

FIG. 28A

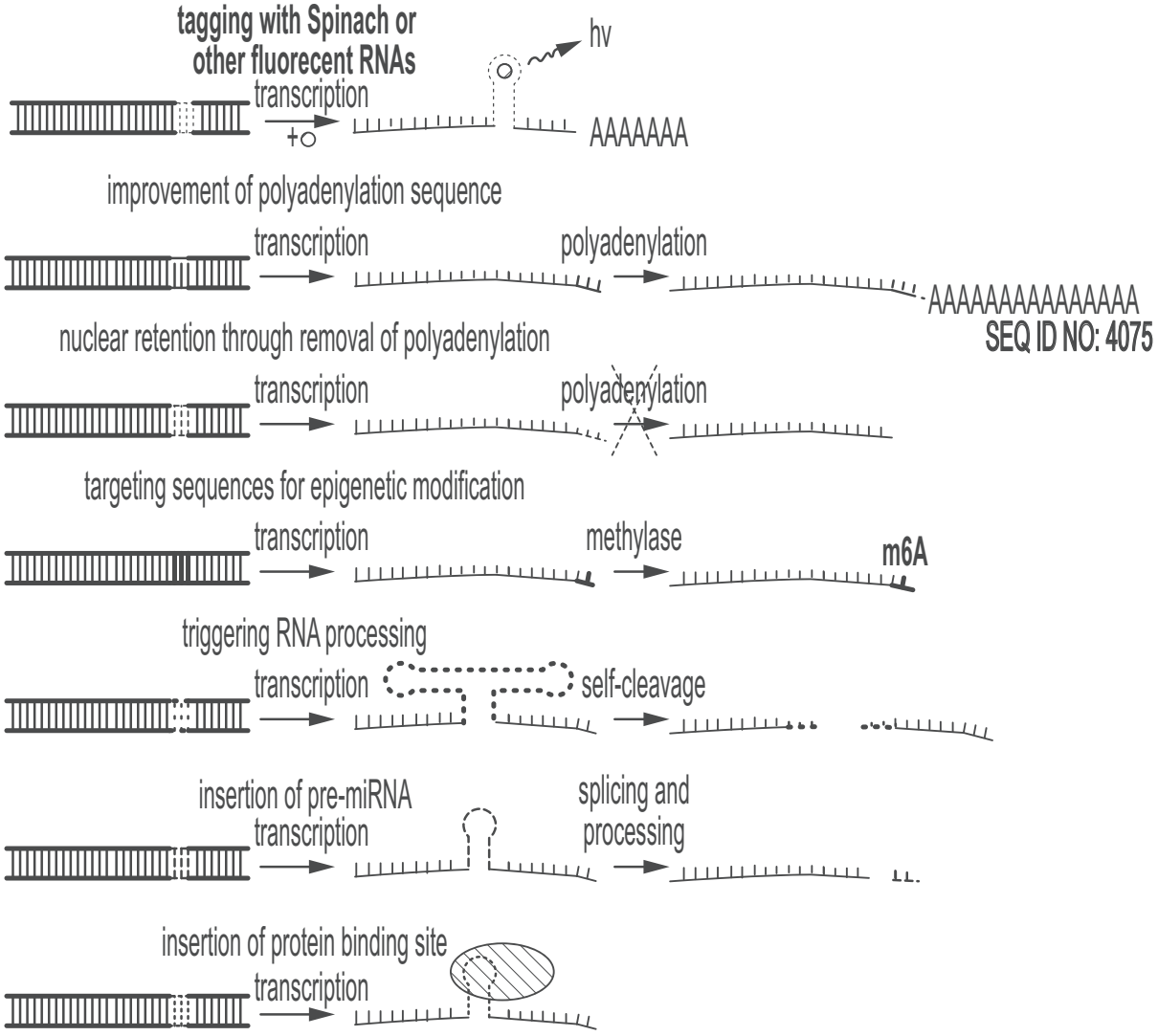


FIG. 28B

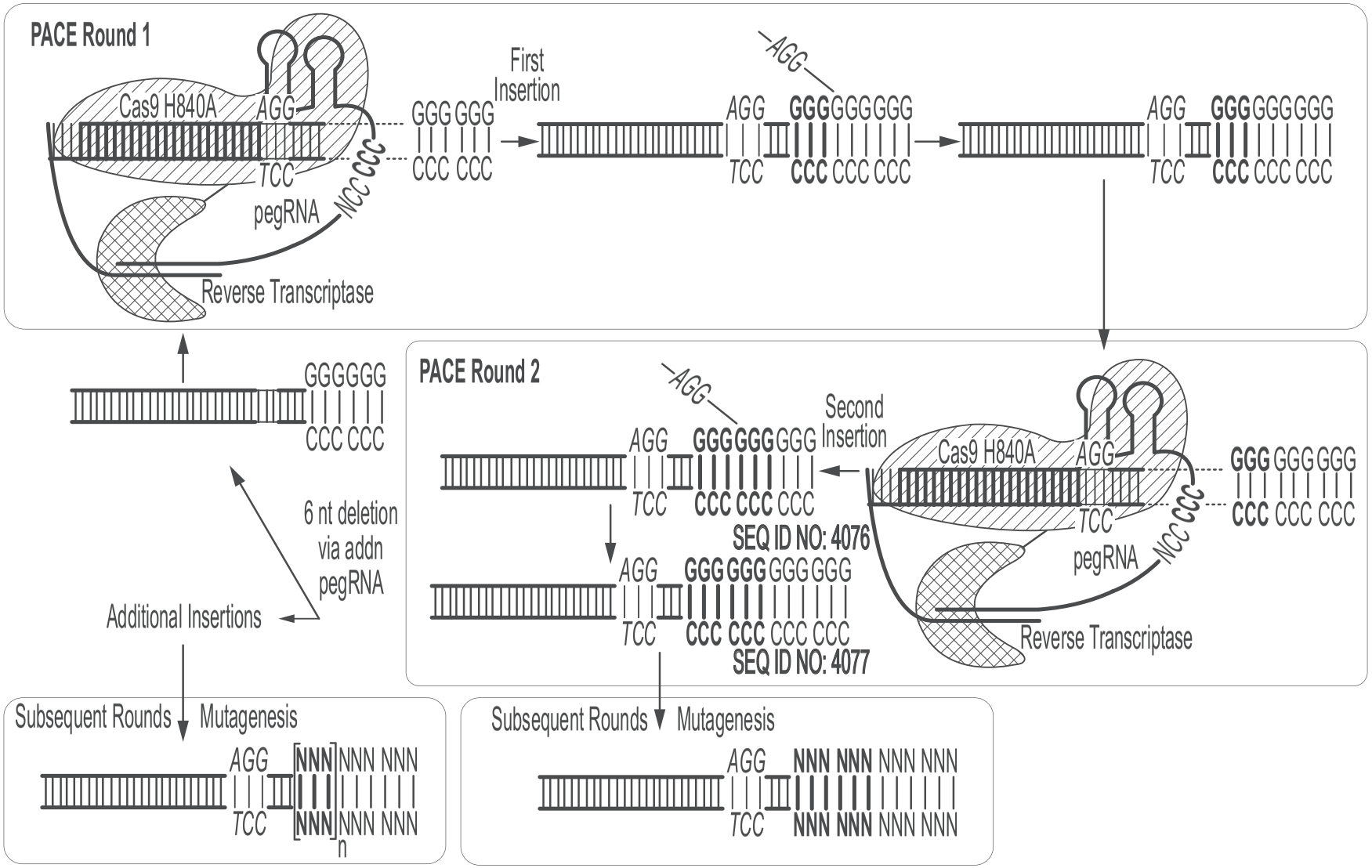

PACE Round 1
Cas9 H840A
AGG
TCC
pegRNA
NCC
Reverse Transcriptase
GGG GGG
CCC CCC
First Insertion
AGG
GGGGGGGGG
TCC
CCC CCC CCC
GGGGGG
CCC CCC
6 nt deletion via addn pegRNA
Additional Insertions
PACE Round 2
Second Insertion
SEQ ID NO: 4076
SEQ ID NO: 4077
Subsequent Rounds
Mutagenesis
NNN NNN NNN NNN
n

FIG. 30

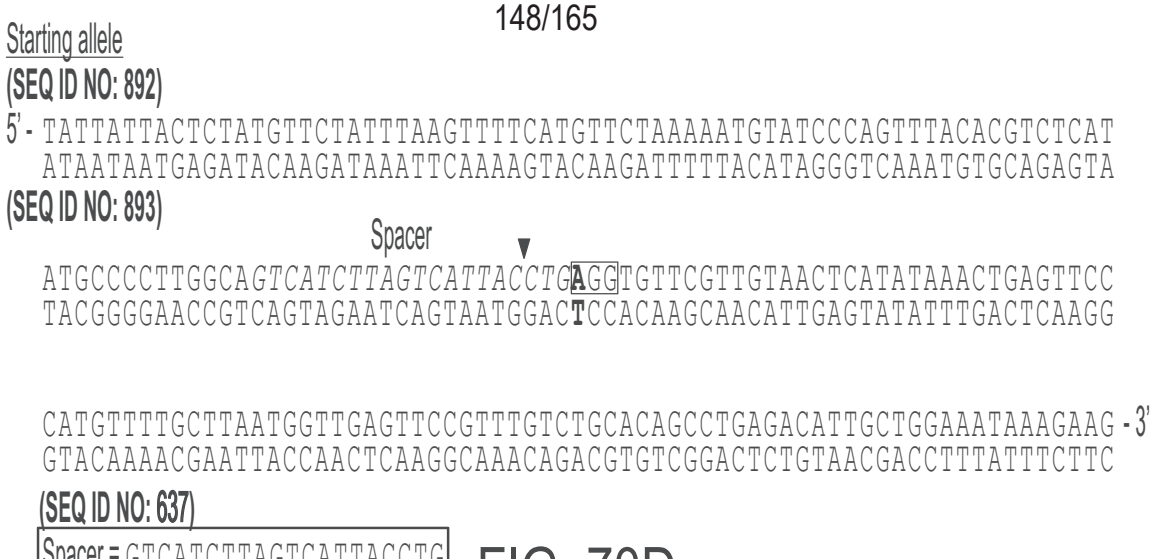


FIG. 70D



FIG. 70E

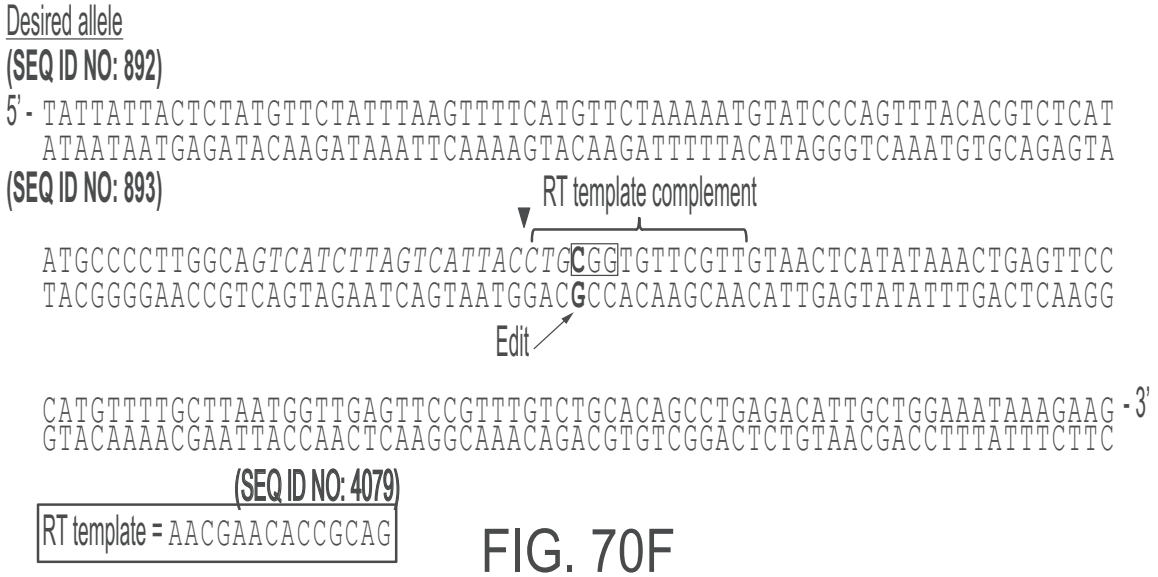


FIG. 70F



FIG. 70G

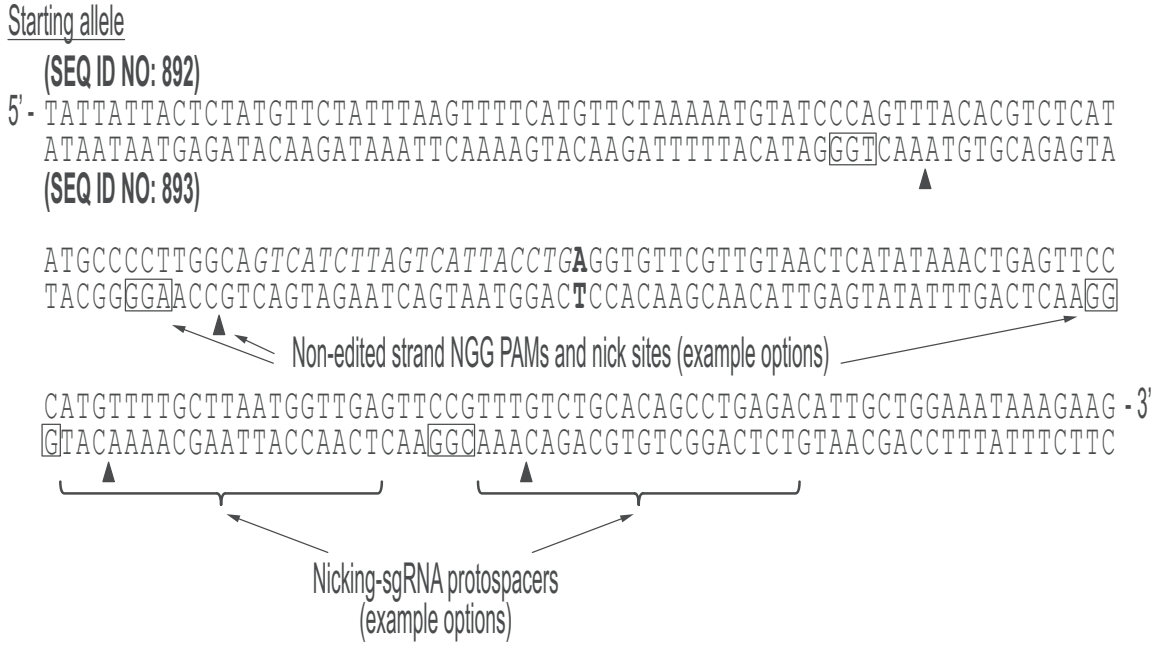


FIG. 70H



FIG. 70I

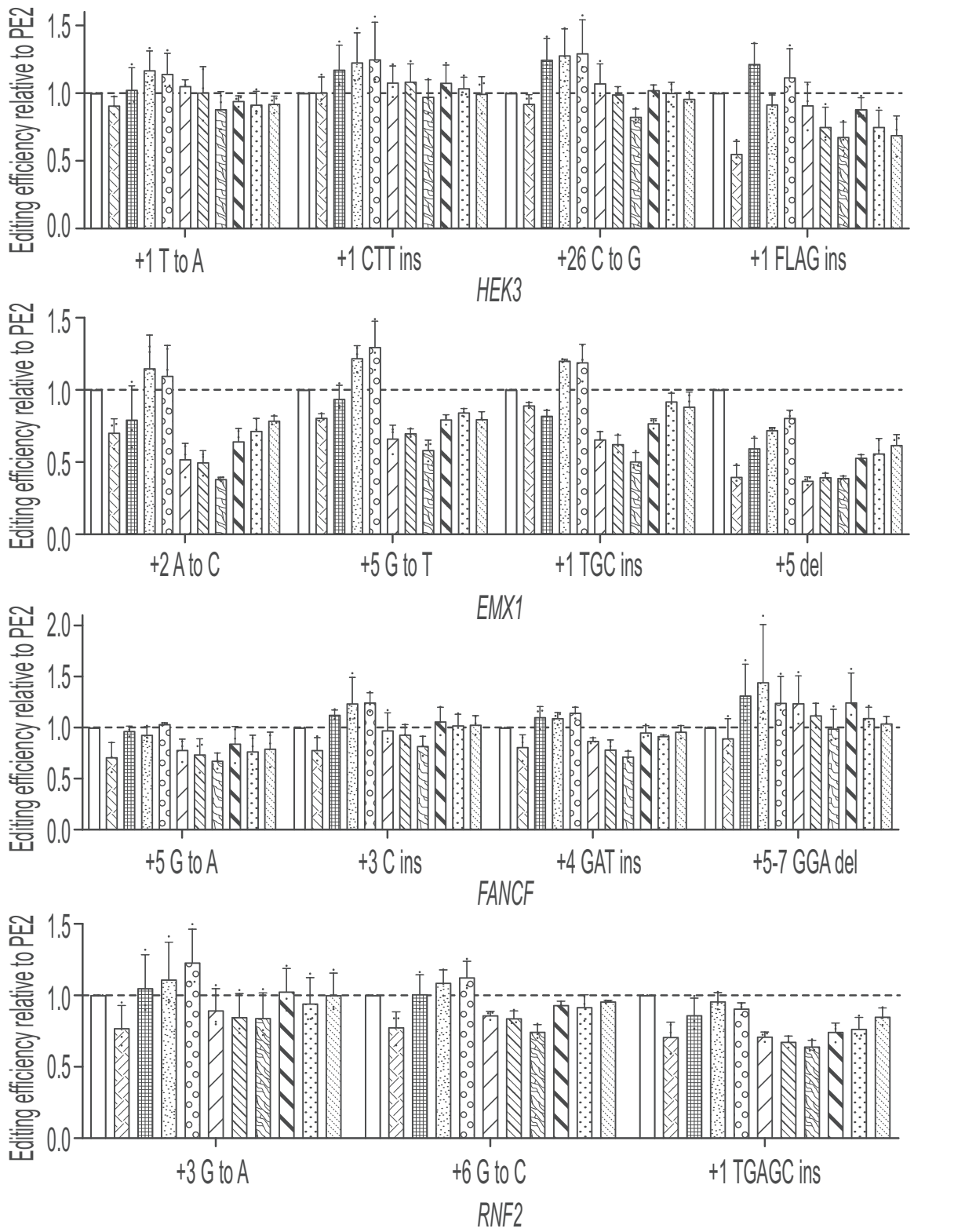

Editing efficiency relative to PE2
1.5
1.0
0.5
0.0
+1 T to A
+1 CTT ins
+26 C to G
+1 FLAG ins
HEK3
Editing efficiency relative to PE2
1.5
1.0
0.5
0.0
+2 A to C
+5 G to T
+1 TGC ins
+5 del
EMX1
Editing efficiency relative to PE2
2.0
1.5
1.0
0.5
0.0
+5 G to A
+3 C ins
+4 GAT ins
+5-7 GGA del
FANCF
Editing efficiency relative to PE2
1.5
1.0
0.5
0.0
+3 G to A
+6 G to C
+1 TGAGC ins
RNF2
PE2
1x SGGS (SEQ ID NO: 174)
2x SGGS (SEQ ID NO: 446)
3x SGGS (SEQ ID NO: 3889)
1x XTEN (SEQ ID NO: 171)
No linker
1x Gly
1x Pro
1x EAAAK (SEQ ID NO: 3968)
2x EAAAK (SEQ ID NO: 3969)
3x EAAAK (SEQ ID NO: 3970)

FIG. 79

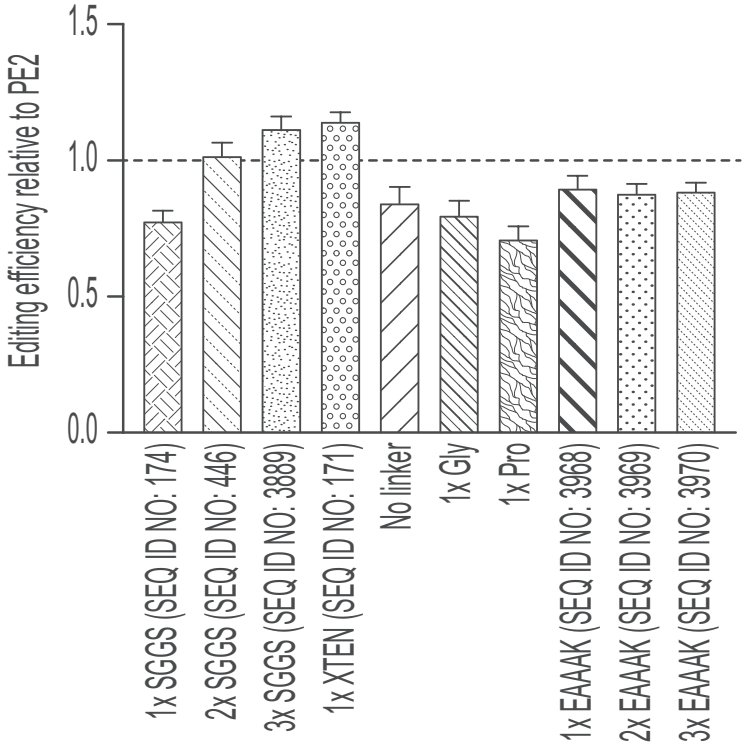

Editing efficiency relative to PE2
1.5
1.0
0.5
0.0
1x SGGS (SEQ ID NO: 174)
2x SGGS (SEQ ID NO: 446)
3x SGGS (SEQ ID NO: 3889)
1x XTEN (SEQ ID NO: 171)
No linker
1x Gly
1x Pro
1x EAAAK (SEQ ID NO: 3968)
2x EAAAK (SEQ ID NO: 3969)
3x EAAAK (SEQ ID NO: 3970)

FIG. 80

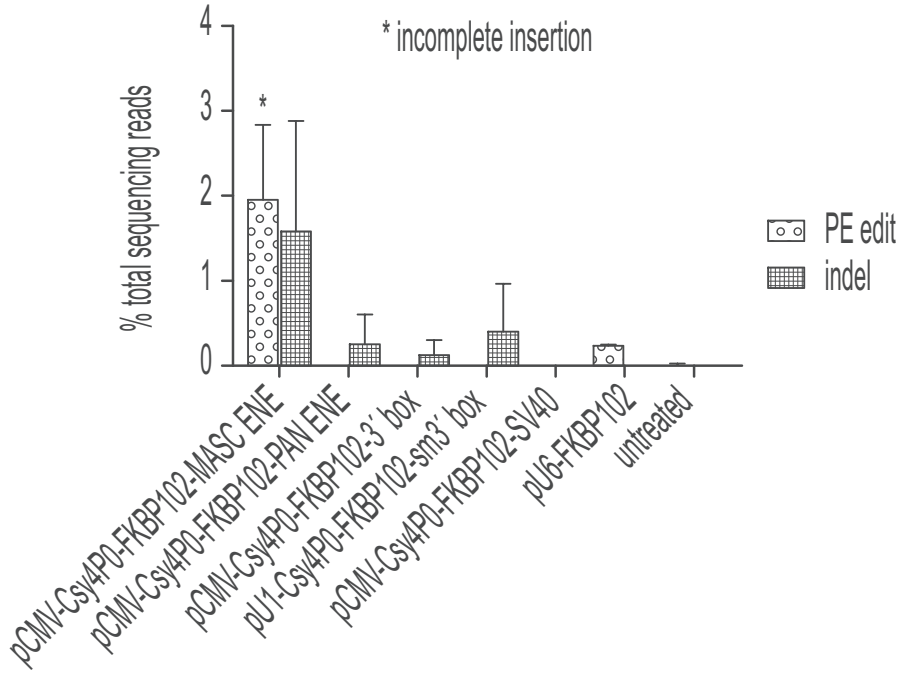

* incomplete insertion
% total sequencing reads
4
3
2
1
0
*
PE edit
indel
pCMV-Csy4P0-FKBP102-MASC ENE
pCMV-Csy4P0-FKBP102-PAN ENE
pCMV-Csy4P0-FKBP102-3' box
pU1-Csy4P0-FKBP102-sm3' box
pCMV-Csy4P0-FKBP102-SV40
pU6-FKBP102
untreated

FIG. 81

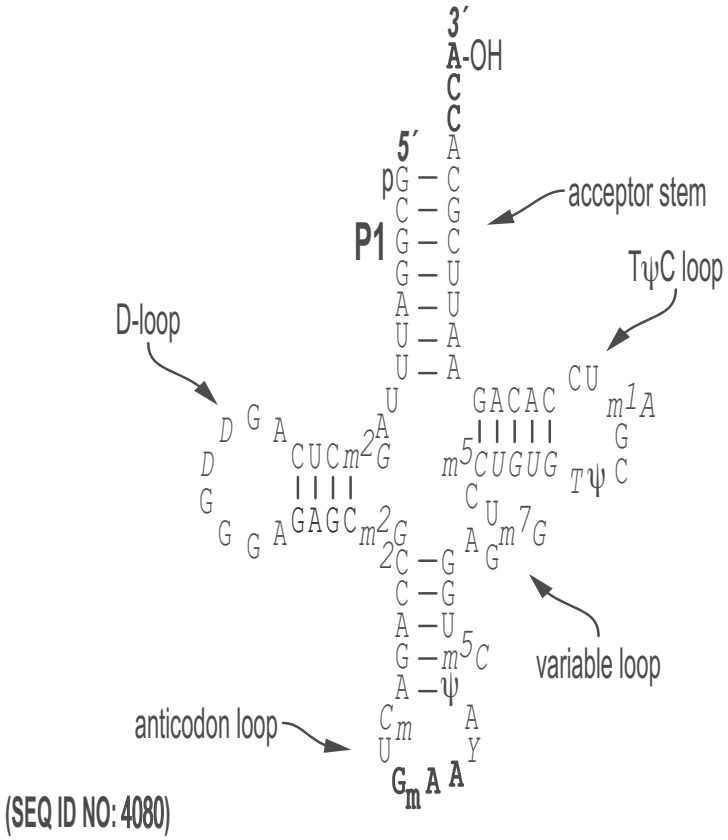


FIG. 84A

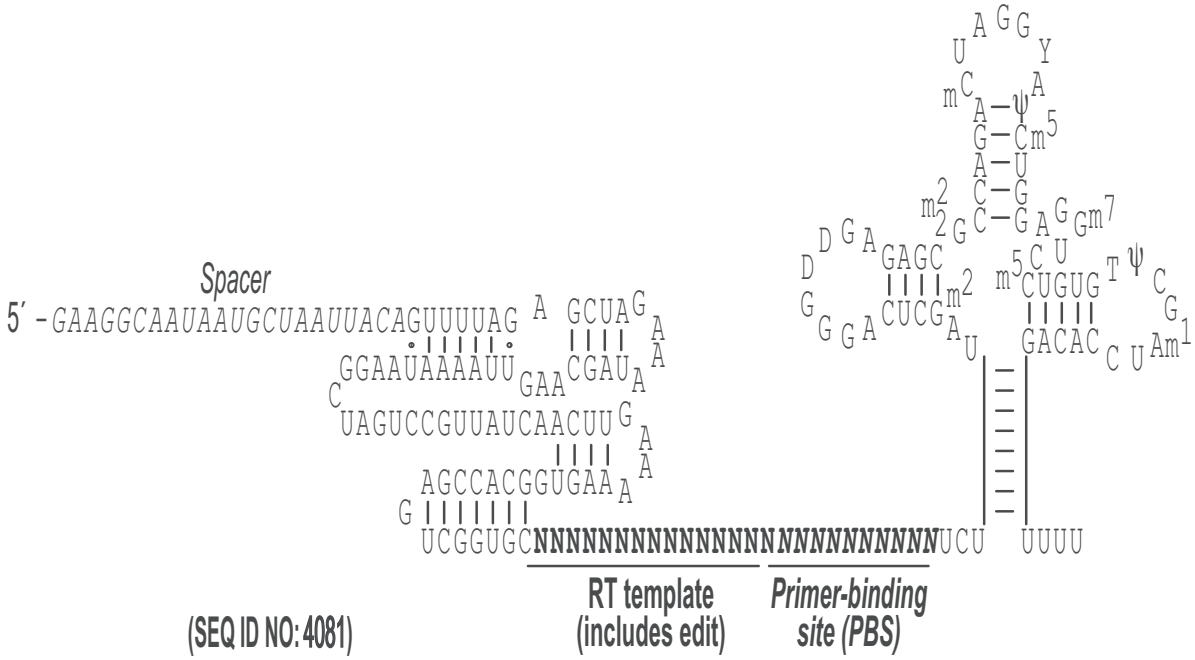


FIG. 84B