

**Supplementary Fig. S4**: Distributions of reads counts by edit distance (mismatches + gaps) between the gRNA and nominated off-target sites for **A**) GUIDE-seq **B**) CIRCLE-seq and **C**) SITE-seq, with no read thresholding applied for all three assays. Numbers in red indicate the number of nominated sites that have a certain edit distance with respect to the gRNA sequence. Dashed horizontal black lines depict average reads in untreated control samples, and dashed grey horizontal lines depict 25% and 75% quartiles of read counts in untreated control samples.