

Supporting Fig. S1. HCV inhibitor causes loss of $\Delta\Psi_m$ and induces mitochondrial fission.

(A) FACS analysis showing restoration of HCV-inhibitor-induced loss of $\Delta\Psi_m$ in the presence of G-Rg3. At 24 hours after treatment with an HCV inhibitor (Sofosbuvir, Telaprevir, or Boceprevir) or G-Rg3 (100 μ M), Huh7 cells were stained with JC-1 dye and then analyzed on a flow cytometer. The graph indicates that G-Rg3 restored the HCV-induced decrease in the level of $\Delta\Psi_m$ (right panel). CCCP was used as a control for mitochondrial depolarization. (B) Confocal-microscope images showing mitochondrial fission in HCV-inhibitor-treated cells. At 24 hours after treatment with an HCV inhibitor (Sofosbuvir, Telaprevir, or Boceprevir), Huh7 cells were stained with MitoTracker (Mito, white). Treated cells (+) are marked. The cells in the zoomed images exhibit a fragmented mitochondrial structure. (C) The graph shows the mitochondrial length in HCV-inhibitor-treated cells.

Supporting Fig. S2. HCV inhibitor induces mitochondrial translocation of p-Drp1.

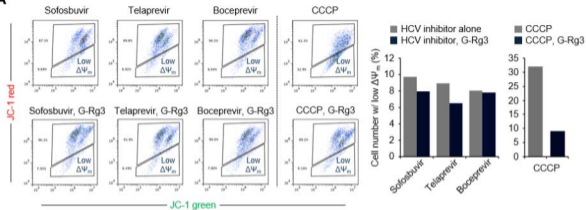
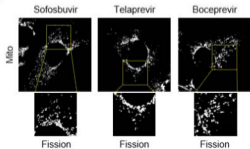
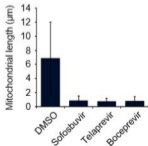
Confocal-microscope image showing p-Drp1 translocation to mitochondria in the presence of Telaprevir and Boceprevir. At 24 hours after treatment with Telaprevir (200 nM, EC_{50}) or Boceprevir (200 nM, EC_{50}), Huh7 cells were prestained with MitoTracker (Mito, red) and then immunostained with an antibody against p-Drp1 (green). Nuclei are demarcated with white dotted circles. Treated cells (+) are marked. In the zoomed images, yellow spots indicate the colocalization of mitochondria and p-Drp1 in cells treated with Telaprevir or Boceprevir.

Supporting Fig. S3. G-Rg3 does not affect IFN response upon HCV infection.

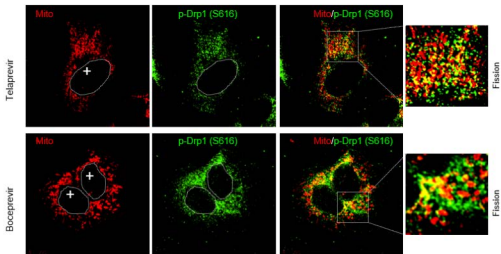
Interferon responses were measured by dual-luciferase assays using reporter plasmids containing interferon-stimulated response element (ISRE). Huh7 cells were transfected with two reporter

plasmids (the one with ISRE promoter followed by firefly luciferase and another with CMV promoter expressing *Renilla* luciferase). After 6 hours, cells were infected with HCV, then treated with G-Rg3 (100 μ M). Interferon responses were measured 24 hrs post-infection. Relative fold change was calculated by normalization of HCV-infected cells to uninfected cells.

Supplementary Fig. 1

A

B

C


Supplementary Fig. 2



Supplementary Fig. 3

