Table S1. List of high-confidence interactors identified by affinity purification and mass spectrometry analysis. Related to Figure 1

Protein name	Accession number	Molecular weight (kDa)
NPM1	P06748	32
SET	Q01105	33
PPM1G/PP2Cγ	O15355	59
hnRNP-F	P52597	46
MePCE/BCDIN3	Q7L2J0	74
DDX21	Q9NR30	87
Sart3/Tip110	Q15020	110
DHX57	Q6P158	155

SUPPLEMENTAL EXPERIMENTAL PROCEDURES

Materials

5,6-dichloro-1-β-ribofuranosylbenzimidazole (DRB) (Sigma, D1916) was used at a final concentration of 100 μM for 4 hrs. TNF-α (Sigma, T6674) was used at final concentration of 50 ng/ml for 1 hr.

Cell culture and treatments

For the heat shock experiment, HeLa cells were heat shocked at 42°C for 2 hrs. To induce the inflammatory pathway, HeLa cells were treated with TNF-α (50 ng/ml) for 1 hr.

RNAi and rescue assay

For the rescue assay (**Figure S5**), HeLa cells were transfected with 100 ng of an empty pcDNA4/TO (–) or pcDNA4/TO-PPM1G:S (PPM1G) plasmid DNA using PolyJet (SignaGen). One day post-transfection, cells were re-transfected with the indicated siRNAs. Two days post-siRNA transfection, cells were induced with TNF-α and used for RNA extraction and gene expression analysis by RT-qPCR and Western Blot.

UV crosslinking of RNA-protein complexes *in vivo*

293T cells were seeded at $2x10^6$ cells into a 10-cm^2 plate and transfected with 5 μg of a Strep-tagged Tat plasmid 24 hrs post seeding. For the experiment in **Figure S1A,** cells were iradiated with 125 mJ/cm^2 using a Spectrolinker XL-1500 UV crosslinker and harvested and lysed using denaturing lysis buffer (150 mM NaCl, 20 mM Tris-HCl pH = 7.0, 5% Glycerol, 1.5 mM $MgCl_2$, 1 mM DTT, 1% NP-40, 0.25% Sodium Deoxycholate and 0.1 % SDS) and sonicated using the Bioruptor water bath Sonicator (Diagenode) with 8 cycles (30 sec on 30 sec off). Tat complexes

were affinity purified using Strep-tactin Superflow Resin (IBA Life Sciences) and washed using denaturing washing buffer (250 mM NaCl, 20 mM Tris-HCl pH = 7.0, 5% Glycerol, 1.5 mM $MgCl_2$, 1 mM DTT, 0.05% NP-40, 0.1 % Sodium Deoxycholate, 0.1 % SDS). Co-immunoprecipitating RNAs were extracted using Proteinase K digestion [0.5 mg/mL Proteinase K, 20mM Tris-HCl pH = 7.0, 5 mM EDTA, 0.5% SDS, 300 pg/μl *in vitro* transcribed β-globin RNA (used as precipitation control, PC)] (Conrad, 2008) followed by Phenol:Chloroform:Isoamylic alcohol (25:24:1) extraction and ethanol precipitation. The immunoprecipitated material was analyzed by Northern blot using a 7SK probe encompassing stem-loop I made with primers P15 and P16 (**Table S4**) and labeled using a PCR DIG DNA labeling kit (Roche).

Table S2. Plasmids used in this study

Gene	Vector / Tag	Restriction sites
Tat	pcDNA-4TO / Strep	BamHI - XhoI
Tat	pcDNA-4TO / Flag	BamHI - XhoI
Larp7	pcDNA-4TO / Strep	BamHI - XhoI
Larp7	pcDNA-4TO / Flag	BamHI - XhoI
Sart3	pcDNA-4TO / Strep	HindIII - XhoI
Sart3	pcDNA-4TO / Flag	HindIII - XhoI
CycT1	pcDNA-4TO / Strep	HindIII - EcoRI
CycT1	pcDNA-4TO / Flag	HindIII - EcoRI
Cdk9	pcDNA-4TO / Strep	HindIII - XhoI
Cdk9	pcDNA-4TO / Flag	HindIII - XhoI
MePCE	pcDNA-4TO / Strep	HindIII - XhoI
MePCE	pcDNA-4TO / Flag	HindIII - XhoI
DDX21	pcDNA-4TO / Strep	BamHI - XhoI
DDX21	pcDNA-4TO / Flag	BamHI - XhoI
NPM1	pcDNA-4TO / Strep	BamHI - XhoI
NPM1	pcDNA-4TO / Flag	BamHI - XhoI
hnRNP-F	pcDNA-4TO / Strep	BamHI - XhoI
hnRNP-F	pcDNA-4TO / Flag	BamHI - XhoI
SET	pcDNA-4TO / Flag	NotI - XhoI
GFP	pcDNA-4TO / Strep	BamHI - XhoI
GFP	pcDNA-4TO / Flag	XhoI - ApaI
PPM1G	pcDNA-4TO / Strep	BamHI - NotI
PPM1G	pcDNA-4TO / Flag	BamHI - NotI

Table S3. siRNAs used in RNAi assays

Gene	Flexitube siRNA product name	Catalog number
Cdk9	Hs_CDK9_5	SI00605066
MePCE	Hs _BCDIN3_1	SI02778265
hnRNP-F	Hs_HNRPF_1	SI00300461
DHX57	Hs_DHX57_5	SI02757839
NPM1	Hs_NPM1_1	SI00300979
PPM1G	Hs_PPM1G_6	SI02658684
PPM1G*	Hs_PPM1G_10	SI05016627
PPM1G*	Hs_PPM1G_11	SI05016634
PPM1A	HS_PPM1A_5	SI02659258
SLC25A5	Hs_SLC25A5_5	SI02654358
CycT1	Hs_CCNT1_1	SI00024073
Larp7	Hs_HDCMA18P_2	SI00434980
SET	Hs_SET_5	SI03021291
DDX21	Hs_DDX21_7	SI04311412
Sart3	Hs_SART3_7	SI04357304
RelA	Hs_RELA_5	SI00301672
Negative control	AllStars Negative Control	SI1027280

* siRNA oligos used in rescue experiments because they target the 3' non-coding region.

Table S4. DNA oligonucleotides used in this study

Gene	Primer number/Sequence (5'–3')	Purpose / Assay
MePCE	**507/**TGAAGCCAGAGCAGTTCAGTTCCTA **508/**TACACAGGACGCTGGAAGCCTTTA	RNAi validation
Larp7	**511/**TCCGGGATACTTTGGCAGCAATCT **512/**AGGATCTCGAGTTTCCAGCAGTGT	RNAi validation
Cdk9	**517/**GTGTTCGACTTCTGCGAGCATGAC **518/**CTATGCAGGATCTTGTTTCTGTGG	RNAi validation
SLC25A5	**519/**GCAGCTGATGTGGGTAAAGCTGG **520/**CCGGAAGCATTCCCTTTGCAGT	RNAi validation
NPM1	**525/**GTTGTGAACTAAAGGCCGACAAAG **526/**TGTGCAACTCATCCTTTGCACCAG	RNAi validation
hnRNP-F	**527/**TGTATTGGTCTCCTGCTCCTAGA **528/**AGGACTGGTTTCTGTTGCTACC	RNAi validation
DDX21	**531/**CTGGGTGTTTGCTTTGATGTACC **532/**AGTTCTGGTTGCTCTGTGG	RNAi validation
DHX57	**537/**CCGCTGTTTGGATCCTGCTCT **538/**GCTGCCATCCCTTATACGCTTG	RNAi validation
SET	**539/**AATATAACAAACTCCGCCAACC **540/**CTGGTCAAATAATGCAGTGCCTC	RNAi validation
PPM1G	**543/**AAAATGGCAACAGCGACAAG **544/**CACCTCATACCCACTGCTA	RNAi validation
Sart3	**549/**CTTTACTCGTGCCTTGGAGTAT **550/**CCGAGCTTTCTGCATGTTATTG	RNAi validation
CycT1	**551/**GCAGACTTTAGGCTTTGAACTAAC **552/**TACTGCAGGCTAAATGTGGT	RNAi validation
7SK RNA	**15/**GGATGTGAGGGCGATCTG **16/**GGAGCGGTGAGGGAGGAAG	RIP assay, Northern blot
U6 snRNA	**9/**CTCGCTTCGGCAGCACATATAC **10/**GGAACGCTTCACGAATTTGCGTG	RIP assay
β-actin	**389/**CCCCCCGGGCCGTCTTCCCCTC **390/**TGAGGATGCCTCTCTTGCTCTG	Internal control RNAi
gapdh	**239/**CCCTGTGCTCAACCAGT **240/**CTCACCTTGACACAAGCC	Internal control RNAi
c-Myc	**860/**ACAGCTACGGAACTCTTGTGCGTA **861/**CAGCCAAGGTTGTGAGGTTGCATT	Internal control RNAi
Rpl19	**354/**ATCGATCGCCACATGTATCA **355/**GCGTGCTTCCTTGGTCTTAG	Internal control RNAi
Hsp90	**838/**CCTTCTATTTGTCCCACG **839/**ATCCTCCGAGTCTACCAC	Heat shock response
Hsp70	**842/**ACCCGCATCCCCAAGGTGCAG **843/**TCAGGGCAGTCATCACGCCTC	Heat shock response
IL-8	**245/**GGGCCATCAGTTGCAAATC **246/**TTCCTTCCGGTGGTTTCTTC	Inflammatory response ChIP (Promoter)
IL-8	**282/**GCCATAAAGTCAAATTTAGCTGGAA **283/**GTGCTTCCACATGTCCTCACA	Inflammatory response ChIP (Gene body)
IκBα	**255/**GATCCGCCAGGTGAAGGG **256/**GCAATTTCTGGCTGGTTGG	Inflammatory response

Table S5. Antibodies used in IF, IP, ChIP and Western blot assays

Protein/Tag	Source (Company)	Catalog Number
CycT1	Santa Cruz Biotechnologies	sc-10750
Cdk9	Santa Cruz Biotechnologies	sc-484
Phospho-Cdk9 (Thr186)	Cell Signaling	2549
STREP-Tag II	Novagen	71591
FLAG M2	Sigma	F1804
MePCE/BCDIN3 (N-17)	Santa Cruz Biotechnologies	sc-82542
Larp7/PIP7S	Sigma	AV40847
Hexim1	Abcam	ab25388
RNA Polymerase II CTD	Active Motif	102660
RNA Polymerase II S5P-CTD	Abcam	ab5131
RNA Polymerase II S2P-CTD	Abcam	ab5095
Normal Rabbit IgG	Santa Cruz Biotechnologies	sc-2027
β-actin (C4)	Santa Cruz Biotechnologies	sc-47778
PPM1G/PP2Cγ	Santa Cruz Biotechnologies	sc-136320
PPM1G/PP2Cγ	Abcam	ab70794
SART3 (C3)	GeneTex	GTX107684
p65/NF-κB/RelA (C-20)	Santa Cruz Biotechnologies	sc-372X
HIV-1 p24 (AG3.0)	AIDS Research and Reference Reagent Program	4121
GST	Santa Cruz Biotechnologies	sc-33613

SUPPLEMENTAL REFERENCES

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