

**Table S1**

LIVER		P/ H	P/ DC	P/ Ctr	P/ SC	H/ DC	H/ Ctr	H/ SC	DC/ Ctr	DC/ SC	SC/ Ctr
	Number of PCs	2	1	2	2	2	2	2	2	2	2
	Q2 value	0.60	neg	0.56	0.40	0.74	0.38	0.76	0.58	0.45	0.68
	R2 value	0.87	0.43	0.83	0.75	0.88	0.83	0.94	0.86	0.79	0.94
FAM	acetate									↘	
NUM	adenosine*	↘		↘		↗		↗	↘		↘
AAM	alanine							↘	↗		↗
AAM	aspartate	↗		↗				↘			↗
CLM	betaine	↘				↗					
CLM	choline					↗	↗				
AAM	creatine										↗
TCA	fumarate				↗			↗		↗	↘
GLY	glucose	↗				↘			↗		
AAM	glutamate			↗		↘		↘	↗		↗
AAM	glutamine										↗
NUM	inosine*	↘		↘		↗		↗	↘		↘
AAM	isoleucine									↘	↗
GLY	lactate			↗		↘		↘	↗		↗
AAM	leucine							↘	↗		↗
CLM	lipid (CH <sub>3</sub> )						↗				↗
CLM	lipid (CH <sub>2</sub> ) <sub>n</sub>						↗				↗
AAM	nicotinurate	↘									
CLM	phosphocholine			↗					↗		↗
TCA	succinate			↗				↘			
AAM	valine									↘	↗
SPLEEN		P/ H	P/ DC	P/ Ctr	P/ SC	H/ DC	H/ Ctr	H/ SC	DC/ Ctr	DC/ SC	SC/ Ctr
	Number of PCs	2	2	2	2	2	2	2	2	2	2
	Q2 value	0.87	0.23	0.85	0.81	0.70	0.72	0.89	0.75	0.60	0.88
	R2 value	0.96	0.89	0.96	0.98	0.96	0.93	0.98	0.94	0.93	0.97
AAM	alanine	↗		↗		↘	↘	↘	↗		↗
AAM	aspartate	↗		↗		↘					
CLM	betaine			↘				↗	↘		↘
AAM	dimethylglycine				↗		↘				↘
MIM	dimethylamine						↘				
FAM	formate	↗									
TCA	fumarate	↗			↗		↘		↘		↘
AAM	glutamate	↗		↗		↘					
AAM	glycine	↗		↗		↘	↘	↘			↗
CLM	glycerophospho- choline	↘	↗		↗	↗		↗	↘		↘
NUM	inosine*	↘		↘	↘	↗		↗	↘		↘
NUM	IMP*			↘	↗	↘	↘	↘	↘	↗	↘
AAM	isoleucine	↗		↗				↘			↗

GLY	lactate	↗		↗		↘		↘			
AAM	leucine	↗	↗					↘	↗	↘	↗
CLM	lipid (CH <sub>2</sub> ) <sub>n</sub>				↘						
AAM	lysine	↗		↗		↘		↘	↗		↗
TCA	malonate*	↘									
IPM	myo-inositol	↘		↘		↗		↗	↘		↘
AAM	nicotinurate						↘				
AAM	phenoacetyl glycine	↗	↗	↗		↘		↘	↗	↘	↗
CLM	phosphocholine				↗			↗			↘
IPM	scyllo-inositol				↗			↗		↗	↘
TCA	succinate	↗		↗							
AAM	taurine						↘	↗	↘		↘
AAM	tyrosine	↗		↗		↘		↘		↘	↗
NUM	uracil	↗						↘	↗		↗
NUM	uridine	↘		↘		↗	↗	↗			↘
AAM	valine	↗	↗	↗				↘	↗		

KIDNEY		P/H	P/DC	P/Ctr	P/SC	H/DC	H/Ctr	H/SC	DC/Ctr	DC/SC	SC/Ctr
	Number of PCs	2	1	2	2	2	2	2	2	2	2
	Q2 value	0.81	neg	0.72	0.64	0.72	0.63	0.69	0.70	0.58	0.51
	R2 value	0.99	0.81	0.97	0.95	0.99	0.96	0.96	0.95	0.93	0.96
FAM	3-hydroxybutyrate	↘				↗					
AAM	alanine	↗									
NUM	inosine*	↘		↘					↘		↘
AAM	aspartate					↘			↗		
CLM	betaine								↘	↘	
CLM	choline	↘		↘		↗	↘		↘		↘
AAM	creatine									↘	
MIM	dimethylglycine							↗			
FAM	formate							↗			
TCA	fumarate										↘
AAM	glutamate	↗		↗		↘		↘	↗		
AAM	glutamine							↘			
AAM	glycine					↗		↘			
NUM	IMP*	↘		↘	↘		↘		↘		
GLY	lactate									↗	
AAM	leucine	↗		↗		↘		↘	↗		↗
AAM	phenylalanine	↗		↗		↘		↘	↗		↗
AAM	taurine							↘			
AAM	tyrosine	↗		↗		↘		↘	↗		↗
AAM	valine	↗		↗		↘		↘	↗		↗

COLON		P/H	P/DC	P/Ctr	P/SC	H/DC	H/Ctr	H/SC	DC/Ctr	DC/SC	SC/Ctr
	Number of PCs	2	1	2	1	1	1	1	2	1	1
	Q2 value	0.47	neg	0.46	neg	0.03	neg	0.15	0.16	neg	0.10
	R2 value	0.91	0.53	0.93	0.39	0.25	0.85	0.35	0.74	0.69	0.30

FAM	3-hydroxybutyrate	↘		↘							
AAM	glutamine							↗			
NUM	inosine*								↗		
AAM	isoleucine	↘						↗			
AAM	leucine	↘									
IPM	myo-inositol			↘							
AAM	tyrosine	↘						↗	↗		
<b>ILEUM</b>											
		<b>P/ H</b>	<b>P/ DC</b>	<b>P/ Ctr</b>	<b>P/ SC</b>	<b>H/ DC</b>	<b>H/ Ctr</b>	<b>H/ SC</b>	<b>DC/ Ctr</b>	<b>DC/ SC</b>	<b>SC/ Ctr</b>
	Number of PCs	1	2	2	1	1	1	1	2	2	1
	Q2 value	neg	0.34	0.33	neg	neg	0.12	neg	0.54	0.30	0.25
	R2 value	0.26	0.81	0.86	0.68	0.29	0.35	0.25	0.84	0.80	0.49
AAM	aspartate								↗		
CLM	choline								↗		
MIM	dimethylamine		↗	↗					↗		
CLM	glycerol								↗		
CLM	glycerophospho- choline								↗	↗	
	methionine		↘						↗		
AAM	taurine			↗							
<b>JEJUNUM</b>											
		<b>P/ H</b>	<b>P/ DC</b>	<b>P/ Ctr</b>	<b>P/ SC</b>	<b>H/ DC</b>	<b>H/ Ctr</b>	<b>H/ SC</b>	<b>DC/ Ctr</b>	<b>DC/ SC</b>	<b>SC/ Ctr</b>
	Number of PCs	2	2	2	1	1	2	1	2	2	2
	Q2 value	0.46	0.63	0.21	neg	neg	0.42	0.09	0.56	0.49	0.32
	R2 value	0.72	0.78	0.76	0.73	0.22	0.80	0.28	0.84	0.79	0.79
FAM	3-hydroxybutyrate			↘					↘		
CLM	choline		↘								
AAM	glutamate									↗	
AAM	glycine									↗	
CLM	glycerophospho- choline	↘	↘				↗	↗	↗	↗	↗
GLY	lactate		↘							↗	
CLM	phosphocholine		↘					↗	↗		
TCA	succinate	↘	↘				↗			↗	
<b>BRAIN FRONTAL CORTEX</b>											
		<b>P/ H</b>	<b>P/ DC</b>	<b>P/ Ctr</b>	<b>P/ SC</b>	<b>H/ DC</b>	<b>H/ Ctr</b>	<b>H/ SC</b>	<b>DC/ Ctr</b>	<b>DC/ SC</b>	<b>SC/ Ctr</b>
	Number of PCs	2	1	1	1	1	1	1	1	1	1
	Q2 value	0.11	neg	neg	neg	0.07	neg	0.11	neg	neg	neg
	R2 value	0.26	0.63	0.23	0.79	0.28	0.22	0.34	0.28	0.69	0.20
AAM	creatine							↘			
AAM	GABA	↗				↘					
AAM	glutamine							↘			
NUM	inosine*	↗				↘					
GLY	lactate	↗				↘		↘			
AAM	N-acetyl-aspartate							↘			
AAM	taurine	↗						↘			

<b>CEREBELLUM</b>		<b>P/ H</b>	<b>P/ DC</b>	<b>P/ Ctr</b>	<b>P/ SC</b>	<b>H/ DC</b>	<b>H/ Ctr</b>	<b>H/ SC</b>	<b>DC/ Ctr</b>	<b>DC/ SC</b>	<b>SC/ Ctr</b>
	Number of PCs	1	1	2	2	1	1	2	1	1	1
	Q2 value	neg	neg	0.31	0.13	neg	0.01	0.22	0.05	neg	neg
	R2 value	0.26	0.40	0.65	0.54	0.36	0.20	0.57	0.18	0.32	0.41
NUM	adenosine*				↘				↘		
AAM	creatine				↘						
AAM	glutamine						↘				
CLM	glycerophospho- choline			↘					↘		
NUM	IMP*			↘	↘				↘		
NUM	inosine*			↘					↗		
IPM	scyllo-inositol			↗	↗		↗				
AAM	taurine				↘						
<b>BRAIN STEM</b>		<b>P/ H</b>	<b>P/ DC</b>	<b>P/ Ctr</b>	<b>P/ SC</b>	<b>H/ DC</b>	<b>H/ Ctr</b>	<b>H/ SC</b>	<b>DC/ Ctr</b>	<b>DC/ SC</b>	<b>SC/ Ctr</b>
	Number of PCs	2	1	2	1	1	1	1	2	1	1
	Q2 value	0.41	neg	0.55	0.26	neg	neg	neg	0.41	neg	neg
	R2 value	0.74	0.60	0.82	0.49	0.53	0.33	0.54	0.87	0.37	0.71
NUM	adenosine*	↘		↘							
AAM	alanine	↗		↗					↗		
CLM	choline	↘		↘							
AAM	creatine	↘									
AAM	glutamine	↘			↘						
CLM	glycerophospho- choline	↘		↘					↘		
NUM	IMP*			↘							
AAM	isoleucine			↗							
GLY	lactate	↗		↗					↗		
AAM	leucine	↗		↗							
IPM	myo-inositol	↘		↘							
AAM	N-acetylaspartate	↘		↘	↘						
AAM	valine	↗		↗					↗		
<b>REMAINING BRAIN TISSUE</b>		<b>P/ H</b>	<b>P/ DC</b>	<b>P/ Ctr</b>	<b>P/ SC</b>	<b>H/ DC</b>	<b>H/ Ctr</b>	<b>H/ SC</b>	<b>DC/ Ctr</b>	<b>DC/ SC</b>	<b>SC/ Ctr</b>
	Number of PCs	1	2	1	1	2	1	1	2	1	1
	Q2 value	0.12	0.26	neg	neg	0.28	0.02	0.08	0.42	0.07	neg
	R2 value	0.36	0.76	0.81	0.56	0.64	0.41	0.39	0.80	0.23	0.62
NUM	adenosine*									↘	
AAM	alanine	↗									
CLM	choline	↘				↗		↗			
TCA	fumarate						↗	↗	↗	↗	
CLM	glycerophospho- choline								↘		
NUM	IMP*						↘				
NUM	inosine*								↗		

AAM	isoleucine							↗			
GLY	lactate	↗				↘					
IPM	<i>myo</i> -inositol	↘									
AAM	valine	↗									

**Table S1.** List of perturbed metabolites across tissues in model comparisons. Key: Arrows indicate changes in the first group compared to the second (i.e. in P in the comparison P/H), ↗, increase; ↘, decrease; \*, tentatively assigned; AAM, amino acid metabolism; CLM, choline and lipid metabolism; FAM, fatty acid metabolism; GLY, glycolysis; GPC, glycerophosphocholine; IMP, inosine monophosphate; IPM, inositol phosphate metabolism; MIM, microbial metabolism; neg, negative/invalid model; NUM, nucleotide metabolism; TCA, tricarboxylic acid cycle. PC, principal component; R<sup>2</sup>, goodness of fit of the data; Q<sup>2</sup>, measure of the predictive power of the model.