microorganisms

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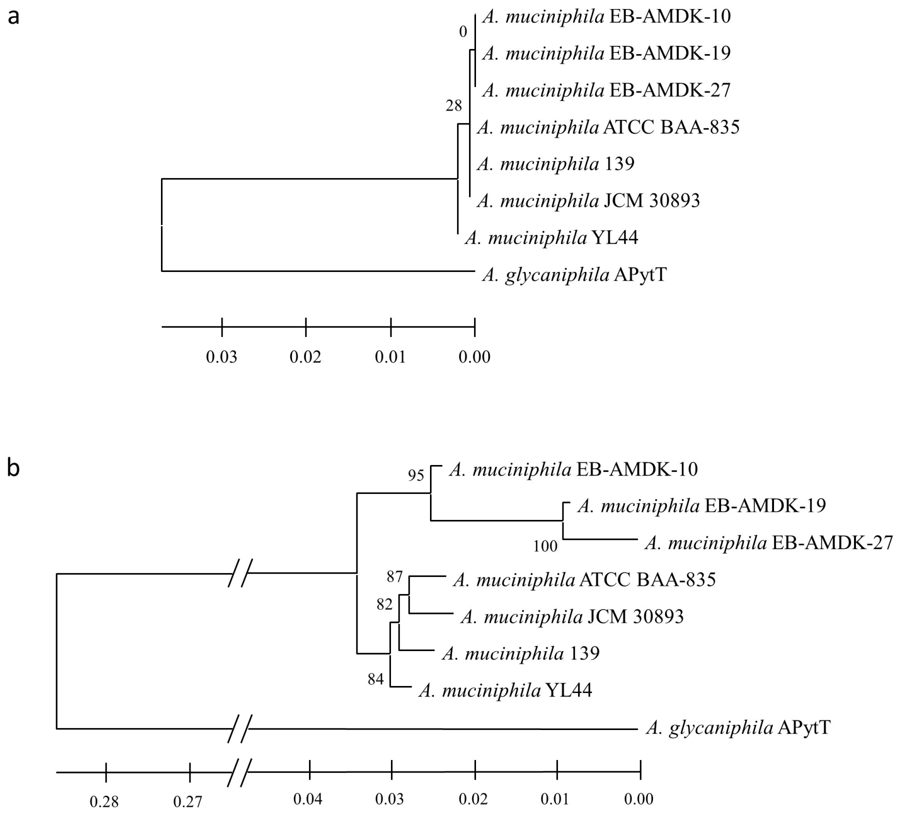
Supplementary Figure 1: Genetic diversity of *A. muciniphila* strains. (a) phylogenetic tree of 16S rRNA gene, and (b) phylogenetic tree of MLST genes.



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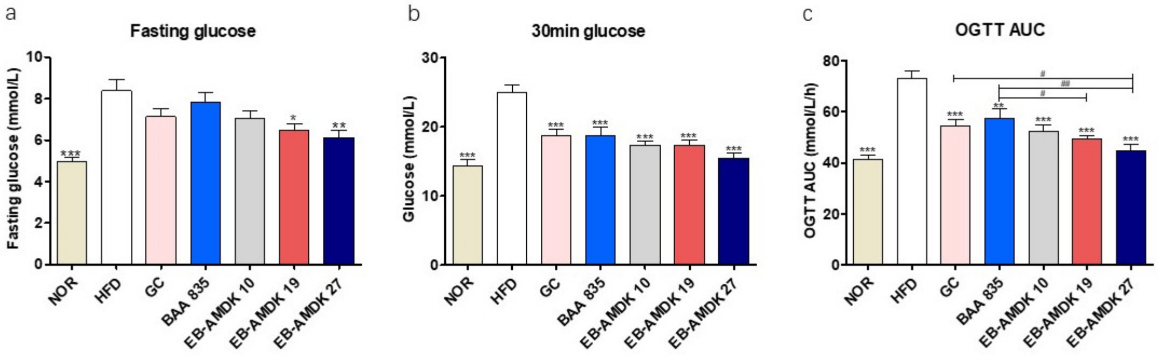
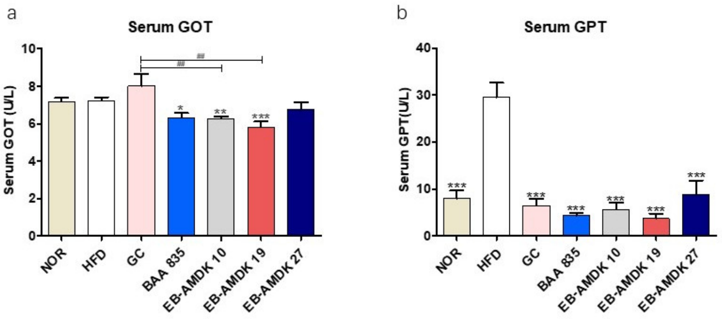
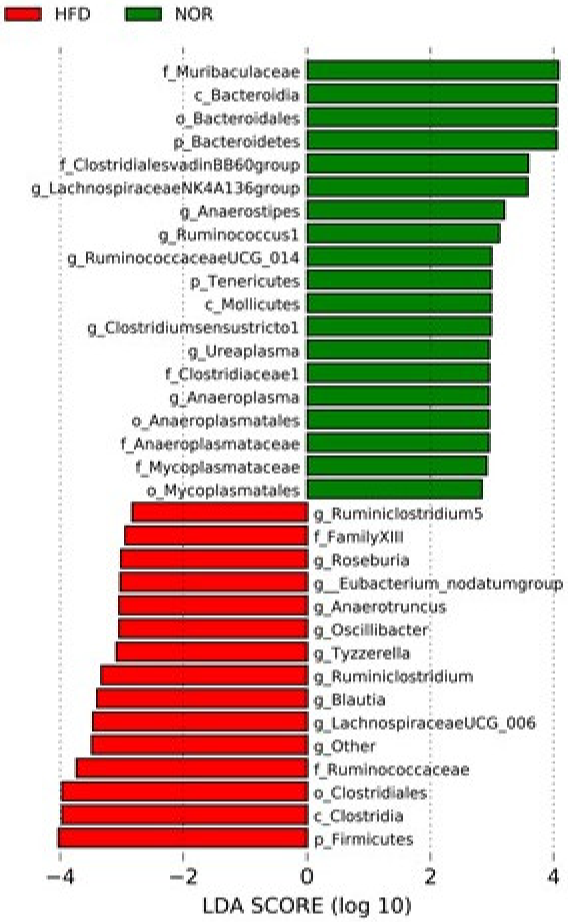
Supplementary Figure 2: *A. muciniphila* strains improved glucose homeostasis in HFD-induced obese mice. (a) Fasting glucose at 0min of OGTT. (b) 30 min glucose level. (c) Areas under the curve of OGTT measured between 0 and 120 min after glucose administration. The data are represented as the mean ± SEM (n = 9-12). Statistical analysis was performed with one-way ANOVA or Student's t-test. *$p < 0.05$, **$p < 0.01$ and ***$p < 0.001$ versus the HFD group. $^{\#}p < 0.05$, $^{\#\#}p < 0.01$.



Supplementary Figure 3: *A. muciniphila* strains mitigate liver injury. (a) Glutamic oxaloacetic transaminase (GOT); (b) Glutamic pyruvic transaminase (GPT) were measured in the serum of each mouse. The data are represented as the mean ± SEM (n = 9-12). Statistics were performed with one-way ANOVA or Student's t-test. $^{*}p < 0.05$, $^{**}p < 0.01$ and $^{***}p < 0.001$ versus the HFD group. $^{\#}p < 0.05$, $^{\#\#}p < 0.01$.



Supplementary Figure 4: *A. muciniphila* treatment modulated the composition of the gut microbiota. LEfSe was used to identify the bacteria represented differentially between the normal group and the HFD group.



Supplementary table 1: Information on the fecal sample from healthy volunteers.

Group	Sample	Unique identification number	Gender	Age	Height (cm)	Body weight (kg)	BMI (kg/m^2)
Group01	AMDK-7	CGT039	F	38	159	54	21.4
Group02	AMDK-29	CGT078	F	38	165	52	19.1
	AMDK-30	CGT078	F	38	165	52	19.1
Group03	AMDK-3	CGT002	F	4	95	12	13.3
	AMDK-4	CGT003	F	61	152	50	21.6
Group04	AMDK-23	CGT068	M	51	173	61	20.4
	AMDK-24	CGT068	M	51	173	61	20.4
	AMDK-25	CGT068	M	51	173	61	20.4
	AMDK-26	CGT068	M	51	173	61	20.4
Group05	AMDK-46	CGT092	F	30	157	58	23.5
	AMDK-47	CGT092	F	30	157	58	23.5
	AMDK-48	CGT092	F	30	157	58	23.5
	AMDK-49	CGT092	F	30	157	58	23.5
Group06	AMDK-1	CGT001	M	35	175	72	23.5
Group07	AMDK-15	CGT060	M	3	95	12.5	13.9
	AMDK-16	CGT060	M	3	95	12.5	13.9
	AMDK-17	CGT060	M	3	95	12.5	13.9
	AMDK-18	CGT060	M	3	95	12.5	13.9
Group08	AMDK-8	CGT031	M	44	173	71	23.7
Group09	AMDK-27	CGT074	F	45	150	52	23.1
	AMDK-28	CGT074	F	45	150	52	23.1
Group10	AMDK-2	CGT001	M	35	175	72	23.5
	AMDK-6	CGT005	F	37	157	46	18.7
	AMDK-10	CGT007	M	7	120	25	17.4
	AMDK-11	CGT007	M	7	120	25	17.4
	AMDK-12	CGT007	M	7	120	25	17.4
	AMDK-13	CGT007	M	7	120	25	17.4
	AMDK-14	CGT007	M	7	120	25	17.4
Group11	AMDK-5	CGT006	M	63	173	67	22.4
	AMDK-19	CGT034	F	35	167	65	23.3
	AMDK-20	CGT034	F	35	167	65	23.3
	AMDK-21	CGT034	F	35	167	65	23.3
	AMDK-22	CGT034	F	35	167	65	23.3
	AMDK-33	CGT079	F	60	157	54	21.9
	AMDK-34	CGT079	F	60	157	54	21.9
	AMDK-35	CGT079	F	60	157	54	21.9
	AMDK-36	CGT079	F	60	157	54	21.9
Group12	AMDK-31	CGT076	F	40	159	62	24.5
	AMDK-37	CGT071	M	14	151	47	20.6

	AMDK-38	CGT071	M	14	151	47	20.6
Group13	AMDK-39	CGT085	F	7	112	25	19.9
	AMDK-40	CGT085	F	7	112	25	19.9
	AMDK-41	CGT085	F	7	112	25	19.9

Supplementary table 2: Primer sequences for PCR.

Gene		Primer Sequence (5'–3')
PPARγ	F:	GCCCTTTGGTGACTTTATGGA
	R:	GCAGCAGGTTGTCTTGGATG
C/EBPα	F:	AGCAACGAGTACCGGGTACG
	R:	TGTTTGGCTTTATCTCGGCTC
Ap2	F:	AGTGAAAACTTCGATGATTACATGAA
	R:	GCCTGCCACTTTCCTTGTG
CD36	F:	TTGTACCTATACTGTGGCTAAATGAGA
	R:	CTTGTGTTTTGAACATTTCTGCTT
ACC1	F:	CCTCCGTCAGCTCAGATACA
	R:	TTTACTAGGTGCAAGCCAGACA
LDLR	F:	GAACTCAGGGCCTCTGTCTG
	R:	CAGGCTGGATGTCTCTGTGA
LPL	F:	TTCCAGCCAGGATGCAACA
	R:	GGTCCACGTCTCCGAGTCC
FAS	F:	AGGGGTCGACCTGGTCCTCA
	R:	GCCATGCCCAGAGGGTGGTT
SREBP1c	F:	GGAGCCATGGATTGCACATT
	R:	GGCCCGGGAAGTCACTGT
GLUT2	F:	GGCTAATTTCAGGACTGGTT
	R:	TTTCTTTGCCCTGACTTCCT
G6Pase	F:	GACTCCCAGGACTGGTTCAT
	R:	GGGCGTTGTCCAAACAGAAT
IRS1	F:	TTTGAAGACCATAACCCACCA
	R:	ATTACACCAGTTCGTCCCTTTC
Leptin	F:	GCCAGGCTGCCAGAATTG
	R:	CTGCCCCCCCAGTTTGATG
TNFα	F:	GACCCTCACACTCAGATCATCTTCT
	R:	CCACTTGGTGGTTTGCTACGA
IL-6	F:	CCTCTGGTCTTCTGGAGTACC
	R:	ACTCCTTCTGTGACTCCAGC
IL-10	F:	ATAACTGCACCCACTTCCCA
	R:	GGGCATCACTTCTACCAGGT
IL-1β	F:	TGCCACCTTTTGACAGTGATG
	R:	AAGGTCCACGGGAAAGACAC
MCP-1	F:	AAGAGATCAGGGAGTTTGCT
	R:	CTGCCTCCATCAACCACTTT
TLR2	F:	AAGGAGGTGCGGACTGTTTC
	R:	GAGCCAAAGAGCTCGTAGC
TLR4	F:	CCTGATGACATTCCTTCTTCAAC
	R:	TTGTTTCAATTTCACACCTGGATAAA
GLP-1	F:	GGCACATTCACCAGCGACTAC

	R:	CAATGGCGACTTCTTCTGGG
PYY	F:	CGGCAGCGGTATGGAAAAA
	R:	TGTGAAGAGCAGTTTGGAGAACA
Lyz1	F:	GCCAAGGTCTACAATCGTTGTGAGTTG
	R:	CAGTCAGCCAGCTTGACACCACG
Muc2	F:	CCATTGAGTTTGGGAACATGC
	R:	TTCGGCTCGGTGTTCAGAG
ZO-1	F:	TTTTTGACAGGGGGAGTGG
	R:	TGCTGCAGAGGTCAAAGTTCAAG
Occludin	F:	ATGTCCGGCCGATGCTCTC
	R:	TTTGGCTGCTCTTGGGTCTGTAT

Supplementary table 3: Effect of *A. muciniphila* on adiposity, liver weight, and energy efficiency in mice.

Parameters	**NOR**	**HFD**	**GC**	**BAA 835**	**EB-AMDK 10**	**EB-AMDK 19**	**EB-AMDK 27**
Energy efficiency (g/kcal/mouse)	$0.0113 \pm 0.0012^{**}$	0.0206 ± 0.0010	0.0171 ± 0.0012	0.0170 ± 0.0015	0.0173 ± 0.0020	$0.0144 \pm 0.0023^{*}$	$0.0155 \pm 0.0014^{*}$
Liver weight (g)	$1.23 \pm 0.07^{***}$	1.77 ± 0.08	$1.07 \pm 0.08^{***}$	$1.16 \pm 0.09^{***,b}$	$1.09 \pm 0.08^{***}$	$1.03 \pm 0.04^{***}$	$0.94 \pm 0.04^{***}$
Subcutaneous fat (g)	$0.47 \pm 0.03^{***}$	1.56 ± 0.05	1.30 ± 0.04	1.35 ± 0.06	1.44 ± 0.09	$0.97 \pm 0.11^{***,a,b}$	$1.09 \pm 0.09^{***,a,b}$
Epididymal fat (g)	$1.47 \pm 0.07^{***}$	2.83 ± 0.10	$2.25 \pm 0.13^{**}$	2.36 ± 0.25	2.40 ± 0.21	$2.00 \pm 0.19^{***}$	$2.27 \pm 0.18^{*}$
Mesenteric fat (g)	$0.48 \pm 0.03^{***}$	1.78 ± 0.12	$1.10 \pm 0.18^{**}$	$0.93 \pm 0.12^{***}$	$1.16 \pm 0.17^{*}$	$0.93 \pm 0.14^{***}$	$0.82 \pm 0.11^{***}$

The data are represented as the mean ± SEM (n=9-12). Statistics were performed with one-way ANOVA or Student's t-test. $^{*}p < 0.05$, $^{**}p < 0.01$ and $^{***}p < 0.001$ versus the HFD group. $^{a}p < 0.05$ versus the BAA 835 group. $^{b}p < 0.05$ versus the GC group.

Supplementary table 4: Modulation of gut microbiota composition by the treatment of *A. muciniphila.*

Parameters	**NOR**	**HFD**	**BAA 835**	**EB-AMDK 10**	**EB-AMDK 19**	**EB-AMDK 27**
Order						
Bacterioidales	$0.667 \pm 0.031^{*}$	0.540±0.024	0.613±0.033	0.544±0.056	0.478±0.057	$0.686 \pm 0.018^{*}$
Clostridiales	$0.284 \pm 0.030^{*}$	0.431±0.022	0.359±0.034	0.401±0.054	0.454±0.052	$0.299 \pm 0.018^{*}$
Lactobacillales	$0.016 \pm 0.004^{*}$	0.029±0.006	$0.014 \pm 0.003^{*}$	$0.011 \pm 0.003^{**}$	$0.007 \pm 0.001^{**}$	$0.011 \pm 0.002^{**}$
Family						
Bacteroidaceae	0.300±0.027	0.259±0.027	0.307±0.035	0.285±0.046	0.190±0.028	$0.411 \pm 0.026^{*,a}$
Muribaculaceae	$0.229 \pm 0.022^{***}$	0.104±0.016	0.162±0.025	0.169±0.012	0.149±0.031	0.151±0.012
Rikenellaceae	$0.116 \pm 0.019^{*}$	0.045±0.011	0.094±0.021	0.082±0.010	$0.112 \pm 0.023^{*}$	$0.113 \pm 0.015^{*}$
Streptococcaceae	$0.006 \pm 0.002^{*}$	0.016±0.003	$0.009 \pm 0.002^{*}$	$0.005 \pm 0.001^{**}$	$0.005 \pm 0.001^{**}$	$0.008 \pm 0.001^{*}$
Prevotellaceae	$0.027 \pm 0.007^{*}$	0.078±0.022	$0.034 \pm 0.009^{*}$	$0.002 \pm 0.001^{***}$	$0.019 \pm 0.008^{*}$	$0.024 \pm 0.012^{*}$
Lachnospiraceae	$0.157 \pm 0.015^{*}$	0.242±0.021	0.171±0.025	0.239±0.029	0.213±0.033	$0.124 \pm 0.010^{**}$
Ruminococcaceae	$0.089 \pm 0.013^{**}$	0.177±0.011	0.156±0.015	0.180±0.025	0.221±0.028	0.124±0.010
Genus						
Bacteroides	0.300±0.027	0.259±0.027	0.293±0.033	0.268±0.043	0.178±0.027	$0.404 \pm 0.024^{*}$
Ruminococcaceae NK4A214 group	$0.0010 \pm 0.0002^{*}$	0.0004±0.0002	$0.0011 \pm 0.0002^{*}$	$0.0010 \pm 0.0001^{**}$	$0.0015 \pm 0.0003^{**}$	$0.0013 \pm 0.0003^{*}$
Lachnospiraceae NK4A136 group	$0.075 \pm 0.008^{***}$	0.024±0.006	$0.081 \pm 0.028^{*}$	$0.100 \pm 0.028^{**}$	$0.105 \pm 0.016^{***}$	$0.046 \pm 0.008^{*}$
Blautia	$0.003 \pm 0.001^{***}$	0.027±0.005	$0.011 \pm 0.003^{**}$	$0.010 \pm 0.003^{**}$	$0.006 \pm 0.003^{**}$	$0.006 \pm 0.002^{***}$
Lactococcus	$0.008 \pm 0.003^{*}$	0.016±0.003	$0.009 \pm 0.002^{*}$	$0.005 \pm 0.001^{**}$	$0.005 \pm 0.001^{**}$	$0.008 \pm 0.002^{*}$
Lactobacillus	$0.005 \pm 0.002^{*}$	0.014±0.004	$0.005 \pm 0.002^{*}$	$0.007 \pm 0.003^{*}$	$0.003 \pm 0.001^{*}$	$0.004 \pm 0.001^{*}$
Roseburia	$0.007 \pm 0.002^{**}$	0.016±0.003	$0.010 \pm 0.002^{*}$	$0.005 \pm 0.002^{**}$	$0.004 \pm 0.001^{***,a}$	$0.003 \pm 0.001^{***,a}$
Ruminiclostridium 5	$0.0011 \pm 0.0004^{**}$	0.0041±0.0009	$0.0019 \pm 0.0003^{**}$	$0.0017 \pm 0.0005^{**}$	$0.0023 \pm 0.0004^{*}$	$0.0015 \pm 0.0002^{**}$
Tyzzerella	$0.0006 \pm 0.0003^{***}$	0.0111±0.0016	0.0077±0.0024	$0.0052 \pm 0.0009^{*}$	0.0077±0.0015	$0.0045 \pm 0.0009^{*}$

The values are presented as the mean ± SEM. Statistics were performed with one-way ANOVA or Student's t-test. $^{*}p < 0.05$, $^{**}p < 0.01$ and $^{***}p < 0.001$ versus the HFD group. $^{a}p < 0.05$ versus the BAA 835 group.