Supplementary Figures

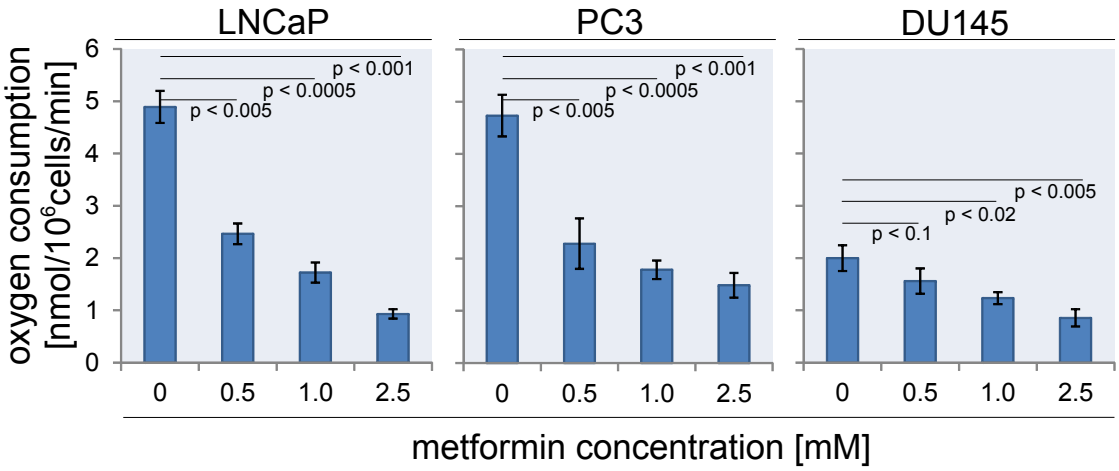

Figure 1: Oxygen consumption rate of prostate cancer cell lines with different concentrations of metformin. Error bars depict the standard deviation. Standard deviation and p-values are calculated from three biological replicates.

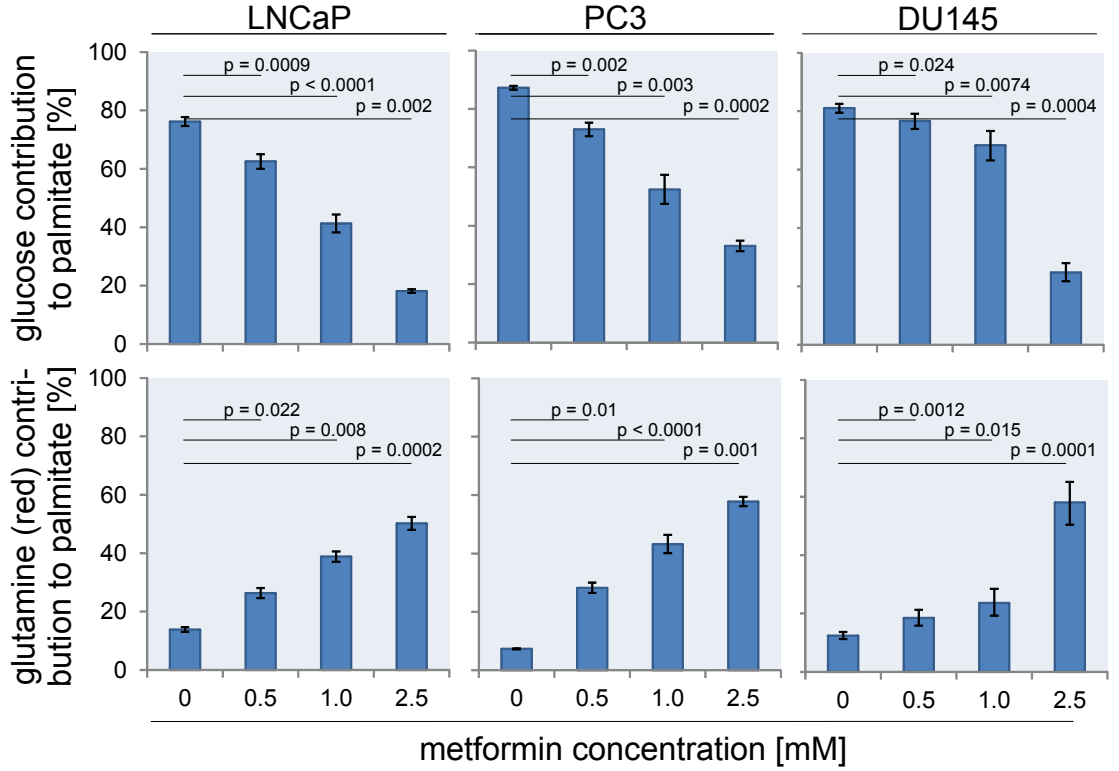

Figure 2: Glucose (upper panel) and reductive glutamine (lower panel) contribution to fatty acids in prostate cancer cell lines treated with metformin fitted from the measured incorporation of [U-^{13}C] labeled glucose or [5-^{13}C] labeled glutamine (reductive glutamine contribution (red)) into palmitate. Error bars depict the 95 % confidence interval. Confidence intervals and p-values are calculated from two biological replicates.

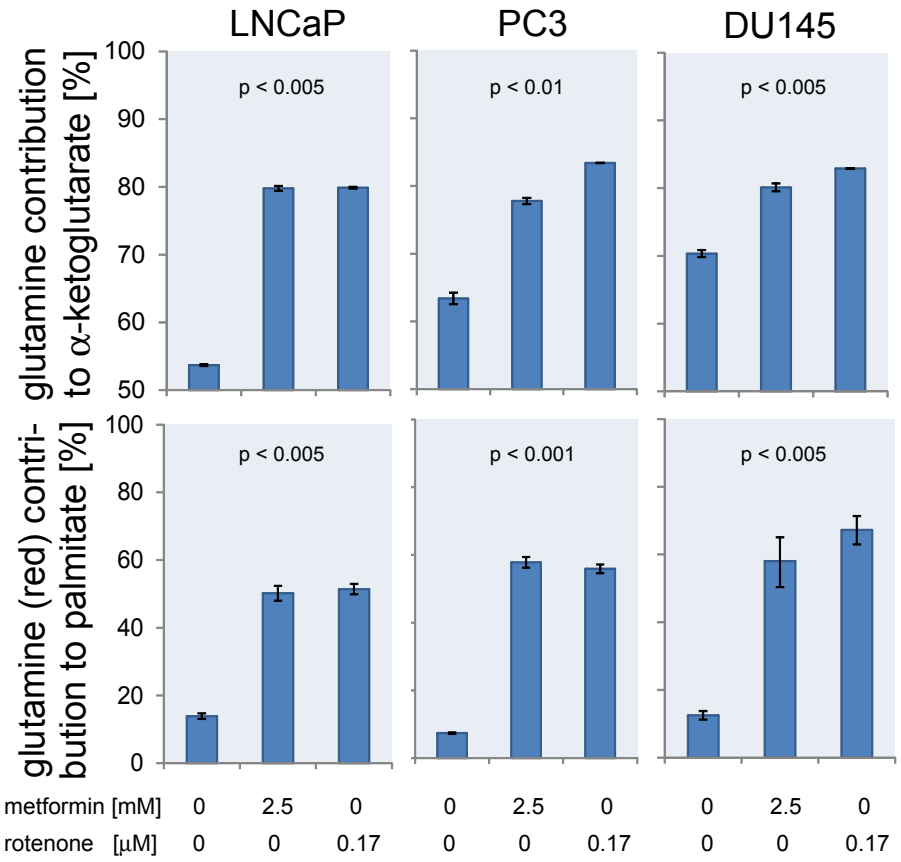

Figure 3: Comparison of glutamine contribution to tricarboxylic acid cycle in prostate cancer cell lines treated with metformin or rotenone measured by the incorporation of [U-^{13}C] labeled glutamine into α-ketoglutarate (upper panel) and reductive glutamine contribution to palmitate using [5-^{13}C] labeled glutamine (lower panel). Confidence intervals and p-values are calculated from two biological replicates.

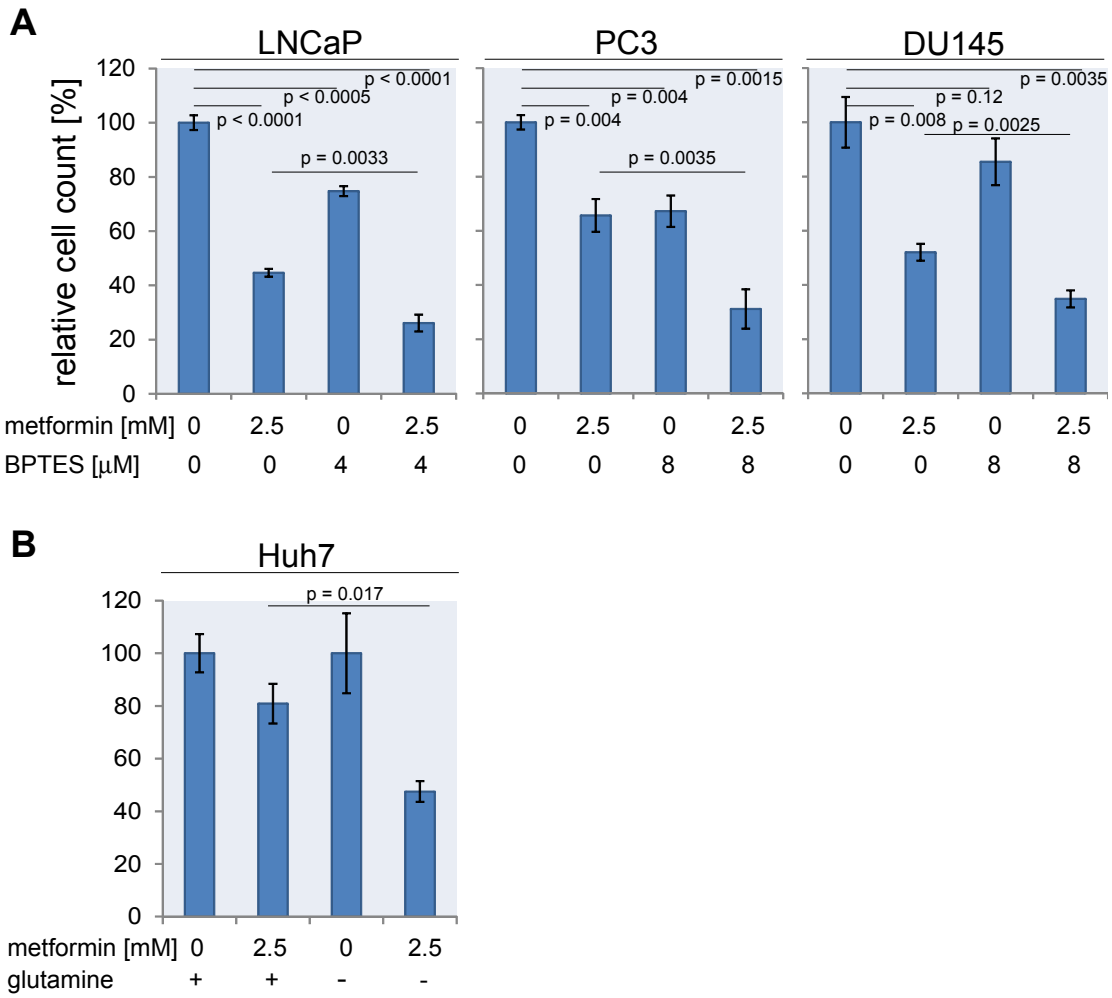

Figure 4: (A) Relative cell count of prostate cancer cell lines treated with a combination of metformin and the glutaminase inhibitor BPTES. Cell counts were normalized to the condition with no metformin and no BPTES added. (B) Relative cell count of Huh7 liver cancer cells, which can grow without glutamine in the presence or absence of metformin. Cell count were normalized to the corresponding condition with no metformin added. Error bars depict the standard deviation. Standard deviation and p-values are calculated from three biological replicates.

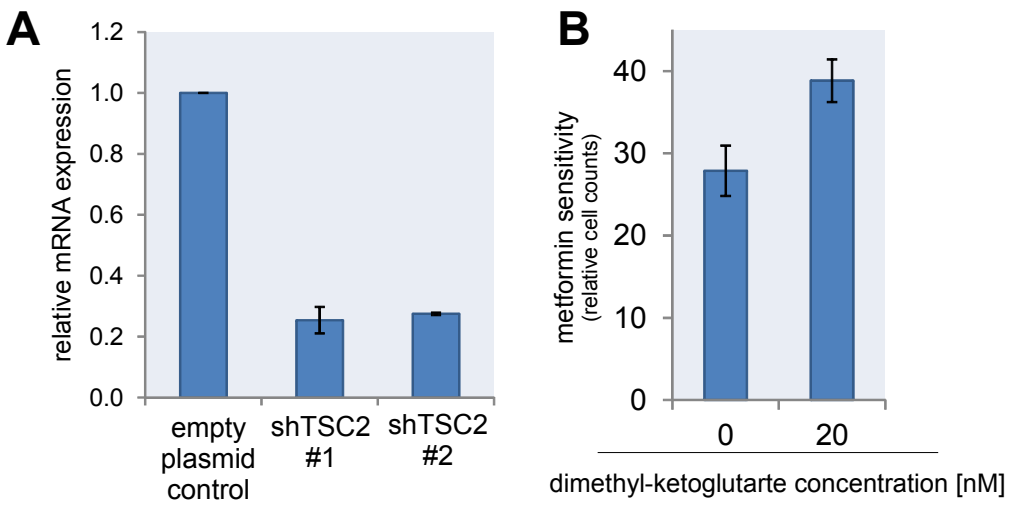

Figure 5: (A) *TSC2* expression in *TSC2* knockdown cells and control. Standard diviation is calculated from three technical replicates. p-values are < 0.005.(B) Metformin sensitivity (2.5mM) in LNCaP cells with and without dimethyl α-ketoglutarate given by cell counts normalized to the corresponding condition with no metformin.Standard deviation and p-values are calculated from at least three biological replicates. p-value is < 0.05. All error bars depict the standard deviation.