

Supplementary Information

Genetic Insights into the Association Between Sunburn Susceptibility and Thoracic Aortic Aneurysm Through Integrated Genomic and Transcriptomic Analyses

Wenhai Pan^{1#}, Wei Xu^{1#}, Liuzexuan Sheng^{1#}, Yiming Zhong¹, Jiawen Zhang¹, Xiangyue Qian¹, Junyi Liang¹, Chenxi Shi¹, Yifan Chen^{1,2,3*}, Zhifen Chen^{2,3*}, Jun Pu^{1*}

¹ Division of Cardiology, State Key Laboratory for Systems Medicine for Cancer, Shanghai Cancer Institute, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China.

² Department of Cardiology, Deutsches Herzzentrum München, School of Medicine and Health, Technical University Munich, 80636 Munich, Germany.

³ Deutsches Zentrum für Herz- und Kreislau fforschung (DZHK), partner site Munich Heart Alliance (MHA), Munich, Germany.

* To whom correspondence should be addressed:

Yifan Chen, M.D., Ph.D.; Division of Cardiology, State Key Laboratory for Systems Medicine for Cancer, Shanghai Cancer Institute, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China. E-mail: yifanchen@sjtu.edu.cn.

Jun Pu, M.D., Ph.D.; Division of Cardiology, State Key Laboratory for Systems Medicine for Cancer, Shanghai Cancer Institute, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China. E-mail: pujun310@sjtu.edu.cn.

Or

Zhifen Chen, Ph.D.; Department of Cardiology, Deutsches Herzzentrum München, School of Medicine and Health, Technical University Munich, 80636 Munich, Germany. E-mail: zhifen.chen@tum.de.

These authors contributed equally as co-first authors.

Supplementary Table 1. Instrumental variants for genetically predicted sunburn susceptibility. Complete results are provided in **Supplementary Table 1**.

Instrumental variants selected for the main two-sample Mendelian randomization analysis of genetically predicted sunburn susceptibility and thoracic aortic aneurysm, including SNP identifiers, harmonized alleles, effect estimates, standard errors, P values, and instrument-strength metrics.

Column definitions:

Column	Definition
exposure	Exposure trait name.
SNP	Single nucleotide polymorphism identifier.
chr	Chromosome.
pos	Genomic position of the variant.
effect_allele	Effect allele for the exposure GWAS association.
other_allele	Non-effect allele for the exposure GWAS association.
effect_allele_frequency	Frequency of the effect allele.
beta	Regression coefficient from the GWAS or PheWAS association.
se	Standard error.
p_value	P value.
Variation_type	Variant type.
minor_allele_frequency	Minor allele frequency.
F_statistic	F statistic used to assess instrumental-variable strength.

Supplementary Table 2. Main Mendelian randomization and sensitivity analyses using 54 instrumental variants. (A) MR effect estimates from the primary IVW model and complementary robust MR models. **(B)** Cochran heterogeneity tests for SNP-specific MR estimates. **(C)** MR-Egger intercept test for directional horizontal pleiotropy. **(D)** Steiger directionality test evaluating the assumed exposure-to-outcome direction. **(E)** MR-PRESSO global and outlier test results for pleiotropy detection. **(F)** Leave-one-out MR sensitivity results assessing single-SNP influence. **(G)** Single-SNP Wald-ratio MR estimates. Complete results are provided in **Supplementary Table 2**.

A

MR effect estimates from the primary inverse-variance weighted model and complementary robust MR models, used to evaluate the association between genetically predicted sunburn susceptibility and thoracic aortic aneurysm risk.

Column definitions:

Column	Definition
id.exposure	Unique identifier for the exposure trait.
id.outcome	Unique identifier for the outcome trait.
outcome	Outcome trait name.
exposure	Exposure trait name.
method	MR method.
nsnp	Number of SNPs included in the MR model.
b	MR effect estimate on the log odds scale.
se	Standard error.
pval	P value.
OR	Odds ratio.
OR_lci95	Lower bound of the 95% confidence interval for the odds ratio.
OR_uci95	Upper bound of the 95% confidence interval for the odds ratio.

B

Cochran heterogeneity statistics for the MR models, used to assess whether SNP-specific causal estimates showed excess variability beyond that expected by chance.

Column definitions:

Column	Definition
id.exposure	Unique identifier for the exposure trait.
id.outcome	Unique identifier for the outcome trait.
outcome	Outcome trait name.
exposure	Exposure trait name.
method	MR method.
Q	Cochran Q statistic for heterogeneity.
Q_df	Degrees of freedom for Cochran Q statistic.
Q_pval	P value for Cochran Q statistic.

C

MR-Egger intercept test results, used to evaluate directional horizontal pleiotropy among the instrumental variants.

Column definitions:

Column	Definition
id.exposure	Unique identifier for the exposure trait.
id.outcome	Unique identifier for the outcome trait.
outcome	Outcome trait name.
exposure	Exposure trait name.
egger_intercept	MR-Egger intercept estimate.
se	Standard error.
pval	P value.

D

Steiger directionality test results, used to examine whether the genetic instruments explained more variance in sunburn susceptibility than in thoracic aortic aneurysm and therefore supported the assumed exposure-to-outcome direction.

Column definitions:

Column	Definition
id.exposure	Unique identifier for the exposure trait.
id.outcome	Unique identifier for the outcome trait.
exposure	Exposure trait name.
outcome	Outcome trait name.
snp_r2.exposure	Variance in the exposure explained by the SNPs.
snp_r2.outcome	Variance in the outcome explained by the SNPs.
correct_causal_direction	Indicator for whether Steiger filtering supports the exposure-to-outcome direction.
steiger_pval	P value from the Steiger directionality test.

E

MR-PRESSO global and outlier test results, used to detect horizontal pleiotropy and identify potential outlier SNPs that might disproportionately influence the MR association.

Column definitions:

Column	Definition
test	MR-PRESSO test component, including the main MR regression result or the global pleiotropy test.
result_type	Type of MR-PRESSO result, such as raw estimate, outlier-corrected estimate, or global test.
beta	MR-PRESSO regression coefficient for genetically predicted

	sunburn susceptibility, when applicable.
se	Standard error of the MR-PRESSO regression coefficient, when applicable.
t_statistic	MR-PRESSO test statistic for the regression coefficient, when applicable.
p_value	P value for the corresponding MR-PRESSO estimate or global test.
RSSobs	Observed residual sum of squares from the MR-PRESSO global test.

F

Leave-one-out MR sensitivity results, showing the IVW estimate after sequentially removing each instrumental SNP to evaluate whether the main association was driven by a single variant.

Column definitions:

Column	Definition
exposure	Exposure trait name.
outcome	Outcome trait name.
id.exposure	Unique identifier for the exposure trait.
id.outcome	Unique identifier for the outcome trait.
samplesize	Sample size for the corresponding GWAS summary dataset.
SNP	Single nucleotide polymorphism identifier.
b	MR effect estimate on the log odds scale.
se	Standard error.
p	P value.
OR	Odds ratio.
OR_lci95	Lower bound of the 95% confidence interval for the odds ratio.
OR_uci95	Upper bound of the 95% confidence interval for the odds ratio.

G

Single-SNP MR estimates, showing the Wald-ratio association for each instrumental variant and supporting visualization of variant-level effect consistency.

Column definitions:

Column	Definition
exposure	Exposure trait name.
outcome	Outcome trait name.
id.exposure	Unique identifier for the exposure trait.
id.outcome	Unique identifier for the outcome trait.
samplesize	Sample size for the corresponding GWAS summary dataset.
SNP	Single nucleotide polymorphism identifier.
b	MR effect estimate on the log odds scale.
se	Standard error.

p	P value.
OR	Odds ratio.
OR_lci95	Lower bound of the 95% confidence interval for the odds ratio.
OR_uci95	Upper bound of the 95% confidence interval for the odds ratio.

Supplementary Table 3. Mendelian randomization after excluding pigmentation and tanning related SNPs. (A) MR effect estimates after excluding 11 pigmentation and tanning related SNPs. (B) Cochran heterogeneity tests in the restricted 43-SNP instrument set. (C) MR-Egger intercept test for residual directional pleiotropy after SNP exclusion. Complete results are provided in **Supplementary Table 3**.

A

MR effect estimates after excluding 11 pigmentation and tanning related SNPs, used to assess whether the observed association was primarily driven by pigmentation and tanning response genetic architecture.

Column definitions:

Column	Definition
id.exposure	Unique identifier for the exposure trait.
id.outcome	Unique identifier for the outcome trait.
outcome	Outcome trait name.
exposure	Exposure trait name.
method	MR method.
nsnp	Number of SNPs included in the MR model.
b	MR effect estimate on the log odds scale.
se	Standard error.
pval	P value.
OR	Odds ratio.
OR_lci95	Lower bound of the 95% confidence interval for the odds ratio.
OR_uci95	Upper bound of the 95% confidence interval for the odds ratio.

B

Cochran heterogeneity statistics after excluding pigmentation and tanning related SNPs, used to evaluate residual heterogeneity in the restricted 43-SNP instrument set.

Column definitions:

Column	Definition
id.exposure	Unique identifier for the exposure trait.
id.outcome	Unique identifier for the outcome trait.
outcome	Outcome trait name.
exposure	Exposure trait name.
method	MR method.
Q	Cochran Q statistic for heterogeneity.
Q_df	Degrees of freedom for Cochran Q statistic.
Q_pval	P value for Cochran Q statistic.

C

MR-Egger intercept test results after excluding pigmentation and tanning related SNPs, used to assess residual directional pleiotropy in the restricted 43-SNP analysis.

Column definitions:

Column	Definition
id.exposure	Unique identifier for the exposure trait.
id.outcome	Unique identifier for the outcome trait.
outcome	Outcome trait name.
exposure	Exposure trait name.
egger_intercept	MR-Egger intercept estimate.
se	Standard error.
pval	P value.

Supplementary Table 4. PheWAS and Visconti-based identification of pigmentation and tanning related SNPs. (A) PheWAS records flagged as pigmentation, tanning, skin color, other pigmentation-related traits, skin cancer, vitamin D, or lifestyle related. (B) Pigmentation and tanning response loci from Visconti et al. 2018. (C) The 11 excluded SNPs in GWAS summary format. Complete results are provided in **Supplementary Table 4**.

A

PheWAS records flagged as pigmentation, tanning, skin color, other pigmentation-related traits, skin cancer, vitamin D, or lifestyle related, used to characterize the phenotypic profile of the instrumental variants and identify potential pleiotropic loci.

Column definitions:

Column	Definition
query_snp	Queried SNP identifier used for PheWAS lookup.
id	PheWAS trait or association identifier.
trait	PheWAS trait name.
chr	Chromosome.
position	Genomic position of the variant.
rsid	Reference SNP identifier returned by the PheWAS source.
ea	Effect allele.
nea	Non-effect allele.
eaf	Effect allele frequency.
beta	Regression coefficient from the GWAS or PheWAS association.
se	Standard error.
p	P value.
n	Sample size or number of observations.
trait_l	Lowercase trait name used for keyword flagging.
flagged_keyword	Keyword category that triggered phenotype flagging.
flagged	Indicator for whether the PheWAS association was flagged.

B

Pigmentation and tanning response loci reported by Visconti et al. 2018, used as an external literature-based reference set for identifying pigmentation and tanning related variants among the sunburn susceptibility instruments.

Column definitions:

Column	Definition
gene	Gene symbol.
rationale	Rationale for including the gene or locus.
primary_support	Primary source supporting the gene or locus.

C

The 11 pigmentation and tanning related SNPs excluded from the sensitivity MR analysis, formatted as a GWAS summary table for transparent reporting of the restricted-instrument analysis.

Column definitions:

Column	Definition
exposure	Exposure trait name.
SNP	Single nucleotide polymorphism identifier.
chr	Chromosome.
pos	Genomic position of the variant.
effect_allele	Effect allele for the exposure GWAS association.
other_allele	Non-effect allele for the exposure GWAS association.
effect_allele_frequency	Frequency of the effect allele.
beta	Regression coefficient from the GWAS or PheWAS association.
se	Standard error.
p_value	P value.
Variation_type	Variant type.
minor_allele_frequency	Minor allele frequency.

Supplementary Table 5. FUMA SNP2GENE annotation and Gene2Func tissue enrichment. (A) Summary of FUMA SNP2GENE mapping. **(B)** FUMA mapped genes and mapping evidence. **(C)** Gene2Func GTEx tissue enrichment results restricted to study-relevant tissues. Complete results are provided in **Supplementary Table 5**.

A

Summary of FUMA SNP2GENE mapping results for the sunburn susceptibility GWAS loci, including the numbers of independent significant SNPs, candidate SNPs, genomic risk loci, and mapped genes.

Column definitions:

Column	Definition
metric	Summary metric.
value	Reported value for the corresponding item.

B

FUMA mapped genes and their supporting annotation evidence, including positional mapping, eQTL mapping, and chromatin interaction mapping where available.

Column definitions:

Column	Definition
ensg	Ensembl gene identifier.
symbol	Gene symbol.
chr	Chromosome.
start	Gene start position.
end	Gene end position.
strand	Genomic strand.
type	Gene biotype.
entrezID	Entrez Gene identifier.
HUGO	HUGO gene symbol.
pLI	Probability of loss-of-function intolerance.
ncRVIS	Noncoding residual variation intolerance score.
posMapSNPs	Number of SNPs mapped to the gene by FUMA positional mapping.
posMapMaxCADD	Maximum CADD score among positionally mapped SNPs.
eqtlMapSNPs	Number of SNPs mapped to the gene by FUMA eQTL mapping.
eqtlMapminP	Minimum P value from FUMA eQTL mapping.
eqtlMapminQ	Minimum q value from FUMA eQTL mapping.
eqtlMapts	Tissues supporting FUMA eQTL mapping.
eqtlDirection	Direction of effect in FUMA eQTL mapping.
ciMap	Indicator for FUMA chromatin interaction mapping.
ciMapts	Tissues supporting FUMA chromatin interaction mapping.
minGwasP	Minimum GWAS P value among SNPs mapped to the gene.
IndSigSNPs	Independent significant SNPs assigned by FUMA.

GenomicLocus	FUMA genomic locus identifier.
mapped_by_pos	Indicator for FUMA positional mapping support.
mapped_by_eqtl	Indicator for FUMA eQTL mapping support.
mapped_by_ci	Indicator for FUMA chromatin interaction mapping support.
mapping_type	Combined FUMA SNP2GENE evidence type supporting the mapped gene, derived row-by-row from positional mapping, eQTL mapping, and chromatin interaction mapping indicators.

C

FUMA Gene2Func GTEx tissue enrichment results restricted to artery, skin, fibroblast, and whole-blood tissues relevant to the vascular and cutaneous components of the study.

Column definitions:

Column	Definition
Category	Gene-set category.
GeneSet	Gene set or tissue label.
N_genes	Number of genes in the gene set.
N_overlap	Number of overlapping genes.
GeneRatio	Ratio of overlapping genes to the query gene set.
p	P value.
adjP	Adjusted P value.
neglog10P	Negative log10-transformed P value.

Supplementary Table 6. GTEx eQTL support for MR instrumental variants. (A) Selected GTEx tissue summary for direct MR SNP eQTL support. **(B)** Direct eQTL records involving the 54 MR instrumental SNPs. Complete results are provided in **Supplementary Table 6**.

A

Selected GTEx tissue summary of direct eQTL support for the 54 MR instrumental SNPs, summarizing whether sunburn susceptibility instruments were associated with gene expression in artery, skin, fibroblast, or whole-blood tissues.

Column definitions:

Column	Definition
tissue	GTEx tissue.
n_direct_mr_snp_eqtl_pairs	Number of direct MR SNP eQTL pairs.
n_unique_mr_snps	Number of unique MR SNPs with eQTL support.
n_unique_eqtl_genes	Number of unique eQTL-supported genes.
min_p	Minimum P value.

B

Direct GTEx eQTL records involving the 54 MR instrumental SNPs in selected study-relevant tissues, used to connect genetic instruments with tissue-specific regulatory effects.

Column definitions:

Column	Definition
rsID	Reference SNP identifier.
variant_id	Variant identifier in GRCh38 format.
variant_id_b37	Variant identifier in GRCh37 format.
chr	Chromosome.
variant_pos	Genomic position of the variant in GRCh38.
ref	Reference allele.
alt	Alternative allele.
symbol	Gene symbol.
ensg_clean	Ensembl gene identifier without version suffix.
gene_id	Ensembl gene identifier used in GTEx.
gtex_gene_name	GTEx gene symbol.
tissue	GTEx tissue.
tissue_n	Sample size for the GTEx tissue.
tss_distance	Distance from variant to transcription start site.
maf	Minor allele frequency.
pval_nominal	Nominal GTEx eQTL P value.
slope	GTEx eQTL effect estimate.
slope_se	Standard error of the GTEx eQTL effect estimate.

neg_log10_p
abs_slope

Negative log10-transformed P value.
Absolute value of the GTEx eQTL slope.

Supplementary Table 7. Integrated FUMA SNP and GTEx eQTL links. Complete results are provided in **Supplementary Table 7**.

Integrated eQTL records involving FUMA candidate SNPs in selected GTEx tissues, used to link FUMA-annotated loci with regulatory evidence in artery, skin, fibroblast, and whole-blood tissues.

Column definitions:

Column	Definition
rsID	Reference SNP identifier.
variant_id	Variant identifier in GRCh38 format.
variant_id_b37	Variant identifier in GRCh37 format.
chr	Chromosome.
variant_pos	Genomic position of the variant in GRCh38.
ref	Reference allele.
alt	Alternative allele.
is_instrument_snp	Indicator for whether the variant is one of the 54 MR instrumental SNPs.
is_fuma_snp	Indicator for whether the variant is a FUMA candidate SNP.
fuma_symbol	Gene symbol assigned by FUMA.
symbol	Gene symbol.
ensg_clean	Ensembl gene identifier without version suffix.
gene_id	Ensembl gene identifier used in GTEx.
tissue	GTEx tissue.
tissue_n	Sample size for the GTEx tissue.
tss_distance	Distance from variant to transcription start site.
maf	Minor allele frequency.
pval_nominal	Nominal GTEx eQTL P value.
slope	GTEx eQTL effect estimate.
slope_se	Standard error of the GTEx eQTL effect estimate.
neg_log10_p	Negative log10-transformed P value.
abs_slope	Absolute value of the GTEx eQTL slope.
eqtl_class	Class of eQTL support.

Supplementary Table 8. Transcriptomic analyses of UV-treated skin and TAAD aortic tissue. (A) ssGSEA summary for MSigDB UV-response gene sets in TAAD aorta. **(B)** Directionality of the 155 overlapping DEGs identified using $|\log_2 \text{ fold change}| > 0.8$ and nominal $P < 0.05$. **(C)** UV-treated skin DEGs defined using $|\log_2 \text{ fold change}| > 0.8$ and nominal $P < 0.05$. **(D)** TAAD aorta DEGs defined using $|\log_2 \text{ fold change}| > 0.8$ and nominal $P < 0.05$. **(E)** FDR-significant UV-treated skin DEGs. **(F)** FDR-significant TAAD aorta DEGs. **(G)** 29 FDR-defined overlapping DEGs and expression directions. Complete results are provided in **Supplementary Table 8**.

A

ssGSEA summary for MSigDB UV-response gene sets in TAAD aortic samples and controls, used to evaluate whether UV-response transcriptional programs were detectable in aortic disease tissue.

Column definitions:

Column	Definition
signature	MSigDB UV-response gene set signature.
n_genes	Number of genes in the signature.
control_mean	Mean ssGSEA score in controls.
TAAD_mean	Mean ssGSEA score in TAAD samples.
TAAD_minus_control	Difference in ssGSEA score between TAAD and controls.
p_value	P value.
FDR	False discovery rate.

B

Directionality summary for the 155 overlapping differentially expressed genes between UV-treated skin and TAAD aortic tissue, classifying genes by concordant or opposite expression changes across the two datasets.

Column definitions:

Column	Definition
gene	Gene symbol.
logFC_skin	Log2 fold change in UV-treated skin.
P_skin	P value in UV-treated skin.
FDR_skin	False discovery rate in UV-treated skin.
direction_skin	Direction of expression change in UV-treated skin.
logFC_aorta	Log2 fold change in TAAD aorta.
P_aorta	P value in TAAD aorta.
FDR_aorta	False discovery rate in TAAD aorta.
direction_aorta	Direction of expression change in TAAD aorta.
concordance	Expression-direction relationship between UV-treated skin and

TAAD aorta.

C

Differentially expressed genes in the UV-treated skin dataset defined using $|\log_2 \text{ fold change}| > 0.8$ and nominal $P < 0.05$, used as the cutaneous UV-response transcriptomic input for exploratory overlap analysis.

Column definitions:

Column	Definition
gene	Gene symbol.
logFC	Log2 fold change.
AveExpr	Average expression.
t	Moderated t statistic from differential expression analysis.
P.Value	P value from differential expression analysis.
adj.P.Val	Adjusted P value from differential expression analysis.
B	Log odds of differential expression.
dataset	Expression dataset.
direction_skin	Direction of expression change in UV-treated skin.

D

Differentially expressed genes in the TAAD aortic tissue dataset defined using $|\log_2 \text{ fold change}| > 0.8$ and nominal $P < 0.05$, used as the aortic disease transcriptomic input for exploratory overlap analysis.

Column definitions:

Column	Definition
gene	Gene symbol.
logFC	Log2 fold change.
AveExpr	Average expression.
t	Moderated t statistic from differential expression analysis.
P.Value	P value from differential expression analysis.
adj.P.Val	Adjusted P value from differential expression analysis.
B	Log odds of differential expression.
dataset	Expression dataset.
direction_aorta	Direction of expression change in TAAD aorta.

E

FDR-significant differentially expressed genes in the UV-treated skin dataset, used as the cutaneous UV-response transcriptomic input for strict overlap analysis.

Column definitions:

Column	Definition
gene	Gene symbol.
logFC	Log2 fold change.

AveExpr	Average expression.
t	Moderated t statistic from differential expression analysis.
P.Value	P value from differential expression analysis.
adj.P.Val	Adjusted P value from differential expression analysis.
B	Log odds of differential expression.
dataset	Expression dataset.
direction_skin	Direction of expression change in UV-treated skin.

F

FDR-significant differentially expressed genes in the TAAD aortic tissue dataset, used as the aortic disease transcriptomic input for strict overlap analysis.

Column definitions:

Column	Definition
gene	Gene symbol.
logFC	Log2 fold change.
AveExpr	Average expression.
t	Moderated t statistic from differential expression analysis.
P.Value	P value from differential expression analysis.
adj.P.Val	Adjusted P value from differential expression analysis.
B	Log odds of differential expression.
dataset	Expression dataset.
direction_aorta	Direction of expression change in TAAD aorta.

G

29 FDR-defined overlapping differentially expressed genes shared by UV-treated skin and TAAD aortic tissue, with expression directions in each dataset for cross-tissue comparison.

Column definitions:

Column	Definition
gene	Gene symbol.
logFC_skin	Log2 fold change in UV-treated skin.
FDR_skin	False discovery rate in UV-treated skin.
direction_skin	Direction of expression change in UV-treated skin.
logFC_aorta	Log2 fold change in TAAD aorta.
FDR_aorta	False discovery rate in TAAD aorta.
direction_aorta	Direction of expression change in TAAD aorta.
concordance	Expression-direction relationship between UV-treated skin and TAAD aorta.

Supplementary Table 9. Functional enrichment and PPI hub-protein analyses for the updated transcriptomic workflow. **(A)** FDR-controlled GO enrichment results for the 155 overlapping DEGs. **(B)** FDR-controlled KEGG enrichment results for the 155 overlapping DEGs. **(C)** FDR-controlled GO enrichment results for the 29 FDR-defined overlapping DEGs. **(D)** STRING PPI hub proteins from the 155 overlapping DEGs, ranked by network degree. Complete results are provided in **Supplementary Table 9**.

A

FDR-controlled GO enrichment results for the 155 overlapping DEGs derived from UV-treated skin and TAAD aorta.

Column definitions:

Column	Definition
ONTOLOGY	GO ontology category.
ID	GO term identifier.
Description	GO term description.
GeneRatio	Ratio of overlapping genes to the query gene set.
BgRatio	Background gene ratio.
RichFactor	Ratio of overlapping genes to genes annotated to the term.
FoldEnrichment	Fold enrichment.
zScore	Enrichment z score.
pvalue	P value.
p.adjust	Multiple-testing adjusted P value.
qvalue	q value.
geneID	Genes contributing to the enriched term.
Count	Number of genes contributing to the term.
source_gene_set	Gene set used for enrichment analysis.

B

FDR-controlled KEGG enrichment results for the 155 overlapping DEGs derived from UV-treated skin and TAAD aorta.

Column definitions:

Column	Definition
category	KEGG pathway category.
subcategory	KEGG pathway subcategory.
ID	KEGG pathway identifier.
Description	KEGG pathway description.
GeneRatio	Ratio of overlapping genes to the query gene set.

BgRatio	Background gene ratio.
RichFactor	Ratio of overlapping genes to genes annotated to the pathway.
FoldEnrichment	Fold enrichment.
zScore	Enrichment z score.
pvalue	P value.
p.adjust	Multiple-testing adjusted P value.
qvalue	q value.
geneID	Genes contributing to the enriched pathway.
Count	Number of genes contributing to the pathway.
source_gene_set	Gene set used for enrichment analysis.

C

FDR-controlled GO enrichment results for the 29 overlapping DEGs identified under the stricter FDR-based DEG threshold.

Column definitions:

Column	Definition
ONTOLOGY	GO ontology category.
ID	GO term identifier.
Description	GO term description.
GeneRatio	Ratio of overlapping genes to the query gene set.
BgRatio	Background gene ratio.
RichFactor	Ratio of overlapping genes to genes annotated to the term.
FoldEnrichment	Fold enrichment.
zScore	Enrichment z score.
pvalue	P value.
p.adjust	Multiple-testing adjusted P value.
qvalue	q value.
geneID	Genes contributing to the enriched term.
Count	Number of genes contributing to the term.
source_gene_set	Gene set used for enrichment analysis.

D

STRING protein-protein interaction hub proteins from the 155 overlapping DEGs, ranked by network degree to highlight highly connected proteins within the broader cross-tissue transcriptomic signal.

Column definitions:

Column	Definition
gene	Gene symbol.
degree	Node degree in the STRING PPI network.
logFC_skin	Log2 fold change in UV-treated skin.
logFC_aorta	Log2 fold change in TAAD aorta.

concordance	Expression-direction relationship between UV-treated skin and TAAD aorta.
-------------	---

Supplementary Table 10. Final exploratory anchored candidate genes. Complete results are provided in **Supplementary Table 10**.

Evidence matrix for HYAL1 and PREPL, the exploratory anchored DEG candidates supported by FUMA SNP2GENE annotation, GTEx eQTL evidence, nominally significant UV-treated skin differential expression, and nominally significant TAAD aortic differential expression.

Column definitions:

Column	Definition
symbol	Gene symbol.
ensg	Ensembl gene identifier.
chr	Chromosome.
FUMA_SNP2GENE	Indicator for FUMA SNP2GENE mapping support.
anchored_GTEx_eQTL_support	Indicator for GTEx eQTL support anchored to MR SNPs or FUMA candidate SNPs.
direct_MR_SNP_eQTL_support	Indicator for direct eQTL support from one of the 54 MR SNPs.
FUMA_SNP_eQTL_support	Indicator for eQTL support from a FUMA candidate SNP.
DEG_UV	Indicator for differential expression in UV-treated skin under the exploratory threshold.
DEG_TAAD	Indicator for differential expression in TAAD aorta under the exploratory threshold.
UV_FDR_DEG	Indicator for FDR-significant differential expression in UV-treated skin.
TAAD_FDR_DEG	Indicator for FDR-significant differential expression in TAAD aorta.
UV_TAAD_opposite	Indicator for opposite expression directions between UV-treated skin and TAAD aorta.
four_evidence_gene	Indicator for support across FUMA mapping, anchored GTEx eQTL, UV skin DEG, and TAAD aorta DEG under the exploratory threshold.
anchored_opposite_candidate	Indicator for exploratory four-evidence support plus opposite expression direction.
evidence_count	Number of evidence categories supporting the gene.
evidence_types	Evidence categories supporting the gene.
priority_group	Final prioritization category.
mapped_by_pos	Indicator for FUMA positional mapping support.
mapped_by_eqtl	Indicator for FUMA eQTL mapping support.
mapped_by_ci	Indicator for FUMA chromatin interaction mapping support.

UVmean_logFC	Mean UV-response log2 fold change across 2J and 4J UV-treated skin comparisons.
UVmean_FDR	False discovery rate for the mean UV-response skin signature.
TAAD_logFC	Log2 fold change in TAAD aorta.
TAAD_FDR	False discovery rate in TAAD aorta.