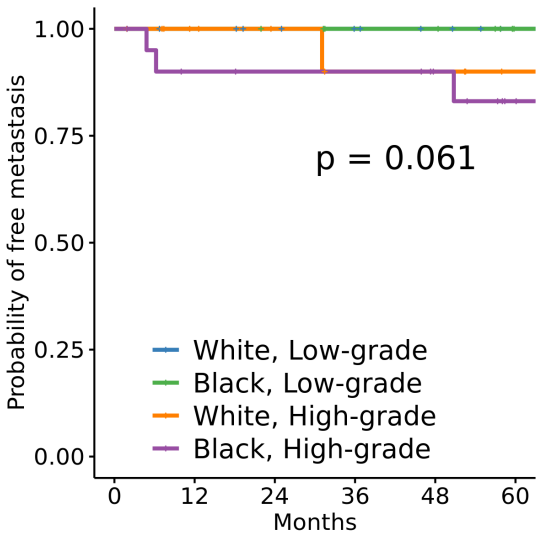


Supplementary Figure 1

Note: all metastasis events are among patients with high-grade PCa (Gleason $\geq 4+3$)



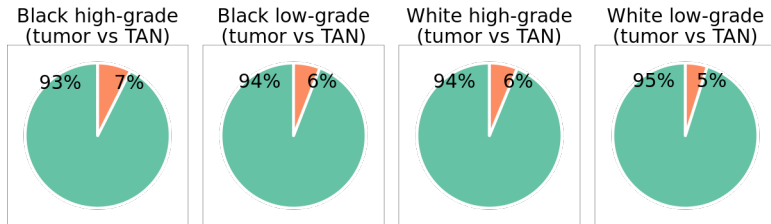
Number at risk

17	16	14	12	10	7
16	16	15	13	13	8
16	12	10	8	8	5
21	17	16	16	13	8

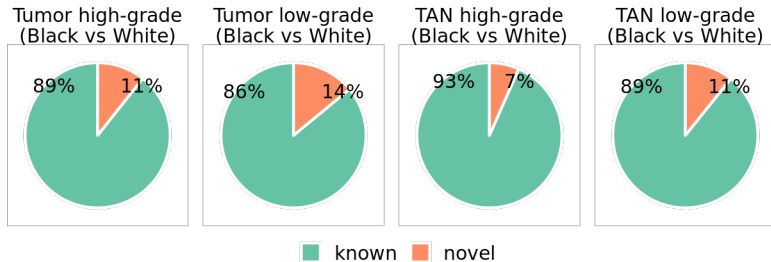
Supplementary Figure 1. Kaplan-Meier plot showing the probability of documented metastasis among Black and White patients with high-grade or low-grade PCa enrolled in GENCADE. The p-value (p) is shown.

Supplementary Figure 2

A

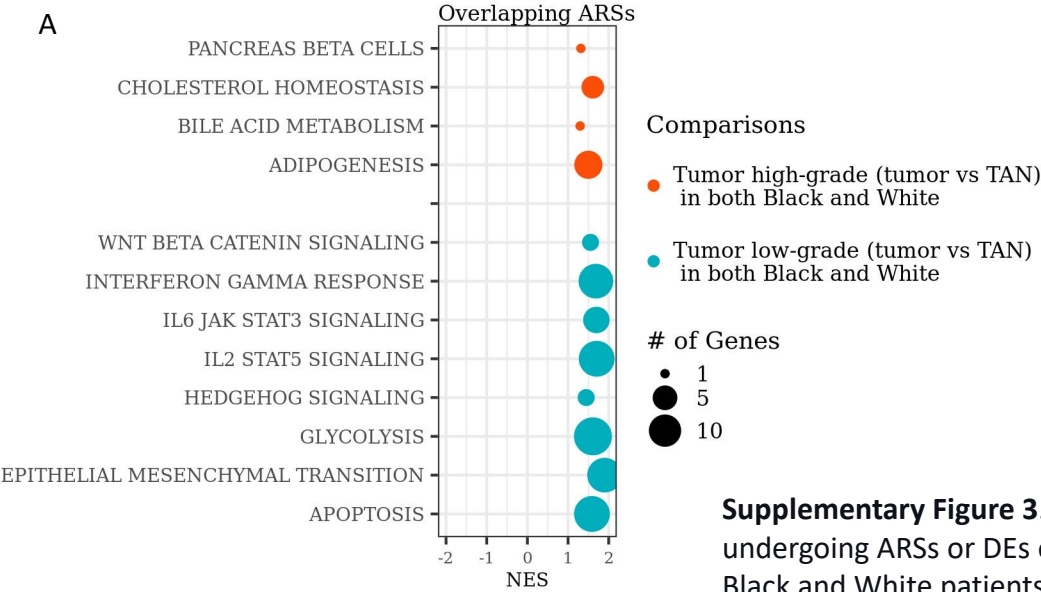


B

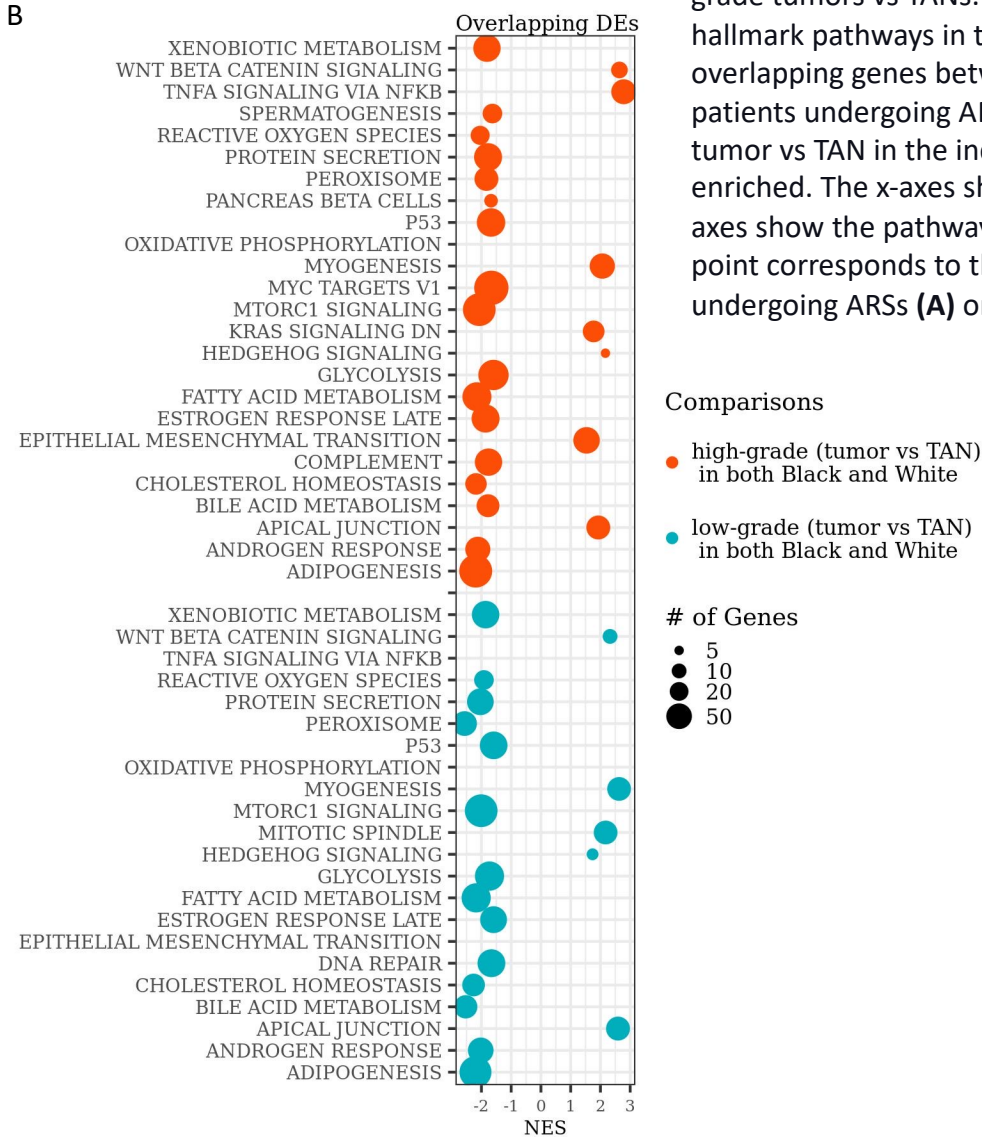


Supplementary Figure 2. Pie charts showing the proportion of novel or known ARSs in the indicated comparisons.

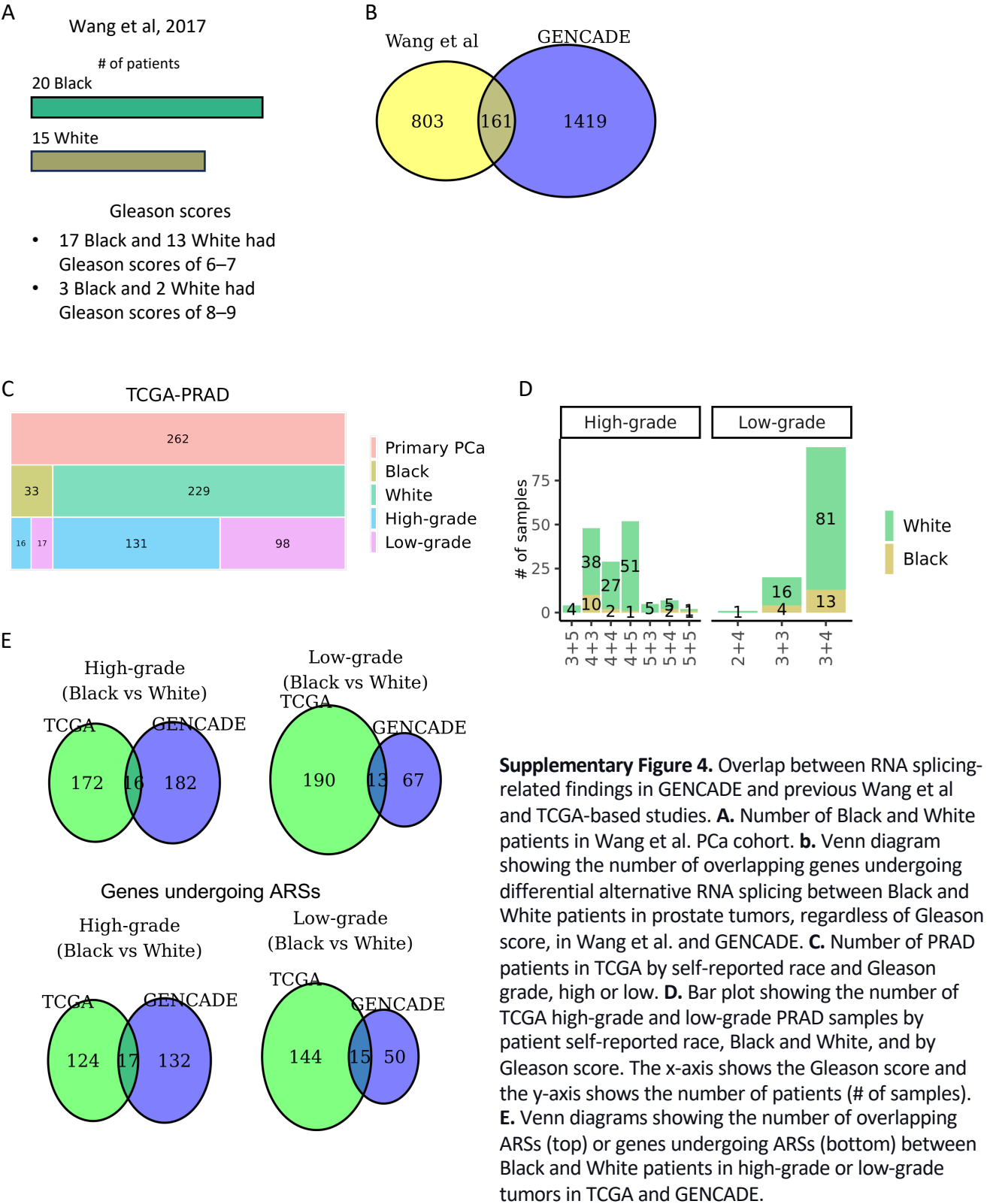
Supplementary Figure 3



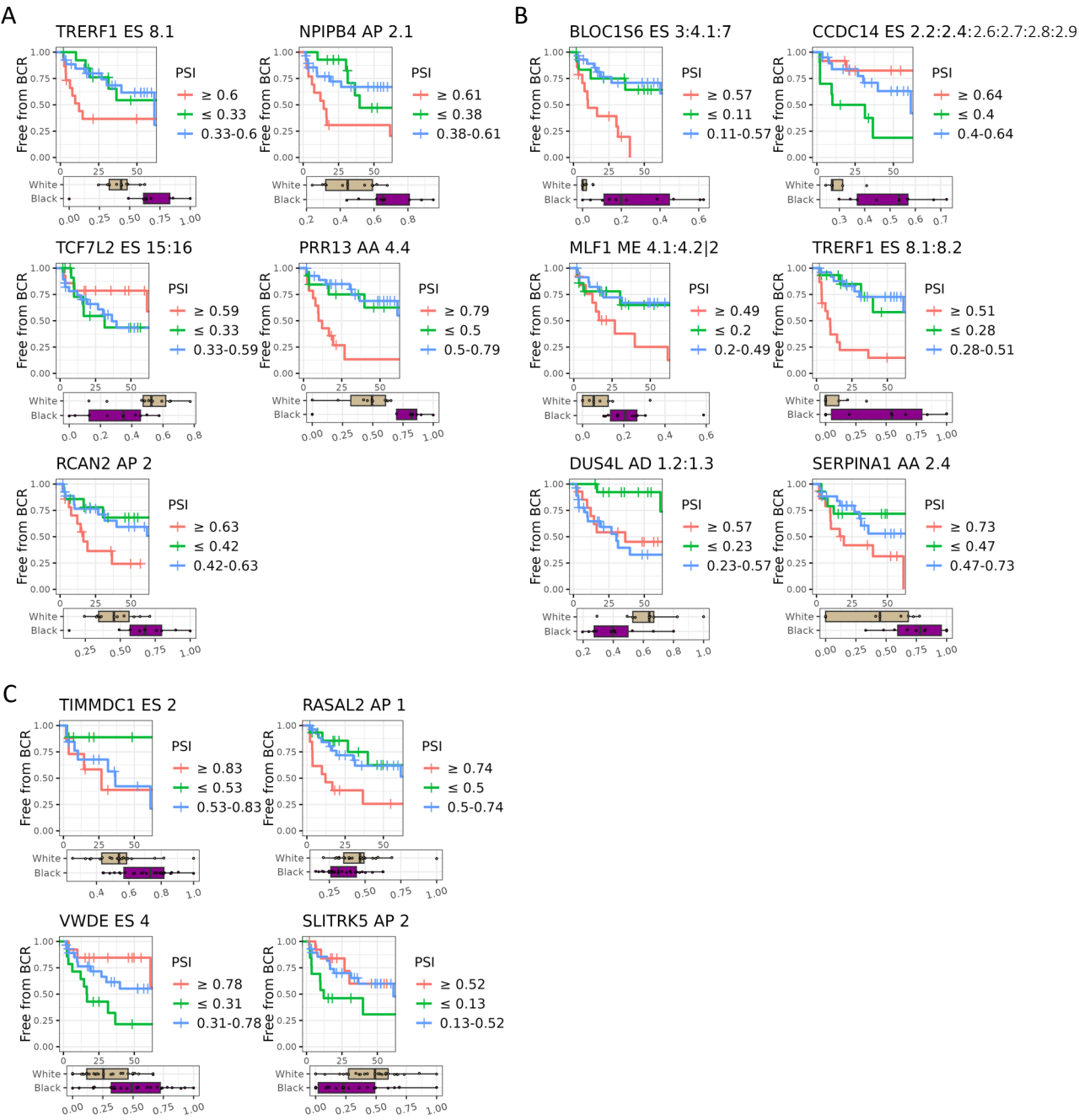
Supplementary Figure 3. GSEA for genes undergoing ARSs or DEs overlapping between Black and White patients in high-grade and low-grade tumors vs TANs. Point plots showing the hallmark pathways in the MSigDB in which overlapping genes between Black and White patients undergoing ARSs (A) or DEs (B) in tumor vs TAN in the indicated comparisons are enriched. The x-axes show the NES and the y-axes show the pathway name. The size of the point corresponds to the number of genes undergoing ARSs (A) or DEs (B).



Supplementary Figure 4

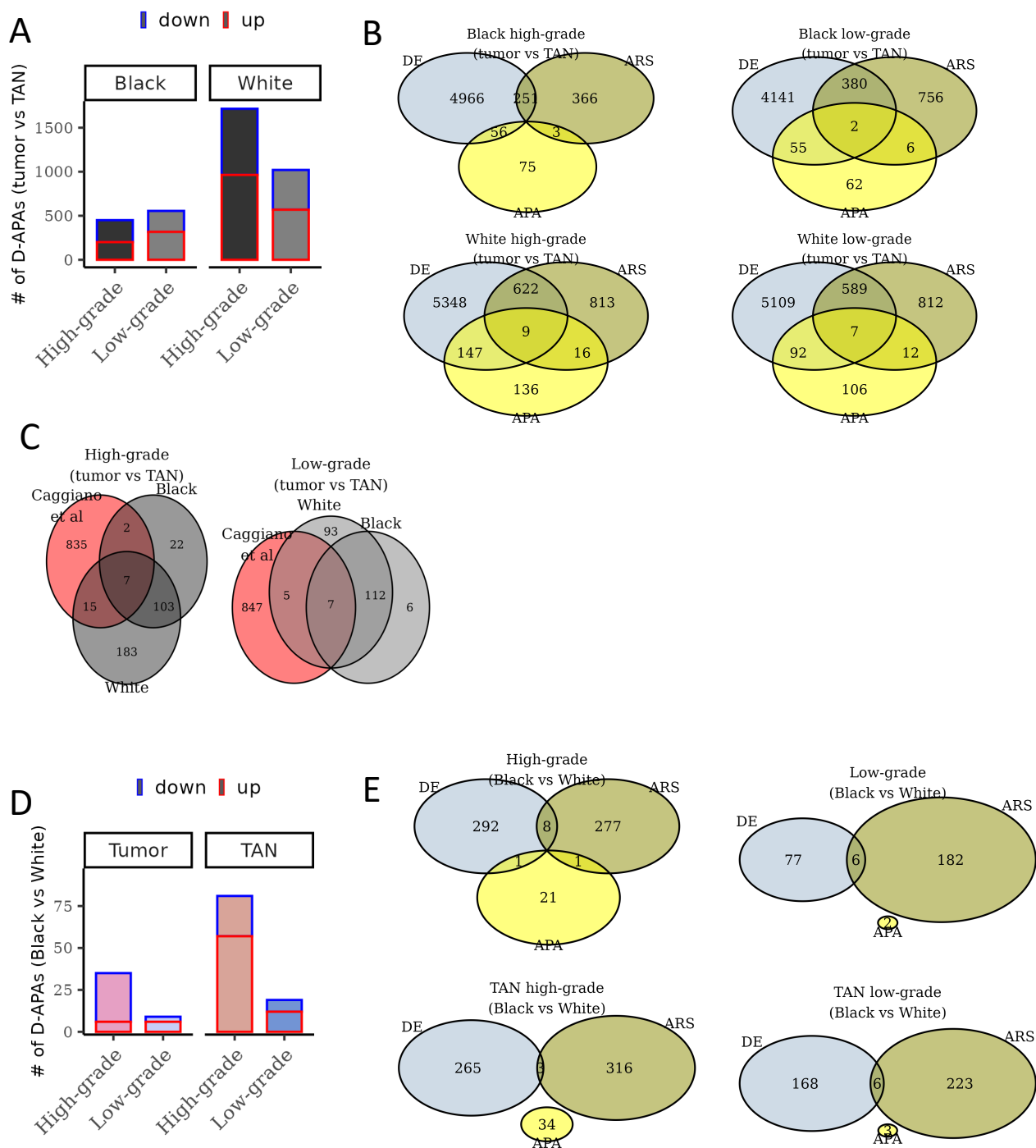


Supplementary Figure 5



Supplementary Figure 5. BCR analysis for the association between genetic ancestry-concordant ARSs and the probability of BCR. Kaplan-Meier plots showing the association between the genetic ancestry-concordant ARSs identified in high-grade tumors **(A)**, low-grade tumors **(B)**, TANs associated with high-grade tumors **(C)**, and TANs associated with low-grade tumors **(D)** with the BCR. The y-axis shows the probability of free BCR and the x-axis represents time in months. Patients were grouped into three groups: 1) PSI larger than the 75th percentile, 2) PSI smaller than the 25th percentile, and 3) PSI between the 75th and 25th percentiles. The box plots under the Kaplan-Meier plots show the PSI of the indicated ARSs between Black patients and White patients. The x-axis shows the PSI level and the y-axis indicates the self-reported race of the patient. Each dot represents a patient.

Supplementary Figure 6



Supplementary figure 6. Genes undergoing D-ARs, DEs, and D-APAs. **A.** Bar plots showing the number of D-APAs in tumor vs TAN in the indicated comparisons. **B.** Venn diagrams showing the number of overlapping genes that undergo D-ARs, DEs, and D-APAs in the indicated comparisons. **C.** Venn diagrams showing the number of overlapping genes undergoing D-APAs in the indicated comparisons and that were reported to be differential in PCa post-enzalutamide treatment by Caggiano et al. **D.** Bar plots showing the number of genetic ancestry-concordant D-APAs in the indicated comparisons. **E.** Venn diagrams showing the number of overlapping genes that undergo genetic ancestry-concordant ARs, DEs, and APAs in the indicated comparisons.

Supplementary Table 1

All GENCADE Patients

	By race		Overall
	Black, N = 39 [†]	White, N = 39 [†]	N = 78 [†]
Age at consent			
Median (IQR)	62 (54, 66)	63 (58, 67)	62 (56, 66)
Range	48, 71	52, 74	48, 74
Ethnicity			
Hispanic or Latino	0 (0%)	1 (2.6%)	1 (1.3%)
Not Hispanic or Latino	38 (97%)	38 (97%)	76 (97%)
Not reported	1 (2.6%)	0 (0%)	1 (1.3%)
PSA			
Median (IQR)	8 (5, 13)	7 (5, 12)	8 (5, 12)
Range	3, 38	3, 55	3, 55
N missing	1	1	2
Surgical Gleason score			
5 – 6	1 (2.6%)	3 (7.7%)	4 (5.1%)
7 (3+4)	15 (38%)	19 (49%)	34 (44%)
7 (4+3)	15 (38%)	9 (23%)	24 (31%)
8 – 10	8 (21%)	8 (21%)	16 (21%)
Gleason score of tissue used for RNA extraction			
5 – 6	11 (28%)	12 (31%)	23 (29%)
7 (3+4)	17 (44%)	16 (41%)	33 (42%)
7 (4+3)	6 (15%)	2 (5.1%)	8 (10%)
8 – 10	5 (13%)	9 (23%)	14 (18%)
T stage			
T2	19 (49%)	20 (51%)	39 (50%)
T3	18 (46%)	19 (49%)	37 (47%)
Unknown	2 (5.1%)	0 (0%)	2 (2.6%)
N stage			
N0	20 (51%)	21 (54%)	41 (53%)
N1	5 (13%)	2 (5.1%)	7 (9.0%)
Unknown	14 (36%)	16 (41%)	30 (38%)
M stage			
M0	1 (2.6%)	0 (0%)	1 (1.3%)
Unknown	38 (97%)	39 (100%)	77 (99%)
NCCN risk group using surgical Gleason			
Low	0 (0%)	1 (2.6%)	1 (1.3%)
Intermediate	16 (41%)	16 (41%)	32 (41%)
High	23 (59%)	22 (56%)	45 (58%)
Unknown	0 (0%)	0 (0%)	0 (0%)
Procedure type			
Biopsy	2 (5.1%)	4 (10%)	6 (7.7%)
RP	37 (95%)	35 (90%)	72 (92%)
[†] n (%)			

Supplementary Table 2

Patients With Progression Data

	By race		Overall
	Black, N = 37 [†]	White, N = 33 [†]	N = 70 [†]
Age at consent			
Median (IQR)	62 (55, 65)	62 (57, 68)	62 (56, 66)
Range	48, 71	52, 74	48, 74
Ethnicity			
Hispanic or Latino	0 (0%)	0 (0%)	0 (0%)
Not Hispanic or Latino	36 (97%)	33 (100%)	69 (99%)
Not reported	1 (2.7%)	0 (0%)	1 (1.4%)
PSA			
Median (IQR)	7.3 (5.3, 10.1)	6.5 (4.8, 10.4)	6.7 (5.0, 10.3)
Range	2.8, 37.7	3.0, 30.0	2.8, 37.7
N missing	1	1	2
Surgical Gleason score			
5 - 6	1 (2.7%)	1 (3.0%)	2 (2.9%)
7 (3+4)	15 (41%)	16 (48%)	31 (44%)
7 (4+3)	13 (35%)	9 (27%)	22 (31%)
8 - 10	8 (22%)	7 (21%)	15 (21%)
Gleason score of tissue used for RNA extraction			
5 - 6	10 (27%)	10 (30%)	20 (29%)
7 (3+4)	17 (46%)	13 (39%)	30 (43%)
7 (4+3)	5 (14%)	2 (6.1%)	7 (10%)
8 - 10	5 (14%)	8 (24%)	13 (19%)
T stage			
T2	18 (49%)	15 (45%)	33 (47%)
T3	18 (49%)	18 (55%)	36 (51%)
Unknown	1 (2.7%)	0 (0%)	1 (1.4%)
N stage			
N0	18 (49%)	20 (61%)	38 (54%)
N1	5 (14%)	2 (6.1%)	7 (10%)
Unknown	14 (38%)	11 (33%)	25 (36%)
M stage			
M0	1 (2.7%)	0 (0%)	1 (1.4%)
Unknown	36 (97%)	33 (100%)	69 (99%)
NCCN risk group using surgical Gleason			
Low	0 (0%)	1 (3.0%)	1 (1.4%)
Intermediate	15 (41%)	12 (36%)	27 (39%)
High	22 (59%)	20 (61%)	42 (60%)
Unknown	0 (0%)	0 (0%)	0 (0%)
Procedure type			
Biopsy	0 (0%)	0 (0%)	0 (0%)
RP	37 (100%)	33 (100%)	70 (100%)
[†] n (%)			

Supplementary Table 3

Cox model for recurrence

Characteristic	HR ¹	95% CI ¹	p-value
Race			
Black	—	—	
White	0.44	0.18, 1.06	0.066
Gleason score			
<=3+4	—	—	
>=4+3	1.38	0.55, 3.45	0.5
log(PSA)	3.82	1.71, 8.53	0.001
T stage			
T2	—	—	
T3	3.95	1.46, 10.7	0.007
Unknown	1.74	0.16, 19.2	0.6

¹ HR = Hazard Ratio, CI = Confidence Interval

Supplementary Table 8. List of genes undergoing ARSs in PCa between Black and White patients and functioning in tumorigenic pathways.

Genes	Oncogenic Gene Sets
NPHP1	GLI1_UP
NDRG4-TPD52-E2F8-ALDH3A1-IL1R1-CALML4-FCHO1-DCAF8-DMBT1-ACTN3-EZH2-APC2-HES6-PTGS1-TK1-FMO3-RUNX1T1-HSPBP1-NUP43-MCM10-PSME3-PDE4DIP-USP10	E2F1_UP
RPS6KA3-E2F8-SPAG1-CARF-IL1R1-EPB41L2-GK-GULP1-AGL-IFI44L-EZH2-P2RY6-PDLIM3-LPP-IFI27-CBFA2T3-CADM1-CHN1-WIPF1	EGFR_UP
IL1R1-RNF138-NMRK1-GULP1-SLC7A2-SERPINA1-AGL-IFI44L-SS18-BNIP3L-NOL8-CAST-CNOT8-SERHL2-METRN-TPK1-IRF7-NDRG1-ST6GALNAC2-LMO3-IFI27-WIPF1	ERBB2_UP
MIPOL1-IRF5-AURKA-CCNJ-LYST-IRF3-GRIN1-E2F8-ATL2-IL1R1-SPDL1-XIAP-DCAF8-UIMC1-PITX2-PIGT-RUNX1T1-EMP1-MCM10-CBFA2T3-WIPF1-IER2	GCNP_SHH_UP_EARLY
AURKA-TTC23-CHP1-E2F8-PARP8-GRIN2C-SLC29A1-NRP2-TK1-CDC25C-B3GAT3-YWHAE-MCM10-MAP3K2-EYA1-AGTRAP-CD6	GCNP_SHH_UP_LATE
DUSP14-GRIN1-PCBP4-PISD-TROAP-ASMT-CNKS2-SNTB1-ADCY10-CACNA1C-COBLL1-GRIN2C-KCNC4-PRG2-ANK1-ETV2-CDH4-PTGS1-ADH6-LGALS3BP-IRF7-CLDN14-IFI27-GDPD5-FARP2	RAPA_EARLY_UP
IL6	HINATA_NFKB_IMMUN_INF
NEK3-CGREF1-APOC1-KDM5C-GLB1-IL1R1-TROAP-ATF7-DIO2-TARBP2-ARCN1-DTNA-CYP24A1-VCAM1-GRIA1-MAD1L1-IFITM1-EYA1	CYCLIN_D1_KE_
ITGB1BP1-NEK3-CGREF1-ZNF133-TPD52-KDM5C-GLB1-MOK-ATF7-HRH1-TARBP2-ARCN1-EZH2-ZNF266-NCSTN-TK2-CYP24A1-MAD1L1-IFITM1	CYCLIN_D1_UP
BRD8-PHLDB1-SCHIP1-FUT10-ADAMTSL4-STX16-APBB3-AMT-UBE2N-BDKRB1	CSR_EARLY_UP
FOXO1-SNTB1-TRERF1-BIRC5-TMEM130-EZH2-KCNC4-GLT8D2-TAGLN3-MT1G-CMC2-DDX60L-TCEAL7	CSR_LATE_UP
NDRG4-IL1R1-DAGLB-CDPF1-ST6GALNAC6-BCS1L-ADHFE1-MYO1G-FMO3-SLC18A1-SLC44A1-TGIF1-MLXIPL-CAP2-PON1-RGS19-RASSF1	AKT_UP_MTOR_DN
NDRG4-GPX2-LDHC-IL1R1-DAGLB-CDPF1-ST6GALNAC6-FUT10-BCS1L-P2RX5-ADHFE1-PDLIM3-MYO1G-KRT15-FMO3-SLC18A1-SLC44A1-TGIF1-MLXIPL-CAP2-PON1-RGS19-RASSF1	AKT_UP
POLR3G-HHAT-CD1E-TSNAXIP1-GPX2-LDHC-CARF-CALML4-GK-SLC43A1-IKZF2-OSMR-DNMT3B-KLHL7-TMEM135-ISOC2-SLC3A2-ZNF180-PDLIM3-KRT15-VNN2-SLC44A1-CBFA2T3-CSAD-IFITM1-BBS1	MTOR_UP
APOC1-UGP2-TTL3-PISD-TROAP-ATP1A3-CACNA1C-RDH11-ZNF646-AGL-TDRD3-NFASC-SLC38A6-DLEC1-POU2F3-RUNX1T1-GRIA1-CBFA2T3-CAMK2B-LY6E	PIGF_UP
IL6-IRF5-TCL1A-UGP2-MTSS1-SLC7A2-RDH11-BIRC5-ETV2-CACNB1-XRCC4-MBD4-EXO1-IL32-AKAP5-LY6E	VEGF_A_UP
RDH5	BCAT_GDS748_DN
SLC3A2-UBE2N	BCAT_GDS748_UP
NDRG4-NBPF10-SORL1-C4orf36-PPP1R1A-SLC3A2-RDH5-CYP24A1-RASAL2-ST6GALNAC2-UBE2N	BCAT
NXT2-TPD52-FOXO1-IL1R1-PISD-COBLL1-SNCAIP-OSMR-EZH2-ADAMTSL4-DLEC1-ARHGAP22-GPR63-PDLIM3-TK1-HAPLN1-VCAM1-ST6GALNAC2-GSG1-COMP-CLDN14-IL32-PDE4DIP	ATF2_S_UP
TPD52-CNTN5-FOXO1-IL1R1-PISD-SNCAIP-ARHGAP22-GPR63-SHOX2-STRA6-PDLIM3-TK1-HAPLN1-CDH13-KCNA2-RPS6KB1-VCAM1-ST6GALNAC2-COMP-IL32-PDE4DIP-CD3D	ATF2_UP

UBXN11-IL6-DNASE1L3-CLN3-DIO2-ADAM12-ST6GALNAC6-SLC7A2-GRIN2C-MAPKBP1-APC2-PPP1R1A-PTPRO-SLC1A6-NSMF-KCNA2-GRM8-LGALS3BP-TPK1-IRF7-PMF1-SEMA5B-CEACAM1-MAP3K2-CD44	WNT_UP
BEST1-NDRG4-CRHR2-NLGN3-XIAP-ADCY10-GRIK1-GDNF-KCNC4-BCL2L11-CLIC5-CRHR1-STAG3-GRM8-CYP24A1-BDKRB1-CLDN14-IFI27-CYP4F3-PSG5-HHLA2-AKAP5	ATM_DN
BEST1-LYST-APOC1-NCALD-RASAL1-LZTS3-IL1R1-SLC4A10-CLEC4M-CHST8-SNTB1-FGF22-RFPL2-ADAM12-ST3GAL5-TDRD3-P2RY6-BCL2L11-SCNN1A-TAGLN3-CDH4-NRP2-MT1G-IL1RN-KRT15-HAPLN1-CDH13-ITGAL-RFX2-NTRK3-IFI27-PPARG-TP73-PPARD-EYA1-PKD2L1	P53_DN
ECEL1-RREB1-NOL4-IDUA-KLK11-KCNC4-P2RY6-KLK7-STAG3-TNC-FOSB-KCNA2-RFX2	RELA_DN
NBPF10-SORL1-RASAL2	BCAT_BILD_ET_AL_DN
NDRG4-C4orf36-CYP24A1-ST6GALNAC2	BCAT_BILD_ET_AL_UP
IL6-GIPR-SAC3D1-TMPRSS6-ZNF646-BCO2-CASP14-HOXC4-TMEM106C-SLC4A3-PPARD-CDC20B	E2F3_UP
IL6-PMM2-CGREF1-SPOCD1-IL1R1-SAC3D1-CALML4-PPM1N-C1orf159-P2RX5-PLK1-ISOC2-ADHFE1-ABCC4-BCO2-HOXC4-TDRD10-PBX4-PPARD	MYC_UP
ACY3-IFITM10-NAALADL1-E2F8-FAM153A-LPO-C1orf159-MORN3-EZH2-APC2-SLC35F4-ST8SIA2-CD70-SULT4A1-TMEM106C-SLC4A9-MLXIPL-PDZD7-CSAD-TMOD1-LEKR1	SRC_UP
PLD3-ABI3BP-STMN4-ESR1-DIO2-KLK11-IFI44L-GDNF-P2RX5-SLC1A6-ELN-LGALS3BP-CELF4-KCNAB1	SNF5_DN
NDRG4-PCMTD1-RREB1-METTL17-KLHDC4-RABGGTA-RNF138-CKMT1A-COPE-PHLDB1-RCHY1-SAT2-ELN-HSPBP1-FOSB-NDRG1-TMEM116-FAM189B-MS4A6A-IFITM1-PDE4DIP	CAMP_UP
UBE3B-RPS6KA3-IL1R1-EPB41L2-NMRK1-SERPINA1-SORL1-IFI44L-BNIP3L-DTNA-BCL2L11-EPS8L1-PDLIM3-SERHL2-TK1-LGALS3BP-IRF7-NUP43-IFI27-CAP2-CBFA2T3-CHN1-WIPF1-IFITM1	LTE2_UP
MOCS2-MEF2C-GPX2-ALDH3A1-SPAG1-NMRK1-AGL-SORL1-IFI44L-NOL8-ABCC4-IRF7-SGCE-ST6GALNAC2-IFI27-PPARG-FHL1-CHN1-WIPF1-IFITM1	MEK_UP
EPB41L2-ZNF331-GULP1-SLC7A2-KLHL7-CAST-ABCC4-SGCE-CBFA2T3-PPARG-CD44	RAF_UP
NXT2-RREB1-FCHO1-RGS6-FAM153A-IKZF2-RFPL2-NCR1-GRIN2C-TPSD1-PTPRO-LRRC36-RDH5-CLDN14-USP46	PRC1_BMI_UP
NDRG4-MTSS1-ZHX3-RFPL2-TNIP1-PLK1-ORC1-SEMA6D-CDHR2-RDH5-MICALL2-GSG1-MCM10-RASSF1-USP46-PKD2L1	PRC2_EED_UP
POLR3G-PTPRB-SLC14A1-ETV1-CPEB1-SLC7A2-MEFV-EZH2-KLK7-RDH5-CD70-CDH13-HCFC1R1-KCNA2-PSRC1-NUP43-MCM10-ELP6-FOLR3	PRC2_EZH2_UP
ALDH3A1-CALML4-FCHO1-SCHIP1-GRIN2C-ORC1-PTPRO-ANK1-IPCEF1-IL1RN-KRT15-CD70-RFX2-CLDN14-CBFA2T3-ELP6-FOLR3-USP46-PKD2L1	PRC2_SUZ12_UP
MDM2-KDM5C-TTLL3-IDUA-ABL2-ADAM12-RIMS1-GRIN2C-PLK1-BCL2L11-RAB40A-KLK7-NRP2-ELN-HOXC4-WIPF1-TULP1-SLC34A1	JNK_DN
MYBPC1-KLK15-HHAT-ASMT-SLC43A1-SPHK2-FGF22-C1orf159-SLC3A1-POU2F3-PDLIM3-TNC-CDH13-GREB1L-KCNA2-THPO-CLDN14-GPR35-CD3D-ICAM4	BRCA1_DN
ABI3BP-TTLL3-NLGN3-FAM153A-SLC43A1-ABLIM2-NCR1-SLC3A1-KCNC4-PTGS1-STAG3-IL1RN-KCNK2-CYP4F3-NPPA-PCDHA5-TULP1-TERT-PKD2L1	CTIP_DN
APOC1-CYGB-NECAB2-ABI3BP-TMPRSS5-SLC14A1-LPO-NXNL2-TMEM135-FBP1-GAS2-RDH5-RFX2-SERINC4-CD44	PKCA_DN

MYBPC1-CD1E-SPDL1-NOL4-SLC14A1-ABLIM2-TMPRSS6-MEFV-NFASC-DGKB-GLT8D2-EMP3-RPGRIP1L-KRT15-LILRA6-SGCE-VCAM1-ST6GALNAC2-ARHGAP33-EMP1-CLDN14-ERN2-WIPF1-IL32-PCDHA5-FARP2-TULP1-FOLR3-TERT-AKAP5-CD3D	PTEN_DN
BEST1-TCL1A-MATN4-ADARB2-TTLL3-GIPR-FGF22-PHLDB1-SERPINA1-NFASC-NOL8-CLIC5-SHOX2-STAG3-IPCEF1-CD70-GRIA1	DCA_UP
PACRGL-PPP1R1A-HES6-SCNN1A-ZFPM2-MOCS1-LPP-SLC18A1-NARF-RRP8-NDRG1-TMEM106C-MAD1L1	ESC_J1_UP_EARLY
E2F8-GPX2-CALML4-MTTP-ACTN3-SULT4A1-SGCE-GYG1-TDGF1-SLC4A3	ESC_J1_UP_LATE
E2F8-GPX2-CALML4-SLC8A3-ZFP1-MTTP-KLK11-PITX2-ACTN3-ZBTB32-ADAMTSL4-HES6-SLC5A11-FBP1-PDLIM3-TNC-GRM8-NARF-RASAL2-SULT4A1-SGCE-NDRG1-MBD4-CLDND1-AQP2-GYG1-EMP1-WIPF1-FAM189B-CD44-CAAP1-TERT	ESC_V6
IL6-GPX2-CHST8-ETV1-DIO2-ADAM12-IFI44L-VNN2-LILRA6-GSG1-SCN1A-IFI27-PDZD7-USP46	ALK_DN
RREB1-IL1R1-ADAM12-P2RX5-SCNN1A-NRP2-HAPLN1-GAS2-CDH13-LMO3-IFI27-TMOD1-IFITM1-LY6E	BMI1_DN_MEL18_DN
RREB1-IL1R1-ETV1-ADAM12-IFI44L-SLC29A1-P2RX5-KCNC4-SCNN1A-NRP2-HAPLN1-GAS2-CDH13-LMO3-IFI27-PSG5-TMOD1-IFITM1-LY6E	BMI1_DN
RREB1-IL1R1-ATXN3-DIO2-ADAM12-GULP1-SNCAIP-SLC29A1-P2RX5-SCNN1A-NRP2-HAPLN1-GAS2-CDH13-LMO3-IFI27-TMOD1-IFITM1-LY6E	MEL18_DN
SLC17A9-GRIN1-CRHR2-CHST8-SLC45A2-DIO2-TMPRSS6-MEFV-ZBBX-GDNF-SCNN1A-CDHR2-RDH5-VNN2-LMO3-RANBP17-MAP3K2-HHLA2-FARP2-PKD2L1	NOTCH_DN
TPD52-SH3YL1-PARP8-TNIP1-APPBP2	EIF4E_DN
PMM2-CNTN4-SNTB1-FBXO4-GEMIN6-ZNF576-ISOC2-NDRG1	EIF4E_UP
UBXN11-DUSP14-IRF5-MEF2C-WDR31-SH3YL1-CKMT1A-MPP6-OSMR-NXNL2-SLC25A25-TCP11-STRA6-PPP1R42-ST3GAL3-FMO3-RDH5-SEMA5B-SERINC4-TMOD1-CD44-EYA1-CAMK2B	CRX_DN
UBXN11-MEF2C-RREB1-MLF1-CKMT1A-BBS9-NXNL2-SLC25A25-BCL2L11-TCP11-EPS8L1-PPP1R42-TNC-METRN-SGCE-RFX2-SERINC4-EYA1-CAMK2B	CRX_NRL_DN
UBXN11-DUSP14-SLAMF9-MEF2C-IFITM10-WDR31-EBPL-RREB1-MLF1-CKMT1A-SLC8A3-MPP6-BBS9-CALU-NXNL2-SLC25A25-APC2-BCL2L11-TCP11-EPS8L1-PPP1R42-ST3GAL3-TNC-METRN-SGCE-RFX2-SERINC4-EYA1-CAMK2B	NRL_DN
DUSP14-MDM2-GAB3-CDIPT-ADAM12-FBP1-TNC-ST8SIA2-GRM8-NDRG1-FHL1-S1PR5-IER2-CD44	RB_DN
PMM2-POLR3G-UBE3B-E2F8-RDH11-MOGS-LGALS3BP-COX6B2-TRPM1	RB_P107_DN
AURKA-IFITM10-EBPL-RAD51D-BIRC5-RAP2C-SLC29A1-ORC1-KLK7-ELOF1-TK1-CSDE1-SEMA5B	RB_P130_DN
DIO2-GRIN2C-ATP13A4-HAPLN1-HEPH	CAHOY_ASTROCYTIC
NOX4-CASP12-EMP3-CAPS2-PSRC1-C11orf88	CAHOY_ASTROGLIAL
MEF2C-CKMT1A-KIAA0319-SLC35F4-METRN-PPFIA2-CELF4-GDA-MLIP-CAMK2B	CAHOY_NEURONAL
GAB3-PHLDB1-FBP1-WIPF1	CAHOY_OLIGODENDROCYTIC
E2F8-SLC43A1-ESPL1-COBL1-SORL1-SLC29A1-KLHL7-PLK1-ORC1-CEACAM8-DOCK9-ISOC2-PTPRO-TK1-ITGAL-RASAL2-EXO1-EMP1-MCM10-CD300A-MS4A6A	RPS14_DN
PMM2-POLR3G-NOX4-GPX2-CALML4-ADAM12-TMPRSS6-MPP6-ZBBX-ZBTB32-GDNF-KCNC4-RAB40A-SEMA6D-ETV2-DNAI2-PAK6-GPR35-AKAP5-EYA1	IL15_UP
PMM2-POLR3G-HTR4-TTC23-GPX2-CALML4-CNKS2-TMPRSS6-SCHIP1-MPP6-ZBTB32-DLEC1-SEMA6D-TAGLN3-WDR62-LMO3-KLHDC8A-TRPM1-PAK6-SLC34A1-EYA1	IL2_UP

HTR4-NDRG4-CYP3A5-GPX2-GIPR-C1orf159-KLK11-CASC1-GDNF-KCNC4-ARHGAP22-SCNN1A-PTPRO-RDH5-FOSB-ST6GALNAC2-FUZ-HAL-KLHDC8A-PCDHA5-CD6	IL21_UP
MAGEA8-PISD-SAC3D1-CALML4-SULT1A1-ASMT-IDUA-MOGS-APC2-KLK7-SLC3A2-TGIF1	PDGF_ERK_DN
TCL1A-NDRG4-GK-TPSD1-CLDND1	PDGF_UP
IRF5-CD1E-YIPF5-CARF-NDST1-PPP2R2B-HRH1-PHLDB1-SCHIP1-MAPKBP1-PRG2-ANK1-HAPLN1-NFATC4-CYP24A1-THPO-LMCD1-MAP3K19-PPARD	TGFB_UP
RHBDL1	YAP1_DN
MOCS2-CDIPT-GTPBP3-NMRK1	YAP1_UP
COPS7A-MAP3K19-PSME3	SIRNA_EIF4GI_DN
CPNE1-CORO1B-CSDE1	SIRNA_EIF4GI_UP
E2F8-EPB41L2-BFAR-UBE2E3-SCHIP1-SLC7A2-SORL1-SLC29A1-KLHL7-ORC1-MT1G-IPCEF1-GPATCH2L-TPK1-THEMIS2-TMEM106C-MCM10-KCTD15-SLITRK5-CD300A-GPR18-MS4A6A	HOXA9_DN
SIDT2-DPH2-CCNJ-NXT2-PROK2-TRIT1-SLC43A1-CCDC125-PCCB-HES6-CEP57-CAST-GAS2-ANKLE1-DNAAF3-CYP4F3-HHLA2	STK33_DN
SIDT2-SLAIN1-NXT2-SIRPB2-PROK2-CKMT1A-SLC43A1-MOGS-PCCB-HES6-ANKLE1-GDA-CYP4F3-HHLA2	STK33_NOMO_DN
WDR20-IL1R1-MTSS1-PTPRO-EMP1-TGIF1-CADM1	STK33_NOMO_UP
FAM186B-DPH2-TPD52-PROK2-TRIT1-SNTB1-SLC43A1-CCDC125-PCCB-SORL1-CAST-FOXP2-GAS2-ANKLE1-DNAAF3-CYP4F3-GPR84-SLITRK5-CD3D	STK33_SKM_DN
TLR10-RHOC-ETV1-CMTM1-NLRC4-SLC38A6-EMP3-PTPRO-TK2	STK33_SKM_UP
TLR10-WDR20-RHOC-MTSS1-CMTM1-NLRC4-SLC38A6-PTPRO-EMP1-TGIF1	STK33_UP
IL6-MEF2C-ECEL1-TCL1A-CGREF1-PDLIM2-NAALADL1-CNTN5-E2F8-RASAL1-RREB1-FAM153B-TTLL3-KLK14-WASF1-FCHO1-RGS6-NOL4-FAM153A-CSF3-IDUA-FBXO4-ETV1-FGF22-NCR1-GULP1-KLK11-RIMS1-NOX5-BBS9-SORL1-GP6-IFI44L-SLC3A1-NPHP1-APC2-GDNF-TMEM135-PRG2-APBB3-EMP3-KLK7-TAGLN3-POU2F3-ETV2-CDH4-FBP1-ASTN1-SERHL2-NRP2-CDHR2-KRT15-NFATC4-TNC-PTPRR-RDH5-ST8SIA2-SLC18A1-PPFIA2-HEPH-KCNA2-GRM8-LILRA6-LGALS3BP-TPK1-CLEC4A-NTRK3-BDKRB1-LMO3-GSG1-TTYH1-HAL-KLHDC8A-GRIA1-EMP1-MLXIPL-IFI27-ATP1B4-CEACAM1-HDAC7-TSGA10-GPR35-CD300A-TMOD1-SNAP91-KLK12-GPR18-MKRN3-TERT-IFITM1-CAMK2B-KCNJ13-CD6	KRAS
DUSP14-ITGB1BP1-GPX2-ALDH3A1-IL1R1-SPDL1-FCHO1-MPHOSPH9-ST3GAL5-SCHIP1-BIRC5-DNMT3B-SLC38A6-P2RX5-EMP3-PTK2-NF2-IL1RN-OSBPL3-APPBP2-RPS6KB1-PSRC1-MAP3K2-SMARCA2-UXS1-USP10-USP46-BBS1	TBK1
RNF212-ZC3H12D-GPX2-ALDH3A1-KIAA0319-CBWD6-PHLDB1-SF1-ORC1-P2RY6-BCL2L11-SLC5A11-ADH6-GAS2-ST8SIA2-PPFIA2-USP6-UBE2N-MCM10-CYP4F3-TP73-TERT	NFE2L2
PDLIM2-ASAP1-SCHIP1-BIRC5-TK1-NDRG1	CORDENONSI_YAP_CONSERVED_SIGNATURE
NPIPB4-MATN4-CARF-MAGEA8-FBXW12-CNKS2-FBXO4-IKZF2-GRIK1-ADAMTSL4-AMT-PTPRO-METRN-SGCE-CSAD	JAK2_DN
MEF2C-CLEC2D-SLC17A9-MPP6-PITX2-SORL1-TMEM135-EMP3-STRA6-ZFPM2-HCFC1R1-EMP1-FHL1-ERN2-TMOD1	LEF1_UP

Supplementary Table 9. List of selected genes undergoing genetic ancestry-related ARSs and DE whose role in cancer biology well-known.

Analysis	Highlighted genes	References
ARS	<i>FGFR2, FGFR3, H6PD, MDM2, RAD51D, CDK7, VEGFA, and XRCC4</i>	(1-10)
DE	<i>FGF10, FAS, SPHK2, CAMK2B, ERG, KLK11, NRG4, SEMA3E, ERAP2, and ABAT</i>	(11-21)

References

1. Wang C, Liu Z, Ke Y, Wang F. Intrinsic FGFR2 and Ectopic FGFR1 Signaling in the Prostate and Prostate Cancer. *Front Genet.* 2019;10:12.
2. Pandey P, Seshacharyulu P, Das S, Rachagani S, Ponnusamy MP, Yan Y, et al. Impaired expression of protein phosphatase 2A subunits enhances metastatic potential of human prostate cancer cells through activation of AKT pathway. *Br J Cancer.* 2013;108(12):2590-600.
3. Leite KR, Franco MF, Srougi M, Nesrallah LJ, Nesrallah A, Bevilacqua RG, et al. Abnormal expression of MDM2 in prostate carcinoma. *Mod Pathol.* 2001;14(5):428-36.
4. Xiao L, Parolia A, Qiao Y, Bawa P, Eyunni S, Mannan R, et al. Targeting SWI/SNF ATPases in enhancer-addicted prostate cancer. *Nature.* 2022;601(7893):434-9.
5. Kovalenko PL, Basson MD. Schlafen 12 expression modulates prostate cancer cell differentiation. *J Surg Res.* 2014;190(1):177-84.
6. Tsachaki M, Mladenovic N, Stamberгова H, Birk J, Odermatt A. Hexose-6-phosphate dehydrogenase controls cancer cell proliferation and migration through pleiotropic effects on the unfolded-protein response, calcium homeostasis, and redox balance. *FASEB J.* 2018;32(5):2690-705.
7. Suszynska M, Ratajska M, Kozłowski P. BRIP1, RAD51C, and RAD51D mutations are associated with high susceptibility to ovarian cancer: mutation prevalence and precise risk estimates based on a pooled analysis of ~30,000 cases. *J Ovarian Res.* 2020;13(1):50.
8. Sava GP, Fan H, Coombes RC, Buluwela L, Ali S. CDK7 inhibitors as anticancer drugs. *Cancer Metastasis Rev.* 2020;39(3):805-23.
9. Parris JLD, Barnoud T, Leu JJ, Leung JC, Ma W, Kirven NA, et al. HSP70 inhibition blocks adaptive resistance and synergizes with MEK inhibition for the treatment of NRAS-mutant melanoma. *Cancer Res Commun.* 2021;1(1):17-29.
10. Yu Y, Sun Y, Li Z, Li J, Tian D. Systematic analysis identifies XRCC4 as a potential immunological and prognostic biomarker associated with pan-cancer. *BMC Bioinformatics.* 2023;24(1):44.
11. Clayton NS, Grose RP. Emerging Roles of Fibroblast Growth Factor 10 in Cancer. *Front Genet.* 2018;9:499.
12. Symes JC, Kurin M, Fleshner NE, Medin JA. Fas-mediated killing of primary prostate cancer cells is increased by mitoxantrone and docetaxel. *Mol Cancer Ther.* 2008;7(9):3018-28.
13. Gestaut MM, Antoon JW, Burow ME, Beckman BS. Inhibition of sphingosine kinase-2 ablates androgen resistant prostate cancer proliferation and survival. *Pharmacol Rep.* 2014;66(1):174-8.

14. Dadwal UC, Chang ES, Sankar U. Androgen Receptor-CaMKK2 Axis in Prostate Cancer and Bone Microenvironment. *Front Endocrinol (Lausanne)*. 2018;9:335.
15. Adamo P, Ladomery MR. The oncogene ERG: a key factor in prostate cancer. *Oncogene*. 2016;35(4):403-14.
16. Fuhrman-Luck RA, Loessner D, Clements JA. Kallikrein-Related Peptidases in Prostate Cancer: From Molecular Function to Clinical Application. *EJIFCC*. 2014;25(3):269-81.
17. Hayes NV, Blackburn E, Smart LV, Boyle MM, Russell GA, Frost TM, et al. Identification and characterization of novel spliced variants of neuregulin 4 in prostate cancer. *Clin Cancer Res*. 2007;13(11):3147-55.
18. Blanc V, Nariculam J, Munson P, Freeman A, Klocker H, Masters J, et al. A role for class 3 semaphorins in prostate cancer. *Prostate*. 2011;71(6):649-58.
19. Yang Z, Tian H, Bie F, Xu J, Zhou Z, Yang J, et al. ERAP2 Is Associated With Immune Infiltration and Predicts Favorable Prognosis in SqCLC. *Front Immunol*. 2021;12:788985.
20. Luchino J, Hocine M, Amoureux MC, Gibert B, Bernet A, Royet A, et al. Semaphorin 3E suppresses tumor cell death triggered by the plexin D1 dependence receptor in metastatic breast cancers. *Cancer Cell*. 2013;24(5):673-85.
21. Chen X, Cao Q, Liao R, Wu X, Xun S, Huang J, et al. Loss of ABAT-Mediated GABAergic System Promotes Basal-Like Breast Cancer Progression by Activating Ca(2+)-NFAT1 Axis. *Theranostics*. 2019;9(1):34-47.

Supplementary Table 10. List of genes from Wang et al., TCGA, and GENCADE studies that undergo differential alternative RNA splicing between Black vs White patients in PCa

Studies	Overlapping genes or events
Wang et al. and GENCADE	NUP62, RSU1, PDHA1, TNIP1, CCDC14, SYNE1, NCOR2, TOP1MT, EDEM2, CRELD2, ABCD3, DCUN1D4, SCAMP3, RFX5, PRDM8, NUB1, AHI1, SS18, HSD3B7, ULK3, LEPR, BTN3A1, MACF1, FAM107B, CAST, CEP63, CYFIP2, PPT1, DUSP12, APOL4, TNFSF10, PLEKHA5, NCAPG2, HCFC2, SLC35C2, GSS, GRK6, ZNF562, FBXW11, EVL, NMT2, ADPGK, UQCRC1, LPXN, PTPN13, MBD6, IDH3B, DAGLA, DDX5, DPYSL4, MBTD1, DMXL1, MED8, CAP2, TGM2, MICAL2, CD44, INTS8, EFTUD2, ANK3, DBNL, ABCA10, DENND3, C12orf4, ZNF330, OVGP1, BAP1, NFE2L1, RANBP10, SLC37A3, HBS1L, CTNND1, FNBP1, ATM, HERC3, UTY, ARHGAP8, TACC1, PLA1A, DNMBP, SLC4A4, ABCA1, CHFR, RAD17, SSX2IP, STT3A, AP3M2, LHPP, ILVBL, PHF20, DST, MYLIP, FES, SPTLC1, GRAMD1C, ADAMTSL1, SRM, MCC, ENY2, WDR13, SCARB2, CCDC88C, NCAPH2, ANXA11, CDH11, ABLIM3, GBP3, MAPK3, MAP3K4, PRKACB, IL16, WDR91, PIK3IP1, TMEM39B, MYO9A, SV2B, FUBP1, TLL1, NFIA, PTK2B, DIP2A, SCMH1, POGZ, PARVB, USP36, DDAH1, ABHD14B, EFNA1, ATP10D, ABI3BP, RPUSD4, IDH2, POLL, RAB24, PFKFB3, SYNE2, ZFP28, PIGK, PHF8, RAP1GAP, EPS15, NPHP4, ST6GALNAC1, FNDC3A, BTN3A2, NOL11, LRSAM1, ABHD11, STX5, UPF2, TAF1C, UBE4B, LARP7, GRB10, ARHGAP30, NUBP2, PRLR, PAAF1, SLC35A2, MAPK10, HACL1
TCGA-PRAD, High-grade and GENCADE	ULK3 AD 14.2, NCALD ES 6, FAM118A AP 7, CMC2 ES 8:9, TSACC AP 1, FAM118A AP 2.1, ETFA ES 2:3, IMPDH1 ES 2:3.2:4.2, TLE6 AT 17, TLE6 AT 3.2, WIZ AP 6, TMC5 AP 2, HSFY2 ES 2:3, TMC5 AP 1.1, TRIM7 AP 1, CNTNAP3B ES 11:12
TCGA-PRAD, Low-grade and GENCADE	NDUFS5 AD 1.2, NCALD ES 6, PSMG4 RI 5.5, ULK3 AD 14.2, SERHL2 ES 8.1:8.2:9, C14orf2 ES 5:6, NEK3 AA 12.1, UBE2I AD 4.3, XRCC4 AA 8.1, RSU1 AD 1.2:1.3, RPS9 AD 1.3, BANF1 AD 2.2, CAST ES 16