SUPPLEMENTAL MATERIALS

Supplemental Methods:

Measurement of the contents of IL-1β, IL-6 and TNF-α in serum and supernatant

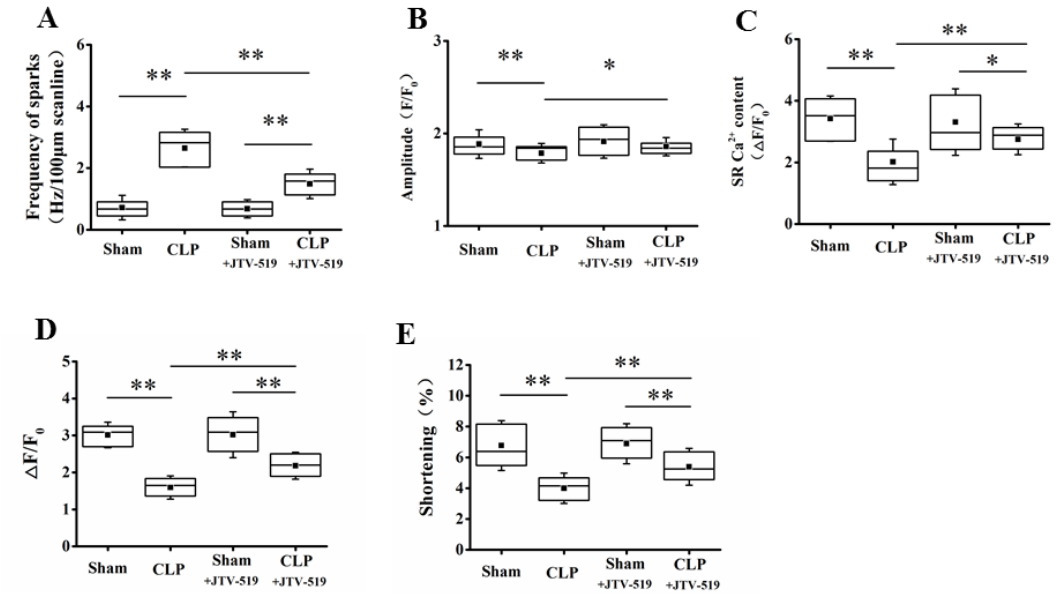
The serum was collected from sham or CLP (cecal ligation and puncture) mice with or without JTV-519 treatment (*in vivo*) under deep anesthesia with pentobarbital sodium (50 mg/kg, i.p). Briefly, the whole blood (~1 ml) was collected from mouse heart under thoracotomy, stood at 4℃ overnight to allow blood coagulation and centrifuged at 2000 g for 15 min. The serum was collected and stored at -80℃ until use.

The cardiomyocytes isolated from sham or CLP mice were seeded on a 96-well plate at the density of $2.5x10^4$ cells per well in 200 μl HEPES-buffered external solution (in mM: 137 NaCl, 5.4 KCl, 1 $CaCl_2$, 1.2$MgCl_2$, 1.2 NaH_2PO_4, 20 glucose and 20 HEPES, pH 7.4) containing JTV-519 (1 μM) or not. The cells were cultured in the incubator (5% CO2) at 37℃ for four hours. Thereafter, the cultural solutions from the four groups (Sham, CLP, Sham+JTV-519 and CLP+JTV-519) were centrifuged at 12000g for 15 min at 4℃. The supernatants were then collected and stored at -80℃ until use.

The contents of IL-1β, IL-6 and TNF-α in serum or supernatants were measured by Milliplex following the manufacturer's instruction (1).

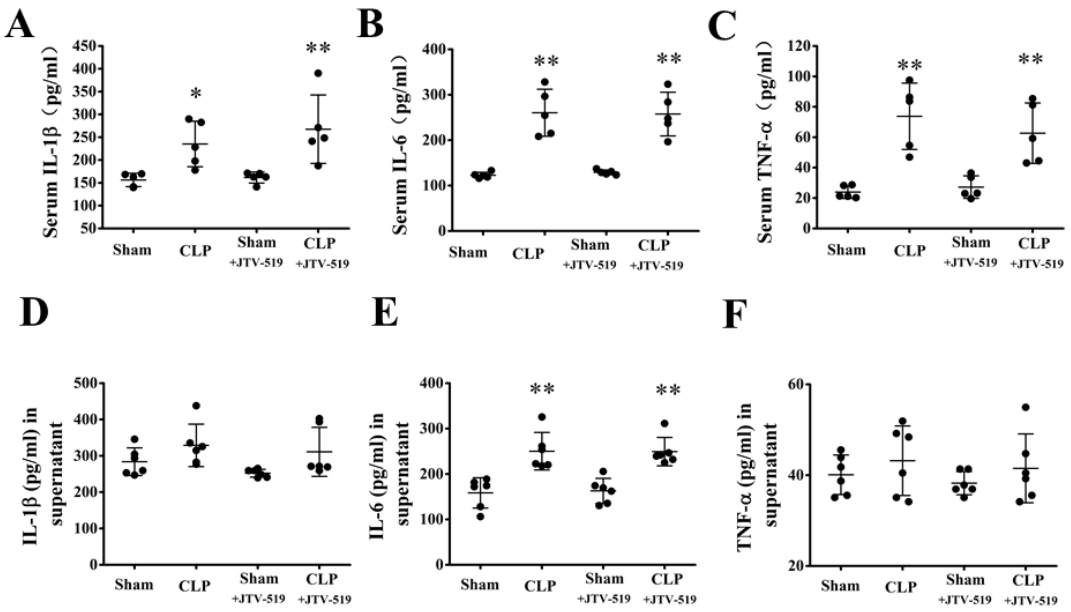
References:

1. Liu, J., Wang, J., Luo, H., Li, Z., Zhong, T., Tang, J., and Jiang, Y. (2017)Screening cytokine/chemokine profiles in serum and organs from an endotoxic shock mouse model by LiquiChip. *Sci China Life Sci* doi: 10.1007/s11427-016-9016-6. [Epub ahead of print]



Supplemental Figure 1. JTV-519 improved Ca^{2+} handling and myocyte contraction in

septic mouse cardiomyocytes. A, averages of the frequency of Ca^{2+} sparks in cardiomyocytes isolated from Sham, CLP (cecal ligation and puncture), Sham+JTV-519, and CLP+ JTV-519 mice. JTV-519 was applied intraperitoneally (i.v., 0.5mg/kg/h) 2 h before the operation of sham or CLP. B and C, statistics of the amplitude (F/F_0) of Ca^{2+} sparks (B, n=32-51 in each group) and SR Ca^{2+} content (C, n=15 to 26 in each group) in the four groups. D and E, images of AP-elicited Ca^{2+} transient and the averages of the amplitude of Ca^{2+} transient (D) and maximum cell shortening (E, n=42 to 67 in each group). **p*<0.05, ***p*<0.01.



Supplemental Figure 2. Effects JTV-519 treatment on the productions of IL-1β, IL-6 and TNF-α. A-C, the concentrations of IL-1β (A), IL-6 (B) and TNF-α (C) (n=5 in each group) in the serum of sham or CLP mice with or without JTV-519 treatment. JTV-519 was applied intraperitoneally (i.v., 0.5mg/kg/h) 2 h before the operation of sham or CLP. D-F, the concentrations of IL-1β (D), IL-6 (E) and TNF-α (F) (n=6 in each group) in the supernatants of cardiomyocytes isolated from sham or CLP mice with or without JTV-519 treatment. JTV-519 (1 μM) was incubated with cardiomyocytes in HEPES-buffered external solution. **p*<0.05.***p*<0.01. *vs* control.