Supplementary Table 1. Physical and metabolic parameters of diabetic patients.

Results are means \pm SE. #p < 0.05 vs. nondiabetic control, *p < 0.05 vs. sedentary diabetics.

Supplementary Table 2. List of antibodies used in the experiments.

Supplementary Figure 1. A: Experimental protocol to assess the effect of aerobic physical exercise on nephroprotection in diabetic rats. B: Experimental protocol to assess the effect of treating exercised diabetic rats with an irisin receptor blocker (CycloRGDyK) on nephroprotection induced by physical exercise. C: Incremental load exhaustion velocity (EV) reached in the initial test and after four and eight weeks of aerobic exercise. D: Incremental load test distance reached in the initial test and after four and eight weeks of aerobic exercise. E: Incremental load test time reached in the initial test and after four and eight weeks of aerobic exercise in diabetic rats. CT, nondiabetic; DM, sedentary diabetic; DM + Exe, exercised diabetic; DM + Cyclo, sedentary diabetic treated intraperitoneally with 1mg/kg of α V integrin receptor inhibitor (CycloRGDyK); DM + Exe + Cyclo, exercised diabetic treated intraperitoneally with 1mg/kg of CycloRGDyK. Results are means \pm SE. #p < 0.05 vs. initial, *p < 0.05 vs. after four weeks.

Supplementary Figure 2. Time course of the effect of high glucose treatment in HK-2 cells. *A* and *B*: Western blot analysis of collagen IV, fibronectin, NF- κ B(p65) pAMPK^(Thr172), AMPK α , pACC^(Ser79), ACC, and vinculin in HK-2 cells treated with high glucose for 24 hours or 48 hours followed by quantitation of collagen IV/vinculin, fibronectin/vinculin, NF- κ B/vinculin, and pAMPK^(Thr172)/vinculin by AMPK α /vinculin ratio, and pACC^(Ser79)/vinculin by ACC/vinculin ratio. The uniformity of protein loading and transfer efficiency were assessed by reprobing the membranes for vinculin. Blots are representative of three independent experiments. Results are means ± SE. NG, normal glucose (5.6 mmol/L); HG, high glucose (30 mmol/L glucose). #p < 0.05 vs. NG (24 h), *p < 0.05 vs. NG (48 h).

Supplementary Table 1

Serum irisin (µg/mL)

| Parameters | Non diabetic control | Sedentary diabetics | Exercised diabetics |
|---------------------------------|----------------------|-----------------------|---------------------|
| Gender (male/female) | 6/9 | 9/6 | 7/8 |
| Age (years) | 47.0 ± 4.8 | 51.7 ± 4.5 | 50.6 ± 3.9 |
| BMI (weight/height²) | 26.8 ± 3.3 | 30.6 ± 3.1# | $29.4\pm3.6^{\#}$ |
| Diabetes diagnosis (years) | - | 4.4 ± 2.0 | 5.5 ± 2.5 |
| Fasting glucose (mg/dL) | 84.9 ± 8.7 | $144.7 \pm 40.8^{\#}$ | 131.8 ± 30.9# |
| Glycated hemoglobin (%) | NA | 7.3 ± 1.3 | 7.2 ± 1.5 |
| Systolic blood pressure (mmHg) | NA | 123.3 ± 12.9 | 113.0 ± 14.6 |
| Diastolic blood pressure (mmHg) | NA | 79.1 ± 7.4 | 73.2 ± 9.0 |

NA

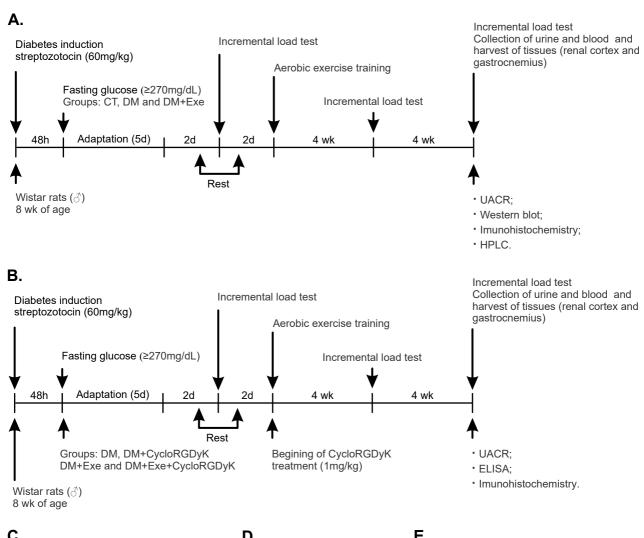
 $1.1\pm0.5\,$

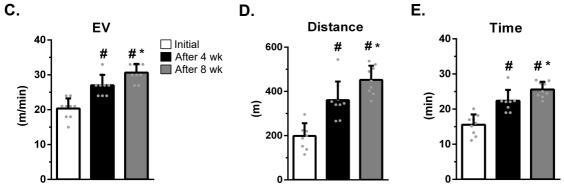
 $1.7\pm0.6^{\color{red}\star}$

Supplementary Table 2

| Antibodies (dilution) | Source | Identifier |
|--|---------------------------|-----------------|
| Anti-rabbit phospho -AMPKa Thr172 (1:1000) | Cell Signaling Technology | Cat. # 2535 |
| Anti-rabbit AMPKa (1:1000) | Cell Signaling Technology | Cat. # 5831 |
| Anti-rabbit phospo-ACC Ser79 (1:1000) | Cell Signaling Technology | Cat. # 11818 |
| Anti-rabbit ACC (1:1000) | Cell Signaling Technology | Cat. # 3676 |
| Anti-rabbit vinculin (1:1000) | Cell Signaling Technology | Cat. # 13901 |
| Anti-rabbit GAPDH (1:1000) | Cell Signaling Technology | Cat. # 5174 |
| Anti-rabbit phopho -NF-κB p65 (1:1000) | Cell Signaling Technology | Cat. # 3033S |
| Anti-rabbit PGC1-α (1:250) | Cell Signaling Technology | Cat. # 2178S |
| Anti-rabbit fibronectin (1:100 - WB, 1:50 - IHC) | Abcam | Cat. # ab2413 |
| Anti-rabbit type IV collagen (1:50 - IHC) | Abcam | Cat. # ab6586 |
| Anti-goat type IV collagen (1:1000) | SouthernBiotech | Cat. # 1340-01 |
| Anti-rabbit acetyl - Lys310 - NF-кB p65 (1:500) | Assay Biotechnology | Cat. # D0018 |
| Anti-mouse NF -kB p65 (1:500) | Santa Cruz Biotechnology | Cat. # sc8008 |
| Anti-mouse TNF -a (1:25 - IHC) | Santa Cruz Biotechnology | Cat. # sc52746 |
| Anti-mouse F4 -80 (1:50 - IHC) | Bio-Rad Laboratories | Cat. # MCA497RT |
| Anti-rabbit FNDC5/irisin (1:1500) | Phoenix Pharmaceuticals | Cat. # G-067-16 |
| Anti-rabbit HRP -linked (1:2000) | Cell Signaling Technology | Cat. # 7074S |
| Anti-goat HRP-linked (1:2000) | Santa Cruz Biotechnology | Cat. # sc2354 |
| Anti-mouse HRP-linked (1:2000) | Thermo Fisher Scientific | Cat. # 31430 |
| Biotinylated anti -rabbit H+L (1:200) | Vector Laboratories | Cat. # BA-100 |
| Biotinylated anti -mouse H+L (1:200) | Vector Laboratories | Cat. # BA-200 |

Supplementary Figure 1





Supplementary Figure 2

