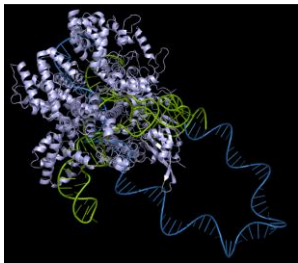
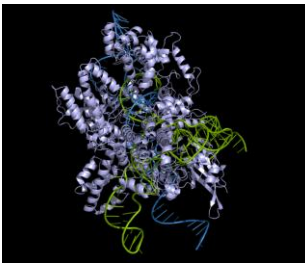


a

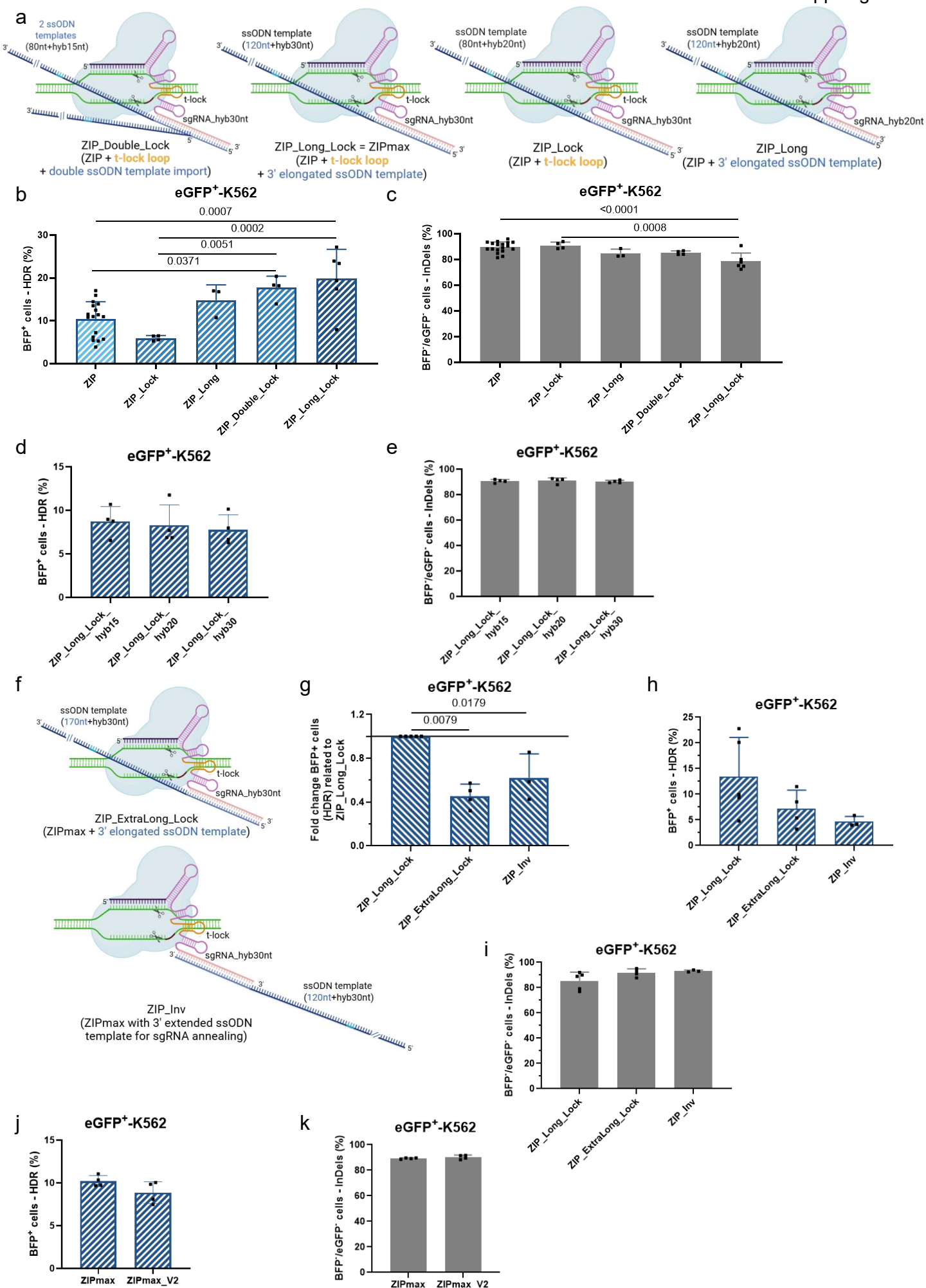


UNZIP (*eGFP* targeting
but template containing only A's)

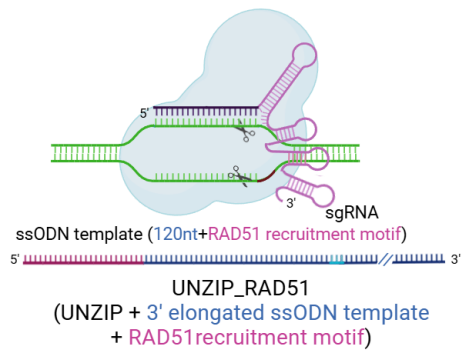
b



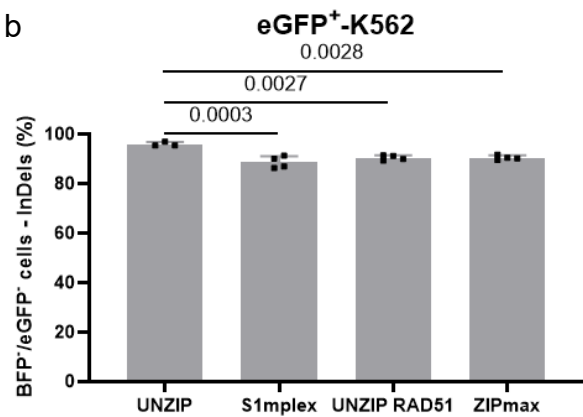
UNZIP (*CFTR* targeting)



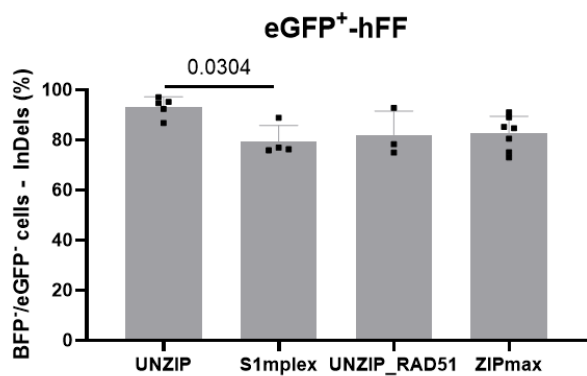
a

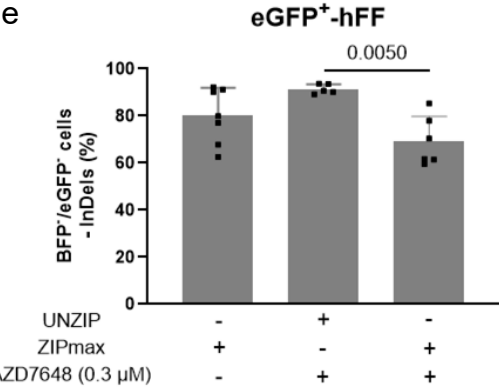
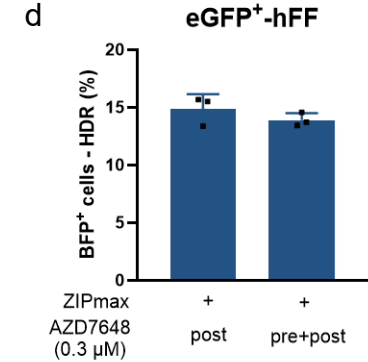
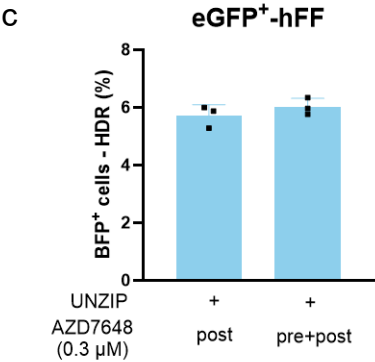
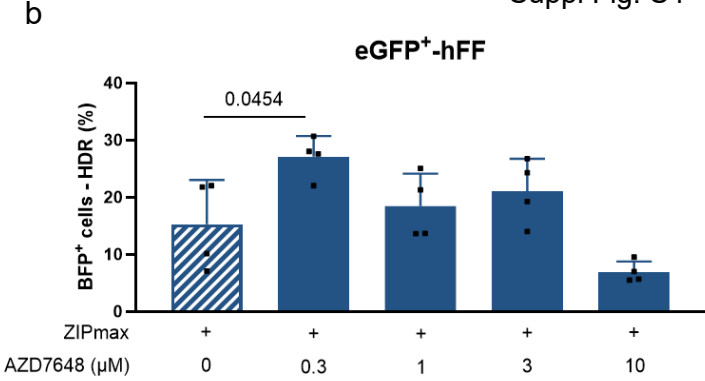
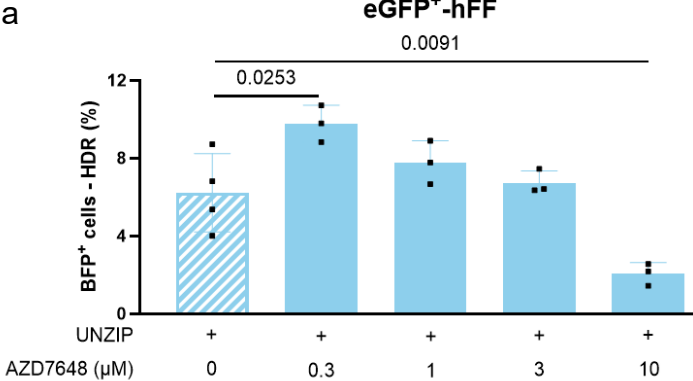


b

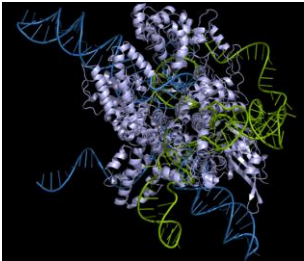


c

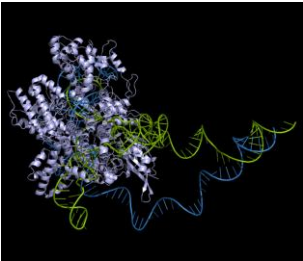




a

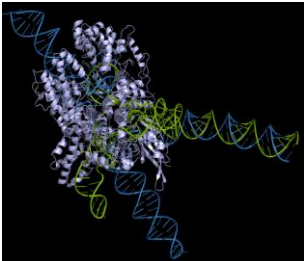


UNZIP_2 (*HBB* targeting)

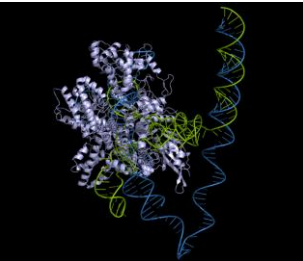


UNZIP_2 (*UROS* targeting)

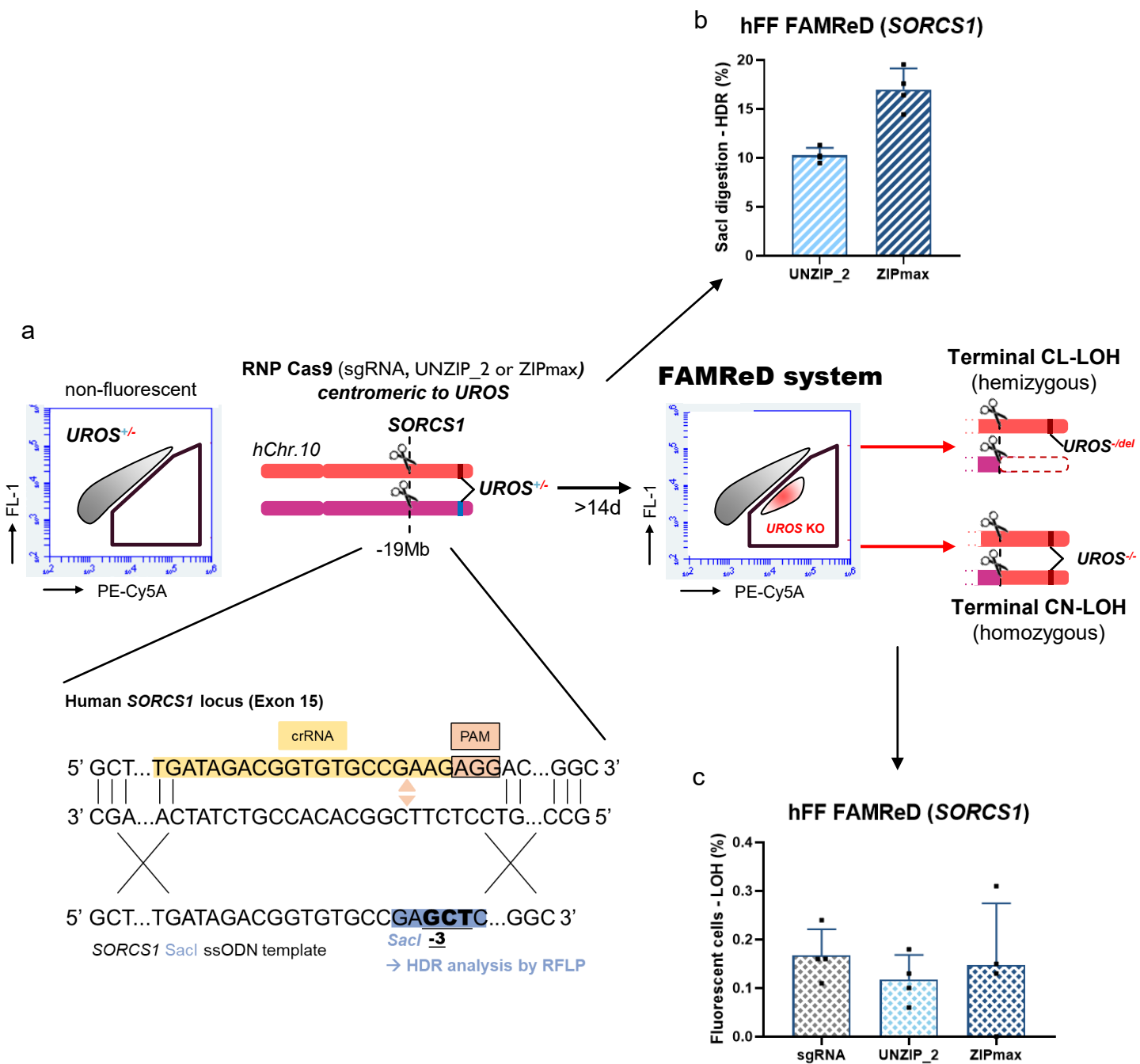
b



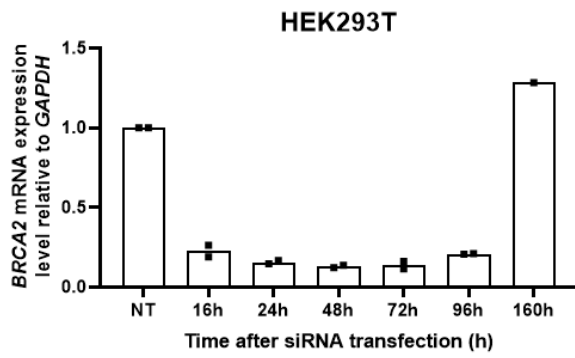
ZIPmax (*HBB* targeting)



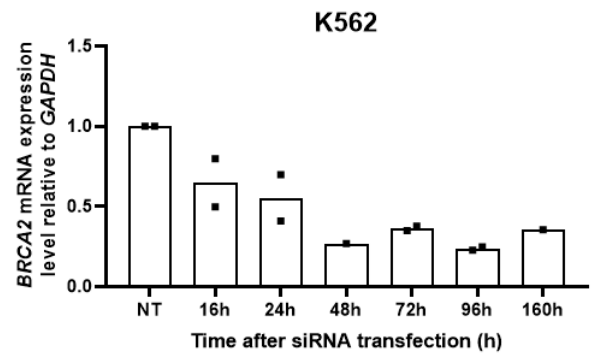
ZIPmax (*UROS* targeting)



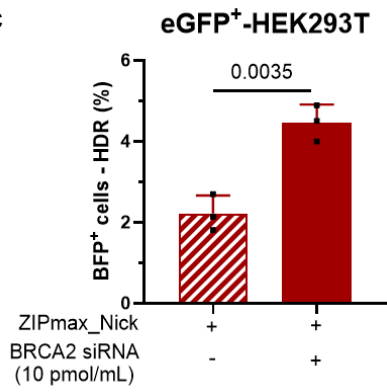
a



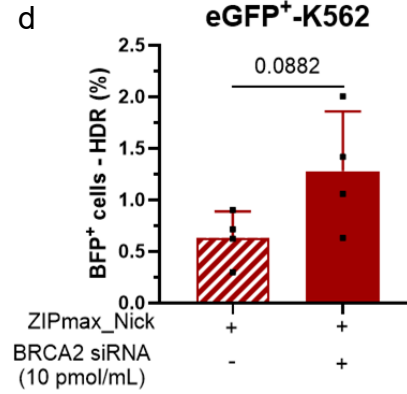
b



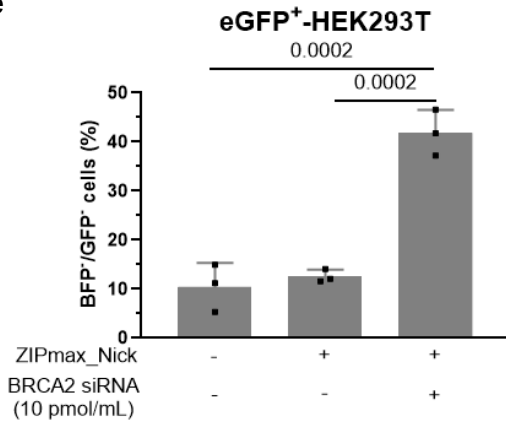
c



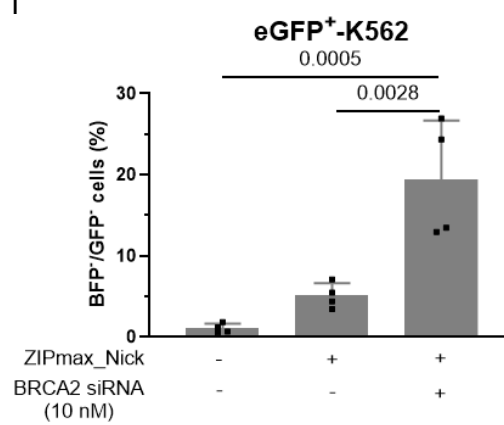
d



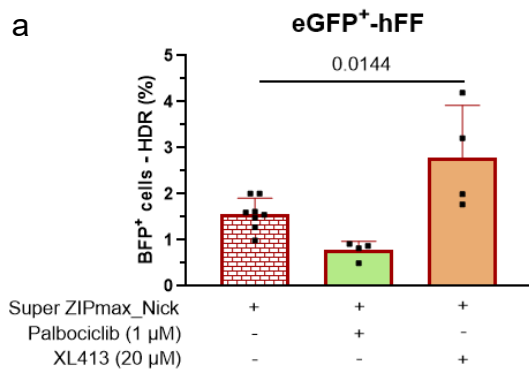
e



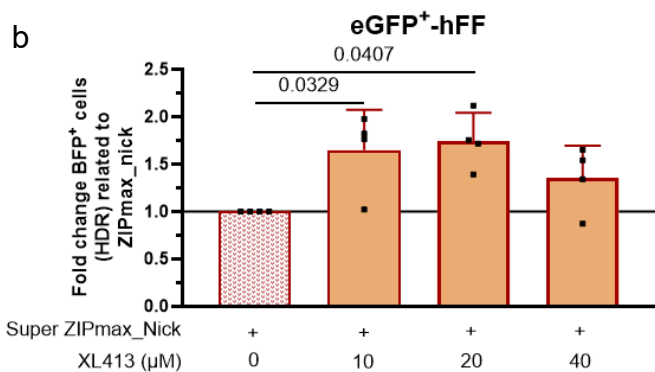
f



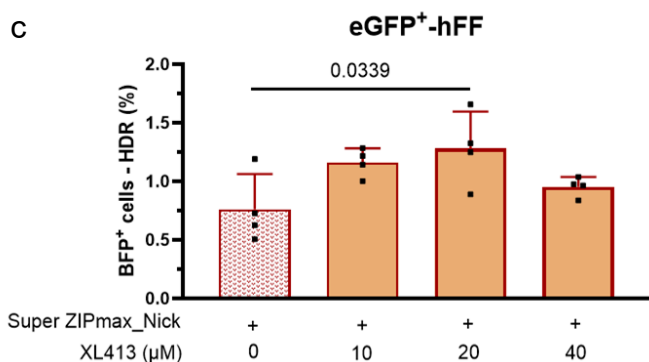
a



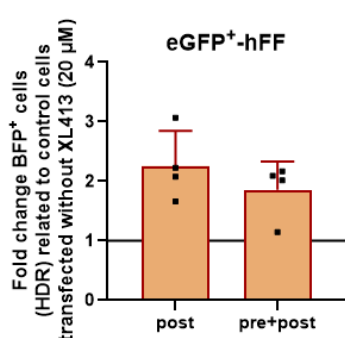
b



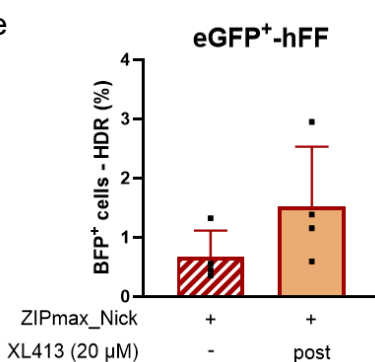
c



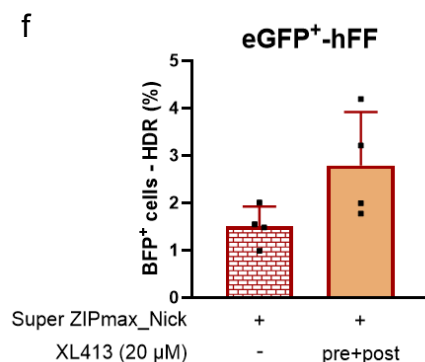
d



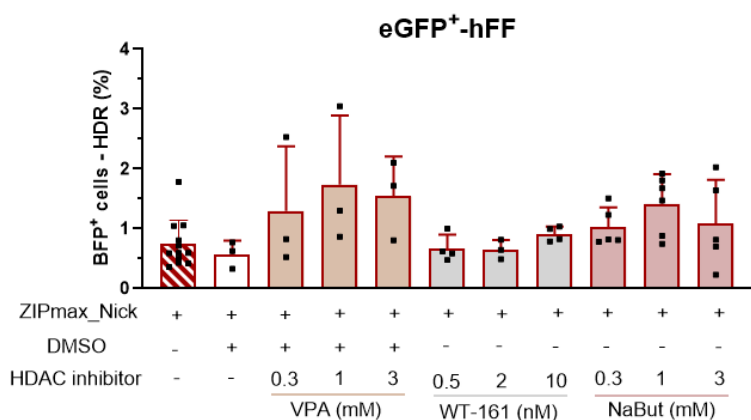
e



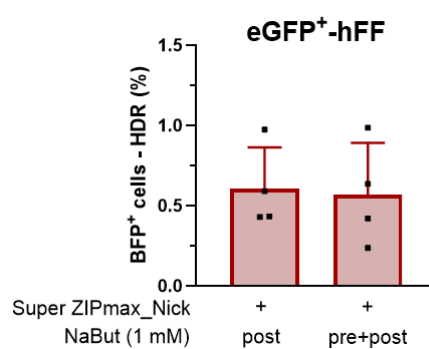
f



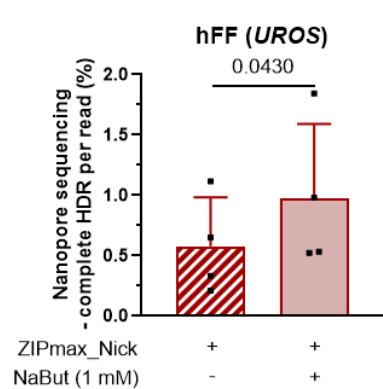
g



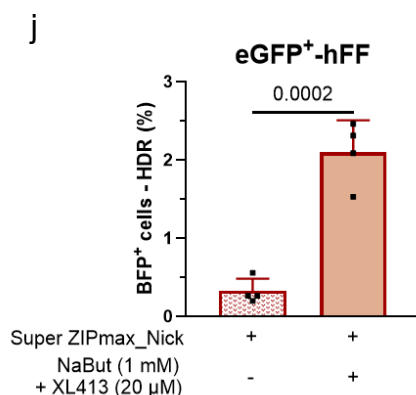
h



i



j



Supplementary Table 1: gRNA sequences for CRISPR-Cas9 editing.

sgRNA	Sequence (5' to 3')
sgRNA eGFP (UNZIP, UNZIP_RAD51, UNZIP_Nick)	CTCGTGACCACCCTGACCTAGTTTTAGAGCTAGAAATAGCAAG TTAAAATAAGGCTAGTCCGTTATCAACTTGAAAAAGTGGCACC GAGTCGGTGCTTTT
sgRNA eGFP (ZIP, ZIP_Long)	CTCGTGACCACCCTGACCTAGTTTTAGAGCTAGAAATAGCAAG TTAAAATAAGGCTAGTCCGTTATCAACTTGAAAAAGTGGCACC GAGTCGGTGCTTTTCTGCCATCAAAGCGTGCTCAGTCT
sgRNA eGFP (ZIP_Lock, ZIP_Double_Lock, ZIPmax, ZIP_ExtraLong_Lock, ZIP_Inv, ZIPmax_Nick, Super ZIPmax_Nick)	CTCGTGACCACCCTGACCTAGTTTTAGAGCTAGAAATAGCAAG TTAAAATAAGGCTAGTCCGTTATCAACTTGGACTTCGGTCCAA GTGGCACCAGAGTCGGTGCTTTTCTGCCATCAAAGCGTGCTCA GTCTGCTGCC
sgRNA eGFP (S1mplex)	CTCGTGACCACCCTGACCTAGTTTAAGAGCTATGCTGCGAATA CGAGATGCGGCCGCCGACCAGAATCATGCCAAGTGCGTAAGA TAGTCGCGGGTTCGGCGGCCGCATCTCGTATTCGCAGCATAGC AAGTTTAAATAAGGCTAGTCCGTTATCAACTTGAAAAAGTGGC ACCGTGACGGTGCTTT
sgRNA eGFP (ZIP_Long_Lock_hyb15)	CTCGTGACCACCCTGACCTAGTTTTAGAGCTAGAAATAGCAAG TTAAAATAAGGCTAGTCCGTTATCAACTTGGACTTCGGTCCAA GTGGCACCAGAGTCGGTGCTTTTCTGCCATCAAAGCGT
sgRNA eGFP (ZIP_Long_Lock_hyb20)	CTCGTGACCACCCTGACCTAGTTTTAGAGCTAGAAATAGCAAG TTAAAATAAGGCTAGTCCGTTATCAACTTGGACTTCGGTCCAA GTGGCACCAGAGTCGGTGCTTTTCTGCCATCAAAGCGTGCTCA
sgRNA eGFP (ZIPmax_V2)	CTCGTGACCACCCTGACCTAGTTTTAGAGCTAGAAATAGCAAG TTAAAATAAGGCTAGTCCGTTATCAACTTGGACTTCGGTCCAA GTGGCACCAGAGTCGGTGCTTTTACGCCGGGTACAACGAGCC TCTTTCTCCG
sgRNA HBB (UNZIP_2, ZIPmax)	GTAACGGCAGACTTCTCCTCGTTTTAGAGCTAGAAATAGCAAG TTAAAATAAGGCTAGTCCGTTATCAACTTGGACTTCGGTCCAA GTGGCACCAGAGTCGGTGCTTTTCTGCCATCAAAGCGTGCTCA GTCTGCTGCC
sgRNA UROS (UNZIP_2, ZIPmax, UNZIP_Nick_2, ZIPmax_Nick)	GGAAGCAGCAGAGTTATGTTGTTTTAGAGCTAGAAATAGCAAG TTAAAATAAGGCTAGTCCGTTATCAACTTGGACTTCGGTCCAA GTGGCACCAGAGTCGGTGCTTTTCTGCCATCAAAGCGTGCTCA GTCTGCTGCC
sgRNA CFTR_G542X_modeling (UNZIP)	GACAATATAGTTCTTGAGAGTTTTAGAGCTAGAAATAGCAAG TTAAAATAAGGCTAGTCCGTTATCAACTTGAAAAAGTGGCACC GAGTCGGTGCTTTT
sgRNA CFTR_G542X_modeling (ZIPmax)	GACAATATAGTTCTTGAGAGTTTTAGAGCTAGAAATAGCAAG TTAAAATAAGGCTAGTCCGTTATCAACTTGGACTTCGGTCCAA GTGGCACCAGAGTCGGTGCTTTTCTGCCATCAAAGCGTGCTCA TTCTGCCATCAAAGCGTGCTCA
sgRNA CFTR_G542X_correction (UNZIP_2, ZIPmax)	GACAATATAGTTCTTTGAGAGTTTTAGAGCTAGAAATAGCAAG TAAAATAAGGCTAGTCCGTTATCAACTTGGACTTCGGTCCAAG TGGCACCAGAGTCGGTGCTTTTCTGCCATCAAAGCGTGCTCAG TCTGCTGCC
sgRNA SORCS1 (UNZIP_2, ZIPmax)	TGATAGACGGTGTGCCGAAGGTTTTAGAGCTAGAAATAGCAA GTTAAAATAAGGCTAGTCCGTTATCAACTTGGACTTCGGTCCA AGTGGCACCAGAGTCGGTGCTTTTCTGCCATCAAAGCGTGCTC AGTCTGCTGCC

Supplementary Table 2: HDR ssODN template sequences for CRISPR-Cas9 HDR editing (eGFP target).

HDR template	Sequence (5' to 3')
BFP (UNZIP, UNZIP_Nick)	AAGCTGCCCCGTGCCCTGGCCCACCCTCGTGACCACCCTGAGCCA CGGCGTGACAGTGCTTCGCCCCGCTACCCCGACCACATGA
BFP (ZIP, ZIP_Lock, ZIPmax_hyb20)	TGAGCACGCTTTGATGGCAGAAGCTGCCCCGTGCCCTGGCCCACC CTCGTGACCACCCTGAGCCACGGCGTGACAGTGCTTCGCCCCGCTA CCCCGACCACAT
BFP (ZIP_Double_Lock 1/2)	GGCAGCAGACTGAGCAAGCTGCCCCGTGCCCTGGCCCACCCTCGT GACCACCCTGAGCCACGGCGTGACAGTGCTTCGCCCCGCTACCCCG ACCACAT
BFP (ZIP_Double_Lock 2/2, ZIP_Long_Lock_hyb15)	ACGCTTTGATGGCAGAAGCTGCCCCGTGCCCTGGCCCACCCTCGT GACCACCCTGAGCCACGGCGTGACAGTGCTTCGCCCCGCTACCCCG ACCACAT
BFP (ZIP_Long, ZIPmax, ZIPmax_Nick)	GGCAGCAGACTGAGCACGCTTTGATGGCAGAAGCTGCCCCGTGCC CTGGCCCACCCTCGTGACCACCCTGAGCCACGGCGTGACAGTGCT TCGCCCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCAAGT CCGCCATGCCCCGAAGGC
BFP-biotin (S1mplex)	Biotin- AAGCTGCCCCGTGCCCTGGCCCACCCTCGTGACCACCCTGAGCCA CGGCGTGACAGTGCTTCGCCCCGCTACCCCGACCACATGA
BFP (UNZIP_RAD51)	AACTCCCCCTCCATCATTCCTGTAAGCTGCCCCGTGCCCTGGCCC ACCCTCGTGACCACCCTGAGCCACGGCGTGACAGTGCTTCGCCCCG CTACCCCGACCACATGAAGCAGCACGACTTCTTCAAGTCCGCCAT GCCCGAAGGC
BFP (ZIP_ExtraLong_Lock)	TGAGCACGCTTTGATGGCAGAAGCTGCCCCGTGCCCTGGCCCACC CTCGTGACCACCCTGAGCCACGGCGTGACAGTGCTTCGCCCCGCTA CCCCGACCACATGAAGCAGCACGACTTCTTCAAGTCCGCCATGCC CGAAGGCTACGTCCAGGAGCGCACCATCTTCTTCAAGGACGACG GCACCTACAAGAC
BFP (ZIP_Inv)	AAGCTGCCCCGTGCCCTGGCCCACCCTCGTGACCACCCTGAGCCA CGGCGTGACAGTGCTTCGCCCCGCTACCCCGACCACATGAAGCAGC ACGACTTCTTCAAGTCCGCCATGCCCGAAGGCTGAGCACGCTTTG ATGGCAG
BFP (ZIPmax_V2)	CGGAGAAAGAGGCTCGTTGTAACCCGGCGTAAGCTGCCCCGTGCC CTGGCCCACCCTCGTGACCACCCTGAGCCACGGCGTGACAGTGCT TCGCCCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCAAGT CCGCCATGCCCCGAAGGC
BFP (Super ZIPmax_Nick)	GGCAGCAGACTGAGCACGCTTTGATGGCAGCACCTACGGCAAGC TGACCCTGAAGTTCATCTGCACCACCGGCAAGCTGCCCCGTGCCCT GGCCCACCCTCGTGACCACCCTGAGCCACGGCGTGACAGTGCTTC GCCCGCTACCCCGACCA

Supplementary Table 3: HDR ssODN template sequences for CRISPR-Cas9 HDR editing (other targets).

HDR template	Sequence (5' to 3')
HBB (UNZIP_2)	TGACACAACCTGTGTTCACTAGCAACCTCAAACAGACACCATGGTGCATC TGACTCCCGAGGAAAAATCCGCAGTCACTGCCCTGTGGGGCAAGGTGA ACGTGGATGAAGTTGGTGGTGAG
HBB (ZIPmax)	GGCAGCAGACTGAGCACGCTTTGATGGCAGTGACACAACCTGTGTTCACT AGCAACCTCAAACAGACACCATGGTGCATCTGACTCCCGAGGAAAAATC CGCAGTCACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGG TGAG
UROS (UNZIP_2, UNZIP_Nick_2)	CTGAAGATTACGGGGGACTCATTTTTACCAGCCCCAGAGCAGTGGAAGC AGCAGAGCTCTGTTTAGAGCAAAACAATAAACTGAAGGTGAGGGTGGG TCTGCTGTGGATTCCACTGGAC
UROS (ZIPmax, ZIPmax_Nick)	GGCAGCAGACTGAGCACGCTTTGATGGCAGCTGAAGATTACGGGGGAC TCATTTTTACCAGCCCCAGAGCAGTGGAAGCAGCAGAGCTCTGTTTAGA GCAAAACAATAAACTGAAGGTGAGGGTGGGTCTGCTGTGGATTCCACT GGAC
CFTR_G542X_ modeling (UNZIP)	ACATCTCCAAGTTTGCAGAGAAAGACAATATAGTTCTTTAGGAGCTCGGA ATCACACTGAGTGGAGGTCAACGAGCAAGA
CFTR_G542X_ modeling (ZIPmax)	TGAGCACGCTTTGATGGCAGAATTTTCTATTTTTGGTAATAGGACATCTC CAAGTTTGCAGAGAAAGACAATATAGTTTAGGAGCTCGGAATCACACTG AGTGGAGGTCAACGAGCAAGAATTTCTTTAGCAAGGTGAAT
CFTR_G542X_ correction (UNZIP_2)	TTCTATTTTTGGTAATAGGACATCTCCAAGTTTGCAGAGAAAGATAACAT CGTCCTCGGAGAGGGTGGAATCACACTGAGTGGAGGTCAACGAGCAAG AATTTCTTTAGCAAGGTGAATA
CFTR_G542X_ correction (ZIPmax)	GGCAGCAGACTGAGCACGCTTTGATGGCAGTTCTATTTTTGGTAATAGG ACATCTCCAAGTTTGCAGAGAAAGATAACATCGTCCTCGGAGAGGGTGG AATCACACTGAGTGGAGGTCAACGAGCAAGAATTTCTTTAGCAAGGTGA ATA
SORCS1 (UNZIP_2)	GCTCTGAATGGCAGCTGGTCAAAGTAGATTACAAGTCCATTTTTGATAGA CGGTGTGCCGAGCTCTACAGACCTTGGCAGCTGCACAGCCAGGTAGGA GGAAAAGAACTGAGACTAAGGC
SORCS1 (ZIPmax)	GGCAGCAGACTGAGCACGCTTTGATGGCAGGCTCTGAATGGCAGCTGG TCAAAGTAGATTACAAGTCCATTTTTGATAGACGGTGTGCCGAGCTCTAC AGACCTTGGCAGCTGCACAGCCAGGTAGGAGGAAAAGAACTGAGACTA AGGC

Supplementary Table 4: PCR primer sequences.

PCR primers	Sequence (5' to 3')
HBB_424pb_F	CTGATGGTATGGGGCCAAGAG
HBB_424pb_R	GTCTCCACATGCCCAGTTTCT
UROS_405pb_F (RFLP analysis)	TAGTTCCAGGCACATAGTAAGCAC
UROS_405pb_R (RFLP analysis)	TCCCAAGGCAGAGTCTGTGA
UROS_1kb_F (Nanopore sequencing)	CTCTAATCCCAGGCTGCGTC
UROS_1kb_R (Nanopore sequencing)	GCCTCCGCTCATCAGTGTA
CFTR_415pb_F (RFLP analysis)	CAGCAATGTTGTTTTTGACCAACT
CFTR_415pb_R (RFLP analysis)	ACCCACTAGCCATAAAACCCC
CFTR_1kb_F (Nanopore sequencing)	AGGTCGTGAGAATGAGGTGC
CFTR_1kb_R (Nanopore sequencing)	TGGAGTGGCAGGGTCTATGA
SORCS1_484pb_F	TGAACGCCCCACAAATGCTC
SORCS1_484pb_R	TTGGATCTGAGTGCTGAACTGG

Supplementary Table 5: Command for nCRISPResso2 analysis.

```

GUIDE="GACAATATAGTTCTTTGAGA"
AMPSEQ_REF="cagcaatgttggttttgaccaactaaataaattgcatttgaaataatggagatgcaatgtt
caaaatttcaactgtggttaaagcaatagtgatataatgattacattagaaggaagatgtgcctttcaaatt
cagattgagcataactaaaagtgactctctaattttctattttttggaatagGACATCTCCAAGTTTGCAGAGA
AAGACAATATAGTTCTTGGAGAAGGTGGAATCACACTGAGTGGAGGTCAACGAGCAAGAATTTCTTTAGCAAG
gtgaataactaattatttggtctagcaagcatttgctgtaaatgtcattcatgtaaaaaaattacagacatttc
tctattgctttatattctgtttctggaattgaaaaaatcctgggggttttatggctagtgggt"
AMPSEQ_HTZ="cagcaatgttggttttgaccaactaaataaattgcatttgaaataatggagatgcaatgtt
caaaatttcaactgtggttaaagcaatagtgatataatgattacattagaaggaagatgtgcctttcaaatt
cagattgagcataactaaaagtgactctctaattttctattttttggaatagGACATCTCCAAGTTTGCAGAGA
AAGACAATATAGTTCTTTGAGAAGGTGGAATCACACTGAGTGGAGGTCAACGAGCAAGAATTTCTTTAGCAAG
gtgaataactaattatttggtctagcaagcatttgctgtaaatgtcattcatgtaaaaaaattacagacatttc
tctattgctttatattctgtttctggaattgaaaaaatcctgggggttttatggctagtgggt"
HDRSEQ="cagcaatgttggttttgaccaactaaataaattgcatttgaaataatggagatgcaatgttcaaa
atttcaactgtggttaaagcaatagtgatataatgattacattagaaggaagatgtgcctttcaaattcaga
ttgagcataactaaaagtgactctctaattttctattttttggaatagGACATCTCCAAGTTTGCAGAGAAAGA
TAACATCGTCCTCGGAGAGGGTGGGAATCACACTGAGTGGAGGTCAACGAGCAAGAATTTCTTTAGCAAGgtga
ataactaattatttggtctagcaagcatttgctgtaaatgtcattcatgtaaaaaaattacagacatttcctta
ttgctttatattctgtttctggaattgaaaaaatcctgggggttttatggctagtgggt"
CRISPResso \
  --fastq_r1 "$fq" \
  --amplicon_seq "$AMPSEQ_HTZ,$AMPSEQ_REF" \
  --amplicon_name "HTZ,REF" \
  --flexiguide_seq "$GUIDE" --flexiguide_homology 90 \
  --ignore_substitutions \
  --expected_hdr_amplicon_seq "$HDRSEQ" \
  --default_min_aln_score 60 \
  --min_bp_quality_or_N 13 \
  --plot_window_size 20 \
  --min_frequency_alleles_around_cut_to_plot 0.1 \
  --quantification_window_size 10 \
  --quantification_window_center 0 \
  --cleavage_offset -3 \
  --exclude_bp_from_left 100 \
  --exclude_bp_from_right 100 \
  --min_average_read_quality 10 \
  -p 20 \
  --name "$name"

```

Supplementary Table 6: RTqPCR primer sequences.

RTqPCR primers	Sequence (5' to 3')
BRCA2_RTqPCR_F	CCAAGTGGTCCACCCCAAC
BRCA2_RTqPCR_R	GGCTGAGACAGGTGTGGAAA
GAPDH_RTqPCR_F	CTGCACCACCAACTGCTTAG
GAPDH_RTqPCR_R	AGGTCCACCACTGACACGTT