Beta-cell regeneration from vimentin⁺/MafB⁺ cells after STZ-induced extreme beta-cell ablation

Yu Cheng^{a,b,e}, Hongjun Kang^{d,e} Jing Shen^{a,b,c,e}, Haojie Hao^b, Jiejie Liu^b, Yelei Guo^b, Yiming Mu^a* and Weidong Han^b*

^aDepartment of Endocrinology, Chinese PLA General Hospital, 28 Fuxing Road, Beijing 100853, China;^bDepartment of Molecular Biology, Institute of Basic Medicine, School of Life Science, Chinese PLA General Hospital, 28 Fuxing Road, Beijing 100853, China; ^cDepartment of Endocrinology, Chinese PLA 309 Hospital, 17 Heishanhu Road, Beijing 100091, China; ^dDepartment of Critical Care Medicine, Chinese PLA General Hospital, 28 Fuxing Road, Beijing 100853, China.

^e*These authors contributed equally to this work*

*Correspondence should be addressed to: MD., Ph.D. Yiming Mu Department of Endocrinology, Chinese PLA General Hospital, Beijing 100853, China E-mail: muyiming@301hospital.com.cn Tel.: +86(10)55499001 Fax: +86(10)68168631

MD., Ph.D. Weidong Han Department of Molecular Biology, Institute of Basic Medicine, School of Life Sciences, Chinese PLA General Hospital, Beijing 100853, China E-mail: hanwdrsw69@yahoo.com Tel.: +86(10)66937463 Fax: +86(10)66937516



Figure S1. A single high dose STZ induced acute and extreme beta-cell injury. (A) Representative islets stained with insulin (red) of normal control SD rats (Nor), and STZ-treated rats at indicated time points (8h, 16h). Nuclei were labeled with DAPI. Scale bars, 50µm. The isosceles triangle: remaining insulin stained cells. (B) Representative islets stained with F480 (red) of STZ-treated rats (8h). Scale bars, 50µm. (C) Representative islets from rat pancreas sections (4µm). The sections were performed with hematoxylin and eosin staining. The isosceles triangle: a group of round-shaped cells. Scale bars, 20µm. (D) Quantification of b-cell number. (E, F) Ins1 and Ins2 gene expression in isolated islets of normal control and STZ-treated rats (16h). Data are shown as means \pm SEM, n=5-6 rats per group. *P < 0.05 and **P < 0.01.



Figure S2. Random blood glucose levels post STZ injection. Data are shown as means \pm SEM, n=10 rats.



Figure S3. The round-shaped vimentin⁺ cells did not express macrophage marker F480. The photomicrographs in the left column showed representative islets stained with anti-F480 (gray), and the right column with anti-vimentin (red) and anti-insulin (green) antibodies of the consecutive slides from normal control SD rats (Nor), and STZ-treated rats at different time points (16 h, 24 h). Nuclei were labeled with DAPI. Scale bars, 50µm.



Figure S4. Very limited recruitment of nestin-positive cells to damaged islets. The photomicrographs stained with anti-vimentin (red) and anti-nestin (green) antibodies from normal control SD rats (Nor), and STZ-treated rats at different time points (16 h, 24 h). Nuclei were labeled with DAPI. Scale bars, $100\mu m$.



Figure S5. Massive beta-cell loss induced limited Ngn3 activation. (A) Expression of Ngn3 gene in pancreas of normal control and STZ-treated rats at indicated time points (8 h, 16 h, and 24 h). (B) Photomicrographs double stained with anti-vimentin (green) and anti-Ngn3 (red) antibodies of normal control and STZ-treated rats (16 h, 24 h). Nuclei were labeled with DAPI. Scale bars, 50 μ m. The isosceles triangle: Ngn3⁺ cells. Data are shown as means ± SEM, n=3 per group; *P < 0.05 and **P < 0.01.