A Novel Inhibitor of Pyruvate Dehydrogenase Kinase Stimulates Myocardial Carbohydrate Oxidation in Diet-Induced Obesity—Supplement

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Supporting Information

A Novel Inhibitor of Pyruvate Dehydrogenase Kinase Stimulates Myocardial Carbohydrate Oxidation in Diet-Induced Obesity

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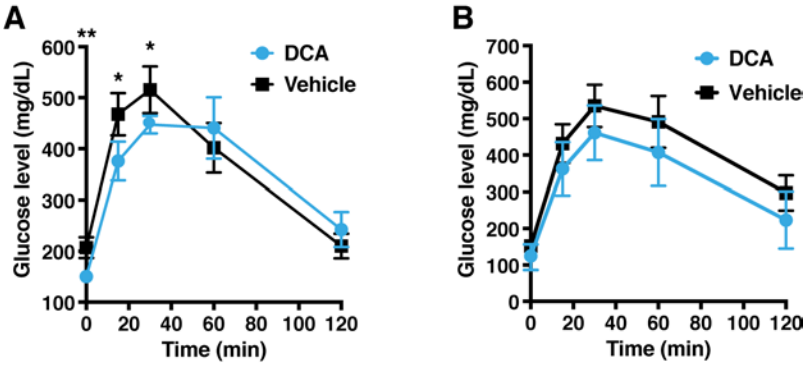

Figure S1. Dose response of glucose tolerance to DCA treatment in diet-induced obese mice. The glucose tolerance test of DCA-treated DIO mice at A. 100mg/kg/day and B. 200mg/kg/day by intraperitoneal administration for two weeks. n=4 in each group. The data is presented as mean±SD. *, P <0.05, **, P <0.01.

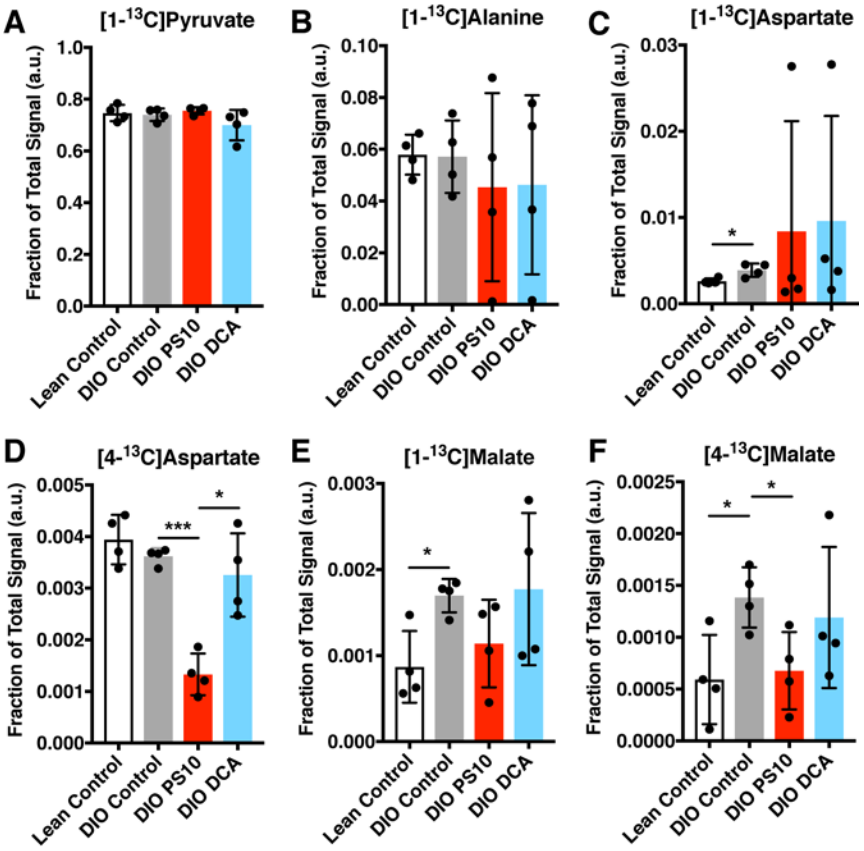

Figure S2. Ratios of metabolite signals following hyperpolarized [1-^{13}C] pyruvate metabolism. The signal to time of each metabolite was plotted as described in Fig. 3. The average AUC of each metabolite from hearts with different were plotted and shown in A. [1-^{13}C] pyruvate; B. [1-^{13}C] alanine; C. [1-^{13}C] aspartate; D. [4-^{13}C]aspartate; E. [1-^{13}C] malate; F. [4-^{13}C] malate. n=4 in each group. Data is presented as mean±SD. *, P<0.05; **, P<0.01; ***, P<0.001.

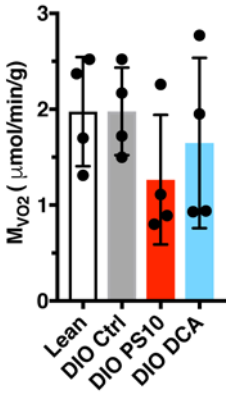

Figure S3. The oxygen consumption rate in hearts treated with different PDK inhibitors. Data is presented as mean ± SD. n = 4 in all groups.

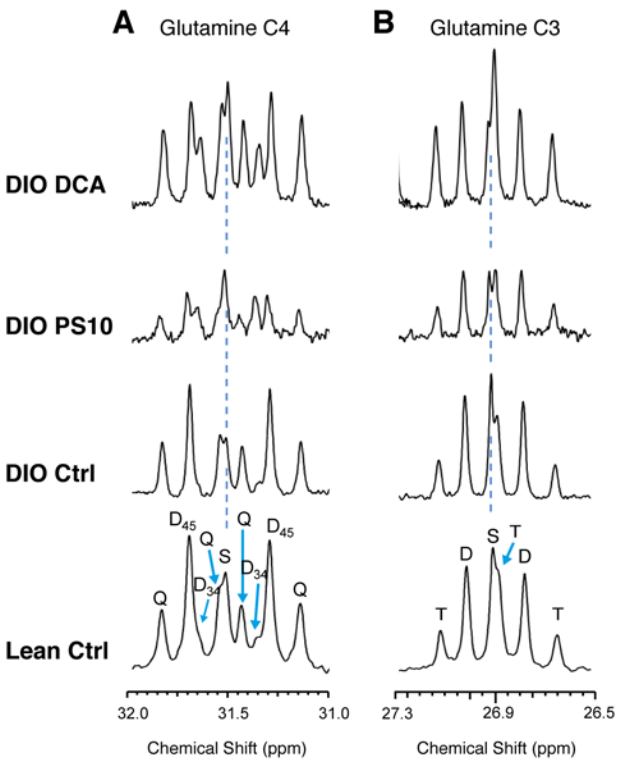

Figure S4. The ^{13}C labeling patterns of glutamine from mouse hearts with different PDK inhibitor treatments. A. ^{13}C signals of C4; B. ^{13}C signals of C3. S denotes singlet, D denotes doublet, T denotes triplet, and Q denotes quartet. The subscript numbers indicate the carbons of coupling.

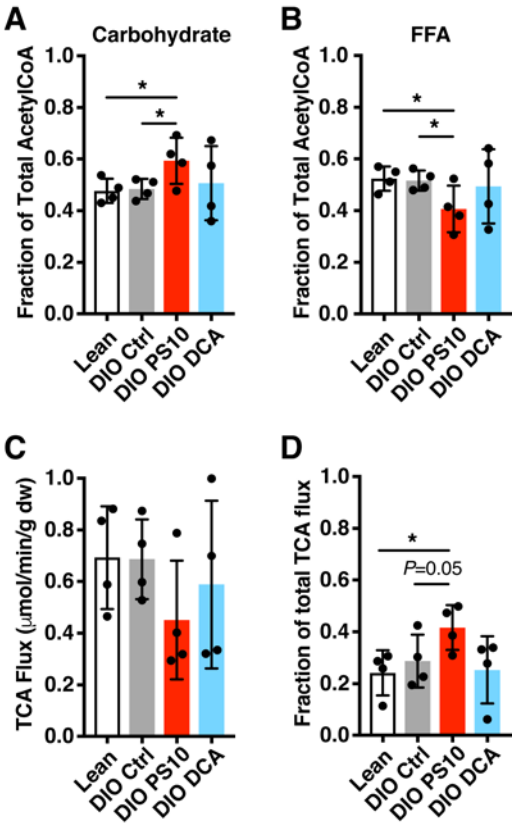

Figure S5. PS10 increases glucose and suppresses free fatty acid utilization in TCA cycle in DIO mouse hearts as measured with a steady state isotopomer analysis of glutamine. A. The contribution of carbohydrate to total Acetyl CoA pool calculated from glutamine data. B. The contribution of free fatty acid to total Acetyl CoA pool calculated from glutamine data. C. TCA flux of hearts with different treatment. D. The PDH fraction of total TCA flux in hearts with different treatment. Data is presented as mean ± SD. n=4 all groups. *, P <0.05.

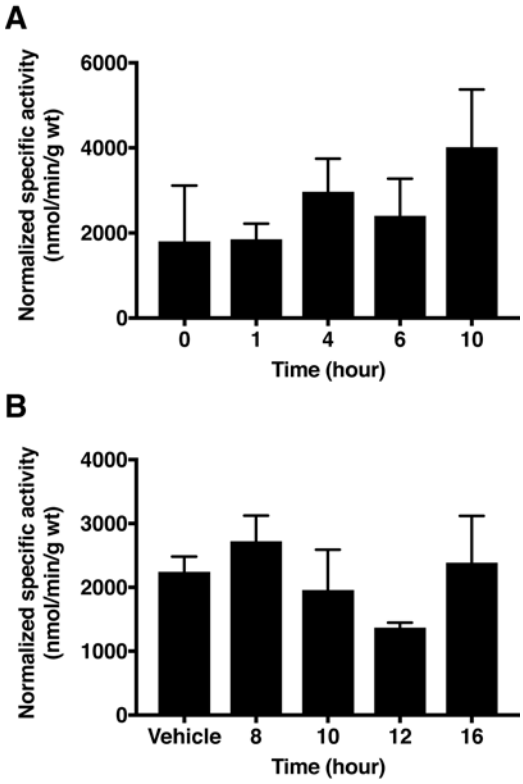

Figure S6. Time-course response of heart PDC activity after PS10 treatment on mice. A single dose of PS10 at 70 mg/kg was administered by intraperitoneal injection to wildtype C57BL/6J mice. After time interval indicated in each plots, tissues were collected for PDC activity assay. A. a time-course from 0 to 10 hours. B. a time course from 8 to 16 hours. Data is presented as mean ± SD. n = 3 in all time points.