Supplementary methods

Study subjects

The CAPS study population was described in detail elsewhere[1-2]. Briefly, we conducted a large-scale population-based case-control study in Sweden, named CAPS (CAncer Prostate in Sweden). Prostate cancer patients were identified and recruited from four of the six regional cancer registries in Sweden. The inclusion criterion for case subjects was pathological or cytological verified adenocarcinoma of the prostate, diagnosed between July, 2001 and October, 2003. Among 3,648 identified prostate cancer case subjects, 3,161 (87%) agreed to participate. DNA samples from blood and TNM stage, Gleason grade (biopsy), and PSA levels at diagnosis were available for 2,899 patients (92%). These case subjects were classified as having advanced disease if they met any of the following criteria: T3/4, N+, M+, Gleason score sum ≥ 8, or PSA > 50 ng/ml; otherwise, they were classified as localized. Control subjects were recruited concurrently with case subjects. They were randomly selected from the Swedish Population Registry, and matched according to the expected age distribution of cases (groups of five-year intervals) and geographical region. A total of 3,153 controls were invited and 2,149 (68%) agreed to participate. DNA samples from blood were available for 1,722 control subjects (80%). Serum PSA level was measured for all control subjects but was not used as an exclusion variable. A history of prostate cancer among first-degree relatives was obtained from a questionnaire for both cases and controls. **Supplementary Table 1a** presents the demographic and clinical characteristics of the study subjects. The study received institutional approval at the Karolinska Institutet, Umeå University, and Wake Forest University School of Medicine.

The Johns Hopkins Hospital (JHH) study population was described in detail elsewhere[3]. Briefly The JHH study Cases were 1,527 men of European 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[4] and staged using the TMN (tumor–node–metastasis) system[5]. 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 482 men of European 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 **Supplementary Table 1b**. In addition, 364 prostate cancer cases and 353 control subjects of African descent (by self report) were recruited using a similar method as for subjects of European descent. The study received institutional approval and complied with Health Insurance Portability and Accountability Act (HIPAA) regulations. Written informed consent was obtained from each participant.

We also utilized data from the National Cancer Institute Cancer Genetic Markers of Susceptibility (CGEMS) study. Individual genotype data from the first stage of CGEMS were obtained through an approved data request application, including 1,172 prostate cancer case subjects and 1,157 control subjects who were selected from the Prostate, Lung, Colon and Ovarian (PLCO) Cancer Screening Trial[6-7]. Summary genotype information from the second stage CGEMS study were downloaded from a public CGEMS website http://cgems.cancer.gov/data/, including four additional study populations: American Cancer Society Cancer Prevention Study II (CPS-II); the Health Professionals Follow-up Study (HPFS); CeRePP French Prostate Case-Control Study (FPCC); and Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (ATBC)[6-7].

Genotyping

Polymerase chain reaction (PCR) and extension primers for these 41 SNPs were designed using the MassARRAY Assay Design 3.0 software (Sequenom, Inc). 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. Duplicate test samples and two water samples (PCR negative controls) that were blinded to the technician were included in each 96-well plate. The rate of concordant results between 100 duplicate samples was >99%.

Statistical methods

Tests for Hardy-Weinberg equilibrium were performed for each SNP separately among case patients and control subjects using Fisher's exact test. Haplotype blocks were estimated

using a computer program Haploview[8], and a default Gabriel method[9] was used to define a haplotype block; i.e. a region in which all (or nearly all) pairs of markers are in "strong LD", which is consistent with no historical recombination. Pairs of markers are defined as being in "strong LD" if the one-sided upper 95% confidence bound on D' is >0.98 and the lower bound is above 0.7. On the other hand, pairs of markers are termed as "strong evidence for historical recombination" if the upper confidence bound on D' is less than 0.9.

We imputed all the known SNPs in the region of interest based on the 41 genotyped SNPs and haplotype information in the HapMap Phase II data (CEU) using a computer program IMPUTE[10]. A posterior probability of 0.9 was used as a threshold to call genotypes.

SequenceLDhot was used to determine recombination hotspots[11]. SequenceLDhot considers a grid of putative hotspot positions, and for each putative hotspot calculates a Likelihood Ratio (LR) statistic for the presence of a hotspot. Haplotype and background recombination rates generated from PHASE (version 2.1) were used as input files. We assumed the putative hotspot with width of 2 kb and the program considers a new hotspot every 1 kb. Seven SNPs were used to calculate the LR statistic for each hotspot.

Allele frequency differences between case patients and control subjects 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. A model-free method was used to estimate ORs and the 95% CI of each risk genotype, compared to the homozygous wildtype. ORs for prostate cancer risk under dominant or recessive model were also estimated using unconditional logistic regression with adjustment for age. Detailed results for each SNPs in the entire fine mapping region are shown in **Supplementary Table 2a-b** for CAPS

and JHH, respectively. Results for two representative SNPs at each locus from CAPS, JHH, as well as 5 study populations from the CGEMS study are shown in **Table 1**.

We fit four genetic models in the combined data from CAPS, JHH, and PLCO where individual genotype data and age information is available using a logistic regression analysis and adjusting for age (5-year group) and study population. These four models include a 2-df general model, and 1-df additive, dominant, and recessive models. The model with the lowest Akaike information criterion (AIC) value is considered as the most parsimonious model (**Supplementary Table 3a)**.

Independence of prostate cancer associations of two representative SNPs at each locus was tested by including both SNPs (assuming a general model at each SNP) in a logistic regression model among three combined populations (CAPS, JHH, and PLCO) where individual genotype data are available. Age (5-year group) and study population were also included in the model (**Supplementary Table 3b**).

The joint effect of two representative SNPs at each locus on prostate cancer risk were explored by estimating ORs for carriers of eight combinations of genotypes (unconstrained model) using men who were homozygous for non-risk alleles at both SNPs as a reference group. Eight dummy variables were created and included in the logistic regression, with adjustment for age (5-year group) in each of the three populations (CAPS, JHH, and PLCO) where individual genotype data are available, as well as in the combined data (adjusting for study and age in the combined analysis). The overall p-value for genetic effects was estimated using the likelihood ratio test (degrees of freedom = 8) **(Supplementary Table 4)**.

We inferred haplotypes for 18 consecutive SNPs that are bounded by rs4430796 at first locus and rs11649743 at the second locus in the CAPS and JHH using PHASE[16]. More than 32

haplotypes with frequencies of 1% and higher were inferred, reflecting a recombination hotspot between the two loci **(Supplementary Table 5)**. Three haplotypes that contain risk alleles of both rs4430796 and rs11649743 (ID: 1, 2, and 20) had higher frequencies in cases than controls (nominal $P < 0.05$); however, the results were not consistent in these two populations. These results suggested that the observed associations at the two independent loci are unlikely due to a single long range haplotype that connects these two alleles (founder effect).

Haplotypes for 18 consecutive SNPs that are bounded by rs4430796 at first locus and rs11649743 at the second locus in the CAPS and JHH were inferred using PHASE (version 2.1)[12]. This computer program implements a Bayesian statistical method for inferring haplotypes from population genotype data.

We tested the association of rs11649743 and rs4430796 with PSA levels in controls assuming a 2-df general model and adjusting for age using a multiple regression analysis. PSA levels were logarithm-transformed to best approximate the assumption of normality (**Supplementary Table 6b**).

We also calculated fraction of total genetic variance explained by rs11649743 and rs4430796, respectively. The total genetic variance (V) for all the susceptibility alleles was estimated based on the equation $\lambda_{monozygotic} = e^{V}$, where $\lambda_{monozygotic}$ stands for the relative risk for prostate cancer in monozygotic twins[13]. When a $\lambda_{monozygotic}$ estimate of 12.3 was used, which was based on a published study by Lichtenstein et al.[14], the V for prostate cancer was calculated to be 2.51. The variance for a specific risk allele can be calculated based on the approach proposed by Pharoah et al.[15]. For rs11649743, assuming the risk allele frequency of 0.83 and the relative risk per allele of 1.19, the variance for the risk allele of the SNP was 0.009. Similarly for rs4430796, assuming the risk allele frequency of 0.58 and the relative risk per allele of 1.23, the variance for

the risk allele of the SNP was 0.01. Therefore, the fraction of total genetic variance explained by rs11649743 and rs4430796 was calculated as 0.3% and 0.5%, respectively.

Supplementary References

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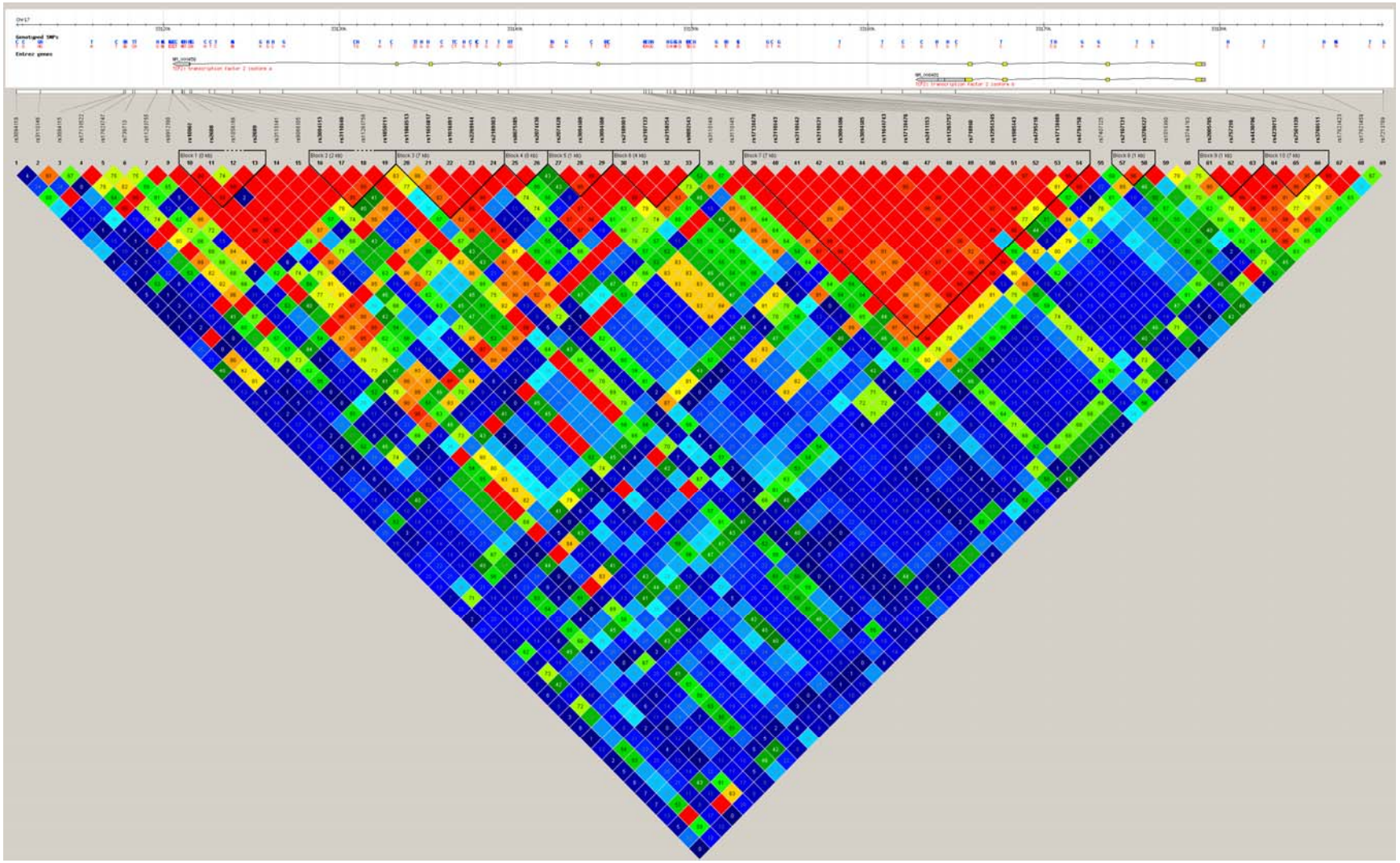
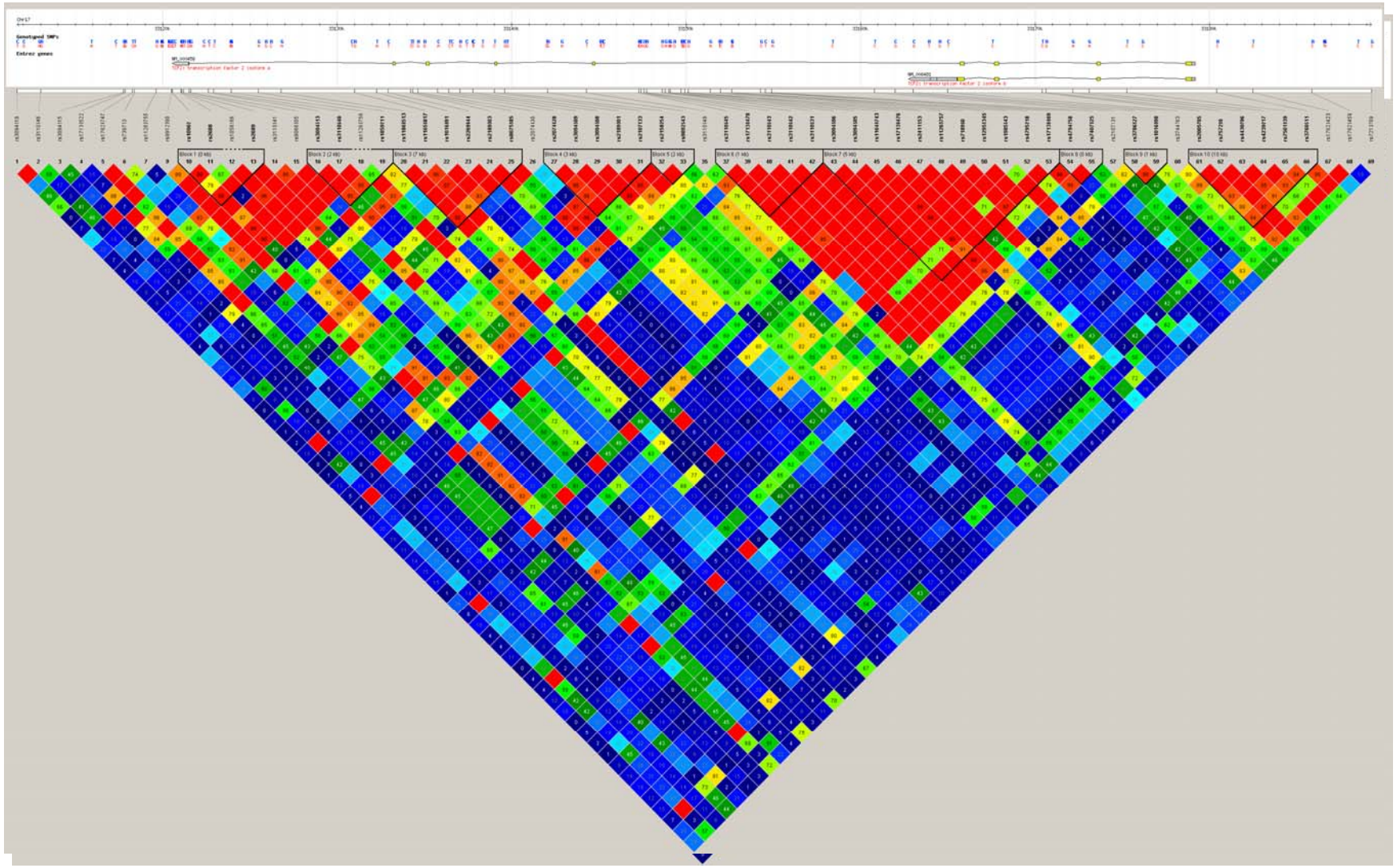
Supplementary figure legend

Supplementary figure 1. Heat map for 64 SNPs in the entire fine mapping region of 17q12 in four study populations. Pair-wise LD (D') for these 64 SNPs were estimated from control subjects in four populations (CAPS, JHH, PLCO, and HapMap) using the computer program Haploview[8]. Results are presented using heat map; with the strongest LD in brightest red. The number in each diamond indicates pair-wise D', except the brightest red square where D' = 1. Eleven haplotype blocks (and size in kb) were estimated using a default Gabriel method[9]. Known transcripts in the region are presented at the top.

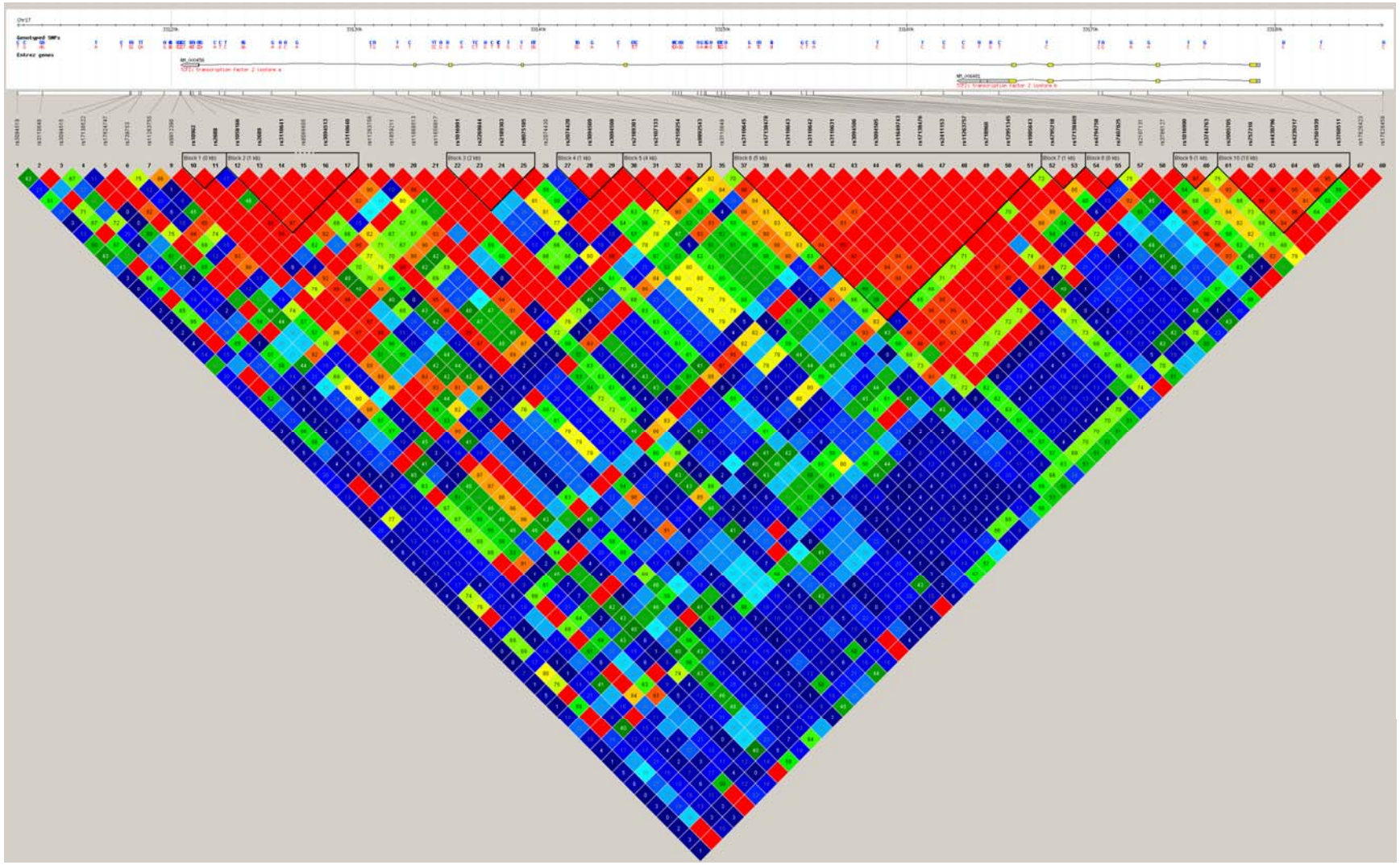
Supplementary Figure 1a (CAPS)



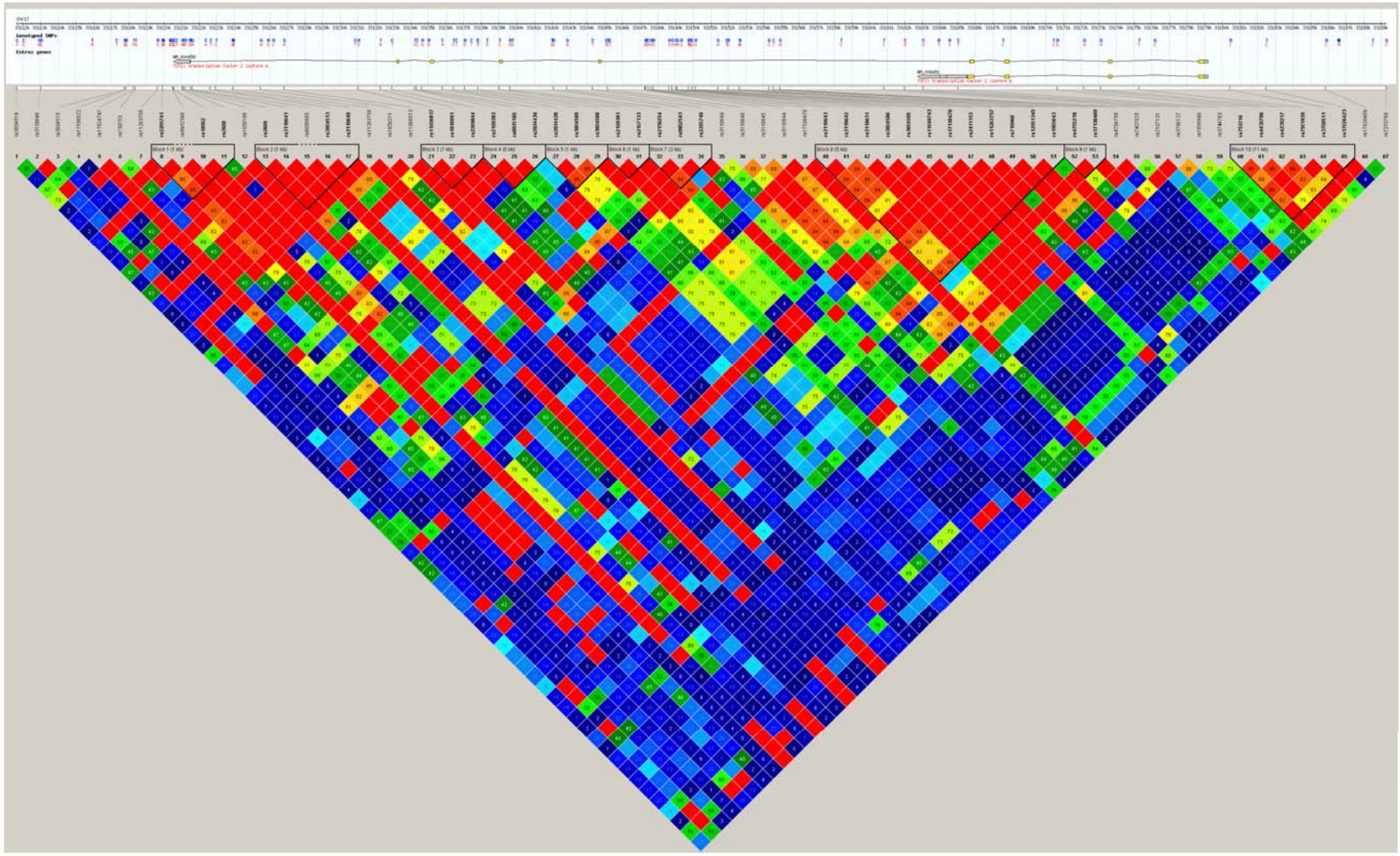
Supplementary Figure 1b (JHH)



Supplementary Figure 1c (PLCO)



Supplementary Figure 1d (HapMap)



Supplementary Table 1a. Clinical and demographic characteristics of subjects in CAPS

	# (%) of cases			# (%) of
Characteristics	**Aggressive (N=1,231)**	**Localized (N=1,619)**	**All cases (N=2,899)**	**controls (N=1,722)**
Age at enrollment (Year)				
Mean (sd)	68.04 (7.32)	65.14 (6.74)	66.36 (7.13)	67.15 (7.39)
Age at disgnosis				
≤ 65	514 (41.75)	926 (57.19)	1469 (50.78)	N/A
> 65	717 (58.25)	693 (42.81)	1424 (49.22)	N/A
Family History (first-degree relatives)				
No	1013 (82.29)	1295 (79.99)	2342 (80.95)	1565 (90.57)
Yes	218 (17.71)	324 (20.01)	551 (19.05)	163 (9.43)
Missing data	0	0	0	0
PSA levels at diagnosis for cases or at enrollment for controls (ng/ml)				
≤ 4	36 (2.95)	185 (11.61)	221 (7.85)	1438 (83.56)
5-9.99	171 (14.00)	755 (47.39)	926 (32.91)	230 (13.36)
10-19.99	216 (17.69)	438 (27.50)	654 (23.24)	37 (2.15)
20-49.99	252 (20.64)	215 (13.50)	467 (16.60)	13 (0.76)
50-99.99	229 (18.76)	0	229 (8.14)	2 (0.12)
≥ 100	317 (25.96)	0	317 (11.27)	1 (0.06)
Missing	10	26	85	1
T-stage				
T0	2 (0.16)	7 (0.44)	9 (0.32)	N/A
T1	147 (12.07)	933 (58.24)	1080 (38.30)	N/A
T2	242 (19.87)	662 (41.32)	904 (32.06)	N/A
T3	724 (59.44)	0	724 (25.67)	N/A
T4	103 (8.46)	0	103 (3.65)	N/A
TX	13	17	79	N/A
N-stage				
N0	222 (70.03)	302 (100.00)	524 (84.65)	N/A
N1	95 (29.97)	0	95 (15.35)	N/A
NX	914	1317	2280	N/A
M-stage				
M0	589 (68.25)	655 (100.00)	1244 (81.95)	N/A
M1	274 (31.75)	0	274 (18.05)	N/A
MX	368	964	1381	N/A
Gleason (biopsy)				
≤ 4	9 (0.83)	98 (6.32)	107 (4.06)	N/A
5	43 (3.96)	247 (15.93)	290 (10.99)	N/A
6	153 (14.08)	832 (53.64)	985 (37.34)	N/A
7	414 (38.09)	374 (24.11)	788 (29.87)	N/A
8	258 (23.74)	0	258 (9.78)	N/A
9	185 (17.02)	0	185 (7.01)	N/A
10	25 (2.30)	0	25	N/A
Missing	144	68	261	N/A

43 patients can not be classifed as aggressive or localized cases because of missing phenotypes

Supplementary Table 1b. Clinical and demographic characteristics of study subjects in the Johns Hopkins Hospital study population*

Characteristic	More aggressive disease	Less aggressive disease	Control subjects
Number of subjects	983	527	482
Mean age, y (SD)	60.1 (6.89)	56.8 (6.46)	59.91 (7.19)
Serum PSA level, No. (%)			
≤ 4.0 ng/mL	71 (8.35)	189 (36.07)	482 (100)
> 4.0 ng/mL	779 (91.65)	335 (63.93)	0 (0)
Missing	133	3	0
Pathologic stage†, No. (%)			
T2N0	174 (24.27)	526 (100)	N/A
pT3 or N1/N2	543 (75.73)	0 (0)	N/A
Missing	266	1	N/A
Gleason score, No. (%)			
≤ 6	72 (7.52)	527 (100)	N/A
= 7	606 (63.32)	0 (0)	N/A
≥ 8	279 (29.15)	0 (0)	N/A
Missing	26	0	N/A

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

†TNM staging as described in the Methods.

Supplemental Table 2a. Associations between prostate cancer risk and SNPs at 17q12 in CAPS

		Allele		Freq. for Allele 1		Allele tests				Dominant				Recessive					Confidence	Call Rate
SNP	Pos*	1	2	Cases	Cont.	*P*	OR	L95	U95	*P*	OR	L95	U95	*P*	OR	L95	U95	Type†	Score^	(%)
rs3094519	33,111,655	A	G	0.23	0.23	0.82	1.01	0.91	1.12	0.94	1.00	0.88	1.13	0.45	1.11	0.85	1.46	genotyped	--	96.10
rs3110646	33,113,030	T	C	0.02	0.02	0.22	1.21	0.89	1.64	0.21	1.22	0.89	1.66	0.89	1.19	0.11	13.11	genotyped	--	98.79
rs3094515	33,117,766	T	C	0.40	0.40	0.54	1.03	0.94	1.12	0.38	1.06	0.93	1.20	0.99	1.00	0.85	1.18	genotyped	--	97.49
rs17138522	33,117,847	G	A	0.05	0.05	0.85	0.98	0.80	1.20	0.41	1.68	0.48	5.80	0.95	1.01	0.82	1.24	genotyped	--	97.49
rs17624747	33,118,267	C	T	0.13	0.13	0.42	0.95	0.84	1.08	0.80	0.94	0.57	1.55	0.34	1.07	0.93	1.23	genotyped	--	97.92
rs739753	33,118,390	T	A	0.18	0.18	0.81	0.99	0.88	1.10	0.76	1.05	0.75	1.48	0.87	1.01	0.89	1.15	genotyped	--	98.03
rs11263755	33,119,634	G	A	0.18	0.18	0.71	0.98	0.88	1.09	0.54	0.90	0.63	1.27	0.51	1.04	0.92	1.19	genotyped	--	97.01
rs9912390	33,120,508	C	G	0.02	0.03	0.41	0.89	0.67	1.17	NA	NA	NA	NA	0.40	1.13	0.85	1.49	imputed	0.98	97.21
rs10962	33,120,564	C	G	0.23	0.24	0.25	0.94	0.85	1.04	0.75	1.04	0.80	1.36	0.21	1.08	0.96	1.22	genotyped	--	97.58
rs2688	33,121,044	G	T	0.36	0.38	0.21	0.94	0.86	1.03	0.06	1.18	1.00	1.40	0.68	1.03	0.91	1.16	genotyped	--	97.40
rs1058166	33,121,104	C	T	0.03	0.04	0.27	0.88	0.69	1.11	0.28	2.24	0.50	10.04	0.33	1.13	0.89	1.43	imputed	0.98	94.31
rs2689	33,121,214	A	T	0.50	0.50	0.74	1.02	0.93	1.11	0.67	1.03	0.90	1.18	0.90	1.01	0.88	1.16	genotyped	--	97.92
rs3110641	33,121,530	A	G	0.21	0.21	0.79	1.01	0.91	1.13	0.99	1.00	0.88	1.13	0.47	1.12	0.83	1.51	genotyped	--	98.05
rs8066605	33,121,614	A	G	0.03	0.03	0.19	0.85	0.67	1.08	0.07	NA	NA	NA	0.24	1.16	0.91	1.48	genotyped	--	98.77
rs3094513	33,122,636	A	G	0.48	0.47	0.33	1.05	0.96	1.14	0.51	1.05	0.91	1.21	0.35	1.07	0.92	1.25	imputed	0.96	90.91
rs3110640	33,122,936	G	A	0.48	0.47	0.44	1.04	0.95	1.13	0.67	1.03	0.90	1.19	0.39	1.07	0.92	1.24	imputed	0.96	89.79
rs11263756	33,123,933	A	G	0.03	0.03	0.37	0.89	0.69	1.15	0.07	NA	NA	NA	0.46	1.10	0.85	1.43	imputed	1.00	99.26
rs1859211	33,125,485	C	T	0.13	0.12	0.04	1.15	1.01	1.31	0.10	1.13	0.98	1.30	0.03	1.77	1.03	3.03	genotyped	--	97.60
rs11868513	33,126,805	A	G	0.22	0.21	0.45	1.04	0.94	1.15	0.61	1.03	0.91	1.17	0.36	1.15	0.85	1.54	genotyped	--	98.74
rs11656817	33,131,012	G	A	0.07	0.07	0.93	0.99	0.84	1.18	0.90	1.05	0.48	2.32	0.94	1.01	0.84	1.20	genotyped	--	97.40
rs1016991	33,132,266	T	A	0.15	0.15	0.71	1.02	0.91	1.16	0.53	1.04	0.91	1.20	0.55	0.88	0.59	1.32	genotyped	--	97.12
rs2269844	33,132,927	A	G	0.15	0.14	0.74	1.02	0.90	1.15	0.51	1.05	0.91	1.20	0.38	0.83	0.55	1.25	imputed	0.99	97.58
rs2189303	33,134,218	A	G	0.26	0.26	0.78	1.01	0.92	1.12	0.97	1.00	0.89	1.13	0.55	1.08	0.85	1.37	imputed	0.98	95.46
rs8075185	33,134,329	T	C	0.42	0.41	0.55	1.03	0.94	1.12	0.31	1.07	0.94	1.21	0.86	0.99	0.84	1.15	genotyped	--	98.85
rs2074430	33,134,628	T	C	0.34	0.34	0.58	1.03	0.94	1.12	0.72	1.02	0.90	1.16	0.56	1.06	0.88	1.28	imputed	0.98	95.95
rs2074428	33,135,772	G	T	0.39	0.39	0.73	0.98	0.90	1.08	0.92	1.01	0.85	1.19	0.68	1.03	0.91	1.16	genotyped	--	97.66
rs3094509	33,136,412	A	G	0.39	0.39	0.77	0.99	0.90	1.08	0.74	1.03	0.87	1.22	0.87	1.01	0.89	1.15	imputed	0.98	97.36
rs3094508	33,137,048	C	T	0.36	0.38	0.22	0.95	0.87	1.03	0.43	1.07	0.90	1.28	0.25	1.08	0.95	1.22	genotyped	--	97.45
rs2189301	33,137,798	A	G	0.13	0.12	0.36	1.06	0.93	1.21	0.26	1.09	0.94	1.25	0.76	0.93	0.59	1.48	genotyped	--	96.95
rs2107133	33,139,010	G	A	0.13	0.12	0.33	1.07	0.94	1.21	0.23	1.09	0.95	1.26	0.69	0.91	0.57	1.45	imputed	0.99	98.85
rs2158254	33,139,608	T	C	0.42	0.43	0.52	0.97	0.89	1.06	0.46	1.06	0.91	1.24	0.72	1.02	0.90	1.16	genotyped	--	97.34
rs9892543	33,142,072	G	A	0.20	0.22	0.04	0.90	0.81	1.00	0.08	1.31	0.97	1.76	0.09	1.11	0.98	1.26	genotyped	--	98.33
rs3110649	33,144,293	A	G	0.24	0.23	0.29	1.06	0.95	1.17	0.22	1.08	0.95	1.23	0.89	1.01	0.83	1.25	genotyped	--	95.82
rs3110645	33,147,289	G	T	0.23	0.21	0.11	1.09	0.98	1.22	0.12	1.11	0.97	1.26	0.40	1.14	0.84	1.54	imputed	0.96	87.04
rs17138478	33,147,433	A	C	0.13	0.12	0.04	1.15	1.01	1.31	0.08	1.14	0.99	1.31	0.06	1.70	0.97	2.96	genotyped	--	97.19
rs3110643	33,147,605	C	T	0.20	0.18	0.04	1.12	1.00	1.25	0.05	1.13	1.00	1.29	0.29	1.20	0.86	1.67	genotyped	--	97.86
rs3110642	33,147,733	C	T	0.19	0.18	0.06	1.11	1.00	1.24	0.07	1.13	0.99	1.28	0.32	1.18	0.85	1.65	imputed	0.99	98.70
rs3110631	33,148,626	C	T	0.19	0.17	0.05	1.12	1.00	1.25	0.08	1.13	0.99	1.28	0.19	1.25	0.89	1.77	imputed	0.97	95.35
rs3094506	33,148,810	T	C	0.19	0.17	0.05	1.12	1.00	1.25	0.08	1.12	0.99	1.28	0.20	1.25	0.89	1.76	imputed	0.97	95.20
rs3094505	33,149,018	T	C	0.19	0.17	0.05	1.12	1.00	1.26	0.08	1.13	0.99	1.28	0.20	1.25	0.89	1.76	imputed	0.97	94.83
rs11649743	33,149,092	A	G	0.20	0.23	4.2E-04	0.83	0.75	0.92	0.03	1.37	1.04	1.82	1.2E-03	1.23	1.08	1.39	genotyped	0.96	91.08
rs17138476	33,149,718	T	C	0.19	0.17	0.04	1.12	1.01	1.25	0.05	1.13	1.00	1.29	0.22	1.24	0.88	1.76	genotyped	--	98.51
rs2411153	33,149,928	G	C	0.35	0.35	0.74	0.98	0.90	1.08	0.74	0.97	0.79	1.18	0.51	1.04	0.92	1.19	imputed	0.95	87.51
rs11263757	33,150,124	A	G	0.18	0.17	0.05	1.12	1.00	1.26	0.07	1.13	0.99	1.29	0.22	1.24	0.88	1.76	imputed	0.96	92.40
rs718960	33,151,392	T	C	0.25	0.28	5.9E-03	0.87	0.79	0.96	0.13	1.20	0.95	1.52	0.01	1.18	1.04	1.33	genotyped	--	97.88
rs12951345	33,151,976	C	A	0.24	0.27	3.8E-03	0.87	0.79	0.95	0.14	1.20	0.94	1.52	4.4E-03	1.19	1.06	1.35	imputed	0.99	96.34
rs1985643	33,152,615	C	T	0.19	0.17	0.07	1.11	0.99	1.25	0.14	1.11	0.97	1.27	0.12	1.32	0.93	1.88	imputed	0.96	89.18
rs4795218	33,152,623	A	G	0.26	0.29	7.6E-03	0.87	0.79	0.96	0.13	1.21	0.95	1.54	0.01	1.18	1.04	1.35	imputed	0.95	85.76
rs17138469	33,154,278	C	G	0.19	0.22	2.4E-03	0.85	0.76	0.94	0.74	1.05	0.78	1.43	5.7E-04	1.25	1.10	1.41	genotyped	--	97.90
rs4794758	33,154,541	T	C	0.26	0.30	1.2E-05	0.81	0.74	0.89	0.01	1.31	1.06	1.62	2.8E-05	1.29	1.15	1.46	genotyped	--	97.75
rs7407025	33,154,923	G	A	0.28	0.25	0.01	1.13	1.02	1.24	0.04	1.13	1.00	1.28	0.05	1.27	1.00	1.61	genotyped	--	98.44
rs2107131	33,160,802	A	G	0.37	0.34	0.04	1.10	1.00	1.20	0.02	1.16	1.03	1.31	0.52	1.06	0.89	1.27	genotyped	--	97.19
rs3786127	33,161,987	C	G	0.17	0.17	0.96	1.00	0.90	1.12	0.91	0.99	0.87	1.13	0.64	1.09	0.76	1.57	genotyped	--	97.60
rs1016990	33,163,028	G	C	0.32	0.35	1.0E-03	0.86	0.79	0.94	0.14	1.15	0.95	1.40	4.9E-04	1.24	1.10	1.40	genotyped	--	97.58
rs3744763	33,164,998	G	A	0.39	0.43	2.0E-04	0.85	0.78	0.93	0.00	1.26	1.08	1.49	1.4E-03	1.23	1.08	1.40	genotyped	--	98.01
rs2005705	33,170,413	A	G	0.37	0.42	1.2E-06	0.79	0.72	0.87	0.02	1.24	1.04	1.48	3.8E-07	1.42	1.24	1.62	imputed	0.95	86.06
rs757210	33,170,628	T	C	0.30	0.36	3.2E-06	0.79	0.72	0.87	0.02	1.28	1.05	1.57	3.5E-06	1.36	1.20	1.56	imputed	0.94	83.94
rs4430796	33,172,153	G	A	0.39	0.44	7.5E-07	0.81	0.74	0.88	0.01	1.24	1.05	1.45	2.1E-07	1.40	1.23	1.60	genotyped	--	99.16
rs4239217	33,173,100	G	A	0.33	0.38	1.0E-05	0.81	0.74	0.89	0.02	1.24	1.03	1.50	8.9E-06	1.33	1.17	1.52	imputed	0.96	91.00
rs7501939	33,175,269	T	C	0.34	0.38	1.3E-05	0.82	0.75	0.90	0.03	1.21	1.01	1.45	5.1E-06	1.33	1.18	1.50	genotyped	--	98.94
rs3760511	33,180,426	G	T	0.41	0.38	5.0E-04	1.17	1.07	1.27	0.05	1.13	1.00	1.28	5.7E-05	1.42	1.20	1.68	genotyped	--	99.11
rs17626423	33,182,480	C	T	0.21	0.20	0.12	1.09	0.98	1.21	0.41	1.05	0.93	1.20	0.02	1.44	1.07	1.95	genotyped	--	97.84
rs17626459	33,185,868	C	A	0.05	0.05	0.38	0.92	0.76	1.11	0.63	0.72	0.19	2.79	0.32	1.10	0.91	1.34	genotyped	--	98.68
rs7213769	33,189,279	G	C	0.43	0.41	0.05	1.09	1.00	1.19	0.10	1.11	0.98	1.26	0.10	1.14	0.97	1.34	genotyped	--	98.01

CAPS: CAncer of the Prostate in Sweden, a population-based case-control study in Sweden

Pos*: Position of SNPs is based on NCBI Build 35

Type†: Indicates whether the SNPs were genotyped directly or imputed

ConfidenceScore^: This is calculated based on the average of the maximum posterior probabilities of the imputed genotypes

"'NA": Denotes the situtaion when the test can not be performed when one or more of the four cells equaled 0.

Supplemental Table 2b. Associations between prostate cancer risk and SNPs at 17q12 in JHH

		Allele		Freq. for Allele 1		Allele tests				Dominant				Recessive					Confidence	Call Rate
SNP	Pos*	1	2	Cases	Cont.	*P*	OR	L95	U95	*P*	OR	L95	U95	*P*	OR	L95	U95	Type†	Score^	(%)
rs3094519	33,111,655	A	G	0.22	0.21	0.26	1.11	0.93	1.33	0.45	1.09	0.88	1.34	0.18	1.44	0.84	2.47	genotyped	--	97.80
rs3110646	33,113,030	T	C	0.02	0.01	0.48	1.24	0.69	2.24	0.60	1.17	0.64	2.13	0.33	NA	NA	NA	genotyped	--	98.95
rs3094515	33,117,766	T	C	0.36	0.37	0.84	0.98	0.85	1.15	0.68	0.94	0.69	1.27	0.58	1.06	0.86	1.31	genotyped	--	98.90
rs17138522	33,117,847	G	A	0.05	0.05	0.46	1.14	0.81	1.59	0.61	1.10	0.77	1.55	0.17	NA	NA	NA	genotyped	--	98.66
rs17624747	33,118,267	C	T	0.11	0.09	0.27	1.15	0.90	1.47	0.51	1.09	0.84	1.42	0.04	6.43	0.86	NA	genotyped	--	99.28
rs739753	33,118,390	T	A	0.20	0.19	0.70	1.04	0.86	1.25	0.94	1.01	0.81	1.25	0.36	1.28	0.75	2.21	genotyped	--	99.28
rs11263755	33,119,634	G	A	0.20	0.18	0.35	1.09	0.91	1.32	0.29	1.12	0.90	1.40	0.92	1.03	0.59	1.79	genotyped	--	98.42
rs9912390	33,120,508	C	G	0.03	0.02	0.38	1.25	0.76	2.05	0.40	1.24	0.75	2.05	0.57	NA	NA	NA	imputed	0.99	96.84
rs10962	33,120,564	C	G	0.21	0.22	0.31	0.91	0.77	1.09	0.35	1.26	0.78	2.04	0.41	1.09	0.89	1.35	genotyped	--	98.75
rs2688	33,121,044	G	T	0.37	0.39	0.28	0.92	0.79	1.07	0.84	1.03	0.77	1.38	0.17	1.16	0.94	1.44	genotyped	--	99.23
rs1058166	33,121,104	C	T	0.04	0.04	0.59	1.11	0.76	1.63	0.65	1.10	0.74	1.62	0.42	NA	NA	NA	imputed	0.98	95.07
rs2689	33,121,214	A	T	0.48	0.46	0.28	1.08	0.94	1.25	0.10	1.21	0.96	1.51	0.92	1.01	0.79	1.30	genotyped	--	99.19
rs3110641	33,121,530	A	G	0.24	0.23	0.52	1.06	0.89	1.26	0.43	1.09	0.88	1.34	0.99	1.00	0.64	1.58	genotyped	--	99.28
rs8066605	33,121,614	A	G	0.04	0.03	0.31	1.23	0.83	1.81	0.32	1.23	0.82	1.82	NA	NA	NA	NA	genotyped	--	99.09
rs3094513	33,122,636	A	G	0.45	0.44	0.40	1.07	0.92	1.24	0.14	1.19	0.94	1.50	0.83	0.97	0.74	1.27	imputed	0.96	90.42
rs3110640	33,122,936	G	A	0.45	0.44	0.50	1.05	0.90	1.23	0.23	1.15	0.91	1.46	0.84	0.97	0.74	1.28	imputed	0.96	89.22
rs11263756	33,123,933	A	G	0.03	0.03	0.41	1.20	0.78	1.84	0.43	1.19	0.77	1.85	0.57	NA	NA	NA	imputed	0.99	98.42
rs1859211	33,125,485	C	T	0.15	0.14	0.69	1.04	0.85	1.29	0.56	1.07	0.85	1.35	0.67	0.86	0.43	1.73	genotyped	--	98.80
rs11868513	33,126,805	A	G	0.21	0.21	0.98	1.00	0.83	1.19	0.78	0.92	0.53	1.60	0.89	1.02	0.82	1.26	genotyped	--	98.85
rs11656817	33,131,012	G	A	0.08	0.09	0.48	0.91	0.70	1.18	0.09	NA	NA	NA	0.29	1.16	0.88	1.52	genotyped	--	98.90
rs1016991	33,132,266	T	A	0.18	0.17	0.34	1.10	0.90	1.33	0.80	1.03	0.83	1.28	0.02	2.69	1.14	6.30	genotyped	--	98.52
rs2269844	33,132,927	A	G	0.18	0.16	0.26	1.12	0.92	1.36	0.66	1.05	0.84	1.31	0.01	3.02	1.19	7.63	imputed	0.99	98.32
rs2189303	33,134,218	A	G	0.23	0.23	0.86	0.98	0.83	1.17	0.51	1.17	0.74	1.85	0.94	0.99	0.80	1.23	imputed	0.98	96.12
rs8075185	33,134,329	T	C	0.42	0.40	0.43	1.06	0.92	1.23	0.50	1.08	0.87	1.34	0.54	1.09	0.83	1.43	genotyped	--	98.95
rs2074430	33,134,628	T	C	0.33	0.31	0.33	1.08	0.92	1.27	0.15	1.17	0.95	1.44	0.81	0.96	0.69	1.35	imputed	0.98	95.83
rs2074428	33,135,772	G	T	0.38	0.38	0.83	1.02	0.87	1.18	0.92	1.01	0.82	1.25	0.79	1.04	0.77	1.40	genotyped	--	99.28
rs3094509	33,136,412	A	G	0.38	0.37	0.70	1.03	0.89	1.20	0.88	1.02	0.82	1.26	0.59	1.09	0.80	1.47	imputed	0.99	97.94
rs3094508	33,137,048	C	T	0.38	0.40	0.54	0.95	0.82	1.11	0.94	1.01	0.76	1.35	0.42	1.09	0.88	1.35	genotyped	--	98.75
rs2189301	33,137,798	A	G	0.14	0.12	0.17	1.17	0.94	1.45	0.14	1.20	0.94	1.53	0.88	1.06	0.48	2.36	genotyped	--	98.56
rs2107133	33,139,010	G	A	0.14	0.12	0.12	1.19	0.95	1.48	0.09	1.24	0.97	1.58	0.96	1.02	0.46	2.27	imputed	0.99	99.04
rs2158254	33,139,608	T	C	0.45	0.45	0.94	1.01	0.87	1.16	0.83	1.02	0.82	1.28	0.92	0.99	0.77	1.27	genotyped	--	98.99
rs9892543	33,142,072	G	A	0.21	0.20	0.62	1.05	0.87	1.26	0.50	1.08	0.87	1.34	0.83	0.95	0.57	1.57	genotyped	--	98.61
rs3110649	33,144,293	A	G	0.26	0.24	0.18	1.13	0.95	1.34	0.28	1.13	0.91	1.40	0.34	1.18	0.84	1.66	genotyped	--	96.12
rs3110645	33,147,289	G	T	0.20	0.20	0.80	0.98	0.81	1.18	0.80	1.08	0.61	1.88	0.84	1.02	0.82	1.28	imputed	0.96	89.85
rs17138478	33,147,433	A	C	0.13	0.13	0.56	1.07	0.86	1.33	0.55	1.08	0.84	1.38	0.91	1.04	0.51	2.13	genotyped	--	98.80
rs3110643	33,147,605	C	T	0.17	0.17	0.70	1.04	0.86	1.26	0.83	1.02	0.82	1.28	0.52	1.25	0.64	2.44	genotyped	--	99.38
rs3110642	33,147,733	C	T	0.17	0.16	0.67	1.04	0.86	1.27	0.79	1.03	0.83	1.29	0.53	1.24	0.63	2.42	imputed	0.99	99.28
rs3110631	33,148,626	C	T	0.16	0.16	0.58	1.06	0.86	1.30	0.64	1.06	0.84	1.33	0.63	1.18	0.60	2.31	imputed	0.97	95.31
rs3094506	33,148,810	T	C	0.16	0.16	0.62	1.05	0.86	1.29	0.69	1.05	0.83	1.32	0.63	1.18	0.60	2.31	imputed	0.97	94.83
rs3094505	33,149,018	T	C	0.16	0.16	0.68	1.04	0.85	1.28	0.76	1.04	0.82	1.31	0.64	1.17	0.60	2.30	imputed	0.97	94.54
rs11649743	33,149,092	A	G	0.16	0.18	1.9E-01	0.88	0.72	1.07	0.73	1.11	0.60	2.06	1.7E-01	1.17	0.94	1.46	genotyped	--	92.00
rs17138476	33,149,718	T	C	0.18	0.16	0.19	1.14	0.94	1.39	0.12	1.20	0.95	1.50	0.95	0.98	0.56	1.71	genotyped	--	98.90
rs2411153	33,149,928	G	C	0.43	0.43	0.93	1.01	0.86	1.18	0.50	1.08	0.86	1.37	0.51	0.91	0.68	1.21	imputed	0.95	86.11
rs11263757	33,150,124	A	G	0.16	0.16	0.82	1.02	0.83	1.26	0.86	1.02	0.81	1.29	0.81	1.09	0.55	2.15	imputed	0.96	91.62
rs718960	33,151,392	T	C	0.20	0.23	2.3E-02	0.82	0.69	0.97	0.28	1.29	0.81	2.06	0.02	1.27	1.03	1.57	genotyped	--	99.14
rs12951345	33,151,976	C	A	0.20	0.23	3.3E-02	0.83	0.69	0.99	0.40	1.23	0.76	1.99	3.0E-02	1.26	1.02	1.56	imputed	0.99	97.84
rs1985643	33,152,615	C	T	0.16	0.16	0.94	1.01	0.82	1.25	0.98	1.00	0.79	1.27	0.85	1.07	0.53	2.19	imputed	0.95	87.93
rs4795218	33,152,623	A	G	0.22	0.24	1.6E-01	0.88	0.73	1.05	0.54	1.16	0.72	1.88	0.15	1.18	0.94	1.47	imputed	0.95	86.16
rs17138469	33,154,278	C	G	0.15	0.18	4.8E-02	0.82	0.68	1.00	0.44	1.26	0.70	2.28	4.9E-02	1.25	1.00	1.56	genotyped	--	99.09
rs4794758	33,154,541	T	C	0.24	0.25	3.0E-01	0.92	0.77	1.08	0.77	1.07	0.70	1.63	2.6E-01	1.13	0.92	1.38	genotyped	--	99.38
rs7407025	33,154,923	G	A	0.27	0.26	0.72	1.03	0.87	1.22	0.88	1.02	0.83	1.25	0.56	1.13	0.76	1.68	genotyped	--	98.85
rs2107131	33,160,802	A	G	0.34	0.35	0.56	0.96	0.82	1.11	0.41	1.14	0.83	1.56	0.81	1.03	0.83	1.26	genotyped	--	98.71
rs3786127	33,161,987	C	G	0.17	0.15	0.20	1.14	0.93	1.40	0.28	1.13	0.90	1.42	0.23	1.59	0.74	3.42	genotyped	--	98.85
rs1016990	33,163,028	C	G	0.32	0.35	1.2E-01	0.89	0.76	1.03	0.07	1.35	0.98	1.86	3.4E-01	1.11	0.90	1.36	genotyped	--	98.71
rs3744763	33,164,998	G	A	0.37	0.39	1.4E-01	0.89	0.77	1.04	0.01	1.43	1.07	1.90	7.2E-01	1.04	0.84	1.29	genotyped	--	99.23
rs2005705	33,170,413	A	G	0.39	0.45	4.2E-03	0.79	0.68	0.93	0.03	1.38	1.03	1.86	1.1E-02	1.36	1.07	1.74	imputed	0.94	82.95
rs757210	33,170,628	T	C	0.29	0.34	1.2E-02	0.80	0.67	0.95	0.02	1.56	1.06	2.28	5.0E-02	1.26	1.00	1.60	imputed	0.93	78.74
rs4430796	33,172,153	G	A	0.42	0.49	7.0E-04	0.78	0.67	0.90	0.01	1.42	1.10	1.83	3.5E-03	1.41	1.12	1.78	genotyped	--	99.57
rs4239217	33,173,100	G	A	0.32	0.38	3.6E-03	0.79	0.67	0.92	0.01	1.60	1.14	2.26	2.3E-02	1.30	1.04	1.63	imputed	0.95	88.22
rs7501939	33,175,269	T	C	0.34	0.40	5.1E-04	0.77	0.66	0.89	0.00	1.57	1.15	2.13	3.2E-03	1.38	1.11	1.71	genotyped	--	99.09
rs3760511	33,180,426	G	T	0.37	0.32	5.6E-03	1.24	1.07	1.45	0.05	1.23	1.00	1.51	5.6E-03	1.63	1.15	2.31	genotyped	--	99.52
rs17626423	33,182,480	C	T	0.22	0.22	0.75	1.03	0.86	1.23	0.71	1.04	0.84	1.28	1.00	1.00	0.60	1.67	genotyped	--	99.23
rs17626459	33,185,868	C	A	0.09	0.08	0.48	1.10	0.84	1.44	0.50	1.10	0.83	1.47	0.77	1.18	0.39	3.57	genotyped	--	98.95
rs7213769	33,189,279	G	C	0.39	0.35	0.02	1.20	1.04	1.40	0.06	1.22	0.99	1.51	0.04	1.37	1.01	1.87	genotyped	--	99.33

JHH: Subjects in JHH were selected from Johns Hopkins Hospital

Pos*: Position of SNPs is based on NCBI Build 35

Type†: Indicates whether the SNPs were genotyped directly or imputed

ConfidenceScore^: This is calculated based on the average of the maximum posterior probabilities of the imputed genotypes

"'NA": Denotes the situtaion when the test can not be performed when one or more of the four cells equaled 0.

Table 3a. Association of prostate cancer risk and SNPs assuming different genetic models

SNP id	Alternative alleles	Genetic Models	Genotype		*P**	AIC
			Reference	Associated		
Combined data from CAPS, JHH, and PLCO						
rs4430796	G, A	Additive	-	-	2.0E-10	11212.97
		dominant	GG	AG/AA	5.0E-04	11241.51
		recessive	GG/AG	AA	3.5E-11	**11209.04**
		2-df general	GG	AG; AA	9.9E-11	11209.14
rs11649743	A, G	Additive	-	-	1.2E-05	**11256.56**
		dominant	AA	AG/GG	2.0E-03	11266.12
		recessive	AG/GG	GG	1.0E-04	11260.52
		2-df general	AA	AG;GG	4.8E-05	11258.10

P* was adjusted for age and study using a logistic regression model

Supplementary Table 3b . Independent prostate cancer association of two 17q12 loci

	Genotypes		Single SNP analysis		Two SNPs analysis	
SNP id	**Reference**	**Risk**	**OR (95% CI)**	***P****	**OR (95% CI)**	***P****
Combined data from CAPS, JHH, and PLCO						
rs4430796	GG	AG	1.08 (0.97-1.22)		1.06 (0.94-1.19)	
	GG	AA	1.47 (1.29-1.68)	9.9E-11	1.42 (1.24-1.62)	4.2E-09
rs1164974	AA	AG	1.28 (1.02-1.62)		1.28 (1.01-1.61)	
	AA	GG	1.50 (1.20-1.88)	4.8E-05	1.40 (1.12-1.76)	0.004

*P is based on the 2-df general tests, adjusted for age and study

Supplementary Table 4. Odds ratios and 95% CI for a joint effect of two SNPs[§]

rs11649743	rs4430796 (1st locus)			Overall
(2nd locus)	GG	AG	AA	*P*-values[†]
Combined data from CAPS, JHH, and PLCO				
	# of cases/controls, OR (95% CI)			
AA	61/57, 1.00 (Referent)	82/69, 1.01 (0.62-1.66)	39/26, 1.31 (0.70-2.43)	
AG	360/251, 1.30 (0.87-1.95)	877/581, 1.33 (0.91-1.95)	399/225, 1.55 (1.04-2.32)	
GG	522/361, 1.30 (0.88-1.92)	1650/995, 1.41 (0.97-2.05)	1443/625, 2.00 (1.37-2.91)	3.59×10^{-9}

[§]Analysis was adjusted for age and study using a logistic regression model

[†]The overall p-value for genetic effects was estimated using the likelihood ratio test (degrees of freedom = 8).

Supplementary Table 5. Inferred haplotypes for SNPs between two prostate cancer associated loci at 17q12

Haplotype[§]		Cases		Controls		
Alleles	**ID**	**Count**	**Frequency**	**Count**	**Frequency**	***P*-value[†]**
CAPS						
GTCGCATGGCGAGCAGCA	1	791	0.136	419	0.122	0.042
GCCACACGGCAGCCAGCA	2	483	0.083	229	0.066	0.0034
GCGGCATGGCAAGCAGCA	3	316	0.055	180	0.052	0.64
GCGGCATGGCAGGCAGCA	4	290	0.050	148	0.043	0.12
GCGGCATGGCAGCCAGCA	5	195	0.034	140	0.041	0.081
GCCGTCTAGCGGGGGGCA	6	97	0.017	42	0.012	0.083
GTCGCATGGCGAGGAGCA	7	78	0.013	44	0.013	0.78
GCCGTCTAGCGAGCAGCA	8	73	0.013	50	0.015	0.43
ACCGTCTACTAGGGGATG	9	484	0.083	337	0.098	0.019
ACCGTCTACTAAGCAGCA	10	250	0.043	139	0.040	0.52
GCGGCATGGTAGGGGATG	11	226	0.039	157	0.046	0.12
GCGGCATGGCAGGGGATG	12	223	0.038	181	0.053	0.0014
GCCACACGGCAGGCGATG	13	130	0.022	61	0.018	0.12
GCCACACGGCAGGCAACG	14	118	0.020	110	0.032	0.0005
GCCACACGGCAGGGGATG	15	104	0.018	57	0.017	0.62
ACCGTCTAGTAGGCAGCA	16	82	0.014	62	0.018	0.15
ACCGTCTACTAAGGGATG	17	78	0.013	72	0.021	0.0061
JHH						
GTCGCATGGCGAGGAGCA	7	396	0.130	109	0.113	0.18
GCGGCATGGCAGGGAGCA	18	194	0.064	52	0.054	0.28
GCGGCATGGCAGCGAGCA	19	180	0.059	52	0.054	0.56
GCCACACGGCAGCGAGCA	20	148	0.048	32	0.033	0.046
GCGGCATGGCAAGGAGCA	21	146	0.048	50	0.052	0.61
GCGGCATGGCAGGCGGCA	22	41	0.013	12	0.012	0.82
GCCACACGGCAGGCGATG	13	45	0.015	22	0.023	0.087
ACCGTCTACTAGGCGATG	23	193	0.063	56	0.058	0.57
GCGGCATGGCAGGCGATG	24	185	0.061	64	0.066	0.51
GCGGCATGGTAGGCGATG	25	141	0.046	45	0.047	0.95
ACCGTCTACTAAGGAGCA	26	101	0.033	43	0.045	0.093
GCCACACGGCAGGGAACG	27	64	0.021	13	0.013	0.14
GCCACACAGCAGGGAACG	28	62	0.020	14	0.015	0.25
GCGGCATGGCGAGCGATG	29	43	0.014	12	0.012	0.70
GCGGCATGGCAGGGAGCG	30	36	0.012	13	0.013	0.68
GCCACACGGCAGCGGATG	31	32	0.010	14	0.015	0.30
ACCGTCTACTAGGGAACG	32	31	0.010	15	0.016	0.17

§SNPs included in the haplotype analysis (from left to right): rs11649743, rs17138476, rs2411153, rs11263757 rs718960, rs12951345, rs1985643, rs4795218, rs17138469, rs4794758, rs7407025, rs2107131, rs3786127 rs1016990, rs3744763, rs2005705, rs757210, rs4430796

†Based on Chi-square test compared with all other haplotypes

Supplementary Table 6a: Association with disease aggressiveness

	Alleles		Freq. of risk allele in	Aggressiveness Freq. of risk alleles		
Variable	**Ref**	**Risk**	**controls**	**More**	**Less**	***P****
CAPS						
rs4430796	G	A	0.56	0.61	0.61	0.51
rs11649743	A	G	0.77	0.80	0.80	0.97
JHH						
rs4430796	G	A	0.51	0.58	0.58	0.74
rs11649743	A	G	0.82	0.84	0.85	0.37

P is based on allelic tests (more aggressive cases vs less aggressive cases)

Supplementary Table 6b. Association of PSA levels with 2 SNPs at 17q12 in control subjects

	Allele (frequency)		# of subjects by genotype			Least square mean PSA (ng/mL)[§]			
	Normal	Risk	NN*	NR*	RR*	NN*	NR*	RR*	*P*[¥]
CAPS									
rs4430796	G (0.44)	A (0.56)	316	883	509	1.35	1.54	1.75	0.0004
rs11649743	A (0.23)	G (0.77)	92	587	1,009	1.72	1.40	1.65	0.003
JHH									
rs4430796	G (0.49)	A (0.51)	106	253	120	1.12	1.08	1.20	0.57
rs11649743	A (0.18)	G (0.82)	316	883	509	1.21	1.19	1.09	0.62

*NN, NR, and RR denote carriers of 0, 1, and 2 risk allele, respectively.

[§]PSA levels were log-transformed and adjusted for age and geographic region. Least sqaure mean for three genotypes were estimated by treating each SNP as a categorical variable. The values presented were back-transformed.

[¥]Tests were based on log-transformed PSA levels and assuming a general model.