

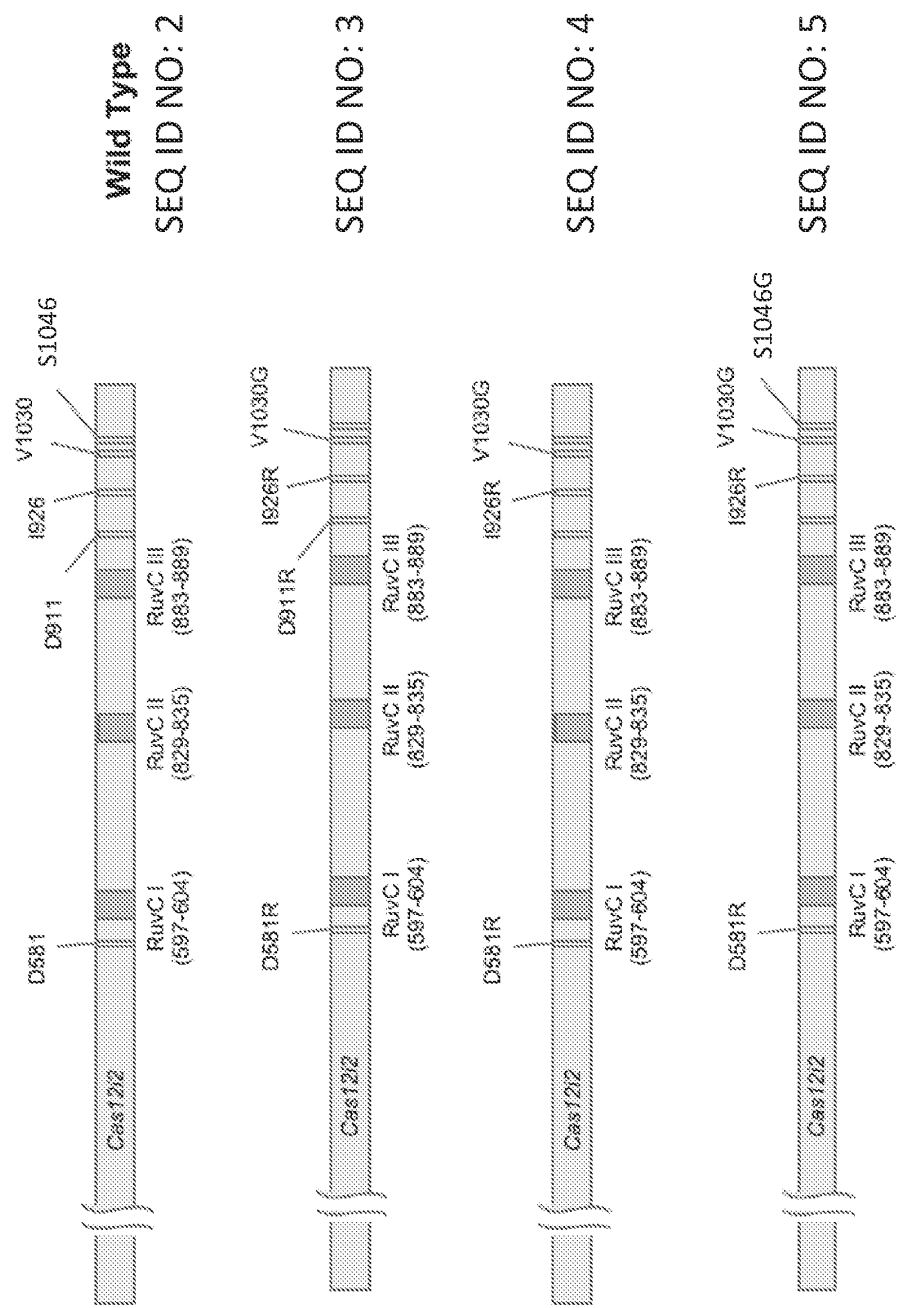


FIG. 1

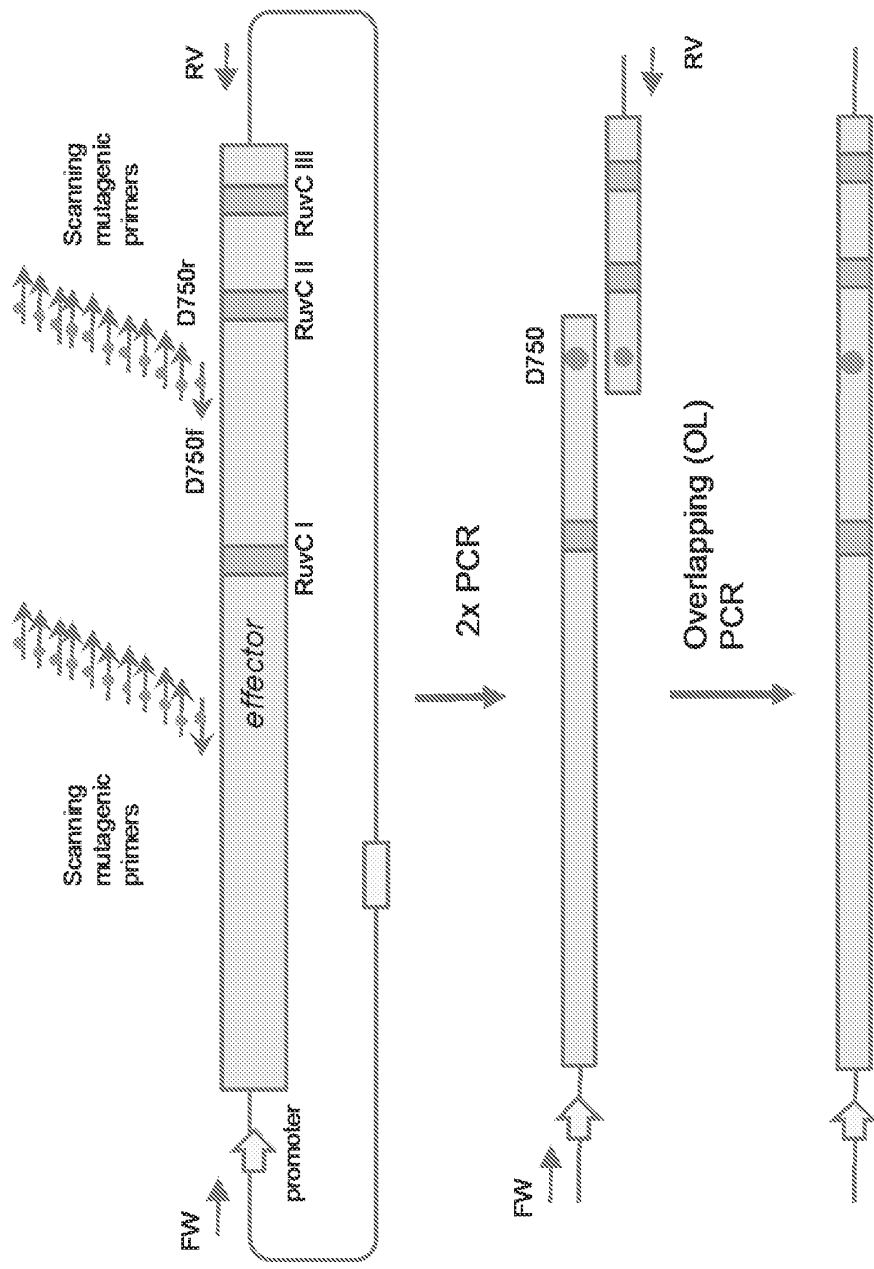


Fig. 2

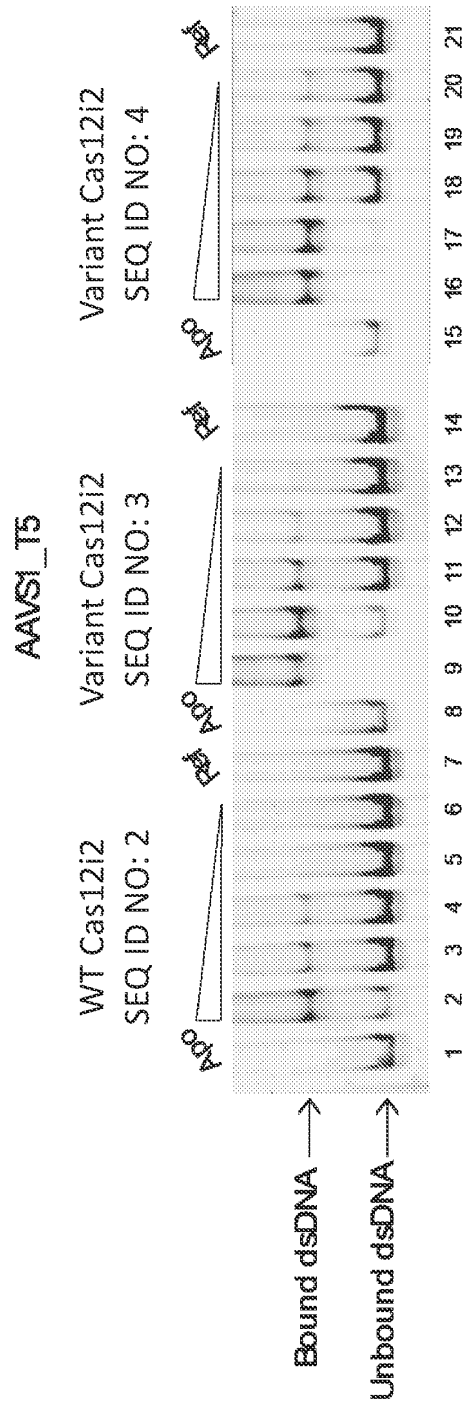


FIG. 3A

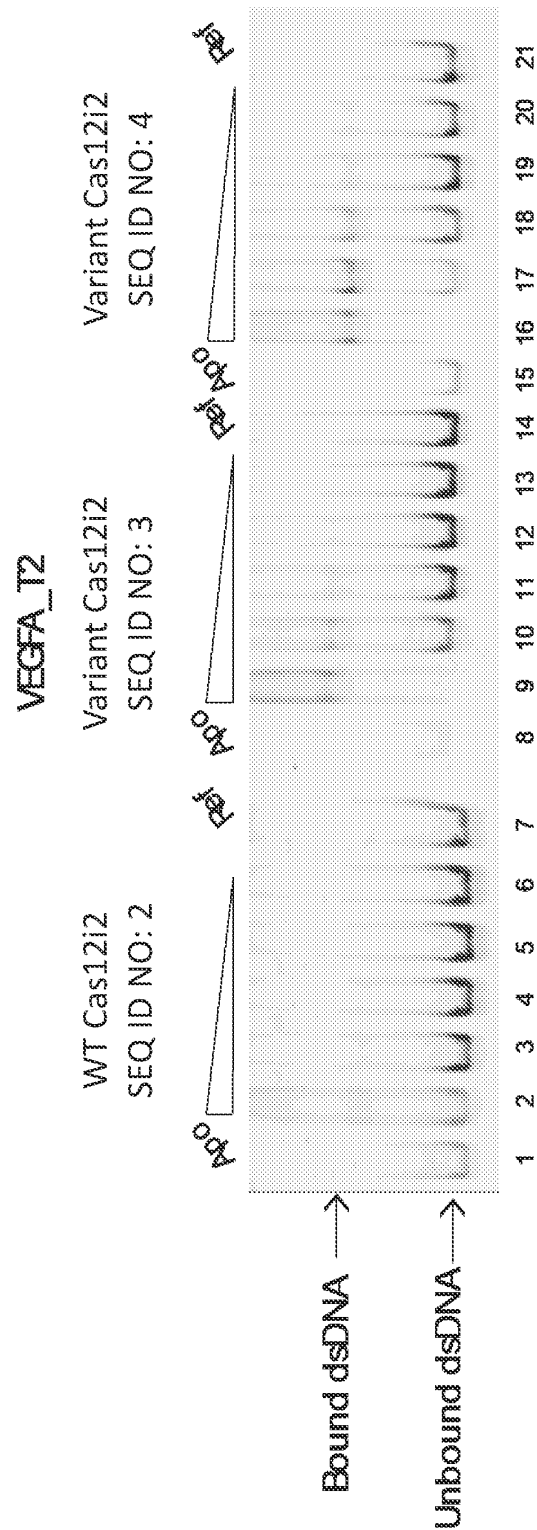


FIG. 3B

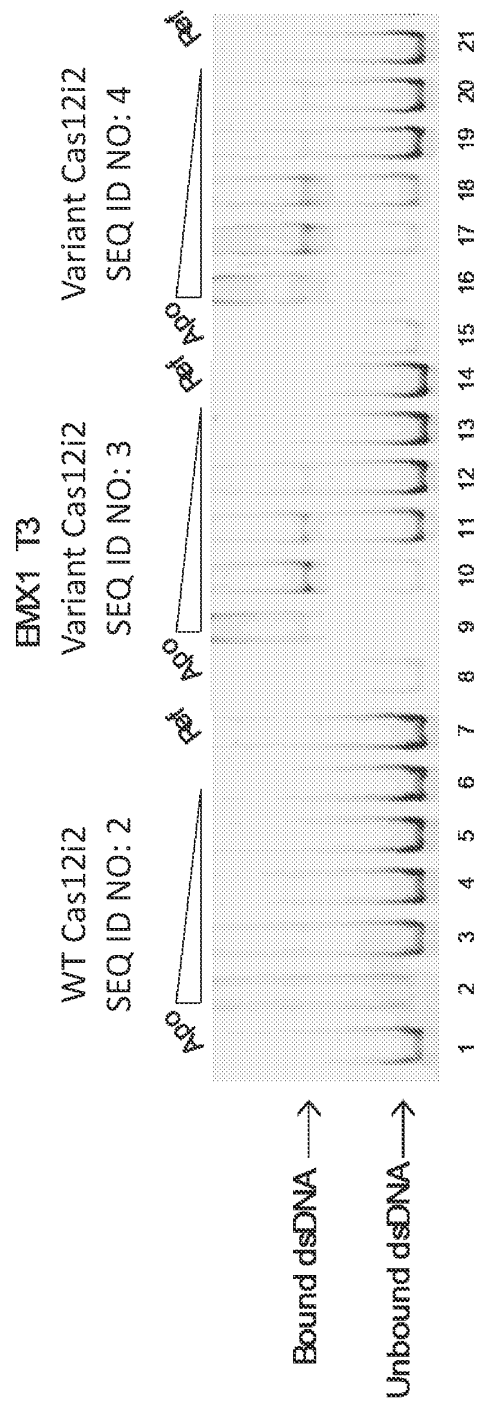


FIG. 3C

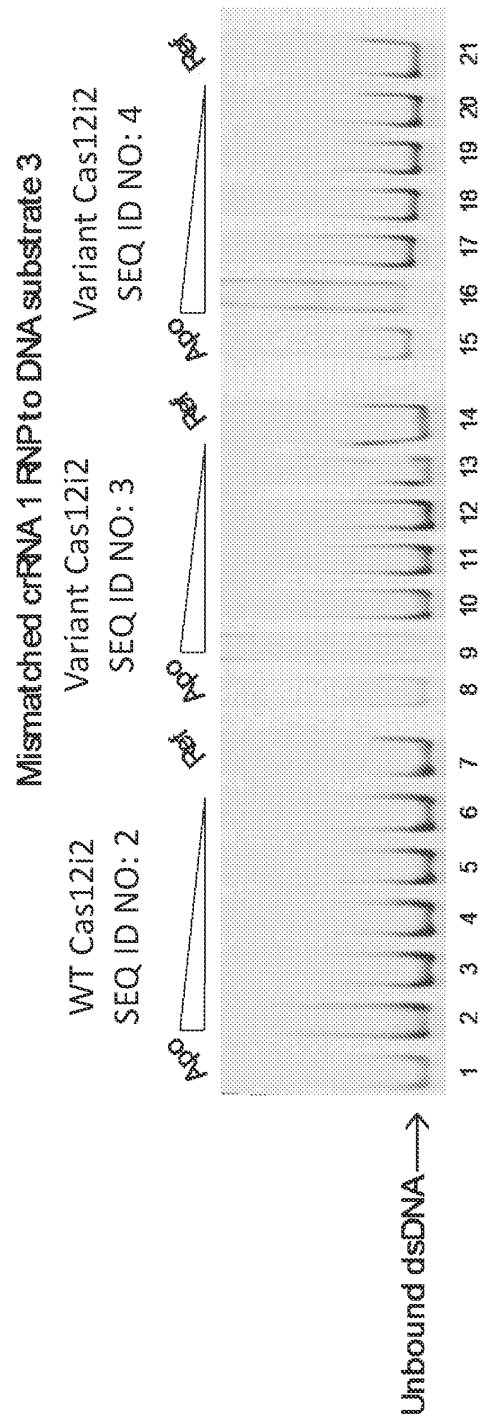
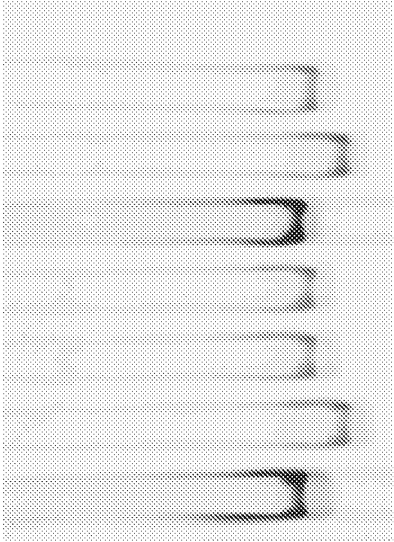


FIG. 3D

crRNA and DNA substrate alone

crRNA 1: DNA 1
crRNA 2: DNA 2
crRNA 3: DNA 3
crRNA 1: DNA 3
crRNA 1: DNA 2
crRNA 2: DNA 3
crRNA 3: DNA 1
crRNA 3: DNA 2
crRNA 2: DNA 1



1 2 3 4 5 6 7

FIG. 3E

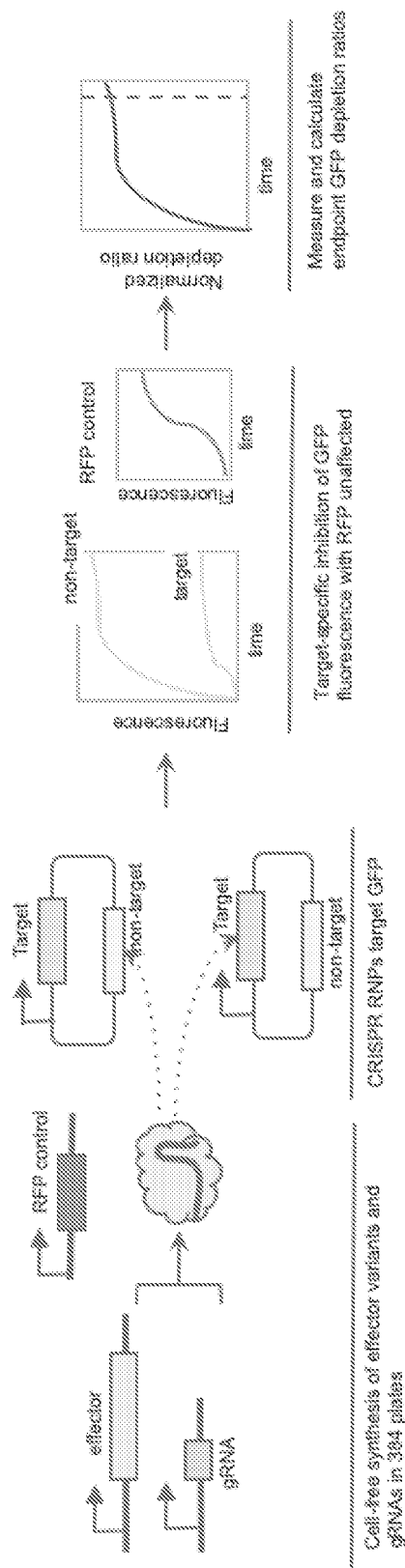


FIG. 4

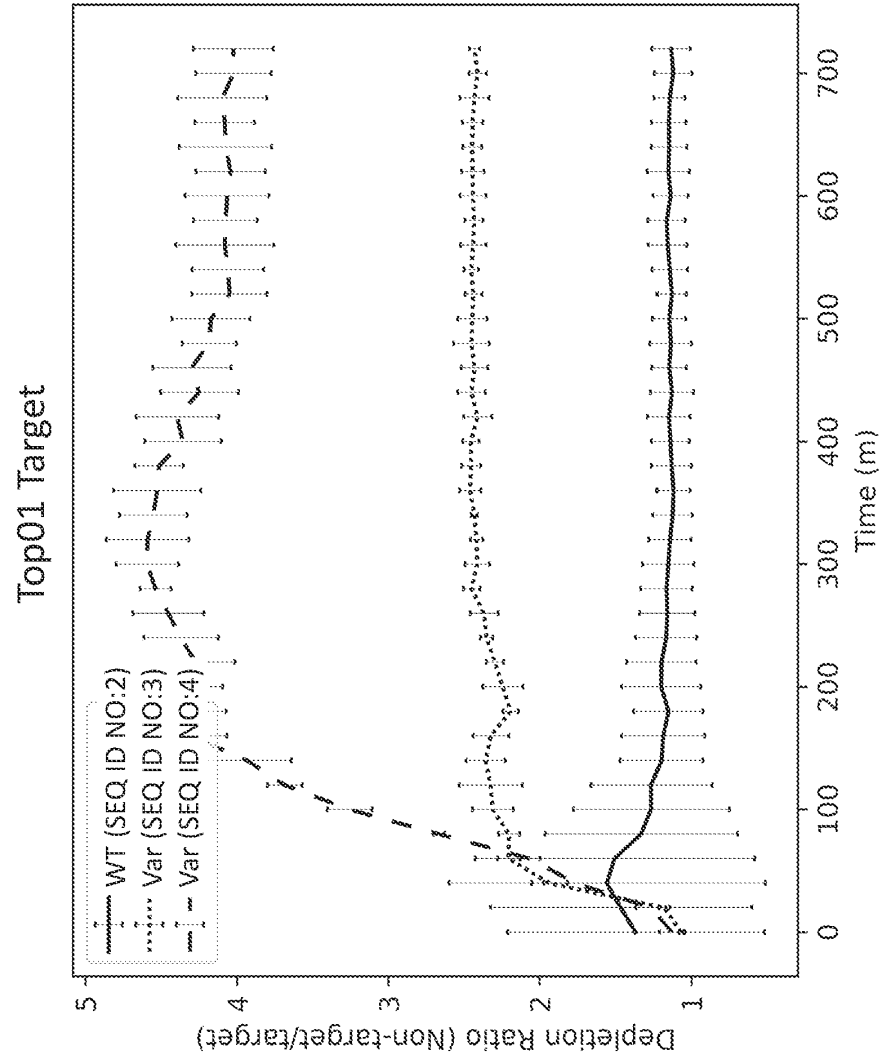


FIG. 5A

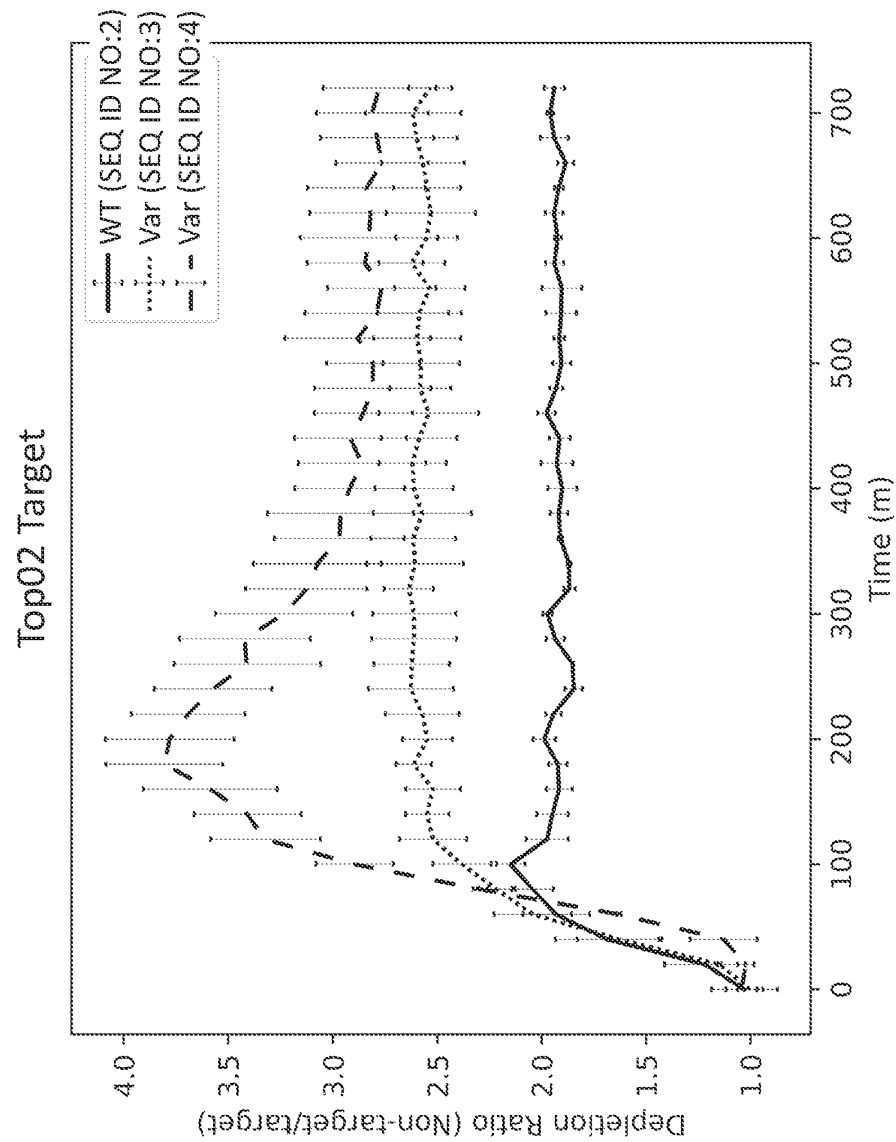


FIG. 5B

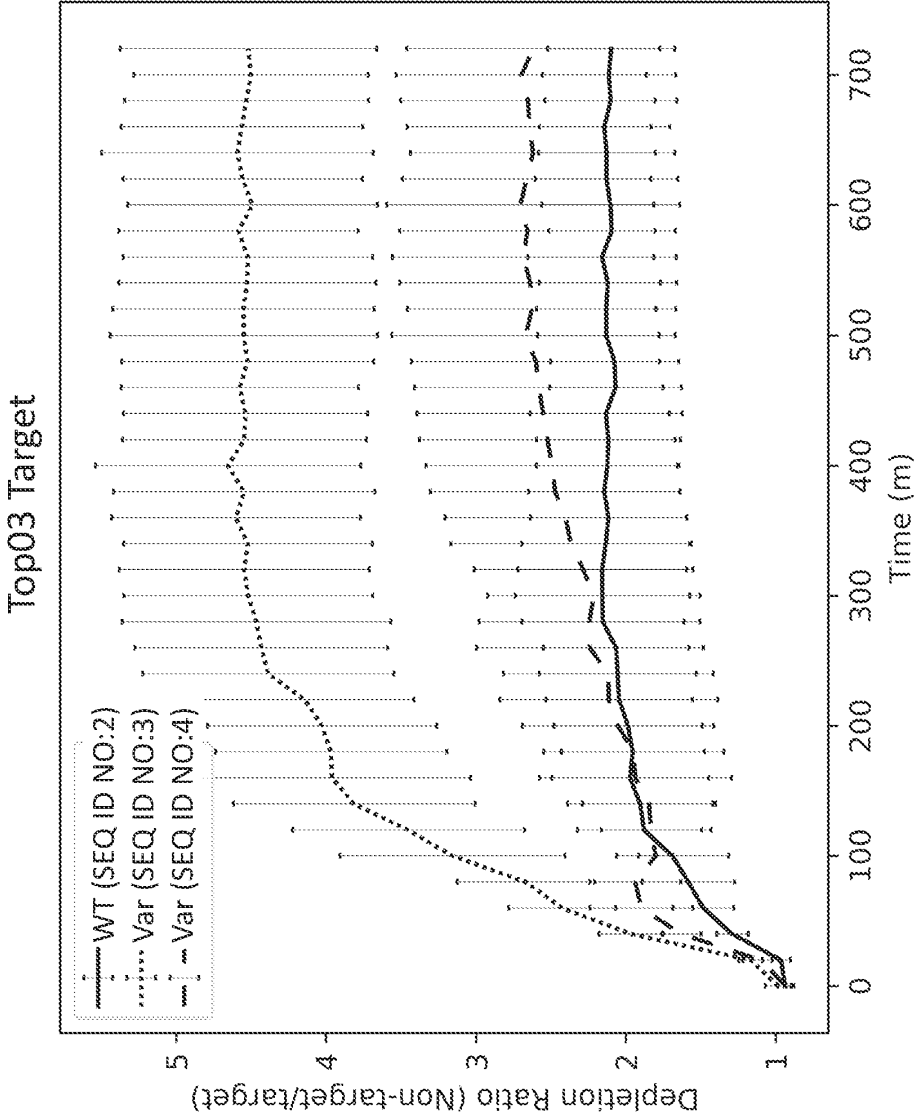


FIG. 5C

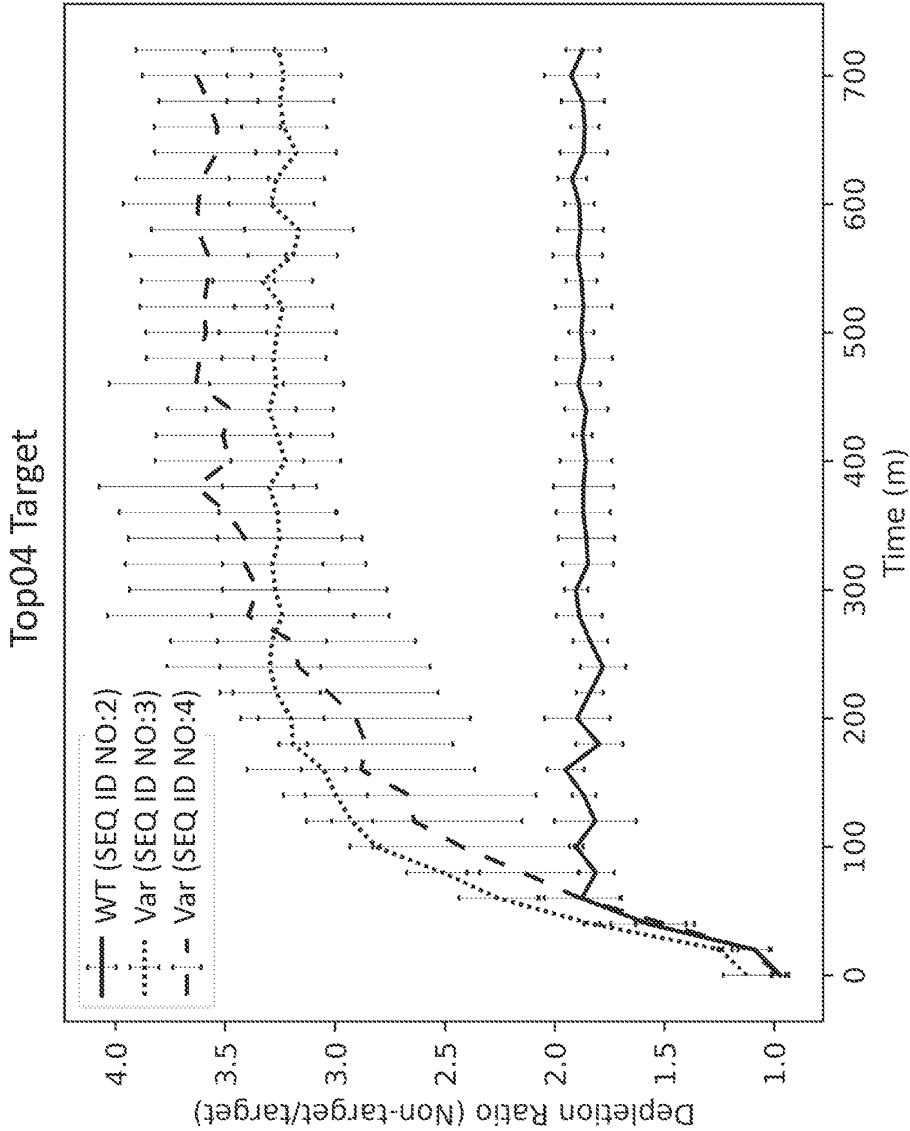


FIG. 5D

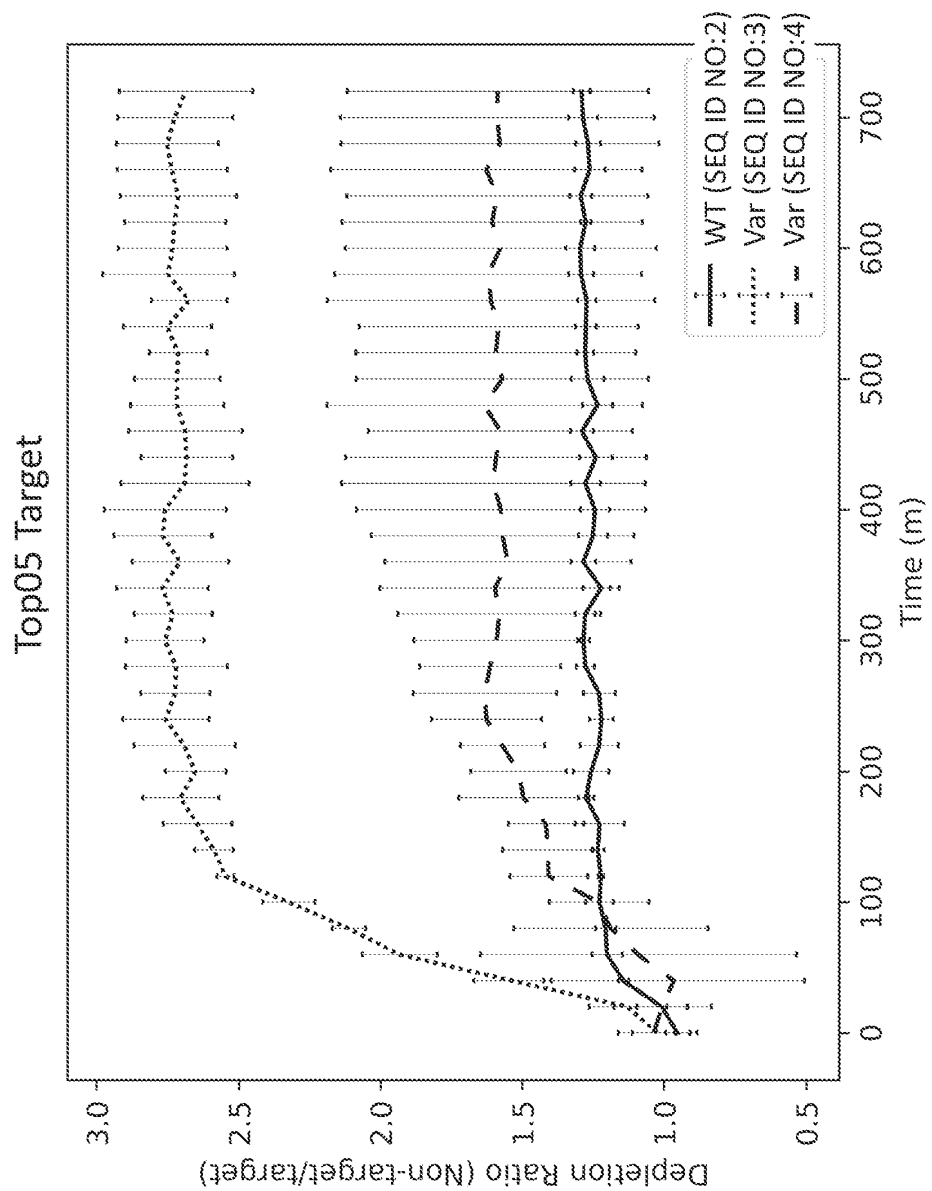


FIG. 5E

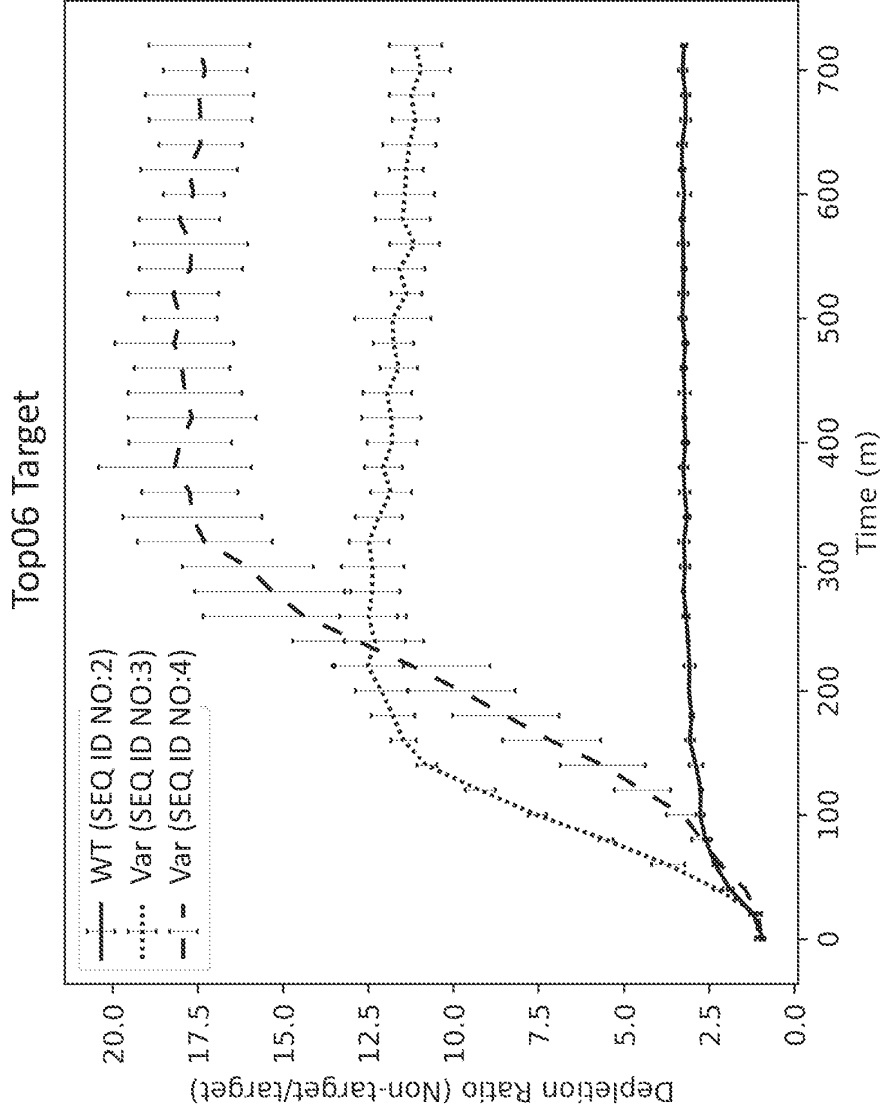


FIG. 5F

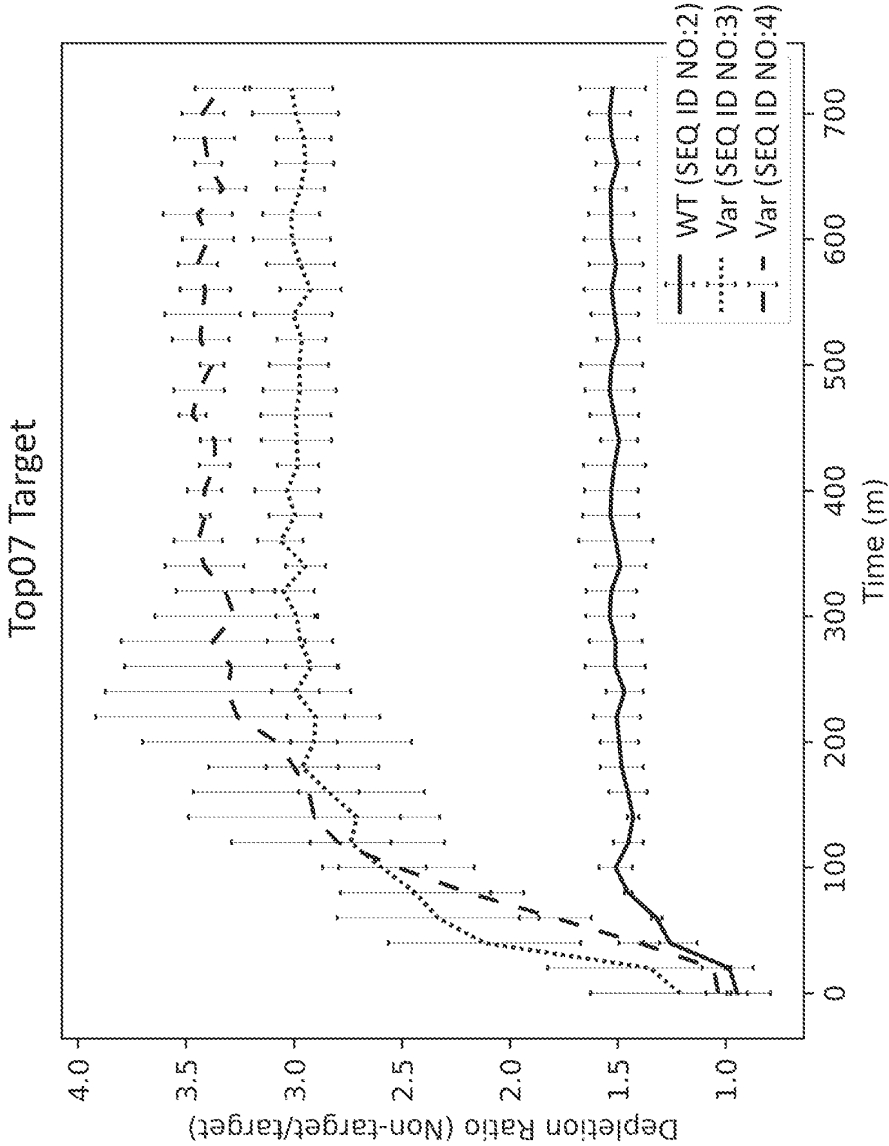


FIG. 5G

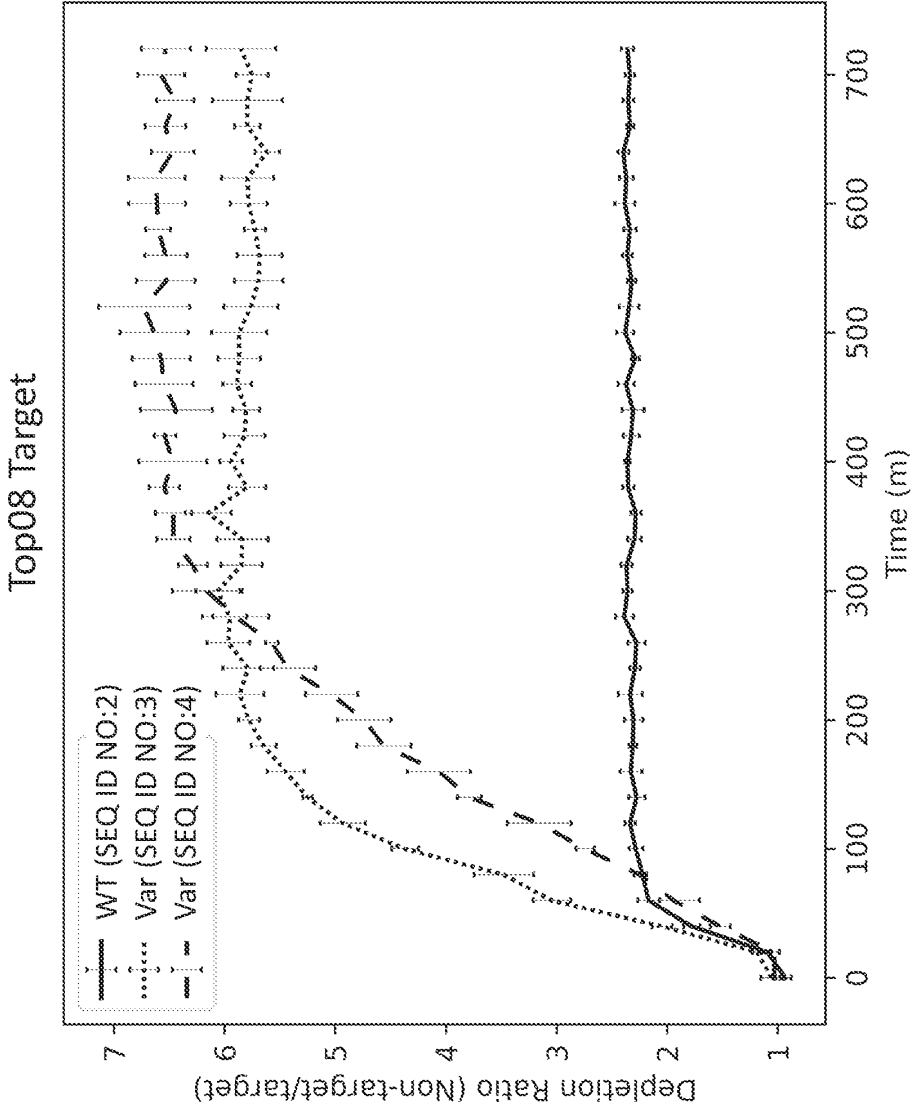


FIG. 5H

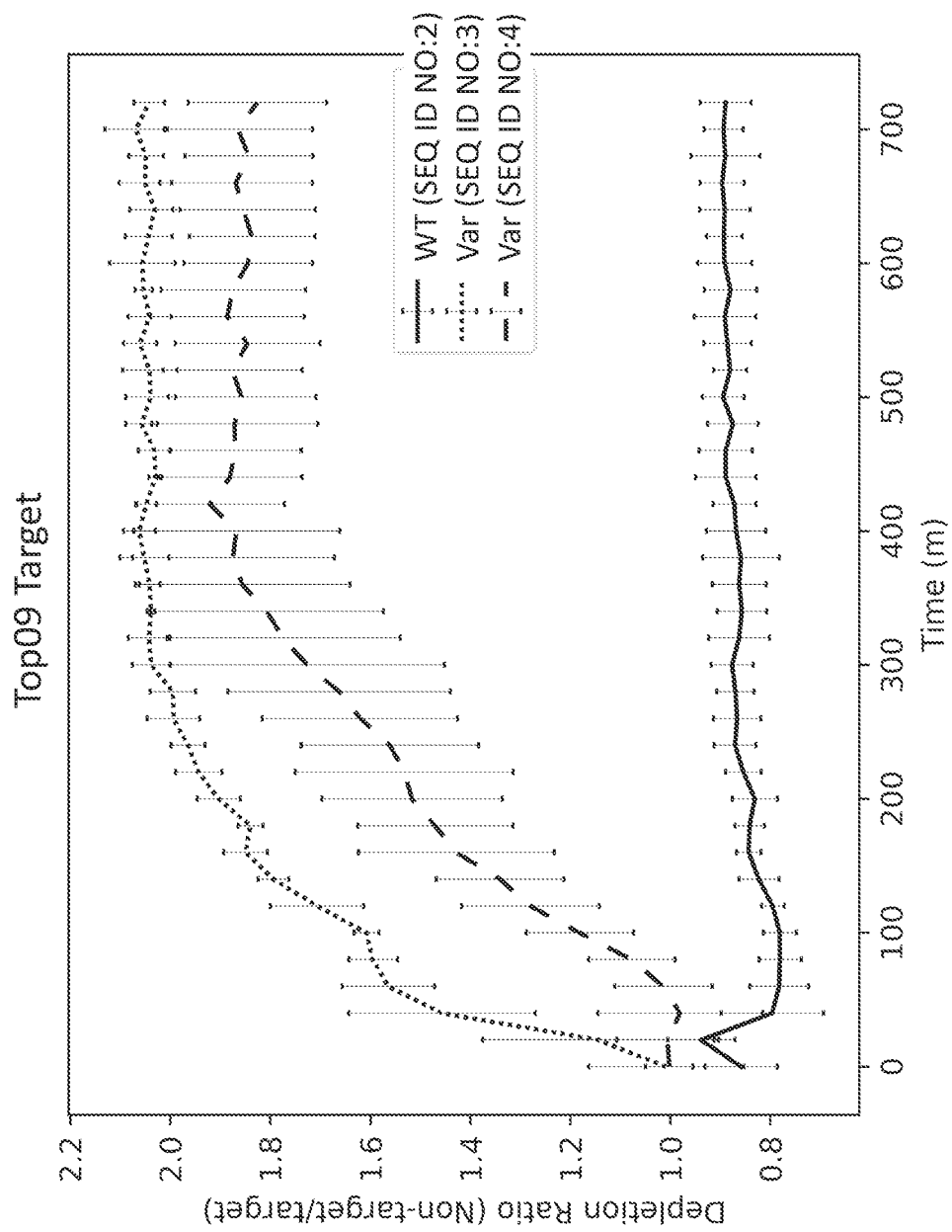


FIG. 5I

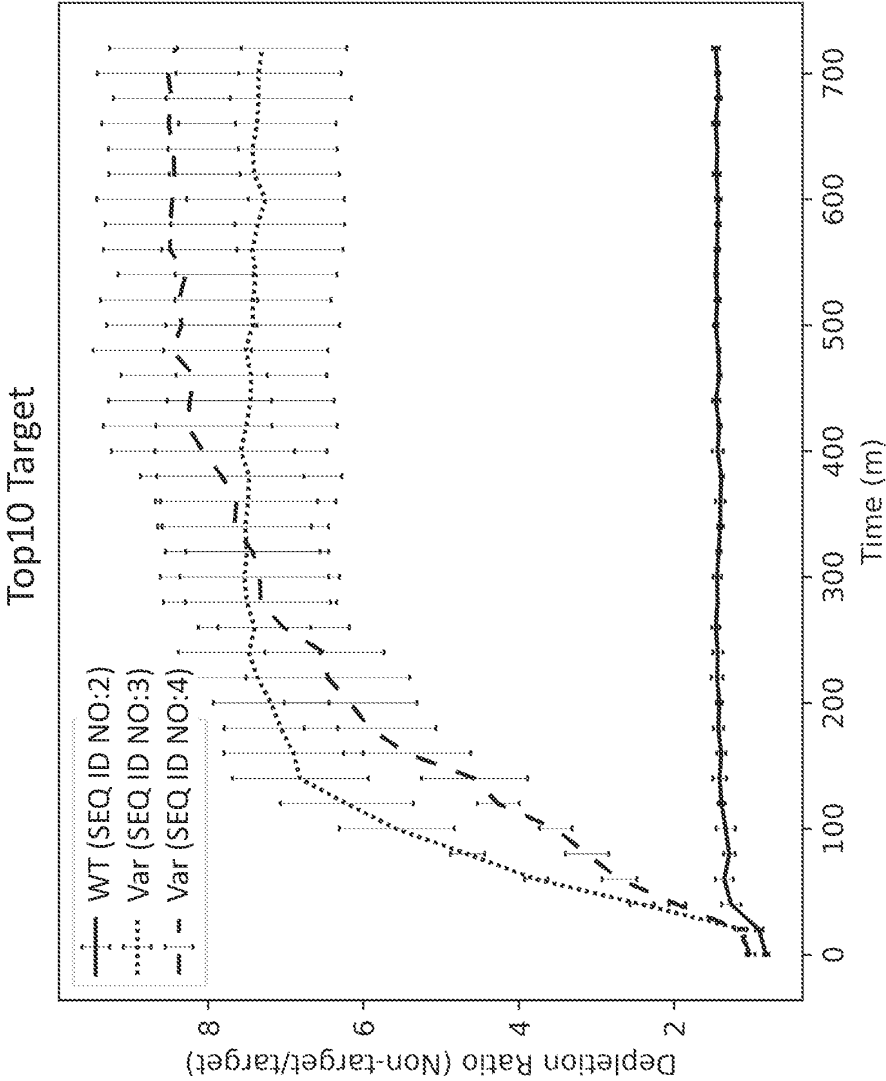


FIG. 5J

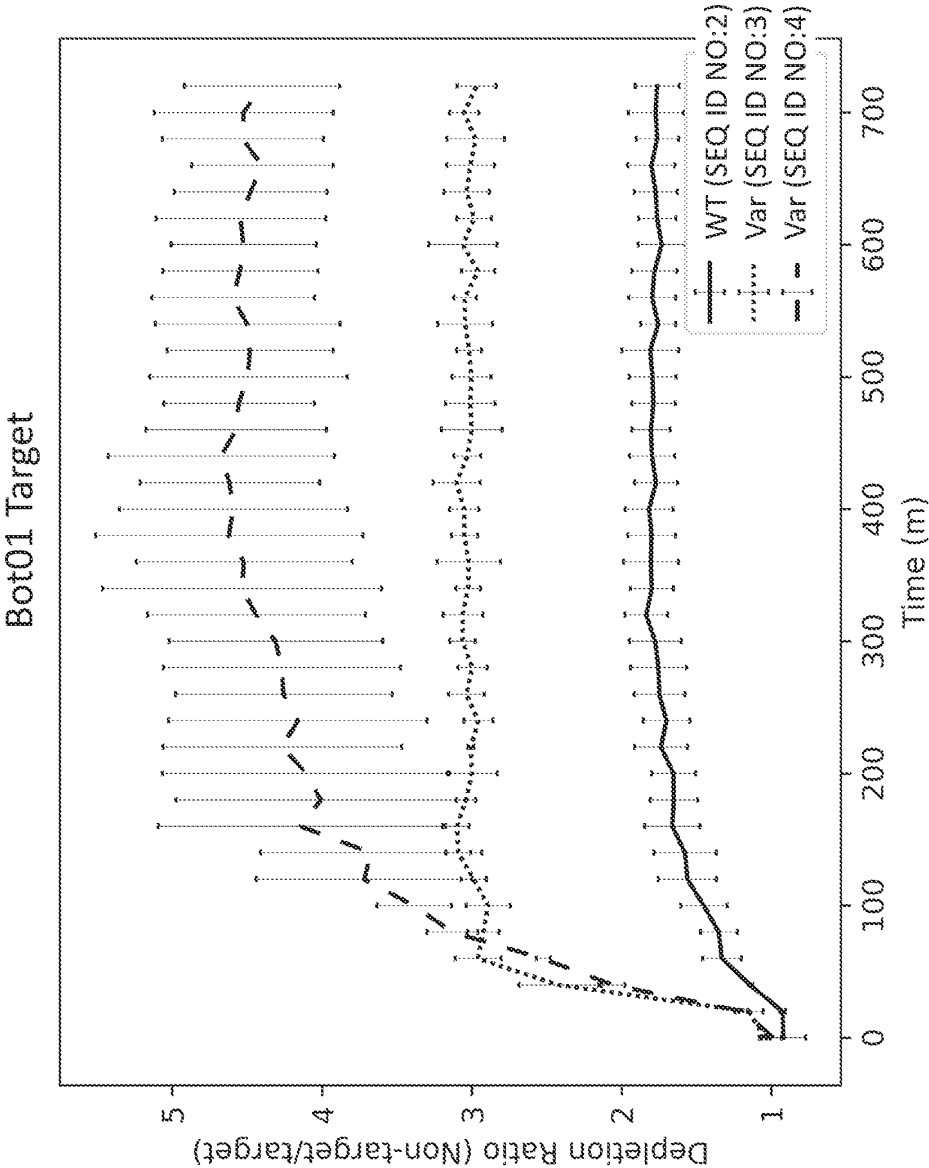


FIG. 5K

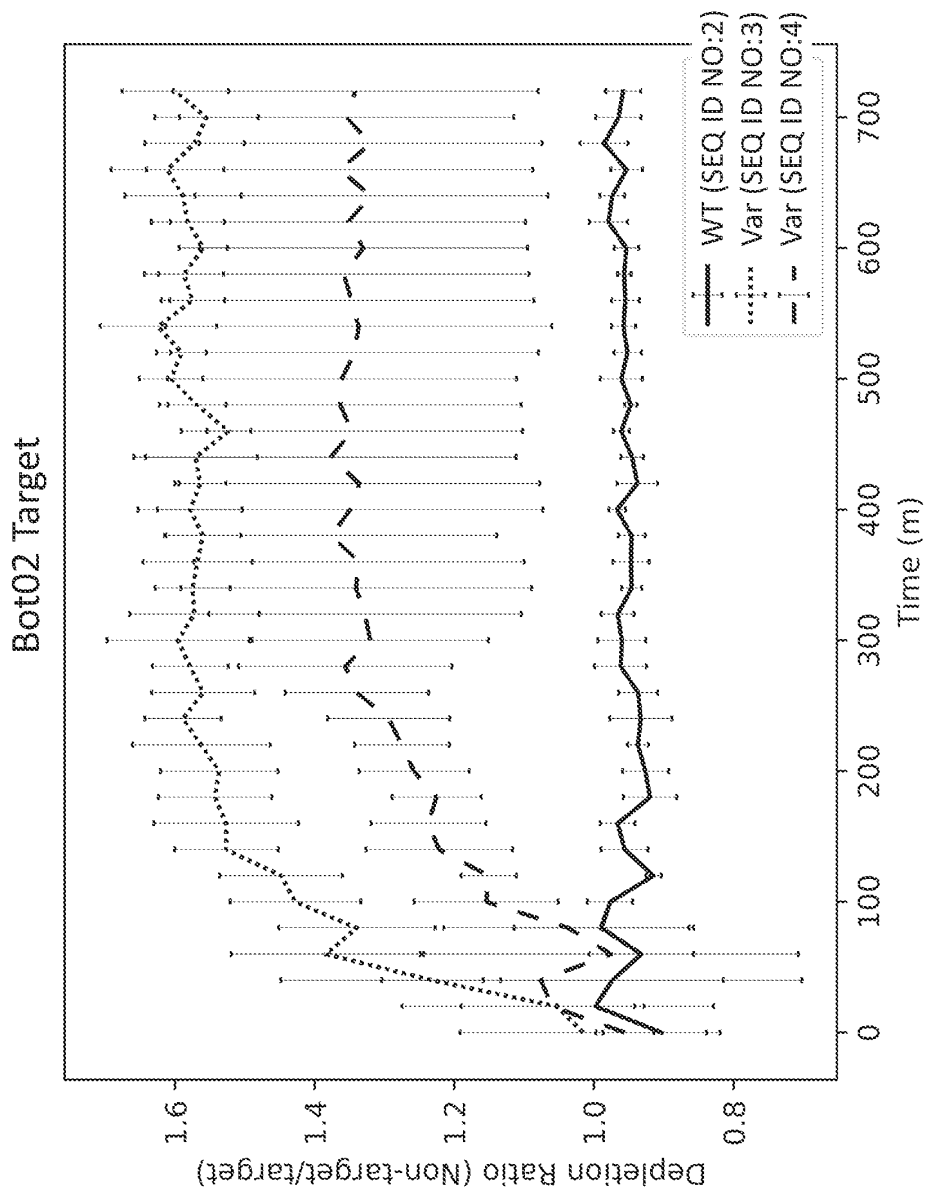


FIG. 5L

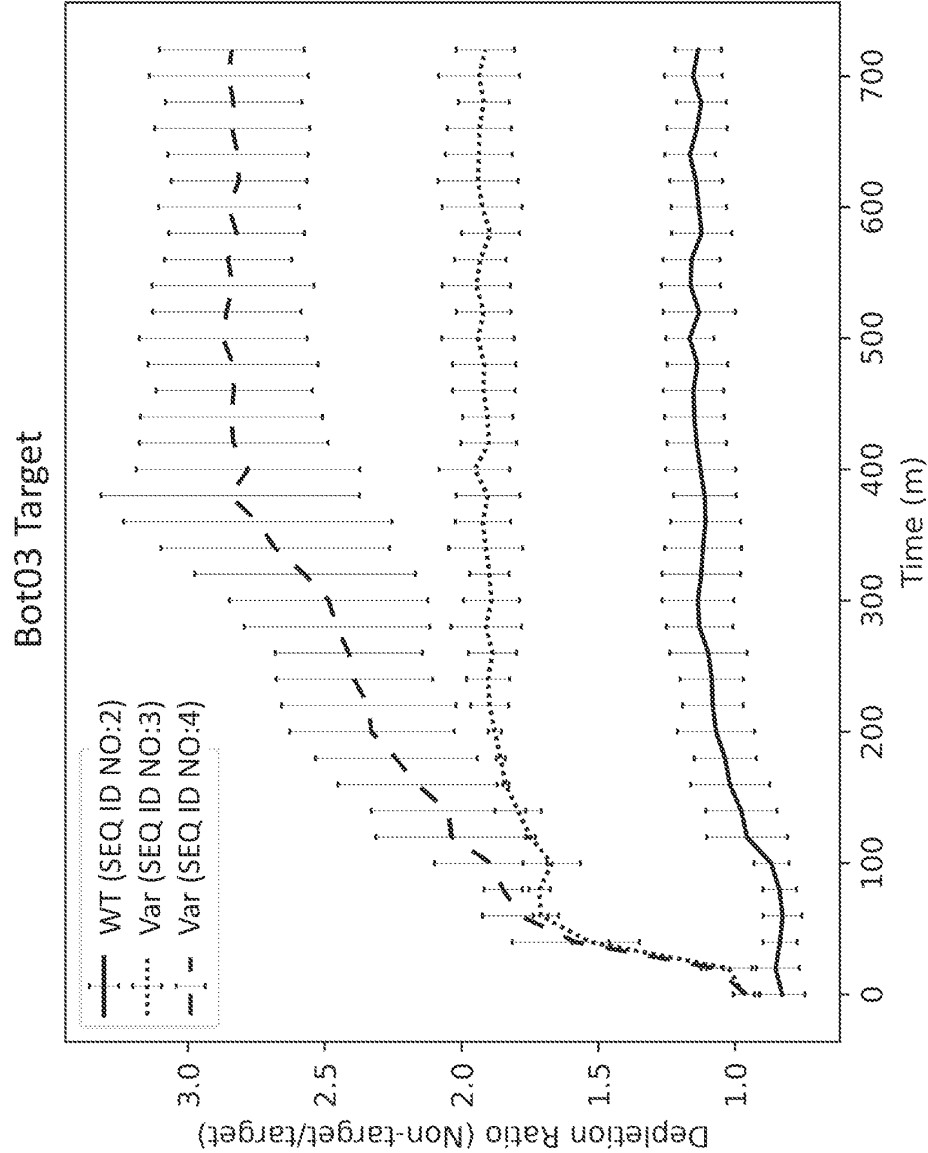


FIG. 5M

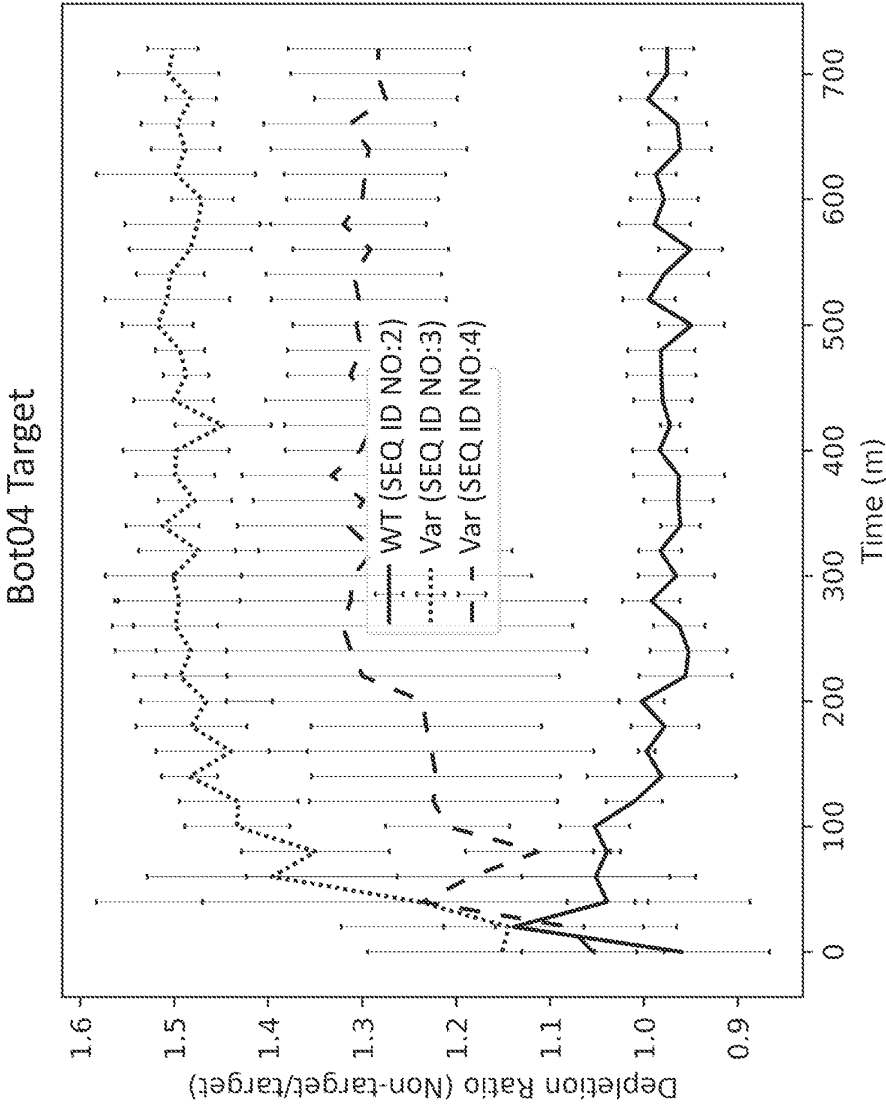


FIG. 5N

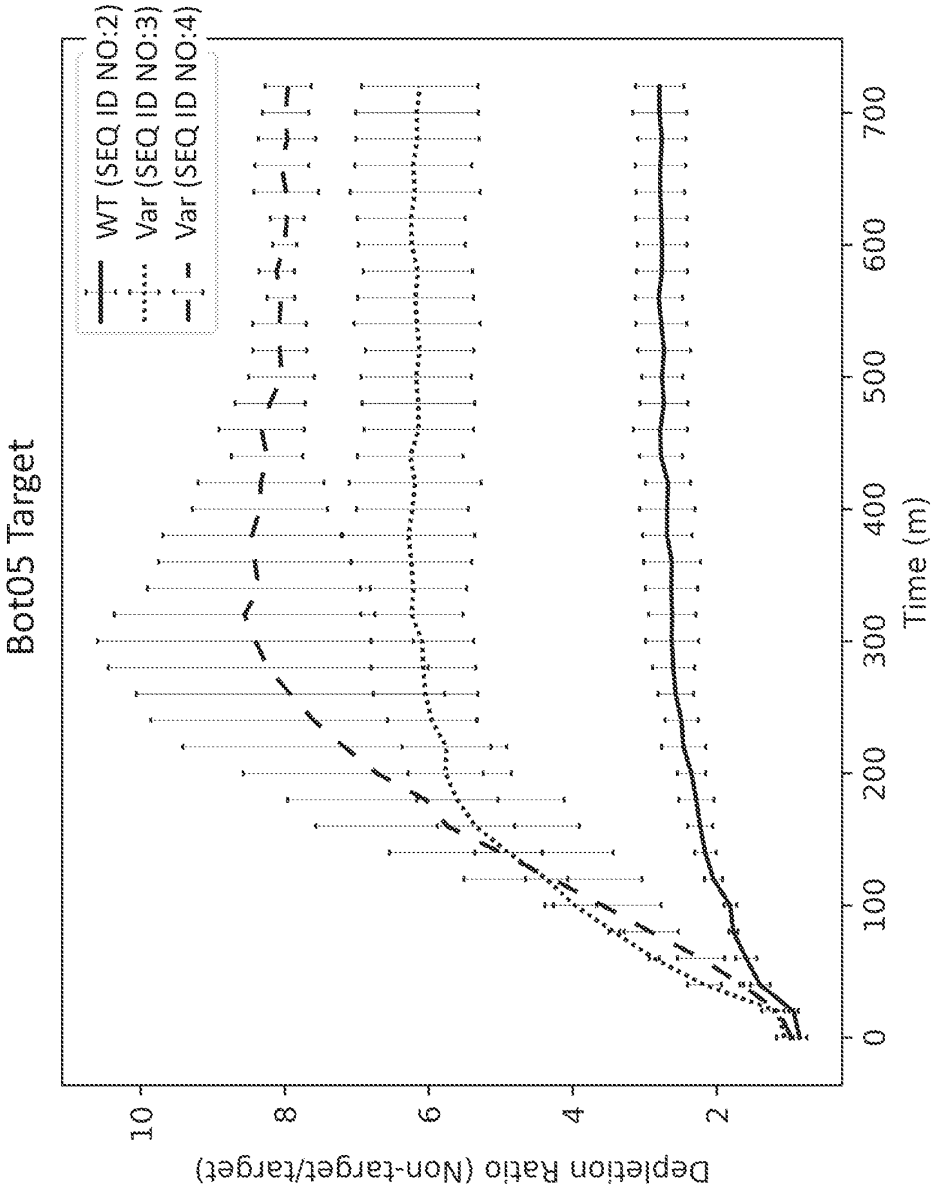


FIG. 50

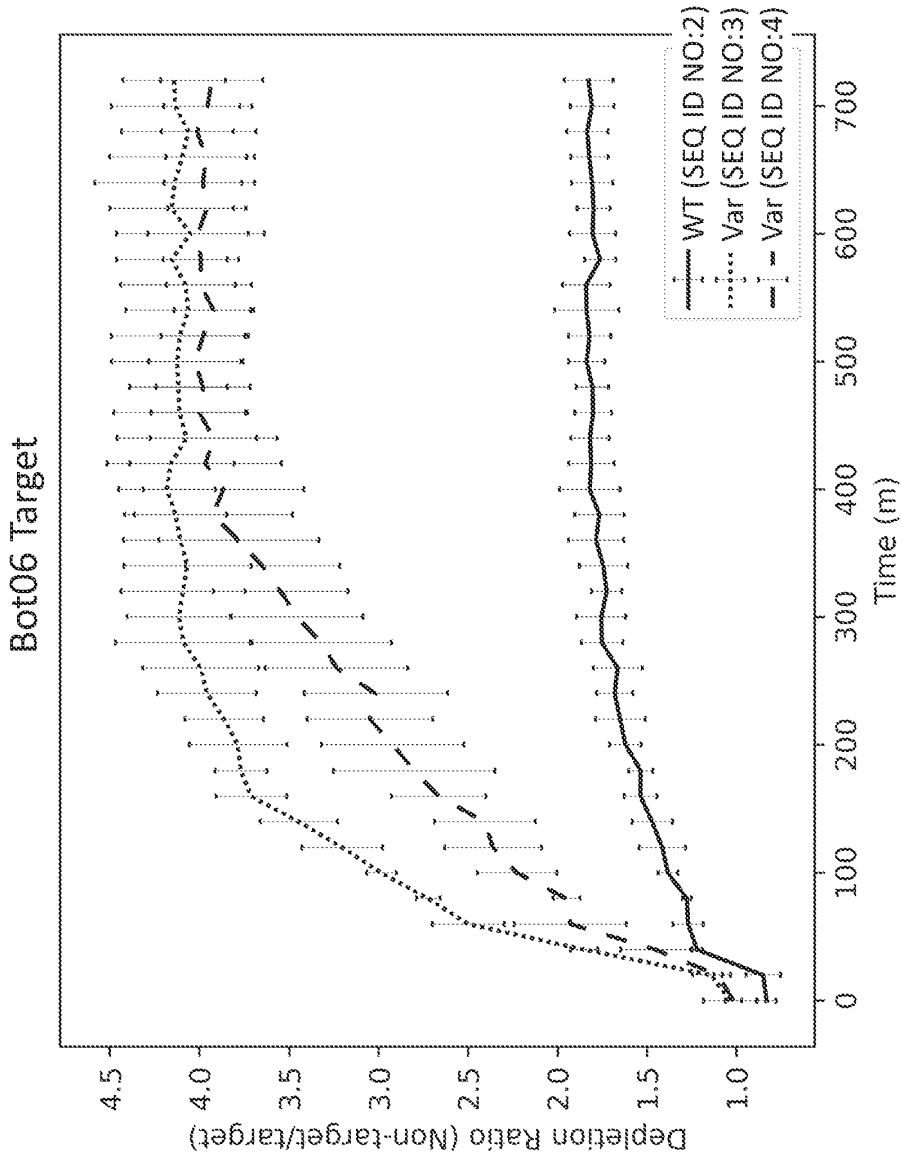


FIG. 5P

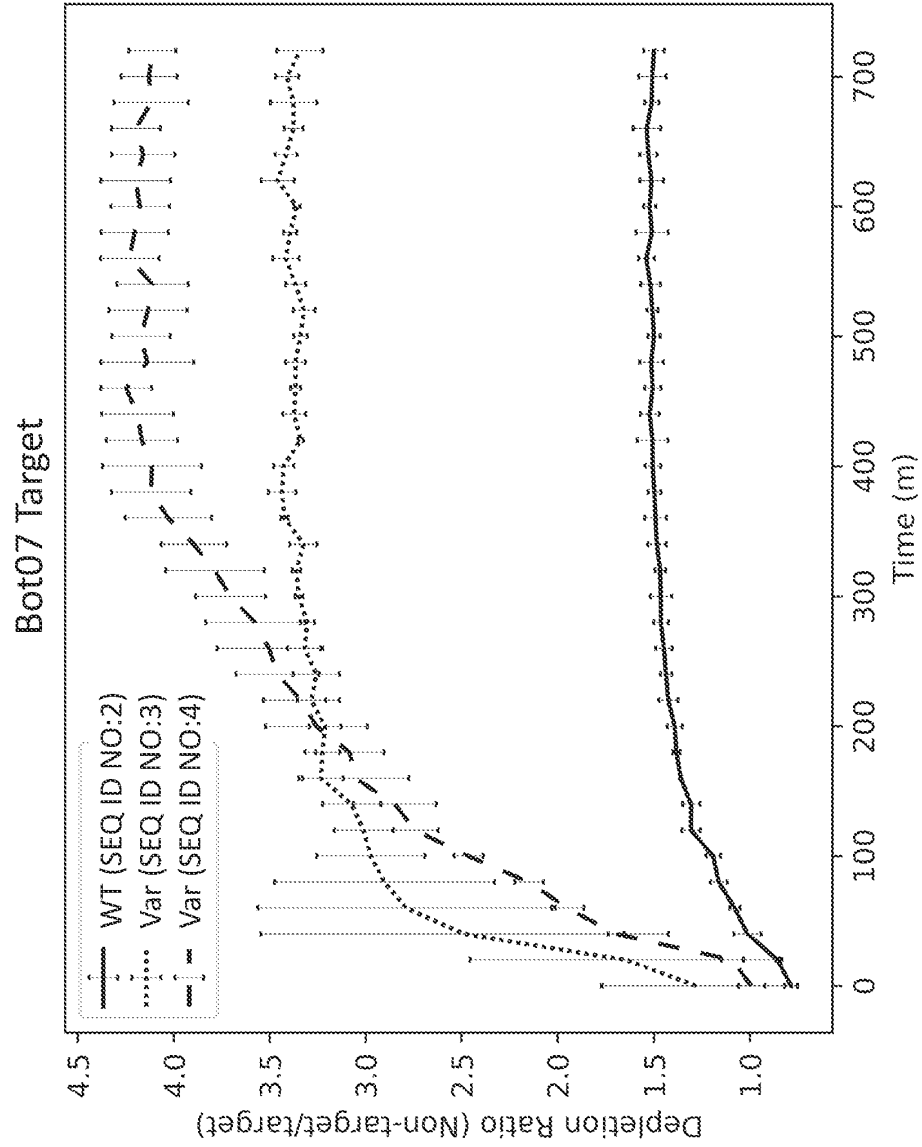


FIG. 5Q

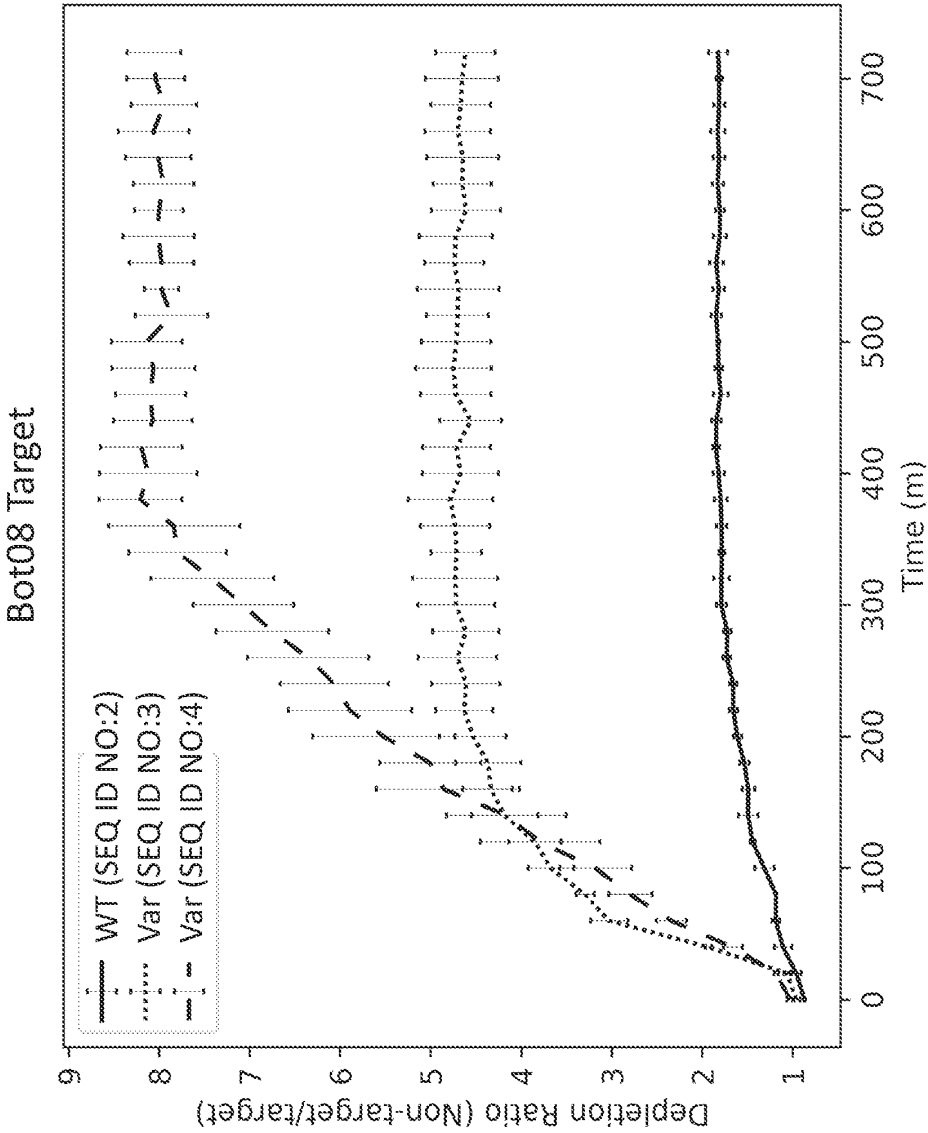


FIG. 5R

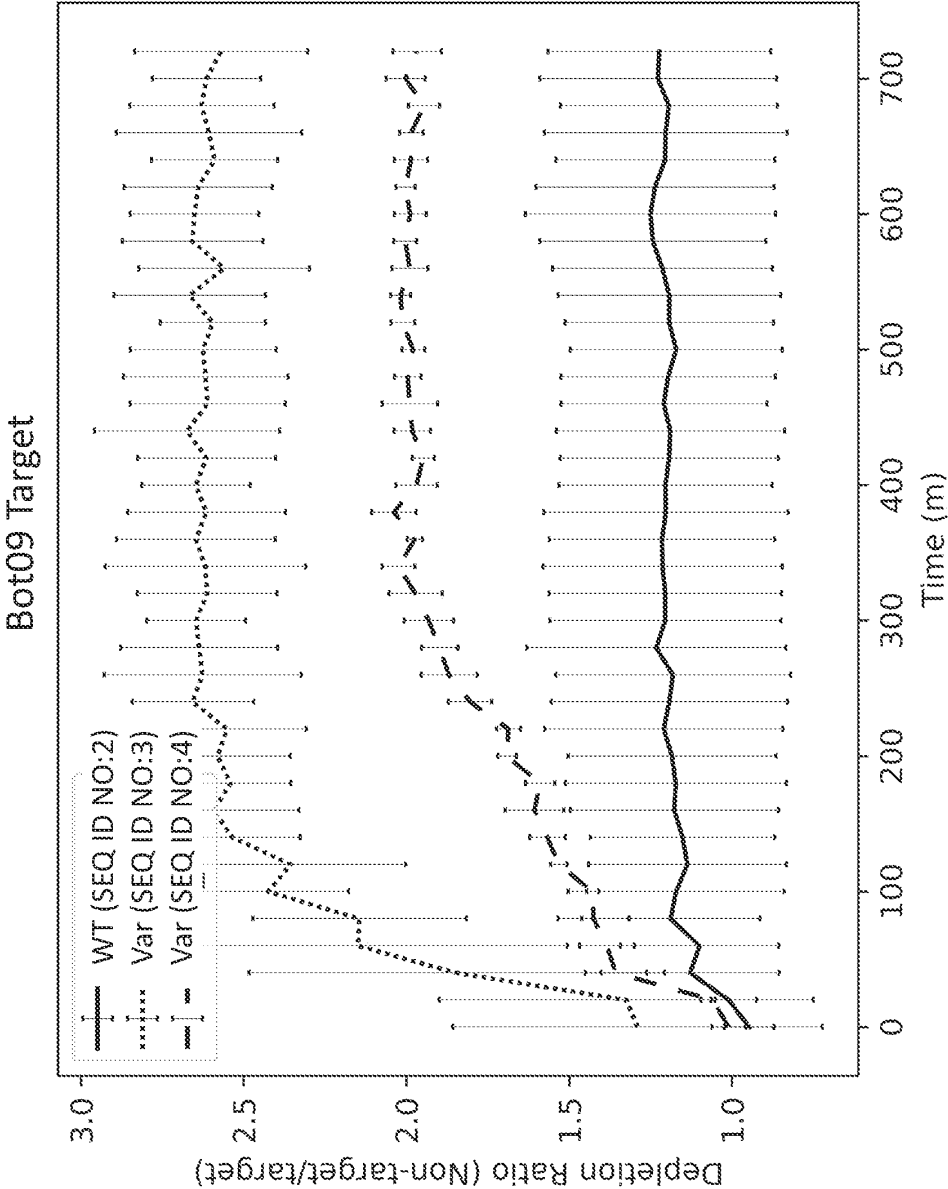


FIG. 5S

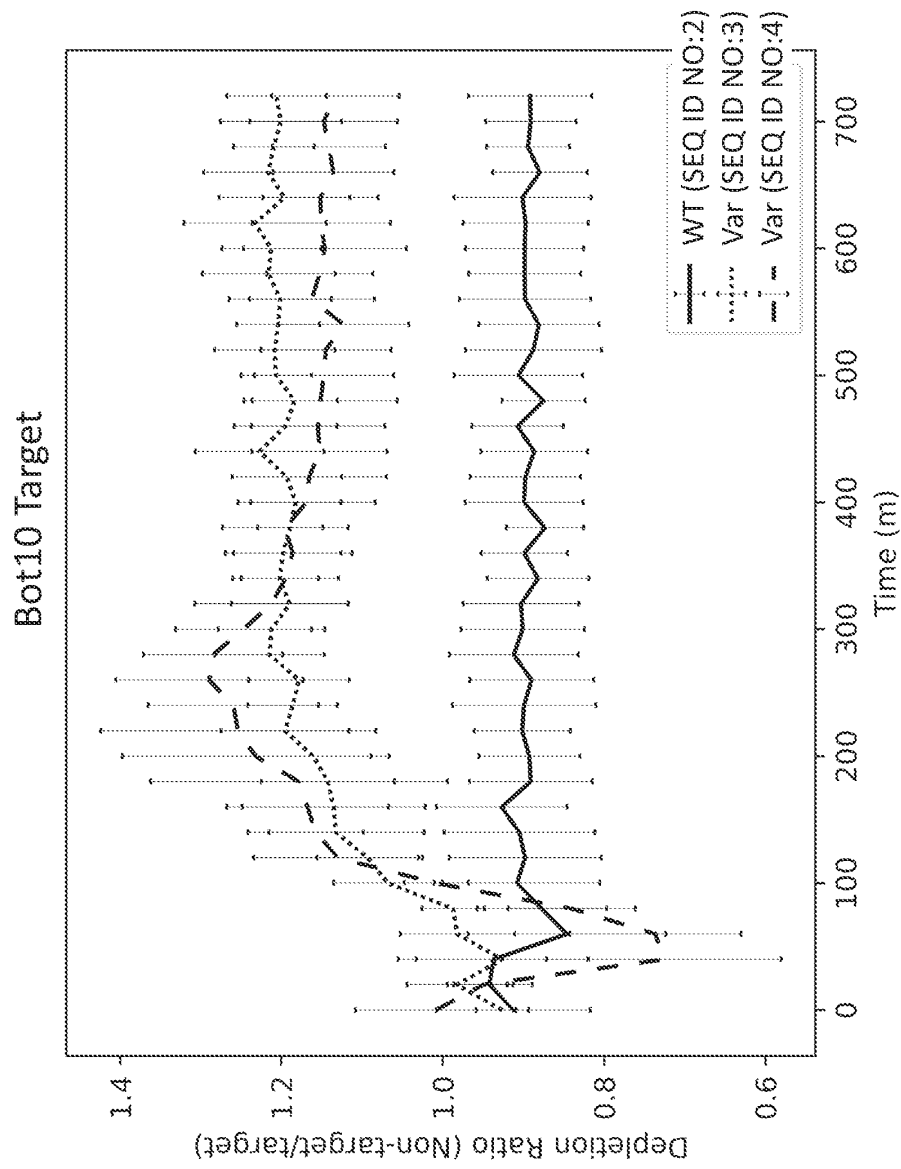


FIG. 5T

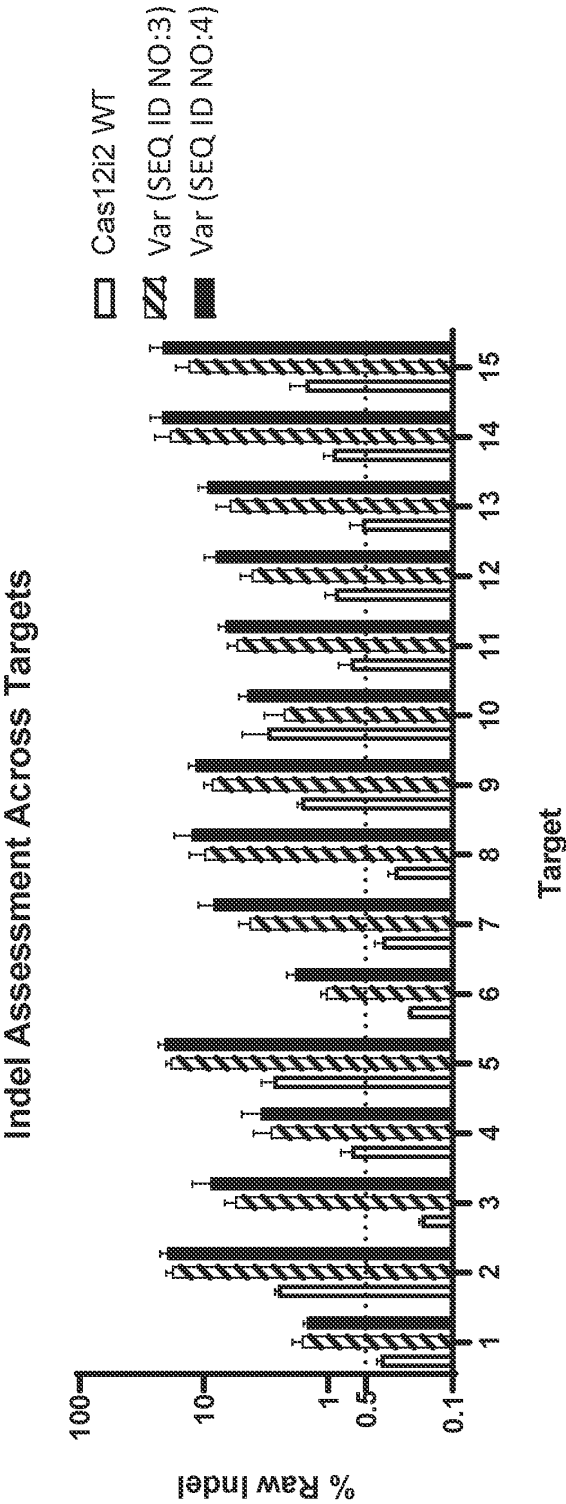


FIG. 6A

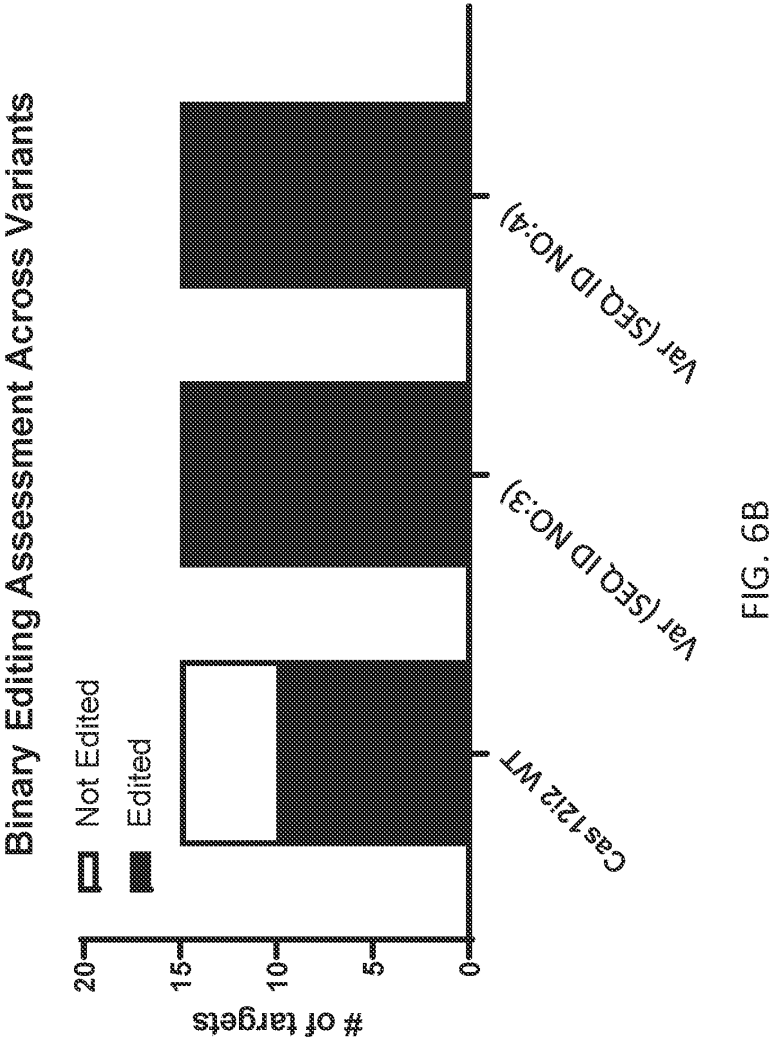


FIG. 6B

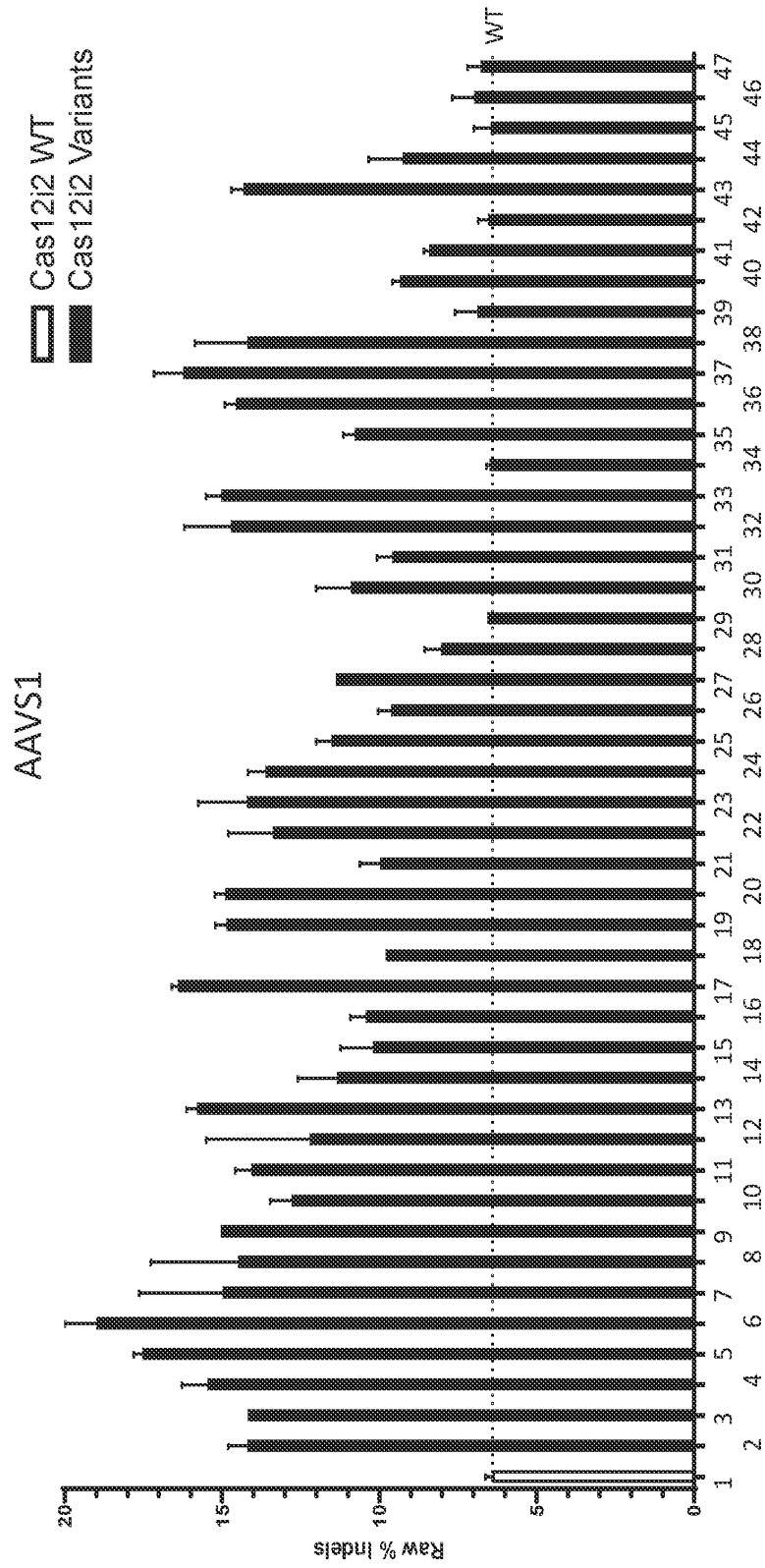


FIG. 7A

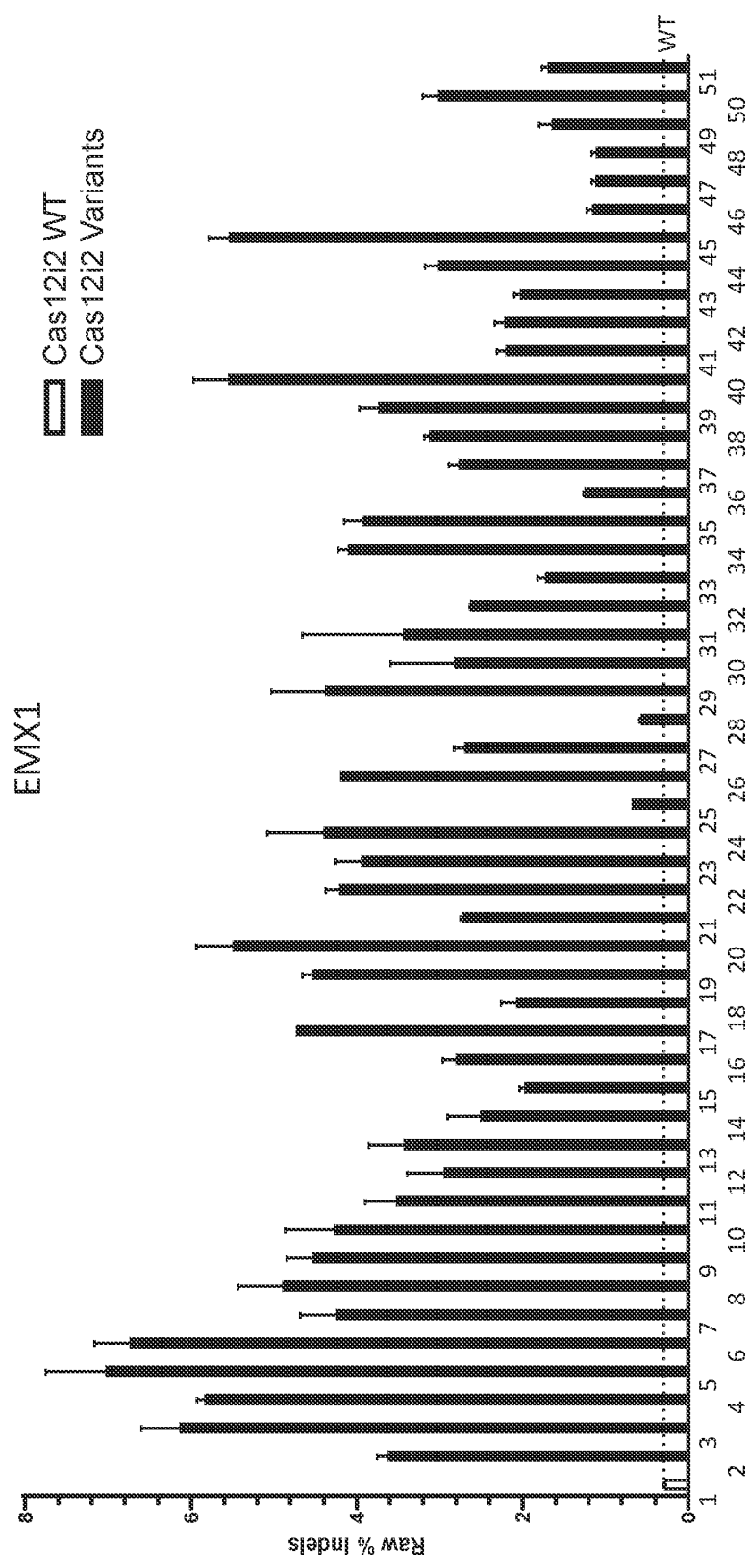


FIG. 7B

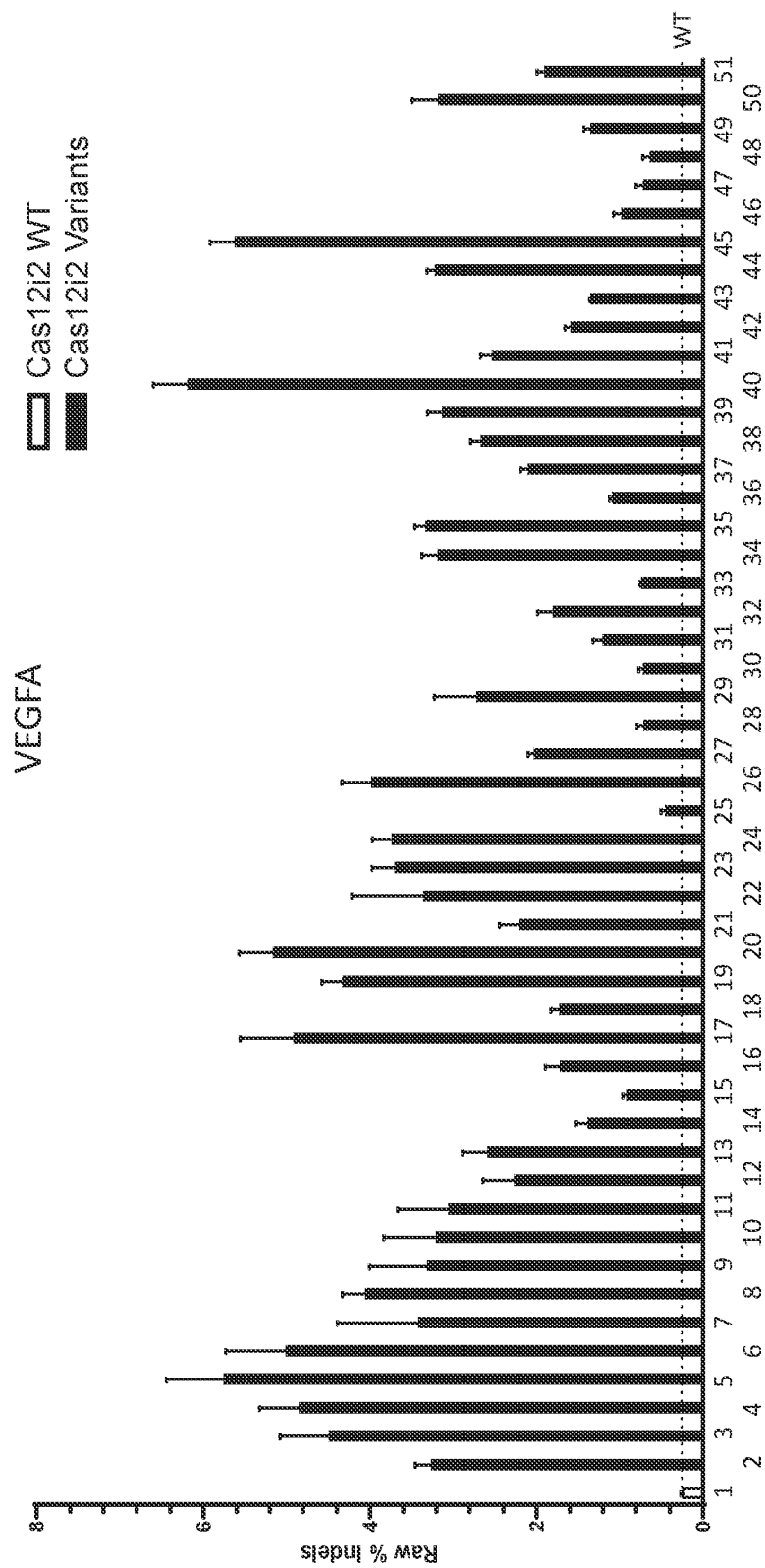


FIG. 7C

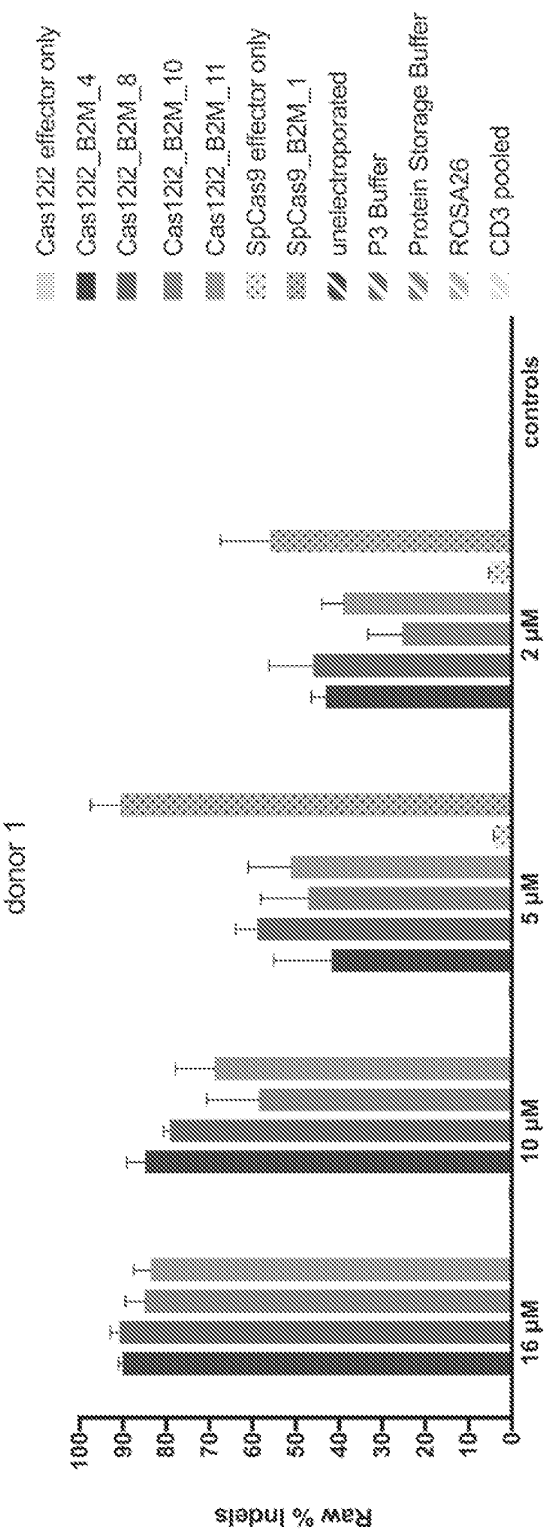


FIG. 8

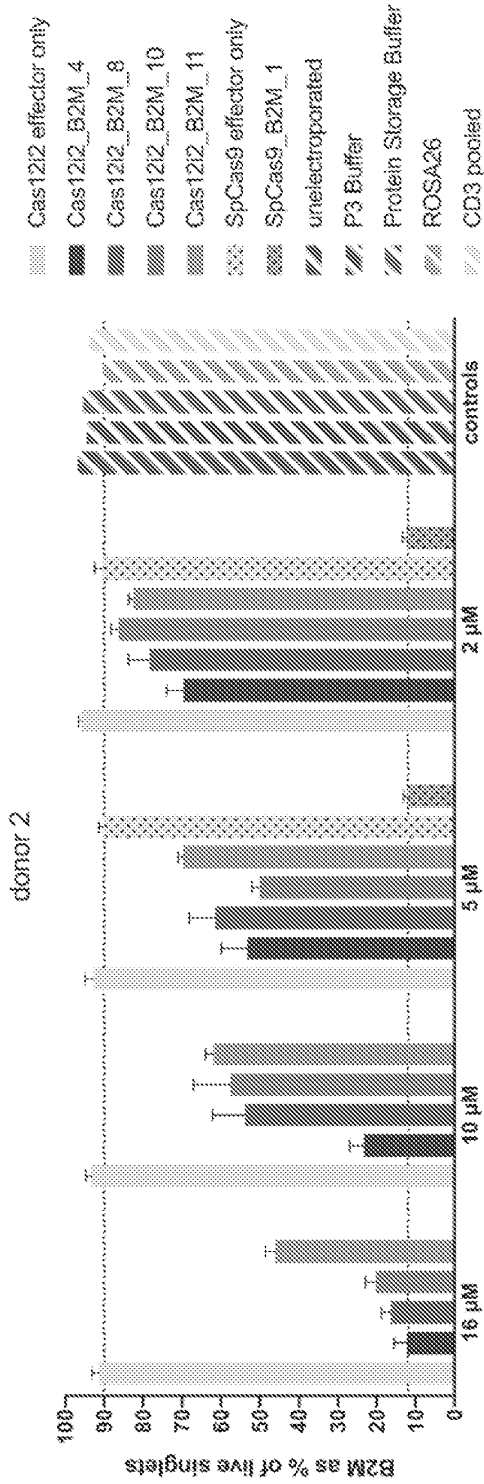


FIG. 9

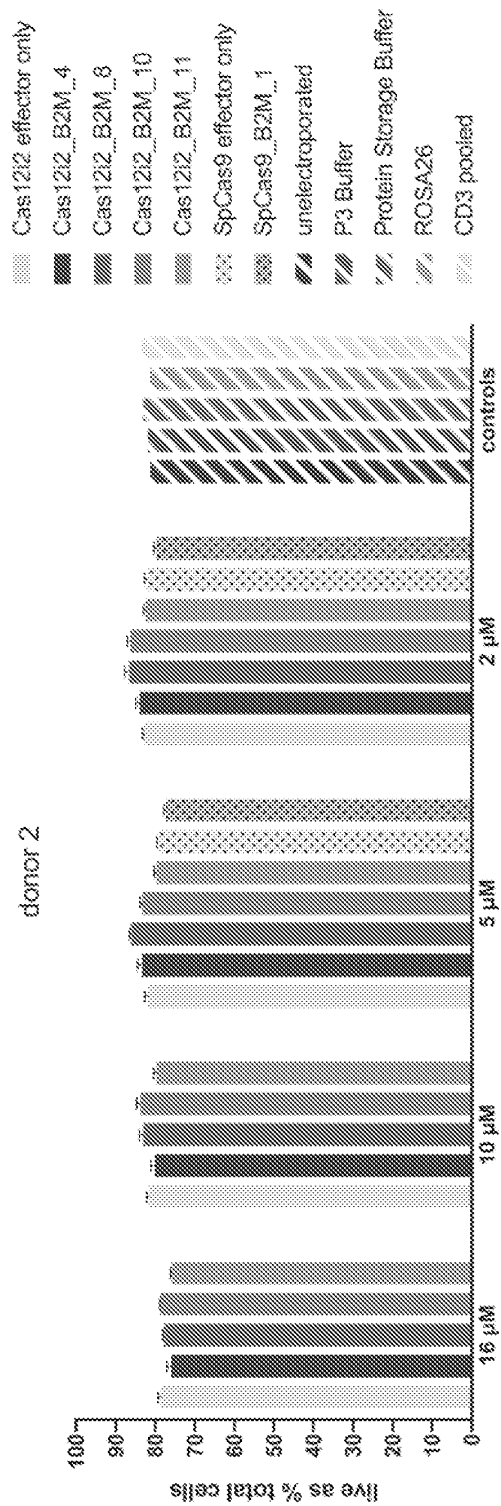


FIG. 10

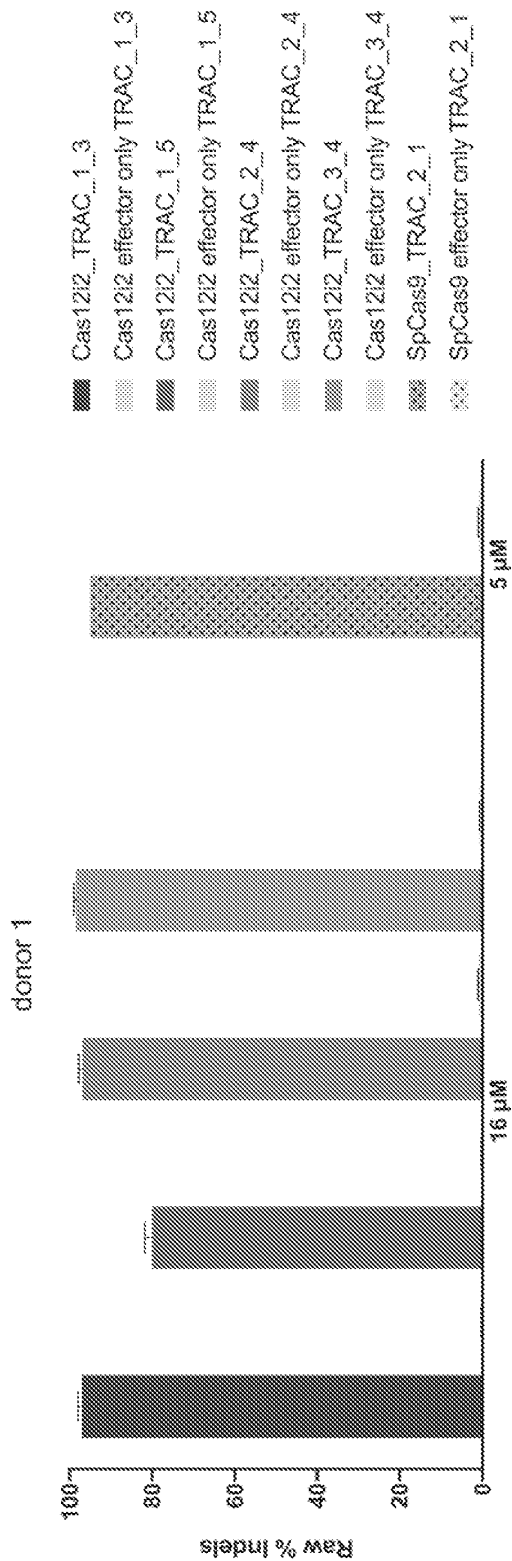


FIG. 11A

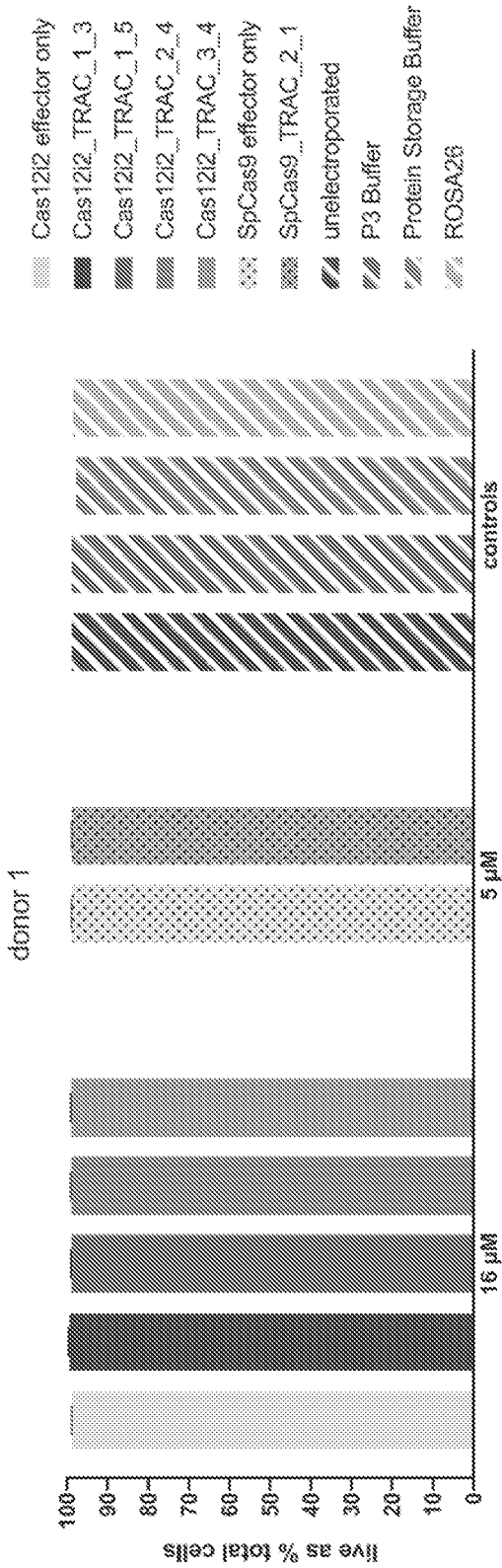


FIG. 11B

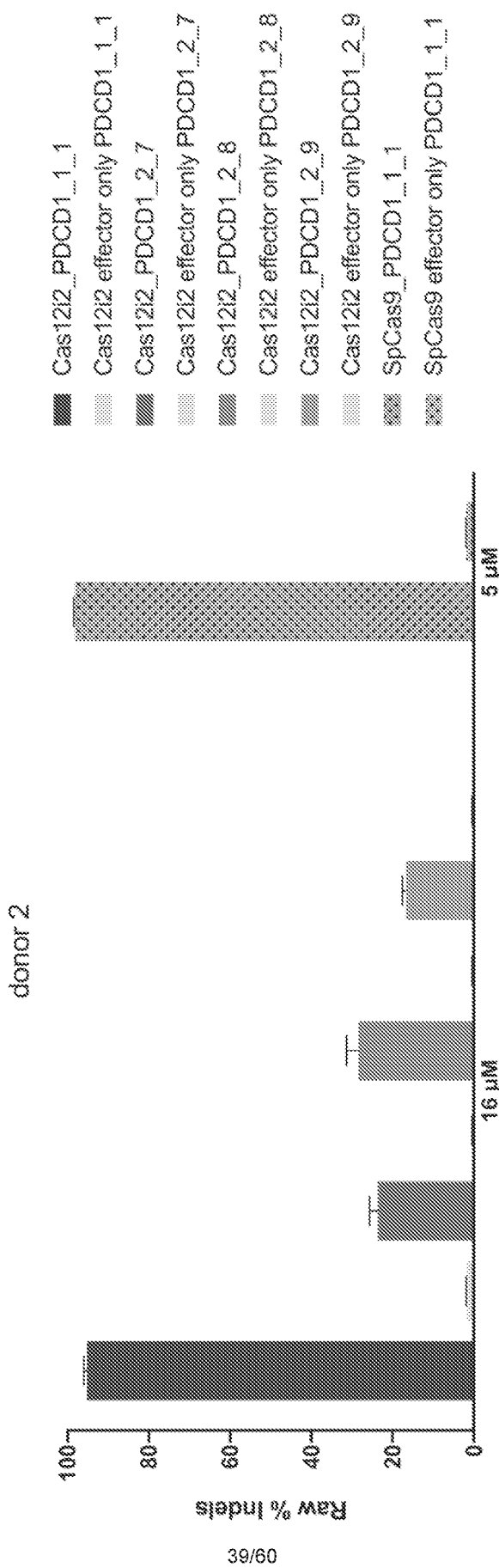


FIG. 12A

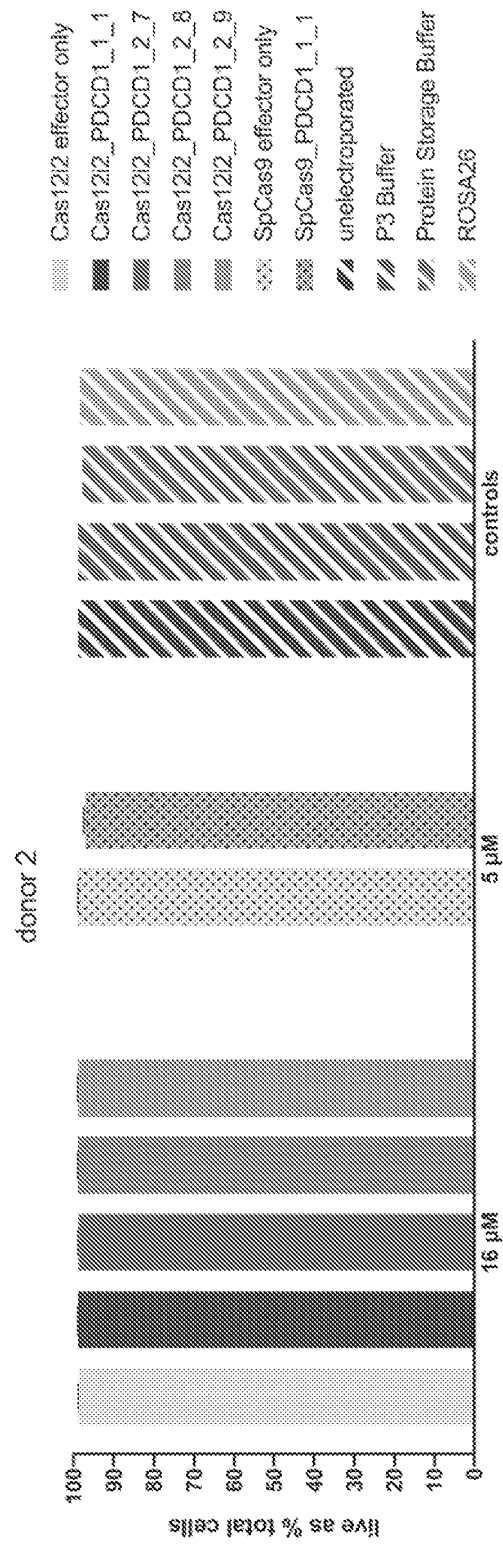


FIG. 12B

PAM		
Target:	TTCACCTGCAGCTTCTCCAACAC (SEQ ID NO: 478)	1 substitution
Edit 1:	TTAACCCT T CAGCTTCTCCAACAC (SEQ ID NO: 479)	
Target:	TTCACCTGCAGCTTCTCCAACAC (SEQ ID NO: 478)	2 substitutions
Edit 2:	TTGACCTGCAG T TTCTCC C ACAC (SEQ ID NO: 480)	
Target:	TTCACCTGCAGCTTCTCCAACAC (SEQ ID NO: 478)	3 substitutions
Edit 3:	TTCA CCCT CAGCTTCTCCA ACTC (SEQ ID NO: 481)	
Target:	TTCACCTGCAGCTTCTCCAACAC (SEQ ID NO: 478)	2 substitutions 1 insertion 1 deletion
Edit 4:	TTT ACCA GCAG T CTTCT-CAACA A (SEQ ID NO: 482)	

FIG. 13

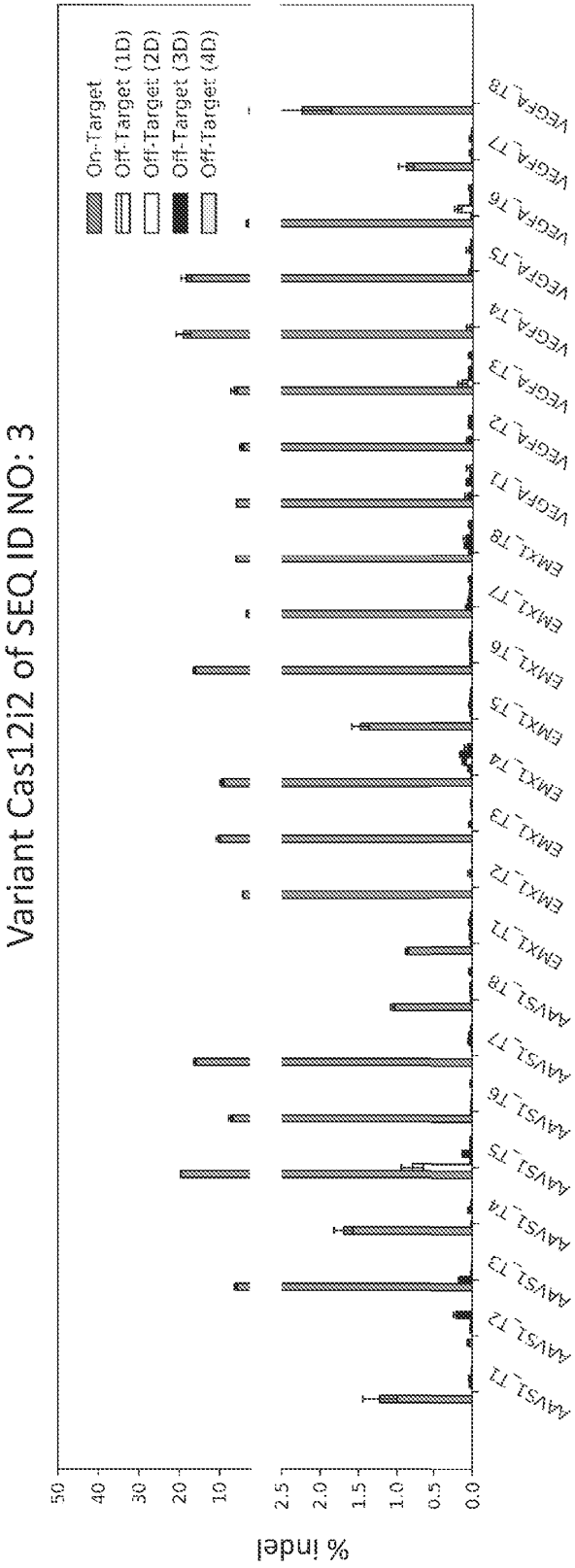


FIG. 14A

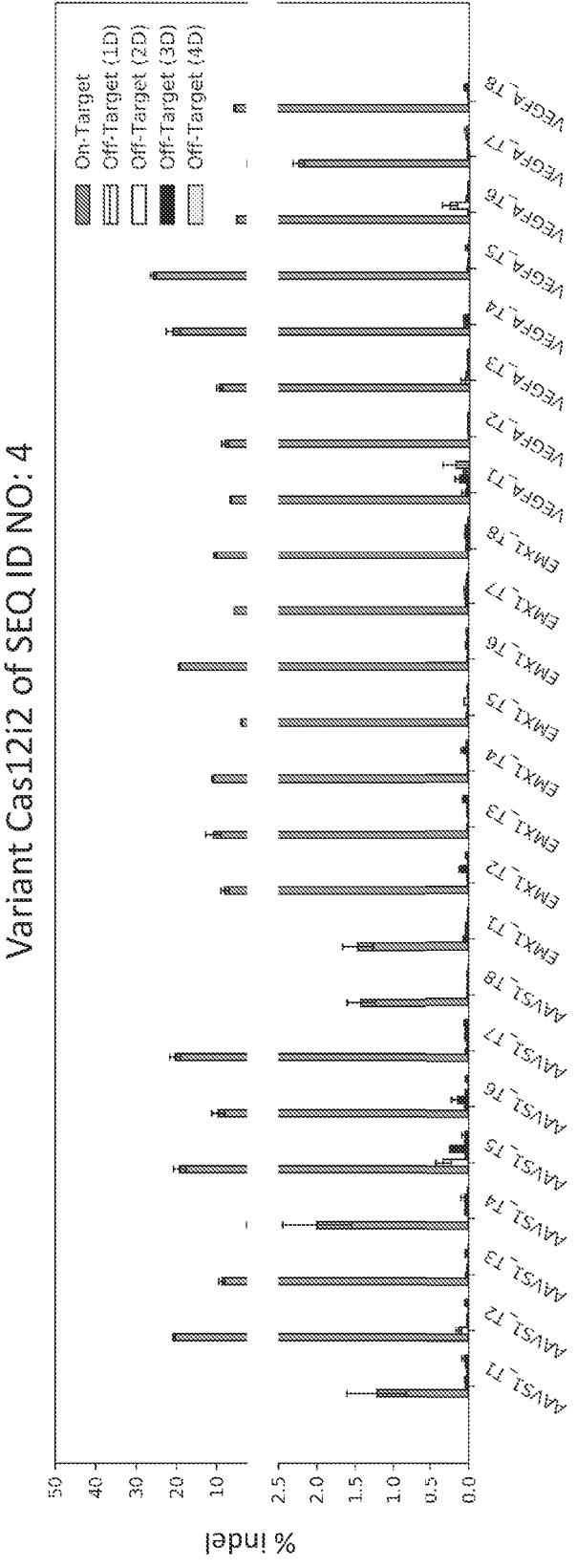


FIG. 14B

Variant Cas12i2 of SEQ ID NO: 5

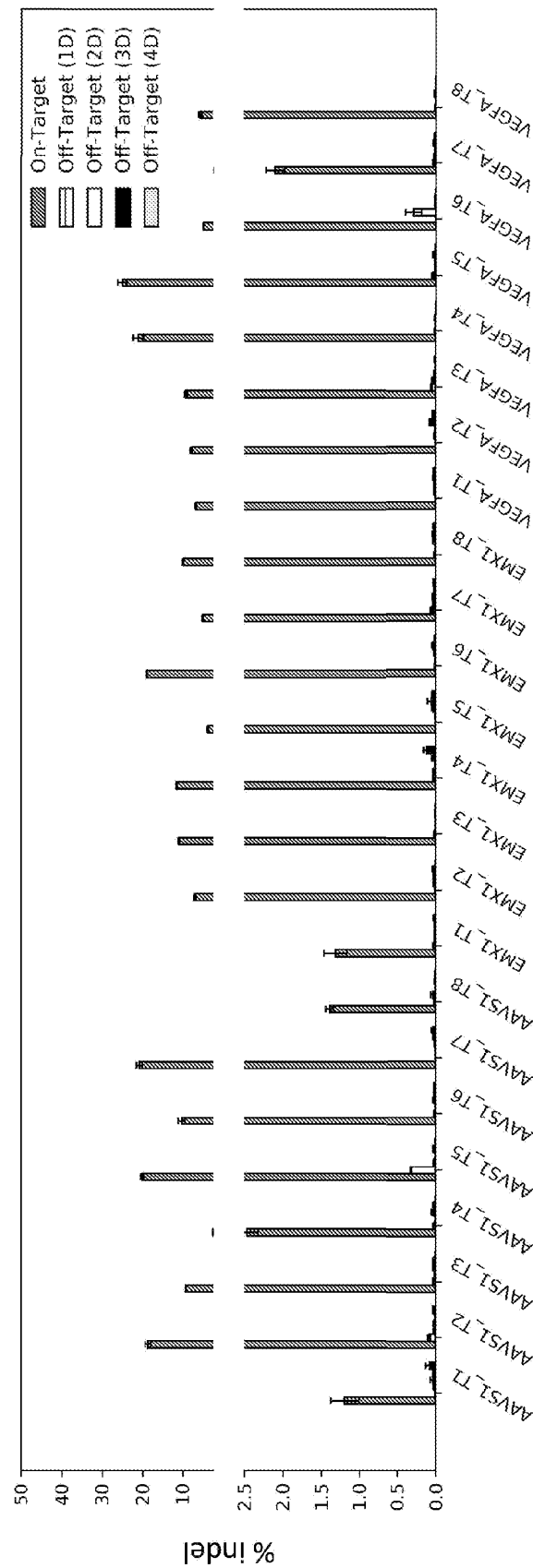


FIG. 14C

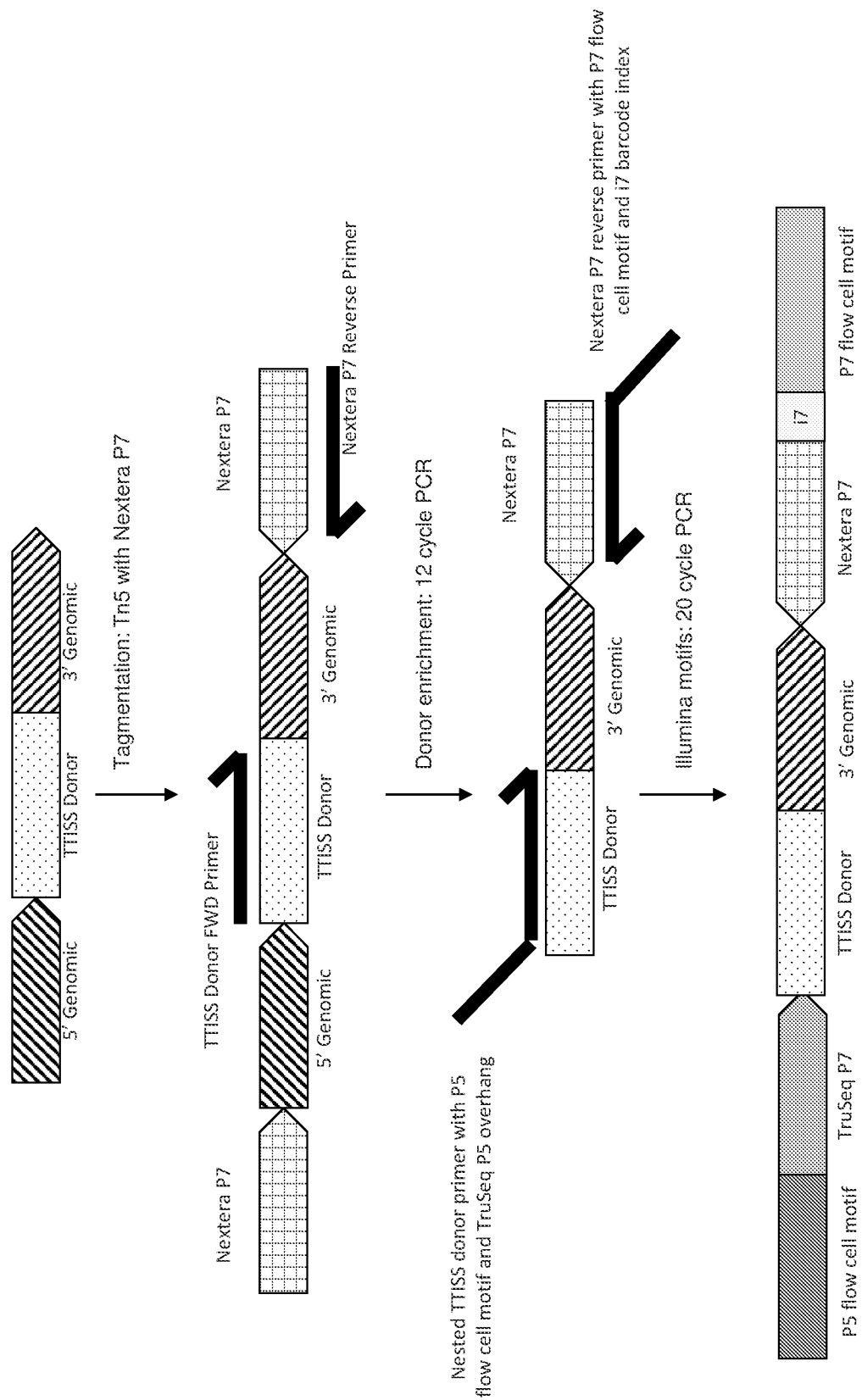


FIG. 15

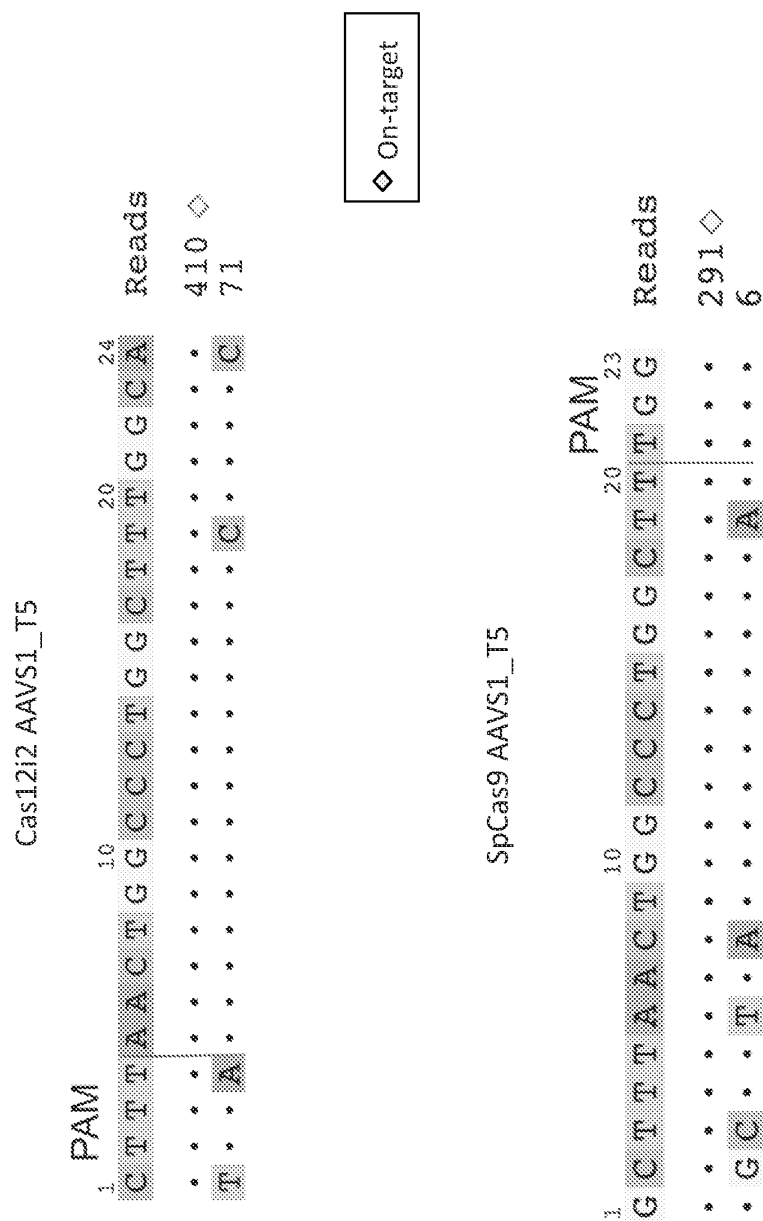


FIG. 16A

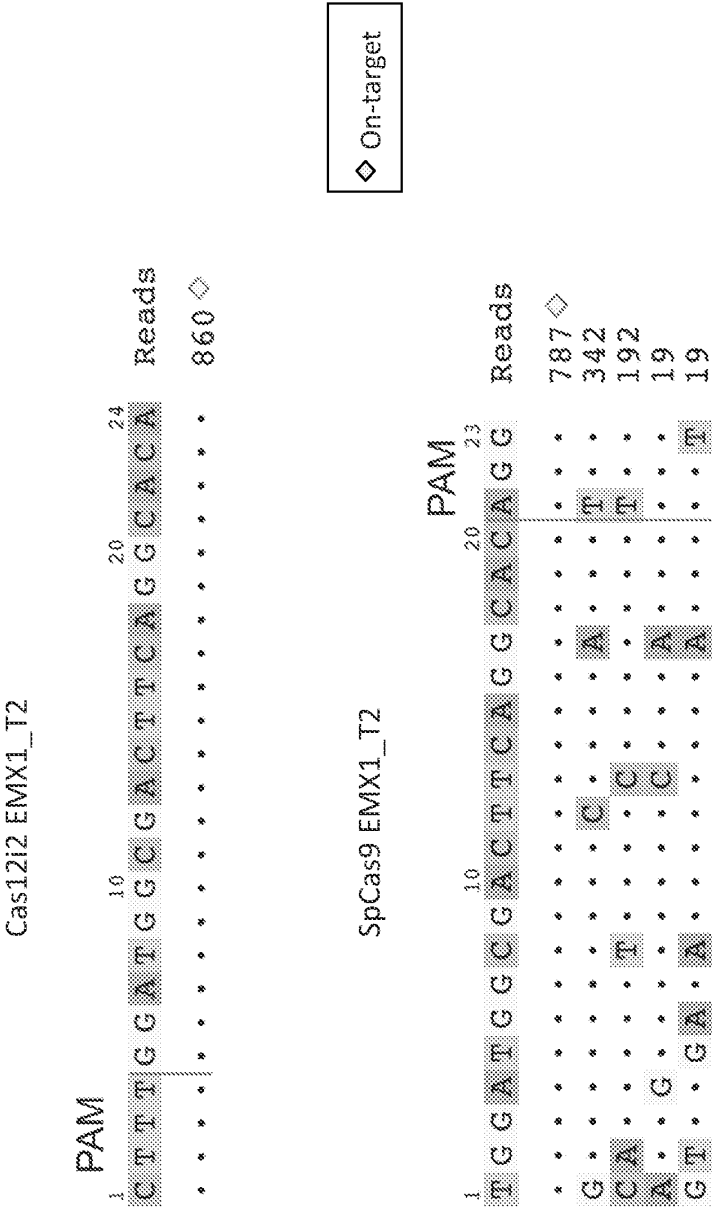


FIG. 16B

Fig. 16C

Cas12i2 EMX1_T4

PAM																							
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
C	T	T	T	G	G	G	G	A	G	G	C	C	T	G	G	A	G	T	C	A	T	G	G
Reads																							
.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
G	.	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.	C	C	A
T	.	A	.	.	.	.	.	.	.	A	.	.	.	.	.	.	.	.	.	C	A	.	.
A	.	.	.	.	A	.	.	.	.	.	.	.	.	.	.	.	.	A	.	A	T	.	.
A	.	.	.	.	.	.	T	.	C	.	.	.	.	.	.	.	.	.	.	.	.	A	C
.	.	.	.	.	.	T	.	.	T	.	A	.	.	.	.	.	.	.	.	.	.	A	.
.	.	G	.	.	A	.	.	.	.	.	.	.	.	.	.	.	.	.	C	A	.	A	.
A	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.	.	.	A	.	.	T	T	.
G	G	G	A	.	.	A	.	.	.	C	C	T	.	.	.	.	A	G	.	.	.	.	.
G	.	C	A	.	.	.	.	A	.	.	.	.	.	.	.	.	.	.	.	A	.	C	.
.	.	A	.	.	.	.	.	.	.	A	.	.	.	.	.	.	G	T	G	T	.	.	.
.	.	A	.	.	A	.	.	.	.	.	.	.	.	.	.	.	.	T	.	C	.	.	.
.	.	G	.	.	.	.	T	.	A	.	.	.	.	.	.	.	.	.	.	.	T	.	.
.	.	.	.	A	.	A	.	.	A	.	.	.	.	.	.	.	.	.	.	.	.	T	.
.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	G	.	A	A	T	.
T	C	.	.	.	.	.	.	A	.	.	.	.	.	.	.	.	.	.	.	.	T	C	.
.	.	C	.	.	A	.	C	.	.	.	.	.	.	.	.	.	.	.	.	A	.	T	.
.	C	A	G	.	.	T	C	A	C	.	A	.	G	.	.	.	.	.	.	.	.	.	.
.	G	.	.	.	.	G	.	T	.	.	.	T	C	.	T	G	.	.	.	.	.	.	.
A	C	A	G	.	.	A	G	.	G	.	A	.	T	.	G	.	.	.	.	.	.	.	.
T	.	C	.	.	.	.	.	.	.	A	.	.	.	.	.	C	.	.	.	.	.	.	.
T	.	.	.	.	T	.	.	.	.	.	A	.	.	.	.	.	.	T	G	T	A	.	.
.	.	.	.	A	.	.	.	.	.	.	.	.	.	.	.	.	.	T	C	A	T	T	.
A	.	G	G	A	.	.	.	.	G	A	G	.	.	.	G	.	.	G	.	.	.	.	.

Reads

495 ◇

54

34

29

20

15

12

10

9

8

8

7

7

7

6

6

6

5

5

5

5

4

4

4



On-target

Fig. 16C
cont.

On-target

PAM																						
1	10	20	23																			
T	T	T	G	G	G	G	A	G	G	C	C	T	G	G	A	G	T	C	A	T	G	G
C	C	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
G	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
G	C	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C	C	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
G	A	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
.	A	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
A	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C	.	C	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
G	A	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C	A	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
A	G	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
A	G	C	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
.	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
A	G	G	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
.	C	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
G	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C	C	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
.	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
A	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
.	C	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C	C	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
G	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
G	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
A	.	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
G	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
A	G	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
G	.	T	T	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
.	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
.	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C	A	A	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
A	G	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C	.	C	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
G	C	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
G	A	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
.	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
G	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C	G	G	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
A	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
A	.	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C	A	G	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
.	G	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
.	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C	C	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
A	A	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

SpCas9 EMX1_T4

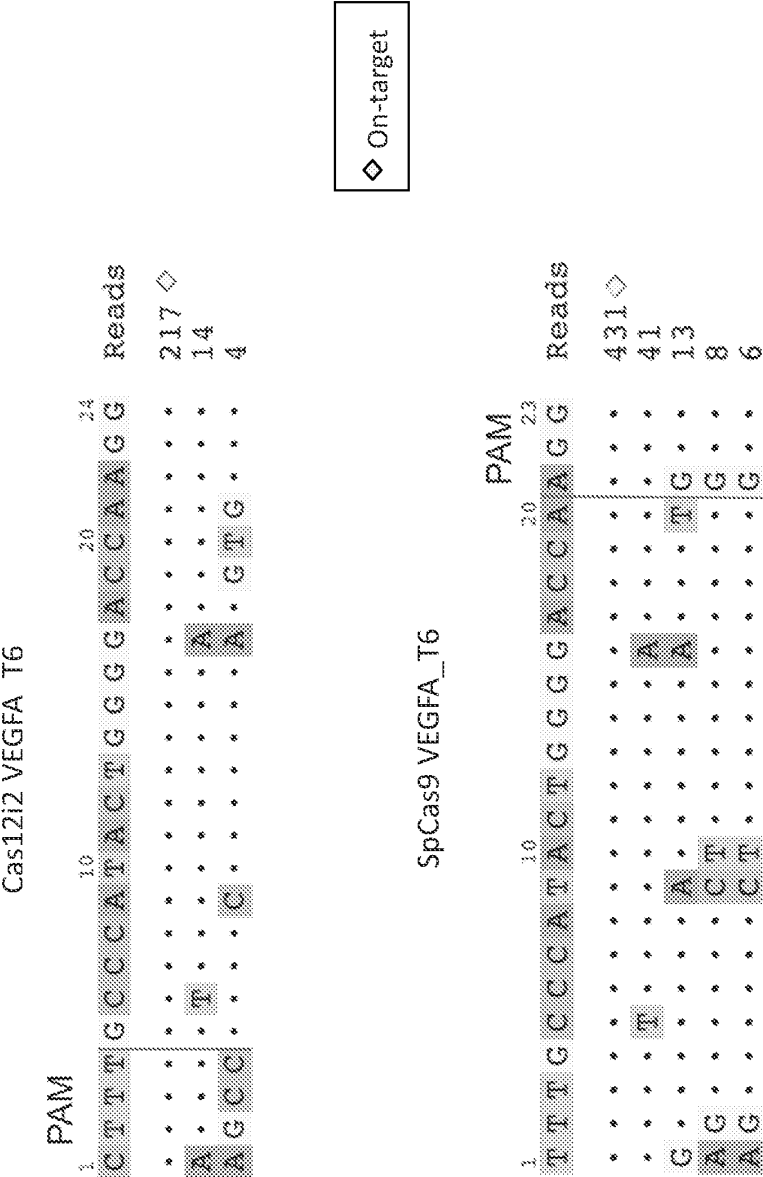


FIG. 16D

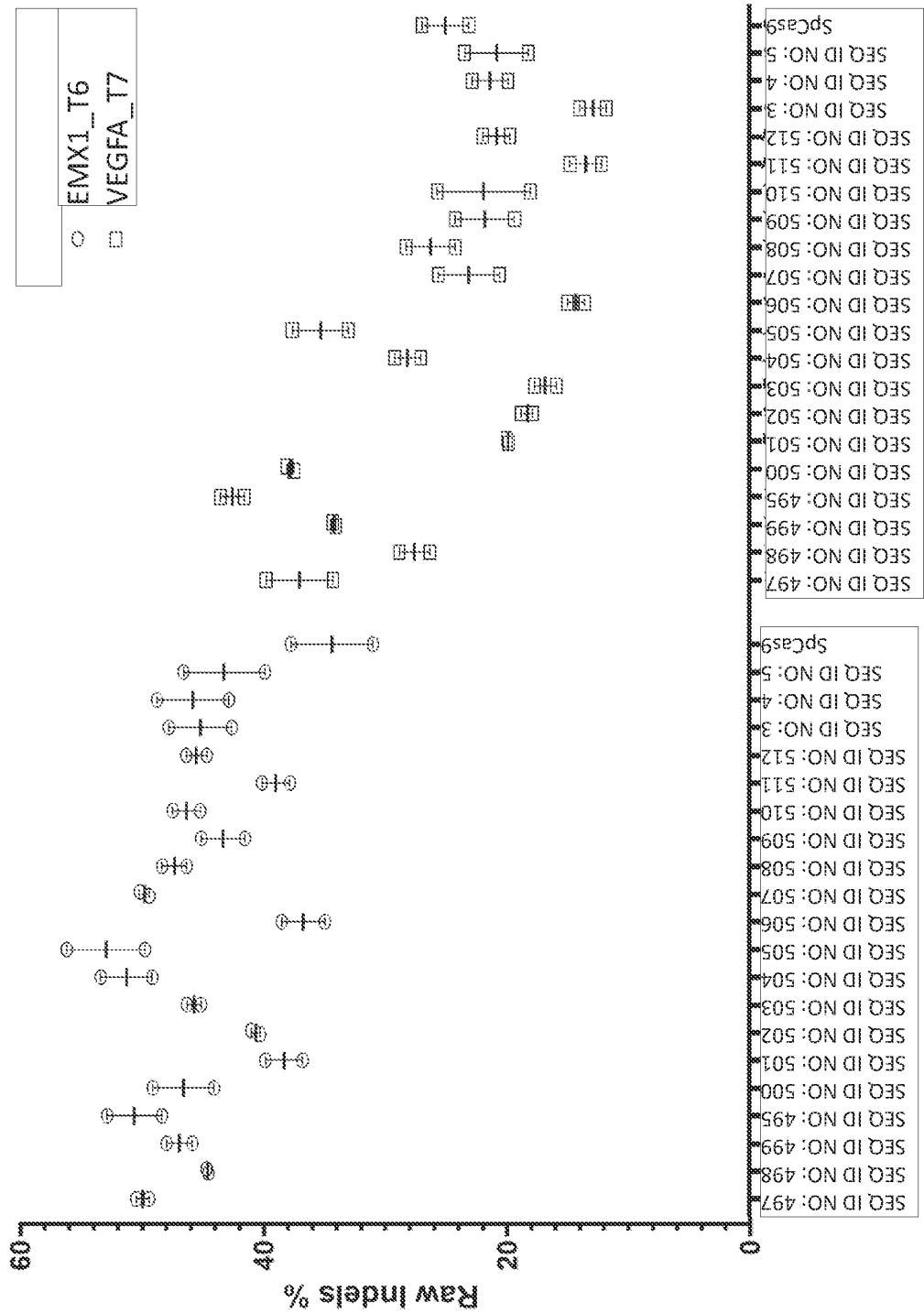


FIG. 17A

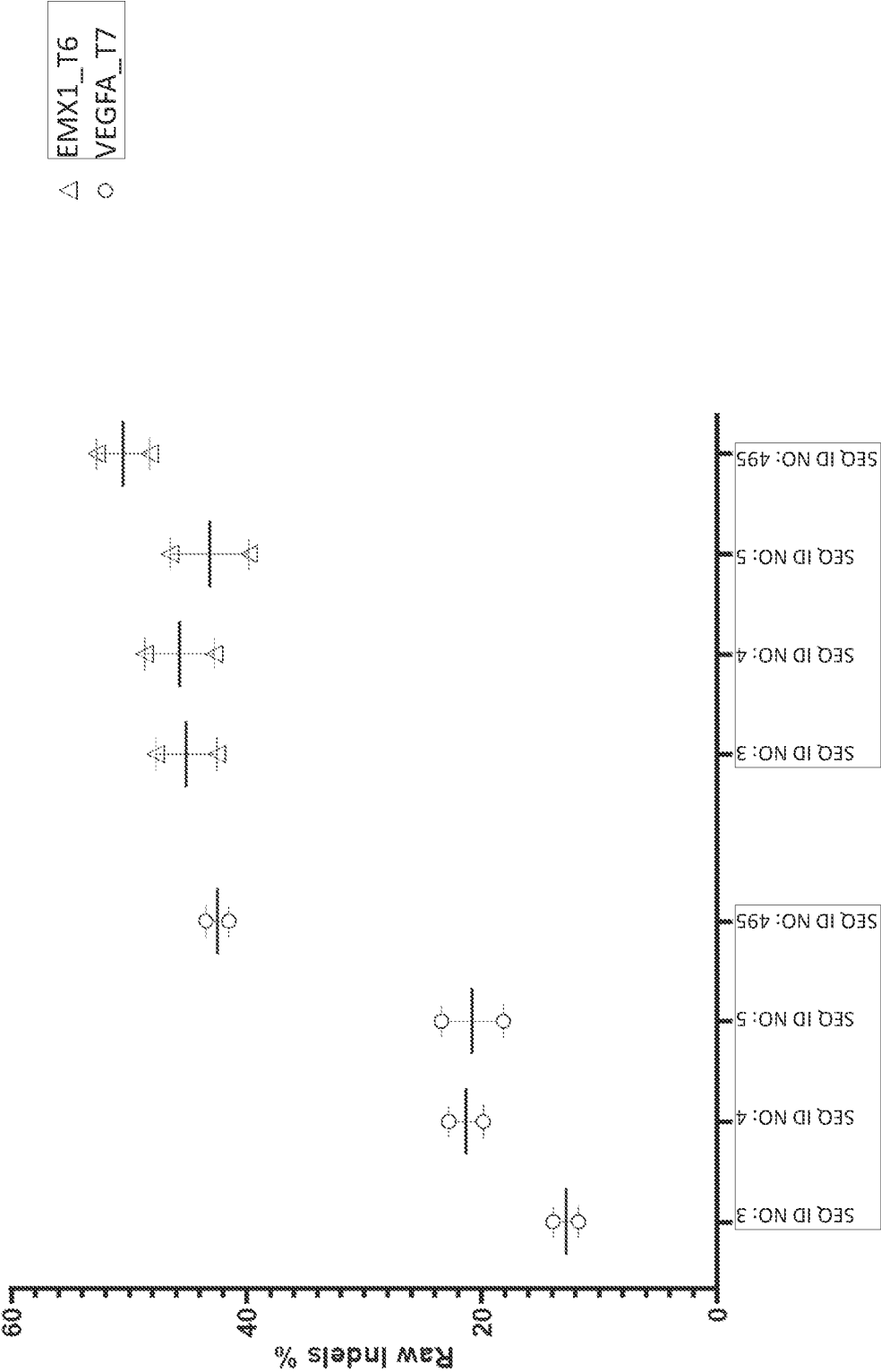


FIG. 17B

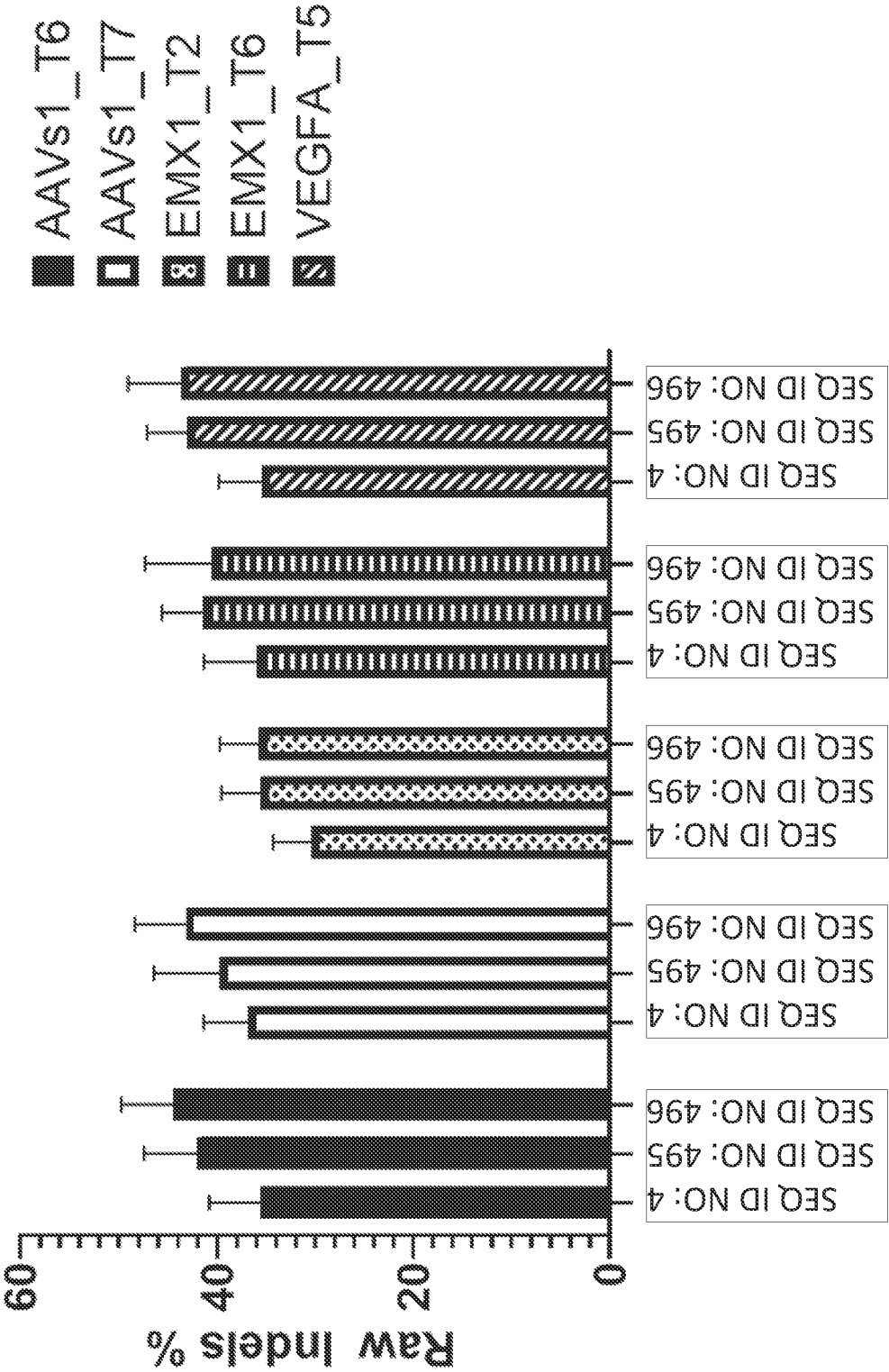


FIG. 18

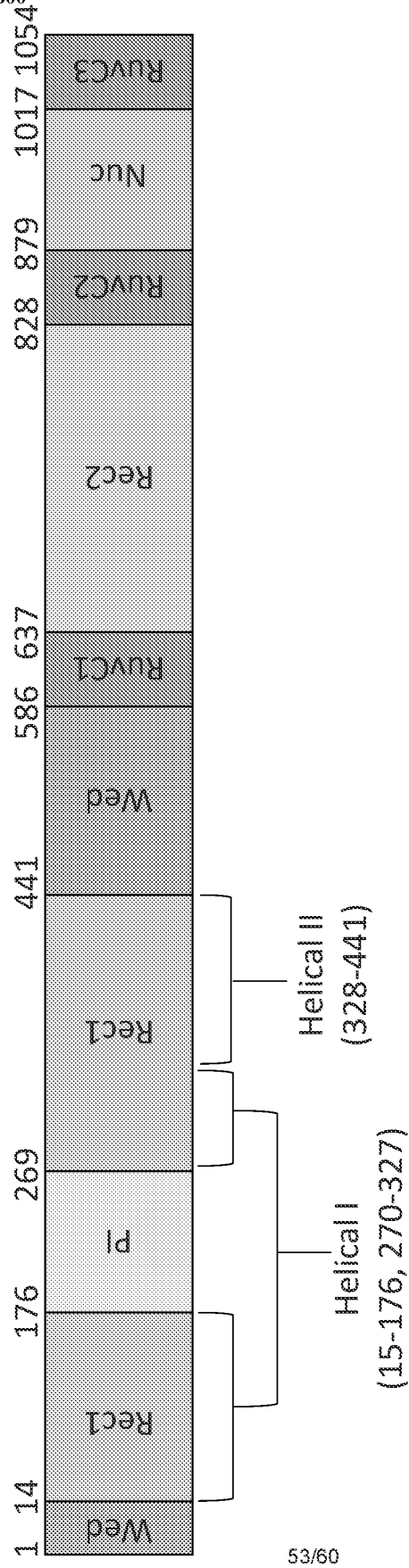


FIG. 19

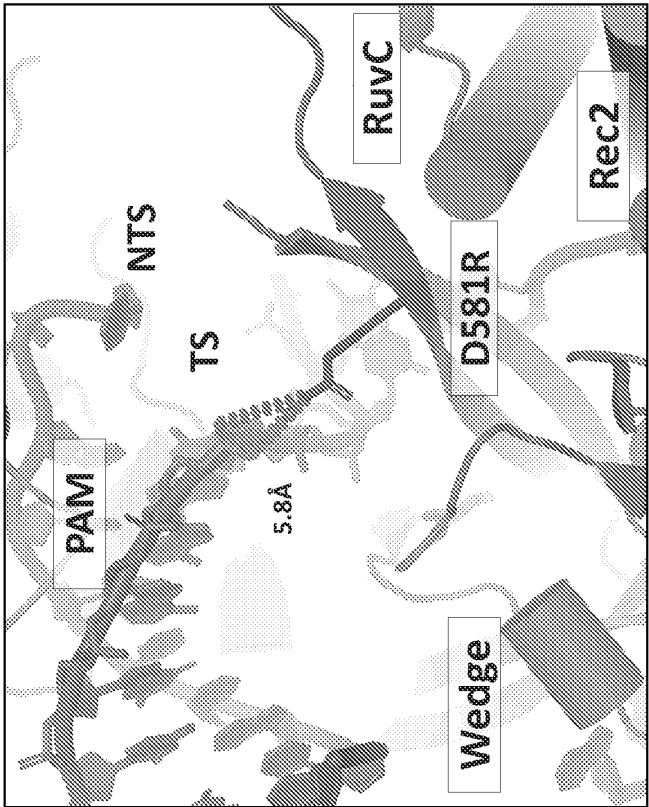
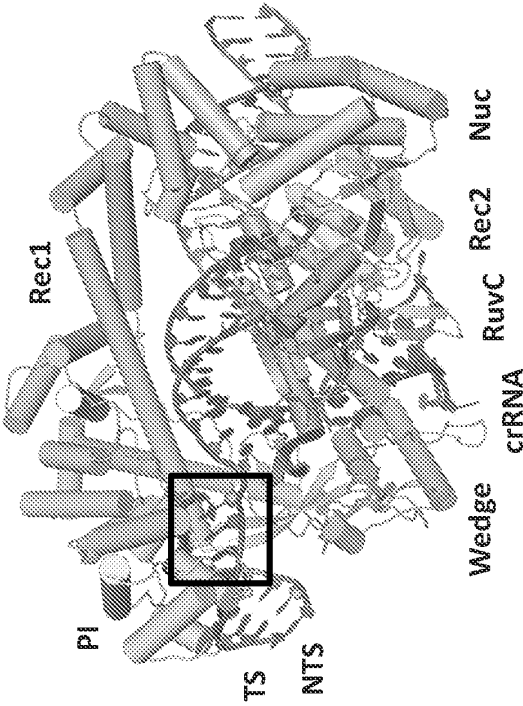


FIG. 20A



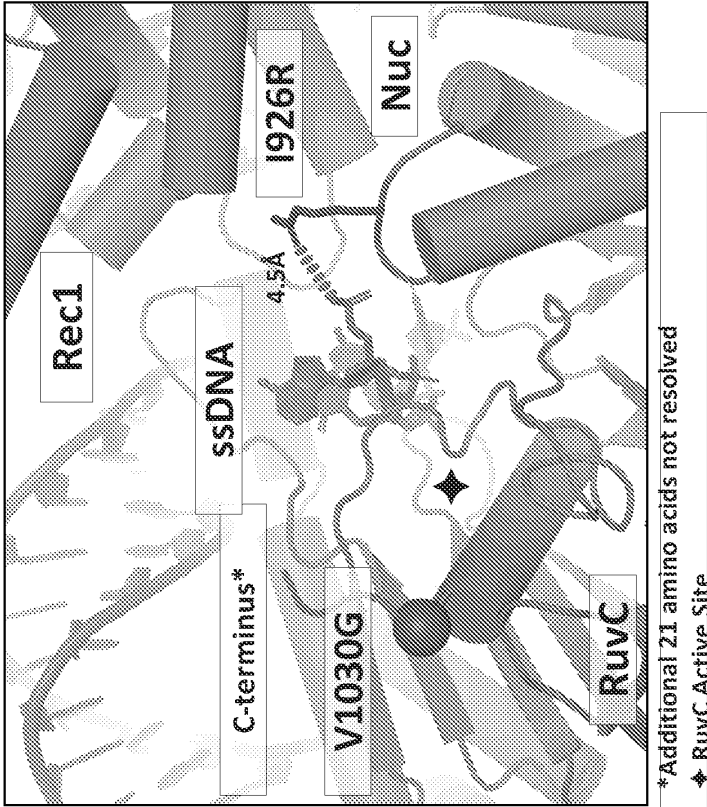
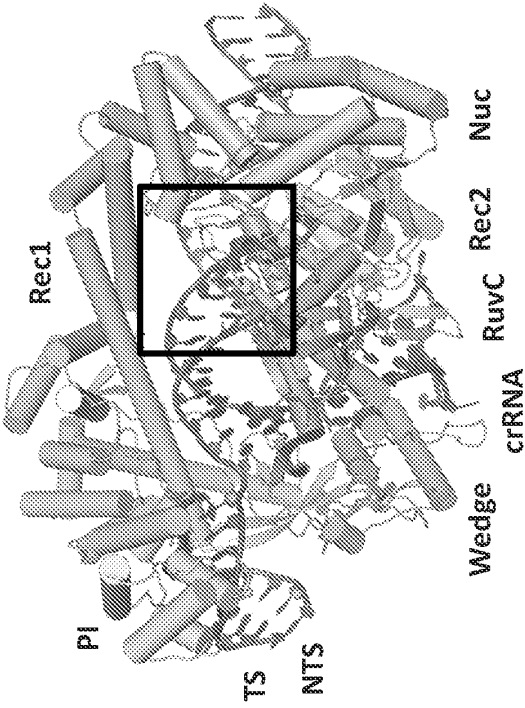


FIG. 20B

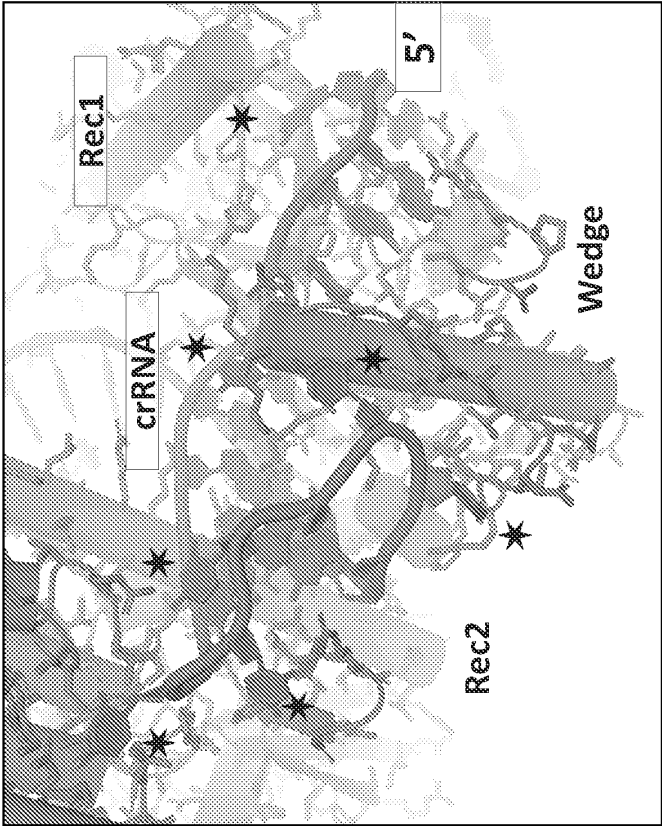


FIG. 20C

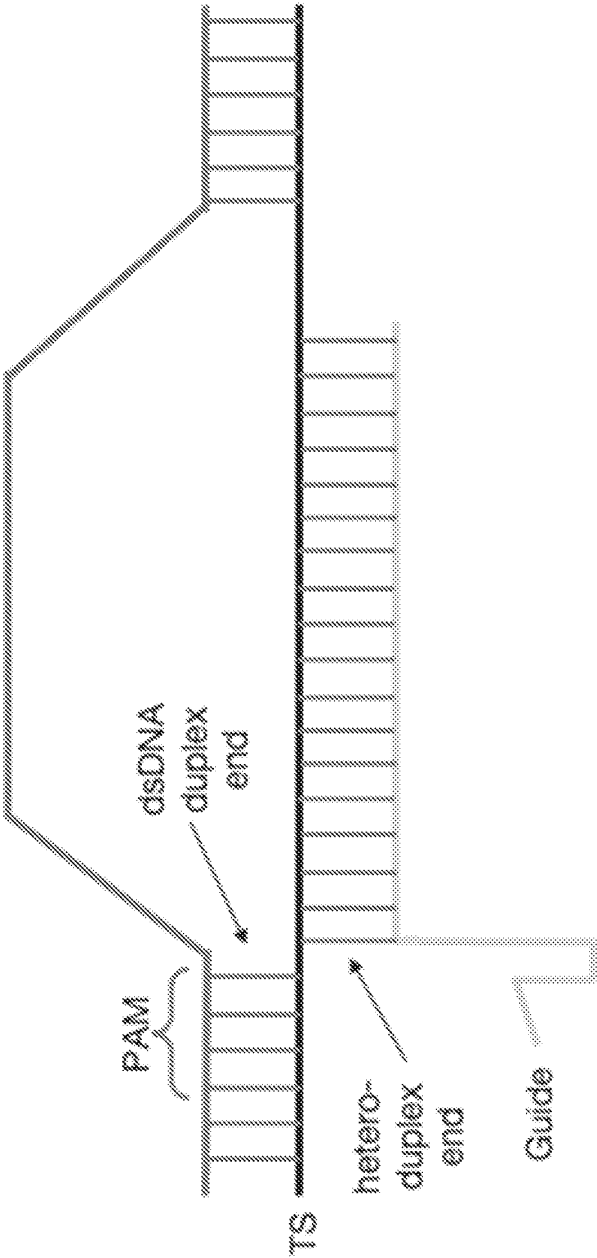


FIG. 21A

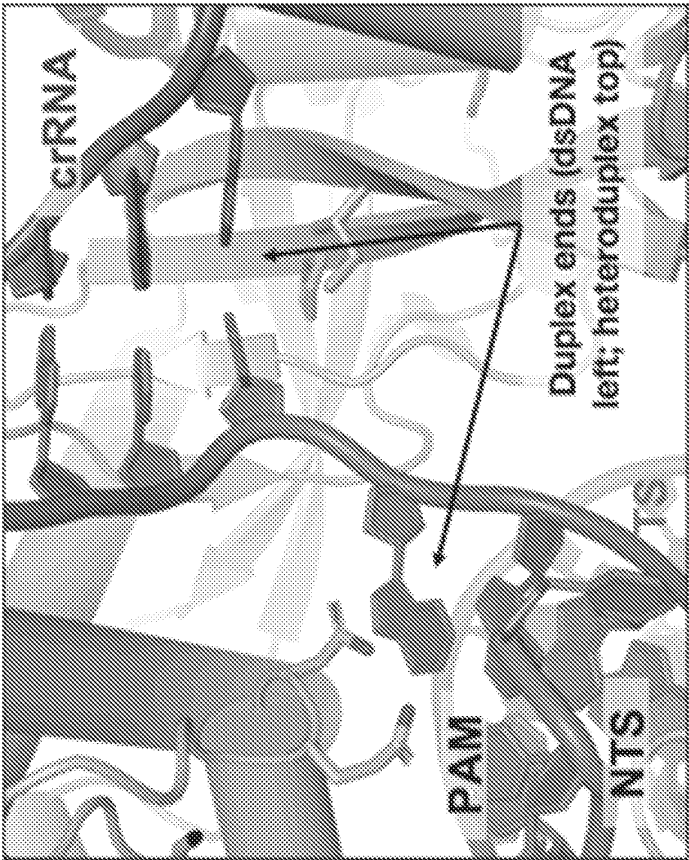


FIG. 21B

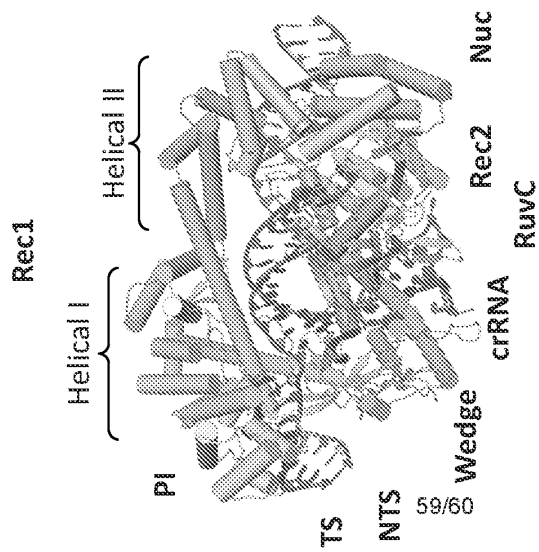
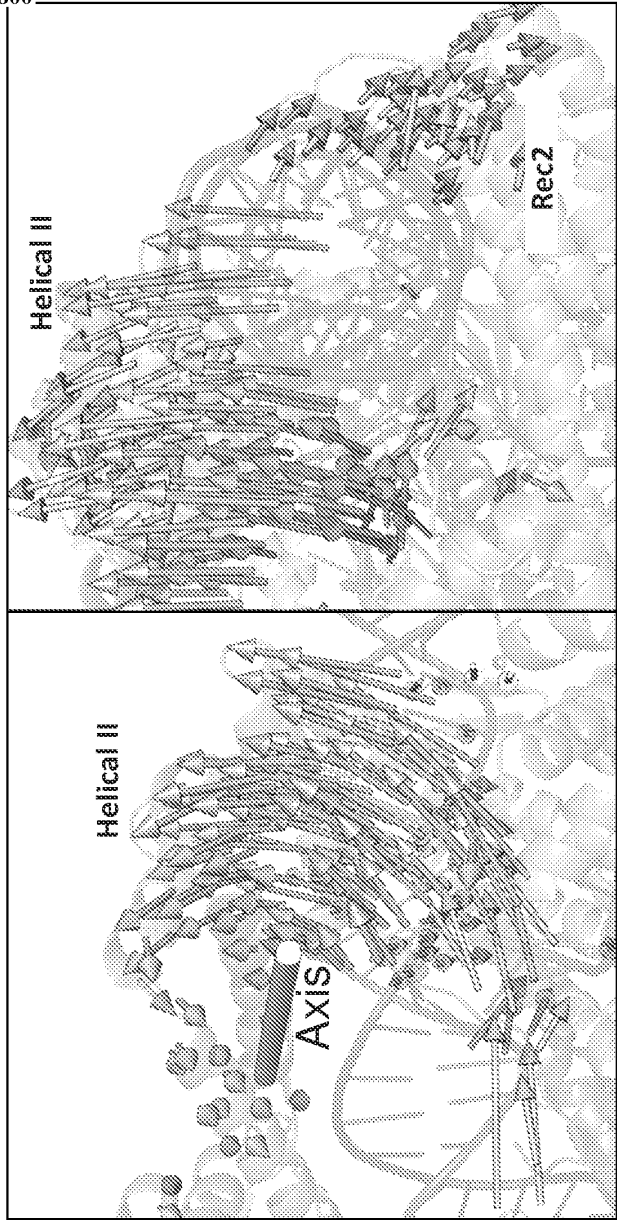


FIG. 22A

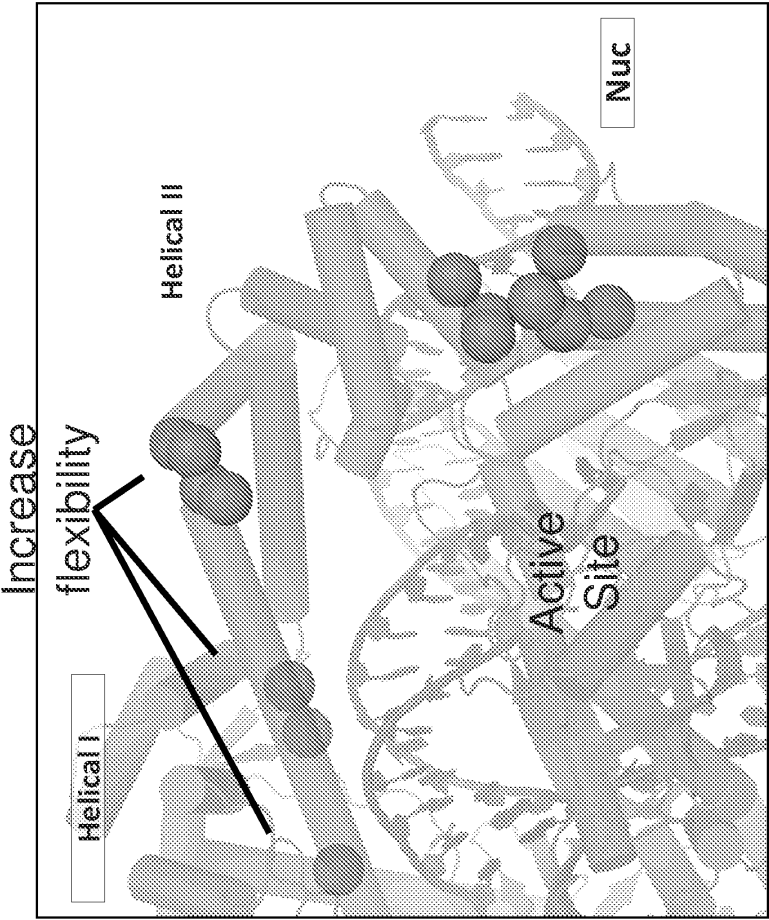
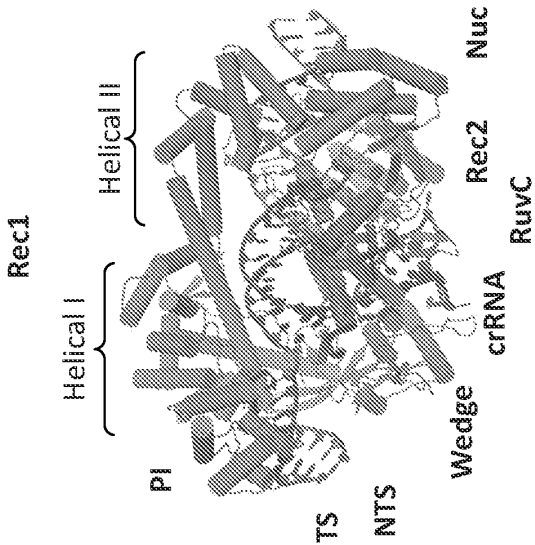


FIG. 22B