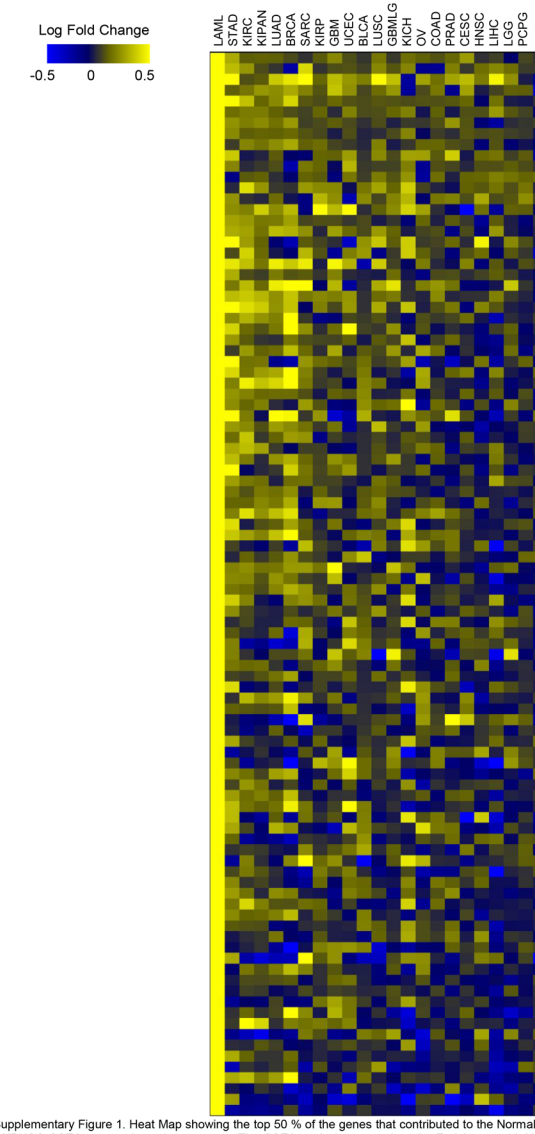

Supplementary Figure 1. Heat Map showing the top 50 % of the genes that contributed to the Normalized Enrichment Score (NES, refer Figure 1A) for the OXPHOS GSEA concept in each tumor type. The GSEA analysis summarizes the Enrichment with Normalized enrichment score (NES) statistics. In addition, it also ranks the genes that contributed to the Normalized enrichment score. Here, an average rank per gene was calculated for each of the 23 cancer types and the genes were ordered based on their average rank. Following this, the heat map was generated using the top 50 % of the average ranked genes in the OXPHOS pathway. The tumors in this heat map are arranged in columns. Rows represent the genes. Genes are arranged in the decreasing order of their expression across all the tumors. Shades of yellow and blue represent up and down regulated genes respectively (refer to color scale). Genes are arranged in the decreasing order of expression within each tumor type. LAML: Acute myeloid leukemia, STAD: Stomach adenocarcinoma, SARC: Sarcoma, HNSC: Head and neck squamous cell carcinoma, KIRC: Kidney renal clear cell carcinoma, LUSC: Lung squamous cell carcinoma, LUAD: Lung adenocarcinoma, LIHC: Live hepatocellular carcinoma, KIRP: Kidney renal papillary cell carcinoma, PRAD: Prostate adenocarcinoma, KICH: Kidney chromophobe, CESC: Cervical squamous cell carcinoma and endocervical adenocarcinoma, GBM: Glioblastoma multiforme, BLCA: Bladder cancer, KIPAN: Pan-kidney cohort, COAD: Colon adenocarcinoma, OV: Ovarian adenocarcinoma, BRCA: Breast cancer, LGG: Brain low grade glioma, GBMLGG: Glioblastoma multiforme low grade glioma, UCEC: Uterine corpus endometrial carcinoma, PCPG: Pheochromocytoma and paraganglioma, and THCA: Thyroid carcinoma.

Supplementary Table 1: Five and ten year survival rates for different cancer types (SEER database)

Cancer site	African-Americans		European-Americans	
	% survival (5y)	% survival (10y)	% survival (5y)	% survival (10y)
Bladder	**63.6**	**55.5**	77.9	70.4
Breast	**79.6**	**70.8**	90.4	84.7
Cervix	**58.1**	**53.2**	69.5	64.4
Colon	**56.1**	**49.8**	64.5	58.2
Brain	39.3	33.4	32.5	27.3
Head and neck	**44.7**	**35.7**	64.4	54.5
Kidney	**71.1**	**63.1**	72	64.3
Acute myeloid leukemia	26.1	23.8	24	21.5
Liver	**12.5**	**7.5**	15.8	11.2
Lung	**14.4**	**9.2**	17.2	11.4
Ovary	**37.2**	**29**	45.5	35.4
Prostate	**96.2**	**93**	98.8	98.2
Sarcoma	**56**	**47**	73.8	67.9
Stomach	28.2	23.3	26.9	22.4
Thyroid	**96.3**	**95.1**	97.9	97.5
Uterus	**61.2**	**55.5**	83.6	80.7

SEER- Surveillance Epidemiology and End Results.

- Survival rates that are lower in African Americans compared to European Americans are highlighted in red.
- Survival data indicates that African Americans perform poorly when compared to European Americans for most cancer types.
- Although the expected trend is not observed in acute myeloid leukemia, stomach cancer, and cancers of the brain, there is evidence in literature to show that racial disparity exists for these cancer types as well (1-5).

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Supplementary Table 3- Normalized enrichment scores for GSEA performed on five independent validation datasets

	BRCA	PRAD	PRAD	LUAD	COAD
Pathway	GSE37751	GSE64331	GSE6956	GSE101929	GSE28000
OXIDATIVE_PHOSPHORYLATION	1.32	6.98	4.3	1.46	-2.07
DNA_REPAIR	1.67	4.87	1.65	2.42	-2.03
G2M_CHECKPOINT	1.5	1.79	1.85	-2.24	-3.63
MTORC1_SIGNALING	1.43	5.07	1.51	1.68	-2.24
E2F_TARGETS	1.52	2.03	2.71	-1.78	-4.52
MITOTIC_SPINDLE	1.56	3.21	-1.58	-2.8	-2.61
MYC_TARGETS_V1	1.62	7.64	-2.59	2.04	-4.62
PROTEIN_SECRETION	NS	5.32	-2.34	-1.24	-2.07
MYC_TARGETS_V2	1.59	3.23	2.01	2.39	NS
UNFOLDED_PROTEIN_RESPONSE	1.57	5.37	1.66	2.2	-1.85
P53_PATHWAY	NS	3.39	1.87	-2.57	1.52
ADIPOGENESIS	NS	5.09	1.35	1.7	NS
PI3K_AKT_MTOR_SIGNALING	NS	4.25	NS	1.63	-1.57
REACTIVE_OXIGEN_SPECIES_PATHWA'	NS	2.7	2.45	1.62	NS
FATTY_ACID_METABOLISM	NS	3.61	NS	-3.38	NS
HEME_METABOLISM	NS	2.76	-1.39	-2.42	NS
CHOLESTEROL_HOMEOSTASIS	NS	2.67	-1.94	1.39	NS
UV_RESPONSE_DN	NS	2.81	NS	-3.56	-2.03
IL2_STAT5_SIGNALING	NS	3.5	3	-2.35	2.06
TNFA_SIGNALING_VIA_NFKB	NS	3.08	4.88	3.05	3.51

Cutoff for enrichment- P< 0.01, FDR <25%

Validate_GSEA_NES

Supplementary Table 6- P values for ERR1 and PGC1α enrichment across 23 cancer types

Cohort	P-value PGC1	p-value ERR1	significance(-log10(p-value)_PGC1	significance(-log10(p-value)_ERR1
CESC	1.22158E-05	9.71018E-39	4.913077666	38.0127725
GBM	3.58509E-05	1.67078E-32	4.445500221	31.77707994
GBMLGG	0.00000753	3.60237E-34	5.123205024	33.4434119
KICH	1.26973E-05	1.41416E-43	4.896288668	42.84950289
KIPAN	0.000456531	5.72679E-37	3.340530195	36.24208896
LAML	1.04406E-05	5.07233E-38	4.98127632	37.29479247
LGG	1.37083E-05	3.66251E-37	4.86301559	36.43622164
LIHC	9.3206E-05	3.18185E-40	4.03055634	39.49731981
PCPG	0.000354548	4.96741E-38	3.450324691	37.30386996
PRAD	1.26973E-05	2.56251E-42	4.896288668	41.59133442
STAD	9.2565E-06	5.07233E-38	5.033552967	37.29479247
SARC	0.0000871	6.91563E-41	4.059981845	40.16016838
UCEC	8.1309E-05	1.46601E-44	4.089861607	43.83386419
THCA	8.416E-05	3.79482E-38	4.074894183	37.42080887
OV	1.31947E-05	6.10262E-41	4.879601676	40.21448389
LUSC	1.12988E-05	5.42979E-39	4.946966162	38.26521731
LUAD	7.32246E-05	1.99812E-42	4.135343287	41.69937843
KIRP	4.71499E-05	2.72747E-40	4.326518999	39.56424003
KIRC	0.000403025	1.71791E-37	3.394667487	36.76499931
HNSC	0.0000127	2.56E-42	4.896196279	41.59176003
COAD	1.65363E-05	6.94781E-44	4.781561518	43.15815196
BRCA	1.65363E-05	5.72679E-37	4.781561518	36.24208896
BLCA	0.0000154	6.69E-43	4.812479279	42.17457388

Supplementary Table 7: Summarized clinical information for prostate cancer samples in the TMA

Variable	African Americans	European Americans	P value
Age	59.9 ± 6.7	62 ± 6.3	0.22246
Body mass index	27.2 ± 3.7	26.5 ± 3.7	0.34722
Pre-operative PSA	6.2 ± 16.5	7.2 ± 10.8	0.34722
Biopsy Gleason score	7 ± 0.9	7 ± 0.6	0.6672
Prostatectomy Gleason score	7 ± 0.7	7 ± 0.5	0.4777
Lymph nodes	0 lymph nodes: 42	0 lymph nodes: 36	0.914217
	1 lymph node: 1	1 lymph node: 1	
Seminal vesicle invasion	Absent: 37	Absent: 32	0.954565
	Present: 6	Present: 5	
Smoking	Smokers: 25	Smokers: 20	0.713419
	Non-smokers: 18	Non-smokers: 17	
Recurrence*	Absent: 28		
	Present: 15	Present: 12	
Prostate cancer associated death	Dead: 1	Dead: -	
	Alive: 42	Alive: 37	

- African Americans (AA): n=53, European Americans (EA): n=51.
- Age, body mass index, PSA, and Gleason scores represented as Median ± Standard Deviation.
- *Data missing for 39 EA patients for recurrence and 51 EA patients for status.
- Data missing for 10 AA and 14 EA patients for all other parameters.
- P values for age, body mass index, PSA, and Gleason scores were calculated using the Wilcoxon rank sum test. A P value< 0.05 was considered significant.
- Data for lymph nodes, seminal vesical invasion, smoking, recurrence and prostate cancer associated death represent number of patients.
- P values for all other frequency variables were calculated using the Chi-Squared test. A P value <0.05 was considered significant.

Supplementary Table 8: Summarized clinical information for laryngeal cancer samples in the TMA

Variable	African Americans	European Americans	P value
Age	67 ± 6.1	57 ± 7.4	0.0018
Gender	Male: 10	Male: 16	0.347627
	Female: 2	Female: 1	
Stage	Stage 2: 1	Stage 2: 3	0.322379
	Stage 3: 2	Stage 3: 6	
	Stage 4: 9	Stage 4: 8	
Lymph nodes	0 lymph nodes: 7	0 lymph nodes: 12	0.350045
	2 lymph nodes: 5	2 lymph nodes: 4	
		3 lymph nodes: 1	
Smoking*	Smokers: 11	Smokers: 16	
		Non-smokers: 1	
Alcohol consumption*	Drinkers: 8	Drinkers: 14	0.544356
	Non-drinkers: 3	Non-drinkers: 3	
Radiation*	Received radiation: 9	Received radiation: 13	0.736268
	No radiation: 2	No radiation: 4	
Status*	Dead: 8	Dead: 12	0.90261
	Alive: 3	Alive: 5	

- African Americans (AA): n=12, European Americans (EA): n=17.
- Age represented as Median ± Standard Deviation.
- * Data missing for one AA patient for these parameters.
- Data for gender, stage, lymph node, smoking, alcohol consumption, radiation and status represent number of patients.
- The P value for age was calculated using a two-tailed Wilcoxon rank sum test. A P value <0.05 was considered significant.
- P values for all other frequency variables were calculated using the Chi-Squared test. A P value <0.05 was considered significant.

Supplementary Table 9: Summarized clinical information for oral cancer samples in the TMA

Variable	African Americans	European Americans	P value
Age	55.5 ± 11.7	63 ± 7.9	0.06876
Gender	Male: 14	Male: 43	
	Female: -	Female: -	
Stage	Stage 1: 2	Stage 1: 9	0.95402
	Stage 2: 6	Stage 2: 16	
	Stage 3: 2	Stage 3: 6	
	Stage 4: 4	Stage 4: 12	
Lymph nodes	0 lymph nodes: 0	0 lymph nodes: 25	0.847516
	1 lymph nodes: 2	1 lymph nodes: 6	
	2 lymph nodes: 3	2 lymph nodes: 11	
	3 lymph nodes: -	3 lymph nodes: 1	
Primary Vs. recurrent	Primary: 13	Primary: 42	0.394866
	Recurrent: 1	Recurrent: 1	
Status	Dead: 13	Dead: 31	0.1077821
	Alive: 1	Alive: 12	

- African Americans (AA): n=14, European Americans (EA): n=43.
- Age represented as Median ± Standard Deviation.
- The P value for age was calculated using a two-tailed Wilcoxon rank sum test. A P value <0.05 was considered significant.
- Data for gender, stage, lymph node, recurrence and status represent number of patients.
- P values for all other variables were calculated using the Chi-Squared test. A P value <0.05 was considered significant.

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	NA
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	8
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	8
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	5
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	5
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	5
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	5
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	5
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	5
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	7
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	7
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	7
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	12

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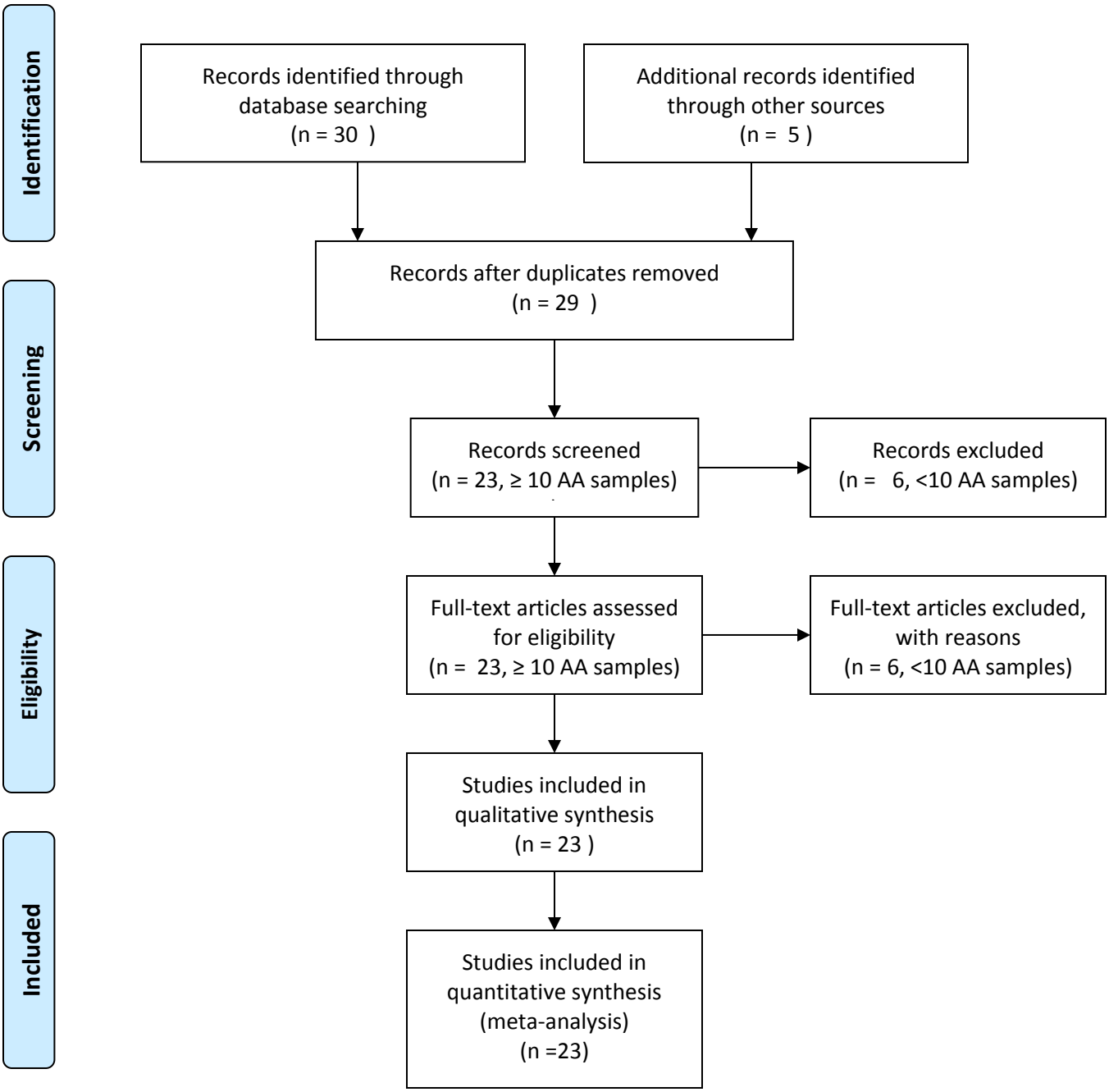
PRISMA 2009 Flow Diagram



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