Supplementary Tables

Supplementary Table 1 **Summary of key signatures provided in the study**

Signature	Gene combination	Cut-off
Two gene signature	*IDO1-BIN1*	25° and 75° quartile
Three gene signature	*IDO1-BIN1-PLXNC1*	25° and 75° quartile
IDO1 top 4 DE gene signature	*GZMH-GNLY-IFIT2-IFIT3*	Median
PLXNC1 top 3 DE gene signature	*IKBKB-FOSL1-TLR9*	Median
7 DE gene signature	*GZMH-GNLY-IFIT2-IFIT3-IKBKB-FOSL1-TLR9*	Median
10 DE gene signature	*IDO1-BIN1-PLXNC1-IKBKB-FOSL1-TLR9-GZMH-GNLY-IFIT2-IFIT3*	Median

Supplementary Table 2 The top 20 differential expressed genes between *IDO1*$^{high/low}$ samples

Gene	Log2 fold change	std error (log2)	Lower confidence limit (log2)	Upper confidence limit (log2)	P-value
IDO1	3.28	0.627	2.06	4.51	< 0.0001
IFI27	4.05	0.78	2.52	5.58	< 0.0001
CXCL1	3.29	0.641	2.04	4.55	< 0.0001
VEGFA	3.04	0.592	1.88	4.2	< 0.0001
IFIT1	3.24	0.663	1.94	4.54	< 0.0001
CXCR2	3.27	0.739	1.82	4.72	< 0.001
IFIT3	2.41	0.567	1.3	3.52	< 0.001
IFIT2	2.15	0.515	1.14	3.16	< 0.001
VCAM1	2.74	0.667	1.44	4.05	< 0.001
GNLY	2.75	0.702	1.37	4.13	< 0.001
GZMH	3.12	0.804	1.54	4.69	< 0.001
RSAD2	2.19	0.578	1.06	3.32	0.001
APOE	2.9	0.781	1.37	4.43	< 0.01
KIR2DL3	2.03	0.557	0.939	3.12	< 0.01
CCL4	2.26	0.624	1.04	3.48	< 0.01
TNFRSF10C	2.98	0.827	1.36	4.6	< 0.01
APOL6	0.757	0.211	0.345	1.17	< 0.01
IRF1	1.01	0.282	0.461	1.57	< 0.01
OASL	2.34	0.662	1.04	3.64	< 0.01
HDC	2.45	0.699	1.08	3.82	< 0.01

Supplementary Table 3 The top 20 differential expressed genes between *PLXNC1*$^{high/low}$ samples

Gene	Log2 fold change	std error (log2)	Lower confidence limit (log2)	Upper confidence limit (log2)	P-value
IL11RA	1.67	0.258	1.16	2.17	< 0.00001
NF1	0.837	0.182	0.481	1.19	< 0.001
APC	0.548	0.123	0.307	0.79	< 0.001
BIRC3	3.29	0.745	1.83	4.75	< 0.001
PARP4	0.646	0.147	0.358	0.933	< 0.001
FZD8	-2.98	0.689	-4.33	-1.63	< 0.001
IKBKB	0.628	0.147	0.34	0.916	< 0.001
TLR9	2.13	0.498	1.15	3.1	< 0.001
FOSL1	-2.03	0.485	-2.98	-1.08	< 0.001
H2AFX	-1.03	0.248	-1.52	-0.548	< 0.001
BAD	-0.397	0.0966	-0.587	-0.208	< 0.001
SNAI1	-1.94	0.478	-2.87	-0.999	< 0.001
TPI1	-0.929	0.236	-1.39	-0.467	< 0.001
EPM2AIP1	0.606	0.155	0.301	0.911	< 0.001
CD79A	2.95	0.784	1.41	4.49	< 0.01
CDKN1A	-2.06	0.55	-3.14	-0.982	< 0.01
CXCR2	2.89	0.772	1.38	4.4	< 0.01
PVRIG	1.05	0.285	0.495	1.61	< 0.01
SRP54	0.357	0.0975	0.165	0.548	< 0.01
ATF3	-2.18	0.601	-3.36	-1	< 0.01

Supplementary Figure Legends

Supplementary Figure 1 **The *RBM25* gene correlates with both *BIN1* and *IDO1* genes in the HOVON cases**

(A) Correlation between *BIN1* and *RBM25* gene expression values in the HOVON cases (r= -0.29, P<0.0001). **(B)** Correlation between *BIN1* and *RBM25* gene expression values in the HOVON cases (r= 0.46, P<0.0001).

Supplementary Figure 2 **The immunological 3-gene signature does not clearly correlate with ELN conventional prognostic risk factors**

(A) *IDO1-BIN1-PLXNC1* score values comparison between ELN cytogenetic risk categories in the HOVON dataset. **(B)** Kaplan-Meier estimates of OS according to *IDO1-BIN1-PLXNC1* score quartiles among patients with ELN favourable cytogenetic risk in the HOVON dataset (P = ns). **(C)** Kaplan-Meier estimates of OS according to *IDO1-BIN1-PLXNC1* score quartiles among patients with ELN intermediate cytogenetic risk in the HOVON dataset (P = ns). **(D)** Kaplan-Meier estimates of OS according to *IDO1-BIN1-PLXNC1* score quartiles among patients with ELN adverse cytogenetic risk in the HOVON dataset (P<0.05). **(E)** *IDO1-BIN1-PLXNC1* score values comparison between *FLT3* mutated vs unmutated cases of the HOVON dataset. **(F)** Kaplan-Meier estimates of OS according to *IDO1-BIN1-PLXNC1* score quartiles among patients with *FLT3*-wilde type in the HOVON dataset (P<0.0001).

Supplementary Figure 3 **The *IDO1-BIN1-PLXNC1* score stratifies AML survival in GSE106291 dataset**

Kaplan-Meier estimates of OS according to *IDO1-BIN1-PLXNC1* score quartiles in the GSE106291 dataset (P<0.05).

Supplementary Figure 4 **AML-TCGA patients showed *IDO1* and *PLXNC1* higher expression by B-cells, T cells and macrophages than corresponding healthy donors.**

The EPIC deconvolution method[34] was applied to the AML-TCGA and Genotype-Tissue Expression (GTEx) datasets to explore the *IDO1* and *PLXNC1* gene sub-expression in single cell-types. **(A)** *IDO1* expression by B-cells, T cells and macrophages is higher in AML patients samples when compared to healthy donor samples. **(B)** *PLXNC1* expression by B-cells, T cells and macrophages is higher in AML patients samples when compared to healthy donor samples.

Supplementary Figure 5 **The 7 DE and 10 DE gene signature predicts survival in the HOVON dataset.**

(**A)** Kaplan-Meier estimates of OS according to 7 DE genes signatures (*GZMH-GNLY-IFIT2-IFIT3-IKBKB-FOSL1-TLR9*) in the HOVON dataset (P<0.05). (**B**) Kaplan-Meier estimates of OS according to 10 DE genes signatures (*IDO1-BIN1-PLXNC1-GZMH-GNLY-IFIT2-IFIT3-IKBKB-FOSL1-TLR9*) in the HOVON dataset (P<0.0001). (**C**) Kaplan-Meier estimates of OS according to 10 DE genes signatures (*IDO1-BIN1-PLXNC1-GZMH-GNLY-IFIT2-IFIT3-IKBKB-FOSL1-TLR9*) among patients with ELN favourable cytogenetic risk in the HOVON dataset (P = ns). (**D**) Kaplan-Meier estimates of OS according to 10 DE genes signatures (*IDO1-BIN1-PLXNC1-GZMH-GNLY-IFIT2-IFIT3-IKBKB-FOSL1-TLR9*) among patients with ELN intermediate cytogenetic risk in the HOVON dataset (P = ns). (**E**) Kaplan-Meier estimates of OS according to 10 DE genes signatures (*IDO1-BIN1-PLXNC1-GZMH-GNLY-IFIT2-IFIT3-IKBKB-FOSL1-TLR9*) among patients with ELN adverse risk in the HOVON dataset (P = ns). (**F**) Kaplan-Meier estimates of OS according to 10 DE genes signatures (*IDO1-BIN1-PLXNC1-GZMH-GNLY-IFIT2-IFIT3-IKBKB-FOSL1-TLR9*) among patients with *FLT3*-wilde type in the HOVON dataset (P<0.001).

Supplementary Figure 6 **Expression of *PLXNC1*-derived genes in TCGA tumor types and in adjacent normal tissues.**

Comparison of the expression of genes in the *PLXNC1*-derived signature between tumor TCGA samples (red boxes) and adjacent normal tissues (grey boxes) from healthy donors available in the Genotype-Tissue Expression (GTEx) project.

Supplementary Figure 7 **Expression of *IDO1*-derived genes in TCGA tumor types and in adjacent normal tissues.**

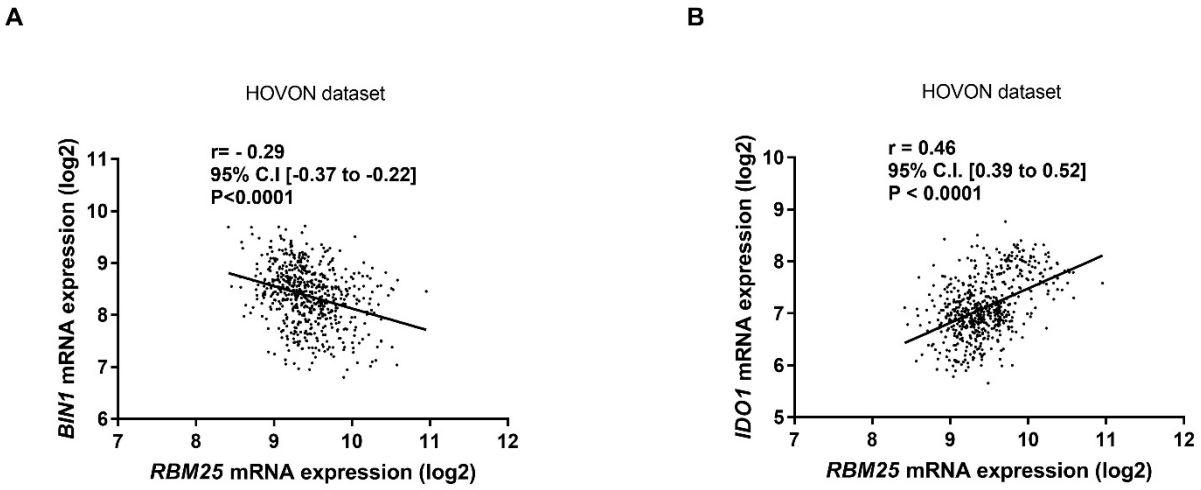
Comparison of the expression of genes in the *IDO1*-derived signature between tumor TCGA samples (red boxes) and adjacent normal tissues (grey boxes) from healthy donors available in the Genotype-Tissue Expression (GTEx) project.

Supplementary Figure 8 **A Pan-cancer analysis of TCGA revealed *PLXNC1*- and *IDO1*-derived signature genes with prognostic relevance in solid tumors**

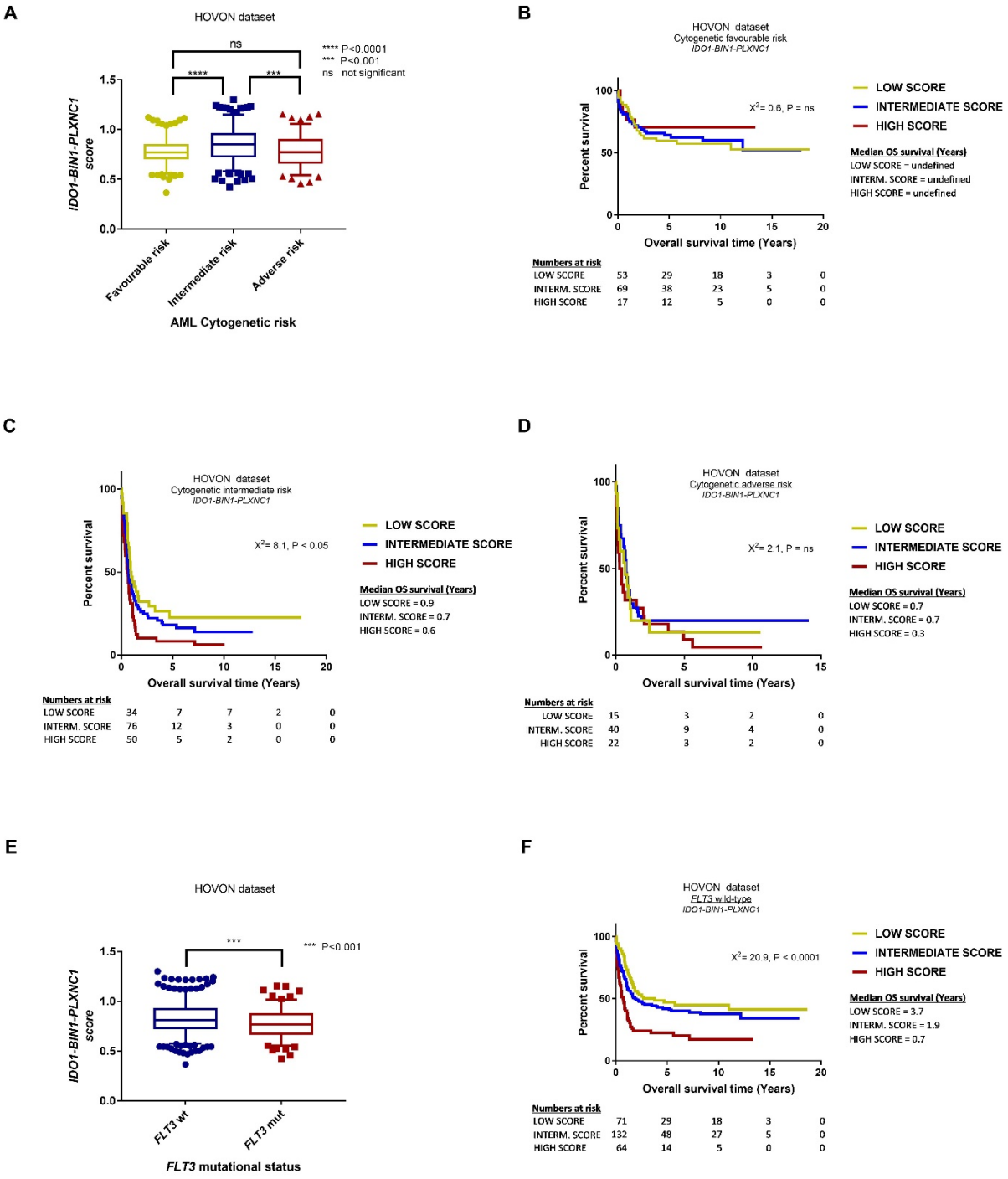
(A) Representation of genes with prognostic relevance in the *PLXNC1*-derived signature identified through a pan-cancer TCGA analysis. **(B)** Representation of genes with prognostic relevance in the *IDO1*-derived signature identified through a pan-cancer TCGA analysis.

Supplementary Figures

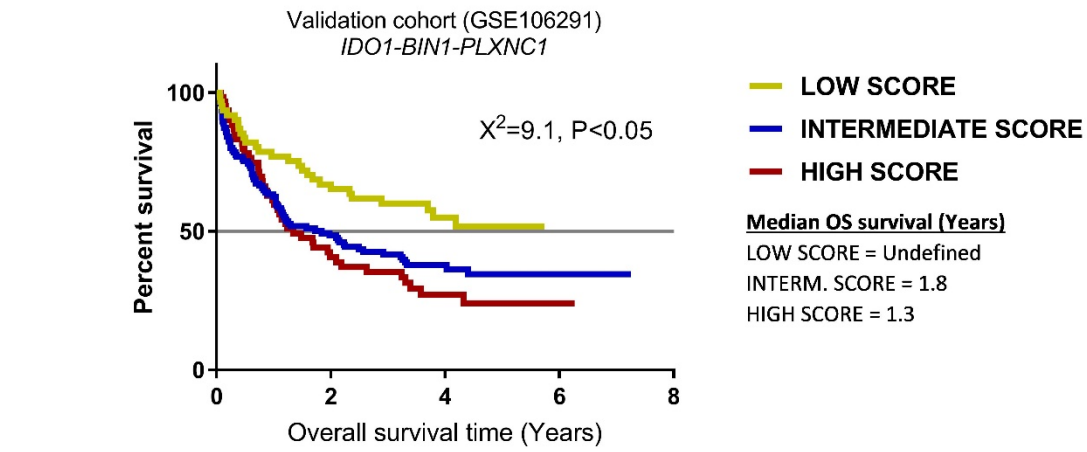
Supplementary Figure 1



Supplementary Figure 2

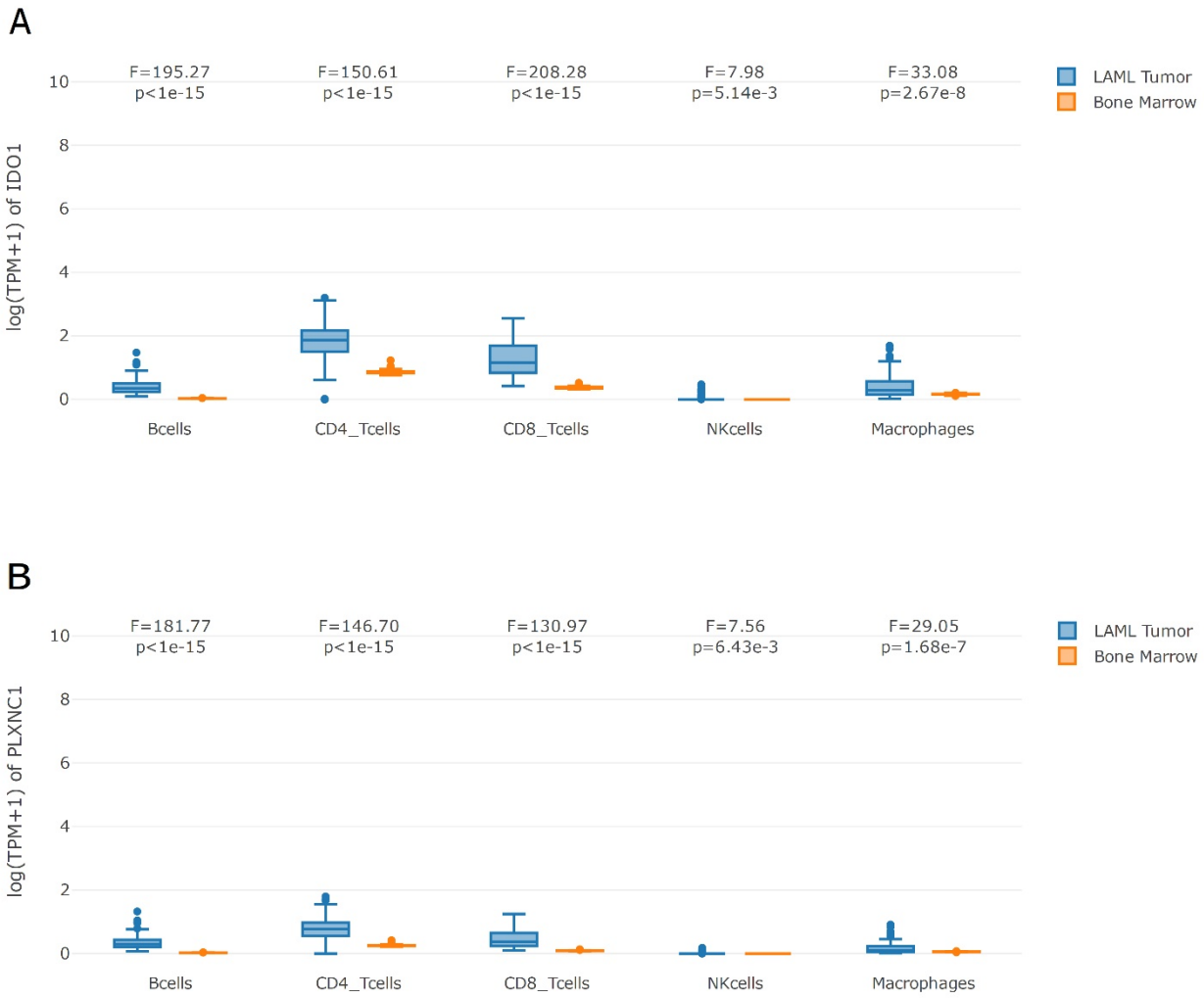


Supplementary Figure 3

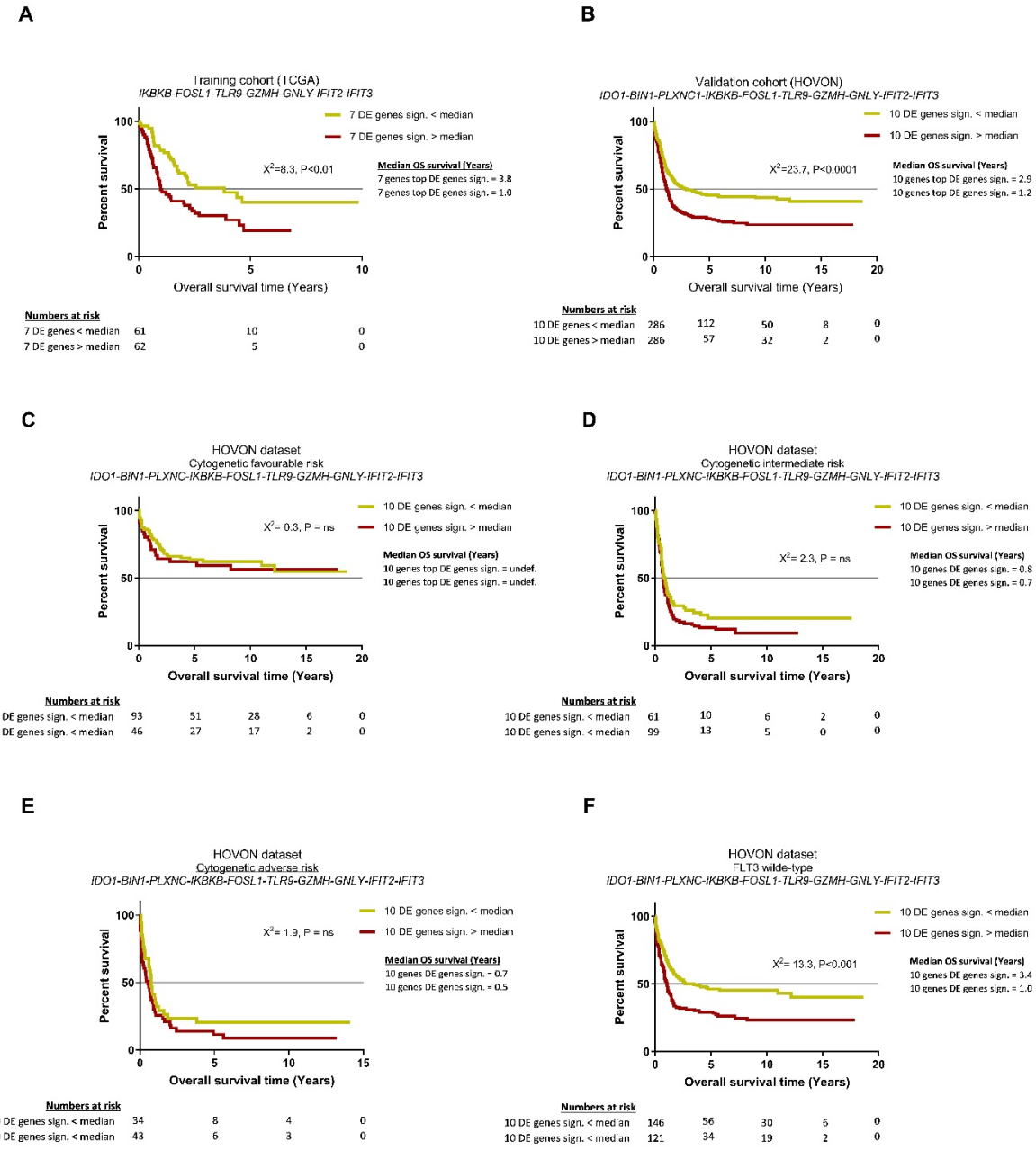


Numbers at risk					
LOW SCORE	61	41	21	0	0
INTERM. SCORE	125	59	26	3	0
HIGH SCORE	62	24	11	2	0

Supplementary Figure 4



Supplementary Figure 5



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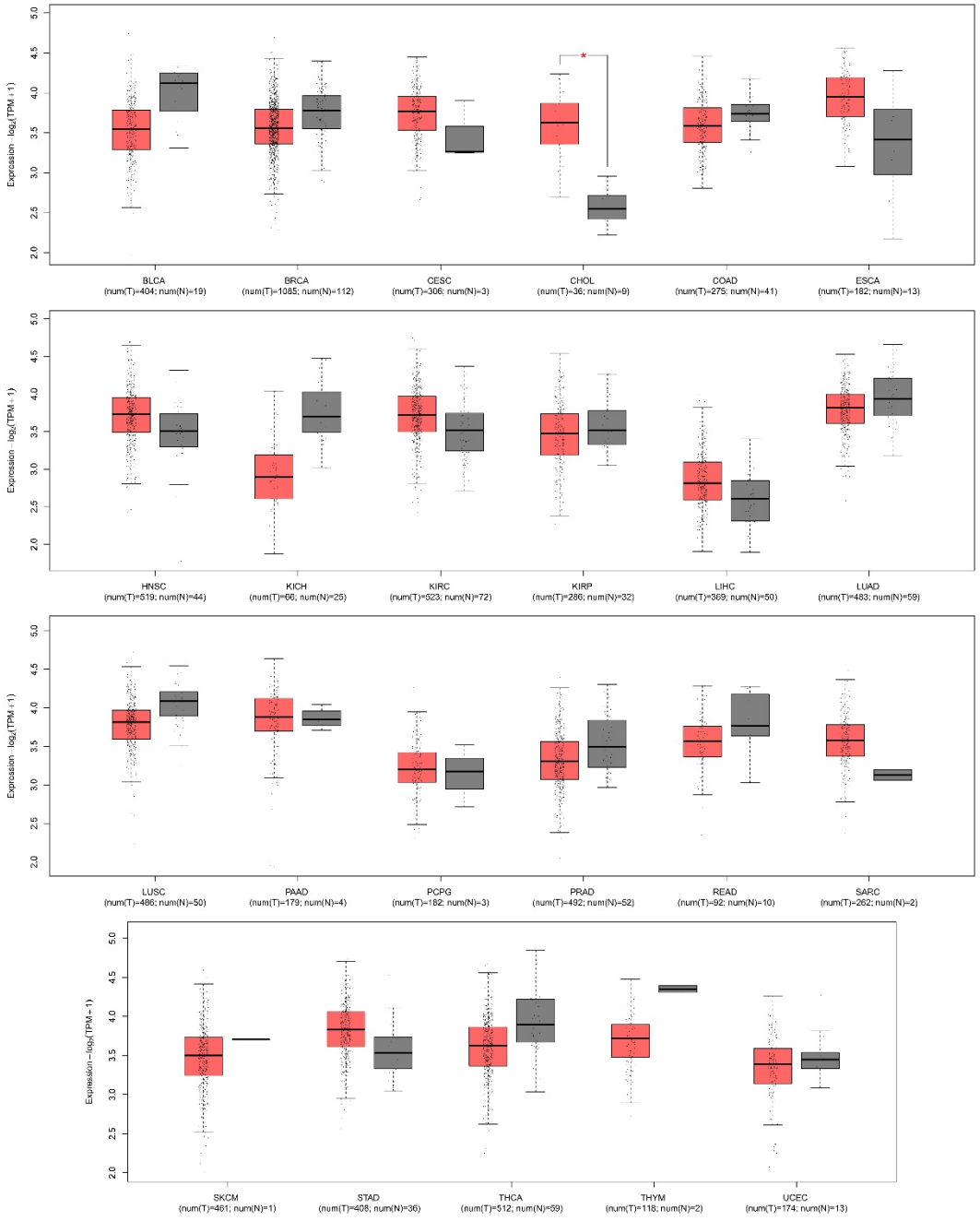
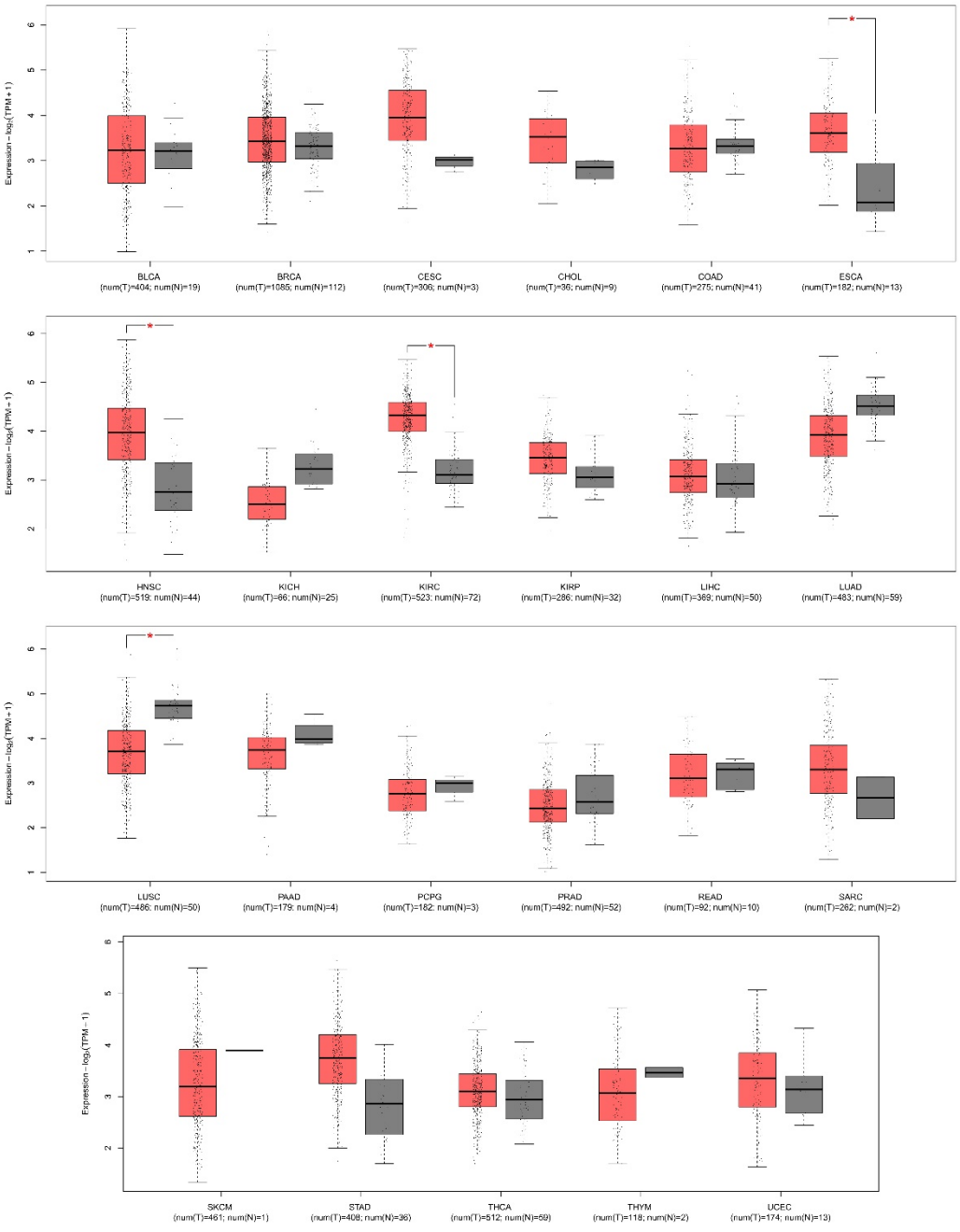


Supplementary Figure 7



Supplementary Figure 8