

Supplementary figures

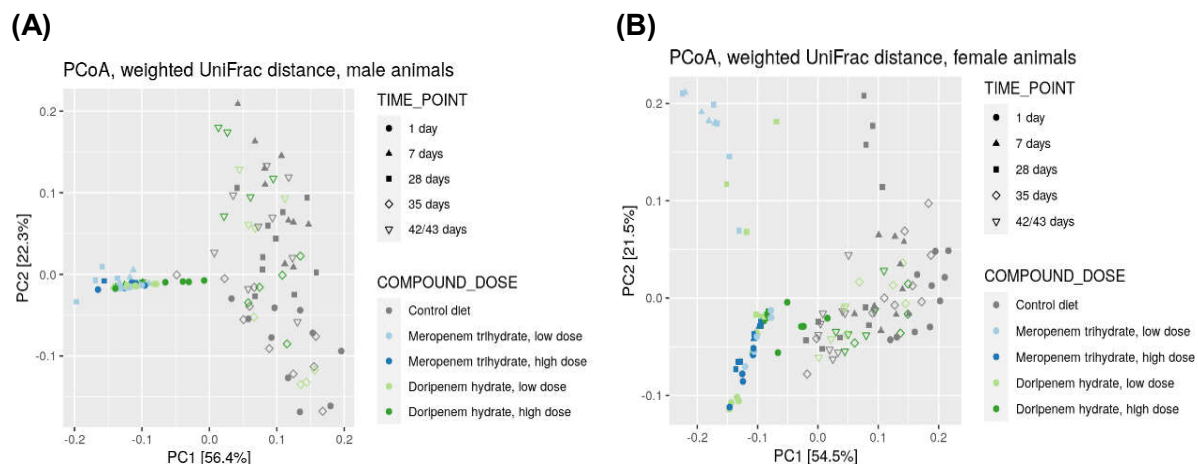
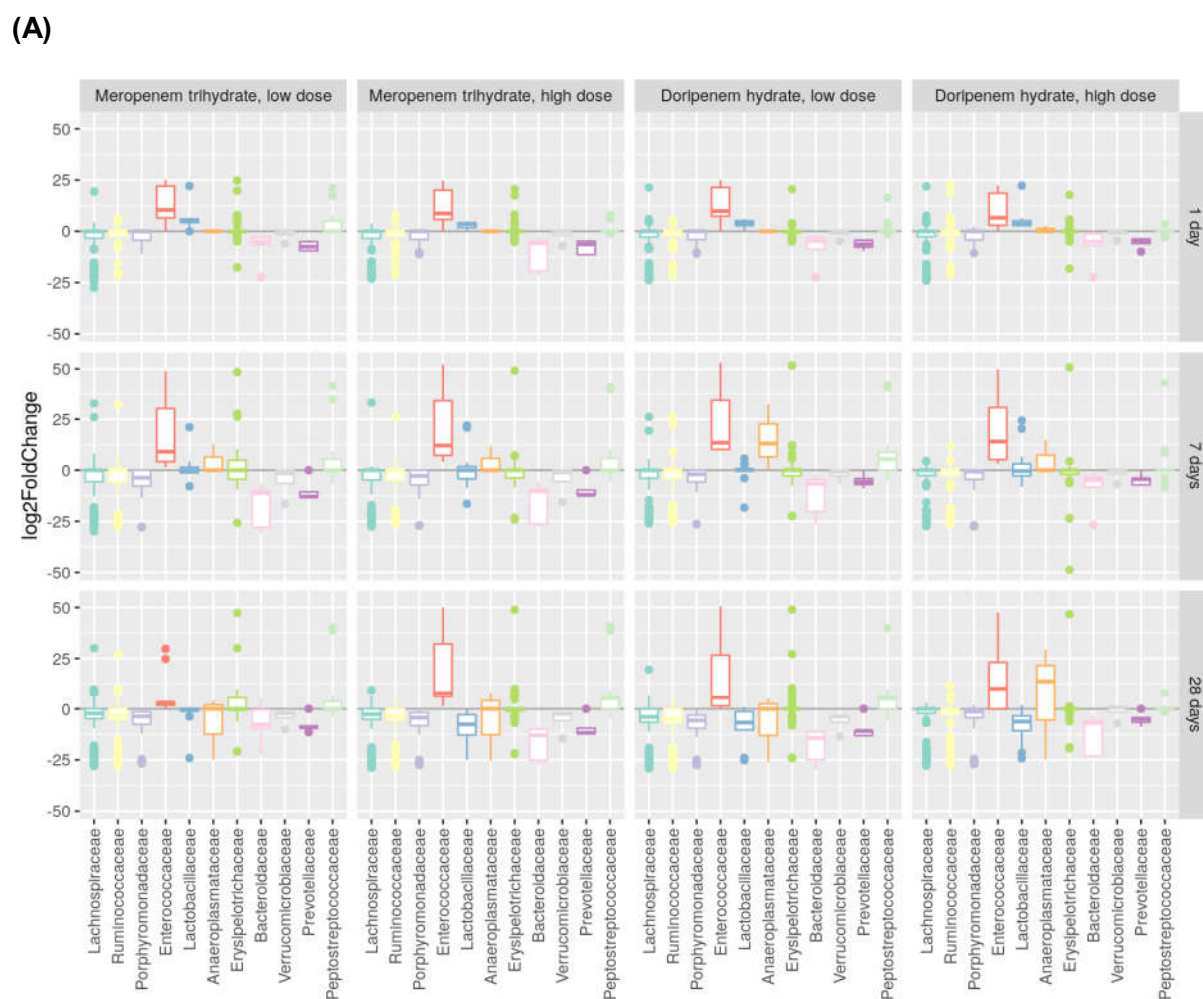


Figure S1: Principal Coordinate Analysis (PCoA) of bacterial families from controls, meropenem and doripenem antibiotic-treated rats at different time points using a phylogenetic-based distance matrix, weighted UniFrac distance, of samples from A) males and B) females are presented. Consistent to Bray-curtis based analysis, samples from day 1 clustered separately from the rest time points and the samples from animals treated with antibiotic from days 7 and 28 all cluster together and are separated both from controls and day 1 treated animals in both the sexes. Finally, samples from control animals at days 35 and 42/43 clustered together with the doripenem-recovery groups at one and two weeks after cessation of doripenem treatment indicating recovery reactions.



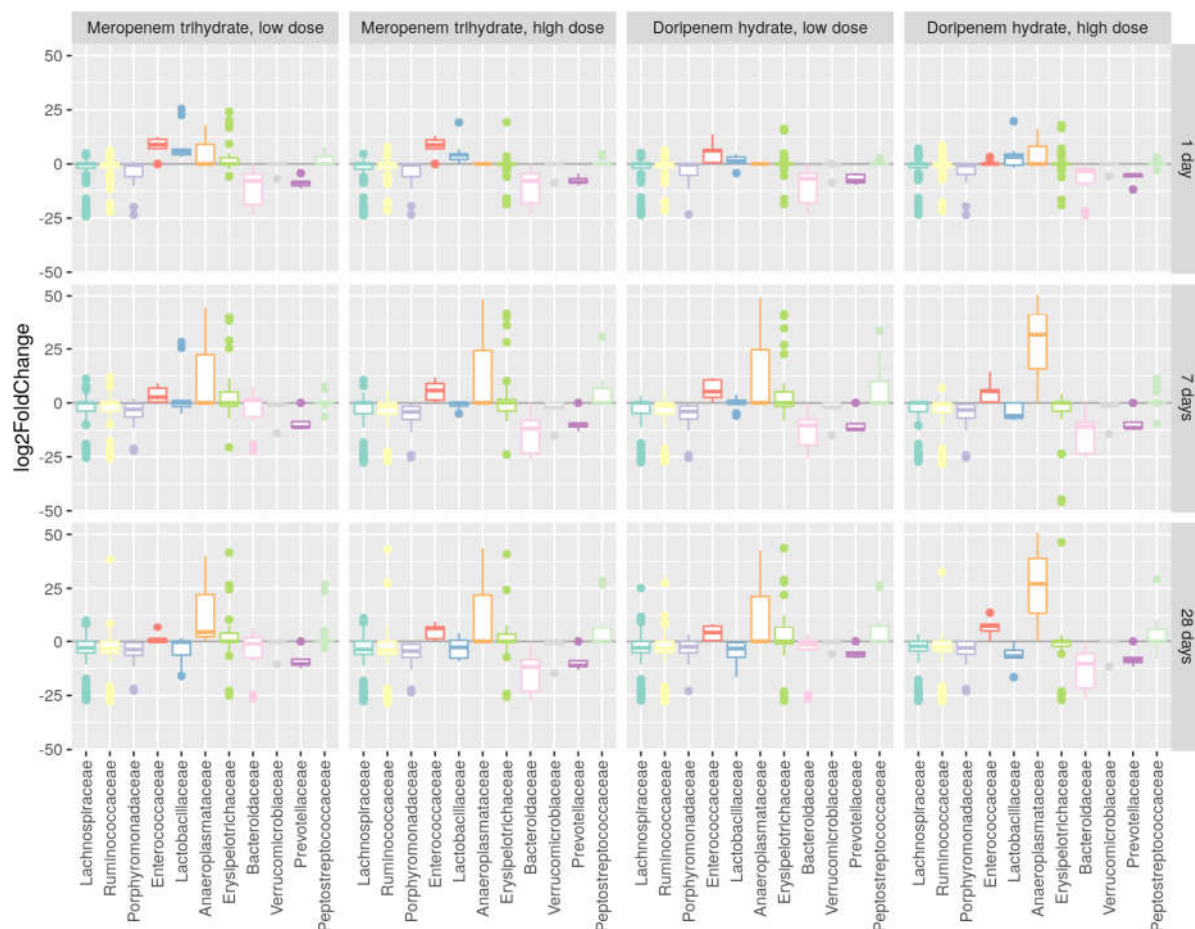
(B)

Figure S2: Differential abundances in dominant bacterial families in carabapenem treated samples from low (LD) and high (HD) dose groups relative to controls in males (A) and females (B). Differential abundance analysis was performed using log2FC (log2 fold change) values.

Supplementary tables

Table S1: Meropenem-induced feces metabolite fold changes in female (f) Wistar rats (N=5 per group) dosed with 100 (LD) and 300 (HD) mg/kg bw/day for 7, 14 and 28 days (f7, f14 and f28). Statistically significant changes (Welch-t-test; p-value < 0.05) are shown in bold numbers where red boxes mean a significant increase in the respective fecal metabolites and yellow a significant reduction compared to control levels.

Metabolite	Class	Meropenem trihydrate HD			Meropenem trihydrate LD		
		f7	f14	f28	f7	f14	f28
1,2-Anhydribose	Carbohydrates and related	4.24	4.94	5.18	3.20	2.33	1.62
1,4-Hydroquinone	Miscellaneous	2.71	2.98	1.82	1.53	1.27	1.09
14-Methylhexadecanoic acid	Complex lipids, fatty acids and related	0.27	0.36	0.25	0.73	0.74	1.15
15-Methylhexadecanoic acid	Complex lipids, fatty acids and related	0.27	0.38	0.40	0.68	0.81	1.69
2-Aminoadipic acid	Amino acids related	3.92	7.00	3.18	2.01	3.05	1.32
2-Hydroxybehenic acid (C22:0)	Complex lipids, fatty acids and related	0.30	0.83	0.55	0.64	0.73	0.77
2-Hydroxycerotic acid (C26:0)	Complex lipids, fatty acids and related	0.38	0.70	0.48	0.52	0.68	0.60

2-Hydroxynervonic acid (C24:1)	Complex lipids, fatty acids and related	0.24	0.85	0.53	0.49	0.95	0.59
2-Hydroxypentacosanoic acid (C25:0)	Complex lipids, fatty acids and related	0.31	0.76	0.50	0.59	0.80	0.69
3-Hydroxybutyrate	Energy metabolism and related	10.8	17.5				
3-Hydroxyphenylacetic acid	Amino acids related	2	9	4.55	4.38	3.45	2.54
4-Hydroxyphenylacetic acid	Amino acids related	0.09	0.05	0.07	0.09	0.04	0.15
4-Hydroxysphinganine (t18:0, Phytosphingosine), total	Complex lipids, fatty acids and related	20.9	11.7	10.6			
5-O-Methylsphingosine (d18:1)	Complex lipids, fatty acids and related	9	3	0	28.18	1.83	0.43
5-Oxoproline	Amino acids related	4.10	9.81	2.93	8.68	7.90	1.83
6-Hydroxynicotinic acid	Vitamins, cofactors and related						
Adenine	Nucleobases and related	1.71	2.65	2.26	3.15	2.83	2.53
Allantoin	Nucleobases and related	13.6	22.6			16.2	
alpha-Amyrin TMS	Unknown	8	9	5.44	6.91	4	4.98
alpha-Tocopherol	Vitamins, cofactors and related			10.7		14.8	19.6
alpha-Tocopherol	Unknown	8.88	7.56	9	7.52	0	9
alpha-Tocotrienol	Unknown	0.33	0.32	0.37	0.29	0.28	0.50
Arabinose	Carbohydrates and related	359.	207.	152.	118.2	16.5	12.6
Arginine	Amino acids	95	31	90	8	4	0
Azelaic acid (Dicarboxylic acid; C9:0)	Complex lipids, fatty acids and related	0.43	1.13	0.43	0.46	0.60	0.65
beta-/gamma-Tocotrienol	Unknown	0.57	0.66	0.80	0.97	0.92	1.18
beta-Alanine	Amino acids related	0.07	0.21	0.07	0.04	0.07	0.13
beta-Amyrin TMS	Unknown	0.09	0.37	0.14	0.06	0.07	0.18
beta-Muricholic acid	Complex lipids, fatty acids and related	3.46	2.48	1.62	2.23	1.92	5.30
beta-Sitosterol, total	Miscellaneous	1.68	3.24	2.71	2.85	2.79	3.22
Bile acid No 05	Complex lipids, fatty acids and related	3.94	1.61	2.04	3.43	3.60	1.75
Bile acid No 07	Complex lipids, fatty acids and related	0.63	0.63	0.95	0.59	0.55	1.11
Biliverdin	Unknown						18.4
bis-Glycerol phosphate, polar fraction	Miscellaneous	9.72	5.63	8.30	25.54	5	0.71
Campesterol, total	Miscellaneous	0.49	1.07	0.56	0.55	0.70	0.82
Cerebronic acid (2-OH-C24:0)	Complex lipids, fatty acids and related	7.76	3.95	3.66	16.51	4.56	2.59
Cholesterol, total	Complex lipids, fatty acids and related	2.93	3.01	3.31	3.80	3.28	2.67
Cholic acid	Unknown					17.5	
Citrulline	Unknown	3.08	2.04	2.34	8.74	3	5.40
Coenzyme Q10	Unknown	0.40	0.27	0.50	0.66	0.46	0.60
Cortisol (lipid)	Unknown	0.43	0.09	0.11	0.93	0.17	0.15
Creatinine	Amino acids related	3.12	1.50	1.30	1.03	1.16	0.66
		3.00	2.80	2.94	3.63	3.60	2.35
		0.32	0.92	0.57	0.57	0.99	0.61
		3.12	2.15	2.29	4.83	2.59	1.34
		10.7					
		8	9.57	7.33	17.48	1.14	0.91
		0.31	0.48	0.37	0.76	0.59	0.97
		0.55	0.63	1.05	0.77	0.82	0.84
		0.75	0.61	0.67	0.62	0.69	0.56
		113.	146.	115.	111.1	152.	175.
		44	37	35	1	38	87

Creatinine	Unknown	137.	138.	48.0		226.	71.9
Cysteine	Amino acids	36	42	9	88.40	47	4
		7.36	7.68	7.82	6.07	5.84	3.41
		10.5					
Cytosine	Nucleobases and related	9	5.41	2.67	4.13	1.64	1.29
Dehydroalanine	Amino acids related	8.09	8.74	5.81	7.21	5.87	3.55
	Complex lipids, fatty acids and related						
Deoxycholic acid	Unknown	0.16	0.06	0.24	0.37	0.26	0.59
Deoxycholic acid	Unknown	0.01	0.01	0.06	0.09	0.16	0.17
	Complex lipids, fatty acids and related						
Eicoasenoic acid (C20:cis[11]1)	Complex lipids, fatty acids and related	0.77	0.54	1.50	0.87	0.69	1.46
	Complex lipids, fatty acids and related						
Eicosadienoic acid (C20:2) No 01	Complex lipids, fatty acids and related	0.30	0.38	0.41	0.45	0.39	0.68
	Complex lipids, fatty acids and related						
Eicosadienoic acid (C20:2) No 02	Complex lipids, fatty acids and related	0.33	0.40	0.37	0.40	0.36	0.38
epsilon-Acetyllysine	Unknown	4.29	5.54	5.55	4.42	4.08	5.99
	Complex lipids, fatty acids and related						
erythro-Dihydrosphingosine (d18:0)	Complex lipids, fatty acids and related	0.18	0.40	0.28	1.46	1.45	2.68
Fucose	Carbohydrates and related	4.89	3.79	2.57	4.06	4.90	3.88
Fucosterol, total	Miscellaneous	2.74	2.16	2.70	2.46	2.32	2.41
	Energy metabolism and related						
Fumarate	Complex lipids, fatty acids and related	3.79	6.63	3.60	2.40	3.74	2.52
	Complex lipids, fatty acids and related						
Galactose, lipid fraction	Hormones, signal substances and related	1.48	1.95	2.46	2.55	1.39	1.55
	Hormones, signal substances and related						
gamma-Aminobutyrate (GABA)	Vitamins, cofactors and related	5.06	2.03	1.71	2.70	2.96	0.78
	Vitamins, cofactors and related						
gamma-Tocopherol	Complex lipids, fatty acids and related	0.60	0.58	0.79	0.64	0.75	0.70
	Complex lipids, fatty acids and related						
Glucose, lipid fraction	Complex lipids, fatty acids and related	1.85	2.25	2.10	3.37	1.80	1.12
Glucose-1-phosphate	Carbohydrates and related	4.38	7.27	2.88	4.32	3.95	3.13
Glucuronic acid	Carbohydrates and related	3.76	4.24	3.88	3.34	1.70	1.63
	Carbohydrates and related		15.7			12.6	
Glutamate	Amino acids	9.24	5	5.45	8.64	3	4.78
Glutamate	Unknown	1.80	3.30	1.78	1.92	2.64	2.05
Glutamic acid 2TMS ME (lipid)	Unknown	2.54	2.52	1.98	2.78	2.48	1.97
Glutamine	Amino acids	5.97	5.45	7.15	4.06	4.56	3.52
Glutarate	Amino acids related	0.45	0.47	0.64	1.44	0.31	0.66
	Complex lipids, fatty acids and related	10.3					
Glycerol-3-phosphate, polar fraction	Complex lipids, fatty acids and related	4	4.53	5.65	7.96	3.79	1.57
Glycine, lipid fraction	Miscellaneous	0.66	0.67	0.66	1.58	1.50	2.18
Glycine, lipid fraction	Miscellaneous	0.50	0.54	0.60	1.67	1.51	2.49
Glycolate	Miscellaneous	4.29	4.11	2.91	1.67	2.22	1.18
	Complex lipids, fatty acids and related						
Heneicosanoic acid (C21:0)	Complex lipids, fatty acids and related	0.40	0.55	0.47	0.59	0.50	0.72
	Complex lipids, fatty acids and related						
Heptadecanoic acid (C17:0)	Complex lipids, fatty acids and related	0.26	0.27	0.34	0.38	0.37	0.83
	Complex lipids, fatty acids and related						
Hexadecanol	Complex lipids, fatty acids and related	0.05	0.21	0.09	0.14	0.08	0.15
	Complex lipids, fatty acids and related						
Hyocholic acid	Complex lipids, fatty acids and related	0.81	0.36	0.28	0.83	0.33	0.64
Hyodeoxycholic acid	Unknown	0.01	0.01	0.01	0.02	0.01	0.04
	Complex lipids, fatty acids and related						
Hyodeoxycholic acid	Complex lipids, fatty acids and related	0.10	0.05	0.47	0.14	0.12	0.59

Indole-3-acetic acid	Amino acids related	11.0		10.0			
isoLCA	Unknown	9	3.86	3	5.12	3.07	1.38
Isopalmitic acid (C16:0)	Complex lipids, fatty acids and related	0.01	0.01	0.01	0.08	0.28	0.31
Kynurenic acid	Unknown	0.27	0.34	0.18	0.81	0.62	1.11
Linoleic acid (C18:cis[9,12]2)	Complex lipids, fatty acids and related	4.23	4.25	5.42	5.83	7.40	7.23
Linolenic acid (C18:cis[9,12,15]3)	Complex lipids, fatty acids and related	4.66	4.63	7.29	6.33	5.57	6.28
Lithocholic acid	Unknown	4.74	4.66	7.03	5.40	4.67	6.46
Mannose	Carbohydrates and related	0.02	0.03	0.02	0.08	0.15	0.15
Methionine	Unknown	11.0	12.3				
Myristic acid (C14:0)	Complex lipids, fatty acids and related	1	2	4.63	12.07	7.01	0.46
N2-Acetyllysine	Amino acids related	0.19	0.23	0.21	0.77	0.76	1.08
N-Acetyl-aspartic acid	Unknown	0.31	0.20	0.53	0.61	0.31	1.03
N-Acetylglucosamine	Unknown	4.82	5.67	4.28	6.23	3.79	3.62
N-Acetylserine	Unknown	5.94	4.76	3.34	1.98	2.37	2.01
N-Methylglutamate	Unknown	0.12	0.13	0.19	0.20	0.36	0.28
Norleucine	Miscellaneous		11.1				
Octadecanol	Complex lipids, fatty acids and related	4.64	6	5.19	4.32	0.99	0.32
Oleic acid (C18:cis[9]1)	Complex lipids, fatty acids and related	0.03	0.05	0.02	0.06	0.03	0.07
omega-Muricholic acid	Complex lipids, fatty acids and related	0.42	0.42	0.36	0.34	0.36	0.46
o-Muricholic Acid	Unknown	0.08	0.37	0.19	0.11	0.09	0.38
Palmitic acid (C16:0)	Complex lipids, fatty acids and related	2.26	2.08	5.19	2.82	2.17	4.55
Pentadecanol	Complex lipids, fatty acids and related	0.51	0.31	0.23	0.88	0.51	0.39
Phosphoenolpyruvate (PEP)	Energy metabolism and related	0.19	0.04	0.03	0.60	0.12	0.13
Pipecolic acid	Unknown	0.71	0.48	1.27	1.16	0.61	1.38
plausible 18:2-Lyso PC (Na-Addukt)	Unknown	0.42	0.45	0.56	0.54	0.50	0.90
plausible 2-Hydroxyarachidic acid (2-OH-C20:0) TMS ME	Unknown	6.07	6.48	4.24	3.52	3.75	3.47
plausible 2-Hydroxytricosanoic acid (2-OH-C23:0) TMS ME	Unknown	0.40	0.23	0.44	0.74	0.47	1.00
plausible Heptadecanol TMS	Unknown	3.02	1.15	2.62	2.48	2.98	1.84
plausible SM (d18:1, C16:0) Na-Addukt	Unknown	0.25	0.69	0.50	0.60	0.70	0.65
proposed Sphingomyelin (d18:2,C16:0)	Unknown	0.29	0.92	0.59	0.66	0.69	0.77
putative 12-Methylmyristic acid TMS	Unknown	0.01	0.10	0.02	0.01	0.11	0.43
putative Anhydroglucuronate 4TMS	Unknown	5.91	4.22	5.33	4.99	3.63	1.54
putative beta-Muricholic acid 3TMS ME (Byprodukt)	Unknown	4.28	3.34	4.27	3.43	2.51	0.98
putative Bis-(glycerol)-phosphate	Unknown	0.02	0.11	0.04	0.91	0.91	1.89
putative Choline plasmalogen (C36:2)	Unknown	3.10	4.24	2.95	3.47	4.12	2.82
putative Deoxycholyglycine deriv #1	Unknown	6.13	2.99	2.10	13.29	4.16	2.55
	Unknown	0.09	0.09	0.13	3.90	3.41	4.51
	Unknown	6.22	1.49	2.68	2.97	1.25	1.59
	Unknown	0.02	0.03	0.04	0.10	0.21	0.30

putative Hydroxy-eicosan OTMS	Unknown	0.17	0.29	0.40	0.17	0.17	0.33
putative Hyodeoxycholic acid 3TMS	Unknown	0.03	0.06	0.08	0.03	0.04	0.11
putative Lithocholic acid OTMS ME	Unknown	0.01	0.02	0.03	0.05	0.18	0.19
putative MeOx impurity (Blank)	Unknown	4.81	6.24	2.63	3.25	3.08	1.43
		71.6	61.0			18.5	
Putrescine	Miscellaneous	0	4	5.54	82.41	2	0.94
	Energy metabolism and related						
Pyruvate	Complex lipids, fatty acids and related	2.81	5.66	3.19	2.37	2.91	1.65
ribo-4-Hydroxy-8E-sphingenine	Amino acids related	0.80	3.04	1.64	1.42	2.16	1.77
Sarcosine		0.67	0.80	0.71	0.63	0.53	0.67
		34.0	22.7				
scyllo-Inositol	Carbohydrates and related	5	5	7.73	5.29	7.42	1.49
Serine, lipid fraction	Miscellaneous	0.62	0.51	0.71	1.31	1.32	2.07
Serine, lipid fraction	Miscellaneous	0.69	0.48	0.63	1.33	1.37	2.39
		1593	1731		1494.	512.	
Shikimic acid	Miscellaneous	.76	.27	3.31	67	47	1.67
	Complex lipids, fatty acids and related						
Stearic acid (C18:0)		0.68	0.50	0.66	0.83	0.56	0.60
Stigmasterol, total	Miscellaneous	2.22	1.85	2.36	2.32	2.26	2.41
		15.0		12.5		15.9	15.1
Taurine	Unknown	0	9.83	0	27.07	5	9
Tauro-b-muricholic Acid	Unknown	3.51	2.01	3.42	2.14	1.30	1.10
Taurochenodeoxycholate	Unknown	2.08	1.43	2.60	1.71	1.56	1.17
		185.	197.	280.		81.4	
Taurocholic Acid 3-sulfate	Unknown	39	22	09	40.98	9	6.10
Taurocholic acid sodium salt	Unknown	4.70	2.04	3.85	3.41	1.87	1.14
Taurolithocholic Acid	Unknown	0.04	0.12	0.15	0.41	0.61	0.78
	Complex lipids, fatty acids and related						
Tetradecanol		0.12	0.13	0.07	0.21	0.08	0.10
Thiamine (Vitamin B1)	Unknown	0.27	0.13	0.18	0.74	0.54	0.59
threo-Sphinganine 3TMS	Unknown	0.13	0.44	0.37	4.20	3.95	6.54
	Complex lipids, fatty acids and related						
threo-Sphingosine (d18:1)		1.86	1.81	1.95	3.26	2.31	2.06
trans-4-Hydroxyproline	Amino acids related	3.59	4.56	3.70	3.59	4.59	3.28
trans-Ferulic acid	Miscellaneous	8.57	5.33	3.48	5.96	4.77	3.18
		41.4	34.4	22.7			
trans-Sinapic acid	Miscellaneous	9	5	6	10.49	8.45	5.06
		16.5	34.3				
Tryptophan	Amino acids	6	5	4.70	3.75	4.53	2.82
		26.4	39.2	12.5			
Tyramine	Amino acids related	4	4	8	6.25	4.51	6.52
Tyrosine	Unknown	0.22	0.24	0.32	0.65	0.87	1.05
Ubichinone-30 (Coenzyme Q6)	Unknown	0.64	0.66	0.98	0.95	0.91	0.81
Ubichinone-35 (Coenzyme Q7)	Unknown	0.63	0.74	0.93	0.89	0.98	0.83
Ubichinone-45 (Coenzyme Q9)	Unknown	0.63	0.70	0.94	0.91	0.97	0.84
Unknown lipid MB (828450473)	Unknown	4.29	4.01	3.13	3.89	3.12	2.23
Unknown lipid MB (828451241)	Unknown	0.10	0.13	0.19	0.30	0.06	0.60
Unknown lipid MB (828451275)	Unknown	0.79	0.32	0.30	0.46	0.36	0.26
Unknown lipid MB (828451312)	Unknown	0.53	0.31	0.57	1.72	0.37	1.04
Unknown lipid MB (828451316)	Unknown	3.45	1.91	3.20	4.35	3.08	1.70
Unknown lipid MB (828451443)	Unknown	0.67	0.58	1.01	0.98	0.81	1.09
Unknown lipid MB (828451445)	Unknown	0.24	0.23	0.36	0.38	0.33	0.86

Unknown lipid MB (828451931)	Unknown	0.00	0.07	0.04	0.01	0.10	0.28
Unknown lipid MB (828451933)	Unknown	0.08	0.10	0.12	0.29	0.09	0.52
Unknown lipid MB (828451940)	Unknown	0.00	0.34	0.05	0.01	0.25	0.24
Unknown lipid MB (828452038)	Unknown	0.01	0.01	0.01	1.98	2.60	3.42
Unknown lipid MB (828452040)	Unknown	0.12	0.09	0.32	1.69	1.59	2.46
Unknown lipid MB (828452041)	Unknown	0.02	0.43	0.11	0.06	0.36	0.30
Unknown lipid MB (828452042)	Unknown	0.01	0.02	0.00	0.01	0.01	0.01
Unknown lipid MB (828452043)	Unknown	0.02	0.47	0.04	0.02	0.41	0.22
Unknown lipid MB (828452047)	Unknown	0.01	0.75	0.09	0.02	0.46	0.34
Unknown lipid MB (828452058)	Unknown	0.11	0.20	0.06	0.19	0.42	0.22
Unknown lipid MB (828452059)	Unknown	0.34	0.18	0.09	0.62	0.20	0.40
Unknown lipid MB (828452060)	Unknown	0.02	0.00	0.02	0.01	0.01	0.11
Unknown lipid MB ESI neg (858450047)	Unknown	3.31	1.37	2.96	1.80	2.05	2.15
Unknown lipid MB ESI neg (858450065)	Unknown	0.06	0.02	0.06	0.08	0.09	0.21
Unknown lipid MB ESI neg (858450068)	Unknown	0.46	0.80	0.50	0.47	0.66	0.49
Unknown lipid MB ESI neg (858450071)	Unknown	5.12	2.20	3.53	4.51	3.90	3.09
Unknown lipid MB ESI pos (848450056)	Unknown	5.71	2.54	3.79	3.44	2.89	3.34
Unknown lipid MB ESI pos (848450067)	Unknown	2.03	1.93	2.38	2.17	1.69	2.15
Unknown lipid MB ESI pos (848450068)	Unknown	3.70	1.43	2.14	3.69	2.46	1.78
Unknown lipid MB ESI pos (848450069)	Unknown	6.06	1.12	2.25	4.61	1.25	1.59
Unknown lipid MB ESI pos (848450083)	Unknown	4.73	2.65	1.80	3.59	2.41	0.82
Unknown lipid MB ESI pos (848450084)	Unknown	3.86	2.42	1.46	2.79	2.69	0.59
Unknown lipid MB ESI pos (848450092)	Unknown	0.40	0.17	0.28	0.55	1.14	1.27
Unknown lipid MB ESI pos (848450093)	Unknown	0.59	0.46	0.55	0.58	1.38	2.01
Unknown lipid MB ESI pos (848450094)	Unknown	4.11	6.98	1.61	1.98	1.51	1.52
Unknown lipid MB ESI pos (848450095)	Unknown	0.58	0.33	0.69	5.63	3.74	1.42
Unknown lipid MB ESI pos (848450096)	Unknown	3.28	1.25	2.19	3.50	11.6	4.24
Unknown lipid MB ESI pos (848450097)	Unknown	7.77	1.87	4.11	3.27	2.61	1.58
Unknown lipid MB ESI pos (848450098)	Unknown	2.55	1.36	1.39	1.58	1.43	1.10
Unknown lipid MB ESI pos (848450100)	Unknown	3.36	1.06	2.00	4.77	2.56	1.48
Unknown lipid MB ESI pos (848450102)	Unknown	4.87	1.46	2.40	2.31	1.74	1.63
Unknown lipid MB ESI pos (848450103)	Unknown	4.91	1.90	3.72	2.68	1.61	1.24
Unknown lipid MB ESI pos (848450105)	Unknown	9.05	2.88	9.13	4.19	4.61	1.57
Unknown lipid MB ESI pos (848450106)	Unknown	8.23	2.10	3.00	5.64	2.42	0.81

Unknown lipid MB ESI pos (848450107)	Unknown	2.97	1.15	2.19	2.62	1.79	2.02
Unknown lipid MB ESI pos (848450108)	Unknown	5.37	1.55	3.81	4.27	2.62	3.26
Unknown lipid MB ESI pos (848450109)	Unknown	5.39	1.56	3.09	3.97	1.80	1.53
Unknown lipid MB ESI pos (848450110)	Unknown	9.35	4.25	3.91	7.78	2.35	0.97
Unknown lipid MB ESI pos (848450111)	Unknown	3.86	2.78	3.17	4.81	3.87	3.66
Unknown lipid MB ESI pos (848450112)	Unknown	3.97	1.17	2.89	3.92	1.54	2.70
Unknown lipid MB ESI pos (848450113)	Unknown	7.26	3.23	6.76	6.65	4.53	6.23
Unknown lipid MB ESI pos (848450114)	Unknown	7.35	1.68	3.87	4.93	2.45	2.20
Unknown lipid MB ESI pos (848450115)	Unknown	4.08	1.26	2.63	2.89	1.01	0.98
Unknown lipid MB ESI pos (848450116)	Unknown	5.77	2.74	2.07	4.00	2.50	0.77
Unknown lipid MB ESI pos (848450120)	Unknown	3.94	1.19	3.12	2.49	1.37	1.27
Unknown lipid MB ESI pos (848450123)	Unknown	3.05	1.30	2.51	3.35	3.15	0.97
Unknown lipid MB ESI pos (848450129)	Unknown	3.67	2.43	2.87	4.01	2.35	0.90
Unknown lipid MB ESI pos (848450130)	Unknown	3.12	1.80	1.89	3.33	1.34	0.87
Unknown lipid MB ESI pos (848450131)	Unknown	6.11	3.39	4.21	6.06	3.02	1.17
Unknown lipid MB ESI pos (848450132)	Unknown	5.87	3.53	3.49	5.40	3.43	0.91
Unknown lipid MB ESI pos (848450133)	Unknown	3.47	2.03	1.57	3.34	1.74	0.63
Unknown lipid MB ESI pos (848450135)	Unknown	3.71	1.73	1.90	3.37	1.97	1.15
Unknown lipid MB ESI pos (848450138)	Unknown	4.33	3.67	2.59	4.52	3.04	0.79
Unknown lipid MB ESI pos (848450144)	Unknown	3.91	3.68	1.96	3.71	3.00	1.18
Unknown lipid MB ESI pos (848450146)	Unknown	3.42	4.32	2.27	2.81	3.83	1.18
Unknown lipid MB ESI pos (848450147)	Unknown	1.42	2.50	1.79	1.96	1.94	1.23
Unknown lipid MB ESI pos (848450148)	Unknown	3.74	5.67	3.07	4.58	4.31	1.31
Unknown lipid MB ESI pos (848450152)	Unknown	3.08	2.74	1.83	3.03	2.29	1.08
Unknown lipid MB ESI pos (848450153)	Unknown	2.24	3.00	1.31	2.35	1.69	1.12
Unknown lipid MB ESI pos (848450156)	Unknown	1.41	2.78	0.86	2.37	1.81	1.18
Unknown lipid MB ESI pos (848450158)	Unknown	2.26	3.46	1.37	4.46	2.40	1.44
Unknown lipid MB ESI pos (848450161)	Unknown	1.58	4.77	1.71	2.75	3.00	2.71
Unknown lipid MB ESI pos (848450162)	Unknown	1.74	3.79	1.54	2.49	2.95	1.66

Unknown lipid MB ESI pos (848450163)	Unknown	1.93	4.61	2.15	3.16	3.66	2.83
Unknown lipid MB ESI pos (848450168)	Unknown	1.67	2.89	1.64	2.78	2.18	1.44
Unknown lipid MB ESI pos (848450169)	Unknown	1.72	7.09	2.14	2.69	3.86	1.79
Unknown lipid MB ESI pos (848450196)	Unknown	12.3	14.9			15.0	11.8
Unknown lipid MB ESI pos (848450201)	Unknown	1	0	9.85	13.22	2	0
Unknown lipid MB ESI pos (848450202)	Unknown		11.5			15.9	10.0
Unknown lipid MB ESI pos (848450204)	Unknown	9.34	2	8.56	10.29	8	8
Unknown lipid MB ESI pos (848450205)	Unknown	4.65	4.08	4.76	4.08	4.94	4.85
Unknown lipid MB ESI pos (848450206)	Unknown	12.2	16.3			20.9	12.0
Unknown lipid MB ESI pos (848450207)	Unknown	1	5	9.62	14.19	6	3
Unknown lipid MB ESI pos (848450208)	Unknown	12.8	10.0			13.1	
Unknown lipid MB ESI pos (848450209)	Unknown	4	8	8.98	12.46	1	9.57
Unknown lipid MB ESI pos (848450210)	Unknown	14.6	25.6	13.6		32.0	16.1
Unknown lipid MB ESI pos (848450211)	Unknown	4	9	6	15.27	2	4
Unknown lipid MB ESI pos (848450212)	Unknown	11.7	18.3	13.6		27.2	15.8
Unknown lipid MB ESI pos (848450213)	Unknown	7	0	4	14.06	7	3
Unknown lipid MB ESI pos (848450214)	Unknown	11.8	16.8	10.6		21.1	11.8
Unknown lipid MB ESI pos (848450215)	Unknown	9	8	1	13.06	4	6
Unknown lipid MB ESI pos (848450216)	Unknown	8.33	8.18	7.42	8.39	9.53	7.81
Unknown lipid MB ESI pos (848450217)	Unknown	11.0				14.9	11.0
Unknown lipid MB ESI pos (848450218)	Unknown	8	9.66	8.96	11.52	2	2
Unknown lipid MB ESI pos (848450219)	Unknown		13.1			13.9	
Unknown lipid MB ESI pos (848450220)	Unknown	8.77	6	7.48	8.72	6	8.21
Unknown lipid MB ESI pos (848450221)	Unknown	11.3	13.3			14.6	10.3
Unknown lipid MB ESI pos (848450222)	Unknown	9	8	9.43	12.40	8	1
Unknown lipid MB ESI pos (848450223)	Unknown		14.5			15.6	
Unknown lipid MB ESI pos (848450224)	Unknown	9.59	1	8.75	9.71	4	9.34
Unknown lipid MB ESI pos (848450225)	Unknown	12.1	15.8			23.1	11.2
Unknown lipid MB ESI pos (848450226)	Unknown	4	4	9.73	10.82	9	8
Unknown lipid MB ESI pos (848450227)	Unknown		10.0			11.7	
Unknown lipid MB ESI pos (848450228)	Unknown	9.81	3	8.72	10.48	2	9.69
Unknown lipid MB ESI pos (848450229)	Unknown	12.4	13.7	10.7		16.2	11.5
Unknown lipid MB ESI pos (848450230)	Unknown	7	5	4	11.05	6	2
Unknown lipid MB ESI pos (848450231)	Unknown		11.0			15.0	10.8
Unknown lipid MB ESI pos (848450232)	Unknown	9.37	2	9.02	9.62	8	5
Unknown polar MB (838450146)	Unknown	4.27	5.06	2.68	1.89	1.47	1.63
Unknown polar MB (838450618)	Unknown	3.08	2.01	2.39	2.73	1.37	1.18
Unknown polar MB (838450621)	Unknown	12.1	10.7				
Unknown polar MB (838450621)	Unknown	3	5	4.98	9.43	3.59	0.92
Unknown polar MB (838450692)	Unknown	0.12	0.25	0.12	0.18	0.13	0.16
Unknown polar MB (838450761)	Unknown	2.55	1.44	2.39	3.93	2.15	1.36
Unknown polar MB (838450807)	Unknown	2.74	1.76	1.89	1.89	2.42	2.33
Unknown polar MB (838450816)	Unknown	0.01	0.01	0.00	0.01	0.00	0.01
Unknown polar MB (838451614)	Unknown	0.01	0.02	0.02	0.02	0.01	0.03
Unknown polar MB (838451982)	Unknown	8.38	3.67	5.01	6.72	3.44	1.85
Unknown polar MB (838452021)	Unknown	0.42	0.39	0.63	0.58	0.40	0.60
Unknown polar MB (838452022)	Unknown	2.48	3.56	2.14	2.12	1.85	1.49
Unknown polar MB (838452079)	Unknown	3.91	3.37	2.35	2.95	2.23	3.63
Unknown polar MB (838452178)	Unknown	0.12	0.17	0.59	0.28	0.21	1.07
Unknown polar MB (838452196)	Unknown	2.80	3.25	2.06	1.73	1.74	1.60

Unknown polar MB (838452482)	Unknown	313.21	115.05	253.60	156.16	16.64	15.63
Unknown polar MB (838452999)	Unknown	53.93	56.90	37.37		20.15	4.97
Unknown polar MB (838453000)	Unknown	7.71	3.49	4.13	4.07	2.52	2.01
Unknown polar MB (838453005)	Unknown	0.18	0.22	0.27	0.64	0.37	1.02
Unknown polar MB (838453006)	Unknown	0.38	0.35	0.48	0.30	0.14	0.24
Unknown polar MB (838453007)	Unknown	0.19	0.21	0.12	0.21	0.09	0.21
Unknown polar MB (838453009)	Unknown	0.03	0.05	0.02	0.01	0.04	0.02
Unknown polar MB (838453011)	Unknown	0.87	0.40	0.26	0.63	0.17	0.35
Unknown polar MB (838453012)	Unknown	187.01	293.71	97.92	164.94	136.84	55.31
Unknown polar MB (838453015)	Unknown	0.20	0.20	0.35	0.27	0.15	0.80
Unknown polar MB (838453017)	Unknown	0.07	0.19	0.07	0.14	0.08	0.17
Unknown polar MB (838453018)	Unknown	0.10	0.20	0.12	0.18	0.10	0.34
Unknown polar MB (838453019)	Unknown	0.06	0.08	0.02	0.03	0.06	0.10
Unknown polar MB (838453026)	Unknown	0.23	0.14	0.14	0.14	0.04	0.09
Unknown polar MB (838453028)	Unknown	0.08	0.08	0.06	0.07	0.08	0.04
Unknown polar MB (838453029)	Unknown	0.08	0.11	0.13	0.09	0.11	0.35
Unknown polar MB (838453030)	Unknown	0.17	0.18	0.15	0.15	0.05	0.09
Unknown polar MB (838453031)	Unknown	0.01	0.02	0.01	0.01	0.01	0.01
Unknown polar MB (838453033)	Unknown	0.06	0.07	0.06	0.09	0.05	0.10
Unknown polar MB (838453035)	Unknown	0.08	0.03	0.01	0.05	0.03	0.02
Unknown polar MB (838453036)	Unknown	0.09	0.12	0.03	0.13	0.09	0.04
Unknown polar MB (838453039)	Unknown	0.08	0.05	0.09	0.08	0.12	0.56
Unknown polar MB (838453040)	Unknown	0.05	0.08	0.31	0.09	0.23	1.11
Unknown polar MB (838453041)	Unknown	0.18	0.21	0.33	0.19	0.25	0.57
Unknown polar MB (838453043)	Unknown	0.07	0.06	0.04	0.10	0.05	0.05
Unknown polar MB (838453044)	Unknown	0.31	0.28	0.77	0.62	0.65	1.09
Unknown polar MB (838453051)	Unknown	0.42	0.24	0.63	0.65	0.57	0.78
Unknown polar MB (838453052)	Unknown	0.21	0.12	0.26	0.28	0.21	0.42
Unknown polar MB (838453053)	Unknown	0.19	0.19	0.31	0.47	0.48	0.76
Unknown polar MB (838453056)	Unknown	0.31	0.15	0.34	0.44	0.36	0.53
Unknown polar MB (838453057)	Unknown	0.17	0.12	0.28	0.28	0.22	0.34
Unknown polar MB (838453058)	Unknown	0.65	0.07	0.10	1.55	0.19	0.38
Unknown polar MB (838453059)	Unknown	2.95	1.43	2.87	3.57	2.14	2.23
Unknown polar MB (838453062)	Unknown	0.50	0.42	0.66	0.76	0.66	0.80
Unknown polar MB (838453063)	Unknown	0.60	0.08	0.12	1.18	0.24	0.28
Unknown polar MB (838453064)	Unknown	0.14	0.09	0.17	0.39	0.19	0.30
Unknown polar MB (838453066)	Unknown	0.01	0.01	0.02	0.01	0.03	0.82
Unknown polar MB (838453067)	Unknown	3.04	3.71	2.18	1.54	1.60	2.21
Unknown polar MB ESI neg (878450071)	Unknown	4.03	1.87	2.36	3.69	3.05	2.52
Unknown polar MB ESI pos (868450018)	Unknown	0.20	0.19	0.40	0.27	0.16	0.63
Unknown polar MB ESI pos (868450034)	Unknown	0.34	0.37	0.72	0.39	0.39	0.63
Uracil	Nucleobases and related	0.17	0.29	0.24	0.30	0.32	0.34
Xanthurenic acid	Amino acids related	0.07	0.12	0.16	0.13	0.10	0.12

Table S2: Meropenem-induced feces metabolite fold changes in male (m) Wistar rats (N=5 per group) dosed with 100 (LD) and 300 (HD) mg/kg bw/day for 7, 14 and 28 days (m7, m14 and m28). Statistically significant changes (Welch-t-test; p-value < 0.05) are shown in bold numbers where red boxes mean a significant increase in the respective fecal metabolites and yellow a significant reduction compared to control levels.

Metabolite	Class	Meropenem trihydrate HD			Meropenem trihydrate LD		
		m7	m14	m28	m7	m14	m28
1,25-Dihydroxy-vitamin D3	Unknown	0.87	0.52	0.61	0.80	0.88	0.92
1,2-Anhydribose	Carbohydrates and related	4.14	5.01	5.10	4.93	4.12	3.49
1,4-Hydroquinone	Miscellaneous	2.89	3.03	2.05	1.57	1.39	1.26
14-Methylhexadecanoic acid	Complex lipids, fatty acids and related	0.33	0.25	0.35	0.65	0.65	1.06
15-Methylhexadecanoic acid	Complex lipids, fatty acids and related	0.32	0.28	0.36	0.39	0.51	0.69
2-Hydroxybehenic acid (C22:0)	Complex lipids, fatty acids and related	0.42	0.38	0.50	0.55	0.71	0.98
2-Hydroxycerotic acid (C26:0)	Complex lipids, fatty acids and related	0.36	0.36	0.54	0.46	0.62	0.84
2-Hydroxynervonic acid (C24:1)	Complex lipids, fatty acids and related	0.35	0.37	0.47	0.45	0.72	0.91
2-Hydroxypalmitic acid (C16:0)	Complex lipids, fatty acids and related	0.54	0.41	0.56	0.67	0.71	0.82
2-Hydroxypentacosanoic acid (C25:0)	Complex lipids, fatty acids and related	0.39	0.40	0.45	0.51	0.59	0.73
2-Methylserine	Unknown	0.46	0.50	0.69	1.08	1.85	1.40
3-Hydroxybutyrate	Energy metabolism and related	7.52	14.7	8.54	4.14	7.90	3.21
3-Hydroxyphenylacetic acid	Amino acids related	0.09	0.13	0.06	0.05	0.06	0.03
4-Hydroxyphenylacetic acid	Amino acids related	33.7	13.9	5.58	24.99	4.27	4.17
4-Hydroxysphinganine (t18:0, Phytosphingosine), total	Complex lipids, fatty acids and related	4.25	3.63	3.08	6.77	5.97	2.68
5-Oxoproline	Amino acids related	13.9	16.4	19.0	11.9	5	9.98
5-Oxoproline, lipid fraction	Miscellaneous	6	4	0	10.82	1.48	2.44
6-Hydroxynicotinic acid	Vitamins, cofactors and related	1.79	1.27	1.70	1.60	14.8	20.7
Adenine	Nucleobases and related	5.81	6.57	7.39	7.42	4	7
Allantoin	Nucleobases and related	0.20	0.29	0.38	0.26	0.25	0.37
alpha-Tocopherol	Vitamins, cofactors and related	239.	134.	291.	373.3	23.5	63.3
alpha-Tocopherol	Unknown	76	81	73	4	0	2
alpha-Tocotrienol	Unknown	0.39	0.54	0.80	0.56	0.77	1.42
a-Muricholic Acid	Unknown	0.04	0.11	0.14	0.05	0.19	0.43
Arabinose	Carbohydrates and related	0.07	0.22	0.20	0.08	0.49	0.58
Arginine	Amino acids	23.8	2.53	2.28	18.70	5.85	2.13
Azelaic acid (Dicarboxylic acid; C9:0)	Complex lipids, fatty acids and related	8	2.87	2.39	2.51	4.44	4.28
Behenic acid (C22:0)	Complex lipids, fatty acids and related	2.00	1.78	2.48	3.48	5.21	3.18
beta-/gamma-Tocotrienol	Unknown	3.81	2.12	2.59	2.03	1.99	1.34
beta-/gamma-Tocotrienol	Unknown	2.12	2.59	2.03	1.99	1.34	1.66
		0.63	0.66	0.70	0.83	0.87	0.96
		0.48	0.61	0.82	0.53	0.80	1.28
		0.51	0.53	0.81	0.51	0.64	1.20

beta-Alanine	Amino acids related	18.7						10.8	31.3
		4.59	4.80	6	19.75	8	1		
beta-Muricholic acid	Complex lipids, fatty acids and related	38.7		13.2					15.9
		9	8.83	5	23.11	3.08	2		
beta-Sitosterol, total	Miscellaneous	3.22	3.78	3.30	3.13	3.78	2.08		
		23.0							
Bile acid No 01	Complex lipids, fatty acids and related	7	2.97	4.41	16.88	2.88	4.34		
Biliverdin	Unknown	0.16	0.08	0.21	0.38	0.13	0.22		
bis-Glyceryl phosphate, polar fraction	Miscellaneous	3.48	4.54	2.00	2.40	1.82	1.34		
b-Muricholic Acid	Unknown	8.16	2.43	2.13	5.03	1.73	3.48		
Campesterol, total	Miscellaneous	3.15	3.33	2.91	3.04	3.20	1.85		
Catechol	Miscellaneous	1.09	0.53	0.39	0.92	0.67	1.06		
Cerebronic acid (2-OH-C24:0)	Complex lipids, fatty acids and related								
		0.44	0.41	0.54	0.57	0.72	0.86		
Cholesterol, total	Complex lipids, fatty acids and related	2.65	3.03	2.36	3.15	3.64	1.26		
		13.7	22.7	33.7					
Cholic acid	Unknown	8	5	8	4.61	5.80	7.61		
Coenzyme Q10	Unknown	0.66	0.40	0.55	0.69	0.71	0.93		
conjugated Linoleic acid (C18:trans[9,11]2)	Complex lipids, fatty acids and related								
		0.38	0.50	0.67	0.64	0.62	1.23		
Cortisol (lipid)	Unknown	0.51	0.49	0.51	0.60	0.62	0.66		
Creatinine	Amino acids related	102.	101.	103.	104.4	84.8	123.		
		63	53	74	9	0	58		
Creatinine	Unknown	280.	184.	228.	151.1	213.	338.		
		14	57	47	0	64	16		
Cysteine	Amino acids	6.54	8.76	6.74	7.44	7.34	8.67		
Cytosine	Nucleobases and related	3.38	6.81	4.32	2.18	1.62	1.52		
Dehydroalanine	Amino acids related	7.23	7.84	5.47	7.48	5.68	4.24		
Deoxycholic acid	Complex lipids, fatty acids and related								
		0.13	0.20	0.17	0.47	0.67	0.44		
Deoxycholic acid	Unknown	0.01	0.01	0.00	0.20	0.21	0.24		
Eicosadienoic acid (C20:2) No 01	Complex lipids, fatty acids and related	0.32	0.30	0.25	0.43	0.48	0.49		
Eicosadienoic acid (C20:2) No 02	Complex lipids, fatty acids and related	0.30	0.22	0.28	0.51	0.42	0.43		
Eicosaenoic acid (C20:1) No 02	Complex lipids, fatty acids and related	0.66	0.46	0.56	0.99	0.87	0.66		
Eicosanoic acid (C20:0)	Complex lipids, fatty acids and related	0.67	0.57	0.63	0.68	0.70	0.87		
epsilon-Acetyllysine	Unknown					10.4			
		6.71	6.62	5.43	8.39	6	9.97		
erythro-Dihydrosphingosine (d18:0)	Complex lipids, fatty acids and related								
		0.22	0.20	0.30	0.29	0.49	0.50		
Fucose	Carbohydrates and related	21.5							
		6	6.28	3.41	4.56	2.05	2.73		
Fucosterol, total	Miscellaneous	2.71	2.28	2.65	2.77	2.06	1.91		
Fumarate	Energy metabolism and related	4.26	6.04	4.69	3.15	3.07	2.93		
Galactose	Carbohydrates and related	6.15	4.66	1.67	5.00	2.63	4.56		
Galactose, lipid fraction	Complex lipids, fatty acids and related								
		3.18	1.79	2.27	2.72	1.98	2.23		
gamma-Aminobutyrate (GABA)	Hormones, signal substances and related								
		5.00	4.37	5.37	3.52	2.32	3.76		

gamma-Tocopherol	Vitamins, cofactors and related	0.50	0.57	0.79	0.63	0.67	0.94
gamma-Tocopherol	Unknown	0.59	0.81	1.32	0.76	0.81	1.65
Glucose, lipid fraction	Complex lipids, fatty acids and related	5.24	2.03	1.91	3.58	3.35	2.13
Glucose-1-phosphate	Carbohydrates and related	6.74	6.31	3.17	3.47	3.50	2.73
Glucuronic acid	Carbohydrates and related	11.6	7	5.94	4.98	2.63	2.57
Glutamate	Amino acids	9.18	2	5	7.76	1	9.88
Glutamate	Unknown	2.50	3.76	3.40	3.57	5.97	4.82
Glutamic acid 2TMS ME (lipid)	Unknown	3.60	2.67	2.77	2.96	2.23	4.55
Glutamine	Amino acids	6.52	5.98	5.34	6.15	4.63	5.14
Glutarate	Amino acids related	0.40	0.34	0.19	0.38	0.47	0.43
Glycerol, lipid fraction	Complex lipids, fatty acids and related	1.44	2.68	2.27	1.81	3.15	3.01
Glycine, lipid fraction	Miscellaneous	0.91	0.68	0.72	1.02	0.81	1.15
Glycine, lipid fraction	Miscellaneous	0.69	0.53	0.63	0.62	0.76	1.07
Glycolate	Miscellaneous	3.90	3.38	2.73	3.12	2.17	1.53
Guanine	Nucleobases and related	2.55	1.48	1.80	1.21	1.60	1.74
Heneicosanoic acid (C21:0)	Complex lipids, fatty acids and related	0.51	0.44	0.42	0.66	0.58	0.68
Heptacosanoic acid (C27:0)	Complex lipids, fatty acids and related	0.75	0.53	0.85	0.83	0.82	1.30
Heptadecanoic acid (C17:0)	Complex lipids, fatty acids and related	0.38	0.28	0.41	0.41	0.42	0.61
Hexadecanol	Complex lipids, fatty acids and related	0.06	0.09	0.10	0.06	0.08	0.38
Hyodeoxycholic acid	Unknown	0.02	0.00	0.00	0.01	0.00	0.01
Hyodeoxycholic acid	Complex lipids, fatty acids and related	0.32	0.09	0.26	0.09	0.04	0.22
Hypoxanthine	Nucleobases and related	3.22	3.24	2.47	4.14	2.76	1.27
Indole-3-acetic acid	Amino acids related	15.8	28.7	46.8			32.5
Inosine	Nucleobases and related	6.02	8.05	4.53	5.43	6	7.05
isoLCA	Unknown	0.01	0.01	0.01	0.14	0.19	0.14
Isopalmitic acid (C16:0)	Complex lipids, fatty acids and related	0.36	0.25	0.25	0.60	0.56	0.80
Kynurenic acid	Unknown	6.60	2.56	5.58	6.67	2.95	5.91
Lignoceric acid (C24:0)	Complex lipids, fatty acids and related	0.70	0.71	0.75	1.08	1.04	0.95
Linoleic acid (C18:cis[9,12]2)	Complex lipids, fatty acids and related	3.60	5.01	5.28	3.29	3.50	8.33
Linolenic acid (C18:cis[9,12,15]3)	Complex lipids, fatty acids and related	4.15	6.57	5.73	5.24	4.81	9.50
Lithocholic acid	Unknown	0.02	0.03	0.02	0.13	0.10	0.08
Mannose	Carbohydrates and related	4.22	7.08	4.32	4.64	4.11	4.40
Methionine	Unknown	0.51	0.11	0.31	0.51	0.66	0.96
myo-Inositol	Carbohydrates and related	4.01	8.10	4.93	9.68	2.90	0.97
Myristic acid (C14:0)	Complex lipids, fatty acids and related	0.40	0.31	0.36	0.44	0.63	1.02
N-Acetyl-aspartic acid	Unknown	5.97	9.55	6	4.18	2.49	2.88

N-Acetylglucosamine	Unknown	0.33	0.21	0.12	0.45	0.48	0.79
N-Acetyl-leucine	Unknown	3.50	6.69	3.32	1.25	0.66	1.42
N-Acetylserine	Unknown	5.94	4.24	1.62	4.23	5.55	1.55
Nervonic acid (C24:cis[15]1)	Complex lipids, fatty acids and related	0.41	0.39	0.64	0.71	0.61	0.94
Niacinamide (Nicotinamide)	Unknown	0.72	0.80	0.63	1.06	1.48	1.03
Nicotinic acid	Vitamins, cofactors and related	2.29	3.44	2.24	1.30	1.29	1.47
Norleucine	Miscellaneous	0.82	0.15	0.49	0.60	0.23	0.61
Octadecanol	Complex lipids, fatty acids and related	0.08	0.09	0.17	0.10	0.13	0.52
Oleic acid (C18:cis[9]1)	Complex lipids, fatty acids and related	0.14	0.07	0.22	0.30	0.30	0.55
o-Muricholic Acid	Unknown	0.35	0.05	0.05	0.14	0.15	0.07
Pentacosanoic acid (C25:0)	Complex lipids, fatty acids and related	0.62	0.53	0.74	0.82	0.79	0.85
Pentadecanol	Complex lipids, fatty acids and related	0.49	0.43	0.55	0.55	0.73	0.80
Phosphate, lipid fraction	Complex lipids, fatty acids and related	1.35	0.45	0.70	0.70	0.72	1.21
Phosphoenolpyruvate (PEP)	Energy metabolism and related	5.39	6.03	4.69	3.62	3.11	2.42
Pipecolic acid	Unknown	0.46	0.37	0.48	0.79	0.76	0.61
plausible 18:2-Lyso PC (Na-Addukt)	Unknown	2.52	4.43	4.56	2.29	2.69	2.89
plausible 2-Hydroxyarachidic acid (2-OH-C20:0) TMS ME	Unknown	0.37	0.31	0.42	0.55	0.60	0.85
plausible 2-Hydroxytricosanoic acid (2-OH-C23:0) TMS ME	Unknown	0.47	0.33	0.50	0.61	0.71	0.98
plausible Heptadecanol TMS	Unknown	0.01	0.02	0.03	0.01	0.20	0.70
plausible SM (d18:1, C16:0) Na-Addukt	Unknown	4.69	2.72	3.21	4.47	2.30	1.89
Proline betaine	Unknown	2.12	0.91	2.40	1.01	1.13	1.25
putative 12-Methylmyristic acid TMS	Unknown	0.03	0.06	0.04	0.04	0.26	0.33
putative Anhydroglucuronate 4TMS	Unknown	4.49	4.72	2.32	2.49	3.03	2.23
putative beta-Muricholic acid 3TMS ME (Byprodukt)	Unknown	23.5	3	8.29	6.11	16.73	7.59
putative Bis-(glycerol)-phosphate	Unknown	0.31	0.21	0.34	0.30	0.79	1.24
putative C16:1 ME	Unknown	1.14	1.67	1.86	1.51	2.71	3.10
putative Choline plasmalogen (C36:2)	Unknown	3.14	3.20	3.83	3.80	1.61	1.64
putative Deoxycholyglycine deriv #1	Unknown	0.01	0.01	0.01	0.22	0.40	0.24
putative Hydroxy-eicosan OTMS	Unknown	0.28	0.26	0.49	0.35	0.38	0.64
putative Hyodeoxycholic acid 3TMS	Unknown	0.02	0.01	0.08	0.02	0.01	0.10
putative Lithocholic acid OTMS ME	Unknown	0.05	0.04	0.04	0.19	0.25	0.07
putative MeOx impurity (Blank)	Unknown	3.15	2.53	3.11	2.81	2.35	3.76
putative Tetracosenoic acid ME	Unknown	0.72	0.36	0.54	1.21	1.08	0.70
Putrescine	Miscellaneous	69.4	3	9.90	3	54.78	15.8
Pyruvate	Energy metabolism and related	2.68	18.2	17.9	25.0	1.64	2.10
scyllo-Inositol	Carbohydrates and related	0	2	1	16.03	6.98	3.70
Serine, lipid fraction	Miscellaneous	0.74	1068	939.	1052	1018.	0.62
Shikimic acid	Miscellaneous	.12	60	.99	27	5.83	2.43

Stearic acid (C18:0)	Complex lipids, fatty acids and related	0.43	0.38	0.60	0.45	0.46	0.66
Stigmastanol, total	Miscellaneous	0.65	0.76	0.74	0.62	0.80	0.84
Stigmasterol, total	Miscellaneous	2.67	2.24	2.22	2.31	2.15	1.93
		29.1	28.1	21.6		42.4	23.2
Taurine	Unknown	6	9	3	42.26	8	6
			26.5	12.7		12.3	
Tauro-b-muricholic Acid	Unknown	3.50	0	0	10.01	4	2.03
		13.1					
Taurocholic acid	Unknown	4	7.95	8.36	22.60	9.78	5.10
		15.2	921.	113.		759.	
Taurocholic Acid 3-sulfate	Unknown	4	65	19	83.21	51	0.13
			110.	12.6		19.4	
Taurocholic acid sodium salt	Unknown	4.49	41	3	8.93	0	0.33
	Complex lipids, fatty acids and related						
Tetradecanol	Complex lipids, fatty acids and related	0.18	0.08	0.13	0.20	0.15	0.40
Thiamine (Vitamin B1)	Unknown	0.18	0.17	0.22	0.22	0.28	0.29
	Complex lipids, fatty acids and related						
threo-Sphingosine (d18:1)	Complex lipids, fatty acids and related	1.74	1.48	2.17	2.41	2.82	2.54
trans-4-Hydroxyproline	Amino acids related	3.96	3.72	3.51	4.77	4.90	2.63
				10.3			
trans-Ferulic acid	Miscellaneous	6.02	9.98	5	2.58	2.80	3.50
		26.1	60.9	43.9		12.9	
trans-Sinapic acid	Miscellaneous	7	8	6	14.85	7	8.36
	Complex lipids, fatty acids and related						
Tricosanoic acid (C23:0)	Complex lipids, fatty acids and related	0.57	0.49	0.56	0.79	0.67	0.87
		51.6	40.2	30.6			
Tryptophan	Amino acids	0	9	1	2.58	3.42	4.78
		34.3	15.9	21.2			
Tyramine	Amino acids related	0	7	6	8.00	8.15	6.30
Tyrosine	Unknown	0.32	0.16	0.24	0.65	0.56	0.41
Ubichinone-30 (Coenzyme Q6)	Unknown	0.69	0.45	0.70	0.74	0.78	0.87
Ubichinone-35 (Coenzyme Q7)	Unknown	0.71	0.39	0.60	0.78	0.67	0.80
Ubichinone-45 (Coenzyme Q9)	Unknown	0.84	0.43	0.66	0.80	0.76	0.80
Unknown lipid MB (828450473)	Unknown	5.14	2.96	2.15	2.74	2.81	3.30
Unknown lipid MB (828451241)	Unknown	0.10	0.04	0.15	0.11	0.13	0.40
Unknown lipid MB (828451312)	Unknown	0.20	0.49	0.15	0.75	1.09	0.44
Unknown lipid MB (828451316)	Unknown	2.28	3.75	2.36	2.11	1.94	3.67
Unknown lipid MB (828451380)	Unknown	0.75	0.39	0.50	1.09	0.94	0.95
Unknown lipid MB (828451443)	Unknown	0.70	0.64	0.68	0.74	0.95	1.02
Unknown lipid MB (828451444)	Unknown	0.68	0.44	0.57	1.44	1.04	0.81
Unknown lipid MB (828451445)	Unknown	0.32	0.31	0.41	0.38	0.44	0.63
Unknown lipid MB (828451931)	Unknown	0.01	0.01	0.04	0.01	0.32	1.60
Unknown lipid MB (828451933)	Unknown	0.10	0.05	0.17	0.09	0.13	0.31
Unknown lipid MB (828451937)	Unknown	0.00	0.00	0.02	0.01	0.18	0.55
Unknown lipid MB (828451940)	Unknown	0.00	0.00	0.02	0.00	0.16	0.51
Unknown lipid MB (828452038)	Unknown	0.02	0.02	0.02	0.03	0.16	0.93
Unknown lipid MB (828452040)	Unknown	0.57	0.19	0.25	0.25	0.31	0.55
Unknown lipid MB (828452041)	Unknown	0.02	0.03	0.09	0.01	0.19	0.70
Unknown lipid MB (828452042)	Unknown	0.00	0.00	0.00	NA	0.01	0.01
Unknown lipid MB (828452043)	Unknown	0.00	0.01	0.05	0.00	0.19	0.60
Unknown lipid MB (828452044)	Unknown	0.71	0.46	0.48	0.97	1.00	1.28
Unknown lipid MB (828452047)	Unknown	0.01	0.01	0.06	0.01	0.21	0.53

Unknown lipid MB (828452050)	Unknown	0.03	0.05	0.05	NA	0.19	0.52
Unknown lipid MB (828452059)	Unknown	0.37	0.07	0.04	0.38	0.11	0.04
Unknown lipid MB ESI neg (858450034)	Unknown	0.49	0.47	0.39	0.59	0.55	0.53
Unknown lipid MB ESI neg (858450047)	Unknown	57.2	26.2	21.3		23.3	
Unknown lipid MB ESI neg (858450068)	Unknown	1	1	8	98.40	7	4.49
Unknown lipid MB ESI neg (858450071)	Unknown	0.48	0.48	0.57	0.58	0.72	0.61
Unknown lipid MB ESI pos (848450056)	Unknown	4.73	6.17	4.29	3.81	3.32	5.15
Unknown lipid MB ESI pos (848450065)	Unknown	4.17	8.14	5.98	5.54	5.29	6.06
Unknown lipid MB ESI pos (848450067)	Unknown	2.49	3.20	3.68	2.54	1.46	2.16
Unknown lipid MB ESI pos (848450068)	Unknown	4.18	3.90	2.31	2.17	1.74	1.62
Unknown lipid MB ESI pos (848450069)	Unknown	2.86	6.16	4.11	2.82	2.68	4.19
Unknown lipid MB ESI pos (848450083)	Unknown	2.90	5.19	5.29	3.19	3.54	5.48
Unknown lipid MB ESI pos (848450084)	Unknown	4.11	3.76	1.89	7.86	3.74	1.47
Unknown lipid MB ESI pos (848450091)	Unknown	2.54	3.06	2.54	3.81	3.69	2.20
Unknown lipid MB ESI pos (848450092)	Unknown	0.44	0.44	1.37	0.62	0.53	0.69
Unknown lipid MB ESI pos (848450094)	Unknown	0.37	0.36	0.27	0.31	0.51	0.35
Unknown lipid MB ESI pos (848450096)	Unknown	4.35	2.99	6.29	2.61	1.37	1.55
Unknown lipid MB ESI pos (848450097)	Unknown	2.72	3.72	2.70	1.85	2.54	2.93
Unknown lipid MB ESI pos (848450100)	Unknown	9.25	9.08	6.92	4.24	1.92	2.00
Unknown lipid MB ESI pos (848450102)	Unknown	4.32	5.37	3.63	3.01	1.64	1.82
Unknown lipid MB ESI pos (848450103)	Unknown	4.06	3.13	2.96	4.82	0.75	1.26
Unknown lipid MB ESI pos (848450105)	Unknown	4.12	4.85	3.26	4.88	1.52	1.37
Unknown lipid MB ESI pos (848450106)	Unknown	11.9	15.2				
Unknown lipid MB ESI pos (848450107)	Unknown	7	6	5.77	9.49	2.50	2.56
Unknown lipid MB ESI pos (848450108)	Unknown	7.04	3.90	3.07	4.84	3.14	1.24
Unknown lipid MB ESI pos (848450109)	Unknown	1.80	2.79	2.07	2.39	2.31	1.64
Unknown lipid MB ESI pos (848450110)	Unknown	3.91	4.07	3.33	4.48	3.14	2.23
Unknown lipid MB ESI pos (848450111)	Unknown	2.41	2.46	2.65	3.39	1.86	1.80
Unknown lipid MB ESI pos (848450112)	Unknown	11.7					
Unknown lipid MB ESI pos (848450113)	Unknown	6	6.96	5.32	6.78	4.08	2.65
Unknown lipid MB ESI pos (848450114)	Unknown	2.47	5.61	3.61	1.67	3.22	3.87
Unknown lipid MB ESI pos (848450115)	Unknown	2.93	2.96	2.99	3.03	2.42	3.00
Unknown lipid MB ESI pos (848450116)	Unknown	3.95	7.50	5.33	3.71	5.00	6.14

Unknown lipid MB ESI pos (848450114)	Unknown	4.58	4.96	4.71	5.12	3.08	2.21
Unknown lipid MB ESI pos (848450115)	Unknown	2.41	2.39	1.90	2.55	1.56	1.05
Unknown lipid MB ESI pos (848450116)	Unknown	6.69	6.06	4.23	6.23	6.30	2.15
Unknown lipid MB ESI pos (848450117)	Unknown	3.60	2.38	2.27	2.05	0.94	0.88
Unknown lipid MB ESI pos (848450119)	Unknown	2.39	2.37	1.59	1.72	0.89	0.87
Unknown lipid MB ESI pos (848450120)	Unknown	2.16	2.24	2.34	2.41	1.38	1.29
Unknown lipid MB ESI pos (848450129)	Unknown	2.42	2.86	2.55	3.43	2.53	1.96
Unknown lipid MB ESI pos (848450131)	Unknown	4.19	5.11	3.70	7.98	3.95	2.09
Unknown lipid MB ESI pos (848450132)	Unknown	3.89	3.33	2.94	5.29	2.85	2.28
Unknown lipid MB ESI pos (848450138)	Unknown	4.18	3.72	3.77	4.65	2.80	2.01
Unknown lipid MB ESI pos (848450139)	Unknown	5.07	8.69	4.45	6.92	2.24	0.86
Unknown lipid MB ESI pos (848450142)	Unknown	7.33	8.84	5.28	7.29	3.16	1.39
Unknown lipid MB ESI pos (848450144)	Unknown	3.93	6.92	5.65	4.72	5.39	3.22
Unknown lipid MB ESI pos (848450146)	Unknown	4.06	4.74	3.57	3.63	3.61	2.25
Unknown lipid MB ESI pos (848450147)	Unknown	1.70	2.23	2.43	1.96	1.87	1.68
Unknown lipid MB ESI pos (848450148)	Unknown	6.10	6.93	5.04	5.57	6.39	2.88
Unknown lipid MB ESI pos (848450170)	Unknown	2.03	1.30	1.50	2.68	2.36	2.15
Unknown lipid MB ESI pos (848450196)	Unknown	9.25	5	0	5.64	5	2
Unknown lipid MB ESI pos (848450201)	Unknown	8.90	8.63	7.76	6.68	10.5	10.6
Unknown lipid MB ESI pos (848450202)	Unknown	3.56	2.98	3.65	2.90	7	3
Unknown lipid MB ESI pos (848450204)	Unknown	11.6	11.7	10.8	2.98	12.9	15.6
Unknown lipid MB ESI pos (848450205)	Unknown	5	3	9	8.19	7	5
Unknown lipid MB ESI pos (848450206)	Unknown	11.0	10.0			12.5	11.8
Unknown lipid MB ESI pos (848450207)	Unknown	2	5	9.95	7.30	1	4
Unknown lipid MB ESI pos (848450208)	Unknown	11.3	18.0	14.7		20.3	18.8
Unknown lipid MB ESI pos (848450209)	Unknown	2	1	1	9.45	1	6
Unknown lipid MB ESI pos (848450210)	Unknown	12.5	15.2	11.8		14.1	15.4
Unknown lipid MB ESI pos (848450211)	Unknown	5	9	1	10.28	5	3
Unknown lipid MB ESI pos (848450212)	Unknown	10.3	11.5				13.3
Unknown lipid MB ESI pos (848450213)	Unknown	9	9	9.44	7.81	9.48	2
Unknown lipid MB ESI pos (848450214)	Unknown	8.03	8.21	5.99	6.48	7.95	7.37
Unknown lipid MB ESI pos (848450215)	Unknown						13.2
Unknown lipid MB ESI pos (848450216)	Unknown	8.10	8.90	9.38	5.61	7.56	1
Unknown lipid MB ESI pos (848450217)	Unknown			10.0			10.5
Unknown lipid MB ESI pos (848450218)	Unknown	7.65	8.92	9	7.13	9.75	3
Unknown lipid MB ESI pos (848450219)	Unknown		10.9	11.1		12.6	13.7
Unknown lipid MB ESI pos (848450220)	Unknown	9.43	8	8	8.34	8	8

Unknown lipid MB ESI pos (848450214)	Unknown	8.04	8.99	10.1	8.08	11.0	12.1
Unknown lipid MB ESI pos (848450215)	Unknown	8.97	11.8	10.5	7.88	11.2	15.2
Unknown lipid MB ESI pos (848450216)	Unknown	8.52	10.1	9.01	7.81	10.3	10.3
Unknown lipid MB ESI pos (848450218)	Unknown	9.06	10.7	9.49	8.20	8.92	11.9
Unknown lipid MB ESI pos (848450219)	Unknown	7.96	8.99	9.37	6.47	9.22	10.3
Unknown polar MB (838450146)	Unknown	3.71	2.96	1.90	1.78	2.07	1.33
Unknown polar MB (838450379)	Unknown	0.83	0.70	0.65	1.00	0.94	0.98
Unknown polar MB (838450566)	Unknown	1.81	3.38	1.67	2.81	1.15	1.06
Unknown polar MB (838450590)	Unknown	0.64	0.14	0.40	0.39	0.27	0.58
Unknown polar MB (838450618)	Unknown	2.55	2.41	1.94	1.67	1.66	0.97
Unknown polar MB (838450621)	Unknown	13.3	10.1	12.5	3	6	3
Unknown polar MB (838450692)	Unknown	3	6	3	5.95	3.91	1.97
Unknown polar MB (838450761)	Unknown	0.16	0.19	0.23	0.17	0.34	0.23
Unknown polar MB (838450807)	Unknown	4.27	2.81	2.59	3.94	2.53	1.09
Unknown polar MB (838450816)	Unknown	2.07	2.19	1.88	2.13	2.14	2.41
Unknown polar MB (838450890)	Unknown	0.01	0.00	0.00	0.01	0.00	0.01
Unknown polar MB (838450990)	Unknown	1.38	1.42	1.33	1.07	0.90	0.91
Unknown polar MB (838451614)	Unknown	0.02	0.10	0.03	0.02	0.05	0.02
Unknown polar MB (838452021)	Unknown	0.41	0.53	0.55	0.50	0.60	0.62
Unknown polar MB (838452022)	Unknown	2.74	2.81	2.47	2.24	2.18	1.98
Unknown polar MB (838452079)	Unknown	2.13	2.19	2.06	3.22	1.90	2.25
Unknown polar MB (838452178)	Unknown	0.12	0.09	0.27	0.17	0.29	0.53
Unknown polar MB (838452196)	Unknown	3.25	2.15	2.01	2.39	1.55	1.21
Unknown polar MB (838452482)	Unknown	380.	161.	245.	397.5	27.1	85.9
Unknown polar MB (838452999)	Unknown	41	12	70	6	0	9
Unknown polar MB (838453005)	Unknown	11.5	43.1	22.5	18.9	1	6
Unknown polar MB (838453006)	Unknown	1	6	9	14.18	8	6.97
Unknown polar MB (838453009)	Unknown	0.23	0.19	0.17	0.13	0.24	0.23
Unknown polar MB (838453012)	Unknown	0.21	0.23	0.32	0.15	0.17	0.29
Unknown polar MB (838453015)	Unknown	0.06	0.03	0.02	0.04	0.02	0.03
Unknown polar MB (838453017)	Unknown	130.	71.0	52.5	217.8	77.7	78.9
Unknown polar MB (838453018)	Unknown	85	3	4	3	1	1
Unknown polar MB (838453019)	Unknown	0.18	0.07	0.27	0.20	0.22	0.32
Unknown polar MB (838453020)	Unknown	0.12	0.09	0.07	0.05	0.07	0.19
Unknown polar MB (838453026)	Unknown	0.10	0.09	0.15	0.07	0.23	0.39
Unknown polar MB (838453028)	Unknown	0.06	0.04	0.03	0.14	0.08	0.02
Unknown polar MB (838453033)	Unknown	1.86	1.62	2.09	1.58	2.79	1.48
Unknown polar MB (838453036)	Unknown	0.13	0.17	0.21	0.17	0.12	0.19
Unknown polar MB (838453040)	Unknown	0.11	0.06	0.04	0.07	0.04	0.05
Unknown polar MB (838453041)	Unknown	0.13	0.05	0.03	0.05	0.04	0.06
Unknown polar MB (838453044)	Unknown	0.03	0.02	0.03	0.05	0.06	0.04
Unknown polar MB (838453047)	Unknown	0.05	0.03	0.03	0.05	0.14	0.11
Unknown polar MB (838453048)	Unknown	0.12	0.10	0.12	0.14	0.11	0.24
Unknown polar MB (838453051)	Unknown	0.46	0.29	0.37	0.48	0.58	0.81
		0.20	0.08	0.15	0.25	0.10	0.18
		0.15	0.11	0.06	0.31	0.16	0.12
		0.41	0.48	0.53	0.71	0.71	0.71

Unknown polar MB (838453052)	Unknown	0.41	0.19	0.15	0.37	0.61	0.31
Unknown polar MB (838453053)	Unknown	0.28	0.22	0.19	0.48	1.88	0.66
Unknown polar MB (838453055)	Unknown	0.16	0.08	0.03	0.07	0.09	0.02
Unknown polar MB (838453056)	Unknown	0.51	0.41	0.19	0.48	0.32	0.32
Unknown polar MB (838453057)	Unknown	0.47	0.37	0.24	0.31	0.21	0.32
Unknown polar MB (838453058)	Unknown	0.58	0.07	0.05	0.43	0.08	0.23
Unknown polar MB (838453059)	Unknown	3.50	3.10	2.86	3.09	3.14	1.63
Unknown polar MB (838453061)	Unknown	0.83	0.71	0.66	0.64	0.75	0.68
Unknown polar MB (838453062)	Unknown	0.42	0.55	0.57	0.58	0.84	0.75
Unknown polar MB (838453063)	Unknown	0.55	0.03	0.05	0.20	0.05	0.09
Unknown polar MB (838453066)	Unknown	0.01	0.00	0.01	0.01	0.00	0.04
Unknown polar MB (838453067)	Unknown	5.07	5.05	2.26	2.17	1.92	1.56
Unknown polar MB ESI neg (878450071)	Unknown	2.74	3.70	3.55	2.80	2.44	3.36
Uracil	Nucleobases and related	0.17	0.06	0.17	0.25	0.14	0.33
Xanthurenic acid	Amino acids related	0.19	0.10	0.10	0.09	0.09	0.08
			11.6				
Xylose	Carbohydrates and related	5.98	3	2.78	1.64	1.64	1.43

Table S3: Doripenem-induced feces metabolite fold changes in female (f) Wistar rats (N=5 per group) dosed with 100 (LD) and 300 (HD) mg/kg bw/day for 7, 14 and 28 days (f7, f14 and f28). Statistically significant changes (Welch-t-test; p-value < 0.05) are shown in bold numbers where red boxes mean a significant increase in the respective fecal metabolites and yellow a significant reduction compared to control levels.

Metabolite	Class	Doripenem HD			Doripenem LD		
		f7	f14	f28	f7	f14	f28
1,25-Dihydroxy-vitamin D3	Unknown	0.74	0.78	0.59	1.06	1.31	1.24
1,2-Anhydroribose	Carbohydrates and related	6.30	4.09	3.44	3.55	2.59	2.18
1,4-Hydroquinone	Miscellaneous	2.27	1.79	1.65	1.47	0.96	1.15
14-Methylhexadecanoic acid	Complex lipids, fatty acids and related	0.30	0.16	0.09	0.17	0.42	1.07
15-Methylhexadecanoic acid	Complex lipids, fatty acids and related	0.27	0.26	0.24	0.30	0.30	1.02
16-Methylheptadecanoic acid	Complex lipids, fatty acids and related	0.68	0.33	0.28	0.66	0.91	1.09
17-Methyloctadecanoic acid	Complex lipids, fatty acids and related	0.61	0.44	0.28	0.51	0.78	0.98
22-Hydroxydocosanoic acid (C22:0)	Complex lipids, fatty acids and related	0.64	0.58	0.63	1.01	0.96	1.10
2-Amino adipic acid	Amino acids related	2.67	4.58	2.26	1.46	2.79	2.97
2-Hydroxybehenic acid (C22:0)	Complex lipids, fatty acids and related	0.27	0.28	0.26	0.58	0.78	0.96
2-Hydroxycerotic acid (C26:0)	Complex lipids, fatty acids and related	0.27	0.31	0.26	0.52	0.71	0.79
2-Hydroxynervonic acid (C24:1)	Complex lipids, fatty acids and related	0.22	0.27	0.28	0.48	0.91	0.81
2-Hydroxypalmitic acid (C16:0)	Complex lipids, fatty acids and related	0.25	0.21	0.16	0.44	0.66	0.63
2-Hydroxypentacosanoic acid (C25:0)	Complex lipids, fatty acids and related	0.29	0.31	0.28	0.51	0.70	0.84
3-Hydroxybutyrate	Energy metabolism and related	24.7	10.2	9.09	1.60	1.11	3.20
3-Hydroxyphenylacetic acid	Amino acids related	0.07	0.01	0.09	0.07	0.04	0.11

4-Hydroxyphenylacetic acid	Amino acids related	6.56	0.39	0.14	30.0	22.1	11.6
4-Hydroxysphinganine (t18:0, Phytosphingosine), total	Complex lipids, fatty acids and related	3.66	2.42	1.72	7.71	3.76	3.11
		12.1	13.2			13.1	11.1
5-Oxoproline	Amino acids related	9	5	4.83	8.43	3	6
	Vitamins, cofactors and related						22.9
6-Hydroxynicotinic acid		1.95	2.42	4.16	6.18	4.12	0
Adenine	Nucleobases and related	0.41	0.25	0.37	0.25	0.21	0.32
Adenosine	Nucleobases and related	0.42	0.20	0.47	0.44	0.45	0.57
Alanine	Amino acids	0.39	7.97	3.68	0.47	0.57	1.07
		87.2	59.6	67.0	222.	291.	69.8
Allantoin	Nucleobases and related	9	7	6	29	94	0
alpha-Amyrin TMS	Unknown	0.47	0.42	0.43	0.61	0.67	0.64
	Vitamins, cofactors and related						
alpha-Tocopherol		0.42	0.67	0.65	0.92	1.06	1.45
alpha-Tocopherol	Unknown	0.04	0.12	0.10	0.35	0.04	0.06
alpha-Tocotrienol	Unknown	0.08	0.21	0.18	0.44	0.05	0.09
	Carbohydrates and related	10.4					
Arabinose		4	2.94	2.22	1.67	1.71	2.54
Arginine	Amino acids	1.40	3.87	4.73	1.53	1.42	2.71
Arginine	Amino acids	2.04	5.16	3.06	0.72	2.15	2.38
	Complex lipids, fatty acids and related						
Behenic acid (C22:0)		0.55	0.60	0.52	0.70	0.90	0.93
beta-/gamma-Tocotrienol	Unknown	0.46	0.68	0.66	0.71	0.76	1.12
beta-/gamma-Tocotrienol	Unknown	0.44	0.72	0.58	0.66	0.72	0.93
beta-Amyrin TMS	Unknown	0.50	0.45	0.53	0.65	0.63	0.81
beta-Sitosterol, total	Miscellaneous	2.65	4.31	3.90	3.57	3.12	3.29
	Complex lipids, fatty acids and related						
Bile acid No 01		0.50	0.55	0.10	2.76	1.46	0.59
	Complex lipids, fatty acids and related						
Bile acid No 07		0.37	0.17	0.18	0.56	0.45	0.49
Campesterol, total	Miscellaneous	2.67	3.68	3.04	3.66	3.06	2.64
Catechol	Miscellaneous	0.66	0.56	0.42	0.98	0.62	0.91
	Complex lipids, fatty acids and related						
Cerebronic acid (2-OH-C24:0)		0.30	0.35	0.28	0.58	0.86	0.92
	Complex lipids, fatty acids and related						
Cerotic acid (C26:0)		0.46	0.48	0.58	0.54	0.79	1.02
	Complex lipids, fatty acids and related						
Cholestenol No 02		0.30	0.31	0.34	0.64	0.69	0.89
	Complex lipids, fatty acids and related						
Cholesterol, total		3.22	2.51	1.54	5.21	2.44	2.15
					15.5	15.7	15.6
Cholic acid	Unknown	3.44	2.81	5.60	0	6	1
Citrulline	Unknown	0.58	4.80	6.89	0.37	0.37	0.44
Coenzyme Q10	Unknown	0.47	0.42	0.43	0.83	0.72	0.98
conjugated Linoleic acid (C18:trans[9,11]2)	Complex lipids, fatty acids and related						
		0.36	0.41	0.36	0.54	0.95	1.65
Cortisol (lipid)	Unknown	0.31	0.27	0.24	0.52	0.51	0.72
		41.9	133.	109.	124.	223.	135.
Creatinine	Amino acids related	1	99	17	25	10	03
		80.6	155.	90.0	49.4	191.	109.
Creatinine	Unknown	8	80	0	7	42	27
Cysteine	Amino acids	4.35	4.37	4.22	4.35	5.20	7.60

Cytosine	Nucleobases and related	9.15	8.87	7.63	4.94	5.05	2.05
Dehydroalanine	Amino acids related	6.02	4.74	3.60	3.88	4.28	5.56
Deoxycholic acid	Complex lipids, fatty acids and related	0.17	0.07	0.10	0.19	0.20	0.33
Deoxycholic acid	Unknown	0.00	0.00	0.00	0.01	0.00	0.03
dihomo-gamma-Linolenic acid (C20:cis[8,11,14]3)	Complex lipids, fatty acids and related	0.43	0.25	0.20	0.58	1.04	2.76
Dihydrocholesterol	Complex lipids, fatty acids and related	0.97	1.45	1.57	0.96	1.16	2.76
Eicoasenoic acid (C20:cis[11]1)	Complex lipids, fatty acids and related	0.52	0.58	1.00	0.76	0.70	1.37
Eicosadienoic acid (C20:2) No 01	Complex lipids, fatty acids and related	0.30	0.28	0.25	0.41	0.43	0.45
Eicosadienoic acid (C20:2) No 02	Complex lipids, fatty acids and related	0.30	0.29	0.24	0.35	0.45	0.51
Eicosaenoic acid (C20:1) No 02	Complex lipids, fatty acids and related	0.32	0.16	0.18	0.28	0.48	0.44
Eicosanoic acid (C20:0)	Complex lipids, fatty acids and related	0.54	0.53	0.51	0.64	0.82	0.92
epsilon-Acetyllysine	Unknown	4.17	4.33	5.55	5.29	5.29	8.96
erythro-Dihydrosphingosine (d18:0)	Complex lipids, fatty acids and related	0.12	0.17	0.16	0.21	0.32	1.14
Fucose	Carbohydrates and related	36.7	6	8.26	4.32	5.22	2.51
Fucosterol, total	Miscellaneous	1.96	3.09	2.65	2.87	2.60	2.61
Fumarate	Energy metabolism and related	2.95	2.89	1.74	3.44	3.29	2.36
Fumarate	Unknown	0.37	0.54	0.60	0.42	0.42	0.73
Galactose	Carbohydrates and related	7.98	2.32	0.85	2.82	2.53	1.45
Galactose, lipid fraction	Complex lipids, fatty acids and related	1.42	1.85	1.88	2.59	1.62	1.90
Galactose, lipid fraction	Complex lipids, fatty acids and related	0.59	0.76	0.78	1.01	0.66	0.96
gamma-Tocopherol	Vitamins, cofactors and related	0.56	0.47	0.32	0.62	0.64	0.75
Glucose-1-phosphate	Carbohydrates and related	15.4	6	8.15	2.99	5.27	6.59
Glucuronic acid	Carbohydrates and related	470.20	7.79	4.44	7.12	1.58	1.49
Glutamate	Amino acids	6.50	4	3.50	5.46	9.99	8.79
Glutamic acid 2TMS ME (lipid)	Unknown	1.97	1.76	1.55	1.64	1.82	1.88
Glutamine	Amino acids	13.5	16.9	1.83	3.82	3.61	4.11
Glutarate	Amino acids related	8	6	0.34	0.20	0.32	0.46
Glycerol phosphate, lipid fraction	Complex lipids, fatty acids and related	0.30	0.36	0.24	0.70	0.47	0.56
Glycine	Amino acids	0.30	24.2	2	6.24	1.59	2.12
Glycine, lipid fraction	Miscellaneous	2.15	0.45	0.53	0.60	0.75	0.67
Glycine, lipid fraction	Miscellaneous	0.45	0.35	0.38	0.44	0.61	0.62
Glycodeoxycholate	Unknown	0.35	0.46	0.33	0.35	0.45	0.26
Glycolithocholic Acid	Unknown	0.46	0.20	0.13	0.06	0.56	0.09
Heneicosanoic acid (C21:0)	Complex lipids, fatty acids and related	0.20	0.33	0.34	0.31	0.41	0.50

Heptacosanoic acid (C27:0)	Complex lipids, fatty acids and related	0.61	0.42	0.44	0.76	0.98	0.94
Heptadecanoic acid (C17:0)	Complex lipids, fatty acids and related	0.18	0.17	0.18	0.23	0.30	0.64
Hexadecanol	Complex lipids, fatty acids and related	0.06	0.03	0.09	0.08	0.12	0.31
Homoserine	Amino acids related	0.77	3.28	3.07	0.55	0.38	0.59
Hyochoholic acid	Complex lipids, fatty acids and related	0.42	0.41	0.07	0.70	0.54	0.36
Hyodeoxycholic acid	Unknown	0.00	0.00	0.00	0.03	0.00	0.01
Hyodeoxycholic acid	Complex lipids, fatty acids and related	0.11	0.08	0.25	0.10	0.28	0.92
Hypoxanthine	Nucleobases and related	26.5	21.0				
		3	9	9.06	2.27	1.29	1.45
					12.3		10.6
Indole-3-acetic acid	Amino acids related	3.06	0.11	0.28	3	5.43	4
isoLCA	Unknown	0.00	0.00	0.01	0.01	0.00	0.02
			51.3	43.3			
Isoleucine	Amino acids	0.53	0	3	0.64	0.80	0.73
			27.4	26.9			
Isoluecine + Leucine	Unknown	0.31	6	2	0.34	0.40	0.61
	Complex lipids, fatty acids and related						
Isopalmitic acid (C16:0)		0.27	0.14	0.07	0.16	0.36	0.91
Kynurenic acid	Unknown	2.18	1.74	2.52	5.53	4.14	7.20
			58.6	34.6			
Leucine	Amino acids	0.43	7	5	0.47	0.66	0.57
	Complex lipids, fatty acids and related						
Lignoceric acid (C24:0)		0.51	0.41	0.41	0.65	0.68	0.91
	Complex lipids, fatty acids and related						
Linoleic acid (C18:cis[9,12]2)		4.61	6.28	5.81	5.27	6.96	6.75
	Complex lipids, fatty acids and related						
Linolenic acid (C18:cis[9,12,15]3)		4.49	5.88	5.29	5.33	6.28	4.97
Lithocholic acid	Unknown	0.01	0.01	0.01	0.02	0.01	0.03
		17.7	23.1	12.5			20.5
Lysine	Amino acids	8	9	0	6.07	4.28	0
	Carbohydrates and related						
Lyxose		8.47	2.07	1.44	1.33	1.20	1.79
	Carbohydrates and related						
Mannose		8.25	8.00	6.59	9.29	4.84	0.30
	Carbohydrates and related						
myo-Inositol		61.6	144.	57.9			
		6	72	1	6.94	3.44	0.97
	Complex lipids, fatty acids and related						
Myristic acid (C14:0)		0.30	0.16	0.23	0.26	0.21	0.98
			10.5				
N2-Acetylhistidine	Unknown	4.57	4	6.29	0.87	2.16	2.26
							20.0
N2-Acetyllysine	Amino acids related	8.85	6.33	4.23	7.06	4.18	9
N-Acetylglucosamine	Unknown	0.08	0.07	0.05	0.26	0.52	0.32
N-Acetyl-leucine	Unknown	4.15	2.81	9.62	2.13	0.68	1.15
	Complex lipids, fatty acids and related						
Nervonic acid (C24:cis[15]1)		0.40	0.31	0.36	0.66	0.63	1.02
Niacinamide (Nicotinamide)	Unknown	0.25	0.49	0.25	0.85	1.64	0.90
N-Methylglutamate	Unknown	0.03	0.02	0.05	0.11	0.10	0.17
Norleucine	Miscellaneous	0.21	0.30	0.30	0.27	0.18	0.27
	Complex lipids, fatty acids and related						
Octadecadienoic acid No 01 (C18:2)		0.49	0.55	0.58	0.65	1.36	1.40

Octadecanol	Complex lipids, fatty acids and related	0.06	0.04	0.13	0.11	0.23	0.31
Oleic acid (C18:cis[9]1)	Complex lipids, fatty acids and related	2.31	2.78	3.69	2.73	2.95	4.65
omega-Muricholic acid	Complex lipids, fatty acids and related	0.28	0.17	0.08	0.62	0.53	0.34
o-Muricholic Acid	Unknown	0.01	0.00	0.01	0.28	0.08	0.08
Ornithine	Amino acids related	8.75	40.8	25.0	1.35	1.34	1.57
Palmitic acid (C16:0)	Complex lipids, fatty acids and related	0.71	0.55	0.82	1.04	0.58	1.32
Pentacosanoic acid (C25:0)	Complex lipids, fatty acids and related	0.44	0.44	0.29	0.55	0.80	0.78
Pentadecanol	Complex lipids, fatty acids and related	0.32	0.34	0.37	0.40	0.38	0.80
Phenylalanine	Amino acids	0.76	73.3	45.4	1.12	1.46	1.38
Phenylalanine	Unknown	2.34	4	8	1.16	1.41	1.22
Phenylalanine	Unknown	0.39	57.5	27.3	0.79	0.79	0.95
Phenylalanine	Unknown	0.41	0	5	0.66	0.85	1.22
Phosphate, lipid fraction	Complex lipids, fatty acids and related	0.40	44.0	28.2	0.55	0.53	0.74
Phosphoenolpyruvate (PEP)	Energy metabolism and related	4.12	7	1	3.02	3.15	3.08
p-Hydroxybenzoic acid	Vitamins, cofactors and related	0.20	45.4	33.2	0.29	0.70	0.41
Pipecolic acid	Unknown	0.14	6	5	0.96	0.63	1.29
plausible 18:2-Lyso PC (Na-Addukt)	Unknown	2.22	0.32	0.24	5.08	1.97	1.55
plausible 2-Hydroxyarachidic acid (2-OH-C20:0) TMS ME	Unknown	0.20	0.12	0.07	0.45	0.67	0.98
plausible 2-Hydroxytricosanoic acid (2-OH-C23:0) TMS ME	Unknown	0.27	0.21	0.24	0.56	0.77	0.85
plausible Heptadecanol TMS	Unknown	0.01	0.28	0.27	0.01	0.30	0.29
plausible SalzCluster (C7H10O8Na3(35)Cl(37)Cl)	Unknown	0.61	0.01	0.03	0.76	0.76	1.01
plausible SM (d18:1, C16:0) Na-Addukt	Unknown	6.19	0.51	0.50	7.05	3.76	3.72
proposed Sphingomyelin (d18:2,C16:0)	Unknown	4.06	2.96	2.44	5.79	2.87	3.11
putative 12-Methylmyristic acid TMS	Unknown	0.01	2.22	2.80	0.02	0.03	0.71
putative 2-Oxobutanedioic acid hexoside 6TMS	Unknown	0.31	0.02	0.02	2.14	2.01	1.06
putative Anhydroglucuronate 4TMS	Unknown	12.7	0.27	0.15	4.17	5.94	3.24
putative Bis-(glycerol)-phosphate	Unknown	0.08	7.39	2.62	0.08	0.15	2.19
putative Choline plasmalogen (C36:2)	Unknown	7.41	0.10	0.06	6.63	1.63	2.22
putative Deoxycholyglycine deriv #1	Unknown	0.01	0.02	0.01	0.03	0.02	0.10
putative Hydroxy-eicosan OTMS	Unknown	0.15	0.02	0.01	0.15	0.27	0.32
putative Hyodeoxycholic acid 3TMS	Unknown	0.03	0.11	0.12	0.05	0.03	0.08
putative Lithocholic acid OTMS ME	Unknown	0.01	0.04	0.08	0.02	0.01	0.05
putative Tetracosenoic acid ME	Unknown	0.39	0.01	0.01	0.40	0.83	0.71
Putrescine	Miscellaneous	11.6	0.28	0.20	43.9	39.6	18.1
		8	0.39	0.20	6	5	2

Pyruvate	Energy metabolism and related	3.88	3.33	3.19	2.45	2.05	2.20
ribo-4-Hydroxy-8E-sphingenine	Complex lipids, fatty acids and related	0.53	0.59	0.82	1.06	1.04	2.01
Sarcosine	Amino acids related	0.59	0.76	0.61	0.89	0.78	0.91
scyllo-Inositol	Carbohydrates and related	14.3	29.2	33.5	10.3	8.54	2.19
Serine, lipid fraction	Miscellaneous	0.56	0.53	0.50	0.66	0.59	1.08
Serine, lipid fraction	Miscellaneous	0.56	0.52	0.43	0.67	0.51	1.03
Shikimic acid	Miscellaneous	911.27	1238.06	1542.15	2535.91	937.46	3.07
Stearic acid (C18:0)	Complex lipids, fatty acids and related	0.59	0.44	0.44	0.74	0.55	0.72
Stigmasterol, total	Miscellaneous	1.82	2.79	2.89	2.67	2.38	2.92
Taurine	Unknown	3.84	8.87	8.09	0	7	3
Tauro-b-muricholic Acid	Unknown	6.80	4.47	2.27	2.02	1.59	1.73
Taurochenodeoxycholate	Unknown	1.65	1.94	1.95	1.63	1.18	1.87
Taurocholic acid	Unknown	2.99	3.73	3.64	1.68	1.35	2.43
Taurocholic Acid 3-sulfate	Unknown	395.06	302.06	28.52	139.94	156.93	16.82
Taurocholic acid sodium salt	Unknown	8.10	6.65	5.78	3.83	2.12	2.46
Taurodeoxycholate	Unknown	0.54	0.46	0.49	0.55	0.48	0.46
Taurolithocholic Acid	Unknown	0.03	0.02	0.01	0.20	0.03	0.40
Tetradecanol	Complex lipids, fatty acids and related	0.12	0.07	0.07	0.17	0.12	0.23
Thiamine (Vitamin B1)	Unknown	0.17	0.17	0.17	0.20	0.20	0.84
threo-Sphinganine 3TMS	Unknown	0.09	0.13	0.08	0.30	0.29	2.80
trans-4-Hydroxyproline	Amino acids related	16.0	43.6	1.88	9	2	2.92
trans-Ferulic acid	Miscellaneous	11.4	7	6.67	9.87	6.69	2.46
trans-Ferulic acid, lipid fraction		0.68	0.44	0.88	0.78	0.70	1.04
trans-Sinapic acid	Miscellaneous	29.9	24.0	23.5	17.5	8.25	4.22
Tricosanoic acid (C23:0)	Complex lipids, fatty acids and related	0.38	0.44	0.37	0.63	0.82	0.92
Tryptophan	Amino acids	59.5	90.2	59.4	2.53	1.56	2.57
Tyramine	Amino acids related	150.42	340.94	198.95	7.30	7.00	9
Tyrosine	Unknown	0.21	0.60	0.43	0.25	0.29	0.61
Ubichinone-30 (Coenzyme Q6)	Unknown	0.59	0.60	0.51	0.96	0.79	0.96
Ubichinone-35 (Coenzyme Q7)	Unknown	0.51	0.58	0.53	0.94	0.76	1.14
Ubichinone-45 (Coenzyme Q9)	Unknown	0.57	0.59	0.53	0.97	0.75	0.96
Unknown lipid MB (828450473)	Unknown	3.39	3.22	2.84	4.77	3.01	2.71
Unknown lipid MB (828450676)	Unknown	0.70	0.82	0.77	0.79	0.87	0.81
Unknown lipid MB (828450834)	Unknown	0.27	0.23	0.17	0.53	0.71	0.88
Unknown lipid MB (828451241)	Unknown	0.06	0.13	0.16	0.08	0.11	0.86
Unknown lipid MB (828451259)	Unknown	0.48	0.23	0.25	0.72	0.95	0.91
Unknown lipid MB (828451275)	Unknown	0.36	0.32	0.45	0.40	0.33	0.24
Unknown lipid MB (828451312)	Unknown	0.31	0.30	0.39	1.46	0.35	1.07
Unknown lipid MB (828451316)	Unknown	0.35	0.58	0.49	3.93	3.60	1.48

Unknown lipid MB (828451380)	Unknown	0.55	0.44	0.28	0.60	1.05	0.93
Unknown lipid MB (828451443)	Unknown	0.48	0.63	0.72	0.93	0.78	0.98
Unknown lipid MB (828451444)	Unknown	0.59	0.39	0.26	0.72	1.04	1.10
Unknown lipid MB (828451445)	Unknown	0.20	0.15	0.21	0.28	0.28	0.71
Unknown lipid MB (828451931)	Unknown	0.00	0.00	0.01	0.01	0.60	0.36
Unknown lipid MB (828451933)	Unknown	0.06	0.14	0.13	0.15	0.11	0.68
Unknown lipid MB (828451937)	Unknown	0.00	0.00	0.02	0.02	0.44	0.31
Unknown lipid MB (828451940)	Unknown	0.00	0.00	0.01	0.01	0.25	0.27
Unknown lipid MB (828452038)	Unknown	0.01	0.01	0.01	0.01	0.01	1.53
Unknown lipid MB (828452040)	Unknown	0.02	0.09	0.06	0.13	0.27	1.10
Unknown lipid MB (828452041)	Unknown	0.03	0.04	0.05	0.03	0.31	0.31
Unknown lipid MB (828452042)	Unknown	0.01	0.01	0.00	0.01	0.01	0.01
Unknown lipid MB (828452043)	Unknown	0.01	0.01	0.01	0.02	0.34	0.13
Unknown lipid MB (828452047)	Unknown	0.00	0.00	0.02	0.02	0.45	0.32
Unknown lipid MB (828452048)	Unknown	0.68	0.54	0.38	0.76	0.92	0.81
Unknown lipid MB (828452050)	Unknown	0.02	0.05	0.04	0.04	0.42	0.55
Unknown lipid MB (828452058)	Unknown	0.08	0.07	0.07	0.08	0.11	0.21
Unknown lipid MB (828452059)	Unknown	0.17	0.10	0.05	0.58	0.16	0.16
Unknown lipid MB (828452060)	Unknown	0.01	0.00	0.00	0.01	0.00	0.04
		12.6					
Unknown lipid MB ESI neg (858450013)	Unknown	0.64	2	9.52	1.03	1.03	0.86
Unknown lipid MB ESI neg (858450034)	Unknown	0.22	0.54	0.06	0.48	0.85	0.17
Unknown lipid MB ESI neg (858450042)	Unknown	0.30	0.24	0.23	1.97	2.11	3.03
Unknown lipid MB ESI neg (858450047)	Unknown	6.89	9.37	4.62	2.24	1.50	1.54
Unknown lipid MB ESI neg (858450065)	Unknown	0.02	0.03	0.01	0.09	0.07	0.07
Unknown lipid MB ESI neg (858450068)	Unknown	0.25	0.33	0.25	0.37	0.68	0.62
Unknown lipid MB ESI neg (858450071)	Unknown	4.39	4.98	3.30	4.29	2.68	2.86
Unknown lipid MB ESI pos (848450056)	Unknown	5.12	3.81	4.99	5.45	3.54	2.30
Unknown lipid MB ESI pos (848450067)	Unknown	2.29	2.61	3.03	3.38	2.32	2.26
Unknown lipid MB ESI pos (848450068)	Unknown	3.71	2.67	2.23	4.74	1.72	1.46
Unknown lipid MB ESI pos (848450069)	Unknown	5.82	1.92	2.50	5.53	1.46	1.49
Unknown lipid MB ESI pos (848450083)	Unknown	5.80	3.39	1.25	6.72	2.75	1.58
Unknown lipid MB ESI pos (848450092)	Unknown	0.28	0.26	0.37	0.55	0.38	0.48
Unknown lipid MB ESI pos (848450093)	Unknown	0.21	0.22	0.48	0.57	0.68	0.88
Unknown lipid MB ESI pos (848450095)	Unknown	0.48	0.43	0.79	0.74	0.50	0.77
Unknown lipid MB ESI pos (848450096)	Unknown	2.04	1.66	2.21	3.90	1.94	3.16
Unknown lipid MB ESI pos (848450097)	Unknown	6.50	6.70	5.20	7.12	3.98	3.18
Unknown lipid MB ESI pos (848450100)	Unknown	4.46	1.85	1.32	4.19	1.49	1.48
Unknown lipid MB ESI pos (848450102)	Unknown	4.76	2.89	2.78	6.85	2.33	1.73
Unknown lipid MB ESI pos (848450103)	Unknown	5.03	3.00	2.21	6.47	2.24	1.64
		11.7					
Unknown lipid MB ESI pos (848450105)	Unknown	2	6.54	6.28	9	4.98	3.71
Unknown lipid MB ESI pos (848450106)	Unknown	7.14	3.23	1.72	6.65	2.40	1.57
Unknown lipid MB ESI pos (848450107)	Unknown	2.94	2.05	2.36	3.59	1.76	1.86
Unknown lipid MB ESI pos (848450108)	Unknown	6.62	3.63	4.70	6.99	2.38	3.25
Unknown lipid MB ESI pos (848450109)	Unknown	5.68	1.74	2.56	6.35	1.97	2.71
		10.5					
Unknown lipid MB ESI pos (848450110)	Unknown	6	3.15	2.06	9.35	2.82	1.92
Unknown lipid MB ESI pos (848450111)	Unknown	2.91	2.92	3.14	3.70	3.33	3.74
Unknown lipid MB ESI pos (848450112)	Unknown	4.88	2.55	2.62	5.41	1.38	2.54

Unknown lipid MB ESI pos (848450113)	Unknown	5.68	5.03	5.22	7.79	4.49	6.13
					10.5		
Unknown lipid MB ESI pos (848450114)	Unknown	8.85	4.78	4.39	1	2.13	3.53
Unknown lipid MB ESI pos (848450123)	Unknown	2.76	1.62	1.38	5.98	1.89	1.29
Unknown lipid MB ESI pos (848450129)	Unknown	3.09	2.43	1.56	4.66	2.73	2.96
Unknown lipid MB ESI pos (848450131)	Unknown	5.98	4.07	2.97	9.41	4.28	3.37
Unknown lipid MB ESI pos (848450132)	Unknown	5.35	2.86	1.66	8.51	3.52	2.74
Unknown lipid MB ESI pos (848450138)	Unknown	4.60	2.89	1.63	6.34	3.26	2.09
Unknown lipid MB ESI pos (848450139)	Unknown	7.32	6.01	1.91	5.91	2.13	1.20
Unknown lipid MB ESI pos (848450142)	Unknown	8.25	8.05	2.30	7.06	2.69	1.11
Unknown lipid MB ESI pos (848450144)	Unknown	4.24	3.20	1.80	5.35	3.16	2.48
Unknown lipid MB ESI pos (848450146)	Unknown	4.02	4.08	2.14	6.14	3.92	2.38
Unknown lipid MB ESI pos (848450147)	Unknown	2.09	1.66	1.34	2.68	2.61	1.63
Unknown lipid MB ESI pos (848450148)	Unknown	5.52	4.00	2.62	7.65	4.98	3.14
Unknown lipid MB ESI pos (848450152)	Unknown	2.77	2.35	1.08	4.72	2.75	2.07
Unknown lipid MB ESI pos (848450154)	Unknown	0.45	0.30	0.14	1.08	1.64	0.55
Unknown lipid MB ESI pos (848450155)	Unknown	0.58	0.41	0.25	1.82	1.59	1.85
Unknown lipid MB ESI pos (848450159)	Unknown	0.58	0.39	0.37	0.93	1.96	2.07
		14.9	16.9	10.9	11.6	14.3	
Unknown lipid MB ESI pos (848450196)	Unknown	5	3	7	6	3	9.58
		10.7	14.6			13.6	
Unknown lipid MB ESI pos (848450201)	Unknown	9	9	9.71	8.49	8	8.42
Unknown lipid MB ESI pos (848450202)	Unknown	3.83	4.57	4.69	3.68	4.88	4.15
		14.2	20.7	10.3	13.0	17.5	
Unknown lipid MB ESI pos (848450204)	Unknown	4	3	7	5	1	9.98
		13.6	13.7	10.1	11.7	11.5	
Unknown lipid MB ESI pos (848450205)	Unknown	3	0	0	8	7	8.38
		15.5	31.0	15.4	13.3	27.5	14.3
Unknown lipid MB ESI pos (848450206)	Unknown	0	4	7	5	2	8
		15.9	24.5	14.3	12.7	20.6	12.6
Unknown lipid MB ESI pos (848450207)	Unknown	6	0	3	3	2	4
		13.2	20.2	12.4	12.2	20.9	
Unknown lipid MB ESI pos (848450208)	Unknown	7	4	7	3	1	9.40
Unknown lipid MB ESI pos (848450209)	Unknown	8.46	9.92	8.19	7.93	9.65	7.07
		10.7	13.4	11.6	10.2	11.4	
Unknown lipid MB ESI pos (848450210)	Unknown	7	9	9	6	7	9.68
			15.8			13.8	
Unknown lipid MB ESI pos (848450212)	Unknown	8.59	0	7.01	8.58	6	7.07
		12.1	16.3		11.2	13.6	
Unknown lipid MB ESI pos (848450213)	Unknown	3	0	9.95	4	2	8.62
			16.9			17.0	
Unknown lipid MB ESI pos (848450214)	Unknown	9.87	4	7.73	9.64	0	7.56
		13.2	24.2	11.3	11.6	19.1	
Unknown lipid MB ESI pos (848450215)	Unknown	4	4	8	3	8	8.54
		10.8	13.6			11.4	
Unknown lipid MB ESI pos (848450216)	Unknown	0	2	8.49	9.93	1	7.88
		12.7	18.0	11.0	11.8	16.7	
Unknown lipid MB ESI pos (848450218)	Unknown	4	0	1	9	3	7.93
			14.2	10.4		11.3	
Unknown lipid MB ESI pos (848450219)	Unknown	9.23	0	5	9.33	8	8.03
Unknown polar MB (838450146)	Unknown	7.98	2.66	2.19	2.18	2.43	1.27
Unknown polar MB (838450566)	Unknown	0.39	0.32	0.38	1.26	0.87	1.18
							26.5
Unknown polar MB (838450590)	Unknown	0.85	0.26	0.36	1.25	0.54	3

Unknown polar MB (838450621)	Unknown	5.66	6.59	5.59	7.14	6.17	1.54
Unknown polar MB (838450677)	Unknown	0.89	0.40	0.50	0.75	0.66	0.63
Unknown polar MB (838450692)	Unknown	0.14	0.08	0.06	0.17	0.24	0.23
Unknown polar MB (838450807)	Unknown	2.21	0.98	1.42	2.15	1.29	2.66
Unknown polar MB (838450816)	Unknown	0.01	0.01	0.00	0.02	0.01	0.01
Unknown polar MB (838451614)	Unknown	0.02	0.01	0.01	0.02	0.01	0.01
Unknown polar MB (838452021)	Unknown	0.37	0.34	0.34	0.47	0.60	0.64
Unknown polar MB (838452022)	Unknown	2.07	1.60	1.44	1.59	1.61	1.34
Unknown polar MB (838452079)	Unknown	4.98	2.38	4.03	3.05	1.61	3.23
Unknown polar MB (838452178)	Unknown	0.10	0.07	0.14	0.10	0.22	0.77
Unknown polar MB (838452196)	Unknown	2.85	3.16	2.68	2.22	1.83	1.60
		36.8	25.0	38.2	208.	241.	118.
Unknown polar MB (838452482)	Unknown	9	6	6	70	92	91
Unknown polar MB (838452804)	Unknown	4.65	2.01	2.10	1.16	0.46	1.94
				13.5	34.8	41.3	10.0
Unknown polar MB (838452999)	Unknown	1.35	6.79	9	6	0	1
Unknown polar MB (838453005)	Unknown	0.26	0.09	0.15	0.07	0.11	0.32
Unknown polar MB (838453006)	Unknown	0.30	0.14	0.22	0.09	0.15	0.30
Unknown polar MB (838453007)	Unknown	0.10	0.16	0.14	0.17	0.31	0.25
Unknown polar MB (838453008)	Unknown	0.34	0.68	0.51	1.19	0.95	1.44
Unknown polar MB (838453009)	Unknown	0.02	0.03	0.01	0.03	0.03	0.02
Unknown polar MB (838453011)	Unknown	1.13	0.27	0.23	1.29	0.43	0.69
		34.4	96.7	33.3	143.	120.	66.6
Unknown polar MB (838453012)	Unknown	3	1	3	00	51	1
Unknown polar MB (838453014)	Unknown	0.51	0.53	0.39	0.77	0.80	1.44
Unknown polar MB (838453015)	Unknown	0.13	0.19	0.24	0.22	0.27	0.85
Unknown polar MB (838453017)	Unknown	0.11	0.03	0.07	0.19	0.23	0.31
Unknown polar MB (838453018)	Unknown	0.07	0.04	0.05	0.12	0.36	0.33
Unknown polar MB (838453019)	Unknown	0.05	0.05	0.02	0.08	0.06	0.03
Unknown polar MB (838453026)	Unknown	0.18	0.07	0.05	0.29	0.12	0.14
Unknown polar MB (838453028)	Unknown	0.13	0.05	0.03	0.08	0.08	0.44
Unknown polar MB (838453029)	Unknown	0.10	0.05	0.08	0.10	0.09	0.35
Unknown polar MB (838453030)	Unknown	0.36	0.07	0.04	0.36	0.16	0.30
Unknown polar MB (838453031)	Unknown	0.00	0.00	0.01	0.01	0.01	0.24
Unknown polar MB (838453033)	Unknown	0.07	0.04	0.02	0.09	0.06	0.23
Unknown polar MB (838453035)	Unknown	0.19	0.03	0.01	0.10	0.05	0.07
Unknown polar MB (838453036)	Unknown	0.26	0.08	0.02	0.11	0.09	0.07
Unknown polar MB (838453039)	Unknown	0.03	0.02	0.02	0.10	0.04	0.07
Unknown polar MB (838453040)	Unknown	0.08	0.03	0.03	0.20	0.07	0.20
Unknown polar MB (838453041)	Unknown	0.13	0.12	0.18	0.19	0.15	0.61
Unknown polar MB (838453043)	Unknown	0.06	0.02	0.06	0.06	0.05	0.08
Unknown polar MB (838453044)	Unknown	0.19	0.13	0.18	0.25	0.35	0.86
Unknown polar MB (838453045)	Unknown	0.28	0.12	0.04	0.46	0.35	0.19
Unknown polar MB (838453047)	Unknown	0.13	0.08	0.10	0.18	0.14	0.72
Unknown polar MB (838453050)	Unknown	1.00	0.16	0.05	1.15	0.82	0.56
Unknown polar MB (838453051)	Unknown	0.29	0.37	0.36	0.37	0.58	0.67
Unknown polar MB (838453052)	Unknown	0.22	0.07	0.12	0.23	0.26	0.37
Unknown polar MB (838453053)	Unknown	0.25	0.10	0.13	0.31	0.24	0.44
Unknown polar MB (838453056)	Unknown	0.34	0.10	0.13	0.36	0.35	0.35
Unknown polar MB (838453057)	Unknown	0.35	0.11	0.18	0.28	0.31	0.58

Unknown polar MB (838453058)	Unknown	0.31	0.10	0.07	0.78	0.26	0.18
Unknown polar MB (838453059)	Unknown	2.60	2.50	2.69	3.02	2.30	2.86
Unknown polar MB (838453062)	Unknown	0.41	0.45	0.51	0.50	0.75	0.81
Unknown polar MB (838453063)	Unknown	0.27	0.04	0.02	0.60	0.22	0.22
Unknown polar MB (838453064)	Unknown	0.18	0.07	0.05	0.21	0.11	0.11
Unknown polar MB (838453066)	Unknown	0.01	0.01	0.01	0.01	0.01	0.68
Unknown polar MB (838453067)	Unknown	2.20	2.27	2.64	3.08	2.23	1.83
Unknown polar MB ESI neg (878450071)	Unknown	3.16	2.62	3.26	3.48	1.78	1.85
Unknown polar MB ESI pos (868450018)	Unknown	0.35	0.35	0.45	0.16	0.27	0.45
Unknown polar MB ESI pos (868450034)	Unknown	0.33	1.98	3.07	0.33	0.38	0.38
Unknown polar MB ESI pos (868450040)	Unknown	4.89	9.87	5.61	1.54	2.06	1.85
Uric acid	Nucleobases and related	11.7	9	4.80	2.76	0.55	1.04
Valine	Amino acids	0.48	45.6	44.7	0.64	0.83	1.01
Valine TMS ME	Unknown	0.61	2.58	2.48	0.84	0.86	0.99
Valine, lipid fraction	Miscellaneous	0.56	2.13	1.90	0.82	0.83	0.86
Xanthine	Nucleobases and related	63.9	37.2	21.1	0.29	0.42	0.74
Xanthurenic acid	Amino acids related	0.08	0.06	0.11	0.08	0.19	0.26
Xylose	Carbohydrates and related	13.5	10.4	13.4			
		8	9	2	2.44	1.74	2.34

Table S4: Doripenem-induced feces metabolite fold changes in male (m) Wistar rats (N=5 per group) dosed with 100 (LD) and 300 (HD) mg/kg bw/day for 7, 14 and 28 days (m7, m14 and m28). Statistically significant changes (Welch-t-test; p-value < 0.05) are shown in bold numbers where red boxes mean a significant increase in the respective fecal metabolites and yellow a significant reduction compared to control levels.

Metabolite	Class	Doripenem HD			Doripenem LD		
		m7	m14	m28	m7	m14	m28
1,25-Dihydroxy-vitamin D3	Unknown	0.74	0.32	0.37	0.71	0.78	0.91
1,2-Anhydroribose	Carbohydrates and related	7.45	3.90	7.11	5.46	4.35	6.14
1,4-Hydroquinone	Miscellaneous	3.06	2.62	1.93	1.53	1.27	1.20
14-Methylhexadecanoic acid	Complex lipids, fatty acids and related	0.34	0.15	0.30	0.31	0.34	0.36
15-Methylhexadecanoic acid	Complex lipids, fatty acids and related	0.33	0.25	0.33	0.24	0.31	0.28
16-Methylheptadecanoic acid	Complex lipids, fatty acids and related	0.69	0.28	0.43	0.49	0.59	0.50
17-Methyloctadecanoic acid	Complex lipids, fatty acids and related	0.67	0.37	0.52	0.61	0.62	0.61
22-Hydroxydocosanoic acid (C22:0)	Complex lipids, fatty acids and related	0.29	0.51	0.81	0.58	0.84	0.66
2-Hydroxybehenic acid (C22:0)	Complex lipids, fatty acids and related	0.40	0.26	0.34	0.36	0.56	0.46
2-Hydroxycerotic acid (C26:0)	Complex lipids, fatty acids and related	0.33	0.22	0.35	0.34	0.42	0.42
2-Hydroxynervonic acid (C24:1)	Complex lipids, fatty acids and related	0.36	0.25	0.36	0.27	0.51	0.43

2-Hydroxypalmitic acid (C16:0)	Complex lipids, fatty acids and related	0.43	0.30	0.39	0.42	0.71	0.61
2-Hydroxypentacosanoic acid (C25:0)	Complex lipids, fatty acids and related	0.33	0.28	0.33	0.32	0.41	0.35
3-Hydroxybutyrate	Energy metabolism and related	22.4	21.3	12.6			
3-Hydroxyphenylacetic acid	Amino acids related	5	5	6	2.67	2.51	2.90
3-Methylxanthine	Miscellaneous	0.06	0.08	0.09	0.06	0.07	0.04
		0.52	0.67	0.67	1.13	1.24	1.70
4-Hydroxyphenylacetic acid	Amino acids related					10.3	
4-Hydroxysphinganine (t18:0, Phytosphingosine), total	Complex lipids, fatty acids and related	1.51	0.14	0.13	6.12	7	9.62
		4.36	2.70	1.64	3.75	6.81	3.11
		19.6	14.1	12.2	10.4	12.8	14.7
5-Oxoproline	Amino acids related	3	1	6	5	5	7
6-Hydroxynicotinic acid	Vitamins, cofactors and related	2.05	3.13	3.85	5.03	5.05	6.95
Adenine	Nucleobases and related	0.65	0.25	0.33	0.27	0.22	0.37
				23.6			
Alanine	Amino acids	4.58	9.59	6	0.91	0.40	1.24
		126.	20.8	36.9	295.	235.	660.
Allantoin	Nucleobases and related	77	2	0	35	87	66
	Vitamins, cofactors and related						
alpha-Tocopherol	Unknown	0.34	0.38	0.52	0.73	0.61	0.84
alpha-Tocopherol	Unknown	0.06	0.04	0.08	0.03	0.03	0.11
alpha-Tocotrienol	Unknown	0.06	0.09	0.15	0.05	0.05	0.13
	Carbohydrates and related	36.5					
Arabinose		9	4.70	4.64	3.37	2.78	2.28
		11.4		10.4			
Arginine	Amino acids	9	8.33	3	2.53	1.10	2.03
			12.8	10.3			
Arginine	Amino acids	7.55	5	8	1.93	1.42	2.15
	Complex lipids, fatty acids and related						
Behenic acid (C22:0)	Unknown	0.62	0.44	0.53	0.74	0.63	0.60
beta-/gamma-Tocotrienol	Unknown	0.30	0.40	0.51	0.63	0.58	0.76
beta-/gamma-Tocotrienol	Unknown	0.29	0.38	0.48	0.67	0.51	0.63
beta-Amyrin TMS	Unknown	0.69	0.63	0.68	0.80	0.92	0.70
beta-Sitosterol, total	Miscellaneous	2.30	2.69	2.62	2.88	3.21	2.75
Biliverdin	Unknown	0.38	0.08	0.40	0.37	0.17	0.26
bis-Glycerol phosphate, polar fraction	Miscellaneous	2.72	2.21	1.26	2.92	1.80	1.74
Campesterol, total	Miscellaneous	2.36	2.02	2.62	2.69	2.86	2.34
	Complex lipids, fatty acids and related						
Cerebronic acid (2-OH-C24:0)	Complex lipids, fatty acids and related	0.41	0.33	0.37	0.39	0.53	0.44
Cerotic acid (C26:0)	Complex lipids, fatty acids and related	0.71	0.50	0.59	0.78	0.74	0.52
Cholestenol No 02	Complex lipids, fatty acids and related	0.53	0.39	0.48	0.69	0.55	0.64
		14.3	26.9		15.3	20.9	14.3
Cholic acid	Unknown	1	2	5.47	4	7	8
Coenzyme Q10	Unknown	0.55	0.44	0.36	0.51	0.79	0.52
conjugated Linoleic acid (C18:trans[9,11]2)	Complex lipids, fatty acids and related	0.42	0.31	0.44	0.35	0.59	0.61
Cortisol (lipid)	Unknown	0.40	0.30	0.33	0.65	0.49	0.68
		159.	92.1	129.	132.	104.	94.5
Creatinine	Amino acids related	09	6	29	71	82	4

Creatinine	Unknown	124.16	192.72	363.87	230.67	168.08	281.58
Cysteine	Amino acids	7.78	5.87	6.38	10.9	3	12.0
Cytosine	Nucleobases and related	8.35	7.28	10.4	3.71	3.95	4.19
Dehydroalanine	Amino acids related	8.23	5.28	4.64	7.97	5.45	6.31
Deoxycholic acid	Complex lipids, fatty acids and related	0.21	0.14	0.25	0.10	0.12	0.11
Deoxycholic acid	Unknown	0.01	0.00	0.01	0.01	0.00	0.00
Eicoasenoic acid (C20:cis[11]1)	Complex lipids, fatty acids and related	0.44	0.44	0.60	0.63	0.53	0.69
Eicosadienoic acid (C20:2) No 01	Complex lipids, fatty acids and related	0.22	0.23	0.20	0.21	0.30	0.26
Eicosadienoic acid (C20:2) No 02	Complex lipids, fatty acids and related	0.20	0.23	0.20	0.25	0.18	0.23
Eicosaenoic acid (C20:1) No 02	Complex lipids, fatty acids and related	0.47	0.23	0.30	0.48	0.63	0.34
Eicosanoic acid (C20:0)	Complex lipids, fatty acids and related	0.58	0.40	0.55	0.77	0.55	0.56
epsilon-Acetyllysine	Unknown	4.65	6.17	5.44	11.1	6	7.59
erythro-Dihydrosphingosine (d18:0)	Complex lipids, fatty acids and related	0.21	0.11	0.15	0.15	0.24	0.21
Ethanolamine	Miscellaneous	1.09	0.55	0.57	0.80	0.59	0.61
Fucose	Carbohydrates and related	31.7	35.3	15.5	4.27	5.43	3.51
Fucosterol, total	Miscellaneous	5	9	4	2.74	2.27	2.25
Fumarate	Energy metabolism and related	2.02	1.53	2.11	4.29	3.18	4.18
Galactose, lipid fraction	Complex lipids, fatty acids and related	4.74	5.10	4.74	1.43	1.81	1.71
gamma-Tocopherol	Vitamins, cofactors and related	1.73	1.70	1.19	0.44	0.50	0.46
gamma-Tocopherol	Unknown	0.34	0.30	0.45	0.82	0.65	0.91
Glucose-1-phosphate	Carbohydrates and related	0.47	0.64	1.01	3.93	6.00	5.07
Glucuronic acid	Carbohydrates and related	23.0	4.62	12.5	4.38	5.14	4.37
Glutamate	Amino acids	1	1	4	10.1	16.0	6
Glutamate	Unknown	1788	23.4	296.	7.07	7.42	3.38
Glutamic acid 2TMS ME (lipid)	Unknown	.81	1	33	1.80	1.64	2.64
Glutamine	Amino acids	10.1	0	8.07	5.82	3.35	4.46
Glutarate	Amino acids related	0	2.79	4.57	0.53	0.51	0.53
Glycerol phosphate, lipid fraction	Complex lipids, fatty acids and related	0.24	0.25	0.20	0.49	0.49	0.48
Glycerol, polar fraction	Complex lipids, fatty acids and related	0.46	0.47	0.23	1.07	0.93	1.65
Glycine	Amino acids	3.04	7.56	5.14	6.97	1.80	3.26
Glycine, lipid fraction	Miscellaneous	29.0	39.8	48.0	0.80	0.67	0.68
Glycine, lipid fraction	Miscellaneous	3	6	1	0.52	0.57	0.56
Heneicosanoic acid (C21:0)	Complex lipids, fatty acids and related	0.47	0.55	0.53	0.46	0.47	0.42

Heptacosanoic acid (C27:0)	Complex lipids, fatty acids and related	0.62	0.44	0.73	0.75	0.66	0.56
Heptadecanoic acid (C17:0)	Complex lipids, fatty acids and related	0.33	0.20	0.28	0.32	0.24	0.34
Hexadecanol	Complex lipids, fatty acids and related	0.06	0.05	0.12	0.04	0.23	0.15
Homoserine	Amino acids related	1.73	2.76	4.43	0.57	0.82	0.72
Hyodeoxycholic acid	Unknown	0.01	0.00	0.01	0.01	0.00	0.01
Hyodeoxycholic acid	Complex lipids, fatty acids and related	0.11	0.10	0.26	0.09	0.06	0.08
Hypoxanthine	Nucleobases and related	51.9	39.2	21.5			
		6	4	0	3.36	2.51	3.04
						12.5	30.2
Indole-3-acetic acid	Amino acids related	0.17	0.21	0.32	6.64	0	5
Inosine	Nucleobases and related	3.23	3.81	3.13	4.10	7.69	8.54
isoLCA	Unknown	0.01	0.00	0.00	0.00	0.00	0.01
		72.1	64.8	127.			
Isoleucine	Amino acids	4	2	40	0.68	0.46	0.83
	Complex lipids, fatty acids and related						
Isopalmitic acid (C16:0)		0.26	0.18	0.21	0.23	0.31	0.23
Kynurenic acid	Unknown	3.05	0.90	2.15	5.06	4.06	6.87
	Carbohydrates and related		23.1				
Lactose		9.76	8	3.01	1.09	0.75	1.49
		63.3	58.7	121.			
Leucine	Amino acids	1	9	57	0.43	0.31	0.63
	Complex lipids, fatty acids and related						
Lignoceric acid (C24:0)		0.84	0.42	0.55	0.67	0.63	0.60
	Complex lipids, fatty acids and related						
Linoleic acid (C18:cis[9,12]2)		2.62	2.94	3.85	3.50	4.09	3.57
	Complex lipids, fatty acids and related						
Linolenic acid (C18:cis[9,12,15]3)		2.89	4.09	4.18	3.77	6.02	3.99
Lithocholic acid	Unknown	0.02	0.02	0.02	0.02	0.02	0.02
		37.0	33.3	19.8	12.4		23.1
Lysine	Amino acids	3	5	8	8	3.31	1
	Carbohydrates and related	34.5					
Lyxose		0	5.17	4.50	2.59	2.08	0.89
	Carbohydrates and related	25.4					
Mannose		3	4.69	7.05	4.44	4.51	6.15
	Carbohydrates and related	299.	350.	152.			
myo-Inositol		98	58	31	3.96	7.51	4.38
	Complex lipids, fatty acids and related						
Myristic acid (C14:0)		0.22	0.22	0.23	0.34	0.32	0.38
N2-Acetylhistidine	Unknown	4.06	5.24	4.73	1.94	0.89	1.33
				16.5			
N-Acetyl-leucine	Unknown	4.32	9.27	2	4.43	3.05	8.96
	Complex lipids, fatty acids and related						
Nervonic acid (C24:cis[15]1)		0.44	0.30	0.47	0.51	0.39	0.59
Niacinamide (Nicotinamide)	Unknown	0.34	0.26	0.16	0.61	0.76	0.40
Norleucine	Miscellaneous	0.44	0.19	0.51	0.44	0.15	0.38
	Complex lipids, fatty acids and related						
Octadecadienoic acid No 01 (C18:2)		0.49	0.38	0.40	0.41	0.70	0.67
	Complex lipids, fatty acids and related						
Octadecanol		0.06	0.06	0.15	0.08	0.53	0.23
	Complex lipids, fatty acids and related						
Oleic acid (C18:cis[9]1)		0.10	0.06	0.14	0.09	0.12	0.34
o-Muricholic Acid	Unknown	0.08	0.00	0.00	0.14	0.03	0.02

Ornithine	Amino acids related	42.2	49.1	32.0	3.16	1.15	1.73
Palmitic acid (C16:0)	Complex lipids, fatty acids and related	2	2	8			
Pentacosanoic acid (C25:0)	Complex lipids, fatty acids and related	0.46	0.52	0.63	0.54	0.68	0.64
Pentadecanol	Complex lipids, fatty acids and related	0.60	0.34	0.57	0.58	0.55	0.51
Phenylalanine	Amino acids	0.40	0.37	0.45	0.49	0.44	0.42
Phenylalanine	Unknown	81.1	87.3	96.4	1.74	0.91	1.30
Phenylalanine	Unknown	2	2	8			
Phenylalanine	Unknown	59.9	45.6	52.3	2.08	0.93	1.92
Phenylalanine	Unknown	2	6	6			
Phenylalanine	Unknown	79.3	46.3	68.3	1.25	0.83	1.15
Phenylalanine	Unknown	1	9	1			
Phenylalanine, lipid fraction	Miscellaneous	76.9	39.3	63.4	0.95	0.56	1.24
Phosphate, lipid fraction	Complex lipids, fatty acids and related	2	6	6	0.78	0.67	0.56
Phosphoenolpyruvate (PEP)	Energy metabolism and related	2.04	1.75	1.99			
Pipecolic acid	Unknown	0.46	0.33	0.34	0.42	0.47	0.55
plausible 2-Hydroxyarachidic acid (2-OH-C20:0) TMS ME	Unknown	4.85	4.04	3.90	5.55	4.19	3.12
plausible 2-Hydroxytricosanoic acid (2-OH-C23:0) TMS ME	Unknown	0.23	0.16	0.08	0.69	0.63	0.61
plausible Heptadecanol TMS	Unknown	0.31	0.22	0.30	0.35	0.54	0.39
plausible SM (d18:1, C16:0) Na-Addukt	Unknown	0.52	0.28	0.35	0.40	0.54	0.45
Proline	Amino acids	0.01	0.01	0.02	0.01	0.04	0.04
Proline betaine	Unknown	4.05	3.35	2.15	2.99	4.18	3.15
putative 12-Methylmyristic acid TMS	Unknown		12.0	34.0			
putative Anhydroglucuronate 4TMS	Unknown	1.64	1	1	1.62	0.92	1.87
putative Bis-(glycerol)-phosphate	Unknown	0.65	0.58	0.69	1.74	0.72	1.30
putative Choline plasmalogen (C36:2)	Unknown	0.04	0.02	0.03	0.03	NA	0.03
putative Deoxycholyglycine deriv #1	Unknown	14.7		10.7			
putative Hydroxy-eicosan OTMS	Unknown	6	7.28	3	3.37	3.94	3.32
putative Hyodeoxycholic acid 3TMS	Unknown	0.28	0.19	0.25	0.24	0.25	0.22
putative Lithocholic acid OTMS ME	Unknown	5.36	2.95	3.16	2.97	2.55	2.06
putative Tetracosenoic acid ME	Unknown	0.02	0.01	0.01	0.02	0.00	0.02
Putrescine	Miscellaneous	0.26	0.17	0.28	0.30	0.40	0.30
Pyruvate	Energy metabolism and related	0.01	0.01	0.08	0.02	0.01	0.05
scyllo-Inositol	Carbohydrates and related	0.05	0.02	0.02	0.04	0.03	0.03
Serine	Amino acids	0.57	0.22	0.38	0.45	0.47	0.41
Serine, lipid fraction	Miscellaneous	11.2			65.3	13.1	26.0
Serine, lipid fraction	Miscellaneous	7	3.64	6.43	7	5	8
Shikimic acid	Miscellaneous	3.69	2.98	3.57	2.93	2.30	2.59
Stearic acid (C18:0)	Complex lipids, fatty acids and related	16.3	23.8	43.0	16.9	13.1	34.7
		3	7	4	5	8	2
		47.1	23.9	49.9			
		9	8	5	1.25	0.82	1.07
		1.16	0.53	0.50	0.96	0.59	0.51
		1.06	0.51	0.59	0.82	0.59	0.52
		738.	504.	1196	1255	829.	1575
		89	54	.46	.66	12	.29
		0.35	0.30	0.44	0.37	0.35	0.46

Stigmastanol, total	Miscellaneous	0.50	0.56	0.67	0.57	0.66	0.68
Stigmasterol, total	Miscellaneous	1.69	1.42	2.09	2.02	1.71	1.87
		24.1	16.9	10.5	21.2	19.9	23.1
Taurine	Unknown	8	3	1	5	3	7
		20.1	148.	40.8			
Tauro-b-muricholic Acid	Unknown	9	81	0	4.03	6.14	2.65
		74.2	81.2	34.2		11.3	
Taurocholic acid	Unknown	4	8	4	6.05	0	5.20
		142.	1738	129.	20.8	85.1	43.3
Taurocholic Acid 3-sulfate	Unknown	02	.70	59	3	1	8
		16.6	73.0	11.5		15.1	
Taurocholic acid sodium salt	Unknown	2	2	1	6.14	3	4.85
	Complex lipids, fatty acids and related						
Tetradecanol		0.17	0.09	0.11	0.17	0.15	0.12
Thiamine (Vitamin B1)	Unknown	0.30	0.09	0.42	0.30	0.15	0.21
		45.8	50.8	87.0			
Threonine	Amino acids	2	3	7	2.42	1.19	2.67
		22.3	112.	134.			
trans-4-Hydroxyproline	Amino acids related	0	85	93	3.42	2.43	1.78
trans-Ferulic acid	Miscellaneous	6.56	7.27	9.78	8.31	7.20	7.57
		18.5	32.1	22.5	33.7	34.5	27.8
trans-Sinapic acid	Miscellaneous	2	3	5	6	0	6
	Complex lipids, fatty acids and related						
Tricosanoic acid (C23:0)		0.55	0.34	0.44	0.54	0.54	0.50
		86.0	120.	92.3	25.0		
Tryptophan	Amino acids	5	14	6	1	2.39	8.98
		401.	132.	317.	180.		11.8
Tyramine	Amino acids related	80	62	71	74	9.83	0
Tyrosine	Unknown	3.56	0.30	0.52	0.21	0.18	0.27
Ubichinone-30 (Coenzyme Q6)	Unknown	0.50	0.54	0.41	0.49	0.71	0.59
Ubichinone-35 (Coenzyme Q7)	Unknown	0.53	0.42	0.40	0.53	0.65	0.59
Ubichinone-45 (Coenzyme Q9)	Unknown	0.61	0.42	0.43	0.55	0.70	0.57
Unknown lipid MB (828450473)	Unknown	4.78	2.90	2.80	3.19	3.02	2.22
Unknown lipid MB (828450676)	Unknown	0.92	0.80	0.87	0.96	0.75	0.90
Unknown lipid MB (828450834)	Unknown	0.45	0.29	0.33	0.49	0.73	0.73
Unknown lipid MB (828451241)	Unknown	0.08	0.06	0.13	0.13	0.05	0.10
Unknown lipid MB (828451316)	Unknown	0.38	0.34	0.46	2.01	2.47	2.47
Unknown lipid MB (828451380)	Unknown	0.71	0.27	0.51	0.55	0.51	0.41
Unknown lipid MB (828451443)	Unknown	0.60	0.43	0.55	0.76	0.67	0.74
Unknown lipid MB (828451444)	Unknown	0.76	0.31	0.49	0.54	0.53	0.43
Unknown lipid MB (828451445)	Unknown	0.26	0.22	0.27	0.30	0.29	0.35
Unknown lipid MB (828451931)	Unknown	0.01	0.00	0.01	0.01	0.00	0.02
Unknown lipid MB (828451933)	Unknown	0.06	0.06	0.10	0.14	0.06	0.09
Unknown lipid MB (828451937)	Unknown	0.00	0.00	0.00	0.00	0.02	0.01
Unknown lipid MB (828451940)	Unknown	0.00	0.00	0.00	0.00	0.01	0.01
Unknown lipid MB (828452038)	Unknown	0.03	0.01	0.02	0.02	0.01	0.02
Unknown lipid MB (828452040)	Unknown	0.37	0.17	0.43	0.14	0.17	0.21
Unknown lipid MB (828452041)	Unknown	0.04	0.07	0.05	0.03	0.08	0.04
Unknown lipid MB (828452042)	Unknown	0.01	0.00	0.00	0.00	0.00	0.00
Unknown lipid MB (828452043)	Unknown	0.01	0.02	0.01	0.01	0.02	0.00
Unknown lipid MB (828452044)	Unknown	0.61	0.33	0.44	0.53	0.59	0.44
Unknown lipid MB (828452047)	Unknown	0.03	0.00	0.00	0.02	0.09	0.02
Unknown lipid MB (828452048)	Unknown	1.09	0.42	0.55	0.72	0.88	0.49

Unknown lipid MB (828452053)	Unknown	0.58	0.51	0.69	0.67	0.64	0.64
Unknown lipid MB (828452059)	Unknown	0.21	0.06	0.03	0.40	0.07	0.03
Unknown lipid MB (828452060)	Unknown	0.01	0.00	0.00	0.01	0.00	0.00
Unknown lipid MB ESI neg (858450013)	Unknown	16.6	14.0	37.5	0.74	0.39	1.14
Unknown lipid MB ESI neg (858450034)	Unknown	0.34	0.16	0.17	1.01	0.52	0.89
Unknown lipid MB ESI neg (858450047)	Unknown	73.0	58.0	56.5	54.2	26.7	
Unknown lipid MB ESI neg (858450065)	Unknown	6	6	0	5	9	6.91
Unknown lipid MB ESI neg (858450068)	Unknown	0.31	0.16	0.28	1.39	0.86	1.54
Unknown lipid MB ESI neg (858450071)	Unknown	0.42	0.36	0.31	0.48	0.60	0.77
Unknown lipid MB ESI pos (848450056)	Unknown	2.45	2.07	2.75	3.71	3.22	2.94
Unknown lipid MB ESI pos (848450083)	Unknown	5.57	3.80	4.60	5.63	4.95	4.79
Unknown lipid MB ESI pos (848450084)	Unknown	4.20	2.83	1.64	3.02	3.41	1.62
Unknown lipid MB ESI pos (848450091)	Unknown	2.51	3.10	2.14	2.04	2.99	2.46
Unknown lipid MB ESI pos (848450092)	Unknown	0.13	0.23	0.39	0.58	0.67	2.08
Unknown lipid MB ESI pos (848450093)	Unknown	0.33	0.18	0.25	0.34	0.27	0.28
Unknown lipid MB ESI pos (848450096)	Unknown	0.36	0.27	0.26	0.81	0.79	0.84
Unknown lipid MB ESI pos (848450097)	Unknown	2.12	2.16	2.13	2.95	3.05	2.15
Unknown lipid MB ESI pos (848450100)	Unknown	7.77	5.44	6.12	8.39	6.77	5.69
Unknown lipid MB ESI pos (848450102)	Unknown	4.45	3.95	3.29	3.66	5.95	3.82
Unknown lipid MB ESI pos (848450103)	Unknown	7.50	2.41	3.35	5.42	3.26	2.48
Unknown lipid MB ESI pos (848450105)	Unknown	6.23	3.76	3.00	5.19	3.47	2.37
Unknown lipid MB ESI pos (848450106)	Unknown	12.9	10.2		15.0	13.2	
Unknown lipid MB ESI pos (848450107)	Unknown	8	9	6.82	0	3	7.67
Unknown lipid MB ESI pos (848450108)	Unknown	6.12	2.96	2.44	3.13	3.79	2.63
Unknown lipid MB ESI pos (848450109)	Unknown	2.30	1.48	1.75	1.35	2.12	1.72
Unknown lipid MB ESI pos (848450110)	Unknown	5.08	2.74	2.99	2.58	2.86	2.64
Unknown lipid MB ESI pos (848450111)	Unknown	3.15	2.05	2.63	1.98	2.46	1.99
Unknown lipid MB ESI pos (848450113)	Unknown	7.61	5.39	4.38	5.29	5.97	8.43
Unknown lipid MB ESI pos (848450114)	Unknown	1.50	2.75	2.58	2.09	3.08	3.30
Unknown lipid MB ESI pos (848450116)	Unknown	3.44	3.72	5.06	3.20	4.44	5.06
		6.47	3.27	3.99	3.27	3.72	3.48
		4.56	3.33	2.16	3.56	6.39	4.97

Unknown lipid MB ESI pos (848450129)	Unknown	2.20	2.33	1.92	1.55	2.99	2.57
Unknown lipid MB ESI pos (848450131)	Unknown	4.68	3.56	3.12	3.13	6.07	3.01
Unknown lipid MB ESI pos (848450132)	Unknown	3.91	3.02	2.49	2.64	4.43	3.27
Unknown lipid MB ESI pos (848450138)	Unknown	2.98	2.43	1.83	2.38	4.26	3.24
Unknown lipid MB ESI pos (848450139)	Unknown	8.65	6.11	4.71	3.82	4.64	2.80
Unknown lipid MB ESI pos (848450142)	Unknown	11.9	1	6.51	4.84	5.92	4.02
Unknown lipid MB ESI pos (848450144)	Unknown	3.66	3.97	2.90	3.06	5.24	5.07
Unknown lipid MB ESI pos (848450146)	Unknown	3.20	2.65	1.89	2.57	3.73	2.89
Unknown lipid MB ESI pos (848450148)	Unknown	4.50	3.55	2.68	3.22	5.94	4.59
Unknown lipid MB ESI pos (848450152)	Unknown	1.97	2.88	1.61	1.76	4.76	3.04
Unknown lipid MB ESI pos (848450154)	Unknown	0.55	0.43	0.31	0.40	0.97	0.50
Unknown lipid MB ESI pos (848450155)	Unknown	0.70	0.33	0.28	0.63	0.76	0.54
Unknown lipid MB ESI pos (848450196)	Unknown	5.29	9.54	8.18	8.93	14.3	1
Unknown lipid MB ESI pos (848450201)	Unknown	5.57	7.29	6.98	9.37	10.2	6
Unknown lipid MB ESI pos (848450202)	Unknown	2.09	2.74	2.70	2.96	3.52	3.20
Unknown lipid MB ESI pos (848450204)	Unknown	7.45	10.2	9	12.7	13.8	6
Unknown lipid MB ESI pos (848450205)	Unknown	7.03	9.67	8.09	11.6	11.3	4
Unknown lipid MB ESI pos (848450206)	Unknown	8.01	13.9	13.7	11.4	20.2	11.6
Unknown lipid MB ESI pos (848450207)	Unknown	7.69	11.5	10.1	13.0	17.7	2
Unknown lipid MB ESI pos (848450208)	Unknown	7.05	0	0	3	11.2	8.94
Unknown lipid MB ESI pos (848450209)	Unknown	5.28	9.59	8.78	9.85	5	7.56
Unknown lipid MB ESI pos (848450210)	Unknown	3.96	6.39	5.23	8.77	8.16	5.73
Unknown lipid MB ESI pos (848450212)	Unknown	5.89	8.29	8.97	7.91	10.1	2
Unknown lipid MB ESI pos (848450213)	Unknown	7.01	9.67	9.44	11.4	11.6	1
Unknown lipid MB ESI pos (848450214)	Unknown	5.94	9.46	10.3	7	5	8.07
Unknown lipid MB ESI pos (848450215)	Unknown	6.71	11.1	8	9.18	10.1	3
Unknown lipid MB ESI pos (848450216)	Unknown	5.58	5	8.18	9.93	11.6	6
Unknown lipid MB ESI pos (848450218)	Unknown	5.65	9.70	8.47	9.45	10.6	9
Unknown lipid MB ESI pos (848450219)	Unknown	4.62	6.93	6.71	7.88	10.0	5
							7.73
							7.04

Unknown polar MB (838450146)	Unknown	5.09	3.02	2.11	2.07	1.69	1.09
Unknown polar MB (838450528)	Unknown	0.60	0.25	0.13	1.00	1.33	1.21
Unknown polar MB (838450590)	Unknown	0.46	0.19	0.71	0.52	0.16	0.42
					12.0		12.6
Unknown polar MB (838450621)	Unknown	6.68	7.46	7.28	7	8.90	1
Unknown polar MB (838450692)	Unknown	0.19	0.24	0.18	0.11	0.23	0.20
Unknown polar MB (838450761)	Unknown	3.89	2.30	1.75	1.92	2.61	2.23
Unknown polar MB (838450816)	Unknown	0.01	0.00	0.01	0.01	0.00	0.01
Unknown polar MB (838450990)	Unknown	1.53	1.47	1.51	1.16	1.05	1.05
Unknown polar MB (838451614)	Unknown	0.04	0.08	0.03	0.02	0.16	0.04
Unknown polar MB (838452021)	Unknown	0.59	0.38	0.49	0.41	0.46	0.52
Unknown polar MB (838452022)	Unknown	2.60	2.14	1.75	2.24	1.62	2.06
Unknown polar MB (838452079)	Unknown	7.37	1.97	2.83	2.98	1.95	2.13
Unknown polar MB (838452178)	Unknown	0.07	0.10	0.18	0.07	0.16	0.34
Unknown polar MB (838452196)	Unknown	3.83	1.85	2.34	2.32	1.44	1.90
		10.4					
Unknown polar MB (838452804)	Unknown	8	2.37	4.70	2.91	2.49	1.31
Unknown polar MB (838452997)	Unknown	0.32	0.55	0.40	0.34	0.59	0.42
Unknown polar MB (838452998)	Unknown	1.86	0.20	0.19	1.04	0.40	0.80
Unknown polar MB (838453005)	Unknown	0.20	0.27	0.26	0.09	0.09	0.09
Unknown polar MB (838453006)	Unknown	0.17	0.24	0.21	0.09	0.30	0.24
Unknown polar MB (838453008)	Unknown	0.18	0.32	0.26	1.19	0.98	1.43
Unknown polar MB (838453009)	Unknown	0.02	0.03	0.02	0.03	0.04	0.02
Unknown polar MB (838453011)	Unknown	0.51	0.69	0.36	0.74	1.06	0.65
		26.4	24.3	11.7	215.	83.2	83.0
Unknown polar MB (838453012)	Unknown	2	3	2	16	7	4
Unknown polar MB (838453014)	Unknown	0.21	0.32	0.61	0.76	0.67	1.06
Unknown polar MB (838453015)	Unknown	0.18	0.11	0.18	0.19	0.12	0.17
Unknown polar MB (838453016)	Unknown	0.33	0.54	0.53	1.27	1.23	2.00
Unknown polar MB (838453017)	Unknown	0.11	0.05	0.10	0.08	0.14	0.09
Unknown polar MB (838453018)	Unknown	0.07	0.11	0.17	0.07	0.17	0.12
Unknown polar MB (838453019)	Unknown	0.10	0.06	0.03	0.08	0.08	0.02
Unknown polar MB (838453026)	Unknown	0.24	0.09	0.17	0.19	0.28	0.40
Unknown polar MB (838453028)	Unknown	0.18	0.08	0.07	0.11	0.07	0.06
Unknown polar MB (838453033)	Unknown	0.14	0.06	0.06	0.05	0.07	0.04
Unknown polar MB (838453036)	Unknown	0.07	0.03	0.02	0.06	0.06	0.04
Unknown polar MB (838453040)	Unknown	0.05	0.03	0.03	0.03	0.06	0.03
Unknown polar MB (838453041)	Unknown	0.07	0.11	0.11	0.10	0.08	0.18
Unknown polar MB (838453044)	Unknown	0.36	0.30	0.36	0.43	0.39	0.40
Unknown polar MB (838453047)	Unknown	0.20	0.04	0.04	0.11	0.10	0.05
Unknown polar MB (838453048)	Unknown	0.12	0.11	0.07	0.15	0.09	0.11
Unknown polar MB (838453051)	Unknown	0.28	0.51	0.50	0.34	0.65	0.75
Unknown polar MB (838453052)	Unknown	0.28	0.15	0.25	0.17	0.17	0.12
Unknown polar MB (838453053)	Unknown	0.32	0.16	0.33	0.17	0.14	0.13
Unknown polar MB (838453055)	Unknown	0.04	0.03	0.02	0.03	0.05	0.02
Unknown polar MB (838453056)	Unknown	0.38	0.29	0.26	0.27	0.19	0.28
Unknown polar MB (838453057)	Unknown	0.44	0.25	0.38	0.25	0.20	0.16
Unknown polar MB (838453058)	Unknown	0.56	0.17	0.21	0.37	0.11	0.12
Unknown polar MB (838453059)	Unknown	2.66	2.95	3.19	2.35	3.17	2.57
Unknown polar MB (838453062)	Unknown	0.30	0.43	0.49	0.43	0.62	0.57

Unknown polar MB (838453063)	Unknown	0.30	0.03	0.03	0.13	0.03	0.05			
Unknown polar MB (838453066)	Unknown	0.01	0.01	0.01	0.01	0.00	0.01			
Unknown polar MB (838453067)	Unknown	3.19	2.27	3.10	4.49	2.27	3.68			
Unknown polar MB ESI pos (868450034)	Unknown	3.53	4.44	3.47	0.52	0.88	0.68			
Unknown polar MB ESI pos (868450040)	Unknown	3.29	4.00	4.83	1.97	0.95	1.49			
Uric acid	Nucleobases and related	10.5	2	8.98	7.47	0.35	1.23	0.72		
Valine	Amino acids	50.7	1	53.5	93.3	0.87	0.44	0.82		
Valine TMS ME	Unknown	2.68	3.55	4.64	0.65	0.70	0.69			
Valine, lipid fraction	Miscellaneous	3.25	3.07	3.89	0.94	0.67	0.62			
Xanthine	Nucleobases and related	88.4	92.2	74.9	4	9	5	0.66	0.55	2.40
Xanthurenic acid	Amino acids related	0.08	0.12	0.05	0.05	0.07	0.11			
Xylose	Carbohydrates and related	11.5	23.6	0	7	4.83	4.22	3.29	2.14	

Table S5: Summarized table indicating the trend of significant alterations in plasma biomarkers including hippuric acid and indole derivatives in samples from animals treated with antibiotics (HD group only) belonging to different classes. Yellow boxes indicate a significant increase and red box indicates a significant decrease in the fold change levels of respective plasma metabolites at p-value<0.1.

Plasma biomarkers	Aminoglycosides			Lincosamides		Fluoroquinolone			Carbapenems	
	Tobramycin	Gentamicin	Neomycin	Clindamycin	Lincomycin	Sparfloxacin	Moxifloxacin	Levofloxacin	Meropenem	Doripenem
3-Indoxylsulfate (3IS)	↓↓	NS	NS	↓↓	↓	NS	↓↓	NS	↓↓	↓↓
Hippuric acid (HA)	↓↓	↓↓	↓↓	↓↓	↓	NS	↓↓	↓↓	↓↓	↓↓
Indole-3-acetic acid (IAA)	↓↓	NS	↓	NS	NS	↓↓	↓↓	↓↓	↑	↓
Indole-3-propionic acid (IPA)	↓↓	NA	↓↓	NA	NA	NA	NS	NS	NS	↓

*NS, non-significant; NA, not applicable