

# Supplementary Material

**Gene coexpression calculation:** In our construction of cancer-specific graphs, we add links to the PPI graph to form a unified one. Here, we describe how data processing is performed.

We download gene expression data from The Cancer Genome Atlas (TCGA) via the Genomic Data Commons (GDC). For each type of cancer, we have gene expression from a set of patients. We process such data following the procedure used in the recommendations from [1]. We represent each gene as a gene expression vector whose coordinates are gene expression across all patients. We calculate the Pearson correlation coefficient (PCC) between each pair of genes. The correlation scores obtained are used to form the KNN graph.

**Multi-omics features:** We adopt four biological features previously used in EMOGI [2] as node features, capturing key molecular mechanisms commonly altered in cancer.

- Somatic mutation rate: Calculated from SNV data in TCGA following the HotNet2 preprocessing pipeline [3]. Samples with abnormal mutation counts (ultramutated) were removed. The SNV frequency of a gene in each type of cancer was defined as the number of nonsilent SNVs divided by the exonic length of the gene.
- Copy number alteration (CNA): CNA data were obtained from TCGA using the GISTIC2 tool [4]. Both gene amplifications and deletions were considered, with ultramutated samples excluded. The CNA rate of a gene was defined as the number of times it was altered (amplified or deleted) in a specific cancer cohort. All CNA types were aggregated into a single feature per gene.
- DNA methylation in promoter regions: Methylation data were collected from Illumina 450k arrays in TCGA (including both tumor and adjacent normal tissues). For each gene, the promoter was defined as the region  $\pm 1,000$  base pairs around the transcription start site, according to GENCODE v28 [5]. The average methylation of the promoter was calculated by averaging the values of  $\beta$  of the CpG sites in this region, after batch effect correction using ComBat [6]. Differential methylation was defined as the difference between tumor and normal tissues, averaged in all samples.
- Gene expression: Gene expression data was derived from the Wang et al. dataset [7], which includes tumor samples from TCGA and normal samples from GTEx [8]. The data were quantile normalized and batch-corrected using ComBat. Differential expression was calculated as the logarithmic<sub>2</sub> fold change between tumor and matched normal samples and averaged for each gene.

**Pathway-derived features:** Pathway membership was encoded as binary vectors using pathway data from the KEGG database [9]. For each gene, a value of 1

indicates its inclusion in a given pathway, while 0 denotes its absence. This representation enables the model to incorporate functional context from curated signaling and metabolic pathways, enhancing its ability to capture biologically meaningful interactions.

**Table S1.** Training hyperparameters for different models

Model	Hidden_channels	# Epochs	Patience	Lr	Weight_decay	Dropout
GCN	64	300	30	0.01	5e-4	0.5
GCN-AE	64	200	-	0.001	-	-
Pretrain	64	300	-	0.001	5e-4	-
Finetune	64	300	30	0.001	5e-3	0.5

**Table S2.** Summary statistics across 12 cancer types. The first three rows report the number of mutation-derived, pathway-derived, and total gene features. The last two rows show the number of driver and passenger genes.

BRCA	BLCA	LUAD	THCA	LIHC	LUSC	ESCA	PRAD	STAD	COAD	UCEC	CESC
4	4	4	4	4	4	4	4	4	4	4	4
8	6	7	5	11	7	5	8	8	9	8	14
12	10	11	9	15	11	9	12	12	13	12	18
202	95	179	72	82	26	89	57	94	155	78	18
2187	2187	2187	2187	2187	2187	2187	2187	2187	2187	2187	2187

**Table S3.** Performance comparison on cancer type-specific driver gene prediction

Cancer	Ours	GAT	Chebnet	EMOGI	MTGCN
BRCA	0.7346	0.4387	0.6507	0.6482	0.6583
BLCA	0.6853	0.2892	0.5394	0.5485	0.6568
LUAD	0.6416	0.3398	0.5771	0.5591	0.6279
LIHC	0.5215	0.2340	0.4215	0.3845	0.4645
THCA	0.3823	0.0976	0.2860	0.2587	0.2907
LUSC	0.4114	0.0673	0.2401	0.2222	0.3099
ESCA	0.5536	0.2478	0.4288	0.4174	0.4721
PRAD	0.6784	0.1777	0.4910	0.5233	0.6143
STAD	0.6329	0.1717	0.4730	0.4604	0.5931
COAD	0.5113	0.1932	0.3490	0.3459	0.3816
UCEC	0.5148	0.1658	0.4021	0.4020	0.4954
CESC	0.5762	0.0839	0.5261	0.5547	0.5972

**Table S4.** Ablation study: performance comparison with and without pathway features, gene expression (GE), and pretraining

Cancer	No Pathway	With Pathway	No GE	With GE	No Pretrain	With Pretrain
BRCA	0.7056	0.7310	0.7152	0.7310	0.7310	0.7346
BLCA	0.6721	0.6808	0.6756	0.6808	0.6808	0.6853
LUAD	0.6146	0.6458	0.6185	0.6458	0.6458	0.6416
LIHC	0.4415	0.4558	0.4205	0.4558	0.4558	0.5215
THCA	0.3362	0.3556	0.3156	0.3556	0.3556	0.3823
LUSC	0.3208	0.3846	0.3185	0.3846	0.3846	0.4114
ESCA	0.5385	0.5523	0.4858	0.5523	0.5523	0.5536
PRAD	0.5363	0.6825	0.6010	0.6825	0.6825	0.6784
STAD	0.5824	0.5662	0.5310	0.5662	0.5662	0.6329
COAD	0.5005	0.4945	0.4926	0.4945	0.4945	0.5113
UCEC	0.4372	0.4189	0.4452	0.4189	0.4189	0.5148
CESC	0.4050	0.5185	0.5320	0.5185	0.5185	0.5762

**Table S5.** Top 100 prioritized genes ranked by the model (with scores)

Rank	Gene	Score	Rank	Gene	Score	Rank	Gene	Score	Rank	Gene	Score
1	SUN5	–	26	WNT5A	0.35	51	CDK1	0.35	76	PTK2	0.45
2	TTN	0.2	27	FZD1	0.25	52	FZD7	0.35	77	WNT11	0.2
3	PCBP4	–	28	WNT3A	0.2	53	EGF	0.45	78	TLE1	0.2
4	SUN3	–	29	GRB2	0.35	54	DKK1	0.35	79	IMPG2	–
5	DVL1	0.2	30	MUC12	–	55	CD44	0.45	80	CDK2	0.35
6	LRP5	0.25	31	MUC6	0.25	56	DNAH1	0.15	81	WIF1	0.3
7	PIK3R3	0.25	32	MAPK9	0.35	57	KDR	0.45	82	MUC7	0.1
8	PIK3R2	0.1	33	PTPRB	0.15	58	PRKCB	0.35	83	STAT3	0.45
9	DVL2	0.2	34	FZD4	0.2	59	FZD9	–	84	MAP4K3	–
10	SYNE3	–	35	MUC20	–	60	SFRP1	0.35	85	CTBP1	0.35
11	DVL3	0.2	36	FZD6	0.2	61	WNT4	0.25	86	WNT7A	0.2
12	SRC	0.45	37	FZD5	0.1	62	RAC2	0.2	87	MUC21	0.25
13	LRP6	0.35	38	FN1	0.35	63	JUN	0.35	88	ANK1	–
14	MUC16	0.35	39	MUC17	0.2	64	WNT1	0.35	89	SHC1	0.35
15	GSK3B	0.35	40	TP53I3	–	65	FZD3	0.2	90	MUC5AC	0.35
16	HDAC1	0.4	41	ITGB1	0.35	66	MUC5B	0.25	91	VANGL2	0.2
17	DIRAS1	0.2	42	CALM3	0.2	67	ZNRF3	0.05	92	TCF7L2	0.4
18	MAPK1	0.45	43	MAML2	0.1	68	DLL1	0.2	93	H3C12	–
19	PRKACA	0.35	44	RNF43	0.15	69	PLCG2	0.2	94	CALML3	0.25
20	PRKACB	–	45	FZD2	0.15	70	PRKCA	0.35	95	SOS1	0.25
21	PRKACG	0.1	46	FZD8	0.2	71	WNT2	0.75	96	CDKN1A	0.5
22	MAPK3	0.35	47	MUC13	–	72	TLE3	0.2	97	MAML1	0.25
23	RBPJ	0.2	48	PDGFRB	0.35	73	PLCG1	0.25	98	WNT5B	0.2
24	MAPK8	0.45	49	BCL2	0.45	74	NOTCH4	0.35	99	SLITRK2	–
25	TRIM55	–	50	TEK	0.35	75	RAC3	0.3	100	WNT6	–

**Table S6.** A summary of the number of nodes and edges for each cancer-specific graph

Cancer	#Nodes	#Edges
BRCA	12 809	148 969
BLCA	12 809	148 915
LUAD	12 809	149 129
LIHC	12 809	148 278
THCA	12 809	149 244
LUSC	12 809	148 789
ESCA	12 809	149 319
PRAD	12 809	149 756
STAD	12 809	149 327
COAD	12 809	148 993
UCEC	12 809	150 037
CESC	12 809	148 798

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