## **Supplementary materials**

**Figure S1. Histopathological changes of tissue and organ of mice injuried by iron overload.** A large amount of iron particles accumulation (Pink arrow), inflammatory infiltration (Green arrow), spotty necrosis (Blue arrow), piecemeal necrosis (Yellow arrow), and hypertrophy of interstitial cells (Orange arrow) were exhibited (400×). (A) Heart. (B) Liver. (C) Islet tissue.

Figure S2. Mice's thoracic aortas constriction to phenylephrine (PE:  $10^{-10}$ - $10^{-4}$  M). Constriction responses to PE did not differ among any group's thoracic aortas (*P*> 0.05). Data are presented as the mean ± SEM. for fifteen individual experiments.

Figure S3. Effects of iron-D and equal concentration Dex on the cell viability and

**LDH activity of HUVECs.** HUVECs viability/LDH activity of iron-D treated were lower/higher in a dose-dependent manner, but cell viability and LDH activity did not change by using Dex of equal concentration gradient, indicating that the changes were the result of iron action and had nothing to do with osmotic pressure. (A) Histogram of the cell viability. (B) Histogram of the LDH activity. Data are presented as the mean  $\pm$  SEM. for eight individual experiments. a: *P*<0.01, *vs* prior dosage.

Figure S4. Effects of Eda/CsA/L-Arg, or up-/downregulated DDAH II expression, or upregulated DDAH II expression added I-NAME on the cell viability and LDH activity of HUVECs. Cell viability and LDH activity did not change by using Eda alone (100  $\mu$ M), CsA alone (1  $\mu$ M), L-Arg alone (1 mM), or up-/downregulated DDAH II expression alone, or upregulated DDAH II expression added 1-NAME (10  $\mu$ M) when compared with the control group (p>0.05). (A) Histogram of the cell viability. (B) Histogram of the LDH activity. Data are presented as the mean  $\pm$  SEM. for eight individual experiments.

Figure S5. Effects of Eda/CsA/L-Arg on the cell viability and LDH activity of HUVECs injuried by 50  $\mu$ M iron-D. Eda/CsA/L-Arg with 50  $\mu$ M iron-D co-treat HUVECs, the cell viability increased and LDH activity decreased. (A) Histogram of the cell viability. (B) Histogram of the LDH activity. Data are presented as the mean  $\pm$  SEM. for eight individual experiments. a: p<0.01, vs. control group; b: p<0.01, vs. iron group.

Figure S6. Effects of up-/downregulated DDAH II expression, or upregulated DDAH II expression added I-NAME on the cell viability and LDH activity of HUVECs injuried by 50  $\mu$ M iron-D. Upregulated DDAH II expression protected HUVECs against iron overload injury, but added I-NAME reversed the effects. Downregulated DDAH II expression could aggravate HUVECs damage induced by iron overload. (A) Histogram of the cell viability. (B) Histogram of the LDH activity. Data are presented as the mean  $\pm$  SEM. for eight individual experiments. a: P < 0.01, vs. control group; b: P < 0.01, vs. iron group.

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Figure S1



Figure S2















Figure S6