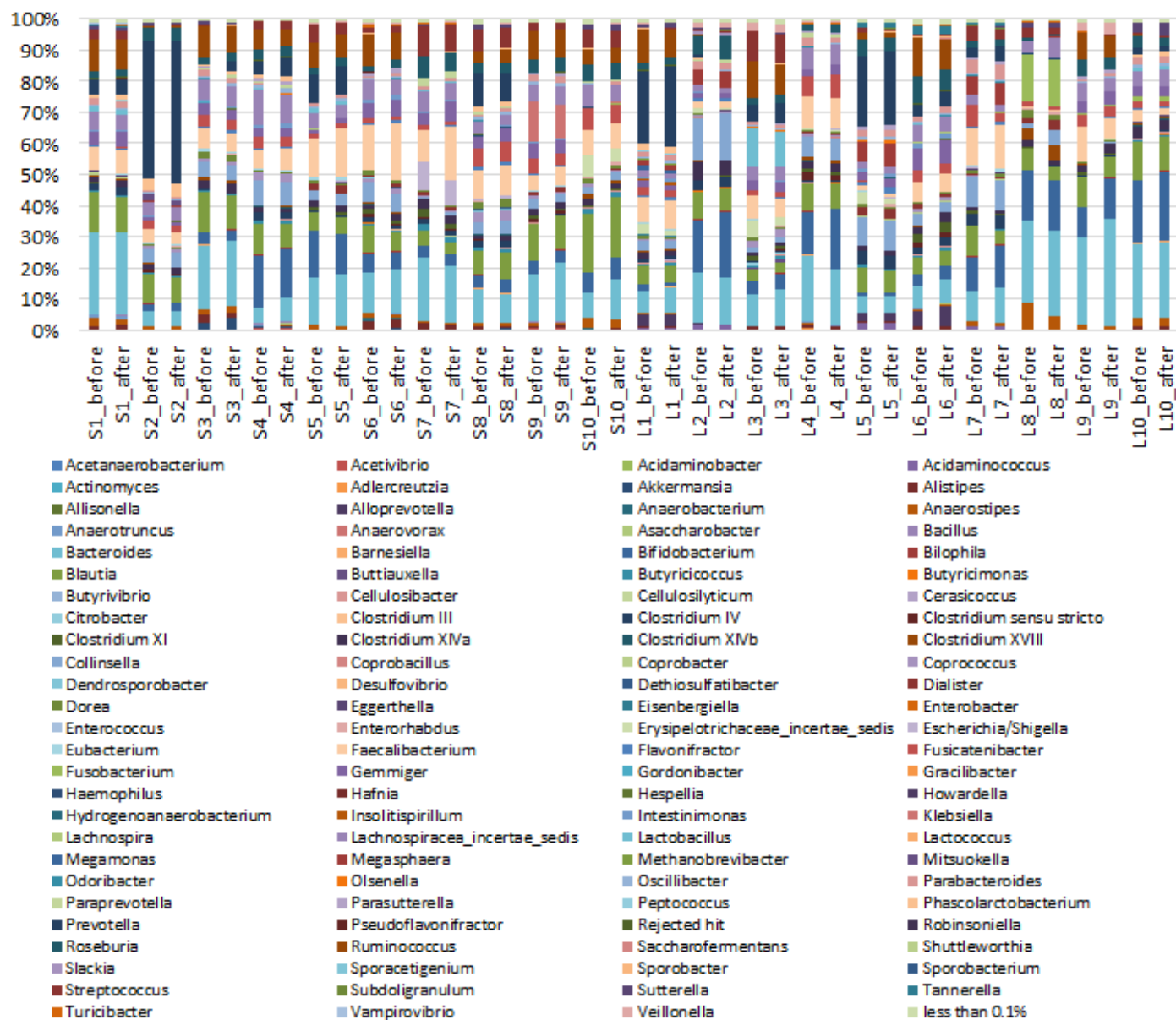


Supplementary Figure 1 The Shannon index of the gut microbiota stratified by VFA in each sex

The data are presented as mean ± standard error. The P-value was calculated using the Wilcoxon rank-sum test.



Group 1	Correlation coefficient	Group 2	Correlation coefficient
S1	0.997	L1	0.990
S2	0.999	L2	0.984
S3	0.986	L3	0.980
S4	0.984	L4	0.972
S5	0.983	L5	0.992
S6	0.979	L6	0.978
S7	0.958	L7	0.953
S8	0.989	L8	0.979
S9	0.986	L9	0.975
S10	0.972	L10	0.994

Supplementary Figure 2 Preservation stability of gut microbiota after storing for 1 year at 4°C

Pearson's correlation coefficient was used to evaluate the stability of the samples before and after preservation for 1 year. Group 1 and Group 2 were evaluated at different times. Gut microbiota with a relative abundance of less than 0.1% is described as < 0.1%.

Supplementary Table 1. Characteristics of the subjects in the main study group stratified by sex and VFA

Characteristics	Men				P value	Women				P value
	VFA<100		100≤VFA			VFA<100		100≤VFA		
Visceral fat area (cm ²)	69.5	± 22.8	140.2	± 31.4		57.5	± 22.2	124.9	± 23.4	
Number	183		208			513		97		
Age (y) ⁺¹	49.1	± 14.8	53.1	± 13.3	0.009**	53.2	± 13.8	59.4	± 12.0	<0.001**
Height (cm) ⁺¹	169.2	± 6.8	169.0	± 6.5	0.966	155.9	± 6.0	154.2	± 6.6	0.015*
Body weight (kg) ⁺¹	62.2	± 7.0	72.9	± 10.8	<0.001**	52.0	± 6.8	65.1	± 9.1	<0.001**
Body mass index (kg/m ²) ⁺¹	21.7	± 2.0	25.5	± 3.0	<0.001**	21.4	± 2.7	27.4	± 3.5	<0.001**
Waist circumference (cm) ⁺¹	76.8	± 5.3	88.3	± 7.3	<0.001**	71.6	± 7.2	87.8	± 8.0	<0.001**
Serum Glucose (mg/dL) ⁺¹	4.4	± 0.6	4.9	± 1.2	<0.001**	4.4	± 0.7	4.8	± 0.7	<0.001**
HbA1c (%) ⁺¹	5.6	± 0.4	5.9	± 0.8	<0.001**	5.7	± 0.4	6.0	± 0.6	<0.001**
SBP (mmHg) ⁺¹	122.5	± 17.0	127.7	± 15.3	0.001**	117.8	± 17.2	129.7	± 17.5	<0.001**
DBP (mmHg) ⁺¹	76.3	± 12.2	80.3	± 10.7	<0.001**	72.1	± 11.1	78.2	± 11.0	<0.001**
Triglyceride (mg/dL) ⁺¹	1.1	± 0.7	1.7	± 1.5	<0.001**	0.9	± 0.4	1.2	± 0.6	<0.001**
Total cholesterol (mg/dL) ⁺¹	5.1	± 0.8	5.5	± 0.8	<0.001**	5.4	± 0.9	5.6	± 0.8	0.005**
HDL cholesterol (mg/dL) ⁺¹	1.7	± 0.4	1.5	± 0.4	<0.001**	1.9	± 0.4	1.6	± 0.4	<0.001**
LDL cholesterol (mg/dL) ⁺¹	109.6	± 27.2	123.1	± 26.8	<0.001**	116.4	± 29.4	129.0	± 26.9	<0.001**
Smoking habit (stick/d) ⁺¹	11.0	± 11.4	12.5	± 12.0	0.240	2.3	± 5.4	2.4	± 5.6	0.741
Sleep time (h/d) ⁺¹	7.1	± 1.3	7.2	± 1.2	0.328	6.8	± 1.0	7.0	± 1.0	0.039*
Walk speed (sec/10m) ⁺¹	3.6	± 0.8	3.6	± 0.7	0.866	4.0	± 0.7	4.5	± 1.0	0.001**
Habitual medicine use (% of Yes) ⁺²	20.1%		36.7%		<0.001**	27.3%		47.4%		<0.001**
Hypertension ⁺²	14.1%		32.4%		<0.001**	20.3%		38.1%		<0.001**
Hyperlipidaemia ⁺²	4.9%		13.5%		0.006**	11.3%		18.6%		0.069
Diabetes ⁺²	2.7%		7.7%		0.049*	1.8%		3.1%		0.637
Rheumatism ⁺²	1.1%		0.5%		0.918	1.8%		4.1%		0.272
Total energy intake (kcal/d) ⁺¹	8879.8	± 2597.8	8810.7	± 2266.7	0.782	6946.2	± 1920.5	7140.5	± 1802.1	0.402
Carbohydrate intake ⁺¹	0.60	± 0.08	0.59	± 0.07	0.119	0.57	± 0.07	0.58	± 0.07	0.042*
Fat intake ⁺¹	0.25	± 0.06	0.26	± 0.05	0.153	0.27	± 0.05	0.26	± 0.05	0.013*
Protein intake ⁺¹	0.15	± 0.03	0.15	± 0.03	0.100	0.16	± 0.03	0.16	± 0.03	0.426
Alcohol consumption (g/d) ⁺¹	19.0	± 21.9	23.9	± 24.6	0.041*	4.5	± 10.7	3.3	± 8.9	0.056
Total dietary fibre intake (g/d) ⁺¹	11.1	± 4.8	11.0	± 4.5	0.975	10.8	± 4.3	10.7	± 4.1	0.864

P<0.05 and <0.01 are indicated by * and **, respectively.

*1 Wilcoxon rank-sum test was used

*2 test for equality of proportions was used

Supplementary Table 3. Relation of the relative abundance of human gut microbial genera and VFA or BMI

Genus	VFA				BMI			
	Men		Women		Men		Women	
	Estimate	P value	Estimate	P value	Estimate	P value	Estimate	P value
Acidaminococcus	0.090	0.075	0.041	0.312	0.101	0.045*	0.060	0.139
Akkermansia	-0.084	0.097	-0.054	0.186	-0.057	0.265	-0.061	0.133
Alistipes	-0.009	0.861	-0.039	0.335	-0.012	0.814	-0.004	0.927
Alloprevotella	0.037	0.466	0.010	0.797	0.008	0.868	-0.013	0.750
Anaerostipes	-0.029	0.564	-0.098	0.015*	-0.016	0.750	-0.111	0.006**
Bacteroides	-0.046	0.365	-0.062	0.128	-0.070	0.165	-0.090	0.027*
Barnesiella	-0.001	0.989	-0.054	0.185	-0.003	0.951	-0.010	0.799
Bifidobacterium	-0.135	0.008**	-0.104	0.010**	-0.104	0.040*	-0.047	0.245
Bilophila	0.018	0.715	0.015	0.707	0.034	0.500	-0.015	0.714
Blautia	-0.154	0.002**	-0.121	0.003**	-0.087	0.086	-0.117	0.004**
Butyricoccus	-0.035	0.493	0.010	0.814	-0.011	0.827	-0.027	0.513
Catenibacterium	0.087	0.086	0.016	0.687	0.084	0.095	0.024	0.549
Clostridium.IV	0.029	0.573	0.047	0.245	0.063	0.216	0.077	0.057
Clostridium.sensu.stricto	0.027	0.599	0.144	<0.001**	0.052	0.306	0.173	<0.001**
Clostridium.XIVa	0.028	0.587	0.018	0.663	0.009	0.866	-0.017	0.668
Clostridium.XIVb	0.090	0.076	-0.082	0.043*	0.093	0.066	-0.085	0.035*
Clostridium.XVIII	0.019	0.713	-0.056	0.168	0.013	0.793	-0.083	0.041*
Collinsella	0.057	0.259	0.015	0.718	0.015	0.761	0.021	0.612
Coprococcus	-0.025	0.618	0.085	0.035*	0.037	0.464	0.062	0.124
Dialister	0.093	0.067	0.044	0.283	0.070	0.167	0.072	0.074
Dorea	0.005	0.919	0.087	0.032*	-0.013	0.793	0.090	0.026*
Eggerthella	-0.061	0.228	-0.129	0.001**	-0.097	0.054	-0.091	0.024*
Enterococcus	-0.069	0.170	0.042	0.297	-0.106	0.036*	0.068	0.094
Erysipelotrichaceae incertae sedis	-0.055	0.274	-0.106	0.009**	-0.126	0.012*	-0.104	0.010*
Escherichia/Shigella	-0.058	0.252	0.038	0.352	-0.103	0.042*	0.040	0.324
Faecalibacterium	-0.053	0.296	0.021	0.603	0.053	0.298	-0.004	0.920
Flavonifractor	-0.028	0.577	-0.145	<0.001**	-0.080	0.113	-0.115	0.004**
Fusicatenibacter	-0.015	0.767	0.047	0.243	0.019	0.706	0.058	0.152
Fusobacterium	0.011	0.833	-0.035	0.394	-0.045	0.378	-0.062	0.126
Gemmiger	-0.073	0.148	0.059	0.148	-0.009	0.860	0.057	0.158
Holdemanella	0.047	0.358	0.078	0.054	0.110	0.030*	0.054	0.185
Intestinibacter	-0.022	0.662	0.043	0.043*	-0.031	0.541	0.096	0.018*
Klebsiella	0.012	0.807	0.023	0.575	-0.012	0.821	0.063	0.123
Lachnospiracea incertae sedis	-0.033	0.510	0.043	0.291	0.005	0.921	0.034	0.405
Lactobacillus	0.010	0.849	0.086	0.034*	0.029	0.354	0.098	0.015*
Megamonas	0.083	0.100	0.049	0.222	0.034	0.503	0.030	0.467
Megasphaera	0.036	0.480	0.114	0.005**	0.031	0.545	0.085	0.036*
Mitsuokella	0.036	0.473	0.068	0.095	0.059	0.242	0.046	0.262
Odoribacter	-0.047	0.358	-0.037	0.365	-0.024	0.632	-0.026	0.518
Oscillibacter	-0.012	0.813	0.001	0.988	0.011	0.834	0.025	0.538
Parabacteroides	-0.067	0.184	-0.046	0.258	-0.072	0.158	-0.052	0.199
Paraprevotella	0.007	0.888	0.046	0.259	0.013	0.796	0.046	0.258
Parasutterella	0.050	0.323	0.099	0.015**	0.060	0.234	0.122	0.003**
Phascolarctobacterium	0.065	0.199	-0.026	0.521	0.026	0.615	-0.017	0.684
Prevotella	0.007	0.888	0.010	0.797	0.168	<0.001**	0.005	0.904
Romboutsia	0.014	0.781	0.109	0.007**	0.066	0.195	0.154	<0.001**
Roseburia	-0.024	0.638	0.104	0.010**	0.011	0.828	0.112	0.006**
Ruminococcus	0.014	0.778	0.091	0.025*	0.053	0.297	0.097	0.017*
Senegalimassilia	-0.016	0.755	0.050	0.217	0.058	0.257	0.047	0.245
Streptococcus	-0.002	0.960	-0.119	0.019**	-0.144	0.004**	0.007	0.871
Sutterella	0.007	0.897	-0.119	0.003**	0.077	0.130	-0.106	0.009**
Turicibacter	0.011	0.834	0.033	0.418	0.030	0.549	0.098	0.016*
Veillonella	-0.122	0.016*	-0.003	0.945	-0.147	0.004**	0.001	0.973

Spearman's correlation coefficient was used.

Supplementary Table 4. Multiple regression analysis of association among Blautia and related factors

MEN			WOMEN		
	Estimate	P value ^{*1}		Estimate	P value ^{*1}
VFA	-1.09E-04	0.032*	VFA	-1.39E-04	0.015*
Age	-2.07E-02	0.175	Age	8.55E-05	0.528
			Smoking habit	6.08E-04	0.070
			Sleeptime	3.20E-03	0.074
			Walk speed	-4.28E-03	0.061

*P<0.05

*1 Step-wise method based on AIC criterion was used

Supplementary Table 5. Characteristics of the subjects in the confirmation group stratified by sex and VFA

Characteristics	Men			Women			P value
		±			±		
Visceral fat area (cm ²)*1	95.4		47.6	63.6		34.4	<0.001**
Number	126			210			
Age (yr) ^{*1}	50.4	±	17.5	51.4	±	17.6	0.623
Height (cm) ^{*1}	168.7	±	6.8	156.0	±	6.7	<0.001**
Body weight (kg) ^{*1}	66.6	±	10.5	54.8	±	9.9	<0.001**
Body mass index (kg/m ²) ^{*1}	23.3	±	3.0	22.5	±	3.7	0.008**
Waist circumference (cm) ^{*1}	81.9	±	8.9	74.6	±	9.8	<0.001**
Serum Glucose (mg/dL) ^{*1}	5.15	±	0.91	5.13	±	1.73	0.030*
HbA1c (%) ^{*1}	5.8	±	0.5	5.9	±	0.9	0.580
SBP (mmHg) ^{*1}	127.0	±	16.0	122.7	±	20.5	0.012
DBP (mmHg) ^{*1}	78.2	±	11.8	72.7	±	11.8	<0.001**
Triglyceride (mg/dL) ^{*1}	1.3	±	0.8	1.0	±	0.8	<0.001**
Total cholesterol (mg/dL) ^{*1}	5.0	±	0.9	5.3	±	1.1	0.054
HDL cholesterol (mg/dL) ^{*1}	1.5	±	0.4	1.7	±	0.4	<0.001**
LDL cholesterol (mg/dL) ^{*1}	2.9	±	0.7	3.0	±	0.9	0.478
Smoking habits (stick/d) ^{*1}	10.9	±	11.2	2.2	±	4.9	<0.001**
Sleep time (h/d) ^{*1}	7.1	±	1.3	6.9	±	1.2	0.138
Walk speed (sec/10m) ^{*1}	3.5	±	1.0	3.9	±	1.0	<0.001**
Habitual medicine use (% of Yes) ^{*2}	28.5%			29.0%			0.805
Hypertension ^{*2}	25.4%			24.3%			0.922
Hyperlipidaemia ^{*2}	11.1%			8.5%			0.565
Diabetes ^{*2}	7.1%			5.2%			0.634
Rheumatism ^{*2}	0.0%			0.5%			1.000
Total energy intake (kcal/d) ^{*1}	9004.1	±	2427.5	7027.9	±	2375.1	<0.001**
Carbohydrate intake ^{*1}	0.59	±	0.08	0.56	±	0.07	0.643
Fat intake ^{*1}	0.26	±	0.06	0.28	±	0.06	<0.001**
Protein intake ^{*1}	0.15	±	0.03	0.16	±	0.03	<0.001**
Alcohol consumption (g/d) ^{*1}	23.6	±	27.7	4.5	±	10.2	<0.001**
Total dietary fibre intake (g/d) ^{*1}	10.9	±	4.8	10.4	±	4.8	0.261
Diversity of intestinal microbiota ^{*1}	9.7	±	3.3	10.1	±	2.2	<0.001**

P<0.05 and <0.01 are indicated by * and **, respectively.

*1Wilcoxon rank-sum test was used

*2 test for equality of proportions was used