

Supplementary Information for

Inhibition of mitochondrial respiration impairs nutrient consumption and metabolite transport in human retinal pigment epithelium

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Running title: *Metabolic signature of dysfunctional mitochondria*

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This PDF file includes:

Figure S1-S5

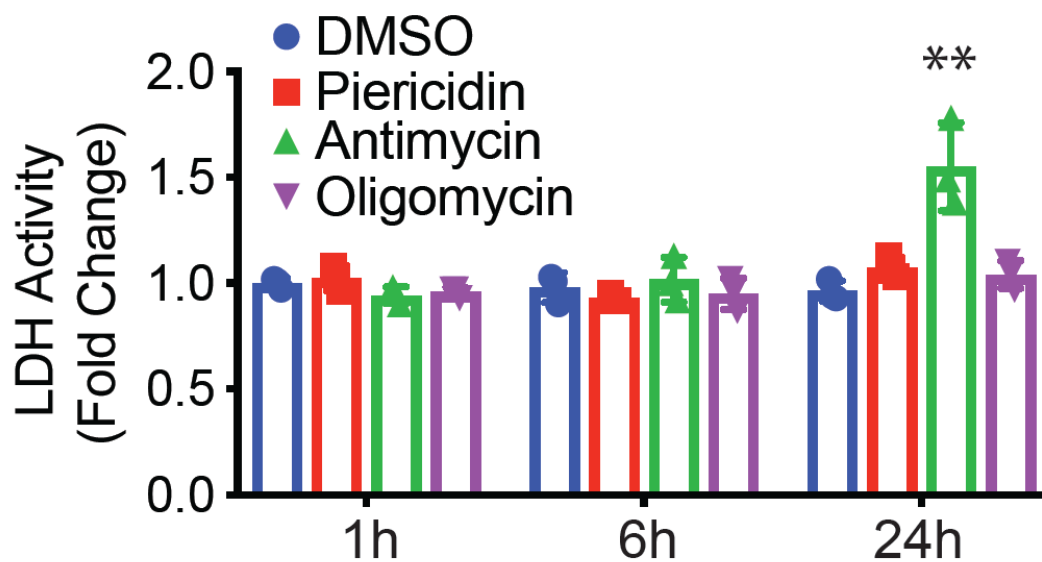


Figure S1. The impact of mitochondrial inhibitors on LDH activity. The data were presented as fold changes of Δ absorbance density at 340nm over the groups with DMSO at different time points. N=3. **P<0.01 vs. the groups treated with DMSO.

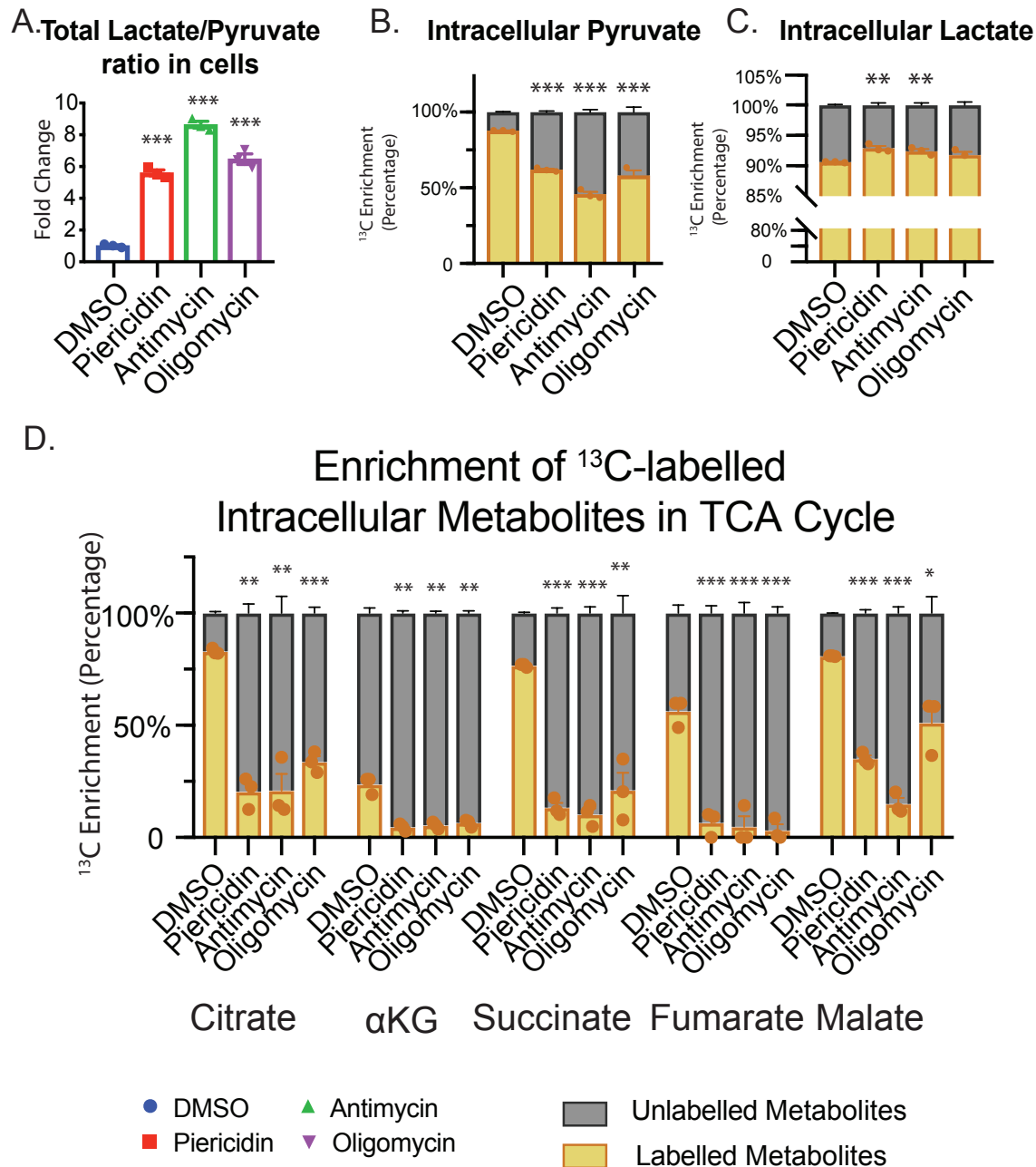


Figure S2. Inhibition of mitochondrial respiration impairs the generation of glycolytic metabolites and TCA cycle intermediates from ^{13}C -labelled glucose. (A) Lactate/pyruvate ratio over the groups with DMSO. **(B-D)** Enrichment of ^{13}C -labelled intracellular metabolites in glycolysis and the TCA cycle. N=3. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ vs. the groups treated with DMSO.

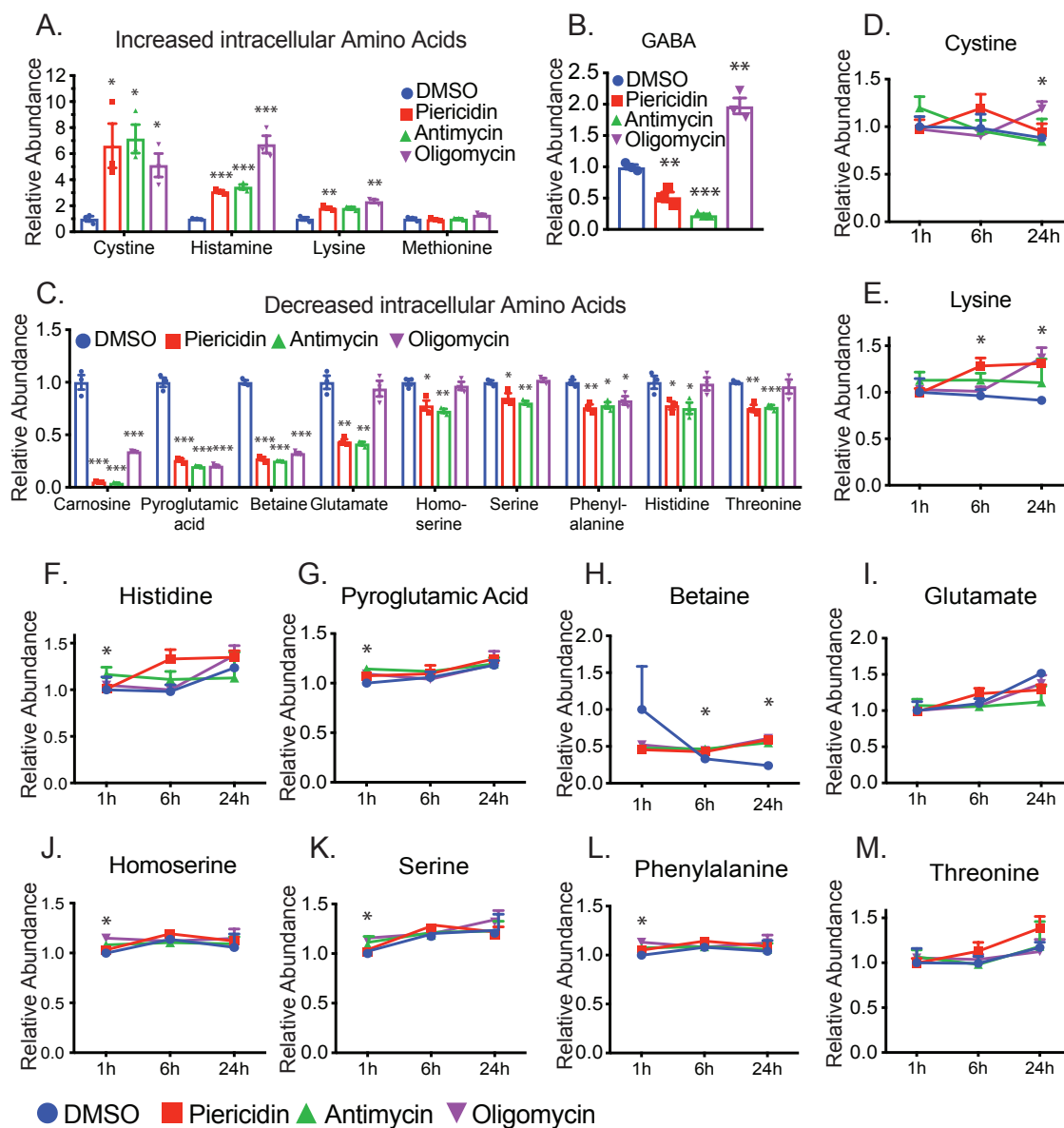


Figure S3. Mitochondrial inhibition impairs the metabolism of amino acids. (A-C) The relative abundance of intracellular amino acids. (D-M) The relative abundance of amino acids in media at different time points. N=3. *P<0.05, **P<0.01, ***P<0.001 vs. the groups treated with DMSO.

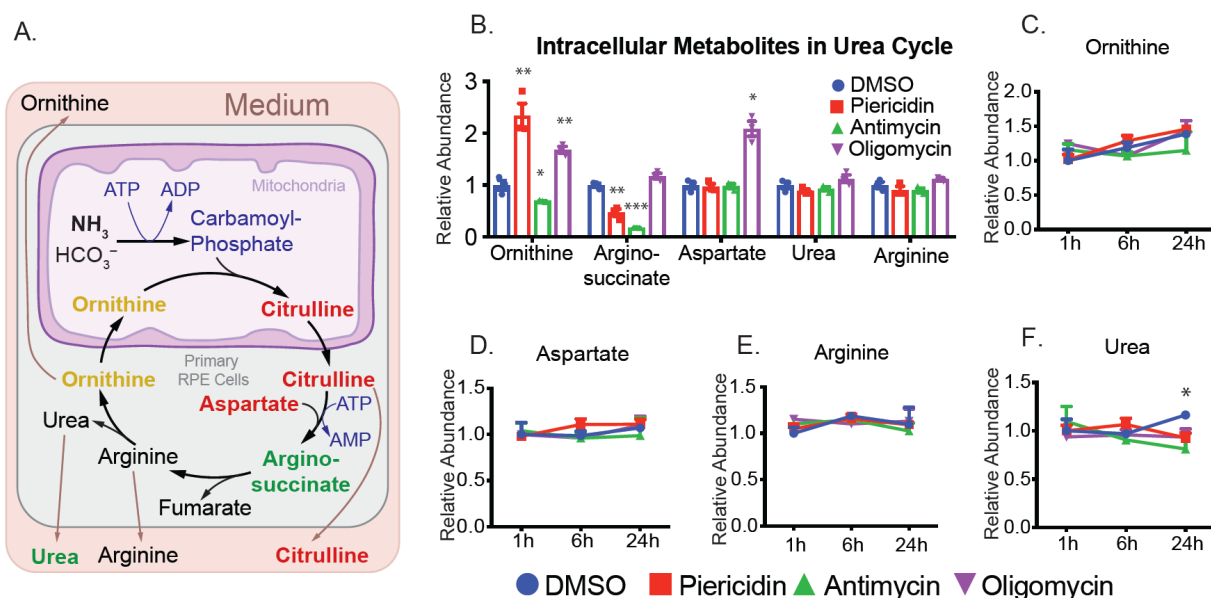


Figure S4. Mitochondrial inhibition impairs the urea cycle. (A) Schematic for the urea cycle. The color of metabolites represents the changes in relative abundance with mitochondrial inhibitors: red for the increased metabolites, green for decreased metabolites, orange for metabolites with mixed changes, and black for no change or not detected. (B) Relative abundance of intracellular metabolites in the urea cycle. (C-F) The relative abundance of metabolites in the urea cycle in media at different time points. N=3. *P<0.05, **P<0.01, *P<0.001 vs the groups treated with DMSO.

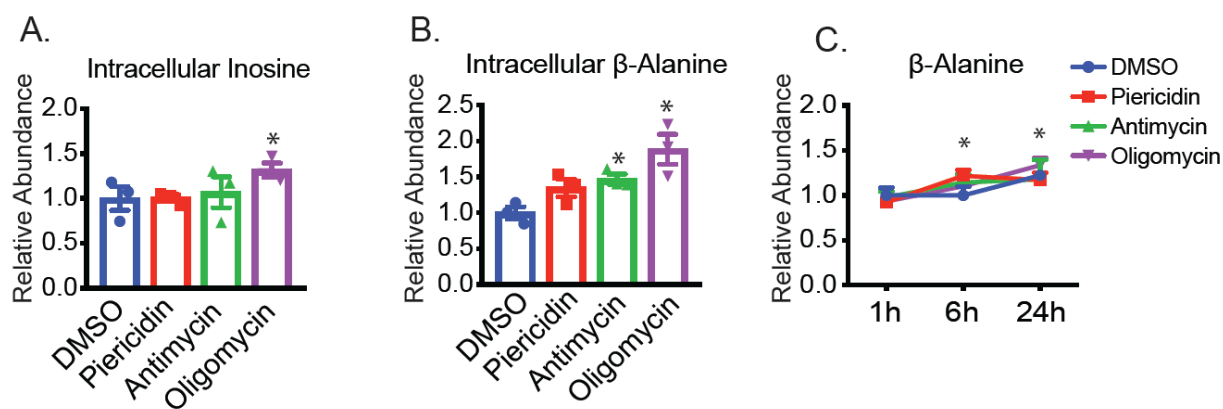


Figure S5. The impact of mitochondrial inhibition on the metabolism of nucleotides. (A-B) The relative abundance of intracellular inosine and β-alanine. (C) The relative abundance of β-alanine in media at different time points. N=3. *P<0.05 vs. the groups treated with DMSO.