SUPPLEMENTARY DATA

EPC Characterization and Enummeration

Heparinized blood samples were stained with saturating concentrations of monoclonal antibodies (mAb): fluorescein isothiocyanate (FITC) conjugated anti-CD31 mAb (Becton Dickinson (BD) Biosciences, San Jose, CA, clone WM59), phycoerythrin (PE) conjugated anti-CD309 (R&D, Minneapolis, MN, clone 89106), phycoerythrin-cyanin dye 5 (PECY5) labeled anti-CD34 (BD Biosciences, clone 581) and allophycocyanin (APC) conjugated anti-CD133 mAb (Miltenyi Biotec, Bergisch Gladbach, Germany, clone AC133) for 45 minutes [17,18]. We may have found different cell numbers compared to other groups due to the different antibody conjugations used. Anti-CD34 mAb is mostly used in FITC, although the general recommendation for stem cell enumeration by ISHAGE [33] is to use Anti-CD34 in a strong (reddish) color such as PE.

All experiments were performed with 30 min of cleaning time of flow cytometer before acquisition. After red blood cell lysis that also reduced the debris (up to 18% of all events in all acquisitions obtained), and removal of excessive antibody by washing, cells were instantly acquired on a FACS Calibur (BD Biosciences). The acquisition goals were $1x10^6$ events in the leukocyte gate. Results were only processed statistically if at least $5x10^5$ events were obtained. Progenitor cells were counted by flow cytometry and expressed in absolute numbers per 10^6 white blood cells to enable in between patient comparison. A gating strategy including four gates was applied in order to identify angiopoietic progenitor cells as reported previously [17,18]. Additionally, a negative control (background noise) was applied with phosphate-buffered-saline, but without antibody.

Data were only included in the analysis if the whole procedure (blood taking, transport, staining, lyse and wash procedure and acquisition on the flow cytometer) had taken less than five hours. Data were analyzed using Paint-a-gate software (BD Biosciences).

SUPPLEMENTARY DATA

Supplementary Table 1. Basic Characteristics of the longitudinal study of patients with Type 1 Diabetes Mellitus.

	Start	End	P value
Age (years)	13.3± 2.8	14.3± 2.8	**<0.001**
Systolic blood pressure (mm Hg)	112±14	114±15	0.281
Diastolic blood pressure (mm Hg)	62±10	63±8	0.705
Pulse	89±16	87±15	0.283
Height (cm)	159±14	163±13	**<0.001**
Weight (kg)	55±15	59±15	**<0.001**
Body mass index (kg/m^2)	21±3	22±3	**<0.001**
Total Cholesterol (mmol/l)	4.5±0.8	4.3±0.8	**0.014**
Triglyceride (mmol/l)	1.2±0.8	1.4±0.9	0.052
HDL cholesterol (mmol/l)	1.7±0.4	1.7±0.5	0.142
LDL cholesterol (mmol/l)	2.3±0.6	1.9±0.7	**<0.001**
VLDL cholesterol (mmol/l)	0.5±0.3	0.6±0.4	**0.001**
Fasting Glucose (mmol/l)	8.2±4.3	9.1±5.4	0.189
HbA1c (rel.%)	7.8±1.2	7.8±1.2	0.660
Creatinine (mg/dl)	0.70±0.13	0.74±0.17	**0.004**
eGFR (ml/min/1.73m^2)	134±21	135±36	0.826
Gamma-Glutamyl-Transferase (U/l)	16±4	14±4	**<0.001**
Aspartat-Aminotransferase (U/l)	25±6	33±49	0.135
Alanin-Aminotransferase (U/l)	31±5	27±17	0.053
C-reactive protein (µg/dl)	305±380	319±160	0.905

Data are given as mean±SD. HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein, estimated glomerular filtration rate after Schwartz Formula; an alpha-level of $p<0.05$ (two-tailed) is considered statistically significant; in bold are those significantly different as assessed by student's paired t-test.

SUPPLEMENTARY DATA

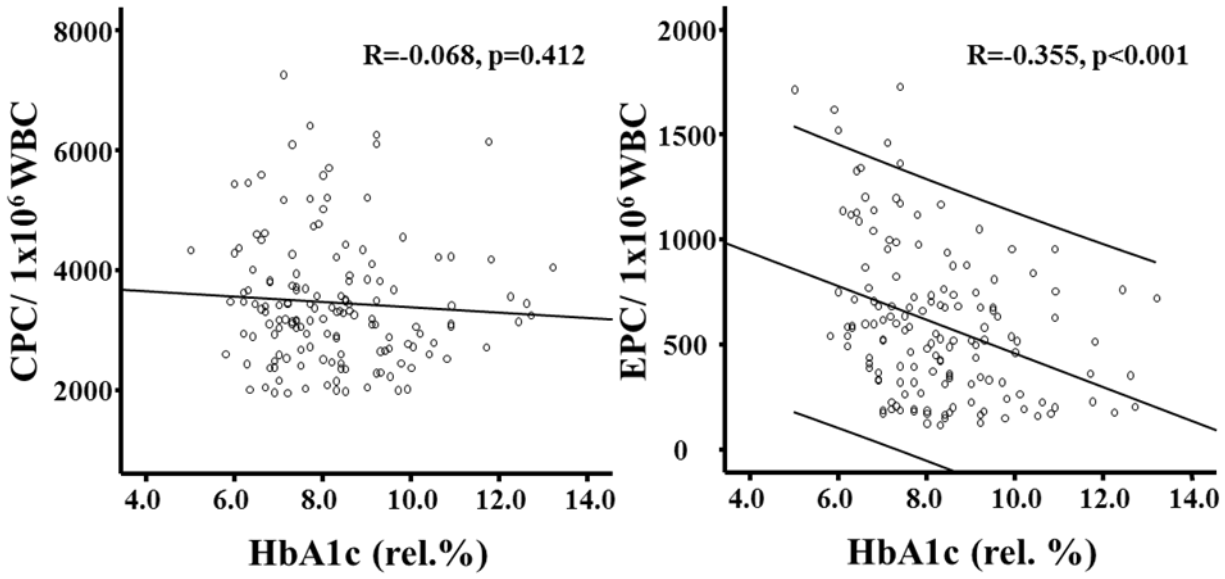
Supplementary Table 2. Multivariate Stepwise Backward Regression Analysis for determinants of EPC at time of inclusion.

		EPC	
Model	determinants	Beta	p-value
1	Systolic Blood Pressure	0.019	0.826
	Fasting Glucose	-0.085	0.317
	HbA1c	-0.354	<0.001
2	Fasting Glucose	-0.086	0.295
	HbA1c	-0.318	<0.001
3	HbA1c	-0.355	<0.001

EPC, endothelial progenitor cell; HbA1c, glycated haemoglobin A1c.

SUPPLEMENTARY DATA

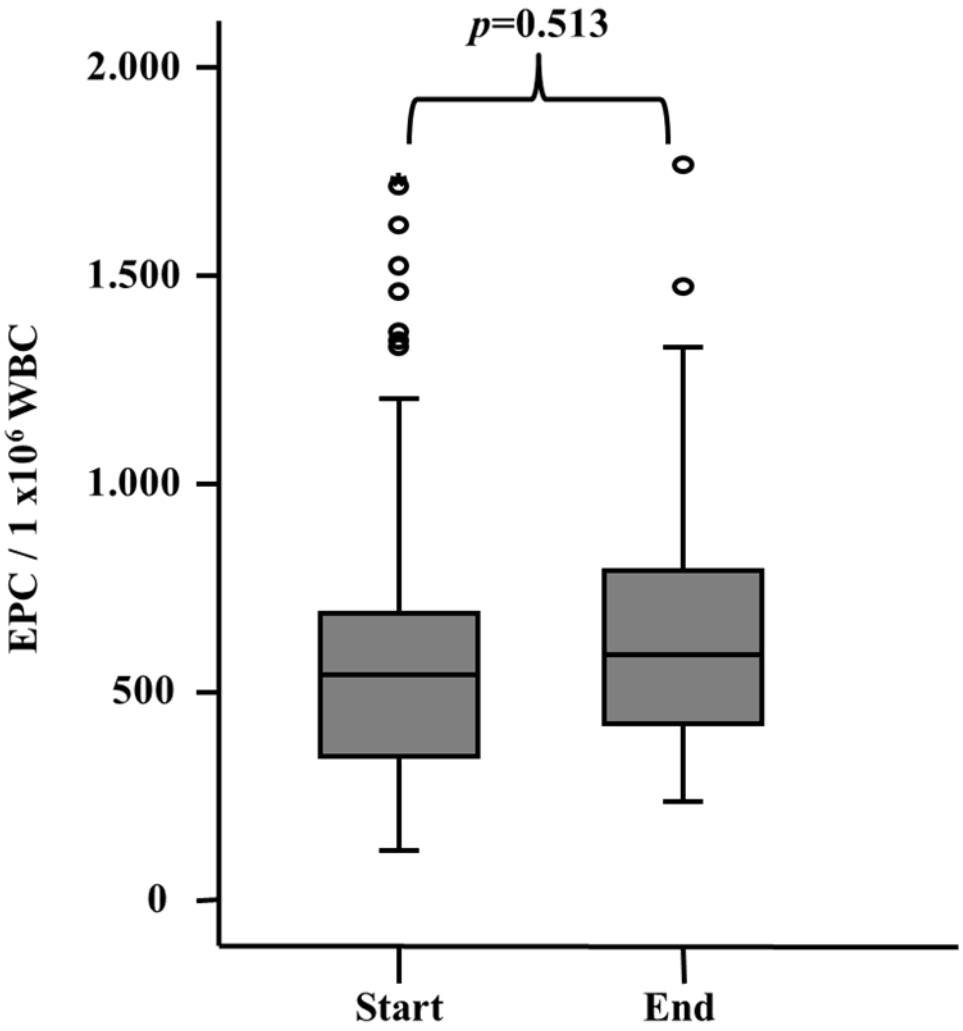
Supplementary Figure 1. Correlation of Progenitor Cells with Glycemic Control at time of inclusion



WBC, white blood cells; CPC, circulating progenitor cells; EPC endothelial progenitor cells; HbA1c, glycated hemoglobin A1c; an alpha-level of $p<0.05$ (two-tailed) is considered statistically significant. Single (left), respectively middle (right) line is line of fit. The two additional lines in the right illustration are 95% confidence intervals.

SUPPLEMENTARY DATA

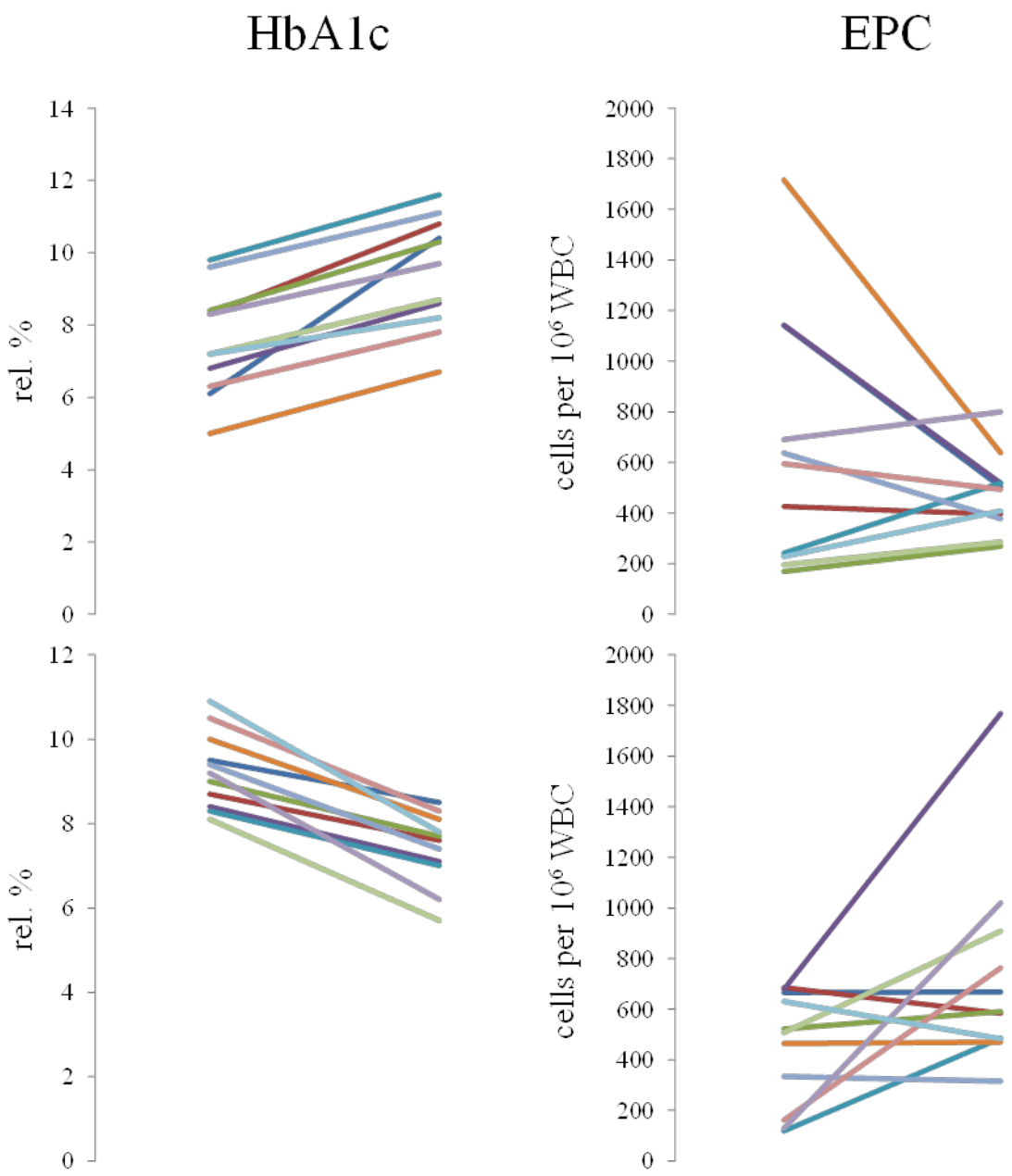
Supplementary Figure 2. Endothelial Progenitor cells during one year of follow up



EPC endothelial progenitor cells; WBC, white blood cells; an alpha-level of $p<0.05$ (two-tailed) is considered statistically significant.

SUPPLEMENTARY DATA

Supplementary Figure 3. Strongest Changes in EPC and HbA1c levels assed with each other



HbA1c, glycated hemoglobin A1c; EPC endothelial progenitor cells, WBC, white blood cells. At the left the most pronounced changes in HbA1c are depicted, at the right the corresponding EPC changes. In the upper row, the individual patients' changes of the patients with the 11 strongest increases in HbA1 are shown, in the lower row, the individual patients' changes of the patients with the 11 strongest decreases in HbA1c.