

Supplemental Figure S1 Excess BMI loss (%) over all cohorts. Boxplots show Excess BMI Loss (EBL, %) in discovery cohort (N = 9), adipose tissue mRNA expression cohort (AT samples, N = 44), and blood validation cohort (validation blood, N = 9). The dashed red line indicates the inclusion cut-off criteria of at least 30% EBL. Significance levels of comparisons were calculated by Wilcoxon rank sum test for unpaired samples. ns: not significant ($P \ge 0.05$).



Supplemental Figure S2 Differentially methylated regions (DMRs) of all tissues. Volcano plots of DMRs in a) blood, b) subcutaneous adipose tissue (SAT), and c) omental visceral adipose tissue (OVAT). Blue points represent hypomethylated DMRs (mean methylation difference < 0, FDR < 0.01) and red points represent hypermethylated DMRs (mean methylation difference > 0, FDR < 0.01) after surgery. Black points show DMRs with FDR between 0.01 and 0.05. Top 20 DMRs (ranked by FDR) are labelled with the annotated gene.



Supplemental Figure S3 | Weight loss in other gene expression studies after bariatric surgery. Violin plots indicate weight loss after bariatric surgery in both studies of a) Kerr et al. (2020, PMID: 32406570) and b) Petrus et al. (2018, PMID: 30332637). Depicted *P*-Values are calculated by Wilcoxon signed rank test for paired data.



Supplemental Figure S4 (Correlation of DNAmAge with chronological age and ageAcc between tissues. a-c) Scatter plots show correlation of DNA methylation age and chronological age (ageAcc) for pre and post-surgery in a) blood, b) subcutaneous adipose tissue (SAT), and c) omental visceral adipose tissue (OVAT). d-f) Scatter plots show correlation of age acceleration (ageAcc) between tissues for pre and post-surgery. Correlations were calculated for ageAcc between d) blood and OVAT, e) blood and SAT, and f) SAT and OVAT. For all correlations Spearman correlation coefficient (R = rho) and nominal significance (p) of correlation are depicted and a linear regression line is added.



Supplemental Figure S5 Cell type distribution. Boxplots show proportions of cell type populations (CD8 T-lymphocytes (CD8T), CD4 T-lymphocytes (CD4T), natural killer cells (NK), B-cells (Bcell), monocytes (Mono), and neutrophils (Neu)) between presurgical (red) and post-surgical (blue) methylation pattern based on Illumina 850K methylation data.

а	0.6	0.004	0.9	0.8	1	Sample_Well
•	0.03	6e-06	8e-07	3e-06	1e-09	Patient
	0.5	0.9	1	0.9	0.9	Group
	0.3	0.8	0.01	0.9	0.08	sex
	0.6	0.6	0.4	0.03	0.02	Age
	0.6	0.1	0.3	0.3	1	weight
	0.4	0.3	0.04	0.2	0.03	height
	0.7	0.2	0.6	0.6	0.8	BMI
	0.3	0.9	0.07	0.9	0.5	BMIgroup
	0.2	0.7	0.1	0.4	0.01	bodyFat
	0.8	0.6	1	0.4	0.2	DiabetesState
	0.6	0.004	0.9	0.8	1	Array
	0.005	0.8	0.7	1	0.8	Slide
	7e-09	0.9	0.6	0.8	0.6	CD8T
	4e-08	0.5	0.5	0.9	0.9	CD4T
	0.1	0.8	0.03	0.7	0.2	NK
	1e-04	0.7	0.2	0.5	0.9	Bcell
	3e-04	0.9	0.09	0.6	0.7	Mono
	2e-08	0.6	0.3	1	0.9	Neu
	1 (22)	2 (9)	3 (9)	4 (8)	5 (7)	
		Principal (Components	(Variation)		

b	0.02	0.3	0.02	0.6	0.5	Sample_Well		
	0.1	0.01	0.008	0.001	1e-05	Patient		
	0.7	0.2	0.5	0.7	0.6	Group		
	0.1	0.8	0.01	0.005	0.9	sex		
	0.3	0.05	0.05	0.5	0.1	Age		
	0.9	0.9	0.4	0.6	0.5	weight		
	0.3	0.6	0.07	0.07	0.7	height		
	0.8	0.8	0.5	0.3	0.5	BMI		
	0.01	0.4	0.2	0.4	0.4	BMIgroup		
	0.4	0.9	0.01	0.3	0.5	bodyFat		
	1	0.1	0.2	0.6	0.8	DiabetesState		
	0.02	0.3	0.02	0.6	0.5	Array		
	0.7	0.8	0.7	0.8	0.2	Slide		
	1 (29)	2 (14)	3 (10)	4 (6)	5 (5)			
Principal Components (Variation)								

С	0.2	0.7	0.4	0.4	0.2	Sample_Well		
	1	0.2	0.02	0.04	0.003	Patient		
	0.005	0.6	0.9	0.5	0.4	Group		
	0.9	0.5	0.001	0.6	0.04	sex		
	0.4	0.2	0.1	0.2	0.4	Age		
	7e-05	0.7	0.8	0.5	0.6	weight		
	0.7	0.4	0.06	0.9	0.06	height		
	2e-04	0.8	0.9	0.9	0.8	BMI		
	0.06	0.8	0.09	0.9	0.5	BMIgroup		
	0.2	0.8	0.07	0.7	0.008	bodyFat		
	0.7	0.009	0.6	0.6	0.3	DiabetesState		
	0.2	0.7	0.4	0.4	0.2	Array		
	0.4	0.8	0.9	0.7	0.2	Slide		
	1 (27)	2 (20)	3 (7)	4 (5)	5 (5)			
	Principal Components (Variation)							

Supplemental Figure S6 | **Principal components of unadjusted DNA methylation data.** Heatmaps show significance level (*P*-value) of associations of top five principal components of normalised EPIC array data with sample annotations in a) blood, b) subcutaneous adipose tissue, and c) omental visceral adipose tissue samples before adjustment.



Supplemental Figure S7 [Correlation of sample annotations. Correlation matrices show interrelation of sample annotations in a) blood, b) subcutaneous adipose tissue, and c) omental visceral adipose tissue samples in order to identify confounding factors. Significance level (*P*-values) of correlations are depicted.

а	0.2	1	1	1	1	Sample_Well		
	1	1	1	1	1	Patient		
	8e-14	0.7	0.7	0.7	0.8	Group		
	1	1	1	1	1	sex		
	0.6	1	0.9	0.9	0.9	Age		
	0.001	0.9	0.8	0.2	0.4	weight		
	0.9	0.9	1	0.9	1	height		
	6e-04	0.9	0.6	0.2	0.2	BMI		
	0.07	0.1	0.5	0.3	0.6	BMIgroup		
	0.2	0.8	0.8	0.3	0.8	bodyFat		
	0.6	0.6	0.7	0.9	0.9	DiabetesState		
	0.2	1	1	1	1	Array		
	2e-09	0.08	0.5	0.5	0.8	Slide		
	0.4	0.8	0.7	0.8	0.8	CD8T		
	0.4	0.6	0.8	0.7	0.9	CD4T		
	0.6	0.5	0.6	0.8	0.8	NK		
	0.1	0.8	1	0.9	0.7	Bcell		
	0.1	0.7	1	0.9	0.8	Mono		
	0.2	0.6	0.9	0.9	0.8	Neu		
	(52)	(15)	(12)	(11)	(11)			
	.	7	б	4	5			
	Principal Components (Variation)							

þ	1	1	1	1	1	Sample_Well
	1	1	1	1	1	Patient
	2e-17	0.8	0.8	3e-11	0.03	Group
	1	1	1	1	0.9	sex
	0.6	0.8	1	0.7	0.7	Age
	5e-04	0.9	1	0.001	0.05	weight
	1	0.9	1	0.9	1	height
	3e-04	0.8	1	4e-04	0.06	BMI
	0.02	0.7	1	0.05	0.2	BMIgroup
	0.2	0.9	0.5	0.3	0.6	bodyFat
	0.6	1	1	0.6	0.8	DiabetesState
	1	1	1	1	1	Array
	6e-13	0.04	0.6	3e-10	0.3	Slide
	1 (77)	2 (12)	3 (11)	4 (0)	5 (0)	
		Principal C	Components	(Variation)		

С	0.8	1	1	1	1	Sample_Well		
	1	1	1	1	0.9	Patient		
	2e-14	0.7	0.7	0.07	0.02	Group		
	1	1	1	1	0.8	sex		
	0.7	1	0.9	0.9	0.7	Age		
	5e-04	1	0.8	0.2	0.1	weight		
	1	0.9	1	1	1	height		
	4e-04	0.7	0.7	0.2	0.2	BMI		
	0.02	0.09	0.5	0.04	0.1	BMIgroup		
	0.1	0.5	0.8	0.6	0.4	bodyFat		
	0.7	0.8	0.3	0.5	0.4	DiabetesState		
	0.8	1	1	1	1	Array		
	1e-04	0.4	0.6	0.3	0.5	Slide		
	1 (68)	2 (23)	3 (9)	4 (0)	5 (0)			
	Principal Components (Variation)							

Supplemental Figure S8| **Principal components after adjustment of DNA methylation data.** Heatmaps show significance level (*P*-value) of associations of top five principal components of normalised EPIC array data adjusted for array and patient factor in a) blood, b) subcutaneous adjusted tissue, and c) omental visceral adjuste tissue samples.



Supplemental Figure S9 Visualisation of Principal Component Analysis (PCA) after adjustment. Three-dimensional PCA plots of normalized EPIC array data adjusted for array and patient factor in a) blood, b) subcutaneous adipose tissue, and c) omental visceral adipose tissue samples show separation of pre (red)- vs post-surgery (blue) samples. PC: principal component.