Supplementary Information

Genome-wide association study of prostate cancer in men of African ancestry identifies a susceptibility locus at 17q21

Christopher A. Haiman, Gary K. Chen, William J. Blot, Sara S. Strom, Sonja I. Berndt, Rick A. Kittles, Benjamin A. Rybicki, William Isaacs, Sue A. Ingles, Janet L. Stanford, W. Ryan Diver, John S. Witte, Ann W. Hsing, Barbara Nemesure, Timothy R. Rebbeck, Kathleen A. Cooney, Jianfeng Xu, Adam S. Kibel, Jennifer J. Hu, Esther M. John, Serigne M. Gueye, Stephen Watya, Lisa B. Signorello, Richard B. Hayes, Zhaoming Wang, Edward Yeboah, Yao Tettey, Qiuyin Cai, Suzanne Kolb, Elaine A. Ostrander, Charnita Zeigler-Johnson, Yuko Yamamura, Christine Neslund-Dudas, Jennifer Haslag-Minoff, William Wu, Venetta Thomas, Glenn O. Allen, Adam Murphy, Bao-Li Chang, S. Lilly Zheng, M. Cristina Leske, Suh-Yuh Wu, Anna M. Ray, Anselm JM Hennis, Michael J. Thun, John Carpten, Graham Casey, Erin N. Carter, Edder R. Duarte, Lucy Y. Xia, Xin Sheng, Peggy Wan, Loreall C. Pooler, Iona Cheng, Kristine R. Monroe, Fredrick Schumacher, Loic Le Marchand, Laurence N. Kolonel, Stephen J. Chanock, David Van Den Berg, Daniel O. Stram, Brian E. Henderson

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Supplementary Table 1. Participating prostate cancer studies in men of African ancestry.

				In Study/In analysis[a]		Mean Age (SD)	
Study Abbreviation	Full Name	Country	Stage	Cases	Controls	Cases	Controls
MEC	Multiethnic Cohort	USA	1	1094/1060	1096/1055	69.3(7.3)	69.7(7.6)
SCCS	Southern Community Cohort	USA	1	212/201	419/412	61.3(7.7)	58.9(7.8)
PLCO	Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial	USA	1	286/231	269/240	67.7(5.8)	63.3(5.3)
CPS-II	The Cancer Prevention Study II Nutrition Cohort	USA	1	76/64	152/112	70.3(6.2)	70.8(5.6)
MDA	Prostate Cancer Case-Control Studies at MD Anderson	USA	1	543/528	474/437	60.0(8.4)	57.4(9.3)
IPCG	Identifying Prostate Cancer Genes	USA	1	368/354	172/157	56.6(7.1)	54.0(14.3)
LAAPC	The Los Angeles Study of Aggressive Prostate Cancer	USA	1	296/288	303/287	63.5(9.2)	63.6(8.6)
CaP Genes	Prostate Cancer Genetics Study	USA	1	75/71	85/85	66.3(8.7)	66.2(8.7)
DCPD	Case-Control Study of Prostate Cancer among African Americans in Washington, DC	USA	1	292/263	359/341	64.0(9.9)	58.5(10.4)
KCPCS	King County Prostate Cancer Study	USA	1	145/141	81/75	59.3(7.1)	54.8(6.4)
GECAP	The Gene-Environment Interaction in Prostate Cancer Study	USA	1	234/224	92/89	61.6(7.4)	61.5(7.4)
			TOTAL	3621/3425	3502/3290		
SFPCS	San Francisco Bay Area Prostate Cancer Study	USA	2	86/86	37/36	63.6(7.8)	60.8(6.6)
FMHS	The Flint Men's Health Study	USA	2	135/126	353/341	62.7(8.8)	56.5(10.4)
MEC-LAC	Multiethnic Cohort / Los Angeles County	USA	2	554/551	557/555	64.6(7.4)	68.8(8.0)
NCPCS	North Carolina Prostate Cancer Study	USA	2	214/214	249/249	59.9(7.5)	53.8(9.7)
WFPCS	Wake Forest University Prostate Cancer Study	USA	2	59/58	66/65	60.1(7.8)	57.3(8.6)
WUPCS	Washington University Prostate Cancer Study	USA	2	75/73	153/153	64.9(10.1)	70.3(4.5)
GHS	The Ghana Men's Health Study	Ghana	2	271/265	968/966	69.2(8.0)	60.2(7.1)
			TOTAL	1396/1373	2383/2365		
SCORE	The Study of Clinical Outcome, Risk and Ethnicity	USA	3	152/146	280/267	62.6(7.9)	59.3(12.1)
PROGRÈS	Prostate-Genetique-Recherche-Senegal	Senegal	3	86/79	414/395	67.6(9.5)	52.3(16.7)
PCBP	Prostate Cancer in a Black Population	Barbados	3	246/246	253/242	66.4(8.9)	66.0(8.8)
			TOTAL	484/471	947/904		
		Stage 1+2+3		5501/5269	6832/6559		

[a]See Online Methods for exclusions in Stage 1. In Stage 2, 18 cases and 18 controls missing data for >3 SNPs were excluded. Also excluded were 5 cases missing age at diagnosis (1 in WUPCS and 4 in GHS). In Stage 3, 12 cases and 41 controls missing data for rs7210100 were excluded. Also excluded was 1 case (SCORE) and 2 controls (PROGRÈS) missing information about age.

Supplementary Table 2. Associations of the 17 SNPs and prostate cancer risk in the stage 1 sample with and without adjustment for population stratification.

Chr., Marker Position, Alleles	Adjusted for age and study Per allele OR (95% CI) P value[a]	Adjusted for age, study and eigenvectors 1-10 Per allele OR (95% CI) P value[a]
1, rs2480677 50350241, T/G	1.30(1.16-1.45) $4.3x10^{-6}$	1.30(1.16-1.45) $3.8x10^{-6}$
1, rs1289830 117646555, A/G	1.14(1.07-1.23) $1.7x10^{-4}$	1.16(1.08-1.25) $2.7x10^{-5}$
2, rs2048844 51708020, G/A	1.35(1.19-1.52) $1.7x10^{-6}$	1.34(1.18-1.51) $3.3x10^{-6}$
3, rs9825965 62855968, T/C	1.17(1.09-1.26) $1.1x10^{-5}$	1.17(1.09-1.26) $1.1x10^{-5}$
3, rs1158540 77349641, T/A	1.21(1.12-1.32) $6.9x10^{-6}$	1.21(1.11-1.32) $1.4x10^{-5}$
4, rs13116912 111391946, C/A	1.26(1.14-1.39) $5.7x10^{-6}$	1.25(1.13-1.38) $1.8x10^{-5}$
5, rs6862488 30309917, C/T	1.16(1.08-1.24) $5.1x10^{-5}$	1.17(1.09-1.26) $1.5x10^{-5}$
5, rs251076 94534764, A/G	1.28(1.16-1.41) $1.4x10^{-6}$	1.28(1.15-1.43) $1.3x10^{-5}$
5, rs686 174801306, G/A	1.19(1.11-1.27) $1.2x10^{-6}$	1.18(1.10-1.26) $5.3x10^{-6}$
9, rs1928474 89269215, A/G	1.20(1.12-1.29) $2.1x10^{-7}$	1.19(1.11-1.28) $1.1x10^{-6}$
10, rs7923229 7618388, A/G	1.16(1.08-1.25) $2.8x10^{-5}$	1.18(1.09-1.26) $9.7x10^{-6}$
10, rs1907342 77833774, G/A	1.22(1.13-1.31) $1.4x10^{-7}$	1.20(1.11-1.30) $4.0x10^{-6}$
10, rs4933314 85970708, T/C	1.24(1.14-1.34) $2.8x10^{-7}$	1.21(1.12-1.32) $4.4x10^{-6}$
14, rs917910 79252720, G/A	1.17(1.09-1.25) $9.3x10^{-6}$	1.16(1.09-1.25) $1.6x10^{-5}$
17, rs7210100 44791748, A/G	1.41(1.22-1.63) $2.4x10^{-6}$	1.40(1.21-1.62) $5.2x10^{-6}$
20, rs297712 4337200, C/T	1.19(1.10-1.30) $2.3x10^{-5}$	1.20(1.11-1.30) $1.4x10^{-5}$
X, rs7880612 53093441, T/C	1.26(1.14-1.40) $8.5\ x10^{-6}$	1.28(1.15-1.41) $2.8x10^{-6}$

[a]Test of trend (1-d.f.).

Supplementary Table 3. Associations with the 17 variants in the stage 1 and stage 2 studies.

				OR (95% CI)[b]			P-value[c]		
Chr., Marker Position, Alleles[a]	Stage	RAF[a] controls	Cases/ Controls	Per allele	Het	Hom	Stage (1df / 2 df)	Combined (1df / 2df)	$P_{Het-study}$[d]
1, rs2480677	1	0.10	3423/3289	1.30(1.16-1.45)	1.30(1.15-1.47)	1.67(1.05-2.67)	$3.8x10^{-6}/2.1x10^{-5}$		0.13
50350241, T/G	2	0.11	1370/2356	0.90(0.77-1.06)	0.89(0.74-1.06)	0.95(0.46-1.99)	0.21/0.40	$1.9x10^{-3}/7.6x10^{-3}$	0.75
1, rs1289830	1	0.56	3425/3288	1.16(1.08-1.25)	1.05(0.91-1.20)	1.32(1.14-1.52)	$2.7x10^{-5}/2.8x10^{-5}$		0.78
117646555, A/G	2	0.55	1368/2348	1.07(0.97-1.18)	1.03(0.85-1.24)	1.14(0.93-1.39)	0.17/0.34	$1.4x10^{-4}/1.5x10^{-4}$	0.15
2, rs2048844	1	0.89	3400/3270	1.34(1.18-1.51)	2.09(0.98-4.44)	2.72(1.29-5.75)	$3.3x10^{-6}8.9x10^{-6}$		0.90
51708020, G/A	2	0.91	1366/2352	1.00(0.85-1.18)	1.00(0.52-1.90)	1.00(0.53-1.87)	0.99/0.99	$1.2x10^{-4}/5.4x10^{-4}$	0.46
3, rs9825965	1	0.58	3425/3289	1.17(1.09-1.26)	1.11(0.97-1.28)	1.35(1.17-1.57)	$1.1x10^{-5}4.4x10^{-5}$		0.35
62855968, T/C	2	0.63	1371/2353	0.85(0.77-0.94)	0.87(0.70-1.07)	0.73(0.59-0.90)	$1.8x10^{-3}/7.3x10^{-3}$	0.06/0.15	0.68
3, rs1158540	1	0.77	3419/3285	1.21(1.11-1.32)	1.10(0.86-1.40)	1.37(1.08-1.74)	$1.4x10^{-5}5.4x10^{-5}$		0.35
77349641, T/A	2	0.80	1370/2356	1.03(0.93-1.16)	1.35(0.94-1.93)	1.29(0.90-1.83)	0.68/0.27	$1.0x10^{-4}/5.0x10^{-4}$	0.10
4, rs13116912	1	0.13	3423/3290	1.25(1.13-1.38)	1.24(1.10-1.39)	1.59(1.12-2.27)	$1.8x10^{-5}$		0.60
111391946, C/A	2	NA[e]	NA	NA	NA	NA	NA	NA	NA
5, rs6862488	1	0.46	3424/3290	1.17(1.09-1.26)	1.12(0.99-1.26)	1.37(1.19-1.58)	$1.5x10^{-5}5.3x10^{-5}$		0.43
30309917, C/T	2	0.46	1368/2350	0.97(0.88-1.08)	1.09(0.92-1.28)	0.93(0.76-1.14)	0.59/0.22	$2.9x10^{-3}/0.012$	0.85
5, rs251076	1	0.85	3425/3289	1.28(1.15-1.43)	1.18(0.83-1.69)	1.53(1.07-2.19)	$1.3x10^{-5}/6.3x10^{-5}$		0.36
94534764, A/G	2	0.88	1370/2360	1.10(0.94-1.29)	1.05(0.57-1.91)	1.16(0.65-2.09)	0.22/0.47	$2.3x10^{-6}/1.2x10^{-5}$	0.53
5, rs686	1	0.54	3424/3290	1.18(1.10-1.26)	1.10(0.96-1.25)	1.36(1.18-1.57)	$5.3x10^{-6}/1.5x10^{-5}$		0.60
174801306, G/A	2	0.58	1372/2360	0.99(0.90-1.10)	0.83(0.69-1.01)	0.94(0.77-1.15)	0.85/0.11	$9.6x10^{-5}/6.2x10^{-5}$	0.43
9, rs1928474	1	0.57	3425/3290	1.19(1.11-1.28)	1.22(1.06-1.40)	1.43(1.24-1.66)	$1.1x10^{-6}6.5x10^{-6}$		0.84
89269215, A/G	2	0.63	1373/2356	1.08(0.97-1.20)	0.90(0.73-1.12)	1.08(0.87-1.35)	0.15/0.06	$2.7x10^{-7}/1.4x10^{-6}$	0.80
10, rs7923229	1	0.37	3425/3289	1.18(1.09-1.26)	1.14(1.03-1.27)	1.40(1.21-1.63)	$9.7x10^{-6}/4.3x10^{-5}$		0.56
7618388, A/G	2	0.37	1364/2345	0.95(0.86-1.05)	0.95(0.82-1.11)	0.90(0.73-1.12)	0.34/0.64	$2.7x10^{-3}/9.7x10^{-3}$	0.25
10, rs1907342	1	0.64	3423/3290	1.20(1.11-1.30)	1.15(0.98-1.35)	1.42(1.19-1.68)	$4.0x10^{-6}/1.9x10^{-5}$		0.24
77833774, G/A	2	0.70	1360/2340	0.99(0.89-1.11)	1.06(0.83-1.36)	1.02(0.80-1.31)	0.92/0.84	$2.1x10^{-5}/1.1x10^{-4}$	0.87
10, rs4933314	1	0.74	3425/3290	1.21(1.12-1.32)	1.14(0.91-1.42)	1.41(1.14-1.75)	$4.4x10^{-6}/2.1x10^{-5}$		0.13
85970708, T/C	2	0.80	1370/2361	1.04(0.92-1.18)	0.95(0.68-1.33)	1.02(0.73-1.42)	0.50/0.67	$2.8x10^{-6}/1.1x10^{-5}$	0.36
14, rs917910	1	0.51	3425/3290	1.16(1.09-1.25)	1.21(1.07-1.37)	1.36(1.18-1.56)	$1.6x10^{-5}/6.9x10^{-5}$		0.27
79252720, G/A	2	0.54	1367/2356	1.03(0.93-1.14)	1.03(0.86-1.24)	1.06(0.87-1.30)	0.56/0.85	$8.3x10^{-5}/3.3x10^{-4}$	0.60
17, rs7210100	1	0.05	3420/3289	1.40(1.21-1.62)	1.37(1.17-1.59)	2.60(1.22-1.53)	$5.2x10^{-6}/1.9x10^{-5}$		0.89
44791748, A/G	2	0.06	1371/2361	1.55(1.26-1.89)	1.57(1.27-1.94)	1.89(0.58-6.16)	$2.5x10^{-5}/1.4x10^{-4}$		0.25
	3	0.05	471/904	2.07(1.49-2.88)	1.97(1.39-2.79)	10.29(1.10-94.40)	$1.5x10^{-5}/5.9x10^{-5}$	$3.4x10^{-13}/2.1x10^{-12}$	0.51
20, rs297712	1	0.76	3422/3290	1.20(1.11-1.30)	1.27(1.01-1.60)	1.50(1.20-1.87)	$1.4x10^{-5}/6.6x10^{-5}$		0.09
4337200, C/T	2	0.77	1361/2333	1.08(0.96-1.21)	1.26(0.90-1.77)	1.30(0.93-1.80)	0.22/0.29	$2.5x10^{-5}7.8x10^{-5}$	0.33
X, rs7880612	1	0.31	3425/3290	1.28(1.15-1.41)	NA	NA	$2.8x10^{-6}/2.8x10^{-6}$		0.99
53093441, T/C	2	0.31	1370/2356	1.04(0.90-1.20)			0.61/0.61	$7.3x10^{-5}/7.2x10^{-5}$	0.49

[a]Risk allele/reference allele (RAF, risk allele frequency in stage 1 sample). [b]Adjusted for age, study and the 1st 10 eigenvalues (stage 1). Adjusted for age and study in stage 2 and stage 3. [c]Test of trend (1-d.f.). Combined p-value is adjusted for age and study. [d]Test of heterogeneity by study in each stage. [e]Deviated from HWE in the stage 2 studies.

Supplementary Table 4. The association of rs7210100 with and without adjustment for European ancestry in the stage 2 and stage 3 studies with available ancestry information.

Study	Ancestry Data (Reference)	Cases/Controls	Adjusted for age and study Per allele OR (95% CI) P value[a]	Cases/Controls (with ancestry information)	Adjusted for age (among those with ancestry information) Per allele OR (95% CI) P value[a]	Adjusted for age and ancestry Per allele OR (95% CI) P value[a]
SFPCS	% European Ancestry[1]	86/36	1.86(0.53-6.55) 0.34	82/36	1.95(0.55-6.90) 0.30	1.92(0.54-6.82) 0.31
FMHS	% European ancestry[1]	125/339	1.70(0.98-2.93) 0.058	125/339	1.70(0.98-2.93) 0.058	1.70(0.99-2.94) 0.056
NCPCS	% European ancestry[2]	214/249	0.92(0.51-1.66) 0.79	160/229	0.86(0.44-1.68) 0.65	0.86(0.44-1.68) 0.65
WFPCS	% European ancestry[2]	58/65	1.90(0.56-6.42) 0.30	58/65	1.90(0.56-6.42) 0.30	1.89(0.56-6.41) 0.31
WUPCS	% European ancestry[2]	73/153	1.96(0.76-5.03) 0.16	66/153	1.88(0.70-5.04) 0.21	1.82(0.68-4.90) 0.23
SCORE	% European ancestry	146/267	1.58(0.88-2.83) 0.13	109/182	1.17(0.55-2.49) 0.68	1.15(0.54-2.46) 0.71
PCBP	Eigenvectors 1-10	246/242	2.02(1.20-3.39) $7.9x10^{-3}$	175/102	2.91(1.35-6.25) $6.2x10^{-3}$	2.88(1.33-6.26) $7.4x10^{-3}$
Meta-Analysis		948/1,351	1.59(1.23-2.05) $4.0x10^{-4}$	779/1,106	1.56(1.16-2.10) $3.3x10^{-3}$	1.54(1.15-2.08) $4.3x10^{-3}$

[a]Test for trend (1-d.f.).

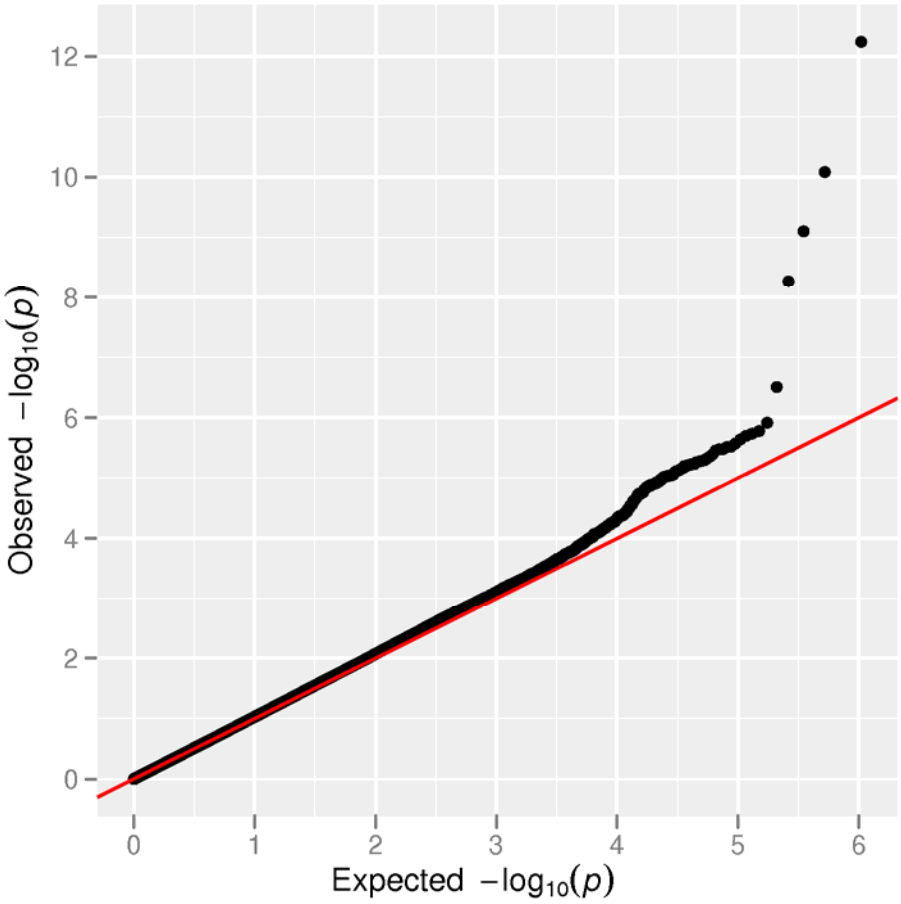
Supplementary Table 5. The association of the 17 variants with and without adjustment for European ancestry in the stage 2 and stage 3 studies with available ancestry information.

		Adjusted for age (among those with ancestry information)		Adjusted for age and % European ancestry	
SNP	Study	OR (95% CI)	P-value	OR (95% CI)	P-value
rs2480677	SFPCS	1.02(0.40-2.63)	0.96	1.01(0.39-2.62)	0.98
	FMHS	0.92(0.57-1.48)	0.74	0.92(0.57-1.48)	0.74
	NCPCS	0.84(0.50-1.40)	0.50	0.84(0.50-1.41)	0.51
	WFPCS	0.89(0.38-2.11)	0.80	0.86(0.36-2.05)	0.73
	WUPCS	1.01(0.45-2.26)	0.98	1.12(0.49-2.55)	0.79
	SCORE	0.96(0.55-1.67)	0.87	0.95(0.54-1.66)	0.86
rs1289830	SFPCS	1.89(1.07-3.33)	0.03	1.98(1.11-3.56)	0.02
	FMHS	1.25(0.94-1.68)	0.13	1.26(0.94-1.68)	0.13
	NCPCS	1.28(0.94-1.75)	0.12	1.29(0.94-1.76)	0.11
	WFPCS	1.31(0.77-2.20)	0.32	1.29(0.76-2.19)	0.34
	WUPCS	0.87(0.55-1.39)	0.56	0.87(0.55-1.39)	0.56
	SCORE	0.82(0.59-1.14)	0.24	0.83(0.59-1.16)	0.27
rs2048844	SFPCS	0.95(0.35-2.57)	0.92	0.92(0.33-2.54)	0.87
	FMHS	0.63(0.40-1.01)	0.05	0.63(0.40-1.01)	0.05
	NCPCS	0.94(0.60-1.49)	0.79	0.94(0.60-1.49)	0.80
	WFPCS	1.40(0.56-3.48)	0.47	1.42(0.57-3.52)	0.45
	WUPCS	1.82(0.75-4.41)	0.18	1.87(0.77-4.54)	0.17
	SCORE	1.64(0.90-2.97)	0.10	1.66(0.91-3.01)	0.10
rs9825965	SFPCS	0.74(0.42-1.30)	0.30	0.74(0.42-1.30)	0.29
	FMHS	0.85(0.63-1.15)	0.30	0.85(0.63-1.15)	0.30
	NCPCS	0.88(0.64-1.21)	0.43	0.88(0.64-1.21)	0.44
	WFPCS	0.59(0.34-1.02)	0.06	0.58(0.34-1.01)	0.05
	WUPCS	1.03(0.64-1.65)	0.90	1.03(0.64-1.67)	0.89
	SCORE	0.60(0.43-0.84)	0.003	0.60(0.43-0.84)	0.003
rs1158540	SFPCS	0.92(0.46-1.85)	0.81	0.93(0.46-1.87)	0.83
	FMHS	1.08(0.76-1.53)	0.68	1.08(0.76-1.54)	0.67
	NCPCS	1.03(0.72-1.47)	0.89	1.02(0.71-1.46)	0.92
	WFPCS	1.45(0.78-2.67)	0.24	1.51(0.81-2.81)	0.20
	WUPCS	0.51(0.30-0.89)	0.02	0.49(0.28-0.86)	0.01
	SCORE	1.17(0.79-1.73)	0.44	1.13(0.76-1.69)	0.55
rs13116912	SFPCS	1.18(0.57-2.44)	0.65	1.17(0.56-2.42)	0.68
	FMHS	1.15(0.81-1.63)	0.43	1.15(0.81-1.64)	0.42
	NCPCS	0.65(0.44-0.96)	0.03	0.65(0.44-0.96)	0.03
	WFPCS	0.59(0.30-1.17)	0.13	0.60(0.30-1.18)	0.14
	WUPCS	0.76(0.43-1.35)	0.35	0.73(0.41-1.31)	0.29
	SCORE	1.14(0.76-1.72)	0.52	1.12(0.74-1.68)	0.60
rs6862488	SFPCS	0.84(0.49-1.44)	0.52	0.84(0.49-1.45)	0.54
	FMHS	0.94(0.71-1.24)	0.65	0.93(0.70-1.24)	0.62
	NCPCS	0.91(0.67-1.22)	0.52	0.91(0.67-1.22)	0.53
	WFPCS	1.19(0.69-2.04)	0.53	1.17(0.68-2.02)	0.58
	WUPCS	0.93(0.57-1.50)	0.75	0.92(0.57-1.49)	0.73
	SCORE	1.18(0.81-1.71)	0.40	1.19(0.82-1.74)	0.36
rs251076	SFPCS	2.06(0.92-4.58)	0.08	2.13(0.92-4.97)	0.08
	FMHS	1.11(0.71-1.72)	0.66	1.11(0.71-1.73)	0.65
	NCPCS	1.19(0.75-1.87)	0.46	1.18(0.74-1.88)	0.49

	WFPCS	0.59(0.26-1.31)	0.19	0.59(0.27-1.32)	0.20
	WUPCS	1.35(0.68-2.68)	0.40	1.24(0.61-2.52)	0.55
	SCORE	1.31(0.80-2.15)	0.28	1.29(0.75-2.20)	0.36
rs686	SFPCS	0.69(0.38-1.26)	0.23	0.68(0.37-1.24)	0.21
	FMHS	0.96(0.71-1.30)	0.80	0.96(0.71-1.30)	0.80
	NCPCS	0.85(0.63-1.15)	0.29	0.84(0.62-1.15)	0.28
	WFPCS	0.74(0.44-1.25)	0.26	0.75(0.45-1.27)	0.29
	WUPCS	1.14(0.70-1.86)	0.59	1.10(0.67-1.81)	0.71
	SCORE	1.02(0.73-1.43)	0.89	0.99(0.70-1.41)	0.96
rs1928474	SFPCS	1.32(0.72-2.41)	0.37	1.29(0.68-2.42)	0.44
	FMHS	1.10(0.82-1.48)	0.53	1.10(0.82-1.49)	0.53
	NCPCS	1.13(0.82-1.54)	0.46	1.12(0.82-1.54)	0.46
	WFPCS	1.38(0.81-2.36)	0.23	1.37(0.80-2.35)	0.25
	WUPCS	1.22(0.74-2.01)	0.43	1.20(0.73-1.98)	0.48
	SCORE	0.74(0.52-1.04)	0.08	0.70(0.49-1.00)	0.05
rs7923229	SFPCS	0.55(0.31-0.98)	0.04	0.55(0.30-1.00)	0.05
	FMHS	1.08(0.79-1.48)	0.64	1.08(0.79-1.48)	0.63
	NCPCS	1.24(0.92-1.67)	0.16	1.24(0.92-1.67)	0.15
	WFPCS	1.16(0.68-1.97)	0.59	1.15(0.67-1.95)	0.62
	WUPCS	0.90(0.54-1.48)	0.67	0.91(0.55-1.50)	0.70
	SCORE	1.19(0.84-1.68)	0.32	1.02(0.85-1.69)	0.31
rs1907342	SFPCS	1.09(0.62-1.94)	0.76	1.08(0.61-1.92)	0.80
	FMHS	0.95(0.69-1.32)	0.78	0.96(0.69-1.33)	0.80
	NCPCS	1.09(0.81-1.48)	0.57	1.09(0.80-1.48)	0.60
	WFPCS	1.22(0.71-2.09)	0.48	1.35(0.75-2.44)	0.31
	WUPCS	0.93(0.57-1.51)	0.77	0.86(0.52-1.42)	0.55
	SCORE	0.91(0.65-1.29)	0.61	0.83(0.57-1.22)	0.35
rs4933314	SFPCS	1.17(0.64-2.15)	0.61	1.16(0.62-2.14)	0.64
	FMHS	1.30(0.92-1.84)	0.14	1.31(0.92-1.86)	0.13
	NCPCS	0.98(0.68-1.42)	0.91	0.97(0.66-1.41)	0.87
	WFPCS	0.79(0.44-1.42)	0.43	0.81(0.45-1.47)	0.49
	WUPCS	0.76(0.44-1.30)	0.32	0.70(0.40-1.22)	0.20
	SCORE	0.93(0.63-1.38)	0.73	0.90(0.61-1.34)	0.61
rs917910	SFPCS	0.90(0.52-1.55)	0.69	0.88(0.51-1.54)	0.66
	FMHS	1.00(0.74-1.36)	0.99	1.00(0.74-1.36)	0.99
	NCPCS	1.47(1.06-2.03)	0.02	1.47(1.06-2.03)	0.02
	WFPCS	1.03(0.62-1.71)	0.92	1.03(0.62-1.72)	0.91
	WUPCS	0.98(0.62-1.55)	0.92	1.00(0.63-1.59)	0.99
	SCORE	0.91(0.64-1.28)	0.59	0.91(0.64-1.28)	0.58
rs7210100	SFPCS	1.95(0.55-6.90)	0.30	1.92(0.54-6.82)	0.31
	FMHS	1.70(0.98-2.93)	0.06	1.70(0.99-2.94)	0.06
	NCPCS	0.86(0.44-1.68)	0.65	0.86(0.44-1.68)	0.65
	WFPCS	1.90(0.56-6.42)	0.30	1.89(0.56-6.41)	0.31
	WUPCS	1.88(0.70-5.04)	0.21	1.82(0.68-4.90)	0.23
	SCORE	1.17(0.55-2.49)	0.68	1.15(0.54-2.46)	0.71
rs297712	SFPCS	1.41(0.75-2.62)	0.28	1.43(0.76-2.67)	0.27
	FMHS	1.42(0.98-2.07)	0.06	1.43(0.98-2.08)	0.06
	NCPCS	0.89(0.62-1.28)	0.53	0.89(0.62-1.28)	0.53
	WFPCS	1.40(0.72-2.75)	0.32	1.39(0.71-2.73)	0.34
	WUPCS	1.45(0.79-2.66)	0.23	1.47(0.80-2.69)	0.21
	SCORE	1.02(0.68-1.55)	0.91	1.02(0.68-1.54)	0.92
rs7880612	SFPCS	0.72(0.31-1.67)	0.44	0.72(0.31-1.67)	0.44
	FMHS	0.98(0.63-1.52)	0.92	0.98(0.63-1.52)	0.91
	NCPCS	0.82(0.53-1.26)	0.36	0.82(0.53-1.26)	0.36

WFPCS	1.16(0.54-2.50)	0.70	1.11(0.51-2.45)	0.79
WUPCS	1.58(0.78-3.20)	0.20	1.56(0.77-3.15)	0.22
SCORE	0.52(0.31-0.87)	0.01	0.52(0.31-0.88)	0.01

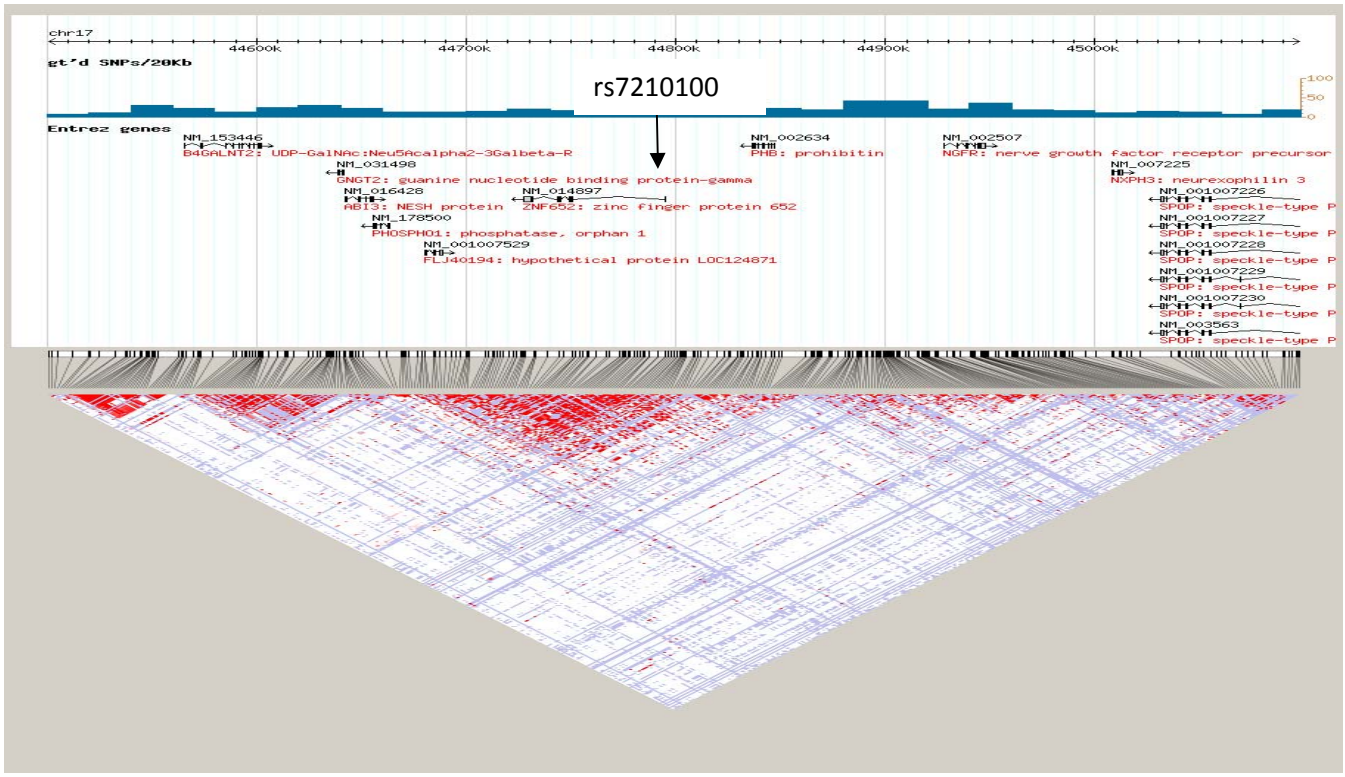
Supplementary Figure 1: Quantile-quantile plot of associations in stage 1 adjusted for population stratification.



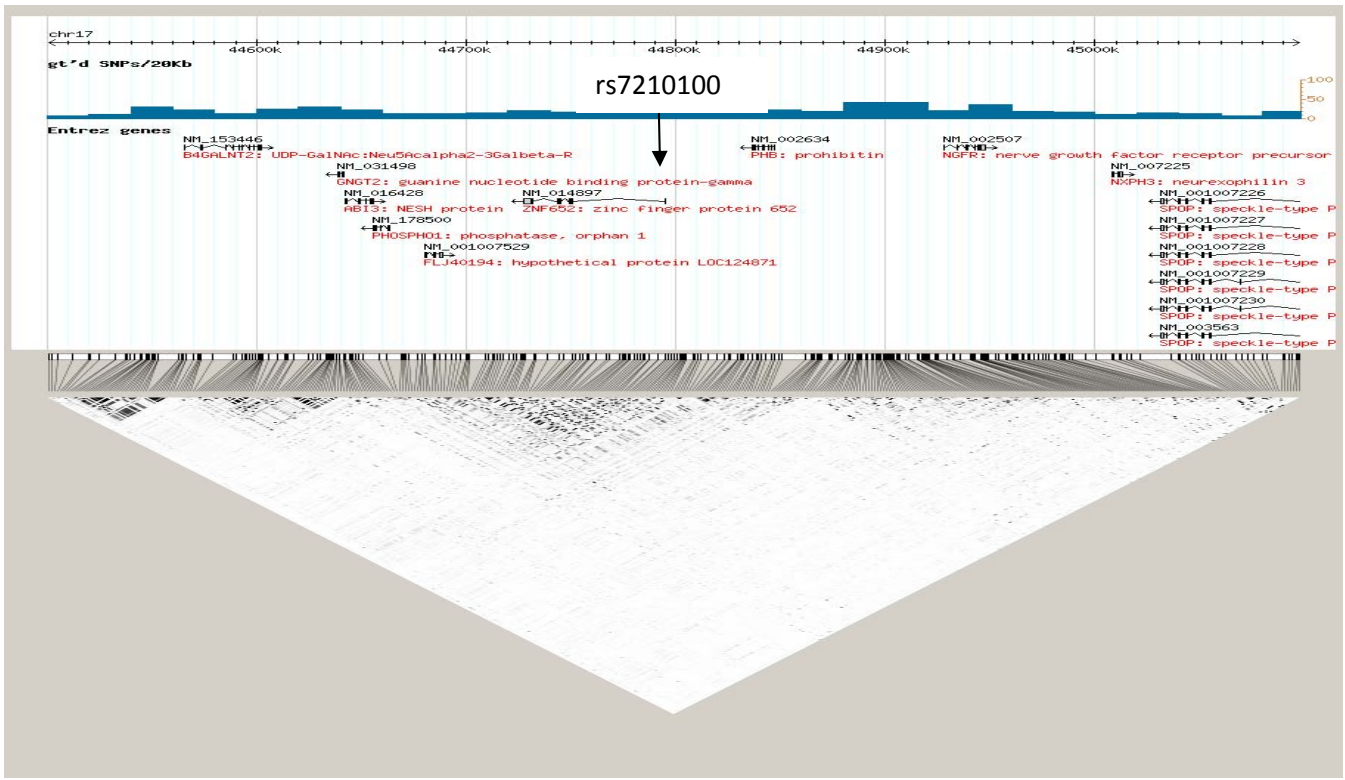
Distribution of p-values (1-df likelihood ratio test) across all genotyped SNPs tested for association with case-control status in models adjusting for age, study and the first 10 eigenvectors calculated from principal components analysis. The genomic inflation factor lambda was calculated as 1.03.

Supplementary Figure 2. D' and r^2 patterns for SNPs with MAF>0.01 at chromosome 17q21 (44.5-45.1 Mb) for the YRI Phase 2 HapMap population estimated in Haploview.[3]

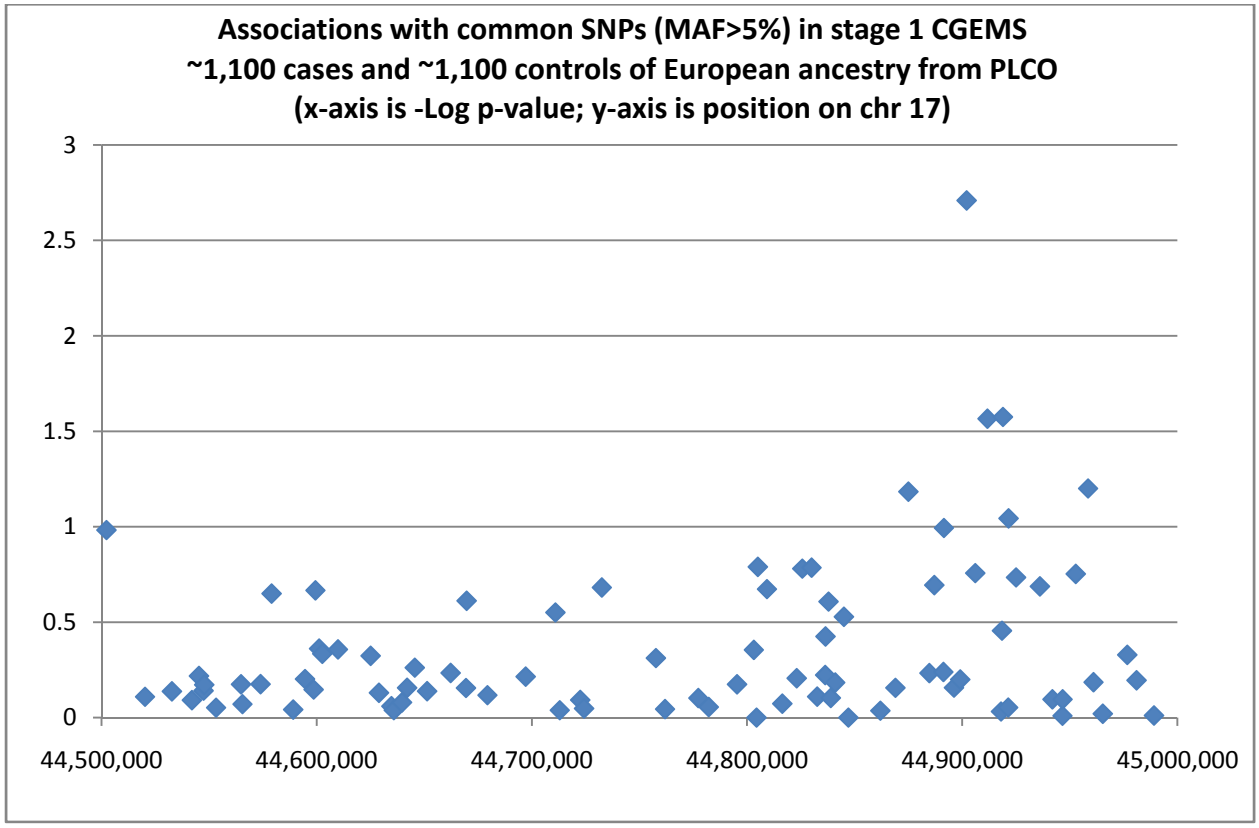
D'



r^2



Supplementary Figure 3. The association of common SNPs at chromosome 17q21 with prostate cancer risk from the NCI CGEMS project.[4]



SNPs with p-values <0.02 were not replicated in stage 2 CGEMS.[4]

Supplementary Note

Eleven studies were included in stage 1, 7 studies in stage 2 and 3 studies in stage 3 as part of the GWAS of prostate cancer in men of African ancestry. Below is a description of each study.

Stage 1 Studies

The Multiethnic Cohort (MEC). The MEC includes 215,251 men and women aged 45-75 years at recruitment from Hawaii and California[5]. The cohort was assembled in 1993-1996 by mailing a self-administered, 26-page questionnaire to persons identified primarily through the driver's license files. Identification of incident cancer cases is by regular linkage with the Hawaii Tumor Registry and the Los Angeles County Cancer Surveillance Program; both NCI-funded Surveillance, Epidemiology, and End Results registries. From the cancer registries, information is obtained about stage and grade. Collection of biospecimens from incident prostate cases began in California in 1995 and in Hawaii in 1997 and a biorepository was established between 2001 and 2006 which includes 67,000 MEC participants. The participation rates for providing a blood sample have been greater than 60%. Through January 1, 2008 the African American case-control study in the MEC included 1,094 cases and 1,096 controls.

The Southern Community Cohort Study (SCCS): The SCCS is a prospective cohort of African and non-African Americans which during 2002-2009 enrolled approximately 86,000 residents aged 40-79 years across 12 southern states[6]. Recruitment occurred mainly at community health centers, institutions providing basic health services primarily to the medically uninsured, so that the cohort includes many adults of lower income and educational status. Each study participant completed a detailed baseline questionnaire, and nearly 90% provided a biologic specimen (approximately 45% a blood sample and 45% buccal cells). Follow-up of the cohort is conducted by linkage to national mortality registers and to state cancer registries. Included in this study are 212 incident African American prostate cancer cases and a matched stratified random sample of 419 African American male cohort members without prostate cancer at the index date selected by incidence density sampling.

The Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO). The Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial[7], is a randomized, two-arm trial among men and women aged 55-74 years to determine if screening reduced the mortality from these cancers. Male participants randomized to the intervention arm underwent prostate specific antigen (PSA) screening at baseline and annually for 5 years and digital rectal examination at baseline and annually for 3 years. Sequential blood samples were collected from participants assigned to the screening arm; participation was 93% at the baseline blood draw (1993-2001). Buccal cell samples were collected from participants in the control arm of the trial; participation was about 85% for this component. Included in this study are 286 African American prostate cancer cases and 269 controls without a history of prostate cancer, matched on age at randomization and study year of the trial.

The Cancer Prevention Study II Nutrition Cohort (CPS-II). The CPS-II Nutrition Cohort includes over 86,000 men and 97,000 women from 21 US states who completed a mailed questionnaire in 1992 (aged 40-92 years at baseline)[8]. Starting in 1997, follow-up questionnaires were sent to surviving cohort members every other year to update exposure information and to ascertain occurrence of new cases of cancer; a >90% response rate has been achieved for each follow-up questionnaire. From 1998-2001, blood samples were collected in a subgroup of 39,376 cohort members. To further supplement the DNA resources, during 2000-2001, buccal cell samples were collected by mail from an additional 70,000 cohort members. Incident cancers are verified through medical records, or through state cancer registries or death certificates when the medical record can not be obtained. Genomic DNA from 76 African American prostate cancer cases and 152 age-matched controls were included in stage 1 of the scan.

Prostate Cancer Case-Control Studies at MD Anderson (MDA): Participants in this study were identified from epidemiological prostate cancer studies conducted at the University of Texas M.D. Anderson Cancer Center in the Houston Metropolitan area since 1996. Cases were accrued from six institutions in the Houston Medical Center and were not restricted with respect to Gleason score, stage or PSA. Controls were identified via random-digit-dialing or among hospital visitors and they were frequency matched to cases on age and race. Lifestyle, demographic, and family history data were collected using a standardized questionnaire. These studies contributed 543 African American cases and 474 controls to this study[9].

Identifying Prostate Cancer Genes (IPCG): Cases in this study were patients 1) undergoing treatment for prostate cancer in the Department of Urology at Johns Hopkins Hospital from 1999 to 2007; 2) undergoing treatment at the Sidney Kimmel Comprehensive Cancer Center from 2003 to 2007; and 3) outside referrals as part of the Hereditary Prostate Cancer Study from 1990 to present. Blood was obtained from groups 2) and 3) while DNA from normal tissue was obtained from group 1). Data are available on age at diagnosis, race, clinical pathology values, and family history. The control subjects were men undergoing disease screening and were not thought to have prostate cancer on the basis of a physical exam. Screenings were performed at the Johns Hopkins Applied Physics Lab, at Bethlehem Steel in Baltimore, and at local African American churches in East Baltimore[10]. A total of 368 African American cases and 172 controls contributed to stage 1.

The Los Angeles Study of Aggressive Prostate Cancer (LAAPC): The LAAPC is a population-based case-control study of aggressive prostate among African Americans in Los Angeles County[11]. Cases were identified through the Los Angeles County Cancer Surveillance Program rapid case ascertainment system and eligible cases included African American men diagnosed with a first primary prostate cancer between January 1, 1999 and December 31, 2003. Eligible cases also had either tumor extension outside the prostate, metastatic prostate cancer in sites other than prostate, or needle biopsy of the prostate with Gleason grade 8 or higher, or Gleason grade 7 and tumor in more than 2/3 of the biopsy cores. Controls were identified by a neighborhood walk algorithm and were men never diagnosed with prostate cancer, and were frequency matched to cases on age (±5 years). For this study, genomic DNA was included for

296 cases and 140 controls. We also included an additional 163 African American controls from the MEC that were frequency matched to cases on age.

Prostate Cancer Genetics Study (CaP Genes): The African American component of this study population comprised 160 men: 75 cases diagnosed with more aggressive prostate cancer and 85 age-matched controls[12]. All subjects were recruited and frequency-matched on the major medical institutions in Cleveland, Ohio (i.e., the Cleveland Clinic, University Hospitals of Cleveland, and their affiliates) between 2001 and 2004. The cases were newly diagnosed with histologically confirmed disease: Gleason score 7; tumor stage T2c; or a prostate-specific antigen level >10 ng/ml at diagnosis. Controls were men without a prostate cancer diagnosis who underwent standard annual medical examinations at the collaborating medical institutions.

Case-Control Study of Prostate Cancer among African Americans in Washington, DC (DCPC): Unrelated men self-described as African American were recruited for several case-control studies on genetic risk factors for prostate cancer between the years 2001 and 2005 from the Division of Urology at Howard University Hospital (HUH) in Washington, DC. Control subjects unrelated to the cases and matched for age (± 5 years) were also ascertained from the prostate cancer screening population of the Division of Urology at HUH[13]. These studies included 292 cases and 359 controls.

King County (Washington) Prostate Cancer Studies (KCPCS): The study population consists of participants from one of two population-based case-control studies among residents of King County, Washington[14,15]. Incident Caucasian and African American cases with histologically confirmed prostate cancer were ascertained from the Seattle-Puget Sound SEER cancer registry during two time periods, 1993-1996 and 2002-2005. Age-matched (5-year age groups) controls were men without a self-reported history of being diagnosed with prostate cancer and were identified using one-step random digit telephone dialing. Controls were ascertained during the same time periods as the cases. A total of 145 incident African American cases and 81 African American controls were included from these studies.

The Gene-Environment Interaction in Prostate Cancer Study (GECAP): The Henry Ford Health System (HFHS) recruited cases diagnosed with adenocarcinoma of the prostate of Caucasian or African American race, less than 75 years of age, and living in the metropolitan Detroit tri-county area[16]. Controls were randomly selected from the same HFHS population base from which cases were drawn. The control sample was frequency matched at a ratio of 3 enrolled cases to 1 control based on race and five-year age stratum. In total, 637 cases and 244 controls were enrolled between January 2002 and December 2004. Of study enrollees, DNA for 234 African Americans cases and 92 controls were included in stage 1 of the scan.

Stage 2 Studies

San Francisco Bay Area Prostate Cancer Study (SFPCS): The SFPCS is a population-based case-control study of advanced prostate among non-Hispanic Whites and African Americans in the San Francisco Bay area[17]. Incident cases of advanced prostate cancer were identified through

the Greater Bay Area Cancer Registry (a SEER registry) and included African American cases aged 40-79 years diagnosed between July 1, 1997 and December 31, 2000. Advanced prostate cancer was defined as a tumor invading and extending beyond the prostatic capsule and/or extending into adjacent tissue or involving regional lymph nodes or distant metastatic sites. Of the 118 eligible African American cases, 105 completed an in-person interview and provided a biospecimen (86 bloods and 19 mouthwash). Control men aged 40-79 years were identified through random-digit dialing and controls aged 65-79 years were identified through random selections from the rosters of beneficiaries of the Health Care Financing Administration (HCFA). In-person interviews and biospecimens were obtained for 85 controls (37 bloods and 48 mouthwash). This study included DNA from blood collected from 86 African American cases and 37 controls.

The Flint Men's Health Study (FMHS): The FMHS was a community-based, case-control study of prostate cancer in African American men living in Genesee County, MI conducted from 1996-2002[18]. Controls were recruited from a probability sample of African American men aged 40-79 years with intentional over-sampling from older age groups. Cases were identified from the Genesee County Community-Wide Hospital Oncology Program registry. All participants provided blood samples from which DNA and serum were isolated and completed detailed interviews which addressed potential risk factors for prostate cancer (family history, environmental exposures, sexual health and fertility, alcohol consumption, smoking history, etc), urinary symptoms, prostate cancer screening history and general medical history, socio-economic factors, and access to and use of health care. Additionally, controls underwent urological examinations and PSA screening and cases provided access to medical records pertaining to their prostate cancer diagnoses. A total of 383 controls participated in all portions of the study. Nineteen of those controls were diagnosed with prostate cancer during the time of the study and subsequently recruited as cases. Genomic DNA was available for 135 African American cases and 353 controls.

The Multiethnic Cohort/Los Angeles County (MEC-LAC): Additional incident African American prostate cases from the MEC were included in the replication sample. Through May 12, 2009 we added 47 cases and 48 age-matched controls. We also included 273 MEC cases whose diagnosis of prostate cancer occurred prior to entering the cohort (prevalent cases) and 273 age-matched controls among eligible African American cohort members. We also included additional African American prostate cancer cases from Los Angeles County (LAC) that are not part of the MEC diagnosed after January 1, 2007. All cases diagnosed with invasive prostate cancer were identified through the Los Angeles County Cancer Surveillance Program. These cases (n=234) were age-matched to controls from the Multiethnic Cohort (n=236).

North Carolina Prostate Cancer Study (NCPCS): NCPCS is a population-based case-control study in the Western part of North Carolina (NC)[2]. This study population included 214 cases and 249 controls that were recruited from November 2006 to November 2008. Cases were identified via the Rapid Case Ascertainment (RCA) center of the North Carolina Central Cancer Registry (NCCCR), which collects standardized demographic and clinical data on every case of cancer

diagnosed in NC, as mandated by state law. Inclusion criteria for cases are a new histological diagnosis of prostate cancer as documented by the NCCCR, age 40 to 70 years, and residence within 12 contiguous NC counties. Case exclusion criteria were prostate cancer incorrectly reported to the NCCCR (false reports), residence in a rest home, hospital, or hospice, any health condition that does not allow completion of the interview, and inability to obtain contact information. Controls were recruited via a friend referral method, and their inclusion criteria required a match to the age, race, and residence county of a case. Control exclusion criteria were a previous diagnosis of prostate cancer, residence in a rest home, hospital, or hospice, and a health condition that does not allow completion of the interview. All cases and controls completed the same participation process, consisting of a blood sample (for DNA and serum), Food Frequency Questionnaire (NIH), and a medical/family history questionnaire.

Wake Forest University Prostate Cancer Study (WFPCS): WFPCS is a hospital-based case-control study from Wake Forest University School of Medicine[19-21]. Prostate cancer cases and controls were recruited from the Departments of Urology and Internal Medicine of the Wake Forest University School of Medicine from September, 26, 1998 to December 15, 2005. All study subjects received a detailed description of the study protocol and provided informed consent, as approved by the medical center's Institutional Review Board. The general eligibility criteria were (i) able to comprehend informed consent and (ii) without previously diagnosed cancer. The exclusion criteria were (i) clinical diagnosis of autoimmune diseases; (ii) chronic inflammatory conditions; and (iii) infections within the past 6 weeks. Blood samples were collected from all subjects. Two groups of controls were recruited from the Urology and Internal Medicine clinics: men with (i) normal prostate-specific antigen (PSA) levels (<4.0 ng/ml) and normal digital rectal exam (DRE); and (ii) abnormal PSA or DRE but negative biopsy results for prostate cancer. Controls recruited from the Urology clinic were mainly follow-up patients with urological problems, such as benign prostatic hyperplasia (BPH), while those from the Internal Medicine clinic were mainly patients coming in for an annual PSA screening without active medical conditions. Epidemiologic information was collected by a self-administered questionnaire. Among the study subjects, 59 cases and 66 controls are African American.

Washington University Prostate Cancer Study (WUPCS): WUPCS is a hospital-based case-control study of prevalent prostate cancer from Washington University School of Medicine. Criteria for case selection in the Washington University (WU) African American population was as follows: the patient must 1) be receiving androgen ablation therapy for prostate carcinoma and 2) have either pathologic or radiologic evidence of metastasis or a PSA of greater than 50ng/ml[2]. These criteria were designed to ensure that all patients had clinically aggressive disease. The criteria for the control population was age $\geq$ 65 years with no history of prostate cancer, PSA <4.0 ng/mL, and a benign digital rectal examination. These criteria were designed so controls were at minimal risk of developing clinically important prostate cancer. Cases from WU consisted of 75 African Americans with advanced prostate cancer recruited from the St. Louis metropolitan area. The control group consisted of 153 African American males all from the St. Louis metropolitan area. Patients and controls were enrolled in the study from January 2001-September 2009. Patients dates of diagnosis ranged from December 1986 until September 2009.

The Ghana Men's Health Study (GHS): The GHS is a population-based study in Ghana that includes 1,038 healthy men aged 55-74 randomly selected from the Accra population for prostate health screening. Between 2006 and 2009, ninety-eight percent of the eligible men selected for the study participated and received a digital rectal examination (DRE) and prostate specific antigen (PSA) testing to assess the prevalence of screened-identified prostate cancer in Ghanaians. Men with positive screening results from DRE or PSA testing underwent a transrectal ultrasound-guided biopsy for histologic confirmation of prostate cancer. To enrich the collection of prostate cancer cases for genetic susceptibility studies, since 2008, the GHS has been expanded to include clinical prostate cancer cases recruited from local hospitals in Accra. To date, the study has amassed 271 cases and 968 population controls. Information on clinical stage and histologic grade was obtained from pathology review and medical records. A structured questionnaire was administered in person to elicit epidemiologic information.

Stage 3 Studies

The Study of Clinical Outcomes, Risk and Ethnicity (SCORE): SCORE is a health system-based case-control study of prostate cancer that utilizes the University of Pennsylvania Health System (UPHS)[22]. In the past 10 years, SCORE have developed the infrastructure for the ascertainment of prostate cancer cases and controls through the UPHS. The SCORE study is comprised of histologically confirmed incident prostate cancer cases identified starting in 1996. Controls are patients seen in general medicine clinics for routine checkups ascertained concurrently to cases at UPHS. A standardized questionnaire is used to collect risk factor information including family history of prostate cancer and demographic information. Whole-genome amplified DNA specimens from 152 African American prostate cancer cases and 280 African American controls were included in stage 3.

Prostate-Genetique-Recherche-Senegal (PROGRÈS): PROGRÈS is a case-control study of prostate cancer in Dakar, Senegal, which utilizes a hospital-based prostate cancer registry at the Hôpital Général de Grand Yoff (HOGGY), a main provider of clinical care in the Dakar metropolitan region[23]. The ethnic (tribal) distribution of men seen at HOGGY is similar to that of the general population of greater Dakar. Controls in this study are also ascertained through HOGGY general medicine practices, which include approximately 70 physicians who see approximately 10,000 potentially eligible control men per year and treat the same population of men who are diagnosed with prostate cancer. Risk factor information is being obtained from a questionnaire interview, a biosample containing DNA is being collected using a non-invasive cheek swab method, and pathology information is being collected using a standardized medical record abstraction approach. For this study, whole-genome amplified DNA was included for 86 cases and 414 controls.

Prostate Cancer in a Black Population (PCBP): The initial project was funded as a pilot study through the National Human Genome Research Institute (NHGRI), NIH, Bethesda, MD, to establish a program to better understand epidemiological and genetic factors influencing the risk of breast and prostate cancer in an Afro-Barbadian population. In 2007, the prostate cancer specific population-based case-control study was funded by the NCI to continue recruitment of

eligible men. The PCBP aims to enroll a total of 960 incident cases of prostate cancer from the Barbados population and 960 age frequency-matched controls, with the vast majority of individuals self identifying as Afro-Barbadian (>90%). The study represents a collaboration with Stony Brook University, the Queen Elizabeth Hospital, Barbados, the University of the West Indies-Cave Hill, Barbados, TGen, Arizona and NHGRI. Blood specimens were collected for genomic DNA to be used for genotyping of potential genetic risk factors for prostate cancer. Admixture Informative Markers (AIMs) are available for many of the participants to assess admixture. This study contributed 246 cases and 253 controls self-reported as Afro-Barbadian to stage 3.

Genetic Susceptibility to Prostate Cancer in African Men: A Study in Uganda (Uganda): This is a hospital-based case-control study of prostate cancer in African men in Kampala, Uganda. Incident cases diagnosed with prostate cancer at Mulago Hospital were recruited starting in January 2010, with recruitment ongoing. Men without prostate cancer are contacted through the orthopedic and surgery clinics at Mulago Hospital. Cases and controls are asked to provide a saliva sample and from controls a blood sample is collected to measure PSA levels to rule out undiagnosed prostate cancer. A total of 111 Ugandan men were genotyped for rs7210100.

References

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