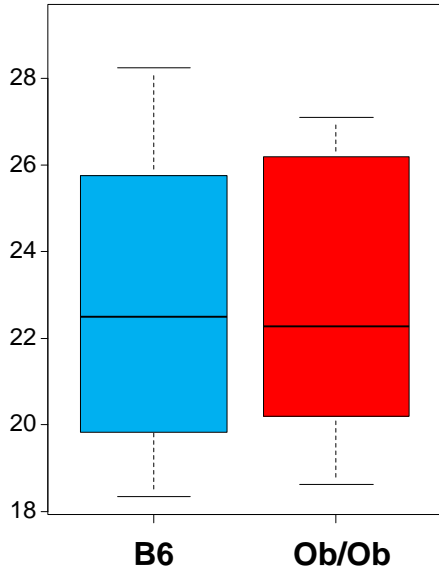
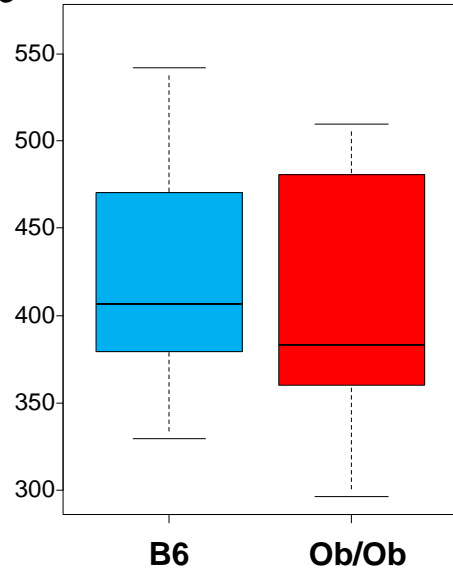
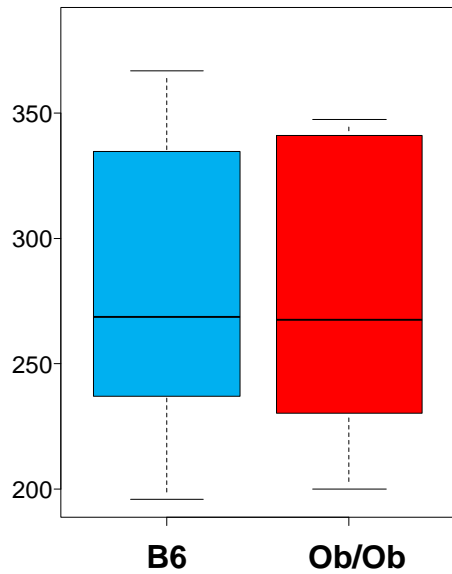
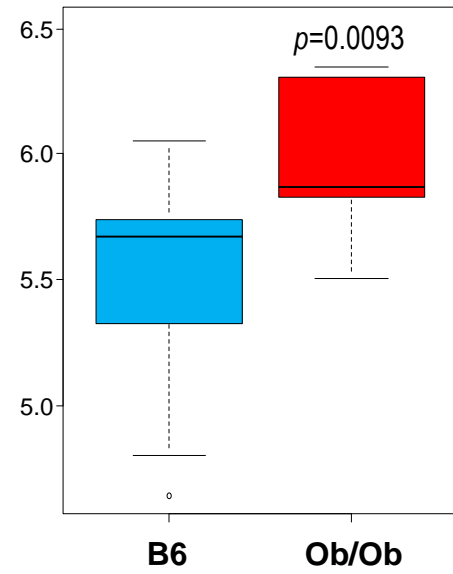


a PD whole tree**b** Chao 1**c** Observed OTUs**d** Shannon

Mann-Whitney U test

Table S1: Primer sequences (mouse) used for real-time PCR (adopted from: PrimerBank: <https://pga.mgh.harvard.edu/primerbank/>)

Gene name	Forward primer (5'→3')	Reverse primer (5'→3')
Bax	TGAAGACAGGGGCCTTTTTG	AATTCGCCGGAGACACTCG
Bad	AAGTCCGATCCCGGAATCC	GCTCACTCGGCTCAAACCTCT
Bcl2	ATGCCTTTGTGGAACCTATATGGC	GGTATGCACCCAGAGTGATGC
Ccnd1	GCGTACCCTGACACCAATCTC	CTCCTCTTCGCACTTCTGCT
Cdk6	GGCGTACCCACAGAAACCATA	AGGTAAGGGCCATCTGAAAACCT
Sox4	CGGCTGCATCGTTCTCTCC	GGTAGACGTGCTTCACTTTCTTG
Lgr5	CCTACTCGAAGACTTACCCAGT	GCATTGGGGTGAATGATAGCA
Olfm4	CAGCCACTTTCCAATTTCACTG	GCTGGACATACTCCTTCACCTTA
Bmi1	ATCCCCACTTAATGTGTGTCCT	CTTGCTGGTCTCCAAGTAACG
Muc2	ATGCCACCTCCTCAAAGAC	GTAGTTTCCGTTGGAACAGTGAA
Muc6	CGGCTGCGTCTGTCCTAAG	GCATAGTCACATGGGCATTCC
Occludin (Ocln)	TTGAAAGTCCACCTCCTTACAGA	CCGGATAAAAAGAGTACGCTGG
Zo1 (Tjp1)	CCGCTAAGAGCACAGCAA	TCCCCACTCTGAAAATGAGGA
Jam	TCTCTTCACGTCTATGATCCTGG	TTTGATGGACTCGTTCTCGGG
18S rRNA	GTAACCCGTTGAACCCATT	CCATCCAATCGGTAGTAGCG

Table S2: Relative abundance of different microbial communities that significantly different in Lepob/ob versus C57BL/6J (B6) mice

	B6		Ob/Ob		P value (T-test)
	Avg	SD	Avg	SD	
	Relative abundance, %				
<i>Bacteroidales</i>	64.16	7.76	50.43	10.94	0.0018
<i>Bacteroidales</i> ;f__S24-7	61.81	7.50	47.38	10.35	0.0008
<i>Bacteroidales</i> ;f__S24-7;g__	61.81	7.50	47.38	10.35	0.0008
<i>Bacteroidia</i>	64.16	7.76	50.43	10.94	0.0018
<i>Clostridia</i>	31.92	8.74	43.01	13.11	0.0233
<i>Clostridiales</i>	31.92	8.74	43.01	13.11	0.0233
<i>Clostridiales</i> ;f__	20.12	5.54	25.88	7.87	0.0502
<i>Clostridiales</i> ;f__;g__	20.12	5.54	25.88	7.87	0.0502
<i>Lachnospiraceae</i>	3.38	1.26	5.18	1.83	0.0102
<i>Lachnospiraceae</i> ;g__	2.40	1.23	4.04	2.22	0.0354
<i>Oscillospira</i>	5.17	2.11	7.38	2.83	0.0412
<i>Ruminococcaceae</i>	7.98	3.00	11.10	4.42	0.0550
<i>Verrucomicrobiaceae</i>	1.33	0.92	3.23	2.42	0.0227
<i>Verrucomicrobiae</i>	1.33	0.92	3.23	2.42	0.0227
<i>Verrucomicrobiales</i>	1.33	0.92	3.23	2.42	0.0227
<i>Akkermansia</i>	1.33	0.92	3.23	2.42	0.0227
<i>Pedobacter kwangyangensis</i>	2.10	1.55	7.49	2.51	0.0000
<i>Blautia hansenii</i>	2.65	1.24	5.19	1.73	0.0004
<i>Akkermansia muciniphila</i>	1.17	0.76	3.19	2.43	0.0163
<i>Alkaliphilus crotonatoxidans</i>	2.78	1.08	0.80	0.35	0.0000

Table S3: Spearman correlation analysis among metabolic, gut permeability, intestinal structural and gene expression analysis with gut microbiome signature of Lepob/ob and C57BL/6J mice.

		Prob > r under H0: Rho=0									
		Number of Observations									
		Body_weight	Blood_glucose	AUC_GTT_	AUC_ITT_	Gut_permeability	Villi_length	Crypt_depth	__budding	Bad	Bax
Bacteroidetes	r	-0.59504	-0.57432	0.29963	0.41844	-0.45722	0.58844	-0.25919	0.37143	-0.31429	-0.71429
Bacteroidetes	p	0.0022	0.0033	0.1549	0.0419	0.0491	0.0441	0.4159	0.4685	0.5441	0.1108
	n	24	24	24	24	19	12	12	6	6	6
Firmicutes	r	0.50054	0.50435	-0.18870	-0.35225	0.39123	-0.60245	0.28021	-0.37143	0.31429	0.71429
Firmicutes	p	0.0127	0.0120	0.3772	0.0914	0.0977	0.0382	0.3777	0.4685	0.5441	0.1108
	n	24	24	24	24	19	12	12	6	6	6
Verrucomicrobia	r	0.46899	0.29508	-0.58268	-0.47138	0.45391	-0.34676	0.38529	-0.65714	0.60000	0.60000
Verrucomicrobia	p	0.0208	0.1616	0.0028	0.0201	0.0509	0.2695	0.2161	0.1562	0.2080	0.2080
	n	24	24	24	24	19	12	12	6	6	6
F_B_ratio	r	0.53165	0.53700	-0.23097	-0.38242	0.41860	-0.59649	0.27018	-0.37143	0.31429	0.71429
F-B ratio	p	0.0075	0.0068	0.2775	0.0651	0.0745	0.0406	0.3957	0.4685	0.5441	0.1108
	n	24	24	24	24	19	12	12	6	6	6
Bacteroidales_f_S24_7	r	-0.63188	-0.61445	0.36522	0.45532	-0.56316	0.70753	-0.42732	0.60000	-0.48571	-0.77143
Bacteroidales;f__S24-7	p	0.0009	0.0014	0.0793	0.0254	0.0121	0.0101	0.1659	0.2080	0.3287	0.0724
	n	24	24	24	24	19	12	12	6	6	6
Lachnospiraceae	r	0.38555	0.64032	-0.25973	-0.27589	0.43108	-0.44483	0.26270	-0.94286	0.82857	0.65714
Lachnospiraceae	p	0.0628	0.0008	0.2203	0.1919	0.0654	0.1473	0.4094	0.0048	0.0416	0.1562
	n	24	24	24	24	19	12	12	6	6	6
Clostridiales_f__	r	0.39182	0.47259	-0.07217	-0.28484	0.31754	-0.52189	0.21366	-0.42857	0.37143	0.77143
Clostridiales;f__	p	0.0583	0.0197	0.7375	0.1773	0.1852	0.0818	0.5049	0.3965	0.4685	0.0724
	n	24	24	24	24	19	12	12	6	6	6
Oscillospira	r	0.49043	0.41694	-0.20448	-0.30527	0.24232	-0.56140	0.30175	-0.08571	0.02857	0.31429
Oscillospira	p	0.0150	0.0427	0.3378	0.1469	0.3175	0.0575	0.3405	0.8717	0.9572	0.5441
	n	24	24	24	24	19	12	12	6	6	6
Lachnospiraceae_g__	r	0.27099	0.53928	-0.17221	-0.21183	0.44142	-0.29072	0.12259	-0.60000	0.48571	0.20000
Lachnospiraceae;g__	p	0.2003	0.0065	0.4210	0.3204	0.0585	0.3593	0.7043	0.2080	0.3287	0.7040
	n	24	24	24	24	19	12	12	6	6	6
Akkermansia	r	0.46899	0.29508	-0.58268	-0.47138	0.45391	-0.34676	0.38529	-0.65714	0.60000	0.60000
Akkermansia	p	0.0208	0.1616	0.0028	0.0201	0.0509	0.2695	0.2161	0.1562	0.2080	0.2080
	n	24	24	24	24	19	12	12	6	6	6

