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A genetic variant rs13293512 in the promoter of let-7 is associated with an increased risk of breast cancer in Chinese women

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INTRODUCTION & AIM

Breast cancer (BC) is the most common invasive cancer and the leading cause of cancer death among women worldwide. However, the exact etiology is still unknown. Therefore, it is of great importance to explore potential genetic biomarkers for effective prevention and treatment of breast cancer. In this study, we sought to evaluate the association of the 2 SNPs with the risk of breast cancer in Chinese women.

MATERIAL & METHODS

In this study, 301 patients with BC were recruited from the hospital of over a period of 3 three years .The study was approved by the ethical committee of the hospital and all participants signed informed consent. About 2 ml of peripheral blood was collected from each subject in EDTA anti-coagulated tubes at room temperature. The rs10877887 polymorphism was analyzed by using polymerase chain reaction and restriction fragment length polymorphism with the restriction enzyme *Fau* I . The rs13293512 polymorphism was analyzed by using a Taq-Man SNP genotyping assay. For quality control, genotype concordance was verified by DNA sequencing. Statistical analysis was done using SPSS version 13.0 software.

RESULTS

The genotype frequencies of rs10877887 and rs13293512 were in line with HWE among healthy controls ($P = 0.65$ and 0.75 , respectively). The differences of the 2 polymorphisms between BC patients and controls were presented in Table 2. A higher frequency of rs13293512 CC genotype and rs13293512 C allele was observed among BC patients than controls. Meanwhile, the frequency of rs13293512 CC genotype was significantly increased in patients with negative estrogen receptor and patients with negative progesterone receptor compared to respective controls. When the data was stratified based on TNM classification, we found a significant association for rs13293512 CC genotype in patients with T1-2 stage .

Table 2. Association between rs10877887 and rs13293512 polymorphisms and BC risk

Polymorphisms	Controls, n = 310 (%)	BC patients, n = 301 (%)	Adjusted OR (95% CI) †	P value †
<u>Genotypes</u>				
TT	140 (45.2)	144 (47.8)	1.00	
CT	134 (43.2)	117 (38.9)	0.85 (0.61-1.20)	0.35
CC	36 (11.6)	40 (13.3)	1.10 (0.66-1.83)	0.72
<u>Alleles</u>				
T	414 (66.8)	405 (67.3)	1.00	
C	206 (33.2)	197 (32.7)	0.99 (0.78-1.25)	0.90
<u>rs13293512</u>				
<u>Genotypes</u>				
TT	110 (35.5)	88 (29.2)	1.00	
CT	147 (47.4)	138 (45.8)	1.20 (0.83-1.73)	0.33
CC	53 (17.1)	75 (24.9)	1.78 (1.14-2.80)	0.012
<u>Alleles</u>				
T	367 (59.2)	314 (52.2)	1.00	
C	253 (40.8)	288 (47.8)	1.33 (1.06-1.67)	0.013

Genotypes	Controls, n (%)	Cases, n (%)		Case I vs. controls		Case II vs. controls	
		Case I	Case II	Adjusted OR (95% CI) †	P value †	Adjusted OR (95% CI) †	P value †
		ER (+)	ER (-)				
TT	110 (35.5)	57 (32.8)	31 (24.4)	1.00		1.00	
CT	147 (47.4)	77 (44.2)	61 (48.0)	1.04 (0.68-1.60)	0.84	1.48 (0.90-2.43)	0.12
CC	53 (17.1)	40 (23.0)	35 (27.6)	1.47 (0.87-2.48)	0.15	2.39 (1.32-4.30)	0.004
		PR (+)	PR (-)				
TT	110 (35.5)	47 (31.5)	41 (27.0)	1.00		1.00	
CT	147 (47.4)	65 (43.6)	73 (48.0)	1.06 (0.68-1.67)	0.79	1.34 (0.85-2.12)	0.20
CC	53 (17.1)	37 (24.8)	38 (25.0)	1.65 (0.96-2.85)	0.07	1.92 (1.11-3.33)	0.02
		T1-2	T3-4				
TT	110 (35.5)	57 (28.1)	31 (31.6)	1.00		1.00	
CT	147 (47.4)	97 (47.8)	41 (41.8)	1.29 (0.85-1.95)	0.22	1.01 (0.59-1.72)	0.97
CC	53 (17.1)	49 (24.1)	26 (26.5)	1.77 (1.07-2.93)	0.03	1.80 (0.96-3.35)	0.07
		N0	N1-3				
TT	110 (35.5)	34 (27.2)	54 (30.7)	1.00		1.00	
CT	147 (47.4)	64 (51.2)	74 (42.0)	1.43 (0.88-2.33)	0.15	1.05 (0.68-1.62)	0.82
CC	53 (17.1)	27 (21.6)	48 (27.3)	1.64 (0.89-2.99)	0.11	1.89 (1.13-3.17)	0.015

Table 5. Combined analysis of rs10877887 and rs13293512 with BC risk

Combined genotypes	Controls (%)	BC patients (%)	OR (95% CI)	P value
rs10877887TT + rs13293512TT	53 (17.1)	43 (14.3)	1.00	
rs10877887TT + rs13293512CC/CT	87 (28.1)	101 (33.6)	1.43 (0.87-2.35)	0.15
rs10877887CC/CT + rs13293512TT	57 (18.4)	45 (15.0)	0.97 (0.56-1.71)	0.92
rs10877887CC/CT + rs13293512CC/CT	113 (36.5)	112 (37.2)	1.22 (0.76-1.97)	0.41

BC, breast cancer; OR, odds ratio; CI, confidence interval.

SUMMARY / CONCLUSION

In conclusion, our assessment of the influence of rs10877887 and rs13293512 on breast cancer showed an increased risk for individuals carrying rs13293512 CC genotype. Since the study population was limited to Chinese Han women, the positive effect cannot be directly extrapolated to other ethnicities. Moreover, the samples are relatively small in this study, especially in subgroup analysis, which provides limited power to obtain precise results. Future investigations with larger samples in diverse ethnic groups are therefore needed to validate our findings. Although there were some limitations in this study, our data provides a first indication that rs13293512 in the promoter of let-7a-1/let-7f-1/let-7d cluster may be a possible biomarker for the development of breast cancer in Chinese women.

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