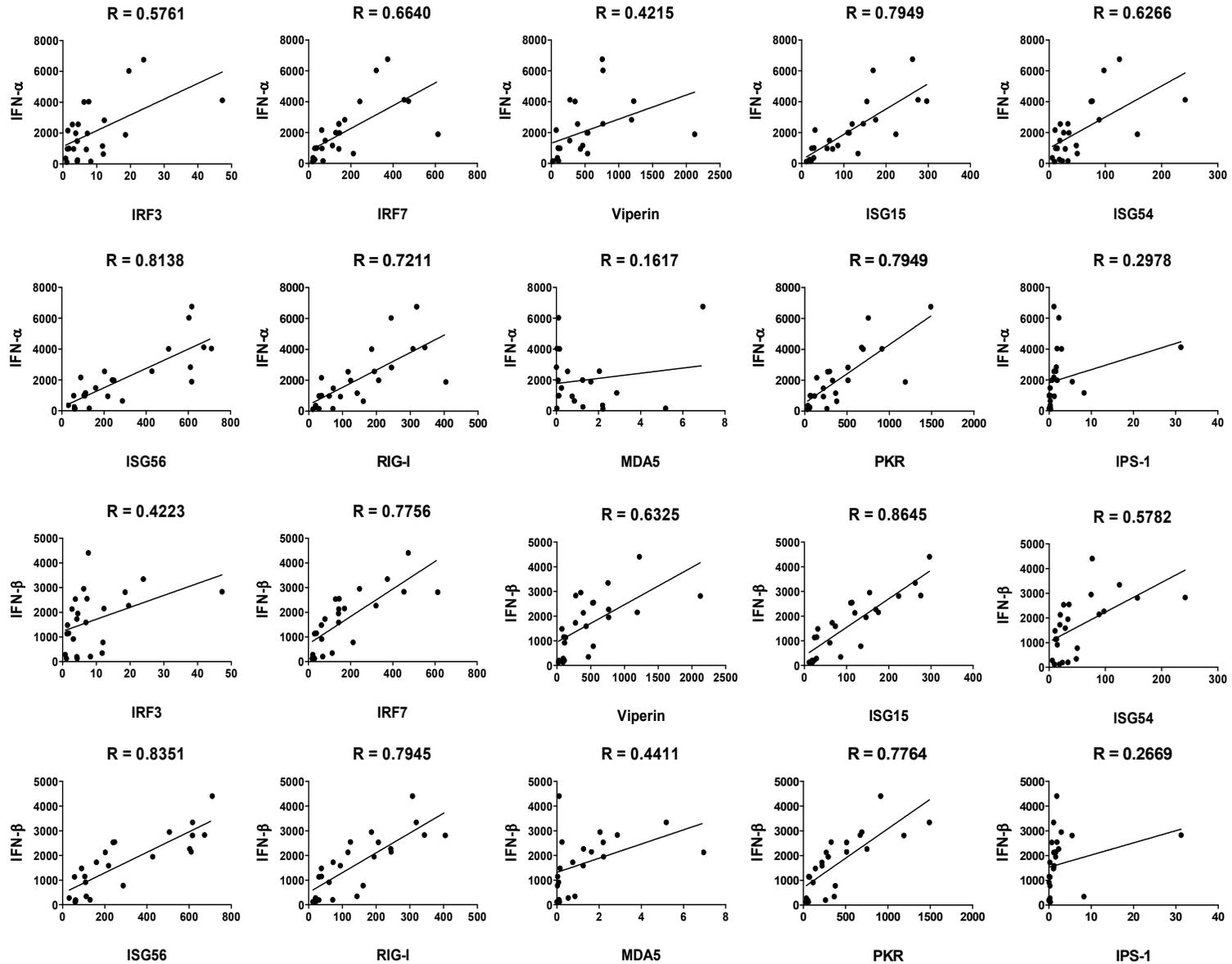


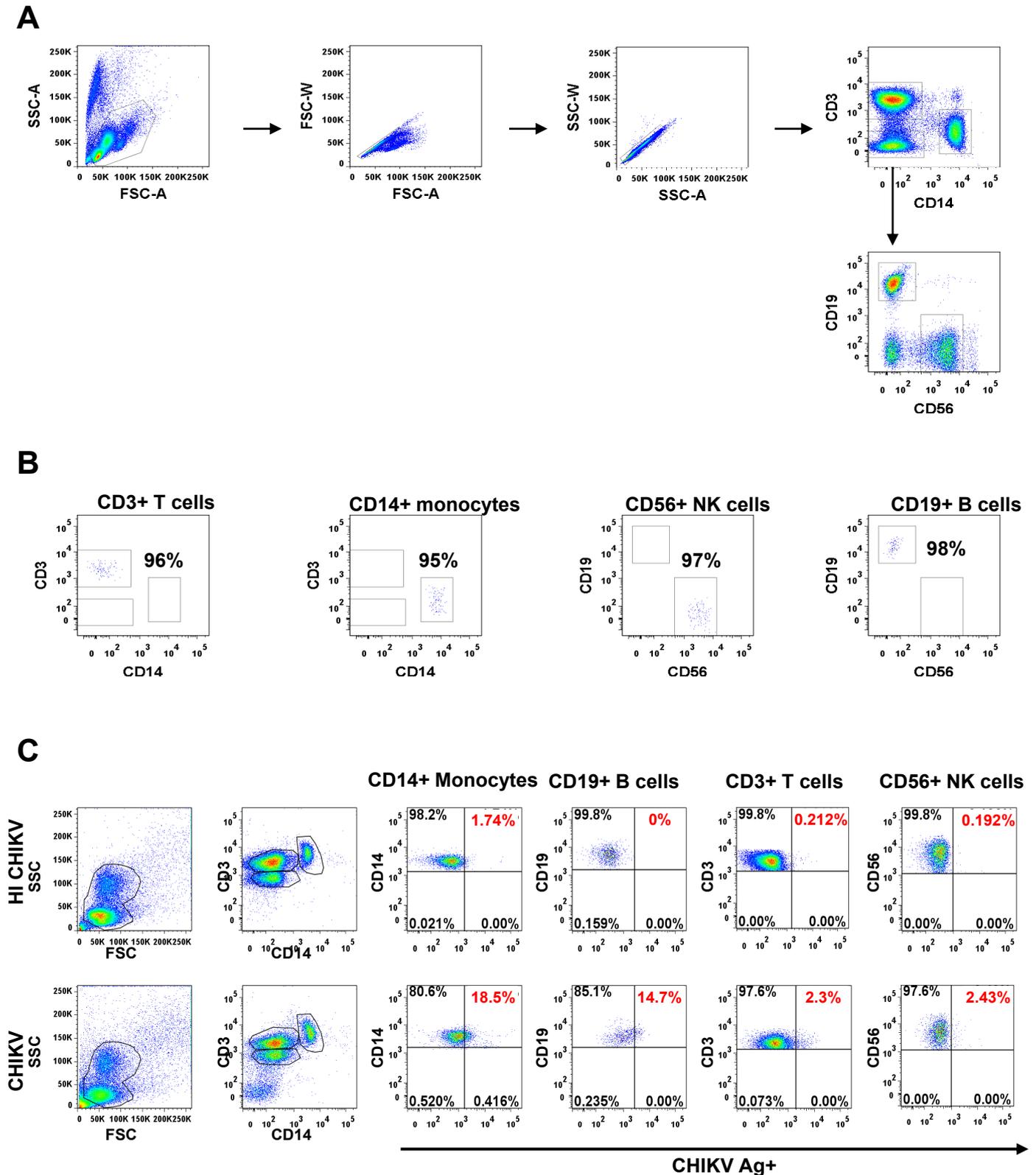
**Supplemental Figure 1**

Transcriptional profiles of innate immune response in CHIKV-infected patients. Expression profiles of IFN- $\alpha$ , IFN- $\beta$ , Viperin, IRF7, IRF3, ISG15, ISG54, ISG56, RIG-I, MDA5, IPS-1 and PKR in PBMCs of CHIKV-infected patients (n = 24) at various time points of the disease were analyzed by qRT-PCR. Data obtained were normalized to GAPDH signal and presented as expression relative to the mean of healthy controls (n = 10). Data are presented in box-and-whisker plot to indicate the ranges. \*  $P < 0.05$ ; \*\*  $P < 0.01$ ; \*\*\*  $P < 0.001$  by Kruskal Wallis test with Dunn's post test.



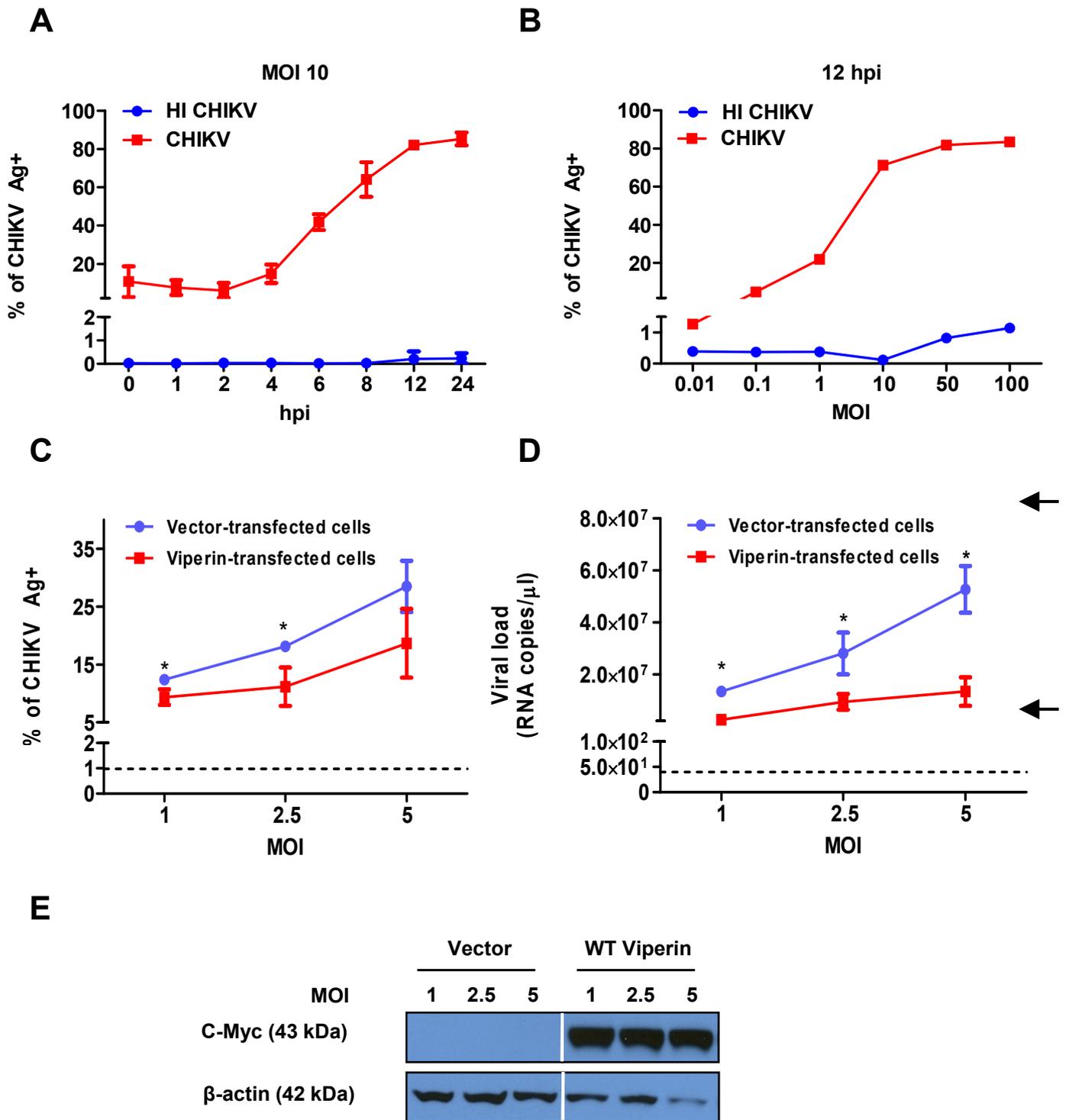
**Supplemental Figure 2**

Correlation analysis of various genes during acute phase of the disease in CHIKV-infected patients. Correlations between the relative expression of IFN-α or IFN-β to the relative expression of either IRF3, IRF7, Viperin, ISG15, ISG54, ISG56, RIG-I, MDA5, PKR and IPS-1 in CHIKV-infected patients (n = 24) were analyzed during the acute phase of the infection. (R) Pearson's correlation coefficient values are as indicated .



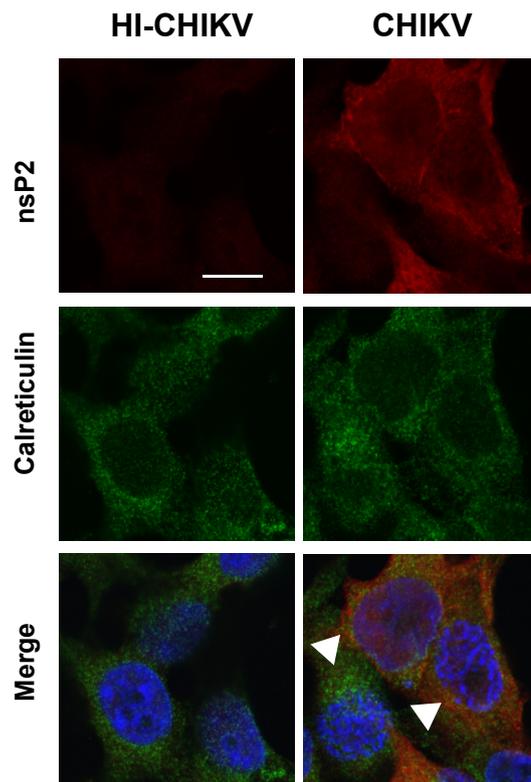
### Supplemental Figure 3

(A) FACS live-cell sorting strategy for PBMC subsets *after* *in vitro* CHIKV infection in human whole blood. Whole blood was collected from healthy donors ( $n = 3$ ) and the total leukocyte count was determined before performing infection with either HI CHIKV as a control or CHIKV (MOI 10) for 12 h. Total PBMCs isolated were stained with CD3-FITC, CD14-PerCP-Cy5.5, CD19-PECy7 and CD56-PE antibodies and sorted with FACS Aria. In the PBMC gate, doublet exclusion was sequentially performed for FSC (FSC-W vs FSC-A plot) and SSC (SSC-W and SSC-A plot). Subsequent gates were designed to isolate the CD3+ T, and CD14+ monocytes, B cells (CD3- CD14- CD19+) and NK cells (CD3- CD14- CD56+). (B) Purity of the sorted PBMC subsets. After sorting as described in (A), each isolated fraction was analyzed by FACS ARIA. % of purity of each sorted subset is as indicated on each gate. (C) A fraction of unsorted PBMCs from (A) was used for flow cytometry analysis as described to determine the % of CHIKV Ag+ in the PBMC subset indicated. Representative dot plots from 1 donor.



#### Supplemental Figure 4

Effect of Viperin over-expression on CHIKV infectivity in HEK 293T cells. (A) Kinetics of CHIKV infection in HEK 293T cells. Cells were infected with CHIKV (MOI 10) or HI CHIKV (control) and harvested at the specific indicated time for analysis by FACS to determine the % of CHIKV Ag<sup>+</sup> cells. Data are presented as mean  $\pm$  SD of % of CHIKV Ag<sup>+</sup> cells, n = 3. (B) HEK 293T cells were infected with CHIKV or HI CHIKV (control) at the different MOI indicated for 12 h and analyzed by FACS for % of CHIKV Ag<sup>+</sup> cells, n = 1. (C) HEK 293T cells were transfected with vector or myc-tagged WT Viperin for 24 h before infection with either CHIKV or HI CHIKV (control) at the different MOI indicated. Cells were harvested at 12 hpi and analyzed by FACS for % of CHIKV Ag<sup>+</sup> cells. Data are presented as mean  $\pm$  SD of % of CHIKV Ag<sup>+</sup> cells, n = 3. \*  $P < 0.05$  by unpaired T test. Horizontal dotted line represents the mean % of CHIKV Ag<sup>+</sup> cells detected in HI CHIKV-infected control. (D) Viral load was quantified using qRT-PCR using specific primers against the negative-strand nsP1 RNA. Data are expressed as mean  $\pm$  SD, n = 3. \*  $P < 0.05$  by unpaired T test. Horizontal dotted line represents the mean amount of RNA detected in HI CHIKV-infected control. (E) Viperin expression was detected with anti-c-Myc antibody (top panel). Detection of  $\alpha$ -actin expression serves as a loading control (bottom panel). All adjacent gel lanes are from the same gel and blot but their order are rearranged for clarity as indicated by the white lines between the lanes.



**Supplemental Figure 5**

Subcellular localization of CHIKV nsP2 and ER during CHIKV infection. HEK 293T cells were infected with either HI CHIKV or CHIKV (MOI 2.5). Cells were fixed at 12 hpi and stained for nsP2 (red), calreticulin (green) and DAPI. Images are representative of 2 independent experiments. Scale bar, 10  $\mu$ m. Co-localization is indicated by arrows.

## Supplemental Material

### Supplemental Table 1

Primer used for qRT-PCR.

Species	Primer name	Sequence
Human	IFN- $\alpha$ F	AGA ATC TCT CCT TTC TCC TG
	IFN- $\alpha$ R	TCT GAC AAC CTC CCA GGC AC
	IFN- $\beta$ F	AAC TTT GAC ATC CCT GAG GAG ATT AAG CAG
	IFN- $\beta$ R	GAC TAT GGT CCA GGC ACA GTG ACT GTA CTC
	IRF3 F	TATG CCC TCT GGT TCT GTG TGG GGG AGT CA
	IRF3 R	GAG TGG GTG GCT GTT GGA AAT GTG CAG GTC
	IRF7 F	CTC CCC ACG CTA TAC CAT CT
	IRF7 R	AAG GAA GCA CTC GAT GTC GT
	RIG-I F	GCT CCT CCA GTG TCT TCT CAG
	RIG-I R	TGA CAA AGT GCT CAC AGT TCC
	MDA5 F	CTG TTT ACA TTG CCA AGG ATC
	MDA5 R	ACA CCA GCA TCT TCT CCA TTT
	ISG15 F	GAC CTG ACG GTG AAG ATG CT
	ISG15 R	GCC CTT GTT ATT CCT CAC CA
	ISG54 F	CTG GTC ACC TGG GGA AAC TA
ISG54 R	GAG CCT TCT CAA AGC ACA CC	
ISG56 F	GCA GCC AAG TTT TAC CGA AG	
ISG56 R	CAC CTC AAA TGT GGG CTT TT	
IPS-1 F	GCA GAG AGA AGG AGC CAA GTT	
IPS-1 R	GGA AGG AGA CAG ATG GAG ACA	
PKR F	GTG ATG CAG CTC ACA ATG CT	
PKR R	GGC ACT GTA AAA TGG GTG CT	
Viperin F	CTT TTG CTG GGA AGC TCT TG	
Viperin R	GTC TCA TCT GGC CCT CTC AG	
GAPDH F	CCA CAT CGC TCA GAC ACC AT	
GAPDH R	GGC AAC AAT ATC CAC TTT ACC AGA GT	
Mouse	IFN- $\beta$ F	CCC TAT GGA GAT GAC GGA GA
	IFN- $\beta$ R	TCC CAC GTC AAT CTT TCC TC
	IFN- $\alpha$ F	TCA TTC TGC AAT GAC CTC CA
	IFN- $\alpha$ R	CAG GGG CTG GTT TCT TCT C
	IRF3 F	GGG GAG CCT CTT CAC TGA AAA CCG TGGA
IRF3 R	TAA CCA CCA GCC TAG ACG CAG TCG ACA GCA	
IRF7 F	GAA GAC CCT GAT CCT GGT GA	
IRF7 R	CCA GGT CCA TGA GGAAGT GT	
ISG15 F	TGG GAC CTA AAG GTG AAG ATG CTG	
ISG15 R	TCA GGC GCA AAT GCT TGA TCAC	

<b>Species</b>	<b>Primer name</b>	<b>Sequence</b>
<b>Mouse</b>	<b>Viperin F</b>	GAC GCT CCA AGA ATG TTT CA
	<b>Viperin R</b>	GAC GCT CCA AGA ATG TTT CA
	<b>RIG-I F</b>	TAC AAT AAT ATG TGC CCC TAC TGG T
	<b>RIG-I R</b>	TCT TTC AAA ATA TCG TGA GAA CAC A
	<b>MDA5 F</b>	ACT TCT GAT TAA CGA TGT CTT GGA C
	<b>MDA5 R</b>	CCT GTT AGT TCT TGG AAT AGT GCA T
	<b>IPS-1 F</b>	AGG GTG GGA TGG ACT GAG AT
	<b>IPS-1 R</b>	CTA GGG GAG AAT GAG GTC GG
	<b>GAPDH F</b>	TTG AGGT CAA TGA AGG GGT C
	<b>GAPDH R</b>	TCG TCC CGT AGA CAA AAT GG

## **Supplemental legends**

### **Supplemental movie 1**

CHIKV infection in HEK 293T cells expressing GFP only. Cells were transiently transfected with GFP and seeded on fibronectin-coated m-slide 8 well (ibidi) before being infected with mCherry-tagged CHIKV (MOI 10). CHIKV infection was monitored by time-lapse confocal microscopy (Fluoview FV1000; Olympus) using 20x NA 0.75 objective. Images were collected as stacks using FV1000-ASW software at 1 frame/15 min for 16 h and presented as movies (15 frames per s). Top left panel: GFP, top right panel: mCherry, bottom left panel: phase contrast and bottom right panel: merge.

### **Supplemental movie 2**

CHIKV infection in HEK 293T cells expressing GFP-WT viperin. Cells were transiently transfected with GFP-WT Viperin and seeded on fibronectin-coated m-slide 8 well (ibidi) before being infected with mCherry-tagged CHIKV (MOI 10). CHIKV infection was monitored by time-lapse confocal microscopy (Fluoview FV1000; Olympus) using 20x NA 0.75 objective. Images were

collected as stacks using FV1000-ASW software at 1 frame/15 min for 16 h and presented as movies (15 frames per s). Top left panel: GFP, top right panel: mCherry, bottom left panel: phase contrast and bottom right panel: merge.

### **Supplemental movie 3**

CHIKV infection in HEK 293T cells expressing GFP-1-42 viperin. Cells were transiently transfected with GFP-1-42 Viperin and seeded on fibronectin-coated m-slide 8 well (ibidi) before being infected with mCherry-tagged CHIKV (MOI 10). CHIKV infection was monitored by time-lapse confocal microscopy (Fluoview FV1000; Olympus) using 20x NA 0.75 objective. Images were collected as stacks using FV1000-ASW software at 1 frame/15 min for 16 h and presented as movies (15 frames per s). Top left panel: GFP, top right panel: mCherry, bottom left panel: phase contrast and bottom right panel: merge.