Supporting Information

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SI Text

Isotopic Mass Balance Equations

Mass Balance:

$d(\text{Citrate})/dt = V_{TCA} - V_{TCA}$
$d(\alpha KG)/dt = V_{TCA} + V_X - (V_{TCA} + V_X)$
$d(\text{Glutamate})/dt = V_X - V_X$
$d(\text{AcetylCoA})/dt = V_{AC} + V_{PDH+FA} - V_{TCA}$

Isotope Balance:

$d(C_4\text{-Cit})/dt = V_{TCA}\ (C_2\text{-AcCoA/AcCoA}) - V_{TCA}(C_4\text{-Cit/Cit})$;
$d(C_4\text{-}\alpha KG)/dt = V_{TCA}(C_4\text{-Cit/Cit}) + V_X(C_4\text{-Glu/Glu}) - (V_{TCA} + V_X)(C_4\text{-}\alpha KG/\alpha KG)$
$d(C_4\text{-Glu})/dt = V_X(C_4\text{-}\alpha KG/\alpha KG) - V_X\ (C_4\text{-Glu/Glu})$;
$d(C_2\text{-AcCoA})/dt = V_{AC}(C_2\text{-AcO/AcO}) + V_{PDH+FA}(C_0\text{-FFA/FFA}) - V_{TCA}(C_2\text{-AcCoA/AcCoA})$

Muscle Metabolite Concentrations:

Acetyl CoA = 0.05 μmol/g
Citrate = 0.2 μmol/g
Glutamate = 2.41 μmol/g
αKG = 0.05 μmol/g

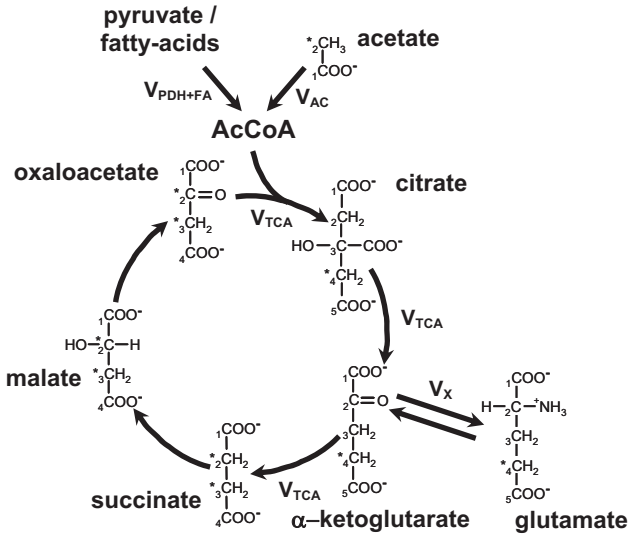

Fig. S1. Schematic of the TCA cycle, depicting the incorporation of ^{13}C label from plasma [2-^{13}C]acetate into the muscle [4-^{13}C]glutamate pool. The carbon position labeled with ^{13}C is denoted by an asterisk (*). A single turn of the TCA cycle is shown, a 2nd turn of the cycle forms [2-^{13}C] and [3-^{13}C]glutamate.