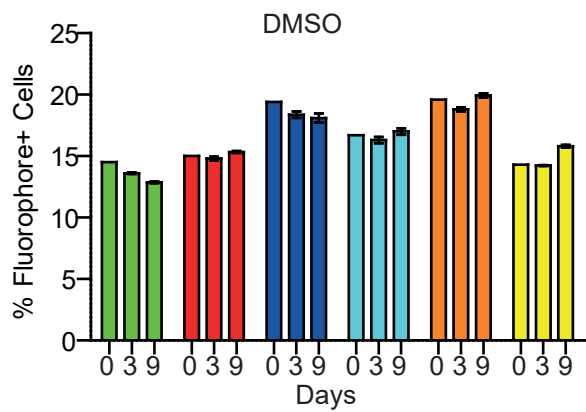
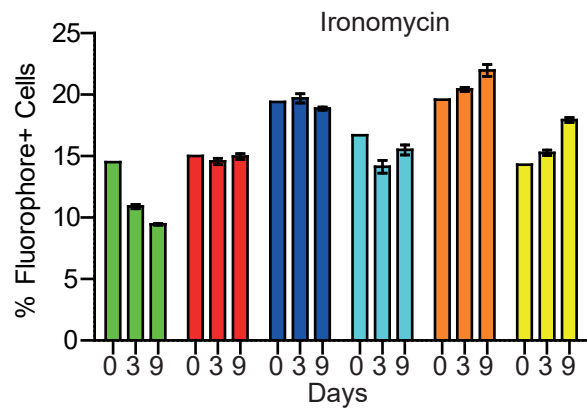


Figure S2

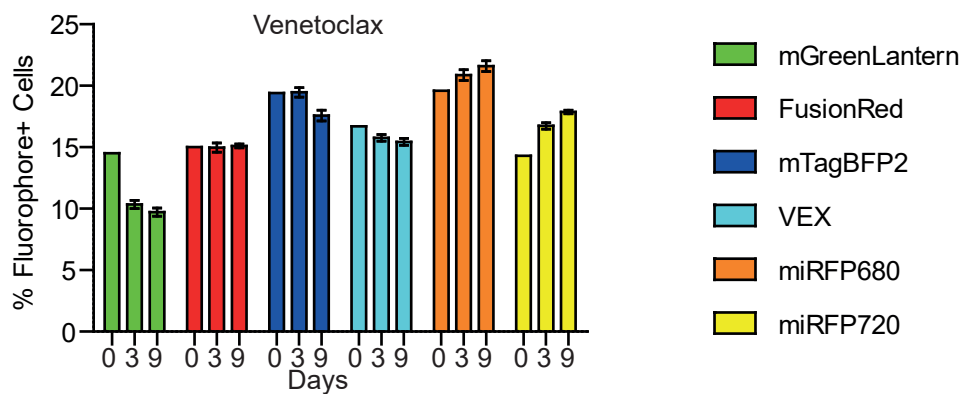
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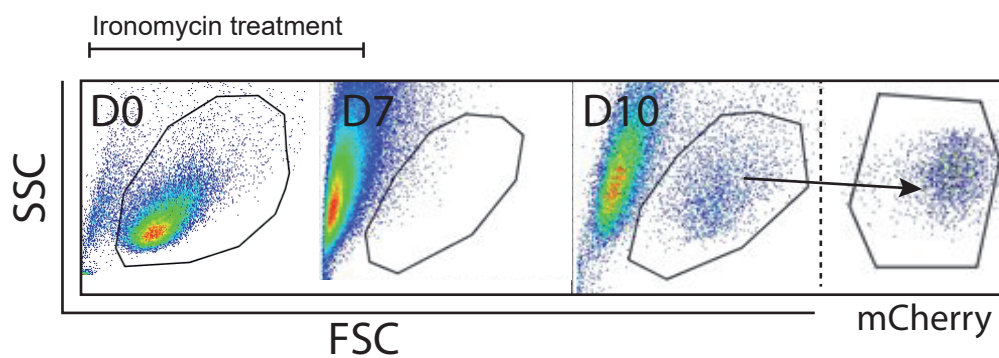
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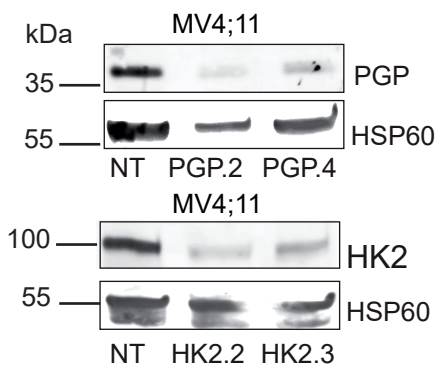
C



D



E



F

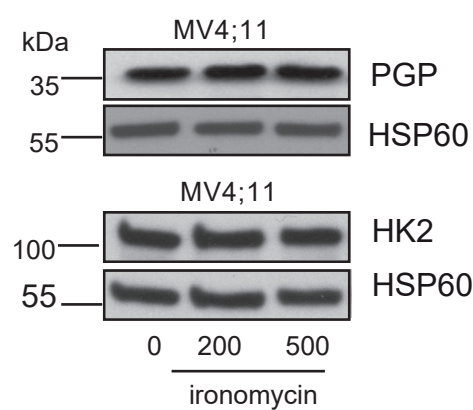


Figure S2| (related to Figure 2). Genome wide CRISPR screen identifies cellular metabolism and mitochondrial homeostasis as key regulators of ironomycin activity. **A-C**, FACS plot showing MV4;11 transduced with lentiviral vectors expressing 6 different fluorochromes. Cells were treated with DMSO (**A**), 200 nM ironomycin (**B**) or 50 nM venetoclax (**C**). After three days, the samples were collected, counted and a small portion was used for FACS analysis. At this stage 100K cells from each well were isolated, washed with PBS and transferred to 6 well plates. The cells were cultured for 6 additional days in absence of drugs and a small proportion was used for FACS analysis (n=3 biological replicates). **D**, FACS plots showing OCI-AML3 Cas9 cells at baseline, day 7 and day 10 in a CRISPR screen replicate (1a). ironomycin (500 nM) induced a strong cell death induction with few surviving cells at day 7. At day 10 reappearance of mCherry positive cells confirmed that a population of resistant OCI-AML3 Cas 9 cells was still expressing selected single guides RNAs (sgRNA) from the CRISPR library. This cell population was collected at day-14 and sequenced. **E**, Immunoblot showing protein expression in MV4;11 expressing Cas9 transfected with a non-targeted sgRNA (NT) and two independent sgRNAs targeting either PGP or HK2. **F**, Immunoblot showing protein expression of PGP and HK2 in MV4;11 cells with or without ironomycin for 24 hours.