

Pooled CRISPR screening in pancreatic cancer cells implicates co-repressor complexes as a cause of multiple drug resistance via regulation of epithelial-to-mesenchymal transition

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Supplemental Figure S1

Supplemental Figure S2

Supplemental Figure S3

Supplemental Figure S4

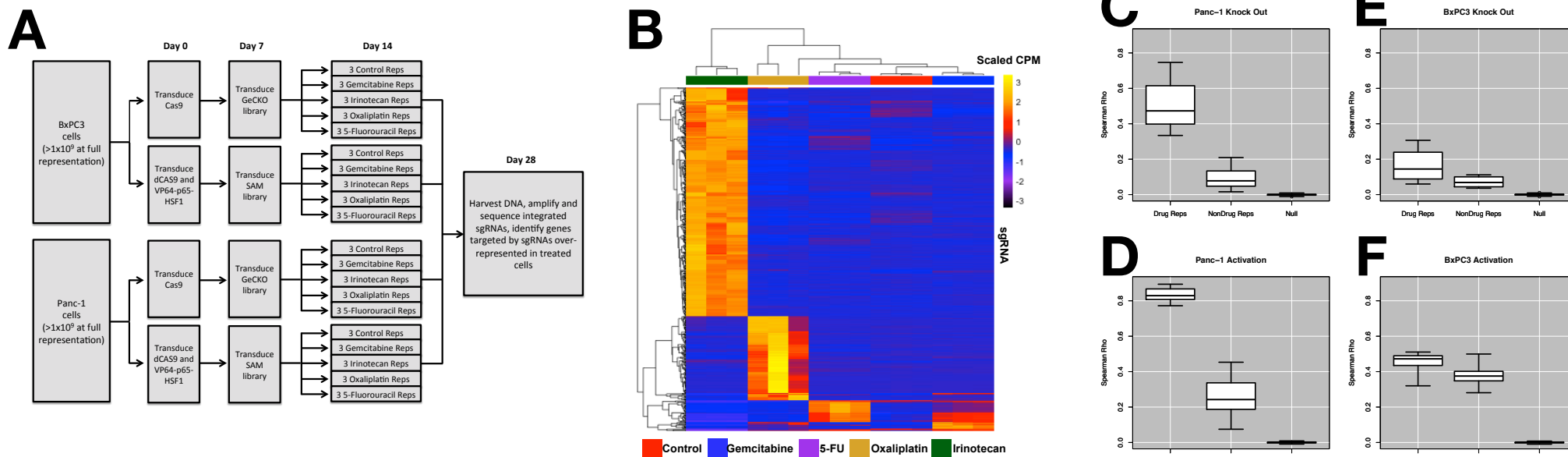


Figure S1. (A) Schematic detailing the screening workflow. (B) A heatmap of the sgRNA count per million, z-scored by row for the most variable 500 sgRNAs across all of our CRISPRa screen replicates in the PANC-1 cell line. (C-F) Boxplots describing the replicate, non-replicate, and scrambled null permutation Spearman correlations for knockout screens in Panc-1 (C) and BxPC3 (E) and activation screens in Panc-1 (D) and BxPC3 (F).

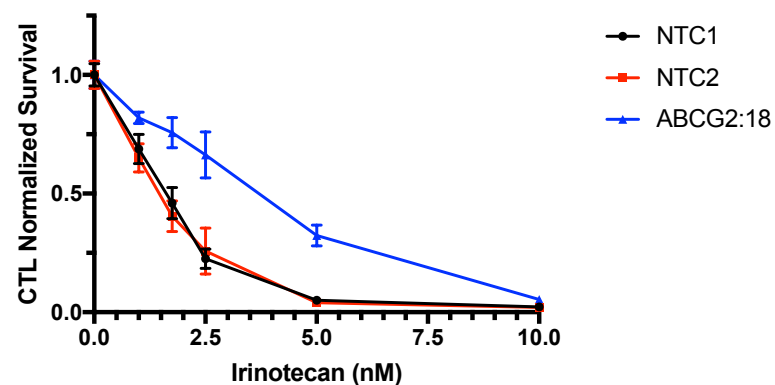
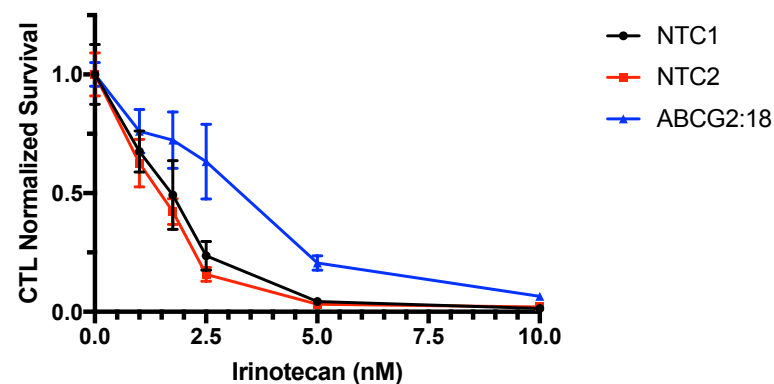
A**BxPC3 ABCG2****B****MiaPaCa2 ABCG2**

Figure S2. Irinotecan resistance following over-expression of ABCG2 compared to controls in two cell lines. A) BxPC-3 cells over expressing ABCG2 show resistance to irinotecan ($p=0.037$, t-test comparing IC₅₀ values for ABCG2 v. NTC2). B) MiaPaca-2 cells over expressing ABCG2 show resistance to irinotecan ($p=0.026$, t-test comparing IC₅₀ values for ABCG2 v. NTC2)

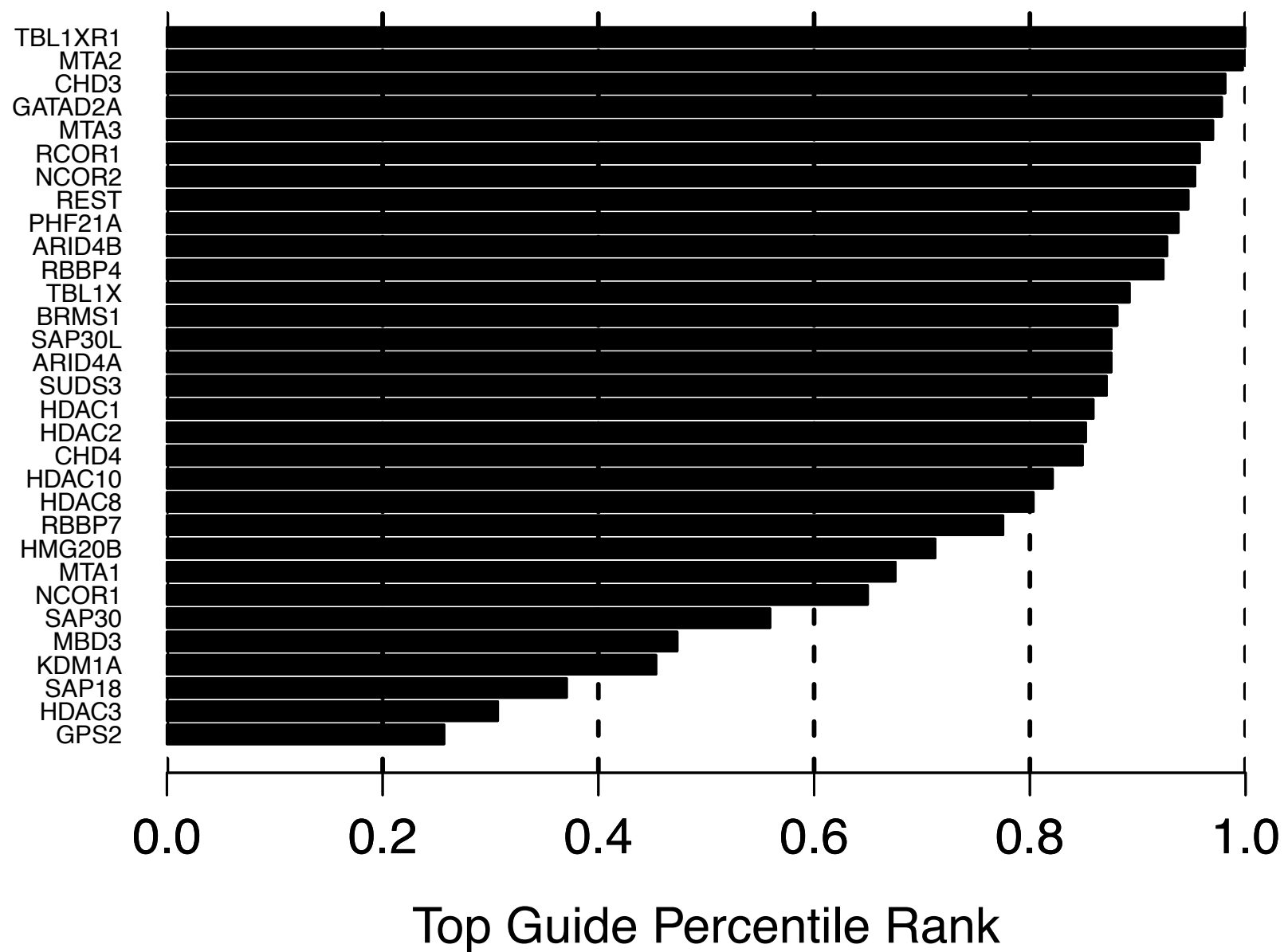


Figure S3. The percentile rank for genes known to be involved in chromatin remodeling. HDAC1 is among the genes in this pathway.

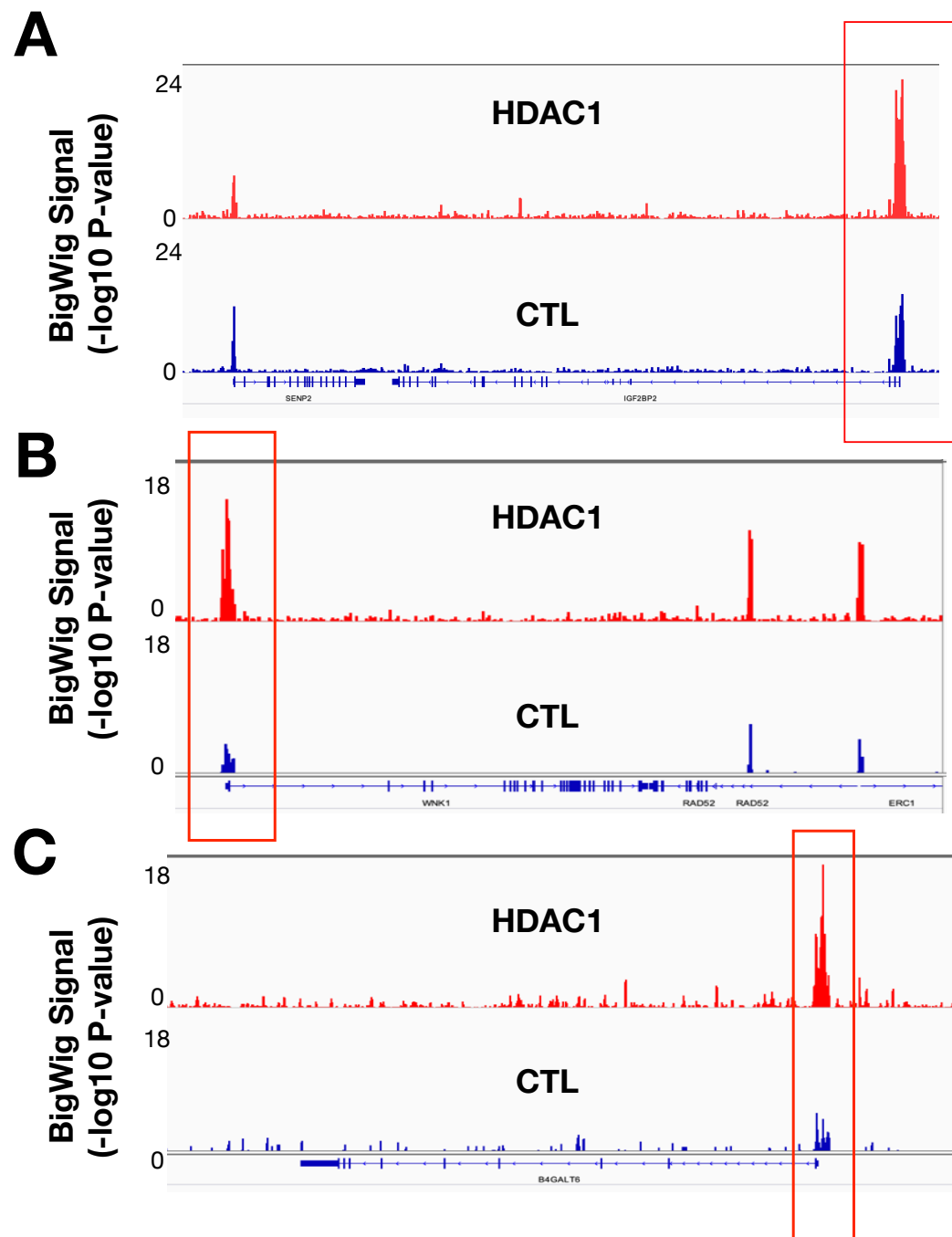


Figure S4. ChIP-seq analysis of HDAC1-overexpressing (red) MiaPaca-2 cells compared to non-targeting controls (blue). HDAC1 overexpressing cells show increased HDAC1 peak height at (A) the IGF2BP2 promoter, (B) the WNK1 promoter, and (C) the B4GALT6 promoter.