Published in final edited form as:
Prostate. 2008 May 15; 68(7): 691–697. doi:10.1002/pros.20754.

Association of variants at two 17q loci with prostate cancer risk in European and African Americans

Jielin Sun[1], **Lina Purcell**[1], **Zhengrong Gao**[1], **Sarah D. Isaacs**[3], **Kathleen E. Wiley**[3], **Fang-Chi Hsu**[2], **Wennuan Liu**[1], **David Duggan**[4], **John D. Carpten**[4], **Henrik Grönberg**[5], **Jianfeng Xu**[1], **Bao-Li Chang**[1], **Alan W. Partin**[3], **Patrick C. Walsh**[3], **William B. Isaacs**[3,†], and **S. Lilly Zheng**[1]

[1]Center for Human Genomics, Wake Forest University School of Medicine, Winston-Salem, NC

[2]Department of Biostatistical Sciences, Wake Forest University School of Medicine, Winston-Salem, NC

[3]Johns Hopkins Medical Institutions, Baltimore, MD

[4]Translational Genomics Research Institute (TGen), Phoenix, AZ

[5]Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

Abstract

Multiple SNPs at 17q12 and 17q24.3 were recently identified to be associated with prostate cancer risk using a genome-wide association study. Although these associations reached genome-wide significance level in a combined analysis of several study populations of European descent in the original report, confirmation in independent populations, including African Americans (AA), is critical to increase confidence that they represent true disease associations and whether the results can be generalized. Therefore, we evaluated these 7 SNPs in two populations recruited from Johns Hopkins Hospital, including European Americans (EA) (1,563 cases and 576 controls) and AA (364 cases and 353 controls). Each of the previously reported risk alleles of these 7 SNPs were more common in cases than in controls among EA and AA. The differences were highly significant in EA ($P = 10^{-4}$) and marginally significant in AA ($P = 0.04$) for 17q12SNPs. In contrast, the differences were not statistically significant in EA or AA for SNPs at 17q24.3, but were marginally significant for two SNPs ($P = 0.04$ - 0.06) when subjects from EA and AA were combined. Similar results were obtained for genotype and haplotype frequencies. These risk variants were not associated with aggressiveness of prostate cancer or other clinical variables such as TNM stage, pre-operative PSA, or age at diagnosis. Our results provide the first confirmation of these novel prostate loci and the first demonstration that these two loci may also play roles in prostate cancer risk among AA.

Keywords

prostate cancer; association; risk; 17q12; 17q24.3

Introduction

Prostate cancer is one of the most common cancers and a major public health problem in the US (1). Genetic susceptibility, age, and race are the risk factors most consistently associated with prostate cancer risk (2). With advances in genome-wide association studies, multiple

[†]Address for correspondence: Marburg 115, Johns Hopkins Hospital, 600 N. Wolfe Street, Baltimore, MD 21287, Phone: (410) 955-2518, Fax: (410) 955-0833, wisaacs@jhmi.edu .

risk variants for prostate cancer have been identified. However, only loci at 8q24 have been confirmed in independent study populations thus far (3-7).

Two novel loci at chromosome 17q were recently reported to be associated with prostate cancer risk by combining genetic linkage and association approaches (8). This study evaluated 310,520 SNPs in the genome using the Illumina Hap300 chip among 1,501 prostate cancer patients and 11,290 control subjects from Iceland. Examining the region at 17q where prostate linkage was previously reported revealed six SNPs at 17q12 and 17q24.3 were significantly associated with prostate cancer risk ($P < 5\times10^{-4}$, ranking from 68 to 100 in the genome). The associations of these SNPs were confirmed in three additional prostate cancer case-control populations of European ancestry. When combining the results from the initial Icelandic population and three confirmation populations, the risk allele of the most significant SNP at 17q12 (rs4430796) conferred an OR of 1.22 (95% CI: 1.15-1.30, $P = 1.4\times10^{-11}$), and at 17q24.3 (rs1859962) conferred an OR of 1.20 (95% CI: 1.14-1.27, $P = 2.5 \times 10^{-10}$).

Although the initial report of prostate cancer associations at 17q12 and 17q24.3 reached genome-wide significance, it remains necessary to confirm these findings to rule out false positive results because these were selected by screening more than 300,000 SNPs in the initial discovery population. Confirmation of these findings in independent studies, including both European Americans (EA) and African Americans (AA) would improve the likelihood they represent true associations. Furthermore, it is important to understand associations of these prostate cancer risk variants, if observed, with clinical characteristics of prostate cancer, including tumor grade, stage, serum PSA levels, and age at diagnosis. In the current study, we address these questions.

Methods

Study subjects

Cases were 1,563 men of European descent and 364 men of African descent (by self report) who underwent radical prostatectomy for treatment of prostate cancer at The Johns Hopkins Hospital from January 1, 1999, through December 31, 2006. Each tumor was graded using the Gleason scoring system (9) and staged using the TMN (tumor–node–metastasis) system (10). We defined more aggressive and less aggressive disease based on tumor stage and Gleason score. Tumors with a Gleason score of 7 or higher or stage pT3 or higher or N+ or M1 (i.e., either high-grade or non–organ-confined disease) were defined as more aggressive. Tumors with a Gleason score of 6 or lower and stage pT2/N0 (i.e., cancer confined to the prostate) were defined as less aggressive. Normal seminal vesicle tissue that was obtained and frozen at the time of surgery was used to isolate DNA for genotyping of case patients.

Men undergoing screening for prostate cancer at The Johns Hopkins Hospital and The Johns Hopkins University Applied Physics Lab (Columbia, MD) during the same time period were asked to participate as control subjects. Blood samples for preparation of DNA, serum prostate-specific antigen (PSA) levels, digital rectal examination (DRE) results, and demographic information were available for these subjects. A total of 576 men of European descent and 353 men of African descent (by self report) met our inclusion criteria as control subjects for this study: normal DRE, PSA levels less than 4.0 ng/mL, and older than 55 years.

The clinical and demographic information for cases and controls is summarized in Table 1. The study received institutional approval and complied with Health Insurance Portability and Accountability Act (HIPAA) regulations. Written informed consent was obtained from each participant.

Selection of SNPs and SNP genotyping

Based on the initial report by Gudmundsson (8), we selected 3 SNPs at 17q12 and 4 SNPs at 17q24.3. Polymerase chain reaction (PCR) and extension primers for these SNPs were designed using MassARRAY Assay Design 3.0 software (Sequenom, Inc), and these 16 SNPs were included in one multiplexing group. The primer information is available at http://www.wfubmc.edu/genomics. PCR and extension reactions were performed according to the manufacturer's instructions, and extension product sizes were determined by mass spectrometry using the Sequenom iPLEX system. Two CEPH subjects (1331-01 and 1331-02) and two water samples (PCR negative controls) that were blinded to the technician were included in each 96-well plate. The average genotype call rates of these 5 SNPs were > 98% and the average concordance rate between samples was >99%.

Statistical Analyses

We used Fisher's exact test to evaluate Hardy–Weinberg equilibrium for each SNP separately among cases and controls of each race group. Tests for pair-wise linkage disequilibrium (LD) among these SNPs in control subjects of each race group (chi-square test, d.f. =1, two-sided) were performed using the SAS/Genetics software (Version 9.0, http://support.sas.com/rnd/papers/sugi27/genetics.pdf).

Because the main purpose of this study was to confirm the association reported by Gudmundsson et al (8), we primarily used the statistical methods that were employed in their report. Allele frequency differences between cases and controls of each race group were tested for each SNP using a chi-square test with 1 degree of freedom. Allelic odds ratio (OR) and 95% confidence interval (95% CI) were estimated based on a multiplicative model. For genotypes, a model-free method was first used to estimate ORs and the 95% CI of each risk genotype, compared to the homozygous wildtype within each race group. A dominant or recessive model was then tested using unconditional logistic regression with adjustment for age and geographic region, and the model that provided the lowest Akaike information criterion (AIC) was selected as the best genetic model (11). The results from EA and AA case-control populations were combined using a Mantel-Haenszel model (12) in which the populations were allowed to have different population frequencies for alleles and genotypes but were assumed to have a common OR. We tested two-locus interaction effects on prostate cancer risk using unconditional logistic regression methods where we fit locus 1, locus 2, and the product of locus 1 and 2 in the regression models. The best-fitting genetic models obtained in the univariate analysis were used in the interaction analysis.

Associations between haplotypes of SNPs and prostate cancer risk were performed using a score test developed by Schaid et al. (13) as implemented in Haplo.stat software (http://mayoresearch.mayo.edu/mayo/research/biostat/schaid.cfm).

Associations of sequence variants with TNM stages and aggressiveness of PCa (more or less aggressive disease) were only tested among cases using a chi-square test of 2xN table. A trend test was used to assess association between proportion of risk genotype with increasing Gleason scores. Associations of sequence variants with mean age at diagnosis was tested only among cases using a two sample t-test. Because serum PSA levels were not normally distributed, a non-parametric analysis (Wilcoxon rank sum test) was used to assess association between SNPs and pre-operative serum PSA level in cases or PSA levels at time of sampling in controls.

To minimize the impact of potential population stratification in AA, we genotyped 30 unlinked ancestry informative microsatellite markers as previously described (3,8). We used the program STRUCTURE to infer the number of ancestral populations and to estimate

proportion of ancestry for each individual (14). The individual ancestry proportion was used as a covariate in the association tests to minimize the effect of potential population stratification.

All reported P-values were based on two-sided tests.

Results

Seven SNPs in the two chromosome17 loci (17q12 and 17q24.3) previously implicated to harbor prostate susceptibility genes were genotyped in this study. Each of the 7 SNPs were in HWE ($P \geq 0.05$) among control subjects of European and African descent, respectively. Significant pair-wise LD ($P < 0.05$) was observed among three SNPs at 17q12 and among four SNPs at 17q24.3 in control subjects.

Allele frequencies of these 7 SNPs in case and control subjects of EA and AA are presented in Table 2. Overall, the results are consistent with the findings from Gudmundsson et al (2007), as each of the reported risk alleles of these 7 SNPs was more common in cases than controls among EA and AA. When statistical significance of allele frequencies between cases and controls were tested, all three SNPs at 17q12 were highly significant ($P = \sim 10^{-4}$) in EA and one SNP (rs4430796) at 17q12 was marginally significant in AA ($P = 0.04$). None of the four SNPs at 17q24.3 were significant in either EA or AA. However, when subjects of both race groups were combined using a Mantel-Haenszel model, two SNPs at 17q24.3 were marginally significant, $P = 0.04$ for rs1859962, and $P = 0.06$ for rs7214479.

Results from genotypic tests also provide confirmation for the associations of prostate cancer risk with sequence variants at these two 17q loci (Table 3). Compared to homozygous non-risk allele carriers, carriers of one risk allele ("0X") or two risk alleles ("XX") had increased risk for prostate cancer for SNPs at 17q12 and 17q24.3 in EA and in AA. When statistical significance of genotypic effect for prostate cancer risk was tested and adjusted for age, the genotypic effect was highly significant ($P = \sim 10^{-4}$) for all three SNPs at 17q12 in EA and marginally significant for one SNP (rs4430796) at 17q12 in AA ($P = 0.05$). For SNPs at 17q24.3, except for one SNP (rs983085) that was marginally significant in AA ($P = 0.04$), none of the remaining SNPs were significant in either EA or AA. Similar results were found in AA after adjustment for individual proportion of African ancestry.

To infer the best fitting model for these risk SNPs, we evaluated associations in the combined race groups under dominant and recessive models. A dominant model appeared to be the best fitting model for all but one SNP. A recessive model was the best fitting model for SNP rs3760511 at 17q12. The most strongly associated SNP at 17q12 was rs4430796 under a dominant model. Compared to men who had a CC genotype, men who had TC or TT had an OR of 1.44 (95% CI: 1.19-1.74) for prostate cancer ($P = 0.0001$). The most strongly associated SNP at 17q24.3 was rs1859962 under a dominant model. Compared to men who had genotype TT, men who had GT or GG had an OR of 1.21 (95% CI: 1.02-1.45) for prostate cancer ($P = 0.03$).

Results from the haplotype analyses within each of the two regions were similar to that of individual SNPs. For EA subjects, the haplotype that had largest difference in frequencies between cases and controls consists of risk alleles of each variant, i.e. T-G-C of rs4430796-rs7501939-rs3760511 at 17q12, with a frequency of 0.35 in cases and 0.30 in controls, $P = 0.0005$, and G-T-A-A of rs1859962-rs7214479-rs6501455-rs983085 at 17q24.3, with a frequency of 0.44 in cases and 0.40 in controls, $P = 0.01$. For AA subjects, three haplotypes at 17q12 (T-A-A, T-A-C, and T-G-A) had significantly different frequencies between cases and controls, and none of the haplotypes at 17q24.3 had significantly different frequencies between cases and controls.

We assessed associations of these risk variants with clinical characteristics of prostate cancer among cases using the best fitting genetic model. Because of strong LD among SNPs within each region, we selected the most strongly associated SNP from 17q12 (rs4430796) and 17q24.3 (rs1859962). We did not observe significant association between these two SNPs with aggressiveness of prostate cancer (more or less aggressive disease as defined under Methods), Gleason score (≤ 6, 7, and ≥ 8), and mean pre-operative PSA (Table 4). However, similar to the findings of Gudmundsson (2007), we found a trend, but not statistically significant, of earlier age at diagnosis among risk allele carriers of rs4430796 at 17q12 in EA and AA cases.

We tested for multiplicative interaction effects on prostate cancer risk between the two most strongly associated SNPs at 17q12 and 17q24.3 using a logistic regression model. No evidence for multiplicative interaction was found; the interaction term was not significant ($P > 0.05$) in EA and AA. We then tested the additive effect of these two risk SNPs on prostate cancer risk. Compared to EA men who had non-risk genotypes at both SNPs, EA men who had a risk genotype at 17q12 alone, risk genotype at 17q24.3 alone, or risk genotype at both SNPs had ORs of 1.01 (95% CI: 0.64-1.61, P=0.97), 0.84 (95% CI: 0.52-1.37, P=0.49), and 1.40 (95% CI: 0.91-2.16, P=0.13), respectively. Compared to AA men who had non-risk genotypes at both SNPs, AA men who had a risk genotype at 17q12 alone, risk genotype at 17q24.3 alone, or risk genotype at both SNPs had ORs of 1.80 (95% CI: 1.22-2.64, P=0.003), 1.66 (95% CI: 1.02-2.70, P=0.04), and 1.60 (95% CI: 1.05-2.44, P=0.03), respectively. These results do not provide evidence for an additive interaction.

Discussion

Overall, our study provides the first independent confirmation of prostate cancer risk association with genetic variants at 17q12 and 17q24.3, although the evidence for variants at 17q24.3 was weaker. Furthermore, our study provides the first evidence that these two 17q loci may also play role in prostate cancer risk among AA.

As with all case-control studies, our study is subject to false positive findings due to multiple testing and population stratification. However, the positive associations in our study are unlikely due to chance alone. Multiple testing is not a major concern in this study because we only evaluated 7 SNPs, with most being dependent because of strong LD among these SNPs. Population stratification is unlikely to contribute considerably to the findings because the association results were similar after adjusting for African ancestry proportion in AA (Table 2). Although we did not have data on ancestry informative markers in EA, the fact that these cases and controls were recruited from the same geographic regions may reduce this concern. Perhaps more importantly, the consistent association findings among EA and AA of our study, both of which have the same direction of association as in the original report (Gudmundsson 2007), strongly suggest these are true prostate cancer associations.

An interesting finding of our study is that the risk variants at 17q12 and 17q24.3 were not associated with clinical characteristics in this study population. One important advantage of the current study population, having underwent radical prostatectomy as the primary treatment modality, is the availability of the prostate specimen in its entirety for systematic and comprehensive pathologic evaluation of tumor grade and stage. The lack of association of risk variants with clinical characteristics is also consistent with that of the original report (Gudmundsson 2007), which noted a non-statistically significant trend for early age at diagnosis among risk allele carriers. Since these variants at 17q12 and 17q24.3 are equally associated with risk for more and less aggressive tumors, it is possible they impact aspects of prostate cancer initiation rather than progression.

Together with the original report by Gudmundsson (2007), our data strongly suggest the presence of prostate cancer risk variants at these two regions. Further fine mapping studies, functional studies, and clinical studies are needed to identify specific causal variants at these two regions and understand their etiology.

Acknowledgments

The authors thank all the study subjects who participated in this study. The study is supported by National Cancer Institute CA106523 and CA95052 to J.X., CA112517 and CA58236 to W.B.I., CA86323 to AWP, and Department of Defense grant PC051264 to J.X.

References

1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics, 2007. CA Cancer J Clin. 2007; 57:43–66. [PubMed: 17237035]
2. Gronberg H. Prostate cancer epidemiology. Lancet. 2003; 361:859–64. [PubMed: 12642065]
3. Amundadottir LT, Sulem P, Gudmundsson J, et al. A common variant associated with prostate cancer in European and African populations. Nat Genet. 2006; 38:652–8. [PubMed: 16682969]
4. Freedman ML, Haiman CA, Patterson N, et al. Admixture mapping identifies 8q24 as a prostate cancer risk locus in African-American men. Proc Natl Acad Sci USA. 2006; 103:14068–73. [PubMed: 16945910]
5. Gudmundsson J, Sulem P, Manolescu A, et al. Genome-wide association study identifies a second prostate cancer susceptibility variant at 8q24. Nat Genet. 2007; 39:631–7. [PubMed: 17401366]
6. Haiman CA, Patterson N, Freedman ML, et al. Multiple regions within 8q24 independently affect risk for prostate cancer. Nat Genet. 2007; 39:638–44. [PubMed: 17401364]
7. Yeager M, Orr N, Hayes RB, et al. Genome-wide association study of prostate cancer identifies a second risk locus at 8q24. Nat Genet. 2007; 39:645–9. [PubMed: 17401363]
8. Gudmundsson J, Sulem P, Steinthorsdottir V, et al. Two variants on chromosome 17 confer prostate cancer risk, and the one in TCF2 protects against type 2 diabetes. Nat Genet. 2007; 39:977–83. [PubMed: 17603485]
9. Epstein JI, Allsbrook WC Jr, Amin MB, Egevad LL, ISUP Grading Committee. The 2005 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma. Am J Surg Pathol. 2005; 29:1228–42. [PubMed: 16096414]
10. Hoedemaeker RF, Vis AN, Van Der Kwast TH. Staging prostate cancer. Microsc Res Tech. 2000; 51:423–9. [PubMed: 11074612]
11. Akaike, H. Information theory and an extension of the maximum likelihood principle. In: Pertaran, BN.; Csaaki, F., editors. International Symposium on Information Theory; Budapest, Hungary: Acadeemiai Kiadi; 1973. p. 267-281.
12. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. J Natl Cancer Inst. 1959; 22:719–48. [PubMed: 13655060]
13. Schaid DJ, Rowland CM, Tines DE, Jacobson RM, Poland GA. Score tests for association between traits and haplotypes when linkage phase is ambiguous. Am J Hum Genet. 2002; 70:425–34. [PubMed: 11791212]
14. Pritchard JK, Stephens M, Rosenberg NA, Donnelly P. Association mapping in structured populations. Am J Hum Genet. 2000; 67:170–81. [PubMed: 10827107]

Table 1

Clinical and demographic characteristics of prostate cancer patients and control subjects*

Characteristic	European Americans			African Americans		
	More aggressive disease	Less aggressive disease	Control subjects	More aggressive disease	Less aggressive disease	Control subjects
Number of subjects	1017	546	576	209	155	353
Mean age, y (SD)	60.1 (6.89)	56.8 (6.46)	59.6 (6.99)	57.95 (6.72)	54.87(7.29)	54.42 (11.88)
Serum PSA level, No. (%)						
≤ 4.0 ng/mL	76 (10)	197 (36)	576 (100)	21 (10.05)	42 (27.10)	316 (89.52)
> 4.0 ng/mL	660 (90)	345 (64)	0 (0)	188 (89.95)	113 (72.90)	37 (10.48)
Pathologic stage†, No. (%)						
T2N0	186 (27)	528 (100)	N/A	80 (40)	152 (100)	N/A
pT3 or N1/N2	502 (73)	0 (0)	N/A	120 (60)	0 (0)	N/A
Gleason score, No. (%)						
≤ 6	50 (6)	528 (100)	N/A	155 (100)	29 (14)	N/A
= 7	572 (70)	0 (0)	N/A	0 (0)	147 (70)	N/A
≥ 8	196 (24)	0 (0)	N/A	0 (0)	33 (16)	N/A

*SD = standard deviation; PSA = prostate-specific antigen; N/A = not applicable.

†TNM staging as described in the Methods. For some patients with more aggressive disease, PSA values, stage, or grade information was not available

Prostate. Author manuscript; available in PMC 2011 September 20.

Table 2

Association of SNPs on chr17 and prostate cancer risk

SNP id	Chromosome (region)	Position[§]	Risk allele	Frequency		OR[†] (95% CI)	*P*[*]
				Cases	Controls		
European American							
rs4430796	17q12	33,172,153	T	0.58	0.52	1.28 (1.11-1.46)	5.1E-04
rs7501939	17q12	33,175,269	G	0.66	0.60	1.31 (1.14-1.51)	1.8E-04
rs3760511	17q12	33,180,426	C	0.37	0.31	1.28 (1.11-1.49)	8.8E-04
rs1859962	17q24.3	66,620,348	G	0.51	0.48	1.12 (0.98-1.28)	0.11
rs7214479	17q24.3	66,702,544	T	0.48	0.45	1.12 (0.97-1.28)	0.11
rs6501455	17q24.3	66,713,406	A	0.56	0.54	1.09 (0.95-1.25)	0.24
rs983085	17q24.3	66,723,656	A	0.56	0.54	1.07 (0.93-1.23)	0.35
African American							
rs4430796	17q12	33,172,153	T	0.38	0.33	1.26 (1.01-1.56)	0.04
rs7501939	17q12	33,175,269	G	0.49	0.48	1.07 (0.87-1.31)	0.54
rs3760511	17q12	33,180,426	C	0.19	0.19	1.03 (0.79-1.34)	0.82
rs1859962	17q24.3	66,620,348	G	0.26	0.24	1.13 (0.89-1.44)	0.31
rs7214479	17q24.3	66,702,544	T	0.20	0.17	1.20 (0.92-1.57)	0.17
rs6501455	17q24.3	66,713,406	A	0.70	0.68	1.07 (0.85-1.34)	0.56
rs983085	17q24.3	66,723,656	A	0.32	0.28	1.20 (0.86-1.50)	0.11
Mantel Haenszel analysis							
rs4430796	17q12	33,172,153	T			1.27 (1.13-1.42)	5.3E-05
rs7501939	17q12	33,175,269	G			1.23 (1.09-1.38)	6.2E-04
rs3760511	17q12	33,180,426	C			1.22 (1.07-1.38)	2.5E-03
rs1859962	17q24.3	66,620,348	G			1.12 (0.99-1.26)	0.06
rs7214479	17q24.3	66,702,544	T			1.14 (1.00-1.28)	0.04
rs6501455	17q24.3	66,713,406	A			1.08 (0.96-1.22)	0.19
rs983085	17q24.3	66,723,656	A			1.10 (0.96-1.22)	0.10

[§]Position is based on NCBI Build 35.

[†]OR is the allelic odds ratio with 95% confidence interval and is based on the multiplicative model

[*]P values shown are two-sided

Table 3

Model-free estimates of genotype OR of SNPs on chr17 and prostate cancer risk

SNP ID	Chromosome (region)	Position[§]	risk allele	Genotypic OR			P*	P&
				00	0X (OR 95%CI)	XX (OR 95% CI)		
European American								
rs4430796	17q12	33,172,153	T	1.00	1.36 (1.05-1.75)	1.66 (1.25-2.20)	2.2E-03	
rs7501939	17q12	33,175,269	G	1.00	1.45 (1.07-1.96)	1.83 (1.34-2.51)	6.6E-04	
rs3760511	17q12	33,180,426	C	1.00	1.17 (0.95-1.44)	1.84 (1.30-2.61)	1.6E-03	
rs1859962	17q24.3	66,620,348	G	1.00	1.26 (1.00-1.60)	1.25 (0.95-1.63)	0.13	
rs7214479	17q24.3	66,702,544	T	1.00	1.17 (0.94-1.47)	1.24 (0.95-1.63)	0.23	
rs6501455	17q24.3	66,713,406	A	1.00	1.00 (0.78-1.29)	1.17 (0.89-1.55)	0.84	
rs983085	17q24.3	66,723,656	A	1.00	0.97 (0.75-1.25)	1.13 (0.86-1.49)	0.81	
African American								
rs4430796	17q12	33,172,153	T	1.00	1.43 (1.04-1.96)	1.47 (0.91-2.37)	0.05	0.06
rs7501939	17q12	33,175,269	G	1.00	1.14 (0.80-1.62)	1.14 (0.76-1.72)	0.72	0.75
rs3760511	17q12	33,180,426	C	1.00	0.98 (0.71-1.36)	1.15 (0.55-2.40)	0.91	0.92
rs1859962	17q24.3	66,620,348	G	1.00	1.14 (0.81-1.60)	1.17 (0.72-1.89)	0.60	0.67
rs7214479	17q24.3	66,702,544	T	1.00	1.37 (0.98-1.91)	0.99 (0.48-2.04)	0.14	0.17
rs6501455	17q24.3	66,713,406	A	1.00	1.77 (1.02-3.07)	1.58 (0.91-2.74)	0.13	0.12
rs983085	17q24.3	66,723,656	A	1.00	1.48 (1.08-2.03)	1.15 (0.67-1.95)	0.04	0.05

[§]Position is based on NCBI Build 35.

*Based on likelihood ratio test (2-df tests, ajusted for age)

&Based on likelihood ratio test (2-df tests, ajusted for age and african acenstry)

Prostate. Author manuscript; available in PMC 2011 September 20.

Table 4

Association of SNPs with clinical characteristics

Clinical characteristics	European Americans				African Americans			
	rs4430796		rs1859962		rs4430796		rs1859962	
	CC	TC/TT	TT	GT/GG	CC	TC/TT	TT	GT/GG
Aggressiveness								
Localized	90 (17.21)	433 (82.79)	126 (24.23)	394 (75.77)	65 (42.21)	89 (57.79)	90 (58.44)	64 (41.56)
Aggressiven	162 (16.51)	819 (83.49)	240 (24.49)	740 (75.51)	71 (34.13)	137 (65.87)	131 (62.68)	78 (37.32)
P [a]		0.73		0.91		0.12		0.41
Gleason score (biopsy)								
≤ 6	102 (16.78)	506 (83.22)	143 (23.64)	462 (76.36)	75 (39.68)	114 (60.32)	110 (58.20)	79 (41.80)
7	97 (16.03)	508 (83.97)	146 (24.17)	458 (75.83)	50 (34.01)	97 (65.99)	92 (62.59)	55 (37.41)
>=8	52 (18.57)	228 (81.43)	72 (25.71)	208 (74.29)	12 (37.50)	20 (62.50)	21 (63.64)	12 (36.36)
P [b]		0.63		0.52		0.45		0.38
PSA levels at diagnosis (ng/ml)								
Median	7.00	6.59	7.19	6.50	5.80	6.00	6.00	5.90
P [c]		0.23		0.21		0.87		0.63
Age at diagnosis (Year)								
Mean	59.36	58.85	58.97	58.94	56.81	56.53	56.52	56.92
P [d]		0.28		0.94		0.72		0.60

p[a] : Pearson Chi-square test, two-sided

p[b] Armitage trend test, two-sided

p[c]: Wilcoxon rank sum test, two-sided

p[d]: Two-sample t test, two-sided