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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.

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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 Brest 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 TNP1and PLSCR3 as a high-risk breast cancer, Because It study was for first time upon our population.

We considered the joint effects of TNP1and PLSCR3genotypes 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.

TNP1 (rs13387042)			bp
F-inner	**CAGAACAGAAAGAAGGCAAATGTAA**	A	250
R-inner	**GGAAATCCTTGGTTTCTGTATCC**	G	362
F-outer	**AGCTCTCATGATTGCTAGCTTTG**		562
R-outer	**GAGAATCACTTGAACCTGGGAG**		
PLSCR3 (rs4784227)			
F-inner	**AAAAGTCCCAATTTGTAGTGTTTTCC**	C	273
R-inner	**GATGGGAGTATTTACATCACAATAAGCA**	T	203
F-outer	**ATGAAAGAATACATGAATGAAAAGTCAGAG**		423
R-outer	**AGTCAGTTCCTGGATCAACAAACATTTA**		

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

TNP1 (rs13387042)	**ER+**	**ER-**	**PR+**	**PR-**	**HER2+**	**HER2-**	**total**
AA	**13**	**2**	**13**	**2**	**5**	**9**	**44**
AG	**20**	**4**	**17**	**4**	**11**	**11**	**67**
GG	**5**	**-**	**5**	**-**	**-**	**5**	**15**
PLSCR3 (rs4784227)							
CC	**21**	**3**	**22**	**3**	**9**	**16**	**75**
CT	**10**	**2**	**10**	**2**	**6**	**5**	**35**
TT	**-**	**5**	**-**	**5**	**-**	**6**	**16**

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

SNP	**Genoty pe**	**Controls (n=160)**	**%**	**Cases, overall**	**%**
TNP1 (rs13387042)	**GG**	**71**	**(44.375%)**	**15**	**(11.9%)**
	AG	**57**	**(35.625%)**	**67**	**(53.18%)**
	AA	**32**	**(20.00%)**	**44**	**(34.92%)**
PLSCR3 (rs4784227)	**TT**	**10**	**(6.25%)**	**16**	**(12.69%)**
	CT	**96**	**(60.00%)**	**35**	**(27.77%)**
	CC	**54**	**(33.75%)**	**75**	**(59.54%)**

Table 4: Test histochemical upon triple $HER2^{-}$, $HER2^{+}$, ER^{-}, ER^{+}, PR^{-} and PR^{+} tumor.

SNP	**Genotype**	**OR**	**95% CL**	**P value**
TNP1 (rs13387042)				
	GG	**5.564**	**2.877-10.759**	**9.056e-08**
	AG	**0.381**	**0.271-0.534**	**1.798e-08**
	AA	**0.855**	**0.480-1.521**	**0.59368**
PLSCR3 (rs4784227)				
	TT	**0.228**	**0.095-0.549**	**0.00053**
	CT	**1.570**	**1.095-2.252**	**0.01391**
	CC	**0.263**	**0.156-0.442**	**2.936e-07**

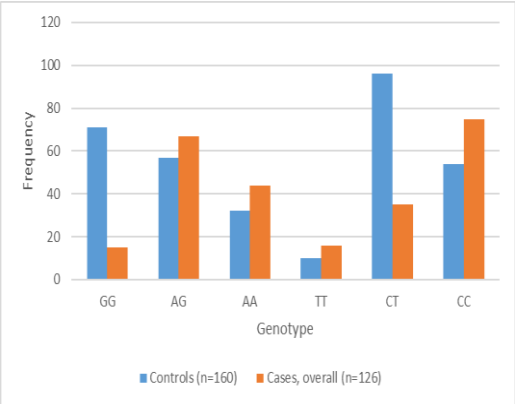

Figure 1. Column Chart genotypes frequencies [n (%)] for cases and control: Analyses of 126 affected women and 160 controls.

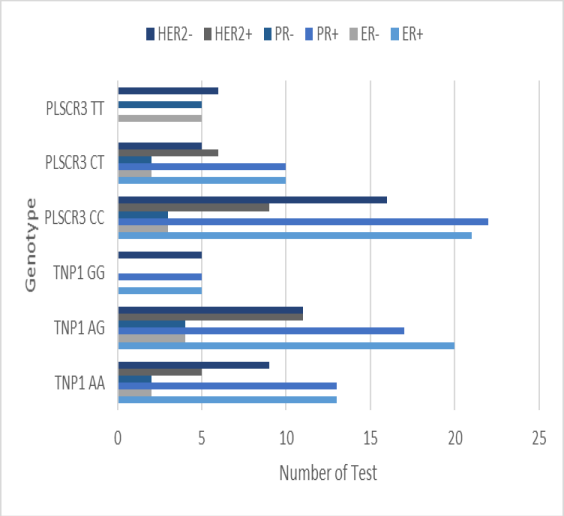

Figure 2. Column Chart Test histochemical Tumor; genotypes were highest positive in, HER2$^{+,}$ ER^{+} and PR+ tumor.

4. DISCUSSION

Current study examined whether 2 SNPs were related with tumor subtypes clear by 3 markers (ER, PR, and HER2). PLSCR3 CC and TNP1 AG genotypes were significantly associated with breast cancer in in our population only in estrogen receptor-positive (ER1), progesterone receptor-positive (PR1) tumors. in Chinese study, confirmed that two SNPs (rs13387042 and rs4415084)were significantly associated with increased risk of breast cancer.

In another study,rs13387042 was first identified as a breast cancer susceptibility SNP Europeans population (Stacey, Manolescu, Sulem, et al. 2008) (Stacey, Manolescu, Sulemet, et. al. 2007). And such as in Europeans and African - American women (Çiftçioğlu & 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 HRE2, 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.

Therefore, PLSCR3 CC strongly associate to breast cancer risk but no any affected to hormonal HER2 (Zheng, Wen, Gao, et al. 2010) (Almasifard, 2013).

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

Almasifard, M. (2013). "An econometric analysis of financial development's effects on the share of final consumption expenditure in gross domestic product", Eastern Mediterranean University.

Bastani, A., Ahmadi, Z., & Damircheli, D. (2013). A radial basis collocation method for pricing American options under regime-switching jump-diffusion models. *Applied Numerical Mathematics*, 65, 79-90.

Çiftçioğlu, S. & Almasifard, M. (2015), The response of consumption to alternative measures of financial development and real interest rate in a sample of central and east European countries. *Journal of Economics*, 3(2), 1-6.

Cui, G. & Kang, K. (2008). Genecentric genomewide association study via entropy, Genetics, 1(179), 637–650.

Dai, J., Hu, Z., Jiang Y., et al. (2012). Breast cancer risk assessment with five independent genetic variants and two risk factors in Chinese women, Breast Cancer Research, 2012. 14, R17.

Ferlay, J., Soerjomataram, I. & Dikshit, R. (2012) Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN. Int J Cancer, 136, 359-386.

Gong, W.-F., Zhong, J.-H., Xiang, B.-D., et al., (2013) Single nucleotide polymorphism 8q24 rs13281615 and risk of breast cancer: metaanalysis of more than 100,000 cases, PLoS ONE, 4.

Khorasani, S. T., & Almasifard, M. (2017). Evolution of Management Theory within 20 Century: A Systemic Overview of Paradigm Shifts in Management. *International Review of Management and Marketing*, 7(3), 134-137

Macintyre, G. Jimeno Yepes, A. Ong, C. S. & Verspoor, K. (2014). Associating disease-related genetic variants in intergenic regions to the genes they impact, *Peer J*, 2, 639-639.

Mersch, J., Jackson, Ma. & Park, M., (2015). Cancers associated with BRCA1 and BRCA2 mutations other than breast and ovarian. Cancer; 121, 269-275.

Reeves, G. K., Travis, R. C., Green, J., et al. (2010) Incidence of breast cancer and its subtypes in relation to individual and multiple low-penetrance genetic susceptibility loci. *The Journal ofthe American Medical Association*, 304, 426–434.

Stacey, S. N., Manolescu, A., Sulem, P. et al. (2008). Common variants on chromosome 5p12 confer susceptibility to estrogen receptorpositive breast cancer, *Nature Genetics*, 40(6), 703–706.

Stacey, S.N., Manolescu, A., Sulemet, P. et. al. (2007). Commonvariantson chromosomes 2q35 and 16q12 confer susceptibility to estrogen receptor-positive breast cancer. *Nature Genetics*, 39, 865–869.

Thomas, G., Jacobs, K. B., Kraft P., et al. (2009). A multistage genomewide association study in breast cancer identifies two new risk alleles at 1p11.2 and 14q24.1 (RAD51L1), *Nature Genetics*, 41, 579–584.

Yu, Y. Chen, Z. Wang, H. & Zhang, Y. (2013). Quantitative assessment of common genetic variants on chromosome 5p12 and hormone receptor status with breast cancer risk, PLoS ONE, 8.

Zheng, W. Wen, W. Gao, Y. et al. (2010). Genetic and clinical predictors for breast cancer risk assessment and stratification among Chinese women, Journal of the National Cancer Institute, 2010.102, 972–981,.

Zheng, W., Cai, Q., Signorello L. B., et al. (2009). Evaluation of 11 breast cancer susceptibility loci in African-American women, Cancer Epidemiology Biomarkers and Prevention,18, 2761–2764.