TNP1 NON-GENE REGION AND INFLUENCES TUMOR CHARACTERISTICS BY LOW-RISK
ALLELES IN BREAST CANCER

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Abstract. Breast cancer affected of multiple molecular by genetic or epigenetic. Single nucleotide polymorphisms lead to genetic differences in breast cancer liability. The present study aimed at investigating the association of SNPs of two genes, PLSCR3 rs4784227 (phospholipid scramblase 3) Gene and TNP1 rs13387042 (transition protein 1) Gene with possibility of breast cancer in Iranian women. Two polymorphic variants are association with breast cancer, rs4784227 in Chromosome 17 and rs13387042 in Chromosome 2. First time, we evaluated these polymorphisms included 126 Patients and 160 controls of Iranian women. So DNA extracted of peripheral blood by Tetra-Primer ARMS –PCR technique also histochemical test HER2 , HER2+ ER- ER+ PR and PR+ upon breast tumor tissue patients.

In the current study TNP1 GG gene and PLSCR3 CT polymorphisms of SNPs variants had statistically significant association with breast cancer (44.375% , 11.9 frequency, Odd Ratio; 5.564, CI; 2.877-10.759, P value; 9.056e-08 * *) and (60.00%,27.77,frequency, Odd Ratio; 1.570, CI; 1.095-2.252, P value; 0.01391 *) respectively .On the other hands, number of total test histochemical in PLSCR3 CC and TNP1 AG then AA were highest positive in ER+ and PR+ .

Keywords: PLSCR3, TNP1, gene, polymorphism, breast cancer.
1. INTRODUCTION

Breast cancer is higher rates of cancer in women of the world (Ferlay, Soerjomataram & Dikshit, 2012). It is a polyfactorial disease included of genetic and peripheral factors (Bastani, Ahmadi & Damircheli, 2013).

In recent paper, Recognition and characterization Disease by gene loci is main in cancer. Because compared to genetic variants located outside genes, to be more likely to alter gene function and disease risk (Mersch, Jackson, & Park, 2015) (Cui, & Kang, 2008). several recent large-scale GWAS of breast cancer (Macintyre, Yepes, Ong & Verspoor, 2014) (Khorasani & Almasifard, 2017) that this coding regions of genes, in first not any seems showing dependent associations with risk of breast cancer but recent study indicated another result. GWAS have well-known some non-genic breast cancer liable loci.

By a recent GWA study, Single nucleotide polymorphisms such as rs13387042 (SNPs) direct to genetic differences in breast cancer and polymorphism has been recognized as breast cancer liability.

We evidence association with the polymorphism and breast carcinoma. Furthermore, the associations of these genotype with breast cancer by 3 markers estrogen, progesterone, and human epidermal growth factor receptor-2 (HER-2) were also assessed.

Thus, 2 SNPs show statistically significant relatives with breast cancer were selected for analysis in this study, one of SNP at 2q35 (rs13387042), and another rs4784227.

2. MATERIALS AND METHODS

2.1 Patients data:

In this study 126 patients Carcinoma Breast Cancer in grade 4 and 160 controls patients of the Khas Medical Center and HAZRAT RASOUL MEDICAL COMPLEX, TEHRAN, Iran were conducted for the genotyped for IGF1 in ages 30-55 years. This study was permitted by the local Ethical Committee of Islamic Azad University samples rights.

Clinical histories included age, cancer type, grade of tumor, lymph node involvement, and family background of cancer.

The blood samples and tissue Breast tumor were collected. The SNPs Extracted from lymphocytes cells by DNA FelxiGene extraction kit (Qiagen Germany).

2.2 Genotyping

To design primers, was included internal primers along with external ones had products with different lengths depending on the polymorphism type. SNPs was examined by Tetra-Primer ARMS –PCR technique. (table 1)

The genotypes of this polymorphisms in Patient and control groups were analyses by HardyWeinberg equilibrium and were assay frequencies, odd ratio. P value, …

3. RESULTS

The present study association TNP1 and PLSCR3 as a high-risk breast cancer, Because It study was for first time upon our population.

We considered the joint effects of TNP1 and PLSCR3 genotypes and 3 marker hormonerelated breast cancer risk factors. (Tables 4, 3 and Graph 1). However, we report statistically significant associations of PLSCR3 CC and TNP1 AG and then AA genotypes in ER+, PR+ tumors (Table 4). That its opposite to has been significant TNP1 GG gene and PLSCR3 CT polymorphisms of SNPs variants.(Table 4, Graph 2)

It is possible that a low-risk, even in outer gene not only influences the chance of developing breast cancer but also influences tumor characteristics such as breast carcinoma.

There was a significant between TNP1 GG polymorphism and breast cancer risk (44.375% , 11.9 frequency, Odd Ratio; 5.564, CI; 2.877-10.759, P value; 9.056e-08 * * *) (Table 2, 3 and figure 1)
3.1. Tables, Graphs

**Table 1:** internal primers and external by Tetra-Primer ARMS –PCR technique.

<table>
<thead>
<tr>
<th>SNP</th>
<th>Genotype</th>
<th>Controls (n=60)</th>
<th>Cases overall (n=126)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNP1 (rs13387042)</td>
<td>GG</td>
<td>71 (44.375%)</td>
<td>15 (11.9%)</td>
</tr>
<tr>
<td></td>
<td>AG</td>
<td>57 (35.625%)</td>
<td>67 (53.18%)</td>
</tr>
<tr>
<td></td>
<td>AA</td>
<td>32 (20.00%)</td>
<td>44 (34.92%)</td>
</tr>
<tr>
<td>PLSCR3 (rs4784227)</td>
<td>TT</td>
<td>10 (6.25%)</td>
<td>16 (12.69%)</td>
</tr>
<tr>
<td></td>
<td>CT</td>
<td>96 (60.00%)</td>
<td>35 (27.77%)</td>
</tr>
<tr>
<td></td>
<td>CC</td>
<td>54 (33.75%)</td>
<td>75 (59.54%)</td>
</tr>
</tbody>
</table>

**Table 2:** Gene genotype frequencies [n (%)] for cases and control

<table>
<thead>
<tr>
<th>SNP</th>
<th>Genotype</th>
<th>OR</th>
<th>95% CL</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNP1 (rs13387042)</td>
<td>GG</td>
<td>5.564</td>
<td>2.877-10.759</td>
<td>9.056e-08</td>
</tr>
<tr>
<td></td>
<td>AG</td>
<td>0.381</td>
<td>0.271-0.534</td>
<td>1.798e-08</td>
</tr>
<tr>
<td></td>
<td>AA</td>
<td>0.855</td>
<td>0.480-1.521</td>
<td>0.59368</td>
</tr>
</tbody>
</table>

**Table 3:** Comparison between genotypes, odds ratio and p value, showed that P ***=P<=0.001, **=P<=0.05

**Table 4:** Test histochemical upon triple HER2−, HER2+, ER−, ER+, PR− and PR+ tumor.
In another study, rs13387042 was first identified as a breast cancer susceptibility SNP in Europeans population (Stacey, Manolescu, Sulem, et al. 2008) (Stacey, Manolescu, Sulemet, et. al. 2007). And such as in Europeans and African - American women (Çiftcioğlu & Almasifard, 2015) (Thomas, Jacobs, Kraft, et al. 2009). However, the findings were inconsistent. For example, Dai et al. find a significant association with increasing risk in Chinese women (Bastani, Ahmadi, & Damircheli, 2013), but Zheng et al. cannot find out any significance (Reeves, Travis, Green, et al. 2010). However, just rs13387042 was statically significant with overexpression in HER2, but it better understanding about mechanisms of development of breast cancer. On the other hands, showed a significance in one or more studies of European, Asian, and/or African populations (Zheng, Cai, Signorello, et al. 2009) (Dai, Hu, Jiang, et al. 2012).

Finally, we observed a significant interaction between PLSCR3 CC but not CT women. These results confirm that PLSCR3 CC are involved by down expression HER2 in breast cancer susceptibility but NOT higher than, among in ER and PR tumors.


Current study, in PLSCR3 CC, not only level of positive ER was matched to PR+ but also strongly its Similar to positive and negative HER2 in TNP1 AG. On the other hands, among positive ER and PR equal to TNP1 AA (Gong, Zhong, Xiang, et al., 2013) (Yu, Chen, Wang, & Zhang, 2013). So, It’s possible that a low-risk allele in TNP1 GG gene and PLSCR3 CT not only influences the chance of developing breast cancer but also, influences tumor.

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REFERENCES


