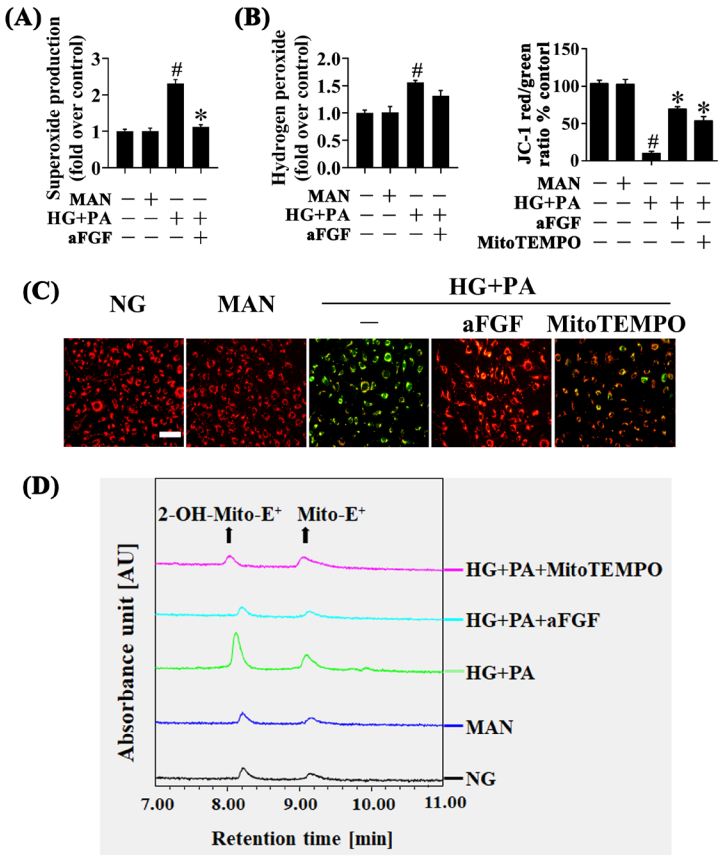


**Fig. S1: aFGF attenuated diabetes-induced endothelial dysfunction in vitro.** (**A, B**) Intracellular superoxide and peroxides levels. (**C**) Mitochondrial membrane potential was detected by JC-1 fluorescence staining, scale bars=1000 μm. (**D**) Chromatogram (UPLC-Abs) of the mixture of 2-OH-Mito-$E^+$ and Mito-$E^+$ in cell lysates.

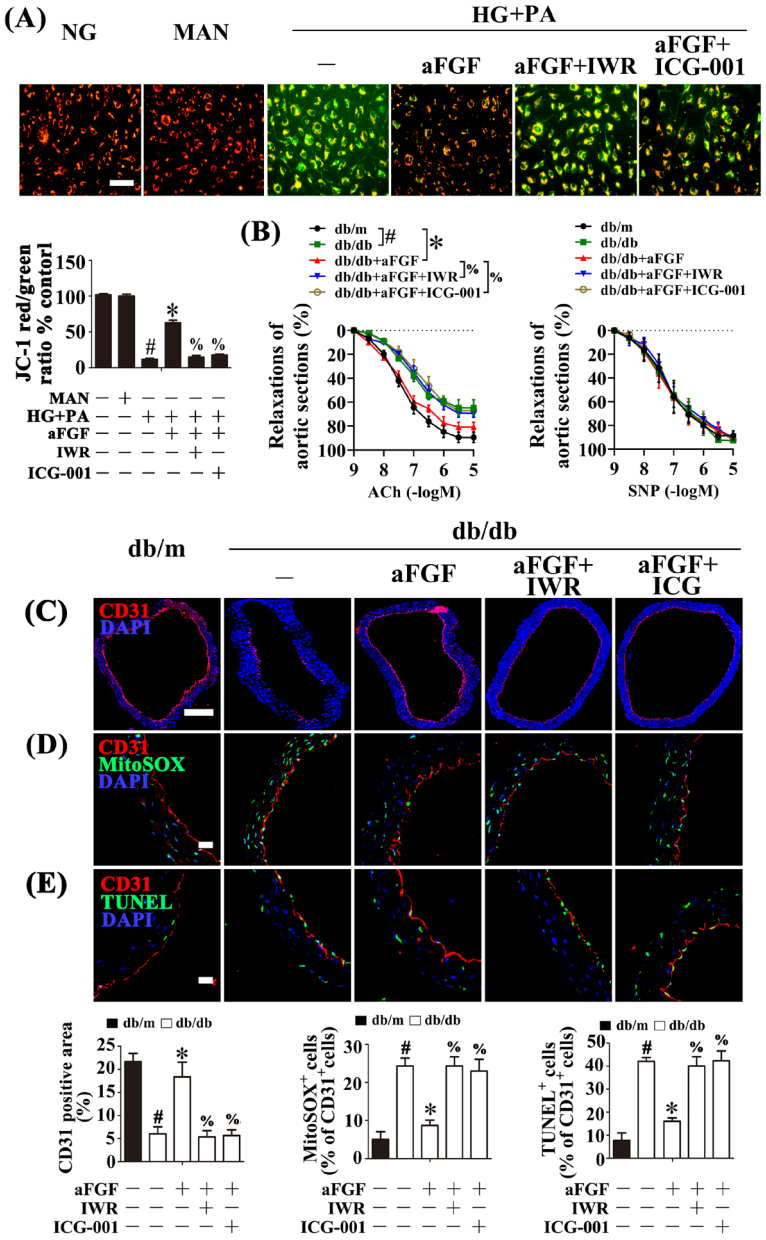


**Fig. S2: The endothelial protective action of aFGF against diabetes is Wnt/β-catenin signaling pathway dependent.** (**A**) Mitochondrial membrane potential was detected by JC-1 fluorescence staining, scale bars=1000 μm. (**B**) Concentration–response curves following Ach or SNP treatments of mice aortic rings. For signaling pathway analysis, IWR and ICG-001 was injected i.p. at 5 mg/kg right after aFGF i.p. injection. (**C**) Representative immunofluorescence with CD31 in aorta tissue sections, scale bars=200 μm. (**D**) Representative confocal images of MitoSOX stained aorta tissue sections, scale bars=20 μm. (**E**) Representative confocal images of TUNEL stained aorta tissue sections, scale bars=20 μm, from db/db mice, and

intraperitoneal aFGF (0.5 mg/kg) treated db/db mice. All values displayed are means ± SEM of 6 independent experiments. For (A)-(B), # $p < 0.05$ vs. NG or MAN; * $p < 0.05$ vs. HG+PA; % $p < 0.05$ vs. HG+PA co-incubated with aFGF; For (C)-(E), # $p < 0.05$ vs. db/m mice; * $p < 0.05$ vs. db/db mice or vehicle treated db/db mice; % $p < 0.05$ vs. aFGF intraperitoneally injected db/db mice.

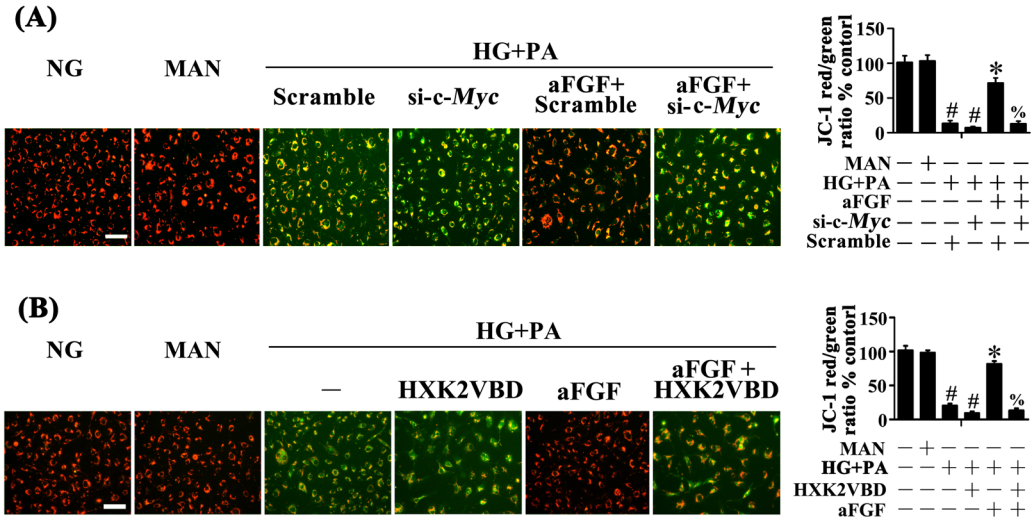


**Fig. S3:** Mitochondrial membrane potential was detected by JC-1 fluorescence staining, scale bars=1000 μm.

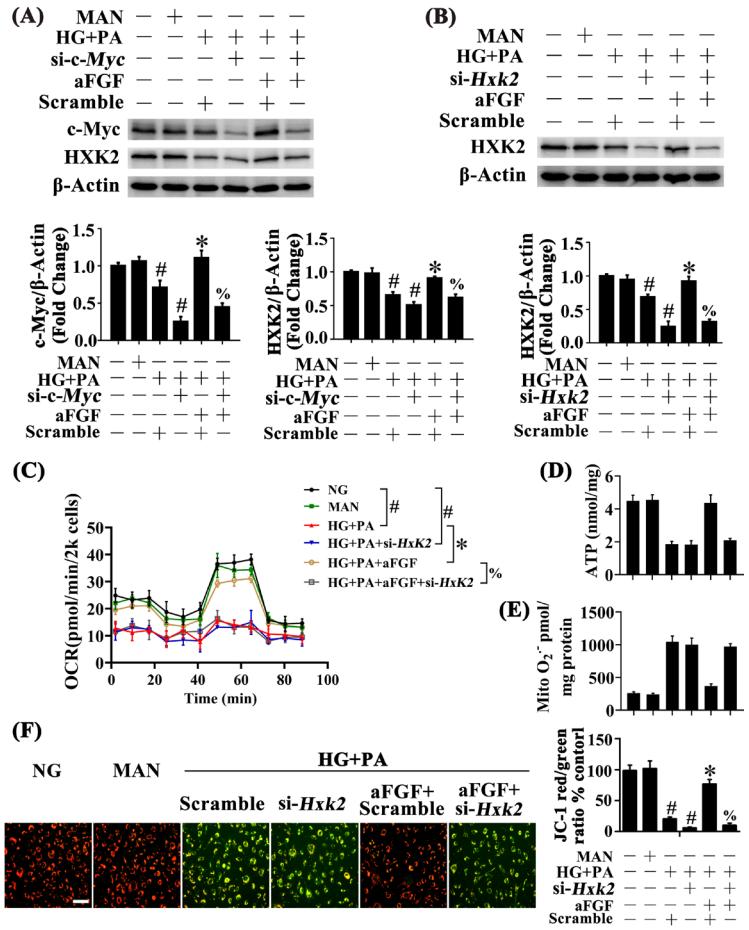


**Fig. S4: aFGF promoted c-Myc expression to increase HXK2 expression.** (**A**) Cell lysates of HUVECs were used to detect the c-Myc, HXK2 protein levels by immunoblotting. (**B**) Cell lysates of HUVECs were used to detect the HXK2 protein levels by immunoblotting, HUVECs were transfected with si-*c-Myc* or si-*HXK2*, respectively. A scrambled sequence was also transfected as control. After transduction, HUVECs were cultured either in NG or HG+PA medium alone or with aFGF (100 ng/mL) for 72 h, MAN was served as the osmotic control for the HG+PA. (**C**) OCR was analysed using a Seahorse XF analyser. (**D**) ATP production in HUVEC. (**E**) Mitochondrial $O_2^{\bullet-}$ in HUVEC was measured by mitochondria targeted probe MitoSOX and UPLC after accumulation of $O_2^{\bullet-}$-specific product 2-OH-Mito-$E^+$. (**F**) Mitochondrial membrane potential was detected by JC-1 fluorescence staining, scale bars=1000 μm. All values displayed are means ± SEM of 6 independent experiments. # $p < 0.05$ vs. NG or MAN; * $p < 0.05$ vs. HG+PA; % $p < 0.05$ vs. HG+PA co-incubated with aFGF.

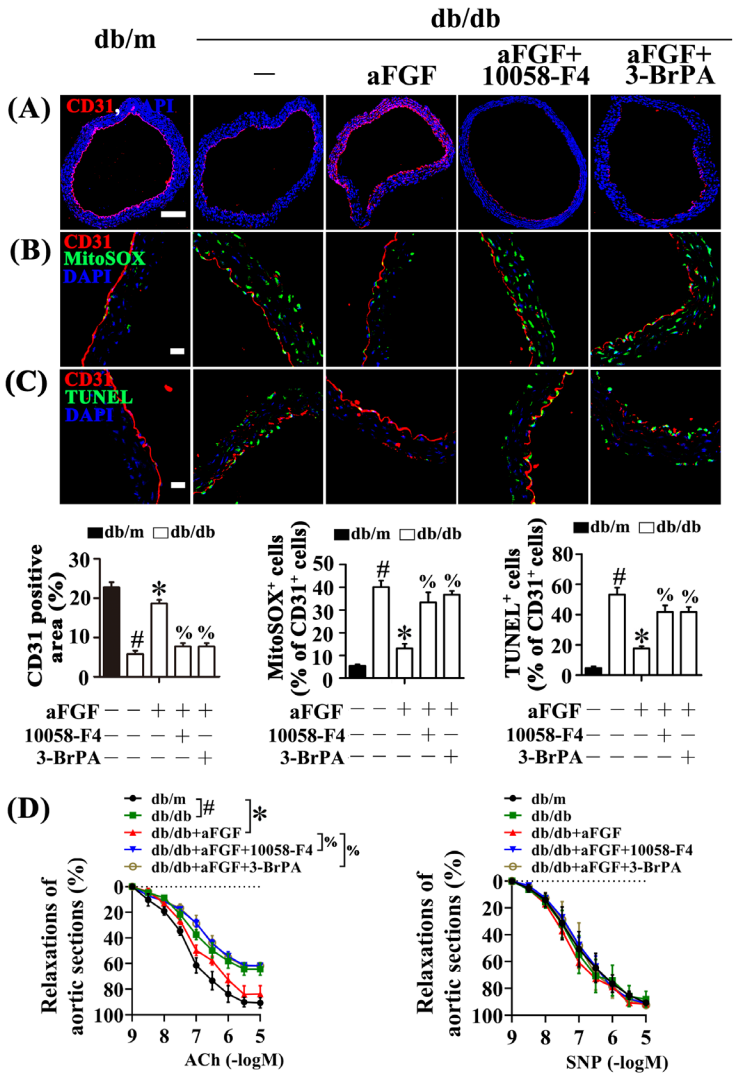


**Fig. S5: aFGF alleviated diabetes-induced endothelial dysfunction via c-Myc/ HXK2.** (**A**) Representative immunofluorescence with CD31 in aorta tissue sections, scale bars=200 μm. For signaling pathway analysis, 10058-F4 was injected i.p. at 30 mg/kg right after aFGF i.p. injection, 3-BrPA was injected i.p. at 8 mg/kg right after aFGF i.p. injection. (**B**) Representative confocal images of MitoSOX stained aorta tissue sections, scale bars=20 μm. (**C**) Representative confocal images of TUNEL stained aorta tissue sections, scale bars=20 μm. (**D**) Concentration–response curves following Ach or SNP treatments of mice aortic rings. All values displayed are means ± SEM of 6 independent experiments. # $p < 0.05$ vs. db/m mice; * $p < 0.05$ vs. db/db mice or vehicle treated db/db mice; % $p < 0.05$ vs. aFGF intraperitoneally injected db/db mice.

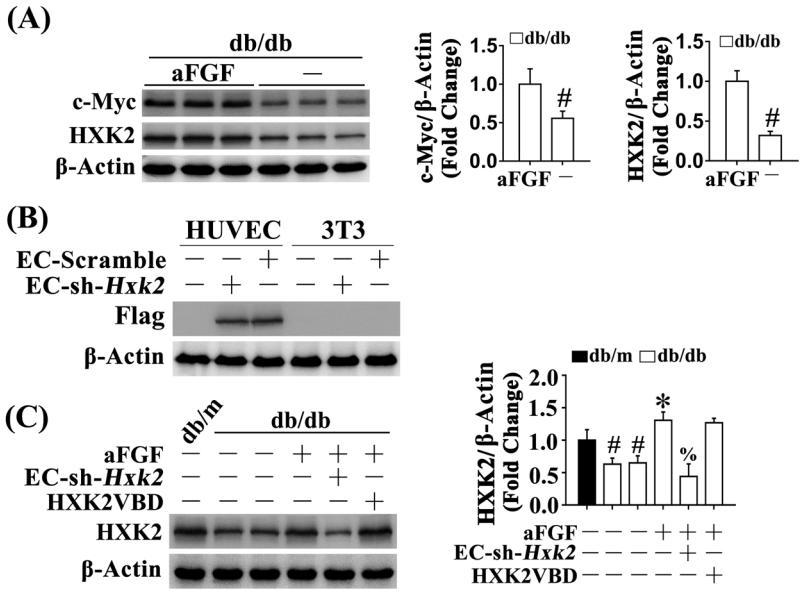


**Fig. S6: aFGF promoted c-Myca and HXK2 expression.** (**A**) Cell lysates of skins from db/db mice and db/db mice receiving aFGF (100 ng/mL) treatment were used to detect the c-Myc and HXK2 protein levels by immunoblotting. **(B)** Cell lysates of HUVECs and mouse fibroblast NIH3T3 cells were used to detect the Flag expression by immunoblotting. HUVECs and mouse fibroblast NIH3T3 cells were infected with Flag-tagged adenovirus vectors carrying a short hairpin RNA against murine HXK2 mRNA or a scrambled sequence under control of the murine vascular Cdh5/Cadherin 5 core promoter in HUVECs or NIH3T3 fibroblasts. **(C)** The lysates of skin wounds from db/m mice, db/db mice and db/db mice receiving aFGF (100 ng/mL) treatment, were used to detect the HXK2 protein levels by immunoblotting. For signaling pathway analysis, Ad-sh-HXK2 was injected intradermally into the wound edges in the mice the day before wounding, HXK2VBD peptide (100 μM) was injected intradermally into the wound edges in the mice after aFGF treated on the wound. All values displayed are means ± SEM of 6 independent experiments. # $p < 0.05$ vs. db/m mice; * $p < 0.05$ vs. db/db mice or vehicle treated db/db mice; % $p < 0.05$ vs. aFGF intraperitoneally injected db/db mice.