Cell Host & Microbe, Volume *16*

Supplemental Information

NRAV, a Long Noncoding RNA, Modulates Antiviral Responses through Suppression of Interferon-Stimulated Gene Transcription

Jing Ouyang, Xiaomei Zhu, Yuhai Chen, Haitao Wei, Qinghuang Chen, Xiaojuan Chi, Baomin Qi, Lianfeng Zhang, Yi Zhao, George Fu Gao, Guoshun Wang, and Ji-Long Chen

Supplemental Figures

Figure S1

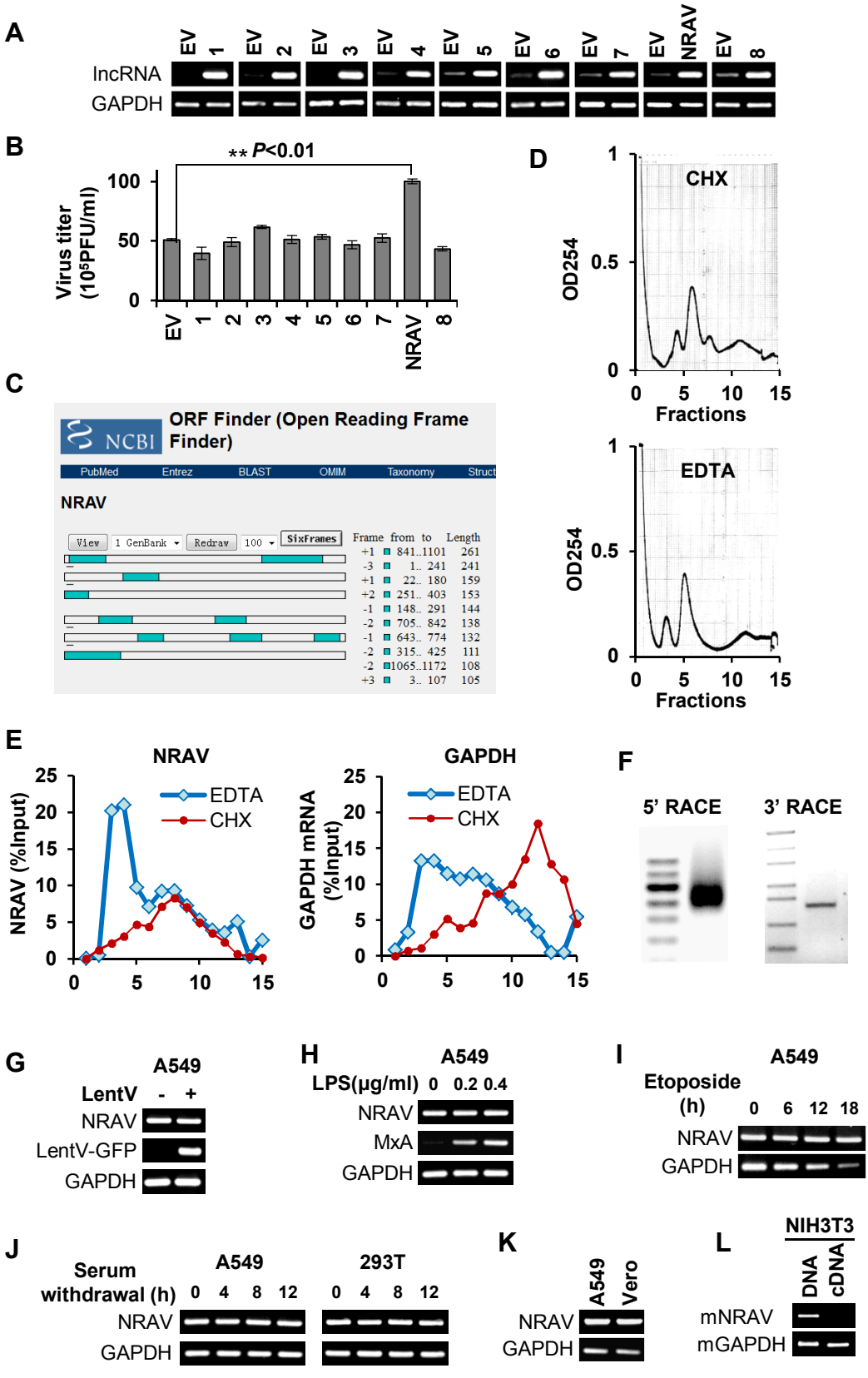


Figure S2

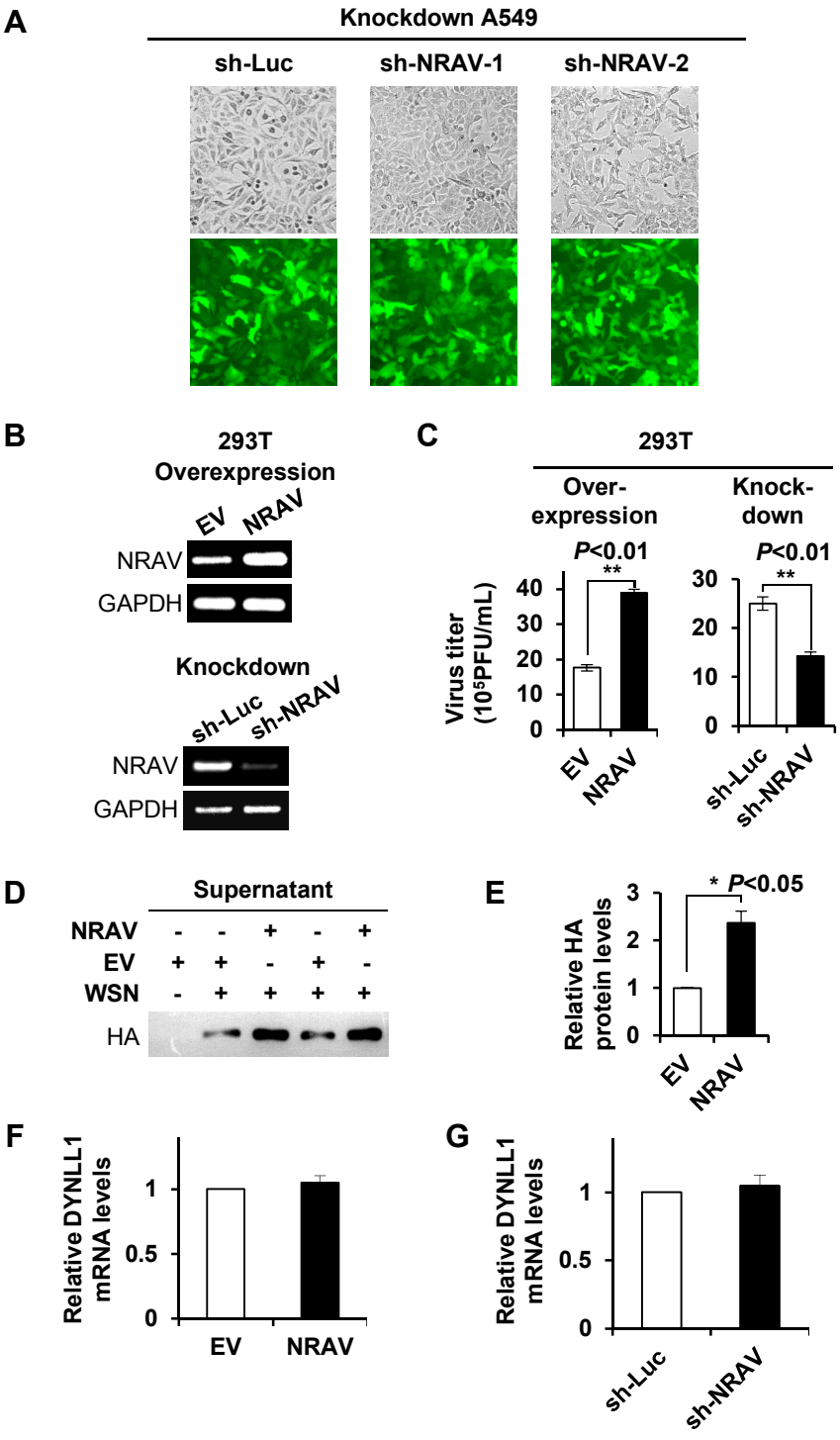

A
Knockdown A549
sh-Luc
sh-NRAV-1
sh-NRAV-2
B
293T
Overexpression
EV
NRAV
NRAV
GAPDH
Knockdown
sh-Luc
sh-NRAV
NRAV
GAPDH
C
293T
Over-expression
Knock-down
P<0.01
**
P<0.01
**
Virus titer (10^5PFU/mL)
40
30
20
10
0
30
20
10
0
EV
NRAV
sh-Luc
sh-NRAV
D
Supernatant
NRAV - - + - +
EV + + - + -
WSN - + + + +
HA
E
* P<0.05
Relative HA protein levels
3
2
1
0
EV
NRAV
F
Relative DYNLL1 mRNA levels
1
0.5
0
EV
NRAV
G
Relative DYNLL1 mRNA levels
1
0.5
0
sh-Luc
sh-NRAV

Figure S3

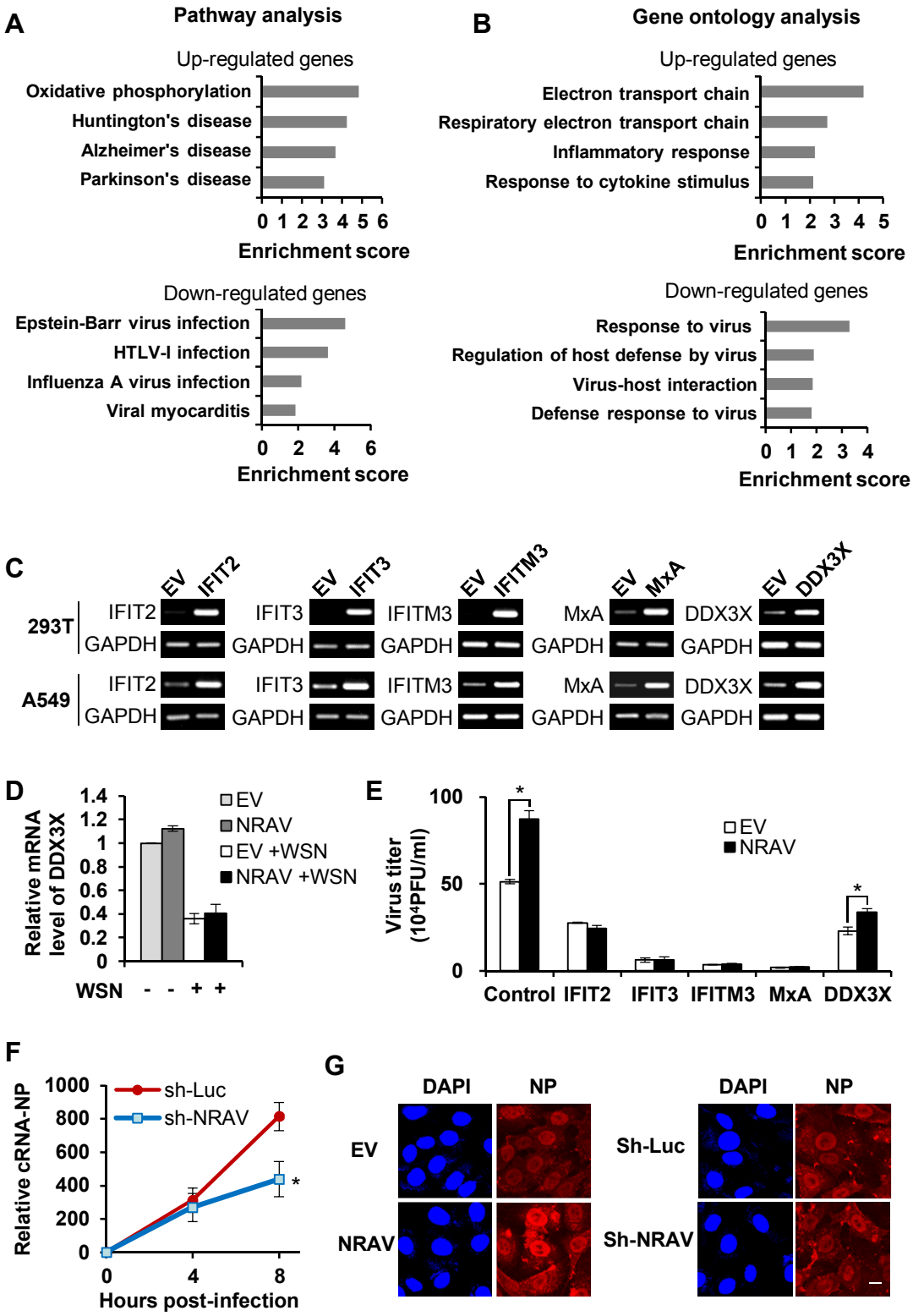

A
Pathway analysis
Up-regulated genes
Oxidative phosphorylation
Huntington's disease
Alzheimer's disease
Parkinson's disease
0 1 2 3 4 5 6
Enrichment score
Down-regulated genes
Epstein-Barr virus infection
HTLV-I infection
Influenza A virus infection
Viral myocarditis
0 2 4 6
Enrichment score
B
Gene ontology analysis
Up-regulated genes
Electron transport chain
Respiratory electron transport chain
Inflammatory response
Response to cytokine stimulus
0 1 2 3 4 5
Enrichment score
Down-regulated genes
Response to virus
Regulation of host defense by virus
Virus-host interaction
Defense response to virus
0 1 2 3 4
Enrichment score
C
EV
IFIT2
IFIT3
IFITM3
MxA
DDX3X
293T
A549
IFIT2
IFIT3
IFITM3
MxA
DDX3X
GAPDH
D
Relative mRNA level of DDX3X
1.4
1.2
1
0.8
0.6
0.4
0.2
0
EV
NRAV
EV +WSN
NRAV +WSN
WSN - - + +
E
Virus titer (10⁴PFU/ml)
100
50
0
EV
NRAV
*
*
Control IFIT2 IFIT3 IFITM3 MxA DDX3X
F
Relative cRNA-NP
1000
800
600
400
200
0
sh-Luc
sh-NRAV
*
0
4
8
Hours post-infection
G
DAPI
NP
EV
NRAV
Sh-Luc
Sh-NRAV

Figure S4

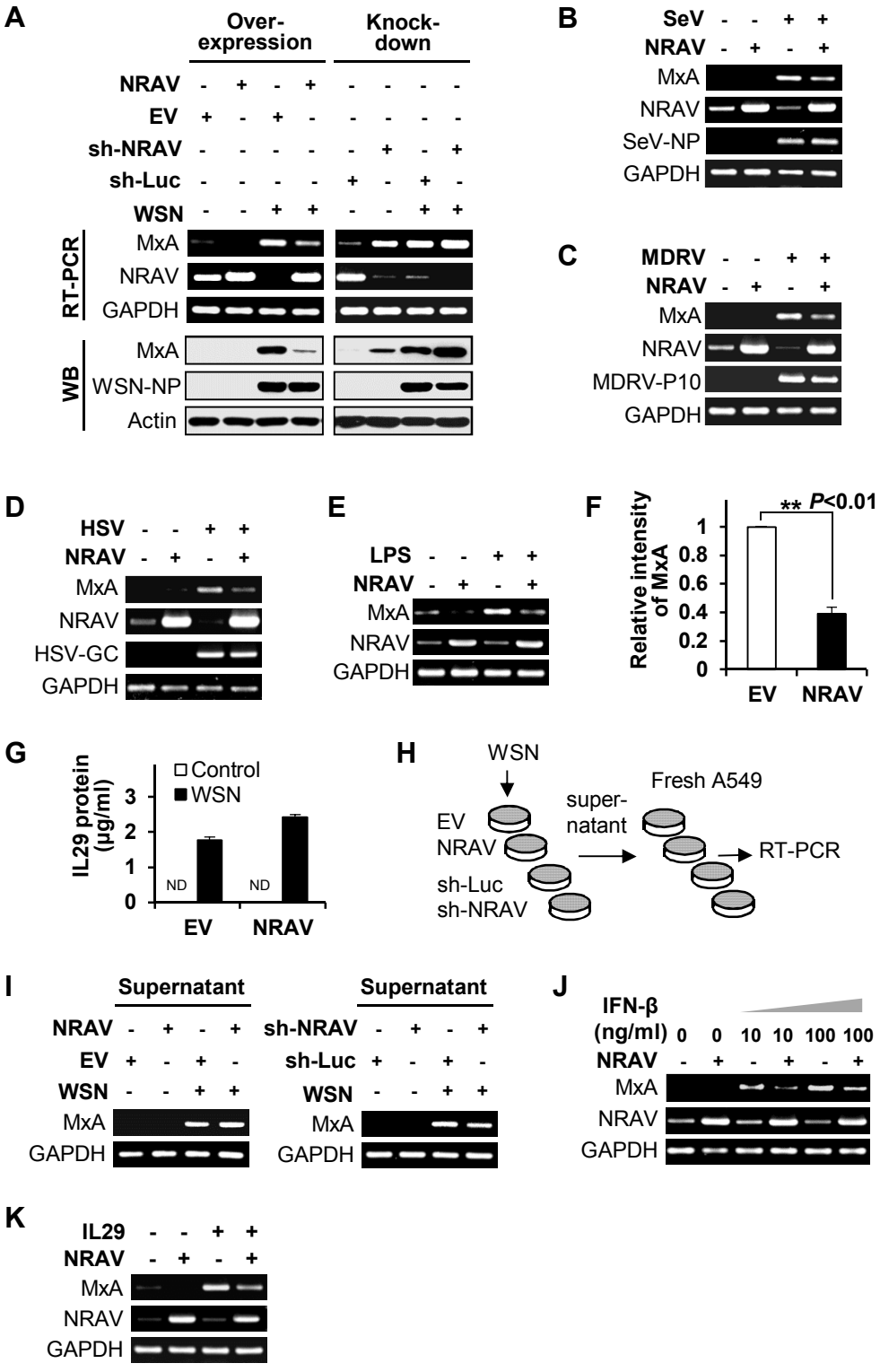

A
Over-expression
Knock-down
NRAV
EV
sh-NRAV
sh-Luc
WSN
RT-PCR
MxA
NRAV
GAPDH
WB
MxA
WSN-NP
Actin
B
SeV
NRAV
MxA
NRAV
SeV-NP
GAPDH
C
MDRV
NRAV
MxA
NRAV
MDRV-P10
GAPDH
D
HSV
NRAV
MxA
NRAV
HSV-GC
GAPDH
E
LPS
NRAV
MxA
NRAV
GAPDH
F
Relative intensity of MxA
** P<0.01
1
0.8
0.6
0.4
0.2
0
EV
NRAV
G
IL29 protein (μg/ml)
Control
WSN
3
2
1
0
ND
ND
EV
NRAV
H
WSN
Fresh A549
super-natant
EV
NRAV
sh-Luc
sh-NRAV
RT-PCR
I
Supernatant
Supernatant
NRAV
EV
WSN
sh-NRAV
sh-Luc
WSN
MxA
GAPDH
MxA
GAPDH
J
IFN-β (ng/ml)
0 0 10 10 100 100
NRAV
MxA
NRAV
GAPDH
K
IL29
NRAV
MxA
NRAV
GAPDH

Figure S5

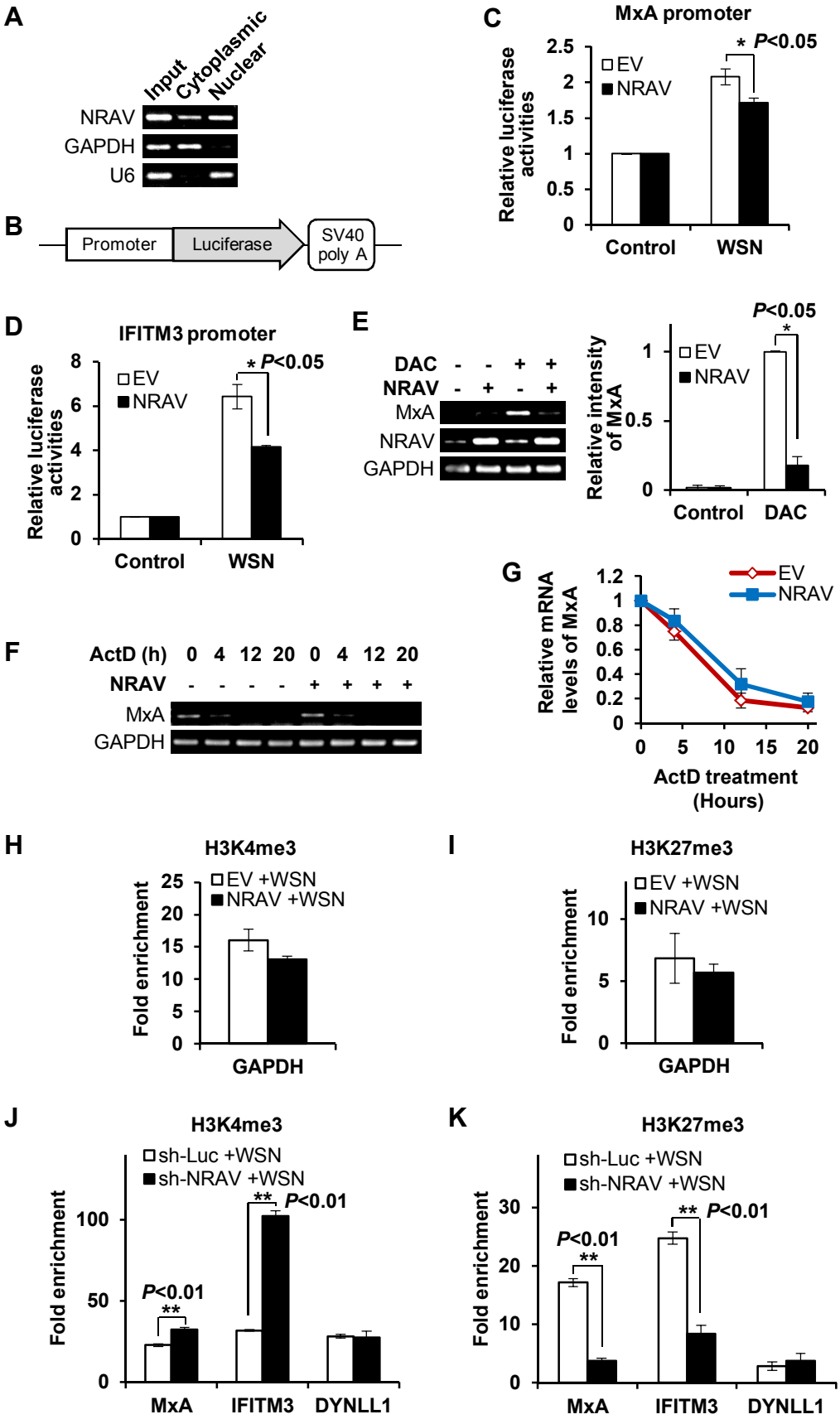

A
Input
Cytoplasmic
Nuclear
NRAV
GAPDH
U6
B
Promoter
Luciferase
SV40 poly A
C
MxA promoter
Relative luciferase activities
EV
NRAV
* P<0.05
Control
WSN
D
IFITM3 promoter
Relative luciferase activities
EV
NRAV
* P<0.05
Control
WSN
E
DAC - - + +
NRAV - + - +
MxA
NRAV
GAPDH
Relative intensity of MxA
EV
NRAV
P<0.05
*
Control
DAC
F
ActD (h) 0 4 12 20 0 4 12 20
NRAV - - - - + + + +
MxA
GAPDH
G
Relative mRNA levels of MxA
EV
NRAV
ActD treatment (Hours)
H
H3K4me3
Fold enrichment
EV +WSN
NRAV +WSN
GAPDH
I
H3K27me3
Fold enrichment
EV +WSN
NRAV +WSN
GAPDH
J
H3K4me3
Fold enrichment
sh-Luc +WSN
sh-NRAV +WSN
** P<0.01
** P<0.01
MxA
IFITM3
DYNLL1
K
H3K27me3
Fold enrichment
sh-Luc +WSN
sh-NRAV +WSN
P<0.01
**
** P<0.01
MxA
IFITM3
DYNLL1

Figure S6

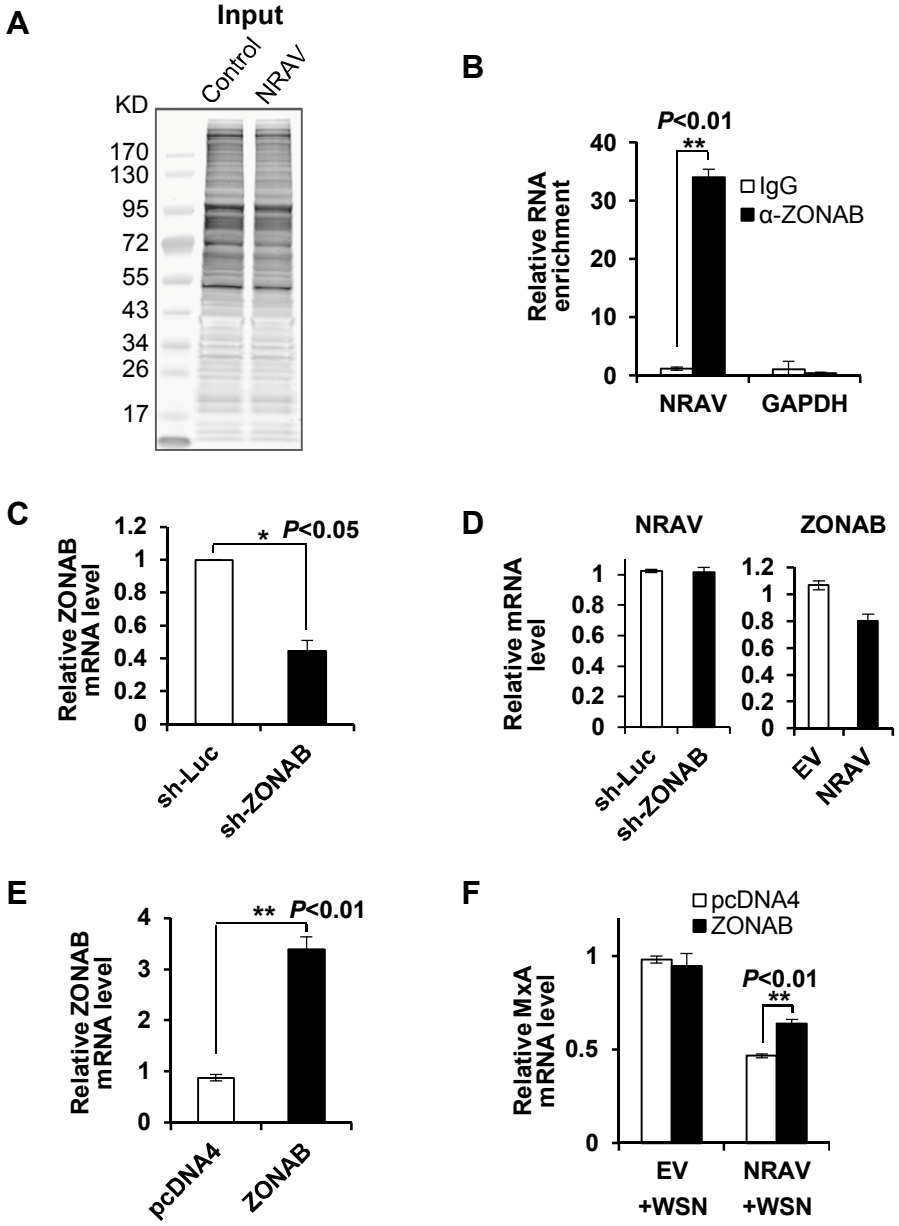
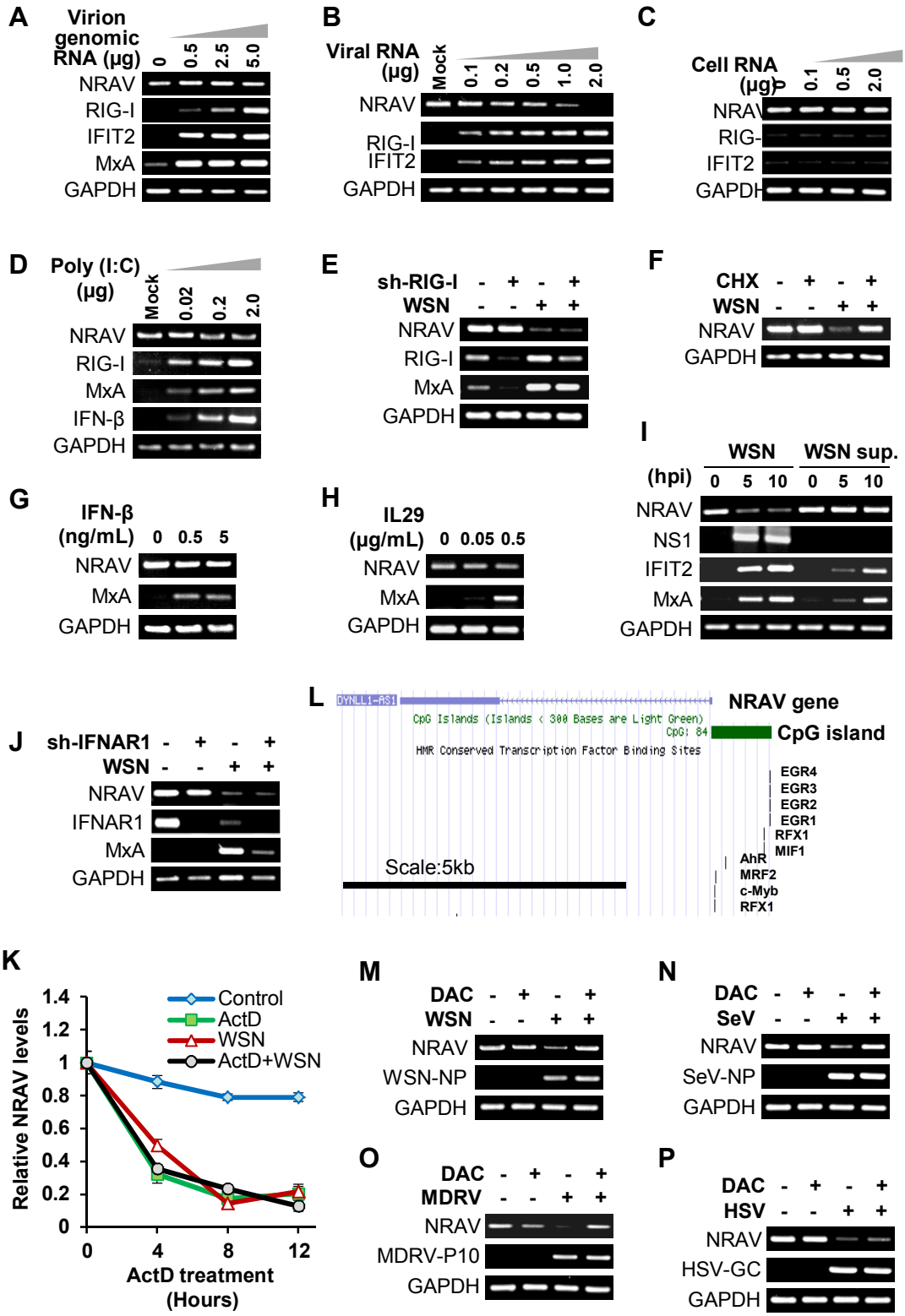

A
Input
Control
NRAV
KD
170
130
95
72
55
43
34
26
17
B
P<0.01
**
IgG
α-ZONAB
Relative RNA enrichment
40
30
20
10
0
NRAV
GAPDH
C
* P<0.05
Relative ZONAB mRNA level
1.2
1
0.8
0.6
0.4
0.2
0
sh-Luc
sh-ZONAB
D
NRAV
ZONAB
Relative mRNA level
1
0.8
0.6
0.4
0.2
0
1.2
1
0.8
0.6
0.4
0.2
0
sh-Luc
sh-ZONAB
EV
NRAV
E
** P<0.01
Relative ZONAB mRNA level
4
3
2
1
0
pcDNA4
ZONAB
F
pcDNA4
ZONAB
P<0.01
**
Relative MxA mRNA level
1
0.5
0
EV
+WSN
NRAV
+WSN

Figure S7


A
Virion genomic RNA (μg)
0 0.5 2.5 5.0
NRAV
RIG-I
IFIT2
MxA
GAPDH
B
Viral RNA (μg)
Mock 0.1 0.2 0.5 1.0 2.0
NRAV
RIG-I
IFIT2
GAPDH
C
Cell RNA (μg)
0 0.1 0.5 2.0
NRAV
RIG-I
IFIT2
GAPDH
D
Poly (I:C) (μg)
Mock 0.02 0.2 2.0
NRAV
RIG-I
MxA
IFN-β
GAPDH
E
sh-RIG-I - + - +
WSN - - + +
NRAV
RIG-I
MxA
GAPDH
F
CHX - + - +
WSN - - + +
NRAV
GAPDH
G
IFN-β (ng/mL) 0 0.5 5
NRAV
MxA
GAPDH
H
IL29 (μg/mL) 0 0.05 0.5
NRAV
MxA
GAPDH
I
WSN WSN sup.
(hpi) 0 5 10 0 5 10
NRAV
NS1
IFIT2
MxA
GAPDH
J
sh-IFNAR1 - + - +
WSN - - + +
NRAV
IFNAR1
MxA
GAPDH
L
DYNLL1-AS1
NRAV gene
CpG Islands (Islands < 300 Bases are Light Green)
CpG: 84
CpG island
HMR Conserved Transcription Factor Binding Sites
EGR4
EGR3
EGR2
EGR1
RFX1
MIF1
AhR
MRF2
c-Myb
RFX1
Scale:5kb
K
Relative NRAV levels
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0 4 8 12
ActD treatment (Hours)
Control
ActD
WSN
ActD+WSN
M
DAC - + - +
WSN - - + +
NRAV
WSN-NP
GAPDH
N
DAC - + - +
SeV - - + +
NRAV
SeV-NP
GAPDH
O
DAC - + - +
MDRV - - + +
NRAV
MDRV-P10
GAPDH
P
DAC - + - +
HSV - - + +
NRAV
HSV-GC
GAPDH

Supplemental Information

Supplemental Figure Legends

Figure S1. Human NRAV Was Identified as a Functional LncRNA through Preliminary Functional Screening, Related to Figure 1

(A) The overexpression efficiencies of lncRNAs in A549 cells were determined by RT-PCR. Fragments of nine lncRNAs, indicated as 1 (BI832838), 2 (GD137531), 3 (D85245), 4 (BC107859), 5 (BX089654), 6 (uc001zcp), 7 (AY927564), NRAV (uc001tyk.1), and 8 (DA418630), amplified from A549 cells were used for ectopic expression as described in **Supplemental Experimental Procedures**.

(B) The lncRNA-overexpressing cells were infected with WSN (MOI=0.3) for 16 hours. The virus titers in culture supernatants were determined through plaque forming assay. Data from three independent experiments are expressed as means±s.e.m. $^{**}P<0.01$.

(C) LncRNA NRAV coding potential was predicted by ORF Finder as described in **Supplemental Experimental Procedures**. No ORF predicted (indicated in green) is longer than 300bp.

(D and E) Sucrose sedimentation and polysome analysis of the cytoplasmic fraction of A549. Cells incubated with cycloheximide (CHX) or mock were lysed as described in **Supplemental Experimental Procedures**. CHX-treated cell lysates were loaded on a 10-50% (weight to volume) sucrose gradient. The cytoplasmic fraction of CHX-untreated cells supplemented with 35 mM EDTA was also loaded on a sucrose gradient. After centrifugation, samples were fractionated from the top of the gradient

into 15 tubes while the absorbance at 254nm (OD254) was measured (D). RNA levels from each fraction were analyzed by qRT-PCR. Relative levels of NRAV (E, *left*) and GAPDH mRNA (E, *right*) are shown as %Input. Representative results from three independent experiments were shown.

(F) Agarose gel analysis of 5' and 3' RACE PCR products. DNA ladders (100, 200, 300, 400, 500,600, and 700 bp) are shown (left lane).

(G-J) A549 cells were transducted with pseudovirus (LentV) prepared by lentivirus expression system (G), or incubated with LPS (100 ng/ml, Invivogen) and sCD14 (300 ng/ml, PeproTech) for 8 h (H), or treated with etoposide (100 μM, Sigma) (I), or cultured in serum-free media for indicated time (J). The expression of NRAV were determined by RT-PCR.

(K) The expressions of NRAV in African green monkey kidney (Vero) cells and human A549 cells were detected by RT-PCR.

(L) The mouse DNA and cDNA prepared from NIH3T3 cells were used as templates to amplify mouse NRAV homolog (mNRAV).

These results shown are representative of at least three independent experiments.

Figure S2. Altering NRAV Expression Has Profound Effects on IAV Replication in Human Cells, Related to Figure 2

(A) Shown are representative phase and fluroscent images of NRAV knockdown A549 cells.

(B) The overexpression and knockdown of NRAV in 293T cells were determined by

RT-PCR. Representative results of three independent experiments are shown.

(C) Influenza virus replication was examined in NRAV-overexpressing and NRAV knockdown 293T cells by plaque forming assay as described in Figure 2E (MOI=0.3, *n*=3, means±s.e.m.) and **Supplemental Experimental Procedures**.

(D) IAV protein HA in supernatants from infected NRAV-overexpressing A549 cells (MOI=1) were detected by Western blotting. Supernatants of same volume at 16 hpi were collected and loaded parallelly. Representative results of three independent experiments are shown.

(E) The protein levels of HA in (D) lane 2 to lane5 were relatively quantitated by densitometry and normalized to GAPDH levels. In each experiment, the level of HA in infected EV control group is 1. Plotted are the average levels from three independent experiments (means±s.e.m.).

(F and G) The expression of DYNLL1 in NRAV-overexpression (F) and knockdown cells (G) were determined by qRT-PCR (*n*=3, means±s.e.m.).

Figure S3. NRAV Acts as a Negative Regulator to Modulate the Expression of Several Key ISGs, Related to Figure 4

(A and B) Pathway analysis (A) and Gene Ontology analysis (B) of up-regulated genes (*upper*) and down-regulated genes (*lower*) from microarray data indicated that many decreased genes were associated with viral infection or host response to virus. Enrichment score is calculated as $-\log_{10}$ (*P*-value), and *P*-value is calculated by Fisher's exact test.

(C) The transient expression of exogenous human IFIT2, IFIT3, IFITM3, MxA or DDX3X in experiments was determined by RT-PCR at 24 hours post-transfection. For each experiment, 1 μg expression plasmid is used for transfection (6 well plate). Representative results of three independent experiments are shown.

(D) The DDX3X mRNA levels in NRAV and EV cells were measured by qRT-PCR (n=3, means±s.e.m.), which was not significantly affected by NRAV overexpression.

(E) Transient expressions of ISGs were performed in NRAV-overexpressing cells or EV cells as described in **Supplemental Experimental Procedures**. 24 hours after transfection, cells were infected with IAV for 16 hours. The virus titers were determined by plaque forming assay (n=3). The empty plasmid was used as control, as well as the expression plasmid of DDX3X.

(F) Viral cRNA of WSN-NP in infected NRAV knockdown cells (MOI=1) were detected by qRT-PCR. Data are shown as means±s.e.m. (n=3). *P< 0.05.

(G) A549 cells stably expressing NRAV or sh-NRAV or controls were incubated with WSN virus (MOI=100) on ice, and then cultured with warm media for 4 h. Immunofluorescence staining was performed using an anti-NP antibody to detect entry of NP (red). The nuclei were stained with DAPI (blue). Scale bar, 10 μm.

Figure S4. NRAV Suppresses the Transcription of MxA without Affecting IFN Signaling, Related to Figure 5

(A) The MxA mRNA (upper) and protein (lower) levels in NRAV-overexpressing or NRAV knockdown cells infected or uninfected with WSN (MOI=3) were measured

by RT-PCR and Western blotting, respectively. Empty vector or sh-Luc expressing plasmid are used as control.

(B-D) The MxA mRNA levels in following NRAV-overexpressing cells or EV control cells were determined by RT-PCR: SeV infected A549 cells (B), MDRV infected 293T cells (C), and HSV infected A549 cells (D). Representative results of three independent experiments are shown.

(E) The MxA mRNA levels in NRAV-overexpressing cells or EV control cells stimulated by LPS (100 ng/ml) and sCD14 (300 ng/ml) were determined by RT-PCR.

(F) Levels of MxA mRNA in (E) lane 3 and lane 4 were quantitated by densitometry as described in Figure S2E. Plotted are the average levels from three independent experiments (means±s.e.m.).

(G) The IL29 protein levels in supernatants of EV and NRAV cells infected with or without WSN (MOI=1) were analyzed by ELISA. Data are shown as means±s.e.m. n=3.

(H) Experimental schematic of cytokine assay. NRAV-overexpressing or NRAV knockdown A549 cells and control cells were infected with or without WSN (MOI=1). The supernatants of above cells were collected at 8 hpi and used to incubate the fresh A549 cells for 1.5 hours.

(I) The MxA mRNA levels in supernanant-incubated cells described in (H) were assessed by RT-PCR. Representative results of three independent experiments are shown.

(J and K) The MxA mRNA levels in NRAV-overexpressing cells and control cells

stimulated by IFN-β (J) or IL29 (K) (50 ng/ml) respectively for 3 h were detected by RT-PCR . Representative results of three independent experiments are shown.

Cells were infected or stimulated as described in **Experimental Procedures.** Data are shown as means±s.e.m. n=3. *P<0.05, **P<0.01.

Figure S5. NRAV Regulates Promoter Activities and Histone Modifications of ISGs, Related to Figure 6

(A) The RNA levels of NRAV, cytoplasmic control transcript (GAPDH mRNA) and nuclear control transcript (U6 RNA) were assessed by RT-PCR in cytoplasmic and nuclear fractions from A549. The total cells were used as input control.

(B) Shown is the schematic diagram of the plasmid construct for luciferase gene reporter assay.

(C and D) 293T cells overexpressing NRAV or EV control were transfected with pGL3-MxAP-Luc (C) or pGL3-IFITM3P-Luc (D) in combination with pRL-TK for 10 h and then infected with WSN for 12 h as described in **Supplemental Experimental Procedures**. Luciferase activity in cell lysates was measured and displayed as mean±s.e.m. of relative luciferase units normalized to Renilla luciferase activity from three independent experiments.

(E) A549 cells overexpressing NRAV were treated with 10 μM decitabine (DAC) as described in **Supplemental Experimental Procedures** and infected with WSN (MOI=3) for 12 h. The mRNA levels of MxA were detected by RT-PCR (*left*). Levels of MxA mRNA were relatively quantitated by densitometry (*right*) as described in

Figure S2E. Plotted are the average levels from three independent experiments.

(F and G) A549 cells overexpressing NRAV were infected with WSN and treated with 2.5 μg/ml actinomycin D (ActD) as described in **Supplemental Experimental Procedures**. Cells were collected at 0, 4, 12, 20 h time points. The mRNA levels of MxA were detected by RT-PCR (F) and qRT-PCR (G).

(H and I) ChIP analysis of H3K4me3 (H) and H3K27me3 (I) levels at the *gapdh* locus in infected NRAV-overexpressing or control A549 cells as described in Figure 6F and **Supplemental Experimental Procedures**.

(J and K) ChIP analysis of H3K4me3 (J) and H3K27me3 (K) levels at the *mxA,ifitm3* and *dynll1* locus in infected NRAV knockdown or control A549 cells.

Representative results of three independent RT-PCR experiments are shown. Data of are shown as means±s.e.m. (n=3, *P<0.05, **P<0.01).

Figure S6. Interaction between NRAV and ZONAB and the Function of ZONAB on MxA Transcription, Related to Figure 6

(A) Silver staining of input proteins of RNA pulldown assay as described in Figure 6H and **Supplemental Experimental Procedures**. Shown is representative result from three independent experiments.

(B) The association of NRAV with ZONAB is verified by RNA immunoprecipitation (RIP). Uninfected cell lysates were immunoprecipitated with anti-ZONAB Ab or control IgG as described in **Supplemental Experimental Procedures**. The enrichments of NRAV or GAPDH mRNA were analyzed by qRT-PCR and

normalized to input and control IgG. The fold enrichment was calculated as $2^{(-\Delta\Delta Ct)}$.

(C) ZONAB was depleted by shRNA sequences through transient transfection with A549 cells. ZONAB mRNA levels were measured by qRT-PCR and normalized to that of control sh-Luc cells.

(D) NRAV expression in ZONAB depleted cells (*left*) as described in (C) and ZONAB mRNA levels in NRAV-overexpressing A549 cells (*right*) were determined by qRT-PCR and normalized to that of control sh-Luc/EV cells respectively.

(E) ZONAB isoform b was transiently expressed in A549 cells by transfecting with transient expression plasmid containing ZONAB isoform b ORF. The mRNA levels were measured by qRT-PCR and normalized to that of control cells transfected with empty vector pcDNA4.

(F) MxA mRNA levels in IAV-infected NRAV-overexpressing A549 cells and EV control cells transfected with transient expression plasmids containing ZONAB isoform b ORF or empty vector pcDNA4 were determined by qRT-PCR and normalized to that of infected EV cells transfected with pcDNA4.

Data are shown as means±s.e.m. (n=3. *P<0.05, **P<0.01).

Figure S7. Down-regulation of NRAV Is Dependent on Virus Replication, Protein Synthesis and Epigenetic Regulation, Related to Figure 6 and Discussion

RT-PCR was performed to examine the RNA expression in following A549 cells:

(A-D) Cells were transfected with WSN virion genomic RNA (A), viral RNA isolated from WSN infected cells (B), cellular RNA derived from uninfected cells (C) and

poly(I:C) (D) of indicated amount for 4 hours. IAV genomic RNA could not affect the NRAV level. By contrast, transfection with viral RNA from IAV infected cells caused marked reduction in NRAV expression. The treatment with poly(I:C) had no effect on NRAV expr ession.

(E) RIG-I knockdown A549 cells generated using specific shRNA targeting RIG-I as described in **Supplemental Experimental Procedures** were infected with WSN. The depletion of RIG-I had no effect on NRAV expression.

(F) Cells were treated with 1μg/ml cycloheximide (CHX) for 30 min before WSN infection. The NRAV level recovered greatly in CHX-pretreated and WSN-infected cells.

(G-I) Cells were stimulated with cytokines IFN-β (G), IL29 (type III IFN) (H) of indicated amount or incubated with culture supernatant (sup.) collected from infected cells (I) for 4 hours. In (I), infected cells were used as control. These virus-induced cytokines could not affect the NRAV level.

(J) The type I IFN receptor IFNAR1 knockdown cells generated using specific shRNA (Invivogen) were infected with WSN. The depletion of IFNAR1 had no effect on NRAV expression.

(K) NRAV RNA decay assay was performed with actinomycin (ActD) treatment of A549 cells infected with WSN (MOI=3) or not. Cells were collected at 0, 4, 8, 12h time points and the NRAV levels were determined by qRT-PCR described in **Supplemental Experimental Procedures (**means±s.e.m. n=3). The turnover rate of NRAV in infected cells did not show difference with that in uninfected cells.

(L) Predicted CpG island in NRAV promoter region and binding sites of transcription factors are shown. Prediction data were from UCSC genome browser database (February 2009 human reference sequence (GRCh37), http://genome.ucsc.edu). Scale bar: 5kb.

(M-P) Cells were treated with 10 μM DNA methyltransferase inhibitor decitabine (DAC) for 2 days before infection with WSN (M), SeV (N), MDRV (O) and HSV (P) as described in **Supplemental Experimental Procedures.** Shown are representative results from three independent experiments. The NRAV levels were obviously recovered in cells pretreated with DAC and infected with IAV, SeV, and MDRV, but less significant in DNA virus HSV infected cells.

Table S1. Full-length sequence of NRAV, Related to Figure 1

NRAV
GGGCAATGGGCCGCACGCTACGAGGCCCACACACCCAGAAGGTGGAGCCCCGGCCGGGTT
ACGCGGACCACCCAGCTGTCTGGAGAGATGAAGAAAATGAGGTTCAAAGAGATGAAGTCT
CTTGCCTAAAGTCAGTGACAGAAAGTGACAGAGCTGGGATGTGAATCCTGGTCTGACTCTA
CAGTCCCACATGGTAGATGGAACCTCCGAGCAACACCTAAACAAAGGGAGTTGATGCCTCC
GAACAGAGTAATGTCGCTGGAGACACTAAGCATCGTCGGCCCCTGGCAGGAGCTCCCTAAA
TATGTGTTGGATGGATGGAAGAAAGGATGGATAGTTCAGAGTACTTCAGCCTTGATTCCTCC
GCAACAGACACCTGAAACTTGACCCTACATTGGTTCTTGGCCATCGTGATCTTCCTTGGACA
GAATCACCTTTCAGCTCCGGTCATCAGACTTTCCCAGGGCCCTCAGAAAGCCCTTCAGAGT
TGTTACTCACAGGCAGGCTGAGGGATTCCTTACGGGGTCTGCAGCTCTCCTCACCTCATCCA
CAAGTAGGACCGTGGCCTGTTCCTCACTACTGCCCCAGGATCACTCTGTTCCCAGCCCAGT
CCAGCAATCACTTGTCTAGCTTTCTGGAACCTTGAGTACTTTCTTGAACCATGAGTCCTGTG
ACCACCCTAGCAGCTCTAACCCTCCCTTATCTGAAAGGAAGTGTGAGGTGACCTTGCAGGT
CCCAGAGTTGATTGAAGACCCCATCCAGAAAGAAGGCACCCTGTGGGAGAGATTGCAAGG
CCTAGGTCTGAATCCGGAAGCTTCCACCCCATGGAGAAGGGCTGGCACCAGCCTGGGGCT
GGCAGTGGAGCTGAGCTTTGGAGCCAAGGACTGTACTGCAGTGCAGGGAGAGTGAGGCCA
GAAAGGCTGAGACAACTCAGGGAAAGAAAACCTCCCTTCTGGCTAATAGTCAAGCACCGC
CTGAGTAGACCAACACTCTCCTGTCCACAGGGGCAGCAGATGAAGACACAACCAGAGAGG
ACTAACAGGCCCCCTCAGCTCTCAGTCAGAGGGCAGAGCAACACAGAATAGACATTAAAG
GAACAGACTTTGAGGCCAGGCAGCCTTGGGTGTGCATCTGTCCCTACTAAGCCATGTGACA
TTAAACAAGTGAGTCCACCTCAAAAAAAAAAAA

The full-length sequence of NRAV is combined the end sequences of NRAV determined by 5’ and 3’ RACE and the middle fragment sequence of NRAV cloned from cDNAs of A549 cells by RT-PCR.

Table S2. ISGs Differentially Expressed in NRAV-overexpressing Cells, Related to Figure 4

Down-regulated ISGs

Entrez Gene ID	Gene Symbol	Description
3433	IFIT2	Interferon-induced protein with tetratricopeptide repeats 2 (IFIT-2) (Interferon-induced 54 kDa protein) (IFI-54K) (ISG-54 K). [Source:Uniprot/SWISSPROT;Acc:P09913]
3437	IFIT3	Interferon-induced protein with tetratricopeptide repeats 3 (IFIT-3) (IFIT-4) (Interferon-induced 60 kDa protein) (IFI-60K) (ISG-60) (CIG49) (Retinoic acid-induced gene G protein) (RIG-G). [Source:Uniprot/SWISSPROT;Acc:O14879]
144383	IFITM3	Interferon-induced transmembrane protein 3 (Interferon-inducible protein 1-8U). [Source:Uniprot/SWISSPROT;Acc:Q01628]
8638	OASL	59 kDa 2-5-oligoadenylate synthetase-like protein (p59 OASL) (p59OASL) (Thyroid receptor-interacting protein 14) (TRIP-14). [Source:Uniprot/SWISSPROT;Acc:Q15646]
4599	MX1	Interferon-induced GTP-binding protein Mx1 (Interferon-regulated resistance GTP-binding protein MxA) (Interferon-induced protein p78) (IFI-78K). [Source:Uniprot/SWISSPROT;Acc:P20591]
58	ACTA1	Actin, alpha skeletal muscle (Alpha-actin-1). [Source:Uniprot/SWISSPROT;Acc:P68133]
8125	ANP32A	Acidic leucine-rich nuclear phosphoprotein 32 family member A (Potent heat-stable protein phosphatase 2A inhibitor I1PP2A) (Acidic nuclear phosphoprotein pp32) (Leucine-rich acidic nuclear protein) (Lanp) (Putative HLA-DR-associated protein I) (PHAPI)
9582	APOBEC3B	Probable DNA dC->dU-editing enzyme APOBEC-3B (EC 3.5.4.-) (Phorbolin- 1-related protein) (Phorbolin-2/3). [Source:Uniprot/SWISSPROT;Acc:Q9UH17]
23780	APOL2	Apolipoprotein-L2 (Apolipoprotein L-II) (ApoL-II). [Source:Uniprot/SWISSPROT;Acc:Q9BQE5]
808	CALM3	Calmodulin (CaM). [Source:Uniprot/SWISSPROT;Acc:P62158]
824	CAPN2	Calpain-2 catalytic subunit precursor (EC 3.4.22.53) (Calpain-2 large subunit) (Calcium-activated neutral proteinase 2) (CANP 2) (Calpain M-type) (M-calpain) (Millimolar-calpain) (Calpain large polypeptide L2). [Source:Uniprot/SWISSPROT;Acc:P17655]
6352	CCL5	Small inducible cytokine A5 precursor (CCL5) (T-cell-specific RANTES protein) (SIS-delta) (T cell-specific protein P228) (TCP228) [Contains: RANTES(3-68); RANTES(4-68)]. [Source:Uniprot/SWISSPROT;Acc:P13501]
894	CCND2	G1/S-specific cyclin-D2. [Source:Uniprot/SWISSPROT;Acc:P30279]
972	CD74	HLA class II histocompatibility antigen gamma chain (HLA-DR antigens- associated invariant chain) (Ia antigen-associated invariant chain) (Ii) (p33) (CD74 antigen). [Source:Uniprot/SWISSPROT;Acc:P04233]
991	CDC20	Cell division cycle protein 20 homolog (p55CDC). [Source:Uniprot/SWISSPROT;Acc:Q12834]
1026	CDKN1A	Cyclin-dependent kinase inhibitor 1 (p21) (CDK-interacting protein 1) (Melanoma differentiation-associated protein 6) (MDA-6). [Source:Uniprot/SWISSPROT;Acc:P38936]
7812	CSDE1	Cold shock domain-containing protein E1 (UNR protein) (N-ras upstream gene protein). [Source:Uniprot/SWISSPROT;Acc:O75534]
1520	CTSS	Cathepsin S precursor (EC 3.4.22.27). [Source:Uniprot/SWISSPROT;Acc:P25774]
1832	DSP	Desmoplakin (DP) (250/210 kDa paraneoplastic pemphigus antigen). [Source:Uniprot/SWISSPROT;Acc:P15924]

1843	DUSP1	Dual specificity protein phosphatase 1 (EC 3.1.3.48) (EC 3.1.3.16) (MAP kinase phosphatase 1) (MKP-1) (Protein-tyrosine phosphatase CL100) (Dual specificity protein phosphatase hVH1). [Source:Uniprot/SWISSPROT;Acc:P28562]
10682	EBP	3-beta-hydroxysteroid-Delta(8),Delta(7)-isomerase (EC 5.3.3.5) (Cholestenol Delta-isomerase) (Delta(8)-Delta(7) sterol isomerase) (D8-D7 sterol isomerase) (Emopamil-binding protein). [Source:Uniprot/SWISSPROT;Acc:Q15125]
1975	EIF4B	Eukaryotic translation initiation factor 4B (eIF-4B). [Source:Uniprot/SWISSPROT;Acc:P23588]
2048	EPHB2	Ephrin type-B receptor 2 precursor (EC 2.7.10.1) (Tyrosine-protein kinase receptor EPH-3) (DRT) (Receptor protein-tyrosine kinase HEK5) (ERK) (Tyrosine-protein kinase TYRO5) (Renal carcinoma antigen NY-REN- 47). [Source:Uniprot/SWISSPROT;Acc:P29323]
3170	FOXA2	Hepatocyte nuclear factor 3-beta (HNF-3B) (Forkhead box protein A2). [Source:Uniprot/SWISSPROT;Acc:Q9Y261]
2294	FOXF1	Forkhead box protein F1 (Forkhead-related protein FKHL5) (Forkhead- related transcription factor 1) (FREAC-1) (Forkhead-related activator 1). [Source:Uniprot/SWISSPROT;Acc:Q12946]
23710	GABARAPL3	Gamma-aminobutyric acid receptor-associated protein-like 1 (GABA(A) receptor-associated protein-like 1) (Glandular epithelial cell protein 1) (GEC-1) (Early estrogen-regulated protein). [Source:Uniprot/SWISSPROT;Acc:Q9H0R8]
2821	GPI	Glucose-6-phosphate isomerase (EC 5.3.1.9) (GPI) (Phosphoglucose isomerase) (PGI) (Phosphohexose isomerase) (PHI) (Neuroleukin) (NLK) (Sperm antigen 36) (SA-36). [Source:Uniprot/SWISSPROT;Acc:P06744]
2987	GUK1	Guanylate kinase (EC 2.7.4.8) (GMP kinase). [Source:Uniprot/SWISSPROT;Acc:Q16774]
3054	HCFC1	Host cell factor (HCF) (HCF-1) (C1 factor) (VP16 accessory protein) (VCAF) (CFF)
3105	HLA-A	HLA class I histocompatibility antigen, A-3 alpha chain precursor (MHC class I antigen A*3). [Source:Uniprot/SWISSPROT;Acc:P04439]
730410	1B18_HUMAN	HLA class I histocompatibility antigen, B-18 alpha chain precursor (MHC class I antigen B*18). [Source:Uniprot/SWISSPROT;Acc:P30466]
3107	1C07_HUMAN	HLA class I histocompatibility antigen, Cw-7 alpha chain precursor (MHC class I antigen Cw*7). [Source:Uniprot/SWISSPROT;Acc:P10321]
3133	NP_005507.3	major histocompatibility complex, class I, E precursor [Source:RefSeq_peptide;Acc:NP_005507]
3135	HLA-G	HLA class I histocompatibility antigen, alpha chain G precursor (HLA G antigen). [Source:Uniprot/SWISSPROT;Acc:P17693]
7184	HSP90B1	Endoplasmin precursor (Heat shock protein 90 kDa beta member 1) (94 kDa glucose-regulated protein) (GRP94) (gp96 homolog) (Tumor rejection antigen 1). [Source:Uniprot/SWISSPROT;Acc:P14625]
8870	NP_003888.2	immediate early response 3 [Source:RefSeq_peptide;Acc:NP_003888]
3460	IFNGR2	Interferon-gamma receptor beta chain precursor (Interferon-gamma receptor accessory factor 1) (AF-1) (Interferon-gamma transducer 1). [Source:Uniprot/SWISSPROT;Acc:P38484]
3576	IL8	Interleukin-8 precursor (IL-8) (CXCL8) (Monocyte-derived neutrophil chemotactic factor) (MDNCF) (T-cell chemotactic factor) (Neutrophil- activating protein 1) (NAP-1) (Protein 3-10C) (Granulocyte chemotactic protein 1) (GCP-1)
3693	ITGB5	Integrin beta-5 precursor. [Source:Uniprot/SWISSPROT;Acc:P18084]
3959	LGALS3BP	Galectin-3-binding protein precursor (Lectin galactoside-binding soluble 3-binding protein) (Mac-2-binding protein) (Mac-2 BP) (MAC2BP) (Tumor-associated antigen 90K). [Source:Uniprot/SWISSPROT;Acc:Q08380]

4061	LY6E	Lymphocyte antigen 6E precursor (Ly-6E) (Retinoic acid-induced gene E protein) (RIG-E) (Thymic shared antigen 1) (TSA-1) (Stem cell antigen 2) (SCA-2). [Source:Uniprot/SWISSPROT;Acc:Q16553]
65108	MARCKSL1	MARCKS-related protein (MARCKS-like protein 1) (Macrophage myristoylated alanine-rich C kinase substrate) (Mac-MARCKS) (MacMARCKS). [Source:Uniprot/SWISSPROT;Acc:P49006]
4605	MYBL2	Myb-related protein B (B-Myb). [Source:Uniprot/SWISSPROT;Acc:P10244]
4771	NF2	Merlin (Moesin-ezrin-radixin-like protein) (Neurofibromin-2) (Schwannomin) (Schwannomerlin). [Source:Uniprot/SWISSPROT;Acc:P35240]
652607	PABPC1	Polyadenylate-binding protein 1 (Poly(A)-binding protein 1) (PABP 1). [Source:Uniprot/SWISSPROT;Acc:P11940]
84333	PCGF5	Polycomb group RING finger protein 5 (RING finger protein 159). [Source:Uniprot/SWISSPROT;Acc:Q86SE9]
5111	PCNA	Proliferating cell nuclear antigen (PCNA) (Cyclin). [Source:Uniprot/SWISSPROT;Acc:P12004]
5329	PLAUR	Urokinase plasminogen activator surface receptor precursor (uPAR) (U- PAR) (Monocyte activation antigen Mo3) (CD87 antigen). [Source:Uniprot/SWISSPROT;Acc:Q03405]
5359	PLSCR1	Phospholipid scramblase 1 (PL scramblase 1) (Ca(2+)-dependent phospholipid scramblase 1) (Erythrocyte phospholipid scramblase) (MmTRA1b). [Source:Uniprot/SWISSPROT;Acc:O15162]
5432	POLR2C	DNA-directed RNA polymerase II subunit RPB3 (RNA polymerase II subunit B3) (RNA polymerase II subunit 3) (DNA-directed RNA polymerase II subunit C) (DNA-directed RNA polymerase II 33 kDa polypeptide) (RPB33) (RPB31). [Source:Uniprot/SWISSPROT;Acc:P19387]
5445	PON2	Serum paraoxonase/arylesterase 2 (EC 3.1.1.2) (EC 3.1.8.1) (PON 2) (Serum aryldialkylphosphatase 2) (A-esterase 2) (Aromatic esterase 2). [Source:Uniprot/SWISSPROT;Acc:Q15165]
5473	PPBP	Platelet basic protein precursor (PBP) (Small inducible cytokine B7) (CXCL7) (Leukocyte-derived growth factor) (LDGF) (Macrophage-derived growth factor) (MDGF)
5514	PPP1R10	Serine/threonine-protein phosphatase 1 regulatory subunit 10 (Phosphatase 1 nuclear targeting subunit) (MHC class I region proline- rich protein CAT53) (FB19 protein) (PP1-binding protein of 114 kDa) (p99). [Source:Uniprot/SWISSPROT;Acc:Q96QC0]
5836	PYGL	Glycogen phosphorylase, liver form (EC 2.4.1.1). [Source:Uniprot/SWISSPROT;Acc:P06737]
5880	RAC2	Ras-related C3 botulinum toxin substrate 2 precursor (p21-Rac2) (Small G protein) (GX). [Source:Uniprot/SWISSPROT;Acc:P15153]
5935	RBM3	Putative RNA-binding protein 3 (RNA-binding motif protein 3) (RNPL). [Source:Uniprot/SWISSPROT;Acc:P98179]
389	RHOC	Rho-related GTP-binding protein RhoC precursor (H9). [Source:Uniprot/SWISSPROT;Acc:P08134]
6124	RPL4	60S ribosomal protein L4 (L1). [Source:Uniprot/SWISSPROT;Acc:P36578]
6175	RPLP0	60S acidic ribosomal protein P0 (L10E). [Source:Uniprot/SWISSPROT;Acc:P05388]
91543	RSAD2	radical S-adenosyl methionine domain containing 2 [Source:RefSeq_peptide;Acc:NP_542388]
5054	SERPINE1	Plasminogen activator inhibitor 1 precursor (PAI-1) (Endothelial plasminogen activator inhibitor) (PAI). [Source:Uniprot/SWISSPROT;Acc:P05121]
29946	SERTAD3	SERTA domain-containing protein 3 (Replication protein-binding trans- activator) (RPA-binding trans-activator). [Source:Uniprot/SWISSPROT;Acc:Q9UJW9]
6774	STAT3	Signal transducer and activator of transcription 3 (Acute-phase response factor). [Source:Uniprot/SWISSPROT;Acc:P40763]
7040	TGFB1	Transforming growth factor beta-1 precursor (TGF-beta-1) [Contains: Latency-associated peptide

		(LAP)]. [Source:Uniprot/SWISSPROT;Acc:P01137]
7083	TK1	Thymidine kinase, cytosolic (EC 2.7.1.21). [Source:Uniprot/SWISSPROT;Acc:P04183]
4071	TM4SF1	Transmembrane 4 L6 family member 1 (Tumor-associated antigen L6) (Membrane component surface marker 1) (M3S1). [Source:Uniprot/SWISSPROT;Acc:P30408]
7127	TNFAIP2	Tumor necrosis factor, alpha-induced protein 2 (Primary response gene B94 protein). [Source:Uniprot/SWISSPROT;Acc:Q03169]
9322	TRIP10	Cdc42-interacting protein 4 (Thyroid receptor-interacting protein 10) (TRIP-10) (Protein Felic) (Salt-tolerant protein) (hSTP). [Source:Uniprot/SWISSPROT;Acc:Q15642]
9246	UBE2L6	Ubiquitin/ISG15-conjugating enzyme E2 L6 (EC 6.3.2.19) (Ubiquitin- protein ligase L6) (Ubiquitin carrier protein L6) (UbcH8) (Retinoic acid-induced gene B protein) (RIG-B). [Source:Uniprot/SWISSPROT;Acc:O14933]
7374	UNG	Uracil-DNA glycosylase (EC 3.2.2.-) (UDG). [Source:Uniprot/SWISSPROT;Acc:P13051]
9100	USP10	Ubiquitin carboxyl-terminal hydrolase 10 (EC 3.1.2.15) (Ubiquitin thioesterase 10) (Ubiquitin-specific-processing protease 10) (Deubiquitinating enzyme 10). [Source:Uniprot/SWISSPROT;Acc:Q14694]
7375	USP4	Ubiquitin carboxyl-terminal hydrolase 4 (EC 3.1.2.15) (Ubiquitin thioesterase 4) (Ubiquitin-specific-processing protease 4) (Deubiquitinating enzyme 4) (Ubiquitous nuclear protein homolog). [Source:Uniprot/SWISSPROT;Acc:Q13107]

Up-regulated ISGs

Entrez Gene ID	Gene Symbol	Description
25841	ABTB2	Ankyrin repeat and BTB/POZ domain-containing protein 2. [Source:Uniprot/SWISSPROT;Acc:Q8N961]
341	APOC1	Apolipoprotein C-I precursor (Apo-CI) (ApoC-I). [Source:Uniprot/SWISSPROT;Acc:P02654]
716	C1S	Complement C1s subcomponent precursor (EC 3.4.21.42) (C1 esterase) [Contains: Complement C1s subcomponent heavy chain; Complement C1s subcomponent light chain]. [Source:Uniprot/SWISSPROT;Acc:P09871]
440068	CASP1	Caspase-1 precursor (EC 3.4.22.36) (CASP-1) (Interleukin-1 beta convertase) (IL-1BC) (IL-1 beta-converting enzyme) (ICE) (Interleukin- 1 beta-converting enzyme) (p45) [Contains: Caspase-1 p20 subunit; Caspase-1 p10 subunit].
6364	CCL20	Small inducible cytokine A20 precursor (CCL20) (Macrophage inflammatory protein 3 alpha) (MIP-3-alpha) (Liver and activation- regulated chemokine) (CC chemokine LARC) (Beta chemokine exodus-1) [Contains: CCL20(1-67); CCL20(1-64); CCL20(2-70)].
629	CFB	Complement factor B precursor (EC 3.4.21.47) (C3/C5 convertase) (Properdin factor B) (Glycine-rich beta glycoprotein) (GBG) (PBF2) [Contains: Complement factor B Ba fragment; Complement factor B Bb fragment]. [Source:Uniprot/SWISSPROT;Acc:P00751]
80347	COASY	Bifunctional coenzyme A synthase (CoA synthase) (NBP) (POV-2) [Includes: Phosphopantetheine adenylyltransferase (EC 2.7.7.3) (Pantetheine-phosphate adenylyltransferase) (PPAT) (Dephospho-CoA pyrophosphorylase); Dephospho-CoA kinase (EC 2.7.1.24) (DPCK)
1390	CREM	cAMP-responsive element modulator (Inducible cAMP early repressor) (ICER). [Source:Uniprot/SWISSPROT;Acc:Q03060]
6376	CX3CL1	Fractalkine precursor (CX3CL1) (Neurotactin) (CX3C membrane-anchored chemokine) (Small

		inducible cytokine D1). [Source:Uniprot/SWISSPROT;Acc:P78423]
731937	EIF1	Eukaryotic translation initiation factor 1 (eIF1) (Protein translation factor SUI1 homolog) (Sui1iso1) (A121). [Source:Uniprot/SWISSPROT;Acc:P41567]
8334	HIST1H2AC	Histone H2A type 1-C. [Source:Uniprot/SWISSPROT;Acc:Q93077]
3108	HLA-DMA	HLA class II histocompatibility antigen, DM alpha chain precursor (MHC class II antigen DMA). [Source:Uniprot/SWISSPROT;Acc:P28067]
3306	HSPA2	Heat shock-related 70 kDa protein 2 (Heat shock 70 kDa protein 2). [Source:Uniprot/SWISSPROT;Acc:P54652]
3308	HSPA4	Heat shock 70 kDa protein 4 (Heat shock 70-related protein APG-2) (HSP70RY). [Source:Uniprot/SWISSPROT;Acc:P34932]
3397	ID1	DNA-binding protein inhibitor ID-1 (Inhibitor of DNA binding 1). [Source:Uniprot/SWISSPROT;Acc:P41134]
3429	IFI27	Interferon-alpha-induced 11.5 kDa protein (p27) (ISG12(a) protein). [Source:Uniprot/SWISSPROT;Acc:P40305]
3434	IFIT1	Interferon-induced protein with tetratricopeptide repeats 1 (IFIT-1) (Interferon-induced 56 kDa protein) (IFI-56K). [Source:Uniprot/SWISSPROT;Acc:P09914]
24138	IFIT5	Interferon-induced protein with tetratricopeptide repeats 5 (IFIT-5) (Retinoic acid- and interferon-inducible 58 kDa protein). [Source:Uniprot/SWISSPROT;Acc:Q13325]
3665	IRF7	Interferon regulatory factor 7 (IRF-7). [Source:Uniprot/SWISSPROT;Acc:Q92985]
3669	ISG20	Interferon-stimulated gene 20 kDa protein (EC 3.1.13.1) (Promyelocytic leukemia nuclear body-associated protein ISG20) (Estrogen-regulated transcript 45 protein). [Source:Uniprot/SWISSPROT;Acc:Q96AZ6]
4149	MAX	Protein max (Myc-associated factor X). [Source:Uniprot/SWISSPROT;Acc:P61244]
4170	MCL1	Induced myeloid leukemia cell differentiation protein Mcl-1 (Bcl-2- related protein EAT/mcl1) (mcl1/EAT). [Source:Uniprot/SWISSPROT;Acc:Q07820]
8202	NCOA3	Nuclear receptor coactivator 3 (EC 2.3.1.48) (NCoA-3) (Thyroid hormone receptor activator molecule 1) (TRAM-1) (ACTR) (Receptor-associated coactivator 3) (RAC-3) (Amplified in breast cancer-1 protein) (AIB-1) (Steroid receptor coactivator protein 3)
9111	NMI	N-myc-interactor (Nmi) (N-myc and STAT interactor). [Source:Uniprot/SWISSPROT;Acc:Q13287]
8204	NRIP1	Nuclear receptor-interacting protein 1 (Nuclear factor RIP140) (Receptor-interacting protein 140). [Source:Uniprot/SWISSPROT;Acc:P48552]
4938	OAS1	2-5-oligoadenylate synthetase 1 (EC 2.7.7.-) ((2-5)oligo(A) synthetase 1) (2-5A synthetase 1) (p46/p42 OAS) (E18/E16). [Source:Uniprot/SWISSPROT;Acc:P00973]
10133	OPTN	Optineurin (Optic neuropathy-inducing protein) (E3-14.7K-interacting protein) (FIP-2) (Huntingtin-interacting protein HYPL) (NEMO-related protein) (Transcription factor IIIA-interacting protein) (TFIIIA- IntP). [Source:Uniprot/SWISSPROT;Acc:Q96CV9]
51131	PHF11	PHD finger protein 11 (BRCA1 C-terminus-associated protein) (Renal carcinoma antigen NY-REN-34). [Source:Uniprot/SWISSPROT;Acc:Q9UIL8]
51296	SLC15A3	solute carrier family 15, member 3 [Source:RefSeq_peptide;Acc:NP_057666]
8651	SOCS1	Suppressor of cytokine signaling 1 (SOCS-1) (JAK-binding protein) (JAB) (STAT-induced STAT inhibitor 1) (SSI-1) (Tec-interacting protein 3) (TIP-3). [Source:Uniprot/SWISSPROT;Acc:O15524]
3431	SP110	Sp110 nuclear body protein (Speckled 110 kDa) (Transcriptional coactivator Sp110) (Interferon-induced protein 41/75). [Source:Uniprot/SWISSPROT;Acc:Q9HB58]

7128	TNFAIP3	Tumor necrosis factor, alpha-induced protein 3 (EC 3.4.19.12) (Putative DNA-binding protein A20) (Zinc finger protein A20). [Source:Uniprot/SWISSPROT;Acc:P21580]
8717	TRADD	Tumor necrosis factor receptor type 1-associated DEATH domain protein (TNFR1-associated DEATH domain protein) (TNFRSF1A-associated via death domain). [Source:Uniprot/SWISSPROT;Acc:Q15628]
11074	TRIM31	Tripartite motif-containing protein 31. [Source:Uniprot/SWISSPROT;Acc:Q9BZY9]
85363	TRIM5	Tripartite motif-containing protein 5 (EC 6.3.2.-) (RING finger protein 88). [Source:Uniprot/SWISSPROT;Acc:Q9C035]

From the cDNA microarray data of NRAV-overexpressing cells, 107 differentially expressed ISGs were identified by using the Interferome analysis with parameters human, lung and A549 cell line. 72 down-regulated and 35 up-regulated ISGs are shown.

Table S3. Mass Spectrometry Analysis of ZONAB, Related to Figure 6

Reference Scan(s)	Peptide	MH+	DeltaM	z	Type	P (pro) P (pep)	**Score** XC	Coverage DeltaCn
ZO-1–associated nucleic acid binding protein (ZONAB) [Homo sapiens]						1.98E-10	**148.30**	
3768	R.NDTKEDVFVHQTAIKK.N	1874.08736	-0.07095	2	CID	2.05E-07	5.12	0.51
3788	K.EDVFVHQTAIKK.N	1415.61915	-0.29085	2	CID	4.81E-05	3.36	0.36
3831	R.PAPAVGEAEDKENQQATSGPNQPSVR.R	2678.81039	0.20204	3	CID	1.98E-10	3.89	0.43
4062	R.NGYGFINRNDTK.E	1399.49353	-0.85896	2	CID	2.17E-06	3.38	0.44
4171	K.DGVPEGAQLQGPVHR.N	1560.69644	0.80263	2	CID	4.17E-07	3.37	0.52
4194	R.NDTKEDVFVHQTAIK.R	1745.91444	-0.04428	2	CID	5.04E-10	4.95	0.47
4272	K.EDVFVHQTAIK.R	1287.44623	-0.59780	2	CID	1.23E-05	3.32	0.41
4273	K.GAEAANVTGPDGVPVEGSR.Y	1783.87794	1.41825	2	CID	2.77E-03	3.81	0.45
4339	K.VLATKVLGTVK.W	1129.41808	0.17279	2	CID	9.02E-07	3.43	0.43
4384	R.NAGEIGEM*KDGVPEGAQLQGPVHR.N	2506.73309	-0.62057	3	CID	4.77E-07	4.56	0.43
4452	R.NGYGFINR.N	941.02532	-0.10120	2	CID	1.21E-04	2.69	0.43
4928	R.NAGEIGEMKDGVPEGAQLQGPVHR.N	2490.73818	-0.05303	3	CID	4.21E-10	5.93	0.57
5326	R.NGYGFINRNDTKEDVFVHQTAIK.R	2667.91717	0.16020	3	CID	1.05E-09	5.21	0.43
6294	K.VLGTVKWFNVR.N	1319.57943	0.33309	2	CID	1.50E-07	3.27	0.48
8163	R.SVGDGETVEFDVVEGEK.G	1796.86702	0.46457	2	CID	5.01E-07	4.95	0.51

Sequence coverage of ZO-1–associated nucleic acid binding protein (ZONAB)

MSEAGEATTTTTTTLPQAPTEAAAAAPQDPAPKSPVGSGAPQAAAPAPAAHVAGNPGGDAAPAATGTAAAASLATAAGSEDAEKKVLATKVLGTVKWFNVRNGYGFINRNDTKED
VFVHQTAIKKNNPRKYLRSVGDGETVEFDVVEGEKGAEAANVTGPDGVPVEGSRYAADRRRYRRGYYGRRRGPPRNAGEIGEMKDGVPEGAQLQGPVHRNPTYRPRYRSRGPPRP
RPAPAVGEAEDKENQQATSGPNQPSVRRGYRRPYNYRRRPRPPNAPSQDGKEAKAGEAPTENPAPPTQQSSAE

Mass Spectrometry was performed as described in Supplemental Experimental Procedures. Machted peptides were listed or shown in Red.

Supplemental Experimental Procedures

Cells, viruses, and antibodies

Cells A549, HeLa, K562, 293T, HepG2, SMMC-7721, QGY-7703, BEL-7402, NIH3T3, and Vero were grown in DMEM or RPMI1640 supplemented with 10% (vol/vol) FBS (Gibco) and antibiotics (penicillin and streptomycin) (Invitrogen) at 37 ℃ in a humidified 5% CO_2 atmosphere as previously described (Guo et al., 2010). Influenza virus A/WSN/33 (H1N1) and Sendai virus (SeV) were propagated in embryonated chicken eggs (Wei et al., 2014). Muscovy Duck Reovirus (MDRV) and Herpes simplex virus (HSV, kindly provided by Prof. Jinhua Yan, Institute of Microbiology, Chinese Academy of Sciences (Zhang et al., 2011)) were propagated in Vero cells. Antibody anti-MxA (Proteintech, 13750-1-AP) is used for Western blot. All other antibodies were obtained as previously described (Wei et al., 2014).

Plasmid construction

The reporter plasmid pGL3-MxAP-FF-Luc carrying the firefly luciferase (FFLuc) gene under the control of the human MxA promoter was kindly provided by Prof. Georg Kochs, Department of Virology, University of Freiburg, Freiburg, Germany (Holzinger et al., 2007). Primers ′5 -TTA AAA GGT ACC GAG CCC TGA ACC GGG ACA GTG-3′ and 5′-TTT GTC AAG CTT TGG TGT CCA GCG AAG ACC AGC-3′ were used to amplify the IFITM3 promoter from A549 genomic DNA (Shen et al., 2013). pGL3-IFITM3P carrying the FF-Luc gene under the control of the IFITM3 promoter was constructed by inserting the IFITM3 promoter into the

XhoI-HindIII sites of pGL3-basic (Promega).

Viral infection

A549 cells were used to infect with IAV WSN, Sendai virus (SeV), or Herpes Simplex Virus (HSV) and 293T cells were infected with Muscovy Duck Reovirus (MDRV). Unless indicated, cells were washed and incubated with virus at a multiplicity of infection (MOI) of 3 for 1 h with medium containing 2 mg/ml TPCK (L-1-tosylamido-2-phenylethyl chloromethyl ketone) -treated trypsin. After adsorption, the supernatant was aspirated and cells were cultured with the medium for 12 h with IAV WSN and SeV, or 24h with MDRV and HSV.

Virus titers assay

Cell culture supernatant was harvested at 16 hpi or indicated time points. Mouse lungs were collected at 6 dpi and homogenized in 1ml DMEM to prepare tissue suspension. Virus titers in supernatants were determined by a standard Hemagglutination assay (HA) or a plaque forming assay (PFU) on MDCK cells as described previously (Wang et al., 2012).

Microarray and data analysis

The microarray experiments were performed as described previously (Guo et al., 2014; Wang et al., 2012). The lncRNA microarray of WSN infected A549 cells and uninfected control was performed using Human lncRNA 100309 (Arraystar,

Rockville, MD). The cDNA microarray of WSN infected NRAV-overexpressing or control A549 cells (MOI=3,16 hpi).was performed using Human 12x135K microarray (Roche NimbleGen, Madison, WI). Expression data were normalized through quantile normalization and the Robust Multichip Average (RMA) algorithm, and transformed into log2 value for calculation. The fold changes of up-regulated genes are calculated as $2^{(\text{mean}[\log2(T1),\ \log2(T2),\ \log2(T3)])}/2^{(\text{mean}[\log2(C1),\ \log2(C2),\ \log2(C3)])}$, and the fold changes of down-regulated genes are calculated as $2^{(\text{mean}[\log2(C1),\ \log2(C2),\ \log2(C3)])}/2^{(\text{mean}[\log2(T1),\ \log2(T2),\ \log2(T3)])}$. Differentially expressed genes were identified through Volcano Plot filtering between two groups, and the threshold is fold change > 2.0 and $P<0.05$. In heatmaps, log2 values have been centered and scaled in the row.

***In Silico* and Primary Functional Screen of LncRNAs**

To identify lncRNAs from the data of microarray, candidates with higher fold change of expression were selected and subjected an *in silico* analysis of genomic locations and sequences (UCSC, http://genome.ucsc.edu, NCBI, http://www.ncbi.nlm.nih.gov), and according to the strict criteria that lncRNA should be longer than 200 nt, have little or no ORFs, and localize in genome antisense to, or intronic of, or intergenic (>5kb away) from adjacent protein-coding genes. No protein-coding potential is performed. The functional primary screen is based on the effects of ectopic lncRNA expression on IAV replication. Fragments of lncRNAs amplified from A549 cell were inserted into modified stable expression system as described in **Supplemental Experimental Procedures** and used for exogenous expression. FACS sorted cells

with fluorescence are maintained. After infection with WSN at MOI=0.3 for 16 hours, the virus titers in cell culture supernatants were determined through plaque forming assay.

Bioinformatics analysis of non-coding potential

Non-coding potential is performed through several programs as described previously (Guo et al., 2014). LncRNA sequences are analyzed by using ORF Finder from NCBI (http://www.ncbi.nlm.nih.gov/gorf/gorf.html) and coding potential calculator (http://cpc.cbi.pku.edu.cn). NRAV homolog sequences from human, chimpanzee, rhesus, guenin pig, and mouse are used for PhyloCSF analysis (Lin et al., 2011) (https://github.com/mlin/PhyloCSF/wiki).

Sucrose sedimentation and polysome analysis

The sucrose sedimentation and polysome analysis was performed as previously described (Carpenter et al., 2013; Ricci et al., 2014). 2×10^7 A549 cells were pretreated with cycloheximide (CHX, 100 μg/ml, Sigma) for 10 min at 37℃ or mock treated. After wash, cells were lysed in 1ml of lysis buffer (10mM HEPES-KOH pH 7.4; 5 mM $MgCl_2$; 300 mM KCl; 0.5% NP-40; 2mM DTT; 100 μg/ml CHX (none for control) and 1 × Protease-Inhibitor Cocktail EDTA-free (Promega)) and incubation at 4ºC for 10 min. After centrifugation at 1300 g for 10 min at 4ºC, the supernatant was recovered. 10 A260 units of mock lysate were treated with 35 mM of EDTA for 20 min, same amount of CHX-treated lysate were not complemented with EDTA, both

were loaded on top of a 10 to 50% (Weight/Volume) sucrose gradient (20mM HEPES-KOH pH 7.4; 5mM $MgCl_2$; 100mM KCl; 2mM DTT; 100 µg/ml CHX) and centrifuged in a SW-41 rotor at 35,000 rpm for 2 h 40 min at 4 ºC. After centrifugation, 15 fractions were collected from the top while absorbance at 254nm was measured. Collected fractions were digested with 1% SDS and proteinase K (200 µg/ml) at 42C for 30 min. RNA was extracted and re -suspended in 50 µl of water. qRT-PCR was performed to quantify the NRAV or GAPDH mRNA distribution in sucrose gradient. The relative RNA levels were normalized to input and shown as %input.

Cell stimulation, Transient transfections and viral transductions

For stimulation, cells were incubated for 2-3 h with the recombinant cytokines or peptides at following concentration IFN-β (0-100 ng/ml), IL-29 (50 ng/ml), for 8 h with LPS (100 ng/ml, Invivogen) and sCD14 (300 ng/ml, PeproTech), for 4 h with etoposide (100 µM, Sigma), or cultured in serum-free media, or transfected with 1 µg/ml RNA or poly(I:C) using Lipofectamine 2000 (Invitrogen) according to the manufacturer's instructions. For transient transfection, cells were transiently transfected with 2 µg plasmids per well of 6-well plate by using Lipofectamine 2000 (Invitrogen). Then, cells were cultured for another 24 hours for transient expression. For viral transductions, cells were transduced with pseudovirus packaged by lentivirus expression system with polybrene (8 µg/ml).

RT-PCR and Quantitative RT-PCR (qRT-PCR)

RNA was isolated with the Total RNA Kit (Omega Bio-Tek). Reverse transcription was performed with oligo-dT primers or random primers by using M-MLV (Promega), and quantitative PCR was performed with SuperReal PreMix Plus (SYBR Green) (Tiangen, Beijing, China). The primer sequences are available upon request. For quantification, the $2^{-\Delta\Delta Ct}$ method was used to calculate the relative RNA levels against GAPDH. Results from three independent experiments were expressed as means ± s.e.m. $P<0.05$ (two-sided Student's *t*-test) was considered statistically significant.

shRNAs

The shRNA target sequences used in supplemental results are sh-RIG-I: TGC AAT CTT GTC ATC CTT TAT (Jiang et al., 2011), sh-MDA5: CCA ACA AAG AAG CAG TGT ATA (Delaloye et al., 2009), sh-TLR3: CAA CAT AGC CAA CAT AAA T (Salaun et al., 2007), sh-VISA: GGC AGG TCA GTT AAC AAT TTA (Jiang et al., 2011), sh-IRF3: CAT TGT AGA TCT GAT TAC CTT C (Manel et al., 2010), sh-IRF7: GCC TCT ATG ACG ACA TCG AGT, sh-STAT1: GCA AGC GTA ATC TTC AGG ATA (Jiang et al., 2011) and sh-ZONAB: GCA GGT GAC CTA AAG AAT TAA and GGA AGA CTA ACC AAG ATT TG. The efficiency of overexpression or knockdown was confirmed by standard RT-PCR or qRT-PCR.

Generation of overexpression and knockdown cell lines

NRAV coding sequence and other lncRNA sequences were cloned from A549 by

RT-PCR. Primers were designed according to the sequences in database of UCSC (http://genome.ucsc.edu) or NCBI (http://www.ncbi.nlm.nih.gov). The stable NRAV-overexpressing cells lines were constructed with a retroviral expression system as described previously (Qiu et al., 2012; Wei et al., 2014; Yang et al., 2013). The expression construct is modified by inserting a bovine growth hormone polyadenylation (BGH-polyA) sequence from pcDNA3.1 into XhoI-EcoRI sites before the GFP coding sequence in the vector. The stable knockdown cells of NRAV were generated using a shRNA-based lentivector system pSIH-H1 (System Biosciences) as provider's protocol. The shRNA target sequences used in this paper are sh-NRAV-1: GCC CTT CAG AGT TGT TAC T, sh-NRAV-2: CCT CCG AAC AGA GTA ATG T. The efficiency of overexpression or knockdown was confirmed by standard RT-PCR or qRT-PCR.

Transgenic mice and virus challenge

The NRAV transgenic C57BL/6 mice (TG) were created as previously described (Lu et al., 2012; Wang et al., 2014; Wei et al., 2014). The NRAV genotype was verified by PCR. The NRAV expression was determined by RT-PCR of mouse tissue after euthanasia. Transgenic lines with high expression were maintained and used in this study. The C57BL/6 wild-type (WT) and NRAV-expressing TG mice (5–6 weeks of age, 5-13 mice/group) were inoculated intranasally with or without 10^3 PFU (about $0.5\times LD_{50}$ for WT mice) of WSN diluted in 50 μL of sterile phosphate buffer saline (PBS). Mice were weighted daily to monitor signs of illness for a period of 14 days.

Mouse lungs (13 mice/group) were collected on 6 dpi and used for further examination. Lung viral loads were measured by standard plaque forming assay, and mouse ISGs mRNA levels in lung were quantified by real-time RT-PCR and RT-PCR. Haematoxylin and Eosin (HE) staining of mouse lung was performed as previously described (Wang et al., 2014).

ISGs transient expression experiment

The transient expression of exogenous human IFIT2, IFIT3, IFITM3 and MxA were performed on NRAV-overexpressing and EV cells by transfecting with plasmids of these ISGs (1 μg/well in 6-well plate) for 24 hours, and followed with IAV infection for 16 hours. The relative virus titer (% of control EV cells) in the culture supernatant of NRAV cells and EV cells was calculated based on the virus titers determined by plaque forming assay. The empty transient expression plasmid was used as control, as well as the expression plasmid of DDX3X. The transient expression efficiency was determined by RT-PCR 24 hours after transfection with expression plasmid containing the coding sequence.

Subcellular fractionation

Cytoplasmic and nuclear fractions were separated as described previously (Yoon et al., 2012). Briefly, A549 cells were lysed with TD buffer (25 mM Tris-HCl pH 7.4; 100 mM NaCl; 5 mM KCl; and 0.7mM Na_2HPO_4) containing 1% NP-40 for 5 min. The lysates were centrifuged with 12,000 rpm for 5 min at 4ºC. The supernatant was

collected and used for the cytoplasmic fraction. The nuclear pellets were washed with TD buffer containing 0.5% NP-40 on ice for 5 min and collected after centrifugation at 4ºC for 5 min at 12,000 rpm.

Luciferase assay

Luciferase assay was performed as previously described (Wei et al., 2014). Briefly, 293T cells stably expressing NRAV in 24-well plate were cotransfected with 0.8μg of pGL3-MxAP or pGL3-IFITM3P, and 30ng of a Renilla luciferase plasmid (pRL-TK, Promega). Luciferase activity was measured using the dual-luciferase reporter assay system according to the manufacturer's instruction (Promega).

5-Aza-2'-deoxycytidine treatment

Cells were treated with or without 10 μM DNA methyltransferase inhibitor 5-Aza-2'-deoxycytidine (decitabine; DAC, Sigma) for 2 days, and supplemented with fresh DAC every 24h. Treated cells were infected with virus (WSN, SeV, MDRV or HSV, MOI=3) for 12 ~ 24 h. RNAs were isolated using Trizol reagent (Tiangen, Beijing, China), reverse transcription were performed using oligo-dT primers and mRNA levels were detected by RT-PCR or qRT-PCR.

RNA stabilization assays

The mRNA expression of MxA in A549 cells were induced by infection with WSN at MOI=1 for 12 h. The infected cells were treated with actinomycin D (ActD, Sigma) at

2.5 μg/ml and collected at 0, 4, 12, 20 h time points. RNAs were extracted using Trizol reagent (Tiangen, Beijing, China), reverse transcription were performed using oligo-dT primers and mRNA levels were determined by RT-PCR or qRT-PCR.

Chromatin immunoprecipitation (ChIP)

A549 cells expressing NRAV or EV control were infected with WSN (MOI=1, 12 hpi) and were subjected to ChIP assays using the Magna ChIP A/G chromatin immunoprecipitation kit (Millipore) following the manufacturer's instruction. Briefly, 10^7 cells were fixed and lysed in 500μl lysis buffer. Nucleus fraction were pelleted and resuspended in 300 μl nucleus lysis buffer, followed by sonication. Sheared chromatin was immunoprecipitated with 3 μg anti-H3K4me3 (Millipore; 17-614), anti-H3K27me3 (Millipore; 07-449) or IgG control (Millipore) antibody and 20μl magentic beads at 4°C for 4 h to overnight. To reverse the cross-links, protein digestion with proteinase K and 0.2 M NaCl were performed. Immunoprecipitated DNA was purified and quantified by qPCR analysis using SYBR Green Supermix (Tiangen). Primers used locate in intron3-exon4 of *mxA* (transcription start site for MxA isoform 2) and exon1 of *ifitm3*. The primer sequences used for the *mxA* gene are 5' CCG AGC TGG GCA ATT GG 3' and 5' TCC TGG CCG GCA ACT G 3'), for *ifitm3* are 5' AAA GGG AGG GCT CAC TGA GAA 3' and 5' CAC CTC GTG CTC CTC CTT GA 3', for *gapdh* are 5' TAC TAG CGG TTT TAC GGG CG 3' and 5' TCG AAC AGG AGG AGC AGA GAG CGA 3', for *dynll1* are 5' GAG CCC GGT CTC ACC GTG GA 3' and 5' GAT GCG CCA CGG CTT CGG TA 3' (Jurado et al.,

2012). Modificated histone enrichment in the ChIP samples were normalized to the input DNA and was calculated as $2^{-\Delta\Delta Ct}$ with normalization against IgG control. Experiments were performed at least three times with independent chromatin samples.

RNA pull-down assay and *Mass Spectrometry*

Three pairs of antisense DNA probes of 20-30 bp binding with NRAV and scramble probes were synthesized and labeled with biotin. 10^8 uninfected A549 cells were lysed in 7ml ice-cold IP Lysis buffer (25mM Tris-HCl pH 7.4; 150mM NaCl; 1mM EDTA; 1% NP-40 and 5% glycerol) complemented with 1 × Protease-Inhibitor Cocktail EDTA-free (Promega) and 7μl of Ribolock RNase inhibitor (Thermo) and incubated on ice for 30min. Supernatant of lysates were incubated with 0.5 nmole of NRAV antisense probes or scramble control probes for 3 h at 4℃ followed by incubation with Streptavidin Dynabeads (Invitrogen) overnight. RNA/protein interacting complexes were immunoprecipated and visualized by silver-staining (Pierce silver stain kit, Thermo). Specific bands were excised and trypsin digested. LC-MS/MS analysis was performed using a ThermoFisher Finnigan LTQ linear ion trap Mass Spectrometer in line with a ThermoFisher Finnigan Survey or MS Pump Plus HPLC system (Beijing Regional center of life science instrument, Chinese Academy of Sciences). The raw MS data were analyzed using SEQUEST v.28 against NCBI human protein database and results were filtered, sorted, and displayed using the Bioworks 3.2.

RNA immunoprecipitation (RIP)

2×10^7 uninfected A549 cells were lysed in 200 µl of ice-cold IP lysis buffer as described in RNA pull-down assay. Lysate was 5 to 10-fold diluted in 1ml RIP buffer (25 mM Tris-HCl pH 7.4; 150mM KCl; 5mM EDTA; 0.5 mM DTT; 0.5% NP-40; 100U/ml RNase inhibitor (Thermo) and 1 × Protease-Inhibitor Cocktail EDTA-free (Promega)) and incubated with 10 µg anti-ZONAB antibody (Bioss, Beijing) or rabbit IgG control (Millipore) overnight at 4°C as previously described (Tsai et al., 2010). Lysate was then incubation with Protein A Dynabeads (Invitrogen) for 3 h at 4°C. RNA/protein complexes were immunoprecpitated and RNA was extracted and measured with qRT-PCR.The relative RNA levels were normalized to input and the fold enrichment was calculated as $2^{-\Delta\Delta Ct}$ with normalization to IgG control.

Predition of CpG island and transcription factor binding

The prediction data of CpG island in NRAV promoter region and binding sites of transcription factors were from UCSC genome browser database (February 2009 human reference sequence (GRCh37)) (Karolchik et al., 2014).

Supplemental References

Delaloye, J., Roger, T., Steiner-Tardivel, Q.G., Le Roy, D., Knaup Reymond, M., Akira, S., Petrilli, V., Gomez, C.E., Perdiguero, B., Tschopp, J*., et al.* (2009). Innate immune sensing of modified vaccinia virus Ankara (MVA) is mediated by TLR2-TLR6, MDA-5 and the NALP3 inflammasome. PLoS pathogens *5*, e1000480.

Guo, G., Qiu, X., Wang, S., Chen, Y., Rothman, P.B., Wang, Z., Chen, Y., Wang, G., and Chen, J.L. (2010). Oncogenic E17K mutation in the pleckstrin homology domain of AKT1 promotes v-Abl-mediated pre-B-cell transformation and survival of Pim-deficient cells. Oncogene *29*, 3845-3853.

Holzinger, D., Jorns, C., Stertz, S., Boisson-Dupuis, S., Thimme, R., Weidmann, M., Casanova, J.L., Haller, O., and Kochs, G. (2007). Induction of MxA gene expression by influenza A virus requires type I or type III interferon signaling. Journal of virology *81*, 7776-7785.

Jiang, L.J., Zhang, N.N., Ding, F., Li, X.Y., Chen, L., Zhang, H.X., Zhang, W., Chen, S.J., Wang, Z.G., Li, J.M*., et al.* (2011). RA-inducible gene-I induction augments STAT1 activation to inhibit leukemia cell proliferation. Proceedings of the National Academy of Sciences of the United States of America *108*, 1897-1902.

Jurado, S., Conlan, L.A., Baker, E.K., Ng, J.L., Tenis, N., Hoch, N.C., Gleeson, K., Smeets, M., Izon, D., and Heierhorst, J. (2012). ATM substrate Chk2-interacting Zn2+ finger (ASCIZ) Is a bi-functional transcriptional activator and feedback sensor in the regulation of dynein light chain (DYNLL1) expression. The Journal of biological chemistry *287*, 3156-3164.

Karolchik, D., Barber, G.P., Casper, J., Clawson, H., Cline, M.S., Diekhans, M., Dreszer, T.R., Fujita, P.A., Guruvadoo, L., Haeussler, M*., et al.* (2014). The UCSC Genome Browser database: 2014 update. Nucleic acids research *42*, D764-770.

Lu, D., Ma, Y., Zhang, W., Bao, D., Dong, W., Lian, H., Huang, L., and Zhang, L. (2012). Knockdown of cytochrome P450 2E1 inhibits oxidative stress and apoptosis in the cTnT(R141W) dilated cardiomyopathy transgenic mice. Hypertension *60*, 81-89.

Manel, N., Hogstad, B., Wang, Y., Levy, D.E., Unutmaz, D., and Littman, D.R. (2010). A cryptic sensor for HIV-1 activates antiviral innate immunity in dendritic cells. Nature *467*, 214-217.

Qiu, X., Guo, G., Chen, K., Kashiwada, M., Druker, B.J., Rothman, P.B., and Chen, J.L. (2012). A requirement for SOCS-1 and SOCS-3 phosphorylation in Bcr-Abl-induced tumorigenesis. Neoplasia *14*, 547-558.

Ricci, E.P., Kucukural, A., Cenik, C., Mercier, B.C., Singh, G., Heyer, E.E., Ashar-Patel, A., Peng, L., and Moore, M.J. (2014). Staufen1 senses overall transcript secondary structure to regulate translation. Nature structural & molecular biology *21*, 26-35.

Salaun, B., Lebecque, S., Matikainen, S., Rimoldi, D., and Romero, P. (2007). Toll-like receptor 3 expressed by melanoma cells as a target for therapy? Clinical cancer research : an official journal of the American Association for Cancer Research *13*, 4565-4574.

Shen, C., Wu, X.R., Jiao, W.W., Sun, L., Feng, W.X., Xiao, J., Miao, Q., Liu, F., Yin, Q.Q., Zhang, C.G*., et al.* (2013). A functional promoter polymorphism of IFITM3 is associated with susceptibility to pediatric tuberculosis in Han Chinese population. PloS one *8*, e67816.

Tsai, M.C., Manor, O., Wan, Y., Mosammaparast, N., Wang, J.K., Lan, F., Shi, Y., Segal, E., and Chang, H.Y. (2010). Long noncoding RNA as modular scaffold of histone modification complexes. Science *329*, 689-693.

Wang, S., Li, H., Chen, Y., Wei, H., Gao, G.F., Liu, H., Huang, S., and Chen, J.-L. (2012). Transport of

influenza virus neuraminidase (NA) to host cell surface is regulated by ARHGAP21 and Cdc42 proteins. Journal of Biological Chemistry *287*, 9804-9816.

Yang, J., Wang, J., Chen, K., Guo, G., Xi, R., Rothman, P.B., Whitten, D., Zhang, L., Huang, S., and Chen, J.L. (2013). eIF4B phosphorylation by Pim kinases plays a critical role in cellular transformation by Abl oncogenes. Cancer research *73*, 4898-4908.

Yoon, J.H., Abdelmohsen, K., Srikantan, S., Yang, X., Martindale, J.L., De, S., Huarte, M., Zhan, M., Becker, K.G., and Gorospe, M. (2012). LincRNA-p21 suppresses target mRNA translation. Molecular cell *47*, 648-655.

Zhang, N., Yan, J., Lu, G., Guo, Z., Fan, Z., Wang, J., Shi, Y., Qi, J., and Gao, G.F. (2011). Binding of herpes simplex virus glycoprotein D to nectin-1 exploits host cell adhesion. Nature communications *2*, 577.