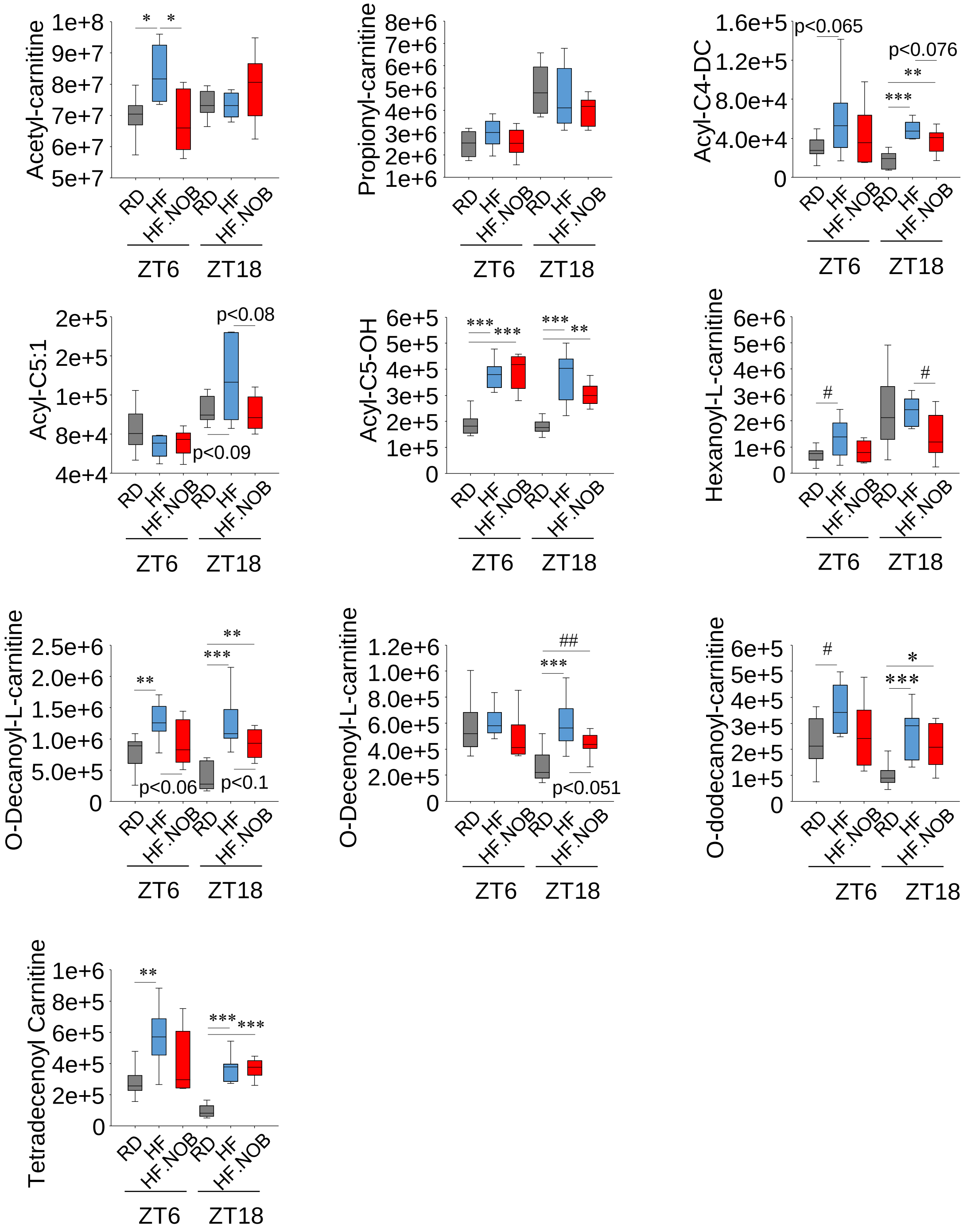
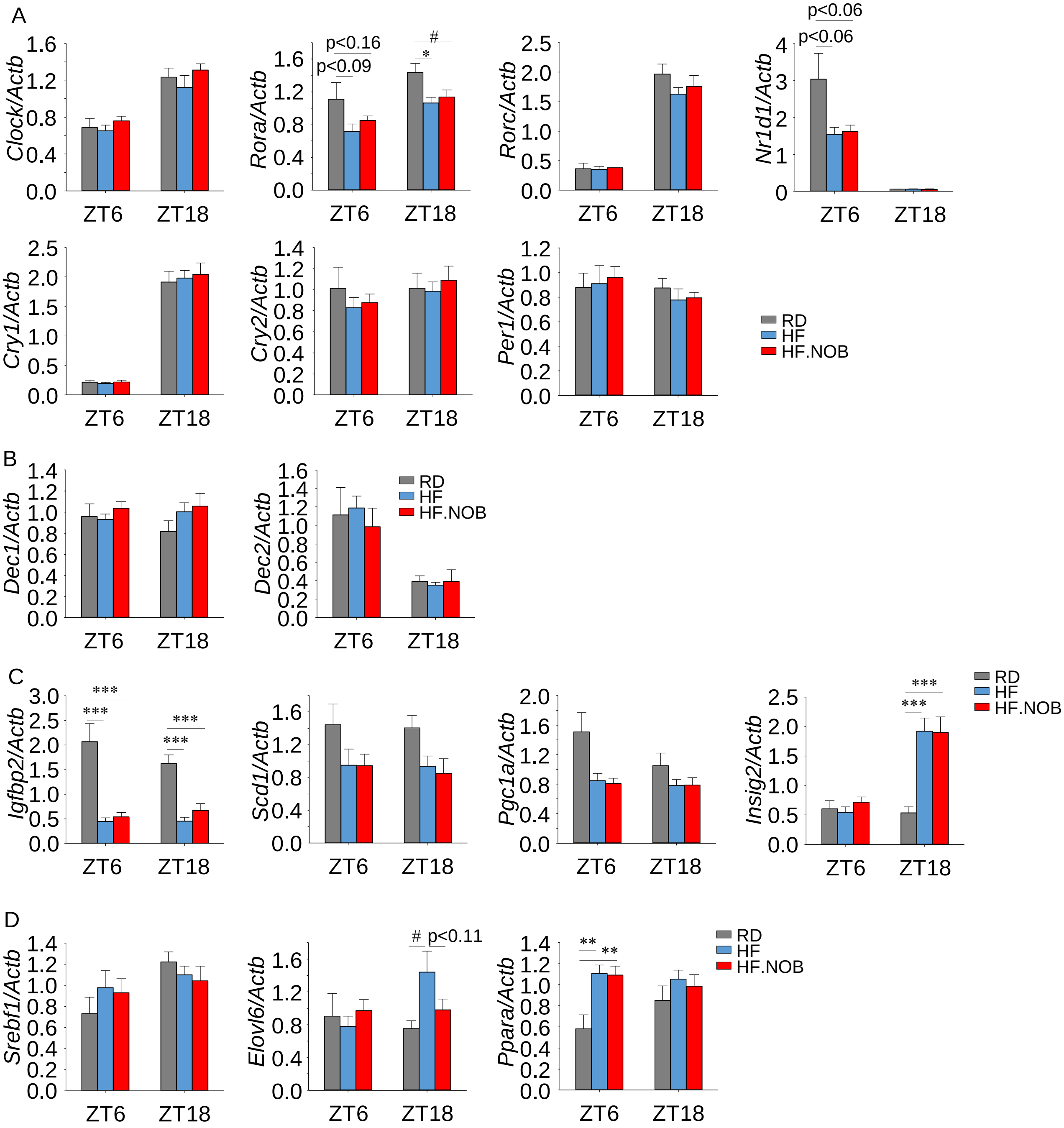
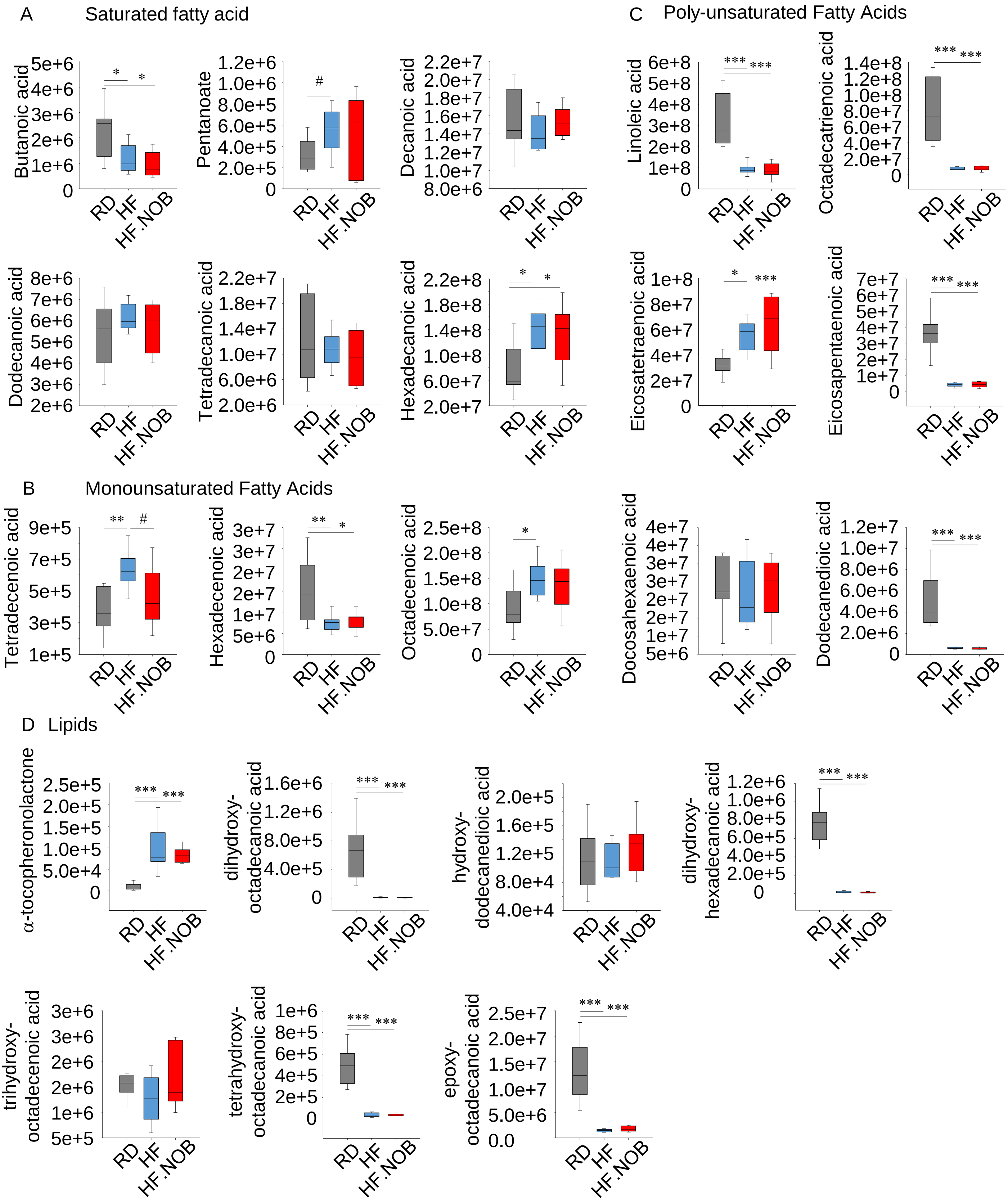


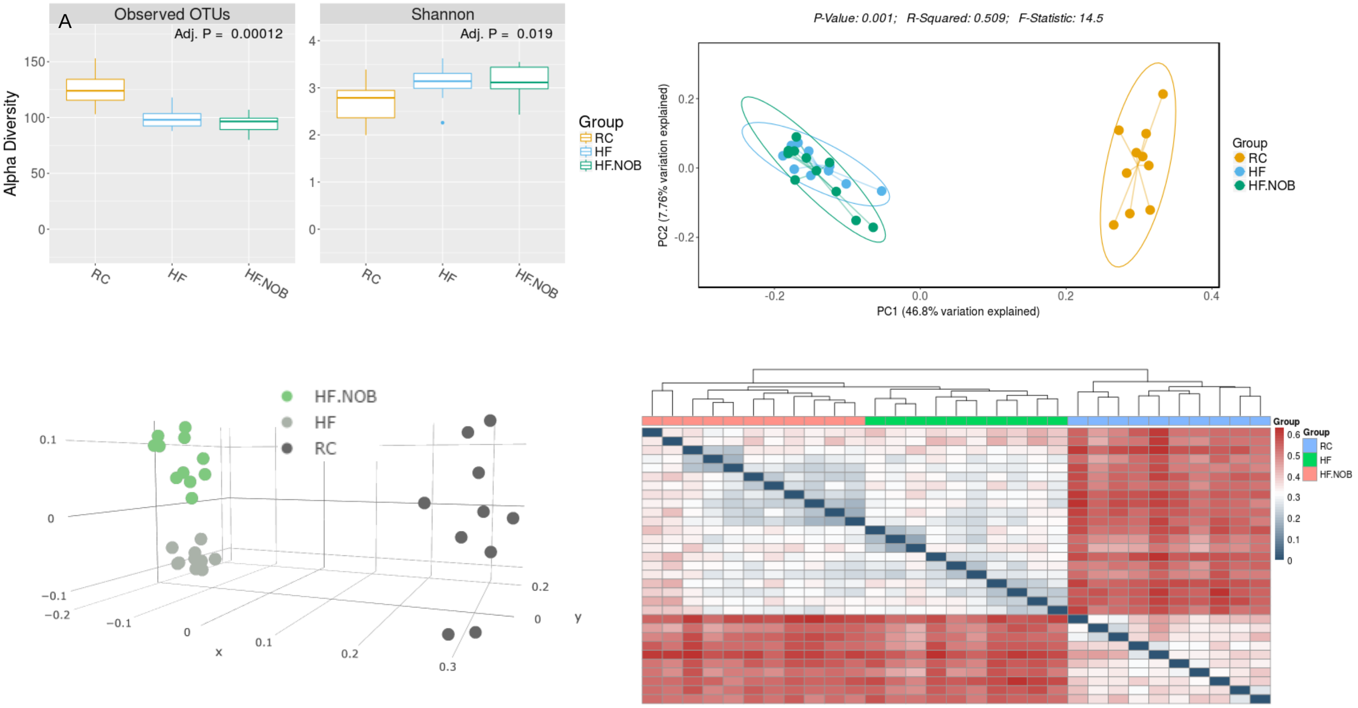
**Supplementary Figure S1. NOB reduces serum carnitine and acyl-carnitine levels.** Serum metabolomic profiles of carnitine and acyl-carnitine levels (n=7-9). RD: regular diet; HF: high-fat diet; HF.NOB: high-fat diet with 0.1% NOB. * $p<0.05$, ** $p<0.01$, *** $p<0.001$, One-Way ANOVA; # $p<0.05$, ## $p<0.001$, t-test. Bar graphs represent Mean ± SEM. For box-whisker plots, box edges correspond to 25th and 75th percentiles, lines inside of box correspond to 50th percentiles and whiskers include extreme data points.



**Supplementary Figure S2. NOB alters circadian and metabolic gene expression in the liver.** (A) Core clock gene expression levels in the liver were analyzed by qPCR (n=7-11). (B) Core clock related Dec1 and Dec2 gene expression levels in the liver were analyzed by qPCR (n=7-11). (C) Fatty acid and lipid metabolism related genes in liver were analyzed by qPCR (n=7-11) (D) Clock output energy homeostasis related gene expression levels in the liver were analyzed by qPCR (n=7-11). RD: regular diet; HF: high-fat diet; HF.NOB: high-fat diet with 0.1% NOB. * $p<0.05$, ** $p<0.01$, *** $p<0.001$, One-Way ANOVA; # $p<0.05$, t-test. Bar graphs represent Mean ± SEM.


A Saturated fatty acid
Butanoic acid
0
1e+6
2e+6
3e+6
4e+6
5e+6
*
*
Pentanoate
0
2.0e+5
4.0e+5
6.0e+5
8.0e+5
1.0e+6
1.2e+6
#
Decanoic acid
8.0e+6
1.0e+7
1.2e+7
1.4e+7
1.6e+7
1.8e+7
2.0e+7
2.2e+7
Dodecanoic acid
2e+6
3e+6
4e+6
5e+6
6e+6
7e+6
8e+6
Tetradecanoic acid
2.0e+6
6.0e+6
1.0e+7
1.4e+7
1.8e+7
2.2e+7
Hexadecanoic acid
2.0e+7
6.0e+7
1.0e+8
1.4e+8
1.8e+8
2.2e+8
*
*
C Poly-unsaturated Fatty Acids
Linoleic acid
0
1e+8
2e+8
3e+8
4e+8
5e+8
6e+8
***
***
Octadecatrienoic acid
0
2.0e+7
4.0e+7
6.0e+7
8.0e+7
1.0e+8
1.2e+8
1.4e+8
***
***
Eicosatetraenoic acid
0
2e+7
4e+7
6e+7
8e+7
1e+8
*
***
Eicosapentaenoic acid
0
1e+7
2e+7
3e+7
4e+7
5e+7
6e+7
7e+7
***
***
B Monounsaturated Fatty Acids
Tetradecenoic acid
1e+5
3e+5
5e+5
7e+5
9e+5
**
#
Hexadecenoic acid
0
5e+6
1e+7
2e+7
2e+7
3e+7
3e+7
**
*
Octadecenoic acid
0
5.0e+7
1.0e+8
1.5e+8
2.0e+8
2.5e+8
*
Docosahexaenoic acid
5e+6
1e+7
2e+7
2e+7
3e+7
3e+7
4e+7
4e+7
Dodecanedioic acid
0
2.0e+6
4.0e+6
6.0e+6
8.0e+6
1.0e+7
1.2e+7
***
***
D Lipids
α-tocopheronolactone
0
5.0e+4
1.0e+5
1.5e+5
2.0e+5
2.5e+5
***
***
dihydroxy-octadecanoic acid
0
4.0e+5
8.0e+5
1.2e+6
1.6e+6
***
***
hydroxy-dodecanedioic acid
4.0e+4
8.0e+4
1.2e+5
1.6e+5
2.0e+5
dihydroxy-hexadecanoic acid
0
2.0e+5
4.0e+5
6.0e+5
8.0e+5
1.0e+6
1.2e+6
***
***
trihydroxy-octadecenoic acid
5e+5
1e+6
2e+6
2e+6
3e+6
3e+6
tetrahydroxy-octadecanoic acid
0
2e+5
4e+5
6e+5
8e+5
1e+6
***
***
epoxy-octadecanoic acid
0.0
5.0e+6
1.0e+7
1.5e+7
2.0e+7
2.5e+7
***
***
RD
HF
HF.NOB

**Supplementary Figure S3. NOB does not influence fatty acid and lipid excretion.** (A) Saturated fatty acid, (B) mono-unsaturated fatty acid, (C) poly-unsaturated fatty acid and (D) other lipid profiles in fecal samples measured by metabolomics (n=10-12). RD: regular diet; HF: high-fat diet; HF.NOB: high-fat diet with 0.1% NOB. * $p<0.05$, ** $p<0.01$, *** $p<0.001$, One-Way ANOVA; # $p<0.05$, t-test. For box-whisker plots, box edges correspond to 25th and 75th percentiles, lines inside of box correspond to 50th percentiles and whiskers include extreme data points.



**Supplementary Figure S4. NOB remodels gut microbiota and protects liver from inflammatory damage.** Taxa abundance distribution at the genus level via 16S rRNA sequencing. Left top: box plot; right top: 2D ordination; left bottom: 3D ordination; right bottom: hierarchical plots. Panels indicate the comparison among all 3 sample groups, namely RD, HF and HF.NOB groups (n=10-12).

# Supplementary Table S1: qPCR Primer sequences for the genes listed, 5’ to 3’.

| | Forward | Reverse |
|---|---|---|
| ***Actb*** | TTGTCCCCCCAACTTGATGT | CCTGGCTGCCTCAACACCT |
| ***Arntl*** | CCACCTCAGAGCCATTGATACA | GAGCAGGTTTAGTTCCACTTTGTCT |
| ***Npas2*** | CAACAGACGGCAGCATCATCT | TTCTGATCCATGACATCCGC |
| ***Clock*** | CCTTCAGCAGTCAGTCCATAAAC | AGACATCGCTGGCTGTGTTAA |
| ***Per1*** | CCCAGCTTTACCTGCAGAAG | ATGGTCGAAAGGAAGCCTCT |
| ***Per2*** | ATGCTCGCCATCCACAAGA | GCGGAATCGAATGGGAGAAT |
| ***Cry1*** | CTGGCGTGGAAGTCATCGT | CTGTCCGCCATTGAGTTCTATG |
| ***Cry2*** | TGTCCCTTCCTGTGTGGAAGA | GCTCCCAGCTTGGCTTGA |
| ***Rora*** | GCACCTGACCGAAGACGAAA | GAGCGATCCGCTGACATCA |
| ***Rorc*** | TCAGCGCCCTGTGTTTTTC | GAGAACCAGGGCCGTGTAG |
| ***Nr1d1*** | CATGGTGCTACTGTGTAAGGTGTGT | CACAGGCGTGCACTCCATAG |
| ***Dec1*** | GCAAGGAAACTTACAAACTGCC | CAATGCACTCGTTAATCCGGT |
| ***Dec2*** | ATTGCTTTACAGAATGGGGAGCG | AAAGCGCGCGAGGTATTGCAAGAC |
| ***Cidec*** | ATGGACTACGCCATGAAGTCT | CGGTGCTAACACGACAGGG |
| ***Ppara*** | AGAGCCCCATCTGTCCTCTC | ACTGGTAGTCTGCAAAACCAAA |
| ***Pparc*** | CGAGGACATCCAAGACAAC | TGTGACGATCTGCCTGAG |
| ***Sreb1f*** | CTGGCTGAGGCGGGATGA | TACGGGCCACAAGAAGTAGA |
| ***Srebf2*** | CACAATATCATTGAAAAGCGCTACCGGTCC | TTTTTCTGATTGGCCAGCTTCAGCACCATG |
| ***Hmgcs1*** | AACTGGTGCAGAAATCTCTAGC | GGTTGAATAGCTCAGAACTAGCC |
| ***Hmgcs2*** | ATACCACCAACGCCTGTTATGG | GTCCACATATTGGGCTGGAAA |
| ***Hmgcr*** | TCTTGTGGAATGCCTTGTGATT | GGGTTACGGGGTTTGGTTTAT |
| ***Igfbp2*** | CAGACGCTACGCTGCTATCC | CCCTCAGAGTGGTCGTCATCA |
| ***Scd1*** | CATCATTCTCATGGTCCTGCT | CCCATTCGTACACGTCATT |
| ***Pgc1a*** | TATGGAGTGACATAGAGTGTGCT | CCACTTCAATCCACCCACAAAG |
| ***Insig2*** | TAAATCACGCCAGTGCTAAAGT | GGTGACAACGGTTGCTAAGAAAG |
| ***Elovl6*** | GAAAAGCAGTTCAACGAGAACG | AGATGCCGACCACCAAAGATA |
| ***Cyp7a1*** | GAACCTCCTTTGGACAACGGG | GGAGTTTGTGATGAAGTGGACAT |
| ***Cyp7b1*** | GGAGCCACGACCCTAGATG | GCCATGCCAAGATAAGGAAGC |
| ***Cyp27a1*** | CCAGGCACAGGAGAGTACG | GGGCAAGTGCAGCACATAG |
| ***Cyp8b1*** | TGCAAAAGAACTGGTGCTCAA | CGAACCTTTAGGCCCTAGCAT |
| ***Tnfa*** | GCCTCTTCTCATTCCTGCTTG | CTGATGAGAGGGAGGCCATT |
| ***Il6*** | ACAACCACGGCCTTCCCTACTT | CACGATTTCCCAGAGAACATGTG |