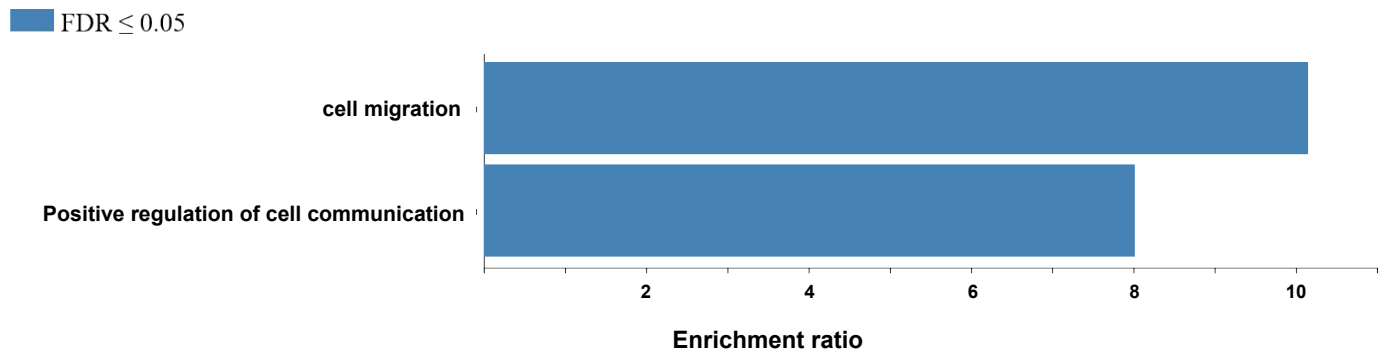
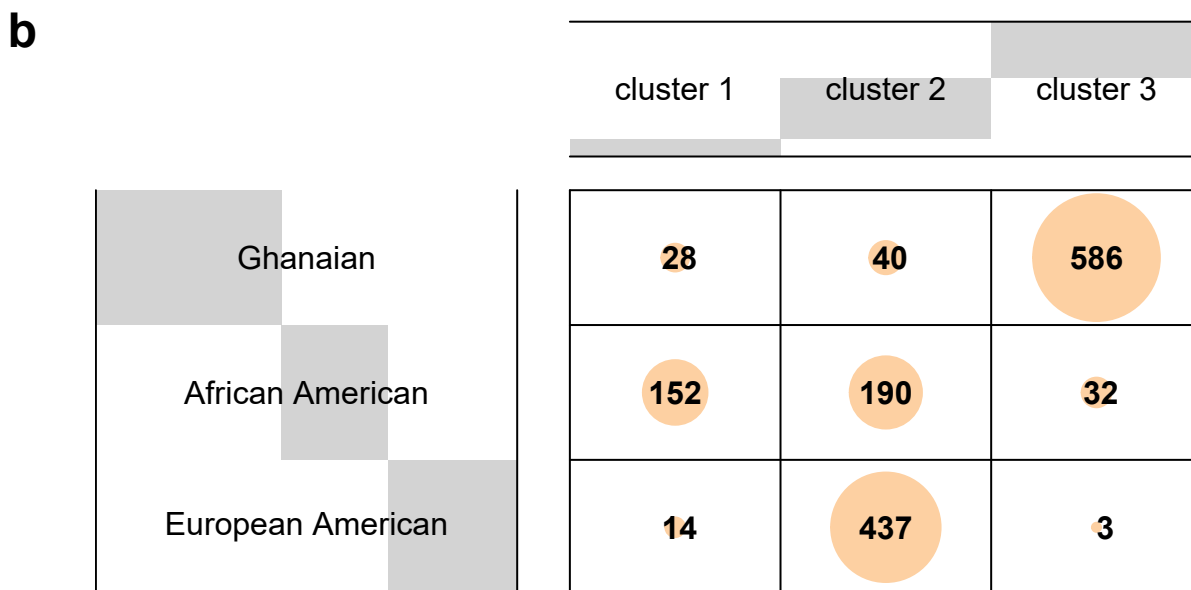
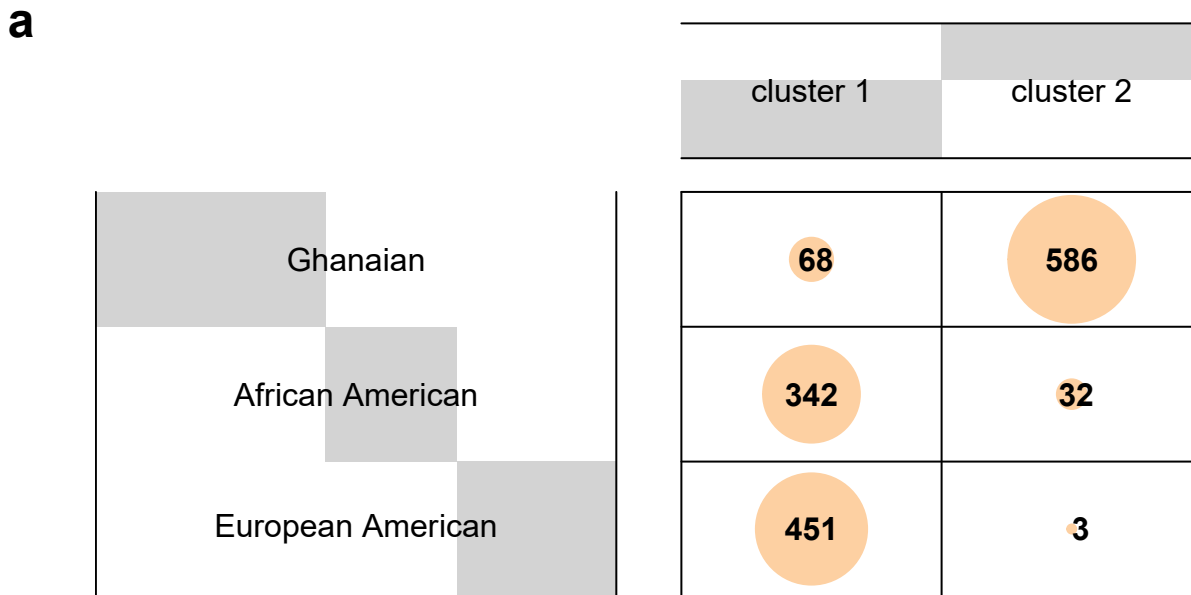


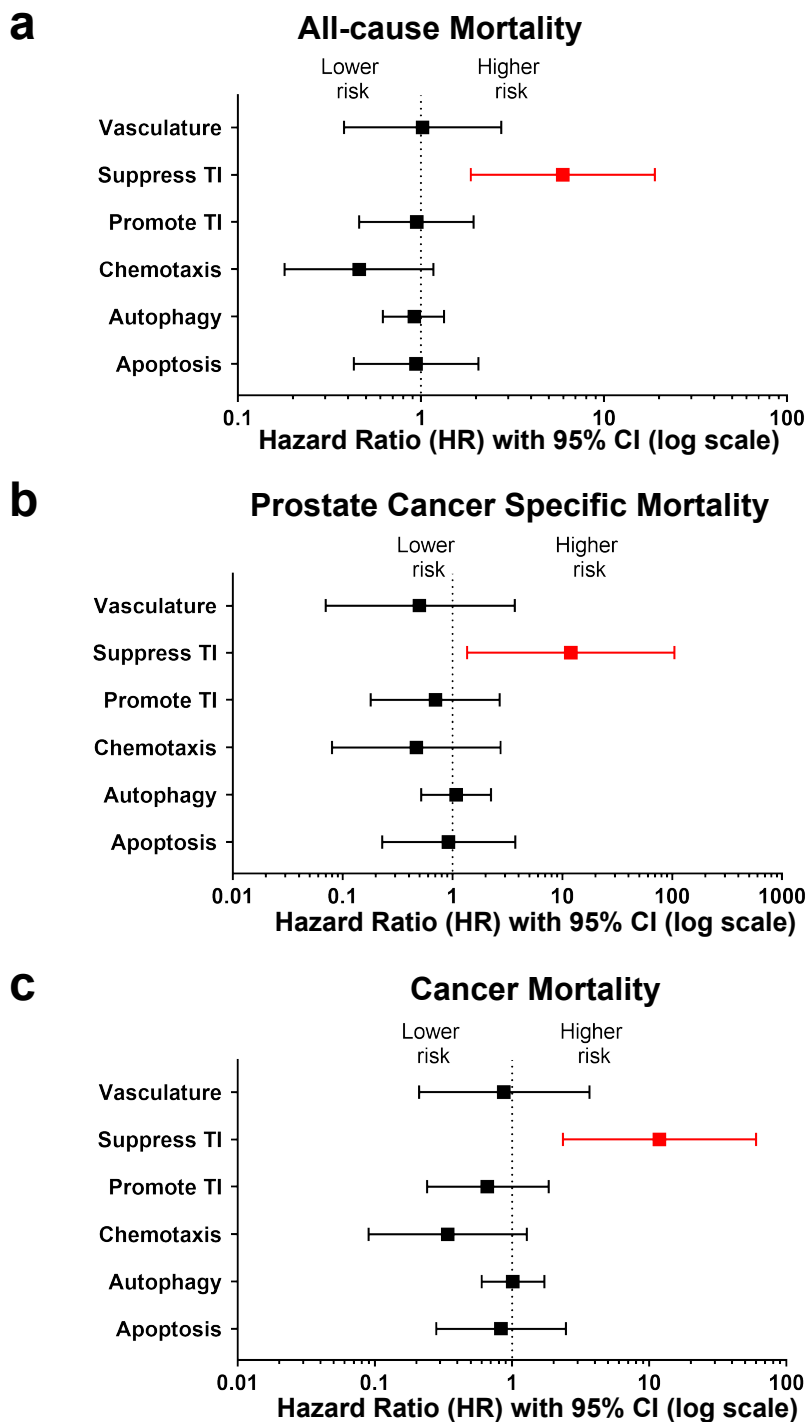
Supplementary Fig. 3 Correlation matrix presenting Pearson pairwise correlations for each of the 82 serum protein pairs. Pearson pairwise correlations were estimated for each serum protein pairs in (a) Ghanaian (n=654) and (b) EA (n=454) population controls and (c) Ghanaian (n=489) and (d) EA (n=425) prostate cancer cases. Source data are provided as a Source Data file.



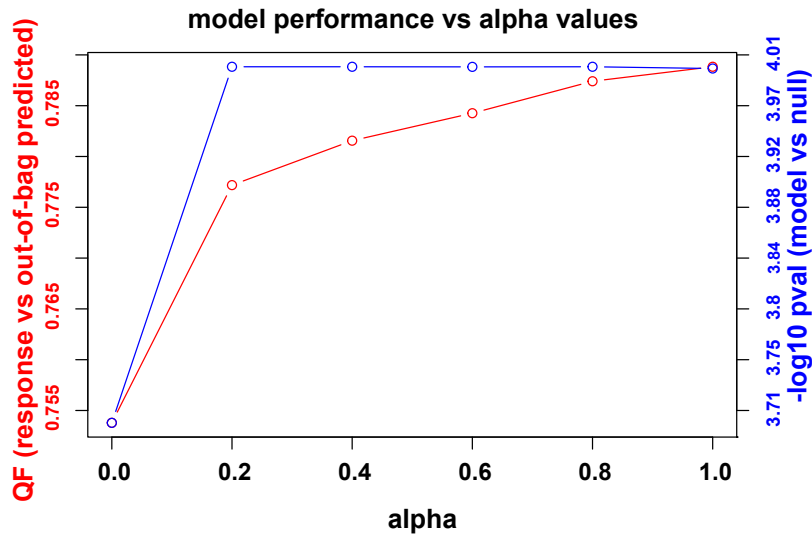
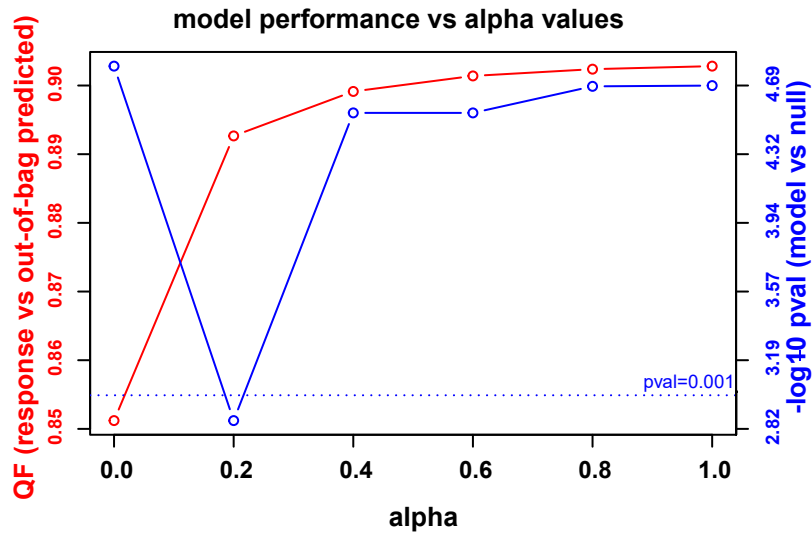
Supplementary Fig. 4. Gene ontology (GO) enrichment analysis. Over-Representation Analysis (ORA) was performed to identify the biological functions over-represented by the serum proteins that were positively associated with aging in all three population cohorts (Ghanaian, AA, and EA). Source data are provided as a Source Data file.



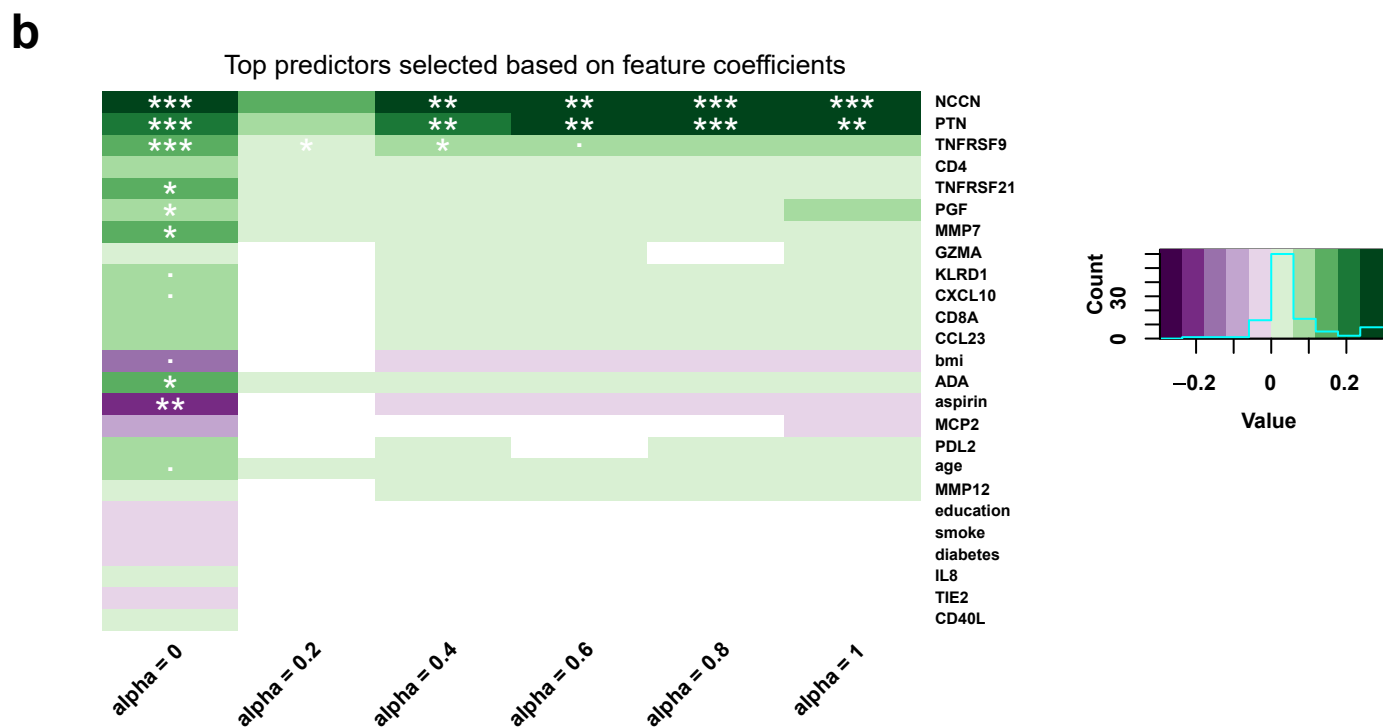
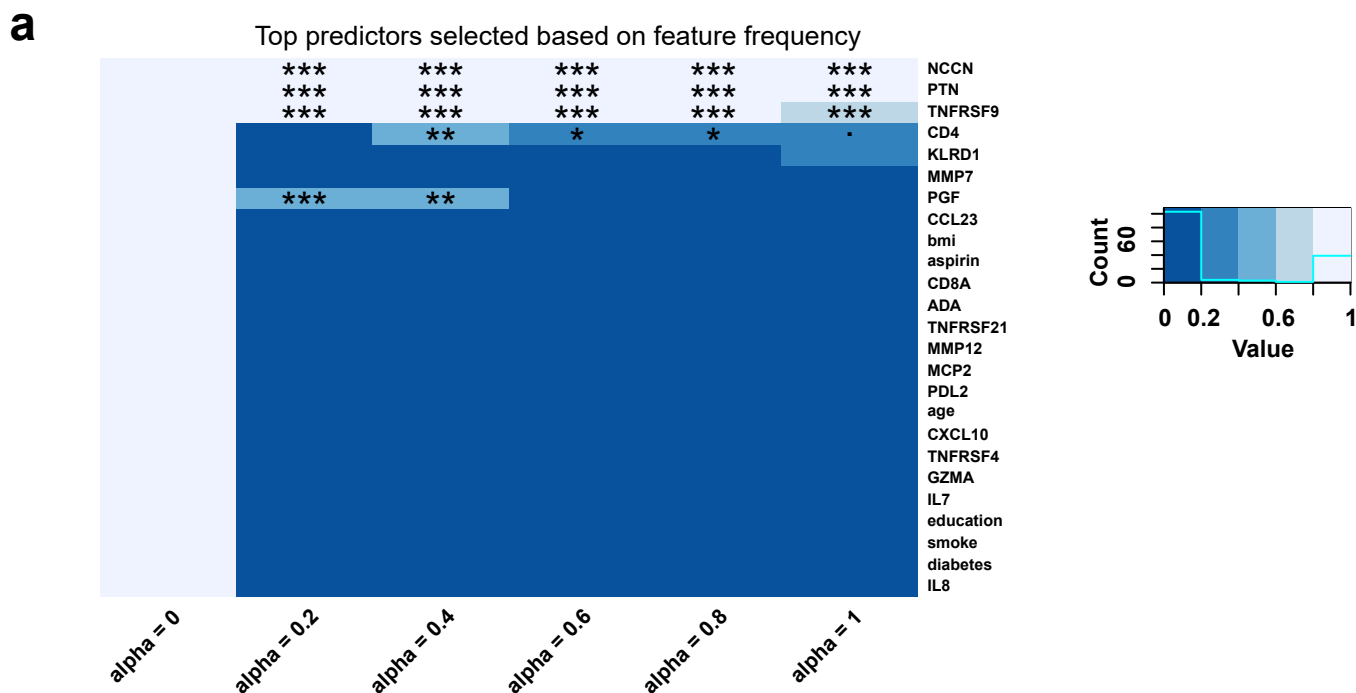
Supplementary Fig. 5. Clusters based on 82-protein profiles are enriched by population group (654 Ghanaian, 374 AA, and 454 EA). The dendrogram obtained from hierarchical clustering was cut to extract K clusters, yielding the contingency tables of cluster assignments vs. population groups shown for (a) K=2 and (b) K=3. For K=2, cluster 1 contains most EA and AA men, while cluster 2 contains most Ghanaian men. For K=3, EA are mostly grouped in cluster 2, AA are chiefly shared between clusters 1 and 2, while most Ghanaian men are in cluster 3. Cluster enrichment by population group was confirmed by Fisher's and chi-squared tests (two-sided $p < 1.e-10$). Source data are provided as a Source Data file.



Supplementary Fig. 6. Suppression of the tumor immunity pathway associates with survival of prostate cancer patients. We assessed the association of the six pathways defined by the 82 immunology markers with all-cause mortality (n=202), prostate cancer-specific mortality (n=57), or mortality due to any cancer after a prostate cancer diagnosis (n=103) out of the 819 prostate cancer patients followed. The pathway scores were evaluated as continuous predictor variables. Suppression of tumor immunity pathway was distinctively associated with all-cause mortality (a), prostate cancer-specific mortality (b), or mortality due to any cancer after a prostate cancer diagnosis (c). Multivariable Cox regression analyses were used to assess if the pathways were independently associated with survival of prostate cancer patients in the NCI-Maryland study. For (a-c), the hazard ratios (HRs) were adjusted for age at study entry (years), body-mass index (BMI, kg/m²), self-reported race (AA/EA), education (high school or less, some college, college, professional school), income (less than \$10k, \$10-30K, \$30-60K, \$60-90k, greater than \$90k), smoking history (never, former, current), diabetes (no/yes), aspirin use (no/yes), treatment (0=none, 1=surgery, 2=radiotherapy, 3=hormone, 4=combination), and NCCN risk score. The HRs indicate the change in risk of dying when the biological process z-score value increases by 1 while holding all the other biological processes' z-scores and covariates constant. Data are presented as hazard ratios +/- 95% Confidence Intervals (CI). Source data are provided as a Source Data file. TI= tumor immunity.

a**b**

Supplementary Fig. 7. Performance of regularized Cox regression models across alpha. Cross-validated, regularized Cox regression models with different elastic net mixture parameter from ridge ($\alpha=0$) to lasso ($\alpha=1$) were implemented to identify a predictive proteomic signature of lethal prostate cancer for AA patients **(a)** without and **(b)** with NCCN risk score. Performance across alpha is shown with the 5-fold cross-validated quality function (QF) or concordance (red) and statistical significance (empirical one-sided p-value of model vs null) (blue). Lasso regression model ($\alpha=1$) had the best out-of-bag performance. Source data are provided as a Source Data file.



Supplementary Fig. 8. NCCN and analytes pleiotrophin (PTN) and TNFRSF9/CD137/4-1BB are the most predictive features for lethal prostate cancer in AA patients. Cross-validated, regularized Cox regression models with different elastic net mixture parameters from ridge ($\alpha=0$) to lasso ($\alpha=1$) were implemented to identify a predictive proteomic signature. One-sided P values were obtained empirically by comparing feature frequencies and coefficients against those obtained from random permutations of the response. **(a)** Heatmaps of feature frequencies across α . Features were ranked by P value for $\alpha=1$. **(b)** Heatmaps of feature coefficients across α . Features were ranked by P value for $\alpha=1$. P value significance was coded as <0.001 (***), <0.01 (**), <0.05 (*), and <0.1 (.). The exact P values are found in the Source Data file. Source data are provided as a Source Data file.

Supplementary Table 1. Characteristics of prostate cancer cases and population controls of the NCI-Maryland and NCI-Ghana Studies

Demographics	Controls			Cases		
	Ghanaian (n=654)	AA ^a (n=374)	EA ^b (n=454)	Ghanaian (n=489)	AA (n=394)	EA (n=425)
Age ^c						
Median (IQR ^d) in years	59 (11)	64 (10)	66.5 (13)	70 (11)	63 (11)	65 (11)
BMI						
Mean(SD ^e) in kg/m2	24.3 (4.4)	29.6 (5.4)	27.8 (4.7)	25.6 (5.1)	28.0 (5.2)	28.0 (4.3)
Education for NCI-MD, N(%)						
High school or less	NA	107 (29)	83 (18)	NA	183 (46)	110 (26)
Some college	NA	109 (29)	93 (20)	NA	130 (33)	110 (26)
College	NA	84 (22)	136 (30)	NA	53 (13)	103 (24)
Graduate	NA	73 (20)	142 (31)	NA	27 (7)	102 (24)
Did not provide	NA	1 (<1)	-	NA	1 (<1)	-
Education for NCI-Ghana, N(%)						
None	75 (11)	NA	NA	39 (8)	NA	NA
Primary	47 (7)	NA	NA	16 (3)	NA	NA
Middle / junior secondary	292 (45)	NA	NA	132 (27)	NA	NA
Secondary/ senior secondary	125 (19)	NA	NA	99 (20)	NA	NA
Higher	86 (13)	NA	NA	190 (39)	NA	NA
Did not provide	29 (4)	NA	NA	13 (3)	NA	NA
Annual household income, N(%)						
Less than \$10,000	NA	18 (5)	5 (1)	NA	58 (15)	16 (4)
\$10,000- \$29,999	NA	63 (17)	37 (8)	NA	131 (33)	79 (19)
\$30,000 - \$59,999	NA	78 (21)	111 (24)	NA	94 (24)	89 (21)
\$60,000-\$90,000	NA	90 (24)	105 (23)	NA	41 (10)	86 (20)
Greater than \$90,000	NA	86 (23)	168 (37)	NA	32 (8)	130 (31)
Don't know/Refused	NA	39 (10)	28 (6)	NA	38 (10)	25 (6)
Baseline Health Factors						
Smoking status ^f , N (%)						
Never	346 (53)	149 (40)	191 (42)	321 (66)	112 (28)	171 (40)
Former	186 (28)	153 (41)	216 (48)	150 (31)	152 (39)	187 (44)
Current	94 (14)	70 (19)	42 (9)	10 (2)	127 (32)	65 (15)
Did not provide	28 (4)	2 (<1)	5 (1)	8 (2)	3 (<1)	2 (<1)
Diabetes, N(%)						
No	602 (92)	260 (70)	377 (83)	397 (81)	282 (72)	360 (85)
Yes	45 (7)	114 (30)	77 (17)	87 (18)	112 (28)	65 (15)
Did not provide	7 (1)	-	-	5 (1)	-	-
Regular aspirin use, N(%)						
No	570 (87)	179 (48)	173 (38)	347 (71)	227 (58)	193 (45)
Yes	66 (10)	195 (52)	281 (62)	78 (16)	167 (42)	232 (55)
Did not provide	18 (3)	-	-	64 (13)	-	-
Gleason score, N (%)						
Gleason score 2-6/ low grade	NA	NA	NA	149 (30)	159 (40)	187 (44)
Gleason score 7/ intermediate grade	NA	NA	NA	175 (36)	167 (42)	165 (39)
Gleason score 8-10/ high grade	NA	NA	NA	158 (32)	68 (17)	73 (17)
Unavailable	NA	NA	NA	7 (1)	-	-
Stage ^g , N (%)						
I	NA	NA	NA	NA	62 (16)	97 (23)
II	NA	NA	NA	NA	280 (71)	264 (62)
III	NA	NA	NA	NA	23 (6)	41 (10)
IV	NA	NA	NA	NA	29 (7)	23 (5)
NCCN risk groups ^h , N (%)						
Low	NA	NA	NA	NA	61 (15)	98 (23)
intermediate	NA	NA	NA	NA	217 (55)	211 (50)
High/ Very high	NA	NA	NA	NA	91 (23)	95 (22)
Regional/ Metastatic	NA	NA	NA	NA	25 (7)	21 (5)
PSA ⁱ						
Median (IQR) in ng/ml	0.98 (1.46)	0.4 (0.6)	0.4 (0.6)	51.9 (101)	6.8 (7.6)	6.0 (4.9)

^a AA: African-American; ^b EA: European American; ^c Age at study interview; ^d IQR: Interquartile range; ^e SD: Standard deviation

^f Smoking status describes cigarette smoking; ^g Pathologically confirmed using American Joint Committee on Cancer (AJCC) 7th Edition

^h Risk stratification based on the 2019 National Comprehensive Cancer Network (NCCN) guideline (see methods)

ⁱ PSA: Prostate specific antigen

Supplementary Table 2. Lower limit of detection for the 92 immuno-oncological proteins assayed

Serum proteins	Lower Limit of Detection (LLOD) in NPX	Missing Data freq. (proportion of samples with protein level below LLOD)	Serum proteins	Lower Limit of Detection (LLOD) in NPX	Missing Data freq. (proportion of samples with protein level below LLOD)
IL33	1.59195	100%	CXCL9	1.86220	0%
IL-35	1.18313	100%	ADA	0.21076	0%
IL-21	1.72309	99%	CXCL1	4.26373	0%
IL2	1.68844	99%	MCP-2	2.38761	0%
IFN-beta	1.84622	95%	HO-1	5.73997	0%
IL13	1.56681	94%	CX3CL1	0.63004	0%
IL-1 alpha	-0.03527	92%	CD70	1.10604	0%
CXCL12	2.22920	87%	CCL23	2.99034	0%
IFN-gamma	1.55567	87%	CCL3	2.05152	0%
TNF	2.15958	85%	NCR1	0.66578	0%
ARG1	5.27490	76%	CCL17	2.84146	0%
IL4	0.54505	75%	ICOSLG	1.66922	0%
IL5	2.01127	62%	CCL20	2.39470	0%
CD28	2.49576	58%	IL8	2.99315	0%
FGF2	1.24047	43%	TNFRSF9	1.21451	0%
NOS3	1.05396	37%	TIE2	2.64389	0%
ADGRG1	1.45257	16%	CD244	1.45933	0%
MIC-A/B	1.23883	9%	PGF	2.42442	0%
CD4	-0.13759	5%	MCP-1	3.78349	0%
IL10	2.30912	5%	TRAIL	1.76455	0%
CD8A	2.55944	4%	CAIX	0.77464	0%
CCL19	2.95390	4%	Gal-9	2.49023	0%
CXCL10	1.42680	3%	VEGFR-2	0.95838	0%
PTN	0.57332	3%	CD40	4.25081	0%
IL12RB1	1.66460	2%	IL18	3.18339	0%
VEGFC	0.05409	2%	TNFSF14	2.16990	0%
MCP-3	1.37635	2%	TWEAK	2.51722	0%
CXCL5	6.60140	2%	PDGF subunit B	4.82460	0%
CXCL11	2.22295	1%	PDCD1	1.80311	0%
PD-L2	1.10516	1%	FASLG	1.83999	0%
LAP TGF-beta-1	0.97475	1%	Gal-1	1.76849	0%
GZMH	2.05211	0%	PD-L1	2.05346	0%
EGF	4.36494	0%	CD27	2.43845	0%
CRTAM	1.07615	0%	HGF	2.23412	0%
MCP-4	3.14076	0%	GZMA	0.65531	0%
CCL4	3.15472	0%	TNFRSF12A	1.92242	0%
DCN	1.24817	0%	CD5	1.08175	0%
GZMB	1.33242	0%	MMP7	5.36396	0%
CD40-L	2.42129	0%	TNFRSF21	2.48109	0%
IL7	1.73351	0%	ANGPT2	1.12478	0%
TNFRSF4	2.60002	0%	LAMP3	2.20090	0%
CASP-8	1.52429	0%	MMP12	0.69984	0%
CXCL13	2.32015	0%	VEGFA	2.15947	0%
IL12	1.44479	0%	KLRD1	1.67210	0%
ANG-1	3.51630	0%	CD83	1.33464	0%
IL6	2.02073	0%	CSF-1	1.43577	0%

Supplementary Table 3. List of 82 immuno-oncological proteins detected in more than 20% of the serum samples

Protein symbol	Protein name	Uniprot ID	Protein symbol	Protein name	Uniprot ID
IL8	Interleukin-8	P10145	Gal-1	Galectin-1	P09382
TNFRSF9	Tumor necrosis factor receptor superfamily member 9	Q07011	PD-L1	Programmed cell death 1 ligand 1	Q9NZQ7
TIE2	Angiopoietin-1 receptor	Q02763	CD27	CD27 antigen	P26842
MCP-3	Monocyte chemotactic protein 3	P80098	CXCL5	C-X-C motif chemokine 5	P42830
CD40-L	CD40 ligand	P29965	IL5	Interleukin-5	P05113
CD244	Natural killer cell receptor 2B4	Q9BZW8	HGF	Hepatocyte growth factor	P14210
EGF	Pro-epidermal growth factor	P01133	GZMA	Granzyme A	P12544
ANG-1	Angiopoietin-1	Q15389	HO-1	Heme oxygenase 1	P09601
IL7	Interleukin-7	P13232	CX3CL1	Fractalkine	P78423
PGF	Placenta growth factor	P49763	CXCL10	C-X-C motif chemokine 10	P02778
IL6	Interleukin-6	P05231	CD70	CD70 antigen	P32970
ADGRG1	Adhesion G-protein coupled receptor G1	Q9Y653	IL10	Interleukin-10	P22301
MCP-1	Monocyte chemotactic protein 1	P13500	TNFRSF12A	Tumor necrosis factor receptor superfamily member 12A	Q9NP84
CRTAM	Cytotoxic and regulatory T-cell molecule (CRTAM)	O95727	CCL23	C-C motif chemokine 23	P55773
CXCL11	C-X-C motif chemokine 11	O14625	CD5	T-cell surface glycoprotein CD5	P06127
MCP-4	Monocyte chemotactic protein 4	Q99616	CCL3	C-C motif chemokine 3	P10147
TRAIL	TNF-related apoptosis-inducing ligand	P50591	MMP7	Matrix metalloproteinase-7	P09237
FGF2	Fibroblast growth factor 2	P09038	NCR1	Natural cytotoxicity triggering receptor 1	O76036
CXCL9	C-X-C motif chemokine 9	Q07325	DCN	Decorin	P07585
CD8A	T-cell surface glycoprotein CD8 alpha chain	P01732	TNFRSF21	Tumor necrosis factor receptor superfamily member 21	O75509
CAIX	Carbonic anhydrase IX	Q16790	TNFRSF4	Tumor necrosis factor receptor superfamily member 4	P43489
ADA	Adenosine Deaminase	P00813	MIC-A/B	MHC class I polypeptide-related sequence A/B	Q29983,Q29980
CD4	T-cell surface glycoprotein CD4	P01730	CCL17	C-C motif chemokine 17	Q92583
NOS3	Nitric oxide synthase, endothelial	P29474	ANGPT2	Angiopoietin-2	O15123
Gal-9	Galectin-9	O00182	PTN	Pleiotrophin	P21246
VEGFR-2	Vascular endothelial growth factor receptor 2	P35968	LAMP3	Lysosome-associated membrane glycoprotein 3	Q9UQV4
CD40	CD40L receptor	P25942	CASP-8	Caspase-8	Q14790
IL18	Interleukin-18	Q14116	ICOSLG	ICOS ligand	O75144
GZMH	Granzyme H	P20718	MMP12	Matrix metalloproteinase-12	P39900
VEGFC	Vascular endothelial growth factor C	P49767	CXCL13	C-X-C motif chemokine 13	O43927
LAP TGF-beta-1	Latency-associated peptide transforming growth factor beta-1	P01137	PD-L2	Programmed cell death 1 ligand 2	Q9BQ51
CXCL1	C-X-C motif chemokine 1	P09341	VEGFA	Vascular endothelial growth factor A	P15692
TNFSF14	Tumor necrosis factor ligand superfamily member 14	O43557	IL4	Interleukin-4	P05112
TWEAK	Tumor necrosis factor (Ligand) superfamily, member 12	O43508	IL12RB1	Interleukin-12 receptor subunit beta-1	P42701
PDGF subunit B	Platelet-derived growth factor subunit B	P01127	CCL20	C-C motif chemokine 20	P78556
PDCD1	Programmed cell death protein 1	Q15116	KLRD1	Natural killer cells antigen CD94	Q13241
FASLG	Fas antigen ligand	P48023	GZMB	Granzyme B	P10144
CD28	T-cell-specific surface glycoprotein CD28	P10747	CD83	CD83 antigen	Q01151
CCL19	C-C motif chemokine 19	Q99731	IL12	Interleukin-12	P29459,P29460
MCP-2	Monocyte chemotactic protein 2	P80075	CSF-1	Macrophage colony-stimulating factor 1	P09603
CCL4	C-C motif chemokine 4	P13236	ARG1	Arginase-1	P05089-1

Supplementary Table 4. Top 10 Pearson pairwise correlations in men with and without prostate cancer

Ghanaian men without prostate cancer			AA men without prostate cancer			EA men without prostate cancer		
Serum protein 1	Serum Protein 2	Correlation (r)	Serum protein 1	Serum Protein 2	Correlation (r)	Serum protein 1	Serum Protein 2	Correlation (r)
PDL2	ICOSLG	0.84	IL8	MCP3	0.89	IL8	MCP3	0.89
ICOSLG	HO1	-0.79	CD83	TNFRSF9	0.85	CCL3	CCL4	0.82
GZMB	GZMH	0.76	TNFRSF4	TNFRSF9	0.85	EGF	CD40L	0.80
HO1	PDL2	-0.73	EGF	CD40L	0.83	IL8	CASP8	0.80
KLRD1	CD244	0.71	IL8	CASP8	0.82	TNFRSF4	TNFRSF9	0.80
CCL3	CCL4	0.71	CD83	TNFRSF4	0.80	GZMB	GZMH	0.78
EGF	CD40L	0.71	PGF	TNFRSF9	0.80	PGF	CD27	0.78
PDL2	TIE2	0.70	PGF	TNFRSF21	0.80	CD83	TNFRSF9	0.76
CXCL10	CXCL9	0.70	PGF	TNFRSF4	0.79	CD83	TNFRSF9	0.76
IL8	CASP8	0.69	PGF	NCR1	0.79	MCP3	CASP8	0.75

Ghanaian men with prostate cancer			AA men with prostate cancer			EA men with prostate cancer		
Serum protein 1	Serum Protein 2	Correlation (r)	Serum protein 1	Serum Protein 2	Correlation (r)	Serum protein 1	Serum Protein 2	Correlation (r)
CD8A	HO1	0.86	MCP3	IL8	0.89	MCP3	IL8	0.84
CXCL10	TWEAK	0.86	EGF	CD40L	0.87	TNFRSF4	TNFRSF9	0.80
TNFRSF9	TNFRSF4	0.85	TNFRSF4	TNFRSF9	0.86	EGF	CD40L	0.77
CCL3	CCL4	0.85	TNFRSF9	PGF	0.84	CCL3	CCL4	0.76
TNFRSF9	PGF	0.85	CD83	TNFRSF9	0.83	PGF	TNFRSF12A	0.75
CXCL10	CXCL11	0.85	CD83	PGF	0.82	TNFRSF21	PGF	0.75
CD8A	TIE2	-0.84	PGF	TNFRSF12A	0.82	TNFRSF14	EGF	0.75
IL6	CCL4	0.84	CD83	TNFRSF4	0.82	PGF	TNFRSF9	0.74
TNFRSF4	PGF	0.83	TNFRSF4	PGF	0.80	PGF	TNFRSF4	0.74
TNFRSF12A	PGF	0.82	CX3CL1	PGF	0.80	MCP3	CASP8	0.75

Supplementary Table 5. The association of blood CRP with clinical/sociodemographic variables estimated using multiple linear regression

	Coefficient [95% CI]	<i>P</i> -value	<i>q</i> -value
BMI (kg/m ²)	59.56 [-29.6, 148.7]	0.19	0.57
age	9.75 [-58.53, 78.02]	0.78	0.96
education (high school or less, some college, college, professional school)	10.9 [-448.8, 427.0]	0.96	0.96
smoke (never, former, vs. current)	891.9 [220.6, 1563.3]	0.01	0.06
diabetes (no vs. yes)	-95.5 [-1391.8, 1200.8]	0.88	0.96
PSA (ng/ml)	-59.3[-507.5, 389.0]	0.79	0.96

Supplementary Table 6. The fraction of variance in each of the serum proteins explained by degree of West African ancestry

Serum Proteins	Number of observations	Root Mean Square		Variance		F-statistics	p-value	†q-value
		Error (RMSE)	fraction	F-statistics	p-value			
CXCL5	795	0.699	0.498	786.48	<0.0001	<0.0001		
CXCL1	795	0.632	0.408	545.60	<0.0001	<0.0001		
MCP2	795	0.648	0.152	141.88	<0.0001	<0.0001		
MCP1	795	0.666	0.147	136.34	<0.0001	<0.0001		
CXCL11	795	1.071	0.128	116.81	<0.0001	<0.0001		
CCL23	795	0.521	0.105	92.68	<0.0001	<0.0001		
PTN	795	1.153	0.100	87.66	<0.0001	<0.0001		
TWEAK	795	0.332	0.090	78.73	<0.0001	<0.0001		
NCR1	795	0.556	0.074	63.32	<0.0001	<0.0001		
CCL17	795	0.781	0.049	40.57	<0.0001	<0.0001		
IL18	795	0.610	0.048	40.11	<0.0001	<0.0001		
CD8A	795	0.790	0.047	38.81	<0.0001	<0.0001		
IL12	795	0.792	0.042	34.53	<0.0001	<0.0001		
CXCL9	795	0.910	0.041	34.04	<0.0001	<0.0001		
TNFRSF4	795	0.509	0.041	33.50	<0.0001	<0.0001		
MCP4	795	0.697	0.039	32.23	<0.0001	<0.0001		
MMP7	795	0.308	0.030	24.28	<0.0001	<0.0001		
CCL3	795	1.464	0.029	23.38	<0.0001	<0.0001		
TNFRSF21	795	0.270	0.024	19.66	<0.0001	<0.0001		
TNFRSF9	795	0.561	0.024	19.44	<0.0001	<0.0001		
HO1	795	0.395	0.023	18.96	<0.0001	0.0001		
PDL2	795	0.405	0.022	17.61	<0.0001	0.0001		
CD70	795	0.460	0.020	16.13	0.0001	0.0002		
CCL20	795	1.255	0.020	16.02	0.0001	0.0002		
TNFSF14	795	0.904	0.019	15.07	0.0001	0.0004		
IL7	795	0.592	0.018	14.74	0.0001	0.0004		
ARG1	795	0.372	0.017	14.04	0.0002	0.0006		
CCL19	795	0.892	0.016	13.15	0.0003	0.0009		
LAMP3	795	0.753	0.012	9.22	0.0025	0.0070		
TRAIL	795	0.326	0.011	8.96	0.0028	0.0078		
HGF	795	0.480	0.011	8.62	0.0034	0.0091		
FGF2	795	0.624	0.010	8.31	0.004	0.0104		
CASP8	795	1.250	0.009	7.51	0.0063	0.0156		
GZMB	795	0.966	0.008	6.59	0.0104	0.0251		
CCL4	795	0.835	0.008	6.53	0.0108	0.0253		
ICOSLG	795	0.286	0.008	6.19	0.0131	0.0290		
PGF	795	0.415	0.008	6.19	0.0131	0.0290		
NOS3	795	0.381	0.007	5.60	0.0182	0.0393		
MICAB	795	1.682	0.007	5.52	0.0191	0.0401		
GZMH	795	1.014	0.006	4.56	0.033	0.0677		
PDCD1	795	0.637	0.006	4.52	0.0339	0.0677		
CD83	795	0.432	0.005	4.30	0.0384	0.0732		
FASLG	795	0.437	0.005	4.32	0.038	0.0732		
CRTAM	795	0.599	0.005	4.03	0.0451	0.0822		
LAPTFbeta1	795	0.336	0.005	4.06	0.0441	0.0822		
CSF1	795	0.239	0.005	3.82	0.0509	0.0907		
CXCL10	795	0.905	0.005	3.72	0.0542	0.0946		
Gal9	795	0.402	0.004	3.41	0.0653	0.1116		
VEGFC	795	0.469	0.004	3.29	0.0702	0.1174		
PDGFsubunitB	795	0.127	0.004	3.12	0.0778	0.1275		
IL6	795	1.181	0.004	2.91	0.0885	0.1423		
Gal1	795	0.238	0.004	2.87	0.0905	0.1426		
ANG1	795	0.292	0.003	2.21	0.1377	0.2130		
IL10	795	0.550	0.002	1.80	0.1807	0.2694		
KLRD1	795	0.615	0.002	1.81	0.1789	0.2694		
CD27	795	0.466	0.002	1.75	0.1859	0.2722		
CX3CL1	795	0.446	0.002	1.56	0.2128	0.3061		
IL8	795	2.693	0.002	1.46	0.227	0.3210		
VEGFR2	795	0.259	0.002	1.19	0.2754	0.3828		
CD5	795	0.410	0.001	1.14	0.2858	0.3906		
CD40	795	0.477	0.001	1.00	0.3187	0.4284		
CD28	795	0.355	0.001	0.94	0.3323	0.4395		
TNFRSF12A	795	0.479	0.001	0.77	0.3792	0.4935		
IL4	795	0.938	0.001	0.72	0.3949	0.5059		
ADA	795	0.594	0.001	0.61	0.4354	0.5275		
ANGPT2	795	0.500	0.001	0.60	0.4385	0.5275		
CD40L	795	0.844	0.001	0.63	0.4283	0.5275		
MCP3	795	2.432	0.001	0.61	0.4359	0.5275		
TIE2	795	0.267	0.001	0.59	0.4439	0.5275		
EGF	795	1.008	0.001	0.55	0.4581	0.5367		
CD4	795	0.372	0.001	0.38	0.5376	0.6111		
IL5	795	1.320	0.001	0.37	0.5441	0.6111		
VEGFA	795	0.515	0.001	0.37	0.5408	0.6111		
GZMA	795	0.484	0.000	0.17	0.6839	0.7578		
CAIX	795	0.651	0.000	0.13	0.7201	0.7873		
MMP12	795	0.763	0.000	0.08	0.7808	0.8424		
ADGRG1	795	1.053	0.000	0.05	0.8243	0.8779		
CD244	795	0.376	0.000	0.03	0.8551	0.8990		
PDL1	795	0.551	0.000	0.02	0.8862	0.9199		
CXCL13	795	0.619	0.000	0.00	0.9678	0.9879		
DCN	795	0.278	0.000	0.00	0.9841	0.9879		
IL12RB1	795	0.433	0.000	0.00	0.9879	0.9879		

Analysis of variance was performed for the levels of each of the 82 immune-oncological cytokines as a function of genetic estimation of West African admixture among men without prostate cancer from the NCI-Maryland study.

†The q-values represent FDR-adjusted p-values for multiple-testing of n=82.

Supplementary Table 7. The fraction of variance in each of the serum proteins explained by degree of West African ancestry after adjusting for differences in age, BMI, aspirin use, education, diabetes status, smoking, and income

Serum Proteins	Number of observations	Root Mean Square Error (RMSE)	Variance fraction	F-statistics	p-value	q-value
CXCL5	726	0.703	0.501	725.43	<0.0001	<0.0001
CXCL1	726	0.628	0.406	494.33	<0.0001	<0.0001
MCP1	726	0.653	0.165	142.58	<0.0001	<0.0001
MCP2	726	0.649	0.146	123.35	<0.0001	<0.0001
CXCL11	726	1.056	0.130	108.20	<0.0001	<0.0001
PTN	726	1.142	0.111	90.36	<0.0001	<0.0001
CCL23	726	0.522	0.108	87.17	<0.0001	<0.0001
TWEAK	726	0.331	0.087	68.55	<0.0001	<0.0001
NCR1	726	0.556	0.076	59.19	<0.0001	<0.0001
IL18	726	0.602	0.056	43.19	<0.0001	<0.0001
CCL17	726	0.778	0.054	40.90	<0.0001	<0.0001
CD8A	726	0.789	0.050	38.29	<0.0001	<0.0001
IL12	726	0.776	0.048	36.62	<0.0001	<0.0001
TNFRSF4	726	0.509	0.048	36.41	<0.0001	<0.0001
CXCL9	726	0.886	0.048	36.37	<0.0001	<0.0001
MCP4	726	0.700	0.037	27.65	<0.0001	<0.0001
MMP7	726	0.307	0.028	20.82	<0.0001	<0.0001
TNFRSF9	726	0.562	0.026	19.31	<0.0001	0.0001
HO1	726	0.396	0.025	18.69	<0.0001	0.0001
TNFSF14	726	0.908	0.024	17.76	<0.0001	0.0001
TNFRSF21	726	0.271	0.024	17.64	<0.0001	0.0001
CCL3	726	1.432	0.022	16.07	0.0001	0.0002
CD70	726	0.457	0.022	16.01	0.0001	0.0002
PDL2	726	0.408	0.021	15.25	0.0001	0.0004
ARG1	726	0.375	0.019	13.83	0.0002	0.0007
HGF	726	0.481	0.016	11.69	0.0007	0.0021
TRAIL	726	0.325	0.016	11.63	0.0007	0.0021
IL7	726	0.592	0.015	11.11	0.0009	0.0026
CCL19	726	0.892	0.014	9.89	0.0017	0.0049
CCL20	726	1.193	0.013	9.80	0.0018	0.0050
CASP8	726	1.244	0.013	9.58	0.002	0.0052
LAMP3	726	0.753	0.013	9.59	0.002	0.0052
FGF2	726	0.630	0.011	8.12	0.0045	0.0112
ICOSLG	726	0.287	0.011	7.96	0.0049	0.0118
GZMB	726	0.967	0.009	6.53	0.0108	0.0254
CXCL10	726	0.887	0.008	5.88	0.0156	0.0355
PGF	726	0.417	0.008	5.59	0.0183	0.0405
NOS3	726	0.372	0.006	4.59	0.0325	0.0701
CD83	726	0.435	0.006	4.36	0.0372	0.0783
LAPTFbeta1	726	0.339	0.006	4.31	0.0382	0.0783
GZMH	726	1.021	0.006	4.02	0.0454	0.0887
PDCD1	726	0.646	0.006	4.03	0.0451	0.0887
MICAB	726	1.661	0.005	3.68	0.0556	0.1039
Gal9	726	0.401	0.005	3.67	0.0558	0.1039
CSF1	726	0.240	0.005	3.56	0.0595	0.1085
CRTAM	726	0.604	0.005	3.39	0.0661	0.1179
VEGFC	726	0.469	0.004	3.07	0.0804	0.1402
CCL4	726	0.812	0.004	2.94	0.0869	0.1484
FASLG	726	0.439	0.004	2.90	0.0889	0.1488
VEGFR2	726	0.257	0.003	2.36	0.1248	0.2047
IL8	726	2.665	0.003	2.27	0.1325	0.2131
Gal1	726	0.240	0.003	2.19	0.1394	0.2199
CD40	726	0.481	0.002	1.55	0.2135	0.3303
IL5	726	1.278	0.002	1.36	0.2436	0.3688
CD5	726	0.409	0.002	1.30	0.2546	0.3728
IL10	726	0.541	0.002	1.34	0.2473	0.3688
CD28	726	0.367	0.002	1.25	0.2643	0.3745
PDGFsubunitB	726	0.127	0.002	1.24	0.2649	0.3745
ANG1	726	0.296	0.002	1.10	0.2949	0.4054
CD27	726	0.464	0.002	1.09	0.2966	0.4054
MCP3	726	2.417	0.002	1.06	0.3044	0.4092
ADA	726	0.576	0.001	0.92	0.3386	0.4407
CX3CL1	726	0.442	0.001	0.92	0.3381	0.4407
IL4	726	0.965	0.001	0.87	0.3503	0.4489
KLRD1	726	0.613	0.001	0.83	0.3616	0.4562
CD40L	726	0.861	0.001	0.75	0.3873	0.4812
IL6	726	1.144	0.001	0.69	0.4053	0.4961
TIE2	726	0.265	0.001	0.55	0.4585	0.5528
EGF	726	1.029	0.001	0.33	0.564	0.6607
IL12RB1	726	0.432	0.001	0.34	0.5576	0.6607
CAIX	726	0.647	0.000	0.30	0.5864	0.6624
CD4	726	0.369	0.000	0.31	0.5773	0.6624
VEGFA	726	0.521	0.000	0.29	0.5897	0.6624
DCN	726	0.278	0.000	0.13	0.7209	0.7882
TNFRSF12A	726	0.483	0.000	0.15	0.701	0.7768
CXCL13	726	0.609	0.000	0.09	0.7663	0.8268
GZMA	726	0.481	0.000	0.04	0.8445	0.8993
ADGRG1	726	1.042	0.000	0.00	0.9783	0.9783
ANGPT2	726	0.497	0.000	0.02	0.8948	0.9058
CD244	726	0.377	0.000	0.02	0.8921	0.9058
MMP12	726	0.757	0.000	0.02	0.8818	0.9058
PDL1	726	0.562	0.000	0.02	0.8764	0.9058

Analysis of variance was performed for the levels of each of the 82 immune-oncological cytokines as a function of genetic estimation of West African admixture among men without prostate cancer from the NCI-Maryland study.

¹The q-values represent FDR-adjusted p-values for multiple-testing of n=82.

Supplementary Table 8. Immune oncological markers that are significantly elevated in both Ghanaian and AA men compared to EA men

markers	EA	AA	Ghanaian	median ratio		median ratio		median ratio	
	median (IQR) (linear NPX)	median (IQR) (linear NPX)	median (IQR) (linear NPX)	(AA/EA)	p-value	q-value	(Ghanaian/EA)	p-value	q-value
CXCL5	6284.05 (4332.56-8943.36)	17648.06 (13969.29-19884.74)	18950.86 (16678.05-21055.39)	2.81	<0.0001	<0.0001	3.02	<0.0001	<0.0001
CXCL1	1794.85 (1347.21-2317.20)	3838.60 (2781.05-5121.68)	4730.16 (3864.12-5615.48)	2.14	<0.0001	<0.0001	2.64	<0.0001	<0.0001
CXCL11	199.81 (140.72-287.12)	390.17 (187.00-674.34)	686.85 (400.24-1293.64)	1.95	<0.0001	<0.0001	3.44	<0.0001	<0.0001
MCP2	401.48 (306.12-535.24)	570.79 (447.25-721.71)	609.02 (479.80-788.77)	1.42	<0.0001	<0.0001	1.52	<0.0001	<0.0001
CCL17	1144.06 (806.42-1613.84)	1515.00 (1077.18-2151.31)	1578.03 (1177.14-2094.19)	1.32	<0.0001	<0.0001	1.38	<0.0001	<0.0001
MCP4	1076.23 (792.86-1444.83)	1358.71 (931.83-1825.48)	1384.04 (1025.71-1929.18)	1.26	<0.0001	<0.0001	1.29	<0.0001	<0.0001
CD70	21.69 (17.71-27.17)	24.56 (20.03-29.46)	32.51 (27.01-38.49)	1.13	<0.0001	0.0001	1.5	<0.0001	<0.0001
PDL2	10.34 (8.69-12.02)	11.50 (9.41-13.74)	15.47 (12.02-28.00)	1.11	0.0120	0.0304	1.5	<0.0001	<0.0001
MMP7	3836.16 (3309.16-4334.54)	4204.66 (3677.46-4856.59)	4470.14 (3889.38-5087.45)	1.10	<0.0001	<0.0001	1.17	<0.0001	<0.0001
CCL19	1075.95 (855.70-1458.43)	1177.98 (854.58-1946.63)	1170.39 (825.52-1615.30)	1.09	0.0194	0.0449	1.09	0.0352	0.0419

Medians were compared using two-sided Wilcoxon rank sum tests.

†The q-values represent FDR-adjusted p-values for multiple-testing.

Supplementary Table 9. Immune oncological markers that are significantly downregulated in both Ghanaian and AA men compared to EA men

markers	EA median (IQR)	AA median (IQR)	Ghanaian median (IQR)	median ratio (AA/EA)	p-value	†q-value	median ratio (Ghanaian/EA)	p-value	†q-value
MCP1	5013.63 (4088.21-6276.75)	3168.62 (2454.90-5211.40)	2316.18 (1999.64-2779.57)	0.63	<0.0001	<0.0001	0.46	<0.0001	<0.0001
IL12	189.78 (136.00-251.02)	134.41 (100.24-187.47)	146.88 (112.96-198.63)	0.71	<0.0001	<0.0001	0.77	<0.0001	<0.0001
CCL23	2303.56 (1869.12-2871.36)	1735.11 (1397.11-2407.05)	1803.47 (1408.06-2344.48)	0.75	<0.0001	<0.0001	0.78	<0.0001	<0.0001
CD8A	1172.34 (859.33-1746.96)	886.06 (674.28-1337.39)	938.37 (586.78-1367.73)	0.76	<0.0001	<0.0001	0.80	<0.0001	<0.0001
NCR1	14.57 (12.02-18.01)	11.63 (9.37-14.23)	10.12 (8.27-12.53)	0.80	<0.0001	<0.0001	0.69	<0.0001	<0.0001
TNFRSF4	26.63 (22.81-31.37)	21.85 (18.42-27.95)	21.90 (17.85-27.63)	0.82	<0.0001	<0.0001	0.82	<0.0001	<0.0001
TNFSF14	140.12 (91.45-210.43)	117.88 (76.88-185.51)	116.26 (84.07-164.84)	0.84	0.0003	0.0010397	0.83	0.0001	0.0002
TWEAK	1031.16 (868.16-1186.18)	872.11 (762.15-1009.09)	889.01 (761.36-1018.81)	0.85	<0.0001	<0.0001	0.86	<0.0001	<0.0001
IL7	96.82 (74.47-127.65)	85.91 (66.26-109.86)	84.68 (65.48-103.35)	0.89	<0.0001	0.0002	0.87	<0.0001	<0.0001
HGF	684.74 (566.67-840.30)	632.71 (533.60-775.66)	612.32 (513.02-734.06)	0.92	0.00162	0.0050	0.89	<0.0001	<0.0001
HO1	7742.15 (6288.28-8830.06)	7200.42 (5827.13-8554.93)	4844.86 (2283.44-6817.24)	0.93	0.0164	0.0390	0.63	<0.0001	<0.0001
TNFRSF21	548.59 (497.35-598.66)	511.27 (456.66-583.68)	489.92 (435.65-557.77)	0.93	<0.0001	<0.0001	0.89	<0.0001	<0.0001
ANG1	2480.61 (2221.52-2734.09)	2397.11 (2139.86-2647.99)	2351.09 (2033.01-2626.74)	0.97	0.0154	0.0378	0.95	0.0003	0.0004

Medians were compared using two-sided Wilcoxon rank sum tests.

†The q-values represent FDR-adjusted p-values for multiple-testing.

Supplementary Table 10. Serum proteins grouped by biological process

Apoptosis	Autophagy	Chemotaxis	Promote TI	Suppress TI	Vasculature
Gal9	ADA	CCL17	CX3CL1	CXCL11	CXCL11
TNFRSF12A	CAIX	CCL19	CXCL10	CXCL13	CXCL1
TWEAK	HO1	CCL20	CXCL11	CD4	CXCL5
MMP7		CCL23	CXCL13	CD5	IL8
CD40L		CCL3	CD40L	IL18	MCP4
TRAIL		CCL4	TRAIL	IL6	Gal9
CASP8		CX3CL1	CD244	CCL17	Gal1
FASLG		CXCL1	CD27	CCL19	MMP12
GZMA		CXCL10	CD28	CCL20	CXCL10
GZMB		CXCL11	CD4	CXCL1	CXCL9
GZMH		CXCL13	CD40	CXCL5	CCL23
TNFRSF21		CXCL5	CD5	IL8	MCP1
		IL8	CD70	MCP4	CAIX
		MCP1	CD83	Gal9	TNFRSF12A
		MCP2	CD8A	MMP7	TWEAK
		MCP3	CRTAM	CSF1	ADGRG1
		MCP4	CXCL9	Gal1	ANG1
			ICOSLG	IL10	ANGPT2
			IL12RB1	IL4	DCN
			IL18	IL5	EGF
			IL6	LAMP3	FGF2
			IL7	LAPTGFbeta1	HGF
			KLRD1	MICAB	IL12
			NCR1	MMP12	NOS3
			TNFRSF4	PDCD1	PDGFsubunitB
			TNFRSF9	PDL1	PGF
			TNFSF14	PDL2	PTN
				ARG1	TIE2
					VEGFA
					VEGFC
					VEGFR2

Supplementary Table 11. Effect of biological processes scores on all-cause mortality of prostate cancer patients

Biological Processes score	Unadjusted Hazard Ratio (95%CI)	p-value	q-value	*Adjusted Hazard Ratio (95%CI)	*Adjusted Hazard Ratio (99%CI)	p-value	[†] q-value
Apoptosis score	0.75 (0.35, 1.59)	0.449	0.659	0.94 (0.43, 2.06)	0.94 (0.34, 2.64)	0.881	0.969
Autophagy score	1.12 (0.78, 1.61)	0.549	0.659	0.92 (0.62, 1.34)	0.92 (0.55, 1.52)	0.651	0.969
Chemotaxis score	0.57 (0.25, 1.30)	0.180	0.539	0.46 (0.18, 1.17)	0.46 (0.13, 1.57)	0.102	0.306
Promote Tumor Immunity Score	0.93 (0.49, 1.78)	0.829	0.829	0.95 (0.46, 1.94)	0.95 (0.37, 2.44)	0.883	0.969
Suppress Tumor Immunity Score	5.66 (2.07, 15.48)	0.001	0.004	5.96 (1.87, 18.95)	5.96 (1.30, 27.26)	0.002	0.012
Vasculature score	1.46 (0.58, 3.69)	0.421	0.659	1.02 (0.38, 2.75)	1.02 (0.28, 3.76)	0.969	0.969

Two-sided multivariable Cox regression analyses were used to assess if the pathways were independently associated with survival.

*Hazard ratios were adjusted for age, BMI, race/ethnicity, education level, income level, smoking status, diabetes status, aspirin use, treatment type, and NCCN risk score.

[†]The q-values represent FDR-adjusted p-values for multiple testing of n=6.

Supplementary Table 12. Effect of biological processes scores on all-cause mortality of population controls

Biological Processes scores	Unadjusted Hazard Ratio (95%CI)	p-value	q-value	*Adjusted Hazard Ratio (95%CI)	*Adjusted Hazard Ratio (99%CI)	p-value	†q-value
Apoptosis score	0.27 (0.10, 0.75)	0.012	0.059	0.47 (0.16, 1.33)	0.47 (0.12, 1.84)	0.153	0.458
Autophagy score	1.19 (0.76, 1.87)	0.457	0.457	1.25 (0.79, 2.00)	1.25 (0.68, 2.31)	0.344	0.516
Chemotaxis score	0.40 (0.15, 1.11)	0.078	0.117	0.77 (0.24, 2.42)	0.77 (0.17, 3.48)	0.649	0.779
Promote Tumor Immunity Score	2.84 (1.18, 6.81)	0.020	0.059	2.04 (0.82, 5.07)	2.04 (0.61, 6.75)	0.127	0.458
Suppress Tumor Immunity Score	3.60 (0.90, 14.44)	0.071	0.117	2.19 (0.48, 9.96)	2.19 (0.30, 16.03)	0.310	0.516
Vasculature score	2.74 (0.70, 10.76)	0.148	0.178	1.12 (0.25, 5.10)	1.12 (0.15, 8.21)	0.866	0.886

Two-sided multivariable Cox regression analyses were used to assess if the pathways were independently associated with survival.

*The hazard ratio was adjusted for age, BMI, education level, smoking status, diabetes status, aspirin use, income level, and race/ethnicity.

†The q-values represent FDR-adjusted p-values for multiple testing of n=6.

Supplementary Table 13. Effect of biological processes scores on prostate cancer-specific mortality

Biological Processes scores	Unadjusted Hazard Ratio (95% CI)	p-value	q-value	*Adjusted Hazard Ratio (95% CI)	*Adjusted Hazard Ratio (99% CI)	p-value	†q-value
Apoptosis score	0.56 (0.13, 2.30)	0.417	0.787	0.92 (0.23, 3.73)	0.92 (0.15, 5.80)	0.907	0.907
Autophagy score	1.20 (0.60, 2.39)	0.601	0.787	1.08 (0.52, 2.24)	1.08(0.41, 2.81)	0.837	0.907
Chemotaxis score	1.38 (0.30, 6.42)	0.683	0.787	0.47 (0.08, 2.74)	0.47 (0.05, 4.77)	0.398	0.907
Promote Tumor Immunity Score	1.32 (0.39, 4.49)	0.652	0.787	0.70 (0.18, 2.69)	0.70 (0.12, 4.11)	0.607	0.907
Suppress Tumor Immunity Score	3.69 (0.55, 24.82)	0.179	0.787	11.94 (1.36, 105.21)	11.94 (0.68, 208.46)	0.026	0.156
Vasculature score	0.79 (0.14, 4.41)	0.787	0.787	0.50 (0.07, 3.70)	0.50 (0.04, 6.96)	0.493	0.907

Two-sided multivariable Cox regression analyses were used to assess if the pathways were independently associated with survival.

*Hazard ratios were adjusted for age, BMI, race/ethnicity, education level, income level, smoking status, diabetes status, aspirin use, treatment type, and NCCN risk score.

†The q-values represent FDR-adjusted p-values for multiple testing of n=6.

Supplementary Table 14. Effect of biological processes scores on mortality from any cancer following a diagnosis with prostate cancer

Biological Processes score	Unadjusted Hazard Ratio (95% CI)	p-value	q-value	*Adjusted Hazard Ratio (95% CI)	*Adjusted Hazard Ratio (99% CI)	p-value	[†] q-value
Apoptosis score	0.61 (0.21, 1.78)	0.365	0.849	0.83 (0.28, 2.47)	0.83 (0.20, 3.48)	0.733	0.957
Autophagy score	1.22 (0.73, 2.04)	0.437	0.849	1.01 (0.60, 1.72)	1.01(0.51, 2.03)	0.957	0.957
Chemotaxis score	0.73 (0.23, 2.34)	0.598	0.849	0.34 (0.09, 1.28)	0.34 (0.06, 1.94)	0.111	0.333
Promote Tumor Immunity Score	0.83 (0.32, 2.15)	0.708	0.849	0.66 (0.24, 1.85)	0.66 (0.17, 2.56)	0.428	0.856
Suppress Tumor Immunity Score	5.67 (1.38, 23.21)	0.016	0.095	11.86 (2.35, 59.93)	11.86 (1.41, 99.69)	0.003	0.018
Vasculature score	1.14 (0.31, 4.20)	0.849	0.849	0.87 (0.21, 3.67)	0.87 (0.13, 5.77)	0.852	0.957

Two-sided multivariable Cox regression analyses were used to assess if the pathways were independently associated with survival.

*Hazard ratios were adjusted for age, BMI, race/ethnicity, education level, income level, smoking status, diabetes status, aspirin use, treatment type, and NCCN risk score.

[†]The q-values represent FDR-adjusted p-values for multiple-testing of n=6.