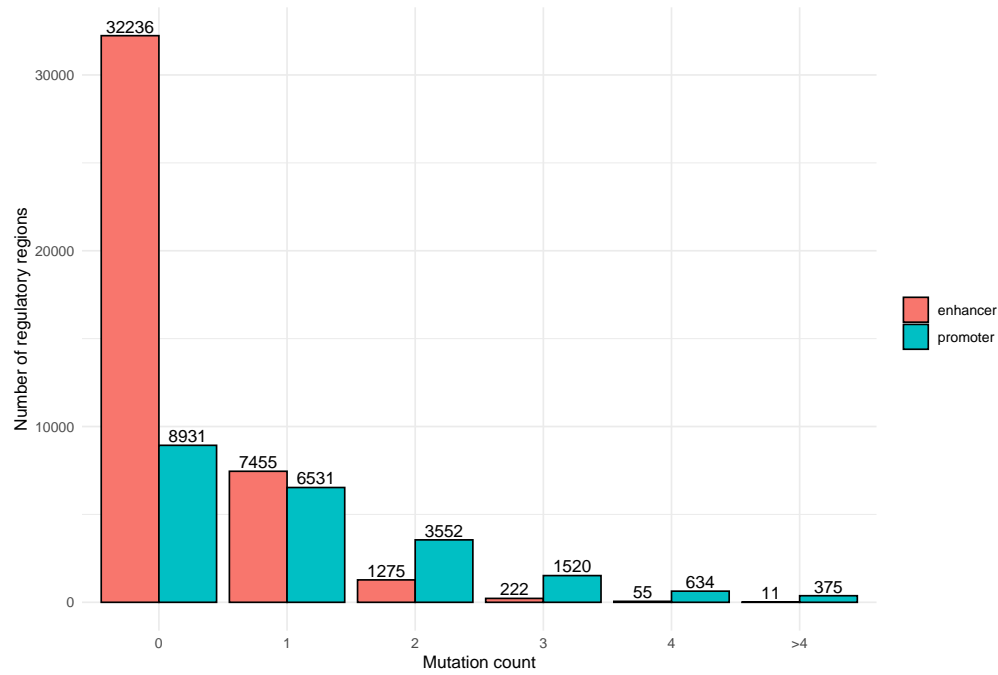
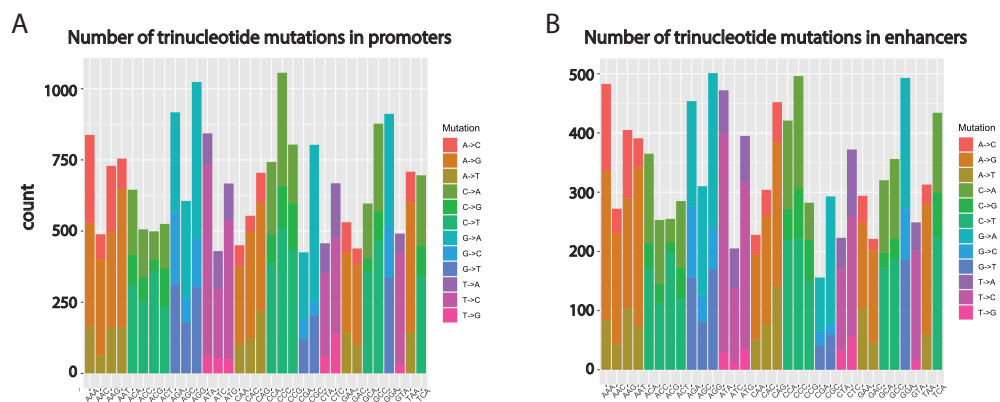


# **Supplemental Figures for “Transcription Factor-Centric Approach to Identify Non-Recurring Putative Regulatory Drivers in Cancer”**

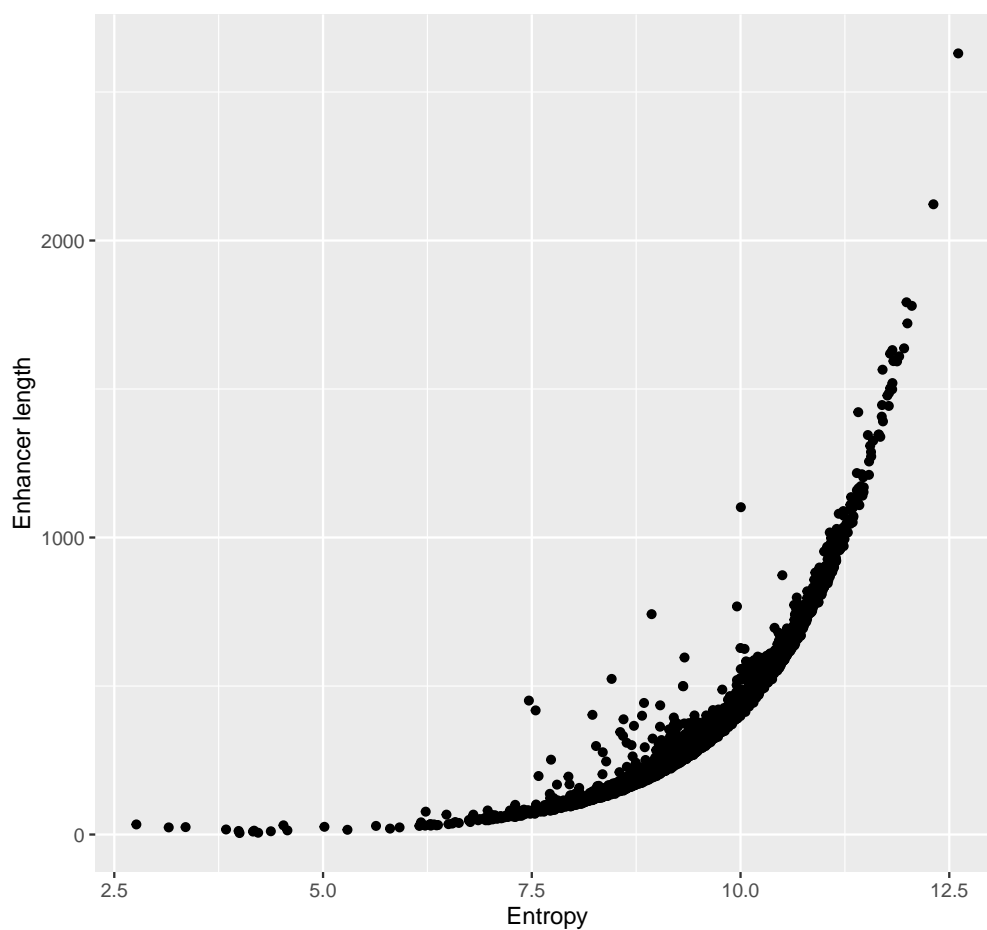
JINGKANG ZHAO, VINCENTIUS MARTIN, RALUCA GORDÂN



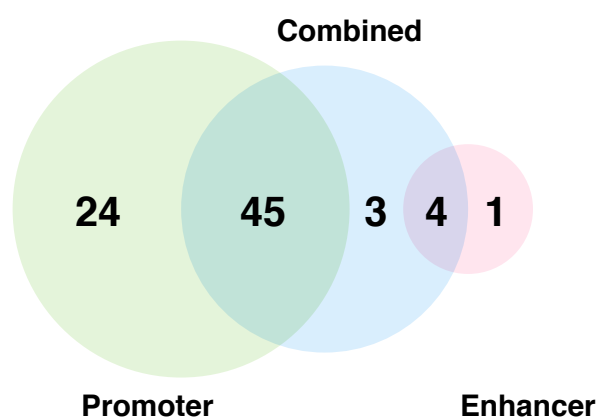
**Fig. S1.** Number of mutations in each regulatory region. The average mutation rate is  $3.6 \times 10^{-6}$  in enhancers and  $2.1 \times 10^{-6}$  in promoters.



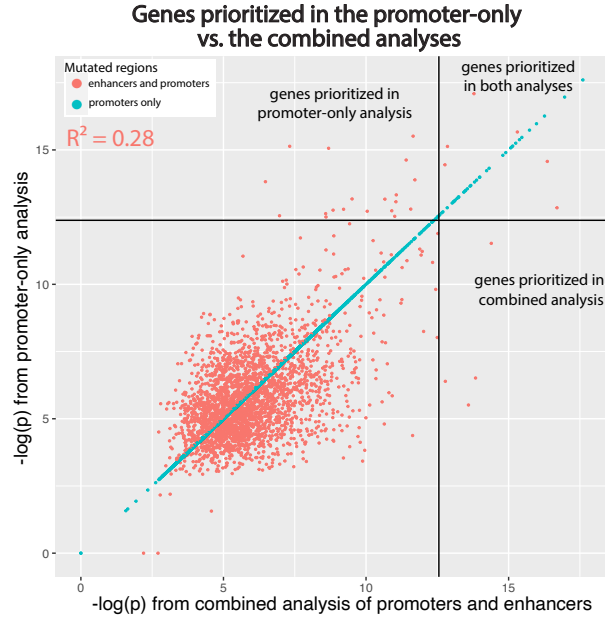
**Fig. S2.** The number of mutations in promoters (A) and enhancers (B), computed for each mutation type in each trinucleotide context .



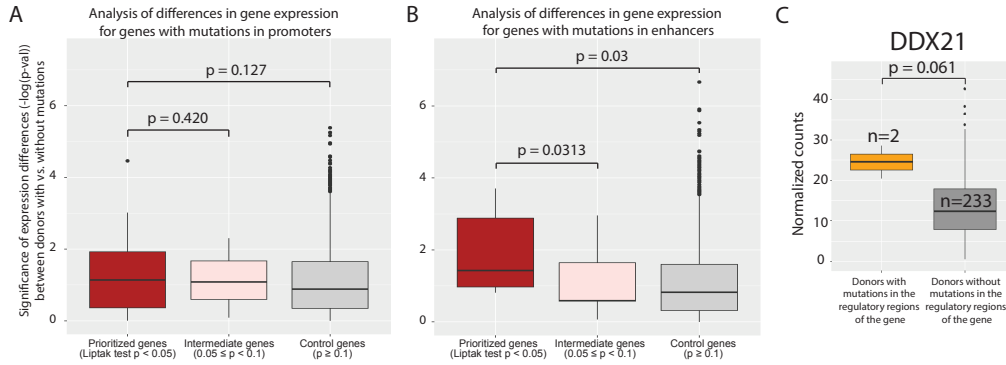
**Fig. S3.** Comparison between the entropy computed for each enhancer, based on the probabilities of all possible mutations, versus the enhancer's length.



**Fig. S4.** Number of prioritized genes in the promoter-only (green), combined (blue), and enhancer-only (pink) analyses.



**Fig. S5.** Comparison between the genes' significance in the promoter-only versus the combined analysis, shown as negative logarithm of the p-value. The  $R^2$  shows the correlation for genes with mutations in both promoters and enhancers (shown in orange).



**Fig. S6.** (A) Significance of gene expression differences between donors with vs. without mutations in promoters, shown for prioritized genes (minimum adjusted Liptak's test  $p < 0.05$ ), intermediate genes ( $0.05 \leq p < 0.1$ ) and control genes ( $p \geq 0.1$ ) genes. (B) Similar to panel A, but analyzing mutations only in enhancers. (C) Only one gene (DDX21) that was prioritized in the promoter-only analysis but not in the combined analysis, has a significant expression difference between donors with vs. without mutations.