

**Inhibition of SGLT-2 rescues bone marrow cell traffic for vascular repair.
Role of glucose control and ketogenesis**

Online Appendix

Table S1. Antibodies for flow cytometry

Antigen	Fluorophore	Clone	Company	Volume/test [μ L]
Lineage Cocktail (CD3, Ly-6G/C, CD11b, CD45R, TER-119)	Pacific blue	17 $^{\circ}$ 2, RB6-8C5, Ra3-6B2, Ter-119, M1/70	BioLegend	10
Isotype control	Pacific blue	Rat IgG2a K	BioLegend	10
CD117 (c-kit)	FITC	2B8	eBioscience	4
Ly-6A/E (Sca-1)	PE	D7	eBioscience	3,5
F40-80	APC/Cy7	BM8	BioLegend	2,5
Ly-6G (GR-1)	PE	RB6-8C5	eBioscience	0,5
CD49	Alexa Fluor 647	R1-2	BD Bioscience	2
CD48	PerPC/Cy5.5	HM48-1	BioLegend	0,5
CD150	PE-Cy7	TC15-12F12.2	BioLegend	2
CD16/32	PerCP-eFluor710	93	Invitrogen	0,5
CD34	eFluor 660	RAM34	eBioscience	5
SIGLEC-F	Brilliant Violet 421 TM	S17007L	BioLegend	1.5

Table S2. Primers for qPCR

Primers name	Sequence (5'-3')
mSGLT2	Fw: TGGTGTGGCTTGTGGTCTA Rv: ATGTTGCTGGCGAACAGAGA
mEPO	Fw: ACTCTCCTTGCTACTGATTCCT Rv: ATCGTGACATTTTCTGCCTCC
mUBC	Fw: GCCCAGTGTTACCACCAAGA Rv: CCCATCACACCCAAGAACA

Figure S1. Expression of the SGLT-2 in mouse tissues. Note the different scale for panel B compared to A and C. The bone marrow column in A and C is reproduced from the same data. The housekeeping gene was ubiquitin (*Ubc*). D) Protein expression of SGLT-2 was not detected by immunofluorescence staining of BM sections, whereas a strong signal was observed in the kidney, as expected.

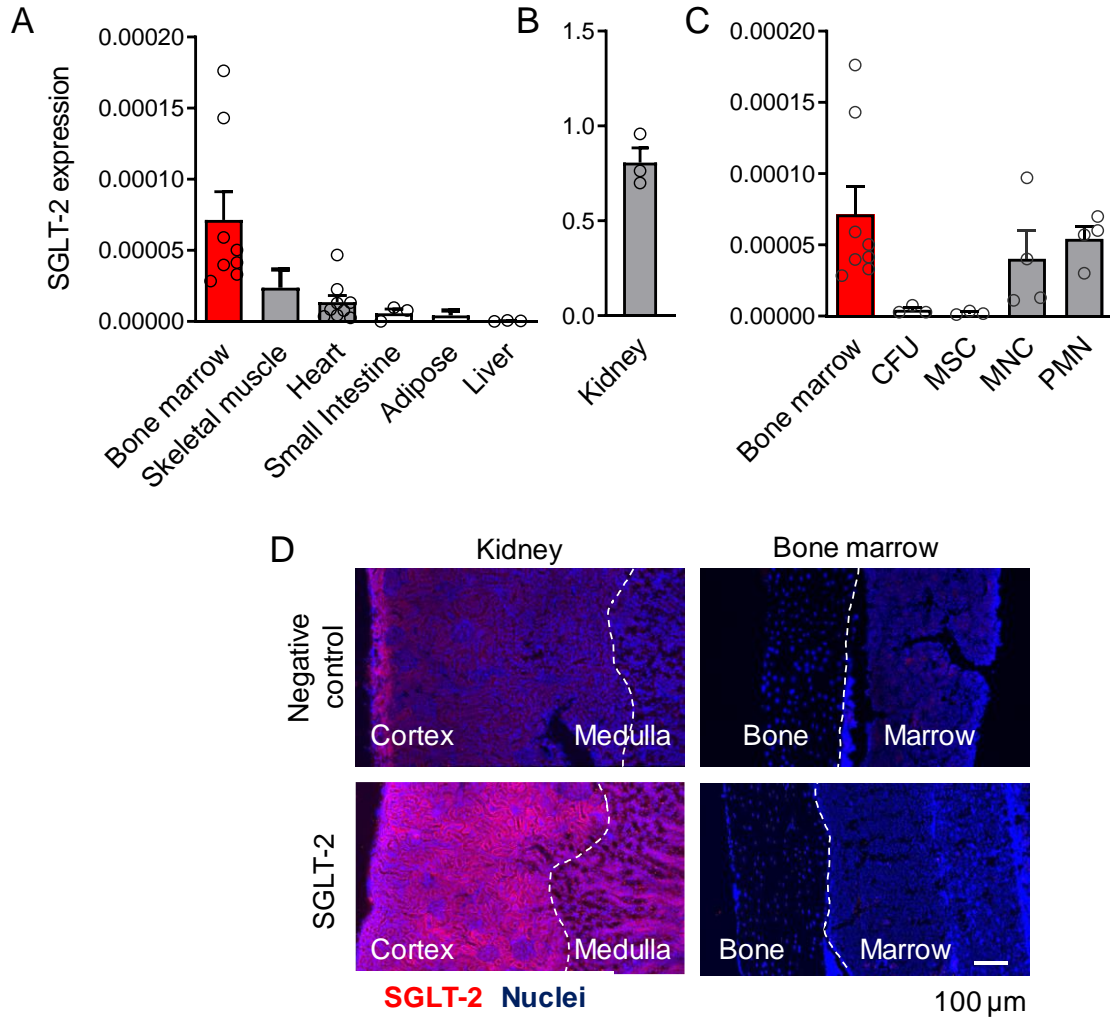


Figure S2. Hematopoietic colonies. The different types of hematopoietic colonies were examined in the ex vivo assay, with bone marrow cells collected from STZ diabetic and non-diabetic control mice treated with dapagliflozin or vehicle (A) and in vitro, by using different concentrations of dapagliflozin (B).

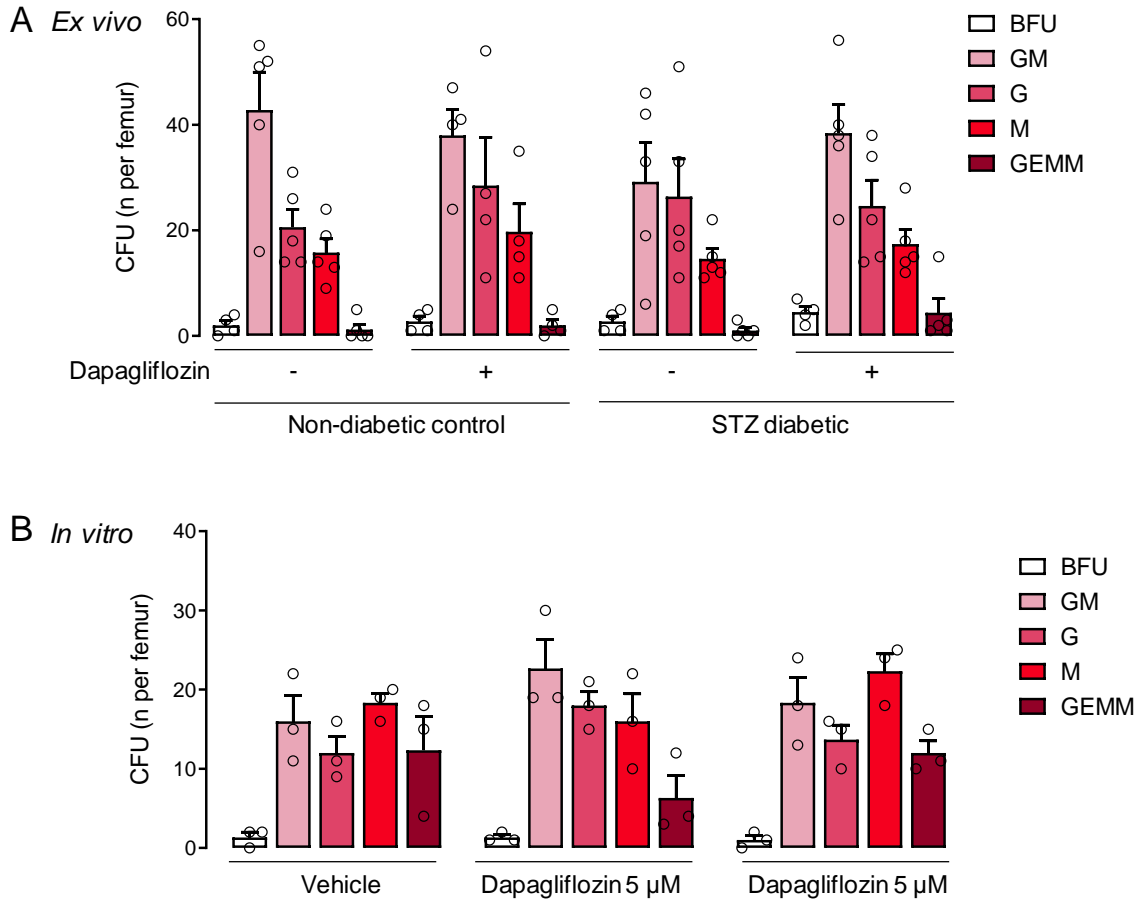


Figure S3. Mobilization and endothelial healing in T2D-like mice. A type 2 diabetes (T2D)-like model was developed by high fat diet (HFD) feeding for 6 weeks, while control mice were kept on a standard diet (SD). A separate batch of mice on HFD were treated with dapagliflozin during the last 2 weeks of HFD. Panel A shows results of the intraperitoneal glucose tolerance test with AUC given in panel C. Change in body weight, along with the effect of dapagliflozin, is shown in panel B. Panel C also reports concentrations of β -hydroxy-butyrate (β -OHB) in the three groups of mice. HSPC mobilization in non-diabetic control mice on SD (D, same data as in Figure 2 of the main manuscript) and HFD mice (E) treated with vehicle or dapagliflozin. F) Carotid endothelial healing in control mice on a SD, mice on HFD, and mice on HFD with dapagliflozin treatment. Representative micro-photographs are shown on the right. * $p < 0.05$ versus control or for the indicated comparison. Bar charts have superimposed individual datapoints and bars indicate standard error. Box plots show median (line), interquartile range (box) and total range (whiskers) with individual lines indicating single mice.

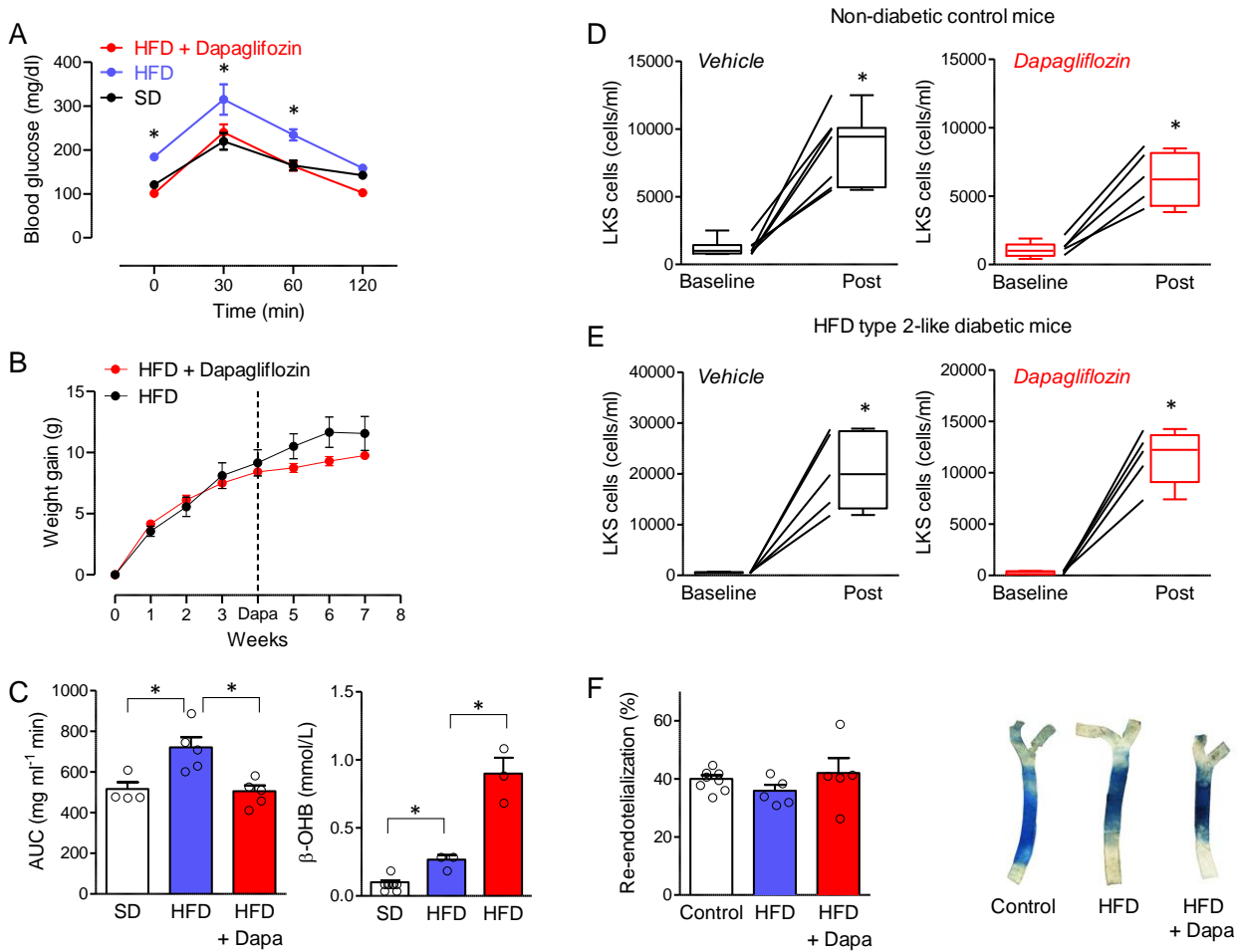


Figure S4. Characterization of bone marrow transplanted mice. A) Degree of chimerism achieved upon reconstitution after transplantation. We compared the % of GFP+ cells in peripheral blood and bone marrow of wild type (WT) control mice and in mice who received a bone marrow transplantation (BMT) from GFP-expressing mice. B) Comparison of white blood cell count (WBC), hemoglobin concentrations, and WBC types in non-diabetic control (Ctrl) mice and in mice examined 4 weeks after bone marrow transplantation (BMT) with GFP+ cells.

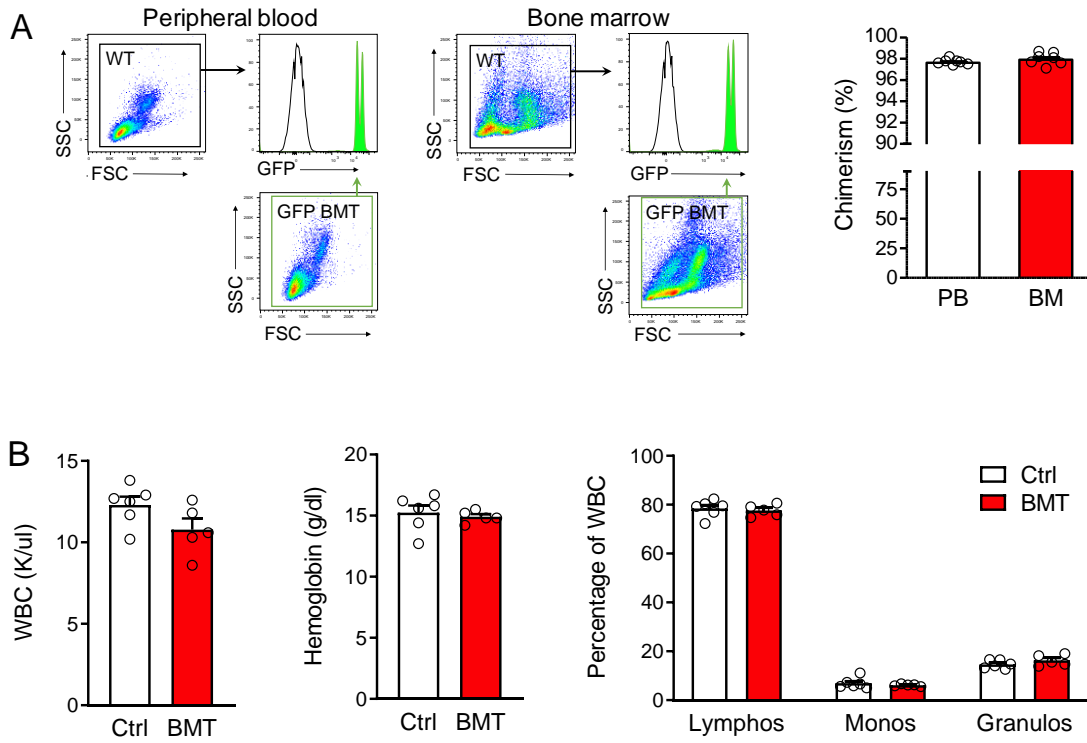


Figure S5. No mobilization effect of low-dose AMD3100. We tested mobilization after administering non-diabetic control mice with low-dose AMD3100 (AMD). Antigenically defined HSPCs ($\text{Lin}^{-\text{c}}\text{-kit}^{+}\text{Sca-1}^{+}$, LKS, cells) were measured at baseline and after AMD treatment. The Y-axis scale is similar to those of figures in the main manuscript is used to show no mobilization of HSPCs. For comparison, panel A, taken from figure in the main manuscript shows the effect of G-CSF, panel B the effect of low-dose AMD on HSPC mobilization. C) Comparison between G-CSF and AMD3100 on the mobilization of CD49d^{+} neutrophils. * $p < 0.05$ versus baseline. Bar charts have superimposed individual datapoints and bars indicate standard error. Box plots show median (line), interquartile range (box) and total range (whiskers) with individual lines indicating single mice.

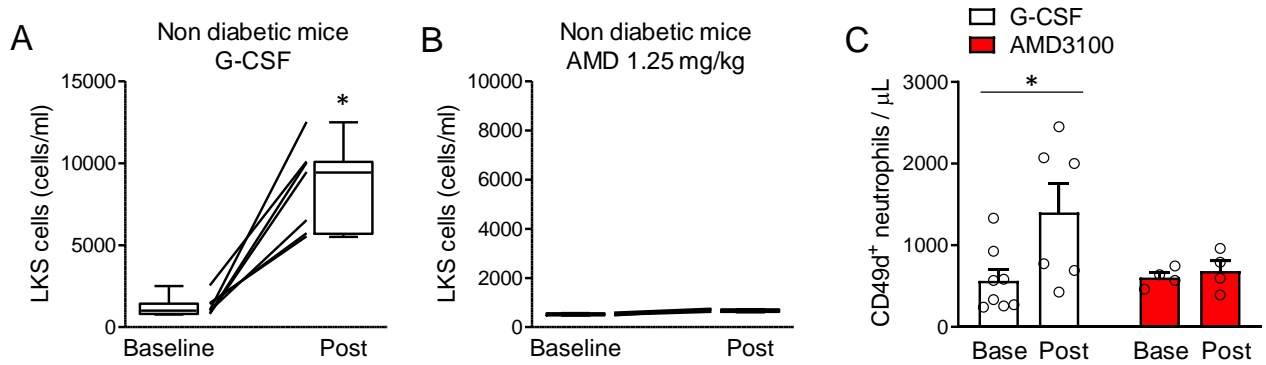


Figure S6. Effects of dapagliflozin on EPO. Dapagliflozin (red columns) versus vehicle (white columns) treatment on EPO gene expression in the kidney (A) or EPO concentration in the plasma (B) of non-diabetic control (Ctrl) mice or type 1 diabetic (T1D) mice. * $p < 0.05$. Bar charts have superimposed individual datapoints and bars indicate standard error.

