

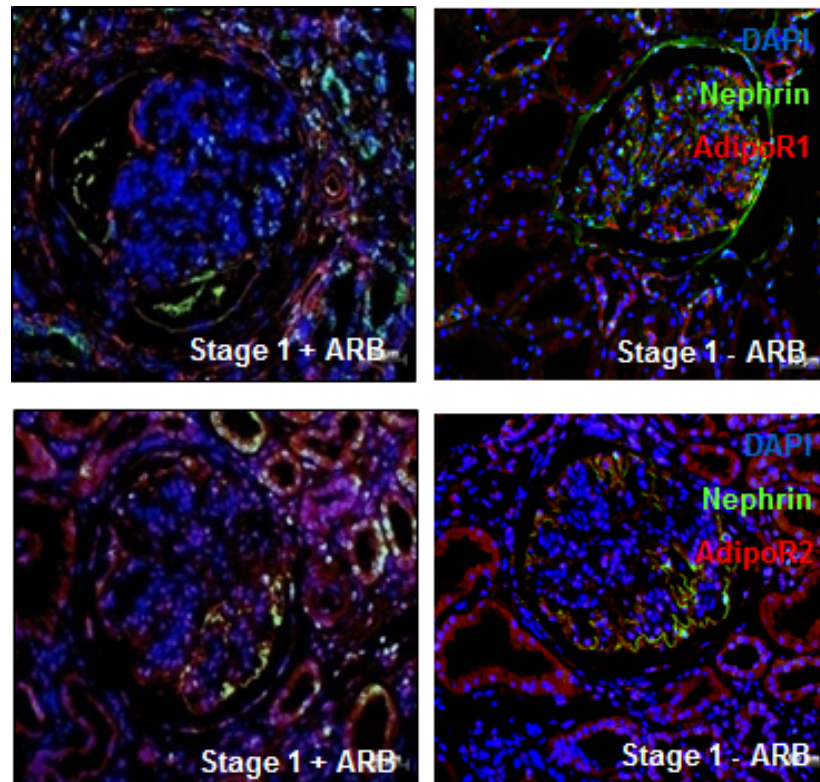
Supplementary Table 1. Biochemical and physical characteristics of healthy normal control subjects (Cont) and patients with DN according to CKD stages.

Characteristics	Cont	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
No. of patient (M)	6 (3)	6 (3)	6 (3)	6 (4)	6 (3)	3 (2)
Age (years)	31 ± 5	32 ± 4	53 ± 5	47 ± 6	60 ± 4	57 ± 5
Medication	NA	ARB (3)	ARB (4) ACEi (2)	ARB (6)	ARB (5) ACEi (1)	ARB (3)
Serum Cr (mg/dl)	0.81 ± 0.08	0.82 ± 0.11	1.25 ± 0.22	1.98 ± 0.73	2.53 ± 0.70	6.45 ± 1.21
eGFR (ml/min/1.73 m ²)	92.3 ± 2.1	91.2 ± 1.8	72.0 ± 3.8	37.9 ± 4.5	19.0 ± 4.4	8.9 ± 1.1
Proteinuria (g/day)	0.1 ± 0.2	1.3 ± 1.3	3.2 ± 1.9	4.3 ± 1.1	3.2 ± 1.7	5.6 ± 2.2
SBP (mmHg)	129 ± 10	135 ± 12	133 ± 9	136 ± 11	136 ± 17	137 ± 11
DBP (mmHg)	74 ± 8	74 ± 9	73 ± 9	83 ± 5	77 ± 5	75 ± 8
DM duration (years)	NA	1.2 ± 1.5	2.2 ± 1.8	6.5 ± 2.4	10.0 ± 5.4	8 ± 3.4

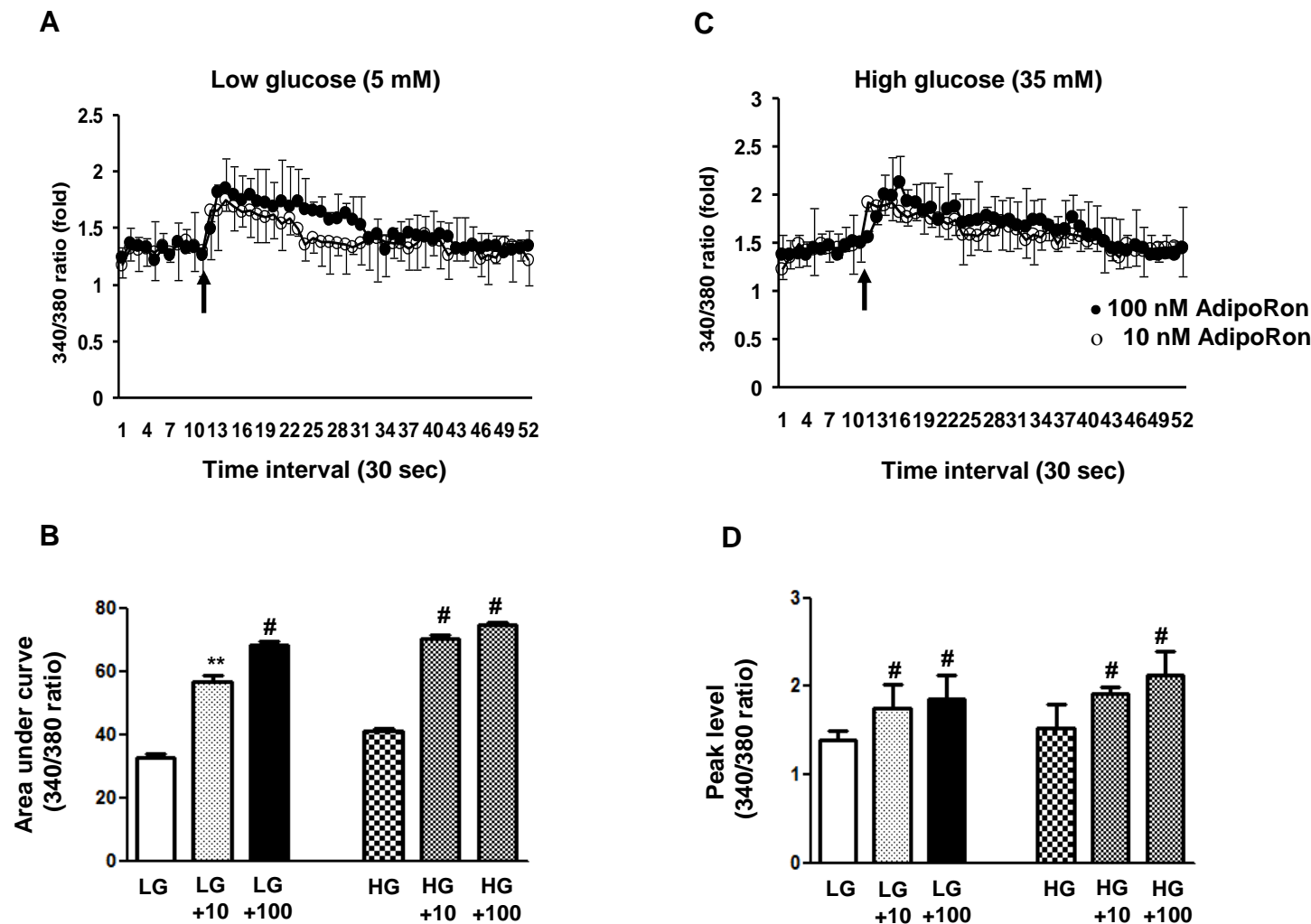
Abbreviation: ACEi; angiotensin-converting enzyme inhibitor, ARB; angiotensin II receptor blocker, Cont; healthy normal control, Cr; creatinine, DM; diabetes mellitus, DBP; diastolic blood pressure, eGFR; estimated glomerular filtration rate, NA; not available, No.; number, SBP; systolic blood pressure.

Supplementary Figure 1.

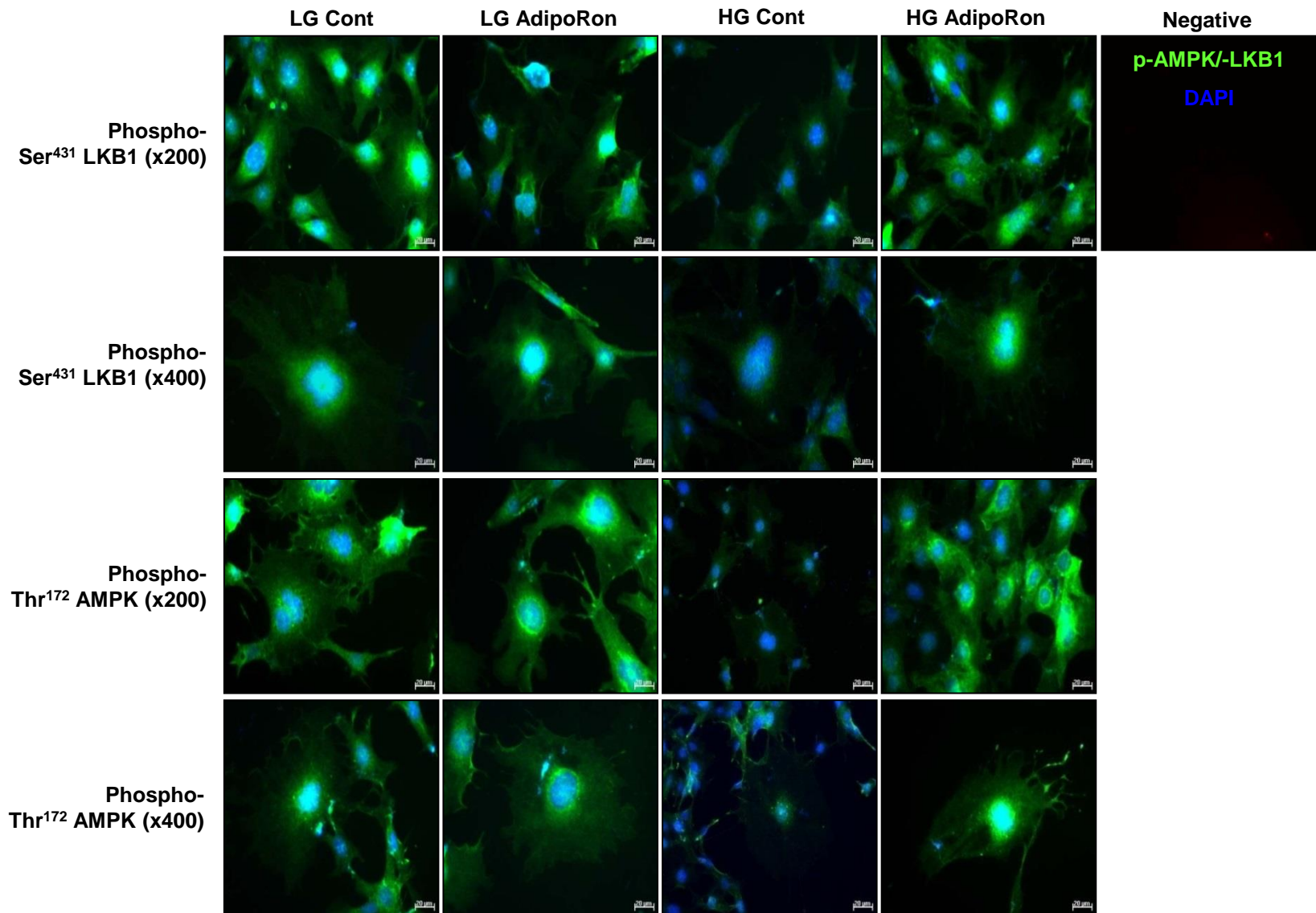
The expression of adiponectin receptor 1 (AdipoR1) and 2 (AdipoR2) in stage 1 patients with or without ARB treatment

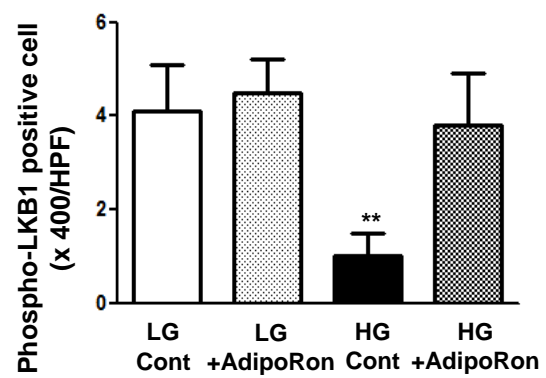
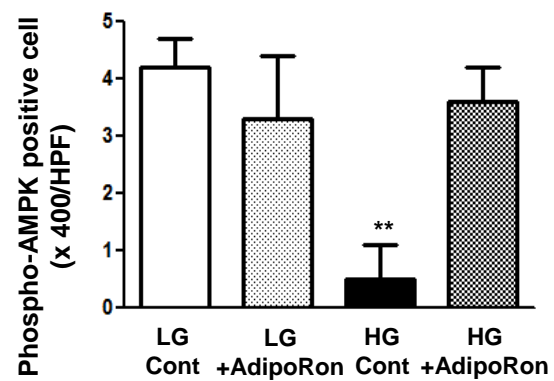


Supplementary Figure 2.

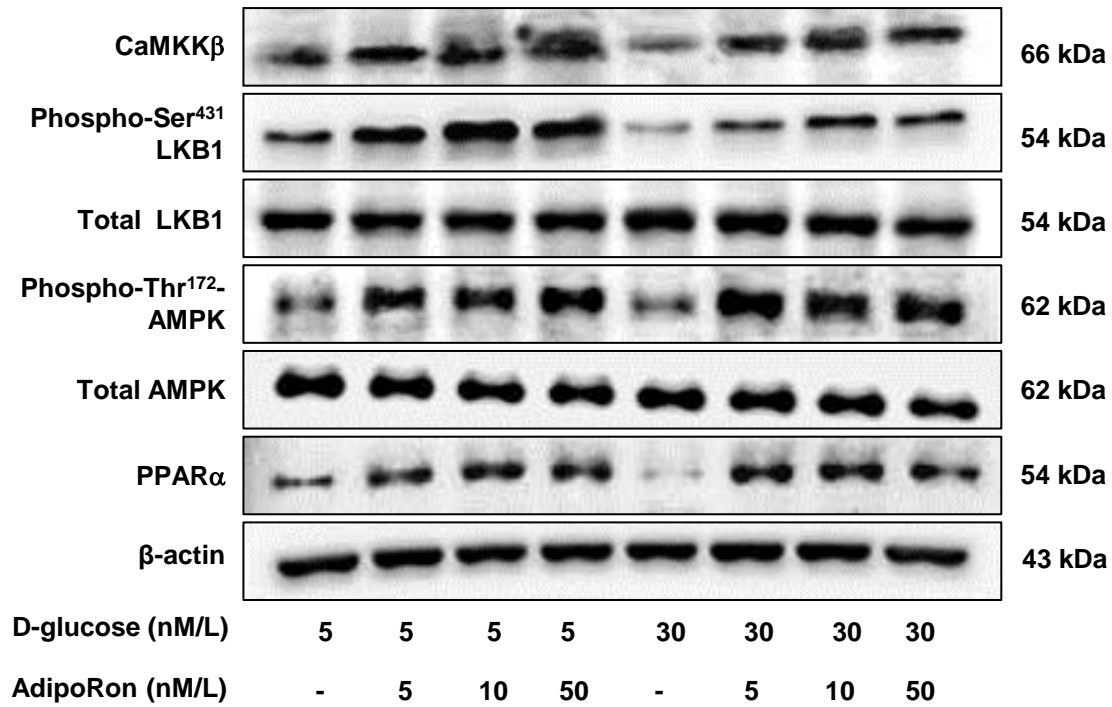


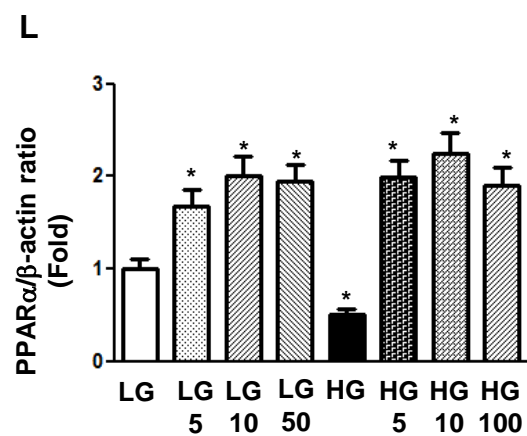
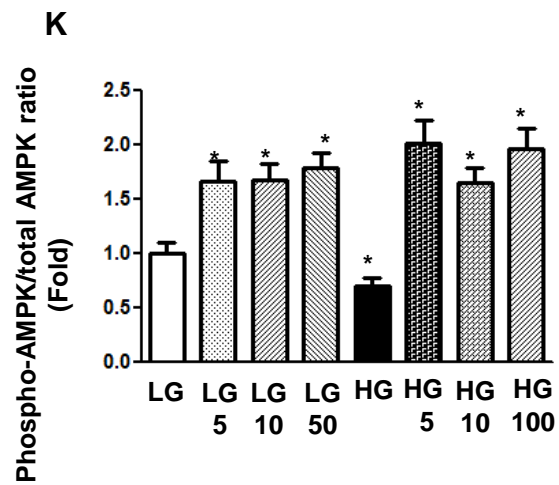
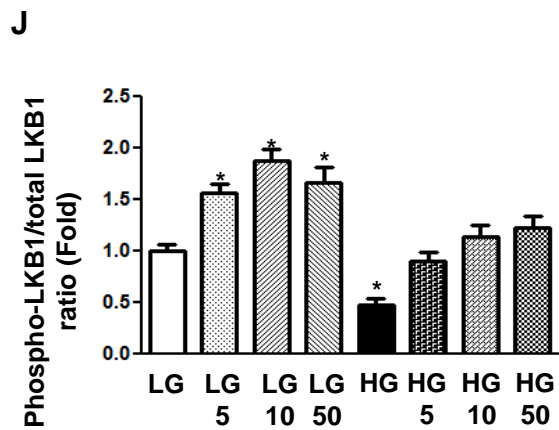
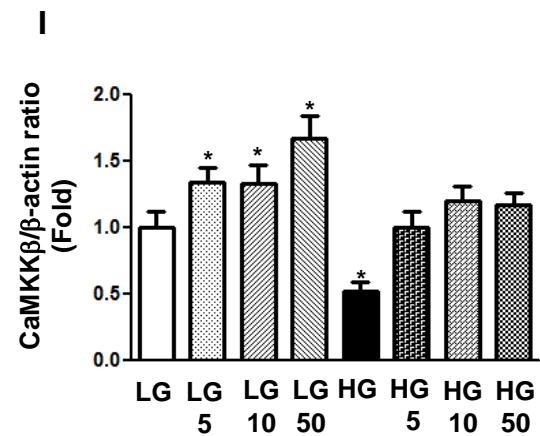
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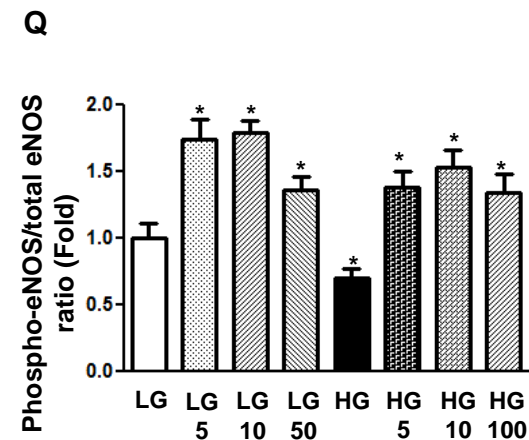
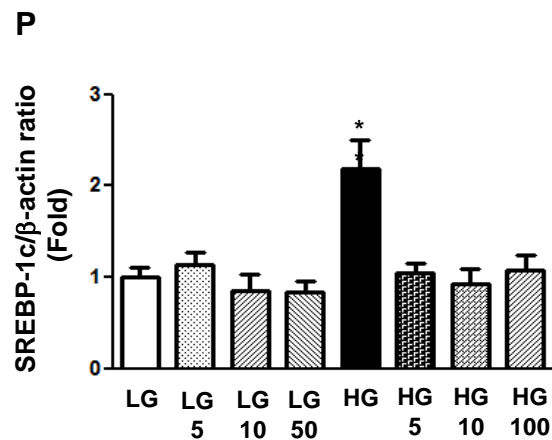
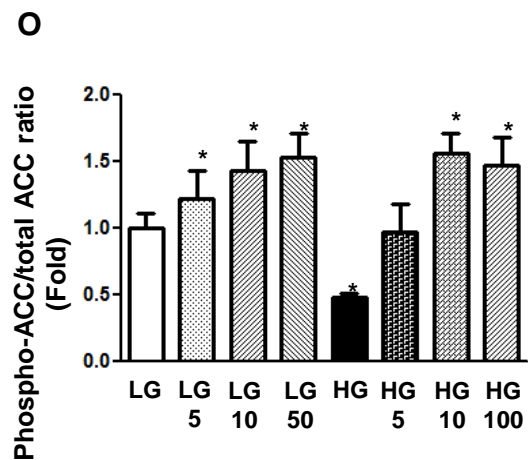
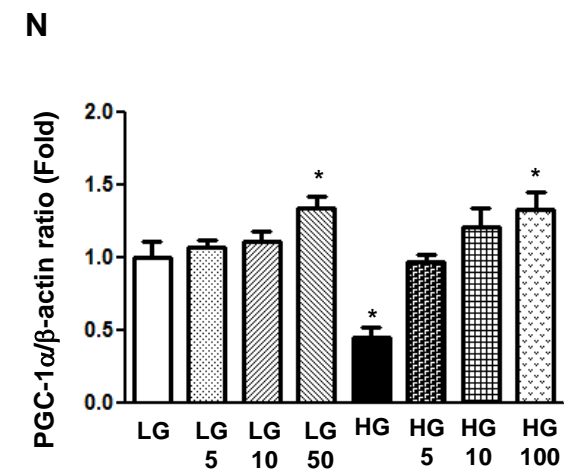
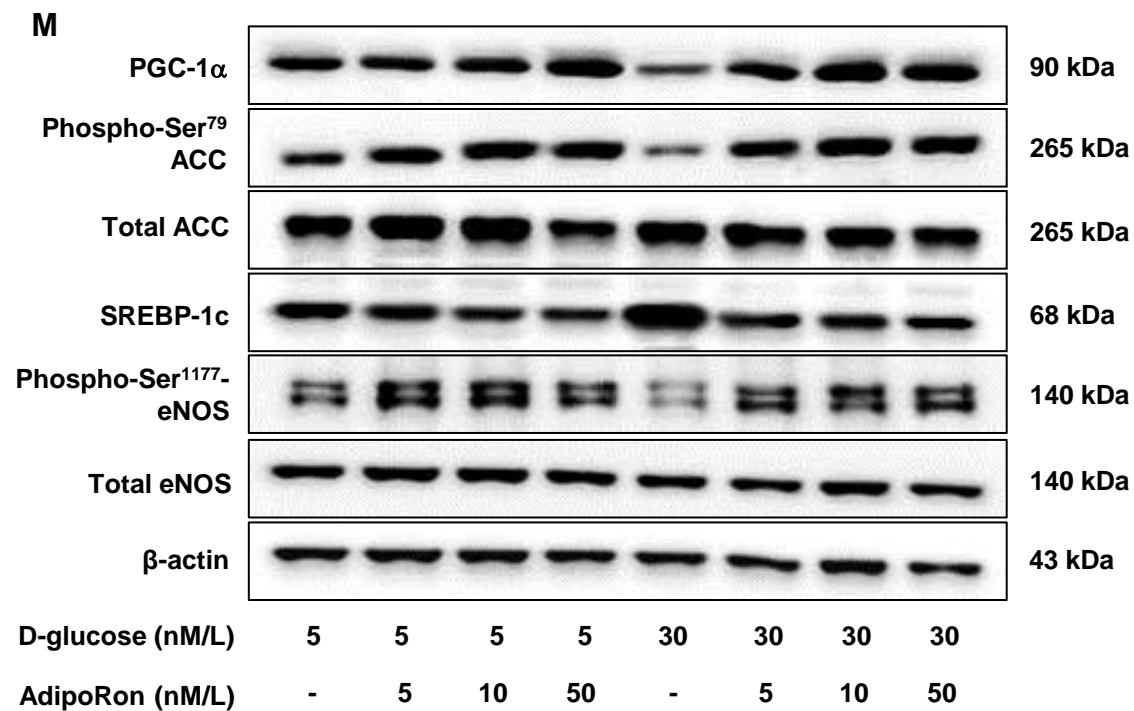


F**G**

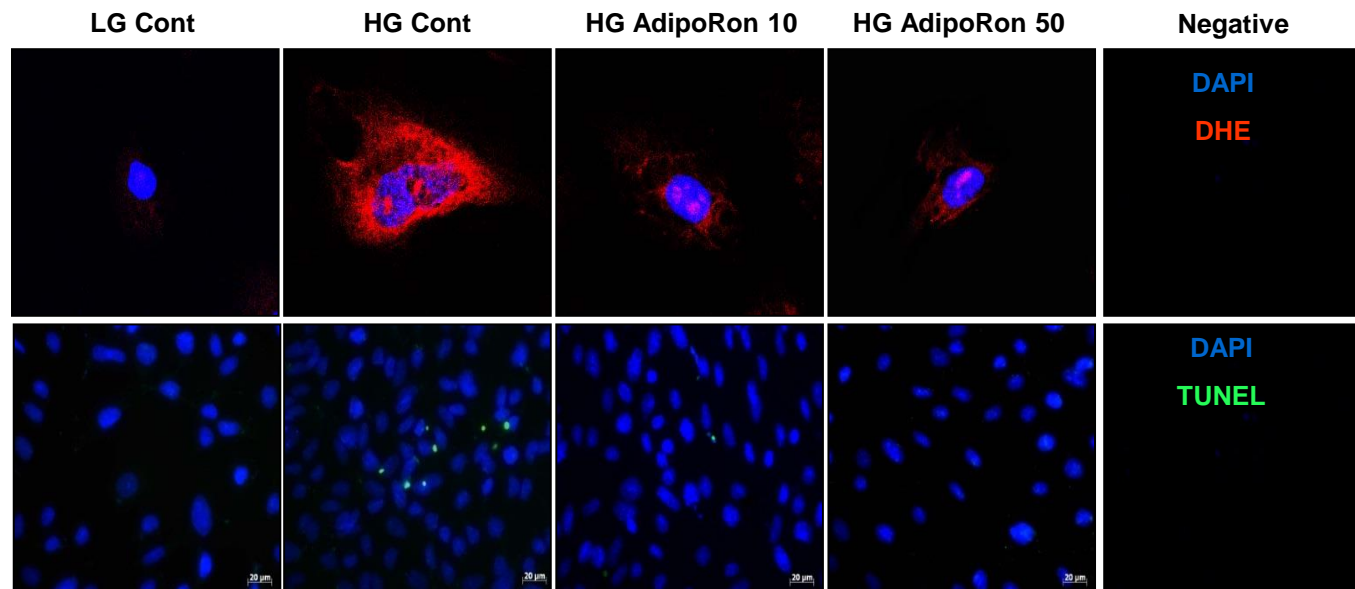
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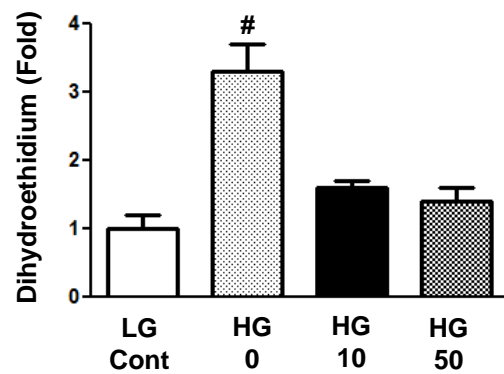




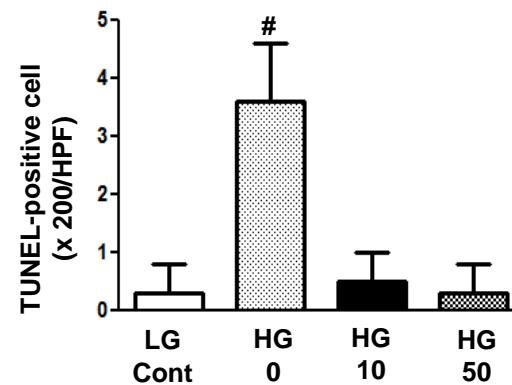
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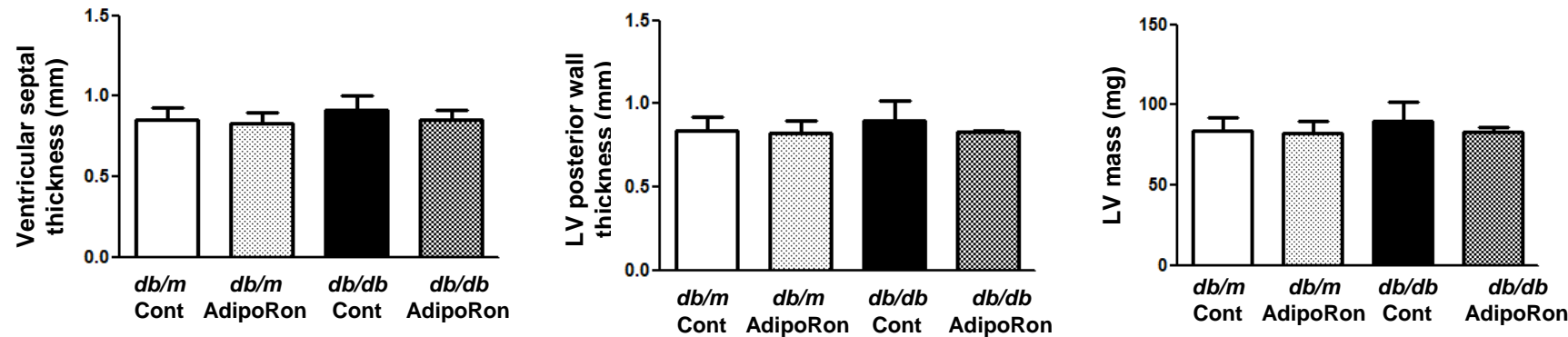


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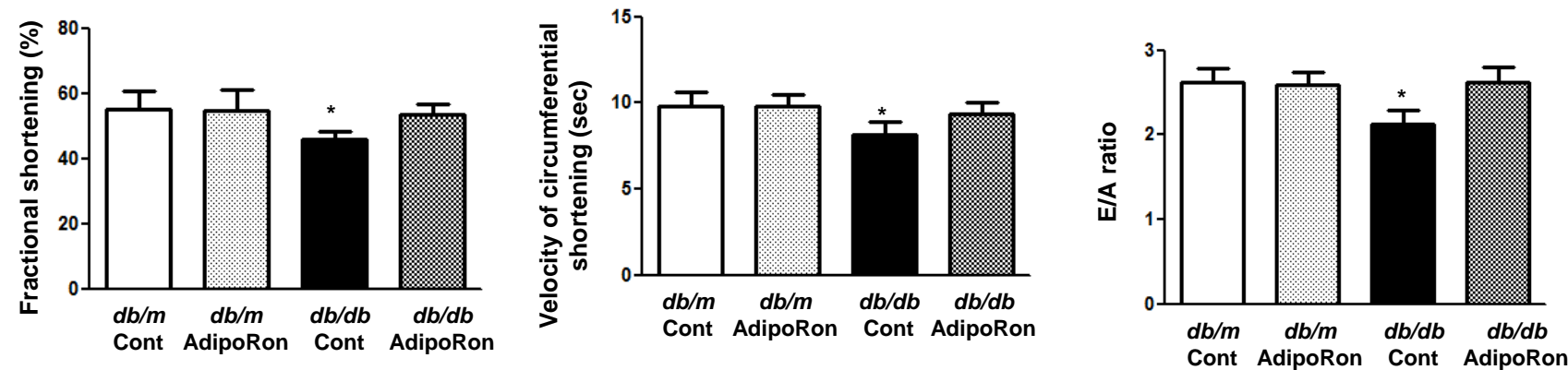


Supplementary Figure 3.

A



B



C

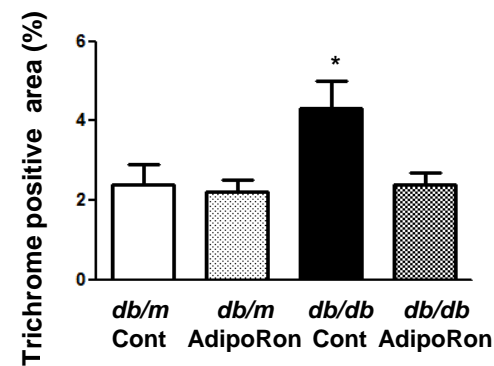
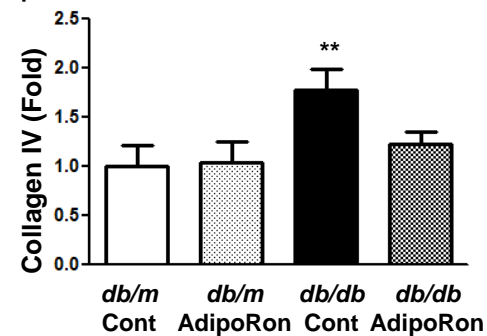
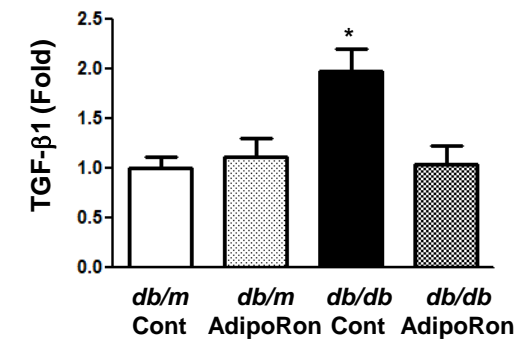
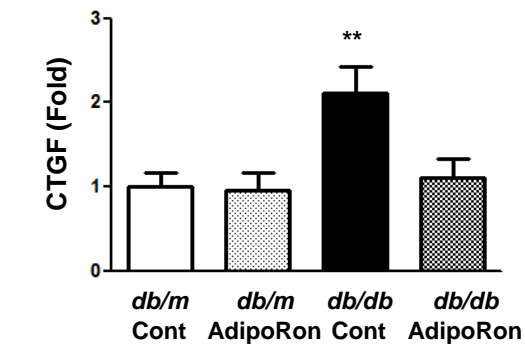
Trichrome

db/m Cont*db/m* AdipoRon*db/db* Cont*db/db* AdipoRon

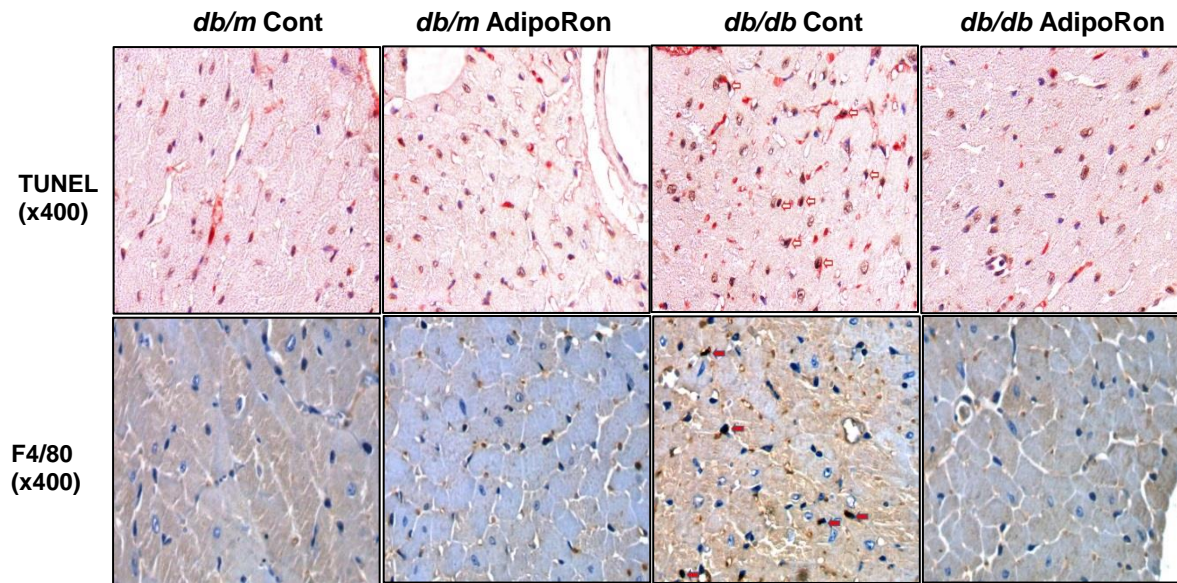
Col IV

TGF- β 1

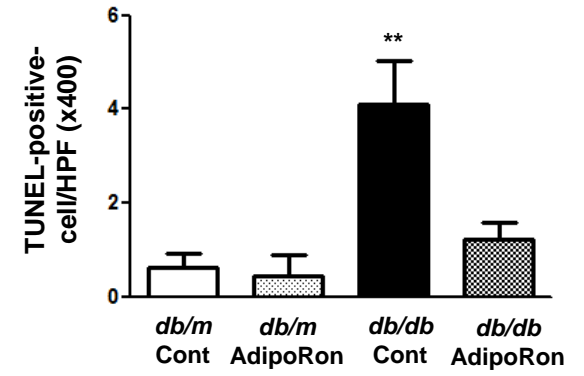
CTGF

D**E****F****G**

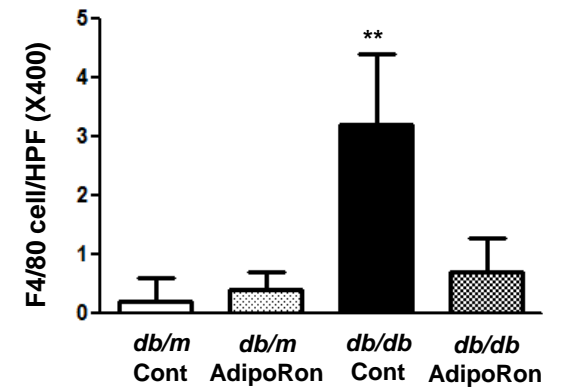
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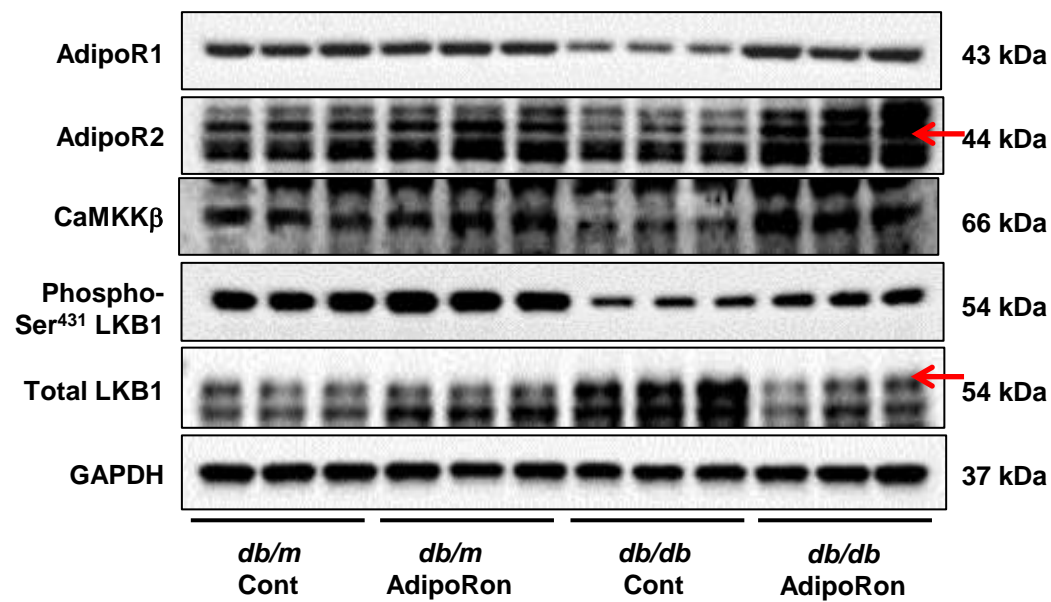
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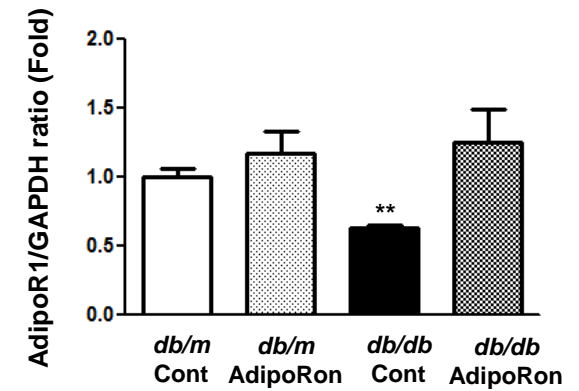
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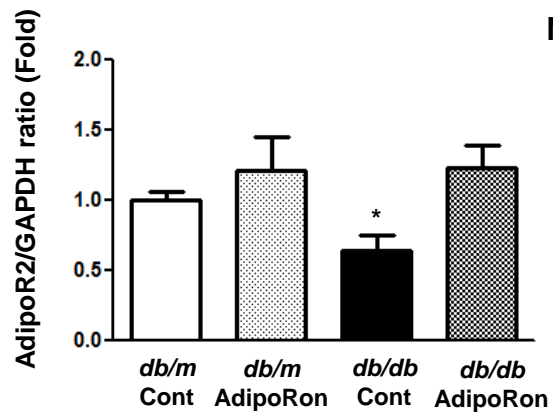
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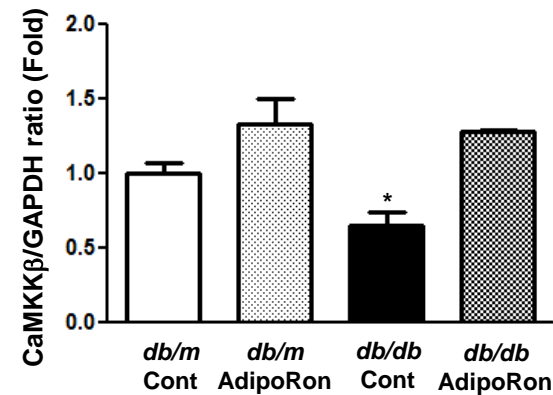
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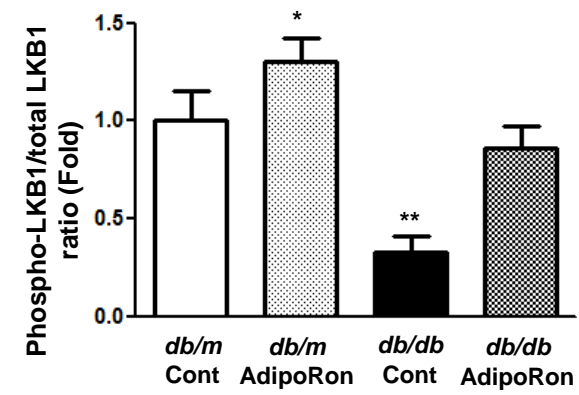
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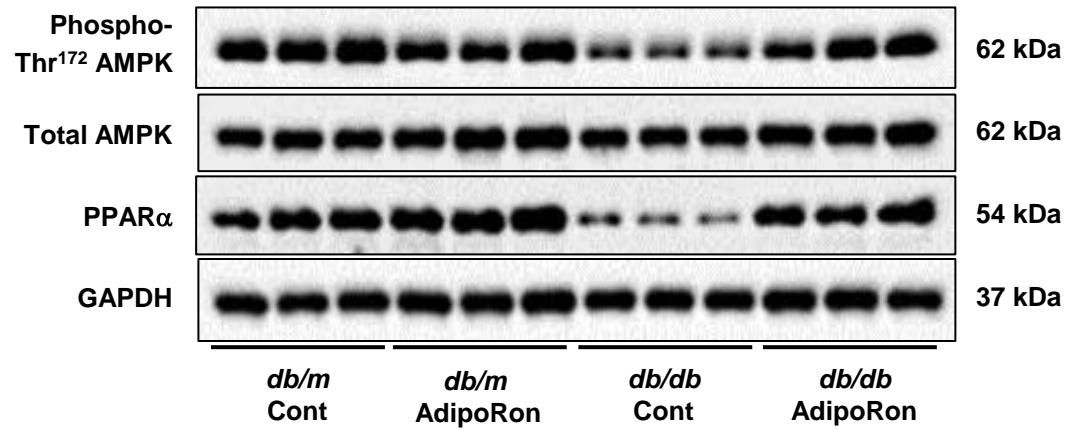
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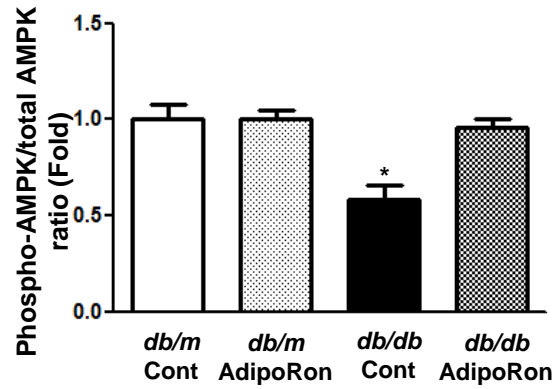
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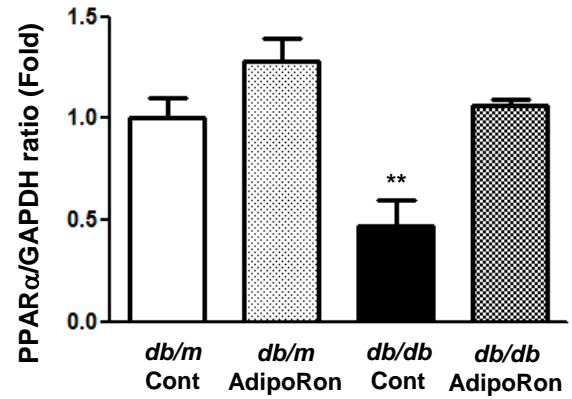
P



Q



R



Supplementary Figure Legends

Figure 1. The expression of adiponectin receptors in CKD stage 1 patients with or without ARB treatment.

Figure 2. Effect of AdipoRon on intracellular Ca^{++} concentration and downstream signaling in murine podocytes cultured in low- or high-glucose medium with or without AdipoRon. Intracellular Ca^{++} concentration in murine podocytes cultured in low- or high-glucose medium with or without AdipoRon (**A–D**). Representative images of immunofluorescence staining and quantitative analyses of phosphorylated Ser⁴³¹LKB1 and phosphorylated Thr¹⁷²AMPK levels (**E–G**). Representative images of western blotting analysis of CaMKK β , phosphorylated Ser⁴³¹LKB1, phosphorylated Thr¹⁷²AMPK, total AMPK, PPAR α , and β -actin levels (**H**) and their quantitative analyses (**I–L**). Representative images of western blotting and quantitative analyses of PGC-1 α , phosphorylated ACC, total ACC, SREBP-1c, phosphorylated Ser¹¹⁷⁷eNOS, total eNOS, and β -actin levels (**M–Q**). Representative images of immunofluorescence staining and quantitative analyses of DHE level and TUNEL-positive cells (**R–T**)

Figure 3. Changes in the cardiac systolic and diastolic function and its phenotypes in *db/m* and *db/db* mice treated with or without AdipoRon. Echocardiographic changes as assessed by ventricular septal thickness, left ventricular (LV) wall thickness, LV mass, fractional shortening, velocity of circumferential shortening, and E/A ratio in cardiac tissues of *db/m* and *db/db* mice treated with or without AdipoRon (**A and B**). Representative sections stained with trichrome are shown to estimate the trichrome positive area (%) (**C**) together with the results of quantitative analysis according to groups (**D**). Immunohistochemical staining and quantitative analyses of type IV collagen- (**C and E**), TGF- β 1- (**C and F**), and CTGF-positive area (**C and G**). Representative images of immunohistochemical staining of TUNEL- and F4/80-positive cardiac myocytes (**H**) and quantitative analyses of the results (**I and J**). Representative images of western blotting and quantitative analyses of AdipoR1, AdipoR2, CaMKK β , phosphorylated Ser⁴³¹LKB1, total LKB1, and GAPDH levels (**K–O**). Representative images of western blotting and quantitative analyses of phosphorylated AMPK Thr¹⁷², total AMPK, PPAR α , and GAPDH (**P–R**).