

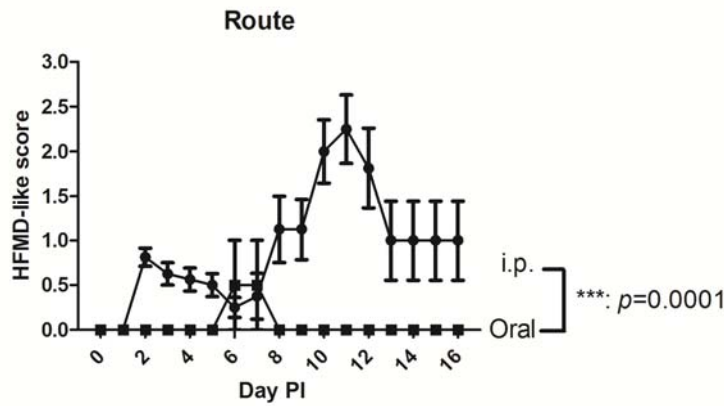
## Supplemental Material

**Table S1 .Comparisons between NOD/SCID and *stat-1* KO mice**

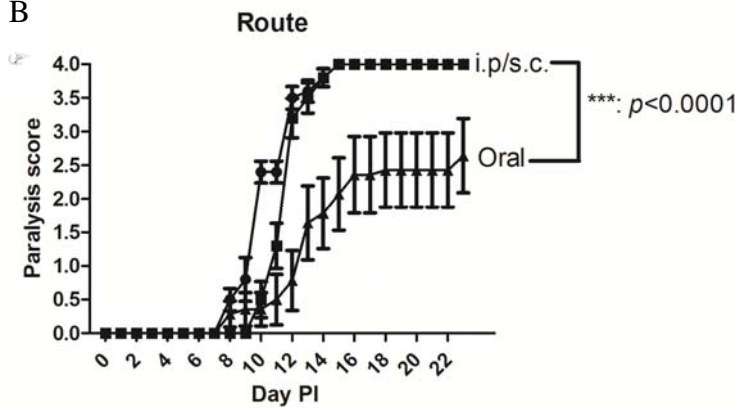
	NOD/SCID	<i>stat-1</i> KO
Intestine	Normal	Dystrophy of villi
Muscle	Destructive structure, severe inflammation and VP1 expression	Dystrophy of muscle fiber, no inflammation and VP1 expression
Brain	Normal	VP1 expression in brainstem and purkinje cell
Spinal cord	Normal	Microglial cell proliferation with VP1 and IBA-1 expression
Skin	Skin rash or hair loss with VP1 expression	Normal
Death	Yes	No

**Fig.S1**

A

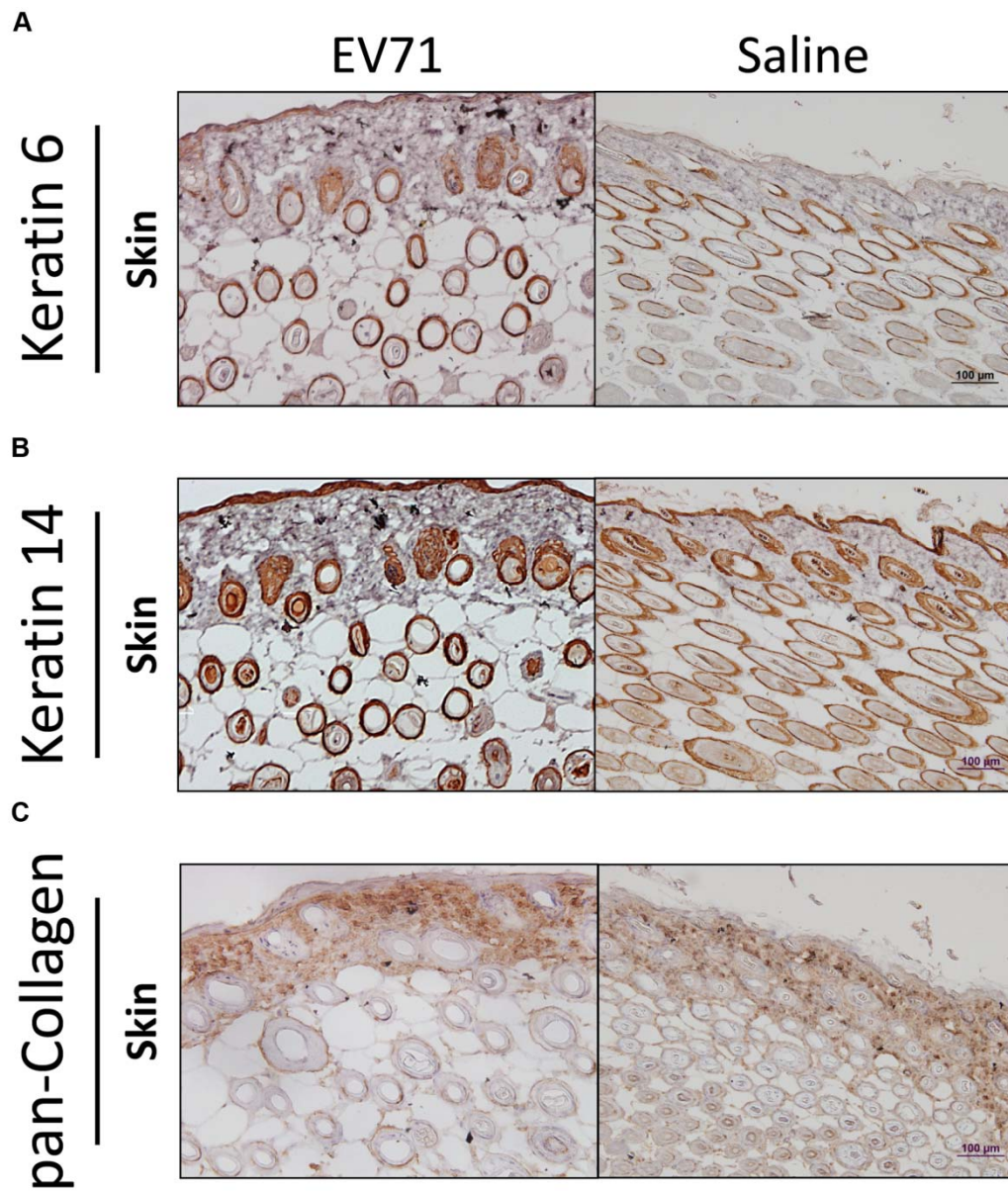


B



**Figure. S1. Comparisons of HFMD-like syndromes and limb paralysis in NOD/SCID mice infected with  $10^8$  pfu of EV71 clinical isolate F23 via different routes.** HFMD-like syndromes (A) and limb paralysis (B) were monitored daily. The HFMD-like scores were defined as follow: 0: healthy; 1: spotty hair-loss; 2: >30% hair loss; 3: Skin rash. The paralysis scores were defined as follow: 0: healthy; 1: limb weakness; 2: one-limb paralysis; 3: two-limb paralysis; 4: >3-limbs paralysis. The statistics were made by Two Way ANOVA test to compare the differences between each route of inoculation.

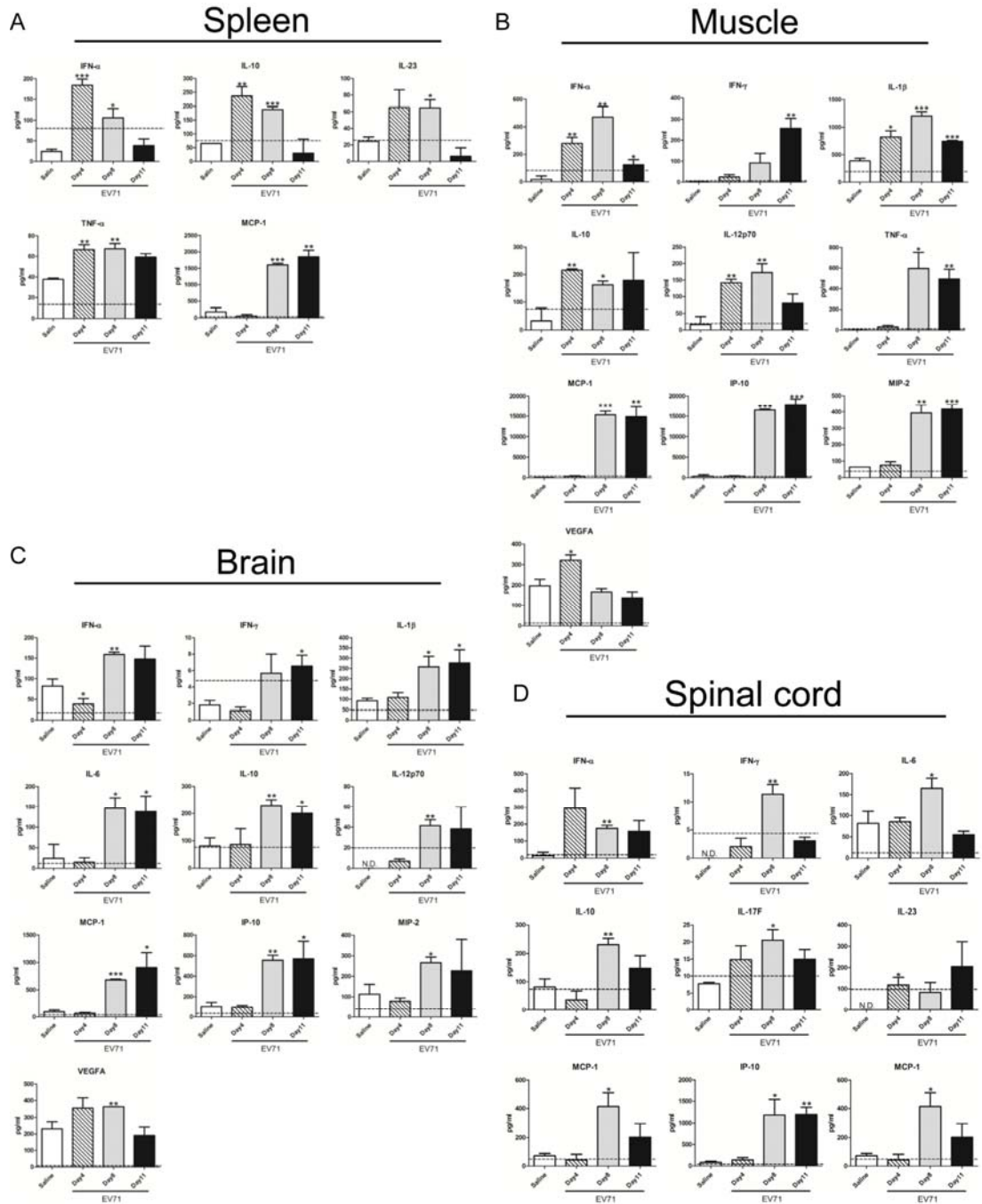
Fig.S2



**Figure S2. Pathological changes in skin tissues of EV71-infected NOD/SCID mice**

**by IHC staining.** 1-week-old NOD/SCID mice were infected i.p. with  $10^8$  pfu of EV71 (left panel) or normal saline (right panel). Mice were sacrificed on day 12 post-infection. The paraffin section were stained with anti-Keratin 6 (A), anti-Keratin 14 (B), and anti-pan-Collagen (C).

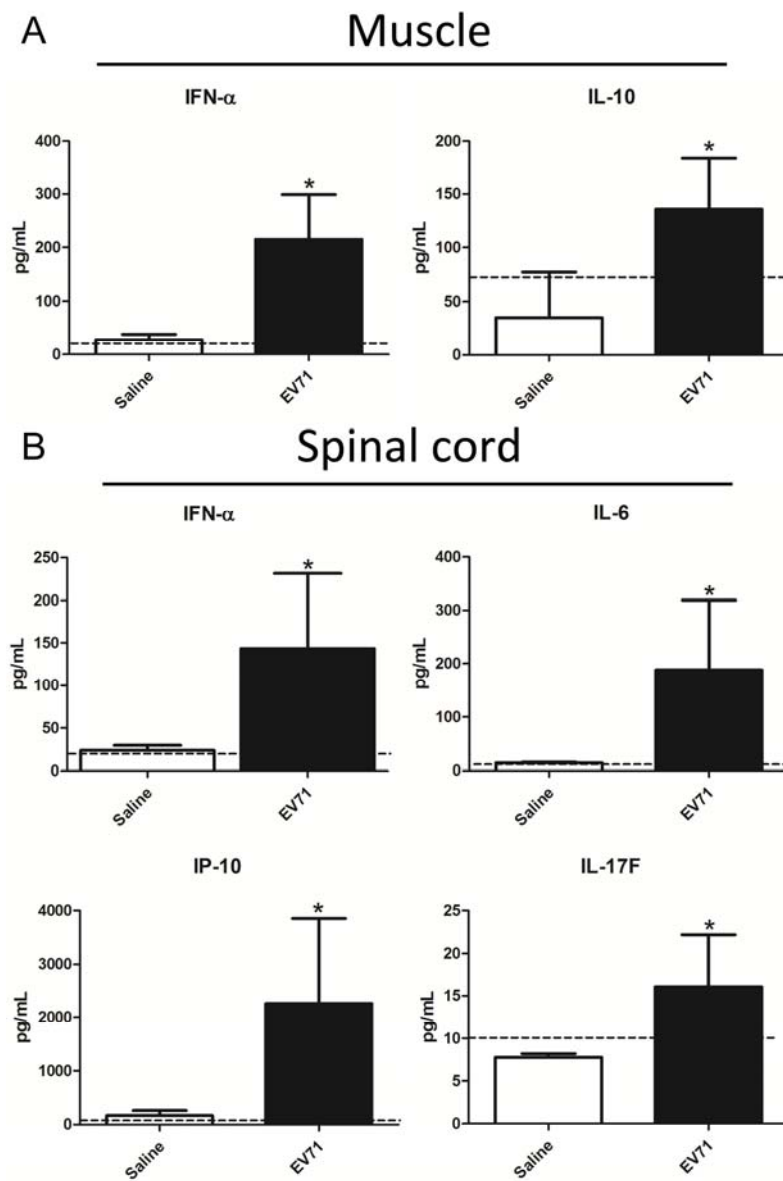
**Fig.S3**



**Fig S3 Cytokine profiles of EV71-infected NOD/SCID mice.** Spleen (A), muscle (B), brain (C), and spinal cord (D) from EV71-infected (black bar; n=3) or saline-injected (open bar; n=2) NOD/SCID mice were dissected on day 4, 8, and 11 post-infection. After homogenization, cytokine levels in tissue homogenates were

measured by Procarta Immunoassay Kit. Dash lines indicated the detection limits of each cytokine according to manufacturer's instruction. The statistic was presented by mean  $\pm$  standard deviation (sd) of each group. \*,  $p < 0.05$ ; \*\*,  $p < 0.01$ ; \*\*\*,  $p < 0.001$  by Student's *t*-test compared with saline control.

**Fig.S4**



**Fig S4 Cytokine profiles of EV71-infected *stat-1* KO mice. Muscle (A) and spinal**

cord (B) from EV71-infected (black bar; n=4) or saline-injected (open bar; n=2) *stat-1* KO mice were dissected at day 19. After homogenization, cytokine levels in tissue homogenates were measured by Procarta Immunoassay Kit. Dash lines indicated the detection limits of each cytokine according to manufacturer's instruction. The statistic was presented by mean  $\pm$  standard deviation (sd) of each group. \*,  $p < 0.05$  by Student's *t*-test compared with saline control