

Legends to Supplementary Figures

Supplementary Figure 1. Panel A. Venn diagrams of the number of genes upregulated or downregulated in DDP-R versus DDP-S ovarian cancer PDXs couples. The genes shared among all the three PDXs couples are listed. Panels B. Venn diagrams of the unique and shared significantly altered metabolites (Mann-Whitney-Wilcoxon Test) identified by targeted and untargeted metabolomics approaches between DDP-R and DDP-S couple of xenografts. Significant shared metabolites are listed.

Supplementary Figure 2. Panel A. Validation real time PCR results of the *PGK2* gene. The mean \pm standard deviation of the normalized gene expression of three biological samples (three technical replicates per sample) is reported. Panel B. Gene expression analysis of the genes coding the lactate transporters MCT1 (*SLC16A1*) and MCT4 (*SLC16A4*), the glucose transporter GLUT1 (*SLC2A1*), and the glutamine transporter ASCT2 (*SLC1A5*). Statistical analysis was performed by Mann-Whitney test (**** $p < 0.0001$, *** $p < 0.005$, ** $p < 0.01$, * $p < 0.05$).

Supplementary Figure 3. Gene expression analysis of genes coding the urea cycle enzymes Ornithine carbamoyltransferase (*OTC*), Arginosuccinate synthase (*ASS1*), Argininosuccinate Lyase (*ASL*), and Arginase 1 (*ARG1*). The mean \pm SD of the normalized gene expression of three different biological samples (three technical replicates per sample) is reported. Statistical analysis was performed by Mann-Whitney test (**** $p < 0.0001$, *** $p < 0.005$, ** $p < 0.01$, * $p < 0.05$).

Supplementary Figure 4. In vivo AMPK activation. Mice bearing tumors were treated for 4 days with metformin 400mg/kg p.o and 30 min after the last dose of metformin, mice were sacrificed and tumors excised. Tumor proteins were processed as described in Material and Methods and pAMPK, total AMPK and actin detected by western blot analysis.