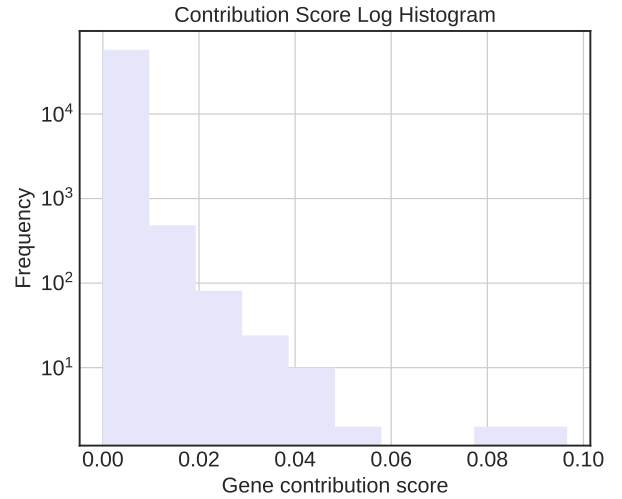


XOmiVAE: an interpretable deep learning model for cancer classification using high-dimensional omics data – Supplementary information



Supplementary Figure 1: Log histogram of the omics latent dimension contribution scores for LUAD prediction



Supplementary Figure 2: Log histogram of the gene contribution scores for LUAD prediction

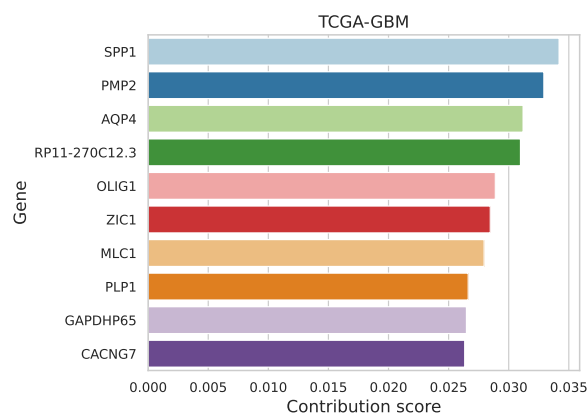
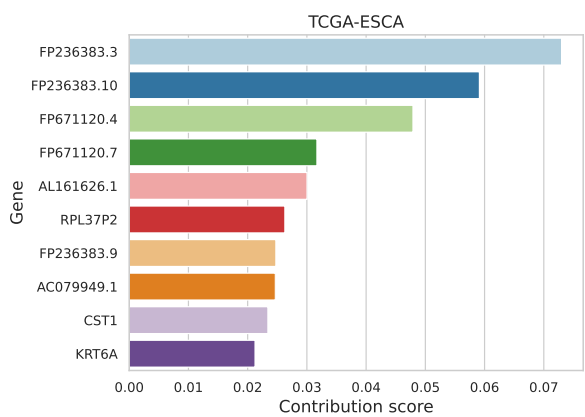
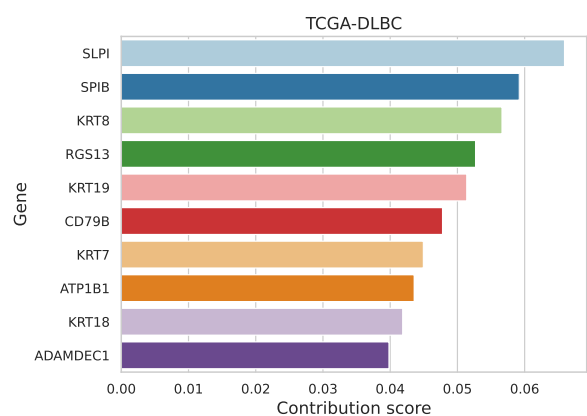
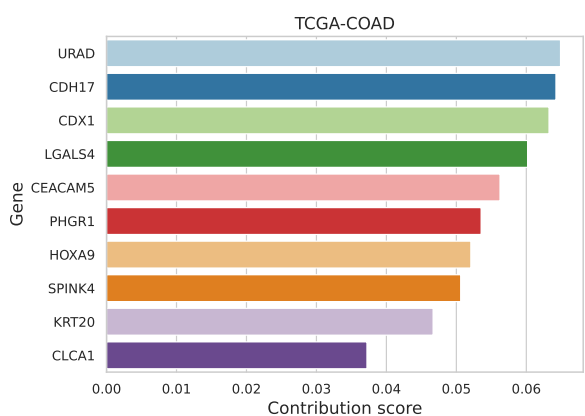
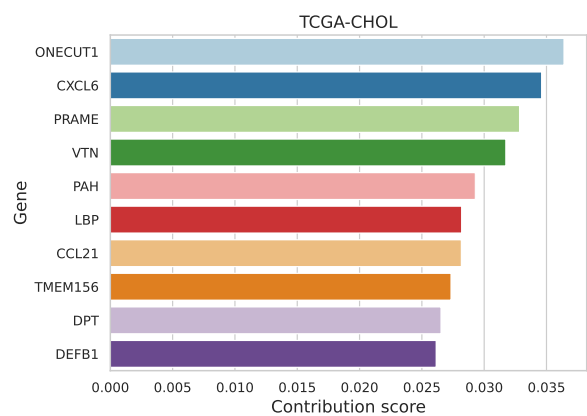
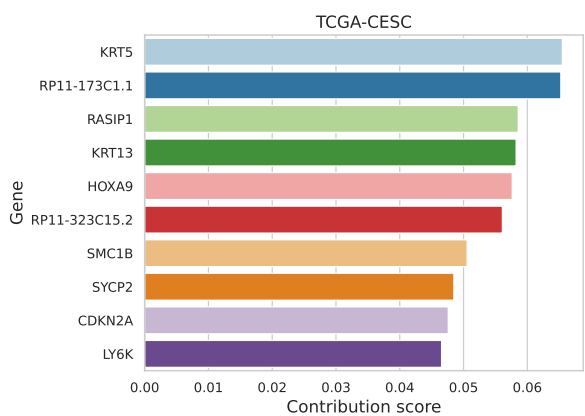
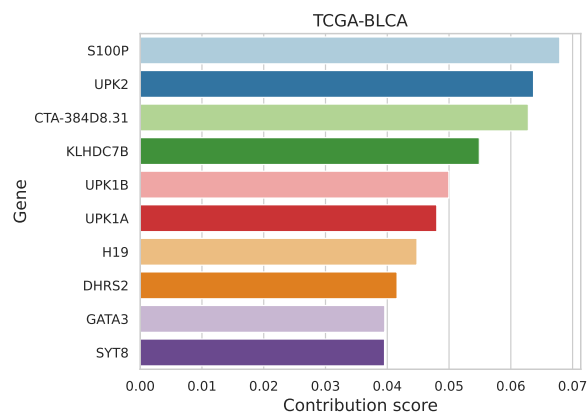
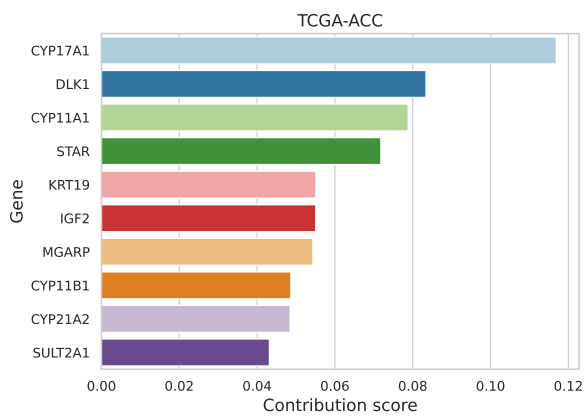
Term ID	Term Name	Padj
GO:0030198	Extracellular matrix organisation	6.450×10^{-11}
GO:0043062	Extracellular structure organisation	6.839×10^{-11}
GO:0005615	Extracellular space	4.048×10^{-12}
GO:0005576	Extracellular region	3.436×10^{-16}
GO:0031012	Extracellular matrix	3.295×10^{-18}

Supplementary Table 1: A list of GO terms that are significantly overrepresented in the top 100 genes with highest contribution scores for BRCA. The GO term definitions were obtained from EMBL-EBI.

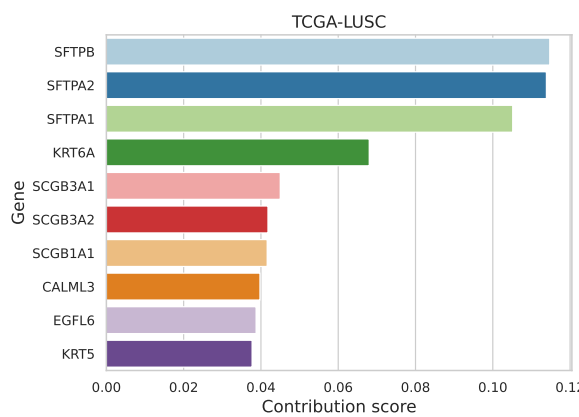
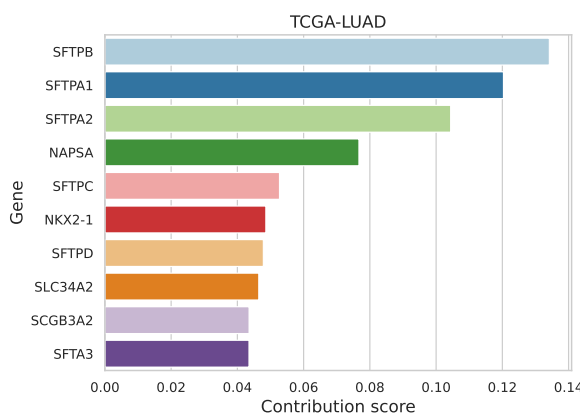
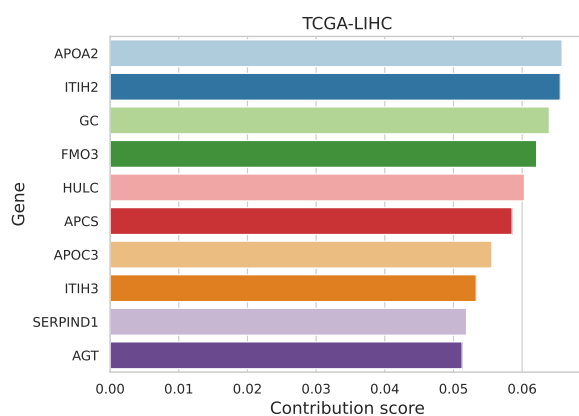
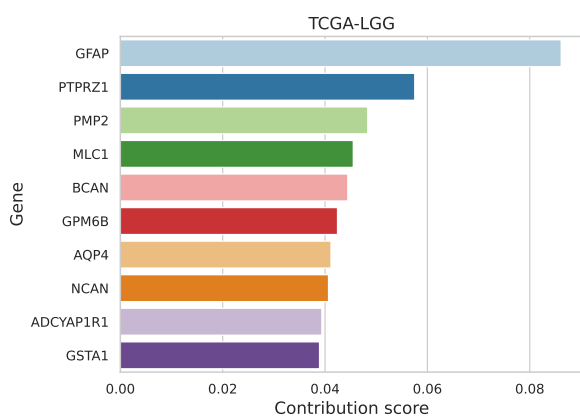
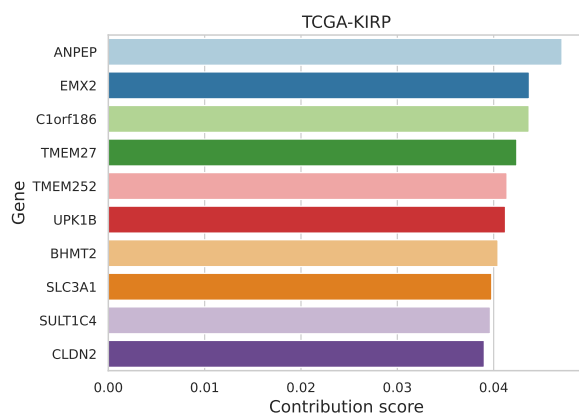
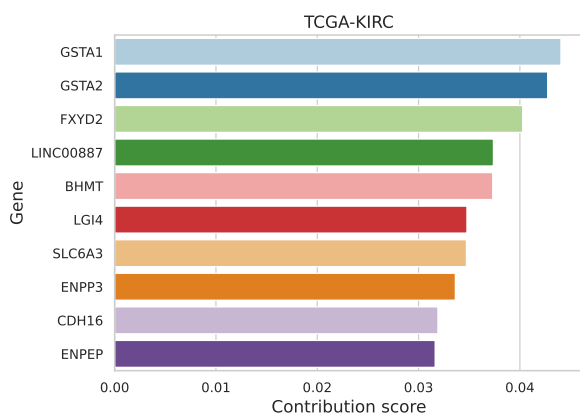
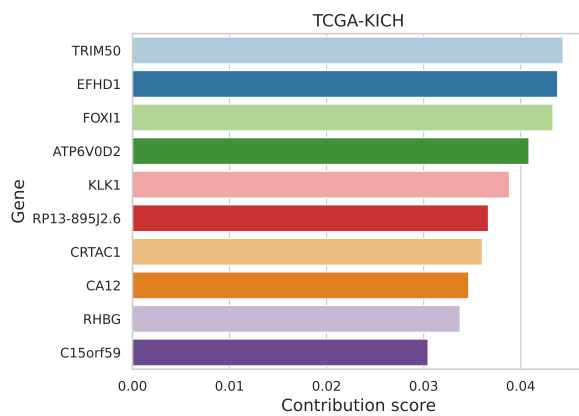
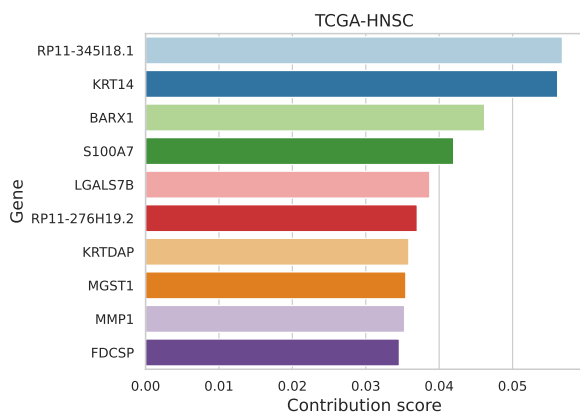
Gene name	Contribution value	DEGs?
LYVE1	0.08802652	True
COMP	0.07973582	True
SCARA5	0.07240529	True
SCGB2A2	0.07231501	False
LPL	0.07080267	True
PAMR1	0.07024122	True
MMP11	0.06332003	True
FABP4	0.06088565	True
CFD	0.06078836	False
CCL21	0.06023567	False
COL10A1	0.05834333	True
MYOC	0.05211987	True
LTF	0.05140609	False
HBB	0.05027783	True
PCOLCE2	0.04830263	True
SCGB1D2	0.0469837	False
AC005152.3	0.04682791	False
HSPB6	0.04676779	True
CES1	0.04491388	True
STAC2	0.04475317	False
RBP4	0.04437602	True

TMEM132C	0.04436617	True
GSTA1	0.04426087	False
KRT81	0.04423712	False
WISP1	0.04395866	True
HSPB7	0.04390443	True
LEP	0.04379686	True
CIDEA	0.04358062	True
IGFBP6	0.04235139	True
MMP3	0.04183716	False
RP11-417E7.2	0.04122007	False
CXCL2	0.04058203	True
NRN1	0.04055257	False
NPY2R	0.04038753	True
HBA2	0.03953991	True
DEGS2	0.0390564	False
MMRN1	0.03803924	True
MFAP4	0.03684358	False
PDLIM3	0.03567977	False
DEFB1	0.03564727	False
MUCL1	0.03556658	False
COX6CP1	0.03456202	False
MYEOV	0.03400248	False
ALDOC	0.03336278	False
CTHRC1	0.03331805	False
RP11-92A5.2	0.031692	False
MYH11	0.03150566	True
RSPO3	0.03146641	False
CYP4Z1	0.03132155	False
AARD	0.03101798	False
ADIPOQ	0.03096839	True
EN1	0.03067887	False
IRX1	0.03019223	False
CNN1	0.0301683	True
CLEC3B	0.02989807	True
CHRDL1	0.02956831	True
RGS2	0.02956212	False
ADH1C	0.02949688	True
PENK	0.02940149	False
NNAT	0.02905503	True
TPSP2	0.02874485	False
FAM162B	0.02874344	False
FMO2	0.02873539	True
NKAIN1	0.02868808	True
DES	0.02867935	False
ANGPTL7	0.02847075	True
PI16	0.02837563	True
TBX15	0.02816985	False
AC097713.3	0.027969	False
FOS	0.02796617	False
SAMD5	0.02795375	False
RP11-736K20.4	0.02790227	False
UBE2Q2P6	0.02789169	False
CBX4	0.02774911	False
KLF4	0.02768696	False
MATN3	0.02767189	False
MAMDC2	0.02758051	True
ALDH1A1	0.02732193	False
HOXA9	0.02702148	False
PPARG	0.026999	True
HRCT1	0.02693174	False
MISP	0.026907	False
HOXC13	0.02684432	False
MAOA	0.02663056	True
SERPINA5	0.02651533	False
CAV1	0.02647178	True
RP11-211G23.2	0.02636731	False
SLC13A2	0.02623627	False
CPB1	0.02623	True
SLC29A4	0.02618126	False
TMEM37	0.02603649	False
PLAC9	0.02602616	False
CTXN1	0.02567291	False
BTNL9	0.0255975	True
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FOSB	0.0251986	True
IGHA2	0.02517499	False

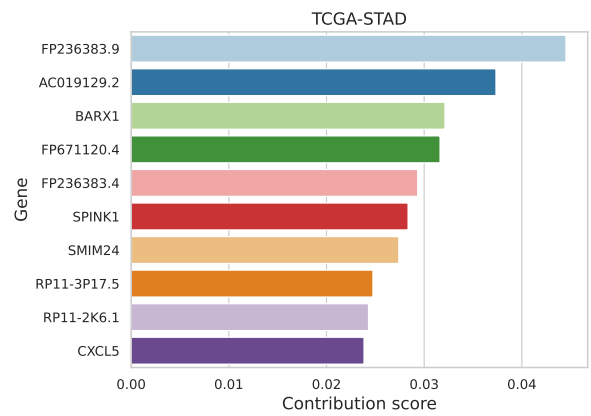
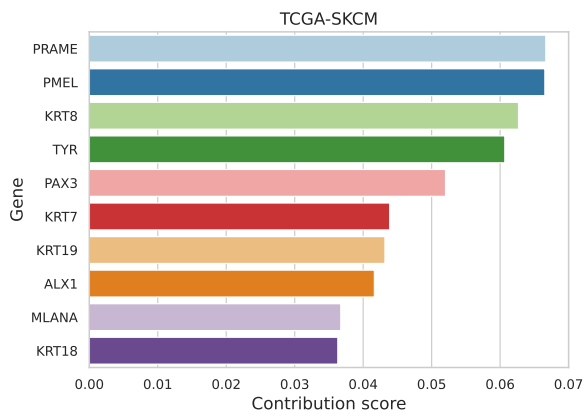
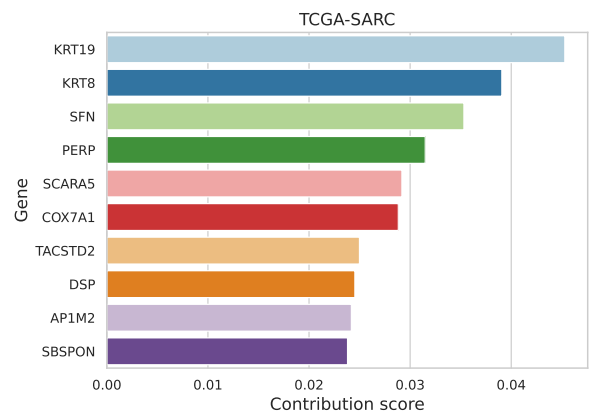
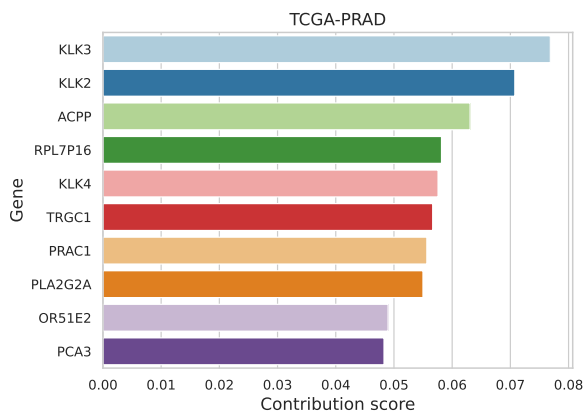
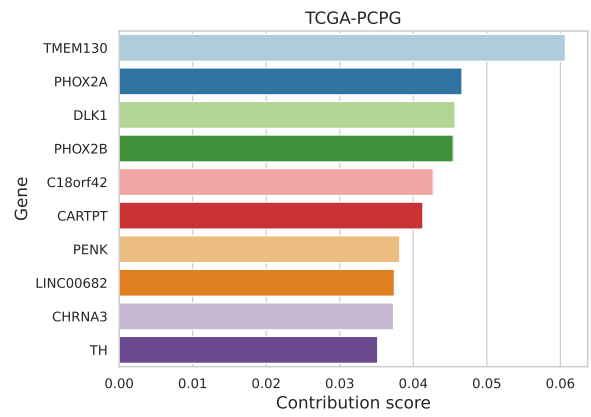
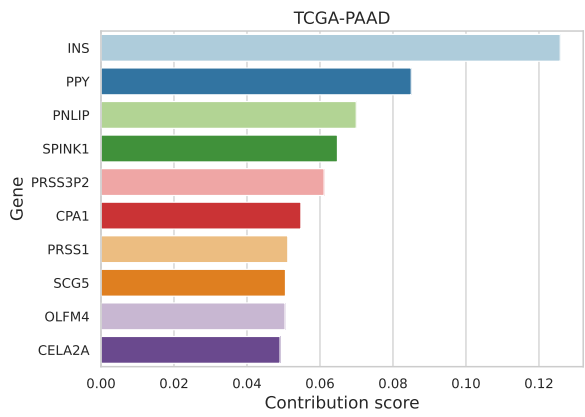
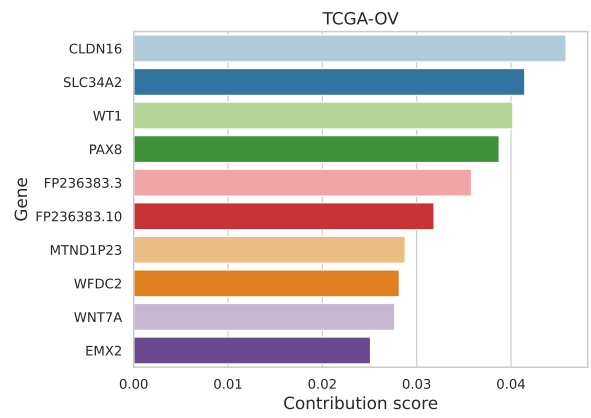
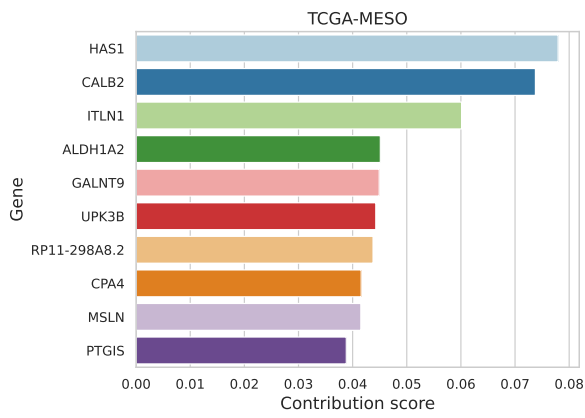
Supplementary Table 2: The top 100 contribution genes for BRCA prediction compared to the differentially expressed genes (DEGs).



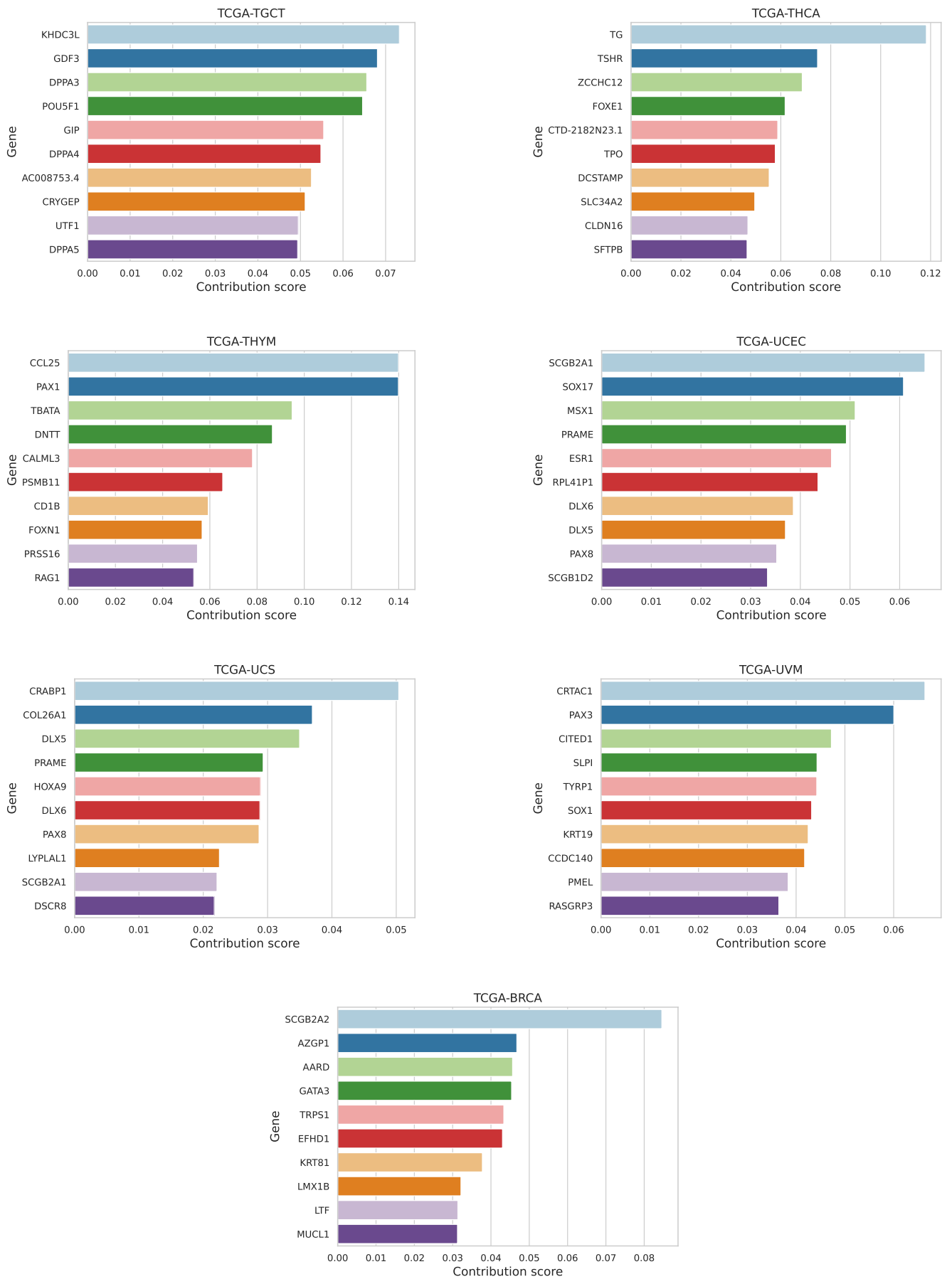
Supplementary Figure 3: The top 10 genes for TCGA tumour types ACC, BLCA, CESC, CHOL, COAD, DLBC, ESCA and GBM.



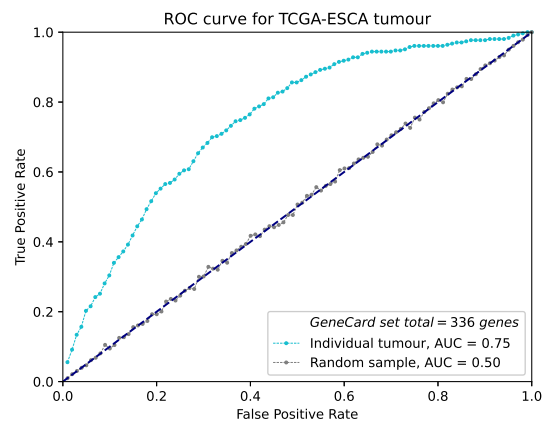
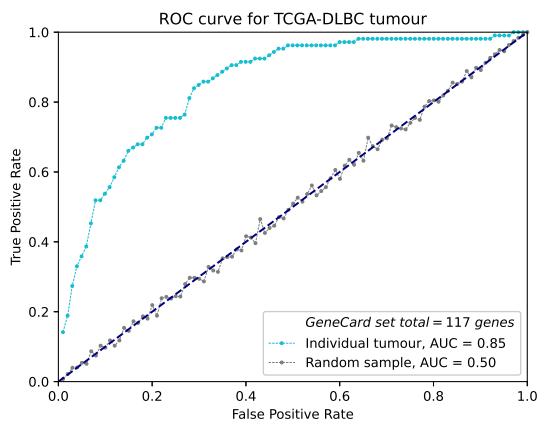
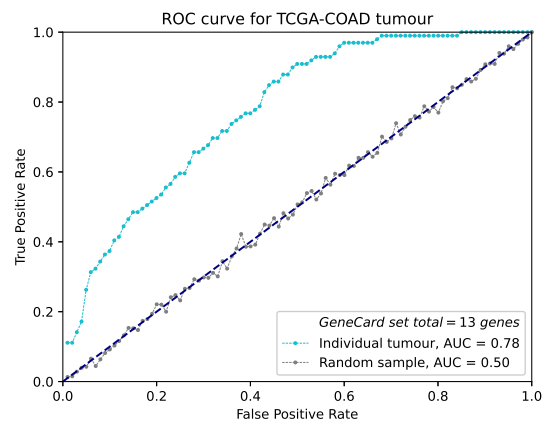
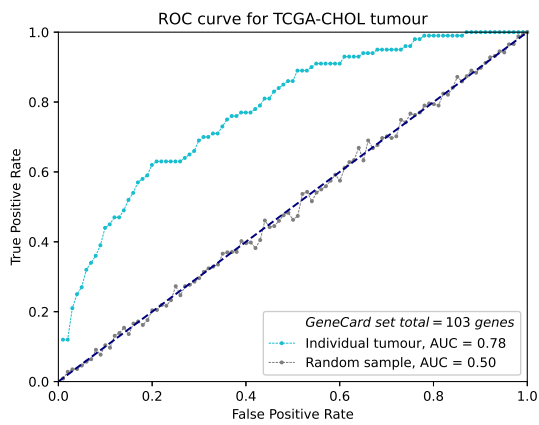
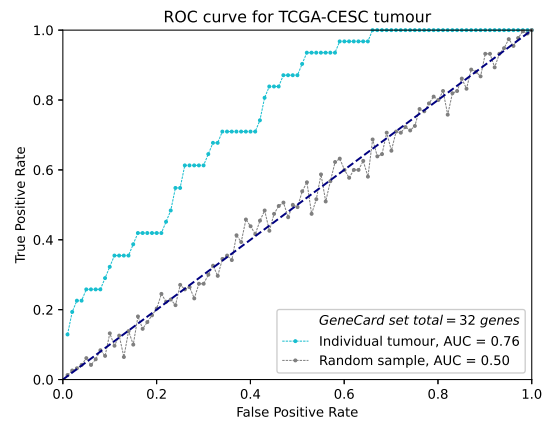
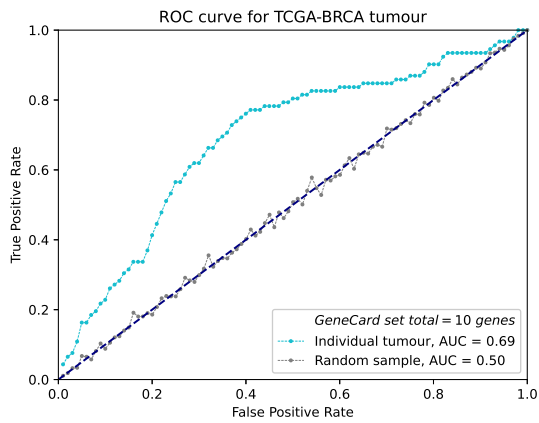
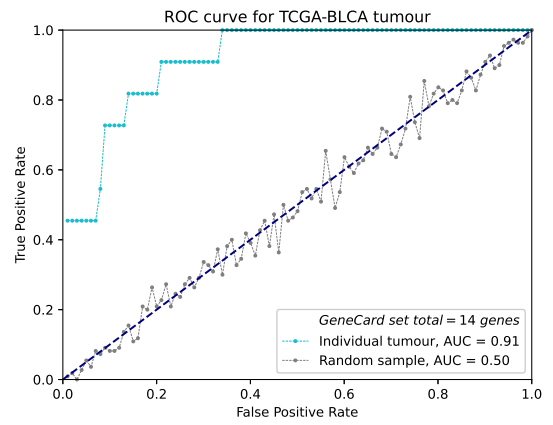
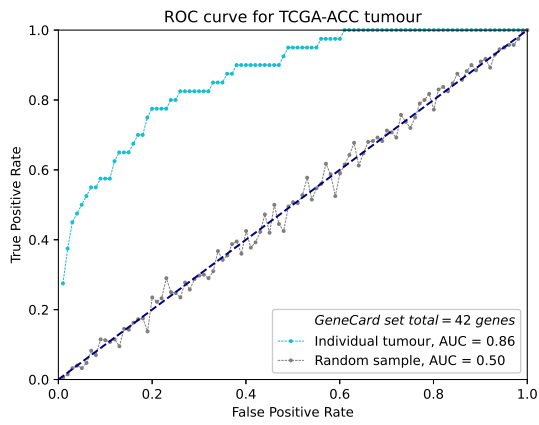
Supplementary Figure 4: The top 10 genes for TCGA tumour types HNSC, KICH, KIRC, KIRP, LGG, LIHC, LUAD and LUSC.



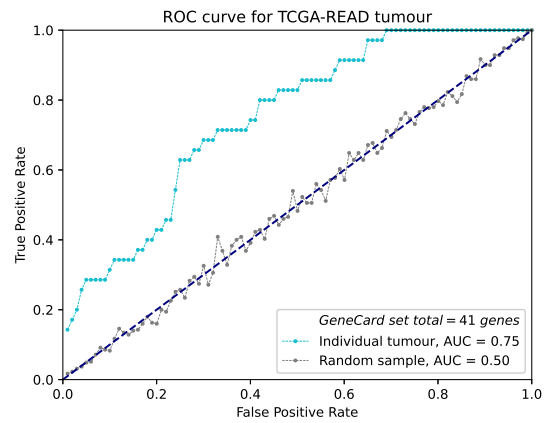
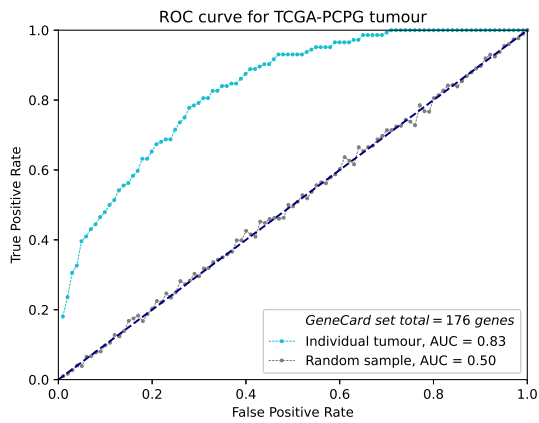
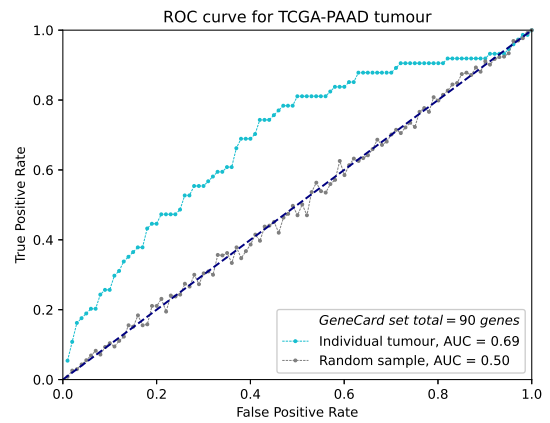
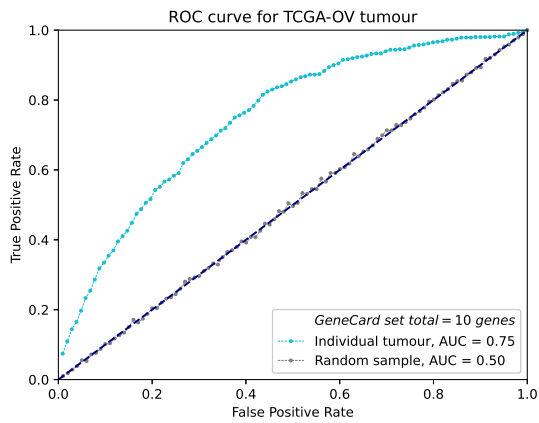
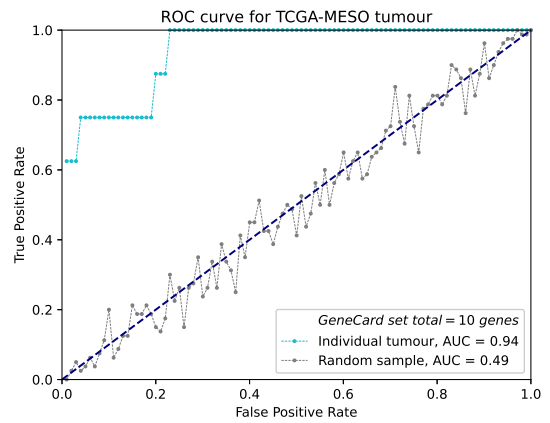
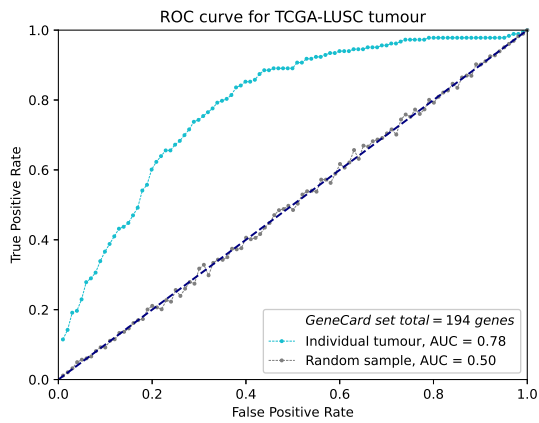
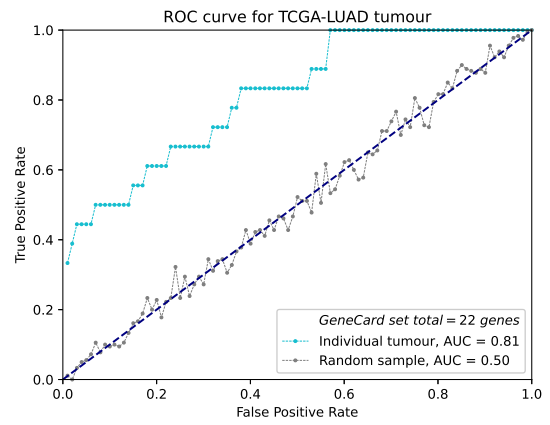
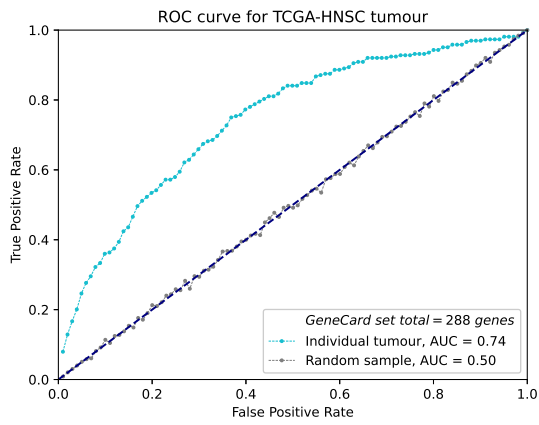
Supplementary Figure 5: The top 10 genes for TCGA tumour types MESO, OV, PAAD, PCPG, PRAD, SARC, SKCM and STAD.



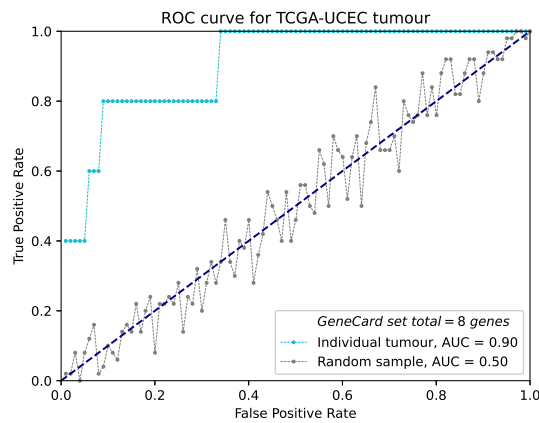
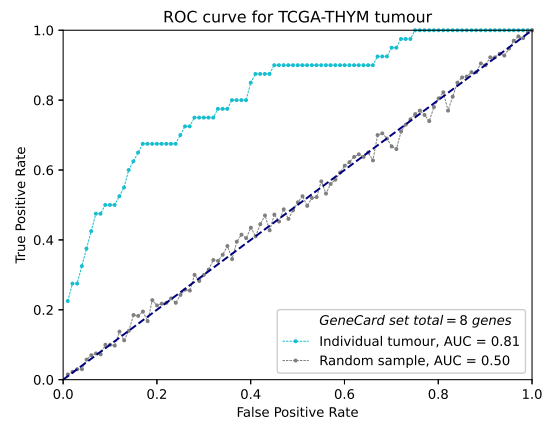
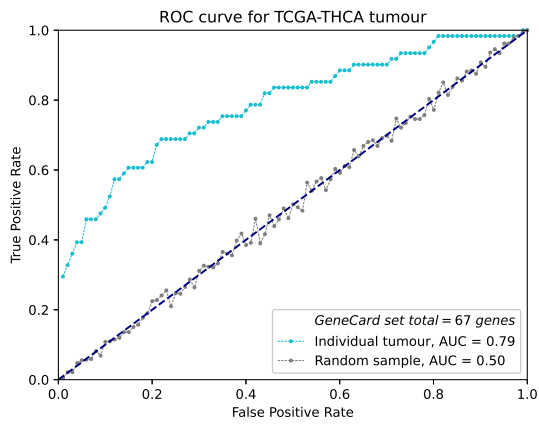
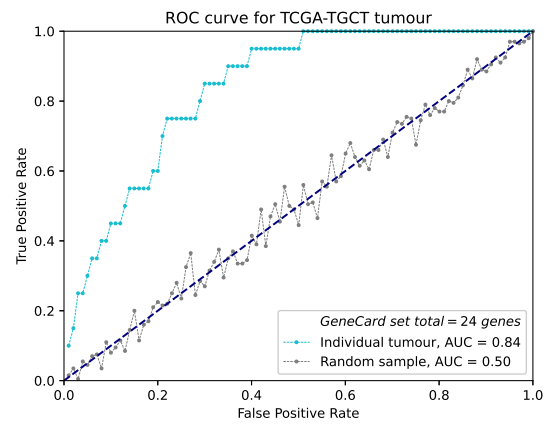
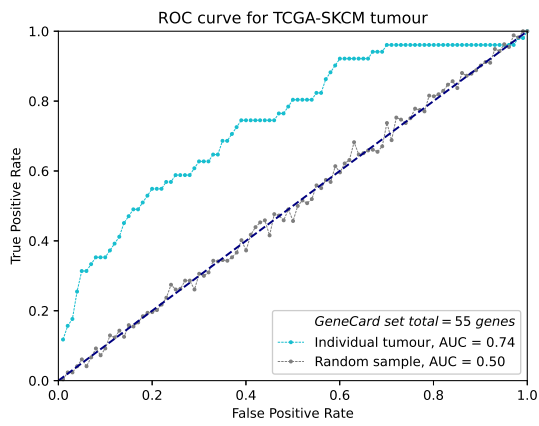
Supplementary Figure 6: The top 10 genes for TCGA tumour types TGCT, THCA, THYM, UCEC, UCS, UVM and BRCA.



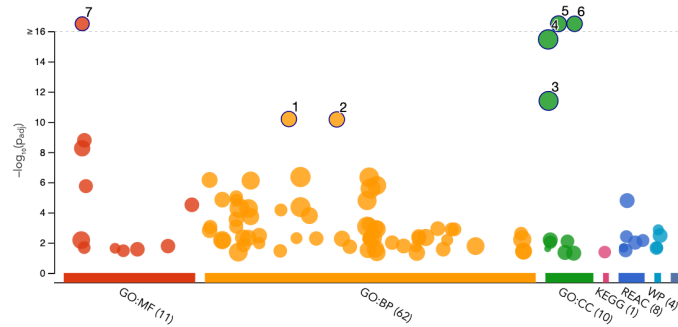
Supplementary Figure 7: AUC-ROC curves for the TCGA tumour most important genes (top SHAP genes) and random samples of genes against the GeneSet gene list for the tumour type. 100 thresholds were used, spaced evenly from 0 to 58,043 (total number of genes). A high AUC score indicates a higher number of genes that matched with the relevant disease genes in the GeneSet database.



Supplementary Figure 8: AUC-ROC curves for the TCGA tumour most important genes (top SHAP genes) and random samples of genes against the GeneSet gene list for the tumour type. 100 thresholds were used, spaced evenly from 0 to 58,043 (total number of genes). A high AUC score indicates a higher number of genes that matched with the relevant disease genes in the GeneSet database.

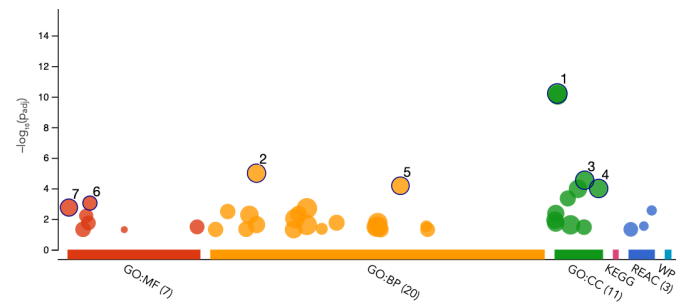


Supplementary Figure 9: AUC-ROC curves for the TCGA tumour most important genes (top SHAP genes) and random samples of genes against the GeneSet gene list for the tumour type. 100 thresholds were used, spaced evenly from 0 to 58,043 (total number of genes). A high AUC score indicates a higher number of genes that matched with the relevant disease genes in the GeneSet database.



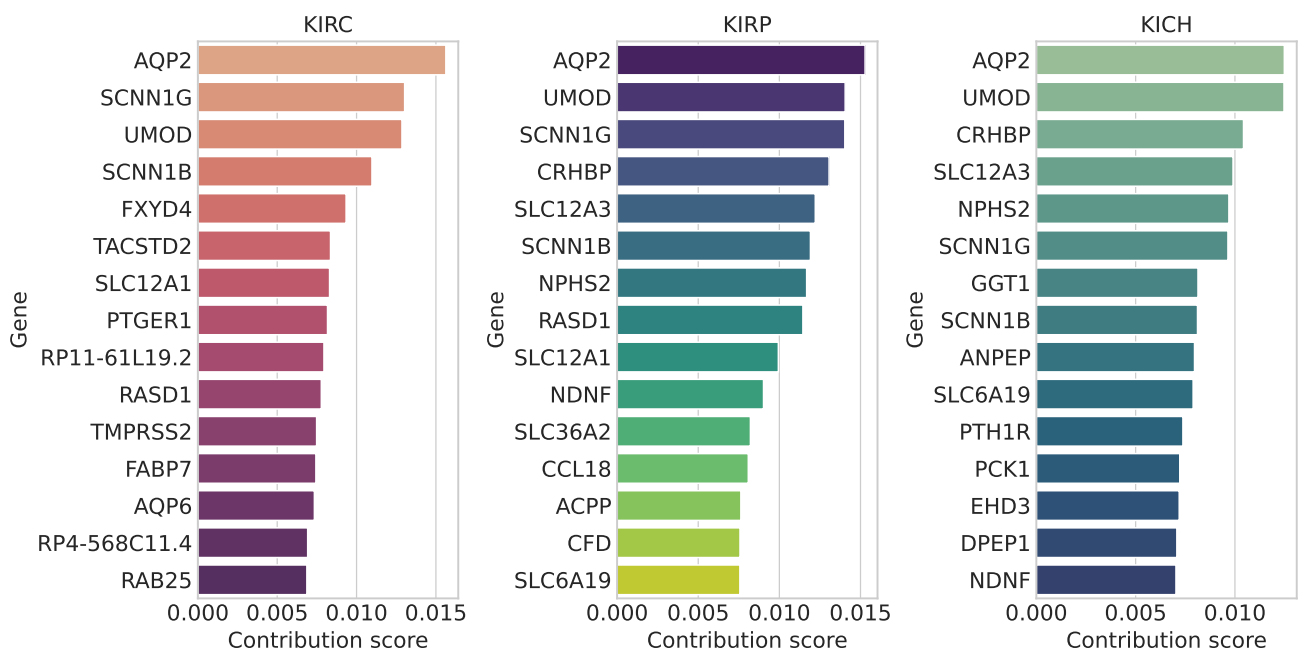
ID	Source	Term ID	Term Name	P _{adj} (query_1)
1	GO:BP	GO:0030198	extracellular matrix organization	6.450×10 ⁻¹¹
2	GO:BP	GO:0043062	extracellular structure organization	6.839×10 ⁻¹¹
3	GO:CC	GO:0005615	extracellular space	4.048×10 ⁻¹²
4	GO:CC	GO:0005576	extracellular region	3.436×10 ⁻¹⁶
5	GO:CC	GO:0031012	extracellular matrix	3.295×10 ⁻¹⁸
6	GO:CC	GO:0062023	collagen-containing extracellular matrix	9.763×10 ⁻¹⁷
7	GO:MF	GO:0005201	extracellular matrix structural constituent	2.717×10 ⁻¹⁷

Supplementary Figure 10: The significant signalling pathways found from the top 100 genes for BRCA when breast normal tissue is used as the reference. Labels 1 to 7 are the most significant pathways and their pathway names listed in the table below, with their respective significance value.



ID	Source	Term ID	Term Name	P _{adj} (query_1)
1	GO:CC	GO:0005576	extracellular region	6.193×10 ⁻¹¹
2	GO:BP	GO:0009888	tissue development	1.005×10 ⁻⁵
3	GO:CC	GO:0070062	extracellular exosome	2.880×10 ⁻⁵
4	GO:CC	GO:1903561	extracellular vesicle	1.005×10 ⁻⁴
5	GO:BP	GO:0060429	epithelium development	6.663×10 ⁻⁵
6	GO:MF	GO:0008201	heparin binding	9.085×10 ⁻⁴
7	GO:MF	GO:0000981	DNA-binding transcription factor activity, RNA ...	1.779×10 ⁻³

Supplementary Figure 11: A detailed view of the top signalling pathways for BRCA classification using a random training sample as the reference sample. There is a decrease in pathways involving the extracellular matrix compared to when normal breast tissue was used as a reference value.



Supplementary Figure 12: The top 15 genes for the common dimension 35 among KICH, KIRC and KIRP. AQP2 is the most important gene in all three cases.