

Supplementary data

Supplementary figures

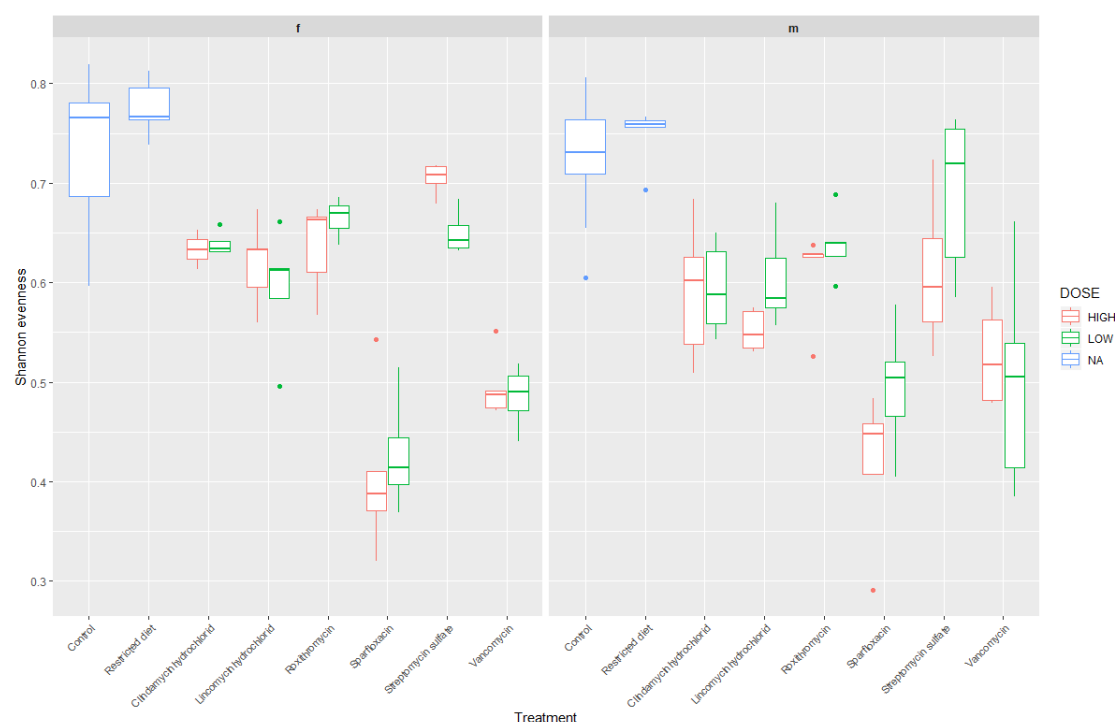


Figure S1: Shannon Evenness for all the treatments including both sexes and dose groups. Ranges from 0 to 1 where 0 means the bacterial diversity is uneven whereas 1 means the evenness in the different bacterial taxa present is higher. (dots are individual samples, solid lines between the boxes are medians)

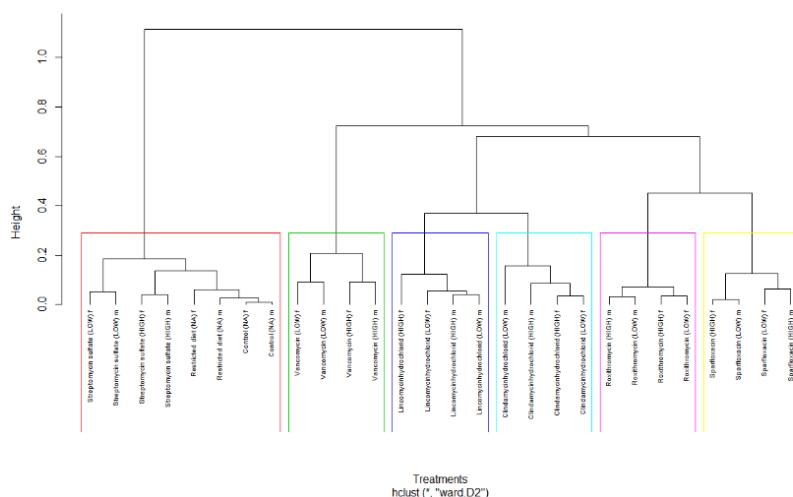


Figure S2: Hierarchical clustering (HCA) analysis of 16S gene sequencing data. Dendrogram showing hierarchical clustering of 16S rDNA gene sequencing of different treatments, dose groups and sex. Euclidean distance was used, and different treatments are depicted, and different colors and dotted boxes show different clusters

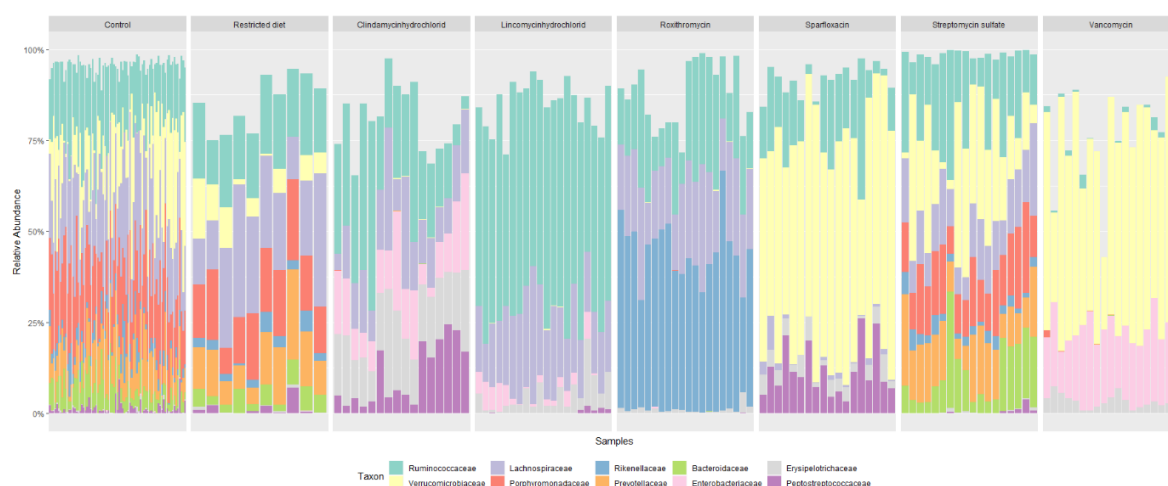


Figure S3: Relative abundance analysis of bacterial families for individual animals. Dose groups and sexes showed very marginal differences hence they were not separated. The most abundant families have higher contributions in the bars. The bars did not add up to 100% as the unclassified bacterial families with no taxonomic assignments were removed. Ten different bacterial families have been observed to be present relatively abundantly in the controls, restricted diet fed and different antibiotic treatments.

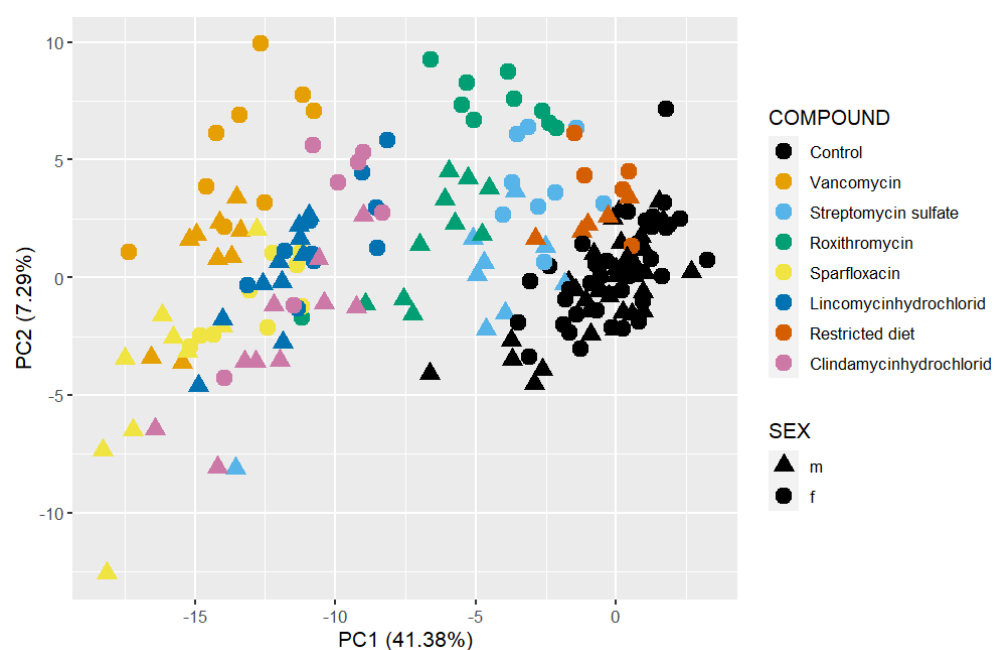


Figure S4: Principle Component Analysis (PCA) of feces metabolites from different treatments. Different colors depict different treatment groups where triangle shaped dots refer to male animals and circles refer to females.

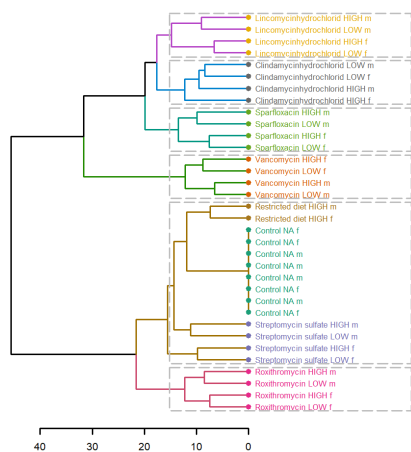


Figure S5: Dendrogram showing hierarchical clustering of cecum metabolites of different treatments, dose groups and sex. Euclidean distance was used, and different treatments are depicted, and different colors and dotted boxes show different clusters.

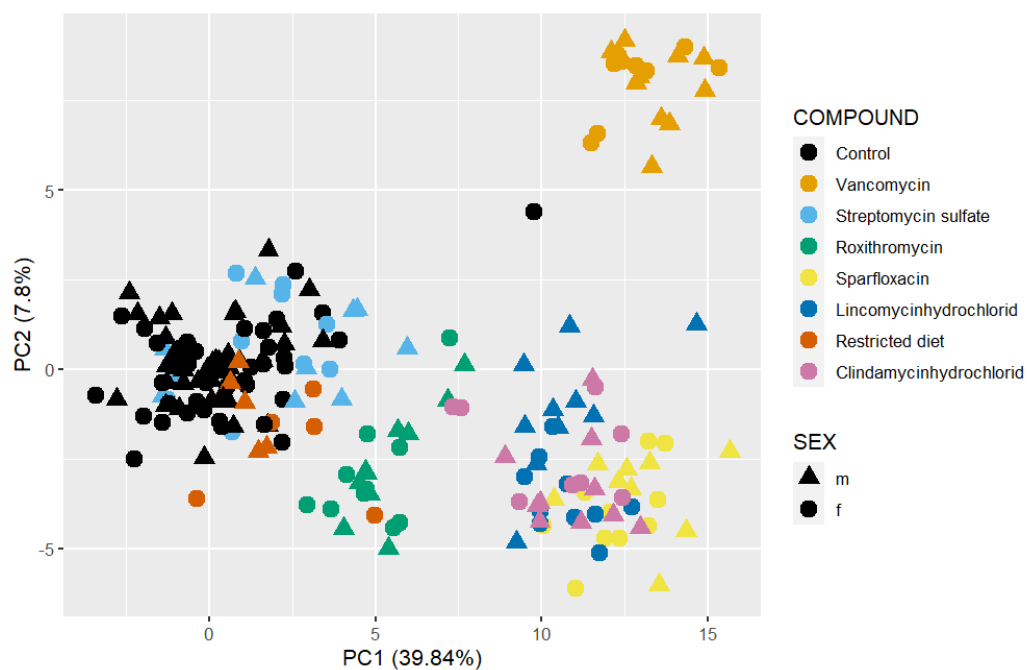


Figure S6: Principle Component Analysis (PCA) of cecum metabolites from different treatments. Different colors depict different treatment groups where triangle shaped dots refer to male animals and circles refer to females.

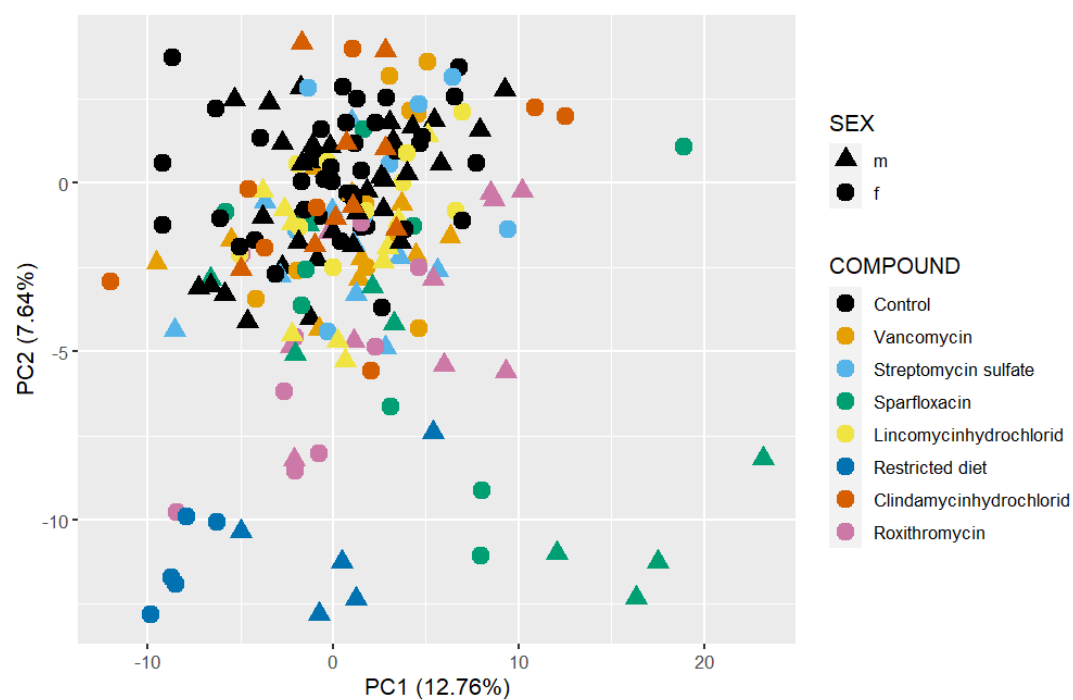


Figure S7: Principle Component Analysis (PCA) of plasma metabolites from different treatments. Different colors depict different treatment groups where triangle shaped dots refer to male animals and circles refer to females.

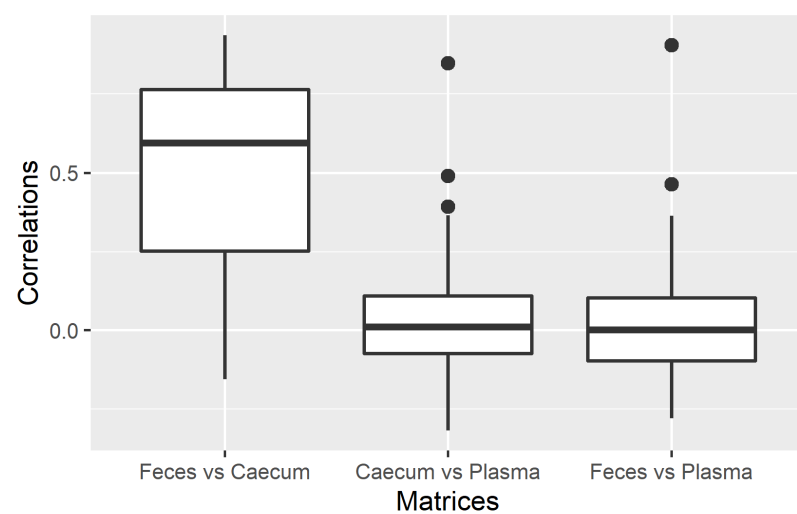


Figure S8: Boxplots comparing between different metabolome matrices. The value refers to correlation coefficient values and the dots represent outliers or metabolites that do not fall in the range of other metabolites.

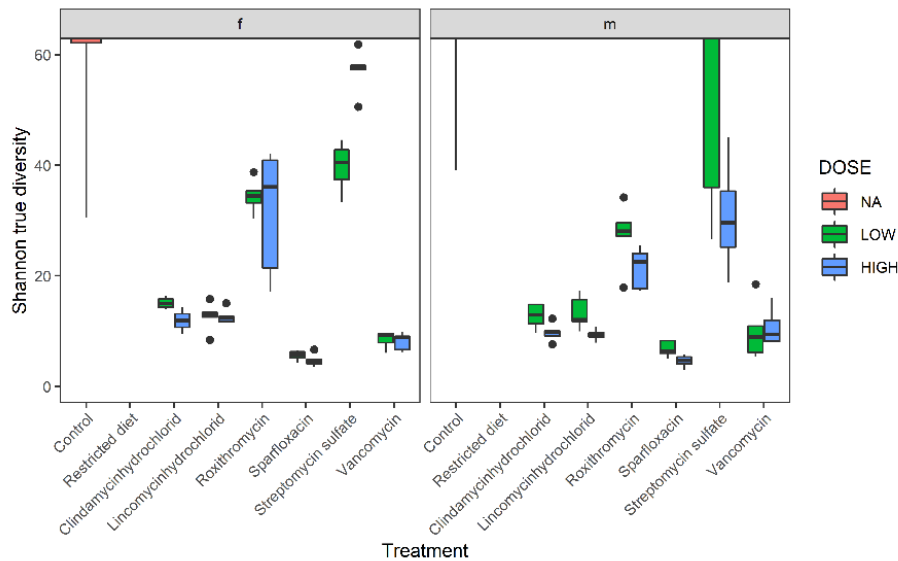


Figure S9: Shannon true diversity analysis of six antibiotic treatments focused for both male and female Wistar rats. Boxplot on the left show the diversity analysis for females (f) and right for the males (m). The colors show different dose groups, where blue box refers to high dose and green refers to low dose groups. The x-axis shows the different treatment groups and y-axis shows Shannon diversity value; whiskers denote standard deviations, solid lines within the boxes indicate the group median and dots lying outside the boxes are outliers. On removing control and restricted diet groups and focusing on the antibiotics only, we zoom in the focus to the fact that high dose groups have majorly lower alpha diversity. Minor differences could be observed but we cannot essentially say if they are statistically significant. Streptomycin sulfate group show higher variability in both the sexes compared to others, this could be mainly due to lack of influence of this antibiotic on the gut bacterial composition.

Supplementary tables

Table S1: Relative changes in body weight and food consumption of male and female Crl:Wi(Han) rats (N = 5 per group) dosed for 28 days compared to the diet controls. Data were collected on study days 6, 13 and 27. Treated animals did not present any significant changes ($p < 0.05$) in body weight compared to the control groups (N = 10 per group).

Antibiotic	Day	Body weight		Food consumption	
		m	f	m	f
Clindamycin	6	0,97	0,99	1,30	0,80
	13	0,95	0,98	1,12	1,19
	27	0,94	1,00	0,99	1,16
Lincomycin	6	1,00	0,99	1,00	0,99
	13	0,98	1,00	1,03	0,92
	27	0,96	1,05	1,18	0,97
Roxithromycin	6	0,98	0,99	0,85	0,80
	13	0,96	1,00	0,86	0,97
	27	0,96	1,01	1,04	1,03
Sparfloxacin	6	0,96	0,98	0,94	0,77
	13	0,94	0,99	0,97	1,01
	27	0,94	0,99	1,01	0,99
Streptomycin	6	0,97	0,98	0,92	0,91
	13	0,96	0,99	0,92	0,99
	27	0,95	0,97	0,97	0,93
Vancomycin	6	0,99	0,98	0,88	0,85
	13	0,97	1,00	0,93	0,92

27 0,95 1,00 0,93 0,95

Table S2: Top 25 (both directions) of plasma altered metabolites (p<0.1) for both females (left) and males (right) respectively for restricted diet treatment. (red = upregulated and yellow = downregulated)

Metabolite	Class	Restricted diet f28	Metabolite	Class	Restricted diet m28
Hippuric acid	Miscellaneous	4,40	dihomo-gamma-Linolenic acid (C20:cis[8,11,14]3)	Complex lipids, fatty acids and related	2,37
Palmitoleic acid (C16:cis[9]1)	Complex lipids, fatty acids and related	2,46	Palmitoleic acid (C16:cis[9]1)	Complex lipids, fatty acids and related	1,95
dihomo-gamma-Linolenic acid (C20:cis[8,11,14]3)	Complex lipids, fatty acids and related	2,32	TAG (C16:0,C16:1)	Complex lipids, fatty acids and related	1,92
TAG (C18:2,C18:3)	Complex lipids, fatty acids and related	2,20	Phosphatidylcholine (C16:0,C20:5)	Complex lipids, fatty acids and related	1,70
Oleic acid (C18:cis[9]1)	Complex lipids, fatty acids and related	2,17	Phosphatidylcholine (C16:1,C18:2)	Complex lipids, fatty acids and related	1,64
TAG (C16:0,C16:1)	Complex lipids, fatty acids and related	2,10	Lysophosphatidylcholine (C18:2)	Complex lipids, fatty acids and related	1,53
Phosphatidylcholine (C16:0,C20:5)	Complex lipids, fatty acids and related	2,00	17-Hydroxypregnenolone	Hormones, signal substances and related	1,47
TAG (C16:0,C18:1,C18:3)	Complex lipids, fatty acids and related	1,96	Hexoses	Carbohydrates and related	1,39
Eicosanoic acid (C20:1) No 02	Complex lipids, fatty acids and related	1,90	Glucose	Carbohydrates and related	1,29
Glycerol, lipid fraction	Complex lipids, fatty acids and related	1,89	Ascorbic acid	Vitamins, cofactors and related	1,25
Lysophosphatidylcholine (C20:4)	Complex lipids, fatty acids and related	1,85	Glucose	Carbohydrates and related	1,22
Coenzyme Q9	Vitamins, cofactors and related	1,83	Phosphatidylcholine (C18:0,C18:1)	Complex lipids, fatty acids and related	1,21
alpha-Tocopherol	Vitamins, cofactors and related	1,73	Hexoses	Carbohydrates and related	1,21
TAG (C18:1,C18:2)	Complex lipids, fatty acids and related	1,66	Lysophosphatidylcholine (C18:1)	Complex lipids, fatty acids and related	1,19
Glycerol phosphate, lipid fraction	Complex lipids, fatty acids and related	1,62	Serine	Amino acids	1,17
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	1,60	3-Methoxytyrosine	Hormones, signal substances and related	1,13
Isopalmitic acid (C16:0)	Complex lipids, fatty acids and related	1,60	Phosphatidylcholine (C18:1,C18:2)	Complex lipids, fatty acids and related	1,08
Unoleic acid (C18:cis[9,12]2)	Complex lipids, fatty acids and related	1,56	Phosphatidylcholine (C18:0,C20:4)	Complex lipids, fatty acids and related	1,06
Coenzyme Q10	Vitamins, cofactors and related	1,52	Phosphatidylcholine (C16:0,C20:4)	Complex lipids, fatty acids and related	1,02
TAG (C16:0,C18:2)	Complex lipids, fatty acids and related	1,51	Elaidic acid (C18:trans[9]1)	Complex lipids, fatty acids and related	0,71
myo-Inositol-2-phosphate, lipid fraction (myo-Inositol)	Complex lipids, fatty acids and related	1,50	Indole-3-lactic acid	Amino acids related	0,71
Lysophosphatidylcholine (C18:2)	Complex lipids, fatty acids and related	1,49	Isoleucine	Amino acids	0,70
Palmitic acid (C16:0)	Complex lipids, fatty acids and related	1,47	Methionine	Amino acids	0,69
Heptadecanoic acid (C17:0)	Complex lipids, fatty acids and related	1,46	Ketoleucine	Amino acids related	0,69
Glucose	Carbohydrates and related	1,46	Cystine	Amino acids	0,69
Phosphatidylcholine (C16:1,C18:2)	Complex lipids, fatty acids and related	1,41	Aspartate	Amino acids	0,67
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	1,40	Tryptophan	Amino acids	0,66
Behenic acid (C22:0)	Complex lipids, fatty acids and related	1,40	3-Hydroxyisobutyrate	Amino acids related	0,65
Tricosanoic acid (C23:0)	Complex lipids, fatty acids and related	1,39	Tyrosine	Amino acids	0,64
Campesterol, total	Miscellaneous	1,35	Ketoleucine	Amino acids related	0,64
Ceramide (d18:1,C24:1)	Complex lipids, fatty acids and related	1,34	3-Phosphoglycerate (3-PGA)	Energy metabolism and related	0,64
4-Hydroxyphinganine (t18:0, Phytosphingosine), total	Complex lipids, fatty acids and related	1,34	Tyrosine	Amino acids	0,64
Erythronic acid	Carbohydrates and related	1,31	Uric acid	Nucleobases and related	0,64
Citrulline	Amino acids related	1,30	TAG (putative)		0,63
Lignoceric acid (C24:0)	Complex lipids, fatty acids and related	1,29	Taurine	Amino acids	0,62
Glucose	Carbohydrates and related	1,28	Metanephine	Hormones, signal substances and related	0,60
Uric acid	Nucleobases and related	0,76	Creatine	Amino acids related	0,60
Lactate	Energy metabolism and related	0,76	DAG (C18:1,C18:2)	Complex lipids, fatty acids and related	0,58
4-Hydroxy-3-methoxyphenylglycol (HMPG)	Hormones, signal substances and related	0,74	Phosphocreatine	Amino acids related	0,55
Normetanephine	Hormones, signal substances and related	0,74	Docosahexaenoic acid (C22:cis[4,7,10,13,16,19]6)	Complex lipids, fatty acids and related	0,54
3-Hydroxybutyrate	Energy metabolism and related	0,74	4-Hydroxyphenylpyruvate	Energy metabolism and related	0,51
Cytosine	Nucleobases and related	0,73	3-Hydroxybutyrate	Amino acids related	0,49
Valine	Amino acids	0,72	2-Hydroxybutyrate	Energy metabolism and related	0,46
Tyrosine	Amino acids	0,72	Creatine	Amino acids related	0,45
Ketoleucine	Amino acids related	0,70	Biotin	Vitamins, cofactors and related	0,43
Uracil	Nucleobases and related	0,69	Creatinine	Amino acids related	0,40
4-Hydroxyphenylpyruvate	Amino acids related	0,68	Adrenaline (Epinephrine)	Hormones, signal substances and related	0,32
Isoleucine	Amino acids	0,68	Cholesterylester C20:4	Complex lipids, fatty acids and related	0,29
Cysteine	Amino acids	0,68			
Indole-3-acetic acid	Amino acids related	0,66			
Metanephine	Hormones, signal substances and related	0,65			
Tyrosine	Amino acids	0,63			
17-Hydroxypregnenolone	Hormones, signal substances and related	0,62			
3-Hydroxybutyrate	Energy metabolism and related	0,60			
3-Hydroxyisobutyrate	Amino acids related	0,59			
2-Hydroxybutyrate	Energy metabolism and related	0,57			
Creatine	Amino acids related	0,55			
Biotin	Vitamins, cofactors and related	0,46			
Creatinine	Amino acids related	0,40			
Adrenaline (Epinephrine)	Hormones, signal substances and related	0,32			
Cholesterylester C20:4	Complex lipids, fatty acids and related	0,29			

Table S3: Plasma altered metabolites (p<0.1) for both females (left) and males (right) respectively for Streptomycin sulfate treatment. (red = upregulated and yellow = downregulated)

Metabolite	Class	Streptomycin sulfate HD f28	Streptomycin sulfate LD f28
18-Hydroxy-11-deoxycorticosterone	Hormones, signal substances and related	1,82	0,66
3-Hydroxyindole	Amino acids related	1,76	1,95
18-Hydroxy-11-deoxycorticosterone	Hormones, signal substances and related	1,56	0,56
3-Hydroxyisobutyrate	Amino acids related	1,14	0,97
Phosphatidylcholine (C16:0,C20:4)	Complex lipids, fatty acids and related	1,06	1,01
Phosphatidylcholine (C16:0,C22:6)	Complex lipids, fatty acids and related	1,04	1
Phosphatidylcholine (C18:0,C18:1)	Complex lipids, fatty acids and related	0,96	1,04
Phosphatidylcholine (C16:0,C16:0)	Complex lipids, fatty acids and related	0,92	0,89
Palmitic acid (C16:0)	Complex lipids, fatty acids and related	0,92	1,15
myo-Inositol	Carbohydrates and related	0,91	1,02
Ethanolamine	Miscellaneous	0,9	1
Stearic acid (C18:0)	Complex lipids, fatty acids and related	0,89	1,14
Unoleic acid (C18:cis[9,12]2)	Complex lipids, fatty acids and related	0,89	1,19
Taurine	Amino acids	0,87	0,86
Cholesterylester, total	Complex lipids, fatty acids and related	0,86	0,98
17-Methyloctadecanoic acid	Complex lipids, fatty acids and related	0,86	1,27
Allantoin	Nucleobases and related	0,85	0,83
Phosphate, lipid fraction	Complex lipids, fatty acids and related	0,82	1,04
alpha-Tocopherol	Vitamins, cofactors and related	0,79	0,95
Creatinine	Amino acids related	0,79	1,06
Coenzyme Q10	Vitamins, cofactors and related	0,78	0,79
beta-Sitosterol, total	Miscellaneous	0,77	0,83
Glucose-6-phosphate	Energy metabolism and related	0,73	0,71
dihomo-gamma-Linolenic acid (C20:cis[8,11,14]3)	Complex lipids, fatty acids and related	0,7	1,16
Kynurenic acid	Amino acids related	0,69	0,65
Lignoceric acid (C24:0)	Complex lipids, fatty acids and related	0,67	0,94
Eicosanoic acid (C20:0)	Complex lipids, fatty acids and related	0,66	1,28
Ceramide (d18:1,C24:1)	Complex lipids, fatty acids and related	0,62	0,78
Indole-3-acetic acid	Amino acids related	0,61	0,51
Coenzyme Q9	Vitamins, cofactors and related	0,55	0,83

Metabolite	Class	Streptomycin sulfate HD m28	Streptomycin sulfate LD m28
Taurocholic acid	Complex lipids, fatty acids and related	2,39	2,29
Malate	Energy metabolism and related	1,34	1,21
Lysophosphatidylcholine (C16:0)	Complex lipids, fatty acids and related	1,18	1,02
Lysophosphatidylcholine (C20:4)	Complex lipids, fatty acids and related	1,04	1,02
Glycolate	Miscellaneous	0,93	0,86
Allantoin	Nucleobases and related	0,91	0,89
Ceramide (d18:1,C24:0)	Complex lipids, fatty acids and related	0,89	0,87
Hexadecanol	Complex lipids, fatty acids and related	0,86	0,83
Taurine	Amino acids	0,85	0,81
Urea	Amino acids related	0,84	0,88
Ceramide (d18:1,C24:1)	Complex lipids, fatty acids and related	0,82	1,01
Fructose-6-phosphate	Energy metabolism and related	0,81	0,72
Taurine	Amino acids	0,79	0,76
Threonic acid	Vitamins, cofactors and related	0,75	0,72
3-Indoxylsulfate	Amino acids related	0,67	0,47
Metanephine	Hormones, signal substances and related	0,59	0,56
Pregnenolone	Hormones, signal substances and related	0,52	0,78
4-Hydroxyphenylpyruvate	Amino acids related	0,49	0,79
Glycochenodeoxycholic acid	Complex lipids, fatty acids and related	0,27	0,22
Cortisol	Hormones, signal substances and related	0,22	0,48
Hippuric acid	Miscellaneous	0,12	0,16
Cholic acid	Complex lipids, fatty acids and related	0,11	NA

Table S4: Plasma altered metabolites (p<0.1) for both females (left) and males (right) respectively for Roxithromycin treatment. (red = upregulated and yellow = downregulated)

Metabolite	Class	Roxithromycin HD	Roxithromycin LD	Metabolite	Class	Roxithromycin m28	Roxithromycin m28
		f28	f28			m28	m28
Taurocholic acid	Complex lipids, fatty acids and related	6.62	3.78	Taurocholic acid	Complex lipids, fatty acids and related	15.28	6.02
Dopamine	Hormones, signal substances and related	2.75	1.29	3-O-Methylsphingosine (d18:1)	Complex lipids, fatty acids and related	3.01	NA
Biotin	Vitamins, cofactors and related	2.09	1.57	Dopamine	Hormones, signal substances and related	2.75	1.13
3,4-Dihydroxyphenylacetic acid (DOPAC)	Hormones, signal substances and related	1.96	1.44	Histamine	Hormones, signal substances and related	2.48	2.01
Histamine	Hormones, signal substances and related	1.84	1.94	Cystine	Amino acids	2.44	0.63
TAG (C16:0,C16:1)	Complex lipids, fatty acids and related	1.67	1.27	3-Hydroxyindole	Amino acids related	2.30	1.64
Phosphate (inorganic and from organic phosphates)	Miscellaneous	1.61	1.37	Pyruvate	Energy metabolism and related	1.91	1.10
Pyruvate	Energy metabolism and related	1.42	1.15	Cysteine	Amino acids	1.67	0.98
trans-4-Hydroxyproline	Amino acids related	1.41	1.15	Pyruvate	Energy metabolism and related	1.64	1.52
Glycine	Amino acids	1.35	0.96	Phosphate (inorganic and from organic phosphates)	Miscellaneous	1.53	1.22
Creatinine	Amino acids related	1.34	1.27	Lactate	Energy metabolism and related	1.49	1.26
Mannose	Carbohydrates and related	1.30	1.59	myo-Inositol-2-phosphate	Carbohydrates and related	1.47	1.40
Taurine	Amino acids	1.30	1.41	Tricosanoic acid (C23:0)	Complex lipids, fatty acids and related	1.45	1.10
Choline plasmalogen (C18-vinyl,C20:4)	Complex lipids, fatty acids and related	1.27	0.77	3,4-Dihydroxyphenylglycol (DOPEG)	Hormones, signal substances and related	1.36	1.29
Phosphatidylcholine (C16:1,C18:2)	Complex lipids, fatty acids and related	1.26	1.01	Ornithine	Amino acids related	1.35	1.01
Citrulline	Amino acids related	1.24	1.44	Citrate	Energy metabolism and related	1.34	1.00
Proline	Amino acids	1.21	1.08	Glucose	Carbohydrates and related	1.33	1.15
Urea	Amino acids related	1.20	1.06	3-Methoxytyrosine	Hormones, signal substances and related	1.31	1.19
Proline	Amino acids	1.20	1.00	Proline	Amino acids	1.31	1.05
Hexoses	Carbohydrates and related	1.18	1.27	Choline plasmalogen (C18-vinyl,C20:4)	Complex lipids, fatty acids and related	1.29	1.09
Sphingomyelin (d18:1,C23:0)	Complex lipids, fatty acids and related	1.16	1.09	Citrulline	Amino acids related	1.28	1.06
Phosphatidylcholine No 02	Complex lipids, fatty acids and related	1.11	1.00	Histidine	Amino acids	1.25	1.07
Phosphatidylcholine (C16:0,C16:0)	Complex lipids, fatty acids and related	1.08	0.95	Hexoses	Carbohydrates and related	1.24	1.23
Lyso phosphatidylcholine (C18:1)	Complex lipids, fatty acids and related	1.06	1.03	Mannose	Carbohydrates and related	1.23	1.17
Phosphatidylcholine (C18:0,C20:4)	Complex lipids, fatty acids and related	0.99	0.98	Alanine	Amino acids	1.21	1.07
Phenylalanine	Amino acids	0.95	1.09	Proline	Amino acids	1.18	0.94
17-Methyltadecanoic acid	Complex lipids, fatty acids and related	0.82	0.72	Isoleucine	Amino acids	0.78	0.85
Lyso phosphatidylcholine (C20:4)	Complex lipids, fatty acids and related	0.81	0.94	Kynurenic acid	Amino acids related	0.78	0.88
Valine	Amino acids	0.80	1.09	3-Hydroxyisobutyrate	Amino acids related	0.77	0.95
Uric acid	Nucleobases and related	0.79	0.96	Dodecanol	Complex lipids, fatty acids and related	0.77	0.86
Stearic acid (C18:0)	Complex lipids, fatty acids and related	0.78	1.06	Theonic acid	Vitamins, cofactors and related	0.76	0.88
Glutamate	Amino acids	0.78	0.94	Lyso phosphatidylcholine (C20:4)	Complex lipids, fatty acids and related	0.74	0.81
Tryptophan	Amino acids	0.78	0.96	Lyso phosphatidylcholine (C20:4)	Complex lipids, fatty acids and related	0.74	0.76
Isoleucine	Amino acids	0.74	1.00	DAG (C18:1,C18:2)	Complex lipids, fatty acids and related	0.74	0.85
16-Methylheptadecanoic acid	Complex lipids, fatty acids and related	0.73	0.64	scyllo-Inositol	Carbohydrates and related	0.70	0.68
Leucine	Amino acids	0.72	1.02	Isopalmitic acid (C16:0)	Complex lipids, fatty acids and related	0.66	0.69
Ketoleucine	Amino acids related	0.65	0.84	4-Hydroxyphenylpyruvate	Amino acids related	0.66	0.73
Glutamine	Amino acids	0.65	0.86	Spermidine	Miscellaneous	0.64	1.04
Metanephrine	Hormones, signal substances and related	0.64	0.68	Glutamate	Amino acids	0.60	0.98
3-Hydroxybutyrate	Energy metabolism and related	0.64	0.70	18-Hydroxy-11-deoxycorticosterone	Hormones, signal substances and related	0.60	1.99
3-Phosphoglycerate (3-PGA)	Energy metabolism and related	0.60	1.01	Glutamate	Amino acids	0.58	0.81
Lysine	Amino acids	0.56	0.99	3-Hydroxybutyrate	Energy metabolism and related	0.56	0.57
Cholesteryl ester C20:4	Complex lipids, fatty acids and related	0.53	0.78	myo-Inositol-2-phosphate, lipid fraction (myo-Inositol)	Complex lipids, fatty acids and related	0.50	0.47
Glucose	Carbohydrates and related	0.39	1.01	2-Hydroxybutyrate	Energy metabolism and related	0.46	0.69
4-Hydroxyphenylpyruvate	Amino acids related	0.39	0.75	3-Hydroxybutyrate	Energy metabolism and related	0.42	0.56
2-Hydroxybutyrate	Energy metabolism and related	0.36	0.82	Androstenedione	Hormones, signal substances and related	0.34	0.31
17-Hydroxyprogesterone	Hormones, signal substances and related	0.31	0.48	Testosterone	Hormones, signal substances and related	0.31	0.28
Adrenaline (Epinephrine)	Hormones, signal substances and related	0.15	0.17	21-Hydroxyprogesterone (11-Deoxycorticosterone)	Hormones, signal substances and related	0.28	1.42
				Adrenaline (Epinephrine)	Hormones, signal substances and related	0.26	1.14
				Progesterone	Hormones, signal substances and related	0.25	1.34
				Hippuric acid	Miscellaneous	0.23	0.21
				Cortisol	Hormones, signal substances and related	0.22	0.22
				Glycochenodeoxycholic acid	Complex lipids, fatty acids and related	0.20	0.07
				1,5-Anhydrosorbitol	Carbohydrates and related	0.17	1.02

Table S5: Plasma altered metabolites (p<0.1) for both females (left) and males (right) respectively for Sparfloxacin treatment. (red = upregulated and yellow = downregulated)

Metabolite	Class	Sparfloxacin HD	Sparfloxacin LD	Metabolite	Class	Sparfloxacin m28	Sparfloxacin m28
		f28	f28			m28	m28
Cholic acid	Complex lipids, fatty acids and related	6.82	0.31	Mannose	Carbohydrates and related	2.54	0.90
3,4-Dihydroxyphenylacetic acid (DOPAC)	Hormones, signal substances and related	3.69	0.82	2-Hydroxybutyrate	Energy metabolism and related	1.55	1.05
Creatinine	Amino acids related	2.50	1.11	Lactate	Energy metabolism and related	1.37	0.82
Noradrenaline (Norepinephrine)	Hormones, signal substances and related	2.20	0.33	Pyruvate	Energy metabolism and related	1.37	1.09
Phosphate (Inorganic and from organic phosphates)	Miscellaneous	1.78	1.05	myo-Inositol-2-phosphate	Carbohydrates and related	1.34	1.02
Coenzyme Q9	Vitamins, cofactors and related	1.78	1.02	Sphingomyelin (d18:1,C16:0)	Complex lipids, fatty acids and related	1.21	0.95
Coenzyme Q10	Vitamins, cofactors and related	1.72	1.17	Uric acid	Nucleobases and related	1.20	0.97
Mannose	Carbohydrates and related	1.65	1.04	TAG (C16:0,C18:2)	Complex lipids, fatty acids and related	1.18	1.12
Ethanolamine plasmalogen (C39:4)	Complex lipids, fatty acids and related	1.64	1.14	Taurine	Amino acids	1.18	1.17
Choline plasmalogen (C18-vinyl,C20:4)	Complex lipids, fatty acids and related	1.49	1.07	Phosphatidylcholine (C18:1,C18:2)	Complex lipids, fatty acids and related	1.12	0.94
Erythronic acid	Carbohydrates and related	1.47	0.98	Phosphatidylcholine (C16:0,C18:2)	Complex lipids, fatty acids and related	1.04	0.96
3-Methoxytyrosine	Hormones, signal substances and related	1.44	0.97	Indole-3-acetic acid	Amino acids related	0.70	1.10
Allantoin	Nucleobases and related	1.37	1.00	Ceramide (d18:1,C24:0)	Complex lipids, fatty acids and related	0.69	1.12
Taurine	Amino acids	1.36	1.38	alpha-Tocopherol	Vitamins, cofactors and related	0.67	1.03
myo-Inositol-2-phosphate	Carbohydrates and related	1.33	1.13	Sphingomyelin (d18:1,C23:0)	Complex lipids, fatty acids and related	0.64	0.92
Glucuronic acid	Carbohydrates and related	1.32	0.99	5-Oxoproline	Amino acids related	0.64	0.95
Deoxyribonucleic acids, total	Carbohydrates and related	1.32	0.83	Kynurenic acid	Amino acids related	0.64	0.93
Arginine	Amino acids	1.25	1.03	Glutamate	Amino acids	0.75	0.64
Glycine	Amino acids	1.22	0.88	Methionine	Amino acids	0.64	0.74
Citrulline	Amino acids related	1.19	1.05	Sphingomyelin (d18:2,C18:0)	Complex lipids, fatty acids and related	0.63	1.13
Phosphatidylcholine (C16:0,C16:0)	Complex lipids, fatty acids and related	1.13	0.99	Glutamine	Amino acids	0.63	0.98
Hexoses	Carbohydrates and related	1.09	1.15	Stearic acid (C18:0)	Complex lipids, fatty acids and related	0.63	1.00
Phosphatidylcholine (C18:0,C22:6)	Complex lipids, fatty acids and related	1.07	0.98	Tyrosine	Amino acids	0.63	0.89
Phosphatidylcholine (C16:0,C20:4)	Complex lipids, fatty acids and related	1.03	0.99	Lyso phosphatidylcholine (C17:0)	Complex lipids, fatty acids and related	0.62	0.94
Kynurenic acid	Amino acids related	0.68	0.82	Indole-3-lactic acid	Amino acids related	0.62	0.88
17-Methyltadecanoic acid	Complex lipids, fatty acids and related	0.67	1.26	Theonic acid	Vitamins, cofactors and related	0.62	0.75
Sphingomyelin (d18:2,C18:0)	Complex lipids, fatty acids and related	0.66	0.98	Tryptophan	Amino acids	0.59	0.69
Glycerol, polar fraction	Complex lipids, fatty acids and related	0.66	1.03	Tryptophan	Amino acids	0.58	0.90
Stearic acid (C18:0)	Complex lipids, fatty acids and related	0.66	1.05	Elaidic acid (C18:trans[9]1)	Complex lipids, fatty acids and related	0.56	0.88
Phosphocreatine	Amino acids related	0.66	0.93	Coenzyme Q10	Vitamins, cofactors and related	0.56	1.29
Malate	Energy metabolism and related	0.66	1.05	Glutamate	Amino acids	0.54	0.87
Cysteine	Amino acids	0.64	1.01	Ketoleucine	Amino acids related	0.49	0.81
Archidonic acid (C20:cis[5,8,11,14]4)	Complex lipids, fatty acids and related	0.64	1.09	Oleic acid (C18:cis[9]1)	Complex lipids, fatty acids and related	0.48	1.13
4-Hydroxy-3-methoxyphenylglycol (HMPG)	Hormones, signal substances and related	0.62	1.03	Heptadecanoic acid (C17:0)	Complex lipids, fatty acids and related	0.47	1.02
3-Hydroxybutyrate	Energy metabolism and related	0.61	1.00	Linoleic acid (C18:cis[9,12]2)	Complex lipids, fatty acids and related	0.47	1.17
Galactose, lipid fraction	Complex lipids, fatty acids and related	0.60	1.34	Glucuronic acid	Carbohydrates and related	0.46	1.23
Metanephrine	Hormones, signal substances and related	0.59	0.76	Arachidonic acid (C20:cis[5,8,11,14]4)	Complex lipids, fatty acids and related	0.41	1.10
Malate	Energy metabolism and related	0.59	0.92	Glycerol, lipid fraction	Complex lipids, fatty acids and related	0.40	0.81
3-Hydroxybutyrate	Energy metabolism and related	0.59	0.99	3-Hydroxybutyrate	Energy metabolism and related	0.39	1.15
3-O-Methylsphingosine (d18:1)	Complex lipids, fatty acids and related	0.56	1.09	Sphingomyelin (d18:2,C16:0)	Complex lipids, fatty acids and related	0.38	1.42
2-Hydroxybutyrate	Energy metabolism and related	0.54	1.09	Isopalmitic acid (C16:0)	Complex lipids, fatty acids and related	0.38	1.29
alpha-Tocopherol	Vitamins, cofactors and related	0.53	1.42	Campesterol, total	Miscellaneous	0.34	1.24
myo-Inositol, lipid fraction	Complex lipids, fatty acids and related	0.52	1.08	3-Hydroxybutyrate	Energy metabolism and related	0.32	1.17
3-Phosphoglycerate (3-PGA)	Energy metabolism and related	0.50	0.80	Pantothenic acid	Vitamins, cofactors and related	0.32	0.40
Pantothenic acid	Vitamins, cofactors and related	0.50	0.44	Myristic acid (C14:0)	Complex lipids, fatty acids and related	0.29	1.06
Lignoceric acid (C24:0)	Complex lipids, fatty acids and related	0.46	0.92	Androstenedione	Hormones, signal substances and related	0.23	0.39
16-Methylheptadecanoic acid	Complex lipids, fatty acids and related	0.44	1.15	Energy metabolism and related	Energy metabolism and related	0.23	1.13
Indole-3-acetic acid	Amino acids related	0.43	0.64	Hormones, signal substances and related	Hormones, signal substances and related	0.21	0.49
5-O-Methylsphingosine (d18:1)	Complex lipids, fatty acids and related	0.39	0.84	Citrate	Energy metabolism and related	0.17	1.02
21-Hydroxyprogesterone (11-Deoxycorticosterone)	Hormones, signal substances and related	0.30	1.87	Biotin	Vitamins, cofactors and related	0.05	0.07
scyllo-Inositol	Carbohydrates and related	0.25	0.86				
myo-Inositol-2-phosphate, lipid fraction (myo-Inosit	Complex lipids, fatty acids and related	0.21	1.50				
Biotin	Vitamins, cofactors and related	0.17	0.45				

Table S6: Plasma altered metabolites (p<0.1) for both females (left) and males (right) respectively for Vancomycin treatment. (red = upregulated and yellow = downregulated)

Metabolite	Class	Vancomycin HD	Vancomycin LD
		f28	f28
Taurocholic acid	Complex lipids, fatty acids and related	4.45	4.86
2-Hydroxybutyrate	Energy metabolism and related	1.74	1.55
Taurine	Amino acids	1.44	0.93
Citrate	Energy metabolism and related	1.57	1.27
17-Methyloctadecanoic acid	Complex lipids, fatty acids and related	1.55	0.91
Dopamine	Hormones, signal substances and related	1.53	1.15
Phosphate (inorganic and from organic phosphates)	Miscellaneous	1.24	1.13
Unolenic acid (C18:cis[9,12,15]3)	Complex lipids, fatty acids and related	1.21	0.90
Lysophosphatidylcholine (C17:0)	Complex lipids, fatty acids and related	0.94	0.90
Ascorbic acid	Vitamins, cofactors and related	0.87	0.98
Tryptophan	Amino acids	0.85	0.85
Glycine	Amino acids	0.83	0.92
Ceramide (d18:1,C24:1)	Complex lipids, fatty acids and related	0.75	0.77
Threonine	Amino acids	0.72	0.89
Proline	Amino acids	0.70	0.85
Indole-3-acetic acid	Amino acids related	0.57	0.58
Kynurenic acid	Amino acids related	0.44	0.58
3,3',5-Triiodothyronine (T3)	Hormones, signal substances and related	0.20	1.20
Hippuric acid	Miscellaneous	0.17	0.63
Cholic acid	Complex lipids, fatty acids and related	0.01	0.19

Metabolite	Class	Vancomycin (MOA89) HD	Vancomycin (MOA89) LD
		m28	m28
17-Hydroxypregnenolone	Hormones, signal substances and related	4.09	2.99
Taurocholic acid	Complex lipids, fatty acids and related	3.12	3.35
Glucosamine	Carbohydrates and related	1.43	1.04
Tryptophan	Amino acids	1.42	1.10
Sucrose	Carbohydrates and related	1.38	1.53
Indole-3-lactic acid	Amino acids related	1.31	1.04
Unknown Lipid (68000024)	Unknown	1.29	1.13
Biotin	Vitamins, cofactors and related	1.29	1.11
Hexoses	Carbohydrates and related	1.16	1.26
Octadecanol	Complex lipids, fatty acids and related	1.14	1.15
Ascorbic acid	Vitamins, cofactors and related	1.12	0.99
Malate	Energy metabolism and related	1.10	1.09
Tryptophan	Amino acids	1.06	0.99
PC No 04 (putative)	Unknown	0.93	0.99
Cytosine	Nucleobases and related	0.88	0.80
3-Hydroxysubutyrate	Amino acids related	0.87	0.93
2-Hydroxybutyrate	Energy metabolism and related	0.86	1.06
3-Hydroxybutyrate	Energy metabolism and related	0.85	0.87
Allantoin	Nucleobases and related	0.84	0.85
Lysophosphatidylcholine (C20:4)	Complex lipids, fatty acids and related	0.83	0.93
3-Hydroxybutyrate	Energy metabolism and related	0.83	1.13
Tyrosine	Amino acids	0.82	0.83
Glycine	Amino acids	0.81	0.89
Glycolate	Miscellaneous	0.79	0.80
Dopamine	Hormones, signal substances and related	0.77	0.87
Spermidine	Miscellaneous	0.77	0.89
Noradrenaline (Norepinephrine)	Hormones, signal substances and related	0.64	0.75
myo-Inositol-2-phosphate, lipid fraction (myo-Inositolphospholipids)	Amino acids related	0.60	0.70
Inositolphospholipids	Complex lipids, fatty acids and related	0.46	0.81
Hippuric acid	Miscellaneous	0.13	0.14
Cholic acid	Complex lipids, fatty acids and related	0.00	0.14

Table S7: Plasma altered metabolites (p<0.1) for both females (left) and males (right) respectively for Clindamycin hydrochloride treatment (red = upregulated and yellow = downregulated)

Metabolite	Class	Clindamycinhydr ochlorid HD	Clindamycinhydr ochlorid LD
		f28	f28
Palmitoleic acid (C16:cis[9]1)	Complex lipids, fatty acids and related	2.37	1.45
Eicosanoic acid (C20:1) No 02	Complex lipids, fatty acids and related	2.08	0.91
Nervonic acid (C24:cis[15]1)	Complex lipids, fatty acids and related	2.00	1.16
Biotin	Vitamins, cofactors and related	1.82	1.54
Threonine	Amino acids	1.74	0.96
2-Hydroxybutyrate	Energy metabolism and related	1.69	1.93
Serine	Amino acids	1.63	1.04
Threonine	Amino acids	1.62	0.88
Oleic acid (C18:cis[9]1)	Complex lipids, fatty acids and related	1.59	0.99
Pregnenolone	Hormones, signal substances and related	1.57	1.40
Aspartate	Amino acids	1.46	0.99
TAG (C16:0,C16:1)	Complex lipids, fatty acids and related	1.40	0.84
alpha-Tocopherol	Vitamins, cofactors and related	1.36	1.02
Glutamate	Amino acids	1.30	1.15
Glycine	Amino acids	1.29	0.91
Methionine	Amino acids	1.27	1.21
Coenzyme Q9	Vitamins, cofactors and related	1.20	1.25
Sphingomyelin (d18:2,C16:0)	Complex lipids, fatty acids and related	1.19	1.13
Arginine	Amino acids	1.18	1.04
TAG (C18:1,C18:2)	Complex lipids, fatty acids and related	1.17	0.66
Deoxyribonucleic acids, total	Carbohydrates and related	1.17	1.12
Leucine	Amino acids	1.17	0.95
Sphingomyelin (d18:1,C24:1)	Complex lipids, fatty acids and related	1.16	1.10
Methionine	Amino acids	1.16	1.07
Phenylalanine	Amino acids	1.16	1.08
3-Methoxytyrosine	Hormones, signal substances and related	1.13	0.94
5-Oxoproline	Amino acids related	1.12	0.88
Palmitic acid (C16:0)	Complex lipids, fatty acids and related	1.12	0.97
Valine	Amino acids	1.11	0.91
Proline	Amino acids	1.08	0.91
Campesterol, total	Miscellaneous	0.82	1.03
3,4-Dihydroxyphenylalanine (DOPA)	Hormones, signal substances and related	0.79	0.81
4-Hydroxy-3-methoxyphenylglycol (HMPG)	Hormones, signal substances and related	0.78	0.82
Phosphatidylcholine (C16:0,C16:0)	Complex lipids, fatty acids and related	0.78	0.92
Tryptophan	Amino acids	0.76	1.24
Heptadecanoic acid (C17:0)	Complex lipids, fatty acids and related	0.74	0.71
Choline plasmalogen (C36:2) (putative)	Unknown	0.73	0.86
Lysophosphatidylcholine (C17:0)	Complex lipids, fatty acids and related	0.68	0.93
Indole-3-lactic acid	Amino acids related	0.65	1.14
beta-Sitosterol, total	Miscellaneous	0.63	0.89
Pyruvate	Energy metabolism and related	0.58	0.74
17-Methyloctadecanoic acid	Complex lipids, fatty acids and related	0.56	0.97
Testosterone	Hormones, signal substances and related	0.52	0.52
Lysio PE (C22:0) (putative)	Unknown	0.52	0.79
Lactate	Energy metabolism and related	0.46	0.48
Malate	Energy metabolism and related	0.40	0.54
Hippuric acid	Miscellaneous	0.14	0.12
1,5-Anhydrosorbitol	Carbohydrates and related	0.11	0.31
Glycochenodeoxycholic acid	Complex lipids, fatty acids and related	0.10	0.21
17-Hydroxypregnenolone	Hormones, signal substances and related	0.00	0.08
Cholic acid	Complex lipids, fatty acids and related	0.00	0.01

Metabolite	Class	Clindamycinhydr ochlorid HD	Clindamycinhydr ochlorid LD
		m28	m28
Indole-3-acetic acid	Amino acids related	6.08	7.34
Serotonin (5-HT)	Hormones, signal substances and related	2.83	3.60
Eicosanoic acid (C20:1) No 02	Complex lipids, fatty acids and related	2.80	1.22
Nervonic acid (C24:cis[15]1)	Complex lipids, fatty acids and related	1.94	1.55
3-O-Methylsphingosine (d18:1)	Complex lipids, fatty acids and related	1.87	1.20
alpha-Tocopherol	Vitamins, cofactors and related	1.84	0.97
5-O-Methylsphingosine (d18:1)	Complex lipids, fatty acids and related	1.75	1.27
Dodecanol	Complex lipids, fatty acids and related	1.69	1.45
erythro-Sphingosine (d18:1)	Complex lipids, fatty acids and related	1.64	1.22
2-Hydroxybutyrate	Energy metabolism and related	1.60	1.45
three-Sphingosine (d18:1)	Complex lipids, fatty acids and related	1.58	1.27
Lignoceric acid (C24:0)	Complex lipids, fatty acids and related	1.57	1.36
alpha-Tocopherol	Vitamins, cofactors and related	1.54	1.34
4-Hydroxyphinganine (t18:0, Phytosphingosine), total	Complex lipids, fatty acids and related	1.50	1.25
Sphingomyelin (d18:2,C18:0)	Complex lipids, fatty acids and related	1.48	1.21
Uric acid	Nucleobases and related	1.48	1.11
Galactose, lipid fraction	Complex lipids, fatty acids and related	1.46	0.98
Cholesterol, total	Cholesterol, total	1.46	1.08
Behenic acid (C22:0)	Complex lipids, fatty acids and related	1.45	1.01
Cholesterol, total	Cholesterol, total	1.44	1.15
Malate	Energy metabolism and related	1.43	1.22
Cholesterol, total	Cholesterol, total	1.36	1.08
myo-Inositol, lipid fraction	Complex lipids, fatty acids and related	1.33	1.11
Glutamate	Amino acids	1.29	1.01
Serine	Amino acids	1.23	1.12
myo-Inositol-2-phosphate, lipid fraction (myo-Inositolphospholipids)	Complex lipids, fatty acids and related	1.23	0.79
Phosphate, lipid fraction	Complex lipids, fatty acids and related	1.23	1.02
alpha-Tocopherol	Vitamins, cofactors and related	1.23	1.01
Ceramide (d18:1,C24:1)	Complex lipids, fatty acids and related	1.22	0.99
Phosphate (inorganic and from organic phosphates)	Miscellaneous	1.20	1.01
Stearic acid (C18:0)	Complex lipids, fatty acids and related	1.20	0.99
Lysine	Amino acids	1.19	1.06
Phosphatidylcholine (C18:0,C18:1)	Complex lipids, fatty acids and related	1.15	1.00
Phosphatidylcholine (C16:1,C18:2)	Complex lipids, fatty acids and related	1.11	1.00
Lysophosphatidylcholine (C18:0)	Complex lipids, fatty acids and related	1.02	1.04
Phosphatidylcholine No 02	Complex lipids, fatty acids and related	0.96	0.97
Creatinine	Amino acids related	0.94	1.25
Methionine	Amino acids	0.93	1.00
Threonine	Amino acids	0.90	0.90
Tyrosine	Amino acids	0.89	0.89
Threonine	Amino acids	0.89	0.89
Phenylalanine	Amino acids	0.88	0.91
Deoxyribonucleic acids, total	Carbohydrates and related	0.87	0.99
Glucose	Carbohydrates and related	0.84	0.84
3-Methoxytyrosine	Hormones, signal substances and related	0.81	0.87
Creatinine	Amino acids related	0.81	1.08
Cytosine	Nucleobases and related	0.79	0.86
Lysophosphatidylcholine (C17:0)	Complex lipids, fatty acids and related	0.73	0.83
DiAG (C18:1,C18:2)	Complex lipids, fatty acids and related	0.67	0.81
Heptadecanoic acid (C17:0)	Complex lipids, fatty acids and related	0.64	0.76
Thyrosine (T4)	Hormones, signal substances and related	0.54	0.57
1,5-Anhydrosorbitol	Carbohydrates and related	0.20	0.47
Hippuric acid	Miscellaneous	0.14	0.10
Cholic acid	Complex lipids, fatty acids and related	0.00	0.00

Table S8: Plasma altered metabolites (p<0.1) for both females (left) and males (right) respectively for Lincomycin hydrochloride treatment (red = upregulated and yellow = downregulated)

		Lincomycinhydrochlorid	Lincomycinhydrochlorid
		HD	LD
Metabolite	Class	f28	f28
Indole-3-acetic acid	Amino acids related	5,65	0,62
Hippuric acid	Miscellaneous	1,78	1,96
Taurolcholic acid	Complex lipids, fatty acids and related	1,58	1,83
Coenzyme Q10	Vitamins, cofactors and related	1,57	1,09
Creatinine	Amino acids related	1,56	1,96
Phosphatidylcholine (C16:0,C18:2)	Complex lipids, fatty acids and related	1,42	1,06
Urea	Amino acids related	1,42	1,10
Creatine	Amino acids related	1,42	1,34
16-Methylheptadecanoic acid	Complex lipids, fatty acids and related	1,41	0,97
TAG (C16:0,C16:1)	Complex lipids, fatty acids and related	1,34	0,63
Arginine	Amino acids	1,31	1,22
Taurine	Amino acids	1,31	1,11
Citrulline	Amino acids related	1,31	1,05
Tricosanoic acid (C23:0)	Complex lipids, fatty acids and related	1,28	1,24
Arginine	Amino acids	1,18	1,13
Oleic acid (C18:cis[9]1)	Complex lipids, fatty acids and related	1,16	0,86
Ornithine	Amino acids related	1,15	0,97
trans-4-Hydroxyproline	Amino acids related	1,14	1,00
Palmitoleic acid (C16:cis[9]1)	Complex lipids, fatty acids and related	1,14	0,72
TAG (C16:0,C18:2)	Complex lipids, fatty acids and related	1,11	1,03
Proline	Amino acids	1,11	1,05
Hexadecanol	Complex lipids, fatty acids and related	1,10	1,07
Phosphatidylcholine (C16:1,C18:2)	Complex lipids, fatty acids and related	1,07	1,03
Cholesteryl ester, total	Complex lipids, fatty acids and related	1,03	1,01
Phosphatidylcholine (C18:0,C20:3)		1,01	1,02
Hexoses	Carbohydrates and related	0,94	0,96
Lysophosphatidylcholine (C17:0)	Complex lipids, fatty acids and related	0,92	0,88
Lysophosphatidylcholine (C20:4)	Complex lipids, fatty acids and related	0,90	0,97
Glycolate	Miscellaneous	0,90	1,03
Glutamine	Amino acids	0,85	0,87
Ketoleucine	Amino acids related	0,81	1,08
Kynurenic acid	Amino acids related	0,81	0,78
Tryptophan	Amino acids	0,81	0,88
3-Methoxytyrosine	Hormones, signal substances and related	0,77	0,96
Indole-3-lactic acid	Amino acids related	0,77	0,84
Lyso PE (C22:0) (putative)	Unknown	0,74	0,81
Histamine	Hormones, signal substances and related	0,73	1,14
Phosphocreatine	Amino acids related	0,73	0,63
Uric acid	Nucleobases and related	0,70	0,87
Fructose-6-phosphate	Energy metabolism and related	0,69	0,83
Uric acid	Nucleobases and related	0,66	1,08
Glucose-6-phosphate	Energy metabolism and related	0,64	0,67
Glucose	Carbohydrates and related	0,58	0,96
1,5-Anhydrosorbitol	Carbohydrates and related	0,44	0,70
Glycochenodeoxycholic acid	Complex lipids, fatty acids and related	0,18	0,18
Serotonin (5-HT)	Hormones, signal substances and related	0,02	0,09
17-Hydroxypregnenolone	Hormones, signal substances and related	0,00	0,00

		Lincomycinhydrochlorid	Lincomycinhydrochlorid
		HD	LD
Metabolite	Class	m28	m28
Taurolcholic acid	Complex lipids, fatty acids and related	4,63	4,22
Hippuric acid	Miscellaneous	2,73	1,30
Serotonin (5-HT)	Hormones, signal substances and related	2,32	1,02
Metanephrene	Hormones, signal substances and related	1,56	1,05
gamma-Linolenic acid (C18:cis[6,9,12]3)	Complex lipids, fatty acids and related	1,56	1,18
Tryptophan	Amino acids	1,49	1,08
Creatinine	Amino acids related	1,48	1,20
Palmitoleic acid (C16:cis[9]1)	Complex lipids, fatty acids and related	1,46	1,31
Uric acid	Nucleobases and related	1,34	0,91
4-Hydroxy-3-methoxyphenylglycol (HMPG)	Hormones, signal substances and related	1,26	1,10
Dopamine	Hormones, signal substances and related	1,24	1,31
Oleic acid (C18:cis[9]1)	Complex lipids, fatty acids and related	1,18	1,29
Citrulline	Amino acids related	1,16	0,99
Phosphatidylcholine (C16:0,C20:5)	Complex lipids, fatty acids and related	1,06	1,05
Lysophosphatidylcholine (C20:4)	Complex lipids, fatty acids and related	1,05	1,03
TAG (C16:0,C18:2)	Complex lipids, fatty acids and related	1,04	1,08
Phosphatidylcholine No 02	Complex lipids, fatty acids and related	1,04	1,04
Phosphatidylcholine (C18:0,C20:4)	Complex lipids, fatty acids and related	0,95	0,96
Glycine	Amino acids	0,95	0,92
Allantoin	Nucleobases and related	0,92	0,87
Tryptophan	Amino acids	0,92	0,82
Ethanolamine plasmalogen (C39:4)	Complex lipids, fatty acids and related	0,91	1,01
Lysophosphatidylcholine (C20:4)	Complex lipids, fatty acids and related	0,91	0,99
Cytosine	Nucleobases and related	0,91	0,96
Deoxyribonucleic acids, total	Carbohydrates and related	0,89	0,94
Lysophosphatidylcholine (C17:0)	Complex lipids, fatty acids and related	0,86	0,93
Isoleucine	Amino acids	0,85	0,87
Phenylalanine	Amino acids	0,82	0,93
Phenylalanine	Amino acids	0,82	0,88
Glutamine	Amino acids	0,82	0,93
Pantothenic acid	Vitamins, cofactors and related	0,81	1,03
Sphingomyelin (d18:1,C23:0)	Complex lipids, fatty acids and related	0,79	0,96
Citrate	Energy metabolism and related	0,79	0,91
Threonine acid	Vitamins, cofactors and related	0,77	0,65
Cystine	Amino acids	0,73	0,75
alpha-Tocopherol	Vitamins, cofactors and related	0,68	1,02
1,5-Anhydrosorbitol	Carbohydrates and related	0,48	0,77
3-Indoxylsulfate	Amino acids related	0,27	0,37
Glycochenodeoxycholic acid	Complex lipids, fatty acids and related	0,04	0,03
Cholic acid	Complex lipids, fatty acids and related	0,01	0,01

Table S9: Feces altered metabolites (p<0.1) for both females (left) and males (right) respectively for restricted diet (red = upregulated and yellow = downregulated)

Metabolite	Class	Restricted diet f28	Metabolite	Class	Restricted diet m28
Linoleic acid (C18:cis[9,12]2)	Complex lipids, fatty acids and related	3,65	TAG (C18:1,C18:2)	Complex lipids, fatty acids and related	6,21
TAG (C16:0,C18:2)	Complex lipids, fatty acids and related	3,62	TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	6,03
Linolenic acid (C18:cis[9,12,15]3)	Complex lipids, fatty acids and related	3,16	TAG (C16:0,C18:2)	Complex lipids, fatty acids and related	4,94
Oleic acid (C18:cis[9]1)	Complex lipids, fatty acids and related	2,76	TAG (C16:0,C18:1,C18:3)	Complex lipids, fatty acids and related	4,90
TAG (C16:0,C18:1,C18:3)	Complex lipids, fatty acids and related	2,70	TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	4,86
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	2,58	Linoleic acid (C18:cis[9,12]2)	Complex lipids, fatty acids and related	3,78
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	2,46	Linolenic acid (C18:cis[9,12,15]3)	Complex lipids, fatty acids and related	3,29
TAG (C18:1,C18:2)	Complex lipids, fatty acids and related	2,01	Oleic acid (C18:cis[9]1)	Complex lipids, fatty acids and related	3,27
beta-Sitosterol, total	Miscellaneous	1,95	TAG (C16:0,C16:1)	Complex lipids, fatty acids and related	2,47
DAG (C18:1,C18:2)	Complex lipids, fatty acids and related	1,89	Palmitoleic acid (C16:ds[9]1)	Complex lipids, fatty acids and related	2,22
Glycerol-3-phosphate, polar fraction	Complex lipids, fatty acids and related	1,86	DAG (C18:1,C18:2)	Complex lipids, fatty acids and related	2,19
Campesterol, total	Miscellaneous	1,62	Cholesteryl ester, total	Complex lipids, fatty acids and related	1,77
trans-4-Hydroxyproline	Amino acids related	1,61	Citrulline	Amino acids related	1,72
Palmitic acid (C16:0)	Complex lipids, fatty acids and related	1,56	Phosphatidylcholine (C16:0,C20:5)	Complex lipids, fatty acids and related	1,66
Glycerol, lipid fraction	Complex lipids, fatty acids and related	1,37	Nervonic acid (C24:cis[15]1)	Complex lipids, fatty acids and related	1,66
alpha-Tocopherol	Vitamins, cofactors and related	1,32	Phosphatidylcholine (C16:1,C18:2)	Complex lipids, fatty acids and related	1,58
Lysophosphatidylcholine (C18:2)	Complex lipids, fatty acids and related	1,22	Lysophosphatidylcholine (C18:1)	Complex lipids, fatty acids and related	1,56
Citrulline	Amino acids related	1,22	alpha-Tocopherol	Vitamins, cofactors and related	1,36
Pyruvate	Energy metabolism and related	1,20	beta-Sitosterol, total	Miscellaneous	1,32
Lysophosphatidylcholine (C20:4)	Complex lipids, fatty acids and related	0,56	alpha-Tocopherol	Vitamins, cofactors and related	1,30
Indole-3-acetic acid	Amino acids related	0,56	Palmitic acid (C16:0)	Complex lipids, fatty acids and related	1,25
threo-Sphingosine (d18:1)	Complex lipids, fatty acids and related	0,56	Hippuric acid	Miscellaneous	1,19
Glucose	Carbohydrates and related	0,54	Tyrosine	Amino acids	0,75
dihomo-gamma-Linolenic acid (C20:cis[8,10,12,14,16,18]6)	Complex lipids, fatty acids and related	0,53	Citrate	Energy metabolism and related	0,75
Eicosanoic acid (C20:1) No 02	Complex lipids, fatty acids and related	0,52	Tricosanoic acid (C23:0)	Complex lipids, fatty acids and related	0,75
Choline plasmalogen (C36:2) (putative)	Unknown	0,51	Hexadecanol	Complex lipids, fatty acids and related	0,74
16-Methylheptadecanoic acid	Complex lipids, fatty acids and related	0,51	Glutamate	Amino acids	0,73
5-O-Methylsphingosine (d18:1)	Complex lipids, fatty acids and related	0,48	Phosphate (inorganic and from organic phospholipids)	Miscellaneous	0,70
Tryptophan	Amino acids	0,47	Glucuronic acid	Carbohydrates and related	0,68
Lignoceric acid (C24:0)	Complex lipids, fatty acids and related	0,47	Octadecanol	Complex lipids, fatty acids and related	0,68
Asparagine	Amino acids	0,46	Asparagine	Amino acids	0,65
erythro-Sphingosine (d18:1)	Complex lipids, fatty acids and related	0,41	Proline	Amino acids	0,65
Ethanolamine plasmalogen (C39:4)	Complex lipids, fatty acids and related	0,40	5-Oxoproline	Amino acids related	0,65
Choline plasmalogen (C18-vinyl,C20:4)	Complex lipids, fatty acids and related	0,40	4-Hydroxyphenylpyruvate	Amino acids related	0,64
Ethanolamine plasmalogen (C39:5)	Complex lipids, fatty acids and related	0,35	Lignoceric acid (C24:0)	Complex lipids, fatty acids and related	0,62
4-Hydroxyphenylpyruvate	Complex lipids, fatty acids and related	0,35	Cytosine	Nucleobases and related	0,60
Kynurenic acid	Amino acids related	0,35	Sphingomyelin (d18:2,C18:0)	Complex lipids, fatty acids and related	0,58
Octadecanol	Complex lipids, fatty acids and related	0,34	Histidine	Amino acids	0,58
Hexadecanol	Complex lipids, fatty acids and related	0,33	Glycolate	Miscellaneous	0,57
Taurine	Amino acids	0,19	Glycerol phosphate, lipid fraction	Complex lipids, fatty acids and related	0,56
			Urea	Amino acids related	0,55
			Ethanolamine plasmalogen (C39:5)	Complex lipids, fatty acids and related	0,54
			Uric acid	Nucleobases and related	0,50
			Glucose	Carbohydrates and related	0,48
			Taurine	Amino acids	0,33

Table S10: Feces altered metabolites (p<0.1) for both females (left) and males (right) respectively for Streptomycin sulfate (red = upregulated and yellow = downregulated)

Metabolite	Class	Streptomycin sulfate HD f28	Streptomycin sulfate LD f28	Metabolite	Class	Streptomycin sulfate HD m28	Streptomycin sulfate LD m28
Taurine	Amino acids	44,24	1,27	Taurine	Amino acids	199,53	8,20
Taurine	Amino acids	32,16	0,79	Taurine	Amino acids	43,32	2,29
Kynurenic acid	Amino acids related	24,01	23,48	Allantoin	Nucleobases and related	39,18	0,76
Sphingomyelin (d18:1,C16:0)	Complex lipids, fatty acids and related	8,70	2,54	Valine	Amino acids	32,83	8,00
Cysteine	Amino acids	8,38	3,81	Indole-3-lactic acid	Amino acids related	25,62	30,65
Valine	Amino acids	8,32	1,13	Kynurenic acid	Amino acids related	21,01	32,15
TAG (C16:0,C18:1,C18:3)	Complex lipids, fatty acids and related	5,39	1,79	Pantothenic acid	Vitamins, cofactors and related	19,76	102,12
Isoleucine	Amino acids	4,89	1,21	Isoleucine	Amino acids	15,20	6,29
Valine	Amino acids	4,69	2,07	Leucine	Amino acids	12,72	3,54
Spermidine	Miscellaneous	4,67	3,77	Isoleucine	Amino acids	11,24	3,19
Taurolithic acid	Complex lipids, fatty acids and related	4,53	4,48	Valine	Amino acids	11,03	3,20
Leucine	Amino acids	4,49	1,46	Threonine	Amino acids	9,87	0,82
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	3,82	2,06	Cysteine	Amino acids	9,56	4,02
TAG (C25:5 (H) or C20:2 (Na)) (putative)	Unknown	3,55	1,80	Biotin	Vitamins, cofactors and related	8,67	1,25
Phenylalanine	Amino acids	3,50	2,03	Taurolithic acid	Complex lipids, fatty acids and related	7,71	0,35
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	3,12	1,18	Malate	Energy metabolism and related	7,26	0,85
TAG (C18:1,C18:2)	Complex lipids, fatty acids and related	3,05	1,44	Glucosamine	Carbohydrates and related	4,07	1,70
Glucose	Carbohydrates and related	2,94	0,84	Spermidine	Miscellaneous	4,07	3,52
Cholic acid	Complex lipids, fatty acids and related	2,87	7,68	Glucose	Carbohydrates and related	3,98	0,96
Isoleucine	Amino acids	2,82	1,33	Alanine	Amino acids	2,93	1,41
DAG (C18:1,C18:2)	Complex lipids, fatty acids and related	2,65	1,07	Oleic acid (C18:cis[9]1)	Complex lipids, fatty acids and related	2,91	3,12
Glucosamine	Carbohydrates and related	2,60	3,67	Hexoses	Carbohydrates and related	2,88	1,40
Ketoleucine	Amino acids related	2,51	0,59	Asparagine	Amino acids	2,74	1,73
Glycerol, polar fraction	Complex lipids, fatty acids and related	2,33	1,11	Phenylalanine	Amino acids	2,69	1,56
Glycerol-3-phosphate, polar fraction	Complex lipids, fatty acids and related	2,27	3,58	Hexoses	Carbohydrates and related	2,67	0,92
Omitine	Amino acids related	1,74	1,63	Linoleic acid (C18:cis[9,12]2)	Complex lipids, fatty acids and related	2,66	4,00
Glucuronic acid	Carbohydrates and related	1,69	1,19	Linolenic acid (C18:cis[9,12,15]3)	Complex lipids, fatty acids and related	2,52	2,02
Lignoceric acid (C24:0)	Complex lipids, fatty acids and related	0,59	0,58	Creatine	Amino acids related	2,28	3,02
myo-Inositol, lipid fraction	Complex lipids, fatty acids and related	0,58	0,96	Methionine	Amino acids	2,24	1,29
Tricosanoic acid (C23:0)	Complex lipids, fatty acids and related	0,58	0,70	Sphingomyelin (d18:1,C24:0)	Complex lipids, fatty acids and related	2,22	1,57
Hexadecanol	Complex lipids, fatty acids and related	0,58	0,95	Tryptophan	Amino acids	2,15	1,21
Threonine	Amino acids	0,58	0,94	Sphingomyelin (d18:2,C16:0)	Complex lipids, fatty acids and related	1,17	1,36
Creatinine	Amino acids related	0,55	1,17	18-Hydroxy-11-deoxycorticosterone	Hormones, signal substances and related	0,78	1,23
Heptadecanoic acid (C17:0)	Complex lipids, fatty acids and related	0,55	0,62	Tryptophan	Amino acids	0,74	0,80
Glutamine	Amino acids	0,53	0,77	Glycerol-3-phosphate, polar fraction	Complex lipids, fatty acids and related	0,49	1,26
3-Hydroxybutyrate	Energy metabolism and related	0,52	0,73	Glutamate	Amino acids	0,48	0,90
Glutamate	Amino acids	0,51	1,04	Sphingomyelin (d18:1,C24:1)	Complex lipids, fatty acids and related	0,41	0,60
myo-Inositol	Carbohydrates and related	0,50	0,47	Stearic acid (C18:0)	Complex lipids, fatty acids and related	0,40	0,40
Myristic acid (C14:0)	Complex lipids, fatty acids and related	0,50	0,78	Glutamate	Amino acids	0,36	0,65
Choline plasmalogen (C18-vinyl,C20:4)	Complex lipids, fatty acids and related	0,47	0,42				
Behenic acid (C22:0)	Complex lipids, fatty acids and related	0,47	0,61				
Ethanolamine plasmalogen (C39:4)	Complex lipids, fatty acids and related	0,44	0,58				
Allantoin	Nucleobases and related	0,43	13,61				
Glutamate	Amino acids	0,40	0,74				
Eicosanoic acid (C20:0)	Complex lipids, fatty acids and related	0,40	0,58				
Octadecanol	Complex lipids, fatty acids and related	0,39	0,53				
Glycerol-3-phosphate, polar fraction	Complex lipids, fatty acids and related	0,36	1,15				
Salicylic acid	Miscellaneous	0,34	0,91				
Glucose-6-phosphate	Energy metabolism and related	0,29	0,83				
Fructose-6-phosphate	Energy metabolism and related	0,27	0,72				
Stearic acid (C18:0)	Complex lipids, fatty acids and related	0,19	0,19				

Table S11: Top metabolites in both the directions of feces altered metabolites (p<0.1) for both females (left) and males (right) respectively for Roxithromycin (red = upregulated and yellow = downregulated)

Metabolite	Class	Roxithromycin HD	Roxithromycin LD
		m28	m28
Creatinine	Amino acids related	108.85	179.63
Creatinine	Amino acids related	31.09	50.20
Taurine	Amino acids	19.68	44.33
Creatinine	Amino acids related	15.97	26.89
Allantoin	Nucleobases and related	12.14	27.81
Taurine	Amino acids	10.48	36.81
Kynurenic acid	Amino acids related	8.88	9.17
Isoleucine	Amino acids	8.69	6.84
Valine	Amino acids	6.86	5.18
Leucine	Amino acids	6.15	7.52
Taurocholic acid	Complex lipids, fatty acids and related	6.13	15.70
Tryptophan	Amino acids	4.38	3.05
Phenylalanine	Amino acids	4.35	2.85
Methionine	Amino acids	3.47	4.07
Phenylalanine	Amino acids	3.42	3.53
Isoleucine	Amino acids	3.39	5.01
Arginine	Amino acids	3.18	3.25
Phenylalanine	Amino acids	3.06	3.51
Ketoleucine	Amino acids related	3.09	2.89
Glucose	Carbohydrates and related	2.92	2.55
Methionine	Amino acids	2.75	4.01
Malate	Energy metabolism and related	2.73	3.23
Glucose	Carbohydrates and related	2.57	3.06
Citrate	Energy metabolism and related	2.55	1.71
Arginine	Amino acids	2.48	2.28
Threonine	Amino acids	2.25	1.11
Citrate	Energy metabolism and related	2.24	2.02
Tyrosine	Amino acids	2.23	2.32
Malate	Energy metabolism and related	2.16	3.24
Tyrosine	Amino acids	2.09	2.08
Hexoses	Carbohydrates and related	1.84	2.54
TAG (C16:0,C18:1,C18:3)	Complex lipids, fatty acids and related	1.82	9.48
Indole-3-lactic acid	Amino acids related	1.73	1.92
Cysteine	Amino acids	0.48	1.06
Hippuric acid	Miscellaneous	0.67	1.21
Ethanolamine	Miscellaneous	0.57	0.60
Sphingomyelin (d18:2,C18:0)	Complex lipids, fatty acids and related	0.56	0.62
Phosphatidylcholine (C16:0,C18:0)	Complex lipids, fatty acids and related	0.55	0.61
Ethanolamine plasmalogen (C18:0)	Complex lipids, fatty acids and related	0.54	0.59
Lysophosphatidylcholine (C18:0)	Complex lipids, fatty acids and related	0.54	0.59
Lysophosphatidylcholine (C18:0)	Complex lipids, fatty acids and related	0.54	1.02
Ulinic acid (C24:0)	Complex lipids, fatty acids and related	0.53	0.44
Phosphatidylcholine (C16:0,C18:0)	Complex lipids, fatty acids and related	0.52	0.56
Lysophosphatidylcholine (C18:0)	Complex lipids, fatty acids and related	0.51	0.96
Heptadecanoic acid (C17:0)	Complex lipids, fatty acids and related	0.51	0.35
Glucosamine	Carbohydrates and related	0.50	0.91
Glutamate	Amino acids	0.50	0.56
Eicosanoic acid (C20:0)	Complex lipids, fatty acids and related	0.49	0.33
Proline	Amino acids	0.48	0.71
18-Hydroxy-11-deoxycorticosterone	Hormones, signal substances and related	0.48	0.64
Hexadecanol	Complex lipids, fatty acids and related	0.46	0.33
Cholic acid	Complex lipids, fatty acids and related	0.46	0.29
Coenzyme Q10	Vitamins, cofactors and related	0.40	0.60
Glutamate	Amino acids	0.39	0.45
Coenzyme Q9	Vitamins, cofactors and related	0.39	0.68
Salicylic acid	Miscellaneous	0.39	0.78
Myristic acid (C14:0)	Complex lipids, fatty acids and related	0.33	0.24
Octadecanol	Complex lipids, fatty acids and related	0.32	0.28
Choline plasmalogen (C18:0)	Complex lipids, fatty acids and related	0.31	0.33
myo-Inositol	Complex lipids, fatty acids and related	0.30	0.20
Stearic acid (C18:0)	Complex lipids, fatty acids and related	0.19	0.11

Metabolite	Class	Roxithromycin HD	Roxithromycin LD
		m28	m28
Creatinine	Amino acids related	112.26	98.05
Taurine	Amino acids	42.04	120.85
Allantoin	Nucleobases and related	39.24	28.15
Creatinine	Amino acids related	38.27	42.57
Taurine	Amino acids	29.34	23.20
Creatinine	Amino acids related	19.40	12.48
Indole-3-lactic acid	Amino acids related	15.40	10.10
Taurocholic acid	Complex lipids, fatty acids and related	14.17	14.89
Kynurenic acid	Amino acids related	12.00	8.29
Lysophosphatidylcholine (C18:0)	Complex lipids, fatty acids and related	6.43	4.57
Glucose-6-phosphate	Energy metabolism and related	5.31	2.99
Leucine	Amino acids	5.30	10.92
Isoleucine	Amino acids	4.68	9.92
Arginine	Amino acids	3.92	5.99
Tryptophan	Amino acids	3.34	4.88
Glucose-6-phosphate	Energy metabolism and related	2.58	1.36
Fructose-6-phosphate	Energy metabolism and related	2.31	1.65
Pyruvate	Energy metabolism and related	0.75	1.25
17-Methyloctadecanoic acid	Complex lipids, fatty acids and related	0.70	0.70
Choline plasmalogen (C18-vinyl,C20:4)	Complex lipids, fatty acids and related	0.69	1.60
18-Hydroxy-11-deoxycorticosterone	Hormones, signal substances and related	0.68	0.65
Salicylic acid	Miscellaneous	0.68	0.69
4-Hydroxyphenylpyruvate	Amino acids related	0.67	1.35
Proline	Amino acids	0.66	1.11
Tricosanoic acid (C23:0)	Complex lipids, fatty acids and related	0.65	0.80
Ceramide (d18:1,C24:0)	Complex lipids, fatty acids and related	0.62	0.83
Lignoceric acid (C24:0)	Complex lipids, fatty acids and related	0.60	0.71
Eicosanoic acid (C20:1) No 02	Complex lipids, fatty acids and related	0.59	0.62
Palmitic acid (C16:0)	Complex lipids, fatty acids and related	0.58	1.01
Tryptophan	Amino acids	0.54	0.87
Glycerol phosphate, lipid fraction	Complex lipids, fatty acids and related	0.51	1.22
Hippuric acid	Miscellaneous	0.48	0.70
Phosphate (inorganic and from organic phosphates)	Miscellaneous	0.47	1.13
Isopalmitic acid (C16:0)	Complex lipids, fatty acids and related	0.47	0.77
16-Methylheptadecanoic acid	Complex lipids, fatty acids and related	0.45	0.91
Eicosanoic acid (C20:0)	Complex lipids, fatty acids and related	0.36	0.64
Hexadecanol	Complex lipids, fatty acids and related	0.32	0.43
Octadecanol	Complex lipids, fatty acids and related	0.30	0.48
Stearic acid (C18:0)	Complex lipids, fatty acids and related	0.30	0.31
Glycochenodeoxycholic acid	Complex lipids, fatty acids and related	0.24	0.53
Cholic acid	Complex lipids, fatty acids and related	0.22	0.42
Indole-3-acetic acid	Amino acids related	0.11	0.26

Table S12: Top metabolites in both the directions of feces altered metabolites (p<0.1) for both females (left) and males (right) respectively for Sparfloxacin (red = upregulated and yellow = downregulated)

Metabolite	Class	Sparfloxacin HD	Sparfloxacin LD
		m28	m28
Allantoin	Nucleobases and related	68.79	4.95
Histidine	Amino acids	46.45	67.75
Creatinine	Amino acids related	26.45	64.20
Glucuronic acid	Carbohydrates and related	24.13	44.54
Cholic acid	Complex lipids, fatty acids and related	20.68	19.20
Valine	Amino acids	20.41	35.71
Threonine acid	Vitamins, cofactors and related	20.21	30.90
Lysine	Amino acids	19.98	4.80
Taurine	Amino acids	18.21	55.21
Asparagine	Amino acids	18.12	20.03
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	16.97	17.86
2-Hydroxybutyrate	Energy metabolism and related	16.91	30.75
Tryptophan	Amino acids	14.32	20.34
Alanine	Amino acids	13.43	35.19
Creatinine	Amino acids related	11.35	10.22
TAG (C16:0,C18:1,C18:3)	Complex lipids, fatty acids and related	11.21	14.95
Tyrosine	Amino acids	11.20	18.27
Glucuronic acid	Carbohydrates and related	10.96	7.03
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	10.98	13.52
TAG (C16:0,C18:2)	Complex lipids, fatty acids and related	10.51	13.04
TAG (C18:1,C18:2)	Complex lipids, fatty acids and related	9.21	10.84
Taurine	Amino acids	8.88	10.41
4-Hydroxyphinganine (t18:0, Phytosphingosine), total	Complex lipids, fatty acids and related	8.87	5.80
Tyrosine	Amino acids	7.64	10.33
Indole-3-lactic acid	Amino acids related	6.47	9.57
Omithine	Amino acids related	6.31	6.70
3-Hydroxybutyrate	Energy metabolism and related	6.28	6.69
Glucose-6-phosphate	Energy metabolism and related	0.70	0.48
Uric acid	Nucleobases and related	0.67	1.02
Deoxyribonucleic acids, total	Carbohydrates and related	0.63	1.81
Dodecanol	Complex lipids, fatty acids and related	0.60	0.51
alpha-Tocopherol	Vitamins, cofactors and related	0.60	0.66
Eicosanoic acid (C20:1) No 02	Complex lipids, fatty acids and related	0.59	0.55
Glycerol-3-phosphate, polar fraction	Complex lipids, fatty acids and related	0.59	0.62
18-Hydroxy-11-deoxycorticosterone	Hormones, signal substances and related	0.57	1.30
Fructose-6-phosphate	Energy metabolism and related	0.55	0.52
16-Methylheptadecanoic acid	Complex lipids, fatty acids and related	0.54	0.55
14-Methylhexadecanoic acid	Complex lipids, fatty acids and related	0.53	0.56
Ulinic acid (C24:0)	Complex lipids, fatty acids and related	0.50	0.56
alpha-Tocopherol	Vitamins, cofactors and related	0.48	0.49
Tricosanoic acid (C23:0)	Complex lipids, fatty acids and related	0.46	0.61
Behenic acid (C22:0)	Complex lipids, fatty acids and related	0.44	0.49
Eicosanoic acid (C20:0)	Complex lipids, fatty acids and related	0.43	0.38
Isopalmitic acid (C16:0)	Complex lipids, fatty acids and related	0.39	0.51
Myristic acid (C14:0)	Complex lipids, fatty acids and related	0.39	0.39
Phosphate (inorganic and from organic phosphates)	Miscellaneous	0.36	0.54
Heptadecanoic acid (C17:0)	Complex lipids, fatty acids and related	0.33	0.36
Stearic acid (C18:0)	Complex lipids, fatty acids and related	0.27	0.22
Indole-3-acetic acid	Amino acids related	0.19	0.23
Octadecanol	Complex lipids, fatty acids and related	0.17	0.15
Hexadecanol	Complex lipids, fatty acids and related	0.12	0.18

Metabolite	Class	Sparfloxacin HD	Sparfloxacin LD
		m28	m28
Lysine	Amino acids	135.60	3.57
Glucuronic acid	Carbohydrates and related	100.95	68.21
Taurine	Amino acids	64.55	107.81
Histidine	Amino acids	63.43	53.36
Allantoin	Nucleobases and related	67.86	4.87
Cholic acid	Complex lipids, fatty acids and related	66.57	26.85
Creatinine	Amino acids related	60.73	77.76
Threonine acid	Vitamins, cofactors and related	39.98	36.97
Tyrosine	Amino acids	35.14	24.95
Alanine	Amino acids	34.48	54.04
Taurine	Amino acids	32.80	20.91
Taurocholic acid	Complex lipids, fatty acids and related	31.06	24.80
Creatinine	Amino acids related	26.97	17.87
Tryptophan	Amino acids	26.05	36.90
Asparagine	Amino acids	24.97	19.27
TAG (C16:0,C18:1,C18:3)	Complex lipids, fatty acids and related	21.27	20.53
Omithine	Amino acids related	20.45	8.86
TAG (C16:0,C18:2)	Complex lipids, fatty acids and related	19.67	15.28
Mannosamine	Carbohydrates and related	19.60	NA
Glucuronic acid	Carbohydrates and related	18.99	31.28
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	18.33	16.88
Creatinine	Amino acids related	17.01	20.99
Glucosamine	Carbohydrates and related	16.91	12.94
4-Hydroxyphinganine (t18:0, Phytosphingosine), total	Complex lipids, fatty acids and related	16.62	5.42
Citrate	Energy metabolism and related	15.84	NA
Tyrosine	Amino acids	15.84	13.96
Indole-3-lactic acid	Amino acids related	7.01	7.23
Tryptophan	Amino acids	2.43	1.53
Glycochenodeoxycholic acid	Complex lipids, fatty acids and related	1.85	1.27
Lysophosphatidylcholine (C16:0)	Complex lipids, fatty acids and related	1.84	0.88
myo-Inositol-2-phosphate	Carbohydrates and related	1.70	2.43
Malate	Energy metabolism and related	1.61	3.01
Lysophosphatidylcholine (C18:2)	Complex lipids, fatty acids and related	1.58	1.26
Glycolate	Miscellaneous	1.58	2.04
Hexoses	Carbohydrates and related	1.52	2.89
Proline	Amino acids	1.46	1.12
Glycerol, lipid fraction	Complex lipids, fatty acids and related	1.46	1.02
Phosphatidylcholine (C16:0,C20:4)	Complex lipids, fatty acids and related	1.42	1.48
Ethanolamine	Miscellaneous	1.27	1.38
Glycerol, polar fraction	Complex lipids, fatty acids and related	1.15	1.11
Lysophosphatidylcholine (C20:4)	Complex lipids, fatty acids and related	0.79	0.95
alpha-Tocopherol	Vitamins, cofactors and related	0.73	0.55
Deoxyribonucleic acids, total	Carbohydrates and related	0.62	1.20
Stearic acid (C18:0)	Complex lipids, fatty acids and related	0.60	0.21
Heptadecanoic acid (C17:0)	Complex lipids, fatty acids and related	0.58	0.29
Glucose-6-phosphate	Energy metabolism and related	0.53	0.63
Ulinic acid (C24:0)	Complex lipids, fatty acids and related	0.47	0.61
14-Methylhexadecanoic acid	Complex lipids, fatty acids and related	0.44	0.51
Isopalmitic acid (C16:0)	Complex lipids, fatty acids and related	0.30	0.43
Myristic acid (C14:0)	Complex lipids, fatty acids and related	0.30	0.16
Indole-3-acetic acid	Amino acids related	0.25	0.54
Octadecanol	Complex lipids, fatty acids and related	0.15	0.15
Hexadecanol	Complex lipids, fatty acids and related	0.07	0.07

Table S13: Top metabolites in both the directions of feces altered metabolites (p<0.1) for both females (left) and males (right) respectively for Vancomycin (red = upregulated and yellow = downregulated)

Metabolite	Class	Vancomycin HD f28	Vancomycin LD f28
trans-4-Hydroxyproline	Amino acids related	114,83	96,42
Creatinine	Amino acids related	113,44	98,70
Taurocholic acid	Complex lipids, fatty acids and related	92,60	0,20
Creatinine	Amino acids related	64,83	76,02
TAG (C16:0,C18:1,C18:3)	Complex lipids, fatty acids and related	50,64	71,84
Valine	Amino acids	49,95	60,56
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	43,06	93,54
Leucine	Amino acids	40,70	42,92
Creatinine	Amino acids related	36,19	48,75
TAG (C18:1,C18:2)	Complex lipids, fatty acids and related	30,69	42,51
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	28,02	40,89
Proline	Amino acids	23,34	18,96
Proline	Amino acids	22,33	16,24
Creatine	Amino acids related	20,78	19,53
TAG (C16:0,C18:2)	Complex lipids, fatty acids and related	18,60	37,19
Histidine	Amino acids	17,36	12,16
Valine	Amino acids	16,43	22,54
Phenylalanine	Amino acids	16,31	10,27
2-Hydroxybutyrate	Energy metabolism and related	16,04	11,53
Phenylalanine	Amino acids	15,12	17,95
Alanine	Amino acids	14,59	15,63
Glycine	Amino acids	14,57	11,37
Taurine	Amino acids	14,37	4,75
3-Hydroxybutyrate	Energy metabolism and related	13,64	1,05
Pantothenic acid	Vitamins, cofactors and related	13,57	17,42
Phenylalanine	Amino acids	13,30	13,10
Kynurenic acid	Amino acids related	12,29	9,73
Indole-3-lactic acid	Amino acids related	2,18	2,01
Tryptophan	Amino acids	1,83	2,22
alpha-Tocopherol	Vitamins, cofactors and related	0,47	0,41
18-Hydroxy-11-deoxycorticosterone	Hormones, signal substances and related	0,46	0,60
Coenzyme Q9	Vitamins, cofactors and related	0,46	0,33
Behenic acid (C22:0)	Complex lipids, fatty acids and related	0,42	0,49
Tricosanoic acid (C23:0)	Complex lipids, fatty acids and related	0,42	0,54
alpha-Tocopherol	Vitamins, cofactors and related	0,41	0,50
alpha-Tocopherol	Vitamins, cofactors and related	0,40	0,54
Heptadecanoic acid (C17:0)	Complex lipids, fatty acids and related	0,37	0,60
Salicylic acid	Miscellaneous	0,36	0,50
5-Oxoproline	Amino acids related	0,35	0,48
Eicosanoic acid (C20:1) No 02	Complex lipids, fatty acids and related	0,34	0,48
Thyroxine (T4)	Hormones, signal substances and related	0,33	0,63
Eicosanoic acid (C20:0)	Complex lipids, fatty acids and related	0,27	0,32
Glycerol-3-phosphate, polar fraction	Complex lipids, fatty acids and related	0,27	0,39
Isopalmitic acid (C16:0)	Complex lipids, fatty acids and related	0,25	0,34
Hexadecanol	Complex lipids, fatty acids and related	0,21	0,29
Myristic acid (C14:0)	Complex lipids, fatty acids and related	0,20	0,25
Octadecanol	Complex lipids, fatty acids and related	0,19	0,31
Stearic acid (C18:0)	Complex lipids, fatty acids and related	0,13	0,15
Glutamate	Amino acids	0,13	0,30
Glutamate	Amino acids	0,11	0,20
Indole-3-acetic acid	Amino acids related	0,10	0,12

Metabolite	Class	Vancomycin HD m28	Vancomycin LD m28
Taurocholic acid	Complex lipids, fatty acids and related	333,19	0,30
Creatinine	Amino acids related	111,69	125,38
Valine	Amino acids	99,27	87,02
trans-4-Hydroxyproline	Amino acids related	95,04	135,85
Leucine	Amino acids	72,19	57,25
Creatinine	Amino acids related	45,47	46,05
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	41,34	46,21
Creatinine	Amino acids related	36,44	43,82
TAG (C18:1,C18:2)	Complex lipids, fatty acids and related	34,82	42,18
TAG (C16:0,C18:1,C18:3)	Complex lipids, fatty acids and related	31,41	39,49
Isoleucine	Amino acids	29,51	30,74
TAG (C16:0,C18:2)	Complex lipids, fatty acids and related	28,07	41,11
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	28,03	34,82
Valine	Amino acids	26,00	23,50
Histidine	Amino acids	25,89	24,98
Creatine	Amino acids related	24,37	27,37
Taurine	Amino acids	23,59	6,05
Pantothenic acid	Vitamins, cofactors and related	22,50	20,16
Phenylalanine	Amino acids	21,97	18,44
Phenylalanine	Amino acids	19,35	15,62
Proline	Amino acids	15,49	41,40
2-Hydroxybutyrate	Energy metabolism and related	13,99	24,66
Proline	Amino acids	13,78	47,18
Alanine	Amino acids	12,18	37,98
4-Hydroxyphenylpyruvate	Complex lipids, fatty acids and related	10,61	6,56
Cholesterylester, total	Complex lipids, fatty acids and related	9,70	8,03
Indole-3-lactic acid	Amino acids related	9,40	13,06
Tryptophan	Amino acids	2,61	2,35
Glycerol, lipid fraction	Complex lipids, fatty acids and related	1,76	1,62
Phosphatidylcholine (C16:0,C20:4)	Complex lipids, fatty acids and related	1,25	1,28
Phosphatidylcholine (C16:0,C18:2)	Complex lipids, fatty acids and related	1,24	1,24
Behenic acid (C22:0)	Complex lipids, fatty acids and related	0,77	0,64
alpha-Tocopherol	Vitamins, cofactors and related	0,65	0,51
Coenzyme Q10	Vitamins, cofactors and related	0,64	0,58
Coenzyme Q9	Vitamins, cofactors and related	0,60	0,62
alpha-Tocopherol	Vitamins, cofactors and related	0,55	0,57
Eicosanoic acid (C20:1) No 02	Complex lipids, fatty acids and related	0,46	0,58
5-Oxoproline	Amino acids related	0,43	0,35
Eicosanoic acid (C20:0)	Complex lipids, fatty acids and related	0,39	0,31
Sphingomyelin (d18:1,C24:1)	Complex lipids, fatty acids and related	0,38	0,44
Glycerol-3-phosphate, polar fraction	Complex lipids, fatty acids and related	0,38	0,33
Glycochenodeoxycholic acid	Complex lipids, fatty acids and related	0,37	0,45
Stearic acid (C18:0)	Complex lipids, fatty acids and related	0,34	0,28
4-Hydroxyphenylpyruvate	Amino acids related	0,30	0,40
Glutamate	Amino acids	0,30	0,23
Glutamate	Amino acids	0,24	0,16
Octadecanol	Complex lipids, fatty acids and related	0,16	0,20
Hexadecanol	Complex lipids, fatty acids and related	0,10	0,13
Indole-3-acetic acid	Amino acids related	0,08	0,18

Table S14: Top metabolites in both the directions of feces altered metabolites (p<0.1) for both females (left) and males (right) respectively for Clindamycin hydrochloride (red = upregulated and yellow = downregulated)

						Clindamycin hydrochlorid HD	Clindamycin hydrochlorid LD
Metabolite	Class	f28	f28			m28	m28
Allantoin	Nucleobases and related	84,31	32,05	TAG (C16:0,C18:1,C18:3)	Complex lipids, fatty acids and related	78,31	30,57
Creatinine	Amino acids related	58,17	55,68	Creatinine	Amino acids related	52,73	64,94
TAG (C16:0,C18:1,C18:3)	Complex lipids, fatty acids and related	57,05	36,65	Allantoin	Nucleobases and related	52,67	23,77
Taurolcholic acid	Complex lipids, fatty acids and related	47,48	119,84	Xylitol	Carbohydrates and related	48,48	12,89
TAG (C16:0,C18:2)	Complex lipids, fatty acids and related	42,45	26,43	Taurine	Amino acids	46,28	18,52
TAG (C18:1,C18:2)	Complex lipids, fatty acids and related	41,89	23,69	Taurolcholic acid	Complex lipids, fatty acids and related	41,20	135,04
Tryptophan	Amino acids	38,49	10,09	TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	35,39	15,27
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	34,78	18,51	Creatinine	Amino acids related	31,18	28,96
Xylitol	Carbohydrates and related	31,52	9,72	TAG (C18:1,C18:2)	Complex lipids, fatty acids and related	30,83	12,77
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	25,14	14,93	TAG (C16:0,C18:2)	Complex lipids, fatty acids and related	30,50	11,58
Taurine	Amino acids	19,21	10,98	Taurine	Amino acids	26,16	22,79
Creatinine	Amino acids related	18,90	18,61	TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	25,47	10,66
2-Hydroxybutyrate	Energy metabolism and related	12,75	16,60	Creatine	Amino acids related	16,52	11,25
Creatinine	Amino acids related	12,61	11,84	Tryptophan	Amino acids	16,07	15,50
4-Hydroxyphosphinganine (t18:0, Phytosphingosin)	Complex lipids, fatty acids and related	12,46	9,09	Cholic acid	Complex lipids, fatty acids and related	15,67	16,10
3-Hydroxybutyrate	Energy metabolism and related	12,16	7,96	Asparagine	Amino acids	13,03	4,78
Creatine	Amino acids related	11,02	8,78	Cystine	Amino acids	11,19	5,33
Ornithine	Amino acids related	10,74	1,18	dihomo-gamma-Linolenic acid (C20:cs[8,11,14])	Complex lipids, fatty acids and related	10,71	5,15
Kynurenic acid	Amino acids related	10,67	12,93	Creatinine	Amino acids related	10,62	12,54
Cholic acid	Complex lipids, fatty acids and related	10,01	16,35	2-Hydroxybutyrate	Energy metabolism and related	10,30	5,48
Linoleic acid (C18:cs[9,12,2])	Complex lipids, fatty acids and related	9,88	9,07	Mannosamine	Carbohydrates and related	10,03	2,63
DAG (C18:1,C18:2)	Complex lipids, fatty acids and related	9,74	7,75	Glutamine	Amino acids	9,92	5,18
Indole-3-lactic acid	Amino acids related	5,64	8,36	TAG (C18:2,C18:3)	Complex lipids, fatty acids and related	9,74	3,73
Phosphatidylcholine (C16:0,C22:6)	Complex lipids, fatty acids and related	0,79	1,06	3-Hydroxybutyrate	Energy metabolism and related	9,64	14,79
Tryptophan	Amino acids	0,77	0,75	Indole-3-acetic acid	Amino acids related	6,02	11,93
myo-Inositol, lipid fraction	Complex lipids, fatty acids and related	0,71	0,77	Indole-3-lactic acid	Amino acids related	4,53	4,64
Salicylic acid	Miscellaneous	0,71	0,90	Glycerol, lipid fraction	Complex lipids, fatty acids and related	2,03	1,08
Uric acid	Nucleobases and related	0,65	0,62	Phosphatidylcholine (C16:0,C18:2)	Complex lipids, fatty acids and related	1,51	1,33
Proline	Amino acids	0,63	0,65	Hexoses	Carbohydrates and related	1,34	0,91
Proline	Amino acids	0,52	0,73	Lysophosphatidylcholine (C16:0)	Complex lipids, fatty acids and related	1,24	1,28
Dodecanol	Complex lipids, fatty acids and related	0,51	0,61	Coenzyme Q9	Vitamins, cofactors and related	0,86	0,70
Sphingomyelin (d18:1,C24:1)	Complex lipids, fatty acids and related	0,50	0,99	Glycolate	Miscellaneous	0,84	0,78
Galactose, lipid fraction	Complex lipids, fatty acids and related	0,50	0,43	Glycerol, polar fraction	Complex lipids, fatty acids and related	0,73	0,78
alpha-Tocopherol	Vitamins, cofactors and related	0,50	0,68	alpha-Tocopherol	Vitamins, cofactors and related	0,71	0,57
Glucose-6-phosphate	Energy metabolism and related	0,50	0,38	Galactose, lipid fraction	Complex lipids, fatty acids and related	0,69	0,50
Ethanolamine plasmalogen (C39:4)	Complex lipids, fatty acids and related	0,46	0,75	Fructose-6-phosphate	Energy metabolism and related	0,69	0,45
Fructose-6-phosphate	Energy metabolism and related	0,45	0,33	Isopalmittic acid (C16:0)	Complex lipids, fatty acids and related	0,63	0,47
Glycchenodeoxycholic acid	Complex lipids, fatty acids and related	0,42	0,70	Proline	Amino acids	0,62	0,82
Phosphate [inorganic and from organic phospholipids]	Miscellaneous	0,33	0,33	18-Hydroxy-11-deoxycorticosterone	Hormones, signal substances and related	0,62	1,16
Glutamate	Amino acids	0,33	1,40	Hippuric acid	Miscellaneous	0,59	0,74
Glutamate	Amino acids	0,30	1,62	18-Hydroxy-11-deoxycorticosterone	Hormones, signal substances and related	0,58	0,90
18-Hydroxy-11-deoxycorticosterone	Hormones, signal substances and related	0,29	0,63	Proline	Amino acids	0,58	0,87
Glycerol-3-phosphate, polar fraction	Complex lipids, fatty acids and related	0,22	0,25	Myristic acid (C14:0)	Complex lipids, fatty acids and related	0,53	0,35
Octadecanol	Complex lipids, fatty acids and related	0,19	0,19	Eicosanoic acid (C20:0)	Complex lipids, fatty acids and related	0,53	0,33
Elaidic acid (C18:trans[9]1)	Complex lipids, fatty acids and related	0,11	0,04	Glucose-6-phosphate	Energy metabolism and related	0,52	0,35
Hexadecanol	Complex lipids, fatty acids and related	0,10	0,12	4-Hydroxyphenylpyruvate	Amino acids related	0,49	0,50
				Tryptophan	Amino acids	0,47	0,51
				Heptadecanoic acid (C17:0)	Complex lipids, fatty acids and related	0,45	0,37
				Biotin	Vitamins, cofactors and related	0,45	0,17
				Stearic acid (C18:0)	Complex lipids, fatty acids and related	0,41	0,24
				Glycerol-3-phosphate, polar fraction	Complex lipids, fatty acids and related	0,34	0,24
				Octadecanol	Complex lipids, fatty acids and related	0,30	0,28
				Hexadecanol	Complex lipids, fatty acids and related	0,17	0,13
				Glycchenodeoxycholic acid	Complex lipids, fatty acids and related	0,13	0,13

Table S15: Top metabolites in both the directions of feces altered metabolites (p<0.1) for both females (left) and males (right) respectively for Lincomycin hydrochloride (red = upregulated and yellow = downregulated)

Metabolite	Class	Uncomycin hydrochlorid HD	Uncomycin hydrochlorid LD
		f28	f28
3-Hydroxybutyrate	Energy metabolism and related	55,43	5,91
Xylitol	Carbohydrates and related	47,84	45,79
Creatinine	Amino acids related	30,15	63,91
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	20,23	23,86
TAG (C16:0,C18:1,C18:3)	Complex lipids, fatty acids and related	24,33	24,63
TAG (C16:0,C18:2)	Complex lipids, fatty acids and related	23,67	27,42
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	23,42	18,81
Taurolcholic acid	Complex lipids, fatty acids and related	22,83	77,83
TAG (C18:1,C18:2)	Complex lipids, fatty acids and related	21,72	24,59
Lysine	Amino acids	20,06	26,61
3-Hydroxybutyrate	Energy metabolism and related	18,65	7,16
Tryptophan	Amino acids	17,35	12,08
Taurine	Amino acids	16,67	35,88
Asparagine	Amino acids	15,80	18,63
2-Hydroxybutyrate	Energy metabolism and related	14,48	16,24
Creatinine	Amino acids related	13,75	27,19
Cholic acid	Complex lipids, fatty acids and related	13,40	13,93
Threonic acid	Vitamins, cofactors and related	9,84	1,86
Valine	Amino acids	9,39	12,81
TAG (C18:2,C18:3)	Complex lipids, fatty acids and related	8,72	7,38
Taurine	Amino acids	8,23	8,48
Indole-3-acetic acid	Amino acids related	7,97	0,53
Indole-3-lactic acid	Amino acids related	6,86	5,11
Creatine	Amino acids related	4,86	6,15
Creatinine	Amino acids related	4,45	7,91
Glucose-6-phosphate	Energy metabolism and related	0,62	0,82
Tricosanoic acid (C23:0)	Complex lipids, fatty acids and related	0,56	0,58
Proline	Amino acids	0,54	0,82
Arachidonic acid (C20:cs[5,8,11,14])	Complex lipids, fatty acids and related	0,54	0,68
18-Hydroxy-11-deoxycorticosterone	Hormones, signal substances and related	0,52	0,85
Ulinic acid (C24:0)	Complex lipids, fatty acids and related	0,50	0,61
Behenic acid (C22:0)	Complex lipids, fatty acids and related	0,49	0,50
Myristic acid (C14:0)	Complex lipids, fatty acids and related	0,48	0,66
Lysophosphatidylcholine (C17:0)	Complex lipids, fatty acids and related	0,45	0,74
Ethanolamine plasmalogen (C39:5)	Complex lipids, fatty acids and related	0,43	1,48
Proline	Amino acids	0,42	0,66
Glycerol phosphate, lipid fraction	Complex lipids, fatty acids and related	0,40	0,72
Isopalmittic acid (C16:0)	Complex lipids, fatty acids and related	0,38	0,60
Eicosanoic acid (C20:0)	Complex lipids, fatty acids and related	0,38	0,43
Glycerol-3-phosphate, polar fraction	Complex lipids, fatty acids and related	0,36	0,37
Uracil	Nucleobases and related	0,35	1,12
Eicosanoic acid (C20:1) No 02	Complex lipids, fatty acids and related	0,35	0,79
Octadecanol	Complex lipids, fatty acids and related	0,27	0,31
Pantothenic acid	Vitamins, cofactors and related	0,26	
Citruiline	Amino acids related	0,25	0,23
Heptadecanoic acid (C17:0)	Complex lipids, fatty acids and related	0,22	0,26
Stearic acid (C18:0)	Complex lipids, fatty acids and related	0,21	0,25
4-Hydroxyphenylpyruvate	Amino acids related	0,21	0,44
Hexadecanol	Complex lipids, fatty acids and related	0,18	0,19

Metabolite	Class	Uncomycin hydrochlorid HD	Uncomycin hydrochlorid LD
		m28	m28
Taurolcholic acid	Complex lipids, fatty acids and related	126,53	125,18
Mannosamine	Carbohydrates and related	68,68	137,48
Creatinine	Amino acids related	60,85	75,14
Lysine	Amino acids	35,59	29,60
Taurine	Amino acids	35,42	67,79
Tryptophan	Amino acids	31,76	5,90
TAG (C16:0,C18:1,C18:3)	Complex lipids, fatty acids and related	26,06	21,17
TAG (C16:0,C18:2)	Complex lipids, fatty acids and related	23,74	16,16
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	20,08	16,16
TAG (C18:1,C18:2)	Complex lipids, fatty acids and related	18,76	18,08
Cholic acid	Complex lipids, fatty acids and related	18,75	27,09
Taurine	Amino acids	17,11	20,67
Threonic acid	Vitamins, cofactors and related	16,98	2,24
TAG (C18:2,C18:2)	Complex lipids, fatty acids and related	16,36	13,79
Creatinine	Amino acids related	15,94	20,99
Asparagine	Amino acids	14,32	18,25
3-Hydroxybutyrate	Energy metabolism and related	13,27	0,92
Creatinine	Amino acids related	13,21	36,19
2-Hydroxybutyrate	Energy metabolism and related	10,07	5,58
Creatine	Amino acids related	9,30	13,53
4-Hydroxyphosphinganine (t18:0, Phytosphingosin)	Complex lipids, fatty acids and related	7,91	5,99
Trans-4-Hydroxyproline	Amino acids related	7,88	8,44
Indole-3-lactic acid	Amino acids related	3,00	1,10
Glycerol, polar fraction	Complex lipids, fatty acids and related	1,67	0,97
Coenzyme Q10	Vitamins, cofactors and related	0,85	0,72
Proline	Amino acids	0,81	0,92
Dodecanol	Complex lipids, fatty acids and related	0,71	0,56
Glycerol-3-phosphate, polar fraction	Complex lipids, fatty acids and related	0,71	0,78
alpha-Tocopherol	Vitamins, cofactors and related	0,69	0,62
Indole-3-acetic acid	Amino acids related	0,57	0,74
Thyroxine (T4)	Hormones, signal substances and related	0,56	0,63
Malate	Energy metabolism and related	0,53	0,57
Palmitic acid (C16:0)	Complex lipids, fatty acids and related	0,52	0,48
Lignoceric acid (C24:0)	Complex lipids, fatty acids and related	0,51	0,63
Galactose, lipid fraction	Complex lipids, fatty acids and related	0,51	0,52
Behenic acid (C22:0)	Complex lipids, fatty acids and related	0,49	0,54
Citrulline	Amino acids related	0,49	0,42
Heleicosanoic acid (C21:0)	Complex lipids, fatty acids and related	0,45	0,60
Tricosanoic acid (C23:0)	Complex lipids, fatty acids and related	0,42	0,47
Eicosanoic acid (C20:1) No 02	Complex lipids, fatty acids and related	0,38	0,54
14-Methylhexadecanoic acid	Complex lipids, fatty acids and related	0,38	0,66
Eicosanoic acid (C20:0)	Complex lipids, fatty acids and related	0,33	0,27
Isopalmittic acid (C16:0)	Complex lipids, fatty acids and related	0,31	0,49
Myristic acid (C14:0)	Complex lipids, fatty acids and related	0,28	0,30
Heptadecanoic acid (C17:0)	Complex lipids, fatty acids and related	0,28	0,22
alpha-Tocopherol	Vitamins, cofactors and related	0,26	0,26
Octadecanol	Complex lipids, fatty acids and related	0,24	0,24
Stearic acid (C18:0)	Complex lipids, fatty acids and related	0,24	0,23
Hexadecanol	Complex lipids, fatty acids and related	0,12	0,14

Table S16: The table below shows DESeq2 analysis results from the low dose (LD) groups of all the treatments. The dots in the scatter plot indicate individual ASVs belonging to respective phyla/families. Color coding of the dots is based on the phyla level. The dots indicate positive or negative relative fold changes of specific bacterial ASV in a treatment group with respect to the control group.

Restricted diet

Streptomycin LD

Clindamycin LD

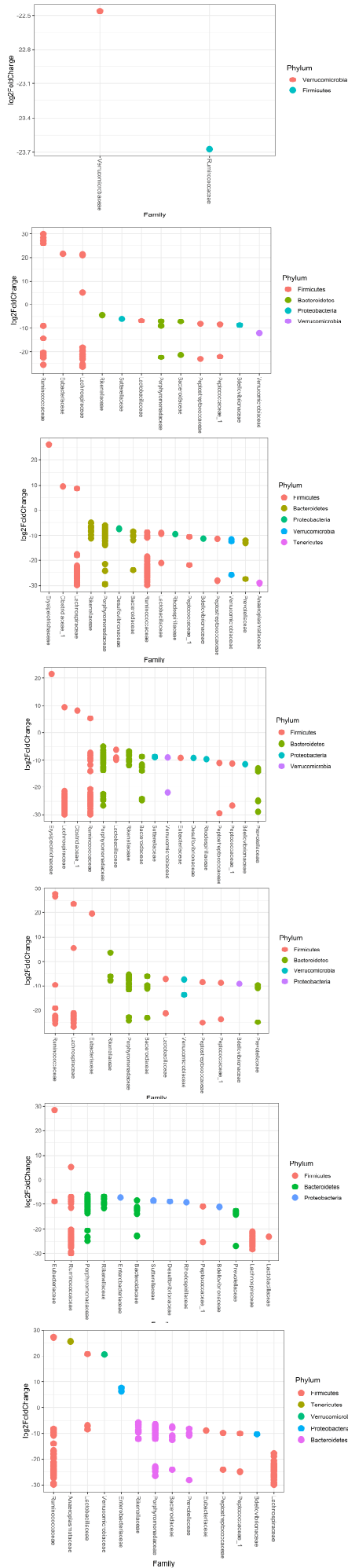
Lincomycin LD

Roxithromycin LD

Sparfloxacin LD

Vancomycin LD

FEMALES



MALES

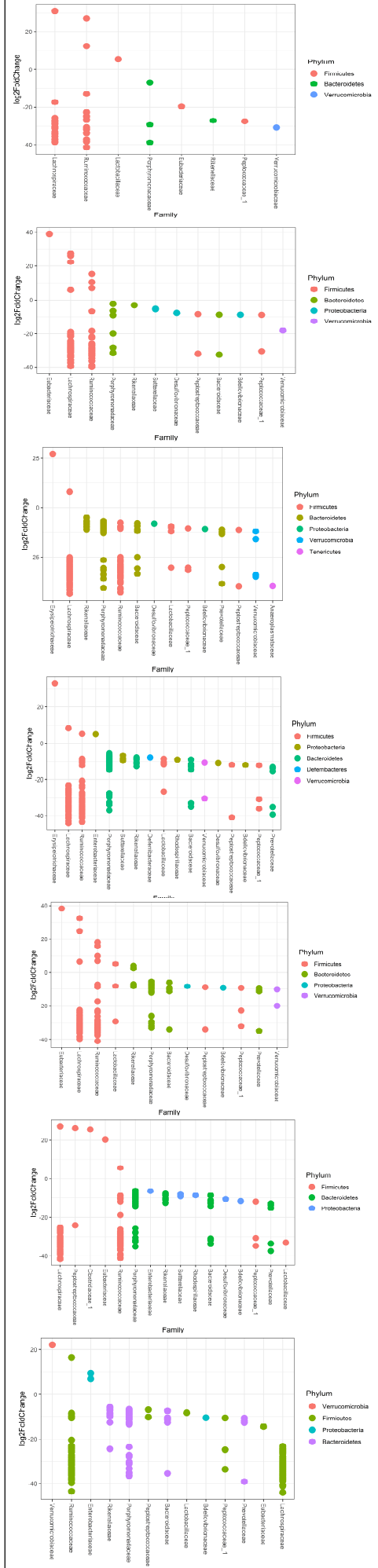


Table S17: Fold changes of different bile acid levels going up (red colored boxes) and down (blue colored boxes) in the feces and plasma matrices of male and female Wistar rats of Lincomycin hydrochloride treatment (p value depends on the shade of the colors, the darkest red is p value<0.01; medium red is p value<0.05 and the lightest shade of red is p value<0.10 and similarly for blue coloring). F represents females, M represents males, 7d, 14d and 28d denote blood sampling time points days 7, 14 and 28 respectively.

METABOLITE NAME	ANALYTE NAME	FECES		PLASMA					
		F	M	F 7d	F 14d	F 28d	M 7d	M 14d	M 28d
Cholate	CA	25,04	48,28	0,00	0,01	0,07	0,01	0,00	0,01
chenodeoxycholate (chenodeoxycholic acid)	CDCA	0,64		0,01	0,01	0,12	0,01		0,03
deoxycholate (deoxycholic acid)	DCA	0,01	0,00	0,26	0,01	0,07	0,00	0,01	0,02
glycocholate, glycocholic acid	GCA	1,18	3,24	0,62	0,06	0,26	0,30	0,18	0,20
glycochenodeoxycholate (glycochenodeoxycholic acid)	GCDCA	0,50	0,28	0,66	0,11	0,69	0,11	0,05	0,21
glycodeoxycholate, -cholic acid	GDCA	1,46	0,63	0,08	0,01		0,00		0,02
Glycolithocholic acid	GLCA	2,69	1,25	7,49			0,15		
Glycoursodeoxycholic acid	GUDCA	2,41	0,78					0,16	0,92
hyodeoxycholate, hyodeoxycholic acid	HDCA	0,00	0,00	0,00			0,00		
lithocholate, lithocholic acid	LCA	0,03	0,01	9,54		0,24	0,09	0,22	0,31
Muricholic acid (alpha)	MCAa	0,24	0,13		0,01	0,11	0,00	0,00	0,01
Muricholic acid (beta)	MCAb	0,88	0,97	0,02	0,09	0,67	0,05	0,05	0,26
Muricholic acid (omega)	MCAo	0,05	0,02	0,02	0,02	0,06	0,01	0,00	0,01
taurocholate, taurocholic acid	TCA	28,03	62,02	4,07	3,73	1,55	7,77	6,80	4,65
taurochenodeoxycholate	TCDCA	4,54	13,40	2,25	1,08	1,00	4,98	2,58	1,68
taurodeoxycholate, -cholic acid	TDCA	0,45		0,02		0,12	0,02		0,01
Taurolithocholic acid	TLCA	0,30			0,04	0,16	0,24		0,34
Tauromuricholic acid (a+b)	TMCA(a+b)	90,84	227,89	3,81	3,21	2,93	5,86	5,93	3,92
Tauroursodeoxycholic acid	TUDCA	5,37	29,02		2,85			3,04	1,74
ursodeoxycholate, ursodeoxycholic acid, ursodiol	UDCA	0,08	0,01		0,02	0,09	0,03		0,04