SUPPLEMENTAL MATERIAL

The NQO1 bioactivatable drug, β-Lapachone, alters the redox state of NQO1+ pancreatic cancer cells causing perturbation in central carbon metabolism

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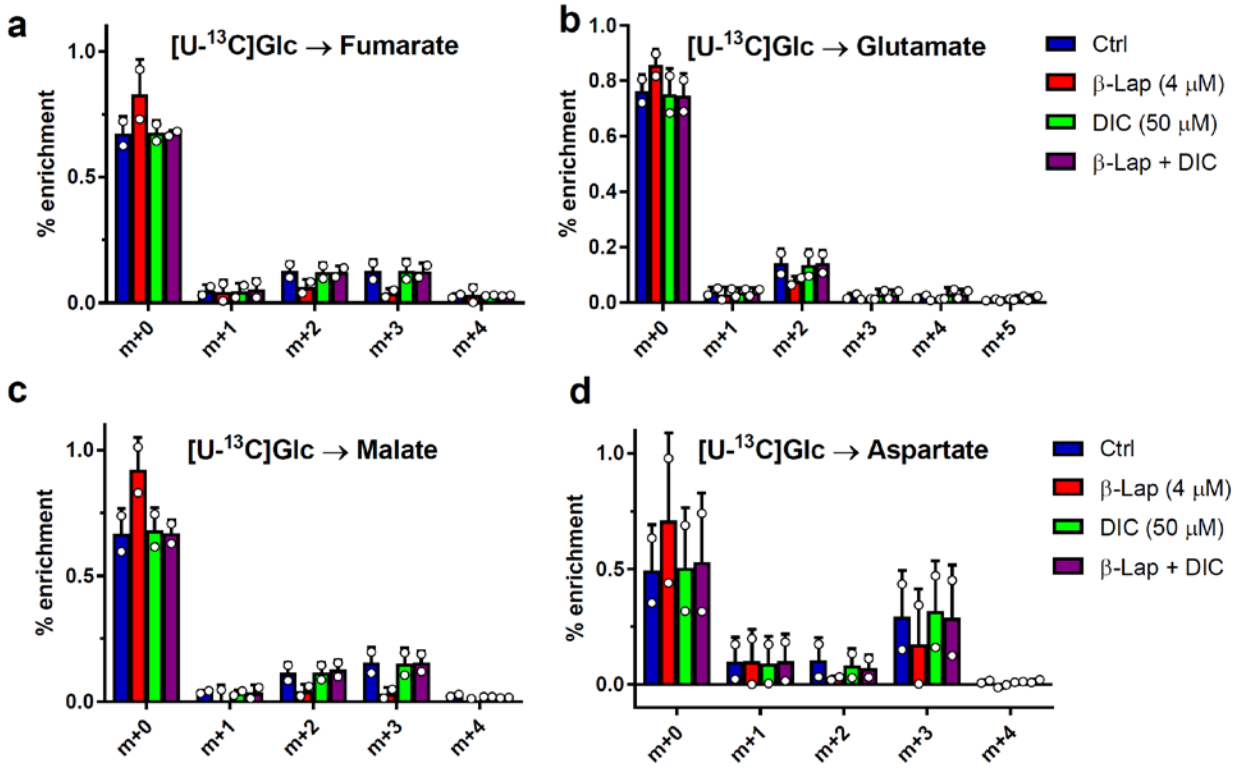

Figure S1. **Labeling of TCA cycle intermediates**. (**a-d**) Plates were incubated with 10 mM U-^{13}C Glucose after a 2 h β-lap (4 μM) treatment, with or without dicoumarol (DIC, 50 μM). Graph shows labeling pattern of isotopomers after a 2 h U-^{13}C Glucose incubation for: (**a**) fumarate, (**b**) glutamate, (**c**) malate, and (**d**) aspartate.

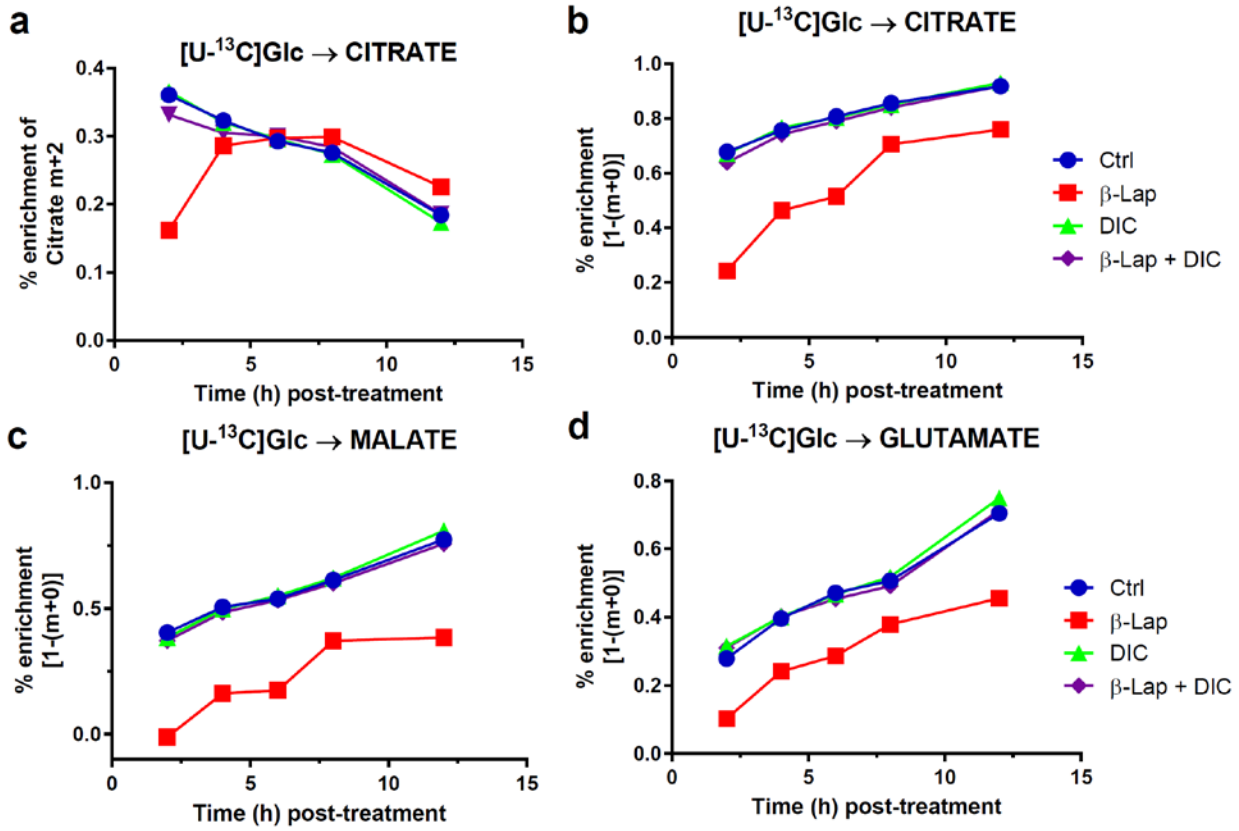

Figure S2. **Time course of labeling of TCA cycle intermediates**. (**a-d**) Plates were incubated with 10 mM U-^{13}C Glucose after a 2 h β-lap (4 μM) treatment, with or without dicoumarol (DIC, 50 μM). (**a**) Time course over 12 h of citrate m+2 labeling. (**b-d**) Time course of labeled isotopomers over 12 h is shown for: (**b**) citrate, (**c**) malate, and (**d**) glutamate.

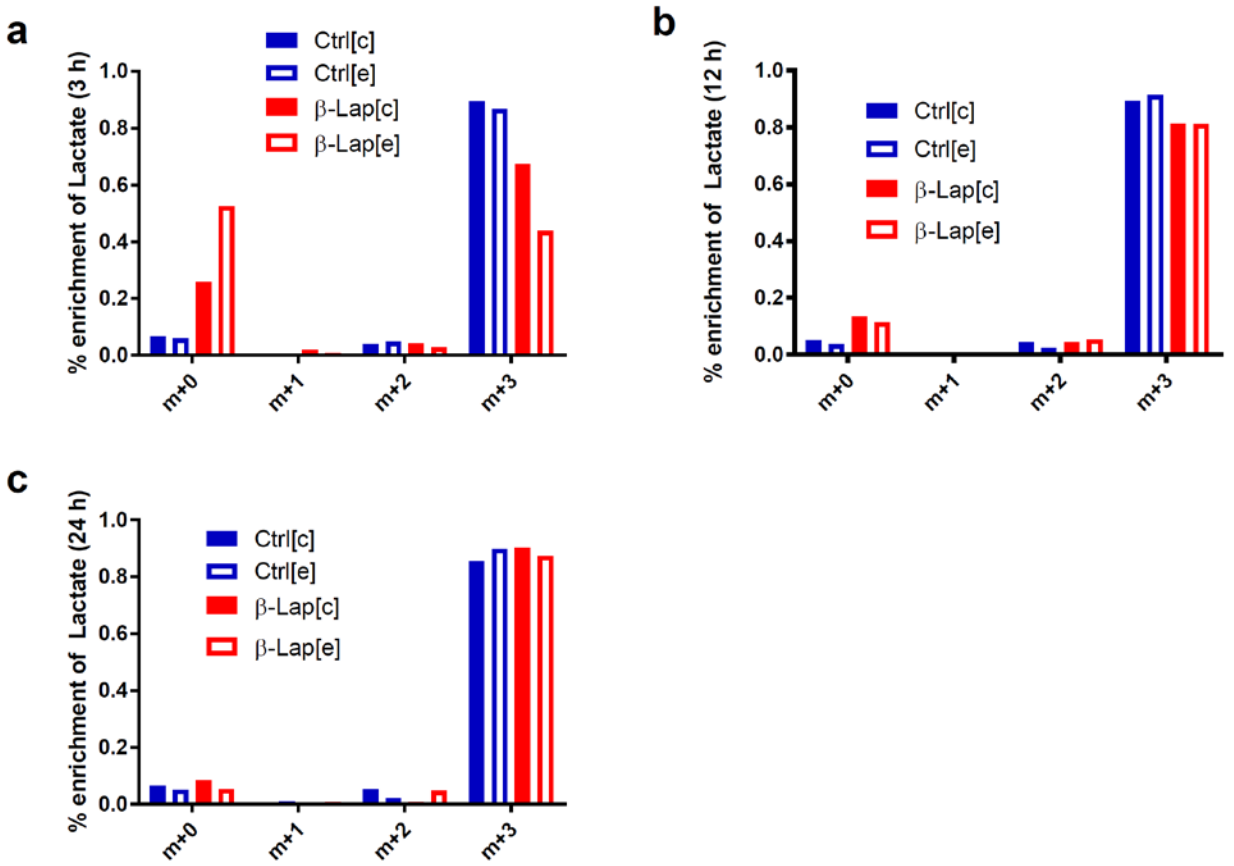

Figure S3. **Lactate enrichment over time after b-lap treatment.** (**a-c**) GC-MS analysis of lactate isotopomers after labeling with U-^{13}C Glucose of both intracellular [c] and extracellular [e] fractions in both control and β-lap (6 μM) cells at 3 h (**a**), 12 h (**b**), and 24 h (**c**).

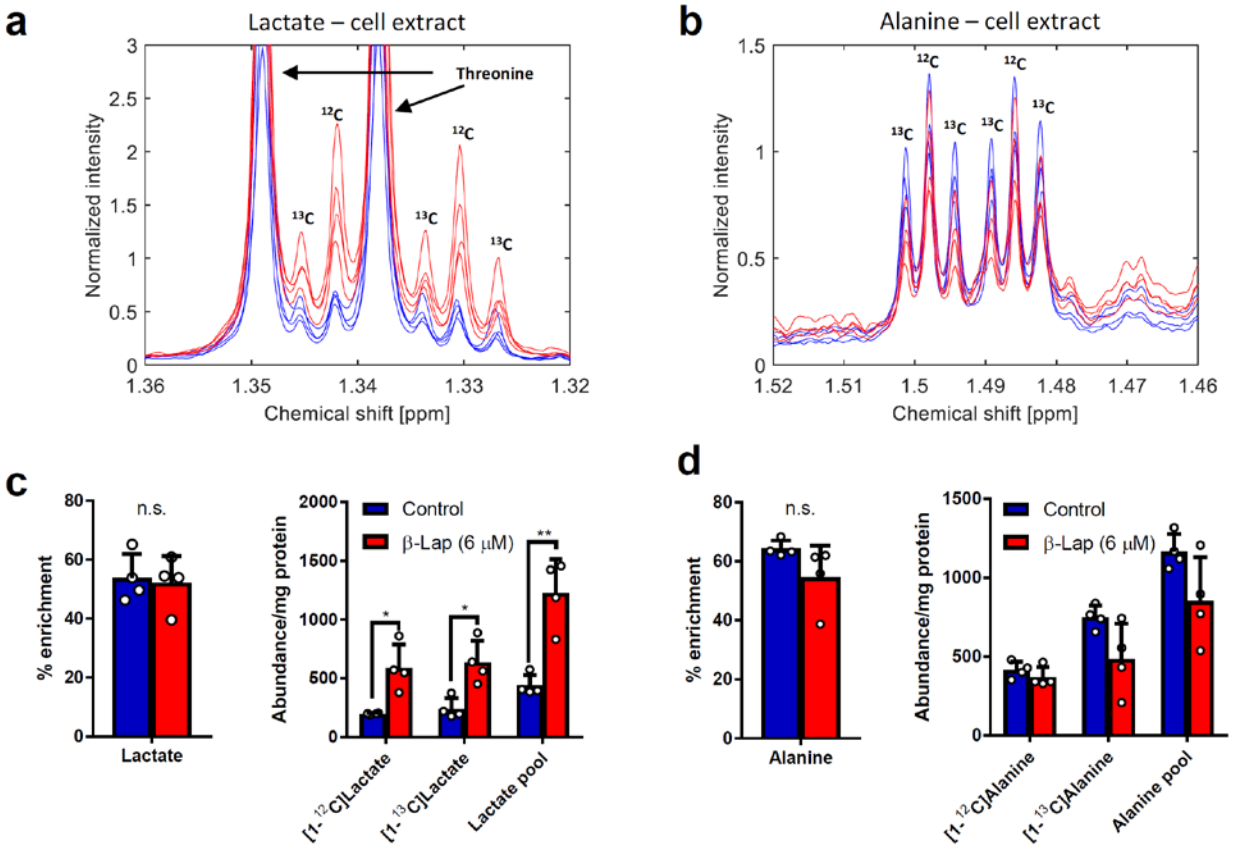

Figure S4. Lactate and Alanine pool sizes. (**a**) Intracellular concentration of enriched (labeled) lactate, unlabeled lactate, and total lactate pool size calculated using ^{1}H NMR after hyperpolarized [1-^{13}C]pyruvate runs. (**b**) Intracellular concentration of enriched (labeled) alanine, unlabeled alanine, and total alanine pool size calculated using ^{1}H NMR after hyperpolarized [1-^{13}C]pyruvate. (**d**) Fractional enrichment and intracellular pools of alanine calculated using ^{1}H NMR after hyperpolarized [1-^{13}C]pyruvate experiments. **p*<0.05, ***p*<0.01

Panel (**c**) is repeated from Figure **4h** for the easier comparison.

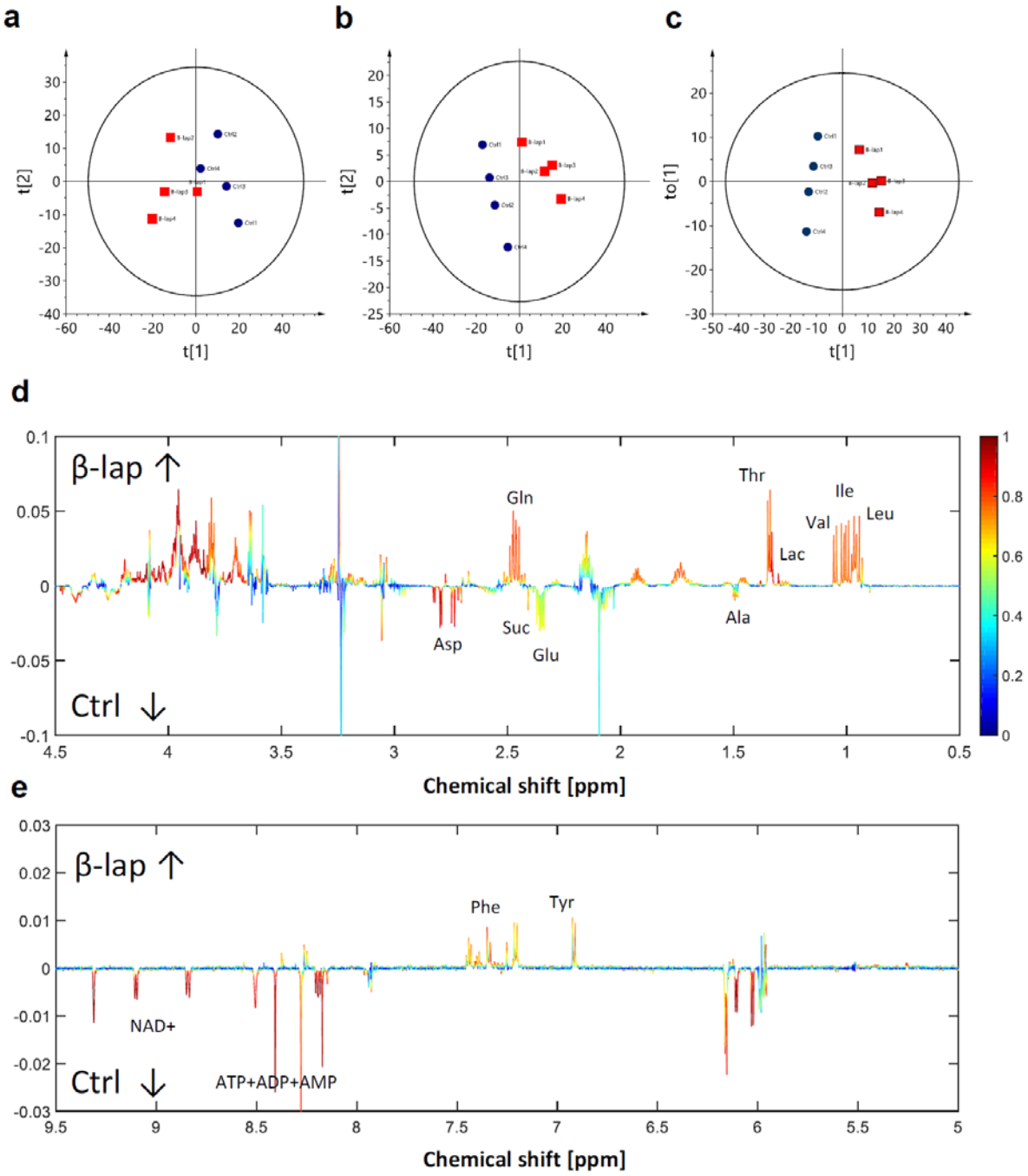

Figure S5. Multivariate data analysis based on whole metabolic profile. Separation between β-lap treated cells (6 μM) and the control were observed using both unsupervised (**a**) (PCA) and supervised (**b**) PLS-DA and (**c**) OPLS-DA models (n=4). (**d**) Aliphatic and (**e**) aromatic spectral region of color-coded loadings of the predictive OPLS-DA component. Signals in the positive y-axis range (Up) were signals found increased in β-lap-treated cells while signals in the negative y-axis range (Down) were metabolites found increased in control (Ctrl) cells. The strength of signals and their overall difference between the two groups is represented by the color bar.

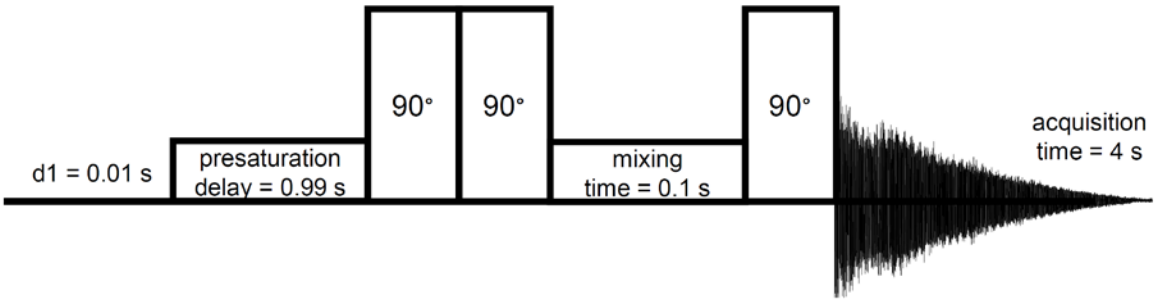

Figure S6. METNOESY pulse sequence.