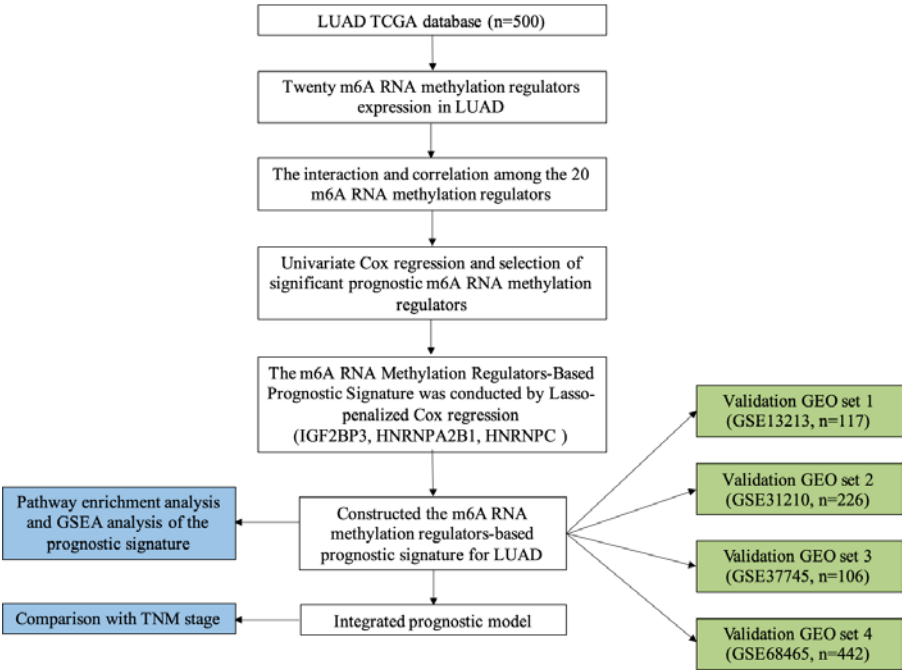**Supplementary Figure 1:** Design and workflow of this study.
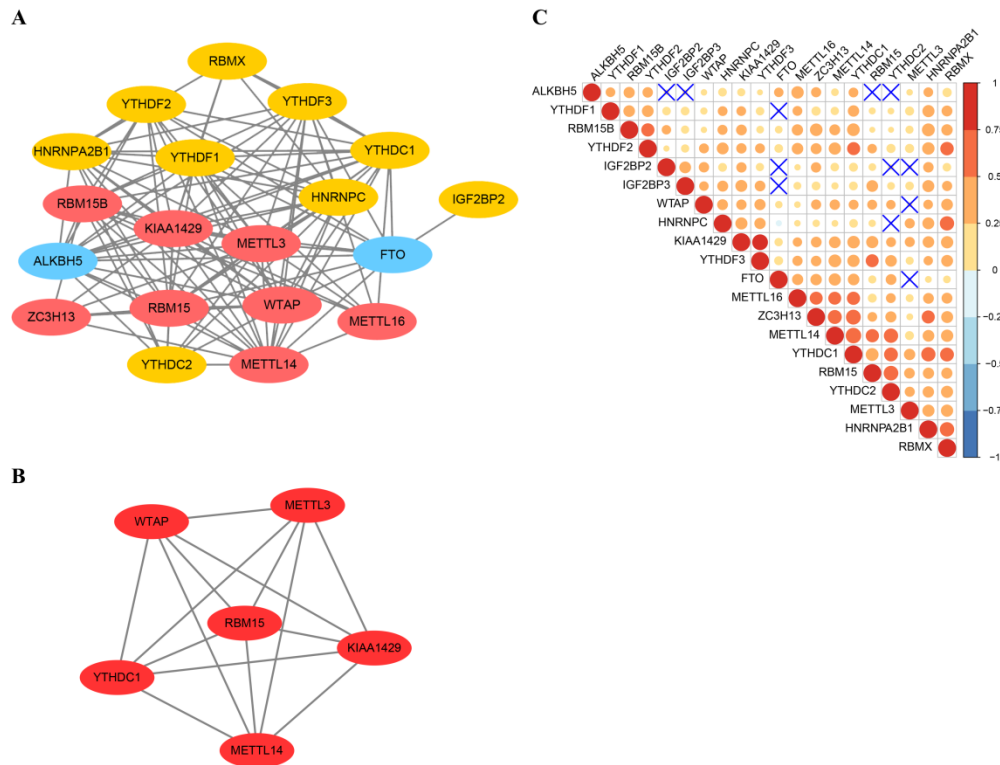

Supplementary Figure 2: Different expression of m6A RNA methylation regulators between LUAD and paired normal tissue. **(A)** The heatmap of 20 m6A RNA methylation regulator expression profile in TCGA-LUAD cohort. **(B)** Different expression of m6A RNA methylation regulators between tumor samples and the normal tissues. Wilcoxon test was used for statistical testing. GEO: Gene Expression Omnibus; GSEA: Gene set enrichment analysis; LUAD: Lung adenocarcinoma; m6A: N6-methyladenosine; TCGA: The Cancer Genome Atlas.
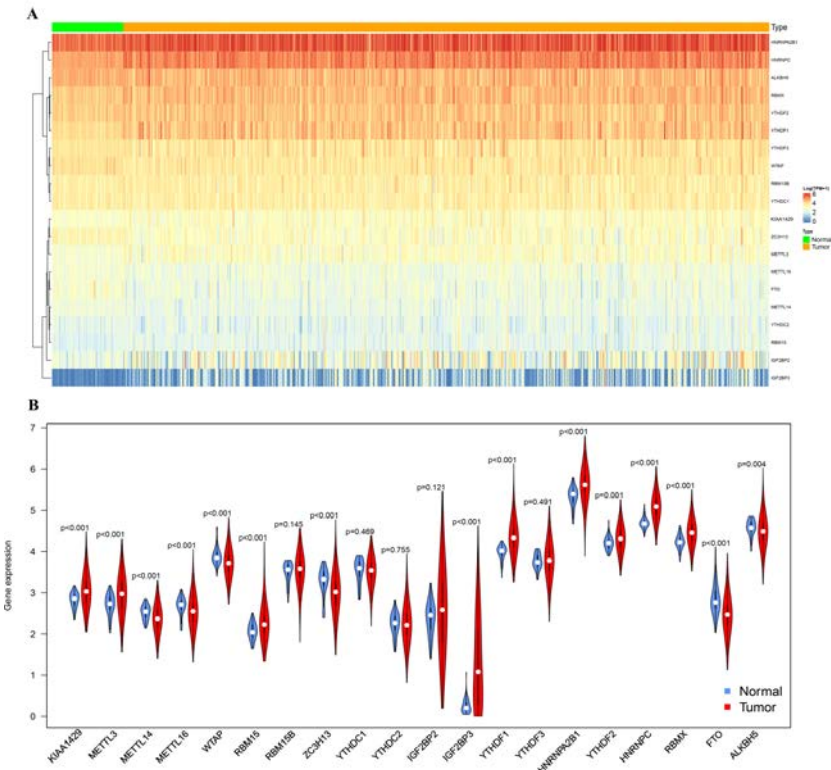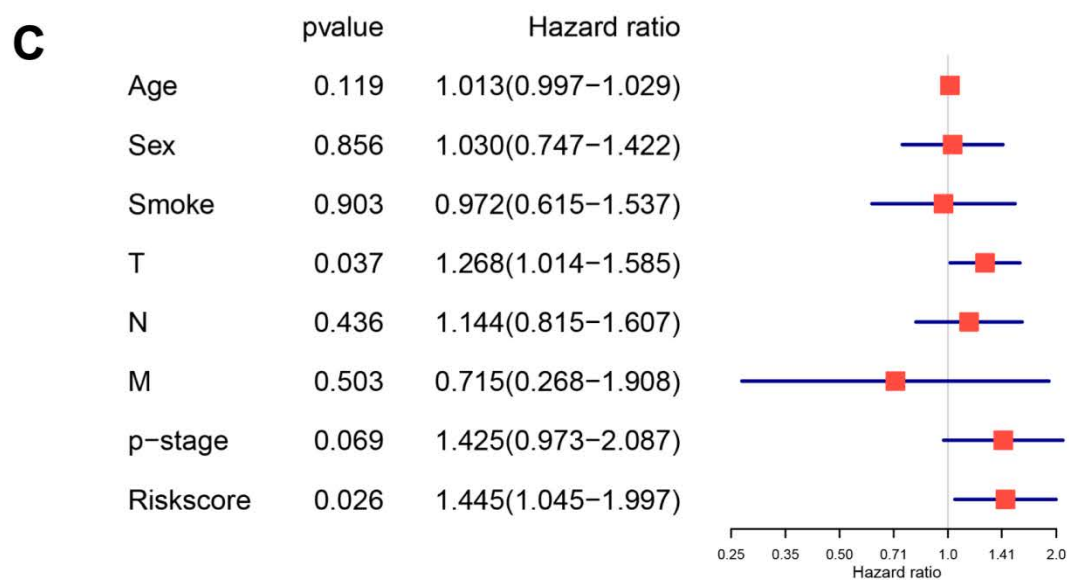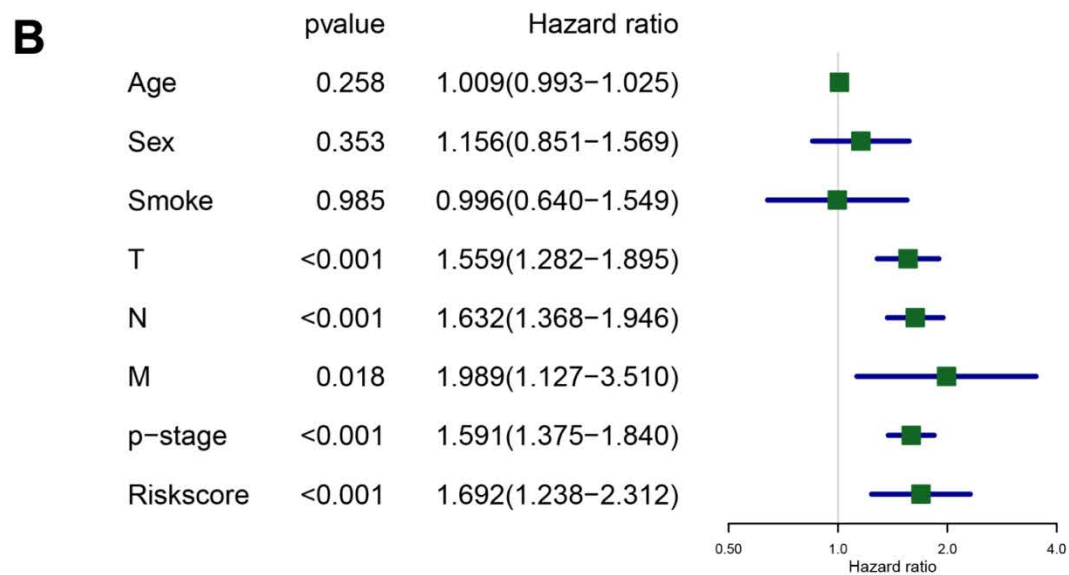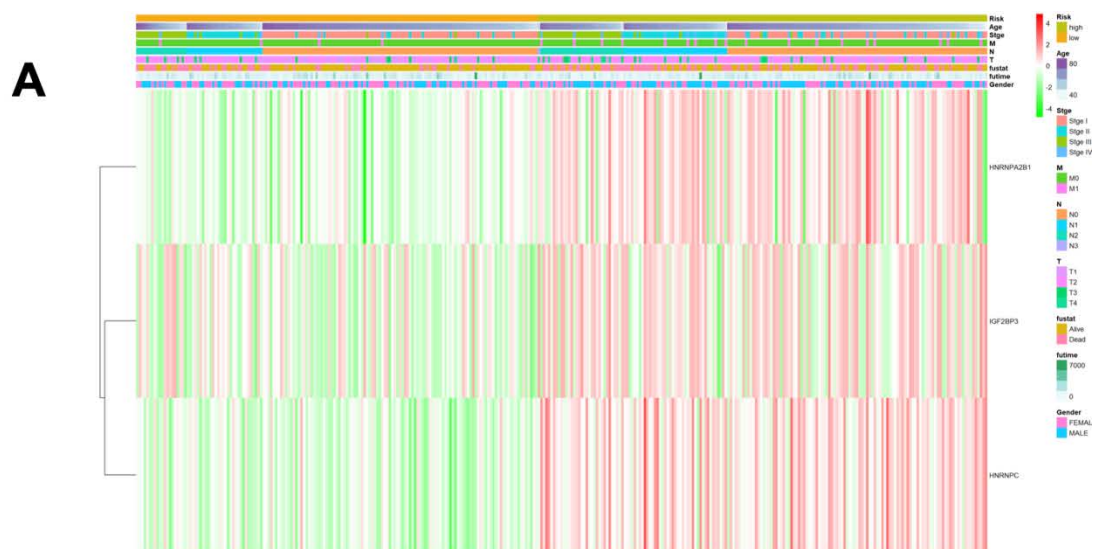
Supplementary Figure 3: The PPI network and correlation analysis among m6A RNA methylation regulators. **(A)** The interaction of 20 m6A RNA methylation regulators visualized by PPI network. **(B)** A densely connected network containing six hub genes was selected based on topology. **(C)** Spearman correlation analysis of the 20 m6A RNA methylation regulators. m6A: N6-methyladenosine; PPI: Protein–protein interaction.

Supplementary Figure 4: The relationship among the clinicopathological characteristics and risk score. **(A)** The heatmap demonstrates the expression level of IGF2BP3, HNRNPC, and HNRNPA2B1 in low- and high-risk LUAD cases. Also, the distribution of clinicopathological characteristics was compared between these two subgroups. **(B)** Univariate and **(C)** multivariate Cox regression analyses of the association between clinicopathological factors and OS of patients in TCGA. LUAD: Lung adenocarcinoma; OS: Overall survival; TCGA: The Cancer Genome Atlas.

A

B

	pvalue	Hazard ratio	
Age	0.258	1.009(0.993–1.025)	
Sex	0.353	1.156(0.851–1.569)	
Smoke	0.985	0.996(0.640–1.549)	
T	<0.001	1.559(1.282–1.895)	
N	<0.001	1.632(1.368–1.946)	
M	0.018	1.989(1.127–3.510)	
p−stage	<0.001	1.591(1.375–1.840)	
Riskscore	<0.001	1.692(1.238–2.312)	

C

	pvalue	Hazard ratio	
Age	0.119	1.013(0.997–1.029)	
Sex	0.856	1.030(0.747–1.422)	
Smoke	0.903	0.972(0.615–1.537)	
T	0.037	1.268(1.014–1.585)	
N	0.436	1.144(0.815–1.607)	
M	0.503	0.715(0.268–1.908)	
p−stage	0.069	1.425(0.973–2.087)	
Riskscore	0.026	1.445(1.045–1.997)	

Supplementary Figure 5: Kaplan–Meier OS analyses for IGF2BP1, HNRNPC, and HNRNPC expressed in patients with LUAD in TCGA cohort. LUAD: Lung adenocarcinoma; OS: Overall survival; TCGA: The Cancer Genome Atlas.
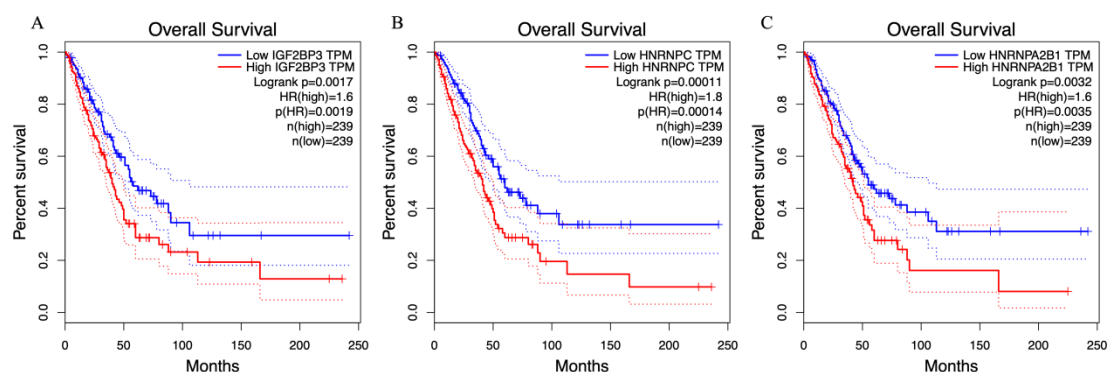
**Supplementary Figure 6:** Kaplan–Meier OS analyses for IGF2BP1, HNRNPC, and HNRNPC expressed in patients with LUAD in KM plotter cohort. LUAD: Lung adenocarcinoma; OS: Overall survival.
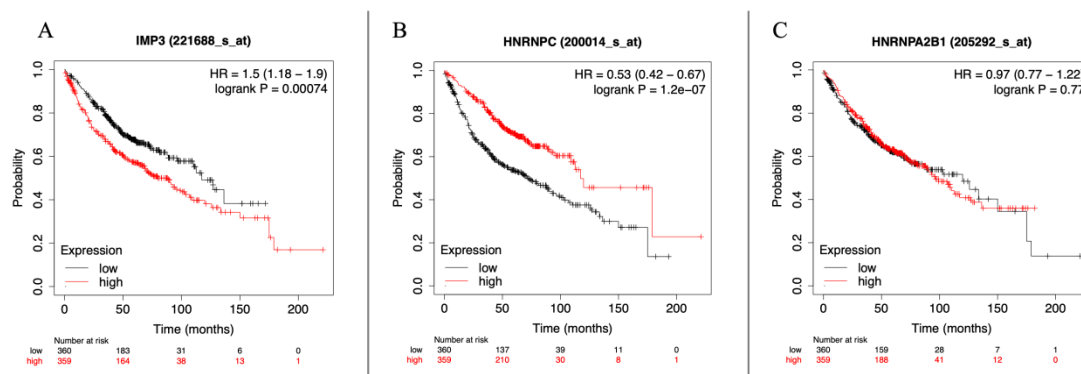
Supplementary Figure 7: Validation of the m6A prognostic signature in independent datasets. Kaplan–Meier curve of OS between low-risk and high-risk groups in **(A)** GSE13213, **(B)** GSE31210, **(C)** GSE37745, and **(D)** GSE68465. Prediction efficiency of the m6A prognostic signature was assessed using AUC in **(E)** GSE13213, **(F)** GSE31210, **(G)** GSE37745, and **(H)** GSE68465. AUC: Area under the curve; m6A: N6-methyladenosine; OS: Overall survival.
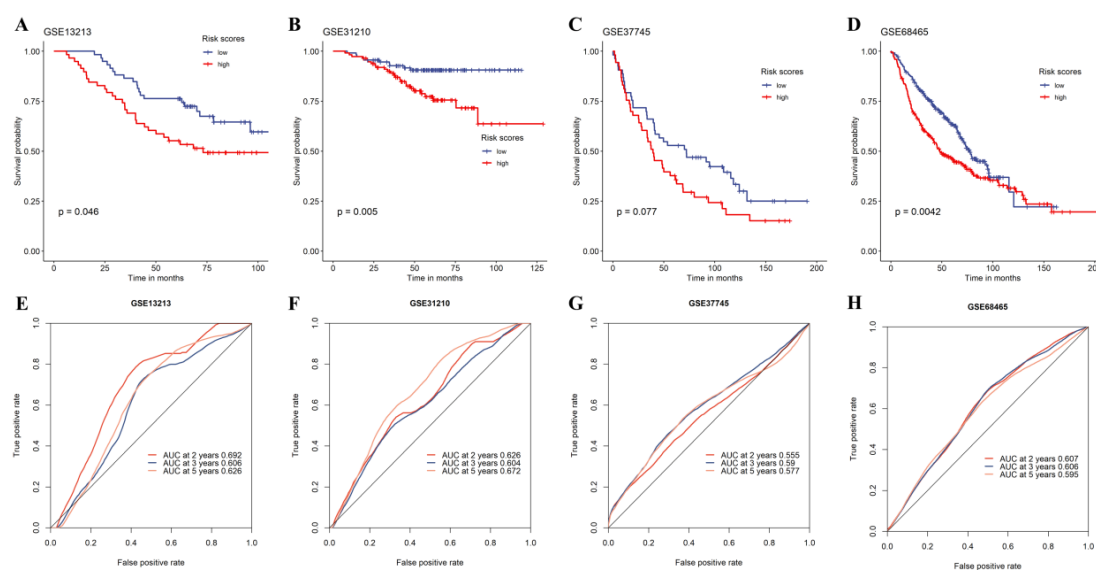
Supplementary Figure 8: Comparisons of predicting the performance of integrated signature with the m6A prognostic signature or TNM staging alone by ROC curve. **(A)** 2-year ROC in TCGA. **(B)** 3-year ROC in TCGA. **(C)** 5-year ROC in TCGA. **(D)** 2-year ROC in GSE13213. **(E)** 3-year ROC in GSE13213. **(F)** 5-year ROC in GSE13213. **(G)** 2-year ROC in GSE31210. **(H)** 3-year ROC in GSE31210. **(I)** 5-year ROC in GSE31210. AUC; Area under the curve; m6A: N6-methyladenosine; ROC: Receiver operating characteristic; TCGA: The Cancer Genome Atlas.

Supplementary Figure 9: The PPI network and functional enrichment analysis of signature constituted genes and closely related genes. **(A)** PPI network of m6A-related genes. **(B)** Functional enrichment analysis of components of the m6A signature using GO biological processes and KEGG. GO: Gene Ontology; KEGG: Kyoto Encyclopedia of Genes and Genomes; m6A: N6-methyladenosine; PPI: Protein–protein interaction.

Supplementary Figure 10: GSEA of LUAD subgroup stratified by the m6A prognostic signature. **(A)** G2M checkpoint. **(B)** E2F targets. **(C)** MTORC1 signaling. **(D)** MYC targets. **(E)** DNA repair. **(F)** Heatmap of the top 50 genes that were most significantly positive or negative correlated with the m6A prognostic signature. GSEA: Gene set enrichment analysis; LUAD: Lung adenocarcinoma; m6A: N6-methyladenosine.

Supplementary Table 1: Correlations between the m6A prognostic signature and clinicopathological parameters in TCGA-LUAD cohort.

Category	Cases	m6A prognostic signature		P-value
		Low (*n* = 228)	High (*n* = 237)	
n	**465**			
Age (mean (SD))		66.1 (9.9)	64.3 (10.1)	0.059
Gender, *n* (%)				0.093
Male	211 (45.4)	94 (41.2)	117 (49.4)	
Female	254 (54.6)	134 (58.8)	120 (50.6)	
Smoking, *n* (%)				0.482
Yes	400 (86.0)	193 (84.6)	207 (87.3)	
No	65 (14.0)	35 (15.4)	30 (12.7)	
T stage, *n* (%)				**0.000**
T1	161 (34.6)	98 (42.2)	63 (27.0)	
T2	245 (52.7)	102 (44.7)	143 (60.3)	
T3	44 (9.4)	24 (10.5)	20 (8.4)	
T4	15 (3.2)	4 (1.8)	11 (4.6)	
N stage, *n* (%)				0.075
N0	314 (67.5)	167 (73.2)	147 (62.0)	
N1	84 (18.1)	35 (15.4)	49 (20.7)	
N2	65 (14.0)	25 (11.0)	40 (16.9)	
N3	2 (0.4)	1 (0.4)	1 (0.4)	
M stage, *n* (%)				**0.010**
M0	444 (95.5)	224 (98.2)	220 (92.8)	
M1	21 (4.5)	4 (1.8)	17 (7.2)	
TNM stage, *n* (%)				**0.002**
I	257 (55.3)	143 (62.7)	114 (48.1)	
II	112 (24.1)	49 (21.5)	63 (26.6)	
III	75 (16.1)	32 (14.0)	43 (18.1)	
IV	21 (4.5)	4 (1.8)	17(7.2)	
Status, *n* (%)				**0.005**
Survival	300 (64.5)	162 (71.1)	138 (58.2)	
Death	165 (35.5)	66 (28.9)	99 (41.8)	

LUAD: Lung adenocarcinoma; m6A: N6-methyladenosine; TCGA: The Cancer Genome Atlas.

Supplementary Table 2: Basic information of included microarray datasets.

Author	Accession	Publication year	Platform	Number of patients
Tomida *et al*	GSE13213	2009	GPL6480	117
Okayama *et al*	GSE31210	2011	GPL570 [HG-U133_Plus_2]	226
Botling *et al*	GSE37745	2012	GPL570 [HG-U133_Plus_2]	106
Heiskanen *et al*	GSE68465	2015	GPL96 [HG-U133A]	442

Supplementary Table 3: Significantly enriched GO terms and KEGG pathways of the m6A prognostic signature.

GO ID	Description	Term *P*-value	Group *P*-value	Number of genes
KEGG:03040	Spliceosome	0	0	9
GO:0045292	mRNA cis splicing, via spliceosome	0	0	3
GO:0006376	mRNA splice site selection	0	0	3
GO:0071774	Response to fibroblast growth factor	0	0	7
GO:0044344	Cellular response to fibroblast growth factor stimulus	0	0	7
GO:0008543	Fibroblast growth factor receptor signaling pathway	0	0	5
GO:0000375	RNA splicing, via transesterification reactions	0	0	16
GO:0000377	RNA splicing, via transesterification reactions with bulged adenosine as nucleophile	0	0	16
GO:0000398	mRNA splicing, via spliceosome	0	0	16
GO:0043484	Regulation of RNA splicing	0	0	10
GO:0050684	Regulation of mRNA processing	0	0	8
GO:0033119	Negative regulation of RNA splicing	0	0	4
GO:1903312	Negative regulation of mRNA metabolic process	0	0	7
GO:0048024	Regulation of mRNA splicing, via spliceosome	0	0	8
GO:0050686	Negative regulation of mRNA processing	0	0	4
GO:0000381	Regulation of alternative mRNA splicing, via	0	0	6

	spliceosome			
GO:0048025	Negative regulation of mRNA splicing, via spliceosome	0	0	4
GO:0043489	RNA stabilization	0	0	4
GO:0033119	Negative regulation of RNA splicing	0	0	4
GO:1902369	Negative regulation of RNA catabolic process	0	0	4
GO:1903312	Negative regulation of mRNA metabolic process	0	0	7
GO:0048255	mRNA stabilization	0	0	4
GO:0050686	Negative regulation of mRNA processing	0	0	4
GO:1902373	Negative regulation of mRNA catabolic process	0	0	4
GO:0048025	Negative regulation of mRNA splicing, via spliceosome	0	0	4
GO:0070935	3′-UTR-mediated mRNA stabilization	0	0	3

GO: Gene Ontology; KEGG: Kyoto Encyclopedia of Genes and Genomes; m6A: N6-methyladenosine.