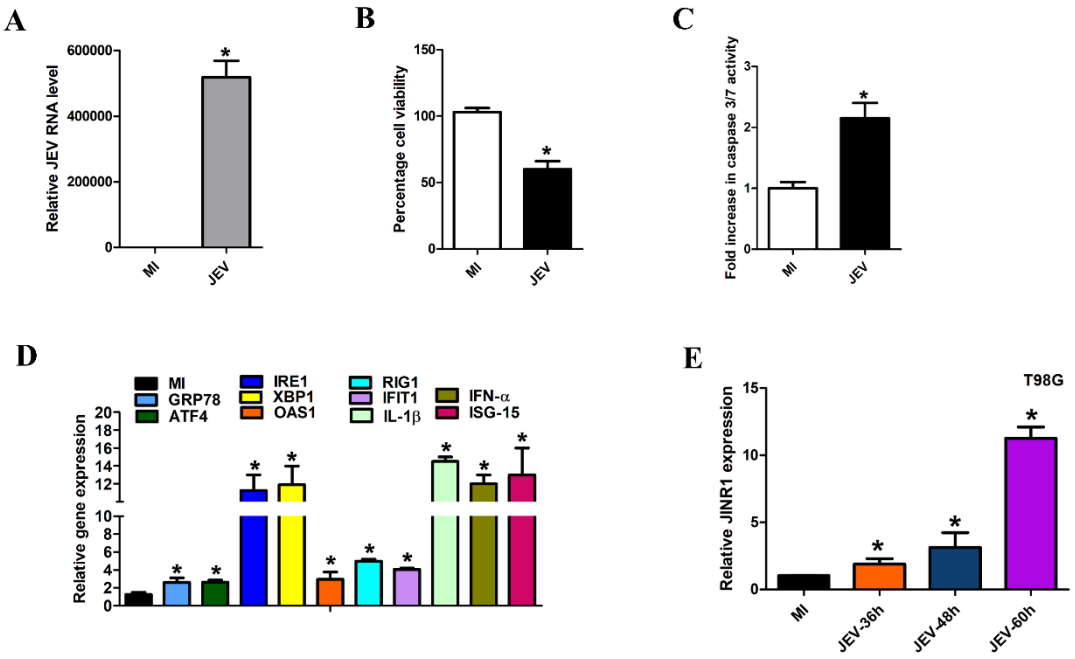
Supplementary Figures

Figure S1. Validation of the JEV infection and DE mRNAs induced upon JEV infection.



A. Verification of JEV infection. Viral infection was confirmed by quantifying the intracellular levels of JEV RNA using qRT-PCR 48 hpi in SH-SY5Y cells.

B. JEV infection reduces cell proliferation. SH-SY5Y cells were analyzed by WST1 assay 48 hpi. The graph represents the percentage of viable cells.

C. JEV infection results in apoptosis in SH-SY5Y cells. The caspase-3/7 activity was determined 48 hpi in SH-SY5Y cells.

D. Validation of JEV-regulated significant DE mRNAs identified from whole transcriptome sequencing using qRT-PCR in SH-SY5Y cells.

E. JEV infection induces *JINR1* expression in astrocytes. T98G cells were infected with JEV (MOI 5), and *JINR1* levels were measured at the indicated time points using qRT-PCR.

Data information:

Error bars represent the mean ± SEM from three independent experiments. *Significant change compared to MI. Statistical comparisons were made using Student's *t*-test.

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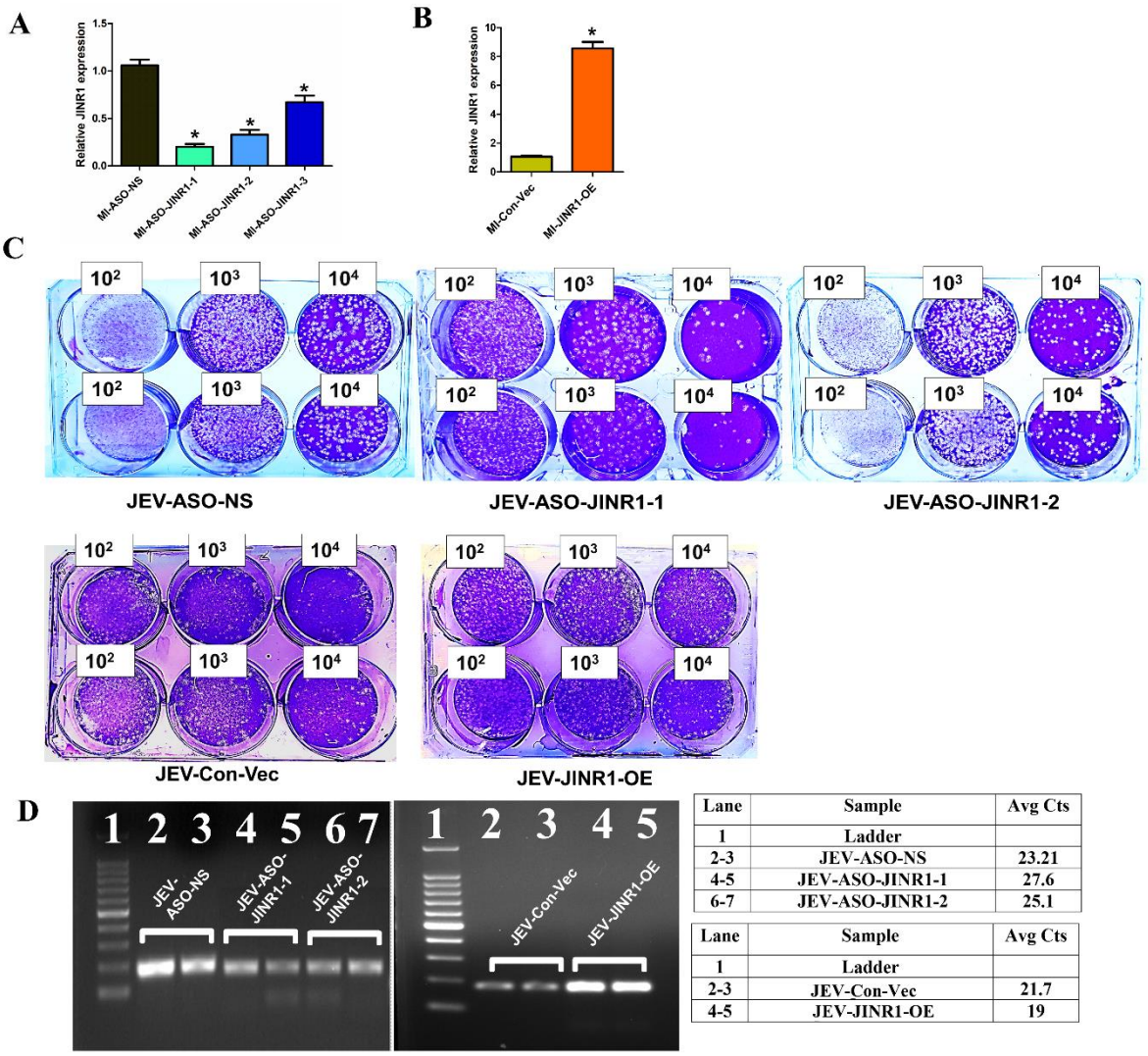
Figure S2. Effect of *JINR1* knockdown and overexpression on JEV replication.



Lane	Sample	Avg Cts
1	Ladder	
2-3	JEV-ASO-NS	23.21
4-5	JEV-ASO-JINR1-1	27.6
6-7	JEV-ASO-JINR1-2	25.1

Lane	Sample	Avg Cts
1	Ladder	
2-3	JEV-Con-Vec	21.7
4-5	JEV-JINR1-OE	19

A. Evaluation of ASO-mediated knockdown efficiency of *JINR1*. SH-SY5Y cells were transfected with ASOs as indicated, and qRT-PCR assays were used to detect *JINR1* expression 48 hours post-transfection.

B. Verification of *JINR1* over-expression in SH-SY5Y cells. SH-SY5Y cells transfected with pCDNA3.1 with full length *JINR1* or empty pcDNA3.1 (Con-Vec) as indicated, and qRT-PCR assays were used to detect *JINR1* expression 48 hours post-transfection.

C. *JINR1* promotes JEV titer. The supernatant from SH-SY5Y cells transfected either with ASO-NS, ASO-*JINR1-1*, ASO-*JINR1-2*, Con-Vec, or *JINR1*-OE was collected 48 hpi. The viral titer in the supernatant was detected using plaque assay in PS cells. Representative images from three independent experiments are shown, and the quantification is shown in figure 3B-C.

D. *JINR1* promotes mature virion RNA release. The supernatant from SH-SY5Y cells transfected either with ASO-NS, ASO-*JINR1-1*/ASO-*JINR1-2*, Con-Vec, or *JINR1*-OE was collected 48 hpi.

The mature virion RNA was detected using qRT-PCR and agarose gel electrophoresis. A representative gel image and table with Ct values from three independent experiments are shown. The viral band was detected at 180bp, 100bp DNA ladder was used. Data represents the mean± SEM from three independent experiments.

Data information: Error bars represent the mean ± SEM from three independent experiments. Statistical comparisons were made using Student's *t*-test. (For A-B) RNA samples were analyzed by qRT-PCR. (For A) *Significant change compared to ASO-NS. (For B) *Significant change compared to empty vector.

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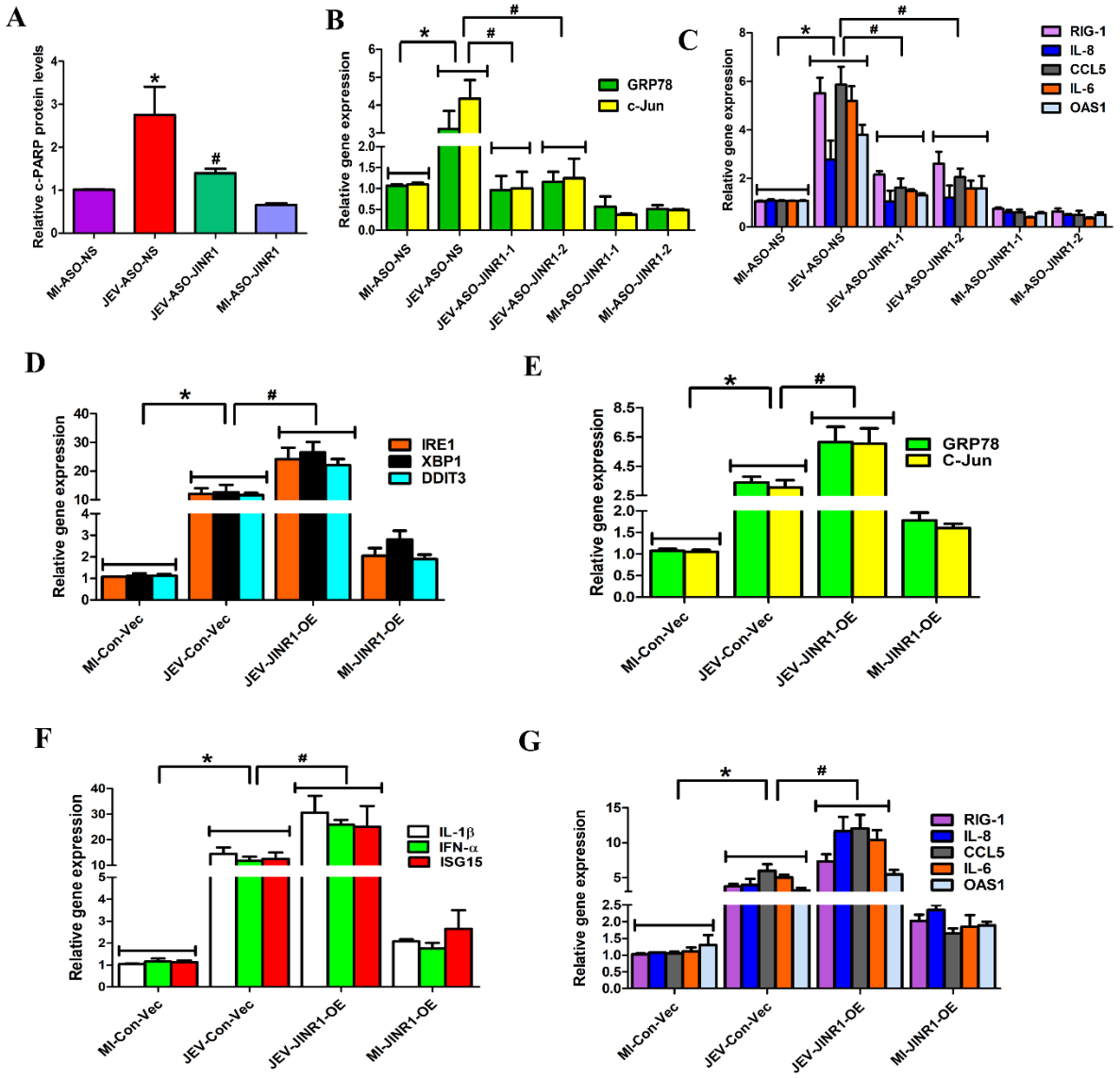
Figure S3. Effect of *JINR1* on neuronal apoptosis, ER stress and inflammatory gene expression.



A. Quantification of cleaved PARP protein levels upon *JINR1* depletion from western blotting (Figure 3E).

B. *JINR1* depletion attenuates JEV-induced ER stress genes. qRT-PCR analysis of indicated ER stress genes upon *JINR1* depletion in SH-SY5Y cells 48 hpi.

C. *JINR1* depletion reduces JEV-induced neuroinflammatory genes. qRT-PCR analysis of indicated neuroinflammatory genes upon *JINR1* depletion in SH-SY5Y cells 48 hpi.

D-E. *JINR1* overexpression enhances JEV-induced ER stress genes. SH-SY5Y cells were transfected with Con-Vec (empty vector) or *JINR1*-OE (pcDNA3.1 with full length *JINR1*), and the indicated ER stress gene transcript levels were measured by qRT-PCR 48 hpi.

F-G. *JINR1* overexpression enhances JEV-induced neuroinflammatory genes. SH-SY5Y cells were transfected with Con-Vec or *JINR1*-OE, and the indicated neuroinflammatory transcript levels were measured by qRT-PCR 48 hpi.

Data information: Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. (For A-G) RNA samples were analyzed by qRT-PCR. (For A-C) *Significant change compared to MI-ASO-NS #significant change compared to JEV-ASO-NS. (For D-G) *Significant change compared to MI-Con-Vec #significant change compared to JEV-Con-Vec.

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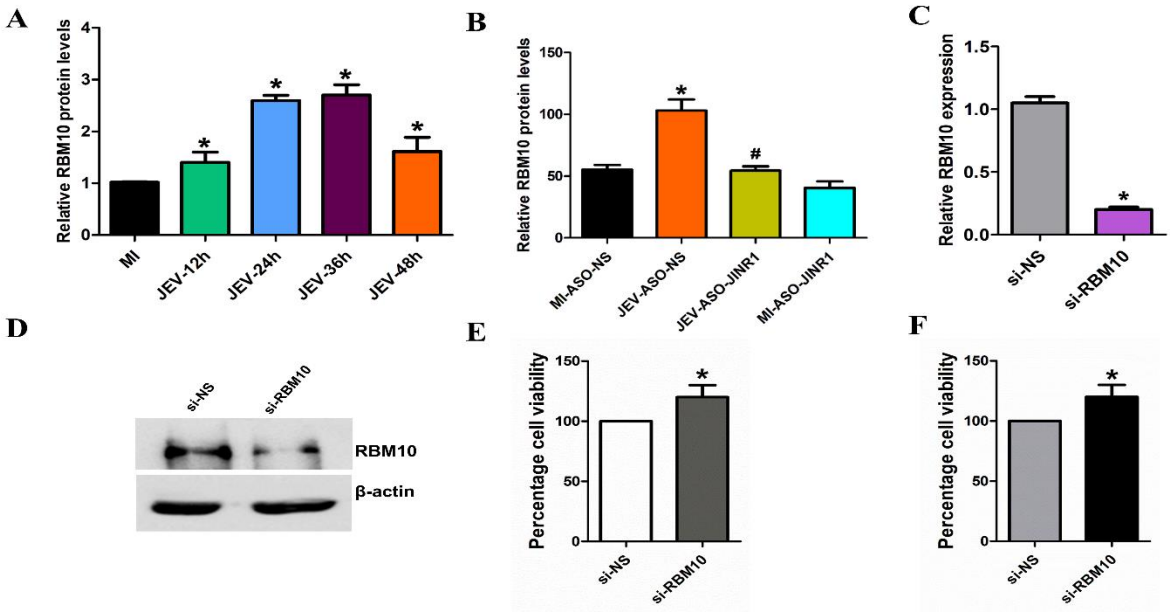
Figure S4. RBM10 Protein levels during JEV infection and validation of RBM10 knock-down in SH-SY5Y cells.



A. Quantification of RBM10 protein levels upon JEV infection from western blotting shown in Figure 4B.

B. Quantification of RBM10 protein levels upon *JINR1* knockdown during JEV infection from western blotting shown in Figure 4E.

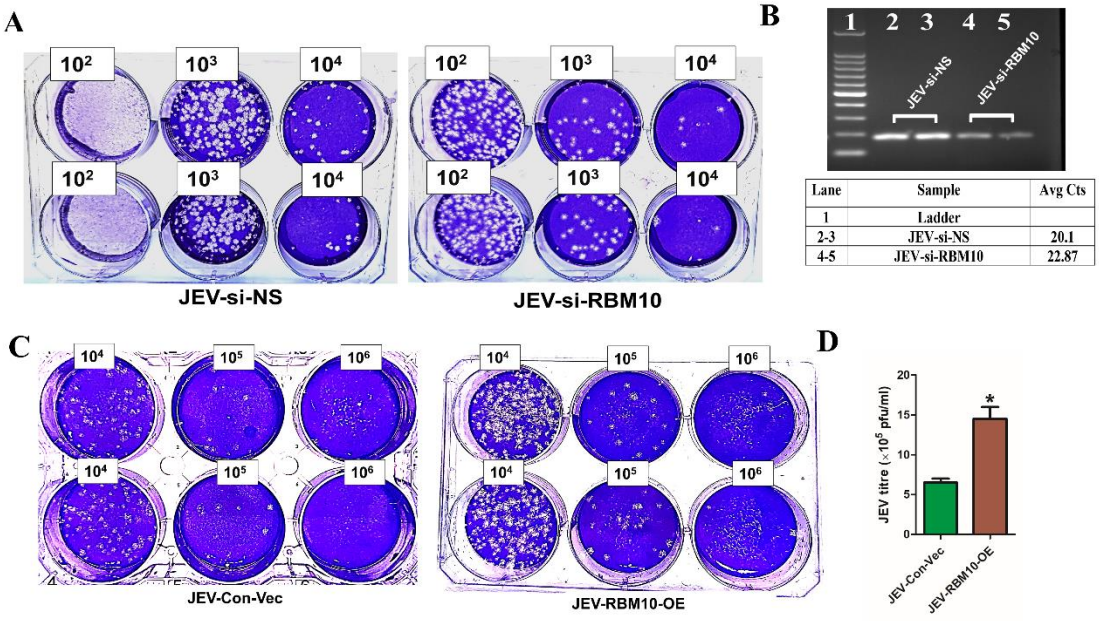
C. Evaluation of siRNA mediated knockdown efficiency of RBM10 in SH-SY5Y cells. RBM10 mRNA levels were detected by qRT-PCR 36 hpi.

D. Evaluation of siRNA mediated knockdown efficiency of RBM10 in SH-SY5Y cells. SH-SY5Y cells were transfected with si-NS or si-RBM10, and protein lysates were collected 36 hpi. RBM10 protein levels were analyzed by western blotting. A representative blot is shown from three independent experiments with similar results. Blots were reprobed for β-actin to establish equal loading.

E-F. RBM10 depletion significantly increases cell proliferation. The proliferation of SH-SY5Y cells and T98G was assessed by WST1 assay upon 48 h post RBM10 knockdown. The graph represents the percentage of viable cells.

Data information: Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. (For A) *Significant change compared to MI. (For B) *Significant change compared to si-NS. (For C) RNA samples were analyzed by qRT-PCR. *Significant change compared to si-NS. (For E-F) *Significant change compared to si-NS.

Figure S5. RBM10 regulates JEV replication in SH-SY5Y cells.



Lane	Sample	Avg Cts
1	Ladder	
2-3	JEV-si-NS	20.1
4-5	JEV-si-RBM10	22.87

A. RBM10 silencing reduces JEV titer. The supernatant from SH-SY5Y cells transfected with si-NS or si-RBM10 was collected 36 hpi. The viral titer in the supernatant was detected using plaque assay in PS cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 6E.

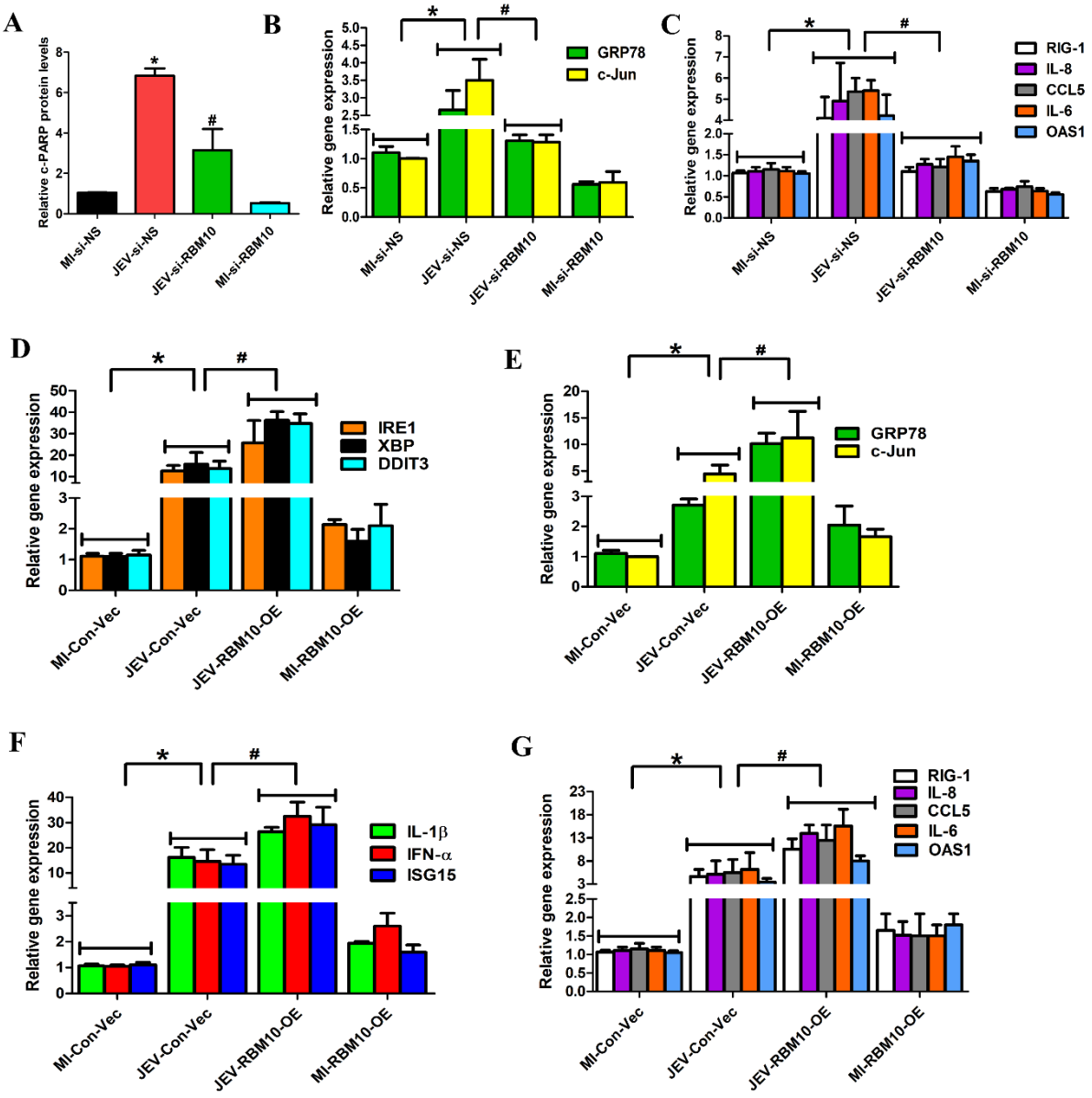
B. RBM10 promotes mature virion RNA release. The supernatant from SH-SY5Y cells transfected with si-NS or si-RBM10 was collected 36 hpi. The mature virion RNA was detected using qRT-PCR and agarose gel electrophoresis. A representative gel image and table with Ct values from three independent experiments are shown. The viral band was detected at 180bp, 100bp DNA ladder was used.

C. RBM10 overexpression promotes JEV titer. The supernatant from SH-SY5Y cells transfected with Con-Vec or RBM10-OE was collected 36 hpi. The viral titer in the supernatant was detected using plaque assay in PS cells. Representative images and quantification from three independent experiments are shown.

D. RBM10 overexpression enhances virion production. Quantification of viral titer upon RBM10 overexpression during JEV infection shown in Figure S5C.

Data information: Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. (For D) *Significant change compared to JEV-Con-Vec.

Figure S6. RBM10 enhances JEV-induced c-PARP protein levels, ER stress, and neuroinflammatory gene expression in SH-SY5Y cells.



A. Quantification of c-PARP protein levels upon RBM10 depletion from western blotting shown in Figure 3E.

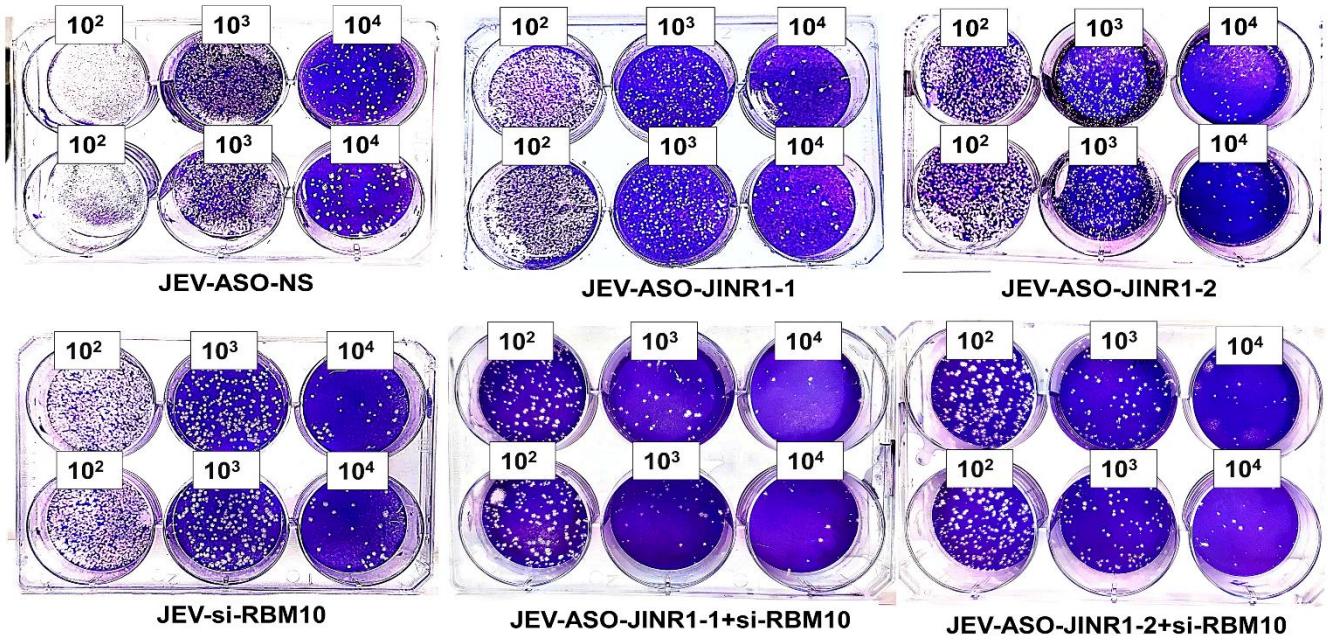
B. RBM10 depletion attenuates JEV-induced ER stress genes. qRT-PCR analysis of indicated ER stress genes upon RBM10 depletion in SH-SY5Y cells 36 hpi.

C. RBM10 depletion reduces JEV-induced neuroinflammatory genes. qRT-PCR analysis of indicated neuroinflammatory genes upon RBM10 depletion in SH-SY5Y cells 36 hpi.

D-E. RBM10 overexpression enhances JEV-induced ER stress genes. qRT-PCR analysis of indicated ER stress genes upon RBM10 overexpression in SH-SY5Y cells 36 hpi.

F-G. RBM10 overexpression enhances JEV-induced neuroinflammatory genes. qRT-PCR analysis of indicated neuroinflammatory genes upon RBM10 overexpression in SH-SY5Y cells 36 hpi.
Data information: Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. (For A-C) *Significant change compared to MI-si-NS. #Significant change compared to JEV-si-NS. (For D-G). *Significant change compared to MI-Con-Vec. #Significant change compared to JEV-Con-Vec.

Figure S7. Impact of co-inhibition of *JINR1* and RBM10 on JEV titer in SH-SY5Y cells.



S7. *JINR1* and RBM10 promotes JEV titer. The supernatant from SH-SY5Y cells transfected ASO-NS/ASO-*JINR1*-1/*JINR1*-2/si-RBM10 or with both ASO-*JINR1*/2 and si-RBM10 was collected 36 hpi. The viral titer in the supernatant was detected using plaque assay in PS cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 4K.

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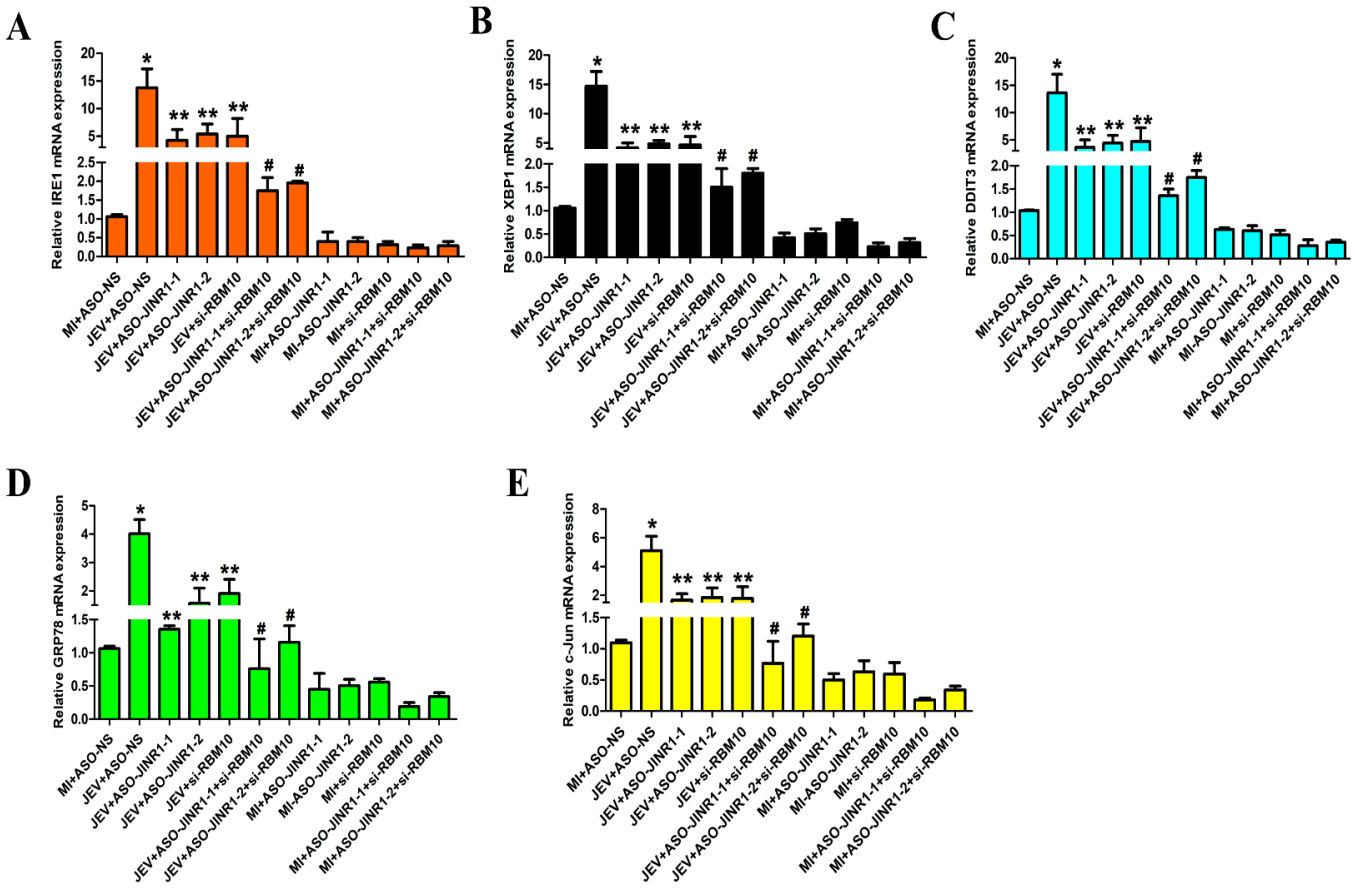
Figure S8. Impact of co-inhibition of *JINR1* and RBM10 on ER stress genes during JEV infection.



A-E. SH-SY5Y cells transfected with one or both ASO-*JINR1*-1/ASO-*JINR1*-2 or si-RBM10, and the indicated ER stress transcript levels were measured by qRT-PCR 48hpi.

Data information: Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. (For A-E) *Significant change compared to MI-ASO-NS, **Significant change compared to JEV-ASO-NS, #significant change compared to JEV-ASO-*JINR1*/2 or JEV-si-RBM10.

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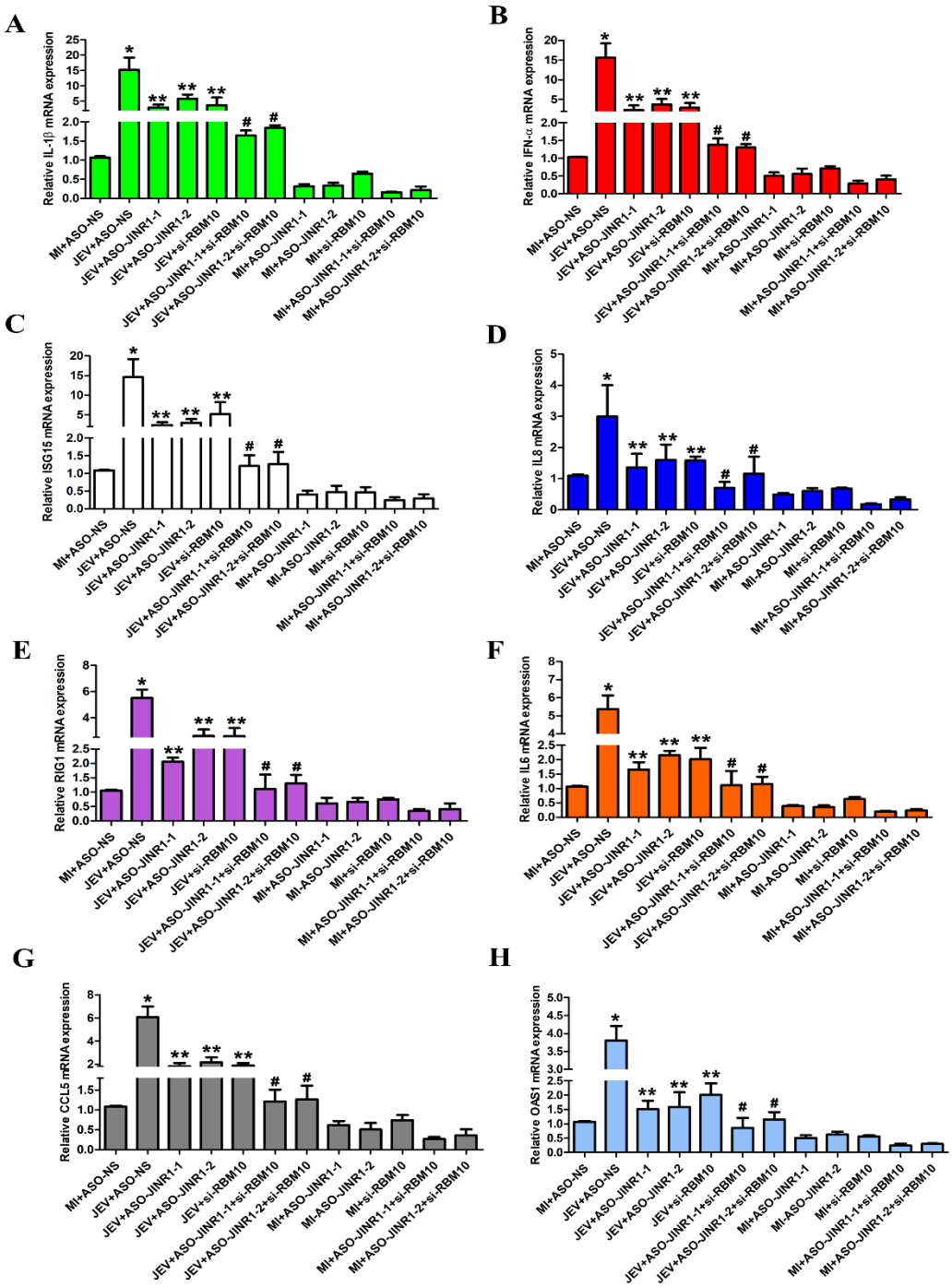
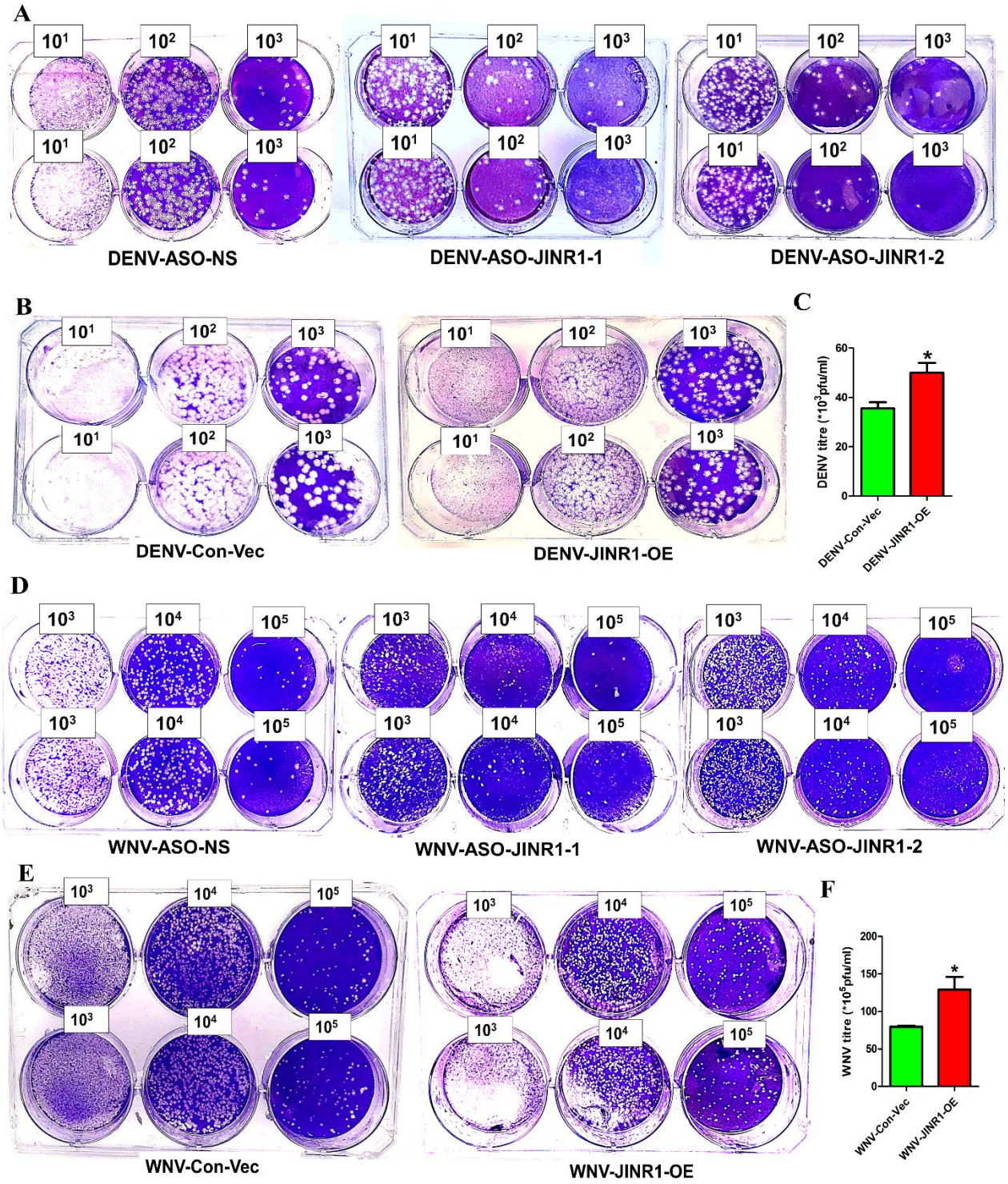
Figure S9. Impact of co-inhibition of *JINR1* and RBM10 on neuroinflammatory genes during JEV infection.



A-H. SH-SY5Y cells transfected with one or both ASO-*JINR1*-1/ASO-*JINR1*-2 or si-RBM10 and the indicated neuroinflammatory transcript levels were measured by qRT-PCR 48hpi.

Data information: Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. (For A-H) *Significant change compared to MI-ASO-NS, **Significant change compared to JEV-ASO-NS, #significant change compared to JEV-ASO-*JINR1*/2 or JEV-si-RBM10.

Figure S10. *JINR1* regulates DENV and WNV replication in SH-SY5Y cells.



A. *JINR1* silencing reduces DENV titer. The supernatant from SH-SY5Y cells, transfected with ASO-NS, ASO-*JINR1-1*, *or* ASO-*JINR1-2*, was collected 48 hpi. The viral titer in the supernatant was detected using plaque assay in PS cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 6F.

B. *JINR1* overexpression promotes DENV titer. The supernatant from SH-SY5Y cells transfected with Con-Vec or *JINR1*-OE was collected 48 hpi. The viral titer in the supernatant was detected using plaque assay in PS cells. Representative images from three independent experiments are shown.

C. *JINR1* overexpression enhances DENV virion production. Quantification of viral titer upon *JINR1* overexpression during DENV infection shown in Figure S10B.

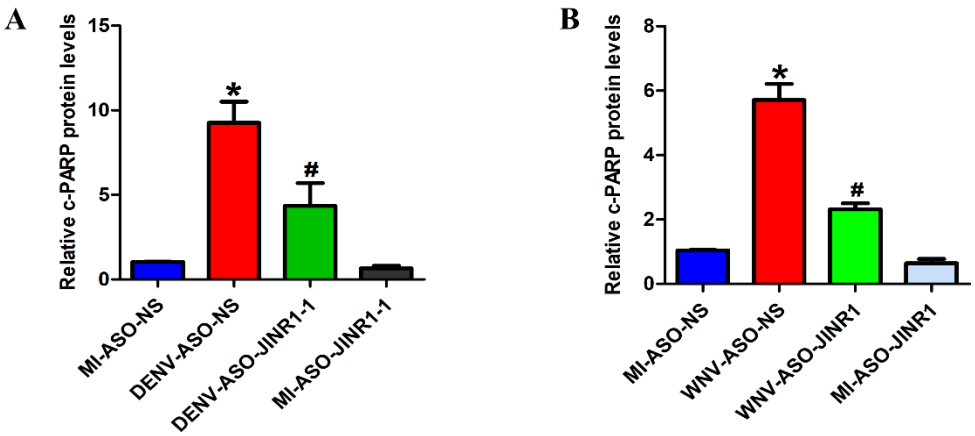
D. *JINR1* silencing reduces WNV titer. The supernatant from SH-SY5Y cells transfected either with ASO-NS, ASO-*JINR1-1*, *or* ASO-*JINR1-2* was collected 48 hpi. The viral titer in the supernatant was detected using plaque assay in Vero cells. Representative images from three independent experiments are shown.

E. *JINR1* overexpression promotes WNV titer. The supernatant from SH-SY5Y cells transfected with Con-Vec or *JINR1*-OE was collected 48 hpi. The viral titer in the supernatant was detected using plaque assay in Vero cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 6G.

F. *JINR1* overexpression enhances WNV virion production. Quantification of viral titer upon *JINR1* overexpression during WNV infection shown in Figure S10E.

Data information: Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. (For C) *Significant change compared to DENV-Con-Vec. (For F) *Significant change compared to WNV-Con-Vec.

Figure S11. *JINR1* depletion reduces DENV and WNV-induced c-PARP protein levels.

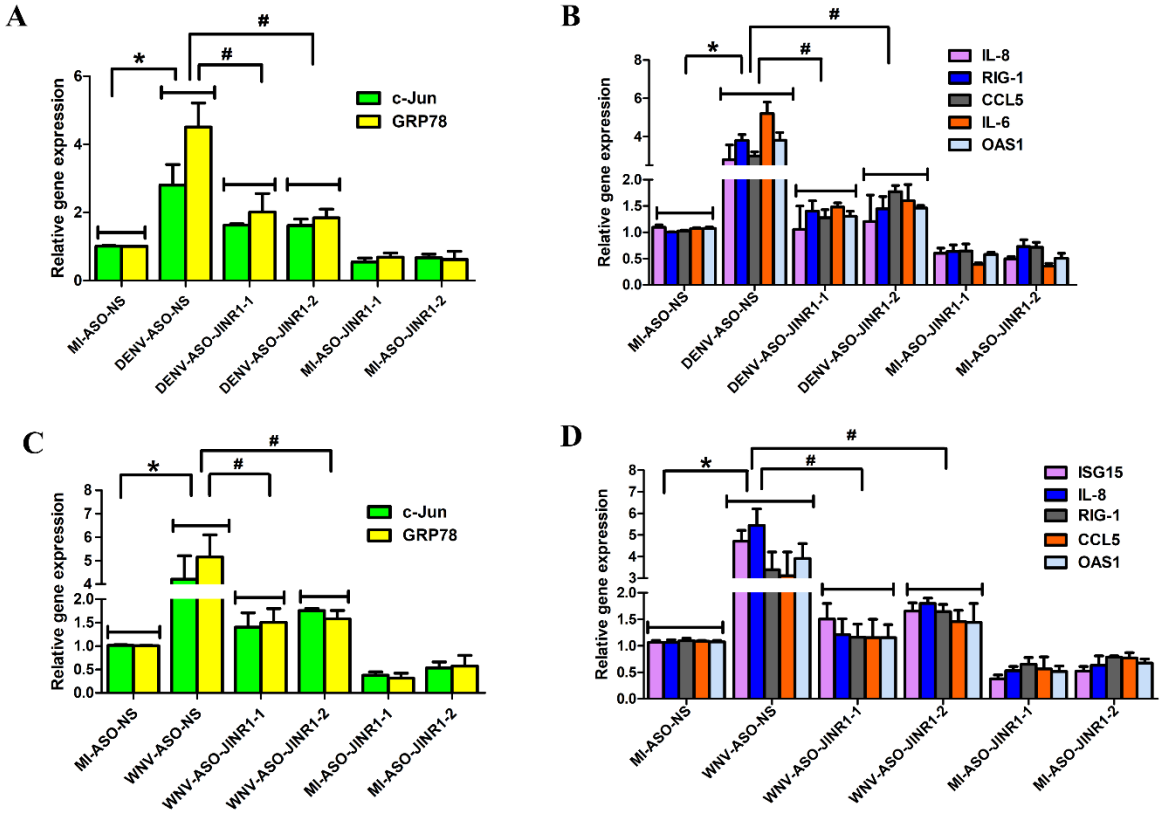


A. Quantification of c-PARP protein levels upon RBM10 depletion during DENV infection from western blotting shown in Figure 6J.

B. Quantification of c-PARP protein levels upon RBM10 depletion during WNV infection from western blotting shown in Figure 6J.

Data information: Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. (For A) *Significant change compared to MI-ASO-NS. #Significant change compared to DENV-ASO-NS. (For B) *Significant change compared to MI-ASO-NS. #Significant change compared to WNV-ASO-NS.

Figure S12. *JINR1* inhibition attenuates DENV and WNV-induced ER stress and neuroinflammatory transcript levels.



A. *JINR1* depletion attenuates DENV-induced ER stress genes. qRT-PCR analysis of indicated ER stress genes upon *JINR1* depletion in SH-SY5Y cells 48 hpi.

B. *JINR1* depletion reduces DENV-induced neuroinflammatory genes. qRT-PCR analysis of indicated neuroinflammatory genes upon *JINR1* depletion in SH-SY5Y cells 48 hpi.

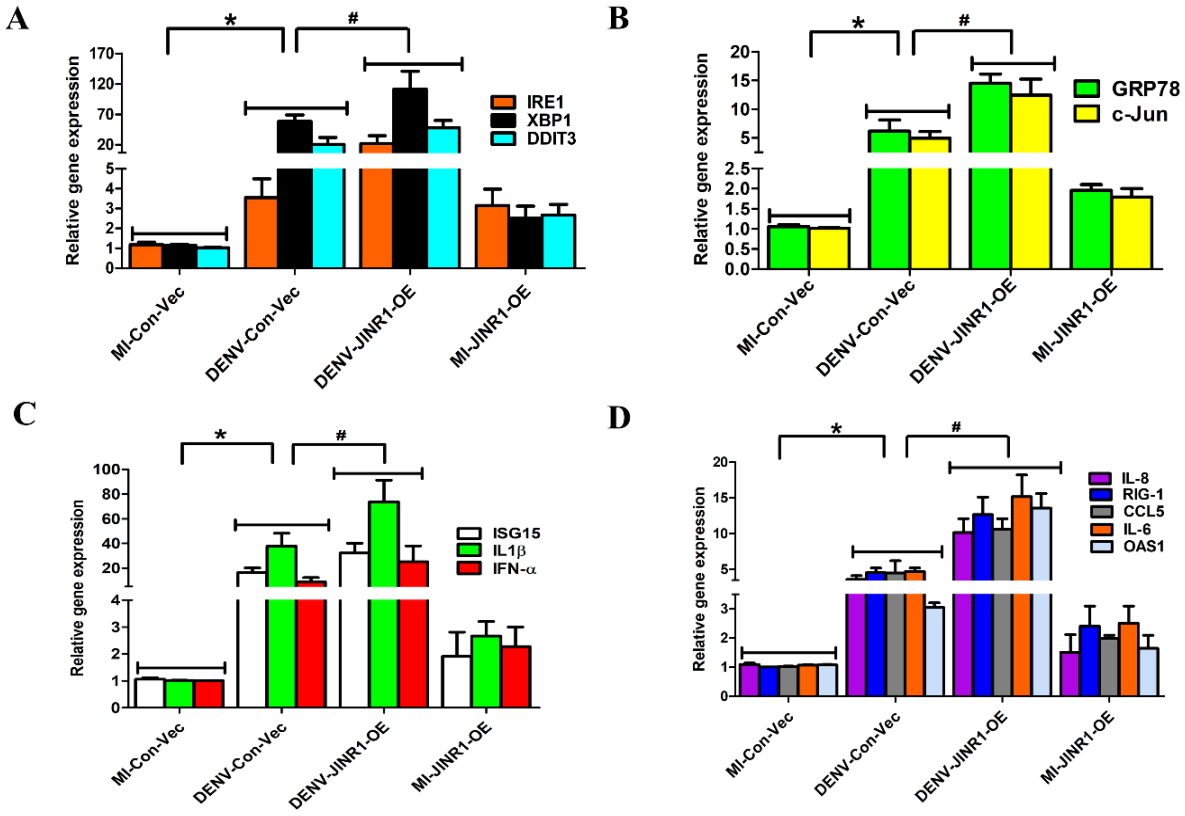
C. *JINR1* depletion attenuates WNV-induced ER stress genes. qRT-PCR analysis of indicated ER stress genes upon *JINR1* depletion in SH-SY5Y cells 48 hpi.

D. *JINR1* depletion reduces WNV-induced neuroinflammatory genes. qRT-PCR analysis of indicated neuroinflammatory genes upon *JINR1* depletion in SH-SY5Y cells 48 hpi.

Data information: RNA samples were analyzed by qRT-PCR. Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-

test. (For A-B) *Significant change compared to MI-ASO-NS #significant change compared to DENV-ASO-NS. (For C-D) *Significant change compared to MI-ASO-NS #significant change compared to WNV-ASO-NS.

Figure S13. *JINR1* overexpression enhances DENV-induced ER stress and neuroinflammatory transcript levels.

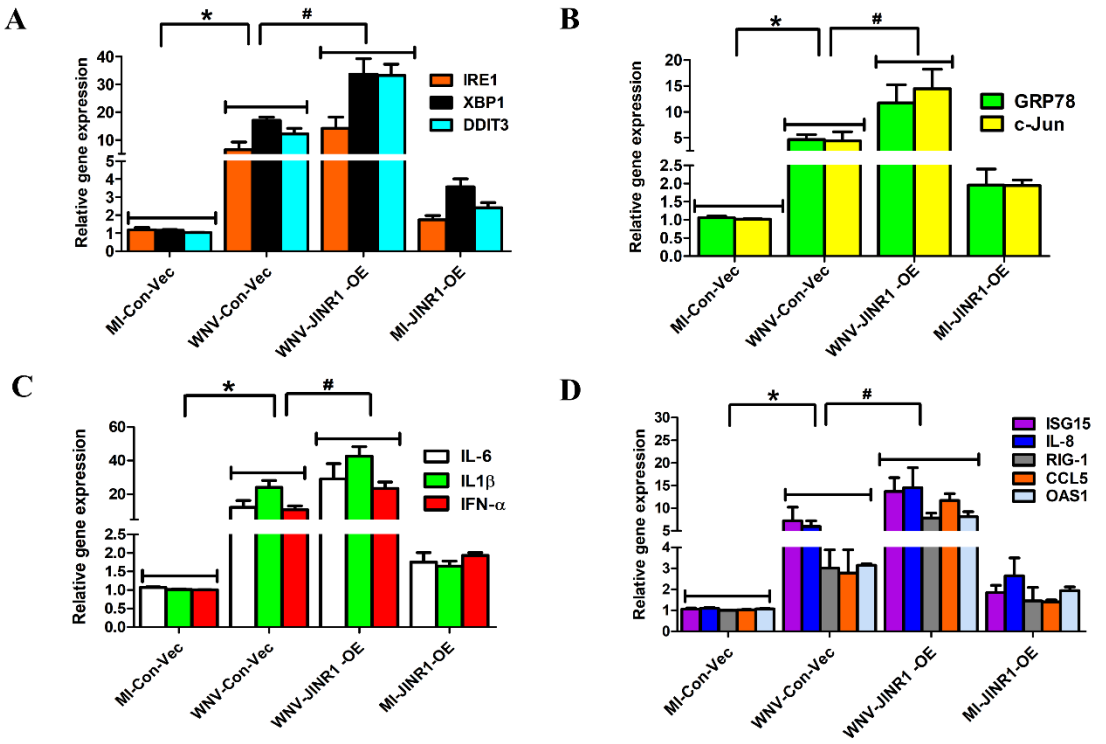


A-B. *JINR1* overexpression enhances DENV-induced ER stress genes. SH-SY5Y cells were transfected with Con-Vec or *JINR1*-OE, and the indicated ER stress gene transcript levels were measured by qRT-PCR 48 hpi.

C-D. *JINR1* overexpression enhances DENV-induced neuroinflammatory genes. SH-SY5Y cells were transfected with Con-Vec or *JINR1*-OE, and the indicated neuroinflammatory transcript levels were measured by qRT-PCR 48 hpi.

Data information: RNA samples were analyzed by qRT-PCR. Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. (For A-D) *Significant change compared to MI-Con-Vec. #significant change compared to DENV-Con-Vec.

Figure S14. *JINR1* overexpression enhances WNV-induced ER stress and neuroinflammatory transcript levels.



A-B. *JINR1* overexpression enhances WNV-induced ER stress genes. SH-SY5Y cells were transfected with Con-Vec or *JINR1*-OE, and the indicated ER stress gene transcript levels were measured by qRT-PCR 48 hpi.

C-D. *JINR1* overexpression enhances WNV-induced neuroinflammatory genes. SH-SY5Y cells were transfected with Con-Vec or *JINR1*-OE, and the indicated neuroinflammatory transcript levels were measured by qRT-PCR 48 hpi.

Data information: RNA samples were analyzed by qRT-PCR. Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. (For A-D) *Significant change compared to MI-Con-Vec. #significant change compared to WNV-Con-Vec.

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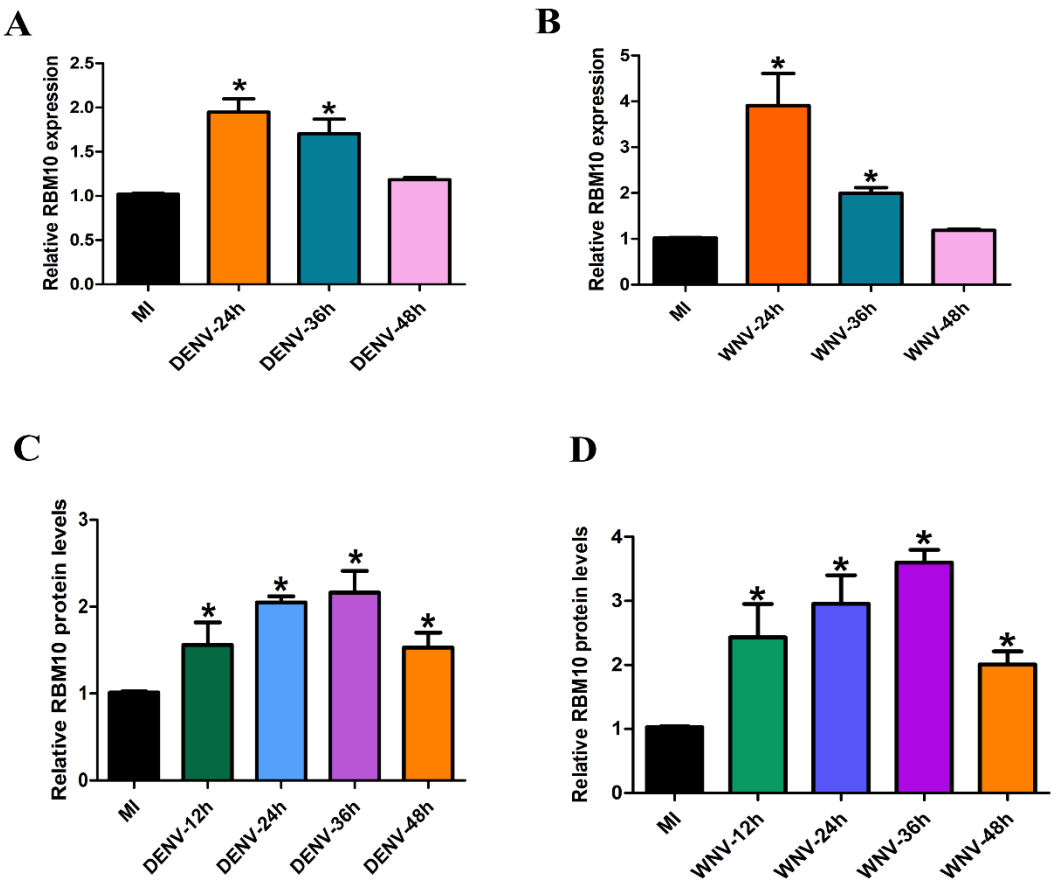
S15. RBM10 transcript and protein levels during DENV and WNV infection in SH-SY5Y cells.



A. DENV infection increases RBM10 mRNA expression. Time course analysis of RBM10 expression at indicated time points during DENV infection was measured using qRT-PCR.

B. WNV infection increases RBM10 mRNA expression. Time course analysis of RBM10 expression at indicated time points during WNV infection was measured using qRT-PCR.

C. Quantification of RBM10 protein levels upon DENV infection from western blotting (Figure 6A).

D. Quantification of RBM10 protein levels upon WNV infection from western blotting (Figure 6A).

Data information: Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. (For A-D) *Significant change compared to MI.

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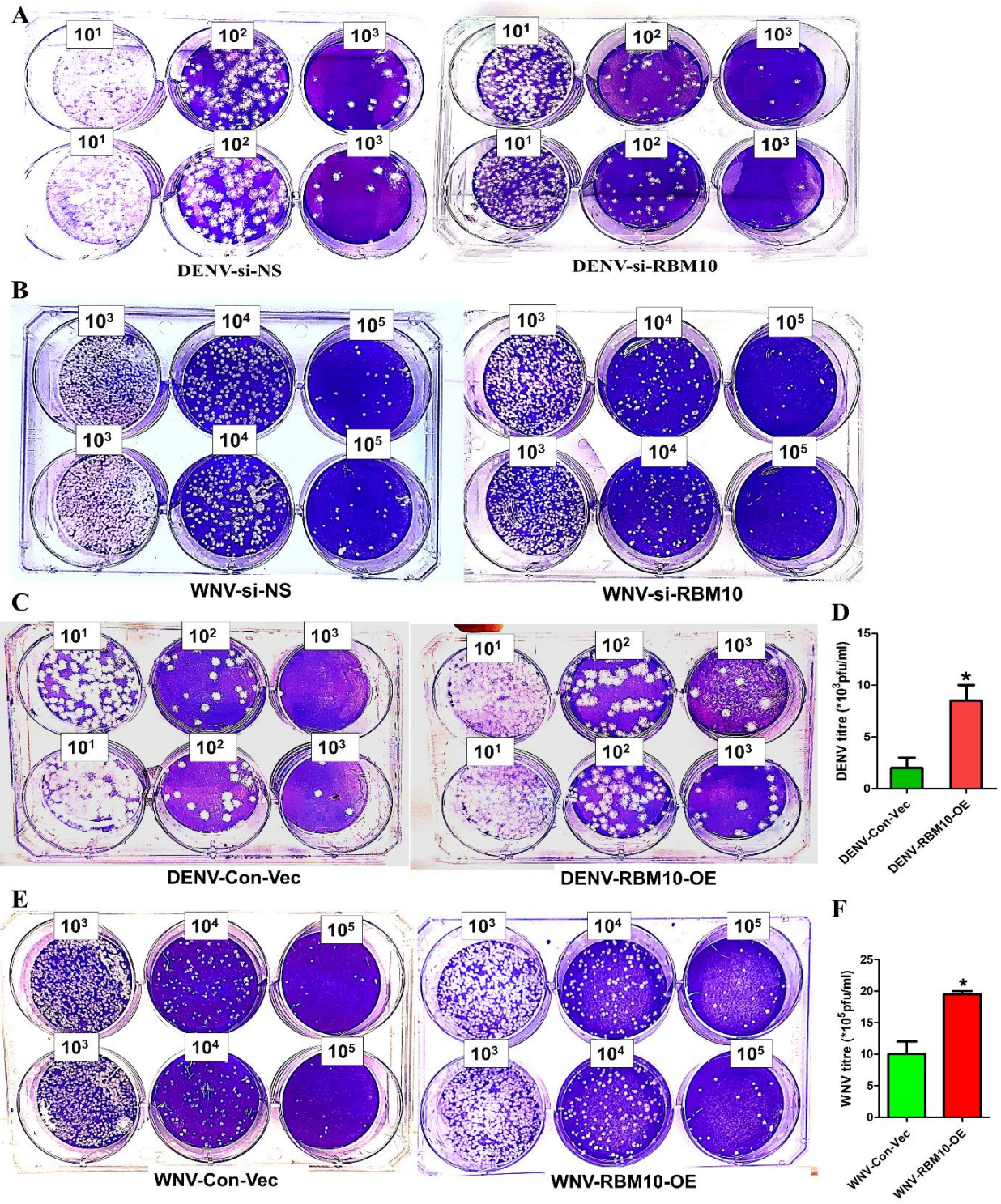
Figure S16. RBM10 regulates DENV and WNV mature virion production.



A. RBM10 promotes DENV titer. The supernatant from SH-SY5Y cells transfected with si-NS or si-RBM10 was collected 36 hpi. The viral titer in the supernatant was detected using plaque assay in PS cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 6F.

B. RBM10 promotes WNV titer. The supernatant from SH-SY5Y cells transfected with si-NS or si-RBM10 was collected 36 hpi. The viral titer in the supernatant was detected using plaque assay in Vero cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 6G.

C. RBM10 promotes DENV titer. The supernatant from SH-SY5Y cells transfected with Con-Vec or RBM10-OE was collected 36 hpi. The viral titer in the supernatant was detected using plaque assay in PS cells. Representative images from three independent experiments are shown.

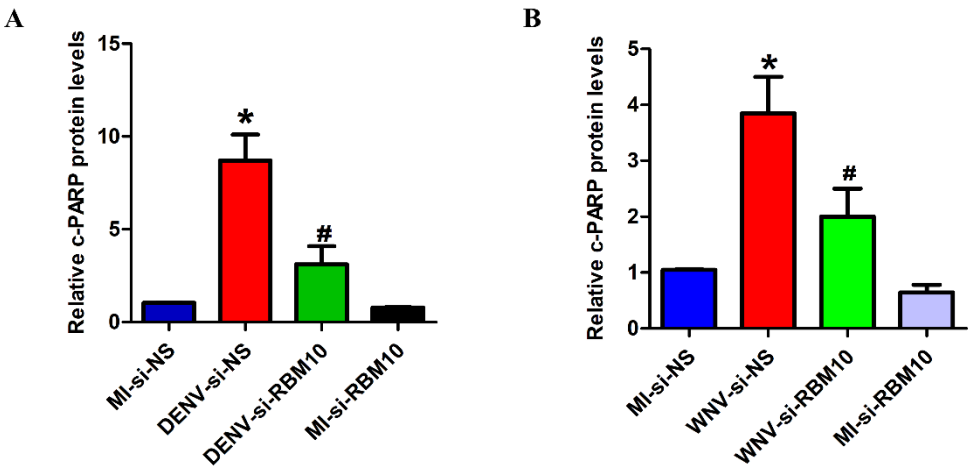
D. RBM10 overexpression enhances DENV virion production. Quantification of viral titer upon RBM10 overexpression during DENV infection shown in Figure S16C.

E. RBM10 promotes WNV titer. The supernatant from SH-SY5Y cells transfected with Con-Vec or RBM10-OE was collected 36 hpi. The viral titer in the supernatant was detected using plaque assay in Vero cells. Representative images from three independent experiments are shown.

F. RBM10 overexpression enhances WNV virion production. Quantification of viral titer upon RBM10 overexpression during WNV infection shown in Figure S16E.

Data information: RNA samples were analyzed by qRT-PCR. Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. (For D) *Significant change compared to DENV-Con-Vec. (For F) *Significant change compared to WNV-Con-Vec.

Figure S17. RBM10 silencing reduces DENV and WNV-induced c-PARP protein levels.

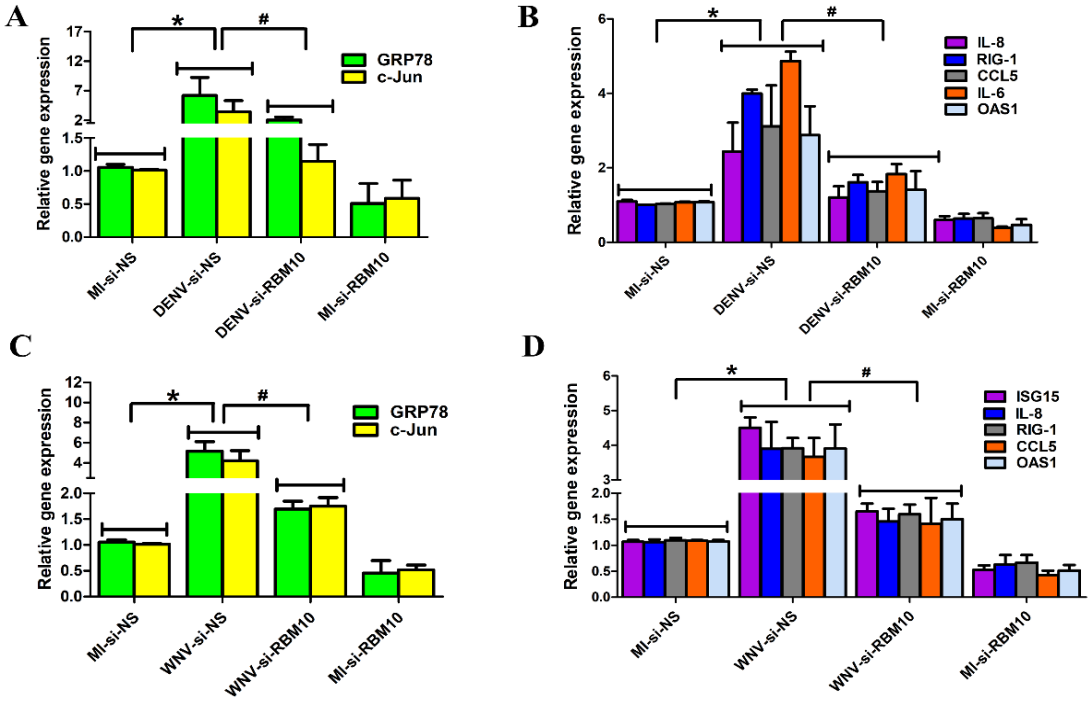


A. Quantification of cleaved PARP protein levels upon RBM10 depletion in DENV-infected SH-SY5Y cells from western blotting shown in Figure 6J.

B. Quantification of c-PARP protein levels upon RBM10 depletion in WNV-infected SH-SY5Y cells from western blotting shown in Figure 6J.

Data information: Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. (For A) *Significant change compared to MI-si-NS. #Significant change compared to DENV-si-NS. (For B) *Significant change compared to MI-si-NS. #Significant change compared to WNV-si-NS.

Figure S18. RBM10 depletion reduces DENV and WNV-induced gene expression in SH-SY5Y cells.



A. RBM10 depletion attenuates DENV-induced ER stress genes. qRT-PCR analysis of indicated ER stress genes upon RBM10 depletion in SH-SY5Y cells 36 hpi.

B. RBM10 depletion reduces DENV-induced neuroinflammatory genes. qRT-PCR analysis of indicated neuroinflammatory genes upon RBM10 depletion in SH-SY5Y cells 36 hpi.

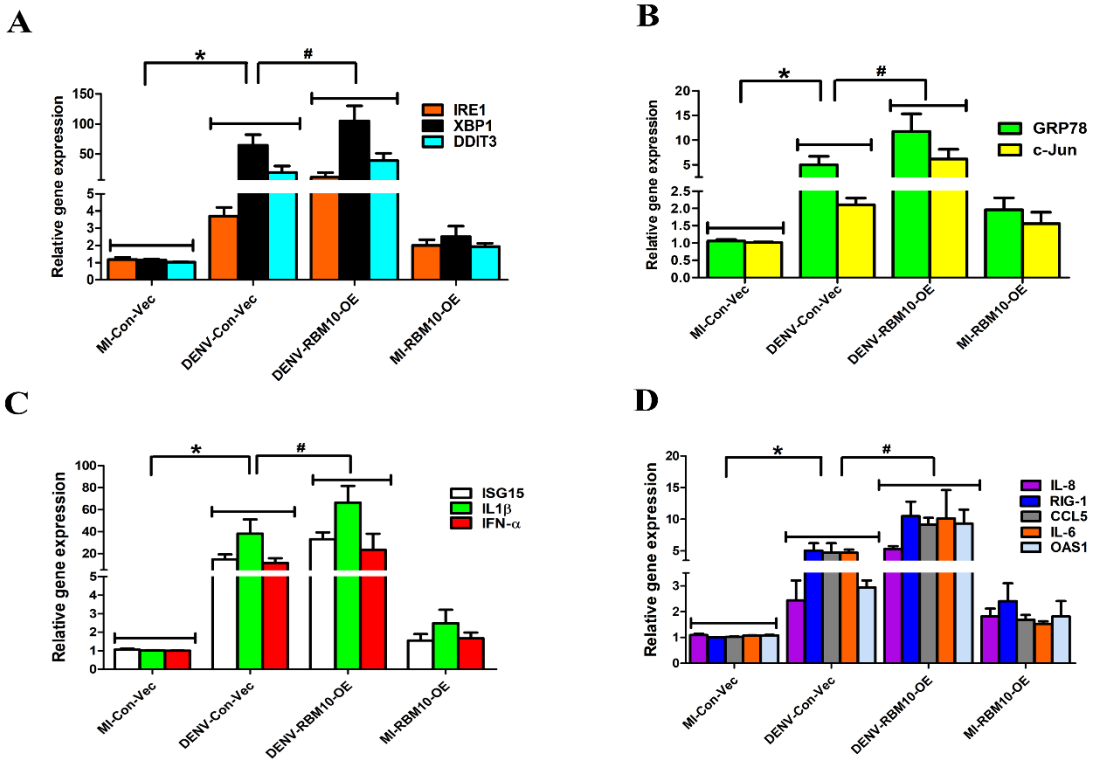
C. RBM10 depletion attenuates WNV-induced ER stress genes. qRT-PCR analysis of indicated ER stress genes upon RBM10 depletion in SH-SY5Y cells 36 hpi.

D. RBM10 depletion reduces WNV-induced neuroinflammatory genes. qRT-PCR analysis of indicated neuroinflammatory genes upon RBM10 depletion in SH-SY5Y cells 36 hpi.

Data information: (For A-D) RNA samples were analyzed by qRT-PCR Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Stu-

dent's t-test. (For A-B) *Significant change compared to MI-si-NS. #Significant change compared to DENV-si-NS. (For C-D) *Significant change compared to MI-si-NS. #Significant change compared to WNV-si-NS.

Figure S19. RBM10 overexpression enhances DENV-induced ER stress and neuroinflammatory gene expression.



A-B. RBM10 overexpression enhances DENV-induced ER stress genes. qRT-PCR analysis of indicated ER stress genes upon RBM10 overexpression in SH-SY5Y cells 36 hpi.

C-D. RBM10 overexpression enhances DENV-induced neuroinflammatory genes. qRT-PCR analysis of indicated neuroinflammatory genes upon RBM10 overexpression in SH-SY5Y cells 36 hpi.

Data information: (For A-D) RNA samples were analyzed by qRT-PCR Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. *Significant change compared to MI-Con-Vec. #Significant change compared to DENV-Con-Vec.

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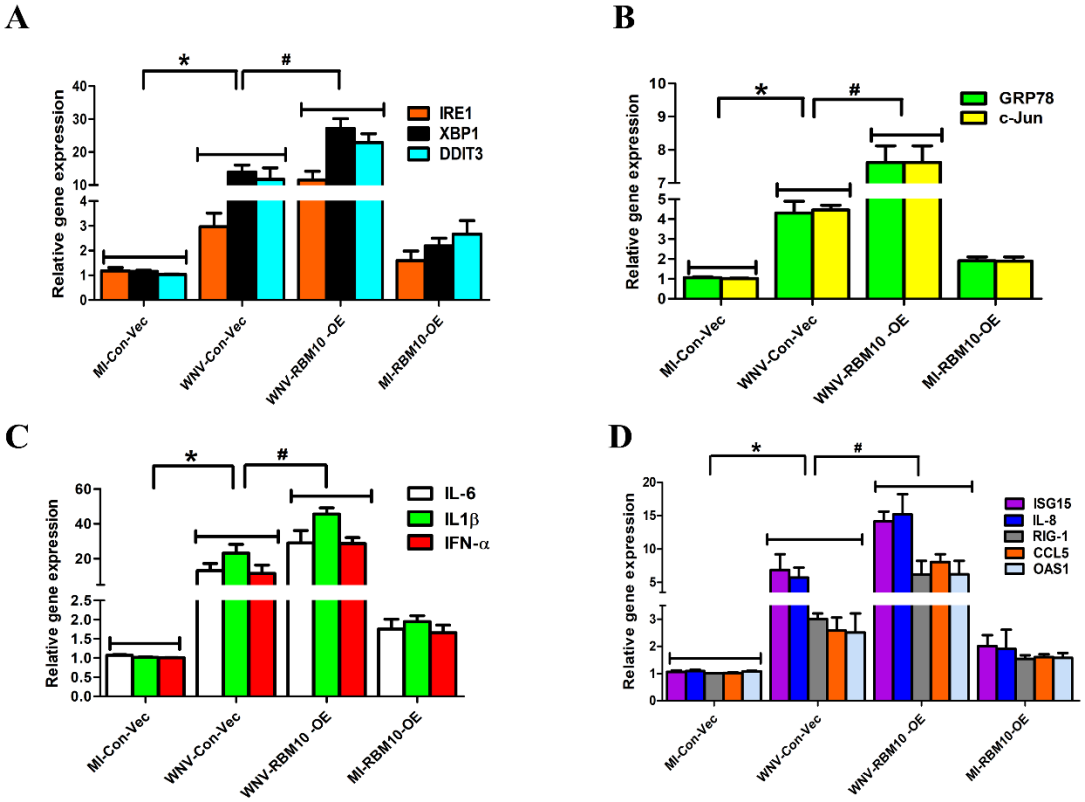
Figure S20. RBM10 overexpression enhances WNV-induced ER stress and neuroinflammatory gene expression.



A-B. RBM10 overexpression enhances WNV-induced ER stress genes. qRT-PCR analysis of indicated ER stress genes upon RBM10 overexpression in SH-SY5Y cells 36 hpi.

C-D. RBM10 overexpression enhances WNV-induced neuroinflammatory genes. qRT-PCR analysis of indicated neuroinflammatory genes upon RBM10 overexpression in SH-SY5Y cells 36 hpi.

Data information: (For A-D) RNA samples were analyzed by qRT-PCR Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. (For A-D) *Significant change compared to MI-Con-Vec. #Significant change compared to WNV-Con-Vec.

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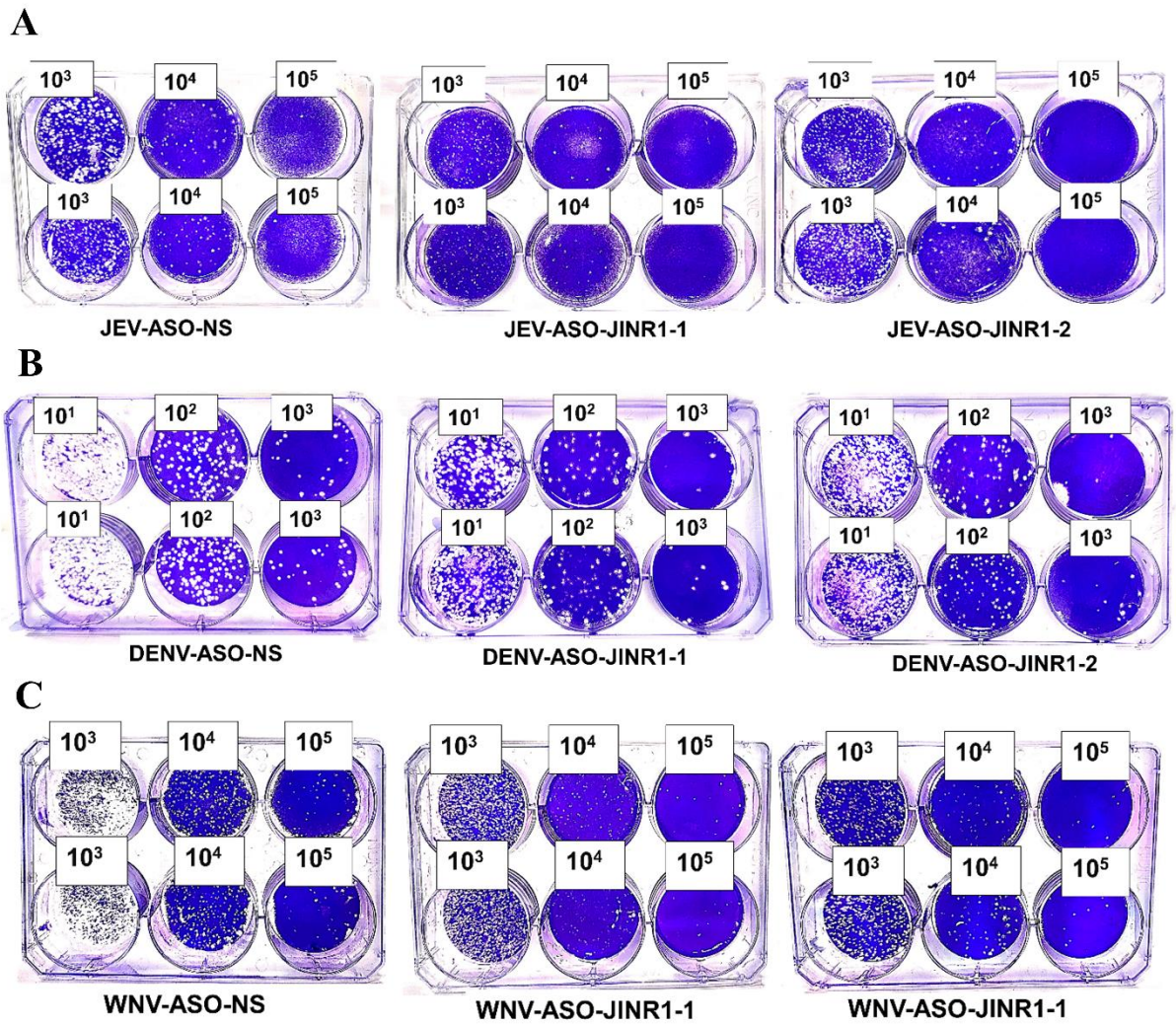
Figure S21. *JINR1* promotes flavivirus replication in T98G cells.

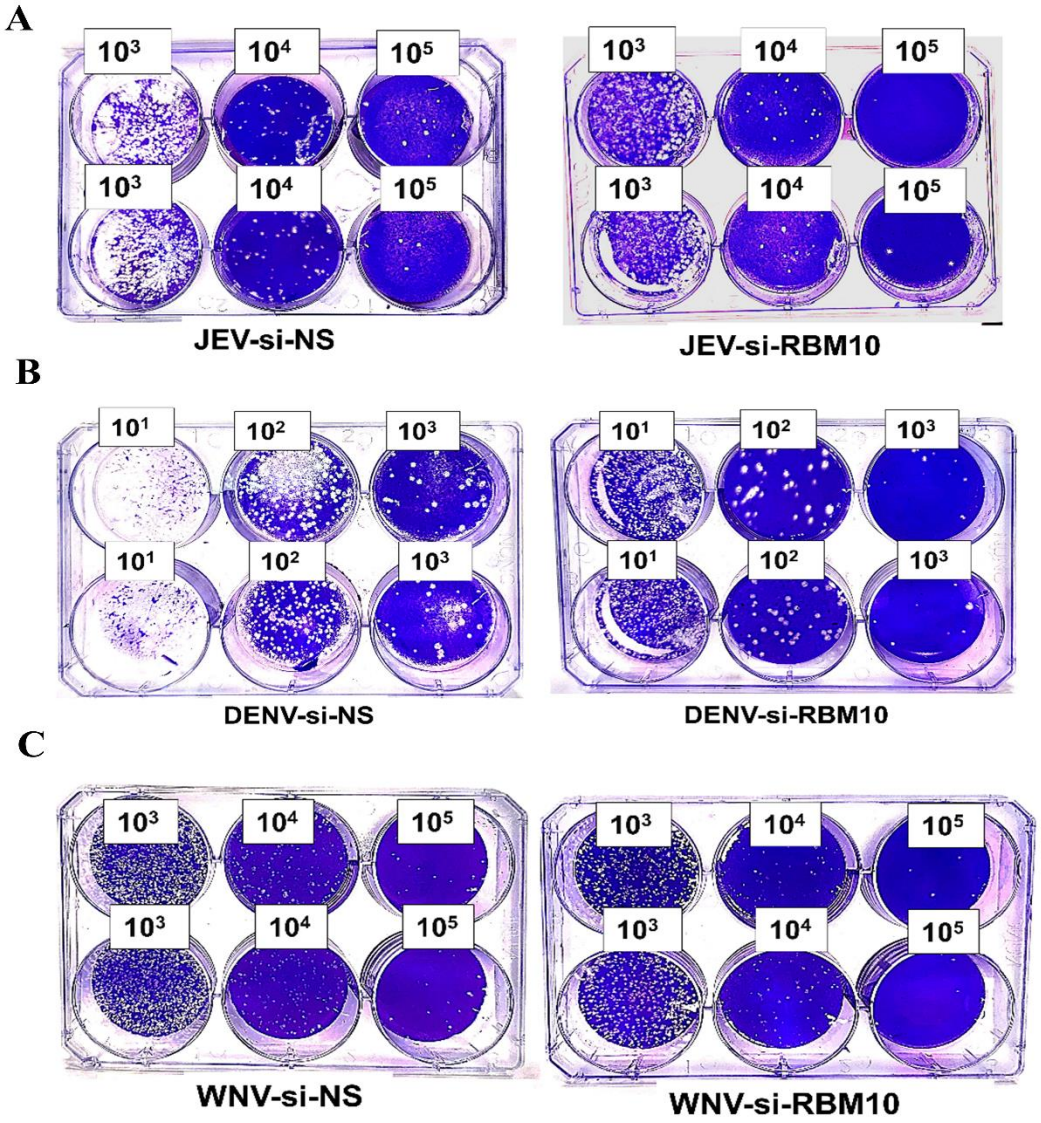


A. *JINR1* silencing reduces JEV titer in astrocytoma cells. The supernatant from T98G cells, transfected with ASO-NS, ASO-*JINR1-1*, *or* ASO-*JINR1-2*, was collected 48 hpi. The viral titer in the supernatant was detected using plaque assay in PS cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 7D.

B. *JINR1* silencing reduces DENV titer in astrocytoma cells. The supernatant from T98G cells, transfected with ASO-NS, ASO-*JINR1-1*, *or* ASO-*JINR1-2*, was collected 48 hpi. The viral titer in the supernatant was detected using plaque assay in PS cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 7E.

C. *JINR1* silencing reduces WNV titer in astrocytoma cells. The supernatant from T98G cells, transfected with ASO-NS, ASO-*JINR1-1*, *or* ASO-*JINR1-2*, was collected 48 hpi. The viral titer in the supernatant was detected using plaque assay in Vero cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 7F.

Figure S22. RBM10 promotes flavivirus replication in T98G cells.

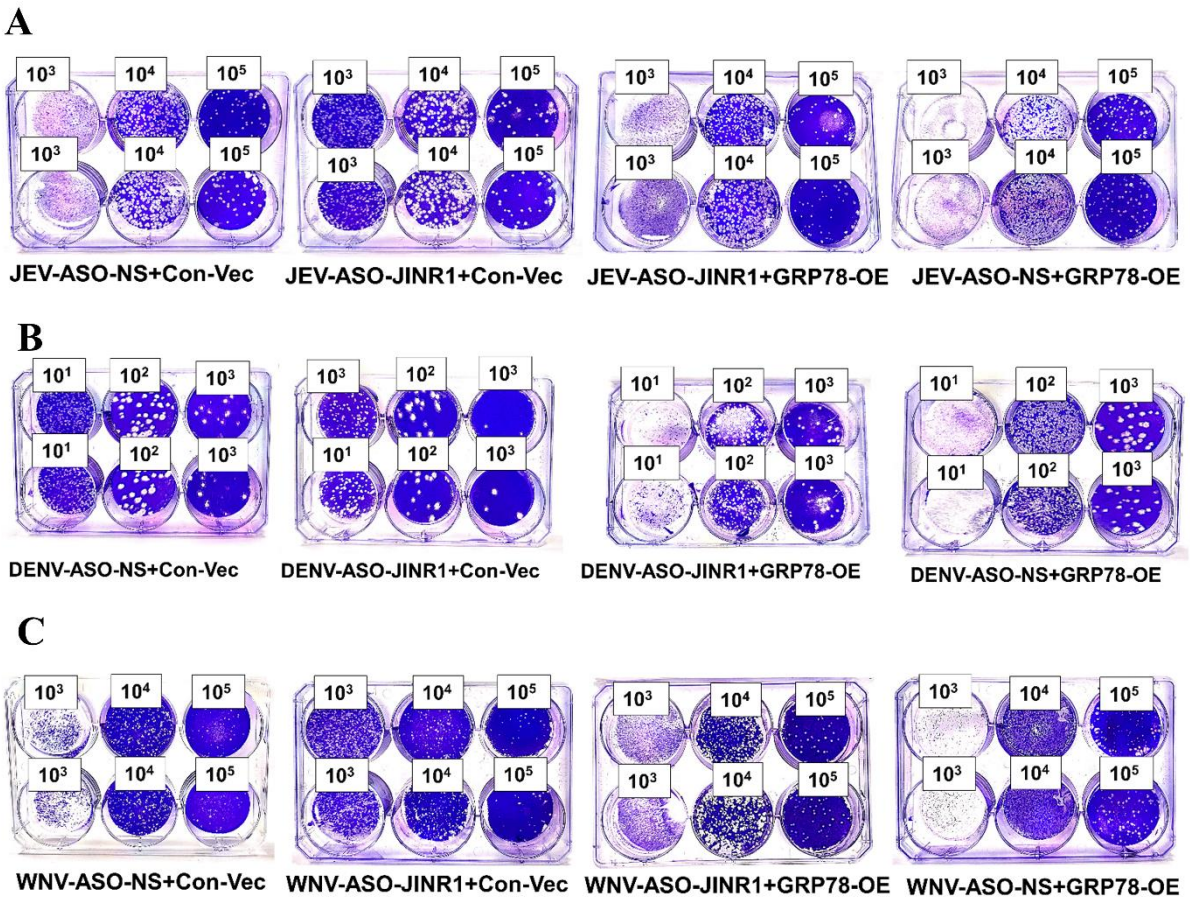


A. RBM10 silencing reduces JEV titer in astrocytoma cells. The supernatant from T98G cells, transfected with si-NS, or si-RBM10, was collected 36 hpi. The viral titer in the supernatant was detected using plaque assay in PS cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 7J.

B. RBM10 silencing reduces DENV titer in astrocytoma cells. The supernatant from T98G cells, transfected with si-NS, or si-RBM10, was collected 36 hpi. The viral titer in the supernatant was detected using plaque assay in PS cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 7K.

C. RBM10 silencing reduces WNV titer in astrocytoma cells. The supernatant from T98G cells, transfected with si-NS, *or* si-RBM10, was collected 36 hpi. The viral titer in the supernatant was detected using plaque assay in Vero cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 7L.

Figure S23. GRP78 regulates *JINR1*-mediated increase in flavivirus replication in SH-SY5Y cells.



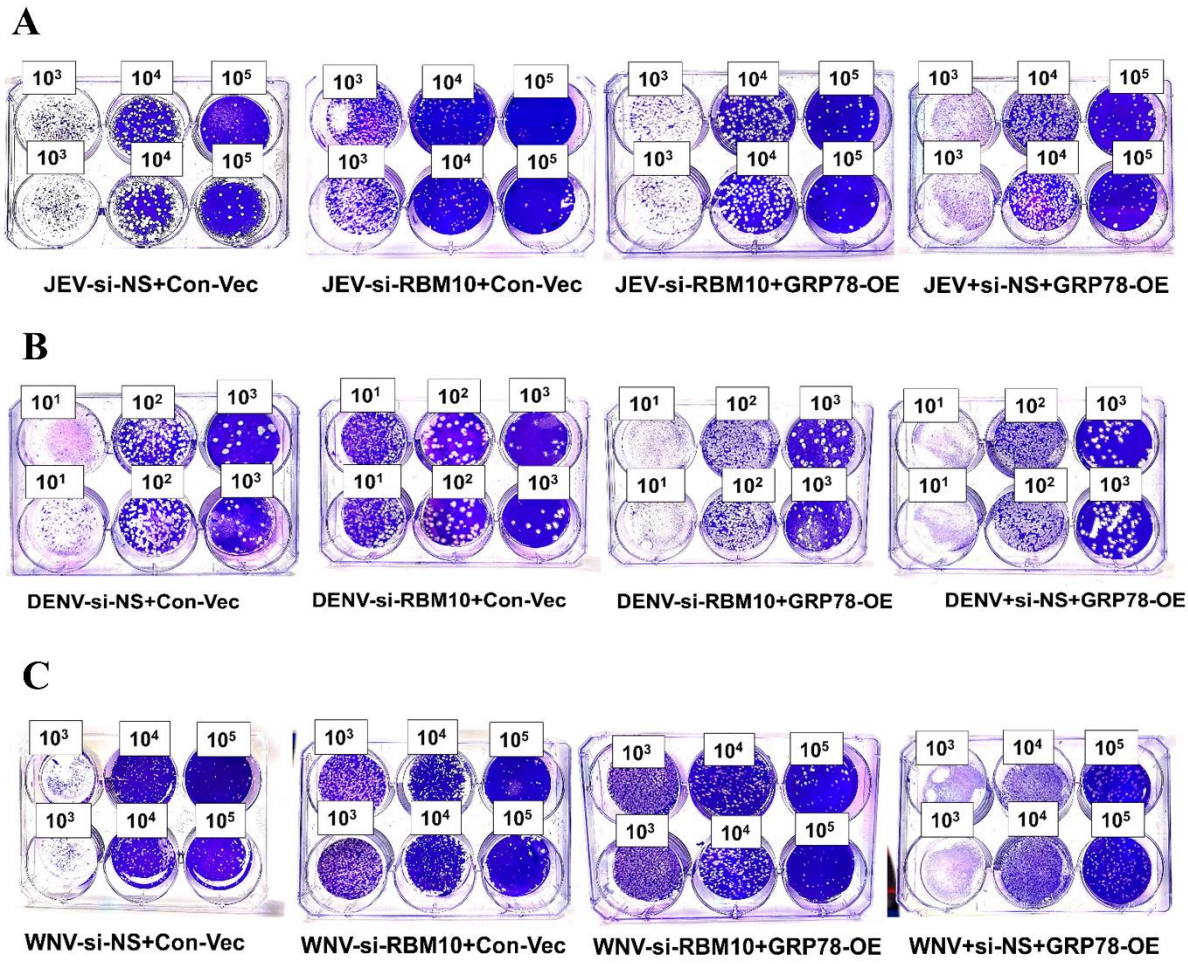
A. GRP78 overexpression prevents the reduction in JEV titer due to *JINR1* depletion in SH-SY5Y cells. The supernatant from JEV-infected SH-SY5Y cells co-transfected with either ASO-NS and Con-Vec or ASO-*JINR1* and Con-Vec or ASO-*JINR1* and GRP78-OE or ASO-NS and GRP78 OE was collected 48 hpi. The viral titer in the supernatant was detected using plaque assay in PS cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 8D.

B. GRP78 overexpression prevents the reduction in DENV titer due to *JINR1* depletion in SH-SY5Y cells. The supernatant from DENV-infected SH-SY5Y cells co-transfected with either ASO-NS and Con-Vec or ASO-*JINR1* and Con-Vec or ASO-*JINR1* and GRP78-OE or ASO-NS and GRP78 OE was collected 48 hpi. The viral titer in the supernatant was detected using plaque assay in PS cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 8E.

C. GRP78 overexpression prevents the reduction in WNV titer due to *JINR1* depletion in SH-SY5Y cells. The supernatant from WNV-infected SH-SY5Y cells co-transfected with either

ASO-NS and Con-Vec or ASO-*JINR1* and Con-Vec or ASO-*JINR1* and GRP78-OE or ASO-NS and GRP78 OE was collected 48 hpi. The viral titer in the supernatant was detected using plaque assay in Vero cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 8F.

Figure S24. GRP78 regulates RBM10 mediated increase in flavivirus replication in SH-SY5Y cells.

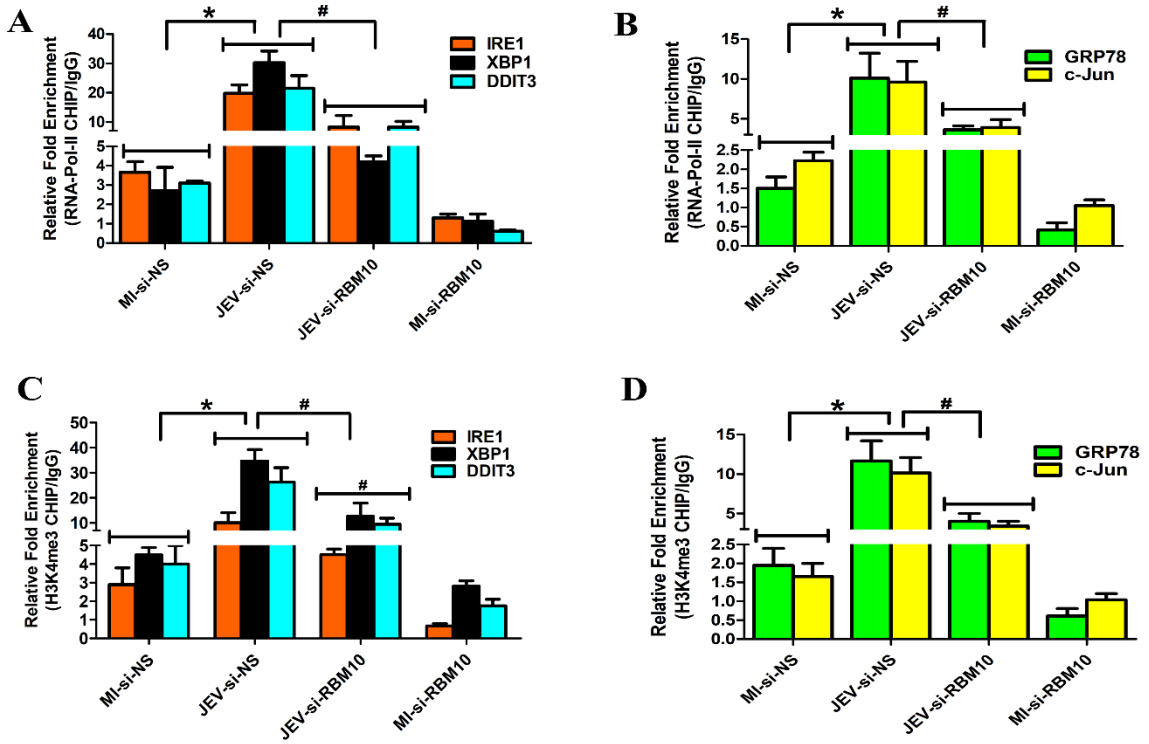


A. GRP78 overexpression prevents the reduction in JEV titer due to RBM10 depletion in SH-SY5Y cells. The supernatant from JEV-infected SH-SY5Y cells co-transfected with either si-NS and Con-Vec or si-RBM10 and Con-Vec or si-RBM10 and GRP78-OE or si-NS and GRP78 OE was collected 36 hpi. The viral titer in the supernatant was detected using plaque assay in PS cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 8J.

B. GRP78 overexpression prevents the reduction in DENV titer due to RBM10 depletion in SH-SY5Y cells. The supernatant from DENV-infected SH-SY5Y cells co-transfected with either si-NS and Con-Vec or si-RBM10 and Con-Vec or si-RBM10 and GRP78-OE or si-NS and GRP78 OE was collected 36 hpi. The viral titer in the supernatant was detected using plaque assay in PS cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 8K.

C. GRP78 overexpression prevents the reduction in WNV titer due to RBM10 depletion in SH-SY5Y cells. The supernatant from WNV-infected SH-SY5Y cells co-transfected with either si-NS and Con-Vec or si-RBM10 and Con-Vec or si-RBM10 and GRP78-OE or si-NS and GRP78 OE was collected 36 hpi. The viral titer in the supernatant was detected using plaque assay in Vero cells. Representative images from three independent experiments are shown, and the quantification is shown in Figure 8L.

Figure S25. RBM10 regulates the transcription of ER stress genes during JEV infection.



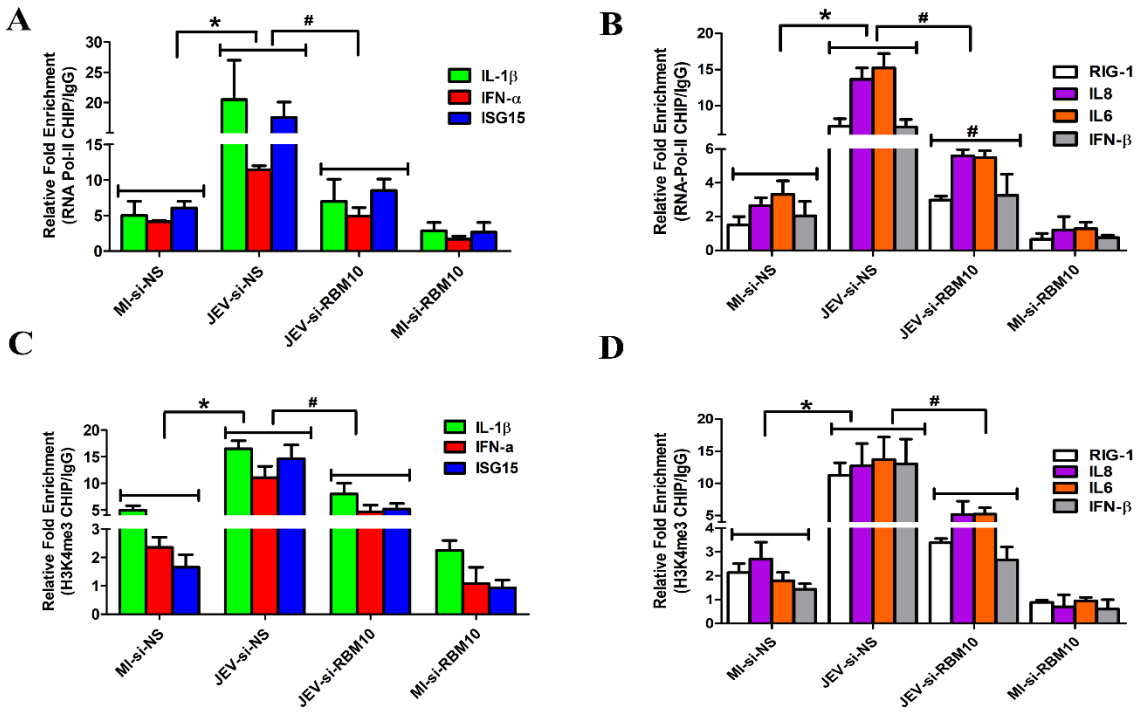
A-B. RBM10 promotes the RNA Pol II recruitment at the promoter of ER stress genes. Relative enrichment of RNA Pol II at the promoter of indicated genes in MI or JEV-infected SH-SY5Y cells transfected with si-NS or si-RBM10 determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-si-NS IgG IP.

C-D. RBM10 promotes the H3K4me3 recruitment at the promoter of ER stress genes. Relative enrichment of H3K4me3 at the promoter of indicated genes in MI or JEV-infected SH-

SY5Y cells transfected with si-NS or si-RBM10 determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-si-NS IgG IP.

Data information: (For A-D) Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. *Significant change compared to MI-si-NS, #significant change compared to JEV-si-NS.

Figure S26. RBM10 regulates the transcription of neuroinflammatory genes during JEV infection.

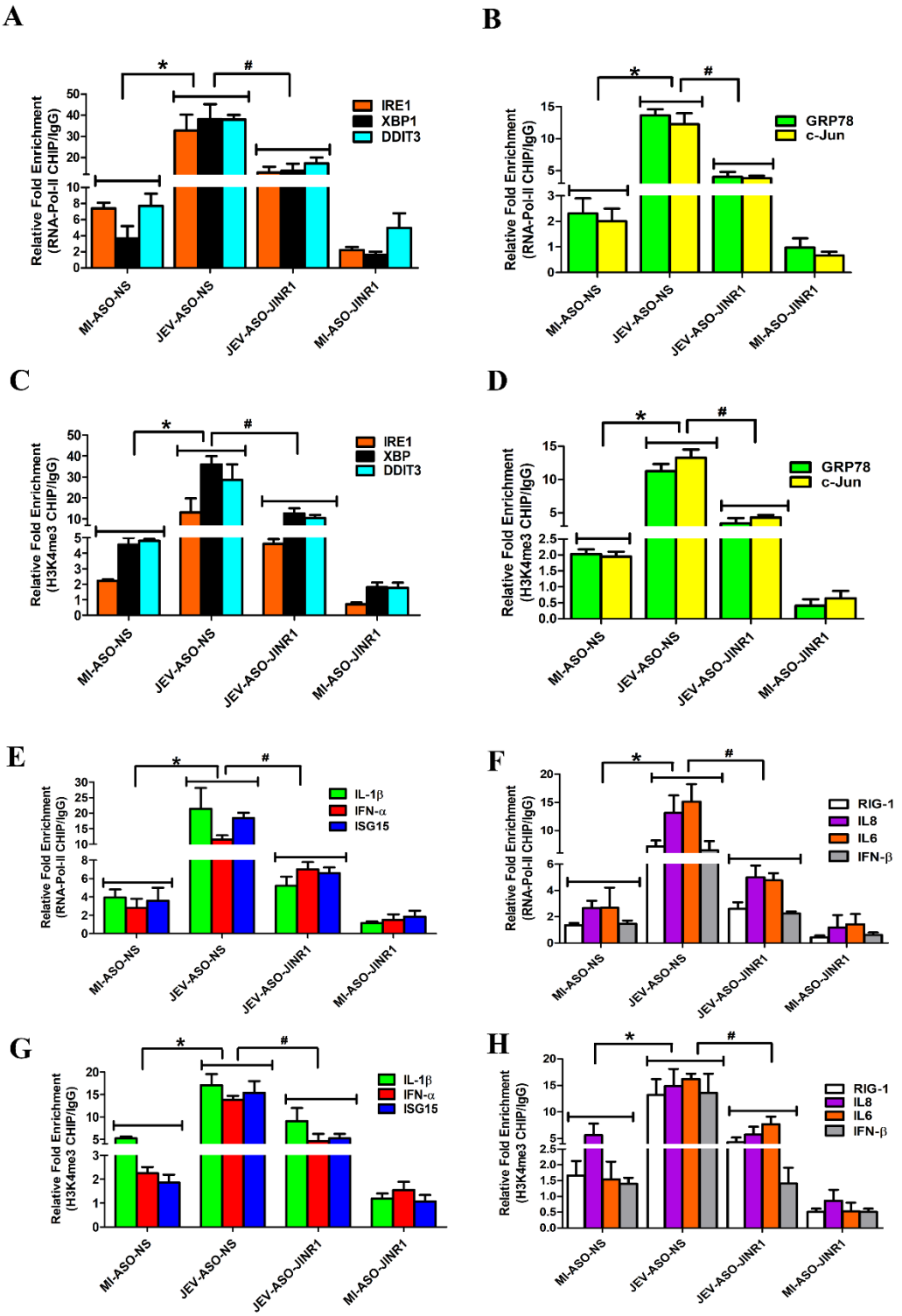


A-B. RBM10 promotes RNA Pol II recruitment at the promoter of inflammatory genes. Relative enrichment of RNA Pol II at the promoter of indicated genes in MI or JEV-infected SH-SY5Y cells transfected with si-NS or si-RBM10 determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-si-NS IgG IP.

C-D. RBM10 promotes the H3K4me3 recruitment at the promoter of inflammatory genes. Relative enrichment of H3K4me3 at the promoter of indicated genes in MI or JEV-infected SH-SY5Y cells transfected with si-NS or si-RBM10 determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-si-NS IgG IP.

Data information: (For A-D) Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. *Significant change compared to MI-si-NS, #significant change compared to JEV-si-NS.

Figure S27. *JINR1* regulates the transcription of ER stress and neuroinflammatory genes during JEV infection.



A-B. *JINR1* promotes RNA Pol II recruitment at the promoter of ER stress genes. Relative enrichment of RNA Pol II at the promoter of indicated genes in MI or JEV-infected SH-SY5Y cells transfected with ASO-NS or ASO-*JINR1* determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-ASO-NS IgG IP.

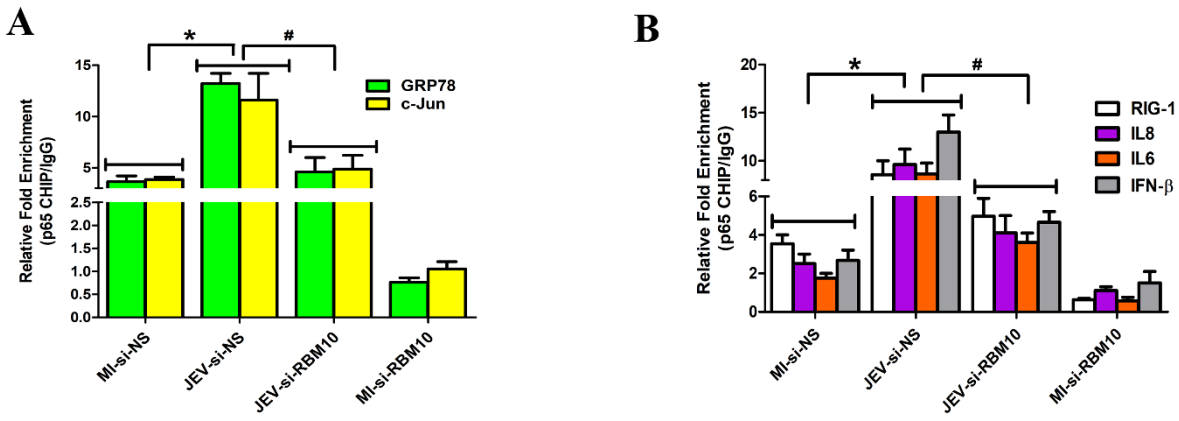
C-D. *JINR1* promotes the H3K4me3 recruitment at the promoter of ER stress genes. Relative enrichment of H3K4me3 at the promoter of indicated genes in MI or JEV-infected SH-SY5Y cells transfected with ASO-NS or ASO-*JINR1* determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-ASO-NS IgG IP.

E-F. *JINR1* promotes RNA Pol II recruitment at the promoter of inflammatory genes. Relative enrichment of RNA Pol II at the promoter of indicated genes in MI or JEV-infected SH-SY5Y cells transfected with ASO-NS or ASO-*JINR1* determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-ASO-NS IgG IP.

G-H. *JINR1* promotes the H3K4me3 recruitment at the promoter of inflammatory genes. Relative enrichment of H3K4me3 at the promoter of indicated genes in MI or JEV-infected SH-SY5Y cells transfected with ASO-NS or ASO-*JINR1* determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-ASO-NS IgG IP.

Data information: (For A-H) Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. *Significant change compared to MI-ASO-NS, #significant change compared to JEV-ASO-NS.

S28. RBM10 recruits p65 at the promoters of ER stress and neuroinflammation genes during JEV infection.



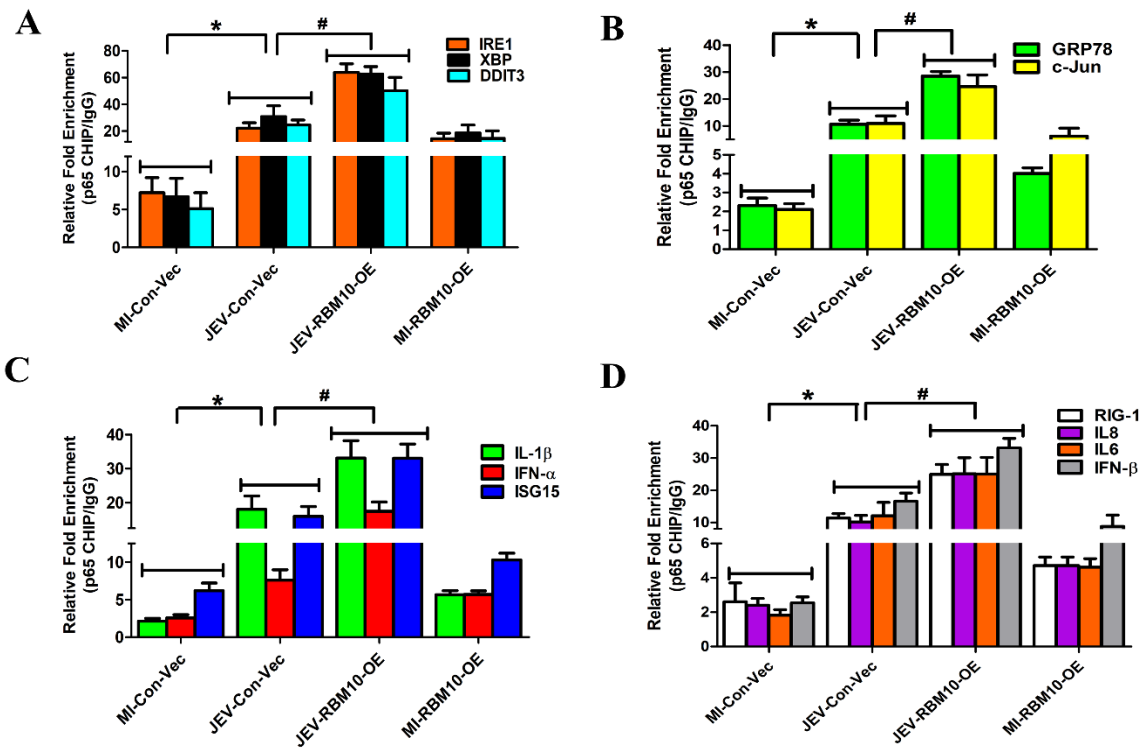
A. RBM10 promotes the p65 recruitment at the promoter of ER stress genes. Relative enrichment of p65 at the promoter of indicated genes in MI or JEV-infected SH-SY5Y cells transfected with si-NS or si-RBM10 determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-si-NS IgG IP.

B. RBM10 promotes the p65 recruitment at the promoter of inflammatory genes. Relative enrichment of p65 at the promoter of indicated genes in MI or JEV-infected SH-SY5Y cells

transfected with si-NS or si-RBM10 determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-si-NS IgG IP.

Data information: (For A-B) Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. *Significant change compared to MI-si-NS, #significant change compared to JEV-si-NS.

Figure S29. RBM10 overexpression enhances the recruitment of p65 at the promoter of ER stress and neuroinflammation genes during JEV infection in SH-SY5Y cells.

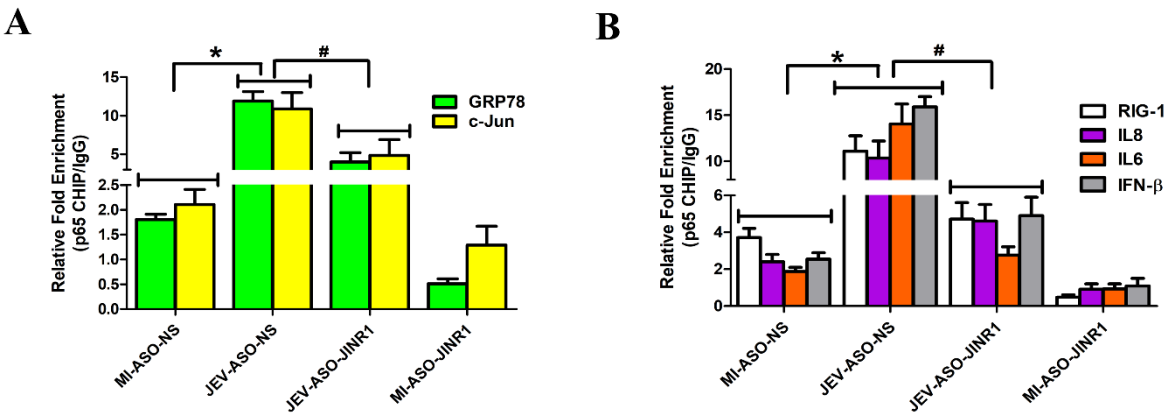


A-B. RBM10 promotes the p65 recruitment at the promoter of ER stress genes. Relative enrichment of p65 at the promoter of indicated genes in MI or JEV-infected SH-SY5Y cells transfected with Con-Vec or RBM10-OE determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-Con-Vec-IgG IP.

C-D. RBM10 promotes the p65 recruitment at the promoter of neuroinflammatory genes. Relative enrichment of p65 at the promoter of indicated genes in MI or JEV-infected SH-SY5Y cells transfected with Con-Vec or RBM10-OE determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-Con-Vec-IgG IP.

Data information: (For A-D) Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. *Significant change compared to MI-Con-Vec, #significant change compared to JEV-Con-Vec.

S30. *JINR1* silencing reduces p65 recruitment at the promoter of ER stress and neuroinflammation genes during JEV infection.



A. *JINR1* promotes the p65 recruitment at the promoter of ER stress genes. Relative enrichment of p65 at the promoter of indicated genes in MI or JEV-infected SH-SY5Y cells transfected with ASO-NS or ASO-*JINR1* determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-ASO-NS IgG IP.

B. *JINR1* promotes the p65 recruitment at the promoter of inflammatory genes. Relative enrichment of p65 at the promoter of indicated genes in MI or JEV-infected SH-SY5Y cells transfected with ASO-NS or ASO-*JINR1* determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-ASO-NS IgG IP.

Data information: (For A-B) Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. *Significant change compared to MI-ASO-NS, #significant change compared to JEV-ASO-NS.

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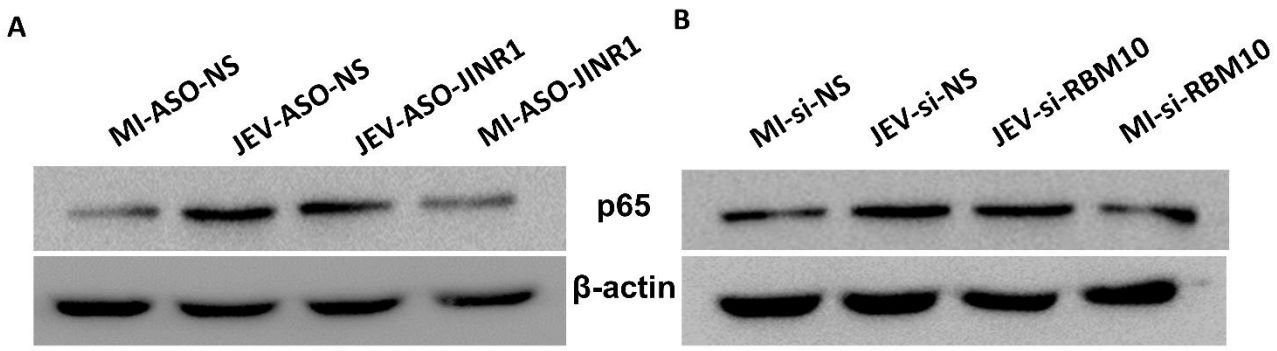
S31. *JINR1*/RBM10 silencing during JEV infection does not change p65 expression.

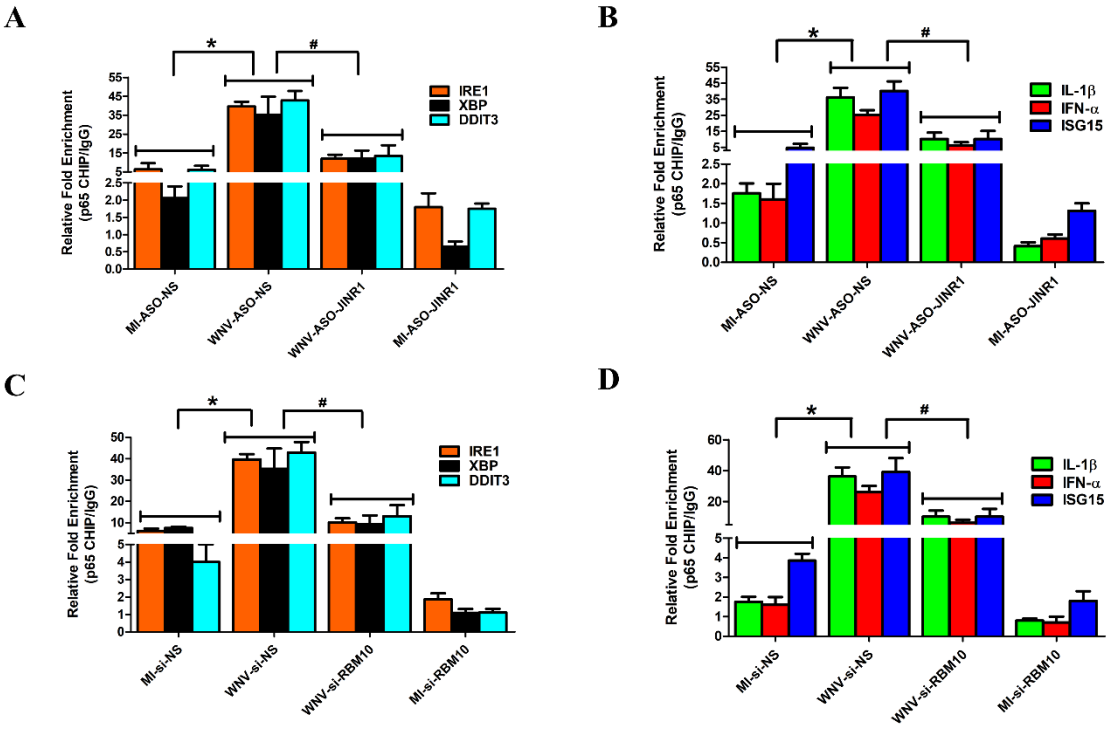


A. *JINR1* depletion during JEV infection did not significantly impact p65 protein expression. SH-SY5Y cells were transfected with ASO-NS, ASO-*JINR1*-1, and protein lysates were collected 48 hpi. p65 protein levels were analyzed by western blotting. A representative blot is shown from two independent experiments with similar results. Blots were reprobed for β-actin to establish equal loading.

B. RBM10 depletion during JEV infection did not significantly impact p65 protein expression. SH-SY5Y cells were transfected with si-NS, si-RBM10, and protein lysates were collected 36 hpi. p65 protein levels were analyzed by western blotting. A representative blot is shown from two independent experiments with similar results. Blots were reprobed for β-actin to establish equal loading.

P.T.O.

S32. *JINR1* and RBM10 silencing reduces the p65 recruitment at the promoters of ER stress and neuroinflammation genes during WNV infection.



A. *JINR1* silencing reduces the p65 recruitment at the promoter of ER stress genes during WNV infection. Relative enrichment of p65 at the promoter of indicated ER stress genes in MI or WNV-infected SH-SY5Y cells transfected with ASO-NS or ASO-*JINR1* determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-ASO-NS-IgG IP.

B. *JINR1* silencing reduces the p65 recruitment at the promoter of inflammatory genes during WNV infection. Relative enrichment of p65 at the promoter of indicated neuroinflammatory genes in MI or WNV-infected SH-SY5Y cells transfected with ASO-NS or ASO-*JINR1* determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-ASO-NS-IgG IP.

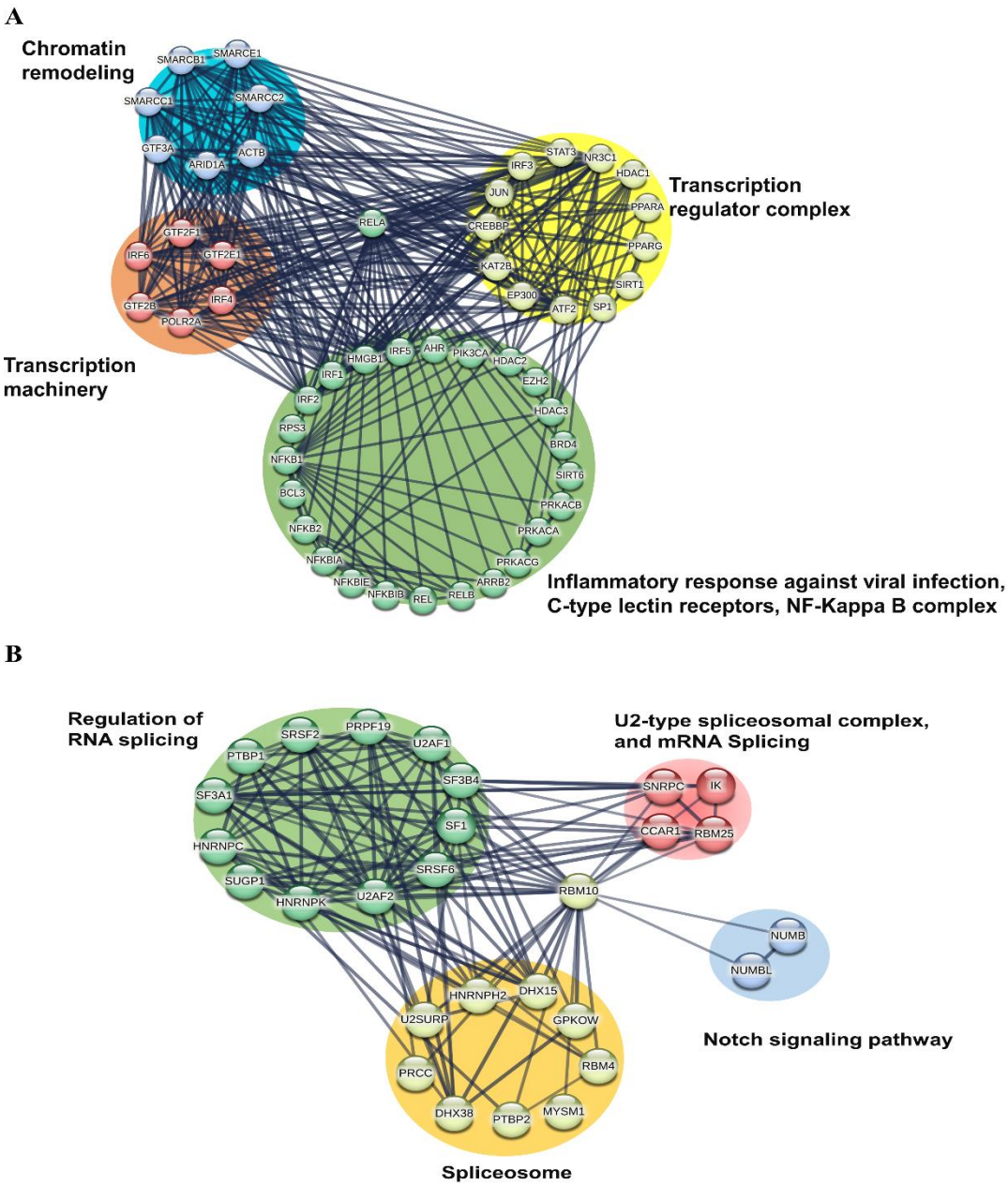
C. RBM10 depletion decreases the p65 recruitment at the promoter of ER stress genes during WNV infection. Relative enrichment of p65 at the promoter of indicated ER genes in MI or WNV-infected SH-SY5Y cells transfected with si-NS or si-RBM10 determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-si-NS IgG IP.

D. RBM10 depletion decreases the p65 recruitment at the promoter of inflammatory genes during WNV infection. Relative enrichment of p65 at the promoter of indicated ER genes in MI or WNV-infected SH-SY5Y cells transfected with si-NS or si-RBM10 determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-si-NS IgG IP.

Data information: (For A-D) Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. For (A-B) *significant change

compared to MI-ASO-NS, #significant change compared to WNV-ASO-NS. For (C-D) *Significant change compared to MI-si-NS, #significant change compared to WNV-si-NS.

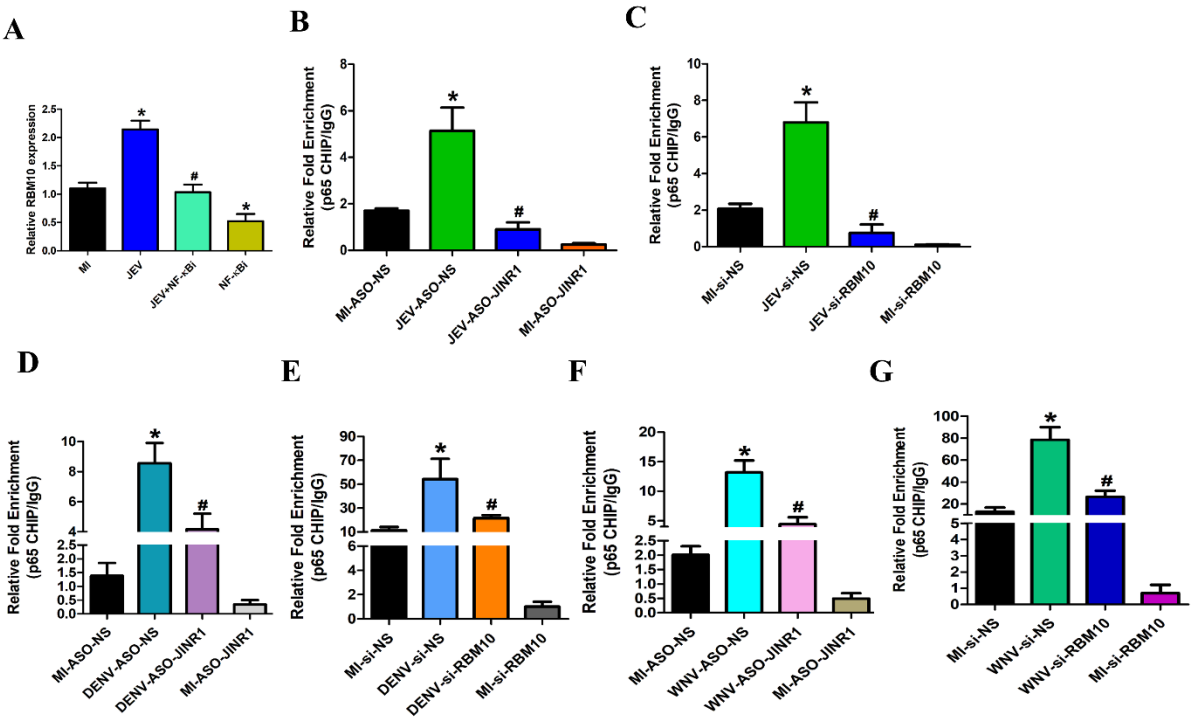
Figure S33. The PPI network of RelA and RBM10.



A. The protein interaction map of RelA/p65 was generated using the STRING database. Proteins (nodes) in the network are connected by edges. Functionally related proteins were clustered together (coloured circles).

B. The protein interaction map of RBM10 was generated using the STRING database. Proteins (nodes) in the network are connected by edges. Functionally related proteins were clustered together (coloured circles).

Figure S34. *JINR1* and RBM10 reciprocally regulate each other's expression through NF-κB.



A. NF-κB inhibition abrogates RBM10 induction upon JEV infection. SH-SY5Y cells were pretreated with 1μM of BAY11-7085 for 2h, followed by JEV infection (MOI 5). RBM10 transcript levels were determined by qRT-PCR 36 hpi.

B. *JINR1* promotes the p65 recruitment at its own promoter during JEV infection. Relative enrichment of p65 at the *JINR1* promoter in MI or JEV-infected SH-SY5Y cells transfected with ASO-NS or ASO-*JINR1* determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-ASO-NS IgG IP.

C. RBM10 promotes the p65 recruitment at its own promoter during JEV infection. Relative enrichment of p65 at the RBM10 promoter in MI or JEV-infected SH-SY5Y cells transfected with si-NS or si-RBM10 determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-si-NS IgG IP.

D. *JINR1* promotes the p65 recruitment at its own promoter during DENV infection. Relative enrichment of p65 at the *JINR1* promoter in MI or DENV-infected SH-SY5Y cells transfected with ASO-NS or ASO-*JINR1* determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-ASO-NS IgG IP.

E. RBM10 promotes the p65 recruitment at its own promoter during DENV infection. Relative enrichment of p65 at the RBM10 promoter in MI or DENV-infected SH-SY5Y cells transfected with si-NS or si-RBM10 determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-si-NS IgG IP.

F. *JINR1* promotes the p65 recruitment at its own promoter during WNV infection. Relative enrichment of p65 at the *JINR1* promoter in MI or WNV-infected SH-SY5Y cells transfected with ASO-NS or ASO-*JINR1* determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-ASO-NS IgG IP.

G. RBM10 promotes the p65 recruitment at its own promoter during WNV infection. Relative enrichment of p65 at the RBM10 promoter in MI or WNV-infected SH-SY5Y cells transfected with si-NS or si-RBM10 determined by ChIP-qRT-PCR 36 hpi. Enrichment values are relative to MI-si-NS IgG IP.

Data information: Error bars represent the mean ± SEM from three independent experiments. Statistical comparison was made using Student's t-test. For (A) *significant change compared to MI, #significant change compared to JEV. For (B) *significant change compared to MI-ASO-NS, #significant change compared to JEV-ASO-NS. For (C) *Significant change compared to MI-si-NS, #significant change compared to JEV-si-NS. (D) *significant change compared to MI-ASO-NS, #significant change compared to DENV-ASO-NS. For (E) *Significant change compared to MI-si-NS, #significant change compared to DENV-si-NS. (F) *significant change compared to MI-ASO-NS, #significant change compared to WNV-ASO-NS. For (G) *Significant change compared to MI-si-NS, #significant change compared to WNV-si-NS.