthy females	442	284	136	170	57	0.749						
Ever-drinking	BC patients	199	87	69	61	13		0.008, 1.60 (1.13-2.26)	0.451, 1.22 (0.73-2.02)	0.006, 2.85 (1.35-6.00)	0.025, 2.35 (1.11-4.95)	0.091, 1.50 (0.94-2.41)	0.008, 2.59 (1.28-5.22)
	CC patients	158	74	50	58	8		0.031, 1.49 (1.04-2.15)	0.776, 0.93 (0.55-1.57)	0.007, 3.36 (1.40-8.03)	0.003, 3.63 (1.53-8.59)	0.435, 1.22 (0.74-2.01)	0.003, 3.50 (1.53-8.00)
	Healthy females	166	116	54	58	29	0.202						
Never-drinking	BC patients	423	251	133	157	47		0.128, 1.18 (0.95–1.47)	0.299, 1.19 (0.86–1.65)	0.152, 1.39 (0.89–2.19)	0.479, 1.17 (0.76–1.81)	0.179, 1.24 (0.91–1.68)	0.268, 1.26 (0.84-1.91)
	CC patients	351	185	121	109	38		0.016, 1.33 (1.06-1.68)	0.012, 1.56 (1.10-2.20)	0.065, 1.57 (0.97-2.52)	0.981, 1.01 (0.63-1.61)	0.009, 1.56 (1.13-2.16)	0.340, 1.24 (0.80-1.92)
	Healthy females	422	296	124	174	61	0.997						

BC, Breast cancer. CC, Cervical cancer.
[a] Genotypic frequency of rs3787016 in healthy females was tested for departure from Hardy-Weinberg equilibrium (HWE) using the χ^2 test.
[b] For each stratified factor, the *P* value and OR(95%CI) were calculated using two-sided χ^2 test and logistic regression analysis. First row for "Breast cancer patients *vs.* Healthy females", second row for "Cervical cancer patients *vs.* Healthy females".

Table 4
Characteristics of the current and previous studies in Chinese population.

References (Author, Year)	Region	Cancer type	Genotyping assay	Case, Control (*n*)			Matching	Quality Control[a]	HWE[b]
				Total	T/C	TT/CT/CC	Y/N	Y/N	
Xu et al, 2017	Jiangsu	Breast Cancer	MassARRAY	439, 439	395/483, 354/524	93/209/137, 64/226/149	Y	Y	0.344
This study_1, 2018	Hubei	Breast Cancer	PCR-RFLP	480, 500	622/338, 588/412	202/218/60, 178/232/90	Y	Y	0.205
This study_2, 2018	Hubei	Cervical Cancer	PCR-RFLP	384, 500	509/259, 588/412	171/167/46, 178/232/90	Y	Y	0.205

HWE, Hardy-Weinberg equilibrium.
[a] Quality control was conducted when sample of cases and controls was genotyped.
[b] Genotypic frequency of rs3787016 in normal controls was tested for departure from Hardy-Weinberg equilibrium (HWE) using the χ^2 test.

1.12–1.64). Moreover, the T allele and TT genotype of rs3787016 conferred an increased risk to BC under three models (T *vs.* C, P = 0.001, OR = 1.25, 95%CI = 1.10–1.43; TT *vs.* CC, P < 0.001, OR = 1.64, 95%CI = 1.25–2.16; TT *vs.* CC + CT, P = 0.001, OR = 1.40, 95%CI = 1.14–1.72).

4. Discussion

The rs3787016 polymorphism is an intronic SNP located in *POLR2E* gene, which encodes a subunit of RNA polymerase II and is responsible for synthesizing messenger RNA [7]. In this study, we confirmed that rs3787016 was a susceptible factor for BC, and firstly identified that rs3787016 was strongly associated with CC risk in a central Chinese population. Specifically, T allele of rs3787016 was the predisposition allele, and the females carrying TT genotype of rs3787016 were more inclined to develop BC and CC compared with females carrying CC and TC + CC genotypes. Although these results proposed that the rs3787016 may be a novel genetic biomarker to predict BC and CC risk, the application value of rs3787016 in clinical practice is still open to debate. Currently, more and more studies demonstrated that a valuable biomarker should have dual roles in diagnosis and prognosis prediction [16,17]. Therefore, the investigations of association between rs3787016 and BC/CC prognosis (survival rate) are needed in the future.

The interesting question is why rs3787016 could affect individual susceptibility to cancer. Recently, there are an increasing number of new pathogenic SNPs located in introns, some of which have been reported to be responsible for aberrant splice processes [18,19]. Interestingly, the SNPnexus database [20] also predicts that the rs3787016 may modulate the splice processes of *POLR2E* gene. Moreover, Studies have reported that the majority of lncRNAs were transcribed by RNA polymerase II, the subunit of which could be affected by *POLR2E* [21]. Therefore, the possible mechanism was that rs3787016 might modulate the splice processes of *POLR2E* gene and produce a dysfunctional POLR2E, which would affect the transcriptional signature of lncRNAs in normal cell, and thereby increase the risk of cancer (such as BC and CC).

It has been largely known that complex diseases are caused by a combination of genetic, environmental, and lifestyle factors [22]. Indeed, we found that the factors of age, smoking and drinking interplayed with rs3787016 in the development of BC and CC. The rs3787016 conferred an increased risk to BC and CC, particularly in ≤60 years old females who smoke and drink, indicating that aging, smoking and drinking might augment the effect of rs3787016 on BC and CC risk. Of note, since the smokers or drinkers carrying rs3787016 TT genotype were particularly in high risk of developing BC and CC, such females would potentially reduce that risk by ceasing smoking or drinking.

BC and gynecological Cancers (*e.g.* CC, ovarian cancer, and uterine cancer) are those specifically occur in female organs. Previously, only one study by Xu et al. explored the association between rs3787016 and the risk of female BC, and their result was repeated in present case-control study. Further, we grouped BC and CC together, and conducted a meta-analysis to increase the statistical power for estimation of the association between rs3787016 and female cancer. The results of meta-analysis confirmed our present findings and provide more precise ORs for each significant genetic comparison models. However, since only three studies that covered two kinds of female cancer were included in this meta-analysis, the findings might not applicable for other types of female cancer (*e.g.* uterine endometrial carcinoma and vagina cancer). Moreover, all the included studies involved only Chinese Han population. Therefore, additional studies with larger sample size in different types of female cancers and in different ethnic populations are warranted.

Collectively, the present study clearly showed that *POLR2E* rs3787016 polymorphism may be strongly associated with the risk of

Table 5
Meta-analysis of the association between *POLR2E* rs3787016 polymorphism and cancer risk.

Genetic Model	Heterogeneity test		Pooled OR (95%CI)	Hypothesis test		Studies (*n*)
	P	I^2		*Z*	*P*	
rs3787016 with overall cancer risk (breast and cervical cancer)						
T *vs.* C	0.650	0.0%	1.29(1.16–1.44)	4.56	< 0.001	3
TT *vs.* TC	0.533	0.0%	1.33(1.12–1.58)	3.19	0.001	3
TT *vs.* CC	0.837	0.0%	1.71(1.36–2.15)	4.61	< 0.001	3
TC *vs.* CC	0.267	24.2%	1.21(0.99–1.48)	1.83	0.067	3
TT *vs.* TC + CC	0.702	0.0%	1.42(1.20–1.67)	4.17	< 0.001	3
TT + TC *vs.* CC	0.243	29.2%	1.35(1.12–1.64)	3.12	0.002	3
rs3787016 with breast cancer risk						
T *vs.* C	0.638	0.0%	1.25(1.10–1.43)	3.34	0.001	2
TT *vs.* TC	0.262	20.5%	1.33(1.06–1.65)	2.52	0.012	2
TT *vs.* CC	0.791	0.0%	1.64(1.25–2.16)	3.54	< 0.001	2
TC *vs.* CC	0.168	47.4%	1.15(0.91–1.45)	1.16	0.248	2
TT *vs.* TC + CC	0.415	0.0%	1.40(1.14–1.72)	3.19	0.001	2
TT + TC *vs.* CC	0.187	42.7%	1.28(1.02–1.59)	2.17	0.030	2

OR, odd ratio; CI, confidence interval.

BC and CC particularly for ≤60 years old females who smoke and drink. Further meta-analysis revealed that *POLR2E* rs3787016 polymorphism may be strongly associated with overall cancer risk and breast cancer risk. Before these reported findings will contribute to clinical decision-making, additional studies with a larger sample size and in different ethnic populations are needed to confirm or further reinforce our present findings.

Declaration of conflict of interest

The authors declare that they have no conflict of interest.

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