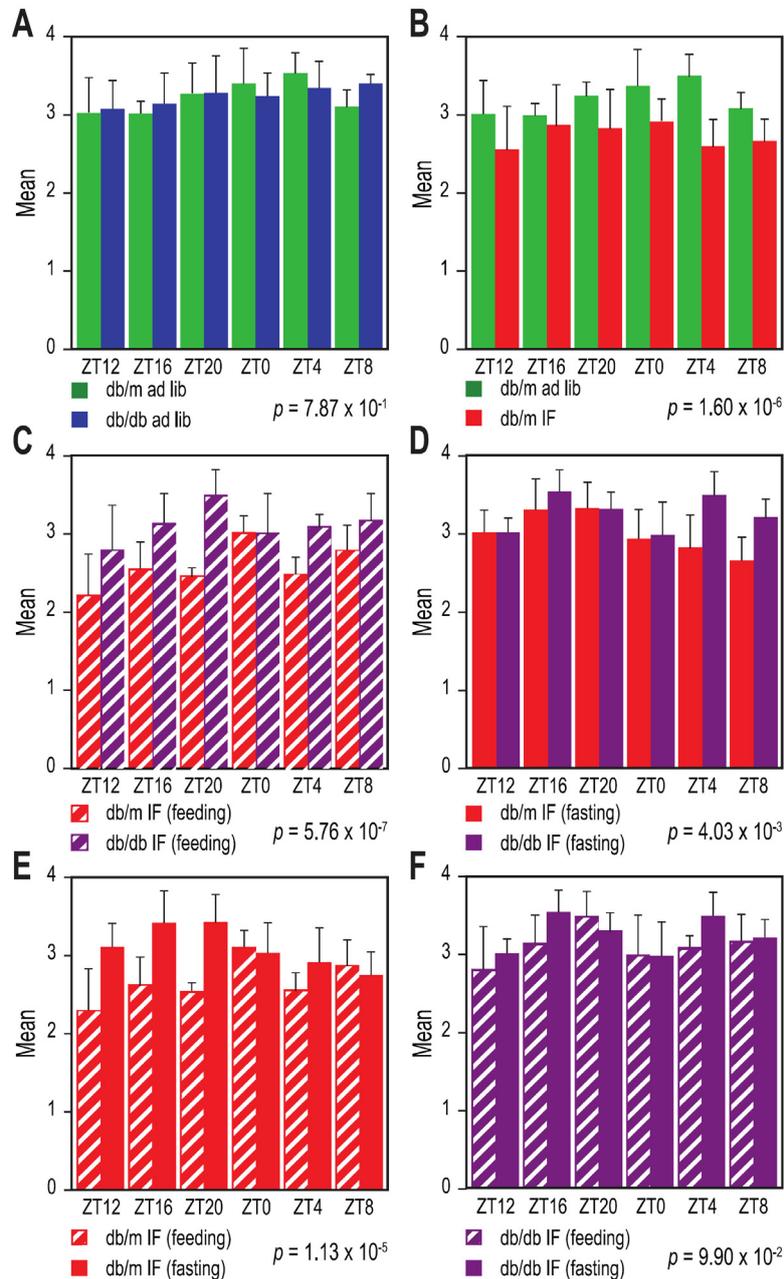


SUPPLEMENTARY DATA

Supplementary Figure S1. Comparison of Shannon diversity in the microbiota of select groups of mice. (A) db/m-AL vs. db/db-AL; (B) db/m-AL vs. db/m-IF; (C) db/m- IF feeding vs db/db-IF feeding; (D) db/m-IF-fasting vs db/db-IF fasting; (E) db/m-IF- feeding vs. db/ m-IF- fasting; (F) db/db- IF feeding vs. fasting. Data are means per respective groups \pm SEM (n = 3-5 mice per group). ANOVA-determined p-values are presented for each comparison.

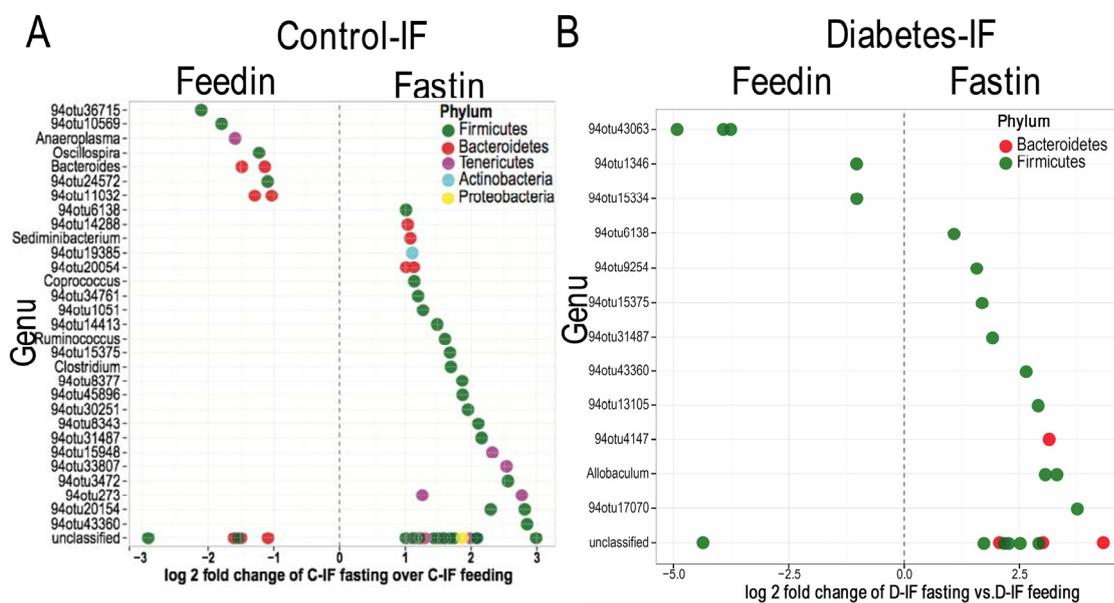


SUPPLEMENTARY DATA

Supplementary Figure. S2. Microbiome analysis. (A) Genera that show statistically significant changes in db/m-IF fasting vs db/m-IF feeding mice. (B) Genera that show statistically significant changes in db/db-IF fasting vs db/db-IF feeding mice.

Microbiome analysis. (C). Venn diagram for the comparison of lists of bacterial species that were significantly increased from their perspective AL diets in order to identify commonly or uniquely increased OTUs among the four data sets of db/m-IF feeding, db/m-IF fasting, db/db-IF feeding, and db/db-IF fasting.

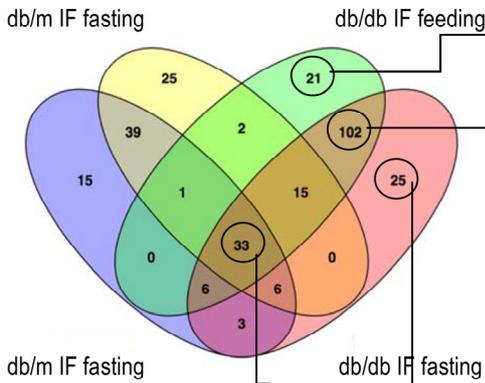
Microbiome analysis. (D) Venn diagram for the comparison of lists of bacteria that were significantly decreased from their perspective AL diets in order to identify commonly or uniquely decreased OTUs.



SUPPLEMENTARY DATA

C

Enriched OTUs



class	order	family	genus (#OTUs)
		Dehalobacteriaceae	Dehalobacterium (1)
		Lachnospiraceae	unclassified (6)
		unclassified	unclassified (3)
Clostridia	Clostridiales	Ruminococcaceae	Oscillospira (7)
		unclassified	Ruminococcus (1)
		unclassified	unclassified (14)
Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	Coprobacillus (1)
Mollicutes	RF39	unclassified	unclassified (1)

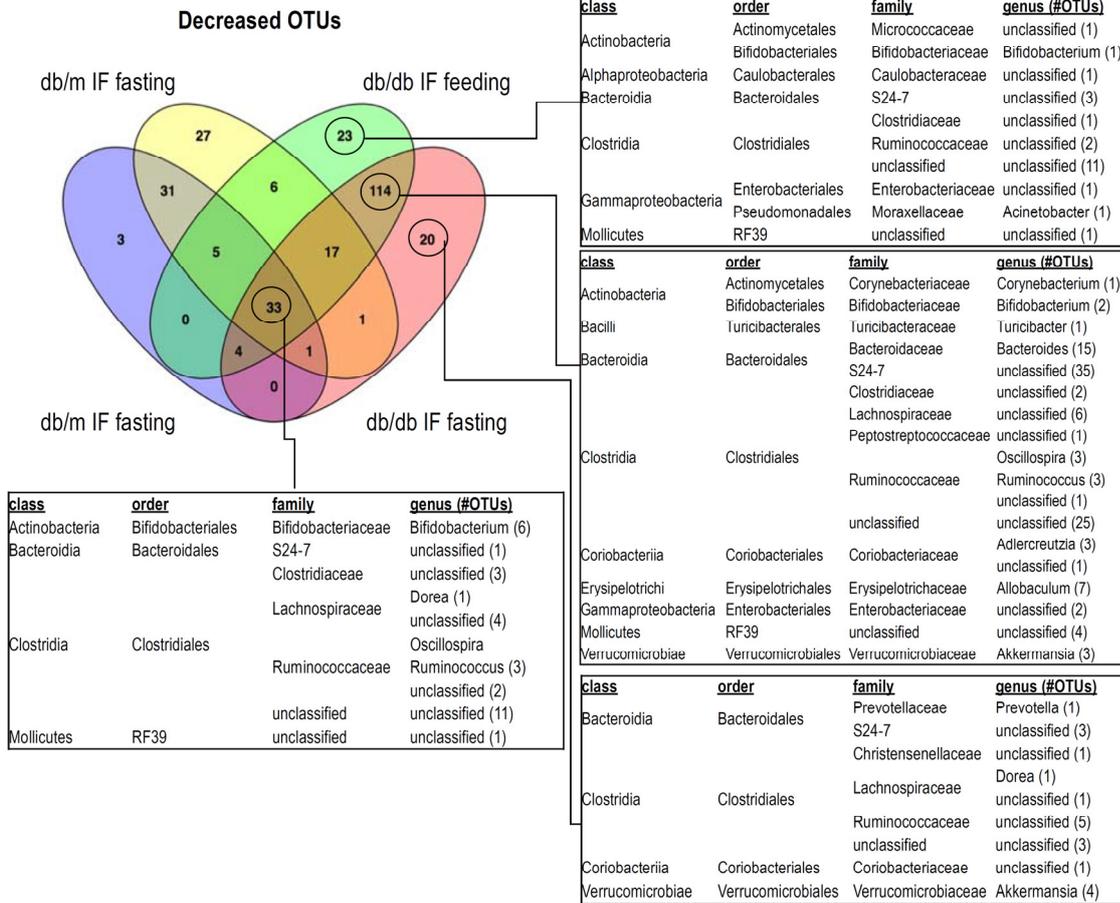
class	order	family	genus (#OTUs)
Bacteroidia	Bacteroidales	S24-7	unclassified (2)
		Lachnospiraceae	Coprococcus (2)
		unclassified	unclassified (2)
Clostridia	Clostridiales	Ruminococcaceae	Oscillospira (5)
		unclassified	Ruminococcus(2)
		unclassified	unclassified(4)
Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	unclassified(3)
Mollicutes	RF39	unclassified	unclassified (1)

class	order	family	genus (#OTUs)
Bacteroidia	Bacteroidales	S24-7	unclassified (9)
		Lachnospiraceae	Dorea (1)
		unclassified	unclassified (14)
Clostridia	Clostridiales	Ruminococcaceae	Oscillospira (7)
		unclassified	Ruminococcus (6)
		unclassified	unclassified (11)
		unclassified	unclassified (52)
Erysipelotrichi	Erysipelotrichales	Erysipelotrichaceae	unclassified (1)
Mollicutes	RF39	unclassified	unclassified (1)

class	order	family	genus (#OTUs)
		Lachnospiraceae	unclassified (3)
Clostridia	Clostridiales	Ruminococcaceae	unclassified (4)
		unclassified	unclassified(17)
Mollicutes	RF39	unclassified	unclassified (1)

SUPPLEMENTARY DATA

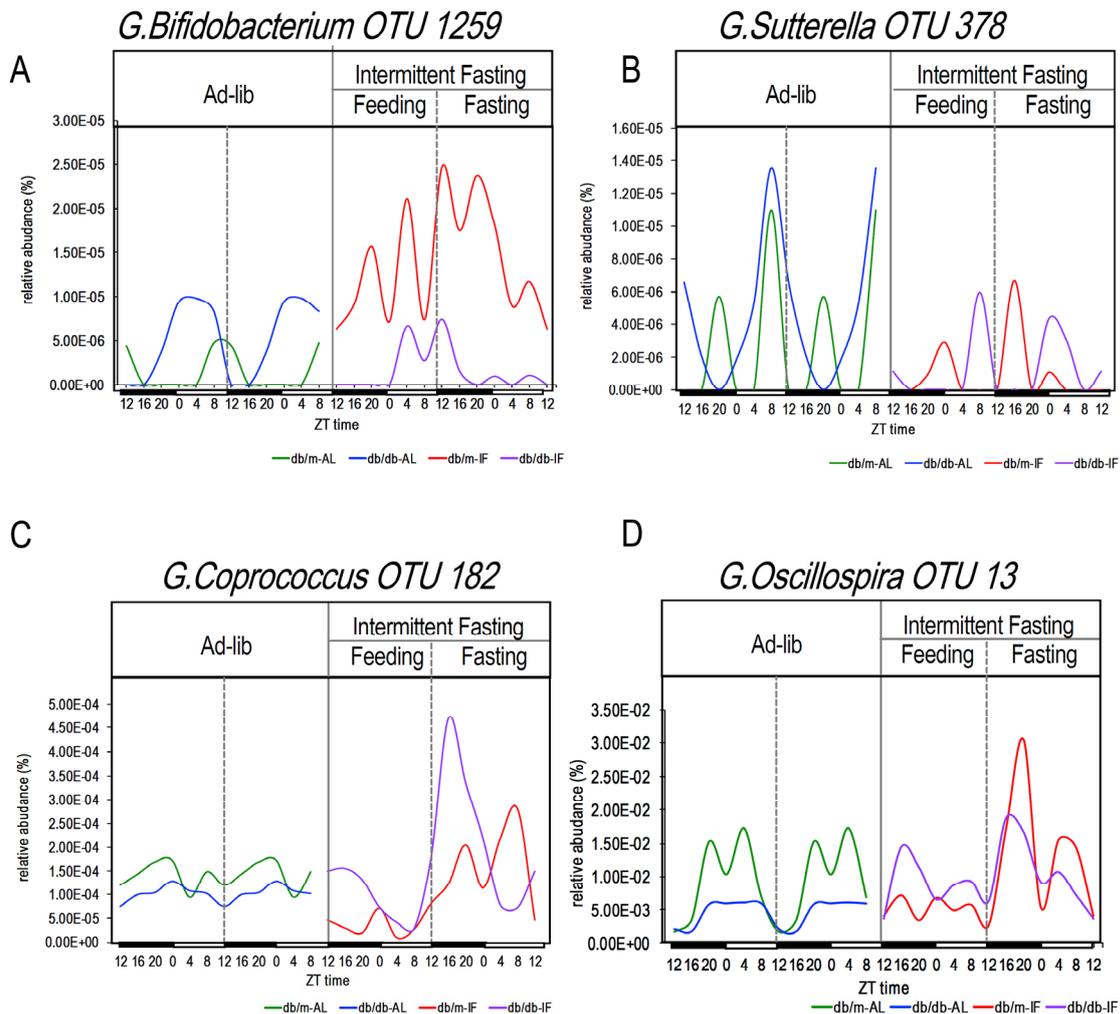
D



SUPPLEMENTARY DATA

Supplementary Figure. S3. Examples of OTUs that show diurnal variations in the AL regimen.

The JTK cycle was used to examine whether a circadian rhythm exists for relative abundance of bacteria in db/m and db/db for each OTU. The comparison of the pattern in relative abundance among (db/m IF, db/db-IF), (db/m-AL, db/db-AL), (db/m-IF, db/m-AL), and (db/db-IF, db/db-AL) was conducted using Kolmogorov–Smirnov test, a nonparametric test of equality of probability distribution. (A) *c_Actinobacteria*, *o_Bifidobacteriales*, *f_Bifidobacteriaceae*, *g_Bifidobacterium*, *s_unclassified_otu1259*. (B) *c_Betaproteobacteria*, *o_Burkholderiales*, *f_Alcaligenaceae*, *g_Sutterella*, *s_97otu21533_otu378*. (C) *c_Clostridia*, *o_Clostridiales*, *f_Lachnospiraceae*, *g_Coproccoccus*, *s_unclassified_otu182*. (D) *c_Clostridia*, *o_Clostridiales*, *f_Ruminococcaceae*, *g_Oscillospira*, *s_97otu13166_otu13*. Green lines: db/m-AL; blue lines: db/db-AL; red lines: db/m-IF; purple lines: db/db-IF. *c*_(class), *o*_(order), *f*_(family), *g*_(genus), *s*_(species).



SUPPLEMENTARY DATA

Supplementary Table S1. Analysis of bile acid content in plasma

bile acids				Ad-libitum		intermittent fasting			
						feeding		fasting	
				db/m (n=4)	db/db (n=4)	db/m (n=5)	db/db (n=4-5)	db/m (n=5)	db/db (n=4-6)
Primary bile	unconjugated	chololate	(CA)	0.166 ± 0.04	11.986 ± 6.3	2.840 ± 1.69	3.923 ± 1.71	4.001 ± 1.96	4.851 ± 1.53
		alpha-muricholate	(α-MCA)	0.192 ± 0.00	1.173 ± 0.62	1.025 ± 0.55	0.920 ± 0.37	3.374 ± 1.90	1.396 ± 0.48
		beta-muricholate	(β-MCA)	0.560 ± 0.13	2.120 ± 1.55	2.275 ± 0.96	1.656 ± 0.67	7.648 ± 3.51	4.304 ± 2.23
		all primary unconjugated bile acids:		0.917 ± 0.16	15.279 ± 7.73	6.140 ± 3.17	6.499 ± 2.69	15.023 ± 7.35	10.551 ± 4.03
	conjugated	glycochololate	(GCA)	0.257 ± 0.10	2.376 ± 1.16	0.438 ± 0.18	2.146 ± 0.60	0.355 ± 0.13	0.941 ± 0.38
		tauro-beta-muricholate	(Tβ-MCA)	0.809 ± 0.20	2.243 ± 0.73	0.418 ± 0.15	5.927 ± 2.47	0.576 ± 0.15	3.405 ± 1.17
		taurochenodeoxychololate	(TCDCOA)	0.697 ± 0.12	1.776 ± 0.52	0.556 ± 0.19	8.961 ± 4.54	0.482 ± 0.11	3.092 ± 1.19
		taurochololate	(TCA)	0.382 ± 0.16	4.868 ± 1.79	0.661 ± 0.27	4.545 ± 1.41	0.426 ± 0.14	2.076 ± 0.60
	all primary conjugated bile acids:		2.144 ± 0.56	11.264 ± 3.70	2.072 ± 0.75	19.936 ± 8.30	1.839 ± 0.49	9.515 ± 2.86	
	all primary bile acids (conjugated and unconjugated):				3.062 ± 0.55	26.543 ± 11.13	8.212 ± 3.74	26.435 ± 7.91	16.862 ± 7.78
Secondary bi	unconjugated	12-dehydrochololate	(12-DCA)	0.053 ± 0.00	0.237 ± 0.11	2.663 ± 1.50	0.686 ± 0.44	9.607 ± 4.09	0.435 ± 0.23
		3-dehydrochololate	(3-DCA)	0.097 ± 0.00	1.103 ± 0.59	0.892 ± 0.55	0.523 ± 0.27	1.711 ± 0.80	0.456 ± 0.18
		7-ketodeoxychololate	(7KDCA)	0.563 ± 0.15	0.974 ± 0.54	5.309 ± 2.89	0.794 ± 0.43	14.628 ± 6.52	2.096 ± 1.25
		deoxychololate	(DCA)	0.209 ± 0.03	0.876 ± 0.27	0.906 ± 0.37	1.524 ± 0.22	2.374 ± 0.96	2.387 ± 0.72
		ursochololate	(UCA)	0.141 ± 0.02	1.228 ± 0.64	1.852 ± 0.92	0.582 ± 0.25	3.773 ± 1.46	0.862 ± 0.28
		ursodeoxychololate	(UDCA)	0.544 ± 0.14	0.631 ± 0.28	3.104 ± 1.26	0.928 ± 0.41	6.770 ± 3.40	2.196 ± 0.97
	all secondary unconjugated bile acids:		1.606 ± 0.27	5.048 ± 2.32	14.727 ± 7.38	5.038 ± 1.83	38.863 ± 16.93	8.431 ± 3.13	
	conjugated	taurodeoxychololate	(TDCA)	0.265 ± 0.09	1.737 ± 0.65	0.415 ± 0.20	1.946 ± 0.39	0.765 ± 0.22	2.280 ± 0.59
		taurohyodeoxychololate	(THDCA)	0.638 ± 0.19	2.990 ± 1.25	0.465 ± 0.15	1.717 ± 0.46	0.687 ± 0.27	2.805 ± 1.09
		tauroursodeoxychololate	(TU DCA)	1.024 ± 0.16	0.913 ± 0.26	0.645 ± 0.10	2.668 ± 1.02	0.664 ± 0.18	2.063 ± 0.28
all secondary conjugated bile acids:		1.927 ± 0.37	5.641 ± 1.80	1.525 ± 0.44	5.973 ± 1.65	2.116 ± 0.61	6.630 ± 1.78		
all secondary bile acids:				3.534 ± 0.44	10.689 ± 4.06	16.252 ± 7.82	11.011 ± 2.62	40.980 ± 17.02	15.061 ± 4.62
all bile acids (primary and secondary)				6.595 ± 0.89	43.490 ± 19.56	24.464 ± 11.54	37.446 ± 10.13	57.842 ± 24.68	35.127 ± 11.05
all conjugated bile acids (primary and secondary)				4.072 ± 0.88	16.905 ± 5.49	3.597 ± 1.11	25.909 ± 9.90	3.956 ± 0.97	16.145 ± 4.59
all unconjugated bile acids(primary and secondary)				2.524 ± 0.40	20.327 ± 10.04	20.867 ± 10.54	11.537 ± 4.48	53.886 ± 24.16	18.982 ± 7.07
ratio of conjugated/ unconjugated				1.889 ± 0.51	1.663 ± 0.61	0.256 ± 0.05	5.028 ± 3.22	0.211 ± 0.13	0.920 ± 0.18
ratio of DCA/CA (indication of 7-α dehydroxylation)				1.579 ± 0.36	0.213 ± 0.09	0.499 ± 0.09	1.877 ± 1.37	1.202 ± 0.41	0.653 ± 0.22
ratio of conjugated /unconjugated secondary bile acids (indication of BSH)				1.453 ± 0.43	1.720 ± 0.51	0.177 ± 0.05	1.855 ± 0.71	0.169 ± 0.11	0.918 ± 0.21