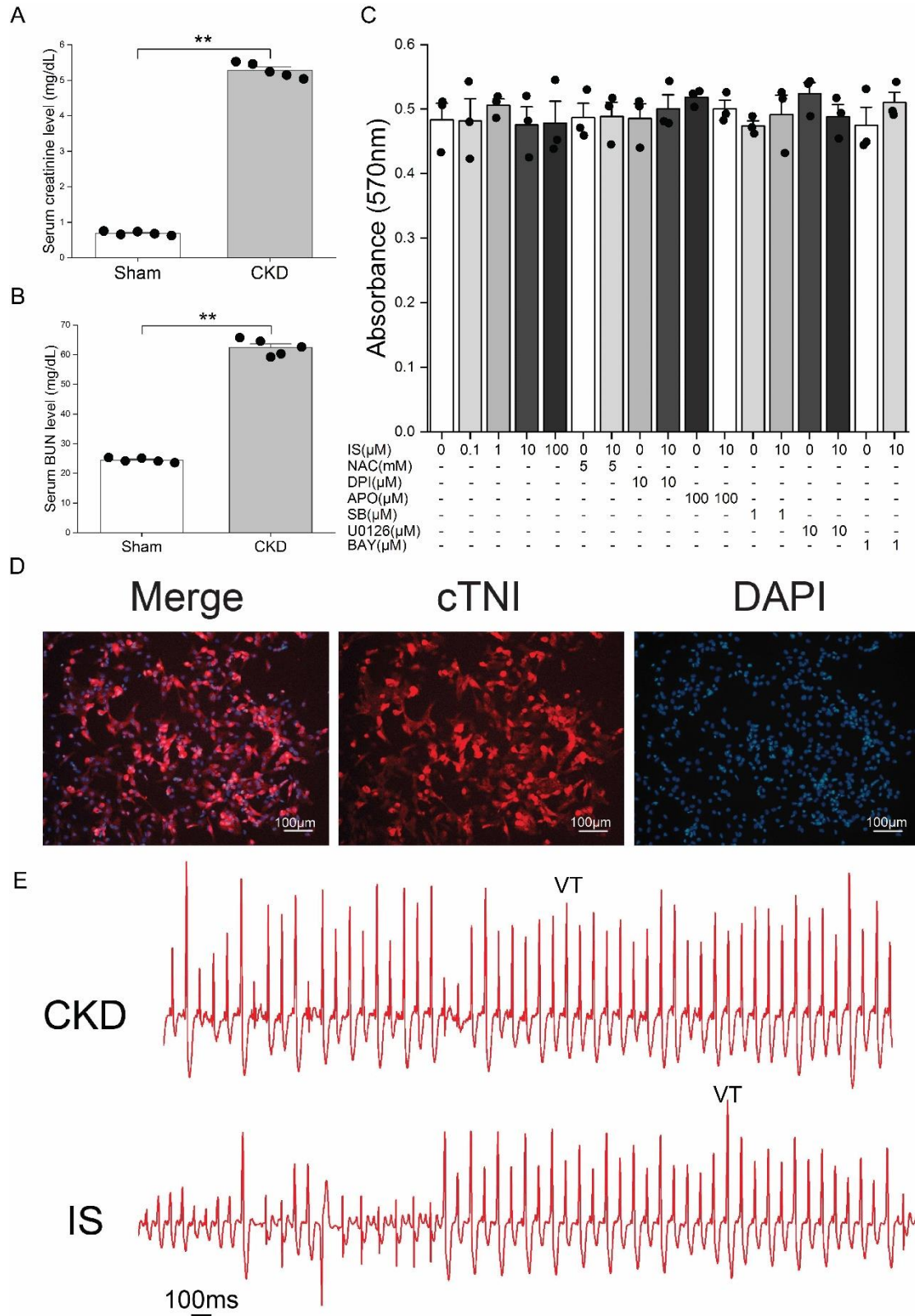


Supplementary materials

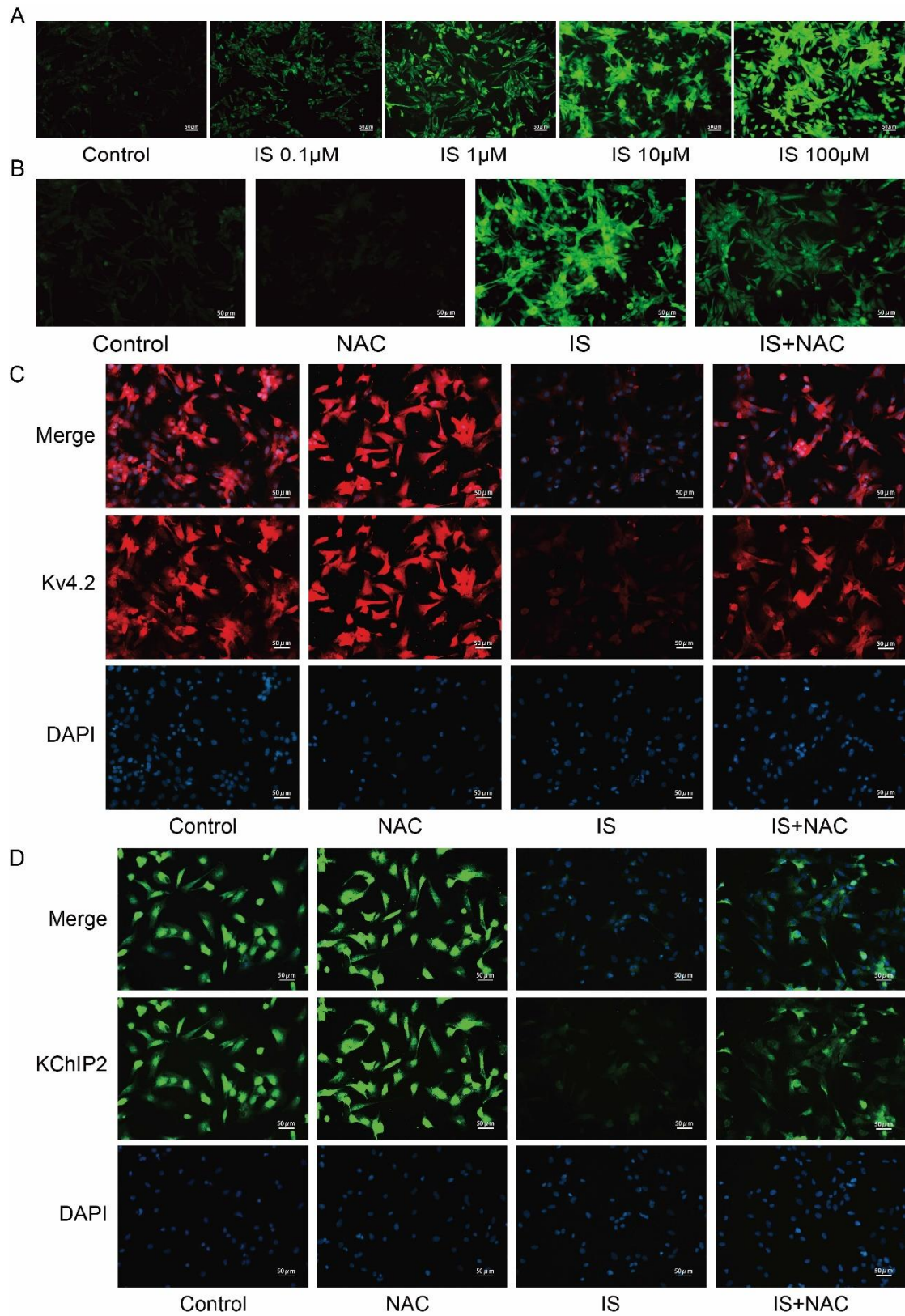
Supplementary Figure 1



Supplementary Figure 1. Measurements of creatinine, BUN and cell viability, identification of cell purity and amplification

of electrocardiogram strips. (A-B) Measurements of serum creatinine (**A**) and BUN (**B**) levels in rats (n=5 per group). (**C**)Determination of cell viability based on 3-(4,5-Dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide (MTT) assay in NRVMs (n=3 per group). (**D**) Representative fluorescence image of cardiac troponin I (cTNI) in NRVMs. Scale bar,100 μ m. (**E**) Enlarged electrocardiogram strips of the rats after the intraperitoneal injection of isoproterenol and caffeine in CKD (n=5) and IS treatment groups (n=6). IS, Indoxyl sulfate; NAC, N-acetylcysteine;DPI, Diphenyleiiodonium chloride;APO,Apocynin;SB, SB203580;U0126, U0126-EtOH;BAY, BAY11-7082;VT,ventricular tachycardia. Data are presented as mean \pm SEM. Statistical analysis was performed using two-tailed Student's t-test (**A** and **B**) and one-way ANOVA followed by Bonferroni post-hoc test (**C**). **P<0.01.

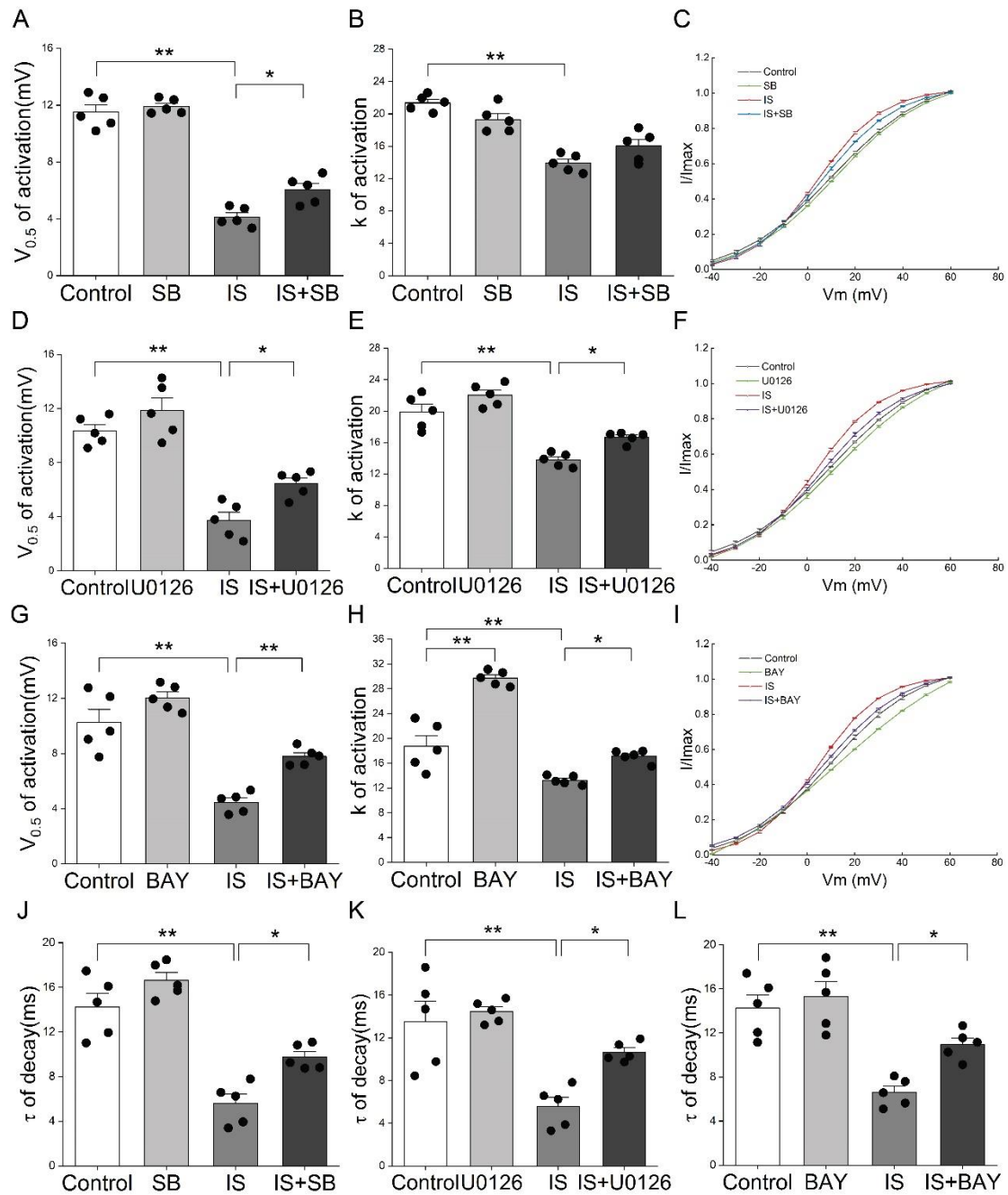
Supplementary Figure 2



Supplementary Figure 2. Measurements of ROS productions, Kv4.2 proteins and KCHIP2 proteins based on Immunofluorescence. (A) Representative images of DCF immunofluorescence in NRVMs treated with different concentrations of IS. Scale bar, 50 μ m. (B) Representative images of DCF immunofluorescence in control, NAC, IS and IS+NAC groups. Scale

bar,50 μm . (C) Representative fluorescence images of Kv4.2 proteins in control, NAC, IS and IS+NAC groups. Scale bar,50 μm . (D) Representative fluorescence images of KChIP2 proteins in control, NAC, IS and IS+NAC groups. Scale bar,50 μm . NAC, N-acetylcysteine.

Supplementary Figure 3



Supplementary Figure 3. IS accelerated the activation and decay of $I_{to,f}$ by activating p38 MAPK, p44/42 MAPK and NF- κ B signaling pathway. (A-B) Average values of half-maximal voltage of activation ($V_{0.5}$, act) (A) and constants (k) of activation (B) in control, SB, IS and IS+SB groups (n=5 per group). (C) Voltage-dependent activation curves of $I_{to,f}$ in control, SB, IS and IS+SB groups (n=5 per group). (D-E) Average values of half-maximal voltage of activation ($V_{0.5}$, act) (D) and constants (k) of activation (E) in control, U0126, IS and IS+U0126 groups (n=5 per group). (F) Voltage-dependent activation curves of $I_{to,f}$ in control, U0126, IS and IS+U0126 groups (n=5 per group). (G-H) Average values of half-maximal voltage of activation ($V_{0.5}$, act) (G) and constants (k) of activation (H) in control, BAY, IS and IS+BAY groups (n=5 per group). (I) Voltage-dependent activation curves of $I_{to,f}$ in control, BAY, IS and IS+BAY groups. (J-L) Average time constants (τ) of decay of $I_{to,f}$ at +60 mV in control, SB, IS and IS+SB groups (J), control, U0126, IS and IS+U0126 groups (K) and control, BAY, IS and IS+BAY groups (L) (n=5 per group). SB, SB203580; U0126, U0126-EtOH; BAY, BAY11-7082. Data are presented as mean \pm SEM. Statistical analysis was performed using one-way ANOVA followed by Bonferroni post-hoc test. * $P < 0.05$, ** $P < 0.01$.