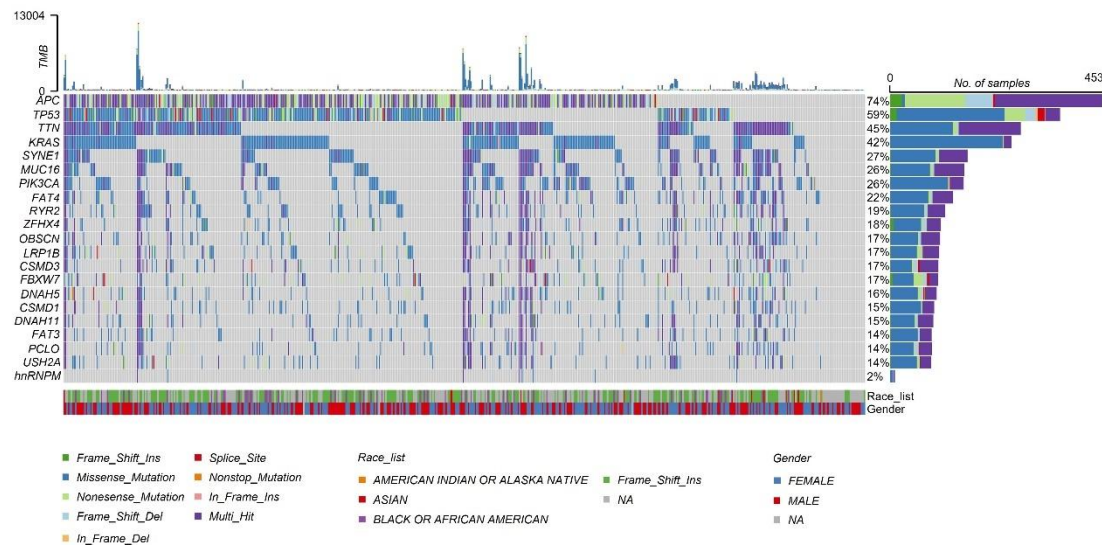


Supplementary File

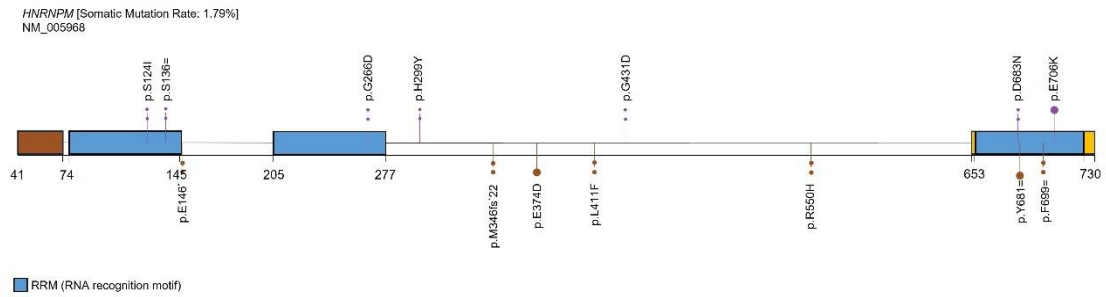
Supplementary Figure 1



Supplementary Figure 1. *In silico* analysis of somatic mutation in CRC samples.

Oncoplot displays the landscape of somatic mutation in CRC cohort from the TCGA datasets. Genes on the left are sorted by mutation frequency, and samples are sorted by race and gender, as shown in the annotation box below. The bar plot on the right presents the $(-\log_{10})$ transformed q-values estimated using MutSigCV algorithm. Mutation information for genes in samples is shown in a waterfall plot, with different colors and specific annotations at the bottom representing different mutation types, races and genders. CRC colorectal cancer, TCGA The Cancer Genome Atlas.

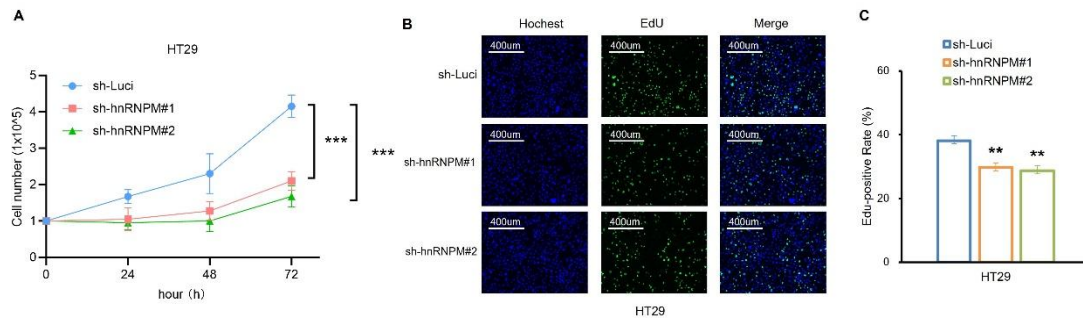
Supplementary Figure 2



Supplementary Figure 2. The mutation distribution of hnRNPM in CRC samples.

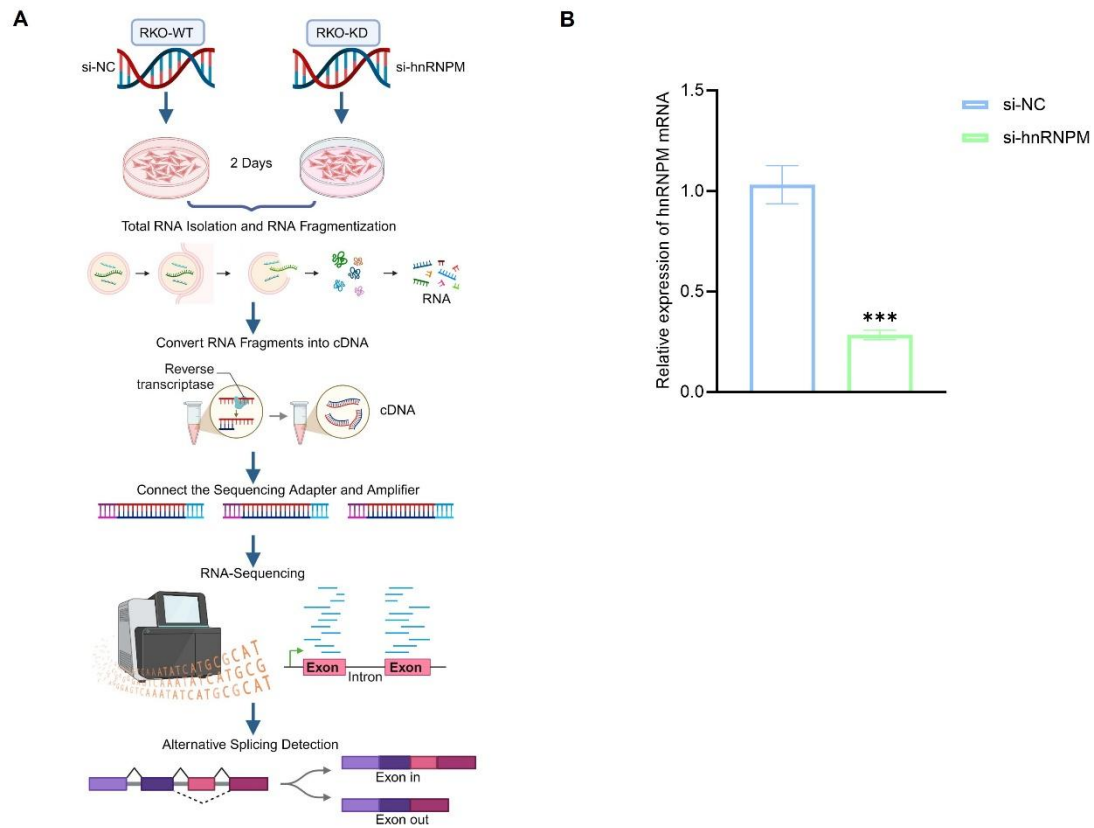
The lollipop plot illustrated the mutation rate and the mutation sites of hnRNPM in CRC samples from the TCGA datasets. hnRNPM heterogeneous nuclear ribonucleoprotein M.

Supplementary Figure 3



Supplementary Figure 3. HnRNPM is essential to the proliferation of colon cancer cells. **A** Colon cancer cell HT29 was stably knockdown using lentiviruses transfected with hnRNPM shRNA (sh-hnRNPM#1, sh-hnRNPM#2) or negative control shRNA (sh-Luci). The growth curves of HT29 cells were shown after stably transfected with indicated shRNAs. *** $p < 0.001$. **B** The representative images showed the EdU staining assay for HT29 cells described in (A). **C** The bar graph presented the results described in (B) and showed as mean $\pm$ SD. ** $p < 0.01$. hnRNPM heterogeneous nuclear ribonucleoprotein M, EdU 5-ethynyl-2'-deoxyuridine.

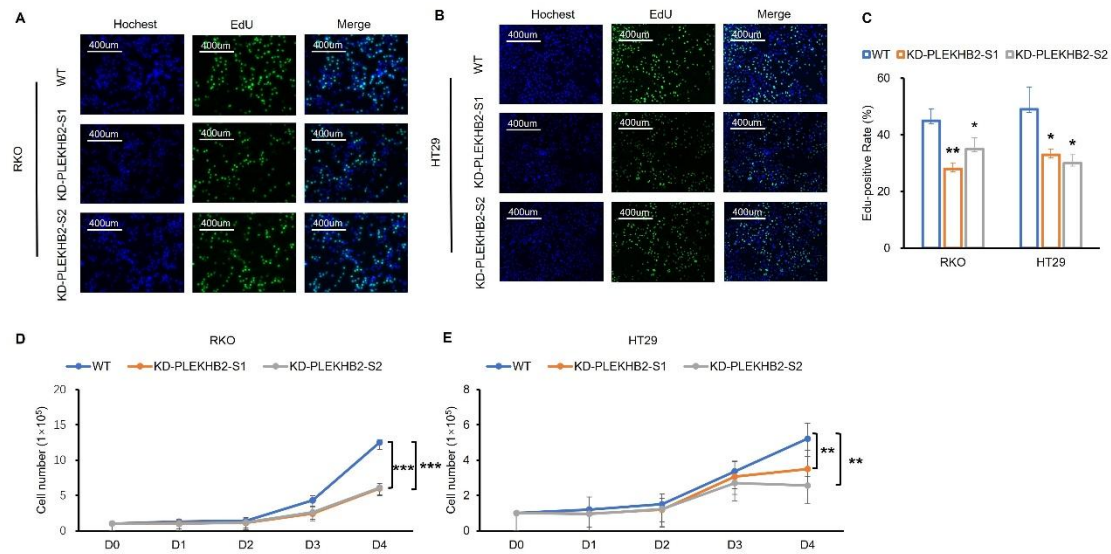
Supplementary Figure 4



Supplementary Figure 4. RNA-seq strategy of RKO cells knockdown by hnRNPM.

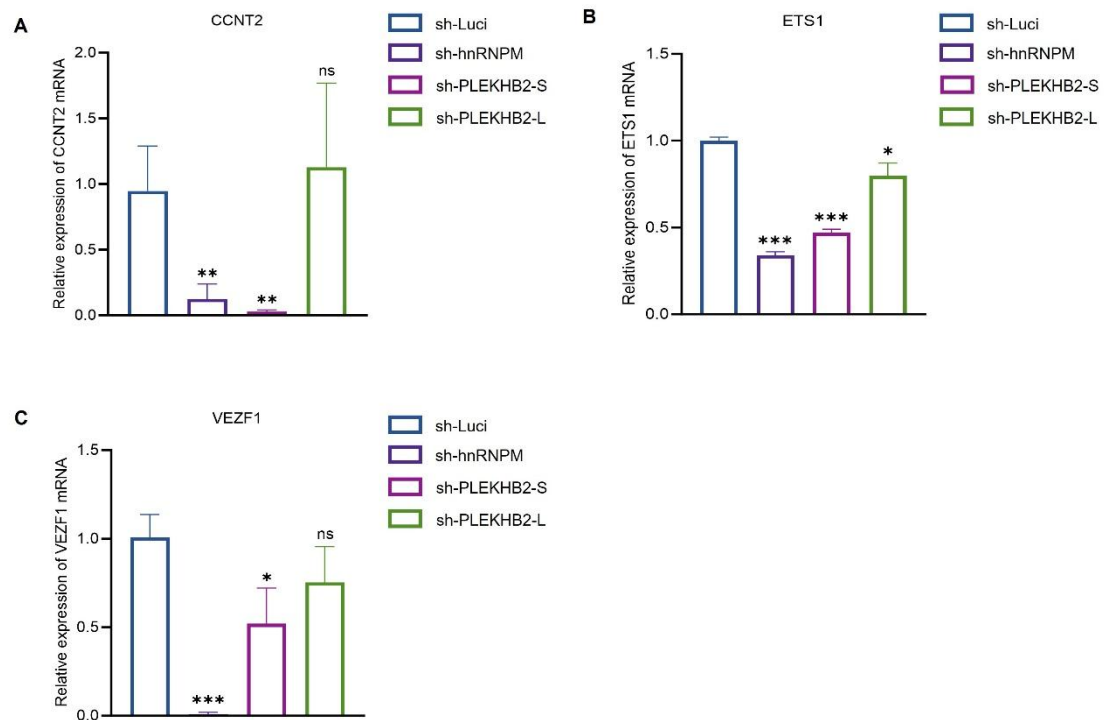
A RNA-seq strategy of RKO cells transiently transfected with si-hnRNPM or si-NC independently. The picture was created with BioRender.com. **B** The knockdown effect of si-hnRNPM in RKO cells was analyzed by qRT-PCR analysis. hnRNPM heterogeneous nuclear ribonucleoprotein M, qRT-PCR quantitative reverse transcriptase PCR.

Supplementary Figure 5



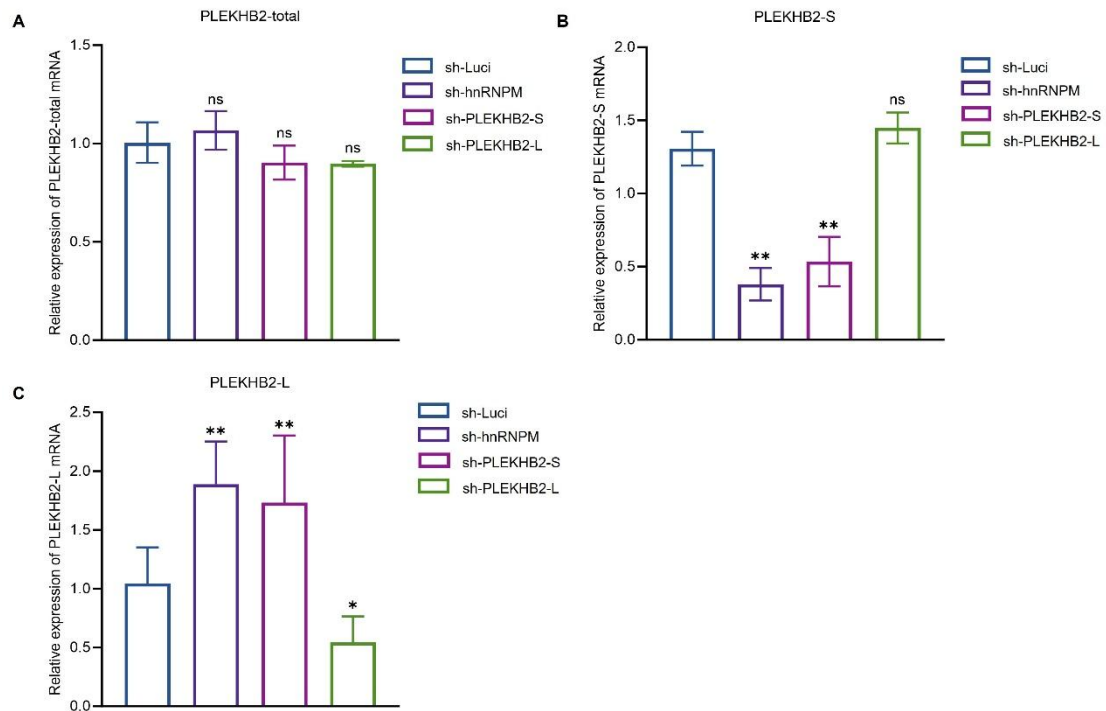
Supplementary Figure 5. Knockdown of PLEKHB2-S splice isoform inhibited the proliferation of colon cancer cells *in vitro*. **A, B** RKO and HT29 cells were stably knockdown using lentiviruses transfected with isoform-specific shRNAs, which targeted against the sh-PLEKHB2-S1 and sh-PLEKHB2-S2 variants independently. The representative images of EdU staining assay for cells described in **(A)** and **(B)** were shown. **C** The results described in **(A)** and **(B)** were presented as mean $\pm$ SD in the bar graph. * $p < 0.05$, ** $p < 0.01$. **D, E** The growth curves of RKO and HT29 cells were shown after stably transfected with indicated shRNAs. ** $p < 0.01$, *** $p < 0.001$. PLEKHB2 pleckstrin homology domain containing B2, EdU 5-ethynyl-2'-deoxyuridine.

Supplementary Figure 6



Supplementary Figure 6. Knockdown of hnRNPM or PLEKHB2-S splice isoforms inhibited the expression of CCNT2, ETS1 and VEZF1. A-C The mRNA expression of CCNT2 (A), ETS1 (B) and VEZF1 (C) were examined via qRT-PCR assay in RKO cells by stably knockdown hnRNPM, PLEKHB2-S or sh-PLEKHB2-L individually. *ns*: no significance, $*p < 0.05$, $**p < 0.01$, $***p < 0.001$. hnRNPM heterogeneous nuclear ribonucleoprotein M, PLEKHB2 pleckstrin homology domain containing B2, qRT-PCR quantitative reverse transcriptase PCR.

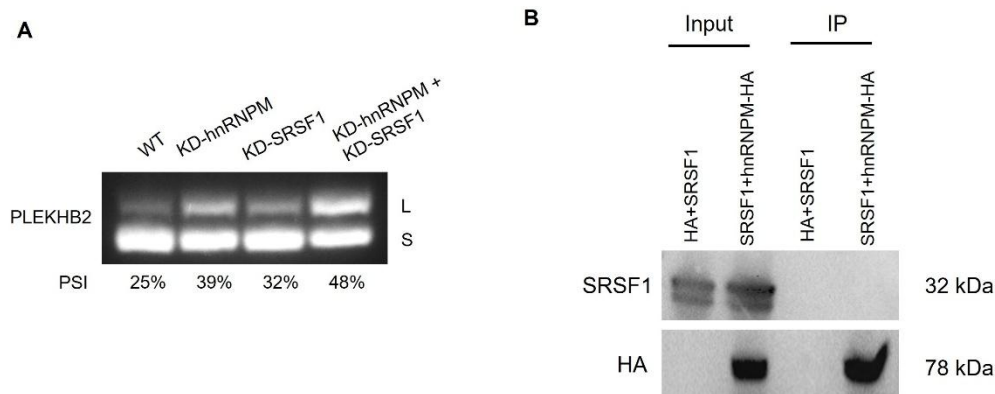
Supplementary Figure 7



Supplementary Figure 7. The mRNA levels of total PLEKHB2, PLEKHB2-S and PLEKHB2-L in hnRNPM, PLEKHB2-S or PLEKHB2-L knockdown RKO cells.

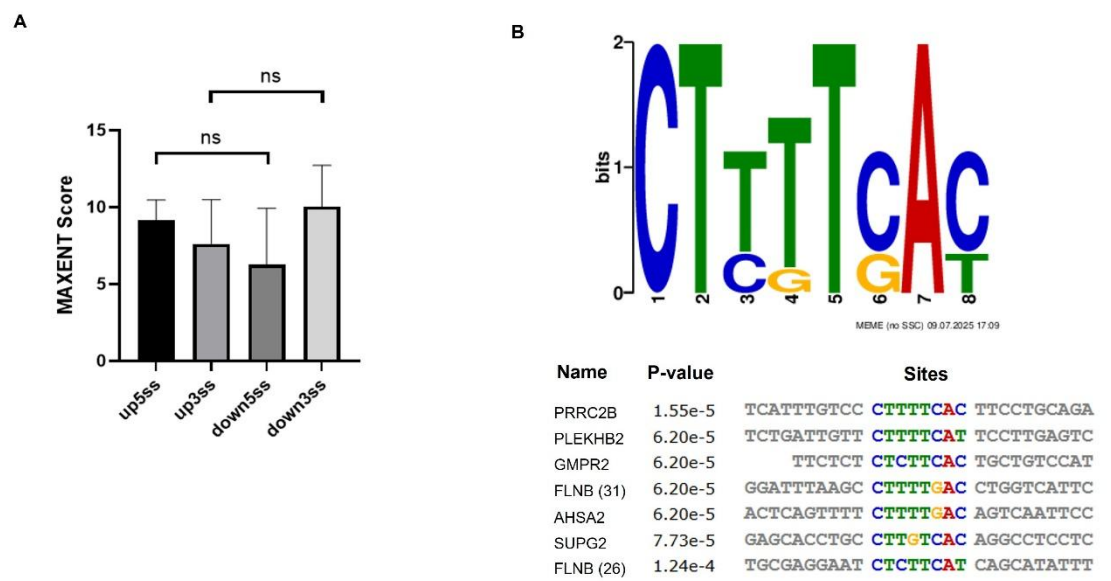
A-C RKO cells were stably knockdown using lentiviruses transfected with sh-hnRNPM, sh-PLEKHB2-S, sh-PLEKHB2-L or negative control shRNA (sh-Luci). The mRNA levels of total PLEKHB2 (**A**), PLEKHB2-S (**B**) and PLEKHB2-L (**C**) were detected by qRT-PCR in sh-hnRNPM, sh-PLEKHB2-S, sh-PLEKHB2-L or sh-Luci cells, respectively. hnRNPM heterogeneous nuclear ribonucleoprotein M, PLEKHB2 pleckstrin homology domain containing B2, qRT-PCR quantitative reverse transcriptase PCR.

Supplementary Figure 8



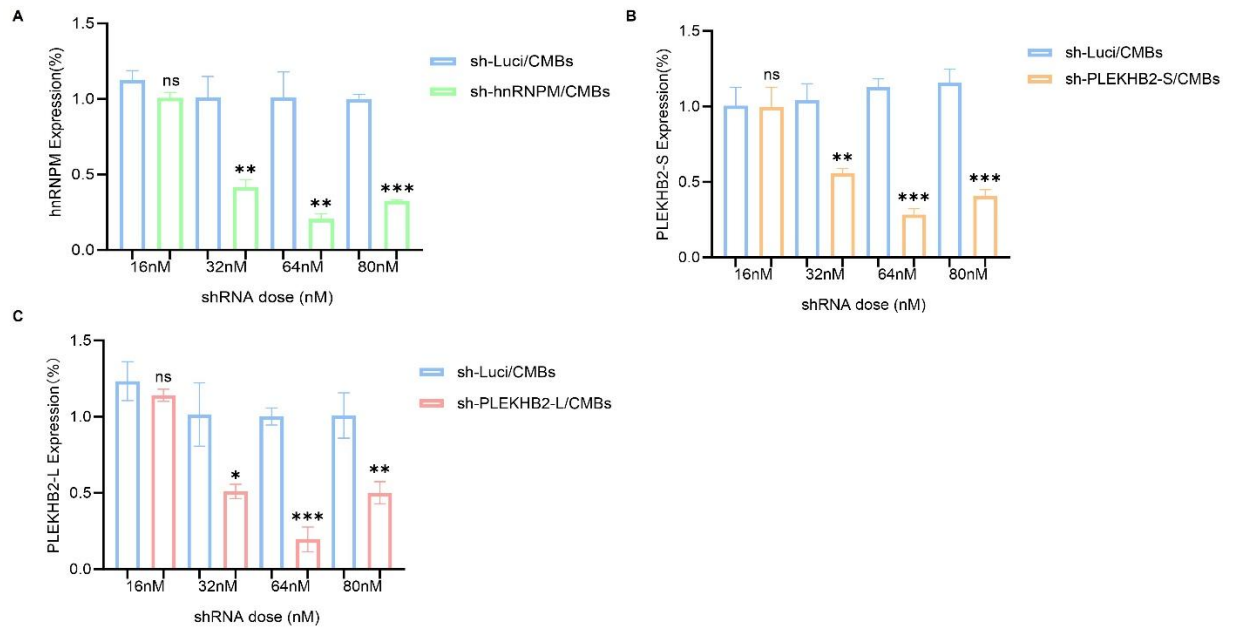
Supplementary Figure 8. The relationship between splicing regulators hnRNPM and SRSF1. **A** The indicated siRNAs (si-NC, si-hnRNPM, si-SRSF1, si-hnRNPM + si-SRSF1) were transiently transfected into RKO cells, and the RNAs were extracted for RT-PCR analysis of PLEKHB2 exon 8 inclusion/exclusion. The quantification of RT-PCR results was measured by PSI (percent of splicing in) and shown under the corresponding RT-PCR image. **B** The indicated plasmids (HA vector + SRSF1, SRSF1 + hnRNPM-HA) were transfected into 293T cells, and the western blot analysis following co-immunoprecipitation (co-IP) assay indicated the interaction between hnRNPM and SRSF1. hnRNPM heterogeneous nuclear ribonucleoprotein M, SRSF1 serine and arginine rich splicing factor 1.

Supplementary Figure 9



Supplementary Figure 9. Motif analysis of hnRNPM-affected alternative splicing events. **A** Splice site strength at the 5'SS and 3'SS of the upstream and downstream introns of the alternative exons was assessed using the MaxEntScan. *ns*, no significance. **B** MEME analysis was performed on the sequences of downstream exons of the validated alternative exons. The height of each letter presents the relative frequency of each base at different positions in the consensus sequence.

Supplementary Figure 10



Supplementary Figure 10. The sh-RNA/CMBs suppress the mRNA expression of hnRNPM, PLEKHB2-S or PLEKHB2-L at the dose over 32nM. A-C The qRT-PCR assay presented the mRNA expression of hnRNPM (A), PLEKHB2-S (B) and PLEKHB2-L (C) in RKO cells which were transfected with sh-Luci/CMBs, sh-hnRNPM/CMBs, sh-PLEKHB2-S/CMBs, sh-PLEKHB2-L/CMBs at different doses. *ns*: no significance, $*p < 0.05$, $**p < 0.01$, $***p < 0.001$. hnRNPM heterogeneous nuclear ribonucleoprotein M, qRT-PCR quantitative reverse transcriptase PCR, PLEKHB2 pleckstrin homology domain containing B2.

Supplementary table 1. Clinical information of 22 CRC patients.

Patient Number	Gender	Age	Tumor site	T	N	M	TNM	Status
1	male	53	Rectum	2	0	0	I	Alive
2	male	68	Rectum	4	0	0	II	Alive
3	male	77	Colon	3	1	0	IIIB	Alive
4	male	51	Rectum	3	2b	0	IIIC	Alive
5	female	66	Rectum	2	0	0	I	Alive
6	male	83	Rectum	3	1	0	IIIB	Alive
7	female	82	Colon	4	2	1	IVA	Alive
8	female	38	Rectum	4	2	0	IIIC	Alive
9	female	55	Colon	3	2	1	IIIC	Alive
10	male	72	Rectum	3	0	0	IIA	Alive
11	female	70	Colon	3	0	0	IIA	Alive
12	female	77	Rectum	3	1	1a	IVA	Alive
13	male	78	Rectum	3	0	0	IIA	Alive
14	female	62	Colon	3	0	0	IIA	Alive
15	male	74	Colon	3	2a	0	III	Alive
16	female	72	Rectum	3	1	0	IIIB	Alive
17	female	61	Colon	3	2	0	IIIB	Alive
18	male	63	Colon	4	1	0	IIIB	Alive
19	male	67	Rectum	3	1	0	IIIB	Alive
20	female	65	Rectum	2	0	0	I	Alive
21	female	58	Rectum	3	1	0	IIIB	Alive
22	male	53	Rectum	2	0	0	I	Alive

Supplementary table 2. The shRNAs used in this study.

Names	Sequences (5'-3')
sh-Luci-F	CCGGTTCCTGGAACAATTGCTTTTACTCGAGTAAAAGCAATTGTTCCA GGAATTTTTG
sh-Luci-R	AATTCAAAAATTCCTGGAACAATTGCTTTTACTCGAGTAAAAGCAAT TGTTCAGGAA
sh-hnRNPM#1-F	CCGGAACAGGAGGGCAACCCATTGACTCGAGTCAATGGGTGCCCCTC CTGTTTTTTTTG
sh-hnRNPM#1-R	AATTCAAAAAAACAGGAGGGCAACCCATTGACTCGAGTCAATGGGT GCCCTCCTGTT
sh-hnRNPM#2-F	CCGGAAGCAACCCATTGATGCCAATCTCGAGATTGGCATCAATGGGT TGCTTTTTTTG
sh-hnRNPM#2-R	AATTCAAAAAAAGCAACCCATTGATGCCAATCTCGAGATTGGCATCA ATGGGTGCTT
sh-PLEKHB2-S-F	CCGGAACAGGACTTTATGGACAGCACTCGAGTGCTGTCCATAAAGTC CTGTTTTTTTTG
sh-PLEKHB2-S-R	AATTCAAAAAAACAGGACTTTATGGACAGCACTCGAGTGCTGTCCAT AAAGTCCTGTT
sh-PLEKHB2-L-F	CCGGAACATGACACGTCATTGCACTCTCGAGAGTGCAATGACGTGTC ATGTTTTTTTTG
sh-PLEKHB2-L-R	AATTCAAAAAAACATGACACGTCATTGCACTCTCGAGAGTGCAATGA CGTGTCATGTT
sh-hnRNPM-F (CMBs)	CCGGAAGGCATCGGAATGGGAAACACTCGAGTGTTTCCCATCCGAT GCCTTTTTTTTTG
Sh-hnRNPM-R (CMBs)	AATTCAAAAAAAGGCATCGGAATGGGAAACACTCGAGTGTTTCCCAT TCCGATGCCTT
sh-PLEKHB2-S-F (CMBs)	CCGGAATGCAGGACTTTATGGACAGCTCGAGCTGTCCATAAAGTCCT GCATTTTTTTTTG
sh-PLEKHB2-S-R (CMBs)	AATTCAAAAAAATGCAGGACTTTATGGACAGCTCGAGCTGTCCATAA AGTCCTGCATT
sh-PLEKHB2-L-F (CMBs)	CCGGAACATGACACGTCATTGCACTCTCGAGAGTGCAATGACGTGTC ATGTTTTTTTTG
sh-PLEKHB2-L-R (CMBs)	AATTCAAAAAAACATGACACGTCATTGCACTCTCGAGAGTGCAATGA CGTGTCATGTT

Supplement table 3. The antibodies used in this study.

Names	Manufacturers	Cat. Number
Anti-hnRNP M1-M4 antibody [EPR13509(B)]	Abcam	ab177957
Alpha Tubulin Polyclonal antibody	Proteintech	11224-1-AP
Anti-HA tag antibody - ChIP Grade	Abcam	ab9110
Anti-HA tag antibody	Abcam	ab18181
ASF/SF2 Monoclonal antibody	Proteintech	66671-1-Ig

Supplementary table 4. The siRNAs used in this study.

Names	Sequences (5'-3')
si-NC	UUCUUCGAACGUGUCACGUTT
si-hnRNPM	GCCAGAUUUUGUGAGAAATT
si-SRSF1	AGGACAUUGAGGACGUGUUTT
si-SRSF2	UCCAAAUCCAGGUCGCGAUTT
si-SRSF3	CCUGUCCAUUGGACUGUAATT
si-SRSF5	GGUUGAGUUUGCCUCUUAUTT
si-SRSF6	CCUCGAAGUAGACCUCAAATT
si-SRSF7	CCUCGACGAUCAAGAUCUATT
si-SRSF9	GAGGACCUGUUCUACAAGUTT
si-SRSF10	GCGUGAAUUUGGUCGUUAUTT
si-hnRNPK	UGGAAACUGAACAGCCAGATT
si-hnRNPH1	GGGACACAGAUUAUGUUGAATT

Supplementary table 5. List of validated alternative splicing events affected by hnRNPM.

AccID	Description	delta_PSI	AS Type	Splicing Type	Junction reads (In::Ex)		Location
					KDM- RKO_Junc_Inclusive ::Exclusive	NC- RKO_Junc_Inclusive ::Exclusive	
ABCC5	ATP-binding cassette, sub-family C (CFTR/MRP), member 5	0.253968254	Exon out	AltEnd	16::47	0::62	chr3:184001171-184001251
AGAP9	ArfGAP with GTPase domain, ankyrin repeat and PH domain 9	-0.75	Exon in	Cassette	0::18	18::6	chr10:47503666-47503754
AHSA2	AHA1, activator of heat shock 90kDa protein ATPase homolog 2 (yeast)	0.198109769	Exon out	Cassette	197::54	186::131	chr2:61183547-61183662
ANKRD13A	ankyrin repeat domain 13A	0.264541636	Exon out	AltEnd	56::86	37::248	chr12:110021108-110021188
ARHGAP17	Rho GTPase activating protein 17	0.490846682	Exon out	Cassette	25::21	1::18	chr16:25013863-25013956
ARHGEF10L	Rho guanine nucleotide exchange factor (GEF) 10-like	-0.156862745	Exon in	Cassette_multi	43::8	89::0	chr1:17607799-17607977
ARMCX5-GPRASP2	ARMCX5-GPRASP2 readthrough	0.75	Exon out	AltStart	12::4	0::16	chrX:102625795-102625875
C7orf55-LUC7L2	C7orf55-LUC7L2 readthrough	0.136153764	Exon out	AltStart	132::2	118::21	chr7:139341132-139341522
CABIN1	calcineurin binding protein 1	0.342857143	Exon out	AltEnd	12::23	0::47	chr22:24068462-24068542
CARM1	coactivator-associated arginine methyltransferase 1	0.285778516	Exon out	Cassette	103::55	67::116	chr19:10921375-10921443
CCDC57	coiled-coil domain containing 57	0.5	Exon out	Cassette	7::7	0::26	chr17:82184958-82185303
CENPN	centromere protein N	0.332142857	Exon out	AltEnd	36::24	15::41	chr16:81022755-81022882
CLEC16A	C-type lectin domain family 16, member A	0.621473354	Exon out	AltEnd	20::9	3::41	chr16:11052640-11052724
CSPP1	centrosome and spindle pole associated protein 1	0.515555556	Exon out	Cassette	25::20	2::48	chr8:67162638-67162762
CTNND1	catenin (cadherin-associated protein), delta 1	-0.207639401	Exon in	Cassette_multi	51::179	152::202	chr11:57791385-57791673
CXXC1	CXXC finger protein 1	-0.317578475	Exon in	Cassette	10::436	34::66	chr18:50287423-50287508
DCAF15	DDB1 and CUL4 associated factor 15	0.490566038	Exon out	Cassette	30::23	4::49	chr19:13953030-13953308
DDHD1	DDHD domain containing 1	0.300086281	Exon out	Cassette	69::26	26::35	chr14:53051844-53051927

DEAF1	DEAF1 transcription factor	0.419730392	Exon out	AltStart	23::28	1::31	chr11:693489-693569
DROSHA	drosha, ribonuclease type III	-0.533333333	Exon in	MXE	2::13	16::8	chr5:31521123-31521215
ENSA	endosulfine alpha	-0.133490974	Exon in	IR	38::411	104::373	chr1:150627070-150627467
ESCO1	establishment of sister chromatid cohesion N-acetyltransferase 1	0.375833333	Exon out	Cassette	18::14	14::61	chr18:21540577-21540700
EXOC2	exocyst complex component 2	-0.243243243	Exon in	Cassette	0::52	18::56	chr6:657163-657250
FLNB	filamin B, beta	0.337582892	Exon out	Cassette	414::174	291::503	chr3:58141858-58141929
FLNB	filamin B, beta	0.21307837	Exon out	Cassette	311::215	253::416	chr3:58131927-58132019
FMNL2	formin-like 2	-0.251402346	Exon in	Cassette	2::104	50::135	chr2:152643419-152643544
FPGS	folylpolyglutamate synthase	0.185185185	Exon out	AltStart	10::44	0::77	chr9:127813027-127813107
FRMD4A	FERM domain containing 4A	0.059031448	Exon out	AltStart	38::435	15::689	chr10:13862470-13862550
FRMD4A	FERM domain containing 4A	-0.076444634	Exon in	AltEnd	111::918	275::1217	chr10:13857697-13857777
GEM	GTP binding protein overexpressed in skeletal muscle	-0.089665653	Exon in	AltEnd	20::356	45::270	chr8:94257915-94257995
GEMIN4	gem (nuclear organelle) associated protein 4	0.378378378	Exon out	Cassette	14::23	0::27	chr17:749814-749909
GMDS	GDP-mannose 4,6-dehydratase	-0.257575758	Exon in	AltEnd	0::44	17::49	chr6:1766371-1766451
GMPR2	guanosine monophosphate reductase 2	0.246708247	Exon out	Cassette	23::51	10::146	chr14:24234107-24234241
GNB1	guanine nucleotide binding protein (G protein), beta polypeptide 1	-0.170131977	Exon in	AltStart	1::197	24::113	chr1:1853152-1853232
GNB1	guanine nucleotide binding protein (G protein), beta polypeptide 1	-0.083333333	Exon in	AltStart	2::198	14::136	chr1:1847878-1847958
GPAT4	1-acylglycerol-3-phosphate O-acyltransferase 6	0.175353925	Exon out	Cassette	33::115	12::240	chr8:41619221-41619351
GPBP1	GC-rich promoter binding protein 1	0.309000763	Exon out	Cassette	124::60	104::181	chr5:57237113-57237172
GTF2IRD1	GTF2I repeat domain containing 1	0.499509804	Exon out	Cassette	46::39	2::46	chr7:74537778-74537978
HDAC9	histone deacetylase 9	-0.168701138	Exon in	AltEnd	43::274	77::176	chr7:18544881-18544961
HGF	hepatocyte growth factor (hepapoietin A; scatter factor)	-0.161439722	Exon in	AltEnd	82::309	157::266	chr7:81742273-81742353
HIBADH	3-hydroxyisobutyrate dehydrogenase	0.09375	Exon out	Cassette	12::116	0::135	chr7:27648548-27648644

HP1BP3	heterochromatin protein 1, binding protein 3	0.095556298	Exon out	AltEnd	14::109	4::215	chr1:20755324-20755404
HSPG2	heparan sulfate proteoglycan 2	0.458333333	Exon out	AltEnd	11::13	0::21	chr1:21873720-21873800
IMPDH1	IMP (inosine 5'-monophosphate) dehydrogenase 1	0.084284542	Exon out	Cassette	16::145	4::261	chr7:128393699-128393738
L3MBTL3	l(3)mbt-like 3 (Drosophila)	0.353993216	Exon out	Cassette	18::29	2::67	chr6:130137286-130137357
LOC100507065	uncharacterized LOC100507065	-0.155720231	Exon in	Cassette_multi	373::549	488::383	chr12:65613179-65613277
LOC100507065	uncharacterized LOC100507065	0.133515743	Exon out	Cassette	71::396	7::371	chr12:65566019-65566117
LOC728730	uncharacterized LOC728730	-0.691876751	Exon in	AltEnd	4::17	15::2	chr2:39474527-39474607
MAP4K4	mitogen-activated protein kinase kinase kinase 4	0.34505772	Exon out	Cassette	43::56	15::153	chr2:101863821-101864051
MED24	mediator complex subunit 24	0.274495017	Exon out	Cassette	95::139	38::251	chr17:40020528-40020619
MIA3	melanoma inhibitory activity family, member 3	0.181818182	Exon out	Cassette	8::36	0::95	chr1:222623307-222623351
MIOS	missing oocyte, meiosis regulator, homolog (Drosophila)	-0.20212766	Exon in	Cassette	0::97	19::75	chr7:7582630-7582819
MRPL14	mitochondrial ribosomal protein L14	0.181695618	Exon out	AltStart	26::107	2::143	chr6:44125953-44126267
MTMR12	myotubularin related protein 12	0.169811321	Exon out	Cassette	9::44	0::93	chr5:32232961-32233020
NAP1L4	nucleosome assembly protein 1-like 4	0.872881356	Exon out	Cassette	30::0	15::103	chr11:2989129-2989271
NAPG	N-ethylmaleimide-sensitive factor attachment protein, gamma	0.173228346	Exon out	Cassette	22::105	0::149	chr18:10529001-10529045
NASP	nuclear autoantigenic sperm protein (histone-binding)	-0.805429864	Exon in	MXE	1::12	15::2	chr1:45594694-45594773
NAV2	neuron navigator 2	-0.154637418	Exon in	Cassette	8::158	43::169	chr11:20056530-20056628
NBPF12	neuroblastoma breakpoint family, member 12	0.583333333	Exon out	Cassette	16::0	10::14	chr1:146946555-146946607
NDEL1	nudE neurodevelopment protein 1-like 1	0.237062937	Exon out	Cassette	15::35	9::134	chr17:8444954-8445040
NDUFV2	NADH dehydrogenase (ubiquinone) flavoprotein 2, 24kDa	0.037322479	Exon out	AltEnd	28::607	6::880	chr18:9103092-9103172
NHEJ1	nonhomologous end-joining factor 1	0.372053872	Exon out	A5SS	18::26	2::52	chr2:219078074-219078089
NPM1	nucleophosmin (nucleolar phosphoprotein B23, numatrin)	0.181260903	Exon out	AltEnd	760::757	752::1600	chr5:171406397-171406731

NR2C2	nuclear receptor subfamily 2, group C, member 2	0.576923077	Exon out	Cassette	15::11	0::28	chr3:15004557-15004613
OPN3	opsin 3	-0.6	Exon in	AltEnd	4::6	29::0	chr1:241635993-241636073
PAQR3	progesterone and adipoQ receptor family member III	0.129032258	Exon out	AltEnd	12::81	0::155	chr4:78923005-78923085
PHC2	polyhomeotic homolog 2 (Drosophila)	-0.210093761	Exon in	AltEnd	30::129	65::98	chr1:33399463-33399543
PLCG1	phospholipase C, gamma 1	0.074745763	Exon out	A3SS	15::162	3::297	chr20:41168974-41169079
PLEKHB2	pleckstrin homology domain containing, family B (evectins) member 2	0.31422895	Exon out	Cassette	132::170	43::307	chr2:131144408-131144449
POLR3G	polymerase (RNA) III (DNA directed) polypeptide G (32kD)	-0.210144928	Exon in	Cassette	0::67	29::109	chr5:90478346-90478455
POP1	processing of precursor 1, ribonuclease P/MRP subunit (S. cerevisiae)	0.467183463	Exon out	Cassette	22::21	2::43	chr8:98151521-98151591
PPP1R14B	protein phosphatase 1, regulatory (inhibitor) subunit 14B	-0.039942939	Exon in	Cassette	0::569	28::673	chr11:64245377-64245418
PPP1R3B	protein phosphatase 1, regulatory subunit 3B	-0.197104283	Exon in	AltStart	80::127	199::142	chr8:9150563-9150710
PRKAB2	protein kinase, AMP-activated, beta 2 non-catalytic subunit	0.745738636	Exon out	Cassette	39::5	9::55	chr1:147160797-147160833
PROCR	protein C receptor, endothelial	-0.03407155	Exon in	AltEnd	567::20	802::0	chr20:35176698-35177362
PRRC2B	proline-rich coiled-coil 2B	0.115290179	Exon out	Cassette	227::29	270::80	chr9:131494405-131494486
PVT1	Pvt1 oncogene (non-protein coding)	-0.119965642	Exon in	AltEnd	2::122	23::146	chr8:128074070-128074150
R3HDM1	R3H domain containing 1	-0.386240786	Exon in	Cassette	18::19	96::14	chr2:135641536-135641790
RAC1	ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)	0.232180329	Exon out	Cassette	210::185	112::262	chr7:6398662-6398718
RBBP8	retinoblastoma binding protein 8	0.412737293	Exon out	AltStart	30::16	17::54	chr18:22933876-22934078
RBCK1	RanBP-type and C3HC4-type zinc finger containing 1	0.100335527	Exon out	AltEnd	813::48	319::59	chr20:410412-410492
RNF41	ring finger protein 41, E3 ubiquitin protein ligase	-0.192771084	Exon in	Cassette	0::66	16::67	chr12:56212996-56213138
RYK	receptor-like tyrosine kinase	0.169142352	Exon out	A5SS	22::94	4::191	chr3:134200353-134202730
SDHAF4	chromosome 6 open reading frame 57	0.102362205	Exon out	AltEnd	13::114	0::145	chr6:70585588-70585668
SEN2	SUMO1/sentrin/SMT3 specific peptidase 2	0.298815202	Exon out	Cassette	29::38	13::84	chr3:185604347-185604437

SERF1A	small EDRK-rich factor 1A (telomeric)	0.172434608	Exon out	AltStart	34::106	15::198	NW_003315917.2:509-659-509739
SIL1	SIL1 nucleotide exchange factor	0.705882353	Exon out	MXE	13::0	5::12	chr5:139196441-139196528
SLC35B1	solute carrier family 35, member B1	0.250090691	Exon out	Cassette	54::100	18::161	chr17:49707343-49707444
SLC44A1	solute carrier family 44 (choline transporter), member 1	0.201362442	Exon out	Cassette	27::76	11::170	chr9:105336567-105336641
SLU7	SLU7 splicing factor homolog (S. cerevisiae)	0.153694387	Exon out	Cassette	16::77	2::107	chr5:160417112-160417241
SNHG16	small nucleolar RNA host gene 16 (non-protein coding)	0.187111534	Exon out	Cassette_multi	492::111	454::268	chr17:76558945-76559043
SPG7	spastic paraplegia 7 (pure and complicated autosomal recessive)	0.239130435	Exon out	AltStart	11::35	0::95	chr16:89535538-89535618
ST6GALNAC4	ST6 (alpha-N-acetyl-neuraminy1-2,3-beta-galactosyl-1,3)-N-acetylglactosaminide alpha-2,6-sialyltransferase 4	0.286809848	Exon out	Cassette	513::74	529::372	chr9:127910415-127910528
STAMBP	STAM binding protein	-0.171434086	Exon in	A5SS	14::143	43::122	chr2:73844888-73845036
STAU2	staufen double-stranded RNA binding protein 2	-0.217921147	Exon in	AltEnd	7::83	55::131	chr8:73653816-73653896
SUGP2	SURP and G patch domain containing 2	0.373895788	Exon out	Cassette	51::56	15::131	chr19:19003496-19003608
SUPT6H	suppressor of Ty 6 homolog (S. cerevisiae)	0.12195122	Exon out	Cassette	20::144	0::192	chr17:28662617-28662685
TFDP1	transcription factor Dp-1	0.346916147	Exon out	AltEnd	59::52	24::106	chr13:113585966-113586046
TMC7	transmembrane channel-like 7	-0.387223587	Exon in	Cassette	22::15	54::1	chr16:19035676-19035823
TOP1MT	topoisomerase (DNA) I, mitochondrial	0.061904762	Exon out	AltStart	13::197	0::201	chr8:143327303-143327383
TRA2B	transformer 2 beta homolog (Drosophila)	-0.156168582	Exon in	Cassette	20::154	61::164	chr3:185931577-185931852
TRIO	trio Rho guanine nucleotide exchange factor	0.415087041	Exon out	Cassette	24::31	2::92	chr5:14507424-14507526
TYW3	tRNA-yW synthesizing protein 3 homolog (S. cerevisiae)	0.17	Exon out	A5SS	17::83	0::217	chr1:74738788-74746864
TYW3	tRNA-yW synthesizing protein 3 homolog (S. cerevisiae)	0.113208995	Exon out	Cassette	26::176	4::254	chr1:74751349-74751689
UAP1	UDP-N-acetylglucosamine pyrophosphorylase 1	0.154200862	Exon out	Cassette	143::458	52::569	chr1:162562470-162562584
UPP1	uridine phosphorylase 1	-0.025542308	Exon in	AltEnd	3::1339	43::1505	chr7:48090791-48090871

UQCRB	ubiquinol-cytochrome c reductase binding protein	0.071782092	Exon out	Cassette	525::3094	389::4919	chr8:96231226-96231515
USP33	ubiquitin specific peptidase 33	0.42760181	Exon out	Cassette	36::16	9::25	chr1:77746399-77746556
VOPP1	vesicular, overexpressed in cancer, prosurvival protein 1	0.33164487	Exon out	Cassette_multi	39::50	13::109	chr7:55492749-55492973
YPEL5	yippee-like 5 (Drosophila)	-0.162098312	Exon in	Cassette	10::137	55::184	chr2:30148245-30148305
ZBTB44	zinc finger and BTB domain containing 44	0.280376766	Exon out	Cassette	16::33	3::62	chr11:130236110-130236216
ZC3H11A	zinc finger CCCH-type containing 11A	0.180934657	Exon out	Cassette	149::7	120::35	chr1:203796293-203796354
ZNF195	zinc finger protein 195	0.400036853	Exon out	Cassette	59::22	22::45	chr11:3373577-3373675
ZNF548	zinc finger protein 548	0.745	Exon out	Cassette_multi	66::14	2::23	chr19:57390722-57392948
ZNF605	zinc finger protein 605	-0.409090909	Exon in	Cassette	13::9	32::0	chr12:132948148-132948270

Supplementary table 6. The primers used in this study.

Names	Sequences
β -actin-F	GCAAAGACCTGTACGCCA
β -actin-R	TGCATCCTGTCGGCAATG
hnRNPM-F	AGGAAGGCCTGCCAGATATT
hnRNPM-R	CTGGCGACTCGAACTTAACC
PLEKHB2-F	CGCCAGGAACTCAAGTTGTC
PLEKHB2-R	CTTGAGGCCCCTAGAAGACC
SUPG2-F	AGGTGGGACCAGAGATCGAA
SUPG2-R	CTTTTGGACATGGGACGACC
PRRC2B-F	ATGAAAGGCTTCCACTTTGC
PRRC2B-R	TCAGGCCTTACTCTCCTCCA
GMPR2-F	GATTCATCGCTACCCCGAGG
GMPR2-R	GGATCTGTTCCAGCTGCTCA
FLNB-F	GGGTGACGACATCCCACTTT
FLNB-R	ACCTCAGTGGGGGCATATCT
FLNB-F	GCCCAAGGACCTGGATTGAA
FLNB-R	CCCTCCTGAGATGGGGTGTA
AHSA2-F	GGAGTGAAGCACAAGGGATT
AHSA2-R	TGCAGGGTATTCCCCTCAG
CCNT2-F	CAGCACAAACAAGGGCAGTC
CCNT2-R	GTTTCACGAGGGTGCTGAGA
ETS1-F	GGAAGAGCTCCTCTCCCTCA
ETS1-R	ATCTCCTGGCCACCTCATCT
VEZF1-F	TCGACCATTGCAGGCATCTT
VEZF1-R	GGCTCTGCCCATGAGTCTTT
PLEKHB2 mini-det-F	CGCCAGGAACTCAAGTTGTC
PLEKHB2 mini-det R	GCGATGCAATTTCTCATT
PLEKHB2-E7-F	CTAATGGGCCTGTTTCTTTTCAG
PLEKHB2-E7-R	AAGGCCGGCGTGAGTTAC
PLEKHB2-E8-F	AGTTGGCTCCTTTGGTTGGA
PLEKHB2-E8-R	GTCCCCAAATCTAGAAAGTCTGCT
PLEKHB2-E9-F	GAGCGCTATCGAGACAACGA
PLEKHB2-E9-R	TCAAGACCTTGAGGCCCCTA
PLEKHB2-total-det-F	CAGCCTGCTAACCAAGTCATC
PLEKHB2-total-det-R	TAGAGACCCTAAGGCCATGC
PLEKHB2-S-det-F	ATGCAGGACTTTATGGACAGCA
PLEKHB2-S-det-R	TCAAGACCTTGAGGCCCCTA
PLEKHB2-L-det-F	CCAGTACCCATATGCAGAGACC

PLEKHB2-L-det-R

TCAAGACCTTGAGGCCCTA

Supplementary table 7. The characteristics of hnRNPM-regulated exons in CRC.

Gene	Type	G	A	T	C	Lenth	GC%
PLEKHB2	Upstream Exon	33	22	23	31	109	58.72%
	Upstream Intron	957	1037	1291	847	4132	43.66%
	Target Exon	9	10	10	13	42	52.38%
	Downstream Intron	508	549	679	451	2187	43.85%
	Downstream Exon	758	791	990	677	3216	44.62%
SUGP2	Upstream Exon	15	17	13	17	62	51.61%
	Upstream Intron	433	464	512	412	1821	46.40%
	Target Exon	25	26	22	40	113	57.52%
	Downstream Intron	167	105	152	135	559	54.03%
	Downstream Exon	150	110	92	127	479	57.83%
FLNB	Upstream Exon	60	26	31	51	168	66.07%
	Upstream Intron	268	241	326	183	1018	44.30%
	Target Exon	23	25	21	24	93	50.54%
	Downstream Intron	164	178	236	210	788	47.46%
	Downstream Exon	34	35	26	29	124	50.81%
FLNB	Upstream Exon	70	59	59	60	248	52.42%
	Upstream Intron	747	880	942	759	3328	45.25%
	Target Exon	25	16	11	20	72	62.50%
	Downstream Intron	146	141	215	218	720	50.56%
	Downstream Exon	30	25	26	22	103	50.49%
PRRC2B	Upstream Exon	21	24	17	30	92	55.43%
	Upstream Intron	562	423	583	576	2144	53.08%
	Target Exon	24	18	16	24	82	58.54%
	Downstream Intron	396	241	303	313	1253	56.58%
	Downstream Exon	1141	938	1174	1199	4452	52.56%
GMPR2	Upstream Exon	28	29	35	28	120	46.67%
	Upstream Intron	80	131	168	129	508	41.14%
	Target Exon	32	28	49	26	135	42.96%
	Downstream Intron	312	380	508	295	1495	40.60%
	Downstream Exon	18	16	27	23	84	48.81%
AHSA2	Upstream Exon	22	32	20	12	86	39.53%
	Upstream Intron	464	521	669	487	2141	44.42%
	Target Exon	36	38	23	19	116	47.41%
	Downstream Intron	229	297	350	173	1049	38.32%
	Downstream Exon	20	34	18	17	89	41.57%

Supplementary table 8. The strength of donor and acceptor splice sites using MaxEntScan.

Gene	5ss	score	3ss	score
>PLEKHB2 up	CAGGTAACT	8.63	CTTCTATTTCTGTCTTGTAGAGA	9.59
>PLEKHB2 down	GGGGTAAGT	9.65	CTATTTTCCTTCTCTTTTAGGAC	13.22
>SUGP2 up	AAGGTATTC	6.8	CTCTTTCTTTTGTCTTCTAGAGG	10.26
>SUGP2 down	CAGGTGAGT	10.67	GAATTTTGTGTGACTGTGCAGGTT	5.66
>PRRC2B up	CAGGTAAAG	9.65	CCTGCCTTTGGTTTTTTCAGGCC	10.39
>PRRC2B down	CAGGTAGAA	6.68	TCCCATTCATCTGTCCAAAGGCA	7.39
>GMPR2 up	AAGGTAGGG	8.76	TAATCTTCCTCTTCTTTAAGTCC	6.06
>GMPR2 down	AAGGTAGAG	6.38	CTTCTTTGTCTTCTCCCCAGTTC	9.86
>FLNB-26 up	GAGGTAAAGT	11.08	TAACAGCCTTTTGATTTTAGCTG	4.43
>FLNB-26 down	CAGGTTTGC	4.86	CCTCTCATCTCTGTCCCTCAGGCT	10.75
>FLNB-31 up	ATGGTAAGG	9.33	CTCCATTTGCCACTGACCAGGCC	3.57
>FLNB-31 down	TGGGTACAA	-0.56	CCACTGCCTTCTGTTTTTAGGTG	12.26
>AHSA2 up	GAGGTATGT	9.81	TCTATTTTCTGATTTGTAGGTC	9.06
>AHSA2 down	CGGGTAAAG	6.23	CTTCCCTTGTTTCTTTATAGAAT	11.15