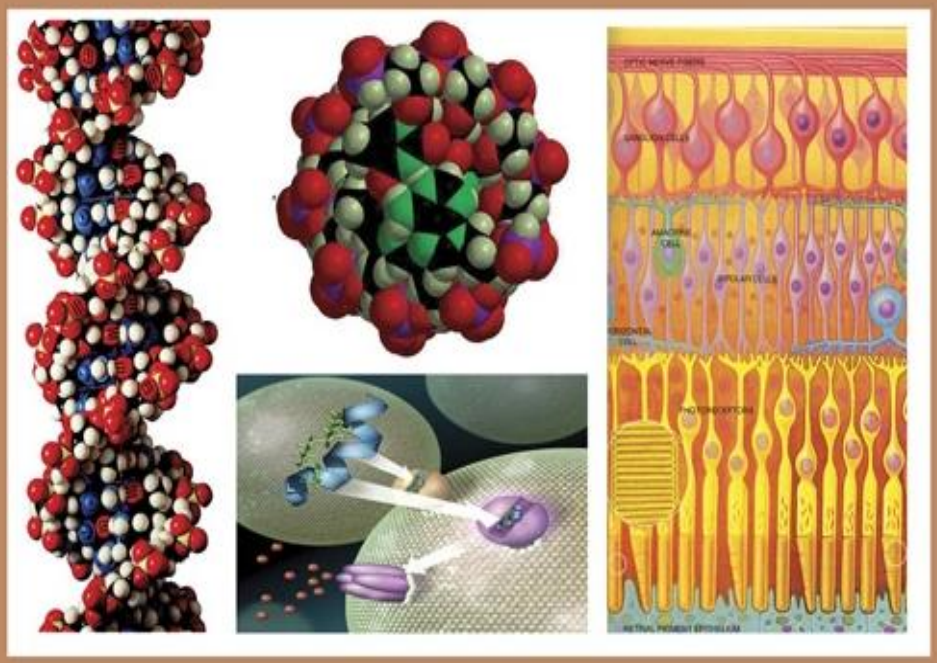
EGYPTIAN ACADEMIC JOURNAL OF

BIOLOGICAL SCIENCES

C

PHYSIOLOGY & MOLECULARBIOLOGY



ISSN
2090-0767

WWW.EAJBS.EG.NET

Vol. 13 No. 1 (2021)

Citation: *Egypt.Acad.J.Biolog.Sci. (C.Physiology and Molecular biology) Vol. 13(1) pp83-91 (2021)*
DOI: 10.21608/EAJBSC.2021.159944

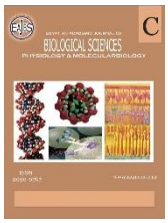
Egypt. Acad. J. Biolog. Sci., 13(1):83-91 (2021)

Egyptian Academic Journal of Biological Sciences

C. Physiology & Molecular Biology

ISSN 2090-0767

www.eajbsc.journals.ekb.eg



The Variant Allele Frequency of the lncRNA Prostate Cancer-Associated Noncoding RNA 1 (PRNCR1) rs1456315 C/T Polymorphism in Saudi Population and Colorectal Cancer Risk

Naseem Akhter

Department of Laboratory Medicine, Faculty of Applied Medical Sciences, Albaha University- Albaha- Saudi Arabia

*E. Mail: Naseem.du@gmail.com; nakhter@bu.edu.sa

ARTICLE INFO

Article History

Received:27/1/2021

Accepted:28/3/2021

Keywords:

Cancer; PRNCR1; rs1456315; single nucleotide polymorphism

ABSTRACT

Single-nucleotide polymorphisms (SNPs) in long noncoding RNA (lncRNA) genes are associated with the onset and progression of multiple cancers in humans. These SNPs are potential biomarkers for predicting cancer risk. The variable frequency of the lncRNA prostate cancer-associated noncoding RNA 1 (PRNCR1) rs1456315 C/T polymorphism may affect different ethnic groups differently, however, the information lacks for the Saudi population. The aim of this study was to assess the allelic distribution and frequency of the PRNCR1 rs1456315 C/T polymorphism in the Saudi Arabian population, as well as compare it to other populations around the world. PUBMED (Medline) and other related web-databases were referred to extract data from epidemiological studies performed in different ethnic groups. The frequency of PRNCR1 rs1456315 variant allele (C) was found to be 34.62% and a significantly different frequency was observed for the USA (p=0.01), Iran (p<0.007) and China (p=0.01) ethnicity, when the Saudi occurrence is compared to those populations. Present results reveal a distinct pattern of lncRNA prostate cancer-associated noncoding RNA 1 (PRNCR1) rs1456315 polymorphism variant allele in the Saudi Arabian population, which may be due to ethnic differences. The findings could assist in the risk assessment of people harbouring risk allele of rs1456315 SNP and their subsequent cancer susceptibility.

INTRODUCTION

Colorectal cancer results from a combination of epigenetic and genetic changes. The transformation of epithelial cells into colorectal adenocarcinoma could be caused by a variety of biological pathways. Colorectal cancer's genetic basis is represented as a multistep model of cancer onset and progression (Fearon and Vogelstein 1990). Long noncoding RNAs have been identified as important genetic regulators of a vital biological procedure central to risk of developing cancer and many other diseases. RNA transcripts longer than 200 nucleotides that do not code for any proteins are known as lncRNAs (Costa 2010). Some lncRNAs, such as Prostate cancer non-coding RNA 1 (PRNCR1), HOTAIR, and UCA1, are thought to play a role in the progression of cancer.

PRNCR1, a long noncoding RNA downregulated in a variety of cancers, is a 13-kb intron-less lncRNA transcribed from the 8q24 gene (Yang *et al.,* 2016). Previous research has revealed that PRNCR1 is essential for the development of prostate cancer risk, and it may also play a key role in prostate cancer progression by altering androgen receptor (AR) activity.

PRNCR1 has been shown to play a significant role in the development of many cancers in recent studies (Cheng *et al.*, 2018; Pang *et al.*, 2019) along with increased prostate cancer susceptibility by altering the AR system (Yang *et al.*, 2013).

PRNCR1 binds to the acetylated region of the androgen receptor, and its interaction with DOT1L appears to be needed for PCGEM recruitment to the DOT1L-mediated methylation of AR at the N-terminus. These overexpressed lncRNAs' interactions could potentially serve as important regulators in prostate cancer. However, the correlation between the lncRNA PRNCR1 and colorectal cancer development is only recently elucidated. Many studies have suggested that 8q24 variants can play a role in colon cancer susceptibility (Cicek *et al.*, 2009). Despite the fact that PRNCR1 is located in this critical genomic region, its function in Saudi populations for any cancer is yet to be elucidated. The current research compared the frequency distribution of the PRNCR1 rs1456315 polymorphism among normal healthy Saudi Arabians to numerous epidemiologic studies conducted around the world.

MATERIALS AND METHODS

Search Criteria Of Gene Variants:

PUBMED (Medline), Web of Science, and EGEMS databases were searched for reports that contained the keywords "PRNCR1" "rs1456315" "polymorphism,". The searches were restricted to human subjects and written in any language. Studies with genotype frequencies for the control population were included, although studies with only allele frequencies and no genotype frequencies were removed.

The first author's name, the year of publication, the nationality of the subjects, the number of controls, the research type, the inclusion/exclusion criteria, and the frequencies of alleles/ genotypes of the subjects were all abstracted for each of the qualifying studies. When there were several reports from the same race, the data from the most recent publication were used.

The prevalence of the PRNCR1 rs1456315 polymorphism was abstracted from eight studies (AlMutairi *et al.*, 2019; Chung *et al.*, 2011; Li *et al.*, 2016; Li *et al.*, 2013; Li *et al.*, 2021; Salinas *et al.*, 2008; Sattarifard *et al.*, 2017; Xu *et al.*, 2017) and included in the current analysis, which was then compared to the Saudi Arabian population.

Statistical Analysis:

Pearson's χ^2 test was used to compare genotype and allelic frequencies of different populations using the SPSS statistical software program (version 21). Hardy-Weinberg equilibrium was studied using Court-Lab (a web-based software program). A statistically significant *p* value of ≤ 0.05 was used.

RESULTS

The minor allele frequency (MAF) of the PRNCR1 rs1456315 polymorphism in the Saudi Arabian population was found to be 34.62 percent according to the genotype distribution, which was in accordance with Hardy–Weinberg equilibrium (HWE) (Table 1). Different minor allele frequencies were found in the genotypic (T/T, T/C, and C/C) and allelic frequency distributions of the studied polymorphism among various populations (Table 2).

When the Saudi Arabian frequency was compared to that of other populations, a substantially different

MAF was observed for the ethnicities of the United States (p=0.01), Iran (p=0.007), and China (p=0.01).

Table 1. Observed and expected genotypic frequencies of PRNCR1 rs1456315 C/T polymorphism in the control group

Study	Genotype observed (n)			Genotype Expected (n)			MAF	p-value (HWE)
	T/T	T/C	C/C	T/T	T/C	C/C		
Al Mutairi *et al,* 2019	61	48	21	56	59	16	0.34	0.04

Table 2. PRNCR1 rs1456315 C/T gene variant genotype and allele frequency distribution in different populations and p-values in contrast to Saudi Arabian population

Study	**Country/ ethnicity**	**(n)**	**Race**	**Tumor type in the cases**	**Genotype**			***P* value**	**MAF**
					T/T	**T/C**	**C/C**		
Al Mutairi *et al.,* 2019	Saudi Arabia	130	Asian	Colorectal Cancer	61	48	21	Ref	34.62
Salinas *et al.,* 2008	USA	1233	Caucasian	Prostate cancer	401	605	227	0.01*	42.94
Chung *et al.,* 2011	Japan	1553	Asian	Prostate Cancer	663	703	187	1	34.67
Li *et al.,* 2013	China	595	Asian	Colorectal Cancer	294	262	39	0.06	28.57
Li *et al.,* 2016	China	394	Asian	Gastric Cancer	179	177	38	0.50	32.11
Sattarifard *et al.,* 2017	Iran	180	Asian	Prostate Cancer	92	88	0	0.007*	24.44
Xu *et al.,* 2017	China	439	Asian	Breast Cancer	244	159	36	0.01*	26.31
Li *et al.,* 2021	China	612	Asian	Lung cancer	288	263	61	0.35	31.45

DISCUSSION

Most diseases are multifactorial, resulting from a complex combination of genetic and environmental factors that influence disease progression during life. An increasing body of evidence indicates that genetic variation leads to vulnerability to common diseases like diabetes, cardiovascular disease, and cancer (Eccles and Tapper 2010; Hanahan and Weinberg 2000; Schmith *et al.,* 2003). The discovery of genetic variation linked to common complex diseases is thus a top priority in understanding the pathophysiological mechanisms that underpin common human illnesses. There has been a growing interest in the potential effect of common, functional germline polymorphisms on cancer risk, development and prognosis of cancer.

The genomic variations seen in a group or species are referred to as genetic variation (Nevo 1978), which is also known as a parameter that influences an individual's phenotype due to the great diversity in the human genome (Kaneko and Furusawa 2006). Genetic diversity refers to variation in individual genes, and it provides a mechanism for population survival by allowing them to adapt to a constantly changing environment. Genetic variation within and between populations has long been considered to be the secret to understanding the biology of human disease (McKeigue 1997; Shriver 1997; Shriver *et al.,* 2005).

The SNP rs1456315 is linked to a higher risk of CRC, particularly in younger people. Previous research has linked the rs1456315 gene to colorectal cancer, gastric cancer, pancreatic cancer and Prostate cancer (Chu *et al.,* 2017; Li et al., 2016; Li et al., 2013). The SNP rs1456315 has also been found to be significantly associated in Saudi population (AlMutairi et al., 2019) which corroborates an early finding (Chung et al., 2011). Further, PRNCR1 regulates AR activity in the prostate and thus plays an important role in the prostate (Chung et al., 2011). Several other studies have found that AR plays a role in pathological growth. TGFβ is also thought to play a role in the development

of CRC (Ferro *et al.,* 2002; Mariani *et al.,* 2012).

Prostate cancer commonly has a genetic component (Bruner *et al.,* 2003; Lichtenstein *et al.,* 2000; Zeegers *et al.,* 2003). Genetic linkage studies have identified a number of putative loci that may harbor prostate cancer susceptibility genes (Xu *et al.,* 2005), and variant alleles in some candidate genes have been reported to be associated with prostate cancer risk (Rawla 2019), but the results have proven difficult to replicate (Schaid 2004).

The 8q24 region's discovery is noteworthy for the effective discovery of multiple markers across different ethnicities (Gudmundsson *et al.,* 2007; Haiman *et al.,* 2007). It's worth noting that the original linkage finding resulted from the investigation of a possible linkage signal (Amundadottir *et al.,* 2006). DG8S737 and rs1447295, the two original markers, have received the most attention, but many other SNPs in the 8q24 region have recently been linked to prostate cancer risk. Fine mapping of the 8q24 region with SNPs from genome-wide association studies (Gudmundsson et al., 2007) and follow-up of an early admixture analysis (McKeigue 1997) have shown that many regions within 8q24 have variants that can influence the susceptibility of prostate cancer (Witte 2007).

The global variation of human genomes is the result of a series of evolutionary events such as migration, admixture, population separation, selective pressure, and genetic drift (Balaresque *et al.,* 2007; Barbujani and Colonna 2010; Henn *et al.,* 2012). Understanding health and disease is supported by genomic imprints conserved in the genomes of diverse populations (Hancock *et al.,* 2011; Scheinfeldt and Tishkoff 2013). The HapMap project and the Human Genome Diversity Project (HGDP) have recently made important contributions to the evolution of a single nucleotide changes database by documenting genetic differences within individuals of an ethnic group as well as between different ethnicities, globally (Li *et al.,* 2008; Rosenberg *et al.,* 2002; The International HapMap 2005).

An exploration of genetic variation in the Saudi population, which is probably diverse, may contribute to early prevention and intervention strategies. The frequency distribution of the PRNCR1 rs1456315 polymorphic variant in the Saudi population was compared to that of other populations around the world in this analysis. PRNCR1 has been steadily studied as a newly discovered lncRNA that affects tumor cell proliferation, invasion, and apoptosis, and it has become a research target for the early diagnosis and treatment of various cancers. SNPs in PRNCR1, such as rs13252298, rs1016343, and rs1456315, have been linked to the risk of multiple cancers in numerous studies (Chu et al., 2017; Huang *et al.,* 2018; Teerlink *et al.,* 2016).

ncRNAs were found to have a range of biological activities during tumorigenesis and development in several studies. MicroRNAs (miRNAs) and lncRNAs are two subgroups of the ncRNA family that could interact to form a ceRNA network (Chen *et al.,* 2018). LncRNAs have the ability to influence the development of cancer by controlling several biological processes in human cancer through various mechanisms. In Saudi population, the current study reveals a 34 percent frequency of a variant allele (C) of rs1456315, which is substantially different from many other countries such as the United States, Iran, and China.The variant allele frequency of Saudi population was discovered to be higher than Japan, Iran, and China, but lower than the United States. When the Saudi population was compared to the Japanese population and a few cohorts of Chinese

citizens, the frequency distribution of the variant allele was found to be almost identical. rs1456315 is linked with a lower risk of colorectal cancer in the Chinese population, but it has been linked to a substantially higher risk of colorectal cancer in the Saudi population (AlMutairi *et al.,* 2019; Li *et al.,* 2013).

Most SNPs are less penetrant, and diseases polygenic in nature, so differences in allele frequencies among independent datasets can influence the final SNP effect. In genetic-association studies, a shift of 0.02 in MAF will result in significant statistical changes. Furthermore, in the case of two interacting SNPs, a difference in allele frequency of less than 0.1 at the second interacting polymorphism will substantially reduce the independent effect of one SNP (Greene *et al.,* 2009). Racial variation, heterogeneity of the studied population, and variable sample sizes can all contribute to variations in allelic frequency in genetic association studies. Previous studies have shown that the PRNCR1 gene has a wide variety of patterns as compared to various populations around the world (Huang et al., 2018). The different prevalence of these SNPs across populations suggests that susceptibility factors have different effects on different populations.

It's worth noting that the allele and genotype frequencies studied in this analysis don't necessarily reflect the full range of variants at a locus. Such studies, on the other hand, could pave the way for the development of epidemiological and clinical databases in the future. Over the last decade, genome-wide association studies (GWAS) and genetic association studies have resulted in the development of vast data repositories (Pearson and Manolio 2008). Multiple genetic association tests are needed to identify important genes and/or their SNPS involved in the development of early disease prevention programs and treatments. However, several bottlenecks, such as statistical and computational trials, as well as the reproducibility factor, must be addressed before novel genetic biomarkers for use in gene-disease-association research can be identified (Hirschhorn and Daly 2005).

Conclusion

The PRNCR1 rs1456315 polymorphism variant allele in the Saudi population varies substantially from that of many other populations around the world. The results may aid in cancer population screening, as well as assessing disease predisposition and significance. Variations in the frequency distribution of the essential Prostate cancer-associated gene in the healthy Saudi population and other racial groups may aid in disease evaluation.

Furthermore, determining the susceptibility factors linked to individual susceptibility and predisposition to diseases such as cancer may reveal details about the etiology of carcinogenesis in the Saudi population. To use this polymorphism as a biomarker for large-scale cancer screening, future large studies investigating gene-gene and gene-environment interactions are needed.

Conflict of interest

The author declares no conflict of interest.

REFERENCES

AlMutairi M, Parine NR, Shaik JP, Aldhaian S, Azzam NA, Aljebreen AM, Alharbi O, Almadi MA, Al-Balbeesi AO, Alanazi M. (2019). Association between polymorphisms in PRNCR1 and risk of colorectal cancer in the Saudi population. *PLoS One,* 14:e0220931.

Amundadottir LT, Sulem P, Gudmundsson J, Helgason A, Baker A, Agnarsson BA, Sigurdsson A, Benediktsdottir KR, Cazier JB, Sainz J and others. (2006). A common variant

associated with prostate cancer in European and African populations. *Nature genetics*, 38:652-8.

Balaresque PL, Ballereau SJ, Jobling MA. (2007). Challenges in human genetic diversity: demographic history and adaptation. *Human Molecular Genetics*, 2:R134-9.

Barbujani G, Colonna V. (2010). Human genome diversity: frequently asked questions. Trends Genet 26:285-95.

Bruner DW, Moore D, Parlanti A, Dorgan J, Engstrom P. (2003). Relative risk of prostate cancer for men with affected relatives: systematic review and meta-analysis. *International journal of cancer*, 107:797-803.

Chen P, Fang X, Xia B, Zhao Y, Li Q, Wu X. (2018). Long noncoding RNA LINC00152 promotes cell proliferation through competitively binding endogenous miR-125b with MCL-1 by regulating mitochondrial apoptosis pathways in ovarian cancer. *Cancer medicine*, 7:4530-4541.

Cheng D, Bao C, Zhang X, Lin X, Huang H, Zhao L. (2018). LncRNA PRNCR1 interacts with HEY2 to abolish miR-448-mediated growth inhibition in non-small cell lung cancer. *Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie* 107:1540-1547.

Chu H, Chen Y, Yuan Q, Hua Q, Zhang X, Wang M, Tong N, Zhang W, Chen J, Zhang Z. (2017). The HOTAIR, PRNCR1 and POLR2E polymorphisms are associated with cancer risk: a meta-analysis. *Oncotarget*, 8:43271-43283.

Chung S, Nakagawa H, Uemura M, Piao L, Ashikawa K, Hosono N, Takata R, Akamatsu S, Kawaguchi T, Morizono T and others. (2011). Association of a novel long non-coding RNA in 8q24 with prostate cancer susceptibility. *Cancer science*, 102:245-52.

Cicek MS, Slager SL, Achenbach SJ, French AJ, Blair HE, Fink SR, Foster NR, Kabat BF, Halling KC, Cunningham JM and others. (2009). Functional and clinical significance of variants localized to 8q24 in colon cancer. *Cancer Epidemiol Biomarkers Prev*, 18:2492-500.

Costa FF. (2010). Non-coding RNAs: Meet thy masters. *BioEssays*, 32:599-608.

Eccles D, Tapper W. (2010). The influence of common polymorphisms on breast cancer. *Cancer treatment and research*, 155:15-32.

Fearon ER, Vogelstein B. (1990). A genetic model for colorectal tumorigenesis. *Cell*, 61:759-67.

Ferro P, Catalano MG, Dell'Eva R, Fortunati N, Pfeffer U. (2002). The androgen receptor CAG repeat: a modifier of carcinogenesis?. *Molecular and cellular endocrinology*, 193:109-20.

Greene CS, Penrod NM, Williams SM, Moore JH. (2009). Failure to replicate a genetic association may provide important clues about genetic architecture. *PLoS One*, 4:e5639.

Gudmundsson J, Sulem P, Manolescu A, Amundadottir LT, Gudbjartsson D, Helgason A, Rafnar T, Bergthorsson JT, Agnarsson BA, Baker A and others. (2007). Genome-wide association study identifies a second prostate cancer susceptibility variant at 8q24. *Nature genetics*, 39:631-7.

Haiman CA, Patterson N, Freedman ML, Myers SR, Pike MC,

Waliszewska A, Neubauer J, Tandon A, Schirmer C, McDonald GJ and others. (2007). Multiple regions within 8q24 independently affect risk for prostate cancer. *Nature genetics*, 39:638-44.

Hanahan D, Weinberg RA. (2000). The hallmarks of cancer. *Cell*, 100:57-70.

Hancock AM, Witonsky DB, Alkorta-Aranburu G, Beall CM, Gebremedhin A, Sukernik R, Utermann G, Pritchard JK, Coop G, Di Rienzo A. (2011). Adaptations to climate-mediated selective pressures in humans. *PLoS Genet*, 7:e1001375.

Henn BM, Cavalli-Sforza LL, Feldman MW. (2012). The great human expansion. *Proceedings of the National Academy of Sciences of the U S A*, 109:17758-64.

Hirschhorn JN, Daly MJ. (2005). Genome-wide association studies for common diseases and complex traits. *Nature Review Genetics*, 6:95-108.

Huang X, Zhang W, Shao Z. (2018). Association between long non-coding RNA polymorphisms and cancer risk: a meta-analysis. *Bioscience reports*, 38 (4): BSR20180365

Kaneko K, Furusawa C. (2006). An evolutionary relationship between genetic variation and phenotypic fluctuation. *Journal of theoretical biology*, 240:78-86.

Li JZ, Absher DM, Tang H, Southwick AM, Casto AM, Ramachandran S, Cann HM, Barsh GS, Feldman M, Cavalli-Sforza LL and others. (2008). Worldwide human relationships inferred from genome-wide patterns of variation. *Science*, 319:1100-4.

Li L, Jia F, Bai P, Liang Y, Sun R, Yuan F, Zhang L, Gao L. (2016). Association between polymorphisms in long non-coding RNA PRNCR1 in 8q24 and risk of gastric cancer. *Tumour Biology*, 37:299-303.

Li L, Sun R, Liang Y, Pan X, Li Z, Bai P, Zeng X, Zhang D, Zhang L, Gao L. (2013). Association between polymorphisms in long non-coding RNA PRNCR1 in 8q24 and risk of colorectal cancer. J*ournal of experimental & clinical cancer research : CR*, 32:104.

Li N, Cui Z, Gao M, Li S, Song M, Wang Y, Tong L, Bi Y, Zhang Z, Wang S and others. (2021). Genetic Polymorphisms of PRNCR1 and Lung Cancer Risk in Chinese Northeast Population: A Case-Control Study and Meta-Analysis. *DNA and cell biology*, 40:132-144.

Lichtenstein P, Holm NV, Verkasalo PK, Iliadou A, Kaprio J, Koskenvuo M, Pukkala E, Skytthe A, Hemminki K. (2000). Environmental and heritable factors in the causation of cancer--analyses of cohorts of twins from Sweden, Denmark, and Finland. *The New England journal of medicine*, 343:78-85.

Mariani M, Zannoni GF, Sioletic S, Sieber S, Martino C, Martinelli E, Coco C, Scambia G, Shahabi S, Ferlini C. (2012). Gender influences the class III and V beta-tubulin ability to predict poor outcome in colorectal cancer. *Clinical cancer research : an official journal of the American Association for Cancer Research*, 18:2964-75.

McKeigue PM. (1997). Mapping genes underlying ethnic differences in disease risk by linkage disequilibrium in recently admixed populations. *American journal of human genetics*, 60:188-96.

Nevo E. (1978). Genetic variation in natural populations: patterns and theory. *Theoretical population biology,* 13:121-77.

Pang D, Hu Q, Lan X, Lin Y, Duan H, Cao S, Li L, Peng F, Pan F. (2019). The novel long noncoding RNA PRNCR12 is involved in breast cancer cell proliferation, migration, invasion and cell cycle progression. *Molecular medicine reports,* 19:1824-1832.

Pearson TA, Manolio TA. (2008). How to interpret a genome-wide association study. *JAMA,* 299:1335-44.

Rawla P. (2019). Epidemiology of Prostate Cancer. *World journal of oncology,* 10:63-89.

Rosenberg NA, Pritchard JK, Weber JL, Cann HM, Kidd KK, Zhivotovsky LA, Feldman MW. (2002). Genetic structure of human populations. *Science* ,298:2381-5.

Salinas CA, Kwon E, Carlson CS, Koopmeiners JS, Feng Z, Karyadi DM, Ostrander EA, Stanford JL. (2008). Multiple independent genetic variants in the 8q24 region are associated with prostate cancer risk. *Cancer Epidemiol Biomarkers Prev,* 17:1203-13.

Sattarifard H, Hashemi M, Hassanzarei S, Narouie B, Bahari G. (2017). Association between genetic polymorphisms of long non-coding RNA PRNCR1 and prostate cancer risk in a sample of the Iranian population. *Molecular and clinical oncology,* 7:1152-1158.

Schaid DJ. (2004). The complex genetic epidemiology of prostate cancer. *Human Molecular Genetics,* 13 Spec No 1:R103-21.

Scheinfeldt LB, Tishkoff SA. (2013). Recent human adaptation: genomic approaches, interpretation and insights. *Nature Review Genetics,* 14:692-702.

Schmith VD, Campbell DA, Sehgal S, Anderson WH, Burns DK, Middleton LT, Roses AD. (2003). Pharmacogenetics and disease genetics of complex diseases. *Cellular and molecular life sciences,* CMLS 60:1636-46.

Shriver MD. (1997). Ethnic variation as a key to the biology of human disease. *Annals of internal medicine,* 127:401-3.

Shriver MD, Mei R, Parra EJ, Sonpar V, Halder I, Tishkoff SA, Schurr TG, Zhadanov SI, Osipova LP, Brutsaert TD and others. (2005). Large-scale SNP analysis reveals clustered and continuous patterns of human genetic variation. *Human genomics,* 2:81-9.

Teerlink CC, Leongamornlert D, Dadaev T, Thomas A, Farnham J, Stephenson RA, Riska S, McDonnell SK, Schaid DJ, Catalona WJ and others. (2016). Genome-wide association of familial prostate cancer cases identifies evidence for a rare segregating haplotype at 8q24.21. *Human genetics,* 135:923-38.

The International HapMap C. (2005). A haplotype map of the human genome. Nature 437:1299-320.

Witte JS. (2007). Multiple prostate cancer risk variants on 8q24. *Nature genetics,* 39:579-80.

Xu J, Dimitrov L, Chang BL, Adams TS, Turner AR, Meyers DA, Eeles RA, Easton DF, Foulkes WD, Simard J and others. (2005). A combined genomewide linkage scan of 1,233 families for prostate cancer-susceptibility genes conducted by the international consortium for prostate cancer genetics. *American journal of human genetics,* 77:219-29.

Xu T, Hu XX, Liu XX, Wang HJ, Lin K, Pan YQ, Sun HL, Peng HX, Chen XX, Wang SK and others. (2017). Association between SNPs in Long Non-coding RNAs and the Risk of Female Breast Cancer in a Chinese Population. *Journal of Cancer,* 8:1162-1169.

Yang L, Lin C, Jin C, Yang JC, Tanasa B, Li W, Merkurjev D, Ohgi KA, Meng D, Zhang J and others. (2013). lncRNA-dependent mechanisms of androgen-receptor-regulated gene activation programs. *Nature,* 500:598-602.

Yang L, Qiu M, Xu Y, Wang J, Zheng Y, Li M, Xu L, Yin R. (2016). Upregulation of long non-coding RNA PRNCR1 in colorectal cancer promotes cell proliferation and cell cycle progression. *Oncology reports ,3*5:318-24.

Zeegers MP, Jellema A, Ostrer H. (2003). Empiric risk of prostate carcinoma for relatives of patients with prostate carcinoma: a meta-analysis. *Cancer,* 97:1894-903.