

**Table S1 Demographics for all samples analyzed for DNA methylation and RNA sequencing**

		<b>AA N(%)</b>	<b>EA N(%)</b>	<b>Overall</b>	<b>P-value</b>
Overall	N (%)	35 (46.1)	41 (53.9)	76 (100%)	
Age at Diagnosis	Mean/Std/N	57.2/7.9/35	57.8/6.6/41	57.5/7.2/76	0.707
	Median/Min/Max	57.0/44.0/73.0	57.0/45.0/72.0	57.0/44.0/73.0	
Smoking Status	Never	13 (37.1%)	18 (43.9%)	31 (40.8%)	0.133
	Former	11 (31.4%)	18 (43.9%)	29 (38.2%)	
	Current	11 (31.4%)	5 (12.2%)	16 (21.1%)	
Clinical Gleason score	< 7	8 (22.9%)	12 (29.3%)	20 (26.3%)	0.724
	7	21 (60.0%)	24 (58.5%)	45 (59.2%)	
	> 7	6 (17.1%)	5 (12.2%)	11 (14.5%)	
Pre-RP PSA	Mean/Std/N	11.0/14.1/35	8.9/6.1/41	9.8/10.6/76	0.621
	Median/Min/Max	6.9/2.8/82.1	6.4/1.7/25.9	6.9/1.7/82.1	
PSA*	< 10	29 (82.9%)	29 (70.7%)	58 (76.3%)	0.221
	10 to <20	2 (5.7%)	8 (19.5%)	10 (13.2%)	
	>= 20	4 (11.4%)	4 (9.8%)	8 (10.5%)	
Clinical T-stage	cT1	19 (54.3%)	23 (56.1%)	42 (55.3%)	1.000
	cT2	14 (40.0%)	16 (39.0%)	30 (39.5%)	
	cT3	2 (5.7%)	2 (4.9%)	4 (5.3%)	
Grade	II	4 (11.4%)	6 (15.0%)	10 (13.3%)	0.742
	III	31 (88.6%)	34 (85.0%)	65 (86.7%)	
Pathological Gleason	< 7	4 (11.4%)	4 (9.8%)	8 (10.5%)	0.814
	7	28 (80.0%)	35 (85.4%)	63 (82.9%)	
	> 7	3 (8.6%)	2 (4.9%)	5 (6.6%)	
Pathological T-stage	pT2	19 (54.3%)	22 (53.7%)	41 (53.9%)	0.271
	pT3	12 (34.3%)	18 (43.9%)	30 (39.5%)	
	pT4	4 (11.4%)	1 (2.4%)	5 (6.6%)	

**Table S2 Demographics for overlapping samples analyzed by both DNA methylation and RNA sequencing**

		EA N(%)	AA N(%)	Overall	P-value
Overall	N	32 (50.8)	31 (49.2)	63 (100%)	
Age at Diagnosis	Mean/Std/N	58.3/6.7/32	56.4/7.5/31	57.4/7.1/63	0.321
	Median/Min/Max	57.5/45.0/72.0	56.0/44.0/73.0	57.0/44.0/73.0	
Smoking Status	Never	15 (46.9%)	12 (38.7%)	27 (42.9%)	0.039
	Former	14 (43.8%)	8 (25.8%)	22 (34.9%)	
	Current	3 (9.4%)	11 (35.5%)	14 (22.2%)	
Clinical Gleason score	< 7	9 (28.1%)	8 (25.8%)	17 (27.0%)	0.819
	7	20 (62.5%)	18 (58.1%)	38 (60.3%)	
	> 7	3 (9.4%)	5 (16.1%)	8 (12.7%)	
Pre-RP PSA	Mean/Std/N	8.6/5.7/32	10.8/14.7/31	9.7/11.1/63	0.815
	Median/Min/Max	6.7/1.7/25.9	6.9/2.8/82.1	6.9/1.7/82.1	
PSA*	< 10	22 (68.8%)	26 (83.9%)	48 (76.2%)	0.141
	20-Oct	8 (25.0%)	2 (6.5%)	10 (15.9%)	
	>= 20	2 (6.3%)	3 (9.7%)	5 (7.9%)	
Clinical T-stage	cT1	19 (59.4%)	16 (51.6%)	35 (55.6%)	0.845
	cT2	11 (34.4%)	13 (41.9%)	24 (38.1%)	
	cT3	2 (6.3%)	2 (6.5%)	4 (6.3%)	
Grade	II	5 (16.1%)	4 (12.9%)	9 (14.5%)	1
	III	26 (83.9%)	27 (87.1%)	53 (85.5%)	
Pathological Gleason	< 7	4 (12.5%)	4 (12.9%)	8 (12.7%)	0.903
	7	26 (81.3%)	24 (77.4%)	50 (79.4%)	
	> 7	2 (6.3%)	3 (9.7%)	5 (7.9%)	
Pathological T-stage	pT2	17 (53.1%)	18 (58.1%)	35 (55.6%)	0.232
	pT3	14 (43.8%)	9 (29.0%)	23 (36.5%)	
	pT4	1 (3.1%)	4 (12.9%)	5 (7.9%)	

**Table S3. Demographics in TMA**

		<b>AA N (%)</b>	<b>EA N (%)</b>	<b>Overall</b>	<b>P-value</b>
Overall	N	107 (44.6)	133 (55.4)	253 (100%)	
Age at Diagnosis	Mean/Std/N	56.0/7.1/107	59.7/6.7/133	58.1/7.1/240	<.001
	Median/Min/Max	55.0/41.0/70.0	60.0/41.0/78.0	58.0/41.0/78.0	
Age*	< 55	46 (43.0%)	29 (21.8%)	80 (31.6%)	<.001
	>= 55	61 (57.0%)	104 (78.2%)	173 (68.4%)	
Tobacco Use	None	42 (39.3%)	49 (37.4%)	92 (38.5%)	<0.01
	Former	32 (29.9%)	63 (48.1%)	95 (39.7%)	
	Current	33 (30.8%)	19 (14.5%)	52 (21.8%)	
pre-RP PSA	Mean/Std/N	9.1/10.3/106	9.1/10.7/132	9.1/10.5/238	0.48
	Median/Min/Max	6.5/0.7/82.1	6.3/0.1/87.9	6.3/0.1/87.9	
PSA*	< 4	16 (15.1%)	24 (18.2%)	40 (16.7%)	0.92
	4 to <10	70 (66.0%)	82 (62.1%)	152 (63.6%)	
	10 to <20	12 (11.3%)	16 (12.1%)	28 (11.7%)	
	>= 20	8 (7.5%)	10 (7.6%)	19 (7.9%)	
Grade	Grade II	32 (29.9%)	33 (24.8%)	65 (25.7%)	0.39
	Grade III	75 (70.1%)	100 (75.2%)	188 (74.3%)	
Clinical Gleason	<= 3+4	61 (57.0%)	76 (58.0%)	138 (57.7%)	0.90
	>= 4+3	46 (43.0%)	55 (42.0%)	101 (42.3%)	
Clinical T-stage	cT1	71 (68.9%)	90 (68.7%)	162 (68.9%)	0.53
	cT2	28 (27.2%)	39 (29.8%)	67 (28.5%)	
	cT3	4 (3.9%)	2 (1.5%)	6 (2.6%)	
Path Gleason	< 3+4	45 (42.5%)	49 (37.1%)	94 (39.3%)	0.43
	> 4+3	61 (57.5%)	83 (62.9%)	145 (60.7%)	
Path T-stage	pT2	71 (68.9%)	75 (57.7%)	146 (62.4%)	0.23
	pT3	27 (26.2%)	46 (35.4%)	74 (31.6%)	
	pT4	5 (4.9%)	9 (6.9%)	14 (6.0%)	
Persistent Disease?	No	84 (78.5%)	106 (79.7%)	200 (79.1%)	0.87
	Yes	23 (21.5%)	27 (20.3%)	53 (20.9%)	

**Table S4. Percent AR positive nuclei in prostate tissues from AA and EA men**

Percent of AR+ve nuclei		AA			EA			Interaction <i>P</i> -value
Tumor		n	Mean (SD)	<i>P</i> -value	n	Mean (SD)	<i>P</i> -value	
Age (range)	<55	46	77.59 (11.80)	0.49	29	80.63 (13.93)	0.07	0.28
	≥ 55	61	75.80 (14.28)		104	74.07 (17.86)		
PSA (range, ng/mL)	<4	16	72.18 (13.65)	0.15	24	75.47 (13.15)	0.96	0.38
	4 to <10	70	77.91 (12.02)		82	75.18 (18.91)		
	10 to <20	12	72.53 (19.51)		16	77.68 (15.49)		
	≥ 20	8	82.51 (5.55)		10	74.49 (17.08)		
Clinical Gleason score	≤ 3+4	61	77.61 (12.30)	0.35	76	73.10 (17.07)	0.06	<0.05
	≥ 4+3	46	75.19 (14.43)		55	78.82 (17.40)		
Pathological T-stage	pT2	71	77.21 (12.59)	0.87	75	75.44 (15.87)	0.7	0.70
	pT3	27	78.58 (11.72)		46	74.41 (19.98)		
	pT4	5	76.52 (9.36)		9	79.72 (9.47)		
Persistent disease	No	84	76.34 (12.96)	0.74	106	75.20 (17.17)	0.69	0.93
	Yes	23	77.39 (14.49)		27	76.70 (17.81)		
Hormone therapy after radical prostatectomy	No	86	76.62 (13.26)	0.93	100	75.32 (17.07)	0.83	0.84
	Yes	21	76.35 (13.49)		33	76.06 (18.02)		
Percent of AR+ve nuclei		AA			EA			Interaction <i>P</i> -value
Adjacent non-tumor		n	Mean (SD)	<i>P</i> -value	n	Mean (SD)	<i>P</i> -value	
Age (range)	<55	46	80.19 (9.90)	0.16	29	78.09 (16.58)	<0.05	0.22
	≥ 55	61	76.63 (14.82)		104	68.68 (19.28)		
PSA (range, ng/mL)	<4	16	74.41 (14.14)	<0.05	24	69.00 (12.61)	0.97	0.5
	4 to <10	70	80.57 (10.70)		82	71.06 (20.26)		
	10 to <20	12	70.36 (21.56)		16	70.71 (20.98)		
	≥ 20	8	75.48 (7.94)		10	71.38 (21.87)		
Clinical Gleason score	≤ 3+4	61	76.66 (12.55)	0.17	76	69.95 (19.27)	0.69	0.63
	≥ 4+3	46	80.15 (13.45)		55	71.31 (19.07)		
Pathological T-stage	pT2	71	79.78 (11.40)	0.28	75	71.28 (13.34)	0.84	0.53
	pT3	27	79.82 (9.59)		46	69.34 (25.53)		
	pT4	5	71.62 (14.02)		9	72.18 (24.53)		
Persistent disease	No	84	79.27 (11.86)	0.09	106	70.05 (18.91)	0.42	0.11
	Yes	23	74.09 (16.18)		27	73.39 (19.80)		
Hormone therapy after radical prostatectomy	No	86	80.45 (10.74)	<0.001	100	70.59 (17.92)	0.88	<0.05
	Yes	21	68.78 (17.03)		33	71.15 (22.47)		

PSA: prostate specific antigen, n: number of samples, SD: standard deviation

**Table S5. Differentially expressed nodes after AR KO between AA and EA men**

Node (Roswell Park cohort)	Pathway	% Change in AUC in AA men	% Change in AUC in EA men	<i>P</i> -value	Adjusted <i>P</i> -value
		Median (Q1 – Q3)	Median (Q1 – Q3)		
SMAD	TGFb pathway	48.5 (43.3 – 120.3)	15.3 (3.6 – 46.3)	0.0401	0.12
IDH1	Nutrient pathway	34.2 (17.8 – 47.7)	9.6 (3.94 – 13.5)	0.00373	0.0629
AR_ERG	AR pathway	-97.4 (-98.4 – -96.2)	-93.4 (-95.6 – -82.7)	0.0140	0.041
ZBTB17	Cell cycle	-95.8 (-97.8 – -89.0)	-78.5 (-84.9 – -50.6)	0.0401	0.252

Node (TCGA)	Pathway	% Change in AUC in AA men	% Change in AUC in EA men	<i>P</i> -value	Adjusted <i>P</i> -value
		Median (Q1 – Q3)	Median (Q1 – Q3)		
SMAD	TGFb pathway	51.9 (33.3 – 76.4)	28.0 (12.1 – 61.3)	0.0108	0.0024
IDH1	Nutrient pathway	19.9 (8.83 – 36.3)	8.90 (1.88 – 20.7)	0.000313	0.0051
E2F1	Cell cycle	-96.8 (-98.4 – -88.0)	-91.0 (-97.7 – -67.1)	0.000817	0.0378
Beta catenin	WNT pathway	-89.5(-95.4 – -44.2)	-65.7 (-88.3 – -24.8)	0.0153	0.107

Table S6. Top GSEA pathways with hazard ratios based on GSA scores for early/elderly and race comparisons

Table with 15 columns: Comparison, Names, NES, Hit, Hit\_AAR, Hit\_ASE, Hit\_AAP-value, Hit\_EAR, Hit\_EAS, Hit\_EAP-value, Total\_EarlyHit, Total\_EarlySE, Total\_EarlyP-value, Hit\_AAR, Hit\_ASE, Hit\_AAP-value, Total\_EarlyHit, Total\_EarlySE, Total\_EarlyP-value. The table lists various GSEA pathways and their associated statistical values for early/elderly and race comparisons.

## **Supplementary Table legends**

**Table S1** Demographics for samples analyzed for DNA methylation and RNA sequencing.

**Table S2** Demographics for overlapping samples analyzed by both DNA methylation and RNA sequencing.

**Table S3** Demographics of clinical samples included in the TMA.

**Table S4** Percent AR positive nuclei in prostate tissues from AA and EA men.

**Table S5** Differentially expressed nodes after AR KO between AA and EA men.

**Table S6** Hazard ratios for GSEA pathways.