Activation of METTL3 promotes white adipose tissue beiging and combats obesity

METTL3 in white adipose tissue beiging

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SUPPLEMENTARY FIGURE 1

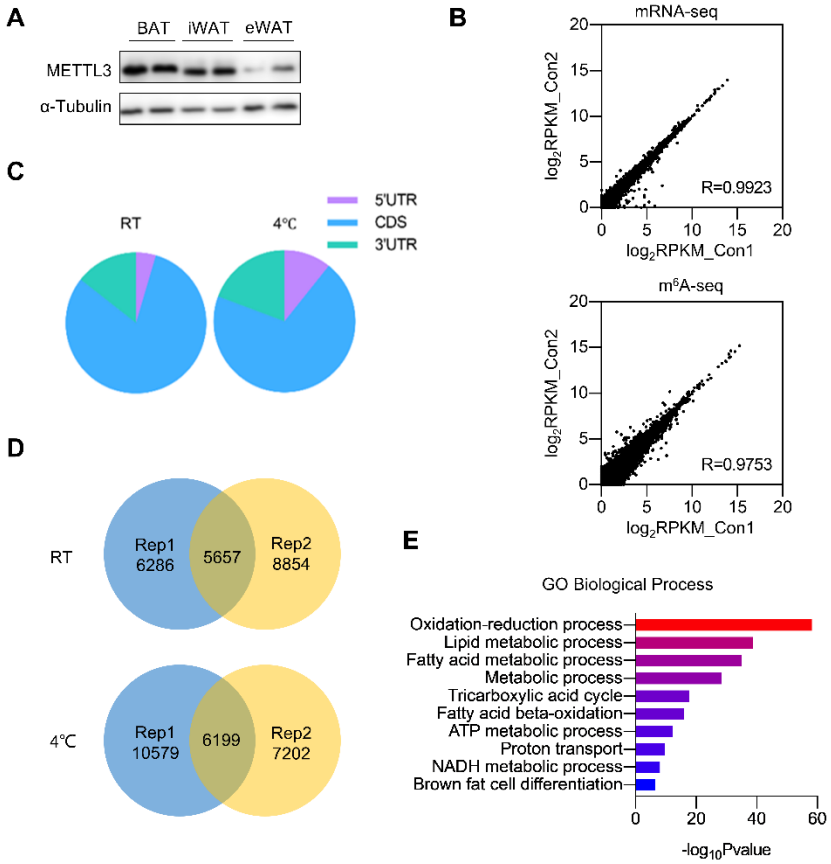

Figure S1. m^{6}A profiling of white and beige adipose tissue

(A) Western blot analysis of METTL3 expression in BAT, iWAT and eWAT from mice housed at room temperature. (B) Pearson's correlation of RNA-seq and m^{6}A-seq data between two independent replicates of iWAT from mice housed at room temperature. (C) Pie chart showing the proportion of m^{6}A peaks among different regions of transcripts in iWAT from mice housed at room temperature or 4 ℃ (two biological replicates). (D) Venn diagram showing the overlap of m^{6}A sites detected from two independent replicates of iWAT from mice housed at room temperature or 4 ℃. (E) Top GO terms (biological process) enriched on transcripts with up-regulated m^{6}A modification during beiging.

SUPPLEMENTARY FIGURE 2

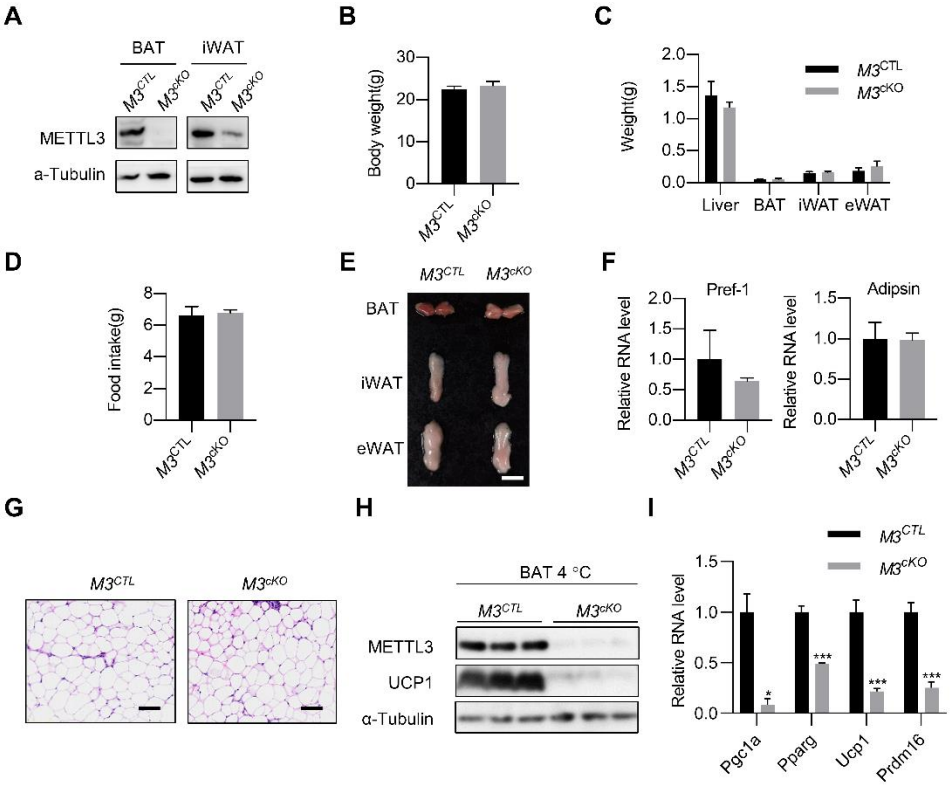

Figure S2. METTL3 is largely dispensable for WAT adipogenesis

(A) Immunoblot analysis of METTL3 expression in BAT and iWAT from *M3*^{CTL} and *M3*^{cKO} mice. (B) Bodyweight of *M3*^{CTL} and *M3*^{cKO} mice at the age of eight weeks (6 mice in each group, t-test, two-tailed). (C) Weight of liver, BAT, iWAT and eWAT from *M3*^{CTL} and *M3*^{cKO} mice at the age of eight weeks (6 *M3*^{CTL} mice, 3 *M3*^{cKO} mice, t-test, two-tailed). (D) Daily food intake of *M3*^{CTL} and *M3*^{cKO} mice at the age of eight weeks (6 mice in each group, t-test, two-tailed). (E) Gross view of BAT, iWAT and eWAT from *M3*^{CTL} and *M3*^{cKO} mice. (F) The mRNA levels of *Pref-1* and *Adipsin* in iWAT from *M3*^{CTL} and *M3*^{cKO} mice (3 independent experiments, t-test, two-tailed). (G) H&E staining of iWAT from *M3*^{CTL} and *M3*^{cKO} mice. Scale bar, 50 μm. (H) Immunoblot analysis of METTL3 and UCP1 expression in BAT of *M3*^{CTL} and *M3*^{cKO} mice housed at 4°C. (I) The mRNA levels of thermogenic genes (*Ppargc1α*, *Pparg*, *Ucp1*, *Prdm16*) in BAT of *M3*^{CTL} and *M3*^{cKO} mice after cold

48 treatment (*P<0.05, ***P<0.001; 3 independent experiments, t-test, two-tailed).
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SUPPLEMENTARY FIGURE 3

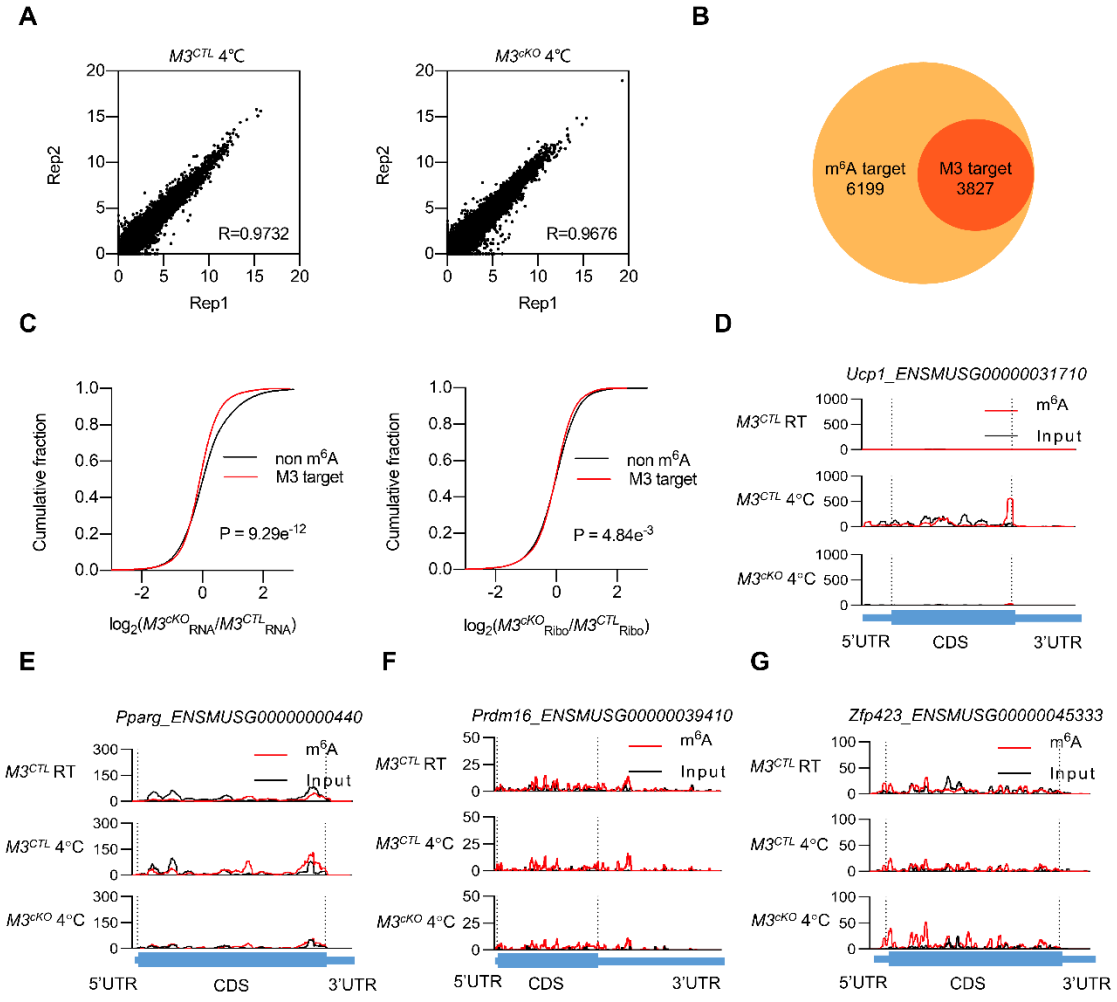

Figure S3. Characteristics of METTL3-targeted mRNA

(A) Pearson's correlation coefficients of Ribo-seq data between two independent replicates in iWAT from *M3*^{CTL} and *M3*^{cKO} mice housed at 4 °C. (B) Venn diagram showing the overlap of m^{6}A sites and METTL3-targeted m^{6}A sites. (C) Cumulative distributions showing the alternation of METTL3-targeted and non-m^{6}A transcripts at mRNA level and translational level between iWAT depots of cold-exposed *M3*^{CTL} and

58 *M3*^{cKO} mice. Mann-Whitney test. (D-G) The m^{6}A distribution within *Ucp1* (D), *Pparg*

59 (E), *Prdm16* (F)*, and Zfp423* (G) transcript (two biological replicates).