	Timepoints for the 1st three participants	Timepoints for other participants
Prior to washout period - collected at home	Day 0 - stool	Day 0 - stool
Washout period	Day 1 - stool, urine, plasma, buffy coat, serum	
Washout period	Day 2 - stool, urine, plasma, buffy coat, serum	
Washout period	Day 3 - stool, urine, plasma, buffy coat, serum	
End of washout period, last samples collected before Randomized diet phase (CMC-containing vs Emulsifier-free diet)	Day 4 - stool, urine, plasma, buffy coat, serum, OGTT, biopsies	Day 4 - stool, urine, plasma, buffy coat, serum, OGTT, biopsies
CMC exposure	Day 5 - stool, urine, plasma, buffy coat, serum	Day 5 - stool, urine, plasma, buffy coat, serum
CMC exposure	Day 6 - stool, urine	Day 6 - stool, urine, plasma, buffy coat, serum
CMC exposure	Day 7 - stool, urine	Day 7 - stool, urine, plasma, buffy coat, serum
CMC exposure	Day 8 - stool, urine, plasma, buffy coat, serum	Day 8 - stool, urine
CMC exposure	Day 9 - stool, urine	Day 9 - stool, urine
CMC exposure	Day 10 - stool, urine, plasma, buffy coat, serum	Day 10 - stool, urine
CMC exposure	Day 11 - stool, urine	Day 11 - stool, urine, plasma, buffy coat, serum
CMC exposure	Day 12 - stool, urine, plasma, buffy coat, serum	Day 12 - stool, urine
CMC exposure	Day 13 - stool, urine	Day 13 - stool, urine, plasma, buffy coat, serum
CMC exposure	Day 14 - stool, urine	Day 14 - stool, urine, plasma, buffy coat, serum, OGTT, biopsies
CMC exposure	Day 15 - stool, urine, plasma, buffy coat, serum	
CMC exposure	Day 16 - stool, urine	
CMC exposure	Day 17 - stool, urine, plasma, buffy coat, serum, OGTT, biopsies	
Post study samples	Day 48 - stool, plasma, buffy coat, serum	Day 48 - stool, plasma, buffy coat, serum
Post study samples	Day 107 - stool	Day 107 - stool

Table S1: Timeline and list of samples collected during the study.

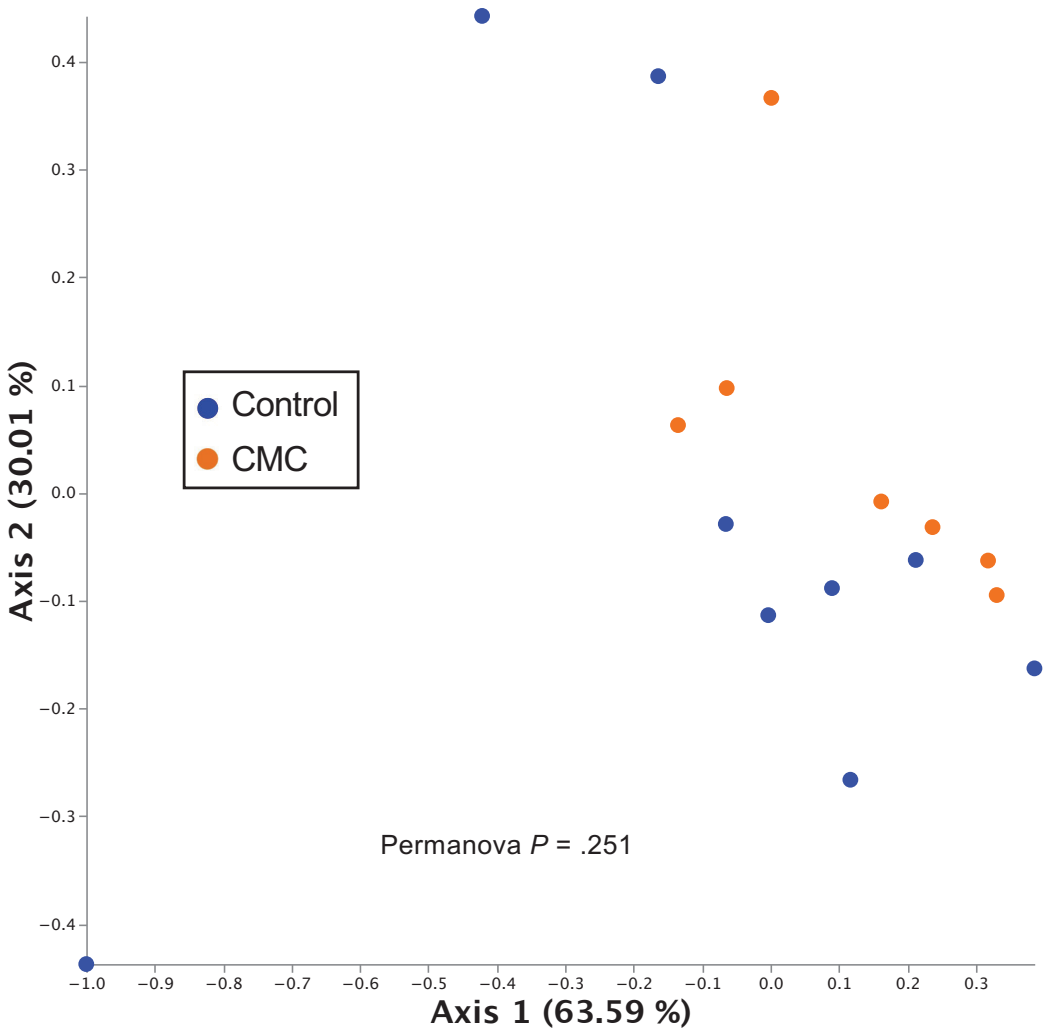


Figure S1: Dietary habits did not significantly differ between groups at the beginning of the study.

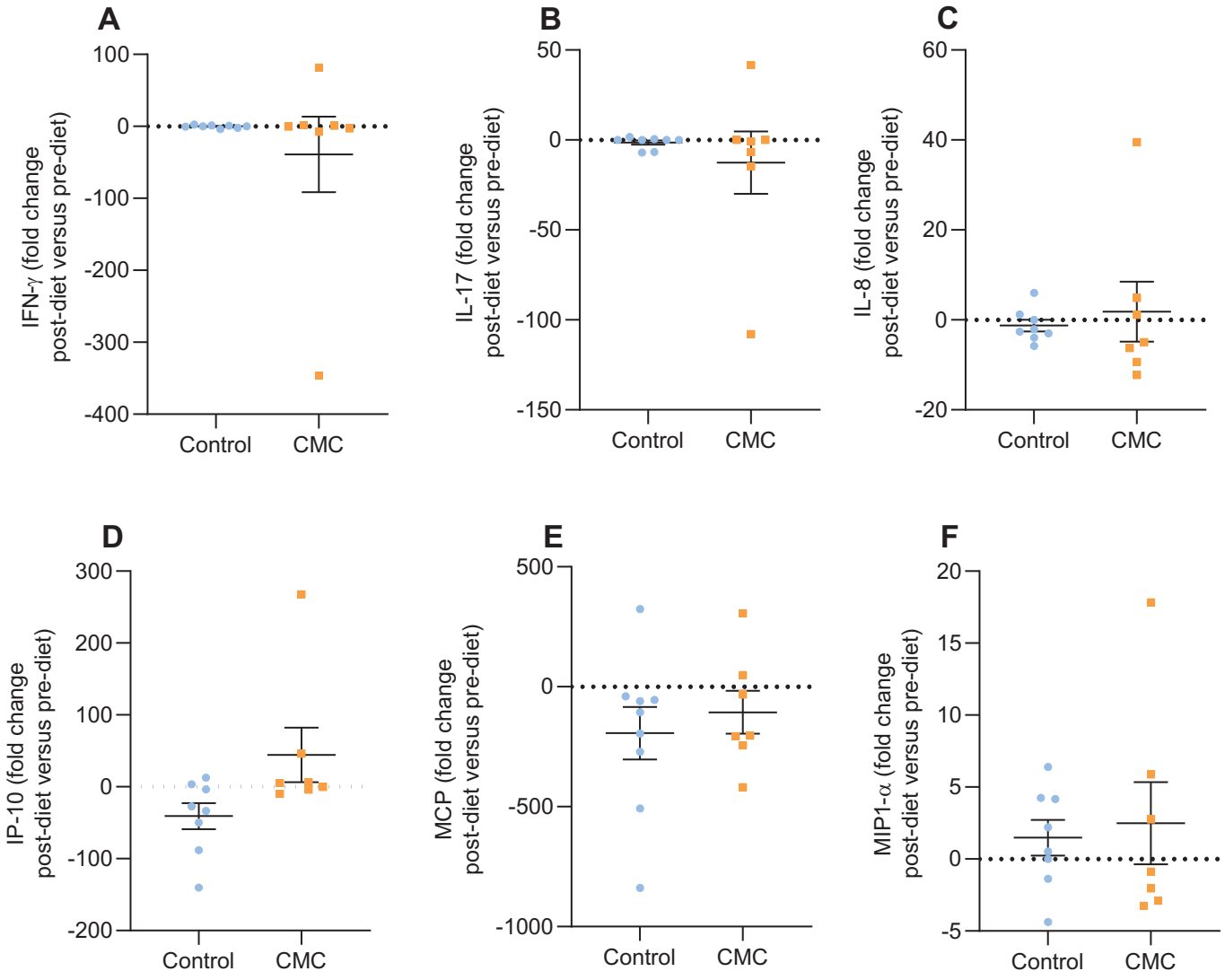


Figure S2: Impact of carboxymethylcellulose exposure on circulating cytokines.

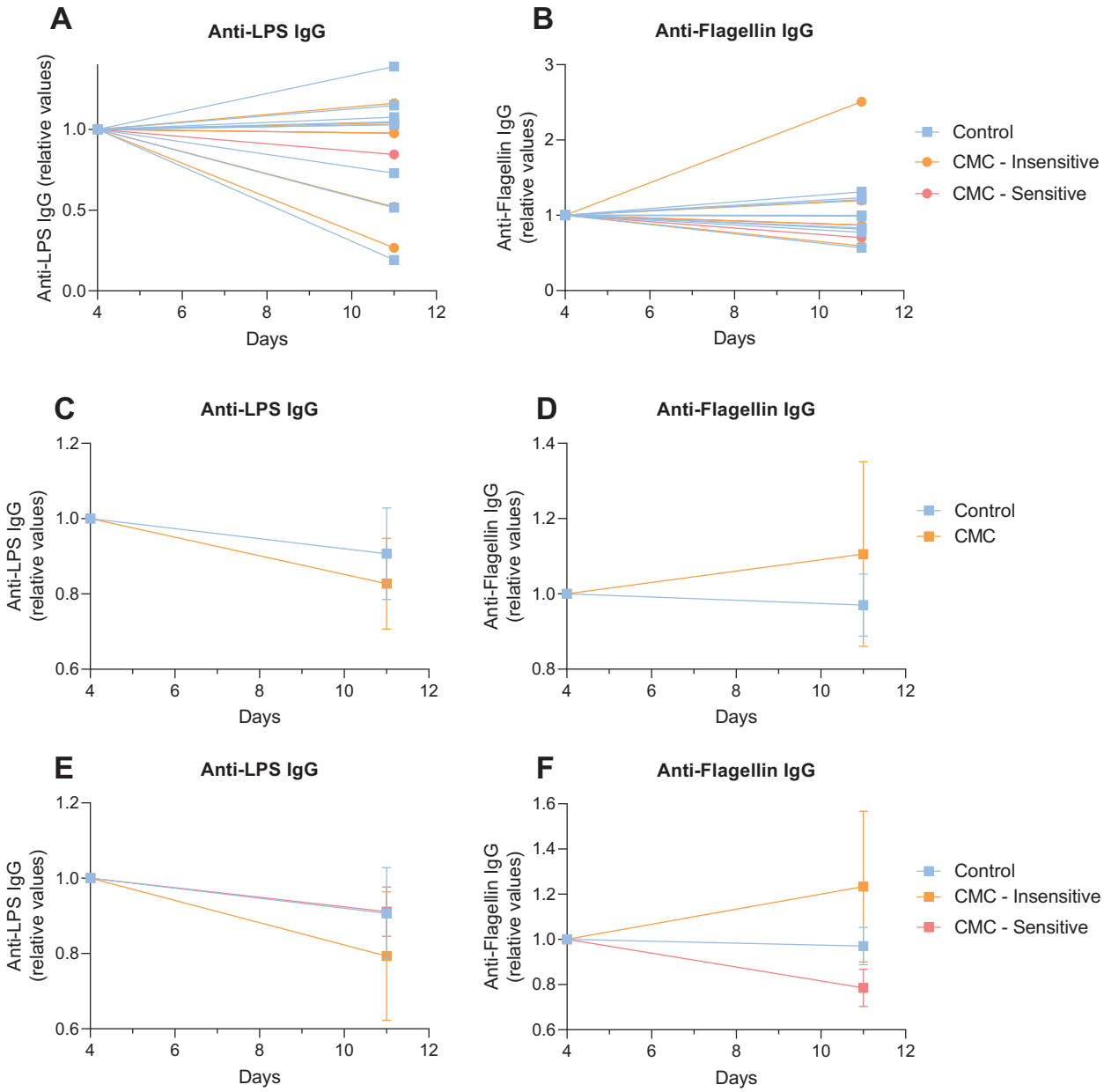


Figure S3: Impact of carboxymethylcellulose exposure on circulating anti-lipopolysaccharide and anti-flagellin IgG.

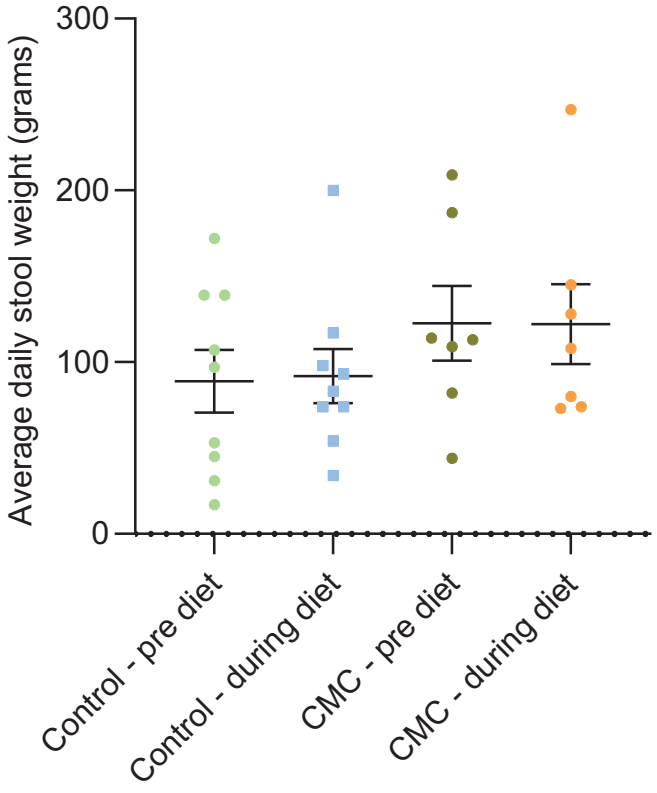
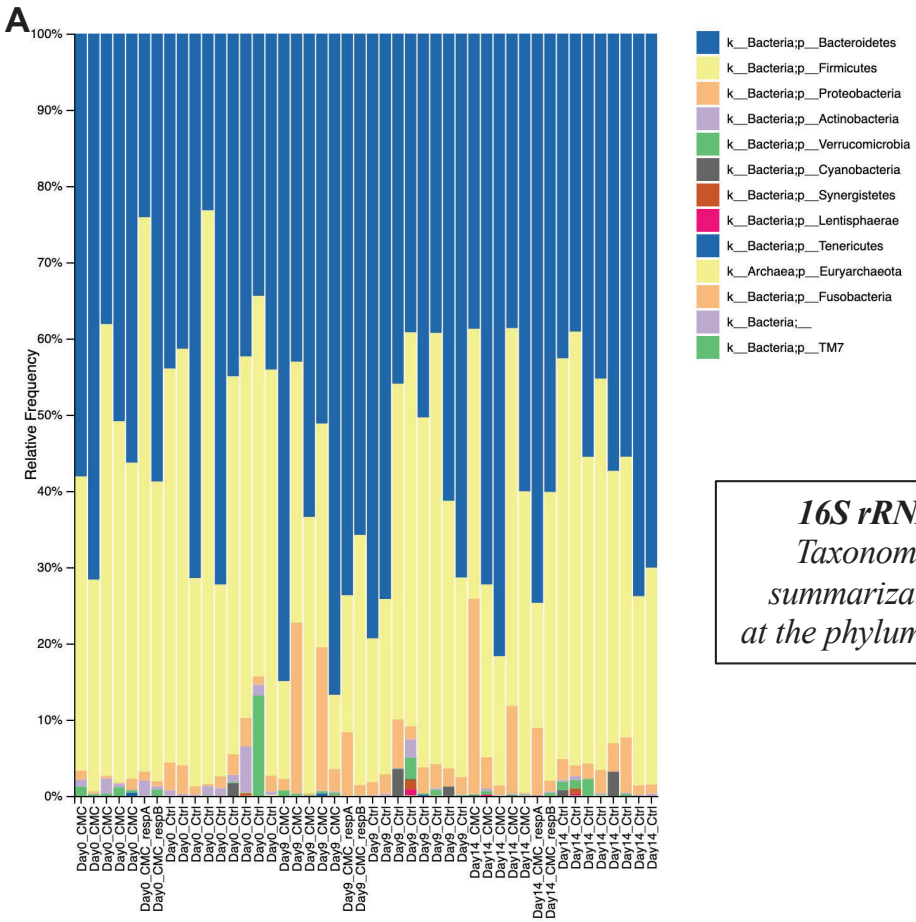
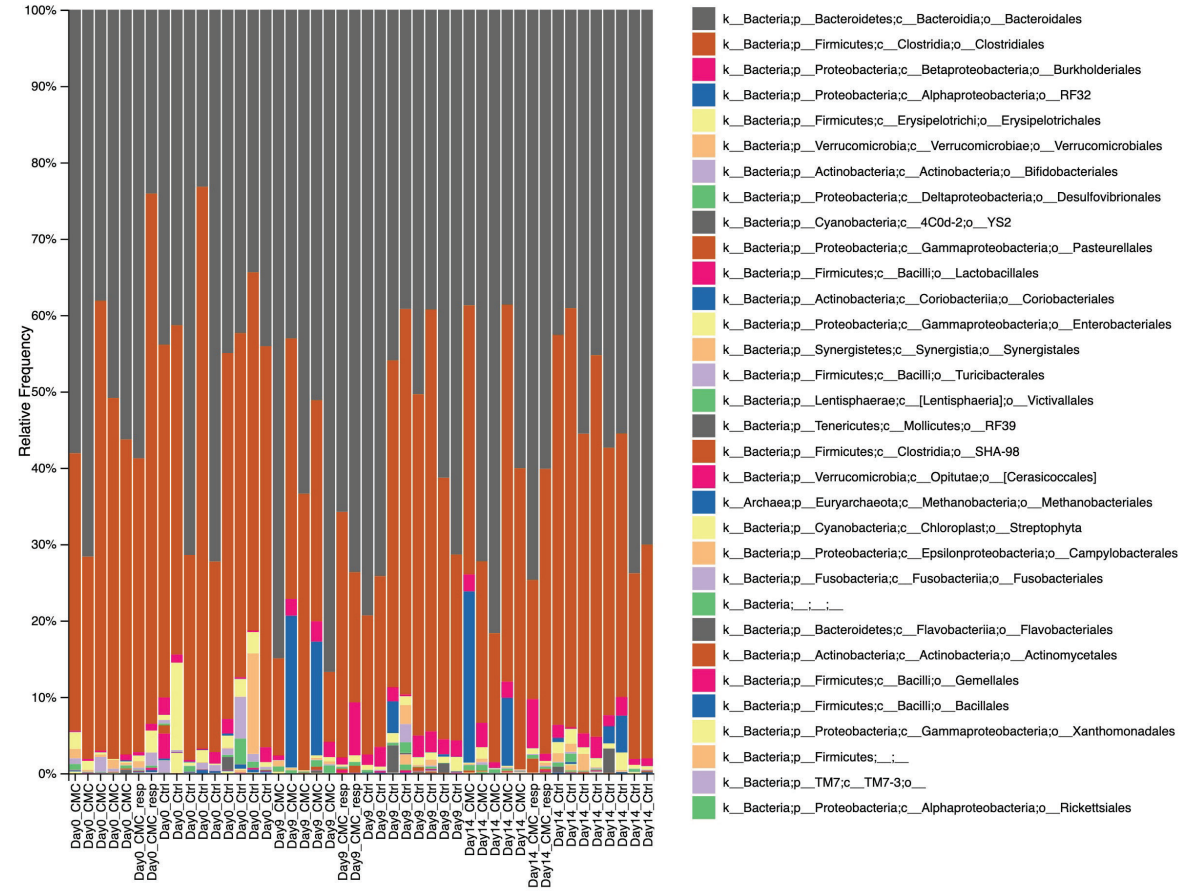


Figure S4: Impact of carboxymethylcellulose consumption on stool weight.



16S rRNA
Taxonomic summarization at the phylum level



16S rRNA
Taxonomic summarization at the order level

Figure S5: Effect of carboxymethylcellulose consumption on microbiota composition.

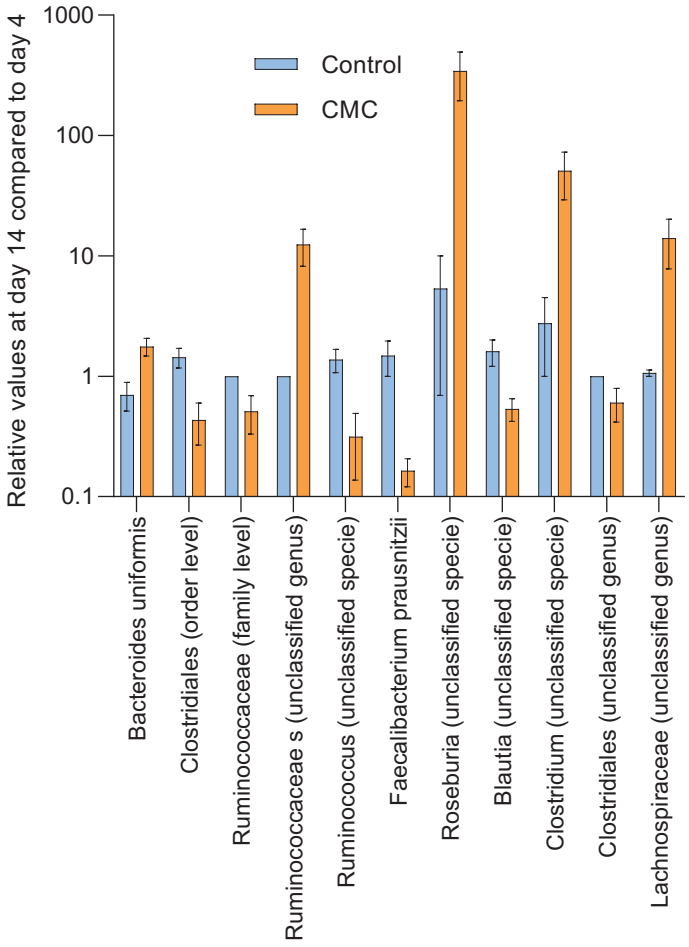


Figure S6: Effect of carboxymethylcellulose consumption on microbiota composition.

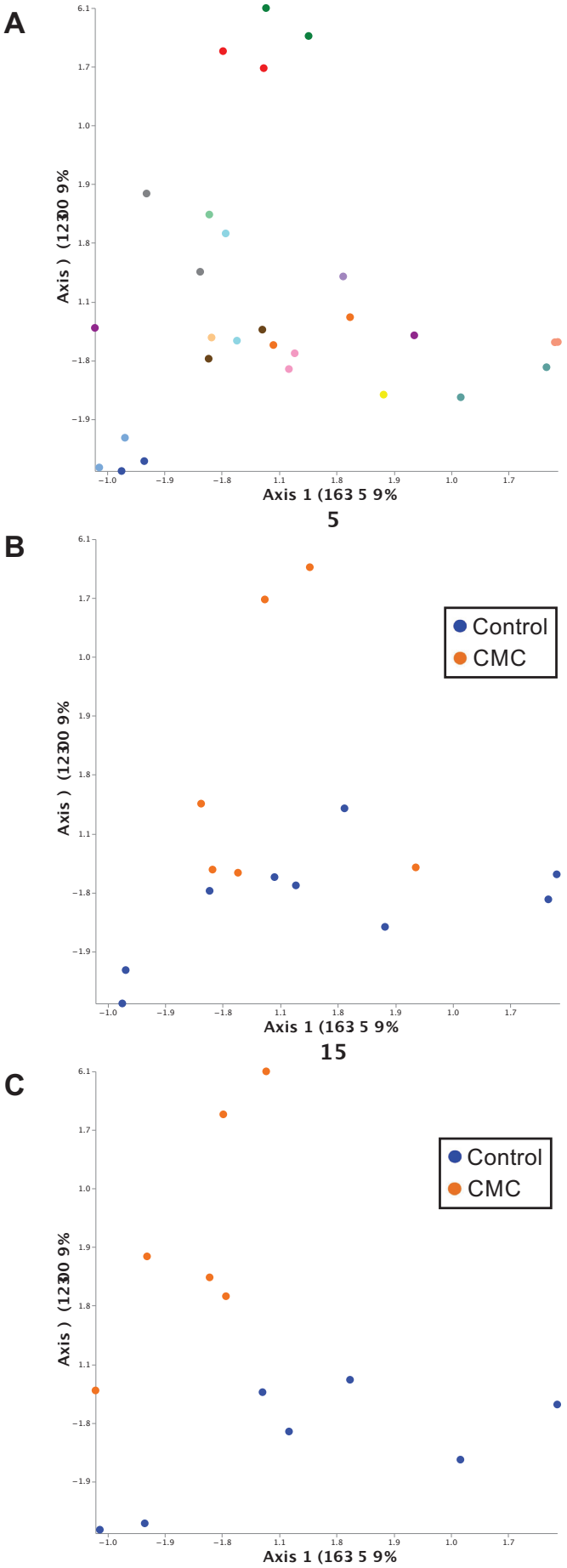


Figure S7: Effect of carboxymethylcellulose consumption on microbiota taxonomic composition based on metagenomic data.

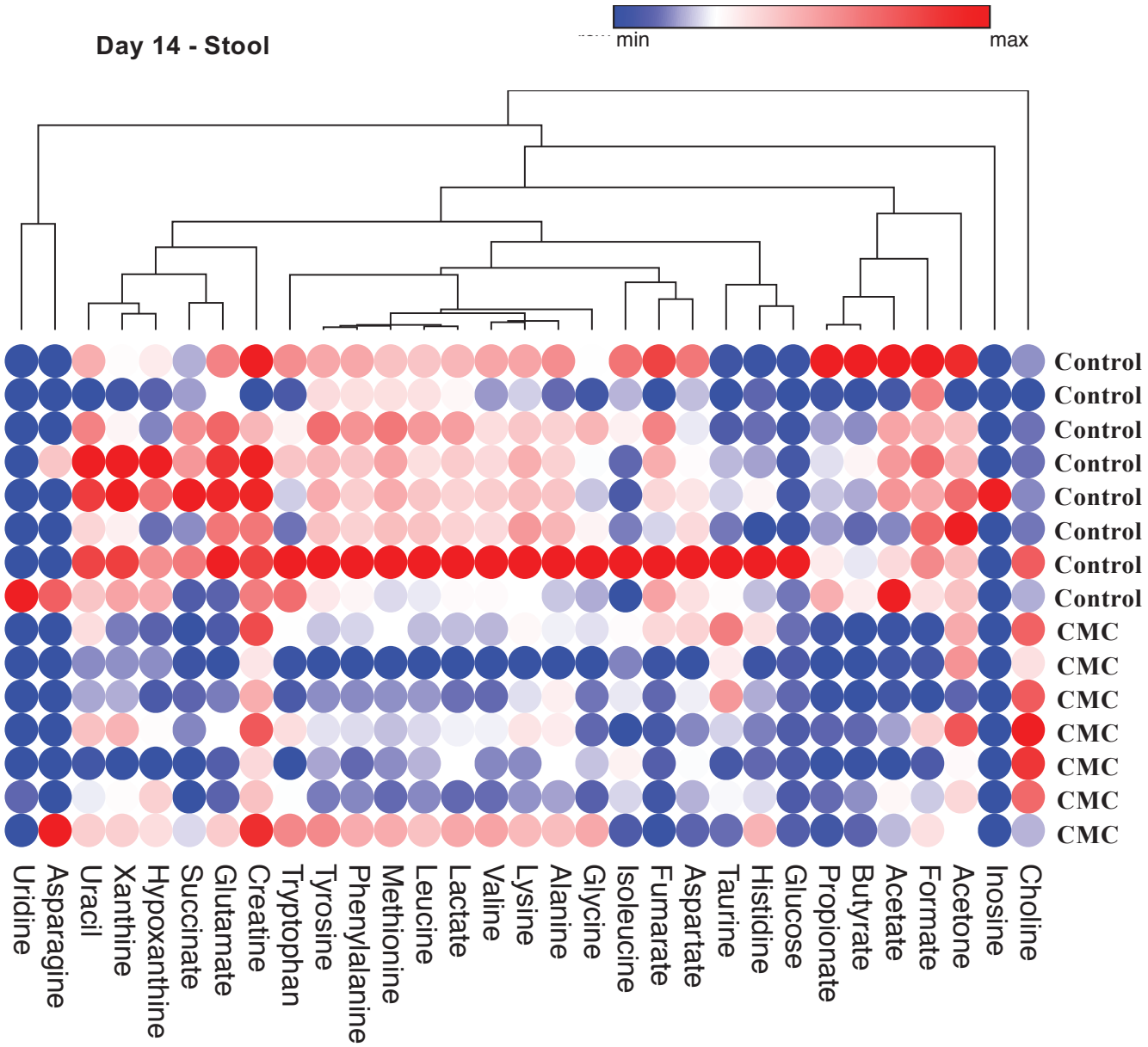


Figure S8: Effect of carboxymethylcellulose consumption on the fecal metabolome.

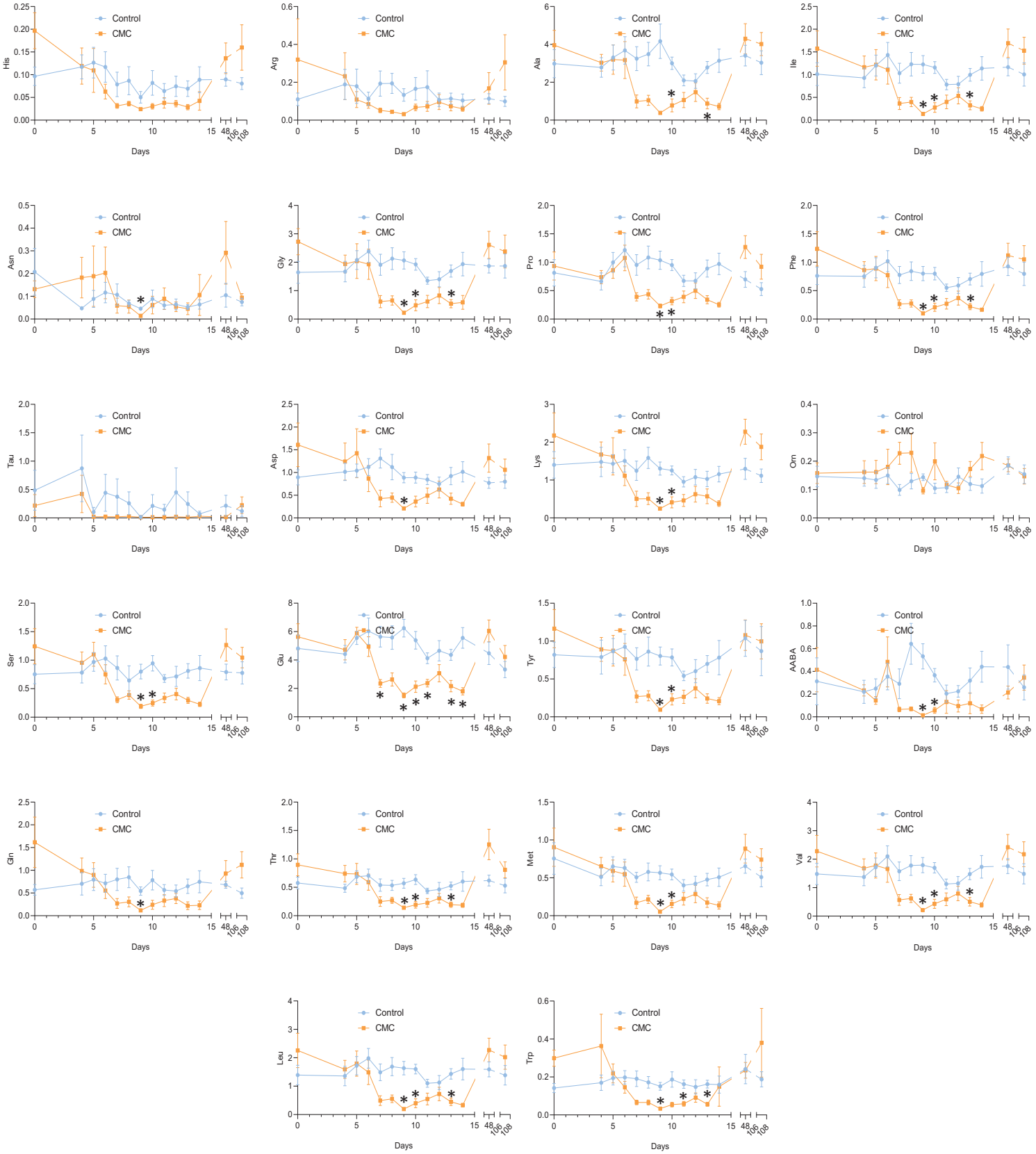


Figure S9: Effect of carboxymethylcellulose consumption on the fecal metabolome

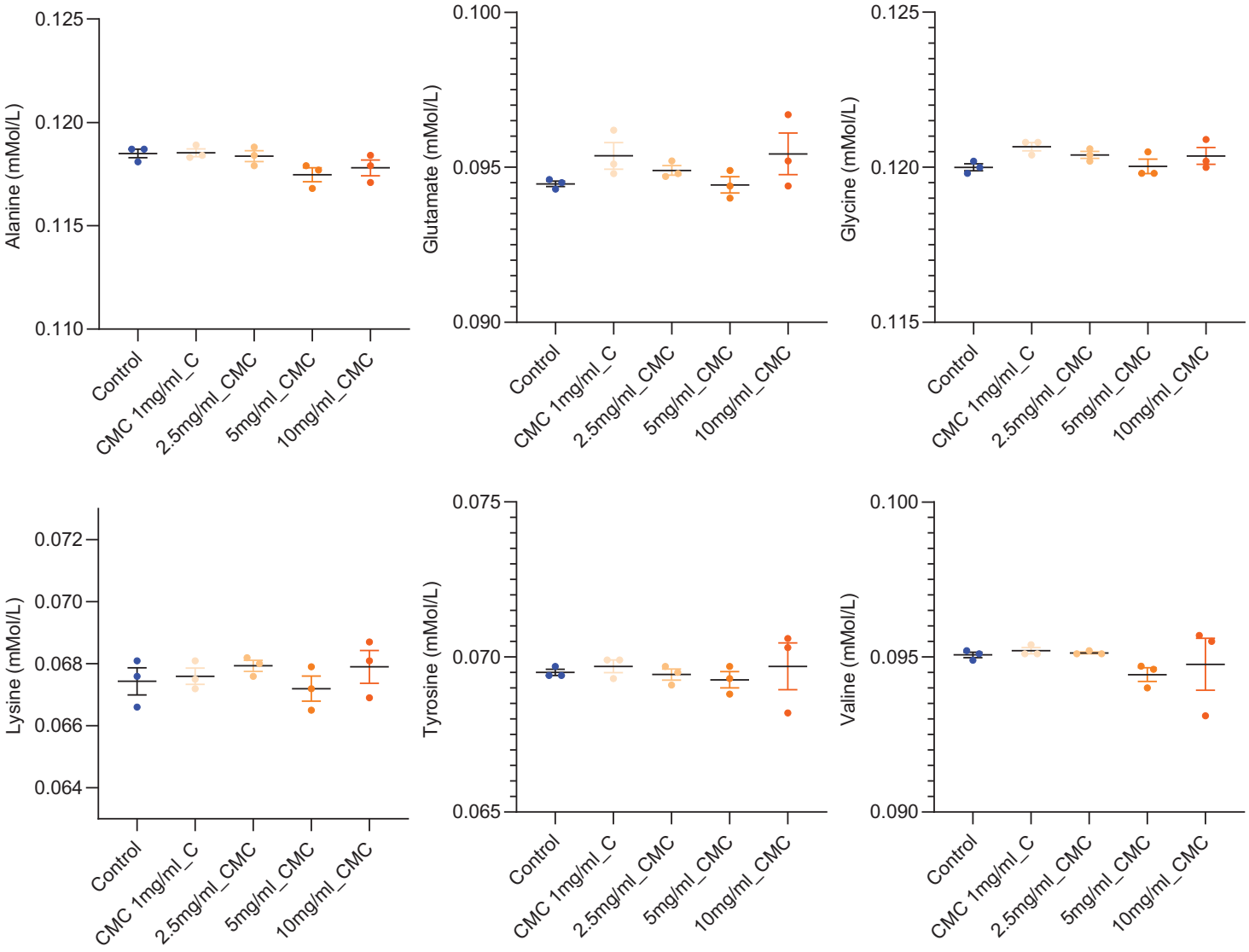
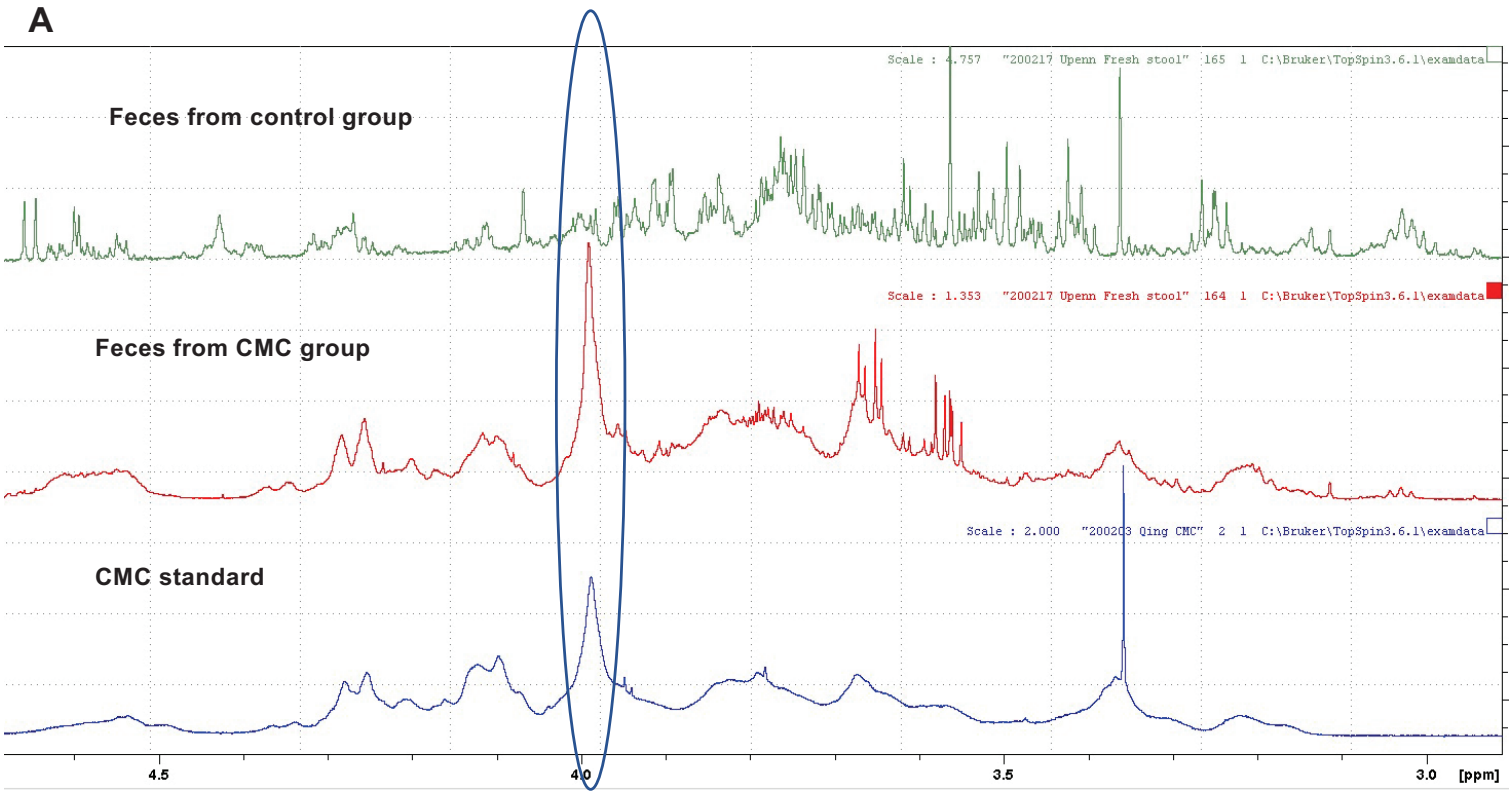
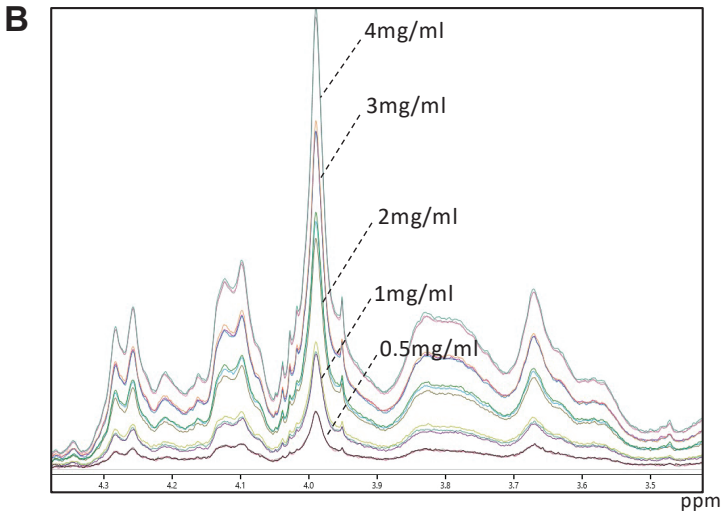


Figure S10: Impact of carboxymethylcellulose on AccQ•Tag-based detection of various amino acids.





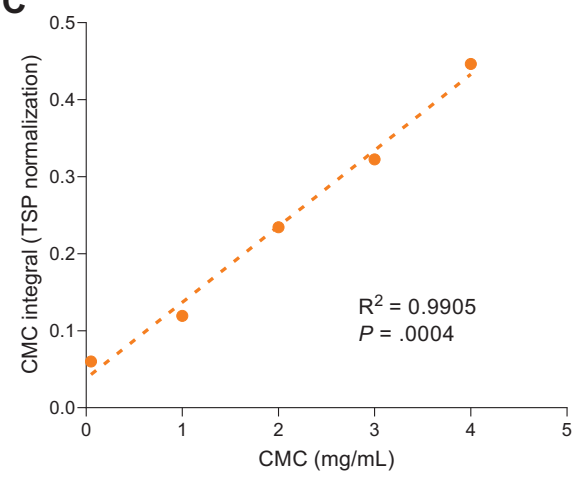


Figure S11: NMR-based detection of carboxymethylcellulose in fecal samples.

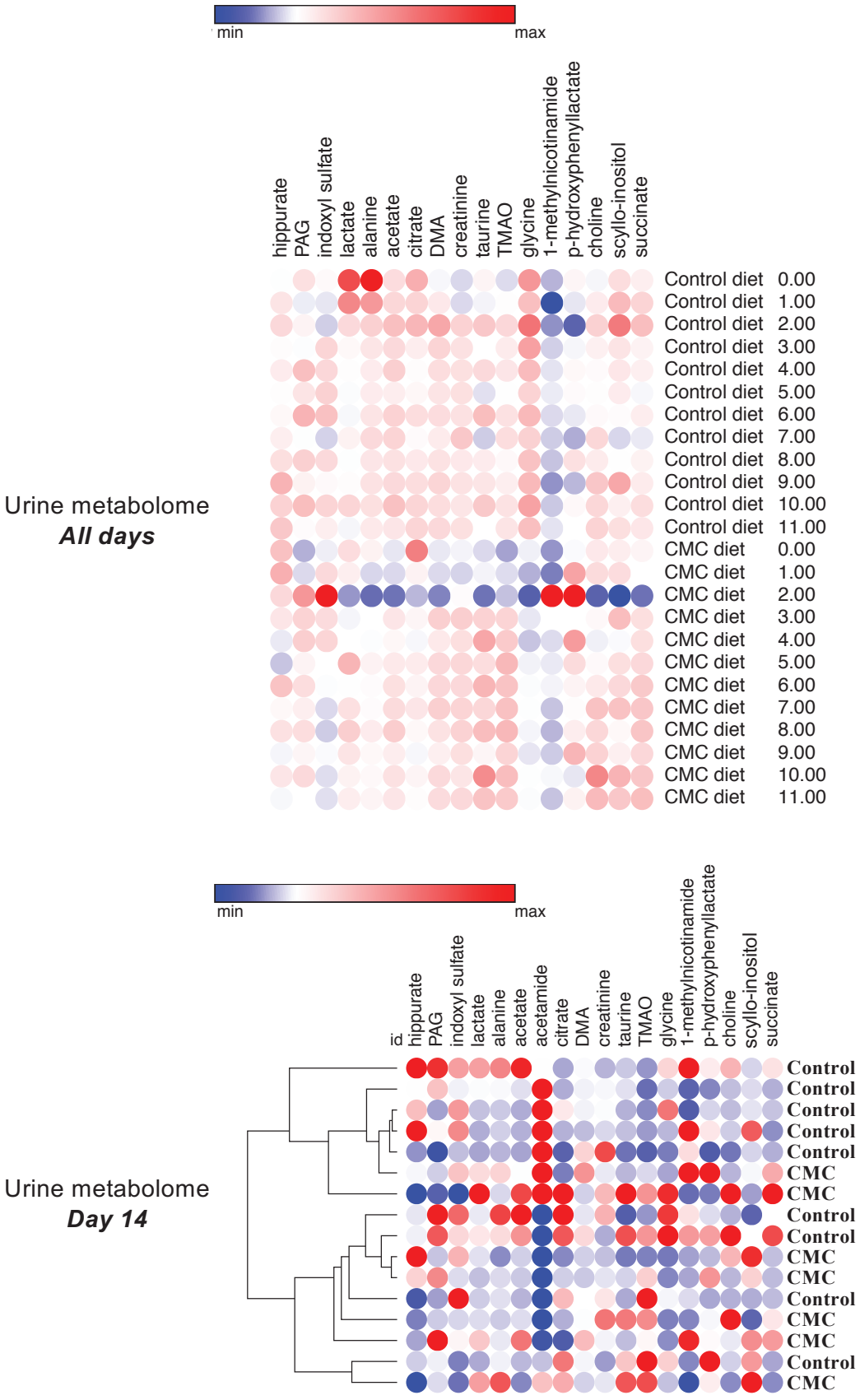
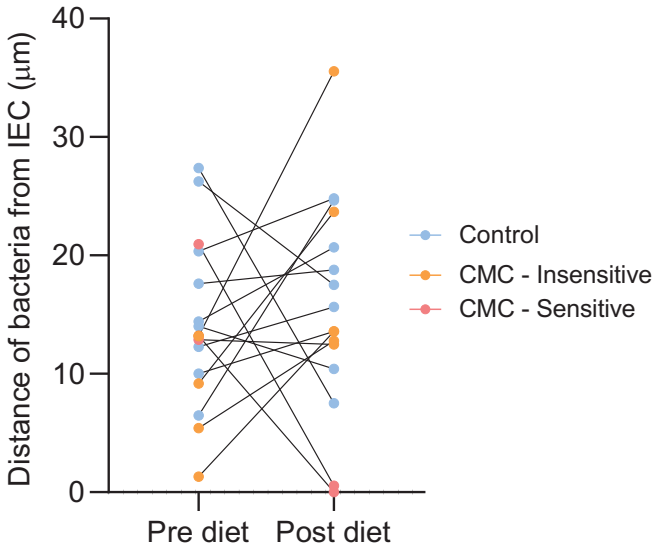
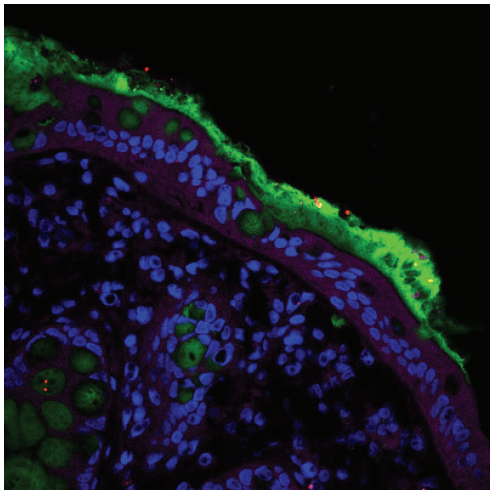
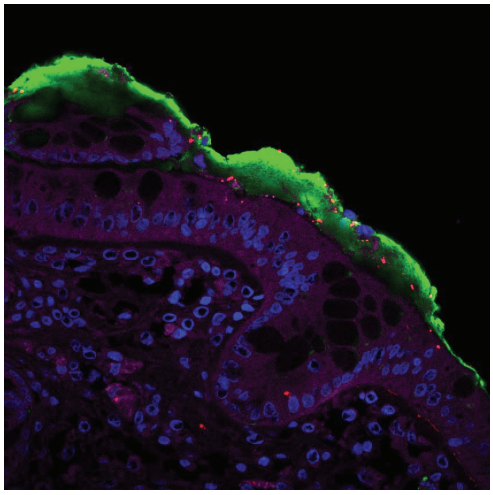


Figure S12: Effect of carboxymethylcellulose consumption on the urine metabolome.

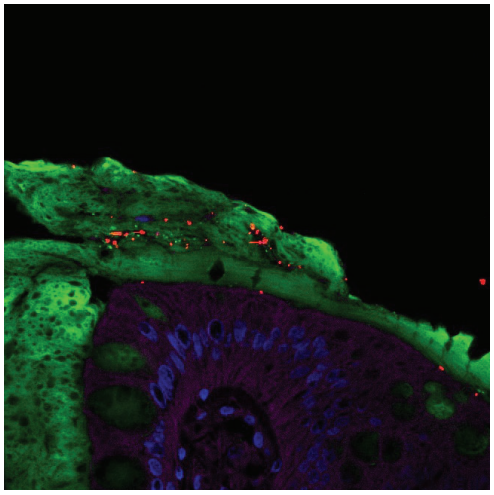




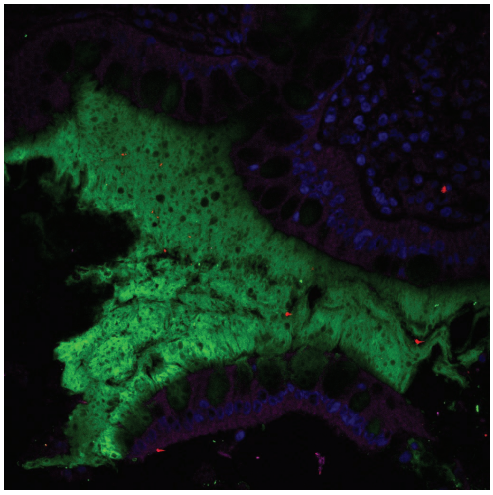
Microbiota - IEC = 14.16μm



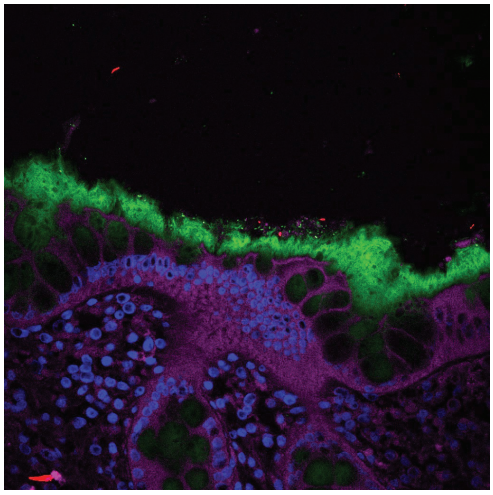
Microbiota - IEC = 2.23μm



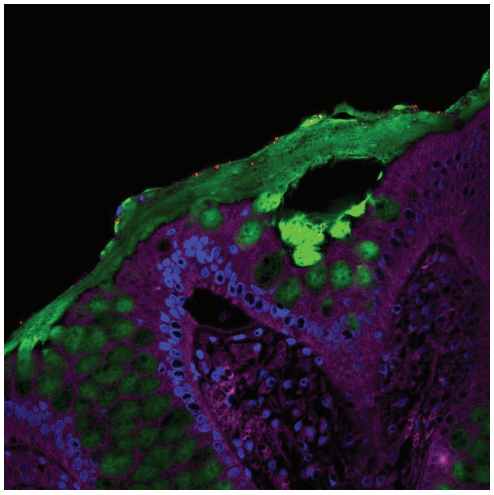
Microbiota - IEC = 0.00μm



Microbiota - IEC = 38.91μm



Microbiota - IEC = 23.86μm



Microbiota - IEC = 22.69μm

Figure S13: Effect of carboxymethylcellulose consumption on microbiota localization

Table S2. NMR data for the metabolites found in stool (S) and urine (U).

NO.	Metabolites	Moieties	δ ^{1}H (ppm)	δ ^{13}C (ppm)	Location	Source*
1	acetone	CH_3	2.23(s)[a]	33.2	S	
2	butyrate	CH_3	0.90(t)	16.3	S	microbial
		βCH_2	1.56(m)	21.5		
		αCH_2	2.15(t)	42.7		
		COOH		186.8		
3	isoleucine	δCH_3	0.94(t)	14.2	S	
		γCH_3	1.01(d)	17.7		
		γCH_2	1.25(m)	27.5		
		$\gamma' CH_2$	1.48(m)	27.5		
		βCH	1.98(m)	37.7		
		αCH	3.67(d)	62.4		
		COOH		177.1		
4	leucine	δCH_3	0.96(d)	24.5	S	
		δCH_3	0.97(d)	23.5		
		γCH	1.69(m)	27.3		
		βCH_2	1.71(m)	42.8		
		αCH	3.74(t)	56.4		
		COOH		178.3		
5	valine	γCH_3	0.99(d)	19.6	S	
		γCH_3	1.04(d)	20.7		
		βCH	2.27(m)	32.0		
		αCH	3.62(d)	63.3		
		COOH		177.1		
6	propionate	CH_3	1.06(t)	13.2	S	microbial
		CH_2	2.19(q)	33.7		
		COOH		187.4		
7	lactate	CH_3	1.33(d)	22.5	S, U	
		CH	4.11(q)	71.9		
		COOH		185.3		
8	alanine	βCH_3	1.48(d)	19.2	S, U	
		αCH	3.79(q)	53.4		
		COOH		178.8		
9	lysine	γCH_2	1.48(m)	23.9	S	
		δCH_2	1.72(m)	29.4		
		βCH_2	1.90(m)	33.0		
		εCH_2	3.03(t)	42.2		
		αCH	3.76(t)	57.6		
		COOH		177.5		
10	acetate	CH_3	1.92(s)	26.2	S, U	microbial
		COOH		184.2		
11	glutamate	βCH_2	2.10(m)	30.1	S	
		$\beta' CH_2$	2.09(m)	30.1		
		γCH_2	2.36(m)	36.4		
		αCH	3.77(m)	57.6		

		C=O		184.0	
		COOH		177.5	
12	methionine	δCH_3	2.14(s)	16.8	S
		βCH_2	2.16(m)	33.2	
		γCH_2	2.65(t)	31.6	
		αCH	3.86(m)	56.9	
		COOH		176.6	
13	succinate	CH_2	2.41(s)	37.6	S, U
		COOH		184.4	
14	citrate	CH_2	2.54(d)	46.5	U
		'CH_2	2.66(d)	46.5	
		C-OH		76.4	
		COOH		181.5	
		COOH		183.9	
15	aspartate	βCH_2	2.68(m)	39.5	S
		β'CH_2	2.82(m)	39.5	
		αCH	3.91(m)	55.3	
		βCOOH		180.5	
		αCOOH		176.9	
16	asparagine	βCH_2	2.86(dd)	37.6	S
		β'CH_2	2.96(dd)	37.6	
		αCH	4.00(m)	54.3	
		C=O		177.1	
		COOH		176.3	
17	dimethylamine (DMA)	CH_3	2.72(s)	39.4	U
18	creatine	CH_3	3.04(s)	40.0	S
		CH_2	3.93(s)	57.1	
		C=NH		159.4	
		COOH		177.2	
19	choline	$N(CH_3)_3$	3.21(s)	56.8	S, U
		NCH_2	3.52(m)	58.5	
		OCH_2	4.07(m)	70.2	
20	taurine	CH_2SO_3	3.25(t)	50.7	S, U
		NCH_2	3.43(t)	38.5	
21	glycine	CH_2	3.57(s)	44.6	S, U
		COOH		175.2	
22	α-glucose	4CH	3.42(dd)	72.7	S
		2CH	3.54(dd)	74.9	
		3CH	3.73(dd)	76.2	
		5CH	3.83(dd)	74.4	
		6CH_2	3.83(dd)	63.7	
		1CH	5.24(d)	95.4	

23	β-glucose	2CH	3.26(dd)	77.5	S
		4CH	3.40(dd)	72.9	
		5CH	3.47(dd)	79.0	
		3CH	3.50(dd)	79.0	
		6CH	3.74(dd)	63.7	
		6CH'	3.90(dd)	63.9	
		1CH	4.45(d)	99.3	
24	uracil	CH	5.81(d)	103.9	S
		CH	7.54(d)	146.5	
		C=O		170.6	
		C=O		155.9	
25	fumarate	CH	6.53(s)	138.1	S
		COOH		179.2	
26	tyrosine	βCH_2	3.06(dd)	38.3	S
		$\beta' CH_2$	3.15(dd)	38.3	
		αCH	3.94(dd)	59.2	
		3 or 5CH	6.91(d)	118.8	
		2 or 6CH	7.20(d)	132.4	
		C(ring)		129.4	
		C-OH(ring)		157.7	
		COOH		177.1	
27	tryptophan	βCH_2	3.31(dd)	29.5	S
		$\beta' CH_2$	3.49(dd)	29.5	
		αCH	4.06(dd)	58.5	
		5CH	7.21(t)	122.5	
		6CH	7.29(t)	125.0	
		2CH	7.33(s)	128.2	
		7CH	7.55(d)	114.9	
		4CH	7.74(d)	121.5	
		COOH		177.4	
28	phenylalanine	βCH_2	3.13(dd)	38.4	S
		$\beta' CH_2$	3.29(dd)	38.4	
		αCH	3.98(dd)	59.3	
		2 or 6CH	7.33(m)	130.7	
		4CH	7.38(m)	131.9	
		3 or 5CH	7.43(m)	132.0	
		C(ring)		139.4	
		COOH		176.4	
29	histidine	βCH_2	3.14(dd)	30.8	S
		$\beta' CH_2$	3.25(dd)	30.8	
		αCH	3.99(dd)	58.7	
		5CH	7.08(s)	120.1	
		3CH	7.83(s)	138.3	
		C(ring)		133.6	
		COOH		176.4	
30	formate	CH	8.45(s)	172.4	S

31	hypoxanthine	8CH	8.20(s)	145.6	S		
		6CH	8.22(s)	149.2			
32	inosine	CH_2	3.85(dd)	63.8	S		
		'CH_2	3.92(dd)	63.8			
		5H'	4.28(q)	88.6			
		4H'	4.44(t)	73.4			
		2H'	6.10(d)	91.4			
		8H	8.24(s)	150.1			
		2H	8.34(s)	143.3			
33	xanthine	8CH	7.89(s)	144.0	S		
34	uridine	CH_2	3.81(d)	64.3	S		
		'CH_2	3.92(d)	64.3			
		4H'	4.14(q)	86.6			
		3H'	4.24(t)	73.1			
		2H'	4.36(t)	78.0			
		5H	5.90(d)	95.2			
		6H	5.91(d)	90.8			
		1H'	7.87(d)	144.1			
35	creatinine	CH_3	3.05(s)	33.2	U		
		CH_2	4.06(s)	59.2			
36	trimethylamine N-oxide (TMAO)	N-CH_3	3.27(s)	62.5	U		microbial
37	hippurate	αCH_2	3.97(s)	47.2	U		
		3 or 5 CH	7.56(dd)	132.1			
		4CH	7.64(t)	135.5			
		2 or 6 CH	7.83(dd)	130.2			
		NH	8.56(brs)				
		C=O		173.3			
		COOH		180.0			
38	phenylacetylglycine (PAG)	CH_2	3.65(s)	45.2	U		
		2 or 6 CH	7.36(m)	132.0			
		4CH	7.36(m)	119.3			
		3 or 5 CH	7.42(m)	132.0			
		C=O		167.8			
39	p-hydroxyphenylacetate	CH_2	3.45(s)	46.9	U		microbial
		2 or 6 CH	6.87(d)	118.2			
		3 or 5 CH	7.16(d)	133.4			
		C-OH		156.9			
		COOH		182.7			
40	indoxyl sulfate	5CH	7.20(m)	123.0	U		microbial
		6CH	7.27(m)	125.2			
		2CH	7.36(s)	118.7			
		7CH	7.50(m)	115.0			
		4CH	7.70(m)	120.3			

41	1-methylnicotinamide	CH_3	4.48(s)	51.3	U
		5CH	8.18(m)	130.9	
		4CH	8.89(dt)	146.4	
		6CH	8.96(m)	150.0	
		2CH	9.27(m)	147.9	
42	*scyllo*-inositol	CHOH	3.35(s)	74.3	U

[a] s, singlet; d, double; t, triplet; q, quartet; m, multiplet; dd, double of doubles; dt, double of triplet.
*Only the microbial metabolic products are indicated. Other metabolites have more complicated sources [18-20].

18. Krautkramer KA, Fan J, Backhed F. Gut microbial metabolites as multi-kingdom intermediates. Nat Rev Microbiol 2021;19:77-94.
19. Hosseinkhani F, Heinken A, Thiele I, et al. The contribution of gut bacterial metabolites in the human immune signaling pathway of non-communicable diseases. Gut Microbes 2021;13:1-22.
20. Vernocchi P, Del Chierico F, Putignani L. Gut Microbiota Profiling: Metabolomics Based Approach to Unravel Compounds Affecting Human Health. Front Microbiol 2016;7:1144.