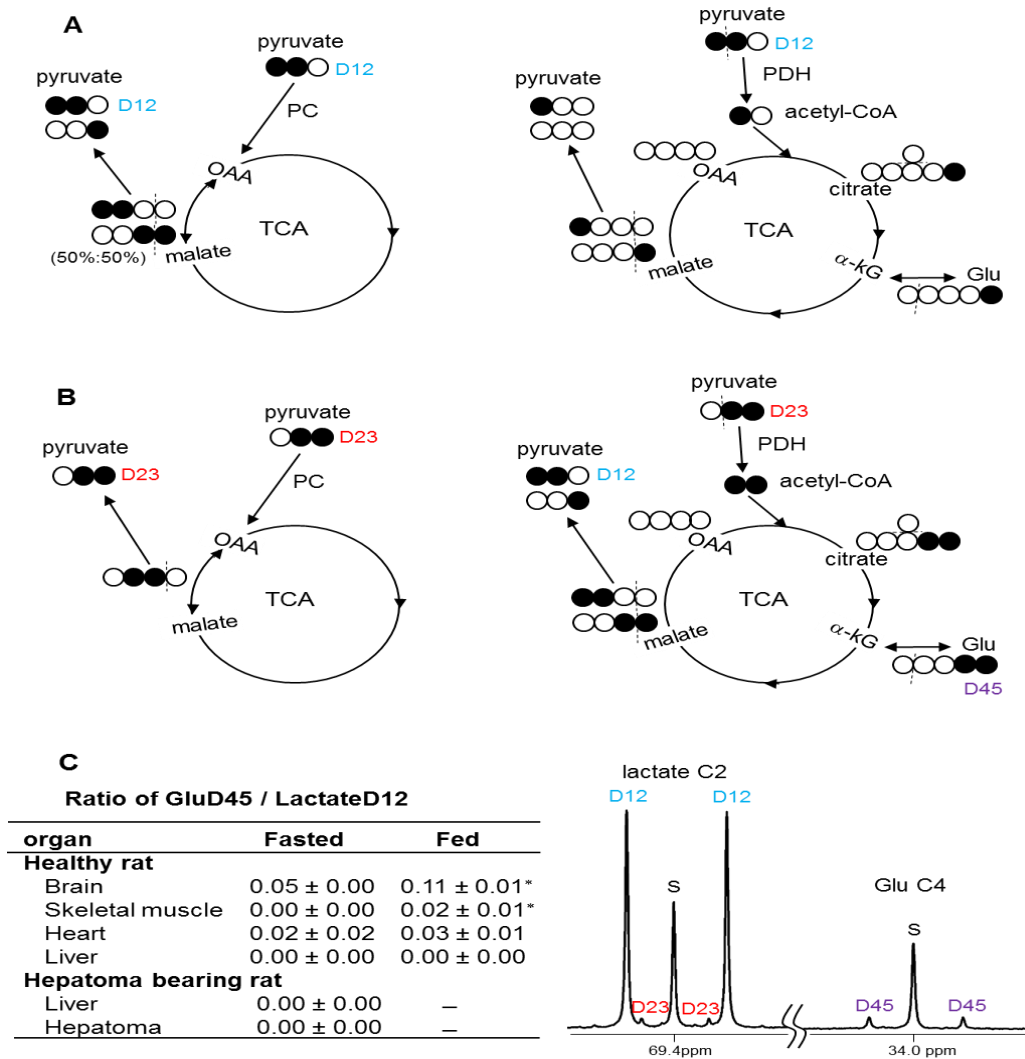


Supplemental Data

Supplemental Table 1. PCR primer sequences.

Gene	Sequence
FAS	5'-GGAAAACATATTGGCAAAGTCC-3'; 5'-CTAGGCCACCAGTGATGATGTA-3'
GAPDH	5'-TGCCACTCAGAAGACTGTGG-3'; 5'-GGATGCAGGGATGATGTTCT-3'
G6PDH	5'-TTTGCAGCAGCTGTCCTCTA-3'; 5'-ACATCGCGGAACTGAAGTCT-3'
SREBP1c	5'-TCGACTACATCCGCTTCTTACA-3'; 5'-TGACACCAGGTCTTTCAGTGAT-3'
TKT	5'-CATCTCCGAGAGCAACATCA-3'; 5'-CTTGGGTAAGACGGTGGA-3'



Supplemental Figure 1. Pyruvate re-generation through the TCA cycle. Pyruvate enters the TCA cycle through pyruvate carboxylase or pyruvate dehydrogenase. Pyruvate carboxylase activity may lead to pyruvate cycling while pyruvate dehydrogenase activity leads to oxidative metabolism through the TCA cycle. (A) After metabolism of [2,3-¹³C₂]glucose via glycolysis, the entry of [1,2-¹³C₂]pyruvate through pyruvate carboxylase or pyruvate dehydrogenase does not produce a competing source of [2,3-¹³C₂]pyruvate. (B) After metabolism of [2,3-¹³C₂]glucose via the PPP, [2,3-¹³C₂]pyruvate can be cycled through pyruvate carboxylase, which re-generates [2,3-¹³C₂]pyruvate. In contrast, the entry of [2,3-¹³C₂]pyruvate into the TCA cycle through pyruvate dehydrogenase produces [1,2-¹³C₂]acetyl-CoA and [4,5-¹³C₂]citrate after condensation with oxaloacetate. This leads to [4,5-¹³C₂]α-ketoglutarate through the TCA cycle, and α-ketoglutarate is in exchange with glutamate. Decarboxylation of the α-ketoglutarate leads to [1,2-¹³C₂]- or [3,4-¹³C₂]succinate/fumarate (50%:50%; symmetric molecules), [1,2-¹³C₂]- or [3,4-¹³C₂]malate, and consequently [1,2-¹³C₂]- or [3-¹³C₁]pyruvate, respectively. (C) The contribution of [1,2-¹³C₂]pyruvate through the TCA cycle to total [1,2-¹³C₂]pyruvate can be roughly estimated by comparing the signal of [4,5-¹³C₂]glutamate (D45) with the signal of [1,2-¹³C₂]lactate (D12) on ¹³C NMR. The ratio of glutamate D45 / lactate D12 is 0.05-0.11 in brain tissues while it is trivial in other organs. ¹³C NMR spectrum of lactate C2 and glutamate C4 is from brain of a fasted rat. Abbreviations: Glu, glutamate; α-kG, α-ketoglutarate; OAA, oxaloacetate; PC, pyruvate carboxylase; PDH, pyruvate dehydrogenase. Data are means ± SEM (n=3-5); *, p<0.05