Supplementary Table S1. Composition of experimental diets (% of diet, w/w).

Ingredients (g)	ND	HFD	ALL
Casein	200.00	200.00	200.00
D,L-methionine	3.00	3.00	3.00
Corn starch	150.00	111.00	111.00
Sucrose	500.00	370.00	320.00
Cellulose powder	50.00	50.00	50.00
Corn oil	50.00	30.00	30.00
Lard	-	170.00	170.00
Mineral Mixture (AIN-76) *	35.00	42.00	42.00
Vitamin mix (AIN-76) †	10.00	12.00	12.00
Choline bitartrate	2.00	2.00	2.00
Cholesterol	-	10.00	10.00
tert-Butylhydroquinone	0.01	0.04	0.04
D-allulose	-	-	50.00
Total (g)	1000.0	1000.0	1000.0
Calories (kcal/kg)	3902	4584	4384
Calories (kcal/g)	3.902	4.584	4.384

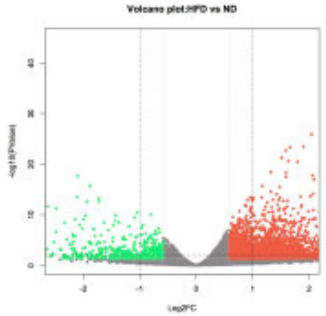
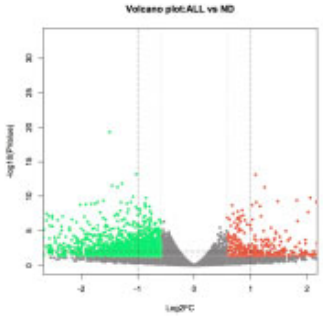
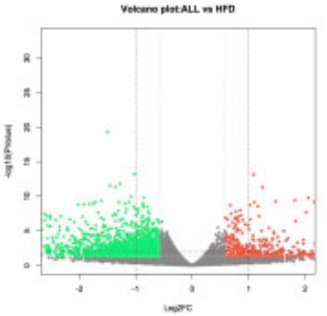
ND, normal diet; **HFD**, high-fat diet; **ALL**, D-allulose, HFD supplemented with 5% D-allulose. * Mineral mixture (AIN-76) calcium phosphate 500 g/kg, NaCl 74 g/kg, potassium citrate 2220 g/kg, potassium sulfate 52 g/kg, magnesium oxide 24 g/kg, manganous carbonate 3·5 g/kg, ferric citrate 6 g/kg, zinc carbonate 1·6 g/kg, cupric carbonate 0·3 g/kg, potassium iodate 0·01 g/kg, sodium selenite 0·01 g/kg, chromium potassium sulfate 0·55 g/kg, sucrose 118·03 g/kg. † Vitamin mixture AIN-76: thiamin HCl 0·6 g/kg, riboflavin 0·6 g/kg, pyridoxine HCl 0·7 g/kg, niacin 3 g/kg, calcium pantothenate 1·6 g/kg, folic acid 0·2 g/kg, biotin 0·02 g/kg, vitamin B_{12} 1 g/kg, vitamin A (500 000 IU/g) 0·8 g/kg, vitamin D3 (400 000 IU/g) 0·25 g/kg, vitamin E acetate (500 IU/g) 10 g/kg, menadione sodium bisulfite 0·08 g/kg, sucrose 981·15 g/kg.

Supplementary Table S2. Effects of 16-week D-allulose supplementation on plasma adipokine and cytokine concentrations in C57BL/6J mice fed a high-fat diet.

	ND			HFD			ERY			ALL		
Leptin (ng/ml)	4.34	⊚⊚	2.39	19.58	⊚⊚	0.20^{**a}	12.89	⊚⊚	0.30^{a}	12.24	⊚⊚	0.47^{b}
Resistin (ng/ml)	1.74	⊚⊚	6.20	2.23	⊚⊚	0.57^{*a}	1.88	⊚⊚	0.39^{ab}	1.72	⊚⊚	1.29^{b}
Adiponectin (ng/ml)	5.27	⊚	11.48	4.75	⊚⊚	0.86^{*b}	4.53	⊚⊚	0.36^{b}	5.23	⊚⊚	2.73^{a}
Leptin: Adiponectin	0.83	⊚⊚	3.93	4.11	⊚⊚	0.39^{*a}	2.85	⊚⊚	0.43^{ab}	2.37	⊚⊚	0.86^{b}
Interleukin 1-β (pg/ml)	75.44	⊚⊚	10.35	186.03	⊚	23.19^{**a}	190.26	⊚	47.99^{a}	79.99	±	14.20^{b}
Interleukin 6 (pg/ml)	2.55	⊚⊚	0.22	4.48	⊚	0.26^{**a}	4.65	⊚	0.43^{a}	3.50	⊚	0.16^{b}
Interleukin 10 (pg/ml)	34.42	⊚⊚	6.68	38.49	⊚	4.40	36.35	⊚	8.42	39.72	⊚	6.49
Interferon-γ (pg/ml)	7.30	⊚⊚	0.75	12.08	⊚	1.88^{**a}	11.76	⊚	1.94^{a}	7.87	⊚	1.15^{b}
Monocyte chemoattractant protein 1 (pg/ml)	503.03	⊚⊚	10.25	553.60	⊚	13.37^{**a}	533.57	⊚	12.89^{ab}	450.51	⊚	9.39^{b}
Tumor necrosis factor–α (ng/ml)	335.13	⊚⊚	0.05	426.60	⊚	0.14^{**a}	401.00	⊚	0.06^{a}	329.52	⊚	0.06^{b}

Data are presented as the mean ± SE. Significant differences between HFD versus ND are indicated; **p < 0.01. ab Means not sharing common letters in the same row are significantly different among the high-fat diet groups, at p < 0.05. ND, normal diet (AIN-76); HFD, high-fat diet (AIN-76, 20 % fat, 1% cholesterol); ERY (HFD + 5% Erythritol); ALL, (HFD + 5% D-allulose).

Supplementary Table S3. The numbers of up- or down-regulated genes in epididymal white adipose tissue D-allulose group compared to the high-fat diet group.

Number of differentially expressed genes identified by mRNA-seq analysis						
Cut off	**HFD vs ND**		**ALL vs ND**		**ALL vs HFD**	
FDR < 0.05 & fold change ≥ 2	**up**	**1285**	**up**	**201**	**up**	**178**
	down	**370**	**down**	**292**	**down**	**812**
	total	**1655**	**total**	**493**	**total**	**990**
						

Differentially expressed genes based on HFD vs ND, ALL vs HFD comparison among to FDR <0.05, fold change ≥2. ND, normal diet (AIN-76); HFD, high fat diet (AIN-76, 20% fat, 1% cholesterol); ALL, (HFD+5% D-allulose).

Supplementary Table S4. The list of up- or down-regulated genes in hepatic tissue by allulose among the high-fat diet-responsive genes.

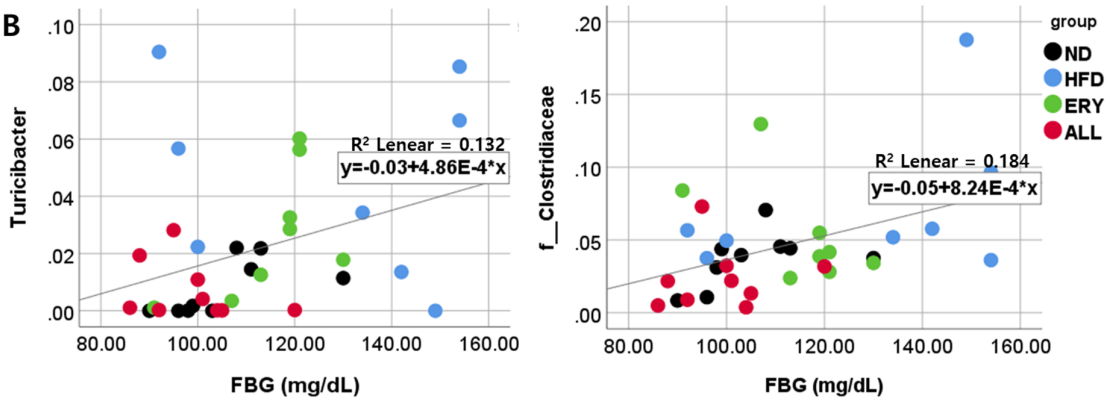
Numbers of differentially expressed genes identified by mRNA-seq analysis	
Among the 1099 genes up-regulated by HFD	
Up 1	Obp2a
Down 175	Aatk, Abcc12, Acod1, Acyp2, Adgrg2, Adgrv1, Anxa2, Apol10b, Aqp7, Atp6v0d2, Atp8b5, B430306N03Rik, Batf3, BC023105, Cbr3, Ccl19ps3, Ccl7, Ccr2, Cd207, Cd274, Cd300lb, Cd52, Ces1g, Chil3, Chst11, Cidea, Ciita, Clec12a, Clec4e, Clec4n, Clec7a, Col12a1, Col3a1, Cotl1, Cpxm1, Csf2rb2, Cxcl10, Cxcl14, Cxcl9, Cyp2a22, Cyp2b13, Cyp2c55, Cyth4, Dcst2, Dfna5, Dgkg, Dhrs9, Diaph3, Dock2, Ear2, Eda2r, Eif4e3, Ephb2, Esco2, Evi2a, Fabp3, Fabp4, Fam65b, Fam83a, Fam83f, Fbxo40, Fgl2, Fgr, Fosb, Gas7, Gbp10, Gbp2, Gbp5, Gbp6, Gins2, Gm10010, Gm12250, Gm13415, Gm15411, Gm16409, Gm37844, Gm44619, Gpr141, H2-DMa,H2-DMb1,H2M2, Haus8, Hk2, Hk3, Ifi209, Ifi211, Ifi27l2b, Ifit2, Igtp, Il27, Insl6, Itga4, Itgb2, Ivl, Kbtbd11, Kif14, Klrk1, Krt8, Ldb3, Lgals1, Lgals3, Limk1, Lrrc14b, Lum, Ly6d, Ly75, Ly86, Ly9, Lyz2, Mas1, Matn2, Mfap3l, Mfi2, Mki67, Mlkl, Mmp12, Mmp13, Mpeg1, Ms4a4c, Ms4a6c, Msrb3, Mthfd1l, Mybl1, Nipa1, Olfr56, Orm2, Orm3, Pcdh18, Plac8, Plek, Plin4, Psd4, Rassf4, S1pr2, Saa1, Saa2, Samsn1, Sdcbp2, Serpina7, Serpinb10, Serpinb9, Sirpb1a, Slamf8, Slc13a3, Slc13a4, Slc15a3, Slc1a4, Slc22a27, Slc28a1, Slc38a1, Slc39a4, Slc41a2, Smpd3, Smpdl3b, Sort1, St18, Tgtp1, Tgtp2, Tifa, Tnc, Tnfrsf19, Top2a, Tpm2, Trem1, Trp53cor1, Ttc39a, Ttc39aos1, Tubb6, Tyrobp, Uap1l1, Ubd, Vldlr, Vsig8, Zfp831, Zfp984
Among the 158 genes up-regulated by HFD	
Up 15	Cyp4a12b, Cyp4a14, E030018B13Rik, Eif4ebp3, Gm28438, Gm43314, Gm44117, Gm7463, Grm8, Hsd3b5, Lrp2, Moxd1, Mup21, RP23-306P12.3, Trpm5
Down 4	Idi1, Pcsk9, RP23-337J18.2, Ugt1a5

Differentially expressed genes based on HFD vs ND, ALL vs HFD comparison among to FDR <0.05, fold change ≥2. ND, normal diet (AIN-76); HFD, high fat diet (AIN-76, 20% fat, 1% cholesterol); ERY (HFD+5% Erythritol); ALL, (HFD+5% D-allulose).

A

Genus level		Turicibacter	Coprococcus
FBG	Spearman Correlation	0.359*	-0.160
	Significance (2-tailed)	0.049	0.366
	N	34	34
Family level		**Clostridiaceae**	**Erysipelotrichaceae**
FBG	Spearman Correlation	.360*	-0.107
	0.546	0.036	0.024
	N	34	34

B



Supplementary Figure S1. The correlation between Turcibacter, Clostridiaceae and fasting blood glucose.