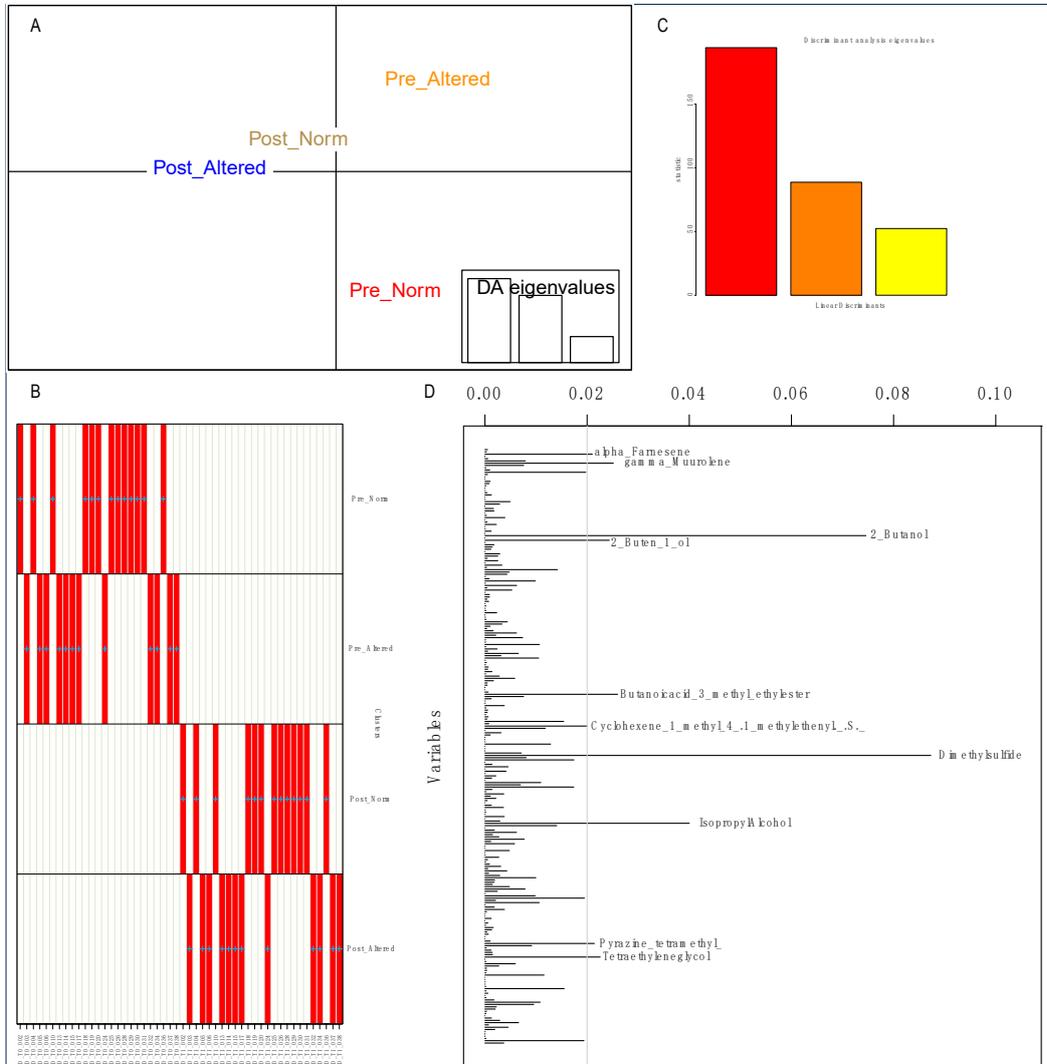
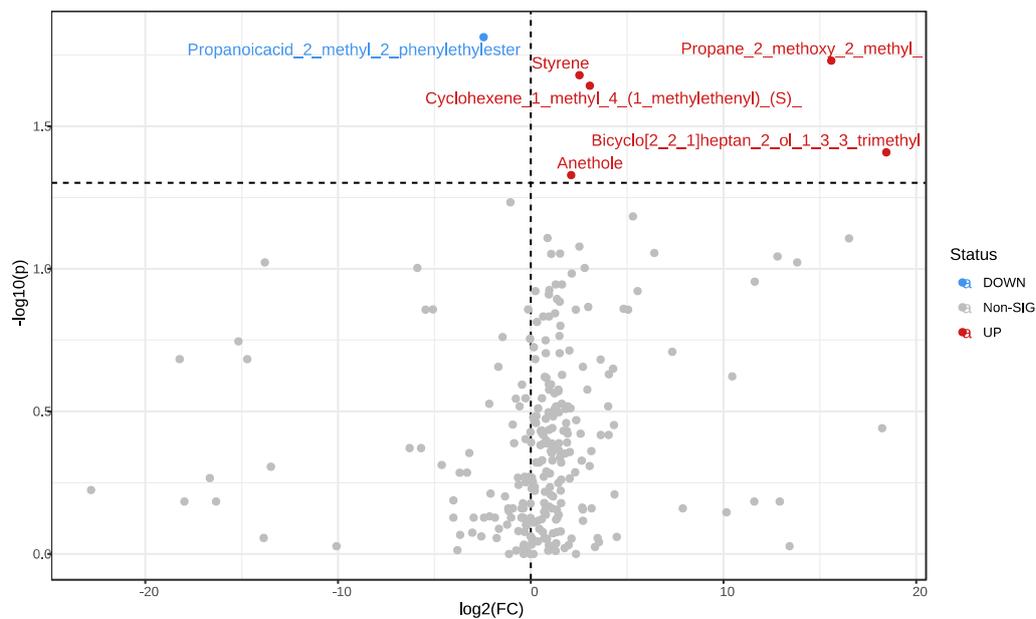


Supplementary Figure S1. Fecal metabolomics DAPC clustering. Discriminant analysis of principal components of volatile organic compounds in obese patients with altered and normal intestinal permeability before (pre) and after (post) VLCKD administration. A) DAPC plot based on discriminant eigen values. B) proportions of successful reassignments (based on the discriminant functions) of individuals to their original cluster. C) DAPC linear discriminants. D) Loading plot reporting the contribution of most impacting var-iables (VOCs) useful in discriminating sample clusters.

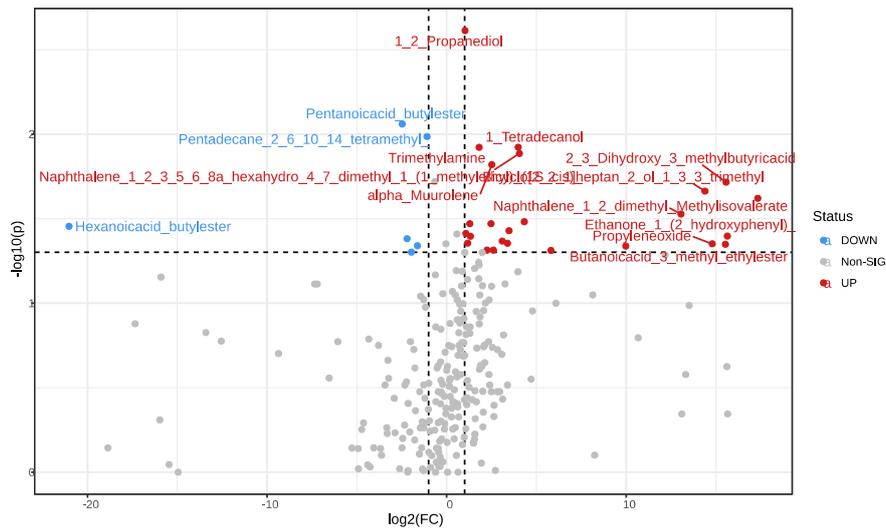


Supplementary Figure S2. Volcano plot of statistically significant fecal VOC fold changes in patients marked by altered intestinal permeability. VOCs in fecal samples from obese patients marked by altered permeability were compared before and after VLCKD administration by meaning of a non-parametric Wilcoxon rank-sum test combined with a fold change analysis. Due to the group comparison direction, increased (up-red) and decreased (down-blue) VOC concentrations are relative to altered phenotype after treatment. Under threshold VOCs are reported as grey dots. The table below the volcano plot reports significant VOC fold change as raw values (FC), log2 fold change (log2FC), corrected p-values and the p-value base-10 logarithm.



fecal sample VOC	FC	log2(FC)	corrected pval	=-LOG10(p)
Propanoic acid, 2-methyl-, 2-phenylethyl ester	0.18358	-2.4455	0.0154	1.8125
Propane, 2-methoxy-2-methyl-	49393	15.592	0.018635	1.7297
Styrene	5.7559	2.525	0.020954	1.6787
Cyclohexene, 1-methyl-4-(1-methylethenyl)-(S)-	8.3695	3.0651	0.022805	1.642
Bicyclo[2.2.1]heptan-2-ol, 1,3,3-trimethyl-	357640	18.448	0.039037	1.4085
Anethole	4.2744	2.0957	0.046962	1.3283

Supplementary Figure S3. Volcano plot of statistically significant fecal VOC fold changes in patients marked by normal intestinal permeability. VOCs in fecal samples from obese patients marked by normal intestinal permeability were compared before and after VLCKD administration using a non-parametric Wilcoxon rank-sum test combined with a fold change analysis. Due to the group comparison direction, increased (up-red) and decreased (down-blue) VOC concentrations are relative to normal phenotype after treatment. Under threshold, VOCs are reported as grey dots. The table below the volcano plot reports significant VOC fold change as raw values (FC), log2 fold change (log2FC), corrected p-values and the p-value base-10 logarithm.



faecal sample VOC	FC	log2(FC)	corrected p-value	$-\text{LOG}_{10}(p)$
1_2_Propanediol	2.0387	1.0276	0.0024389	2.6128
Pentanoicacid_butylester	0.18064	-2.4688	0.0087048	2.0602
Pentadecane_2_6_10_14_tetramethyl_	0.47061	-1.0874	0.010333	1.9858
1_Tetradecanol	15.906	3.9915	0.011949	1.9227
Trimethylamine	3.5047	1.8093	0.011962	1.9222
Naphthalene_1_2_3_5_6_8a_hexahydro_4_7_dimethyl_1_(1_methylethyl)_(1S_cis)_alpha_Murolene	16.66	4.0583	0.013015	1.8856
2_3_Dihydroxy_3_methylbutyricacid	5.7356	2.5199	0.015131	1.8201
Bicyclo[2_2_1]heptan_2_ol_1_3_3_trimethyl	48369	15.562	0.01921	1.7165
Methylisovalerate	21453	14.389	0.021736	1.6628
Naphthalene_1_2_dimethyl_	165400	17.336	0.023971	1.6203
Acetophenone_2_chloro	8520.1	13.057	0.029693	1.5273
1_Undecanol	20.093	4.3287	0.032959	1.482
Caryophyllene	5.549	2.4722	0.033828	1.4707
Hexanoicacid_butylester	2.4484	1.2918	0.033828	1.4707
Tetradecane	4.68E-07	-21.028	0.035093	1.4548
Nonanoicacid	11.156	3.4797	0.037287	1.4284
Ethanone_1_(2_hydroxyphenyl)_	2.1028	1.0723	0.038694	1.4124
Ethylamine	51023	15.639	0.040061	1.3973
Phenol_3_(1_methylethyl)_methylcarbamate	2.5155	1.3308	0.040205	1.3957
Cyclopentadecane	0.21751	-2.2009	0.041539	1.3815
Hexadecane	8.5933	3.1032	0.042908	1.3675
Menthol	2.2513	1.1707	0.044117	1.3554
Propyleneoxide	10.499	3.3922	0.044212	1.3545
Butanoicacid_3_methyl_ethyl_ester	28377	14.792	0.044536	1.3513
Cyclohexene_1_methyl_4_(1_methylethyl)_(S)_	47354	15.531	0.044776	1.349
Carbamicacid_methyl_3_methylphenylester	0.32489	-1.622	0.045759	1.3395
Phenol_3_4_dimethoxy_	1008.5	9.978	0.045924	1.338
Heptadecane	6.0973	2.6082	0.048496	1.3143
1_Hexanol_2_ethyl	4.7572	2.2501	0.048496	1.3143
Pentanoicacid_propylester	56.172	5.8118	0.048768	1.3119
	0.25686	-1.961	0.049886	1.302

Supplementary Table S1. SCFA raw concentration average values and relative standard deviations derived from GC-MS target experiment.

SCFA/group	Post_Norm	Pre_Norm	Post_Altered	Pre_Altered
Acetic acid	325.83 ± 55.35	320.81 ± 56.81	344.08 ± 79.45	310.5 ± 49.69
Propanoic acid	48.43 ± 12.97	51.87 ± 13.58	50.5 ± 13.13	55.86 ± 8.31
Isobutyric acid	16.16 ± 11.27	15.14 ± 6.36	16.48 ± 9.24	19.15 ± 9.18
Butanoic acid	44.74 ± 20.15	59.46 ± 32.13	41.03 ± 20.73	51.23 ± 21.84
Isovaleric acid	11.94 ± 10.49	9.38 ± 3.11	9.32 ± 7	13.69 ± 7.5

Supplementary Table S2. Biochemical parameters expressed as mean and standard deviations.

	Post_Norm	Pre_Norm	Post_Altered	Pre_Altered
%Lac	0.239 ± 0.07	0.235 ± 0.13	0.498 ± 0.14	0.292 ± 0.15
%Man	11.436 ± 3.05	15.311 ± 6.52	13.814 ± 3.08	11.499 ± 2.65
Lac to Man	0.021 ± 0.003	0.015 ± 0.006	0.021 ± 0.005	0.043 ± 0.01
Fecal				
Zonulin	263.928 ± 174.36	255 ± 97.88	221.545 ± 108.48	216.909 ± 135.45
Serum				
Zonulin	44.928 ± 22.58	33 ± 10.49	32.545 ± 11.45	37.545 ± 20.44
I-FAB	2.389 ± 1.11	2.11 ± 1.66	2.347 ± 1.04	2.391 ± 1.22
DAO	54.214 ± 7.86	55.071 ± 6.74	56.209 ± 4.94	55.39 ± 6.55
IL-6	6.117 ± 2.04	6.735 ± 2.93	5.957 ± 2.6	5.818 ± 2.63
IL-8	4.685 ± 1.91	5.23 ± 2.2	5.521 ± 1.21	4.897 ± 1.23
IL-10	3.292 ± 1.42	3.212 ± 1.03	3.251 ± 0.82	2.52 ± 0.79
TNF-α	6.185 ± 2.18	6.894 ± 3.16	5.257 ± 1.33	5.873 ± 1.17
LPS	0.044 ± 0.05	0.031 ± 0.03	0.055 ± 0.07	0.023 ± 0.02
Vitamin D	26.642 ± 14.53	22.357 ± 10.08	24.4 ± 5.96	20.7 ± 6.48