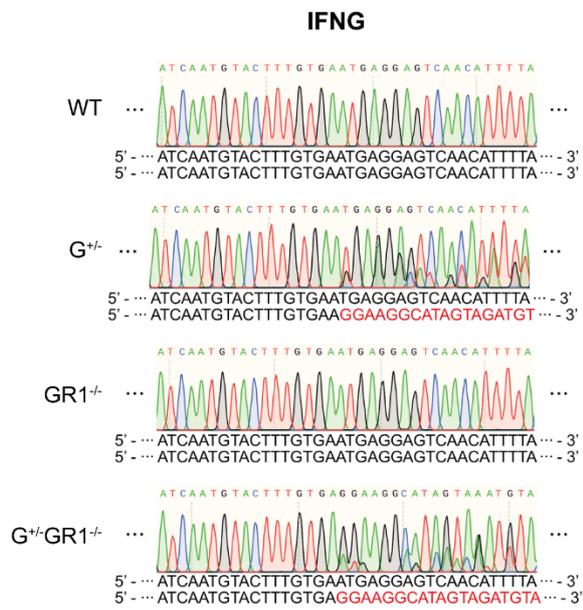
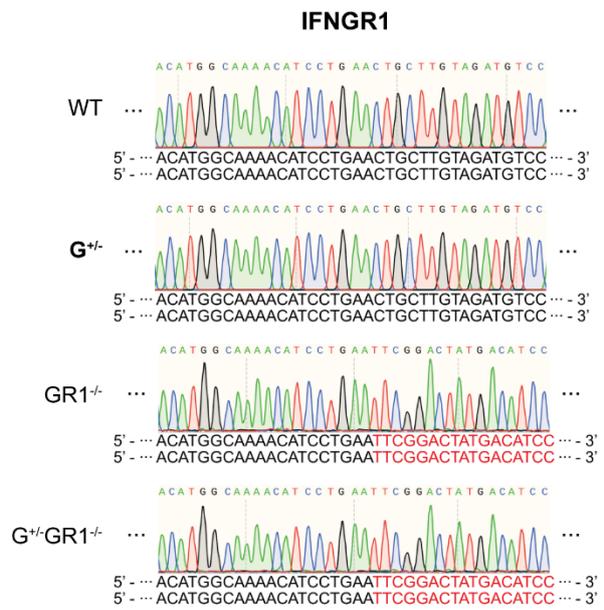
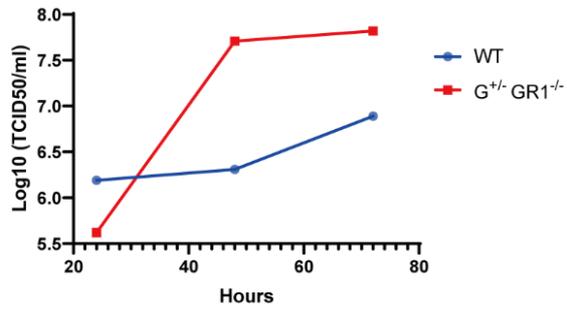
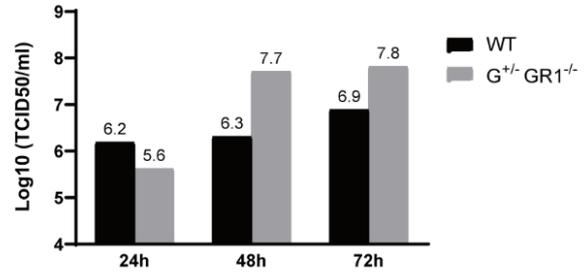
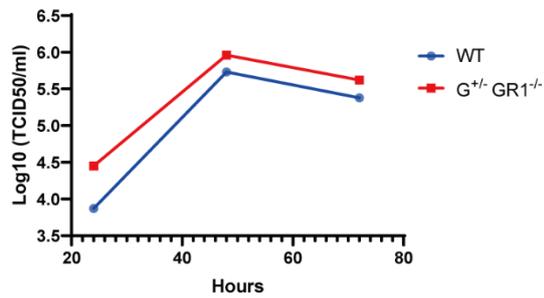
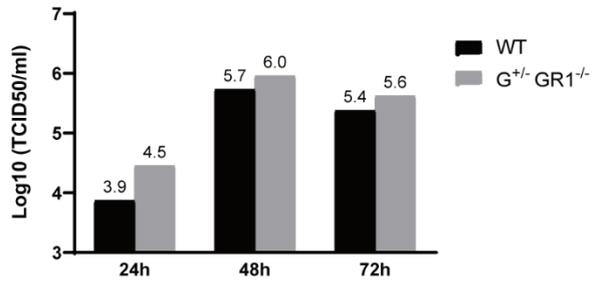


**a****b**

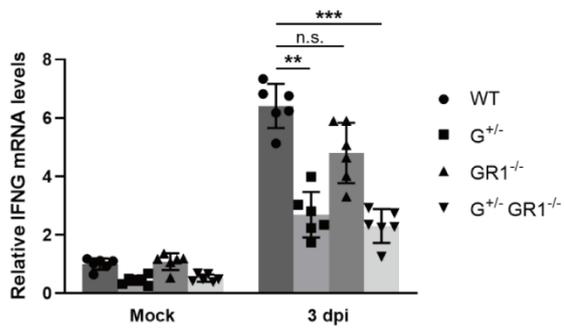
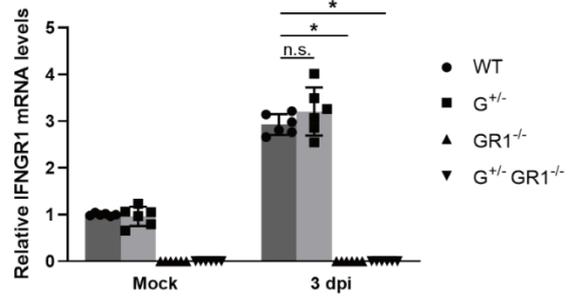
**Supplementary Figure S1. Sanger sequencing analysis of *IFNG*- and *IFNGR1*-knockout Vero cell lines.** (a) Sequencing results of the *IFNG* locus. WT, wild-type Vero cell line;  $G^{+/-}$ , heterozygous deletion of *IFNG* in the Vero cell line;  $GR1^{-/-}$ , homozygous deletion of *IFNGR1* in the Vero cell line;  $G^{+/-}GR1^{-/-}$ , combined deletion of *IFNG* and *IFNGR1* in the Vero cell line. (b) Sequencing results of the *IFNGR1* locus in WT,  $G^{+/-}$ ,  $GR1^{-/-}$ , and  $G^{+/-}GR1^{-/-}$  cell lines.

**a****b**

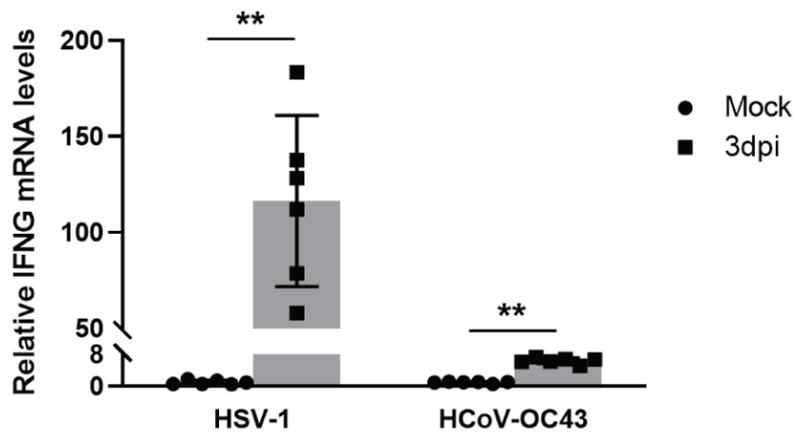
**Supplementary Figure S2. Comparison of HSV-1 virus growth in the wild-type Vero cell line and *IFNG/IFNGR1*-knockout Vero cell line.** (a) HSV-1 growth curves in the wild-type Vero cell line (WT) and *IFNG/IFNGR1*-double-knockout cell line ( $G^{+/-}GR1^{-/-}$ ). Infectious titer was measured at the indicated time points in each cell line by endpoint dilution assay. (b) Bar graph showing TCID<sub>50</sub> values for HSV-1 measured at 24-hour intervals.

**a****b**

**Supplementary Figure S3. Comparison of HCoV-OC43 virus growth in the wild-type Vero cell line and *IFNG/IFNGR1*-knockout Vero cell line. (a)** HSV-1 growth curves in the wild-type Vero cell line (WT) and *IFNG/IFNGR1*-double-knockout cell line (*G<sup>+/-</sup>GR1<sup>-/-</sup>*). Infectious titer was measured at the indicated time points in each cell line by endpoint dilution assay. **(b)** Bar graph showing TCID<sub>50</sub> values for HCoV-OC43 measured at 24-hour intervals.

**a****b**

**Supplementary Figure S4. Relative expression levels of *IFNG* and *IFNGR1* after HCoV-OC43 infection in *IFNG*- and *IFNGR1*-knockout cell lines.** (a) Relative expression levels of *IFNG* in G<sup>+/-</sup>, GR1<sup>-/-</sup>, G<sup>+/-</sup>GR1<sup>-/-</sup> cell lines. *IFNG* mRNA levels were normalized to those of wild-type cells. Results are shown as means  $\pm$  SD of six independent replicates (\* $p$  < 0.05, \*\* $p$  < 0.01, \*\*\* $p$  < 0.001, *n.s.*, not significant). (b) Relative expression levels of *IFNGR1* in G<sup>+/-</sup>, GR1<sup>-/-</sup>, and G<sup>+/-</sup>GR1<sup>-/-</sup> cell lines. *IFNGR1* mRNA levels were normalized to those of wild-type cells.



**Supplementary Figure S5. Relative expression levels of *IFNG* after viral infection.** *IFNG* mRNA levels of infected Vero cells were normalized to those of uninfected cells. *IFNG* mRNA levels were measured by RT-qPCR after 48 hours of HSV-1 infection, and 72 hours of HCoV-OC43, respectively. Results are shown as means  $\pm$  SD of six independent replicates (\*\* $p < 0.01$ ).

**Supplementary Table S1. Deleted sequences in *IFNG*- and *IFNGR1*-knockout cell lines**

<b>Genotype</b>	<b><i>IFNG</i> Sequences</b>	<b>Mutations</b>
Wild-type	5' - ...CTTTGTGAATGAGGAGTC...TACACTACAGGAAGGCAT... - 3'	
G <sup>+/-</sup>	5' - ...CTTTGTGAA-----GGAAGGCAT... - 3'	1,405 bp deletion ( <i>IFNG</i> Δexon1)
GR1 <sup>-/-</sup>	5' - ...CTTTGTGAATGAGGAGTC...TACACTACAGGAAGGCAT... - 3'	
G <sup>+/-</sup> GR1 <sup>-/-</sup>	5' - ...CTTTGTGA-----GGAAGGCAT... - 3'	1,406 bp deletion ( <i>IFNG</i> Δexon1)
<b>Genotype</b>	<b><i>IFNGR1</i> Sequences</b>	<b>Mutations</b>
Wild-type	5' - ...CATCCTGAACTGCTTGTA...GATCCTGTTTTCGGACTAT... - 3'	
G <sup>+/-</sup>	5' - ...CATCCTGAACTGCTTGTA...GATCCTGTTTTCGGACTAT... - 3'	
GR1 <sup>-/-</sup>	5' - ...CATCCTGAA-----TTCGGACTAT... - 3'	1,651 bp deletion ( <i>IFNGR1</i> Δexon3)
G <sup>+/-</sup> GR1 <sup>-/-</sup>	5' - ...CATCCTGAA-----TTCGGACTAT... - 3'	1,651 bp deletion ( <i>IFNGR1</i> Δexon3)

**Supplementary Table S2. gRNA sequences for targeting *IFNG* and *IFNGR1***

<b>Target gene</b>	<b>gRNA sequences with PAM</b>	<b>Target region</b>
<i>IFNG</i>	5'-GATCAATGTACTTTGTGAATG AGG-3'	Exon 1
	5'-GTGACGTAATACTACTACAGGA AGG-3'	Exon 1 ~ Exon 2
<i>IFNGR1</i>	5'-GTGGACATCTACAAGCAGTTC AGG-3'	Exon 2 ~ Exon 3
	5'-GGATGTCATAGTCCGAAAAC AGG-3'	Exon 3 ~ Exon 4

**Supplementary Table S3. Target-specific primers for PCR-based genotyping**

<b>Target gene</b>	<b>Primer sequences</b>		<b>PCR product size</b>
<i>IFNG</i>	Forward	5'-CCTGTGTGGCTTGTATTATATTTC-3'	1,831 bp
	Reverse	5'-GTTCAACAAAGCTGATGATACTCC-3'	
<i>IFNGR1</i>	Forward	5'-GTACCAGATCATGCCACAGG-3'	2,061 bp
	Reverse	5'-ATGCAGACGGTGTGGTAATC-3'	

**Supplementary Table S4. Target-specific primers for Sanger sequencing**

Target gene	Primer sequences	
<i>IFNG</i>	Forward-1	5'-CCTGTGTGGCTTGTATTATATTTTC-3'
	Forward-2	5'-CAAATGCCACAAAACCTTAG-3'
	Forward-3	5'-GGTGAGAACTCATTTCAGATG-3'
	Reverse 1	5'-GTTCAACAAAGCTGATGATACTCC-3'
<i>IFNGR1</i>	Forward-1	5'-GTACCAGATCATGCCACAGG-3'
	Forward-2	5'-AGGCTGAGGCAGGAGAATGG-3'
	Forward-3	5'-TCTGATCACGTTGGTGATCC-3'
	Reverse-1	5'-ATGCAGACGGTGTGGTAATC-3'

**Supplementary Table S5. Gene-specific primers for RT-qPCR analyses**

<b>Target gene</b>	<b>Primer sequences</b>	
<i>IFNG</i>	Forward	5'-TGGAAAGAGGAGAGTGACAG-3'
	Reverse	5'-TCAGCTTTTTCGAAGTCATCC-3'
<i>IFNGR1</i>	Forward	5'-AACTATGGTGTTAAGAATGC-3'
	Reverse	5'-GGTCCAATTTTTCCATCTCG-3'
<i>TNF-<math>\alpha</math></i>	Forward	5'-GCTGCACTTTGGAGTGATCG-3'
	Reverse	5'-CCAGCTGGTTATCTGTCAGC-3'
<i>IL-15</i>	Forward	5'-CCCAGTTGCAAGGTAACAGC-3'
	Reverse	5'-TCCTCACATTCTTTGCATCC-3'
<i>IRF1</i>	Forward	5'-CCATTCACACAGGCCGATAC-3'
	Reverse	5'-GGAATCCCCACATGACTTCC-3'
<i>IL-6</i>	Forward	5'-AAGGAGACATGTAACAGGAG-3'
	Reverse	5'-CTAGGTATACCTCAAACCTCC-3'
<i>Nectin-1</i>	Forward	5'-CTGCAGTATTAGTGTCTCC-3'
	Reverse	5'-GTGCAGGATAAAGGAGATGC-3'
<i>TLR2</i>	Forward	5'-CGAATACACAGTGTAACAGG-3'
	Reverse	5'-GAAAAGAGTCAAGTTGCTCC-3'
<i>TLR3</i>	Forward	5'-GACAAACCTCACTATGCTCG-3'
	Reverse	5'-CCGTTTCAAATTCAGGTACC-3'
<i>TLR7</i>	Forward	5'-TGAGTCTCTTAGAACTCTGG-3'
	Reverse	5'-GGCATACCATCAAAAACCTCC-3'