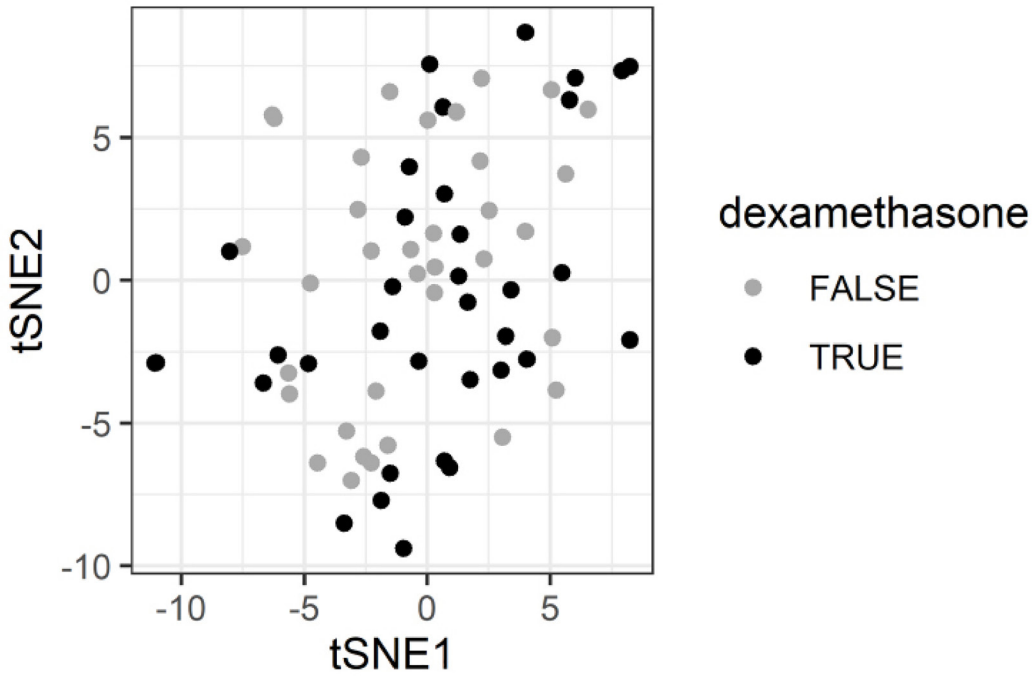
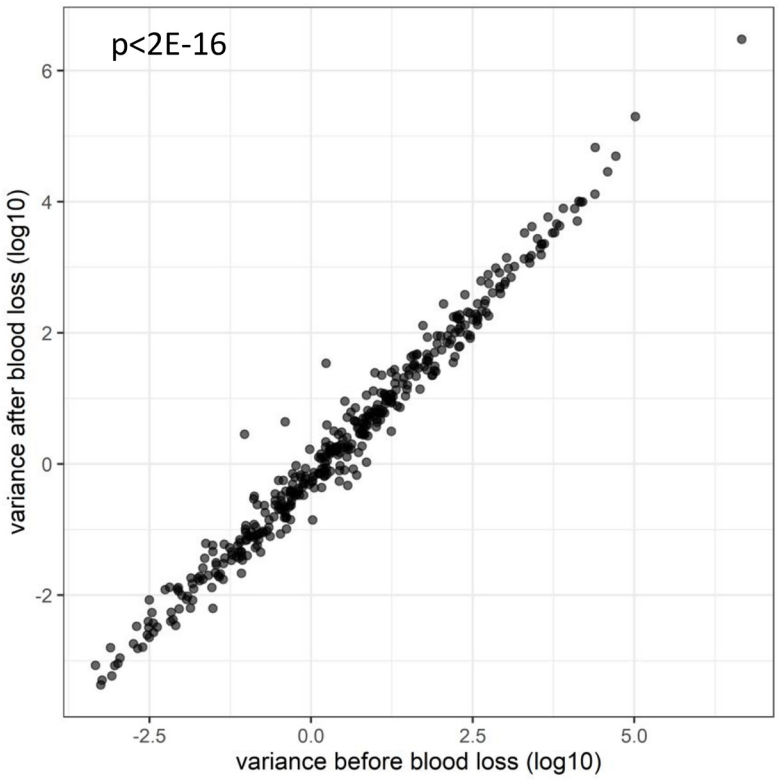
Perioperative changes in the plasma metabolome of patients receiving general anesthesia for pancreatic cancer surgery

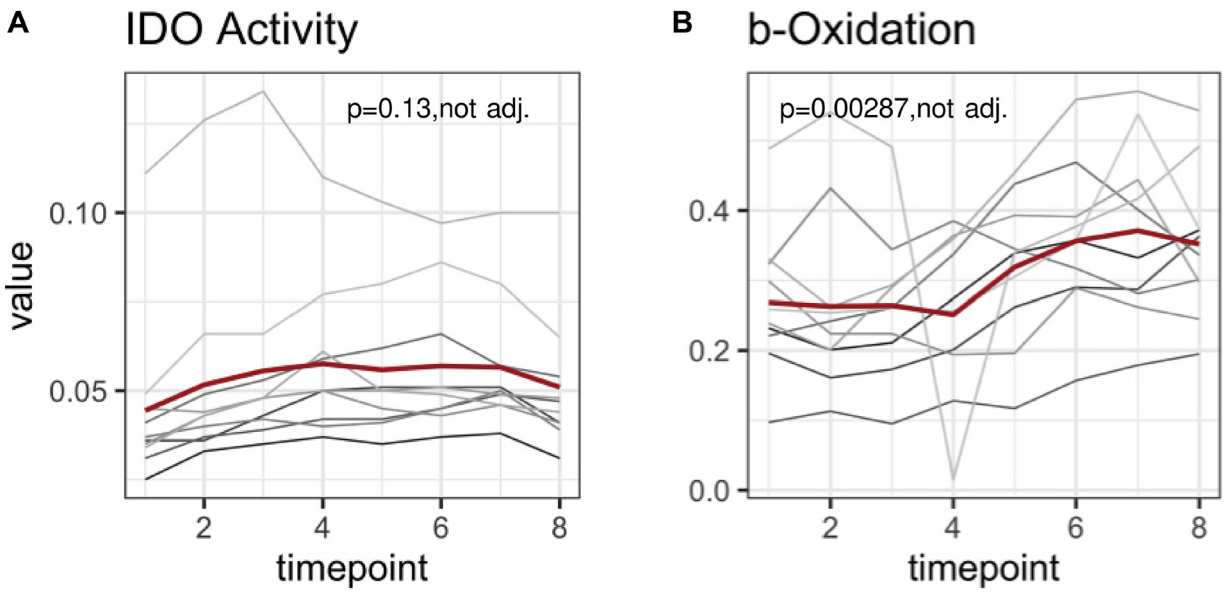
SUPPLEMENTARY MATERIALS



Supplementary Figure 1: Further tSNE plot for unsupervised comparison of the metabolome. Usage of dexamethasone had no systematic effect on the plasma metabolome. Metabolome data from all patients and all timepoints (80 samples) are depicted according to whether dexamethasone was used (black) or not (grey).



Supplementary Figure 2: Variance in plasma metabolite concentrations before and after major blood loss. Linear regression analysis revealed a high concordance between variances (p < 2E-16). Hence, the extent of plasma metabolite changes was not significantly different.



Supplementary Figure 3: Further metabolomic interpretation. Ratios of metabolites are depicted. Mean concentrations are depicted as a red line while individual courses of each patient are depicted in grey lines. *p*-values are not adjusted for multiple testing. (**A**) Ratio of [kynurenine]/[tryptophane] represents Indolamin-2,3-dioxygenase activity (IDO-activity). IDO-activity did not change significantly during observation period. (**B**) The ratio of propionyl carnitine plus acetyl carnitine to carnitine ([propionyl carnitine + acetyl carnitine]/[carnitine]), serves as an indicator for b-oxidation rates. B-oxidation increased during observation period but lost statistical significancy after adjusting for multiple testing.

Supplementary Table 1: List of significantly changing metabolites and MetaboINDICATORS™

Metabolites	class	*p*-val	*p*-adjust	coeff
Carnitine	Acylcarnitines	1,65E-06	9,30E-04	-1,60E+00
Propionyl carnitine	Acylcarnitines	2,88E-07	1,64E-04	-2,37E-02
TMAO	Amine Oxides	8,26E-05	4,40E-02	-5,81E-01
Cysteine	Amino acids	3,97E-05	2,15E-02	-4,30E+00
Tryptophan	Amino acids	1,08E-09	6,24E-07	-3,48E+00
1-Methylhistidine	Amino acids Related	8,85E-07	5,03E-04	-1,73E-01
Kynurenine	Amino acids Related	7,13E-10	4,14E-07	-1,18E-01
t4-Hydroxyproline	Amino acids Related	5,45E-06	3,05E-03	-4,27E-01
Taurine	Amino acids Related	9,07E-05	4,79E-02	2,98E+00
Lactate	Carboxylic Acids	4,73E-06	2,65E-03	1,27E+02
FA(18:1)	Fatty Acids	5,14E-05	2,77E-02	1,59E+01
lysoPC a C16:0	Glycerophospholipids	6,15E-05	3,29E-02	-3,59E+00
lysoPC a C16:1	Glycerophospholipids	1,55E-06	8,79E-04	-1,21E-01
lysoPC a C18:0	Glycerophospholipids	7,76E-05	4,14E-02	-8,59E-01
lysoPC a C18:1	Glycerophospholipids	1,18E-07	6,81E-05	-9,04E-01
lysoPC a C18:2	Glycerophospholipids	1,59E-05	8,78E-03	-9,06E-01
lysoPC a C20:3	Glycerophospholipids	3,27E-07	1,86E-04	-9,07E-02
lysoPC a C20:4	Glycerophospholipids	3,05E-06	1,71E-03	-2,99E-01
3-Indoleaceitic acid	Indoles Derivatives	2,21E-09	1,28E-06	-1,56E-01
TG(16:0_38:7)	Triacylglycerols	3,24E-05	1,77E-02	-4,43E-02
TG(16:0_40:6)	Triacylglycerols	2,28E-06	1,28E-03	-2,18E-01
TG(16:0_40:7)	Triacylglycerols	1,09E-06	6,16E-04	-1,98E-01
TG(16:0_40:8)	Triacylglycerols	3,81E-05	2,07E-02	-7,88E-02
TG(17:1_34:3)	Triacylglycerols	3,71E-05	2,02E-02	-3,70E-02
TG(17:2_36:2)	Triacylglycerols	2,63E-05	1,44E-02	-2,43E-02
TG(18:1_34:1)	Triacylglycerols	8,98E-05	4,76E-02	-2,27E+01
TG(18:1_35:2)	Triacylglycerols	9,27E-05	4,88E-02	-4,16E-01
TG(18:1_38:6)	Triacylglycerols	5,35E-05	2,87E-02	-1,68E-01
TG(18:1_38:7)	Triacylglycerols	7,89E-05	4,20E-02	-2,90E-02
TG(18:3_34:0)	Triacylglycerols	5,53E-06	3,08E-03	-1,04E-01
TG(18:3_34:1)	Triacylglycerols	9,18E-05	4,84E-02	-9,30E-01
TG(20:1_32:1)	Triacylglycerols	8,98E-05	4,76E-02	-6,92E-02
TG(22:5_32:1)	Triacylglycerols	3,64E-05	1,99E-02	-9,30E-02
TG(22:5_34:1)	Triacylglycerols	2,64E-06	1,49E-03	-3,94E-01
TG(22:5_34:2)	Triacylglycerols	2,10E-05	1,15E-02	-1,93E-01
TG(22:6_32:0)	Triacylglycerols	1,32E-05	7,29E-03	-1,76E-01
TG(22:6_32:1)	Triacylglycerols	5,76E-06	3,21E-03	-2,04E-01
TG(22:6_34:1)	Triacylglycerols	2,56E-07	1,46E-04	-7,32E-01
TG(22:6_34:2)	Triacylglycerols	1,10E-05	6,07E-03	-4,09E-01
MC Deficiency (NBS)	INDICATOR	3,93E-05	2,13E-02	1,87E-02
DLD (NBS)	INDICATOR	2,63E-07	1,51E-04	-1,17E-01

Fischer Ratio	INDICATOR	1,54E-10	8,98E-08	9,73E-02
PKU (NBS)	INDICATOR	4,14E-09	2,39E-06	-1,99E-02
Ratio of Non-Essential to Essential AAs	INDICATOR	5,99E-05	3,21E-02	-3,00E-02
Sum of Sulfur-Containing AAs	INDICATOR	8,46E-05	4,49E-02	-4,40E+00
Cit Synthesis	INDICATOR	1,70E-05	9,34E-03	-1,94E-02
GABR	INDICATOR	4,23E-08	2,44E-05	4,29E-02
NO-Synthase Activity	INDICATOR	2,79E-10	1,62E-07	-2,15E-02
Pro Hydroxylation	INDICATOR	2,71E-07	1,55E-04	-1,87E-03
Taurine Synthesis	INDICATOR	2,54E-07	1,46E-04	4,18E-02
Sum of Carboxylic Acids	INDICATOR	5,52E-06	3,08E-03	1,27E+02
Ratio of Hex3Cer to Cer	INDICATOR	4,69E-05	2,54E-02	-1,03E-02
Ratio of DGs to FAs	INDICATOR	7,84E-11	4,58E-08	-7,20E-03
Sum of MUFAs	INDICATOR	5,17E-05	2,78E-02	1,65E+01
Ratio of TGs to FAs	INDICATOR	1,40E-12	8,21E-10	-7,57E-01
Sum of LCFA-LysoPCs	INDICATOR	1,18E-05	6,55E-03	-6,82E+00
Sum of LysoPCs	INDICATOR	1,08E-05	5,98E-03	-6,86E+00
Sum of MUFA-LysoPCs	INDICATOR	5,55E-08	3,20E-05	-1,05E+00
Sum of PUFA-LysoPCs	INDICATOR	6,12E-06	3,40E-03	-1,30E+00
Sum of SFA-LysoPCs	INDICATOR	4,70E-05	2,54E-02	-4,52E+00

Abbreviations: TMAO: Trimethylamine N-oxide; FA: fatty acid; lysoPC: lysophosphatidylcholine; TG: triacylglyceride; MC: Multiple Carboxylase; DPD: Dihydrolipoamide Dehydrogenase Deficiency; PKU: Phenylketonuria; AA: Amino acid; Cit: Citrulline; GABR: Global Arginine Bioavailability Ratio; Pro: Proline; Hex3Cer: Trihexosylceramides; DG: Diglycerides; MUFA: Monounsaturated Fatty Acid; LCFA: Long-Chain Fatty Acid; PUFA: Polyunsaturated Fatty Acid; SFA: Saturated Fatty Acid.