Figure 1

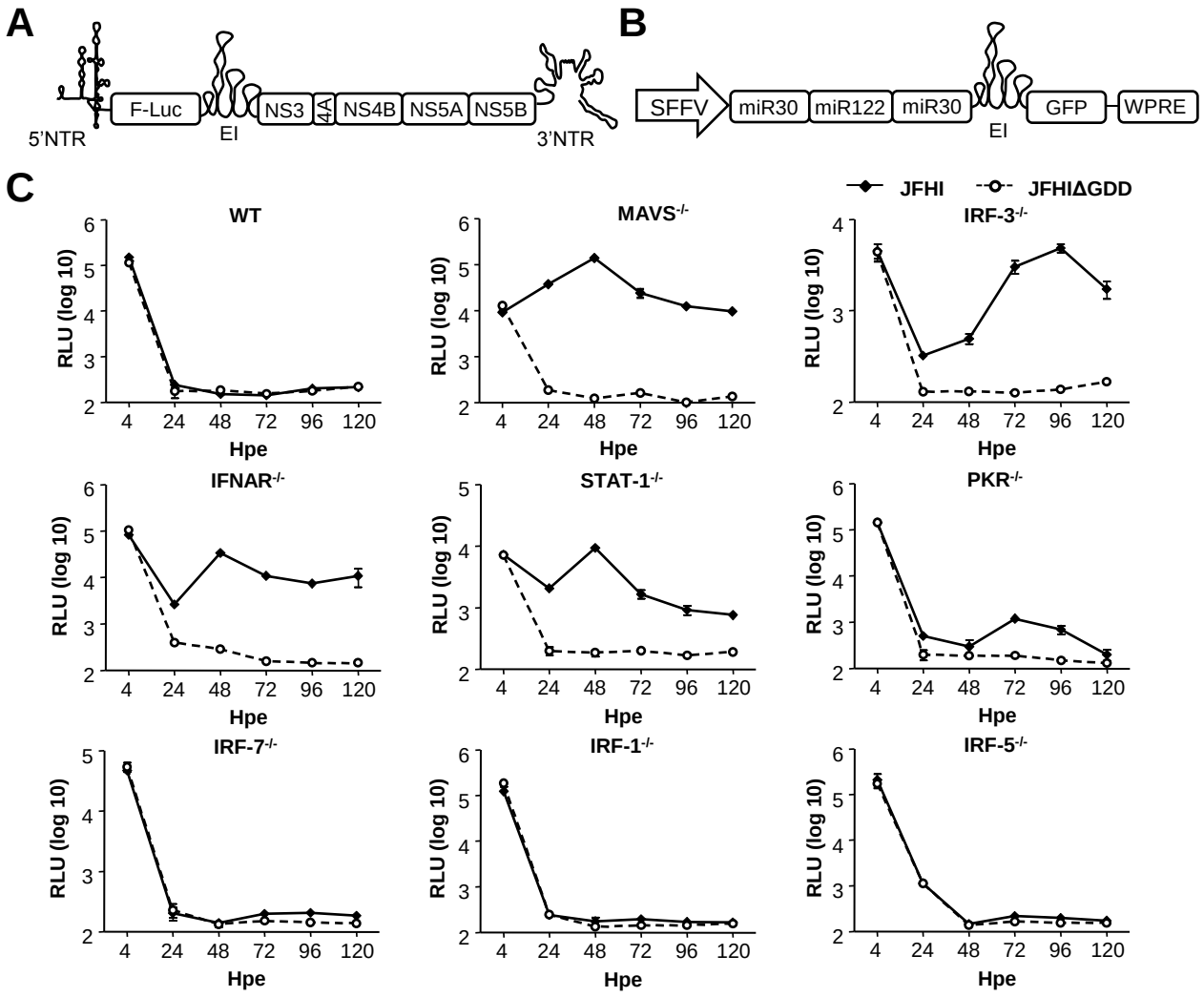

A
5'NTR
F-Luc
EI
NS3
4A
NS4B
NS5A
NS5B
3'NTR
B
SFFV
miR30
miR122
miR30
EI
GFP
WPRE
C
JFHI
JFHIΔGDD
WT
MAVS-/-
IRF-3-/-
IFNAR-/-
STAT-1-/-
PKR-/-
IRF-7-/-
IRF-1-/-
IRF-5-/-
RLU (log 10)
Hpe
4
24
48
72
96
120

Figure 2

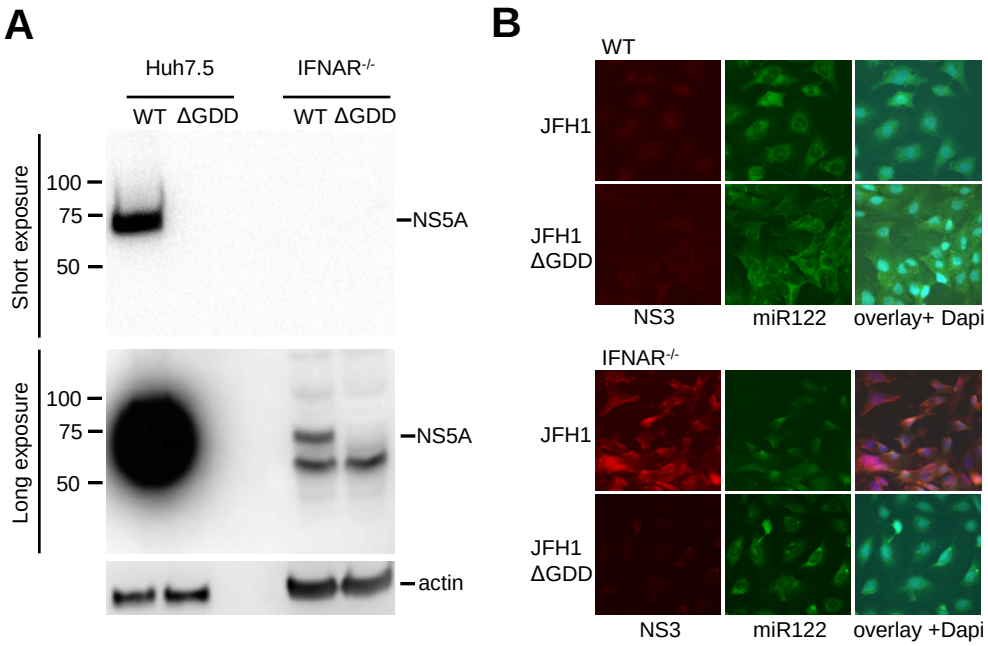

A
Huh7.5
IFNAR-/-
WT ΔGDD
WT ΔGDD
Short exposure
100
75
50
NS5A
Long exposure
100
75
50
NS5A
actin
B
WT
JFH1
JFH1 ΔGDD
NS3
miR122
overlay+ Dapi
IFNAR-/-
JFH1
JFH1 ΔGDD
NS3
miR122
overlay +Dapi

Figure 3

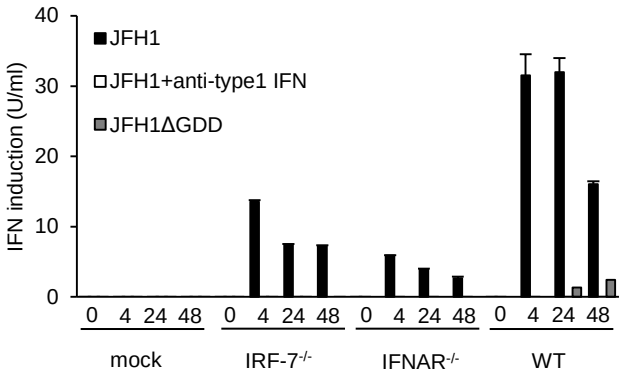

40
30
20
10
0
IFN induction (U/ml)
JFH1
JFH1+anti-type1 IFN
JFH1ΔGDD
0 4 24 48
0 4 24 48
0 4 24 48
0 4 24 48
mock
IRF-7-/-
IFNAR-/-
WT

Figure 4

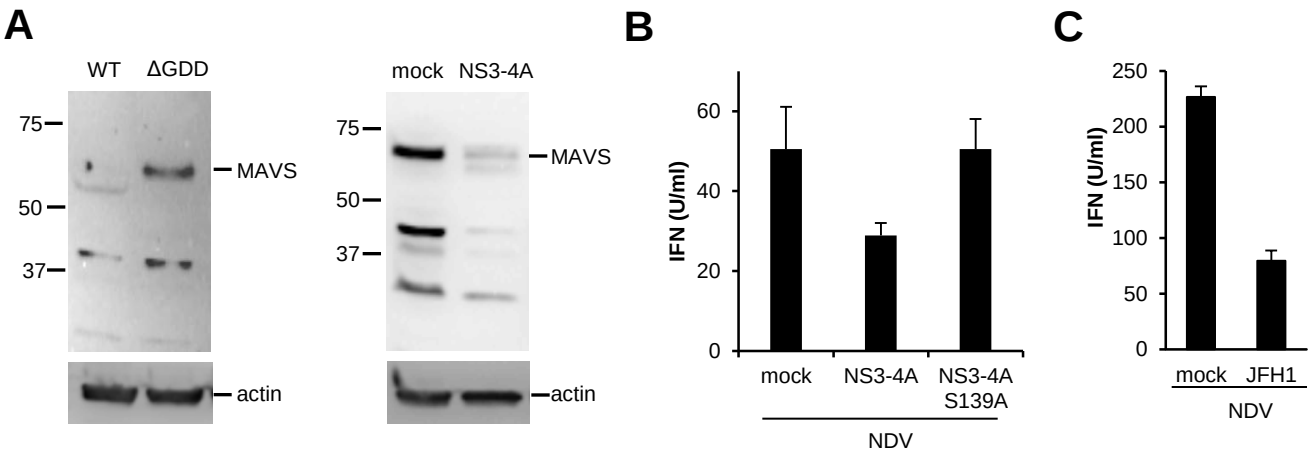

A
WT
ΔGDD
75
50
37
MAVS
actin
mock
NS3-4A
75
50
37
MAVS
actin
B
IFN (U/ml)
60
40
20
0
mock
NS3-4A
NS3-4A S139A
NDV
C
IFN (U/ml)
250
200
150
100
50
0
mock
JFH1
NDV

Figure 5

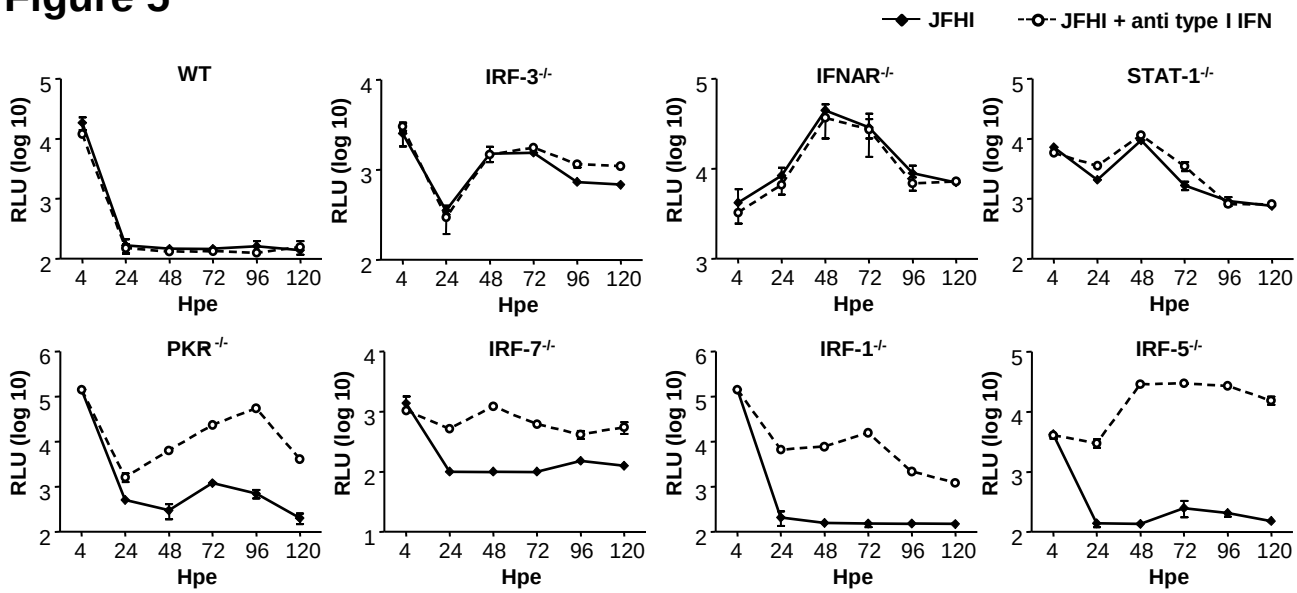

JFHI
JFHI + anti type I IFN
WT
IRF-3-/-
IFNAR-/-
STAT-1-/-
PKR-/-
IRF-7-/-
IRF-1-/-
IRF-5-/-
RLU (log 10)
Hpe
4
24
48
72
96
120

Figure 6

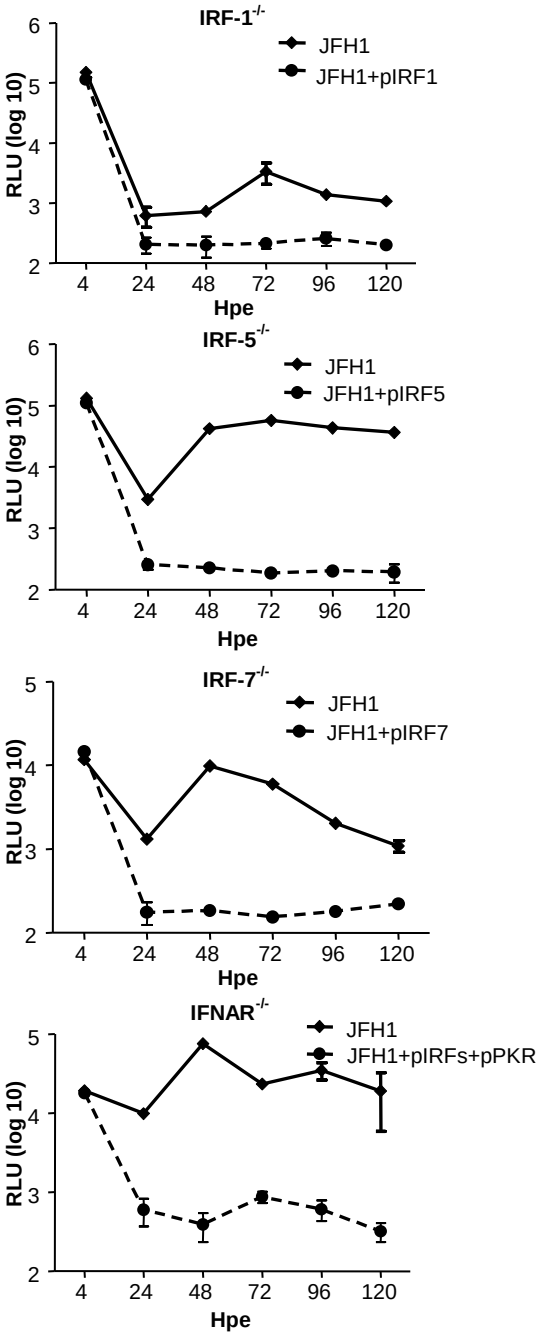
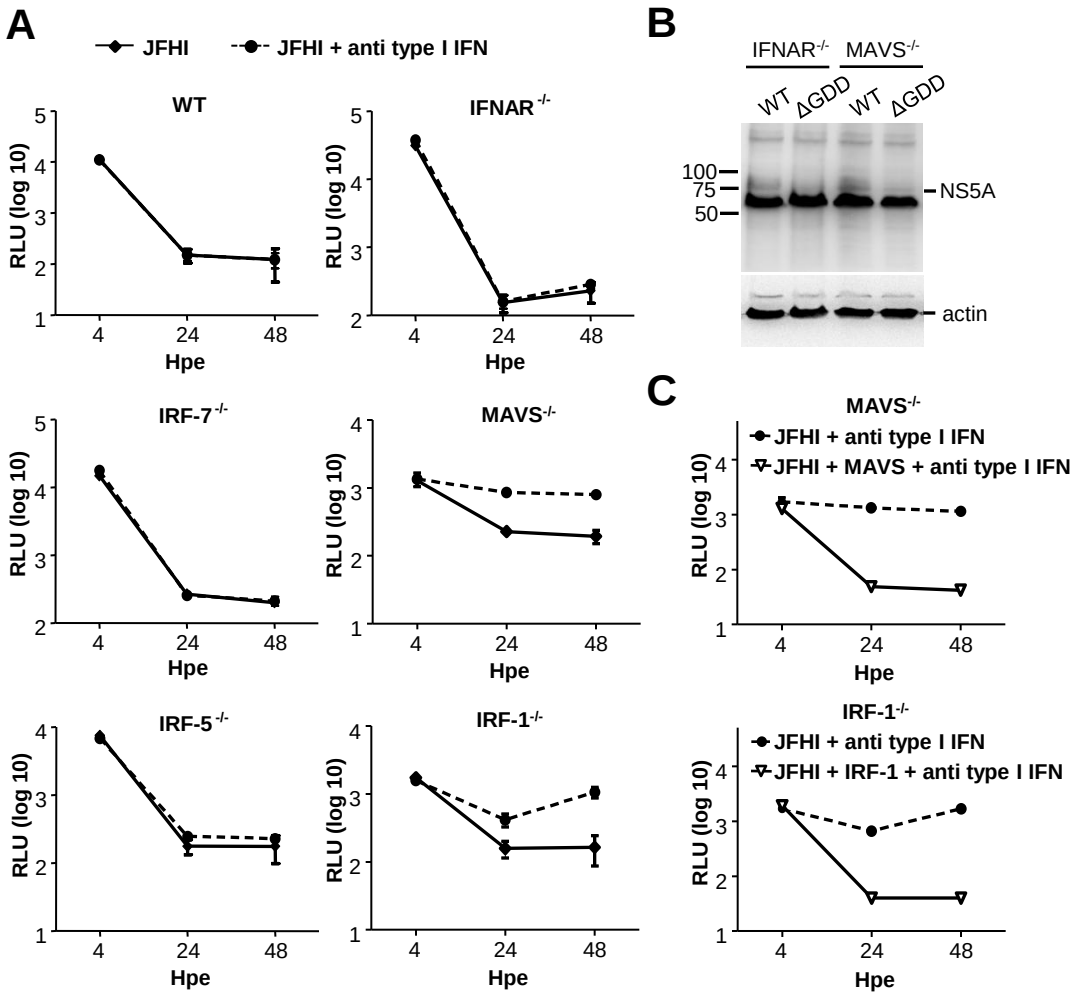
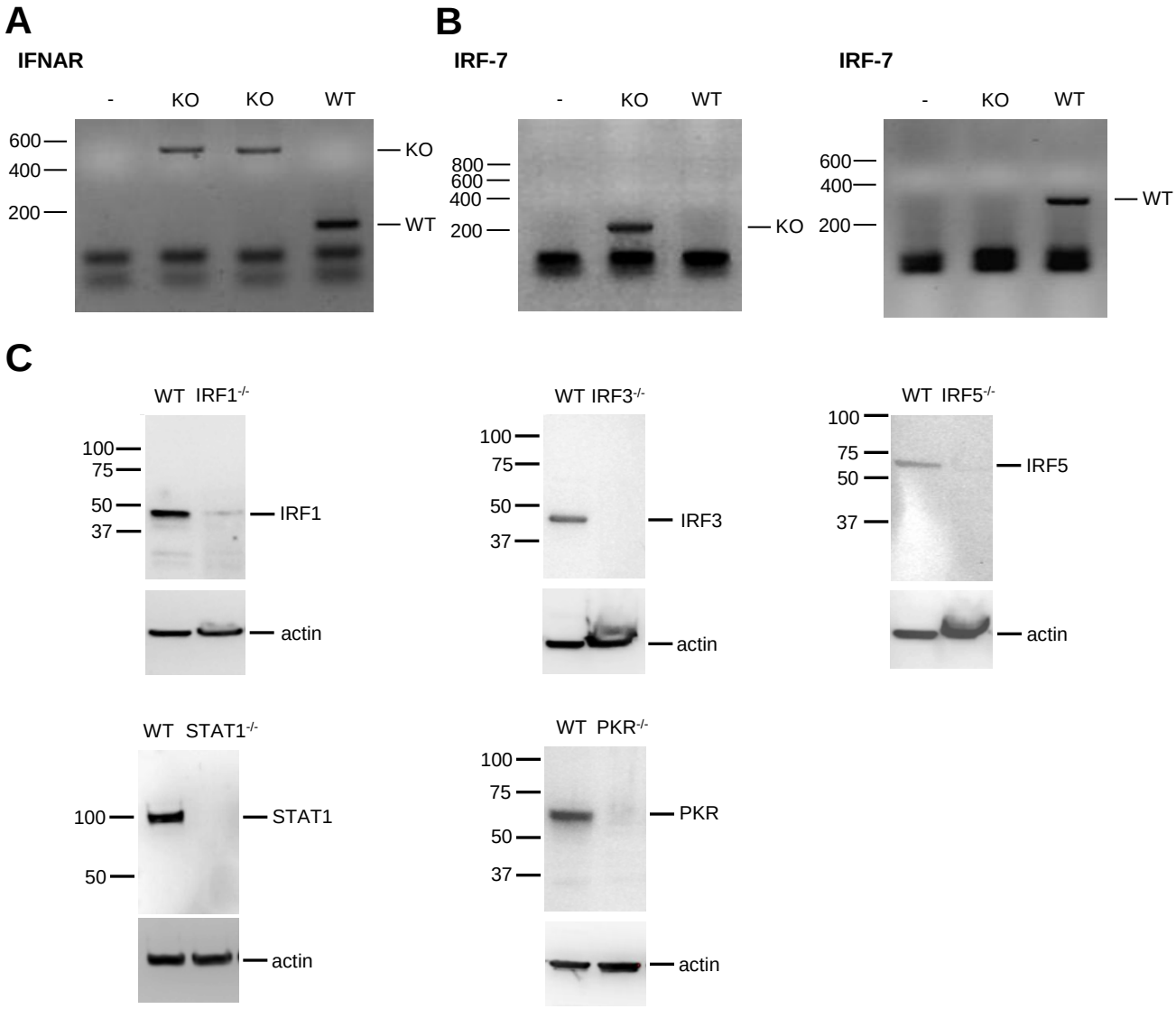

IRF-1-/-
JFH1
JFH1+pIRF1
RLU (log 10)
Hpe
IRF-5-/-
JFH1
JFH1+pIRF5
RLU (log 10)
Hpe
IRF-7-/-
JFH1
JFH1+pIRF7
RLU (log 10)
Hpe
IFNAR-/-
JFH1
JFH1+pIRFs+pPKR
RLU (log 10)
Hpe

Figure 7

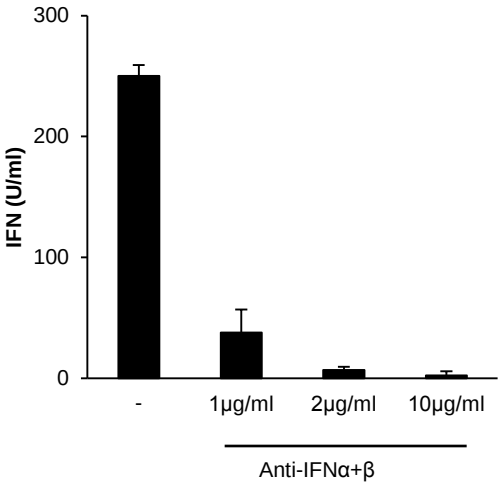

A
JFHI
JFHI + anti type I IFN
WT
IFNAR -/-
IRF-7 -/-
MAVS-/-
IRF-5 -/-
IRF-1-/-
RLU (log 10)
Hpe
4
24
48
B
IFNAR-/-
MAVS-/-
WT
ΔGDD
WT
ΔGDD
100
75
50
NS5A
actin
C
MAVS-/-
JFHI + anti type I IFN
JFHI + MAVS + anti type I IFN
IRF-1-/-
JFHI + anti type I IFN
JFHI + IRF-1 + anti type I IFN

Supplementary Figure 1.



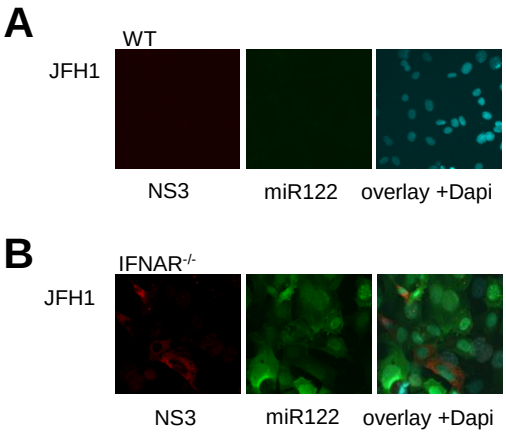
Supplementary Figure 1: Confirmation of the origin of the different knock-out cells.
The different immortalized MEFs were confirmed by genotyping and protein expression analysis. For confirmation of the genotype of IFNAR and IRF-7, genomic DNA was isolated from immortalized IFNAR$^{-/-}$ (A) and IRF-7$^{-/-}$ (B) MEFs and PCRs were performed. C. Cell lysates from immortalized MEFs from different knock outs were prepared and proteins were analyzed by Western blotting using IRF-1, IRF-3, IRF-5, STAT1, and PKR antibodies.

Supplementary Figure 2.



Supplementary Figure 2: Titration of type I IFN depletion antibodies
Mx2 reporter cells were treated with 250 U IFNα/β and the indicated amounts of antibodies against IFNα (4EA1) and IFN-β (7FD3). Luciferase activity was determined after 24h and IFN concentrations were obtained by administering serial dilutions of IFN-β.

Supplementary Figure 3



Supplementary Figure 3: Immunofluorecent staining of WT and miR122 expressing MEFs
Immortalized WT MEFs non-infection with miR122 lentiviral expression vector (A) or Immortalized IFNAR$^{-/-}$ MEFs expressing miR122 combined with GFP by an IRES (B) were electroporated with JFH1 RNA. Fixed cells were stained with a primary antibody against NS3, followed by a secondary anti-mouse Cy5 (red) conjugated antibody. Coverslips were mounted on Mowiol containing DAPI (cyan).