

***KANSL2* and *MBNL3* are regulators of pancreatic ductal adenocarcinoma invasion**

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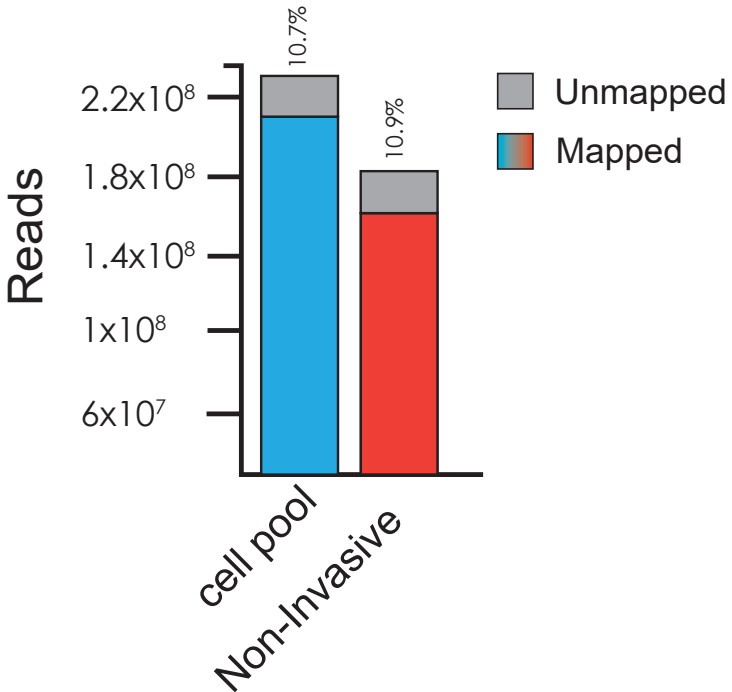
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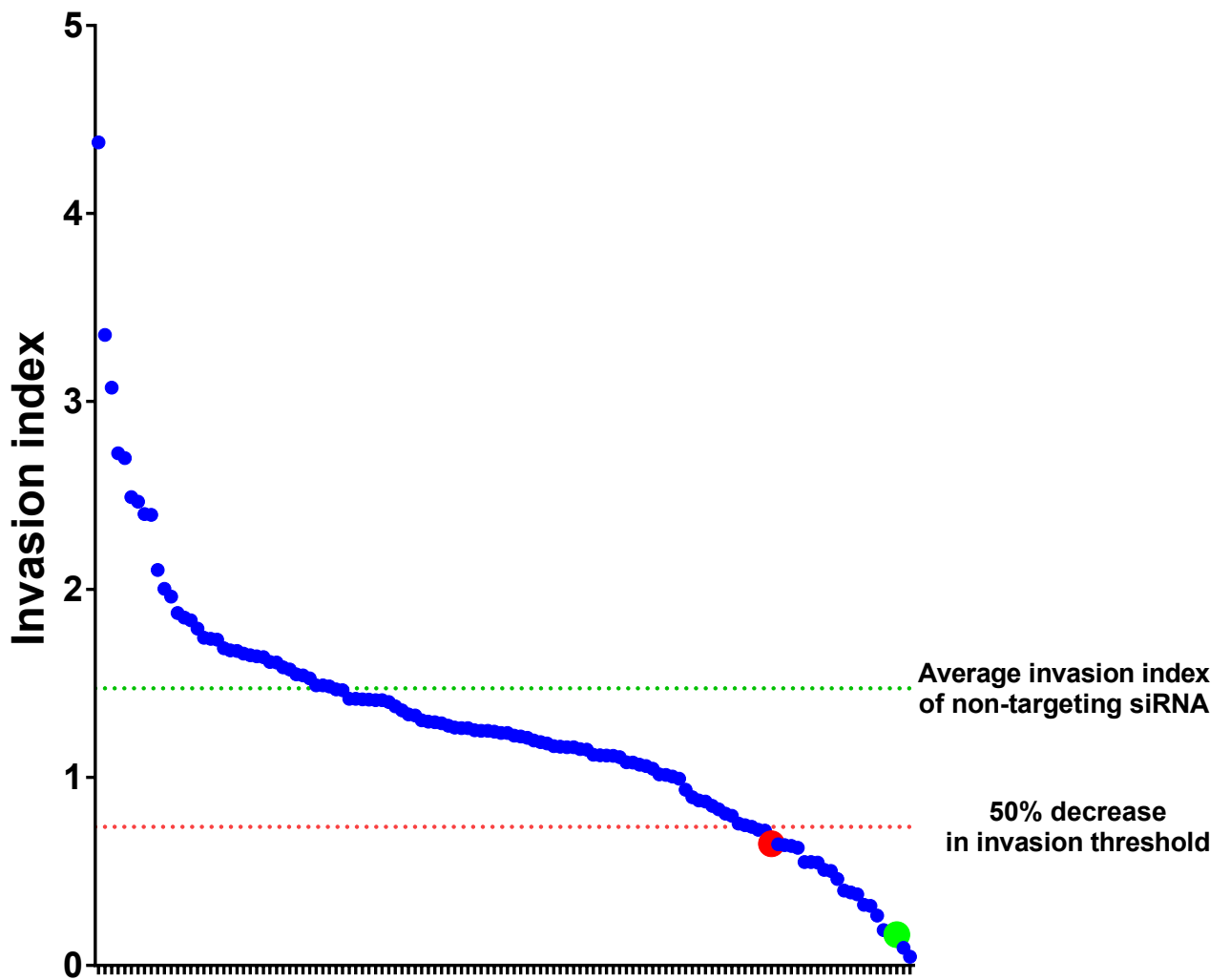
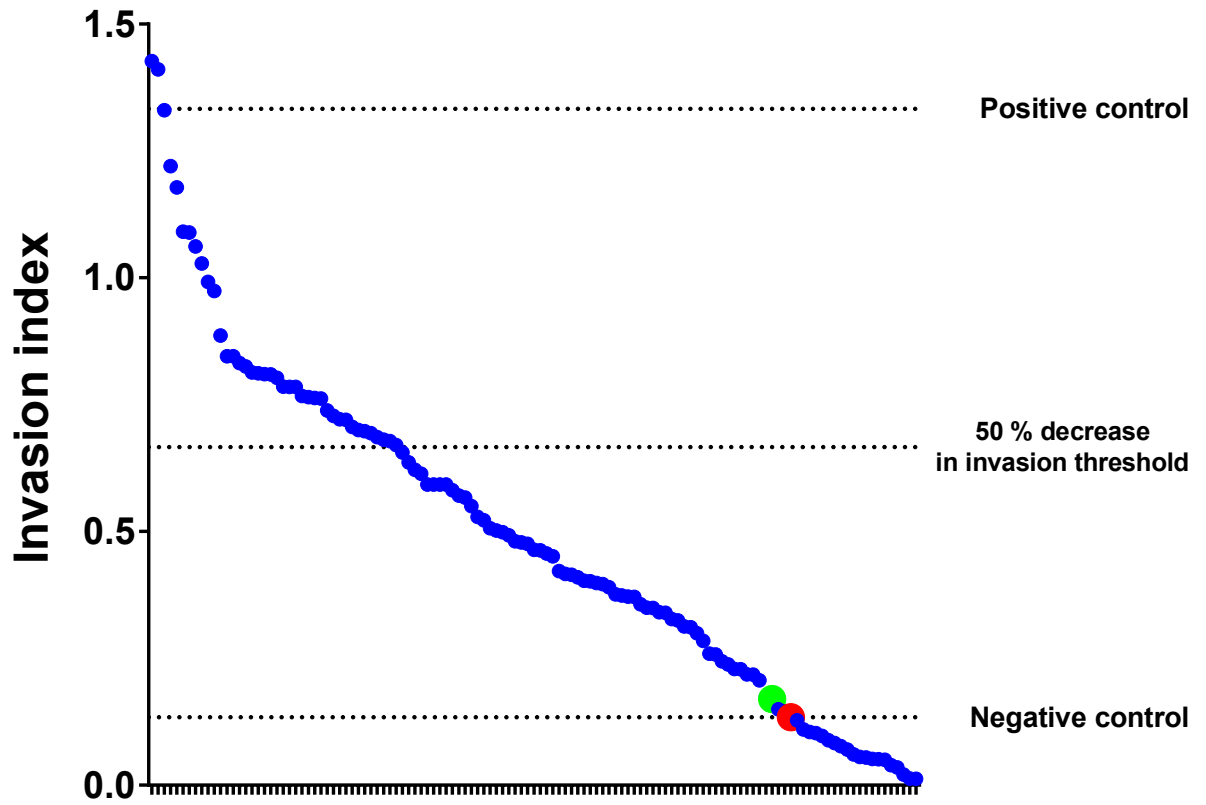
**Supplementary Figure S1. Next-generation sequencing and enrichment results.** (A) Total reads, both mapped and unmapped. (B) Candidate genes were identified after an enrichment CRISPR screen. (C) Gini index (a measure of inequality, with 1 being the most unequal) of the starting cell population and the three replicates of the enrichment screen.

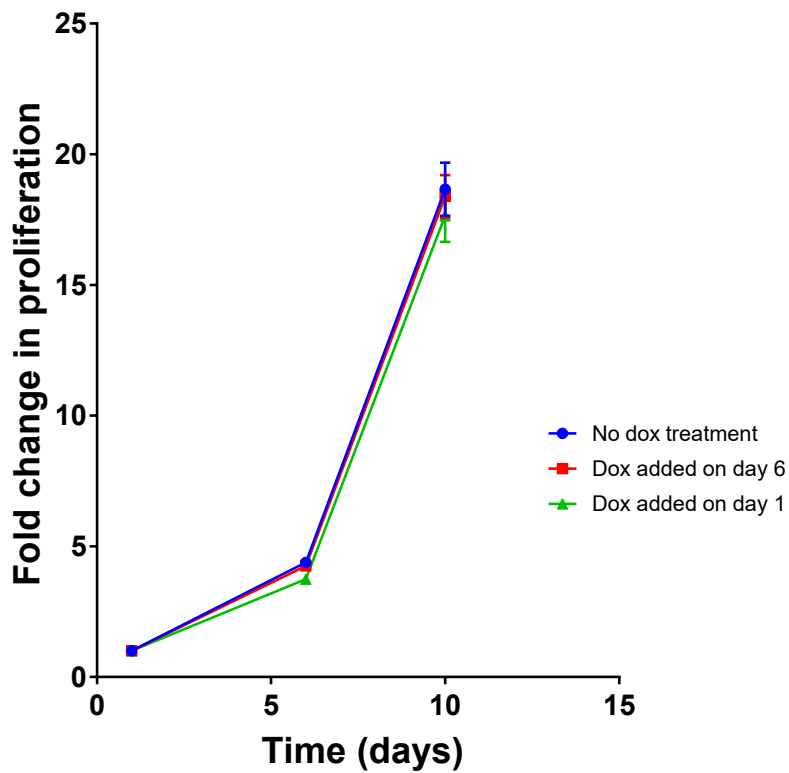
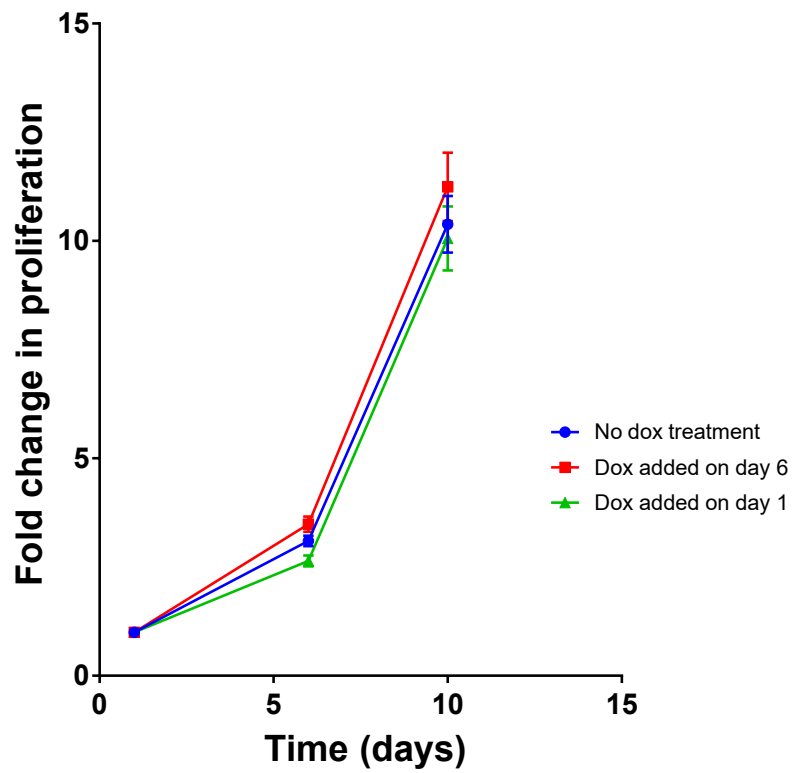
**Supplementary Figure S2. Confirmatory screens of top hits.** Waterfall plot showing the distribution of the top 125 genes selected from the primary screen in a confirmatory CRISPR screen (upper panel) and a confirmatory siRNA screen (lower panel). The red dot is the position of *MBNL3* and the green dot is the position of *KANSL2* after ranking.

**Supplementary Figure S3. Results of spheroid growth assay.** The fold change in proliferation of PANC-1 shScr, PANC-1 shKANSL2, and PANC-1 shMBNL3 cells in spheroids treated with or without doxycycline as described in the Results and Methods sections. The data presented are based on three independent experiments.

**Supplementary Data Set.** Hit list from three independent CRISPR screenings. The first three columns list the ranked genes from each independent CRISPR screen (Rep 1, Rep 2, and Rep 3, respectively). The fourth and fifth columns list the genes having an overlap of at least two positive gRNAs (“pos/goodsgrna”; 1,767 genes) or three positive gRNAs (48 genes) among the three independent CRISPR screens, respectively. Column 6 lists the final hits (959) after removing duplicated genes, with the top 125 hits highlighted in yellow.





**shScramble****shKANSL2****shMBNL3**