

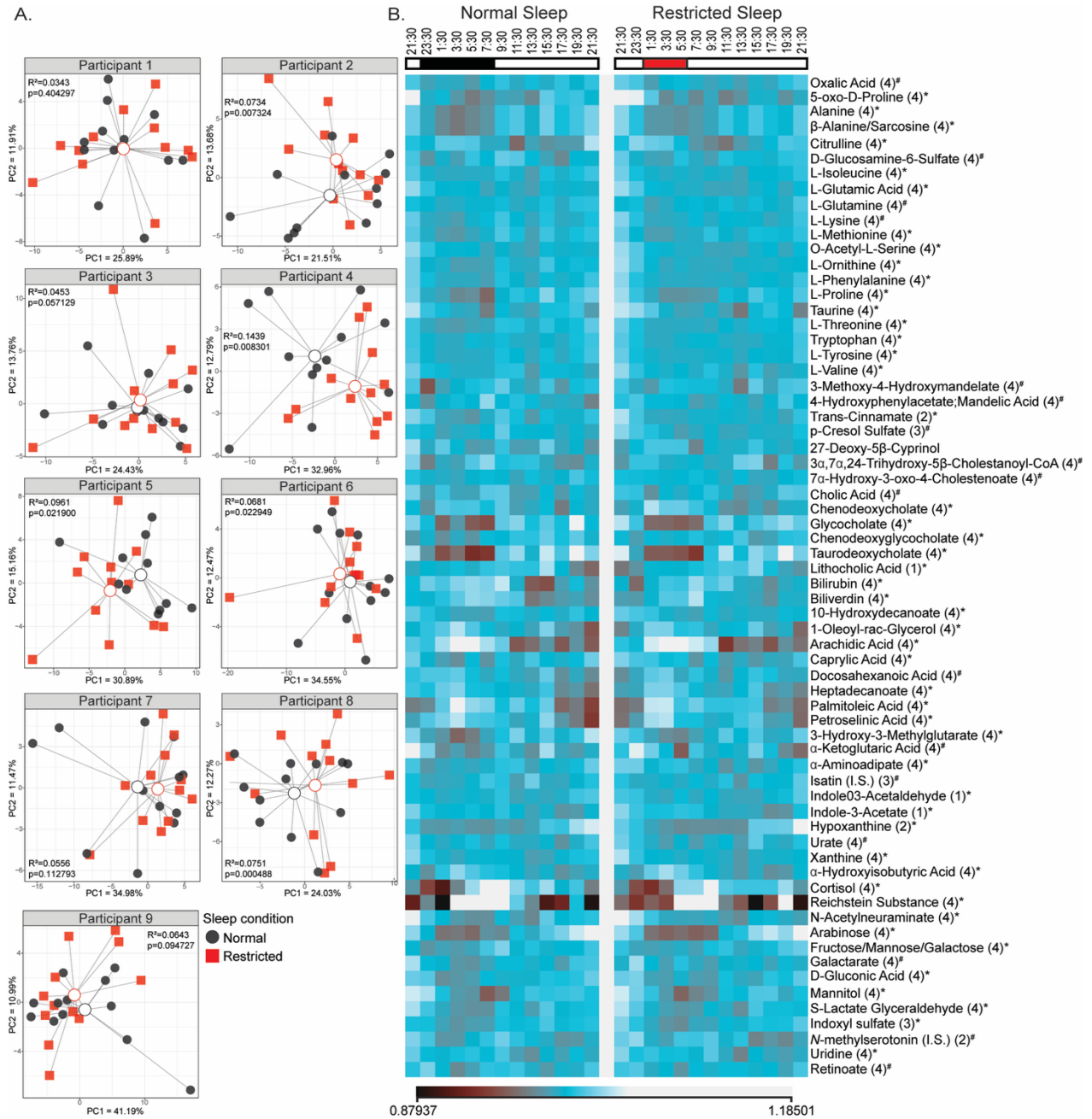


Figure S1. Short-term sleep restriction elicits inter-individual variation in 24-hr metabolite abundances, while rhythmic status remains unchanged in most serum metabolites (A)

Principal Coordinate Analysis (PCoA) of Euclidian distances calculated from the mean relative abundance over 24-hr of metabolites under normal vs. restricted sleep conditions plotted by individual participant. P-value and pseudo- r^2 determined using PERMANOVA implemented via the adonis2 function ($p < 0.05$ considered statistically significant). **(B)** Heatmap representing mean-

normalized relative abundance of metabolites sampled every 2-hrs over 24-hrs. Black and red bars indicate sleep time in normal and restricted sleep conditions. Metabolite category is listed in parentheses and are as follows: 1 = microbially-derived, reflecting metabolites exclusively derived from microbial origin; 2 = microbe/host-derived, representing metabolites produced either by gut microbes or via host enzymatic processes; 3 = derived from host metabolism of microbial metabolites, reflecting products of microbial metabolites that have undergone host modifications; and 4 = diet/host-derived, reflecting metabolites absorbed from the diet and/or further processed via host metabolism. *Indicates rhythmicity under both normal and sleep restricted conditions and # indicates no rhythmicity under both normal and sleep restricted conditions determined via eJTK cycle (GammaBH $p < 0.05$).

Table S1. Metabolites identified in blood collected every 2-hrs over 24-hrs under normal (habitual) or restricted sleep conditions where rhythms were unchanged following the intervention.

Metabolite Type	Category ^A	Metabolite	Normal Sleep GammaBH	Restricted Sleep GammaBH	Rhythm Change from Normal Sleep
Acid	4	Oxalic Acid	0.061	0.068	None
	4	5-oxo-D-Proline	6.27E-05*	0.0002*	None
Amino acids and derivatives	4	Alanine	3.45E-10*	3.35E-08*	None
	4	β-Alanine/Sarcosine	3.45E-10*	3.35E-08*	None
	4	Citrulline	4.52E-05*	3.81E-06*	None
	4	D-Glucosamine-6-Sulfate	0.104	0.147	None
	4	L-Isoleucine	0.0004*	0.006*	None
	4	L-Glutamic Acid	0.008*	7.70E-05*	None
	4	L-Glutamine	0.210	0.136	None
	4	L-Lysine	0.068	0.325	None
	4	L-Methionine	7.99E-05*	0.002*	None
	4	O-Acetyl-L-Serine	0.008*	7.70E-05*	None
	4	L-Ornithine	0.0006*	0.007*	None
	4	L-Phenylalanine	0.0004*	0.0002*	None
	4	L-Proline	3.45E-10*	1.25E-09*	None
	4	Taurine	0.0004*	0.0003*	None
	4	L-Threonine	5.30E-06*	0.0002*	None
	4	Tryptophan	0.031*	0.012*	None
	4	L-Tyrosine	0.005*	0.002*	None
	4	L-Valine	0.351	0.406	None
Aryl acids	4	3-Methoxy-4-Hydroxymandelate	0.163	0.209	None
	4	4-Hydroxyphenylacetate; Mandelic Acid	0.141	0.533	None
	2	Trans-Cinnamate	0.008*	0.011*	None
Aryl Sulfate	3	p-Cresol sulfate	0.248	0.055	None
Bile acids - primary precursors	4	27-Deoxy-5β-Cyprinol	0.248	0.292	None
	4	3α,7α,24-Trihydroxy-5β-Cholestanoyl-CoA	0.383	0.460	None
	4	7α-Hydroxy-3-oxo-4-Cholestenoate	0.097	0.165	None
Bile acids - primary	4	Cholic acid	0.448	0.324	None
	4	Chenodeoxycholate	0.012*	9.50E-08*	None
Bile acids - Glyco-conjugated	4	Glycocholate	3.11E-07*	9.50E-08*	None
	4	Chenodeoxyglycocholate	2.54E-14*	8.95E-12*	None
Bile acids - Tauro-conjugated	4	Taurodeoxycholate	4.52E-14*	7.53E-12*	None
Bile acids - secondary	1	Lithocholic acid	9.16E-07*	4.32E-07*	None
Bile component	4	Bilirubin	8.21E-08*	7.30E-07*	None
	4	Biliverdin	1.01E-08*	7.34E-06*	None
Fatty acids	4	10-Hydroxydecanoate	0.002*	0.004*	None
	4	1-Oleoyl-rac-Glycerol	1.36E-05*	1.28E-05*	None
	4	Arachidic Acid	1.72E-16*	6.00E-21*	None
	4	Caprylic Acid	4.78E-05*	0.0002*	None
	4	Docosahexanoic Acid	0.063	0.141	None
	4	Heptadecanoate	3.20E-05*	1.76E-06*	None
	4	Palmitoleic Acid	1.42E-07*	8.28E-10*	None

	4	Petroselinic Acid	2.11E-05*	1.04E-06*	None
Glutaric acid derivatives	4	3-Hydroxy-3-Methylglutarate	1.82E-08*	0.0003*	None
	4	α -Ketoglutaric Acid	0.064	0.098	None
Homoisocitrate derivative	4	α -Aminoadipate	0.010*	0.002*	None
Indoles and derivatives	3	Isatin (I.S.)	0.532	0.771	None
	1	Indole-3-Acetaldehyde	0.018*	0.018*	None
	1	Indole-3-Acetate	0.001*	1.53E-07*	None
Purines and derivatives	2	Hypoxanthine	2.29E-08*	5.29E-09*	None
	4	Urate	0.071	0.085	None
	4	Xanthine	0.006*	0.0003*	None
SCFA and derivatives	4	α -Hydroxyisobutyric Acid	1.72E-06*	1.22E-10*	None
Steroids and derivatives	4	Cortisol	7.09E-20*	8.06E-14*	None
	4	Reichstein Substance	1.59E-07*	0.0007*	None
Sugars and derivatives	4	N-Acetylneuraminate	2.02E-05*	1.29E-05*	None
	4	Arabinose	1.32E-14*	1.24E-14*	None
	4	Fructose/Mannose/Galactose	0.010*	0.0002*	None
	4	Galactarate	0.064	0.393	None
	4	D-Gluconic Acid	0.001*	0.009*	None
	4	Mannitol	0.001*	0.002*	None
	4	S-Lactate-Glyceraldehyde	3.01E-07*	3.35E-08*	None
Tryptophan catabolites	3	Indoxyl sulfate	6.56E-06*	4.92E-12*	None
	2	N-methylserotonin (I.S.)	0.532	0.080	None
Uracil containing precursor and derivatives	4	Uridine	8.90E-05*	0.0002*	None
Vitamin	4	Retinoate	0.161	0.596	None

^ACategories: 1 = microbially-derived, reflecting metabolites exclusively derived from microbial origin; 2 = microbe/host-derived, representing metabolites produced either by gut microbes or via host enzymatic processes; 3 = derived from host metabolism of microbial metabolites, reflecting products of microbial metabolites that have undergone host modifications; and 4 = diet/host-derived, reflecting metabolites absorbed from the diet and/or further processed via host metabolism. *GammaBH p < 0.05 represents statistically significant rhythm determined via eJTK_Cycle analysis.

Table S2. Detected metabolites mapped to Homo sapien (hsa) KEGG pathways*. Of the 90 compounds searched, 71 compounds** mapped to at least 1 hsa pathway***. Yellow, always rhythmic; Green, gained rhythms from normal sleep; Red, lost rhythms from normal sleep; Grey, never rhythmic. Bolded metabolites are microbially-associated.

[illegible]

*p-cresol sulfate, 1-oleoyl-rac-glycerol, heptadecanoate, alpha-hydroxyisobutyric acid, and indoxyl sulfate do not have KEGG IDs and were excluded from the table.

**2,3-Dihydroxybenzoate (C00196) and 3-Hydroxybenzaldehyde (C03067) do not map to any hsa pathways.

***The following compounds have KEGG IDs but do not map to hsa KEGG pathways: D-glucosamine-6 sulfate (C04132), 2-quinoline-carboxylic acid (C06325), Taurodeoxycholate (C05463) 10-Hydroxydecanoate (C02774), Noanoate (C01601); Petroselinic acid (C08363), 3-Hydroxy-3-methylglutarate (C03761), Indole-3-propionic acid (C22236), Isatin (C11129), Cortisol-21-Acetate (C02821)

****Fructose, Mannose, and Galactose exhibit identical MS fragments that could not be resolved at the individual compound level

Table S4. Metabolites identified in blood collected every 2 hrs over a 24 hr period under normal (habitual) or restricted sleep conditions and corresponding eJTK_cycle rhythms analyses, including time of max and min values, max and min values, and max amplitude.

Metabolite	Time of Max		Time of Min		Max Value		Min Value		Max Amplitude	
	Normal	Restricted	Normal	Restricted	Normal	Restricted	Normal	Restricted	Normal	Restricted
Oxalic Acid	9:30	21:30	15:30	9:30	1.045 ± 0.008	1.048 ± 0.01	0.950 ± 0.006	0.953 ± 0.008	0.094 ± 0.014	0.095 ± 0.012
5-oxo-D-Proline	21:30	21:30	23:30	7:30	1.10 ± 0.014	1.109 ± 0.014	0.947 ± 0.007	0.942 ± 0.006	0.15 ± 0.02	0.168 ± 0.017
Alanine	21:30	21:30	7:30	5:30	1.045 ± 0.004	1.045 ± 0.008	0.957 ± 0.003	0.970 ± 0.003	0.088 ± 0.006	0.076 ± 0.009
Aspartate	9:30	21:30	3:30	5:30	1.04 ± 0.004	1.039 ± 0.009	0.975 ± 0.002	0.973 ± 0.002	0.065 ± 0.006	0.066 ± 0.01
β-Alanine/Sarcosine	21:30	21:30	7:30	5:30	1.045 ± 0.004	1.045 ± 0.008	0.957 ± 0.003	0.969 ± 0.003	0.088 ± 0.006	0.076 ± 0.009
Citrulline	3:30	23:30	1:30	21:30	1.062 ± 0.011	1.057 ± 0.006	0.939 ± 0.008	0.943 ± 0.006	0.123 ± 0.016	0.113 ± 0.010
Cystine	21:30	21:30	23:30	13:30	1.057 ± 0.006	1.043 ± 0.006	0.907 ± 0.035	0.941 ± 0.014	0.149 ± 0.040	0.103 ± 0.017
D-Glucosamine-6-Sulfate	9:30	11:30	11:30	21:30	1.052 ± 0.005	1.056 ± 0.009	0.952 ± 0.004	0.955 ± 0.004	0.100 ± 0.007	0.101 ± 0.013
Isoleucine	9:30	21:30	13:30	3:30	1.029 ± 0.004	1.034 ± 0.007	0.977 ± 0.002	0.982 ± 0.001	0.051 ± 0.005	0.052 ± 0.007
L-Glutamic Acid	21:30	21:30	13:30	13:30	1.038 ± 0.005	1.038 ± 0.008	0.970 ± 0.003	0.977 ± 0.002	0.069 ± 0.007	0.061 ± 0.01
L-Glutamine	9:30	7:30	9:30	1:30	1.030 ± 0.003	1.028 ± 0.003	0.968 ± 0.004	0.978 ± 0.002	0.063 ± 0.005	0.050 ± 0.005
Lysine	21:30	21:30	11:30	3:30	1.032 ± 0.004	1.044 ± 0.01	0.969 ± 0.004	0.975 ± 0.002	0.063 ± 0.007	0.068 ± 0.009
Methionine	21:30	21:30	1:30	11:30	1.035 ± 0.005	1.037 ± 0.008	0.970 ± 0.002	0.973 ± 0.003	0.065 ± 0.005	0.064 ± 0.007
O-Acetyl-L-Serine	21:30	21:30	13:30	13:30	1.038 ± 0.005	1.038 ± 0.008	0.970 ± 0.003	0.977 ± 0.002	0.069 ± 0.007	0.061 ± 0.01
Ornithine	21:30	21:30	13:30	15:30	1.039 ± 0.005	1.044 ± 0.01	0.972 ± 0.002	0.976 ± 0.003	0.067 ± 0.005	0.068 ± 0.01
Phenylalanine	21:30	21:30	1:30	1:30	1.033 ± 0.003	1.036 ± 0.008	0.977 ± 0.001	0.98 ± 0.002	0.056 ± 0.004	0.055 ± 0.008
Proline	15:30	21:30	7:30	5:30	1.046 ± 0.005	1.045 ± 0.005	0.942 ± 0.024	0.965 ± 0.004	0.104 ± 0.027	0.081 ± 0.007
Taurine	21:30	21:30	7:30	13:30	1.045 ± 0.005	1.052 ± 0.012	0.956 ± 0.004	0.950 ± 0.006	0.089 ± 0.006	0.102 ± 0.015
Threonine	13:30	21:30	13:30	9:30	1.039 ± 0.004	1.039 ± 0.008	0.975 ± 0.002	0.979 ± 0.002	0.062 ± 0.004	0.06 ± 0.009
Trans-4-Hydroxyproline	9:30	21:30	9:30	11:30	1.046 ± 0.007	1.043 ± 0.01	0.956 ± 0.007	0.961 ± 0.004	0.090 ± 0.011	0.083 ± 0.011
Tryptophan	19:30	21:30	1:30	5:30	1.025 ± 0.003	1.032 ± 0.007	0.981 ± 0.002	0.982 ± 0.002	0.043 ± 0.005	0.050 ± 0.008
Tyrosine	9:30	21:30	13:30	3:30	1.03 ± 0.004	1.032 ± 0.007	0.978 ± 0.002	0.985 ± 0.001	0.052 ± 0.006	0.048 ± 0.007
Valine	21:30	21:30	13:30	13:30	1.032 ± 0.004	1.044 ± 0.009	0.965 ± 0.006	0.960 ± 0.006	0.067 ± 0.009	0.084 ± 0.013
Hippuric Acid ^B	9:30	9:30	1:30	23:30	1.048 ± 0.007	1.051 ± 0.005	0.953 ± 0.007	0.951 ± 0.007	0.095 ± 0.013	0.100 ± 0.01
2,3-Dihydroxybenzoate	7:30	21:30	9:30	17:30	1.055 ± 0.004	1.063 ± 0.009	0.942 ± 0.008	0.937 ± 0.005	0.112 ± 0.008	0.126 ± 0.012
2-Quinoline-Carboxylic Acid	9:30	5:30	23:30	15:30	1.076 ± 0.01	1.066 ± 0.015	0.91 ± 0.017	0.912 ± 0.01	0.165 ± 0.018	0.154 ± 0.022
3-Methoxy-4-Hydroxy Mandelate	9:30	5:30	23:30	13:30	1.037 ± 0.006	1.035 ± 0.007	0.958 ± 0.008	0.95 ± 0.015	0.08 ± 0.013	0.085 ± 0.019
4-Hydroxy Phenylacetate-Mandelic Acid	13:30	21:30	21:30	21:30	1.053 ± 0.004	1.049 ± 0.006	0.948 ± 0.005	0.948 ± 0.007	0.105 ± 0.007	0.101 ± 0.007
Dihydroxy Mandelic Acid	9:30	21:30	21:30	17:30	1.055 ± 0.009	1.056 ± 0.008	0.906 ± 0.019	0.914 ± 0.014	0.15 ± 0.026	0.143 ± 0.018
Ferulate	15:30	19:30	3:30	9:30	1.142 ± 0.018	1.163 ± 0.01	0.868 ± 0.012	0.874 ± 0.014	0.274 ± 0.027	0.289 ± 0.016
Trans-Cinnamate ^B	21:30	21:30	5:30	5:30	1.04 ± 0.004	1.041 ± 0.011	0.97 ± 0.005	0.968 ± 0.003	0.07 ± 0.008	0.072 ± 0.013
3-Hydroxy Benzaldehyde	9:30	21:30	5:30	21:30	1.041 ± 0.007	1.052 ± 0.005	0.972 ± 0.003	0.97 ± 0.002	0.069 ± 0.008	0.081 ± 0.006
p-Cresol sulfate ^C	9:30	21:30	21:30	5:30	1.038 ± 0.003	1.039 ± 0.008	0.966 ± 0.005	0.966 ± 0.01	0.072 ± 0.007	0.072 ± 0.014
3α,7α,12α-Trihydroxy-5β-Cholestan-26-al	15:30	13:30	3:30	21:30	1.172 ± 0.022	1.184 ± 0.018	0.787 ± 0.020	0.728 ± 0.029	0.385 ± 0.035	0.456 ± 0.039
Coprocholic acid	9:30	21:30	21:30	11:30	1.032 ± 0.004	1.035 ± 0.008	0.961 ± 0.007	0.976 ± 0.003	0.071 ± 0.009	0.059 ± 0.01
27-Deoxy-5β-Cyprinol	21:30	5:30	11:30	21:30	1.074 ± 0.015	1.058 ± 0.012	0.956 ± 0.005	0.954 ± 0.007	0.118 ± 0.016	0.104 ± 0.017
3α,7α,24-Trihydroxy-	21:30	3:30	1:30	21:30	1.071 ± 0.006	1.078 ± 0.009	0.894 ± 0.012	0.900 ± 0.015	0.177 ± 0.015	0.178 ± 0.017

5 β -Cholestanoyl-CoA										
7 α -Hydroxy-3-oxo-4-Cholestenoate	9:30	21:30	9:30	21:30	1.028 $\pm$ 0.005	1.029 $\pm$ 0.007	0.976 $\pm$ 0.002	0.982 $\pm$ 0.002	0.052 $\pm$ 0.007	0.047 $\pm$ 0.008
Cholic Acid	21:30	21:30	5:30	23:30	1.081 $\pm$ 0.015	1.064 $\pm$ 0.007	0.948 $\pm$ 0.005	0.950 $\pm$ 0.003	0.133 $\pm$ 0.015	0.113 $\pm$ 0.008
Chenodeoxycholate	5:30	21:30	11:30	11:30	1.052 $\pm$ 0.003	1.052 $\pm$ 0.008	0.950 $\pm$ 0.003	0.953 $\pm$ 0.004	0.102 $\pm$ 0.005	0.098 $\pm$ 0.011
Glycocholate	19:30	19:30	7:30	5:30	1.086 $\pm$ 0.010	1.073 $\pm$ 0.005	0.928 $\pm$ 0.004	0.902 $\pm$ 0.013	1.158 $\pm$ 0.011	0.170 $\pm$ 0.014
Chenodeoxyglycocholate	15:30	21:30	1:30	23:30	1.048 $\pm$ 0.004	1.041 $\pm$ 0.006	0.955 $\pm$ 0.007	0.933 $\pm$ 0.012	0.093 $\pm$ 0.007	0.108 $\pm$ 0.016
Taurodeoxycholate	19:30	19:30	5:30	5:30	1.092 $\pm$ 0.009	1.083 $\pm$ 0.008	0.908 $\pm$ 0.008	0.899 $\pm$ 0.013	0.184 $\pm$ 0.014	0.183 $\pm$ 0.018
Lithocholic Acid ^B	15:30	23:30	21:30	21:30	1.050 $\pm$ 0.007	1.041 $\pm$ 0.005	0.945 $\pm$ 0.009	0.948 $\pm$ 0.009	0.105 $\pm$ 0.015	0.093 $\pm$ 0.012
Bilirubin	5:30	7:30	9:30	23:30	1.056 $\pm$ 0.01	1.046 $\pm$ 0.006	0.891 $\pm$ 0.032	0.926 $\pm$ 0.026	0.165 $\pm$ 0.039	0.12 $\pm$ 0.029
Biliverdin	5:30	7:30	19:30	23:30	1.047 $\pm$ 0.006	1.05 $\pm$ 0.006	0.924 $\pm$ 0.016	0.932 $\pm$ 0.017	0.123 $\pm$ 0.02	0.118 $\pm$ 0.021
10-Hydroxy decanoate	21:30	21:30	7:30	7:30	1.033 $\pm$ 0.003	1.039 $\pm$ 0.008	0.976 $\pm$ 0.003	0.974 $\pm$ 0.003	0.057 $\pm$ 0.004	0.065 $\pm$ 0.01
1-Oleoyl-rac-Glycerol	3:30	23:30	21:30	21:30	1.055 $\pm$ 0.009	1.05 $\pm$ 0.005	0.937 $\pm$ 0.008	0.937 $\pm$ 0.008	0.119 $\pm$ 0.014	0.112 $\pm$ 0.011
Arachidic Acid	5:30	3:30	21:30	11:30	1.063 $\pm$ 0.007	1.074 $\pm$ 0.007	0.932 $\pm$ 0.003	0.927 $\pm$ 0.004	0.132 $\pm$ 0.007	0.147 $\pm$ 0.01
Caprylic Acid	9:30	21:30	23:30	11:30	1.04 $\pm$ 0.006	1.047 $\pm$ 0.008	0.956 $\pm$ 0.006	0.959 $\pm$ 0.005	0.084 $\pm$ 0.01	0.088 $\pm$ 0.011
Docosahexaenoic Acid	21:30	23:30	17:30	21:30	1.043 $\pm$ 0.004	1.043 $\pm$ 0.006	0.949 $\pm$ 0.011	0.945 $\pm$ 0.013	0.094 $\pm$ 0.013	0.099 $\pm$ 0.017
Gamma Linolenic Acid	15:30	15:30	21:30	21:30	1.079 $\pm$ 0.012	1.077 $\pm$ 0.008	0.905 $\pm$ 0.012	0.913 $\pm$ 0.006	0.174 $\pm$ 0.014	0.164 $\pm$ 0.009
Heptadecanoate	1:30	3:30	17:30	21:30	1.051 $\pm$ 0.007	1.047 $\pm$ 0.007	0.951 $\pm$ 0.004	0.957 $\pm$ 0.004	0.100 $\pm$ 0.011	0.09 $\pm$ 0.01
Linoleate	15:30	23:30	21:30	21:30	1.047 $\pm$ 0.007	1.04 $\pm$ 0.004	0.942 $\pm$ 0.013	0.938 $\pm$ 0.012	0.106 $\pm$ 0.019	0.102 $\pm$ 0.015
Myristic Acid	15:30	13:30	7:30	19:30	1.068 $\pm$ 0.012	1.062 $\pm$ 0.011	0.933 $\pm$ 0.014	0.942 $\pm$ 0.008	0.136 $\pm$ 0.023	0.12 $\pm$ 0.017
Nonanoate	21:30	21:30	7:30	15:30	1.034 $\pm$ 0.003	1.048 $\pm$ 0.009	0.967 $\pm$ 0.006	0.962 $\pm$ 0.004	0.066 $\pm$ 0.008	0.086 $\pm$ 0.012
Palmitate	3:30	3:30	3:30	11:30	1.058 $\pm$ 0.008	1.046 $\pm$ 0.006	0.924 $\pm$ 0.024	0.936 $\pm$ 0.015	0.134 $\pm$ 0.024	0.111 $\pm$ 0.016
Palmitoleic Acid	7:30	1:30	21:30	5:30	1.069 $\pm$ 0.009	1.065 $\pm$ 0.007	0.901 $\pm$ 0.011	0.914 $\pm$ 0.007	0.168 $\pm$ 0.016	0.151 $\pm$ 0.013
Petroselinic Acid	3:30	1:30	21:30	19:30	1.061 $\pm$ 0.008	1.05 $\pm$ 0.008	0.914 $\pm$ 0.016	0.93 $\pm$ 0.012	0.146 $\pm$ 0.02	0.12 $\pm$ 0.018
Stearate	3:30	1:30	11:30	21:30	1.032 $\pm$ 0.003	1.03 $\pm$ 0.002	0.972 $\pm$ 0.003	0.968 $\pm$ 0.004	0.06 $\pm$ 0.004	0.062 $\pm$ 0.005
3-Hydroxy-3-Methyl Glutarate	21:30	21:30	3:30	5:30	1.064 $\pm$ 0.007	1.051 $\pm$ 0.008	0.945 $\pm$ 0.005	0.956 $\pm$ 0.005	0.12 $\pm$ 0.01	0.095 $\pm$ 0.012
α -Ketoglutaric Acid	21:30	23:30	1:30	19:30	1.099 $\pm$ 0.015	1.07 $\pm$ 0.008	0.919 $\pm$ 0.011	0.911 $\pm$ 0.011	0.182 $\pm$ 0.018	0.159 $\pm$ 0.017
α -Aminoadipate	21:30	21:30	23:30	11:30	1.046 $\pm$ 0.004	1.047 $\pm$ 0.007	0.967 $\pm$ 0.003	0.943 $\pm$ 0.017	0.08 $\pm$ 0.006	0.104 $\pm$ 0.018
Isatin (I.S.) ^C	18	21:30	11:30	9:30	1.053 $\pm$ 0.008	1.046 $\pm$ 0.006	0.964 $\pm$ 0.002	0.955 $\pm$ 0.005	0.090 $\pm$ 0.009	0.090 $\pm$ 0.008
Indole-3-Acetaldehyde ^A	9:30	21:30	15:30	13:30	1.032 $\pm$ 0.003	1.04 $\pm$ 0.005	0.969 $\pm$ 0.005	0.972 $\pm$ 0.005	0.064 $\pm$ 0.007	0.068 $\pm$ 0.009
Indole-3-Acetate ^A	21:30	21:30	19:30	15:30	1.034 $\pm$ 0.007	1.04 $\pm$ 0.009	0.971 $\pm$ 0.004	0.971 $\pm$ 0.002	0.063 $\pm$ 0.009	0.07 $\pm$ 0.011
Hypoxanthine ^B	21:30	15:30	13:30	5:30	1.059 $\pm$ 0.005	1.069 $\pm$ 0.008	0.963 $\pm$ 0.003	0.951 $\pm$ 0.005	0.095 $\pm$ 0.007	0.119 $\pm$ 0.009
Urate	21:30	11:30	17:30	13:30	1.055 $\pm$ 0.007	1.064 $\pm$ 0.009	0.961 $\pm$ 0.003	0.961 $\pm$ 0.004	0.095 $\pm$ 0.009	0.103 $\pm$ 0.011
Xanthine	21:30	21:30	15:30	13:30	1.041 $\pm$ 0.004	1.042 $\pm$ 0.01	0.967 $\pm$ 0.007	0.974 $\pm$ 0.002	0.073 $\pm$ 0.009	0.067 $\pm$ 0.011
Butyric Acid ^A	21:30	21:30	19:30	3:30	1.065 $\pm$ 0.005	1.058 $\pm$ 0.008	0.944 $\pm$ 0.006	0.948 $\pm$ 0.005	0.120 $\pm$ 0.010	0.110 $\pm$ 0.011
α -Hydroxy Isobutyric Acid	3:30	21:30	21:30	21:30	1.039 $\pm$ 0.006	1.045 $\pm$ 0.005	0.959 $\pm$ 0.003	0.966 $\pm$ 0.002	0.071 $\pm$ 0.008	0.078 $\pm$ 0.006
3-Methyl-2-oxo Valeric Acid	5:30	21:30	15:30	5:30	1.067 $\pm$ 0.006	1.059 $\pm$ 0.012	0.932 $\pm$ 0.004	0.953 $\pm$ 0.004	0.135 $\pm$ 0.007	0.107 $\pm$ 0.013
Cortisol	9:30	5:30	1:30	1:30	1.067 $\pm$ 0.005	1.064 $\pm$ 0.006	0.903 $\pm$ 0.008	0.909 $\pm$ 0.008	0.164 $\pm$ 0.01	0.154 $\pm$ 0.013
Cortisol 21-Acetate	21:30	23:30	23:30	1:30	1.084 $\pm$ 0.032	1.069 $\pm$ 0.011	0.930 $\pm$ 0.028	0.949 $\pm$ 0.004	0.153 $\pm$ 0.06	0.12 $\pm$ 0.014
Reichstein Substance	5:30	5:30	1:30	7:30	1.26 $\pm$ 0.027	1.298 $\pm$ 0.025	0.766 $\pm$ 0.012	0.768 $\pm$ 0.016	0.496 $\pm$ 0.027	0.53 $\pm$ 0.026
Acetylneuraminate	21:30	21:30	7:30	11:30	1.061 $\pm$ 0.006	1.062 $\pm$ 0.011	0.948 $\pm$ 0.005	0.945 $\pm$ 0.005	0.113 $\pm$ 0.01	0.107 $\pm$ 0.014
Arabinose	21:30	21:30	23:30	9:30	1.07 $\pm$ 0.005	1.074 $\pm$ 0.006	0.921 $\pm$ 0.012	0.907 $\pm$ 0.008	0.15 $\pm$ 0.014	0.167 $\pm$ 0.011
D-Ribose-5-Phosphate	19:30	19:30	1:30	3:30	1.114 $\pm$ 0.019	1.114 $\pm$ 0.015	0.861 $\pm$ 0.031	0.853 $\pm$ 0.037	0.253 $\pm$ 0.045	0.26 $\pm$ 0.05
Fructose/Mannose/Galactose	13:30	19:30	23:30	15:30	1.05 $\pm$ 0.009	1.047 $\pm$ 0.006	0.966 $\pm$ 0.004	0.976 $\pm$ 0.003	0.083 $\pm$ 0.012	0.071 $\pm$ 0.007
Galactarate	13:30	1:30	21:30	9:30	1.072 $\pm$ 0.008	1.069 $\pm$ 0.005	0.933 $\pm$ 0.005	0.92 $\pm$ 0.008	0.139 $\pm$ 0.011	0.149 $\pm$ 0.012
Gluconic Acid	13:30	21:30	3:30	21:30	1.054 $\pm$ 0.011	1.057 $\pm$ 0.009	0.948 $\pm$ 0.008	0.954 $\pm$ 0.006	0.105 $\pm$ 0.018	0.102 $\pm$ 0.014
Mannitol	13:30	21:30	3:30	3:30	1.062 $\pm$ 0.008	1.064 $\pm$ 0.006	0.874 $\pm$ 0.024	0.91 $\pm$ 0.013	0.188 $\pm$ 0.031	0.154 $\pm$ 0.017

S-Lactate- Glyceraldehyde	21:30	21:30	7:30	13:30	1.044 ± 0.004	1.044 ± 0.011	0.968 ± 0.002	0.969 ± 0.002	0.076 ± 0.004	0.075 ± 0.011
Indole-3-propionic acid ^A	23:30	3:30	1:30	23:30	1.046 ± 0.002	1.055 ± 0.008	0.970 ± 0.003	0.954 ± 0.004	0.076 ± 0.005	0.099 ± 0.011
Indoxyl sulfate (indican) ^C	19:30	21:30	21:30	5:30	1.039 ± 0.003	1.039 ± 0.009	0.955 ± 0.017	0.970 ± 0.004	0.083 ± 0.019	0.069 ± 0.011
Kynurenine ^B	19:30	21:30	11:30	9:30	1.043 ± 0.006	1.042 ± 0.005	0.957 ± 0.006	0.966 ± 0.003	0.086 ± 0.011	0.077 ± 0.006
N-methyl Serotonin (I.S.) ^B	9:30	21:30	17:30	21:30	1.070 ± 0.011	1.059 ± 0.009	0.940 ± 0.010	0.938 ± 0.014	0.129 ± 0.020	0.120 ± 0.020
Uridine	9:30	21:30	1:30	13:30	1.034 ± 0.005	1.036 ± 0.008	0.964 ± 0.005	0.958 ± 0.004	0.07 ± 0.008	0.078 ± 0.009
Retinoate	7:30	21:30	3:30	7:30	1.05 ± 0.005	1.056 ± 0.005	0.952 ± 0.004	0.933 ± 0.01	0.098 ± 0.006	0.122 ± 0.012
Creatinine ^D	19:30	1:30	3:30	9:30	1.054 ± 0.006	1.043 ± 0.006	0.940 ± 0.003	0.946 ± 0.005	0.115 ± 0.007	0.098 ± 0.009

^ADerived solely from microbial metabolism. ^BDerived from both microbial and host metabolism. ^CDerived from host secondary metabolism of microbial metabolites. ^DAssociated with shifts in gut microbes.

Table S5. Metabolite identification level

Metabolite type	Metabolite	Metabolite Identification Level
Acid	Oxalic Acid	5
	5-oxo-D-Proline	1
Amino acids and derivatives	Alanine	1
	Aspartate	1
	β -Alanine/Sarcosine	1
	Citrulline	1
	Cystine	1
	D-Glucosamine-6-Sulfate	1
	L-Isoleucine	1
	L-Glutamic Acid	1
	L-Glutamine	1
	L-Lysine	1
	L-Methionine	1
	O-Acetyl-L-Serine	1
	L-Ornithine	1
	L-Phenylalanine	1
	L-Proline	1
	Taurine	1
	L-Threonine	1
	Trans-4-Hydroxyproline	1
	Tryptophan	1
	L-Tyrosine	1
	L-Valine	1
Aryl acids	Hippuric acid	1
	2,3-Dihydroxybenzoate	5
	2-Quinoline-Carboxylic Acid	1
	3-Methoxy-4-Hydroxymandelate	5
	4-Hydroxyphenylacetate; Mandelic Acid	5
	Dihydroxymandelic Acid	5
	Ferulate	1
Aryl aldehyde	Trans-Cinnamate	1
	3-Hydroxybenzaldehyde	5
Aryl Sulfate	p-Cresol sulfate ^C	5
Bile acids primary precursors	3 α ,7 α ,12 α -Trihydroxy-5 β -Cholestan-26-al	5
	27-Deoxy-5 β -Cyprinol	5
	3 α ,7 α ,24-Trihydroxy-5 β -Cholestanoyl-CoA	5
	7 α -Hydroxy-3-oxo-4-Cholestenoate	5
Bile acids primary	Cholic acid	5
	Chenodeoxycholate	1
Bile acids	Glycocholate	1
Glyco-conjugated	Chenodeoxyglycocholate	5
Bile acids Tauro-conjugated	Taurodeoxycholate	5
Bile acids secondary	Lithocholic acid ^A	5
	Coprocholic acid	5
	Bilirubin	1

Bile component	Biliverdin	1
	10-Hydroxydecanoate	1
	1-Oleoyl-rac-Glycerol	1
	Arachidic Acid	5
	Caprylic Acid	5
	Docosahexanoic Acid	5
	Gamma Linolenic Acid	1
Fatty acids	Heptadecanoate	5
	Linoleate	1
	Myristic Acid	5
	Nonanoate	5
	Palmitate/ Hexadexanoic acid	5
	Palmitoleic Acid	5
	Petroselinic Acid	5
	Stearate	1
Glutaric acid derivatives	3-Hydroxy-3-Methylglutarate	5
	α -Ketoglutaric Acid	5
Homoisocitrate derivative	α -Aminoadipate	1
	Isatin (I.S.)	5
Indoles and derivatives	Indole-3-Acetaldehyde	1
	Indole-3-Acetate	1
	Hypoxanthine	1
Purines and derivatives	Urate	1
	Xanthine	1
SCFA and derivatives	Butyric acid	5
	α -Hydroxyisobutyric Acid	5
Short chain keto acids and derivatives	3-Methyl-2-oxovaleric Acid	5
	Cortisol	1
Steroids and derivatives	Cortisol 21-Acetate	1
	Reichstein Substance	5
	N-Acetylneuraminate	1
	Arabinose	5
	D-Ribose-5-Phosphate	1
Sugars and derivatives	Fructose/Mannose/Galactose	1
	Galactarate	1
	D-Gluconic Acid	1
	Mannitol	1
	S-Lactate-Glyceraldehyde	5
	Indole-3-propionic acid	5
Tryptophan catabolites	Indoxyl sulfate	5
	Kynurenine	1
	N-methylserotonin (I.S.)	5
Uracil containing precursor and derivatives	Uridine	1
Vitamin	Retinoate	1
Other	Creatinine	1