

## Additional File 1: Supplementary Tables

### A unique transcriptomic landscape defines African-specific grade group 1 prostate cancer

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#### Supplementary Table S1: Participant clinicopathological characteristics post-filtering for this study (n=107).

<sup>a</sup>Country of origin. <sup>b</sup>Age at diagnosis. <sup>c</sup>PSA at diagnosis. PSA measurement unavailable for one African PCa and six European PCa patients. <sup>d</sup>Grade Group from diagnostic biopsies for African patients and radical prostatectomy for European patients. ASAP = atypical small acinar proliferation; BPH = benign prostatic hyperplasia; IQR = interquartile range; NA = not available; PCa = prostate cancer; PSA = prostate-specific antigen.

Characteristic	African		European
	Non-PCa n = 26	PCa n = 34	PCa n = 47
<b>Country<sup>a</sup>, n (%)</b>			
South Africa	26 (100)	34 (100)	0 (0)
Australia	0 (0)	0 (0)	48 (100)
<b>Age in years, median (IQR)<sup>b</sup></b>	64.5 (58.2-66.8)	64.0 (61.0-67.8)	56.9 (53.0-61.3)
<b>PSA ng/mL, median (IQR)<sup>c</sup></b>	14.4 (7.6-18.8)	11.8 (8.0-36.6)	4.3 (3.4-5.7)
<b>BPH, n (%)</b>	19 (73.1)	1 (2.9)	NA
<b>Prostatitis, n (%)</b>	13 (50)	8 (23.5)	NA
<b>ASAP, n (%)</b>	0 (0)	4 (11.8)	NA
<b>Grade Group<sup>d</sup>, n (%)</b>			
1	NA	30 (100)	47 (100)
NA	26 (100)	0 (0)	0 (0)

**Supplementary Table S2: Clinical characteristics stratified by ancestry and PSA group (n = 107).** PSA measurements unavailable for one African and six European patients (assigned to PSA-unknown groups). ASAP = atypical small acinar proliferation; BPH = benign prostatic hyperplasia; IQR = interquartile range; NA = not available; PCa = prostate cancer; PSA = prostate-specific antigen.

Characteristic	African			European		
	PSA-low n = 30	PSA-high n = 29	PSA-unknown n = 1	PSA-low n = 21	PSA-high n = 20	PSA-unknown n = 6
<b>Age in years, median (IQR)</b>	63.0 (58.2-65.0)	66.0 (61.0-72.0)	80 (NA)	55.4 (51.2-57.6)	58.2 (55.3-62.6)	62.3 (54.6-68.3)
<b>PSA ng/mL, median (IQR)</b>	7.8 (6.1-10.2)	25.7 (17.3-74.0)	NA	3.4 (3.0-3.8)	5.9 (5.0-9.4)	NA
<b>BPH, n (%)</b>	9 (30.0)	11 (37.9)	0 (100)	NA	NA	NA
<b>Prostatitis, n (%)</b>	9 (30.0)	11 (37.9)	1 (100)	NA	NA	NA
<b>ASAP, n (%)</b>	3 (10.0)	1 (3.4)	0 (100)	NA	NA	NA
<b>Grade Group, n (%)</b>						
1	15 (50.0)	14 (48.3)	1 (100)	21 (100)	20 (100)	6 (100)
NA	15 (50.0)	15 (51.7)	0 (0)	0 (0)	0 (0)	0 (0)

**Table S3: Top 20 leading-edge genes for key differentially enriched pathways between African (n = 34) and European (n = 47) prostate tumours.** Leading-edge genes represent the genes driving the enrichment signal and are ordered by their position in the ranked gene list. Pathways are ordered by adjusted *p*-value. NES = normalised enrichment score; padj = adjusted *p*-value.

Leading Edge Genes (Top 20 per Pathway)																			
<b>TNFA SIGNALING VIA NFKB</b> NES: -3.13   padj: 2.6e-35					<b>OXIDATIVE PHOSPHORYLATION</b> NES: -2.67   padj: 3e-19					<b>HYPOXIA</b> NES: -2.54   padj: 7.2e-16					<b>MTORC1 SIGNALING</b> NES: -2.14   padj: 6.5e-09				
FOSB	IL6	FOS	NR4A1	ATF3	PDK4	UQCRCQ	ATP5ME	NDUFA2	NDUFS3	IL6	FOS	ATF3	DUSP1	CCN1	SLC2A3	BTG2	LDLR	BHLHE40	CXCR4
DUSP1	SOCS3	EGR1	CCN1	AREG	ATP5MF	NDUFB6	NDUFA1	NDUFB1	ATP5PD	ZFP36	JUN	SLC2A3	CCN2	ANGPTL4	NAMPT	PPP1R15A	NFIL3	RDH11	PNP
NR4A2	JUNB	GADD45B	ZFP36	NR4A3	NDUFB8	MRPL34	NDUFS7	PDHB	NDUFC1	SERPINE1	VEGFA	TIPARP	PLAUR	CCN5	IDI1	DDIT4	STC1	SORD	CDKN1A
EGR3	SIK1	JUN	SLC2A3	CD69	NDUFA9	NDUFB2	COX8A	ATP6V0B	MDH1	BHLHE40	MAFF	CXCR4	KLF6	IER3	INSIG1	HMGCS1	EBP	HMGCR	CD9
<b>INFLAMMATORY RESPONSE</b> NES: -2.06   padj: 9.1e-08					<b>FATTY ACID METABOLISM</b> NES: -2   padj: 2.9e-06					<b>CHOLESTEROL HOMEOSTASIS</b> NES: -2.08   padj: 1.3e-05					<b>GLYCOLYSIS</b> NES: -1.71   padj: 1.3e-04				
IL6	CSF3	RGS1	SELE	CD69	XIST	TDO2	RDH11	ACAT2	IDI1	ATF3	PLAUR	LDLR	AVPR1A	NFIL3	TFF3	ANGPTL4	VEGFA	CXCR4	IER3
RGS16	VIP	SERPINE1	HBEGF	BTG2	HMGCS1	CRYZ	H2AZ1	CBR1	PDHB	ERRF1	ACAT2	IDI1	HMGCS1	EBP	DDIT4	STC1	BIK	SDC2	CLDN3
PLAUR	OSM	LDLR	TNFSF9	GPR183	ALDH1A1	MDH1	SERINC1	MIF	BLVRA	HMGCR	CD9	FDPS	CYP51A1	ANTXR2	GPC3	GALK1	FAM162A	BPNT1	MDH1
IL1B	FPR1	TNFAIP6	KLF6	NAMPT	PTS	ACADL	SUCLG1	AOC3	ACSL4	SQLE	CTNNB1	CLU	STARD4	SEMA3B	SPAG4	KDELR3	SOD1	TGFBI	MIF
<b>COMPLEMENT</b> NES: -1.59   padj: 1.7e-03					<b>IL2 STAT5 SIGNALING</b> NES: -1.57   padj: 2e-03					<b>IL6 JAK STAT3 SIGNALING</b> NES: -1.66   padj: 4.8e-03					<b>TGF BETA SIGNALING</b> NES: -1.59   padj: 1.7e-02				
IL6	MT3	SERPINE1	PLAUR	MAFF	GADD45B	SLC2A3	RGS16	GPR83	RHOB	IL6	SOCS3	JUN	CXCL3	IL1B	JUNB	THBS1	SERPINE1	PPP1R15A	KLF10
DUSP5	ACTN2	HSPA1A	CDH13	F3	EMP1	BHLHE40	MAFF	IL1RL1	KLF6	CD38	IL2RA	CD14	MAP3K8	PLA2G2A	ID2	CTNNB1	CDKN1C	ID3	TGIF1
LAMP2	OLR1	C1QA	CD55	S100A13	NFKBIZ	IL2RA	NFIL3	IL10	PNP	CD9	HMOX1	IL7	CRLF2	IL17RB	PPM1A	ID1	RHOA	WWTR1	NOG
DUSP6	CALM1	TFP12	CEBPB	ANG	MAP3K8	MYC	PTRH2	PHLDA1	SMPDL3A	LEPR	PIM1	IFNGR1	TNFRSF12A	CD44	TGFBR1				

**Supplementary Table S4: Top 25 significant DEGs in PSA-high Cluster 2 (n = 13) versus Cluster 1 (n = 16).** Clusters were identified by unsupervised clustering of cell type signature scores within PSA-high samples. Positive  $\log_2$  fold changes indicate higher expression in Cluster 2 relative to Cluster 1. Genes are ranked by adjusted  $p$ -value.

Gene	Log <sub>2</sub> Fold Change	Adjusted P-value	P-value
SETP21	23.42	$7.00 \times 10^{-22}$	$2.91 \times 10^{-26}$
CASTOR3P	-22.81	$1.89 \times 10^{-21}$	$1.57 \times 10^{-25}$
ENSG00000259623	26.09	$7.32 \times 10^{-21}$	$9.13 \times 10^{-25}$
ENSG00000256349	-19.56	$1.26 \times 10^{-10}$	$2.09 \times 10^{-14}$
FAM117B	1.96	$1.27 \times 10^{-7}$	$2.64 \times 10^{-11}$
PCDHB2	4.16	$2.36 \times 10^{-7}$	$5.88 \times 10^{-11}$
PIK3CB	1.35	$1.69 \times 10^{-5}$	$4.92 \times 10^{-9}$
ENSG00000310519	3.51	$3.70 \times 10^{-5}$	$1.23 \times 10^{-8}$
DNAJA4	1.28	$7.74 \times 10^{-5}$	$2.89 \times 10^{-8}$
HBB	4.51	$1.25 \times 10^{-4}$	$5.18 \times 10^{-8}$
ENSG00000293025	3.88	$1.43 \times 10^{-4}$	$6.54 \times 10^{-8}$
ZNF613	2.09	$1.74 \times 10^{-4}$	$8.68 \times 10^{-8}$
FXYD6	-1.93	$1.91 \times 10^{-4}$	$1.03 \times 10^{-7}$
TESK2	1.75	$2.19 \times 10^{-4}$	$1.53 \times 10^{-7}$
OPRK1	4.03	$2.19 \times 10^{-4}$	$1.54 \times 10^{-7}$
UNC13B	1.18	$2.19 \times 10^{-4}$	$1.49 \times 10^{-7}$
ENSG00000298932	4.59	$2.19 \times 10^{-4}$	$1.47 \times 10^{-7}$
ARHGAP6	0.96	$3.45 \times 10^{-4}$	$2.58 \times 10^{-7}$
TM6SF2	-4.62	$3.46 \times 10^{-4}$	$2.73 \times 10^{-7}$
EXTL1	-4.25	$3.47 \times 10^{-4}$	$2.89 \times 10^{-7}$
FAM135A	1.82	$3.67 \times 10^{-4}$	$3.20 \times 10^{-7}$
KRAS	1.07	$4.19 \times 10^{-4}$	$3.83 \times 10^{-7}$
CLMP	-1.77	$4.28 \times 10^{-4}$	$4.23 \times 10^{-7}$
MALINC1	1.89	$4.28 \times 10^{-4}$	$4.26 \times 10^{-7}$
VSTM2L	2.36	$4.71 \times 10^{-4}$	$5.23 \times 10^{-7}$