

Figure S1. Zfp217^{+/-} mice exhibit no phenotypic alterations compared to Zfp217^{+/+} mice fed normal chow diet (NC). (A) Food intake of Zfp217^{+/+} and Zfp217^{+/-} mice under NC or HFD (n = 8 per group). (B) Body fat weight or percentage of Zfp217^{+/+} and Zfp217^{+/-} mice (n = 8 per group). (C) Gross appearance of adipose tissues from representative Zfp217^{+/+} and Zfp217^{+/-} mice at 26 weeks. (D) iWAT, eWAT, BAT weight or percentage of Zfp217^{+/+} and Zfp217^{+/-} mice (n = 8 per group). (E) H&E staining of adipose tissue from Zfp217^{+/+} and Zfp217^{+/-} mice (Scale bar: 100 μ m) (n = 6 per group). (F, G) Average cell area (left) and adipocyte size distribution (right) in iWAT (F) and eWAT (G) of Zfp217^{+/+} and Zfp217^{+/-} mice (n = 6 per group). For all statistical plots, data are presented as the mean \pm SEM. **P* < 0.05; ***P* < 0.01 and ns indicates no significance between the two indicated groups.

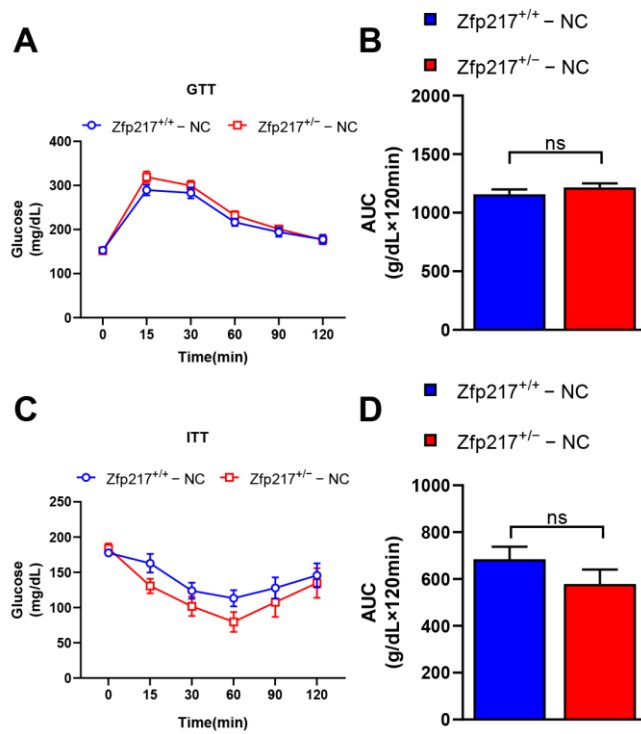


Figure S2. Zfp217^{+/-} mice and Zfp217^{+/+} mice exhibit similar glucose tolerance and insulin sensitivity under NC. (A, B) IP glucose tolerance test (GTT) were performed in Zfp217^{+/+} and Zfp217^{+/-} mice at 14 weeks, and the corresponding areas under the curves were calculated (n = 8 per group). Comparison at each time point was made against Zfp217^{+/+} control mice by Two-way ANOVA. (C, D) IP insulin tolerance test (ITT) were performed in Zfp217^{+/+} and Zfp217^{+/-} mice at 15 weeks, and the corresponding areas under the curves were calculated (n = 8 per group). Comparison at each time point was made against Zfp217^{+/+} control mice by Two-way ANOVA. For all statistical plots, data are presented as the mean \pm SEM. **P* < 0.05; ***P* < 0.01, and ns indicates no significance between the two indicated groups.

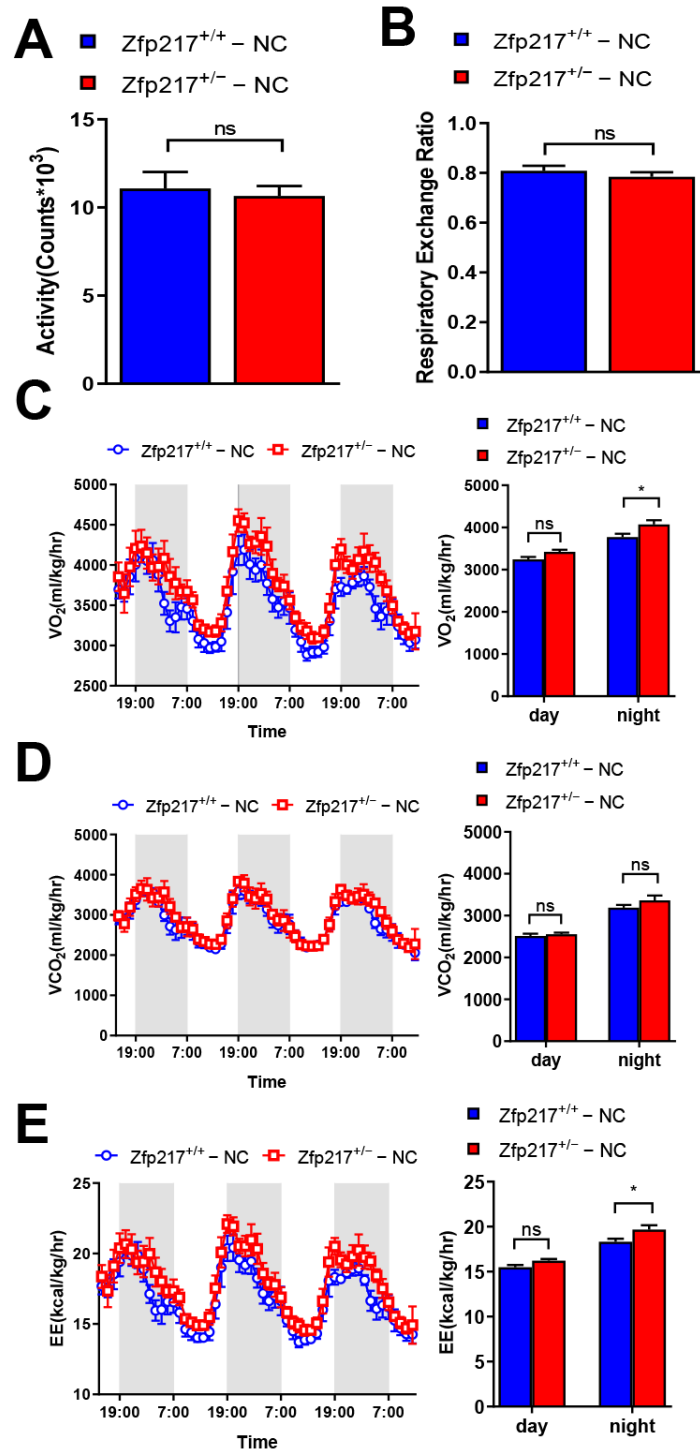


Figure S3. Zfp217^{+/-} mice exhibit no difference compared to the Zfp217^{+/+} mice in energy expenditure under NC. (A) Physical activity, (B) Respiratory exchange ratio, (C) Oxygen consumption (VO₂), (D) Carbon dioxide generation (VCO₂)

and (E) Energy expenditure analyzed by indirect calorimetry in *Zfp217^{+/+}* and *Zfp217^{+/-}* mice after NC feeding for 25 weeks (n=6 per group). For all statistical plots, data are presented as the mean \pm SEM. **P* < 0.05; ***P* < 0.01, and ns indicates no significance between the two indicated groups.

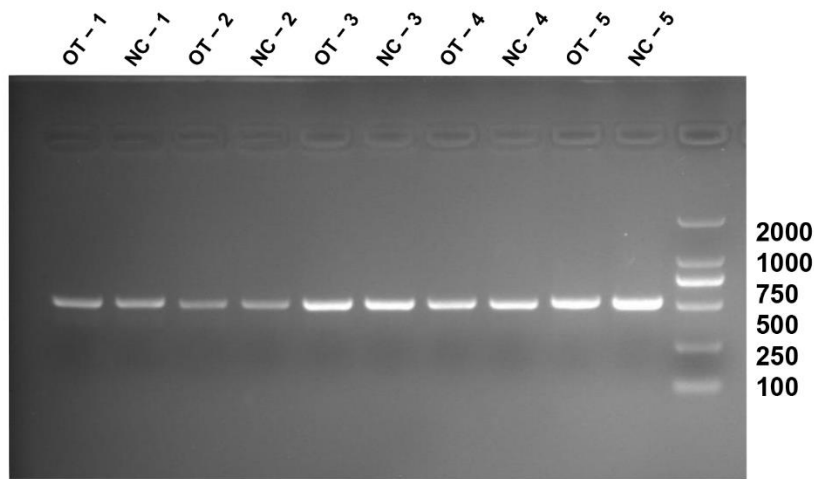


Figure S4. Detection of the five most likely off-target sites of sgRNA2' on the genome by PCR and agarose gel electrophoresis.

Table S1 Quantification real-time PCR primer sequence

Gene	Primer sequence	Retardation temperature, °C	Product length, bp
<i>Zfp217</i>	F: CTCTCTAGGCTCCCAGATGGA R: AGAACATGCAATCCAGGGGC	60	131
<i>PPARγ</i>	F: TCGCTGATGCACTGCCTATG R: GAGAGGTCCACAGAGCTGATT	60	103
<i>Ap2</i>	F: ATCAGCGTAAATGGGGATTTGG R: GTCTGCGGTGATTTTCATCGAA	60	105
<i>C/EBPα</i>	F: CAAGAACAGCAACGAGTACCG R: GTCACTGGTCAACTCCAGCAC	60	124
<i>adiponectin</i>	F: TGTTCCTCTTAATCCTGCCCCA R: CCAACCTGCACAAGTTCCC	60	104
<i>ACOX1</i>	F: TAACTTCCTCACTCGAAGCCA R: AGTTCCATGACCCATCTCTGTC	60	283
<i>ACC1</i>	F: ATGGGCGGAATGGTCTCTTTC R: TGGGGACCTTGTCTTCATCAT	60	148
<i>ELOVL6</i>	F: GAAAAGCAGTTCAACGAGAACG R: AGATGCCGACCACCAAAGATA	60	110
<i>FAS</i>	F: TATCAAGGAGGCCCATTTTGC R: TGTTTCCACCTCTAAACCATGCT	60	195
<i>Perlipin A</i>	F: CTGTGTGCAATGCCTATGAGA R: CTGGAGGGTATTGAAGAGCCG	60	171
<i>HSL</i>	F: GATTTACGCACGATGACACAGT R: ACCTGCAAAGACATTAGACAGC	60	114
<i>LPL</i>	F: GGGAGTTTGGCTCCAGAGTTT R: TGTGTCTTCAGGGGTCCTTAG	60	115
<i>SCD1</i>	F: TTCTTGCGATACACTCTGGTGTC R: CGGGATTGAATGTTCTTGTCGT	60	98

<i>β-actin</i>	F: CACGATGGAGGGGCGGACTCATC	60	241
	R: TAAAGACCTCTATGCCAACACAGT		
18s	F: TTGACGGAAGGGCACCACCAG	60	130
	R: GCACCACCACCCACGGAATCG		

Table S2 Primer design for off-target site

Primer name	Primer sequence	Location on the genome
<i>OT-Zfp217-1</i>	F: AAGTTTAGGTAGCAGGAT	Chr11: +93805835
	R: GATGGAAGAAATGGCAGA	
<i>OT-Zfp217-2</i>	F: TGAGAAGGTTTTGGACTA	Chr18: -65234377
	R: TTTCCCGTGTCACCTTCAT	
<i>OT-Zfp217-3</i>	F: GGACCTGGACCTGTAGTTT	Chr9: -44661009
	R: CATGCCCAAGTATTACCC	
<i>OT-Zfp217-4</i>	F: CTTCAGGCACATAGTCAGC	Chr14: +9351328
	R: TACCTATTGGAGCCTTCT	
<i>OT-Zfp217-5</i>	F: CCTTCCTCCCAGACCATC	Chr16: -144443447
	R: AGGCCATTCTGGA ACTCA	