SUPPLEMENTAL FIGURE LEGENDS

Supplemental Figure 1. Podocyte-specific *Sirt1* knockout (SIRT1$^{pod-/-}$) mice showed normal phenotype without glomerular damage induction. (A) Histological analysis by PAS staining. No severe glomerular injuries were detected in both groups. Scale bars, 50 μm. (B, C) Blood urea nitrogen (BUN) level (B) or urinary albumin per creatinine ratio (U-alb/cre) (C) of wild-type (n=18) and SIRT1$^{pod-/-}$ mice (n=21). n.s., not significant. (D) Representative immunohistochemical pictures of synaptopodin (Synpo) or WT-1 in experimental mice. The results of quantitative analysis were shown in right panels. Difference of the expression between SIRT1$^{pod-/-}$ mice and wild-type mice was not detected. Scale bars, 20 μm.

Supplemental figure 2. Glomerular macrophage infiltration was increased in SIRT1$^{pod-/-}$ mice compared with wild-type mice at 7 days after nephrotoxic serum (NTS) injection. Quantitative analysis of infiltration of macrophage in glomerulus. F4/80-positive cells in the glomeruli were significantly increased in SIRT1$^{pod-/-}$ mice compared with wild-type mice. Scale bar, 50 μm. ***P<0.001. n.s., not significant.

Supplemental figure 3. Pathological phenotypic change in glomeruli at 7 days after NTS injection was not different in between wild-type and SIRT1$^{pod-/-}$ mice. Histological analysis by PAS staining followed by morphometric analysis was performed. (A) Representative images of glomerular damage such as tuft necrosis and/or crescent formation at 7 days after disease induction. Scale bar, 50 μm. (B) Morphometric analysis of the PAS stained glomeruli in the glomerulonephritis-induced wild-type or SIRT1$^{pod-/-}$ mice showed that the proportion of tuft

necrosis and/or crescent formation was similar in the two groups (n=4 for each). Both, tuft necrosis and crescent formation.

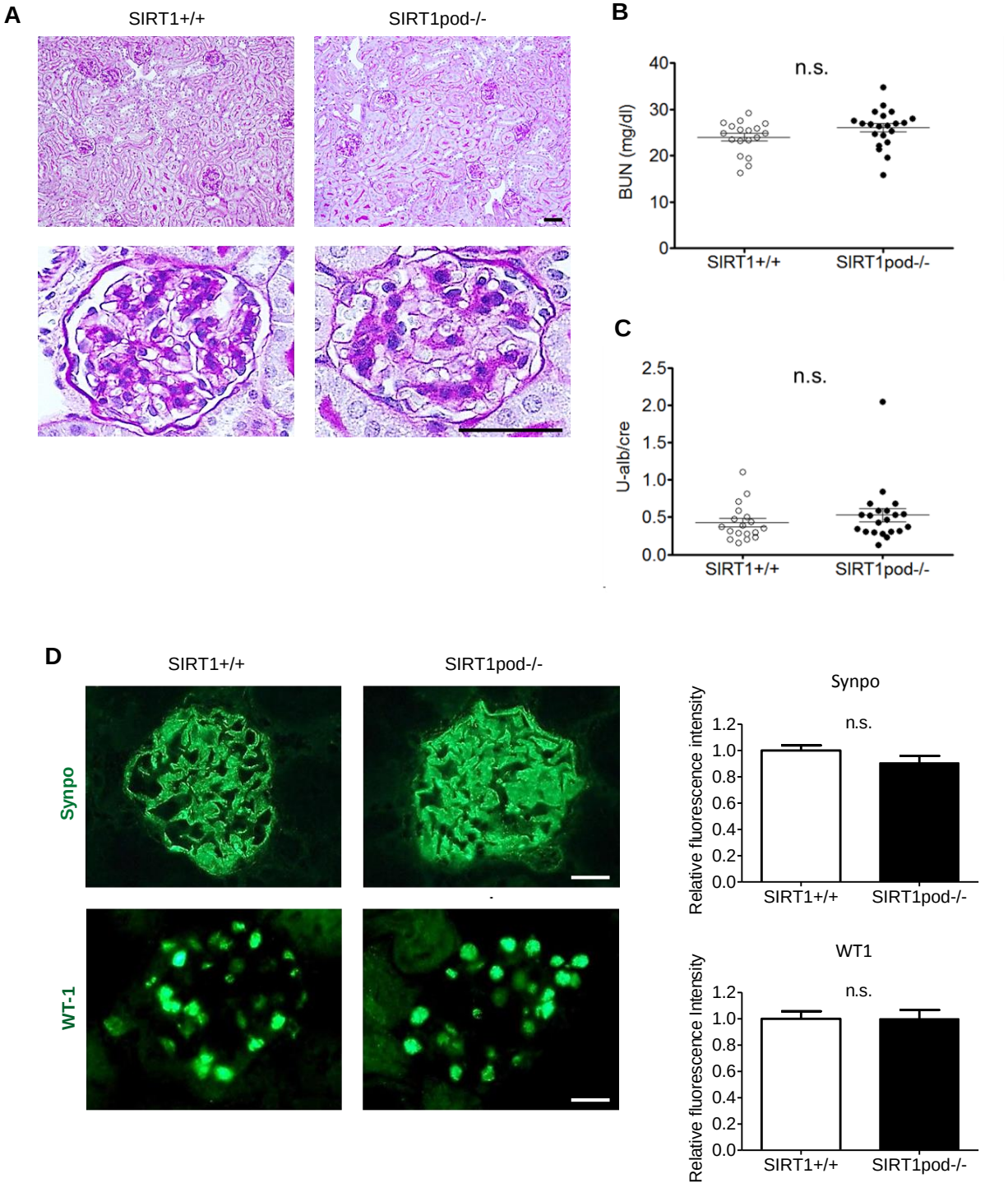
Supplemental figure 4. The immune response to NTS was not different between wild-type and SIRT1$^{pod-/-}$ mice. Representative immunofluorescence images of mouse IgG deposition on glomeruli in the experimental mice. NTS injection increased the IgG deposition on glomeruli. The difference of the IgG intensity was undetectable between wild-type and SIRT1$^{pod-/-}$ mice at 7 days after NTS treatment. Scale bar, 20 μm.

Supplemental figure 5. Glomerular macrophage infiltration was not changed in the experimental mice at an early phase (day 2) of glomerulonephritis induced by NTS. Quantitative analysis of glomerular infiltration of macrophage in the mice at 2 days after NTS injection. Macrophages were stained by Immunohistochemistry for F4/80. F4/80-positive cells per glomerulus were counted in each mouse group. Significant difference was not seen between the two groups. Scale bar, 50 μm. n.s., not significant.

Supplemental figure 6. SIRT1 inhibition deteriorated actin cytoskeleton derangement induced by protamine sulfate. Fluorescein-phalloidin staining of cultured podocytes treated with SIRT1 inhibitor and protamine sulfate (PS). Cultured podocytes were pretreated with SIRT1 inhibitor (EX527, 100 μM) or vehicle (Vehi, ethanol) for 24 h and then treated with PS (300 μg/ml) for 80 minutes. Actin cytoskeleton derangement was markedly deteriorated in podocytes pretreated with EX527 compared with the vehicle group. Scale bar, 50 μm.

Supplemental Figure 7. Cytoplasmic cortactin is crucial for maintenance of actin cytoskeleton. (A, B) Immunofluorescence images of cultured podocytes treated with leptomycin B. Staining of cortactin (using rabbit anti-cortactin antibody purchased from Abcam (A) or rabbit anti-cortactin antibody purchased from Cell Signaling Technology (B)), actin fibers (Phalloidin), nuclei (Hoechst33258), and their merged images are shown as Figure 10J. Scale bars, 100 μm. (C, D) Immunofluorescence images of cultured podocytes treated with leptomycin B. Staining of cortactin (using mouse anti-cortactin antibody purchased from Millipore (C) or rabbit anti-cortactin antibody purchased from Cell Signaling Technology (D)), nuclei (Hoechst33258), and their merged images are shown as Figure 10K. Scale bars, 100 μm.

Supplemental figure 8. SIRT1 expression was increased by glomerular damage *in vivo* or by H2O2 *in vitro*. (A) Western blot analysis for detection of SIRT1 in mice with glomerulonephritis induced by NTS. Isolated glomeruli from wild-type mice with or without NTS injection were used for quantitative analysis of SIRT1. SIRT1 expression was significantly increased by NTS treatment. *P<0.05 versus untreated mice (control). (B) Western blot analysis for detection of SIRT1 in cultured murine podocytes treated with H_2O_2. Cultured podocytes with or without H_2O_2 (300 μM) treatment were analyzed. SIRT1 expression was significantly increased by H_2O_2 treatment. *P<0.05 versus control. (C) Quantitative analysis of *Sirt1* mRNA expression in cultured podocytes treated with H_2O_2. Real-time PCR analysis showed the *Sirt1* expression was significantly increased by H_2O_2 in a dose dependent manner. ***P<0.001 versus control.



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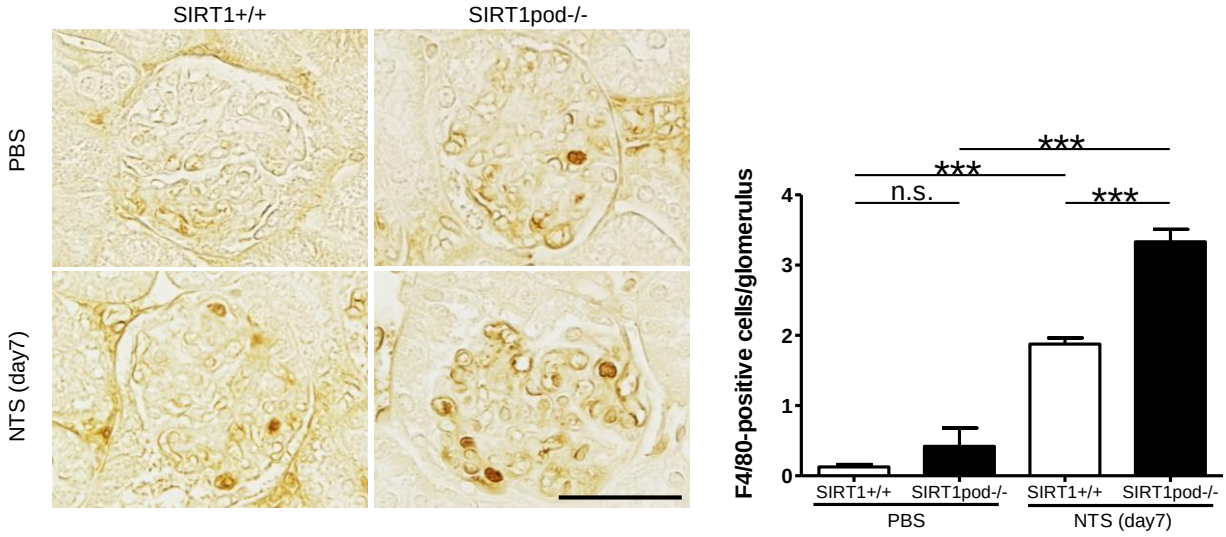

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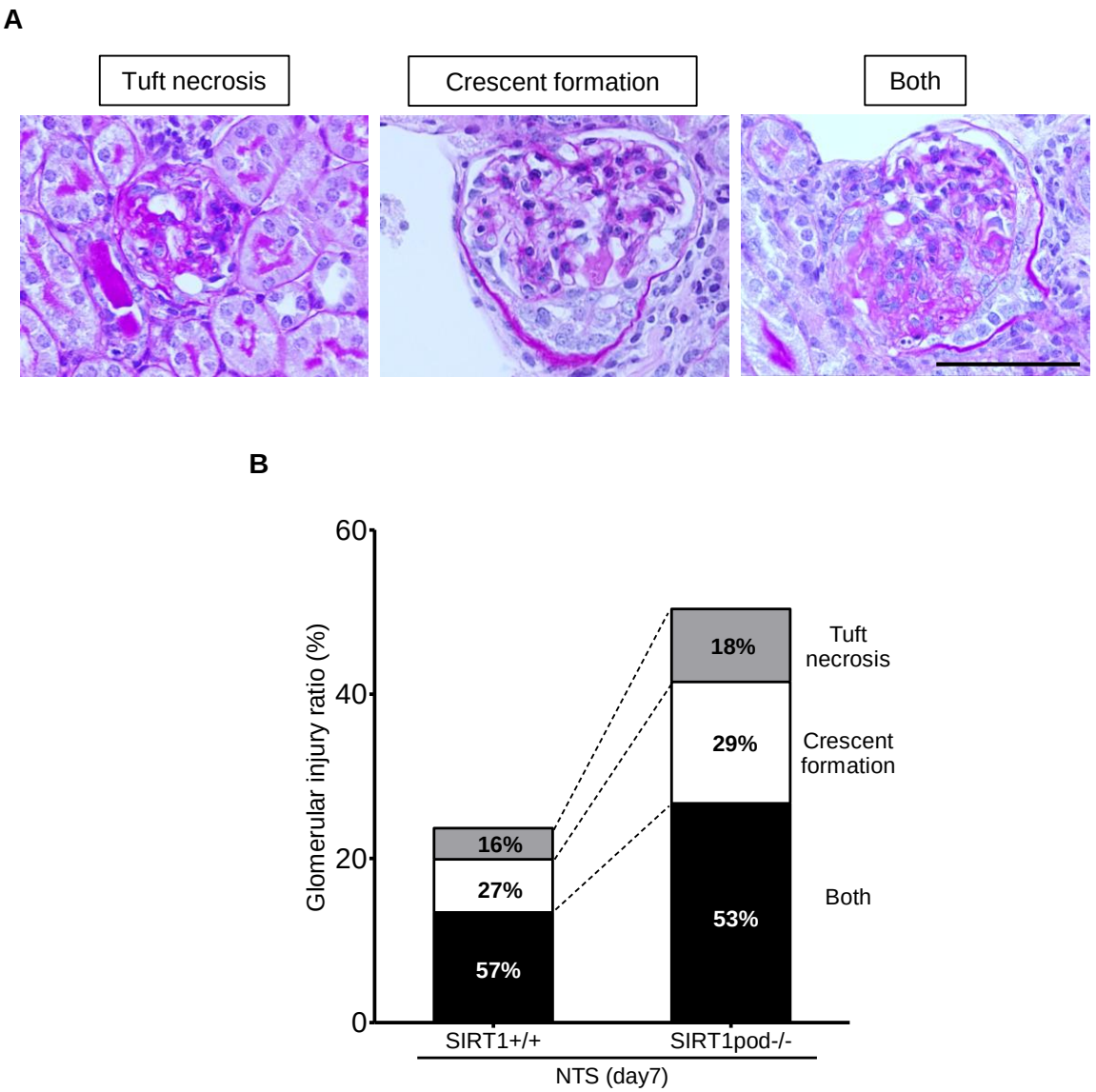

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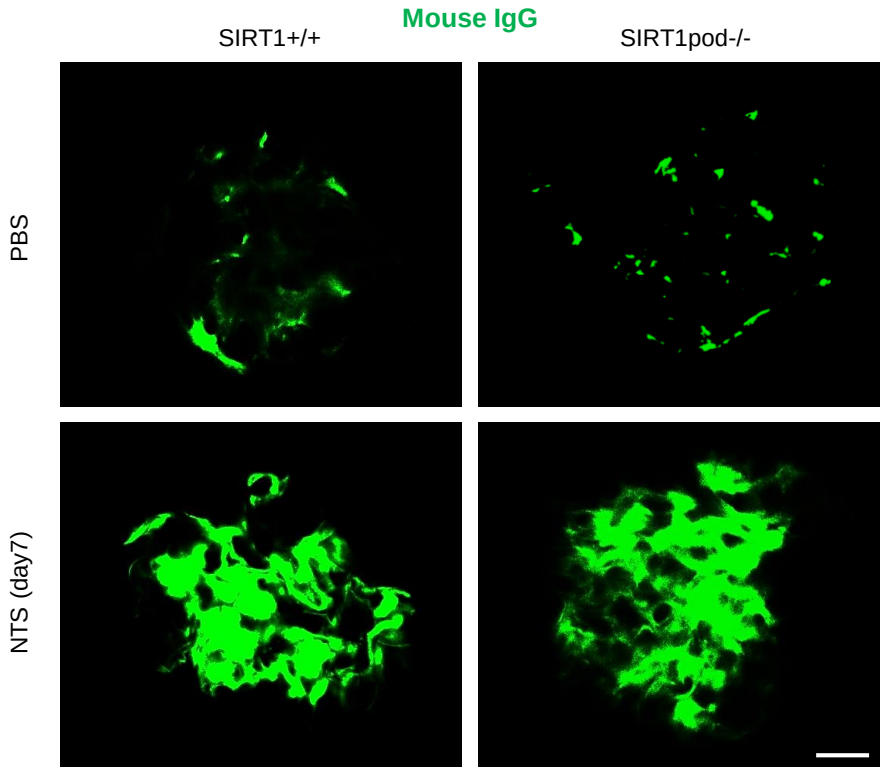

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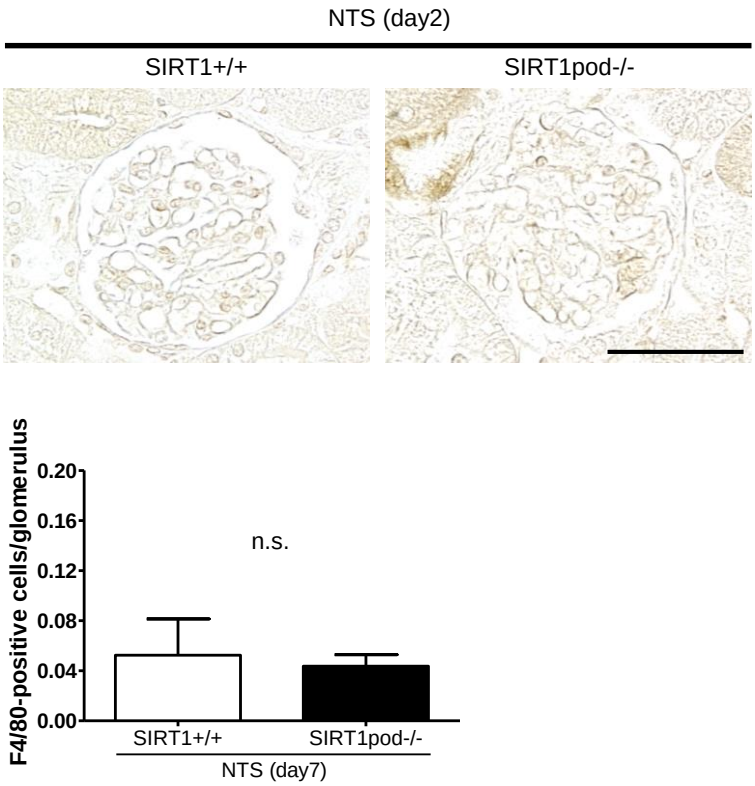

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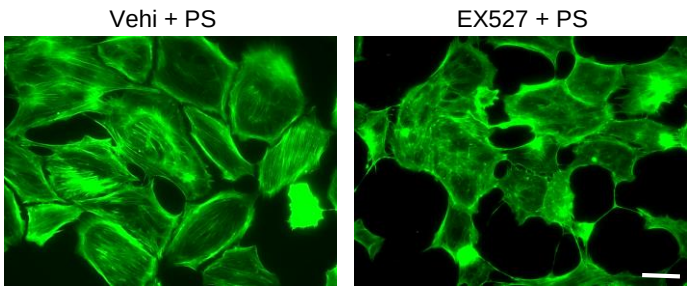

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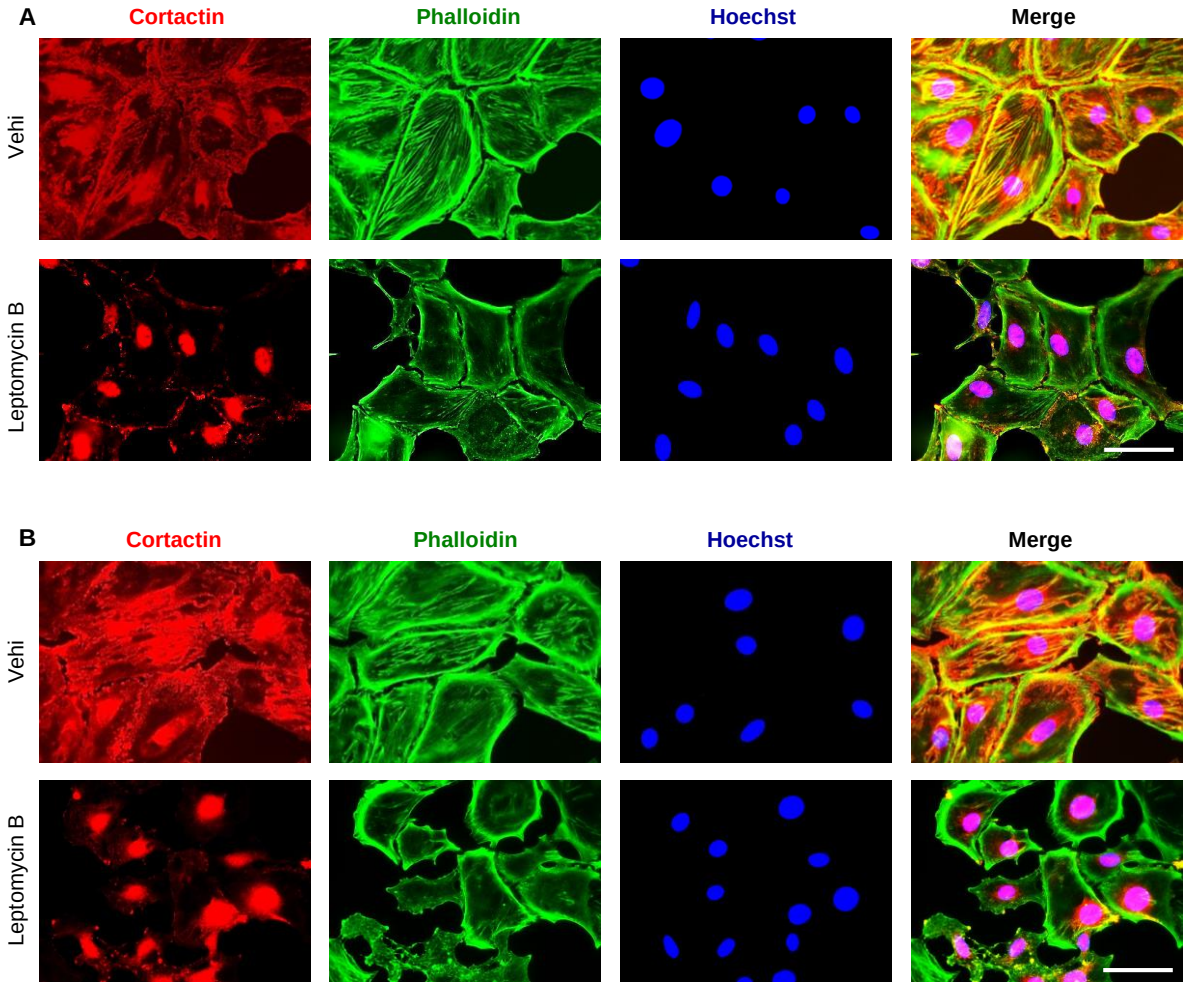

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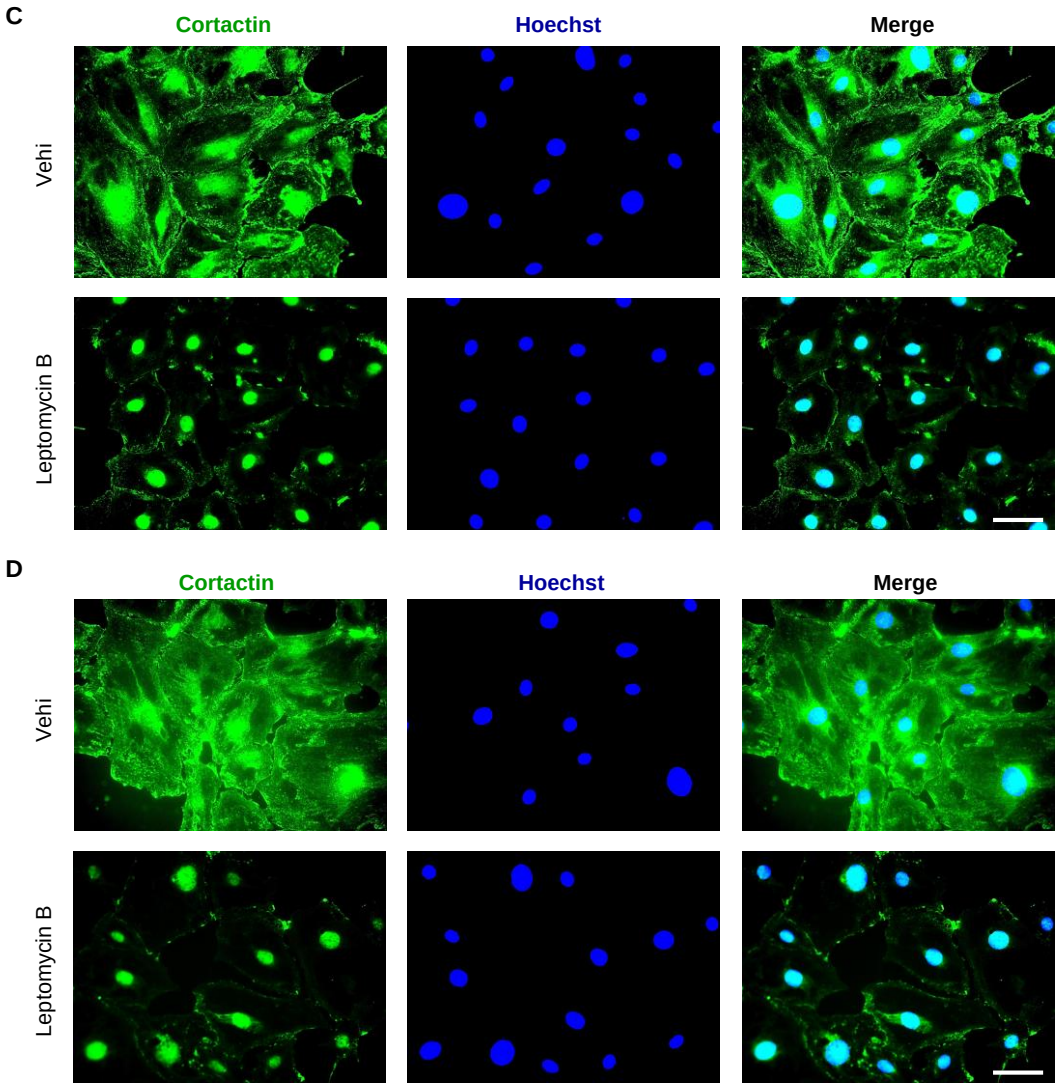
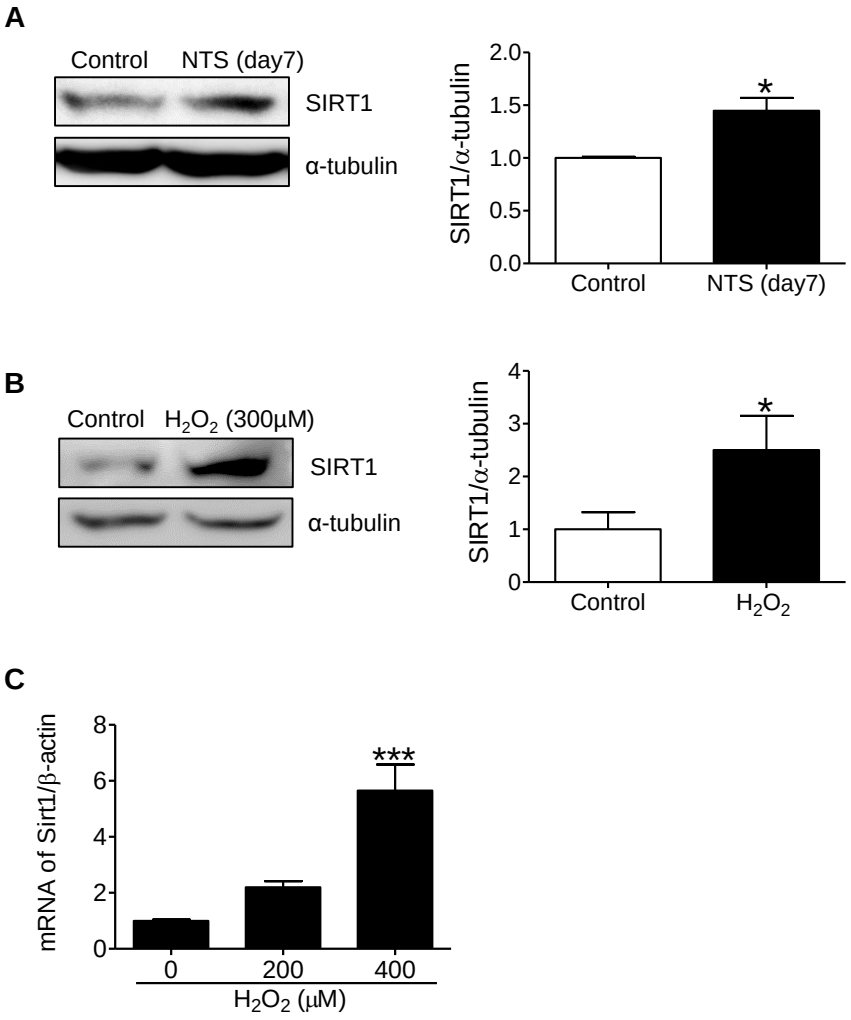


Supplemental Figure 7 (cont.). (C, D) Immunofluorescence images of cultured podocytes treated with leptomycin B. Staining of cortactin (using mouse anti-cortactin antibody purchased from Millipore (C) or rabbit anti-cortactin antibody purchased from Cell Signaling Technology (D)), nuclei (Hoechst33258), and their merged images are shown as Figure 10K. Scale bars, 100 μm.



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