

Obesity Development in a Miniature Yucatan Pig
Model – a multi-compartmental Metabolomics
Study on Cloned and Normal Pigs Fed Restricted
or *Ad Libitum* High-Energy Diets.

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Figure S1. Position of CT abdominal cross-section used in quantifying of total abdominal fat area; marked by red dotted line.

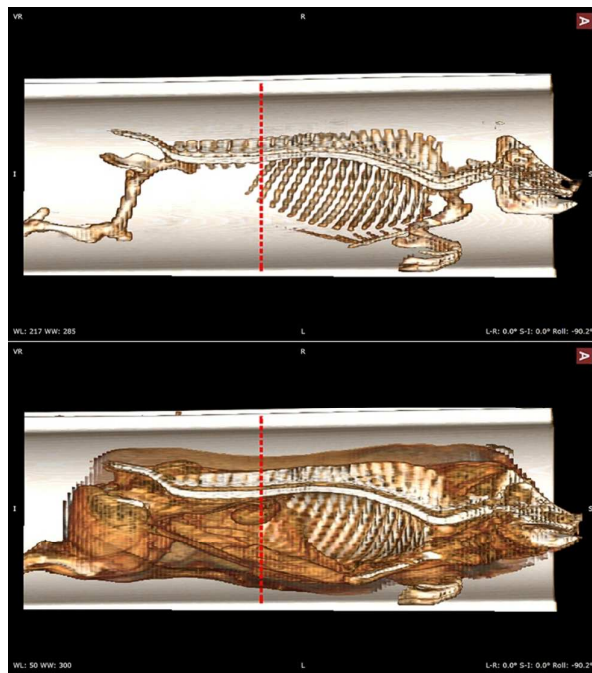


Table S1. Partial Least Squares Discriminant Analysis models information

<i>Model name</i>	<i>Model type</i>	<i>Initial feature no.^a</i>	<i>Final feature no.^b</i>	<i>PC^c (no.)</i>	<i>evY calibrated</i>	<i>evY^d validated</i>	<i>R^{2e}</i>	<i>PC1 (%)^f</i>	<i>PC2 (%)^f</i>
<i>Serum_pos_diet</i>	Ad Libitum vs Restricted	2395 ^g	1145	3	96.2	56.00	0.4982	14.8	12.8
<i>Serum_neg_diet</i>	Ad Libitum vs Restricted	1420 ^g	699	4	99	31.80	0.2485	17.5	13.7
<i>Serum_pos_clone</i>	clone vs control	2396 ^h	908	5	99.8	33.40	0.2815	17.2	15.4
<i>Serum_neg_clone</i>	clone vs control	1420 ^g	736	4	99.8	58.20	0.5788	9.6	9.6
<i>Urine_pos_diet</i>	Ad Libitum vs Restricted	5422 ^g	1843	3	96.5	73.50	0.7018	40.1	7.9
<i>Urine_neg_diet</i>	Ad Libitum vs Restricted	5079 ^g	1435	3	97.3	71.70	0.6806	28.7	15.3
<i>Urine_pos_clone</i>	clone vs control	5422 ⁱ	1649	2	82.9	8.60	0.042	10.2	14.8
<i>Urine_neg_clone</i>	clone vs control	5079 ⁱ	1304	2	85	9.40	0.033	13.4	25.5
<i>Liver_pos_diet</i>	Ad Libitum vs Restricted	2633 ⁱ	1048	3	48.2	28.00	0.4066	26.4	28.2
<i>Liver_neg_diet</i>	Ad Libitum vs Restricted	4036 ⁱ	713	2	46.4	32.00	0.5456	19.8	8.3
<i>Liver_pos_clone</i>	clone vs control	2633 ⁱ	1023	4	96.9	75.30	0.7303	27.6	19.9
<i>Liver_neg_clone</i>	clone vs control	4036 ⁱ	810	2	94	56.10	0.5211	17.8	11.7

^a Number of features post data pre-treatment; ^b Number of features after variable selection, used in calculating the models; ^c Number of principal components used in calculating the model; ^d Explained variance in Y matrix.; ^e coefficient of determination; ^f Variance explained by PLS principal components 1 and 2 in the score plot.; ^g VIP < 0.1 excluded; ^h VIP < 0.2 excluded; ⁱ VIP < 0.5 excluded.

Table S2. List of metabolic features detected from metabolomics analysis of serum, liver, and urine in pigs fed ad libitum or restricted a Western Style Diet.

Mo de ¹	M/Z ² ratio	RT ³ (min)	VIP score	Level ID	Compound ID	Pval ⁴	FC ⁵	Regu lation (vs restric ted)	Qval ⁶	Compound class ⁷	Subclass ⁷	KEGG ⁷
Serum ⁸												
POS	548.3719	9.95	5.34	Level 2	[M+K] 1-heptadecanoyl-sn-glycero-3-phosphocholine	0.010	-1.36	Down	0.089	Lipids and lipid-like molecules	Glycerophospholipids	C04230
POS	153.0661	1.39	2.00	Level 1	N-Methyl-4-pyridone-3-carboxamide	0.015	1.44	Up	0.089	Organoheterocyclic compounds	Pyridines and derivatives	C05843
POS	409.1873	2.6	3.42	Level 1	[2M+H] L-Tryptophan	0.015	1.13	Up	0.089	Organoheterocyclic compounds	Indoles and derivatives	C00078
POS	80.9479	0.93	2.67	Level 4	Unknown	0.015*	1.59	Up	0.089	n/a	n/a	n/a
POS	226.0454	1.11	1.23	Level 4	Unknown	0.021*	1.31	Up	0.089	n/a	n/a	n/a
POS	205.0973	2.61	35.96	Level 1	L-Tryptophan	0.021	1.19	Up	0.089	Organoheterocyclic compounds	Indoles and derivatives	C00078
POS	132.0809	2.61	1.99	Level 1	3-Methylindole	0.021	1.2	Up	0.089	Organoheterocyclic compounds	Indoles and derivatives	C08313
POS	146.1177	2.33	3.50	Level 2	2-amino-heptanoic acid	0.046*	-1.68	Down	0.168	Organic acids and derivatives	Carboxylic acids and derivatives	n/a
POS	357.2796	7.49	6.84	Level 2	Nisinic acid; C24:6n-3,6,9,12,15,18	0.059*	-2.02	Down	0.191	Lipids and lipid-like molecules	Fatty Acyls	n/a
POS	118.0864	1.02	3.15	Level 2	Valine	0.090	1.3	Up	0.224	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00183
POS	116.0707	0.68	2.61	Level 1	L-Proline	0.093*	1.2	Up	0.224	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00148
POS	205.0799	4.05	5.62	Level 4	Unidentified	0.093*	-4.56	Down	0.224	Organic acids and derivatives	Carboxylic acids and derivatives	n/a
POS	510.3565	9.91	3.29	Level 3	1-heptadecanoyl-sn-glycero-3-phosphocholine LPC (17:0/0:0)	0.140	-1.19	Down	0.313	Lipids and lipid-like molecules	Glycerophospholipids	C04230
POS	524.3720	10.58	75.03	Level 1	PC(0:0/18:0) / LysoPC(0:0/18:0)	0.167*	-1.1	Down	0.346	Lipids and lipid-like molecules	Glycerophospholipids	C04230
POS	524.3720	10.32	7.90	Level 3	Unknown	0.167*	-1.1	Down	0.346	Lipids and lipid-like molecules	Glycerophospholipids	n/a
POS	269.0885	1.29	1.77	Level 1	Inosine	0.188	1.21	Up	0.363	Nucleosides, nucleotides, and analogues	Purine nucleosides	C00294
POS	498.3469	9.29	2.72	Level 3	LysoPC(16:0)	0.207*	-1.09	Down	0.375	Lipids and lipid-like molecules	Glycerophospholipids	n/a
POS	132.0770	0.68	5.32	Level 1	Creatine	0.236*	1.21	Up	0.402	Organic acids and derivatives	Carboxylic acids and derivatives	C00300
POS	166.0864	1.94	11.21	Level 1	L-Phenylalanine	0.287	1.06	Up	0.438	Organic acids and derivatives	Carboxylic acids and derivatives	C00079

POS	450.3172	6.34	3.31	Level 3	Glycoursodeoxycholic acid	0.321*	-1.5	Down	0.457	Steroids and steroid derivatives	Bile acids, alcohols and derivatives	n/a
POS	194.0813	3.63	2.77	Level 1	Phenylacetyl glycine	0.331	-1.16	Down	0.457	Organic acids and derivatives	Carboxylic acids and derivatives	C05598
POS	525.3755	10.32	2.01	Level 3	2-Oleoylglycerophosphocholine	0.500*	-1.06	Down	0.651	Lipids and lipid-like molecules	Glycerophospholipids	n/a
POS	132.1021	1.23	11.23	Level 1	L-Leucine	0.532	1.08	Up	0.651	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00123
POS	522.3564	9.64	11.31	Level 3	LysoPC(18:1(9Z))	0.539	-1.05	Down	0.651	Lipids and lipid-like molecules	Glycerophospholipids	C04230
POS	182.0815	1.13	5.96	Level 1	L-Tyrosine	0.597	1.05	Up	0.693	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00082
POS	165.0550	1.13	5.29	Level 2	2-Hydroxycinnamic acid	0.626	1.05	Up	0.698	Phenylpropanoids and polyketides	Hydroxycinnamic acids	C01772
POS	466.3174	5.98	2.67	Level 2	Glycocholic acid	1.000*	-1.53	Down	1.000	Steroids and steroid derivatives	Bile acids, alcohols and derivatives	C01921
NEG	611.2618	2.60	2.54	Level 1	[3M-H] L-Tryptophan	0.001*	1.28	Up	0.025	Organoheterocyclic compounds	Indoles and derivatives	C00078
NEG	203.0825	2.60	91.68	Level 1	L-Tryptophan	0.002*	1.15	Up	0.025	Organoheterocyclic compounds	Indoles and derivatives	C00078
NEG	144.0456	4.66	6.11	Level 1	Indole-3-carboxaldehyde	0.002	1.37	Up	0.025	Organoheterocyclic compounds	Indoles and derivatives	C08493
NEG	150.8866	0.68	5.87	Level 4	Unknown	0.006	-1.1	Down	0.045	n/a	n/a	n/a
NEG	152.8837	0.68	6.70	Level 4	Unknown	0.008*	-1.1	Down	0.045	n/a	n/a	n/a
NEG	253.0176	4.16	5.72	Level 4	Unknown	0.008	1.82	Up	0.045	n/a	n/a	n/a
NEG	218.1033	2.08	7.58	Level 1	Pantothenic Acid	0.009	1.32	Up	0.045	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00864
NEG	499.2912	6.50	2.20	Level 4	Unknown	0.012	1.48	Up	0.051	n/a	n/a	n/a
NEG	592.3619	9.94	3.82	Level 3	PC(16:0/5:0(CHO))	0.022	-1.33	Down	0.080	Lipids and lipid-like molecules	Glycerophospholipids	n/a
NEG	338.0880	2.89	7.46	Level 4	Unknown	0.025	-2.69	Down	0.080	n/a	n/a	n/a
NEG	204.0668	4.33	10.52	Level 1	Indolelactic acid	0.026	1.39	Up	0.080	Organoheterocyclic compounds	Indoles and derivatives	C02043
NEG	387.1662	5.23	2.20	Level 3	Unknown	0.027*	2.11	Up	0.080	Lipids and lipid-like molecules	Fatty Acyls	n/a
NEG	258.0077	2.17	4.22	Level 4	Unknown	0.034	2.02	Down	0.092	n/a	n/a	n/a
NEG	187.0072	4.04	26.22	Level 1	p-Cresol sulfate	0.051	1.62	Up	0.119	Organic acids and derivatives	Organic sulfuric acids and derivatives	C01468
NEG	147.0453	4.07	2.56	Level 2	Unknown	0.059*	1.64	Up	0.122	Benzene and substituted derivatives	n/a	n/a
NEG	165.0559	4.07	11.81	Level 1	Phenyllactic acid	0.059*	1.8	Up	0.122	Phenylpropanoids and polyketides	Phenylpropanoic acids	C05607
NEG	212.0023	3.51	68.87	Level 1	Indoxyl sulfate	0.124	1.35	Up	0.218	Organic acids and derivatives	Organic sulfuric acids and derivatives	
NEG	151.0402	5.55	10.69	Level 2	3-Cresotinic acid	0.125	1.44	Up	0.218	Benzenoids	Benzene and substituted derivatives	C14088
NEG	131.0715	3.58	5.02	Level 3	5-Hydroxyhexanoic acid, 3-hydroxyhexanoic acid	0.162	1.24	Up	0.270	Organic acids and derivatives	Hydroxy acids and derivatives	n/a
NEG	164.0717	2.10	5.14	Level 1	L-Phenylalanine	0.200*	1.56	Up	0.318	Organic acids and derivatives	Carboxylic acids and derivatives	C00079

NEG	283.0824	3.78	20.15	Level 2	p-Cresol glucuronide	0.235	-1.2	Down	0.358	Benzenoids	Phenols	C01468
NEG	192.0667	3.64	18.49	Level 1	Phenylacetyl glycine	0.267	-1.17	Down	0.374	Organic acids and derivatives	Carboxylic acids and derivatives	C05598
NEG	226.0180	4.56	48.65	Level 3	L-Glutamyl 5-phosphate	0.313	-1.27	Down	0.422	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C03287
NEG	103.0400	1.24	3.73	Level 3	3-Hydroxybutyric acid	0.370*	-1.31	Down	0.463	Hydroxy acids and derivatives	Alpha hydroxy acids and derivatives	C01089
NEG	181.0506	2.69	6.40	Level 1	Hydroxyphenyllactic acid	0.423*	1.19	Up	0.511	Phenylpropanoids and polyketides	Phenylpropanoic acids	C03672
NEG	267.0732	1.29	8.36	Level 1	Inosine	0.481*	1.1	Up	0.561	Nucleosides, nucleotides, and analogues	Purine nucleosides	C00294
NEG	180.0665	1.13	4.36	Level 1	L-Tyrosine	0.877	-1.01	Down	0.915	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00082
NEG	175.0248	0.80	2.32	Level 2	L-Ascorbic acid	0.888*	-1.56	Down	0.915	Dihydrofurans	Furanones	C00072
Urine ⁹												
POS	202.1079	3.34	5.65	Level 1	[M+Na] Hippuric acid	< 0.0001*	2.9	Up	0.001	Benzene and substituted derivatives	Benzoic acids and derivatives	C01586
POS	251.1028	3.77	4.56	Level 4	Unknown	< 0.0001	2.63	Up	0.001	n/a	n/a	n/a
POS	181.0611	2.77	6.27	Level 2	Picolinoyl glycine	0.0002*	1.77	Up	0.001	Organic acids and derivatives	Carboxylic acids and derivatives	n/a
POS	190.0503	2.77	4.47	Level 1	Kynurenic acid	0.0002	2.16	Up	0.001	Organoheterocyclic compounds	Quinolines and derivatives	C01717
POS	213.1493	5.23	4.26	Level 2	7-Oxo-11-dodecenoic acid	0.0002*	2.28	Up	0.001	Lipids and lipid-like molecules	Fatty Acyls	n/a
POS	257.1753	4.04	3.41	Level 4	Unknown	0.0003*	2.15	Up	0.002	n/a	n/a	n/a
POS	389.1814	5.23	4.58	Level 3	HpODE	0.001*	2.38	Up	0.004	Lipids and lipid-like molecules	Fatty Acyls	C04717
POS	424.2184	4.42	5.30	Level 3	HpODE	0.001	2.57	Up	0.004	Lipids and lipid-like molecules	Fatty Acyls	C04717
POS	153.066	1.40	28.14	Level 1	N-Methyl-4-pyridone-3-carboxamide [M-NH4] 452.2495 Unknown tetrapeptide	0.001	2.11	Up	0.004	Organoheterocyclic compounds	Pyridines and derivatives	C05843
POS	435.2233	5.04	9.79	Level 3	Unknown tetrapeptide	0.001	1.88	Up	0.004	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	n/a
POS	263.103	3.18	4.64	Level 4	Unknown	0.001	2.23	Up	0.004	n/a	n/a	n/a
POS	245.1597	1.10	4.61	Level 4	Unknown	0.001	1.75	Up	0.004	n/a	n/a	n/a
POS	220.1184	2.08	11.34	Level 1	Pantothenic Acid	0.001	2.09	Up	0.004	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00864
POS	452.2495	5.05	6.21	Level 3	Unknown tetrapeptide	0.001	2.06	Up	0.004	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	n/a
POS	247.1079	4.30	5.94	Level 2	N-Acetyl-DL-tryptophan	0.002	1.72	Up	0.004	Organic acids and derivatives	Carboxylic acids and derivatives	HMDB0013713
POS	468.2448	4.04	6.75	Level 3	Unknown tetrapeptide	0.006	2.15	Up	0.015	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	n/a
POS	259.1911	5.05	4.27	Level 2	Tetradecanedioic acid	0.006	1.53	Up	0.015	Lipids and lipid-like molecules	Fatty Acyls	C11002
POS	324.1084	3.11	1.75	Level 3	Unknown tripeptide	0.007	-2.07	Down	0.015	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	n/a
POS	210.0765	2.38	14.88	Level 1	Hydroxyphenylacetyl glycine	0.009	1.83	Up	0.019	Organic acids and derivatives	Carboxylic acids and derivatives	C05596

											derivatives	
POS	252.0873	3.46	9.55	Level 2	4-Hydroxy-3-methoxy-cinnamoylglycine	0.010	2.54	Up	0.020	Organic acids and derivatives	Carboxylic acids and derivatives	C02564
POS	338.0876	1.65	3.87	Level 2	3-Indole carboxylic acid glucuronide	0.014	-2.11	Down	0.028	Organic oxygen compounds	Organooxygen compounds	C19837
POS	302.124	3.79	15.15	Level 2	Unknown	0.015*	1.62	Up	0.029	n/a	n/a	n/a
POS	324.1086	3.37	0.89	Level 3	Unknown tripeptide	0.017	-1.72	Down	0.030	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	n/a
POS	324.1081	4.21	1.80	Level 3	Unknown tripeptide	0.018	-2.59	Down	0.031	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	n/a
POS	326.0874	2.49	3.98	Level 2	Dihydroxy-1H-indole glucuronide	0.018	2.1	Up	0.031	Organic oxygen compounds	Organooxygen compounds	C04185
POS	290.1603	2.00	9.34	Level 2	3-Methylglutarylcamitine	0.020	1.67	Up	0.032	Lipids and lipid-like molecules	Fatty Acyls	n/a
POS	340.1034	1.93	2.58	Level 2	6-Hydroxy-5-methoxyindole glucuronide	0.024	-1.66	Down	0.036	Organic oxygen compounds	Organooxygen compounds	C03033
POS	328.1033	3.37	9.03	Level 2	p-Acetamidophenyl glucuronide	0.025	-1.97	Down	0.036	Organic oxygen compounds	Organooxygen compounds	n/a
POS	329.2471	6.55	1.40	Level 2	Docosahexaenoic acid	0.025	-2.88	Down	0.036	Lipids and lipid-like molecules	Fatty Acyls	C06429
POS	146.0598	3.46	0.63	Level 2	4-formyl Indole	0.028	-1.99	Down	0.039	Organoheterocyclic compounds	Indoles and derivatives	n/a
POS	560.3075	4.97	10.92	Level 2	3-Hydroxy-5, 8-tetradecadienylcamitine-glucuronate	0.054	1.9	Up	0.073	Organic acids and derivatives	Hydroxy acids and derivatives	n/a
POS	132.0768	0.67	9.86	Level 1	Creatine	0.061	2.76	Up	0.080	Organic acids and derivatives	Carboxylic acids and derivatives	C00300
POS	164.0709	2.87	1.45	Level 3	3-Methyldioxyindole	0.063	-1.5	Down	0.080	Organoheterocyclic compounds	Indoles and derivatives	C05834
POS	229.1551	1.28	16.52	Level 3	Unknown dipeptide	0.072	1.49	Up	0.089	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	n/a
POS	340.1032	2.87	4.83	Level 2	6-Hydroxy-5-methoxyindole glucuronide	0.075	-1.5	Down	0.090	Organic oxygen compounds	Organooxygen compounds	C03033
POS	146.0602	5.25	1.17	Level 1	1H-Indole-3-carboxaldehyde	0.096	-1.93	Down	0.111	Organoheterocyclic compounds	Indoles and derivatives	C08493
POS	114.0662	0.67	30.80	Level 1	Creatinine	0.119	1.21	Up	0.135	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00791
POS	160.097	2.78	4.21	Level 3	Valerylglycine	0.194	1.3	Up	0.214	Organic acids and derivatives	Carboxylic acids and derivatives	HMDB0000927
POS	137.0459	0.86	5.41	Level 1	Hypoxanthine	0.200*	2.53	Up	0.215	Imidazopyrimidines	Purines and purine derivatives	C00262
POS	180.0656	3.27	8.25	Level 1	Hippuric acid	0.270	1.22	Up	0.284	Benzene and substituted derivatives	Benzoic acids and derivatives	C01586
POS	194.0813	3.63	42.99	Level 1	Phenylacetyl glycine	0.370	1.23	Up	0.379	Organic acids and derivatives	Carboxylic acids and derivatives	C05598
POS	130.0651	5.18	7.01	Level 2	3-Methylene-indolenine	0.579	-1.18	Down	0.579	Organoheterocyclic compounds	Indoles and derivatives	HMDB0011664
NEG	204.0305	2.54	0.81	Level 1	Xanthurenic acid	< 0.0001	2.33	Up	0.001	Organoheterocyclic compounds	Quinolines and derivatives	C02470
NEG	445.0785	4.17	2.78	Level 2	Baicalin (Baicalein 7-glucuronide)	0.0001*	1.95	Up	0.001	Phenylpropanoids and polyketides	Flavonoids	C10025
NEG	446.0819	4.17	0.67	Level 2	[M+H] ⁺ Baicalin, Baicalein 7-glucuronide	< 0.0001*	1.96	Up	0.001	Phenylpropanoids and polyketides	Flavonoids	C10025

NEG	269.0462	4.17	0.19	Level 2	[M-176] Baicalein	< 0.0001*	1.93	Up	0.001	Phenylpropanoids and polyketides	Flavonoids	C10025
NEG	218.1036	2.07	8.61	Level 1	Pantothenic Acid	0.000	1.85	Up	0.001	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00864
NEG	175.0978	3.12	1.06	Level 4	Unknown	0.000	2.02	Up	0.001	n/a	n/a	n/a
NEG	429.0833	3.91	1.17	Level 3	Daidzein 4'-O-glucuronide	0.000*	2.08	Up	0.001	Phenylpropanoids and polyketides	Flavonoids	n/a
NEG	387.1669	5.22	10.95	Level 2	7-Oxo-11-dodecenoic acid glucuronide	0.000*	1.86	Up	0.002	Lipids and lipid-like molecules	Fatty Acyls	n/a
NEG	429.0833	3.55	1.54	Level 2	Daidzein 7-O-glucuronide	0.000*	1.9	Up	0.002	Phenylpropanoids and polyketides	Flavonoids	n/a
NEG	369.0832	2.69	4.04	Level 3	Ferulic acid 4-O-glucuronide	0.001	2.85	Up	0.002	Organic oxygen compounds	Organooxygen compounds	n/a
NEG	188.9865	2.72	1.43	Level 2	Pyrocatechol sulfate	0.001	2.27	Up	0.002	Organic acids and derivatives	Organic sulfuric acids and derivatives	n/a
NEG	160.0616	1.46	0.31	Level 2	DL-2-Aminoadipic acid	0.001	2.36	Up	0.002	Organic acids and derivatives	Carboxylic acids and derivatives	C00956
NEG	194.0462	4.02	1.10	Level 2	Hydroxyhippuric acid	0.001*	2.37	Up	0.002	Benzenoids	Benzene and substituted derivative	n/a
NEG	345.0828	2	0.78	Level 4	Unknown	0.001*	2.72	Up	0.002	n/a	n/a	n/a
NEG	227.0441	0.66	0.47	Level 4	Unknown	0.001*	3.76	Up	0.002	n/a	n/a	n/a
NEG	559.3032	6.38	0.33	Level 3	PG(22:4(7Z,10Z,13Z,16Z)/0:0)	0.001*	4.66	Up	0.002	Lipids and lipid-like molecules	Fatty Acyls	n/a
NEG	150.0563	4.02	0.32	Level 2	Leukoaminochrome, 2-Phenylglycine	0.001*	2.3	Up	0.002	Organoheterocyclic compounds	Indoles and derivatives	C17756
NEG	557.2875	6.57	0.27	Level 4	Unknown	0.001*	3.77	Up	0.002	n/a	n/a	n/a
NEG	188.0355	2.78	0.90	Level 1	Kynurenic acid	0.001	2.17	Up	0.002	Organoheterocyclic compounds	Quinolines and derivatives	C01717
NEG	222.0775	2.73	0.36	Level 1	N-Acetyl-L-tyrosine	0.001*	1.53	Up	0.003	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C01657
NEG	330.1928	4.21	3.47	Level 4	Unknown	0.001	2.06	Up	0.003	n/a	n/a	n/a
NEG	361.1509	4.55	5.95	Level 4	Unknown	0.002	1.84	Up	0.004	n/a	n/a	n/a
NEG	322.0939	3.1	3.64	Level 2	3-Methyloxindole glucuronide (2)	0.004	-2.37	Down	0.010	Organoheterocyclic compounds	Indoles and derivatives	C02366
NEG	379.1615	3.91	4.15	Level 2	3,7-Dimethyl-3-octene-1,2,6,7-tetrol glucuronide	0.004	1.63	Up	0.010	Lipids and lipid-like molecules	Fatty Acyls	n/a
NEG	405.1772	4.41	14.07	Level 2	Dodecanedioic acid glucuronide	0.005	1.83	Up	0.011	Lipids and lipid-like molecules	Fatty Acyls	n/a
NEG	322.0938	4.21	2.77	Level 2	3-Methyloxindole glucuronide (3)	0.010	-2.94	Down	0.023	Organoheterocyclic compounds	Indoles and derivatives	C02366
NEG	459.2245	5.57	9.09	Level 4	Unknown glucuronide	0.010	1.71	Up	0.023	n/a	n/a	n/a
NEG	387.1665	4.54	4.52	Level 4	Unknown	0.011	2.16	Up	0.024	n/a	n/a	n/a
NEG	187.0073	3.93	20.79	Level 1	p-Cresol Sulphate	0.014	2.56	Up	0.029	Organic acids and derivatives	Organic sulfuric acids and derivatives	C01468
NEG	338.0885	2.88	13.15	Level 2	5-Hydroxy-6-methoxyindole glucuronide	0.015	-1.82	Down	0.029	Organic oxygen compounds	Organooxygen compounds	C03033
NEG	181.0508	2.66	9.70	Level 1	Hydroxyphenyllactic acid	0.015*	1.4	Up	0.029	Phenylpropanoids and polyketides	Phenylpropanoic acids	C03672
NEG	461.24	6.26	3.68	Level 2	Hexadecanedioic acid glucuronide (2)	0.015*	1.7	Up	0.029	Lipids and lipid-like molecules	Fatty Acyls	C19615

NEG	354.083	1.47	1.96	Level 2	Adrenochrome glucuronide	0.015	-2	Down	0.029	Organoheterocyclic compounds	Indoles and derivatives	n/a
NEG	250.0724	3.45	5.38	Level 2	N-Phenylacetylaspatic acid	0.021*	1.95	Up	0.036	Organic acids and derivatives	Carboxylic acids and derivatives	n/a
NEG	258.135	2.97	4.30	Level 4	Unknown sulphate	0.021*	1.44	Up	0.036	n/a	n/a	n/a
NEG	363.2545	6.55	1.11	Level 4	Unknown	0.021	-2.7	Down	0.036	n/a	n/a	n/a
NEG	541.2656	4.77	5.41	Level 2	Cortolone-3-glucuronide	0.027	1.67	Up	0.045	Lipids and lipid-like molecule	Steroids and steroid derivatives	n/a
NEG	208.0617	2.38	8.44	Level 1	Hydroxyphenylacetylglutamine	0.030	1.47	Up	0.048	Organic acids and derivatives	Carboxylic acids and derivatives	C05596
NEG	326.0886	3.36	1.27	Level 2	2-Phenylglycine / Leukoaminochrome glucuronide	0.030	-1.97	Down	0.048	Organoheterocyclic compounds	Indoles and derivatives	C17756
NEG	449.2034	4.03	17.41	Level 2	3-Hydroxytetradecanedioic acid glucuronide	0.031	1.59	Up	0.049	Lipids and lipid-like molecules	Fatty Acyls	n/a
NEG	326.0883	2.78	5.80	Level 2	Leukoaminochrome glucuronide	0.037	1.55	Up	0.056	Organoheterocyclic compounds	Indoles and derivatives	C17756
NEG	309.1353	5.08	3.76	Level 2	8,12-Epoxy-4(15),7,11-eudesmatrien-1-one Sulphate	0.039	-1.86	Down	0.058	Lipids and lipid-like molecules	Prenol lipids	n/a
NEG	322.0939	4.72	4.98	Level 2	3-Methyloxindole glucuronide	0.040	-2.03	Down	0.058	Organoheterocyclic compounds	Indoles and derivatives	C02366
NEG	433.2087	5.39	16.74	Level 2	Tetradecanedioic acid glucuronide	0.043	1.41	Up	0.061	Lipids and lipid-like molecules	Fatty Acyls	C11002
NEG	324.0727	2.45	11.57	Level 2	Dihydroxy-1H-indole glucuronide I	0.044	1.76	Up	0.061	Organic oxygen compounds	Organooxygen compounds	C04185
NEG	258.0079	2.12	7.90	Level 2	Adrenochrome sulphate	0.047	-1.67	Down	0.063	Organoheterocyclic compounds	Indoles and derivatives	n/a
NEG	338.0882	1.92	3.07	Level 2	6-Hydroxy-5-methoxyindole glucuronide	0.052	-1.62	Down	0.069	Organic oxygen compounds	Organooxygen compounds	C03033
NEG	165.056	4.07	5.37	Level 1	Phenyllactic acid	0.058	2.13	Up	0.075	Phenylpropanoids and polyketides	Phenylpropanoic acids	C05607
NEG	201.1135	3.71	12.05	Level 2	3-Methylazelaic acid	0.065	1.44	Up	0.082	Lipids and lipid-like molecules	Fatty Acyls	n/a
NEG	215.1293	5.92	7.24	Level 2	Undecanedioic acid	0.114*	-2.23	Down	0.141	Lipids and lipid-like molecules	Fatty Acyls	n/a
NEG	212.0025	3.31	40.76	Level 1	Indoxyl sulfate	0.150	1.4	Up	0.182	Organic acids and derivatives	Organic sulfuric acids and derivatives	n/a
NEG	417.2131	6.08	6.32	Level 2	3-Oxotetradecanoic acid glucuronide	0.178	1.39	Up	0.212	Lipids and lipid-like molecules	Fatty Acyls	n/a
NEG	158.0825	2.78	5.31	Level 2	2-Methylbutyrylglutamine	0.184	1.23	Up	0.215	Organic acids and derivatives	Carboxylic acids and derivatives	HMDB0000339
NEG	226.0184	4.43	7.04	Level 2	3-Methyloxindole sulphate	0.228	-1.33	Down	0.262	Organoheterocyclic compounds	Indoles and derivatives	C02366
NEG	230.0131	2.64	2.21	Level 2	Leukoaminochrome sulphate	0.249	-1.34	Down	0.281	Organoheterocyclic compounds	Indoles and derivatives	C17756
NEG	231.9922	2.71	6.93	Level 1	3-Hydroxyanthranilic acid sulphate	0.277*	1.14	Up	0.303	Benzenoids	Benzene and substituted derivatives	C00632
NEG	308.0779	3.19	9.00	Level 3	Indoxyl glucuronide	0.281	-1.2	Down	0.303	Organic oxygen compounds	Organooxygen compounds	C03033
NEG	192.0667	3.62	12.77	Level 1	Phenylacetylglutamine	0.284	1.1	Up	0.303	Organic acids and derivatives	Carboxylic acids and derivatives	C05598
NEG	431.1931	4.76	10.44	Level 2	5-Nonyltetrahydro-2-oxo-3-furancarboxylic acid glucuronide	0.305	1.23	Up	0.321	Organoheterocyclic compounds	Lactones	n/a
NEG	338.0886	3.38	1.13	Level 2	5-Hydroxy-6-methoxyindole glucuronide	0.332	-1.31	Down	0.343	Organic oxygen compounds	Organooxygen compounds	C03033

NEG	201.1136	5.29	12.97	Level 1	Sebacic acid	0.436	-1.27	Down	0.443	Lipids and lipid-like molecules	Fatty Acyls	C08277
NEG	283.0823	3.76	9.38	Level 2	p-Cresol glucuronide	0.568	1.05	Up	0.568	Benzenoids	Phenols	C01468
Liver¹⁰												
POS	615.1756	0.92	5.15	Level 1	[2M+H] Glutathione	0.001	1.18	Up	0.003	Organic acids and derivatives	Carboxylic acids and derivatives	C00051
POS	308.0914	0.92	57.30	Level 1	Glutathione	0.001	1.12	Up	0.003	Organic acids and derivatives	Carboxylic acids and derivatives	C00051
POS	450.3221	7.70	8.85	Level 1	Glycochenodeoxycholate	0.009	1.43	Up	0.018	Steroids and steroid derivatives	Bile acids, alcohols and derivatives	HMDB0000708
POS	148.0607	0.71	2.37	Level 1	L-Glutamate	0.037	1.19	Up	0.056	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00025
POS	104.0707	0.70	5.13	Level 2	Choline	0.114*	-8.16	Down	0.137	Organonitrogen compounds	Quaternary ammonium salts	C00114
POS	268.1044	1.13	8.70	Level 1	Adenosine	0.350	1.04	Up	0.350	Nucleosides, nucleotides, and analogues	Class Purine nucleosides	C00212
NEG	308.0986	0.75	0.92	Level 1	N-Acetylneuraminic Acid	0.001	1.22	Up	0.007	Organic oxygen compounds	Organooxygen compounds	C19910
NEG	165.0404	0.74	2.35	Level 2	Arabinonic acid, L-Xylonate	0.002*	1.39	Up	0.007	Organic oxygen compounds	Organooxygen compounds	C00878
NEG	306.0764	0.94	32.69	Level 2	Glutathione	0.002	1.07	Up	0.007	Organic acids and derivatives	Carboxylic acids and derivatives	C00051
NEG	613.16	0.94	9.26	Level 2	[2M-H] Glutathione	0.003	1.15	Up	0.007	Organic acids and derivatives	Carboxylic acids and derivatives	C00051
NEG	245.0432	0.74	5.58	Level 2	Glycerophosphoglycerol	0.003*	1.19	Up	0.007	Organic acids and derivatives	Hydroxy acids and derivatives	C03274
NEG	448.3066	7.73	43.93	Level 1	Glycochenodeoxycholate	0.004*	1.39	Up	0.009	Steroids and steroid derivatives	Bile acids, alcohols and derivatives	HMDB0006898
NEG	337.0441	1.13	2.50	Level 2	Imidazoleacetic acid ribotide	0.006	-1.3	Down	0.012	Organic oxygen compounds	Organooxygen compounds	C04437
NEG	147.0299	1.03	0.80	Level 1	D-2-Hydroxyglutaric acid	0.009	1.3	Up	0.016	Organic acids and derivatives	Hydroxy acids and derivatives	C01087
NEG	146.0459	0.72	5.58	Level 1	L-Glutamic acid	0.035	1.18	Up	0.055	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00025
NEG	565.0471	1.44	75.80	Level 2	Uridine diphosphate glucose	0.045	-1.37	Down	0.063	Nucleosides, nucleotides, and analogue	Pyrimidine nucleotides	C00029
NEG	102.0561	0.72	0.62	Level 3	L-Alpha-aminobutyric acid	0.050	1.17	Up	0.063	Organic acids and derivatives	Carboxylic acids and derivatives	C02356
NEG	264.934	0.63	0.73	Level 4	Unknown	0.075*	-1.23	Down	0.087	n/a	n/a	n/a
NEG	259.0224	0.75	3.44	Level 2	D-Glucose 6-phosphate	0.088	1.12	Up	0.094	Organic oxygen compounds	Organooxygen compounds	C00092
NEG	273.0381	0.74	4.24	Level 2	1-Deoxy-D-altro-heptulose phosphate ⁷⁻	0.094	1.21	Up	0.094	Organic oxygen compounds	Organooxygen compounds	C04359

¹Ionisation mode (ESI+, ESI-)

²Mass-to-charge

³Retention Time (* p-value with (W) is calculated by the Wilcoxon Mann Whitney test)

⁴values calculated using Student T-test; values with * are calculated by the Wilcoxon Mann Whitney test;

⁵FC – fold change (ad libitum vs restricted), positive values reflect an upregulation in the ad libitum feeding strategy

⁶False-discovery-rate (FDR) corrected P-values

⁷N/A – not available

⁸ $N_{\text{ad libitum}}(\text{ESI}^+) = 7$, $N_{\text{ad libitum}}(\text{ESI}^-) = 8$, $N_{\text{restricted}} = 9$

⁹ $N_{\text{ad libitum}} = 8$, $N_{\text{restricted}} = 8$;

¹⁰ $N_{\text{ad libitum}} = 7$, $N_{\text{restricted}} = 9$;

Table S3. List of metabolic features detected from metabolomics analysis of serum and liver in cloned and control Yucatan minipigs.

Mo de ¹	M/Z ² ratio	RT ³ (min)	VIP score	Level ID	Compound ID	Pval ⁴	FC ⁵	Regu lation (vs wild- type)	Qval ⁶	Compound class ⁷	Subclass ⁷	KEGG ⁷
Serum ⁸												
POS	160.0758	1.73	13.4	Level 1	[M-NH4] Serotonin	0.002	1.82	Up	0.031	Indoles and derivatives	Tryptamines and derivatives	C00780
POS	177.1026	1.73	1.6	Level 1	Serotonin	0.003	1.63	Up	0.031	Indoles and derivatives	Tryptamines and derivatives	C00780
POS	219.0828	0.61	1.0	Level 3	Prolyl-Cysteine; Cysteinyl-Proline	0.004	-1.53	Down	0.031	Organic acids and derivatives	Carboxylic acids and derivatives	N/A
POS	161.0791	1.73	1.3	Level 1	[M-NH4+H] Serotonin	0.004	1.74	Up	0.031	Indoles and derivatives	Tryptamines and derivatives	C00780
POS	166.0864	1.94	43.9	Level 1	L-Phenylalanine	0.005	-1.14	Down	0.031	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00079
POS	268.1045	1.11	25.8	Level 1	Adenosine	0.006	2.07	Up	0.034	Purine nucleosides	Not Available	C00212
POS	560.1546	1.29	0.6	Level 1	[2M+Na+H] Inosine	0.007	2.02	Up	0.034	Nucleosides, nucleotides, and analogues	Purine nucleosides	C00294
POS	692.4435	5.46	2.6	Level 4	[M+NH4] 675.4146 Unknown	0.008	1.27	Up	0.034	N/A	N/A	N/A
POS	156.0771	0.56	0.3	Level 3	L-Histidine	0.011	-1.22	Down	0.043	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00135
POS	132.0770	0.68	15.3	Level 1	Creatine	0.014	-1.50	Down*	0.051	Organic acids and derivatives	Carboxylic acids and derivatives	C00300
POS	154.0587	0.69	1.6	Level 1	[M+Na] Creatine	0.016	-1.72	Down	0.053	Organic acids and derivatives	Carboxylic acids and derivatives	C00300
POS	291.0705	1.29	2.5	Level 1	[M+Na] Inosine	0.022	1.33	Up	0.068	Nucleosides, nucleotides, and analogues	Purine nucleosides	C00294
POS	343.2640	7.73	2.9	Level 2	TrHA / Docosaheptaenoic Acid methyl ester	0.025	1.31	Up	0.068	Lipids and lipid-like molecules	Fatty acid esters	N/A
POS	192.0610	0.79	0.3	Level 3	Pyridoxine (standard available,	0.025	-1.15	Down*	0.068	Pyridines and derivatives	Pyridoxines	C00314

					confirm RT)							
POS	204.1235	0.86	6.7	Level 1	Acetylcarnitine	0.026	-1.25	Down	0.068	Lipids and lipid-like molecules	Fatty acid esters	C02571
POS	392.0346	0.74	0.8	Level 1	[M+2Na] Adenosine 5'-phosphate	0.029	2.05	Up	0.069	Nucleosides, nucleotides, and analogues	Purine nucleotides	C00020
POS	150.0587	0.91	3.4	Level 1	L-Methionine	0.033	-1.21	Down*	0.069	Organic acids and derivatives	Carboxylic acids and derivatives	C00073
POS	113.0211	0.93	4.0	Level 4	Unknown	0.033	-1.19	Down	0.069	N/A	N/A	N/A
POS	380.2569	8.04	1.8	Level 2	Sphingosine-1-phosphate	0.034	1.34	Up	0.069	Lipids and lipid-like molecules	Sphingolipids	C06124
POS	112.0872	0.56	10.6	Level 1	Histamine	0.037	1.56	Up	0.071	Organonitrogen compounds	Amines	C00388
POS	370.0529	0.74	1.4	Level 1	[M+Na] Adenosine monophosphate	0.038	2.02	Up	0.071	Nucleosides, nucleotides, and analogues	Purine nucleotides	C00020
POS	348.0709	0.73	2.2	Level 1	Adenosine monophosphate	0.041	1.97	Up	0.074	Nucleosides, nucleotides, and analogues	Purine nucleotides	C00020
POS	162.0763	0.70	3.0	Level 2	N-Methylglutamic acid	0.055	2.82	Up*	0.095	Organic acids and derivatives	Carboxylic acids and derivatives	C01046
POS	229.1551	1.34	1.3	Level 2	Leucylproline	0.070	-1.50	Down*	0.115	Organic acids and derivatives	Carboxylic acids and derivatives	HMDB0011175
POS	205.0973	2.61	16.0	Level 1	L-Tryptophan	0.080	-1.13	Down	0.126	Organoheterocyclic compounds	Indoles and derivatives	C00078
POS	269.0885	1.29	5.8	Level 1	Inosine	0.106	1.27	Up	0.161	Nucleosides, nucleotides, and analogues	Purine nucleosides	C00294
POS	118.0865	0.77	11.6	Level 1	L-Valine	0.124	1.20	Up	0.178	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00183
POS	152.0569	1.27	1.2	Level 2	Guanine	0.126	1.18	Up	0.178	Organoheterocyclic compounds	Imidazopyrimidines	C00242
POS	466.3174	5.98	4.8	Level 1	Glycocholic acid	0.133	1.35	Up*	0.182	Steroids and steroid derivatives	Bile acids, alcohols and derivatives	C01921
POS	116.0707	0.68	2.9	Level 1	L-Proline	0.161	-1.20	Down	0.213	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00148
POS	180.0655	3.28	0.7	Level 1	Hippuric acid	0.184	1.37	Up	0.236	Benzene and substituted derivatives	Benzoic acids and derivatives	C01586
POS	496.3409	9.29	33.9	Level 2	LysoPC(16:0)	0.230	-1.07	Down*	0.277	Lipids and lipid-like molecules	Glycerophospholipids	C04230
POS	520.3408	8.88	44.1	Level 2	LysoPC(18:2(9Z,12Z))	0.289	-1.09	Down	0.329	Lipids and lipid-like molecules	Glycerophospholipids	C04230
POS	524.3720	10.58	27.6	Level 2	LysoPC(18:0)	0.516	-1.06	Down	0.550	Lipids and lipid-like molecules	Glycerophospholipids	C04230
POS	132.1021	1.23	11.6	Level 1	L-Leucine	0.536	1.04	Up*	0.550	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00123
POS	137.0460	0.91	5.8	Level 1	Hypoxanthine	0.536	1.20	Up*	0.550	Imidazopyrimidines	Purines and purine derivatives	C00262
POS	205.0799	4.05	1.9	Level 2	gamma-Glutamylglycine	0.962	-1.98	Down*	0.962	Organic acids and derivatives	Carboxylic acids and derivatives	HMDB0011667
NEG	131.0351	2.29	3.1	Level 2	Methylsuccinic acid	0.000	3.96	Up	0.009	Lipids and lipid-like molecules	Fatty Acyls	C08645

NEG	228.9936	0.75	2.4	Level 4	Unknown	0.003	-1.38	Down	0.032	N/A	N/A	N/A
NEG	415.1973	5.59	9.4	Level 4	Unknown	0.003	-1.41	Down	0.032	N/A	N/A	N/A
NEG	226.9963	0.75	6.4	Level 4	Unknown	0.003	-1.38	Down	0.032	N/A	N/A	N/A
NEG	173.0092	0.77	3.7	Level 4	Unknown	0.003	-1.37	Down	0.032	N/A	N/A	N/A
NEG	215.0327	0.75	91.9	Level 1	[M+Cl] Glucose	0.007	2.31	Up*	0.053	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	C00031
NEG	302.0657	1.12	10.6	Level 1	[M+Cl] Adenosine	0.009	1.95	Up	0.059	Purine nucleosides	Not Available	C00212
NEG	325.0318	1.29	2.2	Level 4	Unknown	0.010	1.5	Up	0.059	N/A	N/A	N/A
NEG	243.1967	8.04	4.5	Level 2	2-Hydroxymyristic Acid	0.014	1.36	Up*	0.071	Lipids and lipid-like molecules	Fatty Acyls	HMDB0002261
NEG	404.0141	0.73	4.5	Level 1	[M+CH3COOH] Adenosine monophosphate	0.018	2.16	Up	0.071	Nucleosides, nucleotides, and analogues	Purine nucleotides	C00020
NEG	423.2751	7.73	3.1	Level 3	[M+FA] Norchenodeoxycholic acid	0.022	1.33	Up	0.071	Steroids and steroid derivatives	Bile acids, alcohols and derivatives	N/A
NEG	151.0402	5.55	18.2	Level 2	3-Cresotinic acid	0.022	-1.68	Down	0.071	Benzenoids	Benzene and substituted derivatives	C14088
NEG	377.2698	7.73	4.8	Level 3	Norchenodeoxycholic acid	0.024	1.31	Up	0.071	Steroids and steroid derivatives	Bile acids, alcohols and derivatives	N/A
NEG	346.0556	0.73	10.1	Level 1	Adenosine monophosphate	0.025	2.12	Up	0.071	Nucleosides, nucleotides, and analogues	Purine nucleotides	C00020
NEG	218.1033	2.08	5.0	Level 1	Pantothenic Acid	0.026	-1.27	Down	0.071	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00864
NEG	321.1472	6.84	3.0	Level 4	Unknown	0.033	-1.65	Down*	0.086	N/A	N/A	N/A
NEG	245.049	5.1	5.0	Level 4	Unknown	0.041	-2.46	Down*	0.098	N/A	N/A	N/A
NEG	378.2415	8.03	4.6	Level 2	Sphingosine-1-phosphate	0.042	1.33	Up	0.098	Lipids and lipid-like molecules	Sphingolipids	C06124
NEG	267.0732	1.29	64.4	Level 1	Inosine	0.045	1.41	Up	0.100	Nucleosides, nucleotides, and analogues	Purine nucleosides	C00294
NEG	87.0088	0.86	3.3	Level 3	Pyruvic acid	0.055	-1.28	Down*	0.118	Keto acids and derivatives	Alpha-keto acids and derivatives	C00022
NEG	446.2912	6.58	6.8	Level 3	Unknown	0.109	1.3	Up*	0.213	Steroids and steroid derivatives	Bile acids, alcohols and derivatives	N/A
NEG	464.3018	5.96	34.6	Level 1	Glycocholic Acid	0.133	1.38	Up*	0.250	Steroids and steroid derivatives	Bile acids, alcohols and derivatives	C01921
NEG	178.051	3.29	26.2	Level 1	Hippuric acid	0.148	1.39	Up	0.267	Benzene and substituted derivatives	Benzoic acids and derivatives	C01586
NEG	204.0668	4.33	4.4	Level 1	Indolelactic acid	0.157	-1.26	Down	0.267	Organoheterocyclic compounds	Indoles and derivatives	C02043
NEG	134.0613	3.29	3.7	Level 3	2-Phenylacetamide	0.159	1.37	Up	0.267	Benzenoids	Benzene and substituted derivatives	C02505
NEG	158.0824	2.79	4.2	Level 2	2-Methylbutyrylglycine	0.169	-1.44	Down	0.268	Organic acids and derivatives	Carboxylic acids and derivatives	HMDB0000339

NEG	195.8108	0.7	2.7	Level 4	Unknown	0.187	-1.04	Down	0.283	N/A	N/A	N/A
NEG	297.2436	9.89	2.2	Level 3	3-Oxo-octadecanoic acid	0.201	-1.67	Down	0.286	Lipids and lipid-like molecules	Fatty Acyls	HMDB0010736
NEG	165.0559	4.07	4.3	Level 1	D-Phenyllactic acid	0.230	-1.69	Down*	0.317	Phenylpropanoids and polyketides	Phenylpropanoic acids	C05607
NEG	203.0825	2.6	14.0	Level 1	L-Tryptophan	0.305	-1.06	Down	0.410	Organoheterocyclic compounds	Indoles and derivatives	C00078
NEG	135.0312	0.91	2.4	Level 1	Hypoxanthine	0.337	1.16	Up	0.440	Imidazopyrimidines	Purines and purine derivatives	C00262
NEG	514.2842	5.47	2.8	Level 3	Taurocholic acid	0.417	1.44	Up*	0.503	Steroids and steroid derivatives	Bile acids, alcohols and derivatives	C05122
NEG	230.0129	3.63	2.8	Level 3	Benzeneacetamide-4-o-sulphate	0.417	1.56	Up*	0.503	Organic acids and derivatives	Organic sulfuric acids and derivatives	N/A
NEG	283.0824	3.78	8.2	Level 2	p-Cresol glucuronide	0.527	1.11	Up	0.607	Benzenoids	Phenols	C01468
NEG	192.0667	3.64	13.9	Level 1	Phenylacetyl-glycine	0.584	1.08	Up	0.649	Organic acids and derivatives	Carboxylic acids and derivatives	C05598
NEG	187.0072	4.04	2.4	Level 1	p-Cresol sulfate	0.608	-1.13	Down	0.649	Organic acids and derivatives	Organic sulfuric acids and derivatives	C01468
NEG	407.2804	6.94	2.1	Level 2	1b,3a,7a-Trihydroxy-5b-cholanoic acid	0.813	1.03	Up*	0.814	Steroids and steroid derivatives	Bile acids, alcohols and derivatives	N/A
Liver⁸												
POS	150.0586	0.94	3.5	Level 1	L-Methionine	< 0.0001	1.2	Up	0.000	Organic acids and derivatives	Carboxylic acids and derivatives	C00073
POS	166.0867	2.11	12.3	Level 1	L-Phenylalanine	0.000	1.22	Up	0.002	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00079
POS	188.071	2.87	3.4	Level 2	3-amino-2-naphthoic acid	0.003	1.08	Up	0.012	Organoheterocyclic compounds	n/a	n/a
POS	205.0975	2.87	1.1	Level 1	L-Tryptophan	0.009	1.08	Up	0.030	Organoheterocyclic compounds	Indoles and derivatives	C00078
POS	254.0192	0.67	0.7	Level 4	Unknown	0.011	1.23	Up	0.030	n/a	n/a	n/a
POS	147.1131	0.60	0.6	Level 1	L-Lysine	0.000	1.13	Up	0.011	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00047
POS	126.0221	0.74	0.8	Level 2	2-Aminoethylphosphonic acid	0.015	-1.39	Down	0.030	Organic acids and derivatives	Organic phosphonic acids and derivatives	C03557
POS	176.067	0.71	0.3	Level 2	Guanidinosuccinic acid	0.019	1.23	Up*	0.032	Organic acids and derivatives	Carboxylic acids and derivatives	C03139
POS	296.0662	0.65	7.1	Level 1	[M+K] Glycerophosphocholine	0.031	1.22	Up	0.042	Lipids and lipid-like molecules	Glycerophospholipids	C00670
POS	219.0268	0.68	1.4	Level 3	Unknown, possible fragment of peptide	0.032	-1.18	Down	0.042	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	n/a
POS	405.0099	1.21	0.3	Level 4	Unknown	0.033	1.3	Up	0.042	n/a	n/a	n/a
POS	146.1179	2.68	0.9	Level 2	3-Dehydroxycarnitine	0.037	1.19	Up	0.043	Lipids and lipid-like molecules	Fatty Acyls	C05543
POS	258.1105	0.69	14.8	Level 1	Glycerophosphocholine	0.046	1.2	Up	0.050	Lipids and lipid-like molecules	Glycerophospholipids	C00670
POS	216.0635	0.72	0.5	Level 3	Unknown peptide	0.066	1.15	Up	0.066	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	n/a
NEG	124.0074	0.72	23.5	Level 1	Taurine	0.011	-1.38	Down	0.030	Organic sulfonic acids and	Organosulfonic acids and	C00245

										derivatives	derivatives	
NEG	195.051	0.74	14.8	Level 1	Gluconic acid	0.018	1.12	Up	0.035	Organooxygen compounds	Carbohydrates and carbohydrate conjugates	C00257
NEG	215.0328	0.72	12.4	Level 2	sn-glycero-3-Phosphoethanolamine	0.012	-1.13	Down	0.030	Lipids and lipid-like molecules	Glycerophospholipids	HMDB59660
NEG	164.0717	2.15	8.1	Level 1	DL-Phenylalanine	0.001	1.24	Up	0.006	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00079
NEG	259.0224	0.75	7.0	Level 1	D-Glucose 6-phosphate	0.025	-1.16	Down	0.036	Organic oxygen compounds	Organooxygen compounds	C00092
NEG	180.0666	1.19	6.8	Level 1	L-Tyrosine	0.081	1.1	Up	0.081	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00082
NEG	179.0561	0.7	6.7	Level 1	D-Glucose	0.006	-1.15	Down	0.023	Organic oxygen compounds	Organooxygen compounds	C00031
NEG	686.141	2.53	4.0	Level 2	Dephospho-CoA	0.013	1.23	Up	0.030	Nucleosides, nucleotides, and analogues	Purine nucleotides	C00882
NEG	130.0873	1.27	3.6	Level 1	Leucine	< 0.0001	1.17	Up	0.000	Organic nitrogen compounds	Organonitrogen compounds	C03065
NEG	304.0707	0.72	3.0	Level 4	Unknown	0.033	-1.47	Down	0.039	n/a	n/a	n/a
NEG	203.0827	2.91	2.2	Level 1	L-Tryptophan	0.007	1.08	Up	0.023	Organoheterocyclic compounds	Indoles and derivatives	C00078
NEG	452.0492	0.74	1.6	Level 4	Unknown	0.002	1.27	Up	0.010	n/a	n/a	n/a
NEG	309.1707	7.85	1.5	Level 4	Unknown	0.048	-1.3	Down	0.050	n/a	n/a	n/a
NEG	311.1863	8.82	1.4	Level 4	Unknown	0.034	-1.66	Down	0.039	n/a	n/a	n/a
NEG	161.0461	0.7	1.3	Level 3	2-Hydroxyadipic acid	0.001	-1.17	Down	0.009	Lipids and lipid-like molecules	Fatty Acyls	C02360
NEG	309.1708	8.42	1.2	Level 4	Unknown	0.026	-1.28	Down	0.036	n/a	n/a	n/a
NEG	193.0353	0.74	0.9	Level 1	D-Glucuronic acid	0.026	1.18	Up	0.036	Organic oxygen compounds	Organooxygen compounds	C00191
NEG	237.0881	1.84	0.6	Level 3	Glycyl-Tyrosine	0.020	1.23	Up	0.035	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	n/a
NEG	154.0622	0.63	0.4	Level 1	L-Histidine	0.026	1.06	Up	0.036	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00135
NEG	75.0089	0.74	0.2	Level 3	Glycolic acid	0.005	1.16	Up	0.021	Organic acids and derivatives	Hydroxy acids and derivatives	C03547
NEG	148.0437	0.98	0.2	Level 1	L-Methionine	0.036	1.27	Up	0.039	Organic acids and derivatives	Carboxylic acids and derivatives	C00073
NEG	118.051	0.69	0.1	Level 1	L-Threonine	0.032	1.08	Up	0.039	Organic acids and derivatives	Carboxylic acids and derivatives	C00188
NEG	174.052	0.74	0.1	Level 2	Guanidosuccinic acid	0.015	1.44	Up	0.031	Organic acids and derivatives	Carboxylic acids and derivatives	C03139
POS	150.0586	0.94	3.5	Level 1	L-Methionine	< 0.0001	1.2	Up	0.000	Organic acids and derivatives	Carboxylic acids and derivatives	C00073
POS	166.0867	2.11	12.3	Level 1	L-Phenylalanine	0.000	1.22	Up	0.002	Carboxylic acids and derivatives	Amino acids, peptides, and analogues	C00079
POS	188.071	2.87	3.4	Level 2	3-amino-2-naphthoic acid	0.003	1.08	Up	0.012	Organoheterocyclic compounds	n/a	n/a

¹ Ionisation mode (ESI+, ESI-)

²Mass-to-charge

³Retention Time (* p-value with (W) is calculated by the Wilcoxon Mann Whitney test)

⁴values calculated using Student T-test; values with * are calculated by the Wilcoxon Mann Whitney test;

⁵FC – fold change (ad libitum vs restricted), positive values reflect an upregulation in the ad libitum feeding strategy

⁶False-discovery-rate (FDR) corrected P-values

⁷N/A – not available

⁸ $N_{\text{cloned}} = 10$, $N_{\text{control}} = 7$.

Table S4. Metabolic pathway analysis using MetaboAnalyst 4.0: ad libitum versus restrictive fed Yucatan minipigs in serum, liver and urine metabolomics.

No.	Pathways	Cmpd ¹	Hits ²	Raw P ³	FDR ⁴	Impact	Compounds in pathway ⁵
Serum							
1	Pantothenate and CoA biosynthesis	27	2	0.068	0.29	0.180	Pantothenic Acid; Valine
2	Arginine and proline metabolism	77	3	0.316	0.51	0.134	L-Glutamyl 5-phosphate; L-Proline; Creatine
3	Phenylalanine metabolism	45	5	0.645	0.64	0.129	L-Phenylalanine; L-Tyrosine; Phenyllactic acid; 2-Hydroxycinnamic acid; Phenylacetyl glycine
4	Tryptophan metabolism	79	2	0.003	0.07	0.109	L-Tryptophan; Indolelactic acid
5	Tyrosine metabolism	76	2	0.586	0.63	0.047	L-Tyrosine; Hydroxyphenyllactic acid
6	Ubiquinone and other terpenoid-quinone biosynthesis	36	2	0.586	0.63	0.037	L-Tyrosine; Hydroxyphenyllactic acid
7	Valine, leucine and isoleucine biosynthesis	27	2	0.527	0.63	0.027	Valine; L-Leucine
8	Valine, leucine and isoleucine degradation	40	2	0.527	0.63	0.022	Valine; L-Leucine
9	Ascorbate and aldarate metabolism	45	1	0.396	0.59	0.016	L-Ascorbic acid
10	Primary bile acid biosynthesis	47	1	0.292	0.51	0.008	Glycocholic acid
11	Phenylalanine, tyrosine and tryptophan biosynthesis	27	3	0.258	0.51	0.008	L-Phenylalanine; L-Tyrosine; L-Tryptophan
12	Butanoate metabolism	40	1	0.296	0.51	0.005	3-Hydroxybutyric acid
13	Purine metabolism	92	1	0.188	0.51	0.004	Inosine
14	Glycine, serine and threonine metabolism	48	2	0.012	0.08	0.001	L-Tryptophan; Creatine
15	beta-Alanine metabolism	28	1	0.009	0.08	0.000	Pantothenic Acid
16	Nicotinate and nicotinamide metabolism	44	1	0.015	0.08	0.000	N-Methyl-4-pyridone-3-carboxamide
17	Propanoate metabolism	35	1	0.090	0.32	0.000	Valine
18	Nitrogen metabolism	39	3	0.258	0.51	0.000	L-Tryptophan; L-Phenylalanine; L-Tyrosine
19	Synthesis and degradation of ketone bodies	6	1	0.296	0.51	0.000	3-Hydroxybutyric acid
20	Aminoacyl-tRNA biosynthesis	75	6	0.505	0.63	0.000	L-Phenylalanine; Valine; L-Leucine; L-Tryptophan; L-Tyrosine; L-Proline
21	Thiamine metabolism	24	1	0.597	0.63	0.000	L-Tyrosine
Liver							
1	Glutathione metabolism	38	2	0.001	0.01	0.248	L-Glutamate; Glutathione
2	Alanine, aspartate and glutamate metabolism	24	1	0.037	0.06	0.177	L-Glutamate
3	Starch and sucrose metabolism	50	2	0.045	0.06	0.139	Uridine diphosphate glucose; D-Glucose 6-phosphate
4	D-Glutamine and D-glutamate metabolism	11	1	0.037	0.06	0.112	L-Glutamate
5	Amino sugar and nucleotide sugar metabolism	88	1	0.045	0.06	0.093	D-Glucose 6-phosphate
6	Aminoacyl-tRNA biosynthesis	75	1	0.037	0.06	0.056	L-Glutamate
7	Arginine and proline metabolism	77	1	0.037	0.06	0.036	Choline

8	Glycerophospholipid metabolism	39	1	0.170	0.18	0.021	L-Glutamate
9	Histidine metabolism	44	2	0.033	0.06	0.009	Imidazoleacetic acid ribotide; L-Glutamate
10	Purine metabolism	92	1	0.350	0.35	0.009	Adenosine
11	Cysteine and methionine metabolism	56	1	0.001	0.01	0.007	Glutathione
12	Pentose and glucuronate interconversions	53	1	0.045	0.06	0.006	D-Glucose 6-phosphate
13	Galactose metabolism	41	1	0.045	0.06	0.001	D-Glucose 6-phosphate
14	Butanoate metabolism	40	1	0.037	0.06	0.000	D-Glucose 6-phosphate
15	Porphyryn and chlorophyll metabolism	104	1	0.037	0.06	0.000	L-Glutamate
16	Nitrogen metabolism	39	1	0.037	0.06	0.000	D-Glucose 6-phosphate
17	Ascorbate and aldarate metabolism	45	1	0.045	0.06	0.000	
18	Pyrimidine metabolism	60	1	0.045	0.06	0.000	
19	Glycerolipid metabolism	32	1	0.045	0.06	0.000	D-Glucose 6-phosphate
20	Inositol phosphate metabolism	39	1	0.088	0.10	0.000	
21	Glycine, serine and threonine metabolism	48	1	0.170	0.18	0.000	Choline
Urine							
1	Pantothenate and CoA biosynthesis	27	1	0.000	0.001	0.180	Pantothenic Acid
2	Lysine biosynthesis	32	1	0.001	0.002	0.068	DL-2-Aminoadipic acid
3	Tryptophan metabolism	79	4	0.508	0.508	0.061	Kynurenic acid; Xanthurenic acid; 3-Methyldioxyindole; 3-Hydroxyanthranilic acid sulphate
4	Arginine and proline metabolism	77	2	0.110	0.129	0.038	Creatine; Creatinine
5	Ubiquinone and other terpenoid-quinone biosynthesis	36	1	0.011	0.022	0.037	Hydroxyphenyllactic acid
6	Phenylalanine metabolism	45	3	0.263	0.284	0.032	Phenylacetyl glycine; [M+Na] Hippuric acid
7	Lysine degradation	47	1	0.001	0.002	0.016	DL-2-Aminoadipic acid
8	Starch and sucrose metabolism	50	1	0.024	0.038	0.013	6-Hydroxy-5-methoxyindole glucuronide
9	Pentose and glucuronate interconversions	53	1	0.024	0.038	0.009	6-Hydroxy-5-methoxyindole glucuronide
10	Purine metabolism	92	1	0.079	0.101	0.008	Hypoxanthine
11	Tyrosine metabolism	76	3	0.001	0.002	0.007	Hydroxyphenyllactic acid; Hydroxyphenylacetyl glycine; Dihydroxy-1H-indole glucuronide
12	Glycine, serine and threonine metabolism	48	1	0.034	0.047	0.001	Creatine
13	beta-Alanine metabolism	28	1	0.000	0.001	0.000	Pantothenic Acid
14	Nicotinate and nicotinamide metabolism	44	1	0.001	0.002	0.000	3-Methyldioxyindole

¹Cmpd – total number of compounds included in the respective pathway;

²Hits – number of compounds identified that match the metabolites in the pathways;

³Raw P – calculated P-value of the enrichment analysis (low p-values describing significant changes of the metabolites involved in that metabolic pathway);

⁴FDR – false discovery rate;

⁵Name of compounds identified in the pathway.

Table S5. Metabolic pathway analysis using MetaboAnalyst 4.0: cloned versus wild-type Yucatan minipigs in serum and liver metabolomics.

No	Pathways	Cmpd ¹	Hits ²	Raw P ³	FDR ⁴	Impact	Compounds in pathway ⁵
Serum							
1	Phenylalanine metabolism	45	5	0.006	0.02	0.186	L-Phenylalanine; D-Phenyllactic acid; 2-Phenylacetamide; Hippuric acid; Phenylacetylglutamine
2	Pantothenate and CoA biosynthesis	27	2	0.122	0.16	0.180	Pantothenic acid; L-Valine
3	Histidine metabolism	44	2	0.012	0.03	0.172	L-Histidine; Histamine
4	Tryptophan metabolism	79	3	0.079	0.11	0.166	L-Tryptophan; Serotonin, Indolelactic acid
5	Arginine and proline metabolism	77	2	0.017	0.04	0.134	L-Proline; Creatine
6	Purine metabolism	92	5	9E-04	0.02	0.112	Adenosine monophosphate; Adenosine; Inosine; Hypoxanthine; Guanine
7	Vitamin B6 metabolism	32	1	0.046	0.07	0.104	Pyridoxine
8	Cysteine and methionine metabolism	56	1	0.019	0.04	0.038	L-Methionine
9	Valine, leucine and isoleucine biosynthesis	27	2	0.636	0.64	0.027	L-Leucine; L-Valine
10	Sphingolipid metabolism	25	1	0.034	0.06	0.026	Sphingosine 1-phosphate
11	Valine, leucine and isoleucine degradation	40	2	0.636	0.64	0.022	L-Leucine; L-Valine
12	Starch and sucrose metabolism	50	1	0.006	0.02	0.017	D-Glucose
13	Primary bile acid biosynthesis	47	2	0.469	0.51	0.017	Glycocholic acid; Taurocholic acid
14	Galactose metabolism	41	1	0.006	0.02	0.003	D-Glucose
15	Glycine, serine and threonine metabolism	48	2	0.04	0.06	0.001	Creatine; L-Tryptophan
16	Phenylalanine, tyrosine and tryptophan biosynthesis	27	2	0.008	0.02	0.001	L-Phenylalanine; L-Tryptophan
17	Glycolysis or Gluconeogenesis	31	1	0.006	0.02	0.000	D-Glucose
18	Pentose phosphate pathway	32	1	0.006	0.02	0.000	D-Glucose
19	Amino sugar and nucleotide metabolism	88	1	0.006	0.02	0.000	D-Glucose
20	Nitrogen metabolism	39	4	0.008	0.02	0.000	L-Phenylalanine; Tryptophan; L-Histidine; Adenosine monophosphate
21	beta-Alanine metabolism	28	2	0.024	0.04	0.000	Pantothenic acid; L-Histidine
22	Propanoate metabolism	35	1	0.124	0.16	0.000	L-Valine
23	Aminoacyl-tRNA biosynthesis	75	7	0.224	0.27	0.000	L-Histidine; L-Phenylalanine; L-Valine; L-Methionine; L-Leucine; L-Tryptophan; L-Proline
24	Taurine and hypotaurine metabolism	20	1	0.456	0.51	0.000	Taurine

Liver							
1	Taurine and hypotaurine metabolism	20	1	0.011	0.021	0.3309	Taurine
2	Lysine degradation	47	1	0.014	0.022	0.1468	L-Lysine
3	Histidine metabolism	44	1	0.026	0.032	0.1399	L-Histidine
4	Phenylalanine metabolism	45	2	0.000	0.001	0.1191	L-Phenylalanine; L-Tyrosine
5	Tryptophan metabolism	79	1	0.007	0.015	0.1085	L-Tryptophan
6	Lysine biosynthesis	32	1	0.014	0.022	0.0999	L-Lysine
7	Glycine, serine and threonine metabolism	48	2	0.007	0.015	0.0966	L-Tryptophan; L-Threonine
8	Pentose and glucuronate interconversions	53	1	0.026	0.032	0.0872	D-Glucuronic acid
9	Pentose phosphate pathway	32	2	0.007	0.015	0.0864	D-Glucose
10	Aminoacyl-tRNA biosynthesis	75	8	0.000	0.001	0.0563	L-Histidine; L-Phenylalanine; L-Methionine; L-Lysine; L-Leucine; L-Threonine; L-Tryptophan; L-Tyrosine
11	Tyrosine metabolism	76	1	0.081	0.081	0.0472	L-Tyrosine
12	Cysteine and methionine metabolism	56	1	0.000	0.000	0.0381	L-Methionine
13	Ascorbate and aldarate metabolism	45	1	0.026	0.032	0.0332	D-Glucuronic acid
14	Valine, leucine and isoleucine degradation	40	1	0.000	0.000	0.0223	L-Leucine
15	Starch and sucrose metabolism	50	3	0.007	0.015	0.0173	D-Glucose; D-Glucose 6-phosphate; D-Glucuronic acid
16	Valine, leucine and isoleucine biosynthesis	27	2	0.000	0.000	0.0133	L-Threonine
17	Glycerophospholipid metabolism	39	1	0.046	0.051	0.0099	L-Leucine
18	Primary bile acid biosynthesis	47	1	0.011	0.021	0.0082	Butyric acid
19	Phenylalanine, tyrosine and tryptophan biosynthesis	27	3	0.000	0.001	0.0080	L-Phenylalanine; L-Tyrosine; L-Tryptophan
20	Galactose metabolism	41	1	0.006	0.015	0.0028	D-Glucose
21	Nitrogen metabolism	39	5	0.000	0.002	0.0000	L-Histidine; L-Phenylalanine; L-Tyrosine; L-Tryptophan; L-Taurine
22	Fatty acid metabolism	50	1	0.005	0.015	0.0000	omega-Hydroxy fatty acid
23	Amino sugar and nucleotide sugar metabolism	88	2	0.006	0.015	0.0000	D-Glucose; D-Glucuronic acid
24	Glycolysis or Gluconeogenesis	31	1	0.006	0.015	0.0000	D-Glucose
25	Pantothenate and CoA biosynthesis	27	1	0.013	0.022	0.0000	Dephospho-CoA
26	Biotin metabolism	11	1	0.014	0.022	0.0000	L-Lysine
27	Inositol phosphate metabolism	39	2	0.024	0.032	0.0000	D-Glucose 6-phosphate; D-Glucuronic acid
28	beta-Alanine metabolism	28	1	0.026	0.032	0.0000	L-Histidine
29	Porphyrin and chlorophyll metabolism	104	1	0.032	0.038	0.0000	L-Threonine
30	Ether lipid metabolism	23	1	0.046	0.051	0.0000	sn-Glycero-3-phosphocholine
31	Ubiquinone and other terpenoid-quinone biosynthesis	36	1	0.081	0.081	0.0000	L-Tyrosine
32	Thiamine metabolism	24	1	0.081	0.081	0.0000	L-Tyrosine

¹Cmpd – total number of compounds included in the respective pathway;

²Hits – number of compounds identified that match the metabolites in the pathways;

³Raw P – calculated P-value of the enrichment analysis (low p-values describing significant changes of the metabolites involved in that metabolic pathway);

⁴FDR – false discovery rate;

⁵Name of compounds identified in the pathway;