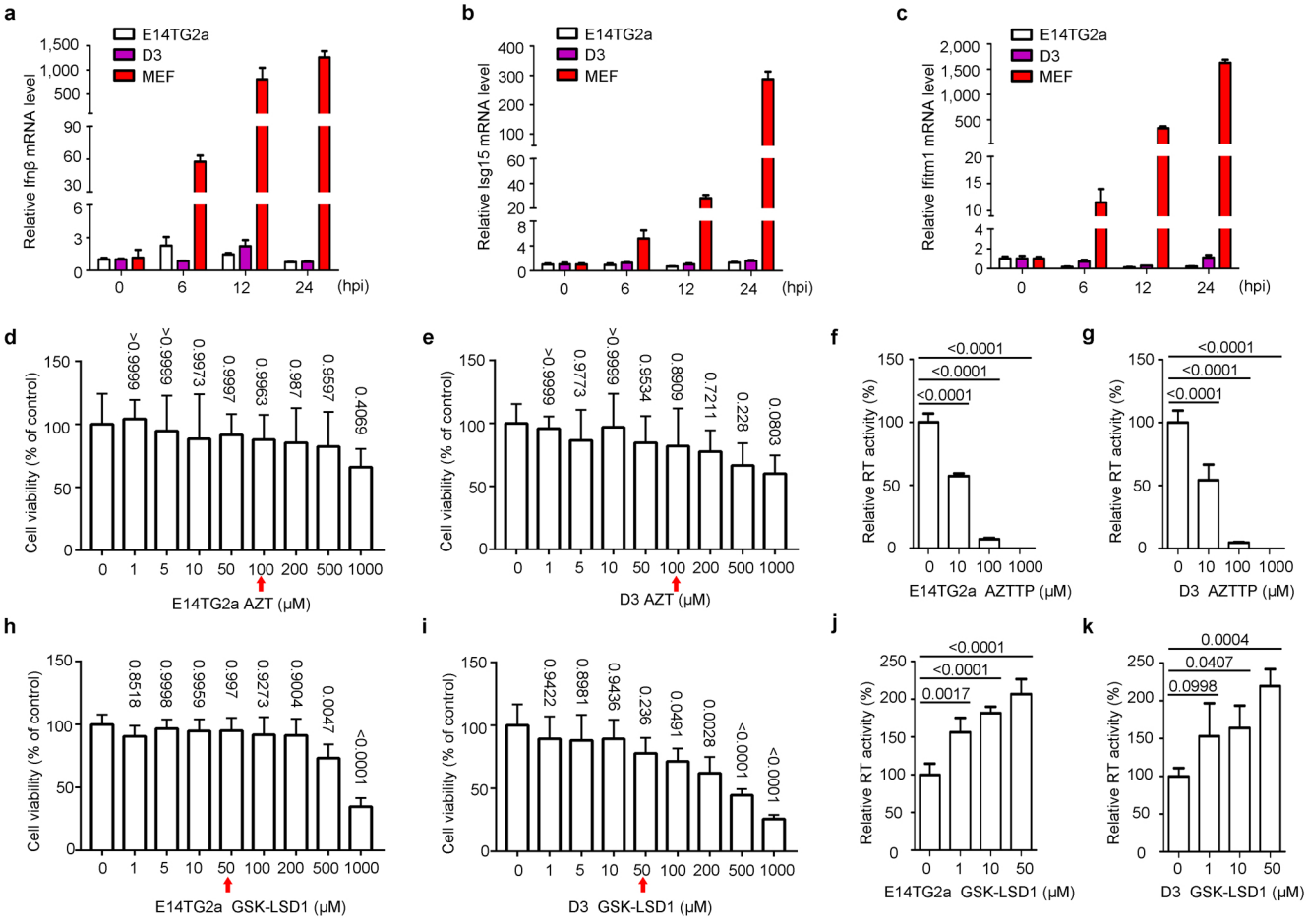
a
E14TG2a
D3
MEF
Relative Ifnβ mRNA level
1,500
1,000
500
90
60
30
6
3
0
0 6 12 24 (hpi)
b
E14TG2a
D3
MEF
Relative Isg15 mRNA level
400
300
200
100
60
40
20
8
4
0
0 6 12 24 (hpi)
c
E14TG2a
D3
MEF
Relative Ifitm1 mRNA level
2,000
1,500
1,000
500
20
15
10
4
2
0
0 6 12 24 (hpi)
d
Cell viability (% of control)
150
100
50
0
>0.9999
>0.9999
0.9973
0.9997
0.9963
0.987
0.9697
0.4069
0 1 5 10 50 100 200 500 1000
E14TG2a AZT (μM)
e
Cell viability (% of control)
>0.9999
0.9773
>0.9999
0.9534
0.8906
0.7211
0.228
0.0803
0 1 5 10 50 100 200 500 1000
D3 AZT (μM)
f
Relative RT activity (%)
<0.0001
<0.0001
<0.0001
150
100
50
0
0 10 100 1000
E14TG2a AZTTP (μM)
g
Relative RT activity (%)
<0.0001
<0.0001
<0.0001
150
100
50
0
0 10 100 1000
D3 AZTTP (μM)
h
Cell viability (% of control)
0.8518
0.9898
0.9959
0.997
0.9273
0.9004
0.0047
<0.0001
150
100
50
0
0 1 5 10 50 100 200 500 1000
E14TG2a GSK-LSD1 (μM)
i
Cell viability (% of control)
0.9422
0.8981
0.9436
0.236
0.0491
0.0028
<0.0001
<0.0001
150
100
50
0
0 1 5 10 50 100 200 500 1000
D3 GSK-LSD1 (μM)
j
Relative RT activity (%)
<0.0001
<0.0001
0.0017
250
200
150
100
50
0
0 1 10 50
E14TG2a GSK-LSD1 (μM)
k
Relative RT activity (%)
0.0004
0.0407
0.0998
250
200
150
100
50
0
0 1 10 50
D3 GSK-LSD1 (μM)

Fig. S1: mESCs are deficient in interferon signaling.

a-c, mESCs (E14TG2a and D3) and MEF cells were infected with EMCV (moi=1) for the indicated time periods. The mRNA levels of the IFNβ (**a**), ISG15 (**b**) and IFITM1 (**c**) were determined by qRT-PCR. **d, e**, The cytotoxicity analysis of AZT to mESCs. E14TG2a (**d**) and D3 (**e**) cells were plated in 96-well plate and treated with increasing concentrations AZT ranging from 0 to 1000 μM for 24 h. Cell viability was tested by using Cell Counting Kit-8 (CCK-8) which measures the activity of mitochondrial dehydrogenase. Red arrows indicate working concentration of AZT. **f, g**, The inhibition of RTase activity by AZTTP, which is the active form of AZT in cells. The cell lysates of E14TG2a (**f**) and D3 (**g**) cells (10 μg) were incubated with AZTTP at the indicated concentrations for 30min. The RT reactions were set up as described in the "Methods" with MS2 RNA as templets. The levels of MS2 cDNA were determined by qRT-PCR with commercial reverse transcriptase, M-MLV, as positive control. The relative RT activity was presented by setting the no drug group as 100%. **h, i**, The cytotoxicity of GSK-LSD1 to mESCs. E14TG2a (**h**) and D3 (**i**) cells were treated with increasing concentrations GSK-LSD1 for 24h. Cell viability was tested by using CCK-8. Red arrows indicate working concentration of GSK-LSD1.**j, k**, The promotion of endogenous RTase activity by GSK-LSD1. E14TG2a (**j**) and D3 (**k**) cells were pre-treated with GSK-LSD1 at the indicated concentrations. Cells were lysed and the RTase activity was measured as described above. The graphs represent means ± SD from three (**a-c**), four (**f, g, j, k**) or five (**d**, **e**, **h**, **i**) independent replicates measured in triplicate. Statistics were calculated by the one-way ANOVA with Tukey's post hoc tests.