Supplementary Table S1. Clinical characteristics of prostate cancer cases analyzed in this study. For each case used in this study, the patient's race and age at time of surgery is shown. Also shown are tissue-specific parameters, including the fixative used, the Gleason score of the radical prostatectomy (RP), the pathologic T stage at RP, the extent of tumor involvement of the prostate, % of Gp4 in the overall tumor, Gp4 histologic subtype, and immunoreactivity of index tumor to anti-ERG antibody.

Case	Race	Age	Fixative	Gleason Score of RP	Stage of RP	Tumor Volume (%)	% of Gp4 in Overall Tumor	ERG Status (IHC)	Gp4 Histologic Subtype
10-01	Caucasian	52	formalin	3+4=7	pT2c	10	30	positive	mucinous cribriform
11-01	Caucasian	66	formalin	3+4=7	pT2c	5-10	40	positive	cribriform and glomeruloid
11-02	Caucasian	54	formalin	3+4=7	pT2c	20	20	positive	mucinous cribriform and glomeruloid
11-03	African American	63	PAXgene	3+4=7 & Tertiary 5	pT3b	40	40	positive	cribriform, ill-defined, and glomeruloid
11-04	Caucasian	64	PAXgene	4+3=7 & Tertiary 5	pT3b	30-40	50	negative	cribriform and glomeruloid
11-05	Caucasian	55	PAXgene	3+4=7	pT3a	10	30	negative	cribriform and glomeruloid
11-06	Caucasian	65	PAXgene	4+3=7 & Tertiary 5	pT3a	30	50	positive	cribriform and ill-defined
11-07	Caucasian	66	PAXgene	4+3=7	pT2c	5-10	60	negative	cribriform and glomeruloid
11-09	Caucasian	43	PAXgene	4+3=7	pT3a	10	60	negative	cribriform and fused
11-10	Caucasian	50	formalin	3+4=7	pT3b	35	40	positive	cribriform and fused (area 1) cribriform and glomeruloid (area 2)
11-12	Caucasian	58	PAXgene	3+4=7	pT2c	10	10	positive	cribriform and fused
11-13	Hispanic	72	PAXgene	4+5=9	pT3a	25	80	negative	cribriform and microacinar
11-14	Caucasian	69	PAXgene	4+3=7	pT2c	<5	60	negative	ill-defined, fused, and cribriform
12-01	Caucasian	50	PAXgene	3+4=7	pT3a	10-20	30	positive	ill-defined, fused, glomeruloid and cribriform
12-02	Caucasian	54	PAXgene	3+4=7	pT3a	10-15	40	positive	mucinous cribriform, ill-defined, and glomeruloid
12-03	Unknown	64	PAXgene/formalin	4+3=7	pT2c	15-20	60	negative	fused and cribriform

Supplementary Table S2. Shared mutations in each case. For each Gs7 PCa case, all somatic mutations shared by each focus are shown, with the total depth of coverage, variant allele frequency and computed cancer cell fraction (CCF) for each tumor sample. For the benign control, depth of coverage and variant allele frequency are shown.

Case	Genomic Coordinates	Classification	Gene Symbol	Effect	Description	Normal coverage (freq.)	Gp3 tumor coverage (freq.)	Gp4 Focus 1 tumor coverage (freq.)	Gp4 Focus 2 tumor coverage (freq.)	Gp3 tumor CCF	Gp4 Focus 1 tumor CCF	Gp4 Focus 2 tumor CCF
10-01	g.chr7:134253042G>T	Missense Mutation	AKR1B15	p.A95S	aldo-keto reductase family 1, member B15	71 (0.00)	71 (0.27)	95 (0.29)	N/A	0.53	0.79	N/A
10-01	g.chr21:11064776C>A	RNA	BAGE2		B melanoma antigen family, member 2	45 (0.02)	42 (0.14)	42 (0.12)	N/A	0.38	0.32	N/A
10-01	g.chr10:68687216G>A	Missense Mutation	LRRTM3	p.R181H	leucine rich repeat transmembrane neuronal 3	59 (0.00)	67 (0.48)	72 (0.33)	N/A	1.27	0.89	N/A
10-01	g.chr6:170871040A>G	Silent	TBP	p.Q72Q	TATA box binding protein	25 (0.00)	21 (0.19)	28 (0.29)	N/A	0.51	0.76	N/A
10-01	g.chr21:42871382G>A	Intron	TMPRSS2		transmembrane protease, serine 2	99 (0.01)	152 (0.29)	162 (0.26)	N/A	0.77	0.69	N/A
10-01	g.chr21:42873082C>T	Intron	TMPRSS2		transmembrane protease, serine 2	99 (0.01)	104 (0.33)	124 (0.30)	N/A	0.87	0.80	N/A
10-01	g.chr2:179585117A>C	Missense Mutation	TTN	p.F7791C	titin	90 (0.00)	122 (0.40)	144 (0.27)	N/A	1.07	0.72	N/A
11-01	g.chr19:17122463G>A	Silent	CPAMD8	p.D171D	C3 and PZP-like, alpha-2-macroglobulin domain containing 8	23 (0.00)	26 (0.58)	39 (0.26)	N/A	1.54	0.68	N/A
11-01	g.chr7:27181615G>A	Missense Mutation	HOXA5	p.R218C	homeobox A5	103 (0.01)	67 (0.75)	101 (0.48)	N/A	1.99	1.27	N/A
11-01	g.chr12:55969047G>T	Missense Mutation	OR2AP1	p.L283F	olfactory receptor, family 2, subfamily AP, member 1	71 (0.00)	45 (0.58)	84 (0.33)	N/A	1.54	0.89	N/A
11-01	g.chr18:60021761C>T	Missense Mutation	TNFRSF11A	p.H141Y	tumor necrosis factor receptor superfamily, member 11a, NFKB activator	17 (0.00)	30 (0.40)	65 (0.45)	N/A	1.07	1.19	N/A
11-02	g.chr2:91888374A>G	RNA	AC027612.3			34 (0.03)	28 (0.21)	31 (0.13)	18 (0.39)	0.57	0.34	1.04
11-02	g.chr3:195395533C>T	lincRNA	LINC00969		long intergenic non-protein coding RNA 969	34 (0.03)	56 (0.29)	45 (0.16)	72 (0.11)	0.76	0.41	0.30
11-02	g.chr7:78325229T>C	Intron	MAGI2		membrane associated guanylate kinase, WW and PDZ domain containing 2	23 (0.00)	29 (0.31)	35 (0.43)	4 (0.75)	0.83	1.14	2.00
11-02	g.chr7:103180662G>T	Missense_Mutation	RELN	p.S2304R	reelin	58 (0.00)	63 (0.37)	23 (0.48)	13 (0.77)	0.97	1.28	2.05
11-03	g.chr15:77472927C>T	Missense Mutation	PEAK1	p.V448I	pseudopodium-enriched atypical kinase 1	59 (0.00)	78 (0.09)	46 (0.17)	N/A	0.24	0.46	N/A
11-03	g.chr2:234247364G>A	Silent	SAG	p.V329V	S-antigen; retina and pineal gland (arrestin)	29 (0.00)	11 (0.36)	31 (0.87)	N/A	0.97	2.32	N/A
11-10 Area 1	g.chr6:20488432C>T	Missense Mutation	E2F3	p.T363I	E2F transcription factor 3	46 (0.00)	30 (0.33)	28 (0.39)	N/A	0.89	1.05	N/A
11-10 Area 1	g.chr2:237405962G>A	Silent	IQCA1	p.Y60Y	IQ motif containing with AAA domain 1	65 (0.02)	41 (0.37)	32 (0.53)	N/A	0.98	1.42	N/A
11-10 Area 2	g.chr2:27930812C>A	Missense Mutation	AC074091.13	p.W74L		129 (0.01)	358 (1.00)	5 (0.80)	N/A	2.66	2.13	N/A
11-10 Area 2	g.chr10:70726923C>T	Nonsense Mutation	DDX21	p.Q352*	DEAD (Asp-Glu-Ala-Asp) box helicase 21	55 (0.00)	284 (0.40)	6 (0.50)	N/A	1.07	1.33	N/A
11-10 Area 2	g.chr21:39816721G>A	Intron	ERG		v-ets avian erythroblastosis virus E26 oncogene homolog	38 (0.00)	4 (0.75)	749 (0.27)	N/A	2.00	0.72	N/A
11-10 Area 2	g.chr21:39816763G>A	Intron	ERG		v-ets avian erythroblastosis virus E26 oncogene homolog	33 (0.00)	4 (0.75)	518 (0.38)	N/A	2.00	1.00	N/A
11-10 Area 2	g.chr3:49159398G>A	Silent	LAMB2	p.D1634D	laminin, beta 2 (laminin S)	35 (0.03)	332 (0.90)	20 (0.20)	N/A	2.39	0.53	N/A
11-10 Area 2	g.chr7:79050991T>C	Intron	MAGI2		membrane associated guanylate kinase, WW and PDZ domain containing 2	55 (0.02)	29 (0.97)	71 (0.96)	N/A	2.57	2.55	N/A

11-10 Area 2	g.chr4:120474859A>G	Silent	PDE5A	p.Y372Y	phosphodiesterase 5A, cGMP-specific	26 (0.00)	12 (0.92)	56 (0.23)	N/A	2.44	0.62	N/A
11-10 Area 2	g.chr5:171472006G>C	Missense Mutation	STK10	p.N929K	serine/threonine kinase 10	29 (0.00)	153 (0.99)	4 (0.75)	N/A	2.65	2.00	N/A
11-10 Area 2	g.chr5:75596718G>T	Missense Mutation	SV2C	p.A601S	synaptic vesicle glycoprotein 2C	143 (0.00)	306 (0.93)	6 (0.50)	N/A	2.48	1.33	N/A
11-12	g.chr6:135769513G>T	Missense Mutation	AHI1	p.A514E	Abelson helper integration site 1	160 (0.01)	418 (0.17)	10 (0.30)	N/A	0.45	0.80	N/A
11-12	g.chr17:65214783C>T	Silent	HELZ	p.G46G	helicase with zinc finger	55 (0.02)	201 (1.00)	20 (0.25)	N/A	2.65	0.67	N/A
11-13	g.chr10:101943585A>G	Silent	ERLIN1	p.A41A	ER lipid raft associated 1	74 (0.00)	484 (0.22)	15 (0.27)	N/A	0.59	0.71	N/A
11-13	g.chr5:76646896C>T	Nonsense Mutation	PDE8B	p.Q342*	phosphodiesterase 8B	15 (0.00)	94 (0.80)	9 (0.33)	N/A	1.59	0.89	N/A
11-13	g.chr7:77203804A>G	Intron	PTPN12		protein tyrosine phosphatase, non-receptor type 12	120 (0.00)	326 (0.99)	4 (0.75)	N/A	2.65	2.00	N/A
11-14	g.chr6:135769534G>A	Missense Mutation	AHI1	p.S507F	Abelson helper integration site 1	128 (0.01)	350 (0.79)	5 (0.60)	N/A	2.12	1.60	N/A
11-14	g.chr9:66458640G>A	lincRNA	RP11-262H14.1			21 (0.00)	58 (0.19)	47 (0.15)	N/A	0.51	0.40	N/A
11-14	g.chr11:117789342T>C	Missense Mutation	TMPRSS13	p.Q78R	transmembrane protease, serine 13	20 (0.00)	312 (0.62)	10 (0.50)	N/A	1.67	1.33	N/A
11-14	g.chr11:117789345G>C	Missense Mutation	TMPRSS13	p.A77G	transmembrane protease, serine 13	20 (0.00)	312 (0.61)	9 (0.44)	N/A	1.62	1.19	N/A
12-01	g.chr1:144018134G>A	RNA	SRGAP2B		SLIT-ROBO Rho GTPase activating protein 2B	19 (0.00)	29 (0.31)	23 (0.17)	N/A	0.83	0.46	N/A
12-01	g.chr12:53457177C>A	Missense Mutation	TENC1	p.S1249Y	tensin like C1 domain containing phosphatase (tensin 2)	139 (0.00)	227 (0.15)	293 (0.15)	N/A	0.40	0.41	N/A
12-02	g.chr10:63852756G>A	Silent	ARID5B	p.Q1178Q	AT rich interactive domain 5B (MRF1-like)	47 (0.00)	26 (0.23)	13 (0.69)	N/A	0.62	1.85	N/A
12-02	g.chr12:42512938T>A	Missense Mutation	GXYLT1	p.H117L	glucoside xylosyltransferase 1	18 (0.00)	29 (0.69)	19 (0.32)	N/A	1.84	0.84	N/A
12-02	g.chr1:152192219G>C	Missense Mutation	HRNR	p.T629S	hornerin	48 (0.00)	176 (0.11)	288 (0.13)	N/A	0.39	0.35	N/A
12-02	g.chr4:128625402T>G	Missense Mutation	INTU	p.M508R	inturned planar cell polarity protein	79 (0.00)	79 (0.47)	21 (0.62)	N/A	1.25	1.65	N/A
12-02	g.chr7:78644843G>A	Intron	MAGI2		membrane associated guanylate kinase, WW and PDZ domain containing 2	118 (0.00)	48 (0.19)	33 (0.27)	N/A	0.50	0.73	N/A
12-02	g.chr14:82383115G>A	lincRNA	RP11-666E17.1			21 (0.00)	8 (0.62)	15 (0.33)	N/A	1.67	0.89	N/A
12-02	g.chr4:154702787G>A	Missense Mutation	SFRP2	p.S235L	secreted frizzled-related protein 2	30 (0.00)	21 (0.38)	95 (0.57)	N/A	1.02	1.52	N/A
12-03	g.chr16:74443526C>T	Missense Mutation	CLEC18B	p.V418M	C-type lectin domain family 18, member B	15 (0.00)	233 (0.19)	145 (0.20)	14 (0.29)	0.50	0.53	0.91
12-03	g.chr11:533874T>C	Missense Mutation	HRAS	p.Q61R	Harvey rat sarcoma viral oncogene	28 (0.04)	154 (0.28)	155 (0.52)	4 (0.25)	0.75	1.39	0.67
12-03	g.chr14:106780672T>G	RNA	IGHV4-28		immunoglobulin heavy variable 4-28	20 (0.00)	151 (0.23)	85 (0.48)	35 (0.26)	0.60	1.29	0.69
12-03	g.chr14:106780684G>T	RNA	IGHV4-28		immunoglobulin heavy variable 4-28	23 (0.00)	164 (0.20)	79 (0.47)	38 (0.24)	0.54	1.25	0.63
12-03	g.chr14:71209301C>T	Missense Mutation	MAP3K9	p.R139H	mitogen-activated protein kinase kinase kinase 9	12 (0)	51 (0.41)	35 (0.11)	15 (0.47)	1.09	0.29	1.25

Supplementary Table S3. Resequencing of a subset of shared mutations. For each mutation shown, the total number of reads covering each position and the number of reads confirming the alteration are shown. Also shown are the locus-specific sequences of the primer pairs for each alteration. Loci that failed to amplify during verification are omitted from this list. 10 of 12 loci (83%) verified successfully.

Case	Chr	Position	Gene Symbol	Ref Allele	Alt Allele	Effect	Norm Cov	Gp3 Cov	Gp4 Focus 1 Cov	Gp4 Focus 2 Cov	Norm Alt Reads	Gp3 Alt Reads	Gp4 Focus 1 Alt Read	Gp4 Focus 2 Alt Reads	Forward Seq	Reverse Seq
10-01	7	134253042	*AKR1B15*	G	T	Coding	4315	2225	6362	N/A	7	223	2343	N/A	GCCATTGATGCAGAATATCGCCA	GCCCACCCGATCCAGATACT
10-01	10	68687216	*LRRTM3*	G	A	Coding	16921	12539	17292	N/A	26	3077	4165	N/A	GAACAGTTTCGGGGCTTGCG	TGTGCTCCAGGTGAAGTTCTTTGA
10-01	21	42871382	*TMPRSS2*	G	A	Non-coding	4809	3510	5961	N/A	1	1336	1492	N/A	AAGCCGCATTCTGACATCACTCT	TGAGGAACCCGATCAGATATCCAG
10-01	21	42873082	*TMPRSS2*	C	T	Non-coding	13934	17334	27532	N/A	45	7449	10729	N/A	ATCAATACTCAAAACCCACACTTGC	AACTGACTTGGGCACACGGAA
11-01	7	27181615	*HOXA5*	G	A	Coding	80057	58726	75717	N/A	61	50628	25920	N/A	TTCCACTTCATTCTCCGGTTTTGG	GCAGACAACATAGGCGGCCC
11-02	7	78325229	*MAGI2*	T	C	Non-coding	502	1116	2506	1634	0	214	546	551	CTGCTGCCCCATCAGGAGG	CTCAGGGCTGCAGTGAGCTA
11-02	7	103180662	*RELN*	G	T	Coding	3051	7821	3114	754	11	48	1637	266	AGTTAATCCTGAAGGGACTGACCT	GCCTCTCGTGGAGTCTTCTTCA
11-10	6	20488432	*E2F3*	C	T	Coding	5590	6056	6547	N/A	14	1906	3076	N/A	TTGGCAAGTACCCAAGGGC	GCTTGTGGTTCCAATACAGATGGT

12-02	1	152192219	*HRNR*	G	C	Coding	9939	8325	17586	N/A	2075	4796	8394	N/A	GGCCGCGACT AGGAGACTG	CACGGATCTAG CTCGGGTCATT
12-02	4	154702787	*SFRP2*	G	A	Coding	62389	23501	67278	N/A	228	6695	29967	N/A	TGACCAGATA GGGCGCGTTG	AGGAGATAACC TACATCAACCG AGA
12-03	11	533874	*HRAS*	T	C	Coding	2388	4206	16186	1852	4	4110	1700	1325	AGACTTGGTG TTGTTGATGG CAAAC	ACGGAAGGTCC TGAGGGGGT
12-03	14	71209301	*MAP3K9*	C	T	Coding	20855	10403	12846	2504	34	9660	2427	1942	GCTCCCGTTC CAGGATGTCA A	CTCTCAGGCCT CACCCCAG