ORIGINAL RESEARCH

Evaluation of Vitamin D Polymorphism in Assessing the Susceptibility of Breast Cancer Patients

Kalidas Ponnusamy[1], Sureshkumar Muthusamy[2], Dheebalakshmi Narayanaswamy[3], Nirmala Appadurai[4*]

[1]Professor and Head, Department of Social and Preventive Medicine, Coimbatore Medical College, Coimbatore-14, Tamil Nadu, India.
[2]Research Scientist, Multi-Disciplinary Research Unit, Coimbatore Medical College, Coimbatore-14, Tamil Nadu, India.
[3]Professor and Head Department of Biochemistry, Coimbatore Medical College, Coimbatore-14, Tamil Nadu, India.
[*4]Dean, Coimbatore Medical College, Coimbatore-14, Tamil Nadu, India

Corresponding Author
Dr. Nirmala Appadurai
Dean, Coimbatore Medical College, Coimbatore-14, Tamil Nadu, India

Received: 01February, 2024 Accepted: 02April, 2024

ABSTRACT

Background: Vitamin D plays a vital role in mediating various metabolisms which include bone and cell growth. It binds with the vitamin D receptor (VDR) and regulates calcium homeostasis. It promotes cell differentiation. The converse correlation between vitamin D and the development of breast cancer was demonstrated in various studies. Breast cancer is also considered the leading cause of mortality among women around the world and its incidence is annually increasing. Several studies were conducted to determine its association with VDR. **Aim:** To determine the contribution of the VDR polymorphism to breast cancer risk in patients and the control group.**Methods:**Genomic DNA was isolated from blood samples of 100 women with breast cancer and 100 healthy women. After the amplification of five positions of VDR gene, the prepared amplicons were digested with BsmI, FokI, TaqI, ApaI, and poly A restriction enzymes.**Result:**Subsequently, the digested products were electrophoresed on the 2 % agarose gel. Odds ratios (ORs) for breast cancer were calculated for genotypes and estimated haplotypes. The distribution of VDR BsmI (rs1544410), FokI (rs2228570) and ApaI (rs7975232) polymorphisms was more significant among the patients than to the normal group. Analysis of linkage disequilibrium for all pairs of SNPs showed the significance between BsmI and TaqI. The major haplotypes of BsmI, FokI, ApaI, TaqI and PolyA SNPs were significantly in high frequency.**Conclusion:**Our results showed that BsmI, FokI and ApaI of VDR polymorphisms are associated with the risk of breast cancer progression.

Key words: Vitamin D Receptor, VDR Polymorphism, Breast cancer, PCR-RFLP.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

INTRODUCTION

The vitamin D receptor (VDR) ligand is the vitamin D metabolite, 1,25 dihydroxy vitamin D3 (1,25-D), the biologically active form of vitamin D3 that mediates cell growth and differentiation. Dietary availability of vitamin D3 is low among natural foods. While exposed to ultraviolet rays, cholesterol metabolites in the skin get converted into vitamin D3[1]. The VDR has gained increasing relevance during the past two decades and is responsible for the transcriptional regulation of hormone-mediating genes as a part of the steroid hormone regulating nuclear receptor. As an intracellular hormone receptor, VDR binds to calcitriol yielding multiple biological effects by interacting with specific loci of some specific genes. VDR mediates the expression of specific genes in tissue through 1,25D modulators by binding to vitamin D receptors[2]. This gene expression contributes to the regulation of a quiescent, differentiated phenotype which mediates apoptosis, cellular proliferation and differentiation in various cell types[3]. Various laboratory-based studies have demonstrated the inhibition of cell proliferation by 1,25-D and its analogues promote apoptosis in cultured breast cancer cells[4]. Apart from cellular differentiation, vitamin D and vitamin D receptors (VDR) are also well-known as the driving forces for their roles in calcium homeostasis and metabolism. vitamin D combined with VDR modulated TGF-β signaling pathway is involved in a tumor suppressor

©2024Int. J. LifeSci.Biotechnol.Pharma.Res.

role[5]. Alterations in VDR expression and activity could lead to deregulation of vitamin D uptake, metabolism, and serum levels of biologically active vitamin D[6]. VDR gene located on chromosome 12q13 encompasses more than 470 single-nucleotide polymorphisms (SNPs) that affect the structural and functional activity of the VDR[7]. Vitamin D deficiency will lead to SNP in the VDR increasing in the risk of prognosis and carcinogenesis[8].

Numerous studies have unveiled the association between low serum 1,25D levels and increased risk of various health complications including carcinoma. The conceivable link between polymorphic variants in genes of vitamin D receptors and increased susceptibility for primary and metastatic breast cancer was reported in various studies[9]. An increase in the incidence of cancer that was reported worldwide was reported by The World Health Organization (WHO) in 2020. Breast cancer was found to be significantly increased, reaching about 2,261,419 out of 19,292,789 new cases in 2020[10]. An increase in breast cancer susceptibility correlating with VDR gene variants has reportedly been noticed in the last decade. Among the multiple polymorphic genes, four SNP are VDR-BsmI (rs1544410), VDR-FokI (rs2228570), VDR-ApaI (rs7975232), VDR-TaqI (rs731236) located in exon 2 and 39UTR region show significant involvement in breast cancer in different populations[11-14]. The functional role of each VDR is not as clear. However, few studies recommend that these polymorphisms may amend the polyadenylation of the VDR mRNA transcript which affect mRNA stability[15]. Some studies found an association of breast cancer with these SNPs, whereas several studies reported contradictory results[16–20]. Hence, this study aimed to determine the contribution of these VDR polymorphisms to breast cancer risk in patients.

MATERIALS AND METHODS

Study Setting: This study was approved by the Institutional Human Ethics Committee and carried out from the period 1st December 2022 to 30th November 2023. The case-control study included 100 breast cancer women and 100 healthy women. The controls were approved through clinical examinations and mammography and have no prior history of cancer. Written informed consent was obtained from each participants during the time of sampling. The age restriction was not involved in sample collection of the patients. Cases with other types of cancer were excluded from the study. Patients diagnosed with breast cancer in IP and OP department were included in the study. Patients under treatment were also included. Patients treated and reported with no proliferation and progression were excluded from the study.

Sample collection

A total of 3mL of the peripheral blood samples from the patients and control females were collected in a sterile ethylene diamine tetraacetic acid (EDTA) tube for DNA extraction.

DNA extraction

Genomic DNA was extracted from whole blood samples using QIAamp DNA Blood Mini Kit (Qiagen, Germany) according to the manufacturer's instructions. About 20 µl of proteinase K and 200 µl of lysis buffer were added to 200 µl whole blood and incubated for 10 min at 60 ºC. Phenol (100 µl) was added to this mixture. Then, the whole lysate transferred into a DNA purification column. After centrifuging at 8000 rpm at 4 ºC for 1 min, the column was washed two times with 500 µl wash buffers. Finally, centrifugation was performed at 8000 rpm for 1 min and DNA was eluted by 100 µl elution buffer. DNA concentration and purity were measured using a UV-Vis spectrophotometer (Thermo Fisher Scientific, USA) and DNA samples were stored at -20 °C for further use.

Genotyping

Polymerase chain reaction-restriction fragment polymorphism (PCR-RFLP) was used to analyze VDR BsmI, FolkI, ApaI, TaqI and PolyA genotypes. The Flanking region of VDR genes was amplified by PCR using specified primers published previously (Table 1 amd Table 2) [21]. The PCR was performed in a 50 µL reaction with 25µL Taq polymerase master mix (Amplicon, Denmark), 2 µL of 50 ng template DNA and 2 µL of each primer (10pmol). Following amplification condition was followed for PCR amplification: initial denaturation at 94 °C for 5 min, then denaturation at 94°C for 30 s, followed by annealing at 58 °C (for BsmI) 55 (for FokI) and 60 °C (for TaqI and ApaI) for 30s, 72 °C for 30s extension for 35 cycles, then final elongation at 72°C for 8 min and final hold at 4°C. The PCR product was digested with BsmI, FokI, ApaI and TaqI (Thermo Scientific FastDigest).

The restriction was performed using the following mixture (1 µl restriction enzyme+34 µl nuclease-free water+10 µl PCR product (0.2 µg)+5 µl 10× buffer) was incubated as mentioned in the product catalog. The restricted PCR products were visualized using 2% agarose gel containing ethidium bromide under ultraviolet transillumination. Nested PCR was performed to determine the VDR PolyA polymorphism. The PCR was started initially with genomic DNA amplified using the first set of primers and amplified for 35 cycles with an annealing temperature of 62 °C. Nested PCR was performed using 5 µl of the first PCR product of 1:200 dilution along with 2.5 pmol IR770dATP by following the conditions 94 °C for 2 minutes, followed by 35 cycles with 30 seconds each at 94 °C, 66 °C, and 72 °C, concluding with 3 minutes at 72 °C.

©2024Int. J. LifeSci.Biotechnol.Pharma.Res.

Table 1. Primers used for detecting the VDR SNP and restriction enzymes.

SNP	*Primer Sequence*	*Restriction Enzyme*
Bsm I	F- 5'-CGGGGAGTATGAAGGACAAA-3' R- 5'-CCATCTCTCAGGCTCCAAAG-3'	Hha-I
FokI	5'-AGCTGGCCCTGGCACTGACTCtGGCTCT-3' 5'-ATGGAAACACCTTGCTTCTTCTCCCTC-3'	Fok-I
ApaI	5'-GGATCCTAAATGCACGGAGA-3' 5'-AGGAAAGGGGTTAGGTTGGA-3'	Apa-I
Taq1	5'-GGATCCTAAATGCACGGAGA-3' 5'-AGGAAAGGGGTTAGGTTGGA-3'	Taq-I
Poly (A)	F5'-GACAGAGGAGGGCGTGACTC-3' R 5'- GTGTAGTGAAAAGGACACCGGA-3' 1F 5'-GAGACCAACCTGACCA-3' 1R 5'-CCTCAGCCTCCTGAGT-3'	

Table 2. Genotyping Pattern

SNP	**Pattern**
BsmI	Bb heterozygote: 348, 243, 105 bp, bb homozygote: 243, 105 bp, Amplicon: 348 bp
FokI	FF homozygote: 267 bp, Ff heterozygote: 267, 198, 69 bp ff homozygote: 198, 69 bp, Amplicon: 267 bp
ApaI	AA homozygote: 630 bp, Aa heterozygote: 630, 484, 146 bp aa homozygote: 484, 146 bp, Amplicon: 630 b
Taq1	TT homozygote: 425, 205 bp, Tt heterozygote: 425, 225, 205, 200 bp, tt homozygote: 225, 205, 200 bp, Amplicon: 630 bp
Poly(A)	113 to 116 bp, 120–123 bp

Statistical Analysis

Using chi-square test, the genotype distribution among subjects in the control group was analyzed for Hardy–Weinberg equilibrium (HWE) for each SNP; with the same test, the p-value for age and gender was established; standard errors of the mean (SEMs) were counted for age. SHEsis software is used for performing the linkage disequilibrium analysis (LD), construction of haplotype and genetic association. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to set the association between alleles and genotypes.

RESULT

Population characteristics

Assessing vitamin D polymorphism for determining the susceptibility of breast cancer patients was performed as a case-control study. In this study, about 200 women were analyzed, 100 women with breast cancer (BC group), and 100 women as control groups. The mean value of women's age in this study was 41.4 ± 17.7. We genotyped five SNPs of the VDR gene in our population.

Association between genotypes and alleles

The distribution of genotype, allele frequency and SNP polymorphisms of VDR genes in the selected population was studied. The BB genotype (homozygous allele 1) of BsmI polymorphism distribution was observed higher among breast cancer cases (36.5%) than controls (28.3%). The heterozygous genotype (Ff) of FokI polymorphism occurrence was higher among breast cancer cases (33.4%) than among controls (8.3%). The incidence percentage of Aa heterozygous genotype of ApaI polymorphism was more in breast cancer cases than controls (38.5%: 19.6%). Tt heterozygous genotype was more prevalent among breast cancer cases (59.9%) than the control group (37.2%). The genotype distribution and allele frequency of the control population confirmed the Hardy-Weinberg equilibrium (P = 0.62, P = 0.51, P = 0.24), whereas the FokI and PolyA allele frequencies missed the Hardy-Weinberg equilibrium (P = 0.0001, P = 0.0001).

Table 3: Genotypes and Allele Frequency of VDR SNPs

SNP	**Genotype & Allele**	**BC Frequency (%)**	**Control Frequency (%)**
BsmI	BB	36.5	28.3
	Bb	6.2	42.8
	bb	11.8	24.6
	B	61.2	55.7
	b	33.4	42.8
FokI	FF	31.7	21.8
	Ff	33.4	8.3
	ff	35.1	73.7
	F	50.2	73.8
	f	47.8	25.2
ApaI	AA	44.6	58.4
	Aa	38.5	19.6
	aa	15.2	18.9
	A	63.5	69.1
	a	34.7	30.2
TaqI	TT	14.3	12.9

©2024Int. J. LifeSci.Biotechnol.Pharma.Res.

	Tt	59.9	37.2
	tt	29.7	40.4
	T	57.8	61.5
	t	43.6	35.7
PolyA	LL	42.7	41.8
	LS	40.3	42.1
	SS	16.9	18
	L	64.7	65.3
	S	36.4	34.3

Association of VDR polymorphism with breast cancer risk

The odd ratios associating VDR polymorphism and breast cancer in the study population were calculated. The association of BsmI (rs1544410) with breast cancer between the two study groups was performed by Univariate logistic regression statistical analysis representing significant variation under the recessive and codominant models of inheritance. The Bb genotype in the recessive model had a defensive effect on the controls, resulting in low chance among the patients (OR: 2.74, 95% CI = 1.29–4.76, $p < 0.01$). As a codominant model, genotype BB was more prevalent among cancer patients (36.5%) than controls (28.3%). The genotype bb had the least prevalence among cancer patients (11.8% in breast cancer vs 24.6% in controls) with OR = 2.85, 95% CI = 1.34–5.96, $P < 0.05$. In FokI, the genotype frequency difference was significant between two groups. The Ff and FF genotypes show a high chance among the patients (OR = 0.27 95% CI = 0.13–0.43, $p = 0.001$). The genotype ff shows more prevalence among control than patients (OR 0.29, 95% CI 0.13–0.44, $P = 0.0001$). In recessive condition, the genotype distribution of VDR ApaI was not found to be significant among test groups whereas, as codominance Aa was more commonly found among cancer cases 38.5% than controls 19.6% (OR = 0.42, 95% CI = 0.25–0.73, $P = 0.01$). Also, aa genotype was commonly found in breast cancer patients in the recessive model (OR 0.27, 95% CI = 0.15–0.49, $P < 0.01$). TaqI and PolyA polymorphisms exhibit no significant distribution between the two groups.

DISCUSSION

VDR polymorphisms are more associated with various health complications which also include multiple cancers. We aimed to evaluate the VDR polymorphism and susceptibility of breast cancer among the patients in our hospital setup. VDR is one of the steroid hormone receptors, regulate cell proliferation. The pathogenesis of breast cancer not only includes various genetic and environmental factors affecting the cellular signalling pathways. As various studies have found a highly significant association between progression of breast cancer and VDR polymorphism. Hence, we selected five variants of VDR for determining the association of VDR with susceptibility to breast cancer. The VDR selected for the genotype study are BsmI (rs1544410), FokI (rs2228570), ApaI (rs7975232), TaqI (rs731236), and PolyA. Genotype distribution, allele frequency and its association with breast cancer for 5 selected SNPs were analyzed in this study.

In this study, 100 breast cancer cases and 100 healthy controls were analyzed for VDR polymorphism. The distribution of BsmI, FokI and ApaI polymorphisms showed a significant distribution among the patient samples than the control cases. The genotype distribution of BsmI, FokI and ApaI was in the Hardy-Weinberg equilibrium whereas the TaqI and PolyA weres not in the equilibrium. Lack of heterozygosity among the alleles in the genes among the study population could be a hypothesized cause of disrupting the equilibrium. Many studies have been deployed for understanding the association of candidate genes involvement in breast cancer. In contrast, varying reports on the association between VDR and the risk of breast cancer[22-24]. The frequency of the B allele showed an association of increase in risk with breast cancer was reported in one Hispanic study[17,25-26], whereas no association was reported in a few studies[12, 27]. One study reported the significant association of b allele of BsmI with an increased breast cancer risk[28]. In a study, an evaluation of the association of VDR polymorphisms of Bsm1, Apa1, Taq1, and Fok1 with the risk of breast cancer showed no significant association between these SNPs and the risk of breast cancer[18]. In another study, it is reported that Bsm1 polymorphism and breast cancer incidence are significantly associated, but no significant association was noticed for Fok1 in Iranian populations[29]. The present study results confirm that both BsmI and FokI have a significant association with the risk of breast cancer. In contrast to the present study, Yiallourou et al. reported, polymorphism of FokI was associated with the risk of staging breast cancer and survival among the patients[30].

Concerning the ApaI polymorphism and breast cancer risk, we observed a significant association between the risk of breast cancer and the Aa genotype. This result is accept by Curran et al.[19] study which found to be significantly increased risk of breast cancer with ApaI Aa genotype. Similarly, Dalessandri et al.[31] reported that the women carrying VDR Apa1A2/A2 genotype show increased susceptibility to breast cancer, whereas no significant associations between breast cancer and the ApaI polymorphisms were reported by McCullough et al.[18] and Mishra et al.[32].

©2024Int. J. LifeSci.Biotechnol.Pharma.Res.

In a study, Perna et al. reported that rare homozygotes alleles of TaqI polymorphism had an augmented the risk of mortality in breast cancer women.[33]. The absence of an association of TaqI and breast cancer susceptibility was reported in numerous studies. In a population-based case-control study, the low frequency of association or no association of breast cancer was reported towards TaqI VDR genotype[34, 35]. Overall, a meta-analysis study showed that all FokI, BsmI, ApaI, and TaqI variants of VDR polymorphisms were not associated with risk of breast cancer[36, 37]. Our results showed that BsmI, FokI and ApaI could be associated with breast cancer.

CONCLUSION

Determining genotype and allele frequency will help us in creating the panel which might contribute to screening the people at great risk for cancer progression and also help us in conducting oncological surveys among the susceptible population. This study indicates that VDR polymorphisms are associated with the risk of progression of breast cancer. This study will be conducted with screening more populations and will help in the early prediction and diagnosis of the disease and more effective treatment.

Acknowledgement

The study was supported by Multi-Disciplinary Research Unit, Department of Health Research. We acknowledge DHR was for providing funds and infrastructure for doing the study. Authors would like to thank all the members who have participated in the research.

Conflicts of Interest

There are no conflicts of interest.

REFERENCES

1. Trang HM, Cole DE, Rubin LA, Pierratos A, Siu S, Vieth R. Evidence that vitamin D3 increases serum 25-hydroxyvitamin D more efficiently than does vitamin D2. Am J Clin Nutr. 1998; 68(4):854-858.
2. D Bretherton-Watt D, Given-Wilson R, Mansi JL, Thomas V, Carter N and Colston KW. Vitamin D receptor gene polymorphisms are associated with breast cancer risk in a UK Caucasian population. British Journal of Cancer, 2001; 85(2), 171–175.
3. Jurutka PW, Whitfield GK, Hsieh JC, Thompson PD, Haussler CA and Haussler MR. Molecular nature of the vitamin D receptor and its role in regulation of gene expression. Rev Endocr Metab Disord. 2001; 2(2):203-216.
4. Uitterlinden A, Fang Y, van Meurs J, Pols H and van Leeuwen, J. Genetics and biology of vitamin D receptor polymorphisms. Gene; 338, 143-156.
5. Jiang YJ, Teichert AE, Fong F, Oda Y and Bikle DD. 1α, 25(OH)2-dihydroxyvitamin D3/VDR protects the skin from UVB-induced tumor formation by interacting with the β-catenin pathway. J Steroid Biochem Mol Biol. 2013; 136:229-32.
6. Mishra DK, Wu Y, Sarkissyan M, Sarkissyan S, Chen Z, et al. Vitamin D Receptor Gene Polymorphisms and Prognosis of Breast Cancer among African-American and Hispanic Women. PLoS ONE 8(3): e57967.
7. Haidan M El-Shorbagy, Nada H Mahmoud and Salwa Sabet. Association of vitamin D receptor gene polymorphisms with breast cancer risk in an Egyptian population. Tumor Biology, 2017: 1-9.
8. Köstner K, Denzer N, Müller CS, Klein R, Tilgen W, Reichrath J. The relevance of vitamin D receptor (VDR) gene polymorphisms for cancer: a review of the literature. Anticancer Res. 2009; 29(9):3511-36.
9. Li J, Li B, Jiang Q, Zhang Y, Liu A, Wang H, Zhang J, Qin Q, Hong Z, Li BA. Do genetic polymorphisms of the vitamin D receptor contribute to breast/ovarian cancer? A systematic review and network meta-analysis. Gene. 2018 Nov 30;677:211-227.
10. GLOBOCAN. Summary statistics 2020: World. https://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf3.
11. Kazemi SM, Esmaieli-Bandboni A, Veisi Malekshahi Z, Shahbaz Sardood M, Hashemi M, Majidzadeh K, Kadkhodazadeh M, Esmaili R, Negahdari B. Vitamin D receptor gene polymorphisms and risk of breast cancer in Iranian women. Ann Med Surg (Lond). 2021; 4:73:103150.
12. McKay JD, McCullough ML, Ziegler RG, Kraft P, Saltzman BS, Riboli E, Barricarte A, Berg CD, Bergland G, Bingham S, Brustad M, Bueno-de-Mesquita HB, Burdette L, Buring J, Calle EE, Chanock SJ, Clavel-Chapelon F, Cox DG, Dossus L, Feigelson HS, Haiman CA, Hankinson SE, Hoover RN, Hunter DJ, Husing A, Kaaks R, Kolonel LN, Le Marchand L, Linseisen J, McCarty CA, Overvad K, Panico S, Purdue MP, Stram DO, Stevens VL, Trichopoulos D, Willett WC, Yuenger J, Thun MJ. Vitamin D receptor polymorphisms and breast cancer risk: results from the National Cancer Institute Breast and Prostate Cancer Cohort Consortium. Cancer Epidemiol Biomarkers Prev. 2009; 18:297–305.
13. Zhang K. and Song L. Association between vitamin D receptor gene polymorphisms and breast cancer risk: A meta-analysis of 39 studies. PLoS One, 2014; 9, e96125.
14. Shaikhn F, Baig S and Jamal Q. Do VDR gene polymorphisms contribute to breast cancer? Asian Pac. J. Cancer Prev. 2016; 17, 479-483.
15. Xu Y, Shibata A, McNeal JE, Stamey TA, Feldman D, Peehl DM. Vitamin D receptor start codon polymorphism (FokI) and prostate cancer progression. Cancer Epidemiol Biomarkers Prev. 2003; 12(1):23-7.
16. Uitterlinden AG, Fang Y, Van Meurs JB, Pols HA, Van Leeuwen JP. Genetics and biology of vitamin D receptor polymorphisms. Gene. 2004; 338(2): 143– 56.
17. Ingles SA, Garcia DG, Wang W, Nieters A, Henderson BE, Kolonel LN, Haile RW, Coetzee GA. Vitamin D receptor genotype and breast cancer in Latinas (United States). Cancer Causes Control. 2000; 11(1):25-30.
18. McCullough ML, Stevens VL, Diver WR, Feigelson HS, Rodriguez C, Bostick RM, Thun MJ, Calle EE. Vitamin D pathway gene polymorphisms, diet, and risk of postmenopausal breast cancer: a nested case-control study. Breast Cancer Res. 2007; 9(1):R9.
19. Curran JE, Vaughan T, Lea RA, Weinstein SR, Morrison NA, Griffiths LR. Association of A vitamin D receptor polymorphism with sporadic breast cancer development. Int J Cancer. 1999; 83(6):723-6.
20. Guy M, Lowe LC, Bretherton-Watt D, Mansi JL, Peckitt C, Bliss J, Wilson RG, Thomas V, Colston KW. Vitamin D receptor gene polymorphisms and breast cancer risk. Clin Cancer Res. 2004;10(16):5472-81.
21. Latacz M, Rozmus D, Fiedorowicz E, Snarska J, Jarmołowska B, Kordulewska N, Savelkoul H, Cieślińska A. Vitamin D Receptor (VDR) Gene Polymorphism in Patients Diagnosed with Colorectal Cancer. Nutrients. 2021; 13(1):200.
22. Chen WY, Bertone-Johnson ER, Hunter DJ, Willett WC and Hankinson SE. Associations between polymorphisms in the vitamin D receptor and breast cancer risk. Cancer Epidemiol Biomarkers Prev 2005, 14:2335-2339.

©2024Int. J. LifeSci.Biotechnol.Pharma.Res.

23. Ruggiero M, Pacini S, Aterini S, Fallai C, Ruggiero C, Pacini P. Vitamin D receptor gene polymorphism is associated with metastatic breast cancer. Oncol Res 1998, 10:43-46.
24. Buyru N, Tezol A, Yosunkaya-Fenerci E, Dalay N. Vitamin D receptor gene polymorphisms in breast cancer. Exp Mol Med 2003, 35:550-555.
25. Huang AJ, Yu KD, Li J, Fan L, Shao ZM. Polymorphism rs4919510:C>G in mature sequence of human microRNA-608 contributes to the risk of HER2-positive breast cancer but not other subtypes. PLoS One. 2012; 7(5):e35252.
26. Mavaddat N, Antoniou AC, Easton DF, Garcia-Closas M. Genetic susceptibility to breast cancer. Mol Oncol. 2010 Jun;4(3):174-91.
27. Mishra DK, Wu Y, Sarkissyan M, Sarkissyan S, Chen Z, Shang X, et al. Vitamin D receptor gene polymorphisms and prognosis of breast cancer among African-American and Hispanic women. PLoS One 2013; 8(3):e57967.
28. Rashid MU, Muzaffar M, Khan FA, Kabisch M, Muhammad N, Faiz S, et al. Association between the BsmI Polymorphism in the Vitamin D Receptor Gene and Breast Cancer Risk: Results from a Pakistani Case-Control Study. PLoS ONE, 2015; 10(10): e0141562.
29. Shahbazi S, Alavi S, Majidzadeh-A K, Ghaffarpour M, Soleimani A, Mahdian R. BsmI but not FokI polymorphism of VDR gene is contributed in breast cancer. Med Oncol. 2013 Mar;30(1):393.
30. Yiallourou AI, Ekonomou E, Tsamadias V, Nastos K, Karapanos K, Papaconstantinou I, Theodosopoulos T, Contis J, Papalambros E, Voros D, Psychogios J. Association of FokI and PvuII polymorphisms with breast cancer staging and survival among Caucasian women: a prospective study. J BUON. 2014; 19(3):633-42.
31. Dalessandri KM, Rei M, Wiencke JK, Farren G, Pugh TW, Manjeshwar S, et al. Vitamin D receptor polymorphisms and breast cancer risk in a high-incidence population: a pilot study. J Am Coll Surg. 2012; 215(5):652–7.
32. Mishra DK, Wu Y, Sarkissyan M, Sarkissyan S, Chen Z, Shang X, et al. Vitamin D receptor gene polymorphisms and prognosis of breast cancer among African-American and hispanic women. PLoS One. 2013; 8(3):e57967.
33. Perna L, Butterbach K, Haug U, Schöttker B, Müller H, Arndt V, Holleczek B, Burwinkel B, Brenner H. Vitamin D receptor genotype rs731236 (Taq1) and breast cancer prognosis. Cancer Epidemiol Biomarkers Prev. 2013;22(3):437-42.
34. John EM, Schwartz GG, Koo J, Wang W and Ingles SA: Sun exposure, vitamin D receptor gene polymorphisms, and breast cancer risk in a multiethnic population. Am J Epidemiol 166: 1409-1419, 2007
35. Hou MF, Tien YC, Lin GT, et al: Association of vitamin D receptor gene polymorphism with sporadic breast cancer in Taiwanese patients. Breast Cancer Res Treat. 2002; 74: 1-7,.
36. D. Lu, L. Jing, S. Zhang, Vitamin D receptor polymorphism and breast cancer risk: a meta-analysis, Medicine (Baltim.) 95 (18) (2016) e3535.
37. Kazemi SM, Esmaieli-bandboni A, Malekshahi ZV, ShahbazSardood M, Hashemi M, Majidzadeh K, Kadkhodazadeh M, Rezvan Esmaili R, Negahdari B, 2022. Vitamin D receptor gene polymorphisms and risk of breast cancer in Iranian women. Ann. of Med Sur, 2022; 73, 103150.

©2024Int. J. LifeSci.Biotechnol.Pharma.Res.