

**Table W1.** Clinical Parameters of Samples Used in ERRBS.

PCa	STID No.	Serum PSA (ng/ml)	Age at Diagnosis	Gleason Score (H&E)	Pathological Stage	EST-Fusion Status	Year of Radical Prostatectomy
1	508	7.8	57	3 + 4 = 7	T2c	NEG	2007
2	581	9.2	69	4 + 5 = 9	T3b	POS	2007
3	1701	2.1	62	3 + 4 = 7	T3a	POS	2007
4	1783	9.8	66	4 + 4 = 8	T2c	NEG	2008
5	2832	6.6	66	3 + 4 = 7	T2c	POS	2007
6	3027	10.2	66	4 + 4 = 8	T3b	NEG	2008
7	3043	7.2	69	3 + 4 = 7	T2c	NEG	2008

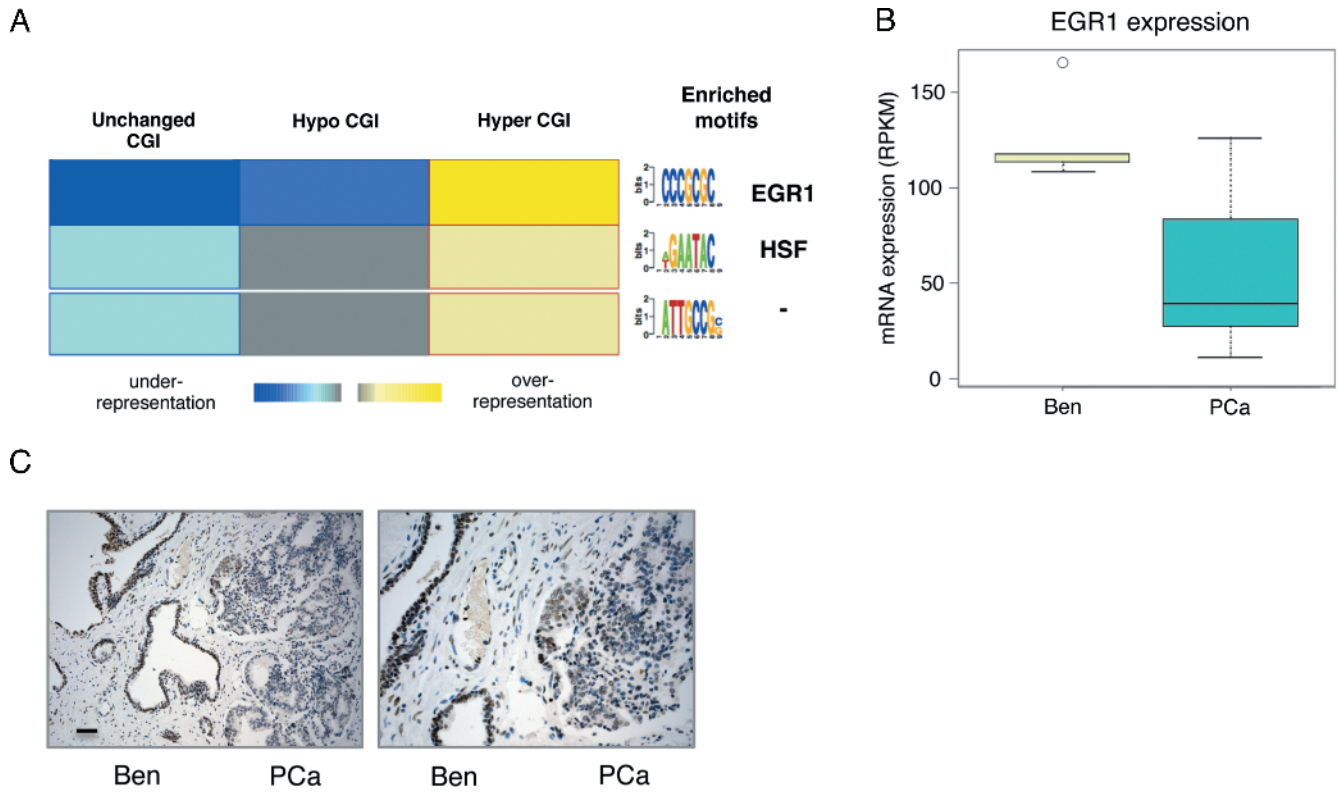
CRPC	STID No.	Serum PSA (ng/ml)	Age at Diagnosis	Metastatic	AR Status	Overall Survival	EST-Fusion Status	Tissue Type
1	4240	1.93	74	–	(–)	13 months	NEG	NEPC
2	7520	0.06	56	Yes	(–)	Alive	POS	NEPC
3	7820	–	–	–	(–)	9 months	NEG	NEPC
4	7821	–	–	–	(–)	9 months	NEG	NEPC
5	8220	–	–	–	(–)	–	NEG	NEPC
6	8740	48.5	59	Yes	(–)	3 months	NEG	NEPC

**Table W2.** Clinical Parameters of FFPE Samples of PCa and CRPC Used in the Validation Cohort.

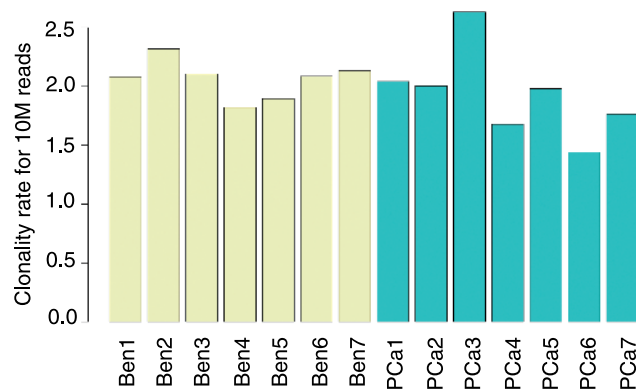
PCa	STID No.	Serum PSA (ng/ml)	Age at Diagnosis	Gleason Score (H&E)	Pathological Stage	Benign in the Cohort	Year of Radical Prostatectomy
FF23	S10-25464	15	74	4 + 3 = 7	T2c	FF22	2010
FF25	S10-17814	5.94	70	3 + 4 = 7	T2a	FF24	2010
FF29	S10-29475	7.4	69	4 + 5 = 9	T3a	FF28	2010
FF31	S09-21599	5.6	62	3 + 4 = 7	T2c	FF30	2009
FF33	S08-6573	–	65	3 + 4 = 7	T2c	FF32	2008
FF35	S08-25678	4.98	68	4 + 3 = 7	T2c	FF34	2008
FF37	S08-15334	–	58	4 + 3 = 7	T3a	FF36	2008
FF39	S07-30717	8.8	63	3 + 4 = 7	T3b	FF38	2007
FF41	S07-29284	5.4	61	3 + 4 = 7	T2c	n/a	2007
FF43	S07-30675	–	50	3 + 4 = 7	T2c	FF42	2007
FF45	S07-28150	–	58	3 + 4 = 7	T2c	FF44	2007
FF47	S07-28191	–	57	3 + 4 = 7	T2c	FF46	2007
FF49	S07-30522	–	63	3 + 4 = 7	T2c	FF48	2007
FF51	S07-31303	–	60	3 + 4 = 7	T2c	FF50	2007
FF53	S07-29250	–	55	3 + 3 = 6	T2a	FF52	2007
FF63	S06-1447	3.15	55	5 + 4 = 9	T4	n/a	2006

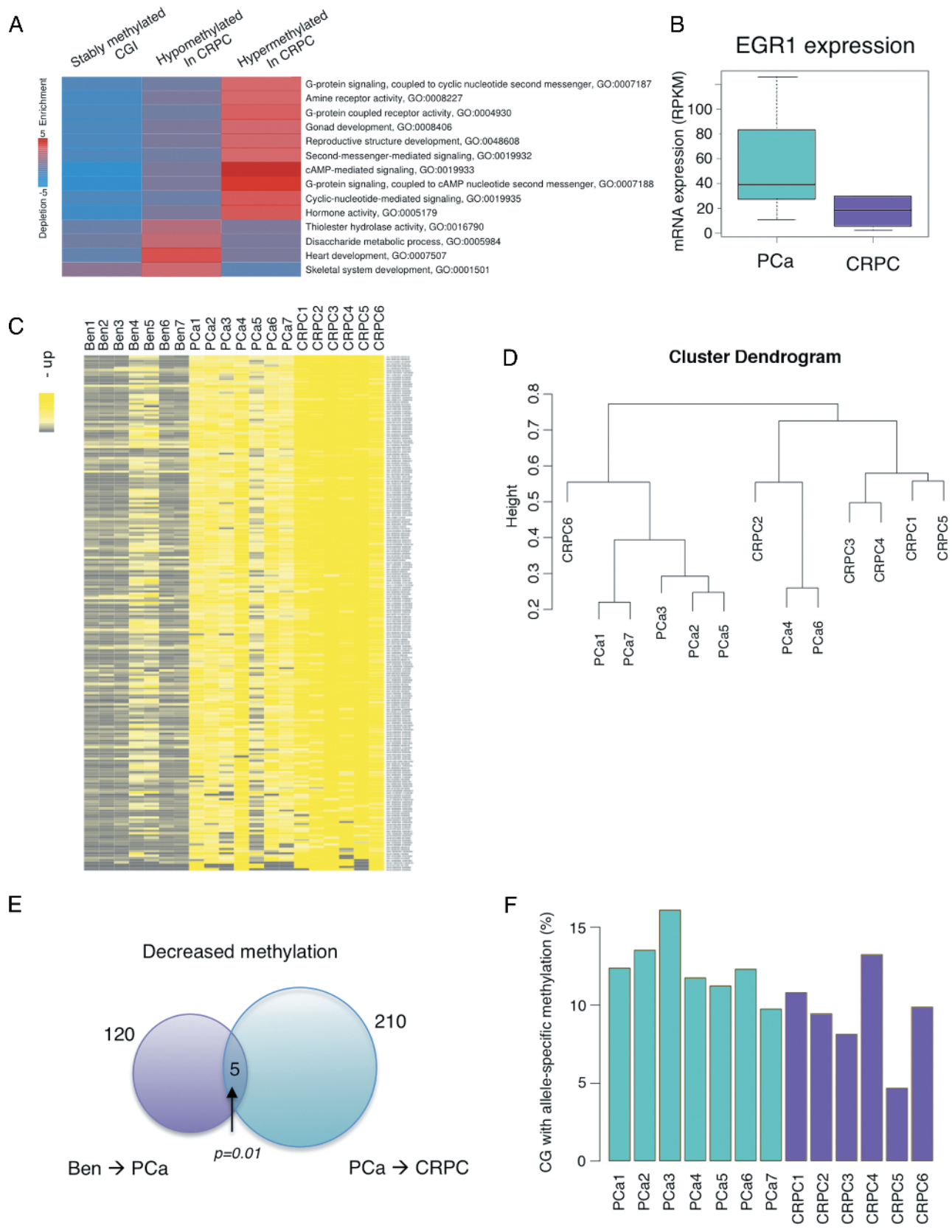
CRPC	STID No.	Tissue Type	Serum PSA (ng/ml)	Age at Diagnosis	Metastatic	Prior Chemotherapy	AR Status	Benign in the Cohort
FF12	1633/04	NEPC	–	–	–	–	(+)	n/a
FF14	10586	NEPC	–	–	–	–	(–)	FF13
FF16	21771/07	NEPC	–	–	–	–	(+)	FF15
FF18	S05-31294	NEPC	5.9	63	–	No	(+)	FF17
FF20	S10-5780	NEPC	–	69	yes	Yes	(–)	FF19
FF55	S97-1161	NEPC	–	78	–	No	(+)	n/a
FF57	S02-1928	NEPC	–	79	yes	No	(+)	n/a
FF59	S12-2609	NEPC	0.7	65	yes	No	(–)	FF58



**Figure W1.** Possible involvement of EGR1 in DNA hypermethylation. (A) Motif analysis of hypermethylated and hypomethylated CGIs. (B) EGR1 mRNA expression between benign prostate tissues and PCa. (C) Immunohistochemistry staining of EGR1 in patient 4 is shown here. Left:  $\times 20$ ; scale bar,  $100 \mu\text{m}$ ; right:  $\times 40$ .



**Figure W2.** PCR duplicates and clonal reads do not explain differences in ASM. Clonality rate for 10 million reads in benign prostate tissue and PCa.



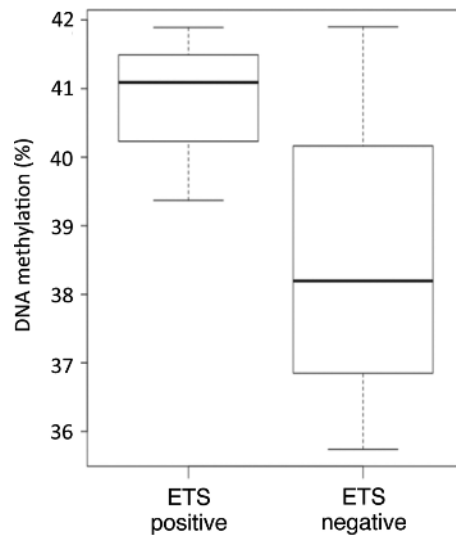
**Figure W3.** Pathway analysis and comparison between PCa and CRPC. (A) The enriched pathways associated with DNA methylation status in CRPC; red, enrichment; blue, depletion. (B) EGR1 mRNA expression between PCa and CRPC. (C) Heat map of the 228 CGIs. (D) Cluster dendrogram of PCa and CRPC using the 228 CGIs. (E) Venn diagram displays the methylation overlap observed between two sections: decreased methylation from benign prostate tissues to PCa and decreased methylation from PCa to CRPC; the inset number represents the coverage in each section. Five CGIs appear in both sections with  $P = .01$ . (F) Percentage of CpG with ASM in PCa and CRPC. Only CpG with nearby SNPs are used for this analysis.

**Table W3.** The Panel of the 13 CGIs and the Associated Genes.

No.	Chr	Start	End	Gene	Description	DIST	EXP	Benign	PCa	CRPC
1	chr12	75601081	75601752	<i>KCNC2</i>	Potassium voltage-gated channel subfamily C	2095	Up	4.644	6.035	11.677
2	chr16	67427284	67428950	<i>ZDHHC1</i>	Probable palmitoyltransferase ZDHHC1	204	Down	8.21	7.266	5.733
3	chr22	19746924	19747141	<i>TBX1</i>	T-box transcription factor TBX1 isoform C	2808	Up	2.078	3.865	9.733
4	chr2	85640969	85641259	<i>CAPG</i>	Macrophage-capping protein	83	Down	22.958	11.654	8.677
5	chr7	150037459	150039031	<i>RARRES2</i>	Retinoic acid receptor responder protein 2	518	Down	77.08	48.548	15.319
6	chr12	52400467	52401696	<i>GRASP</i>	General receptor for phosphoinositides	335	Down	9.953	4.452	2.018
7	chr11	64815040	64815722	<i>SAC3D1</i>	SAC3 domain-containing protein 1	3081	Up	4.907	6.564	19.878
8	chr19	16186789	16188275	<i>TPM4</i>	Tropomyosin $\alpha$ -4 chain isoform 2	398	Down	42.185	23.212	14.138
9	chr11	67350928	67351953	<i>GSTP1</i>	Glutathione S-transferase P	376	Down	168.097	62.937	42.57
10	chr14	36991594	36992488	<i>NKX2-1</i>	Homeobox protein Nkx-2.1 isoform 2	2611	Up	0.014	1.817	66.708
11	chr3	58572478	58572903	<i>FAM107A</i>	Downregulated in renal cell carcinoma	9200	Down	18.921	3.797	1.016
12	chr20	45279781	45280169	<i>SLC13A3</i>	Solute carrier family 13 member 3 isoform a	125	Down	6.766	6.334	3.648
13	chr3	99594969	99595215	<i>FILIP1L</i>	Filamin A interacting protein 1-like isoform 1	46	Down	22.005	5.101	1.525

**Table W4.** MassARRAY EpiTYPER Primers of the 13 CGIs.

No.	Chr	Start	End	Gene	DIST	Forward	Reverse
Epi1	chr12	75601081	75601752	<i>KCNC2</i>	2095	aggaagagagGTAGTATTTTAAAGATTTTGTTTGGAAT	cagtaatacgactcactataggagaaggctATACCCCAAAAAACCAACTCCT
Epi2	chr16	67427284	67428950	<i>ZDHHC1</i>	204	aggaagagagGGTTTTTGGAGAAATAGTTTTTTA	cagtaatacgactcactataggagaaggctTACTCCAAACTCTAAATCCTACCCA
Epi3	chr22	19746924	19747141	<i>TBX1</i>	2808	aggaagagagAAGAGGGTTTTGTATTTTAGGGTG	cagtaatacgactcactataggagaaggctCTAAAAACTCACCTTCCATATCCCT
Epi4	chr2	85640969	85641259	<i>CAPG</i>	83	aggaagagagGGTTGTTATTAGTTTTAAAGTGGGGG	cagtaatacgactcactataggagaaggctACCTAAAAACTCACCTTCCATATCC
Epi5	chr7	150037459	150039031	<i>RARRES2</i>	518	aggaagagagGGAGATTTAGGGAGAGATATAATGGG	cagtaatacgactcactataggagaaggctATAAAATTCCTCCAAAACCACCTAC
Epi6	chr12	52400467	52401696	<i>GRASP</i>	335	aggaagagagAGGATAGAGATAGTTTTAGGTAAGTTGA	cagtaatacgactcactataggagaaggctAAAAATCCAAAAACAATAACCCTC
Epi7	chr11	64815040	64815722	<i>SAC3D1</i>	3081	aggaagagagTTTTTTTATTTTTTTGGTTGATAGAGAAG	cagtaatacgactcactataggagaaggctAAAAACCAATAATCTTTCTCCCT
Epi8	chr19	16186789	16188275	<i>TPM4</i>	398	aggaagagagGAGGAAAAGATGTGAAAATTTTATT	cagtaatacgactcactataggagaaggctCCACAACACTATAAAAAATACCCCTT
Epi9	chr11	67350928	67351953	<i>GSTP1</i>	376	aggaagagagTTTTGTTGTTGTTTATTTTTTAGG	cagtaatacgactcactataggagaaggctTACTAAAAACTCTAAACCCCATCCC
Epi10	chr14	36991594	36992488	<i>NKX2-1</i>	2611	aggaagagagGGGAAGAGAAGGATATTTGTATTTTT	cagtaatacgactcactataggagaaggctTTAAACCCTACCCTACCCTAACC
Epi11	chr3	58572478	58572903	<i>FAM107A</i>	9200	aggaagagagGTTTTTTTATTGTAGAGTTAGTATTGTTGG	cagtaatacgactcactataggagaaggctACACCTACCCTAACCCCTACCC
Epi12	chr20	45279781	45280169	<i>SLC13A3</i>	125	aggaagagagGATTTAGAAGGTAGGGTGGGATTTA	cagtaatacgactcactataggagaaggctCTTTTCTCCAAAAAACAACAAAA
Epi13	chr3	99594969	99595215	<i>FILIP1L</i>	46	aggaagagagGATTTGTTATTTGGTTGTTGATAG	cagtaatacgactcactataggagaaggctTACCTCCCAATAACTTTTATTAACCC



**Figure W4.** DNA methylation levels in *TMPRSS2:ERG* fusion-positive and fusion-negative samples.