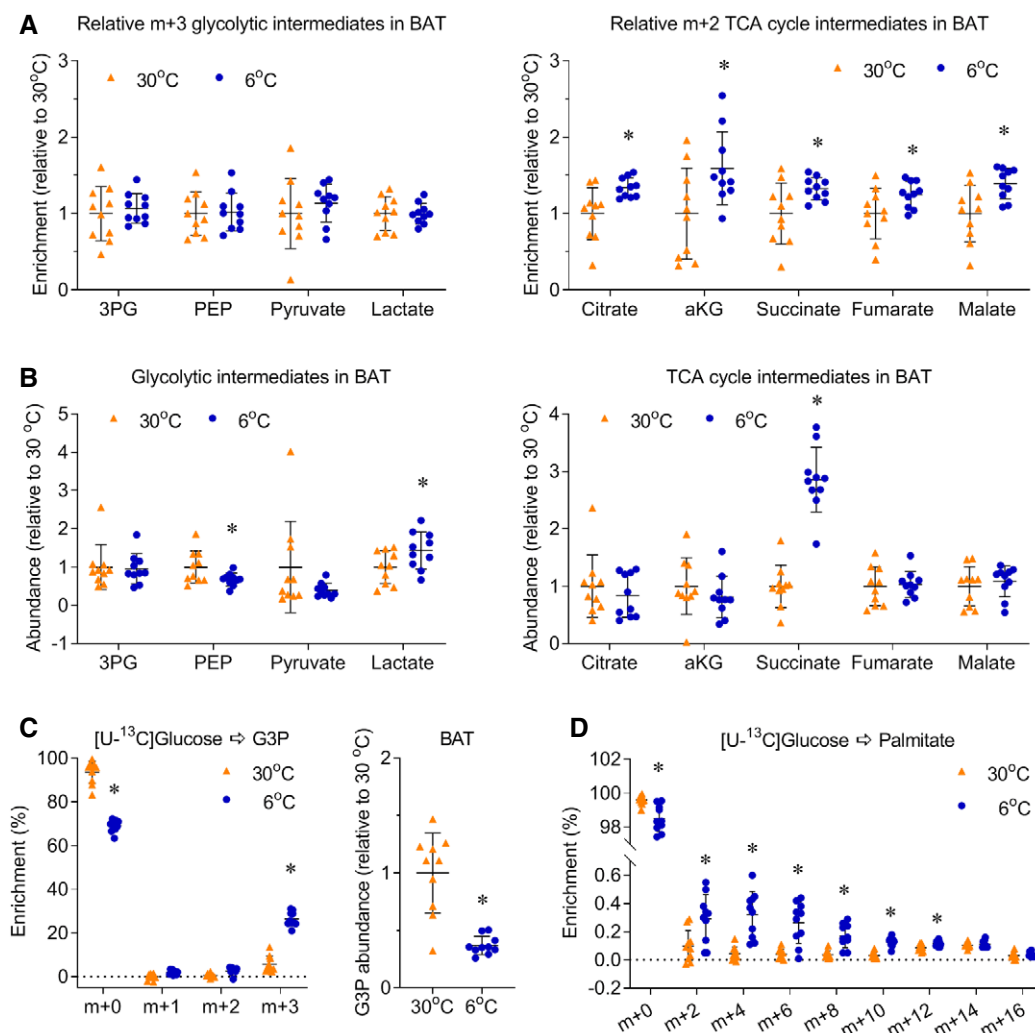


Expanded View Figures

**Figure EV1. Chronic cold exposure induces glucose metabolism in BAT.**

Mice, housed at 30°C or 6°C for 10 days, were administered with [U-¹³C]glucose (2 g/kg, IP). 15 minutes after injection, BAT was harvested for metabolic enrichment assay.

A To directly compare the change of enrichment between different metabolites, the relative metabolic ¹³C enrichments in BAT of male mice are normalized to the average enrichment of each metabolite in 30°C group.

B Relative abundance of glycolytic and TCA cycle intermediates in BAT.

C The enrichment and relative abundance of glyceraldehyde 3-phosphate (G3P).

D The enrichment of palmitate.

Data information: $n = 10$, data are represented as the mean \pm SD. Statistical analysis was performed using two-tailed Student's t -test, $*P < 0.05$.

Source data are available online for this figure.

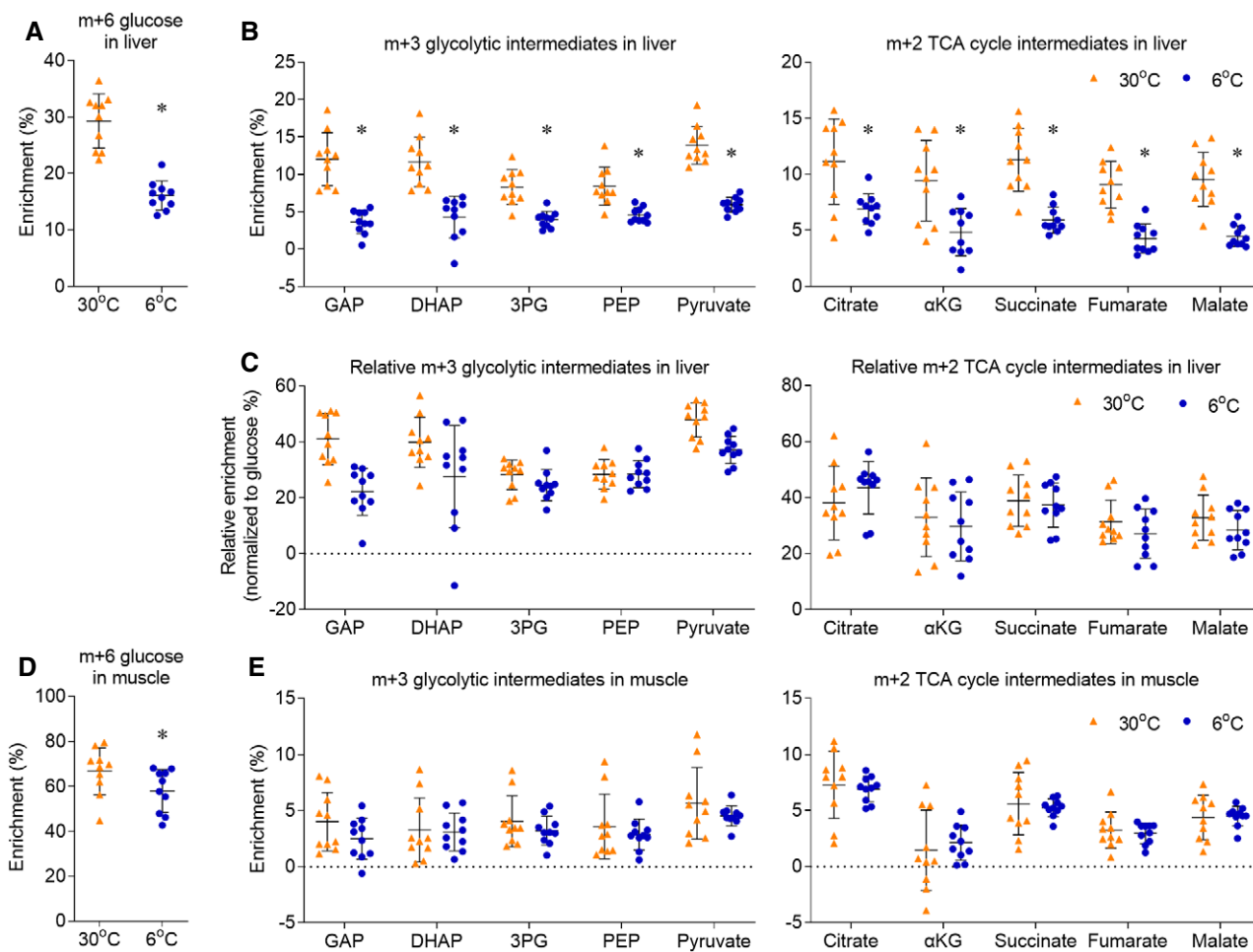


Figure EV2. Chronic cold exposure does not induce oxidative metabolism in liver or muscle.

Mice, housed at 30°C or 6°C for 10 days, were administered with [^{13}C]glucose (2 g/kg, IP). 15 minutes after injection, liver and muscle were harvested for metabolic enrichment assay.

A m+6 glucose enrichment in liver.

B Metabolic ^{13}C enrichments in liver are shown as m+3 glycolysis intermediates, m+2 TCA cycle intermediates. GAP, glyceraldehyde 3-phosphate; DHAP, dihydroxyacetone phosphate.

C After normalizing to the glucose enrichment in the liver of each mouse, the relative metabolic ^{13}C enrichments were shown as m+3 glycolysis intermediates and m+2 TCA cycle intermediates.

D m+6 glucose enrichment in muscle.

E Metabolic ^{13}C enrichments in muscle are shown as m+3 glycolysis intermediates, m+2 TCA cycle intermediates.

Data information: $n = 10$, data are represented as the mean \pm SD. Statistical analysis was performed using two-tailed Student's t -test, $*P < 0.05$.

Source data are available online for this figure.

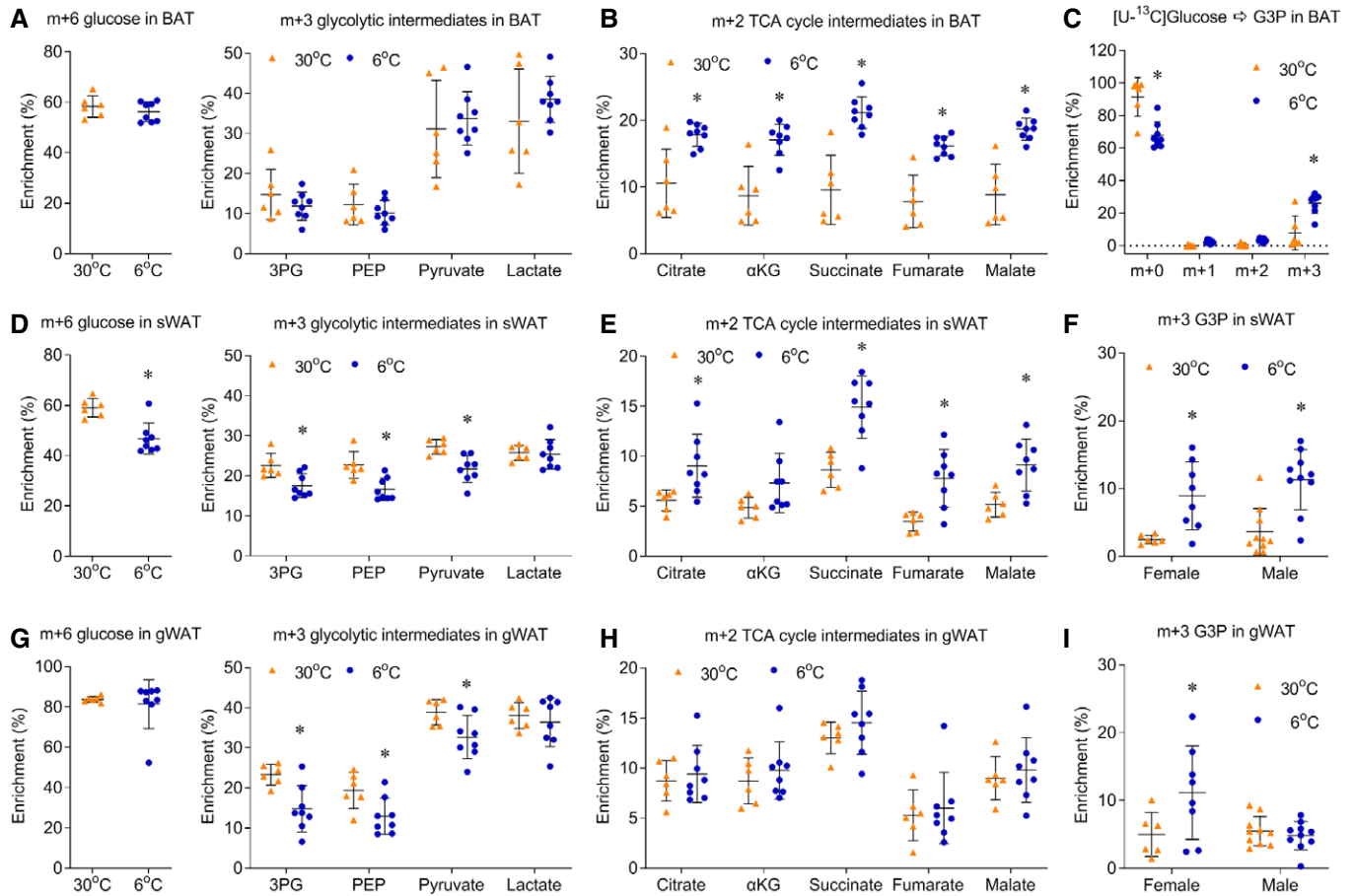


Figure EV3. Chronic cold exposure induces oxidative metabolism in BAT and sWAT of female mice.

Mice, housed at 30 or 6°C for 10 days, were administered with [U-¹³C]glucose (2 g/kg, IP). 15 minutes after injection, BAT, sWAT, and gWAT were harvested for metabolic enrichment assay.

A–C Metabolic ¹³C enrichments in BAT of female mice are shown as m+6 glucose and m+3 glycolytic intermediates (A), m+2 TCA cycle intermediates (B), and the enrichment of G3P (C).

D, E Metabolic ¹³C enrichments in sWAT of female mice are shown as m+6 glucose and m+3 glycolysis intermediates (D), m+2 TCA cycle intermediates (E).

F The m+3 enrichment of G3P in sWAT of both female and male mice.

G, H Metabolic ¹³C enrichments in gWAT of female mice are shown as m+6 glucose and m+3 glycolysis intermediates (G), m+2 TCA cycle intermediates (H).

I The m+3 enrichment of G3P in gWAT of both female and male mice.

Data information: $n = 6–8$ female mice, and $n = 10$ male mice, data are represented as the mean \pm SD. Statistical analysis was performed using two-tailed Student's t -test, $*P < 0.05$.

Source data are available online for this figure.

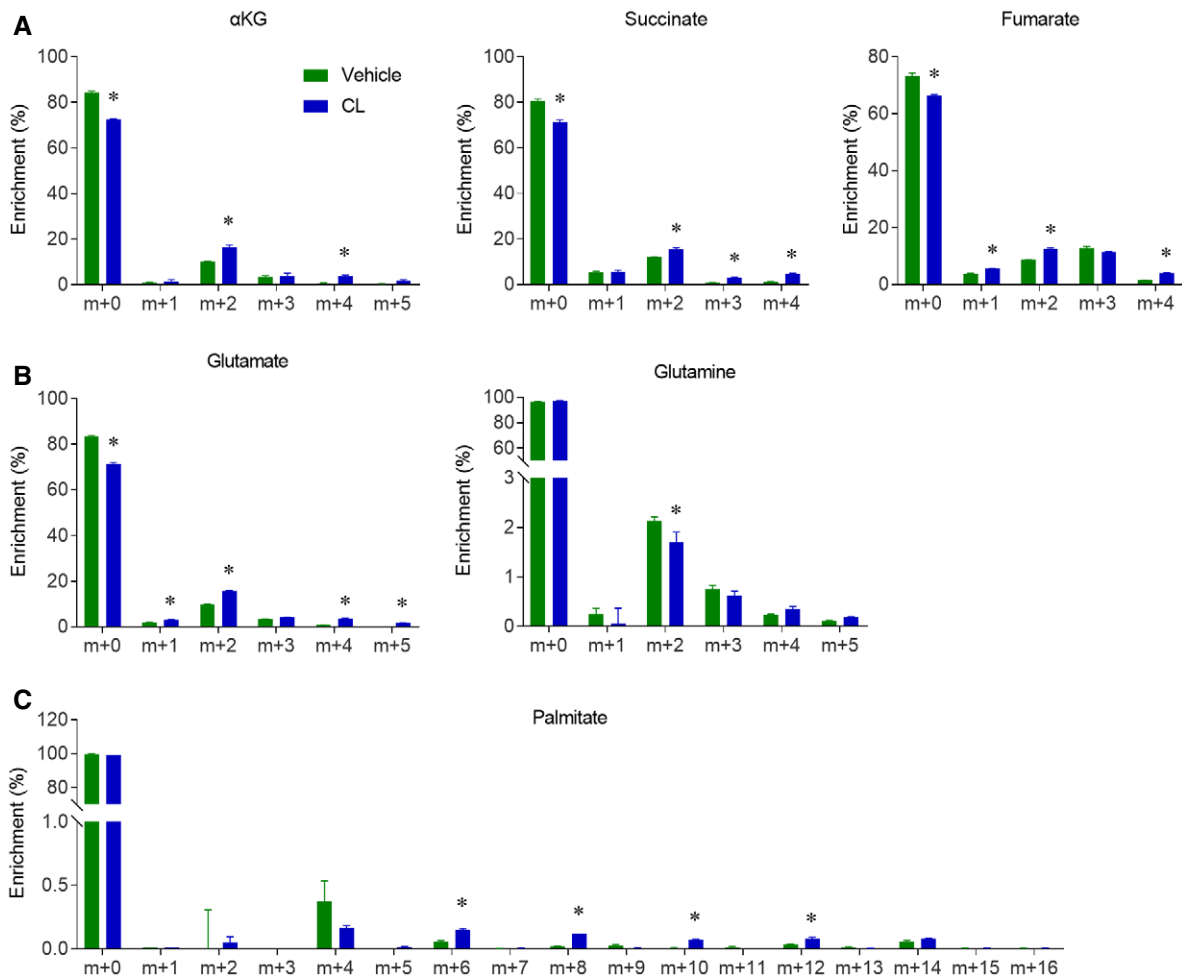


Figure EV4. β 3-AR agonist activates glucose oxidation in differentiated primary brown adipocytes.

A–C In the sample [U - ^{13}C]glucose experiment as shown in Fig 5, the enrichments of other metabolites were used for MFA modeling. $n = 3$ biological repeats, data are represented as the mean \pm SD. Statistical analysis was performed using two-way ANOVA followed by Tukey's multiple comparisons test, * $P < 0.05$.

Source data are available online for this figure.

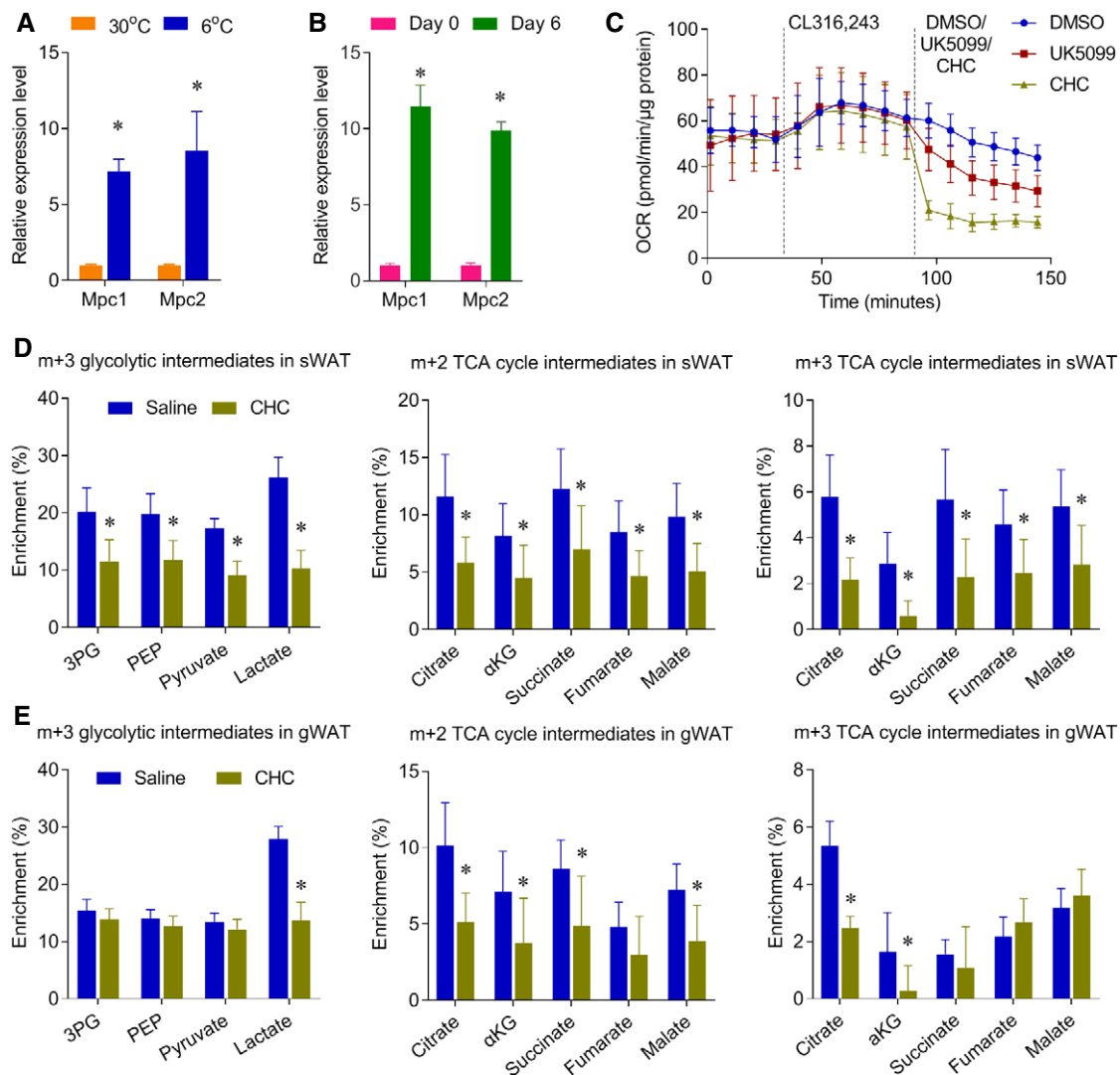


Figure EV5. CHC represses glucose metabolism in multiple adipose tissues.

- A Relative mRNA levels of Mpc1/2 expression were measured by qPCR in BAT of the mice, housed at 30 or 6°C for 10 days. $n = 5-6$ biological replicates.
- B Relative mRNA levels of Mpc1/2 expression were measured by qPCR in the pre-differentiated day 0 and fully differentiated brown adipocytes day 6. $n = 4$ biological replicates.
- C Oxygen consumption rate (OCR) of mouse brown adipocytes treated with MPC inhibitor CHC (2 mM) or UK5099 (2 μ M), $n = 6-7$ biological repeats. CL, CL316,243.
- D, E Mice were housed at 6°C for 10 days, and mice were IP injected with PBS or CHC (500 mg/kg). 30 minutes after CHC treatment, mice were administered with [13 C]glucose (2 g/kg, IP). Metabolic 13 C enrichments in sWAT (D) and gWAT (E) of male mice are shown as m+2 and m+3 TCA cycle intermediates. $n = 7$ biological replicates.

Data information: data are represented as the mean \pm SD, except that (C) is represented as the mean \pm SEM. Statistical analysis was performed using two-tailed Student's t -test, * $P < 0.05$.

Source data are available online for this figure.