

Supplementary Table 1. Results of three-way ANOVA test

Variable	p-value						
	BMI	TM	Time	BMI× TM	BMI× Time	TM× Time	3-way
TNF- α (pg/mL)	0.0015 †	0.8994	0.0460 †	0.4472	0.4271	0.6679	0.8061
IFN- γ (pg/mL)	0.0018 †	0.2349	0.5634	0.4419	0.4950	0.3154	0.9892
IL-1 β (pg/mL)	0.6583	0.8723	0.8535	0.1207	0.9248	0.1127	0.5201
IL-6 (pg/mL)	0.0282 ‡	0.0495 ‡	0.4186	0.3164	0.0421 ‡	0.3922	0.8628
IL-8 (pg/mL)	0.0052 ‡	0.1368	0.8152	0.2859	0.8313	0.3557	0.7692
IL-10 (pg/mL)	0.0135 ‡	0.4186	0.0101 ‡	0.7814	0.0341 ‡	0.8697	0.5069
Active Ghrelin (pg/mL)	0.1008	0.5554	0.9207	0.8078	0.8429	0.7086	0.0211 ‡
Total Ghrelin (pg/mL)	0.0475 ‡	0.5011	0.7102	0.6776	0.9740	0.5640	0.8876
Active/Total Ghreline (%)	0.8676	0.9694	0.7404	0.5914	0.8788	0.5196	0.7247
Leptin (ng/mL)	0.0008 †	0.9296	0.3478	0.5342	0.0004 †	0.7005	0.7625
GIP (pg/mL)	0.1593	0.0981	0.4409	0.6915	0.5178	0.5262	0.7253
GLP-1 (pg/mL)	0.0181 ‡	0.3653	0.8682	0.8695	0.9860	0.0454 ‡	0.7780
PYY (pg/mL)	0.4364	0.1737	0.2895	0.0959	0.0071 ‡	0.0959	0.0396 ‡
ApoE (mg/dL)	0.6489	0.2211	0.4808	0.1701	0.8805	0.2827	0.6382
ApoA-1 (mg/dL)	0.0060 ‡	0.1004	0.4094	0.7748	0.2054	0.4068	0.9077
Trail Making Test A	0.8663	0.8703	0.0001 †	0.7266	0.0207 †	0.7276	0.4498
Trail Making Test B	0.7776	0.4708	0.007†	0.1228	0.3664	0.6568	0.1134
Digit Span Test Forward score	0.3775	0.0186 †	0.0042 †	0.3775	0.3757	0.6958	0.2227
Digit Span Test Backward score	0.4382	0.2674	0.0006 †	0.2762	0.1038	0.033†	0.1038
AUC _{0–2h} (uM*h) BZ	0.1551	0.0391 †	0.0001 †	0.0019 †	0.0927	0.0032 †	0.3332

BMI: Lean or overweight/obese, TM: Treatment (Placebo or Probiotics), Time: Week 0 or Week 8.
†p<0.05, ‡p<0.01 based on 3-way ANOVA test after log transformation.

Supplementary Table 2: Mediation analysis of selected microbiota species and inflammation and hormone markers within the overweight/obese probiotic participants with the highest (n=5) and lowest (n=5) AUC_{0-2h} in gallotannin-metabolites systemic exposure at W8.

Pair	ACME Estimate	ACME p-value	ADE Estimate	ADE p-value	Total Estimate	Total p-value	Proportion Mediated
TNFa vs f_lachnospiraceae	-0.168	0.712	0.242	0.704	0.074	0.880	-0.028
TNFa vs f_clostridiaceae	0.434	0.312	-0.383	0.568	0.051	0.908	0.152
TNFa vs g_lactobacillus	-0.058	0.898	0.134	0.820	0.077	0.906	0.030
TNFa vs g_streptococcus	0.033	0.960	0.030	0.976	0.063	0.918	-0.009
TNFa vs g_oscillospira	-0.076	0.794	0.130	0.810	0.054	0.918	0.036
TNFa vs g_clostridium	0.020	0.948	0.052	0.956	0.072	0.916	0.035
IL-1 β vs f_lachnospiraceae	-0.043	0.430	-0.092	0.258	-0.135	0.052	0.257
IL-1 β vs f_clostridiaceae	0.081	0.100	-0.215	0.004	-0.135	0.056	-0.476
IL-1 β vs g_lactobacillus	0.025	0.516	-0.162	0.002	-0.138	0.038	-0.099
IL-1 β vs g_streptococcus	-0.028	0.726	-0.105	0.288	-0.133	0.066	0.157
IL-1 β vs g_oscillospira	-0.012	0.764	-0.120	0.084	-0.132	0.062	0.051
IL-1 β vs g_clostridium	-0.021	0.580	-0.112	0.058	-0.133	0.050	0.116
IL10 vs f_lachnospiraceae	-0.415	0.092	0.732	0.056	0.317	0.390	-0.502
IL10 vs f_clostridiaceae	0.445	0.116	-0.149	0.668	0.297	0.422	0.863
IL10 vs g_lactobacillus	0.168	0.482	0.147	0.620	0.315	0.392	0.399
IL10 vs g_streptococcus	-0.127	0.798	0.438	0.454	0.311	0.424	-0.133
IL10 vs g_oscillospira	-0.061	0.802	0.370	0.336	0.310	0.416	-0.003
IL10 vs g_clostridium	-0.151	0.554	0.474	0.156	0.323	0.424	-0.027
Active Ghrelin vs f_lachnospiraceae	-17.462	0.884	-27.596	0.882	-45.058	0.690	0.028
Active Ghrelin vs f_clostridiaceae	-1.503	0.984	-31.596	0.826	-33.099	0.830	0.020
Active Ghrelin vs g_lactobacillus	9.759	0.882	-50.867	0.662	-41.108	0.694	0.013
Active Ghrelin vs g_streptococcus	290.440	0.002	-325.999	<0.001	-35.559	0.726	-1.313
Active Ghrelin vs g_oscillospira	66.700	0.420	-111.877	0.084	-45.176	0.614	0.017
Active Ghrelin vs g_clostridium	-6.732	0.916	-30.835	0.746	-37.567	0.724	0.043
Total Ghrelin vs f_lachnospiraceae	-136.775	0.112	-43.111	0.642	-179.886	0.124	0.698
Total Ghrelin vs f_clostridiaceae	49.122	0.862	-234.990	0.388	-185.868	0.168	-0.168
Total Ghrelin vs g_lactobacillus	54.141	0.498	-233.632	0.012	-179.492	0.124	-0.159
Total Ghrelin vs g_streptococcus	-20.744	0.862	-153.144	0.464	-173.888	0.190	0.116
Total Ghrelin vs g_oscillospira	2.907	0.986	-180.950	0.116	-178.043	0.164	0.009
Total Ghrelin vs g_clostridium	-18.654	0.848	-158.544	<0.001	-177.199	0.126	0.181
Leptin vs f_lachnospiraceae	1.302	0.352	-1.162	0.606	0.140	0.956	0.020
Leptin vs f_clostridiaceae	0.061	0.954	0.046	0.990	0.107	0.946	0.009
Leptin vs g_lactobacillus	-0.219	0.844	0.337	0.882	0.118	0.964	0.014
Leptin vs g_streptococcus	2.626	0.168	-2.572	0.256	0.054	0.966	0.130
Leptin vs g_oscillospira	0.703	0.572	-0.595	0.738	0.108	0.976	0.114
Leptin vs g_clostridium	0.497	0.606	-0.491	0.804	0.006	0.948	0.114
GLP-1 vs f_lachnospiraceae	29.437	0.254	-16.172	0.682	13.265	0.672	0.440
GLP-1 vs f_clostridiaceae	-18.053	0.508	32.788	0.454	14.734	0.684	-0.099
GLP-1 vs g_lactobacillus	-9.343	0.656	25.105	0.464	15.762	0.676	0.008

GLP-1 vs g_streptococcus	79.334	<0.001	-63.352	0.026	15.983	0.618	2.094
GLP-1 vs g_oscillospira	20.890	0.376	-4.308	0.872	16.583	0.614	0.670
GLP-1 vs g_clostridium	8.128	0.626	5.889	0.852	14.017	0.660	0.118
PYY vs f_lachnospiraceae	4.207	0.808	31.611	0.164	35.818	0.068	0.056
PYY vs f_clostridiaceae	-2.835	0.914	37.595	0.134	34.760	0.070	-0.039
PYY vs g_lactobacillus	-5.380	0.624	40.535	0.008	35.154	0.046	-0.078
PYY vs g_streptococcus	37.731	0.014	-1.598	0.934	36.134	0.038	1.017
PYY vs g_oscillospira	6.379	0.534	28.761	0.092	35.140	0.062	0.130
PYY vs g_clostridium	-0.337	0.984	35.120	0.060	34.782	0.076	0.002

Average Causal Mediation Effects (ACME), Average Direct Effects (ADE), total effects, and the proportion mediated.