

Figure S1 *in vivo* secondary structure determination of different cell-lines using optimized icSHAPE

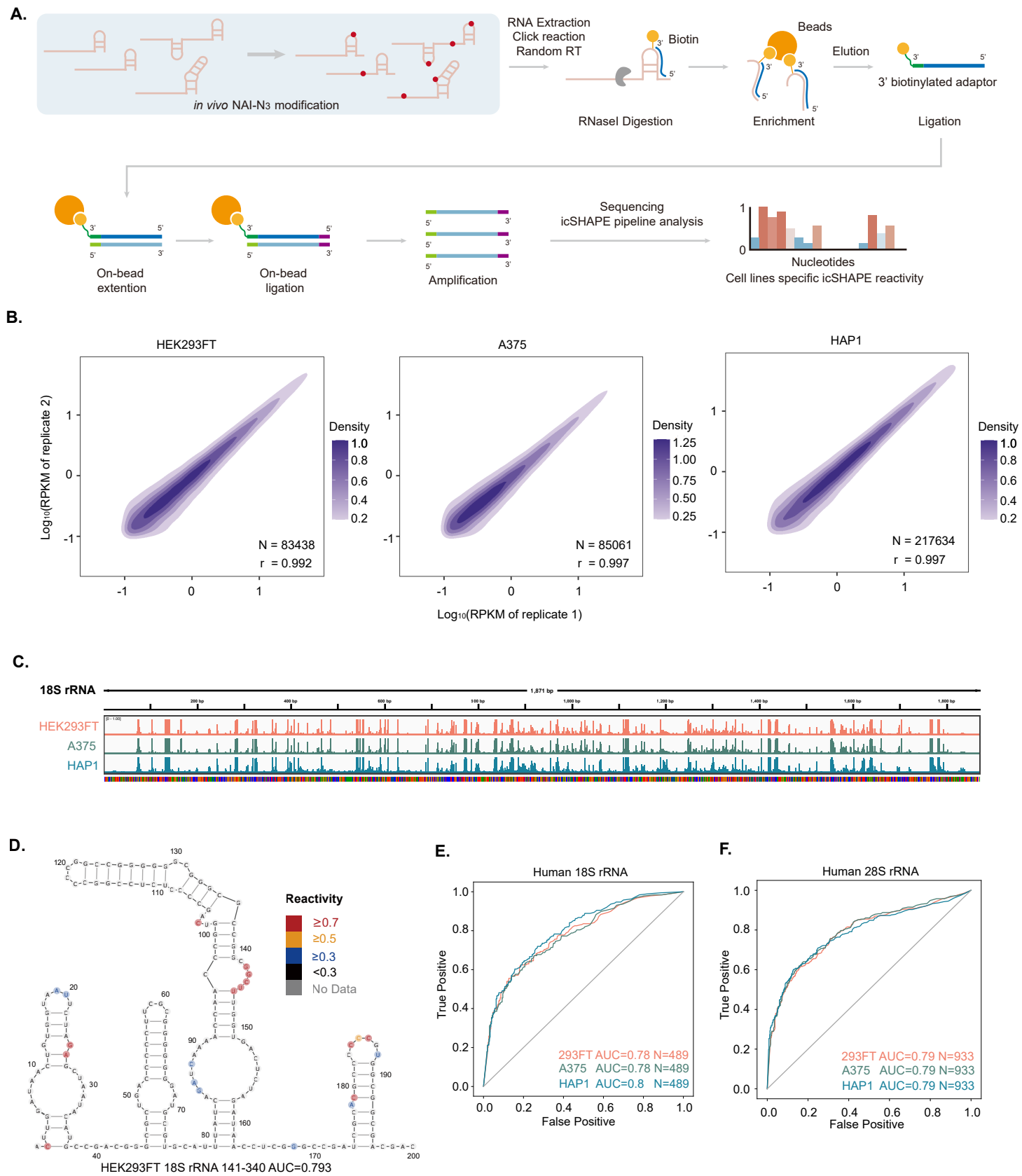


Figure S2 Target structure is an important *in vivo* factor affecting gRNA efficacy

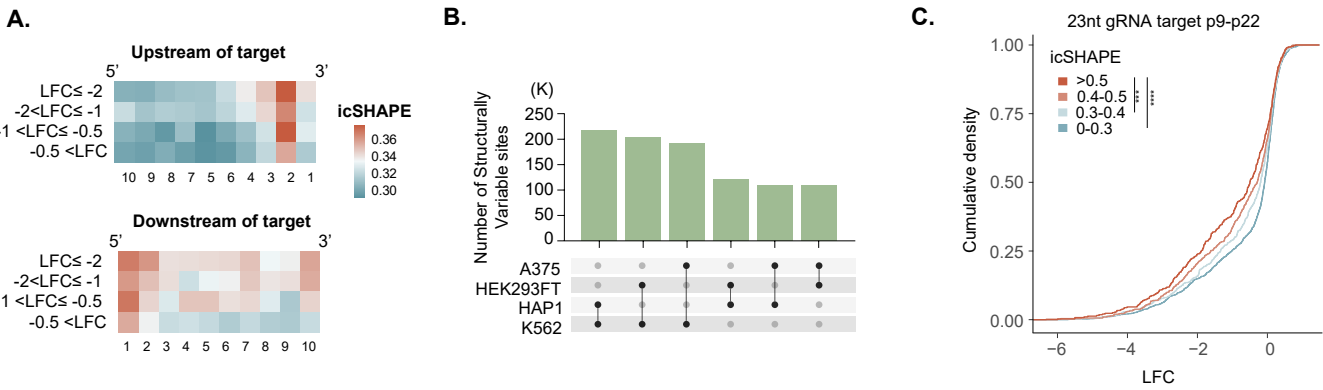


Figure S3 Protein binding around the target sites promotes gRNA efficacy

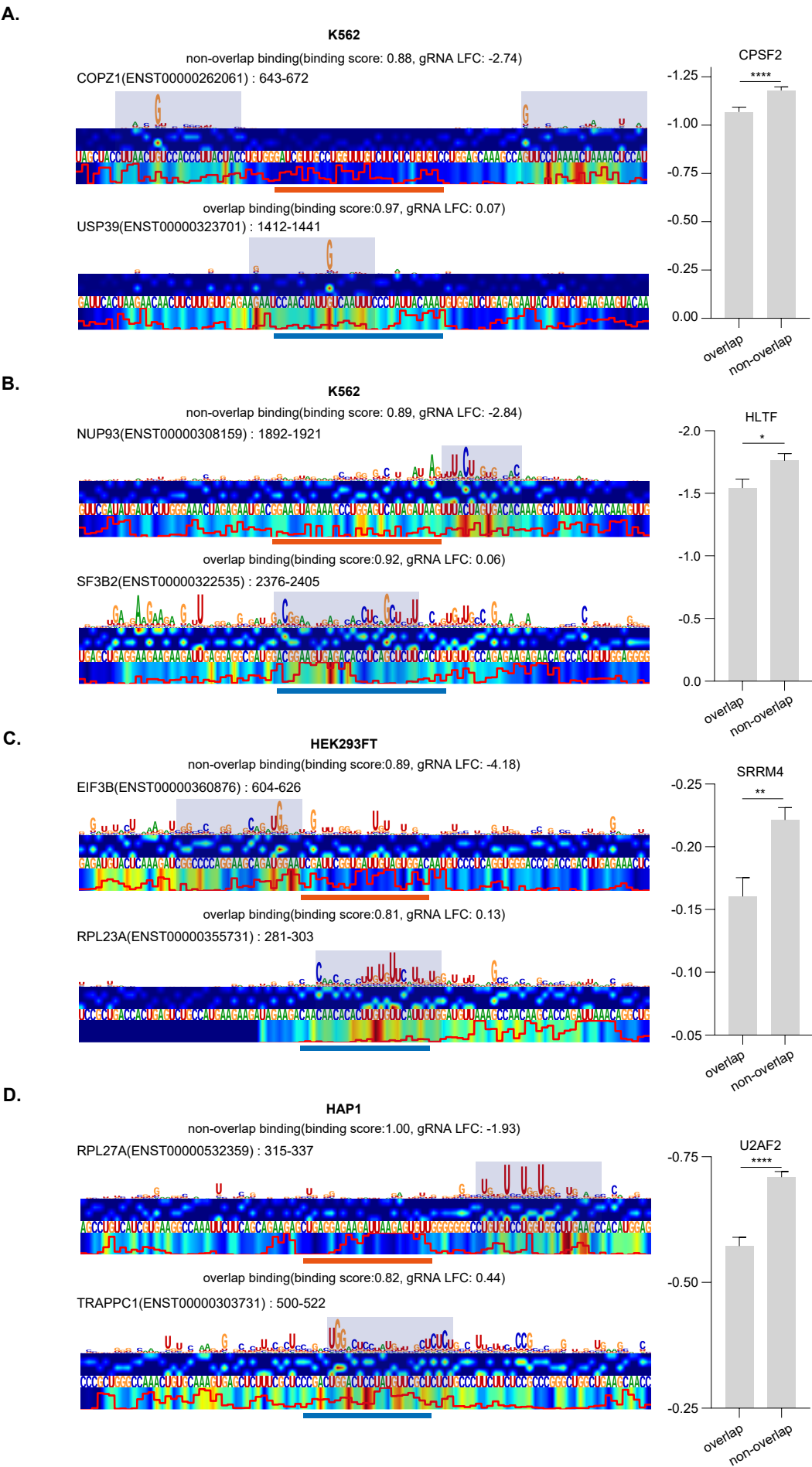
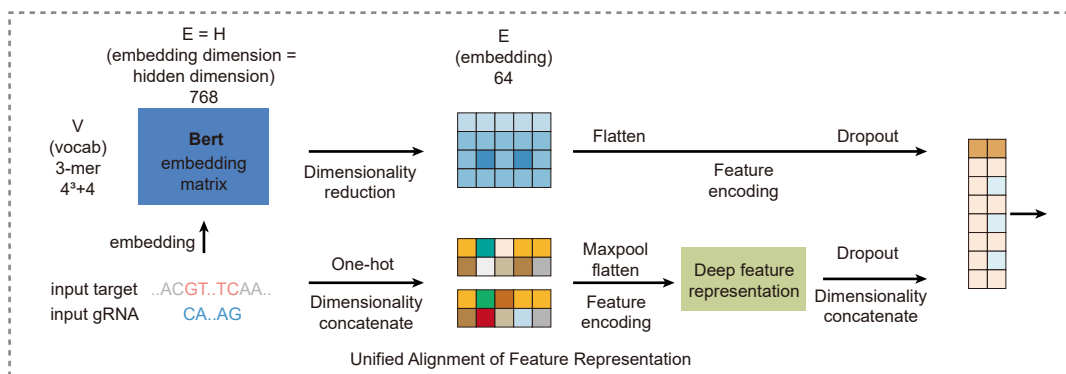
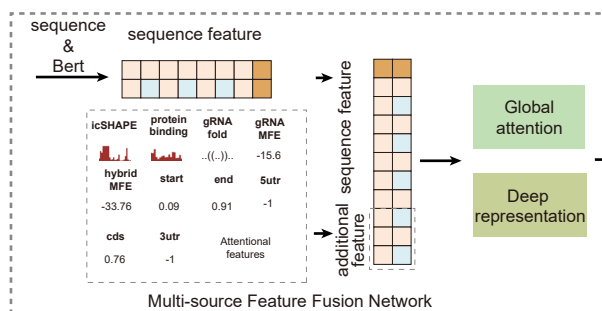


Figure S4 SCALPEL architecture and performance

A.



B.



C.

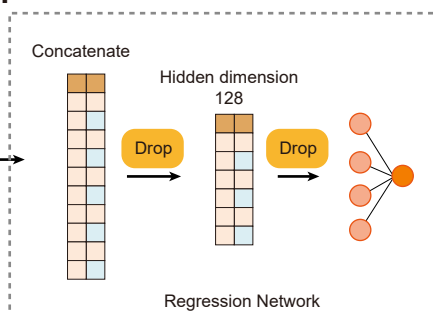


Figure S5 CRISPR screen quality control

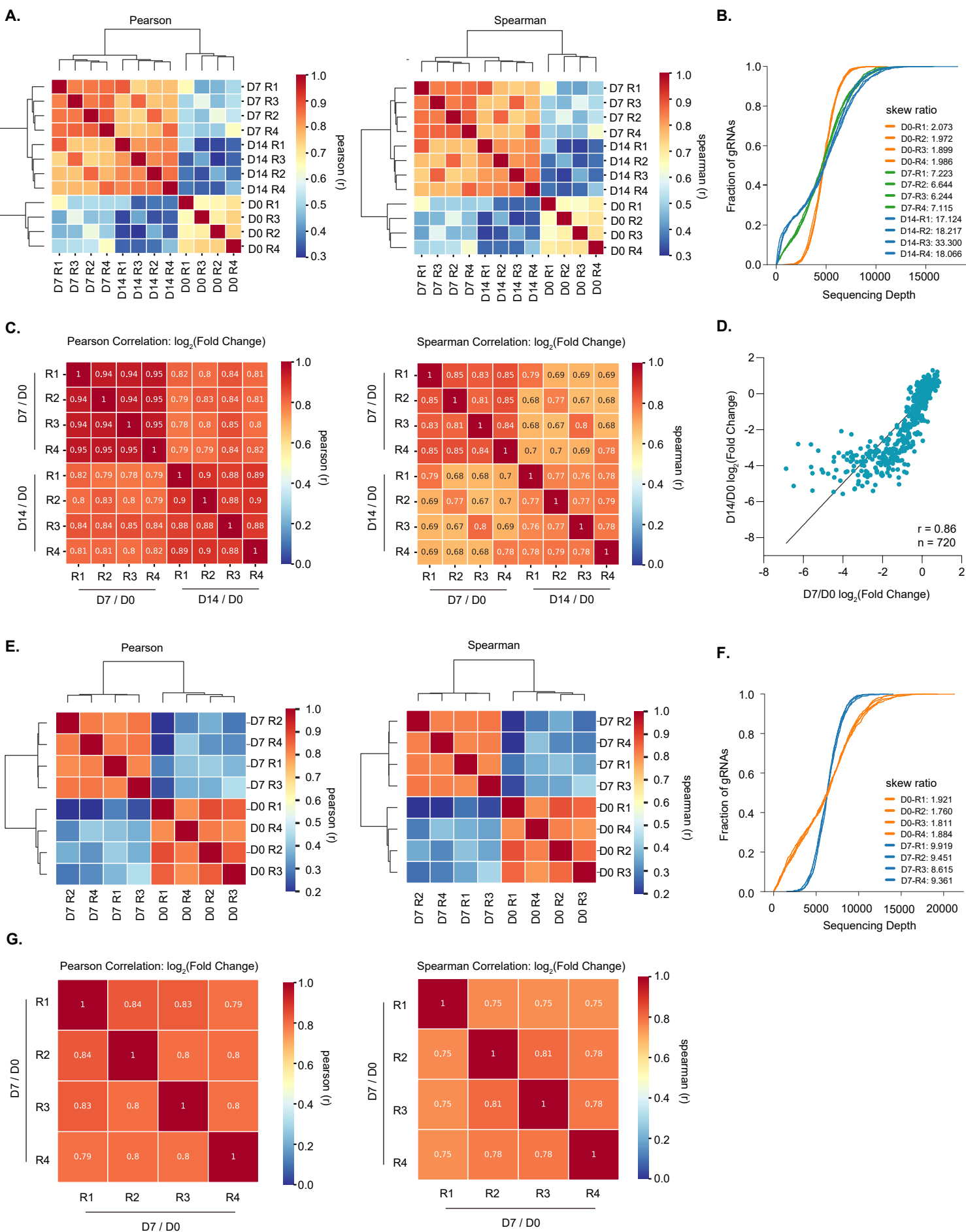


Figure S6 CRISPR screen results

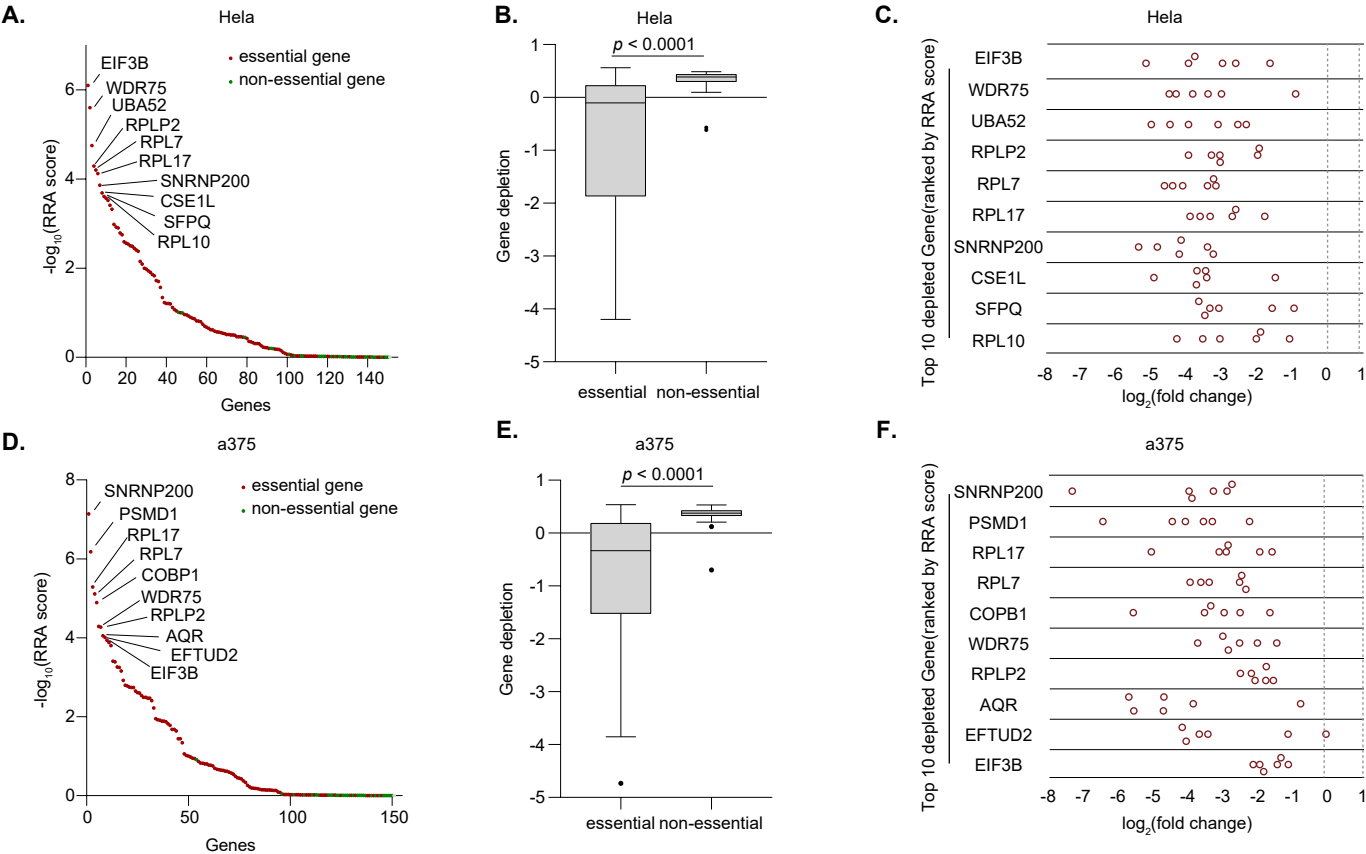


Figure S7 SCALPEL outperforms existing models in our screening data

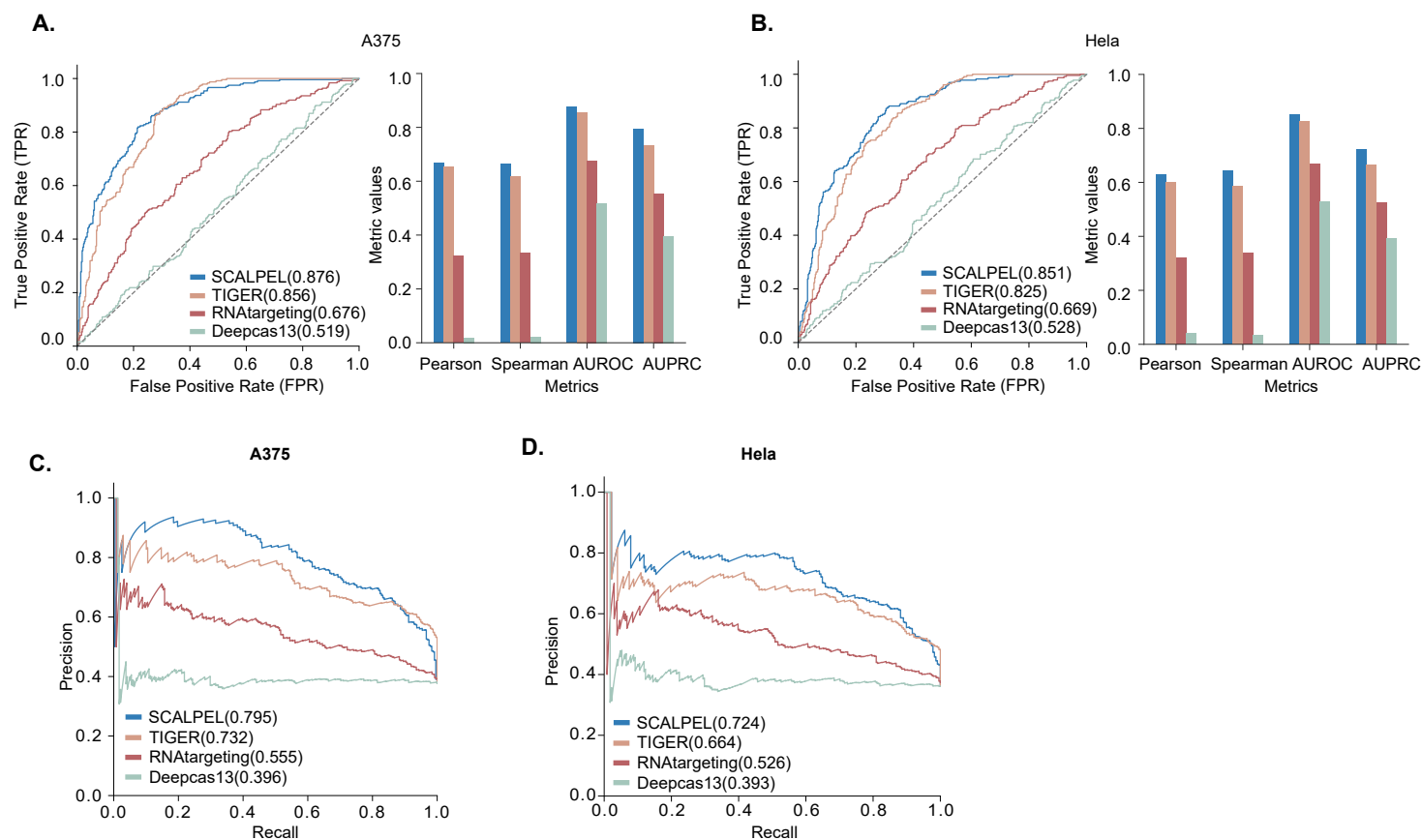


Figure S8 Target structure and protein binding probability affect gRNA efficacy in our screen

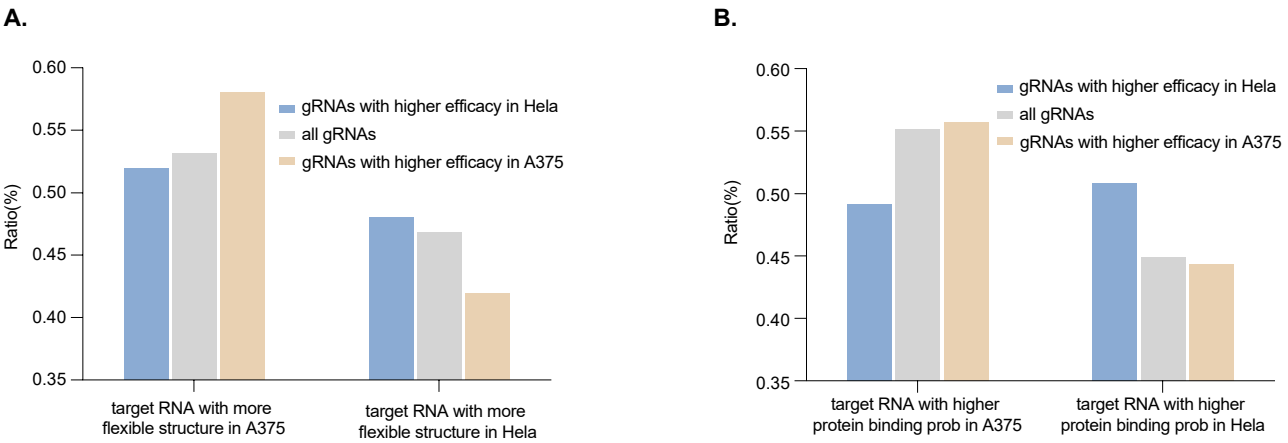


Figure S9 Targeting structural dynamic regions results in different efficacy

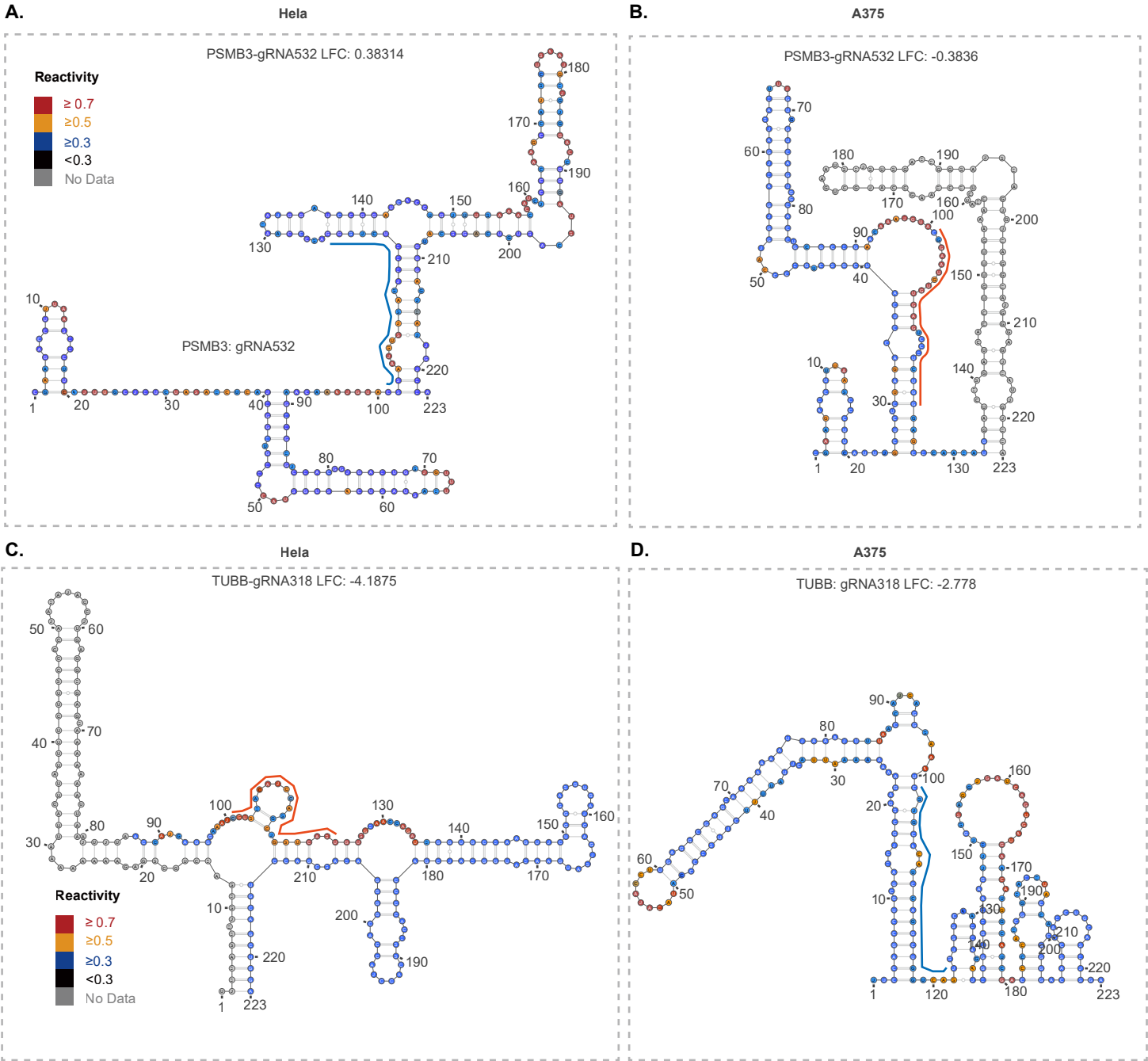


Figure S10 SCALPEL designs high efficacy gRNAs for virus inteference

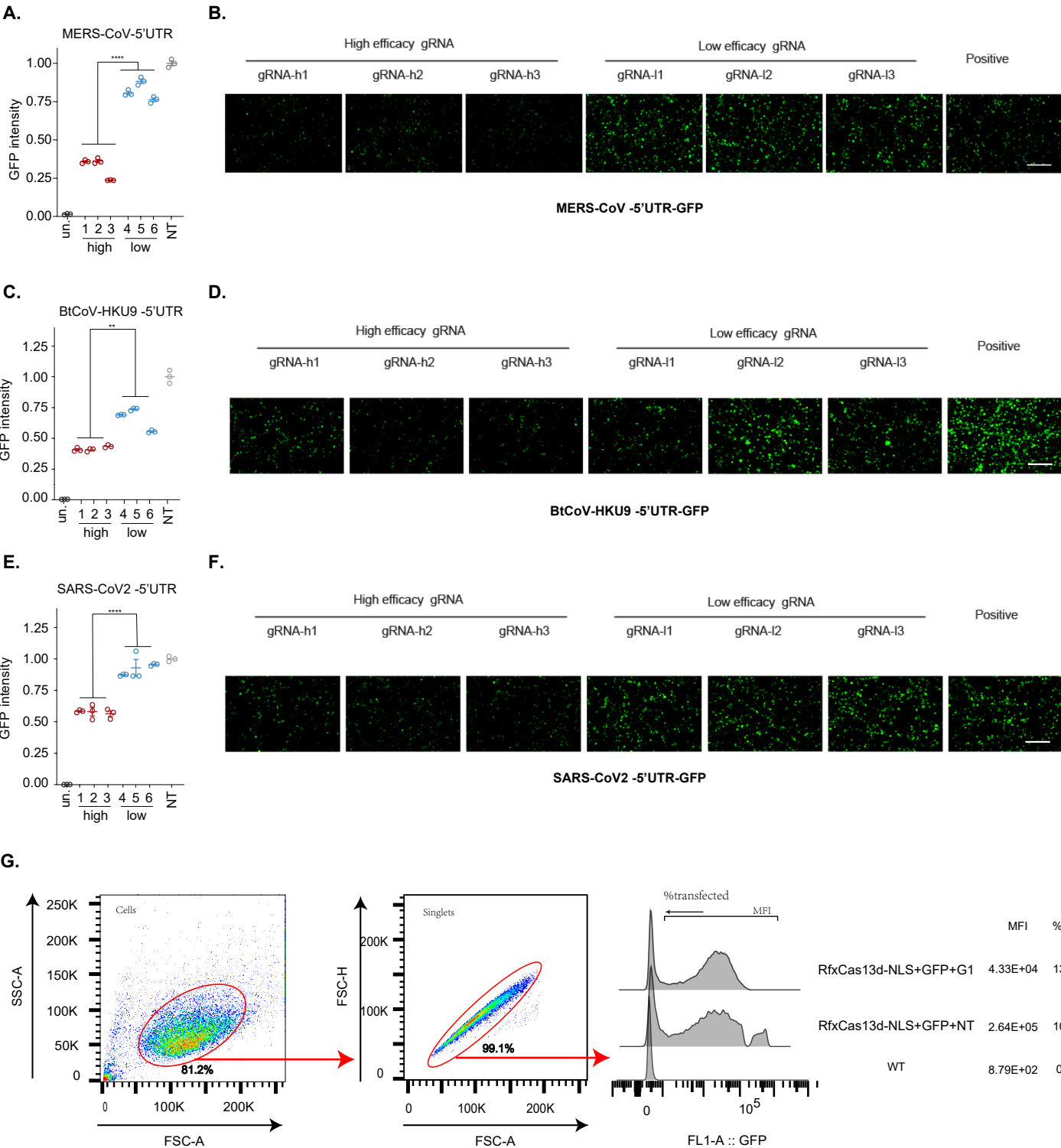


Figure S11 SCALPEL designs high efficacy gRNAs for zebrafish maternal transcript

