Molecular Pharmacology

Supplemental Figures for

Functional CRISPR and shRNA screens identify involvement of mitochondrial electron transport in the activation of evofosfamide

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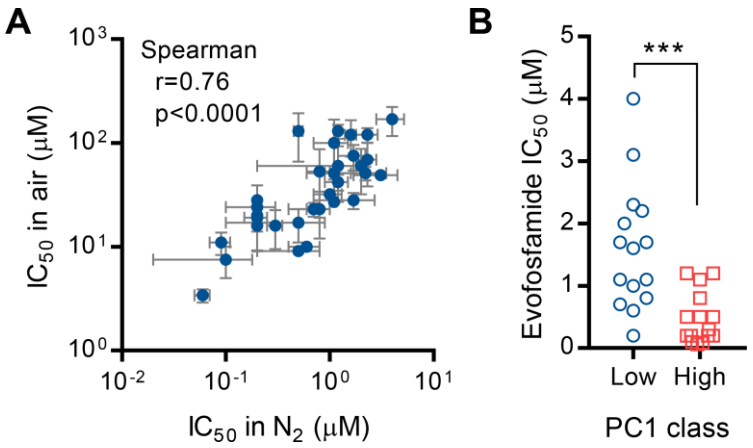
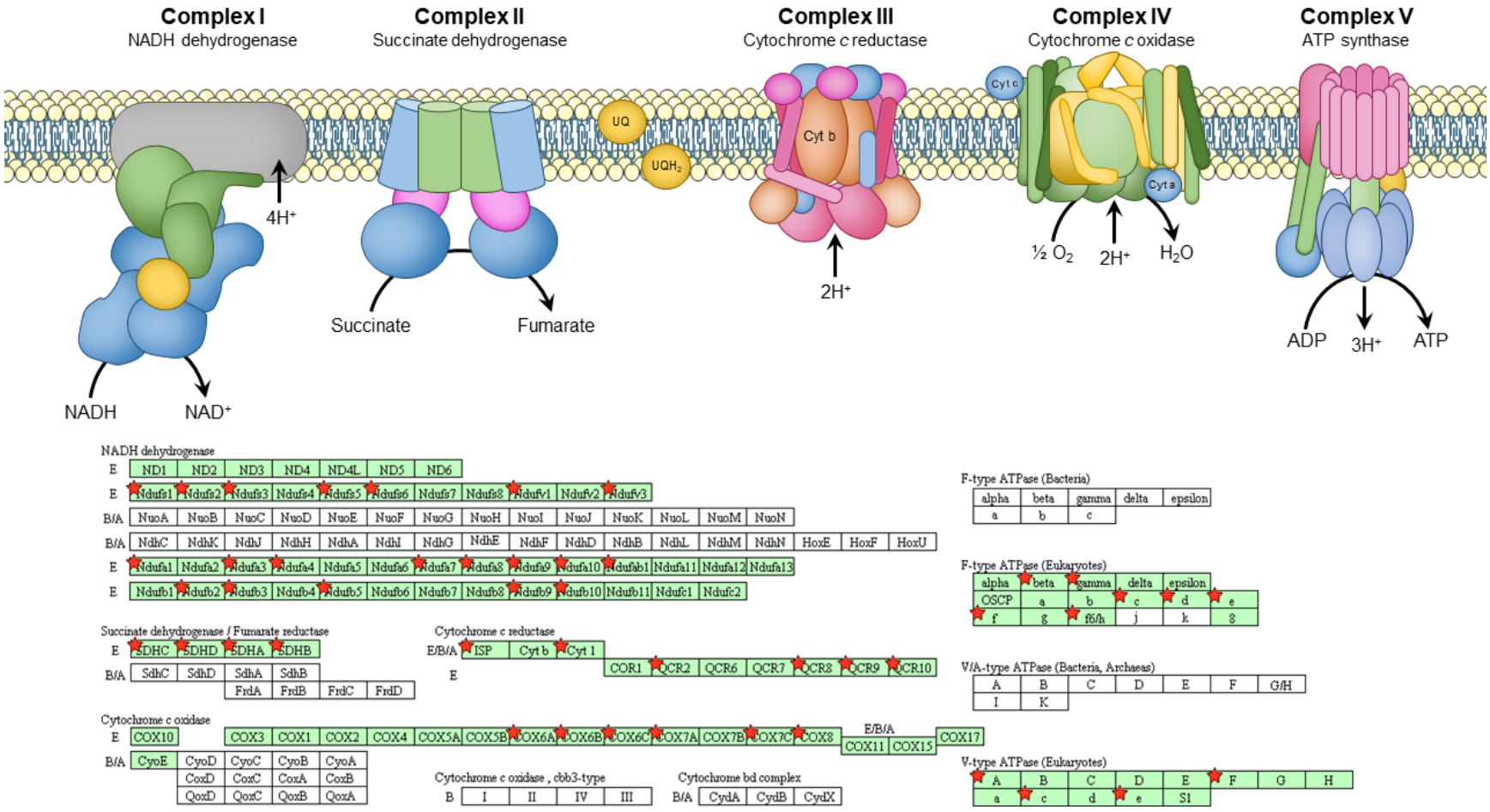
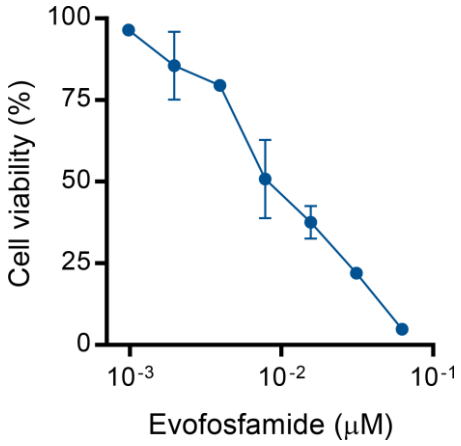


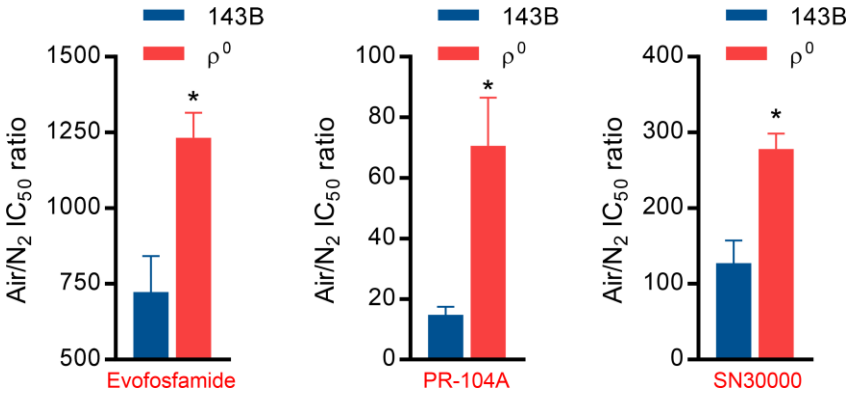
Supplemental Figure 1. (A) Correlation between the sensitivity of 32 cancer cell lines to evofosfamide when challenged under anoxia ("N_2") or 20% O2 ("air") and as assessed by 7-d regrowth assay. Data points are the mean + SEM of IC_{50} determinations from three independent experiment for each cell line. Data correspond to Figure 1B in the main text. (B) Comparison of evofosfamide sensitivity under anoxia between cell lines dichotomised by the first principal component of expression values for 173 genes correlated with evofosfamide potency (Pearson coefficient <-0.4; illustrated in Figure 2B in the main text). Statistical significance of differences in the distribution of IC_{50} values between groups was assessed by Mann−Whitney U-test.



Supplemental Figure 2. Mitochondrial electron transport chain components correlated with evofosfamide potency in 30 genomically diverse cancer cell lines. The expression of all genes marked with red stars correlated with evofosfamide potency (Pearson coefficient <-0.4).



Supplemental Figure 3. Concentration-dependent inhibition of cell viability in KBM-7 cells exposed to evofosfamide. Cells (2,000 per well in 96-well format) were challenged with an evofosfamide dilution series under anoxia for 2 h, re-oxygenated then cultured for 5 d before assessing viability using alamarBlue. Data points are the mean ± SEM of determinations from three independent experiments.



Supplemental Figure 4. Hypoxia selectivity of evofosfamide, PR-104A and SN30000 in parental and ρ^0 143B osteosarcoma cells. Data are the mean + SEM of the intra-experiment ratio of IC_{50} values for cells challenged with evofosfamide under 20% O_2 ("air") or anoxia ("N_2") in three independent pairs of assays. Statistical significance of differences in IC50 ratios was assessed by Mann−Whitney U-test.