SUPPLEMENTARY DATA

Supplementary Table 1. Multivariable analysis with circulating $CD34^+$ cell level as dependent variables and clinical characteristics identified by univariate analysis as explanatory variables.

Variable	**Beta-coefficient**	**p-value**
DAN	-0.377	<0.001
Age	-0.101	0.297
Diabetes type	0.151	0.121
HbA1c	-0.141	0.085
Retinopathy	0.096	0.289
Heart rate	0.023	0.791

Supplementary Table 2. Clinical characteristics of patients with available measure of PBMC expression of *p66Shc* and *Sirt1* (extracted from table 1).

Characteristic	**No DAN**	**DAN**
Age, years	60.0±14.0	59.7±15.0
Sex male, %	70	70
Type 1 / type 2 diabetes	3/7	3/7
Disease duration, years	10.0±7.8	12.9±7.8
HbA1c, %	7.7±1.8	7.9±1.4
p66Shc / β-actin expression	1.01±0.15	1.63±0.95
Sirt1 / β-actin expression	1.09±0.29	0.75±0.17

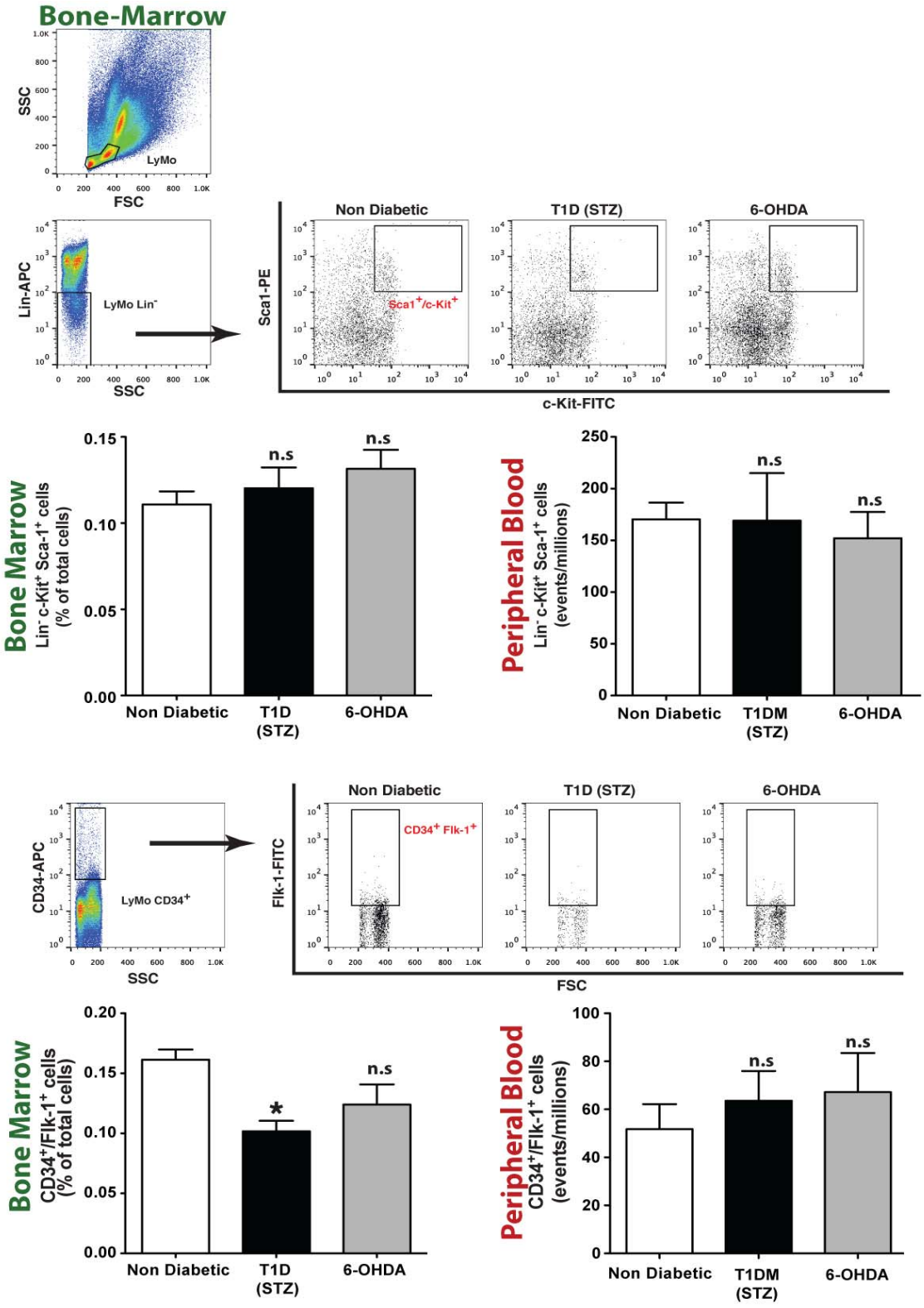
SUPPLEMENTARY DATA

Supplementary Table 3. Primer sequences.

Genes	FW primer sequence	RV primer sequence	Sequence accession number
Mouse genes			
vascular cell adhesion molecule 1 *(Vcam1)*	TATGTCAACGTTGCCCCCAA	GCTGTCTGCTCCACAGGATT	NM_011693.3
src homology 2 domain-containing transforming protein C1 (*Shc1*) – p66shc	TGACAGGATGGCTGGCTT	ACGGACTTCATGGTCTCC	NM_001113331.2
intercellular adhesion molecule 1 (*Icam1*)	AGCTCGGAGGATCACAAACG	TCCAGCCGAGGACCATACAG	NM_010493.2
integrin alpha L (*Itgal*) – CD11a	ACTTCCACTTCCCGATCTGC	CCACCTTTTGGTCCCTTGGT	NM_001253872.1
integrin alpha 4 (*Itga4*) – CD49d	GTTCTCCACCAAGAGCGCAT	GATGAGCCAGCGCTTCGAC	NM_010576.3
integrin alpha 5 (*Itga5*) – CD49e	GAACCCTGTGTCCTGCATCA	TTGGAGTTCCACCTCGAAGC	NM_010577.3
selectin, lymphocyte (*Sell*) – CD62L	TGATGCAGGGTATTACGGGC	CACTGGACCACTTGGCAGAT	NM_001164059.1
integrin alpha X (*Itgax*) – CD11c	TCTTCTGCTGTTGGGGTTTGT	GAGCACACTGTGTCCGAACT	NM_021334.2
Sirtuin 1 (*Sirt1*)	CAGTAGCACTAATTCCAAGTTCTA	TTGGCATATTCACCACCTAGC	NM_001159589.1
ubiquitin C (*Ubc*)	GCCCAGTGTTACCACCAAGA	CCCATCACACCCAAGAACA	NM_019639.4
Human Genes			
sirtuin 1 (*SIRT1*)	TACCGAGATAACCTTCTGTTCG	GTTCGAGGATCTGTGCCAAT	NM_012238.4
selectin L (*SELL*) – CD62L	GCCCTCTGTTACACAGCTTCT	GGCCCATAGTACCCCACATC	NM_000655.4
actin, beta (*ACTB*)	GGATGCCACAGGACTCCA	AGAGCTACGAGCTGCCTGAC	NM_001101.3
src homology 2 domain-containing transforming protein C1 (*SHC1*) – p66shc	AATCAGAGAGCCTGCCACATT	CTCTTCCTCCTCCTCATC	NM_001130040

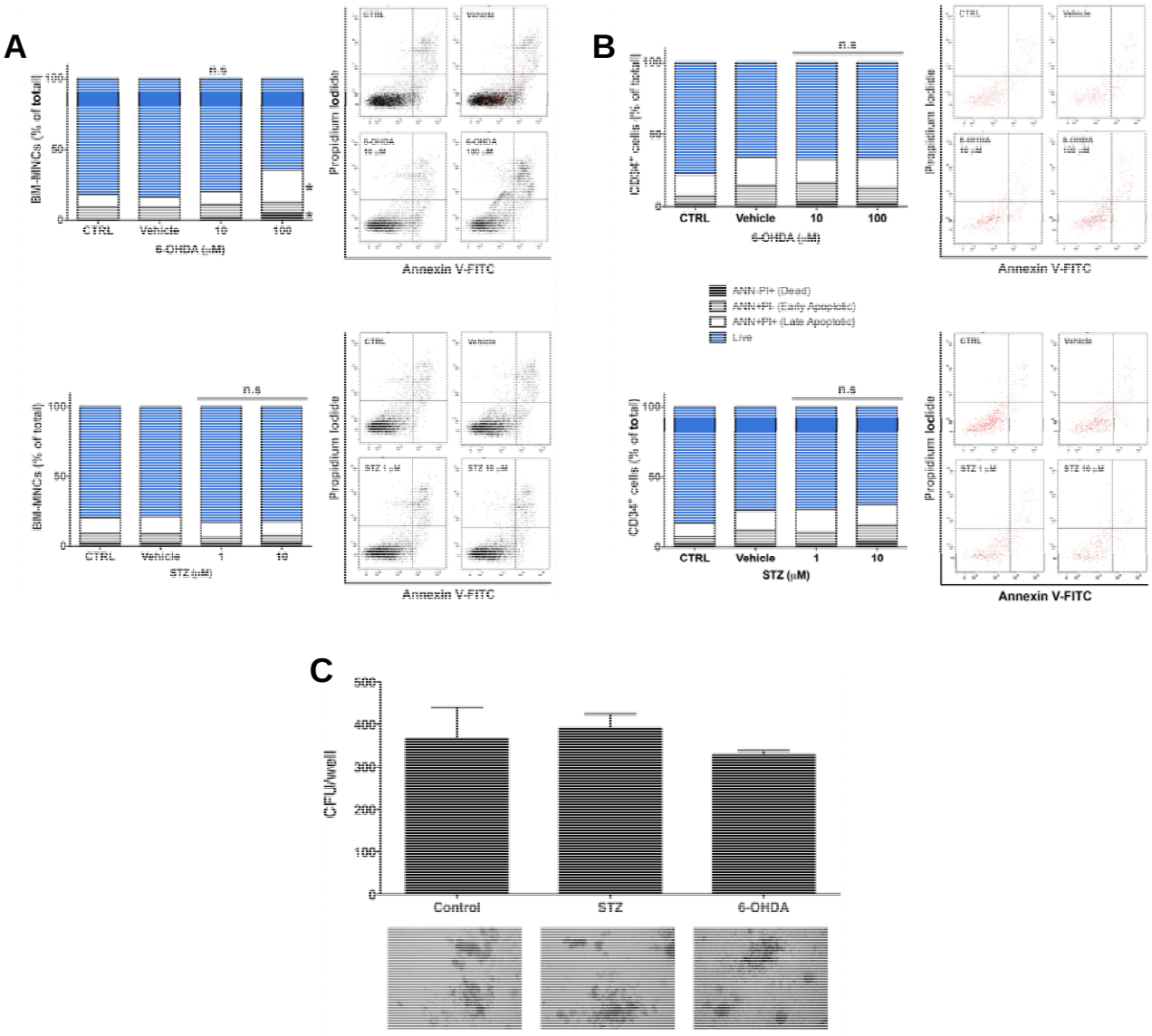
SUPPLEMENTARY DATA

Supplementary Figure 1. Baseline levels of EPC and LKS cells in diabetic and sympathectomized (6-OHDA) mice. * p<0.05 versus non-diabetic control mice. “n.s.” stands for “not significant” compared with non-diabetic control mice.



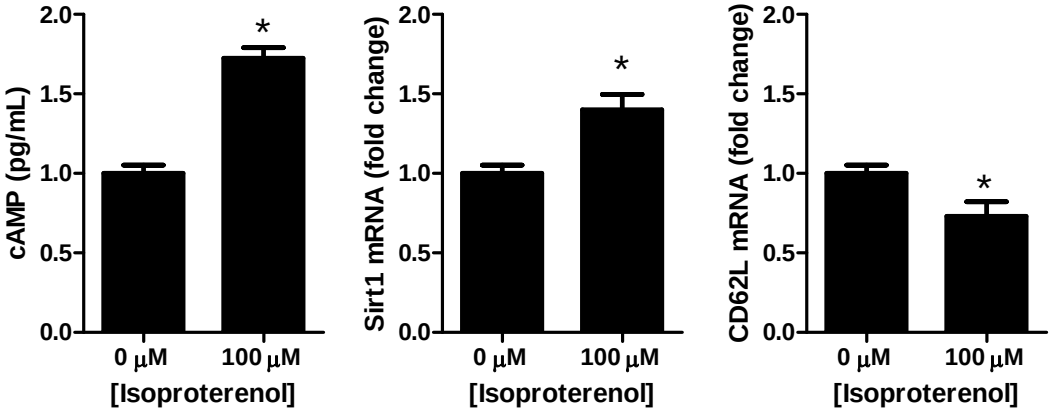
SUPPLEMENTARY DATA

Supplementary Figure 2. Effects of STZ and 6-OHDA in vitro on apoptosis and necrosis of total murine bone marrow cells (A), murine CD34+ bone marrow cells (B) and growth of hematopoietic colonies from murine bone marrow cells (C). In panel (A), *p<0.05 versus percentages in the control (CTRL) condition. In (C), both STZ and 6-OHDA were incubated at 10 microM concentration.

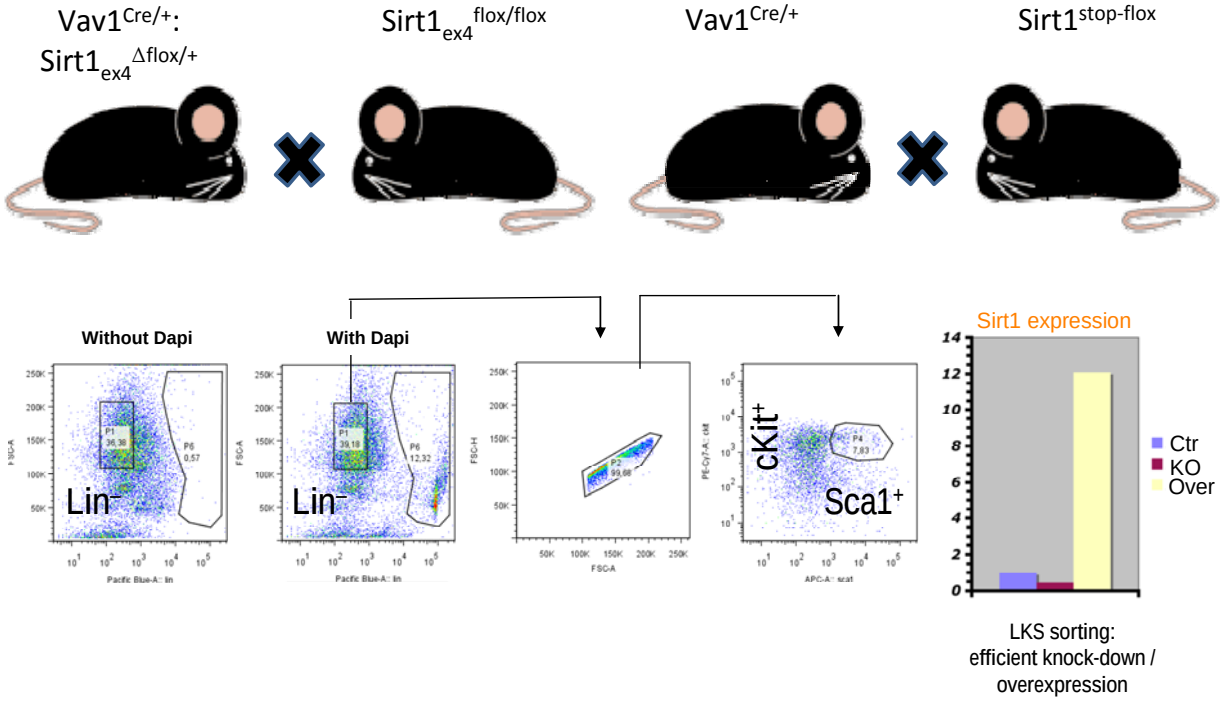


SUPPLEMENTARY DATA

Supplementary Figure 3. Effects of isoproterenol on PBMC Sirt1 and CD62L expression. PBMC of healthy human donors were incubated without or with isoproterenol 100 µM and gene expression of Sirt1 and CD62L (L-selectin, Sell), were analyzed. The cellular concentration of cyclic AMP (cAMP) were also determined to select isoproterenol concentrations that result in increased cAMP production. *p<0.05 100 vs 0 µM isoproterenol.

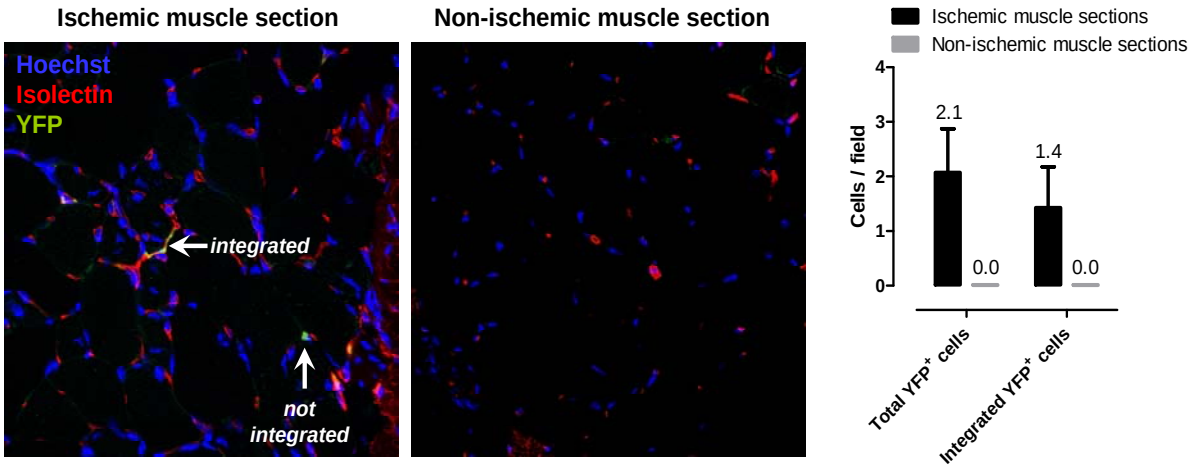


Supplementary Figure 4. Generation and characterization of transgenic animals. The breeding strategy used to generate Vav1-Sirt1$^{-/-}$ and Vav1-Sirt1^{TG} mice is shown. Knock-out and overexpression of Sirt1, respectively, was confirmed by real time PCR on LKS cells isolated by FACS.

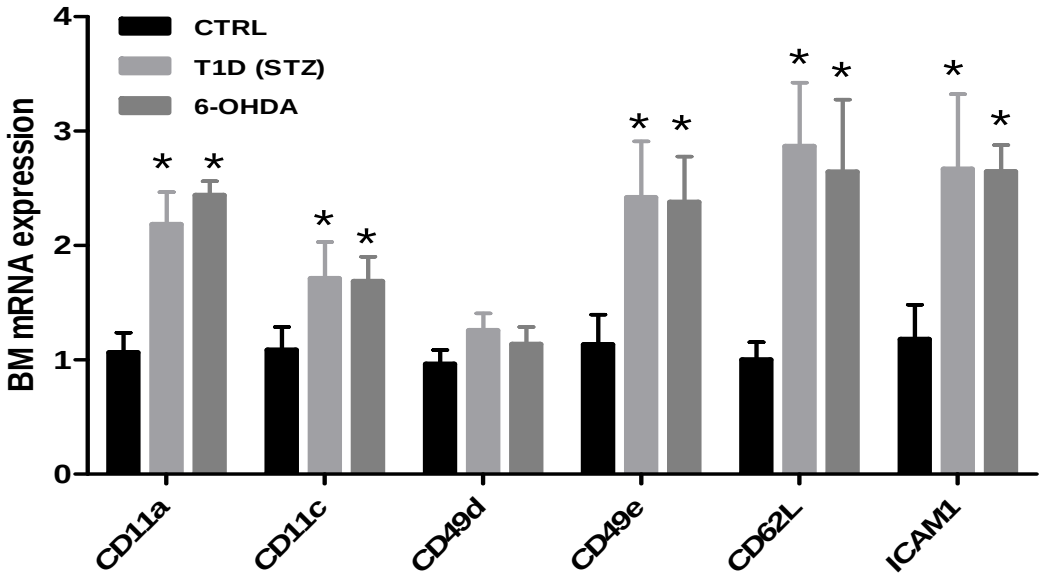


SUPPLEMENTARY DATA

Supplementary Figure 5. Contribution of Vav1$^+$ cells to the microvasculature of ischemic muscles. Vav1-YFP mice were subjected to hind limb ischemia and muscle sections stained for Isolectin B4 (red) to visualize the vascular network (nuclei counterstained in blue with Hoechst); the green/yellow signal represents the spontaneous YFP fluorescence. Merged figures are shown. YFP-expressing cells, indicating Vav1$^+$ cells were only found in sections of ischemic muscles and not of non ischemic contralateral control muscles. Some YFP$^+$ cells were clearly integrated into the vasculature co-staining with Isolectin, while other YFP$^+$ cells did not co-localize with the red Isolectin signal and were considered not integrated (likely intravascular). The right panel shows quantification of total (integrated and non integrated) and integrated cells in ischemic and non ischemic muscle sections.



Supplementary Figure 6. Expression of niche adhesion molecules in the BM. mRNA was extracted from BM cells of control non diabetic, T1D (STZ) and sympathectomised (6-OHDA) mice and analyzed for expression of typical niche genes encoding for adhesion molecules (n=5/group). *p<0.05 versus non diabetic control.



SUPPLEMENTARY DATA

Supplementary Figure 7. Time course analysis of bone marrow neuropathy development and upregulation of adhesion molecules in T1D mice from 1 to 4 weeks after STZ administration. In the lower panel, *p<0.05 versus basal; **p<0.05 versus 1 week.