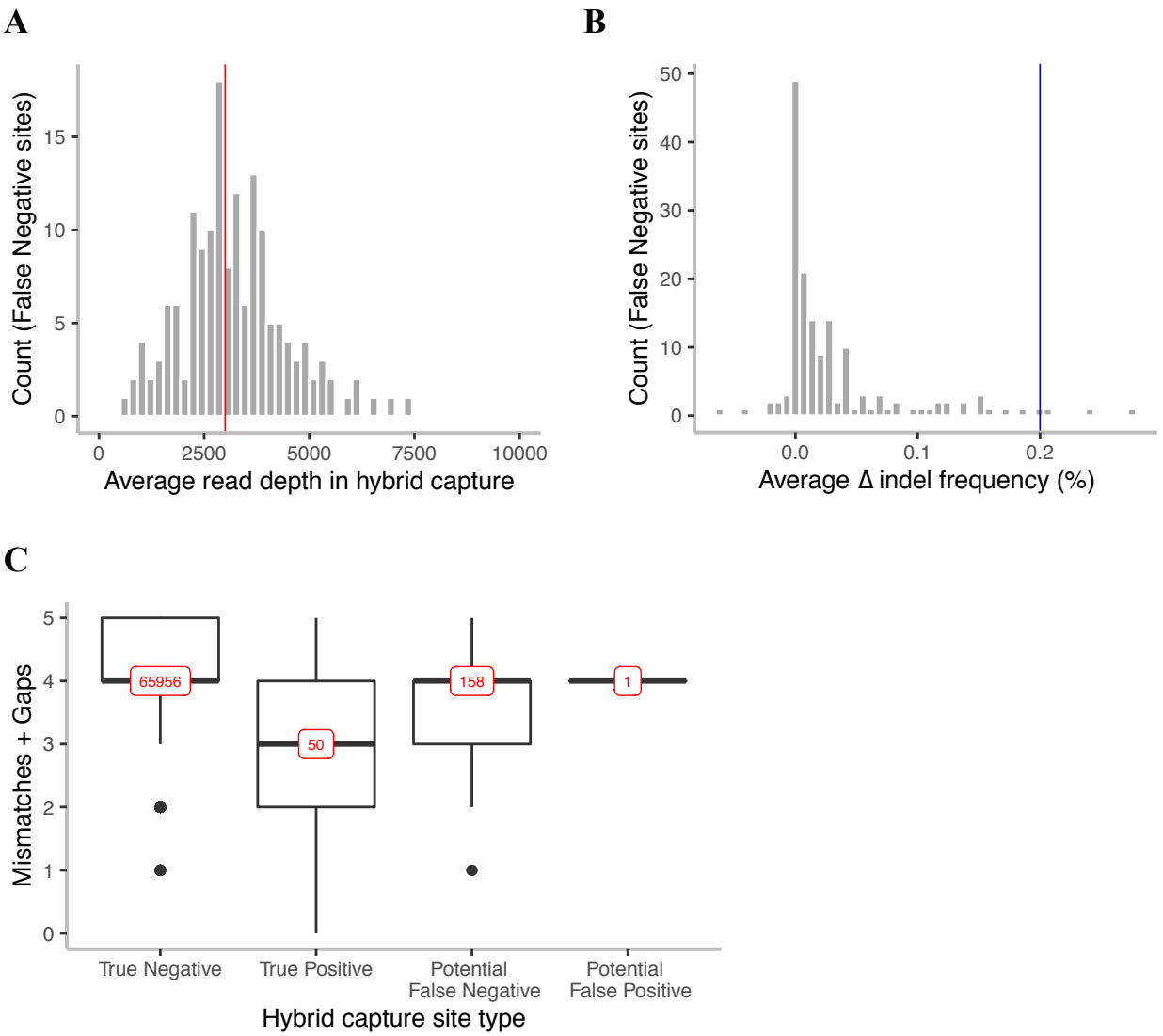

Supplementary Fig. S8: A) Read depth from hybrid capture sequencing in HEK293T/Cas9 cells for 158 sites that were nominated by all three genome-wide assays but not sequence-confirmed as edited by hybrid capture, averaged across three replicates of treated and untreated samples. Red line denotes median of 3000 reads. **B)** Average difference in indel frequency between treated samples and untreated controls in HEK293T/Cas9 cells for 158 sites across eight gRNAs that were nominated by all three genome-wide assays but not sequence-confirmed as edited by hybrid capture. Blue line marks 0.2% indel frequency difference. **C)** Edit distances for all sites sequenced after hybrid capture enrichment in HEK293T/Cas9 cells. 50 sites were sequence-confirmed as edited and nominated by three genome-wide assays (true positive). 158 sites were nominated by all three genome-wide assays but were not sequence-confirmed as edited (potential false negatives of hybrid capture). One site, a potential false positive of the sequence-confirmation step, was sequence-confirmed but not nominated by any genome-wide assay. Distribution of edit distances was statistically significantly different between true positives and