

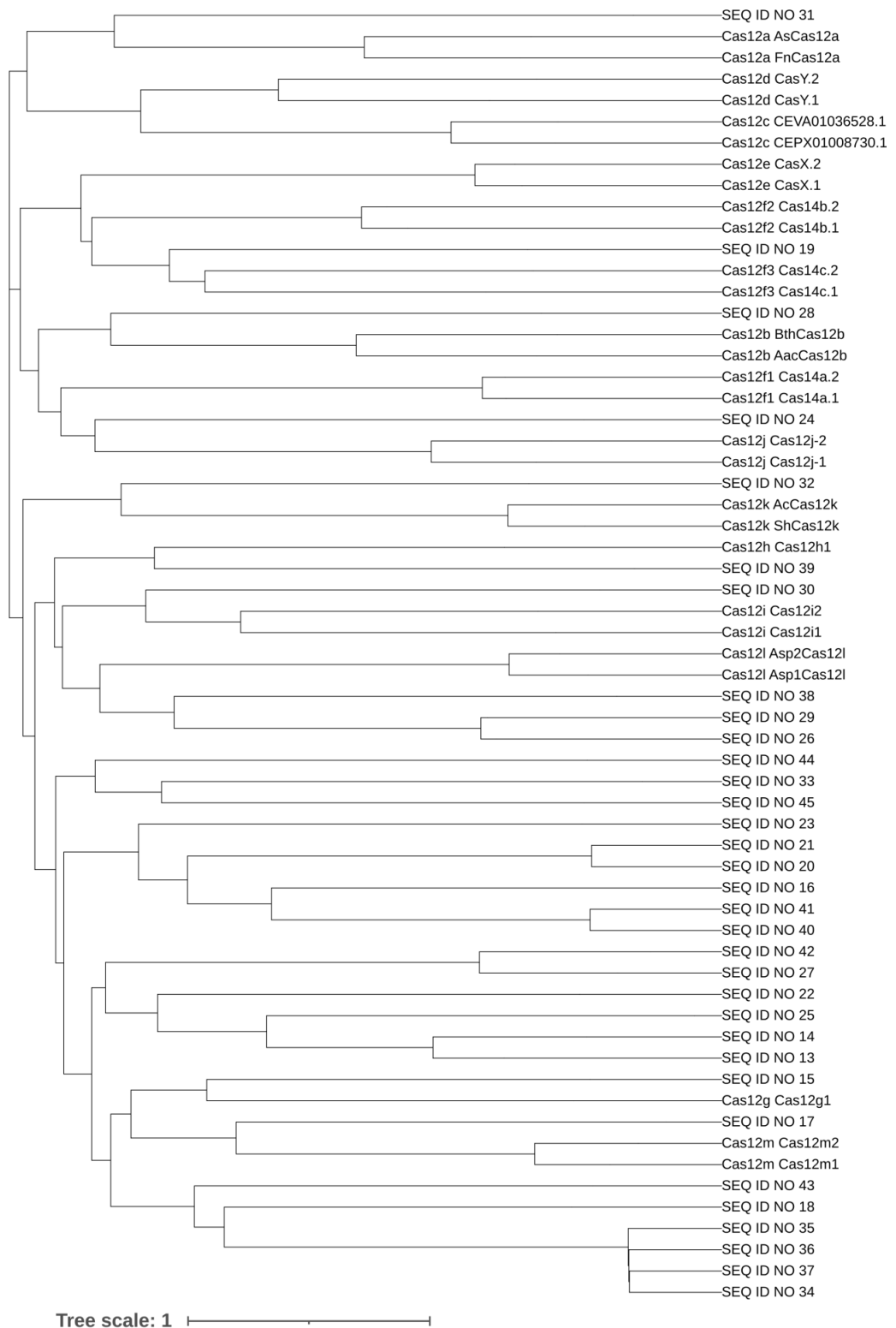


FIG. 1A

CLUSTER	Protein
CLUSTER1	SEQ ID NO: 31
CLUSTER2	SEQ ID NO: 28
CLUSTER3	SEQ ID NO: 24
CLUSTER4	SEQ ID NO: 32
CLUSTER5	SEQ ID NO: 29
CLUSTER6	SEQ ID NO: 30
CLUSTER7	SEQ ID NO: 38、 29、 26
CLUSTER8	SEQ ID NO: 44、 33、 45
CLUSTER9	SEQ ID NO: 23、 21、 20、 16、 41、 40
CLUSTER10	SEQ ID NO: 42、 27、 22、 25、 14、 13
CLUSTER11	SEQ ID NO: 15
CLUSTER12	SEQ ID NO: 17
CLUSTER13	SEQ ID NO: 43、 18、 34、 35、 36、 37

FIG. 1B

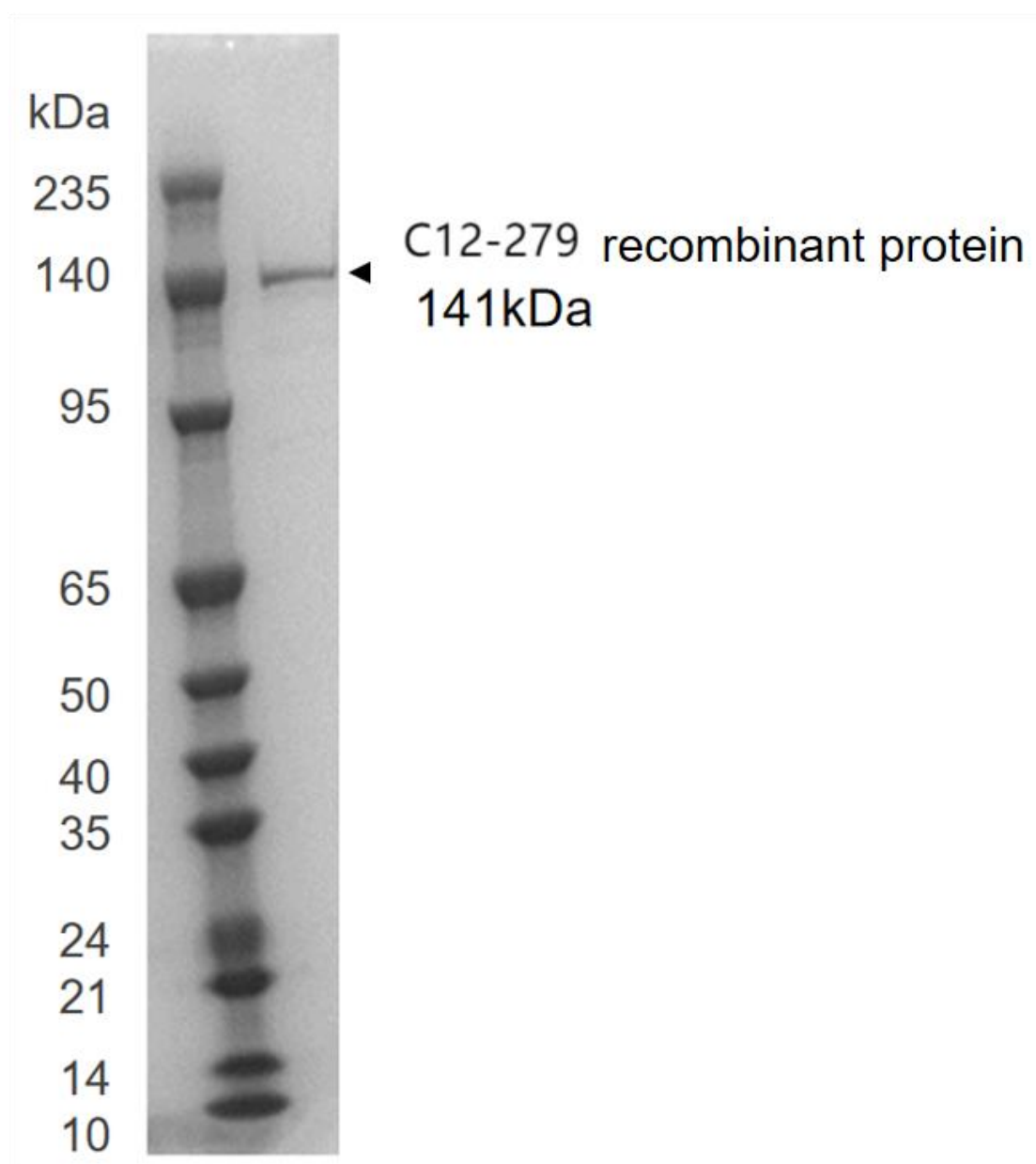
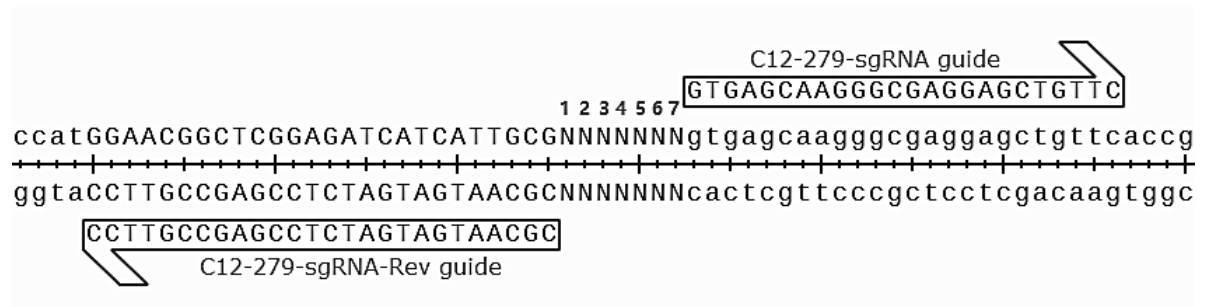
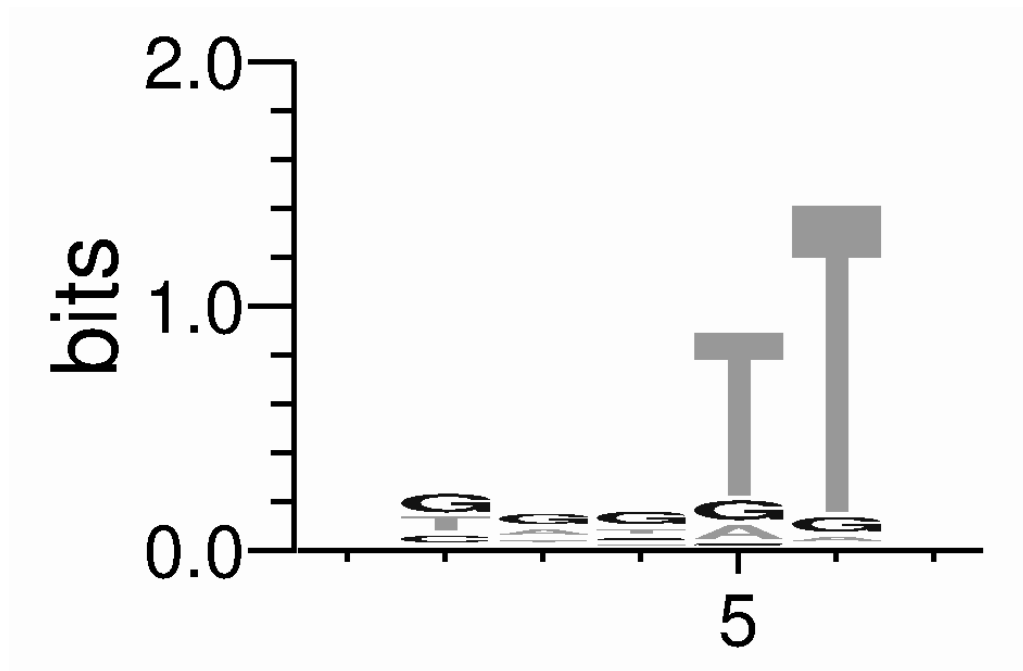


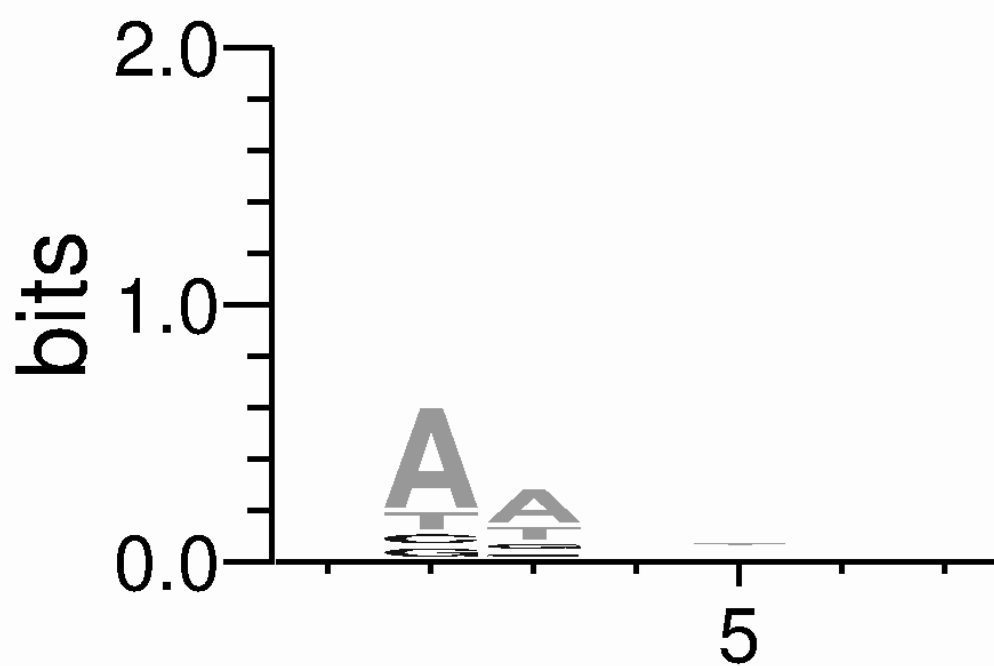
FIG. 2

**FIG. 3**



	N1	N2	N3	N4	N5	N6	N7
A	23	6	27	13	8	2	21
T	22	33	19	23	77	90	35
G	29	40	41	45	11	5	18
C	24	20	10	17	3	1	24

FIG. 4



	N1	N2	N3	N4	N5	N6	N7
G	34	8	13	34	25	29	31
T	25	14	23	24	37	27	25
A	17	67	51	19	15	17	19
C	22	9	10	21	21	24	23

FIG. 5

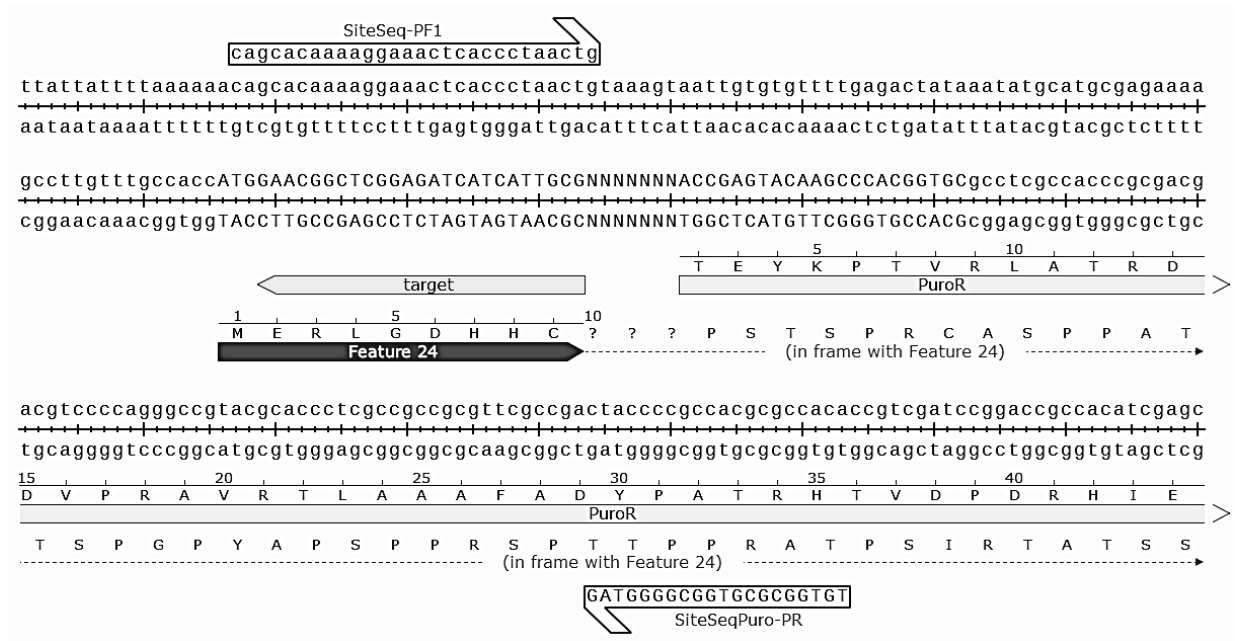
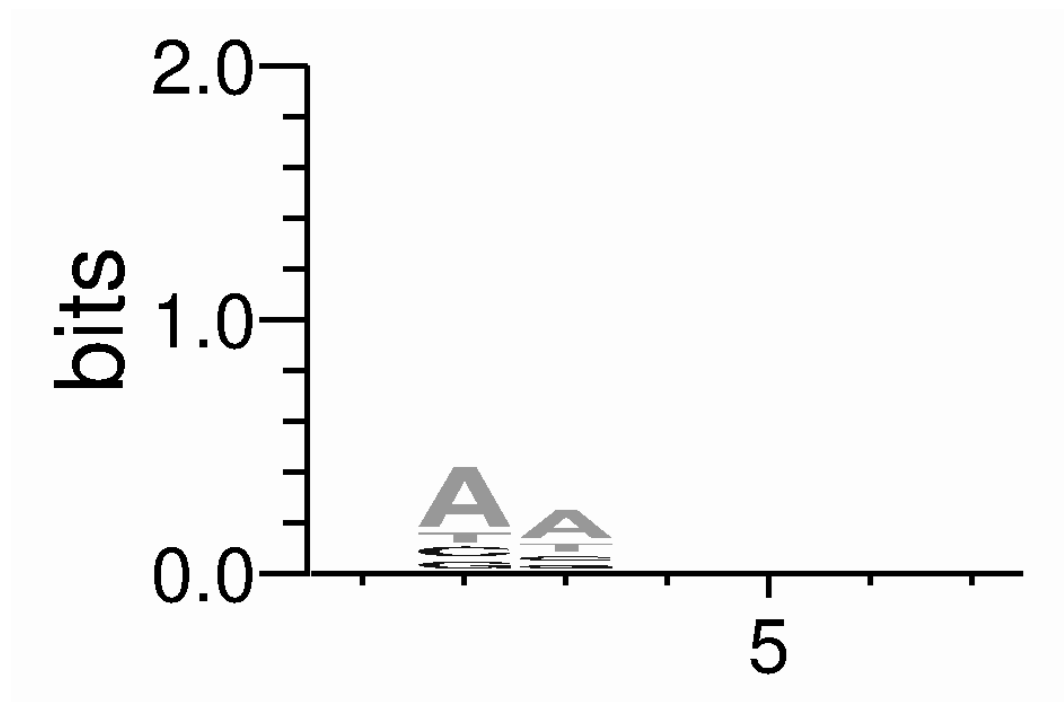


FIG. 6



	N1	N2	N3	N4	N5	N6	N7
A	25	60	51	21	20	20	25
G	23	11	13	28	24	27	24
C	23	13	14	27	25	29	24
T	27	14	20	21	29	22	24

FIG. 7

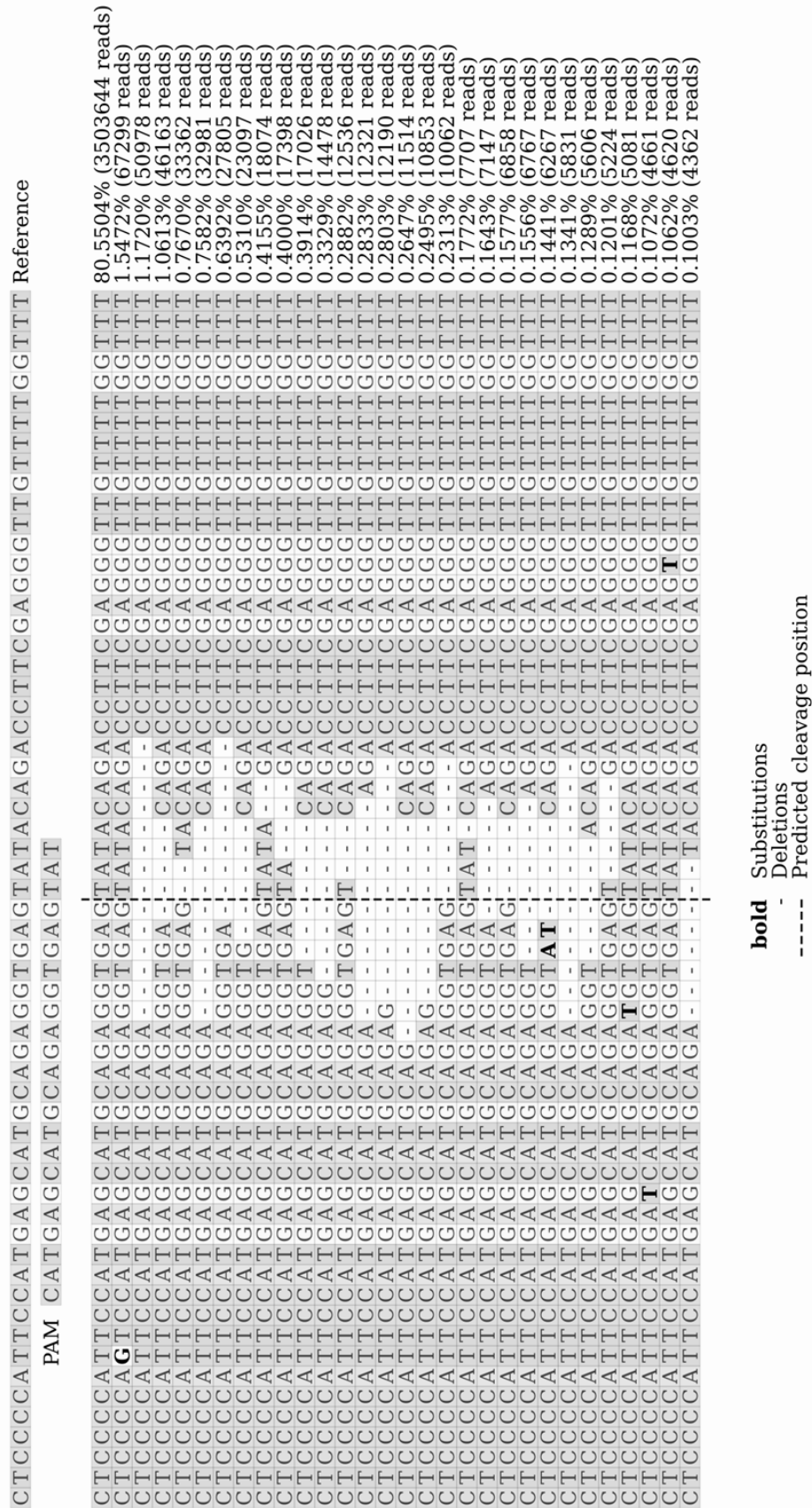


FIG. 8

	N1	N2	N3	N4	N5	N6	N7
T	14	21	4	27	16	32	22
A	0	32	95	60	22	17	24
G	85	26	NaN	12	33	27	25
C	NaN	18	NaN	NaN	28	23	28

FIG. 9

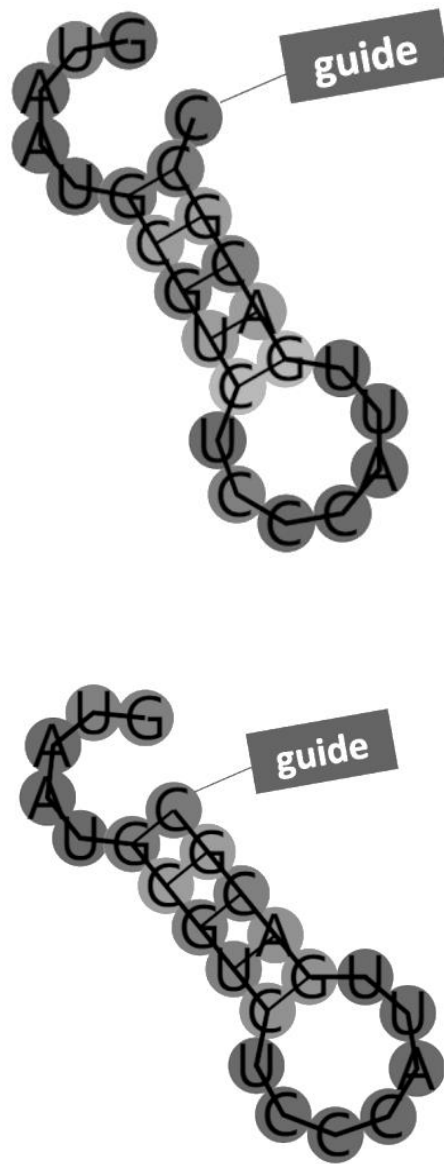
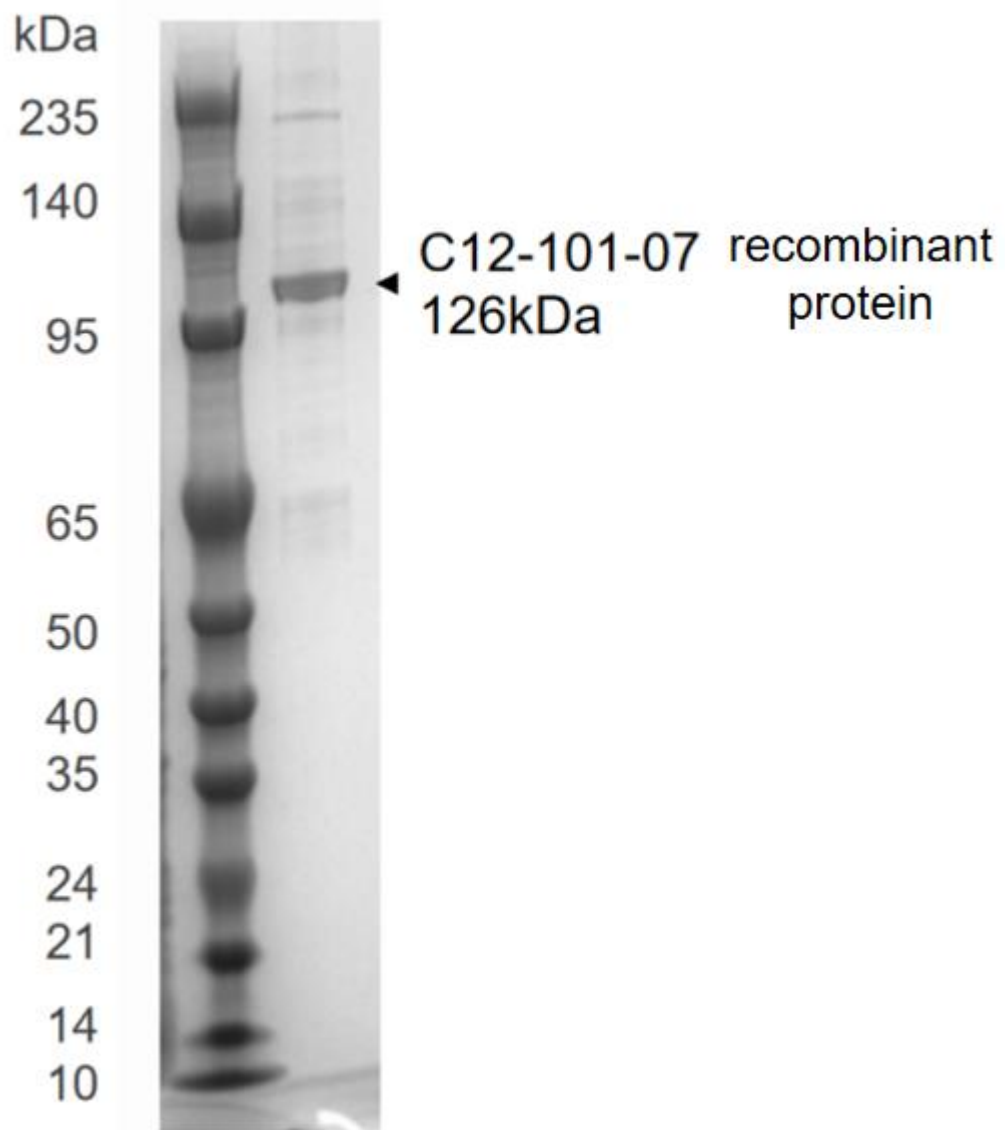
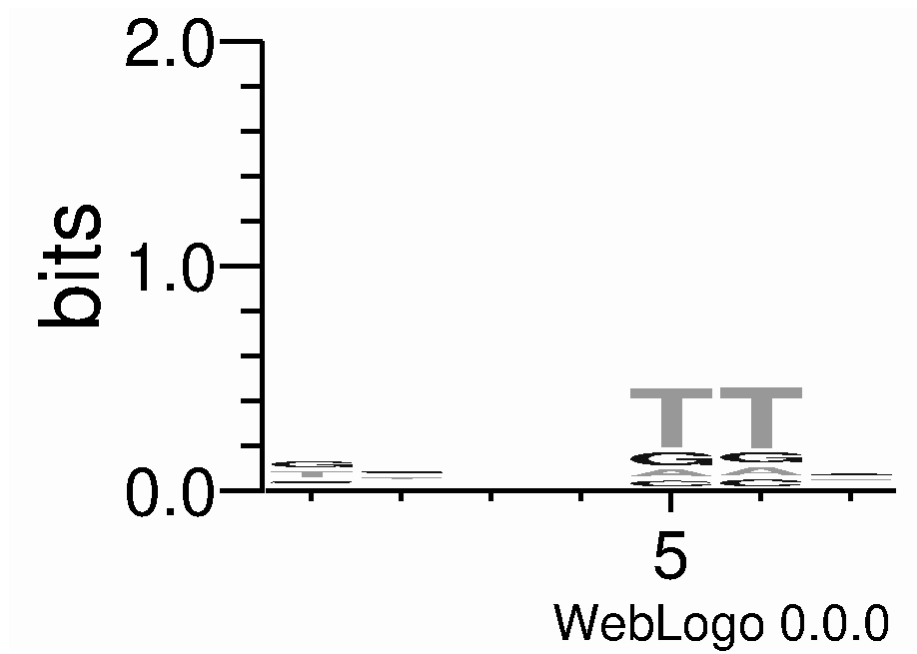


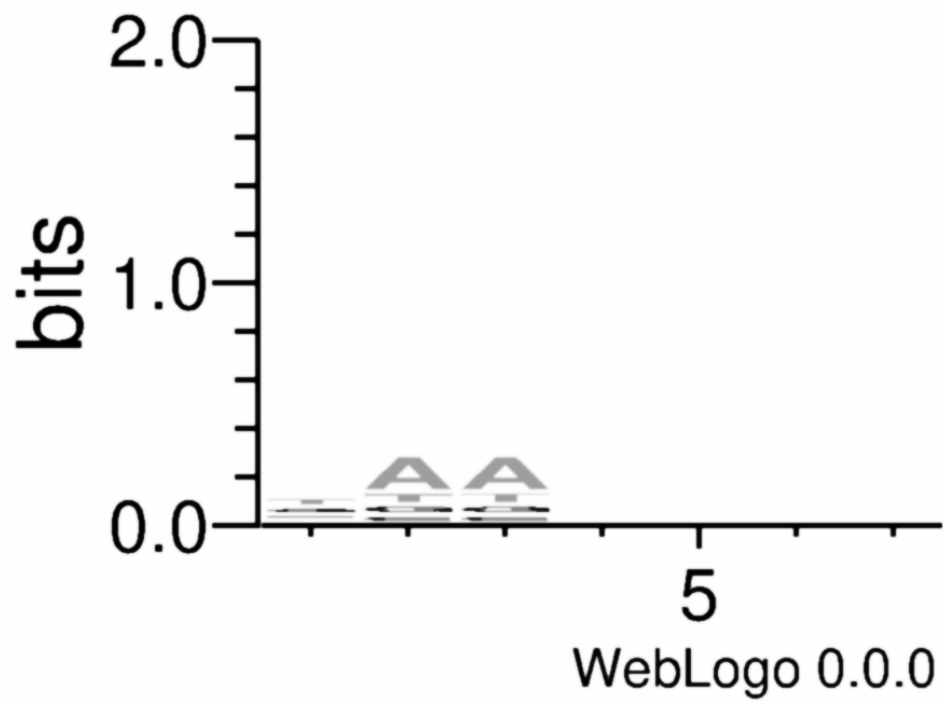
FIG. 10

**FIG. 11**



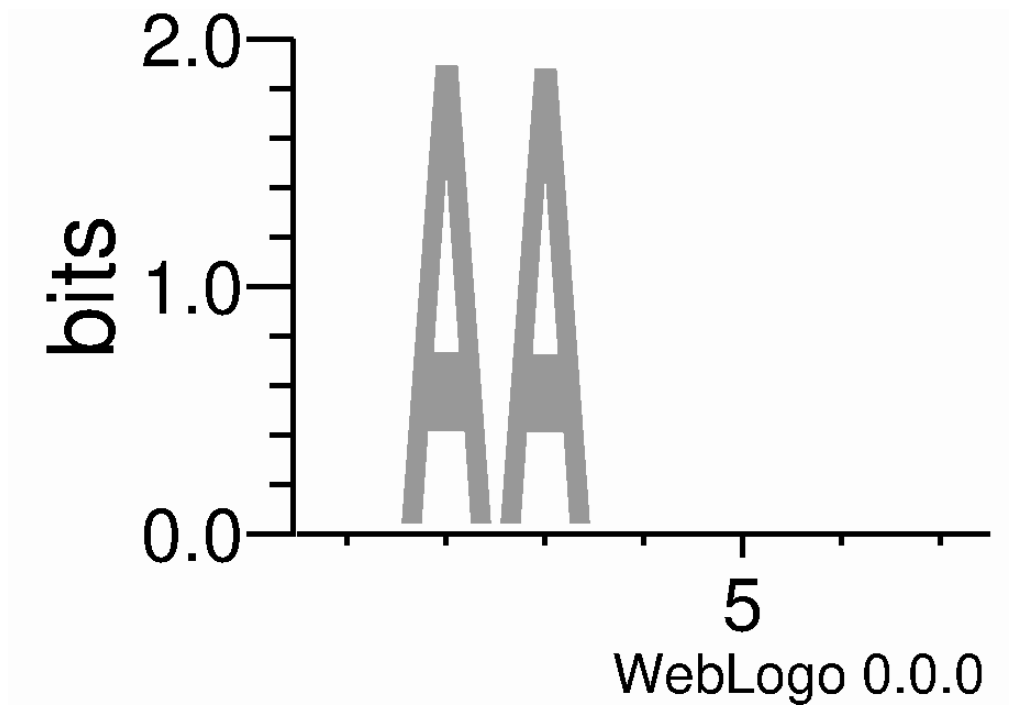
	N1	N2	N3	N4	N5	N6	N7
T	33	33	28	31	61	62	30
G	34	33	32	30	17	14	35
C	21	20	16	21	9	10	19
A	9	13	22	17	11	12	15

FIG. 12



	N1	N2	N3	N4	N5	N6	N7
T	36	18	19	34	30	27	28
C	22	12	11	19	22	24	23
G	28	15	14	26	30	25	25
A	11	53	53	20	16	22	22

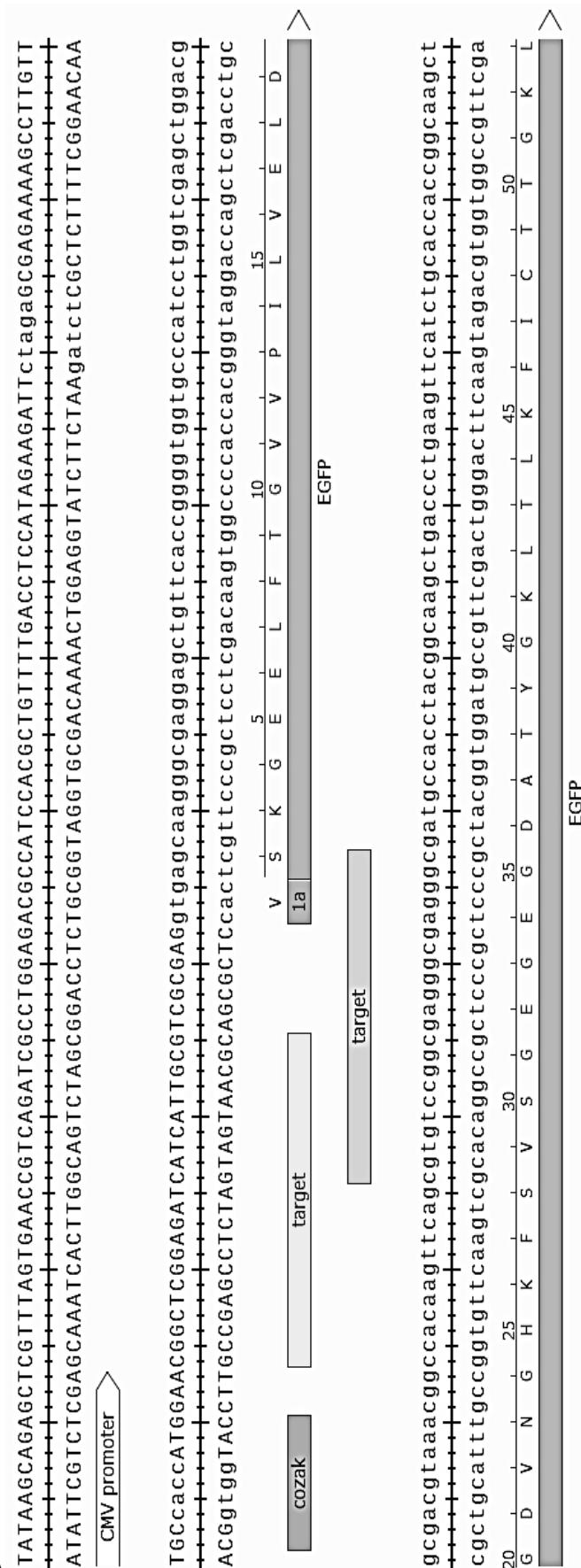
FIG. 13



	N1	N2	N3	N4	N5	N6	N7
T	22	0	0	23	23	22	24
G	25	0	0	23	25	27	23
C	24	0	0	24	24	23	25
A	27	98	98	28	26	26	26

FIG. 14

FIG. 15A



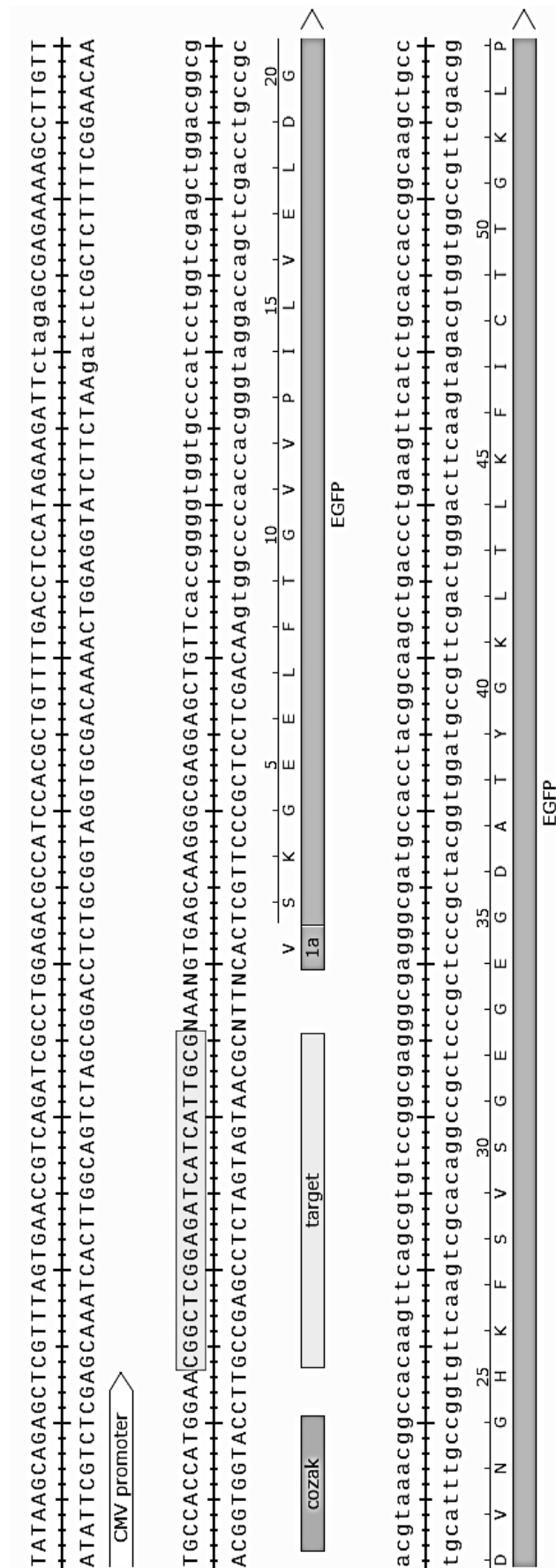


FIG. 15B

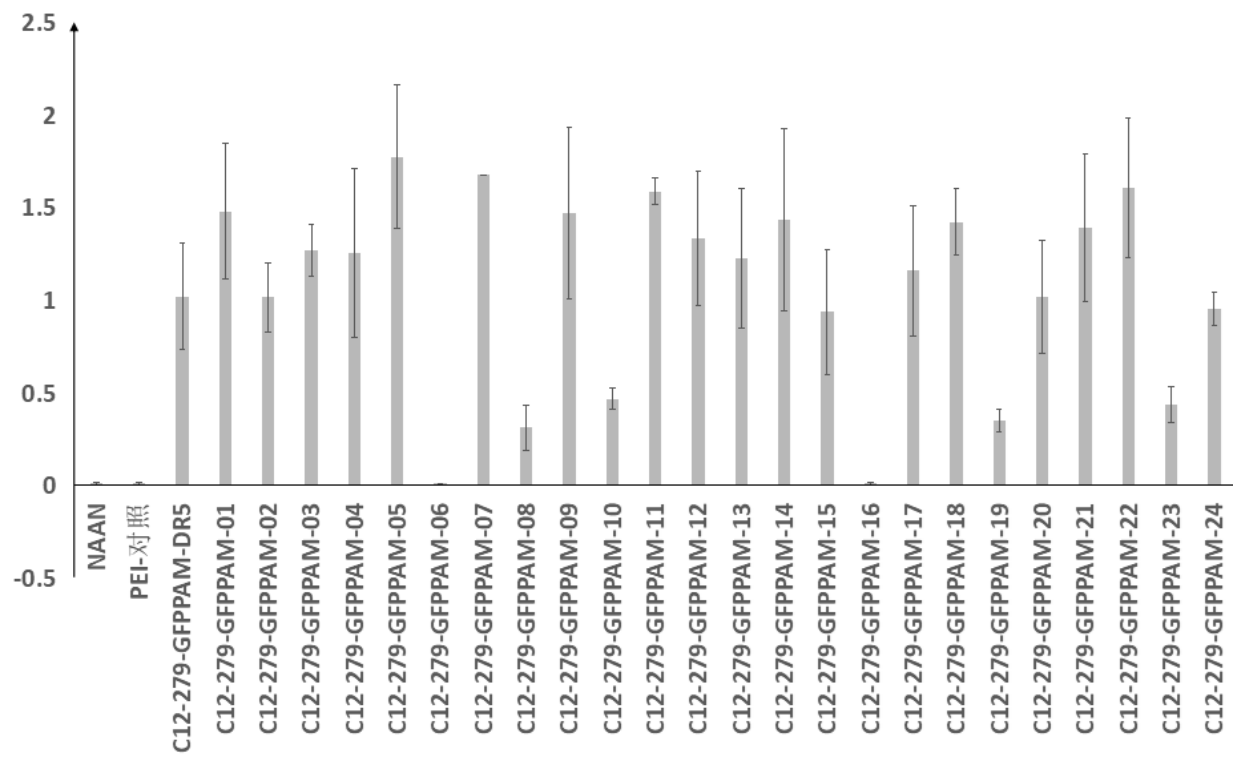


FIG. 16

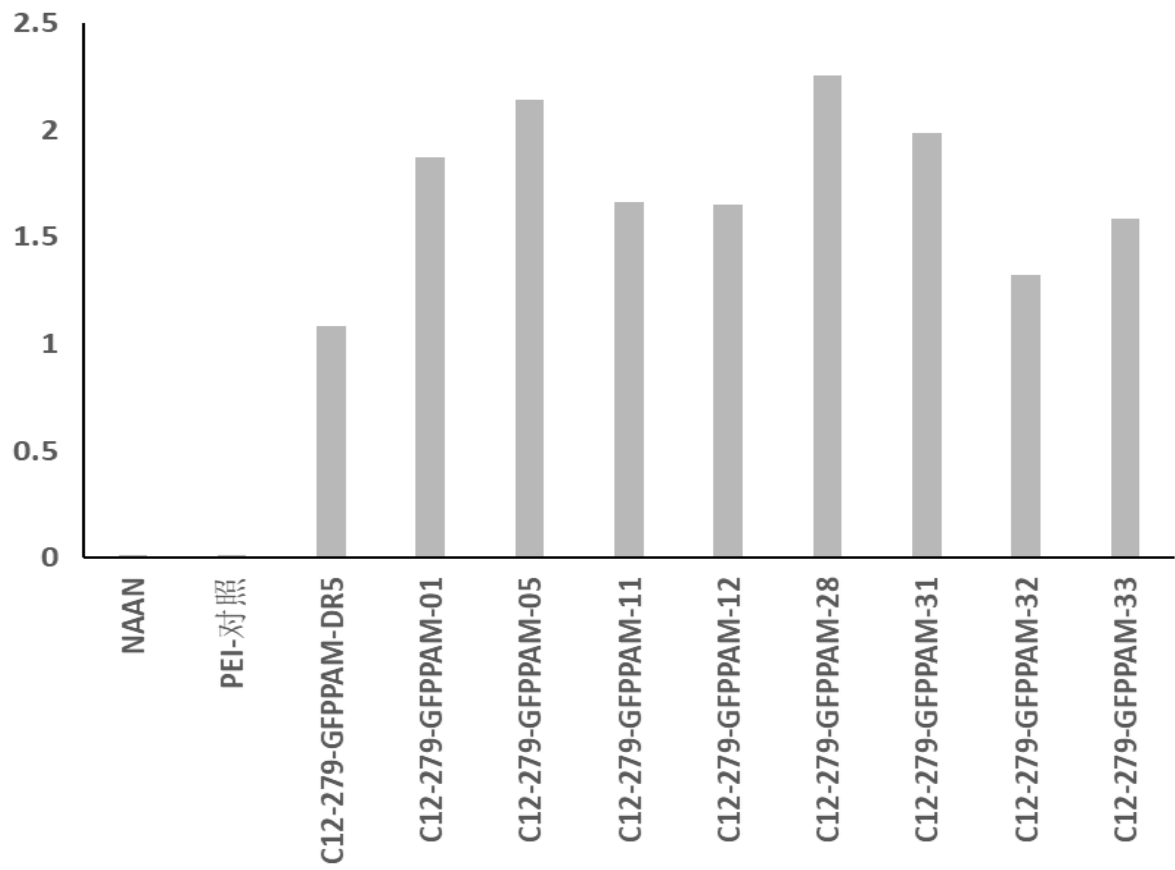
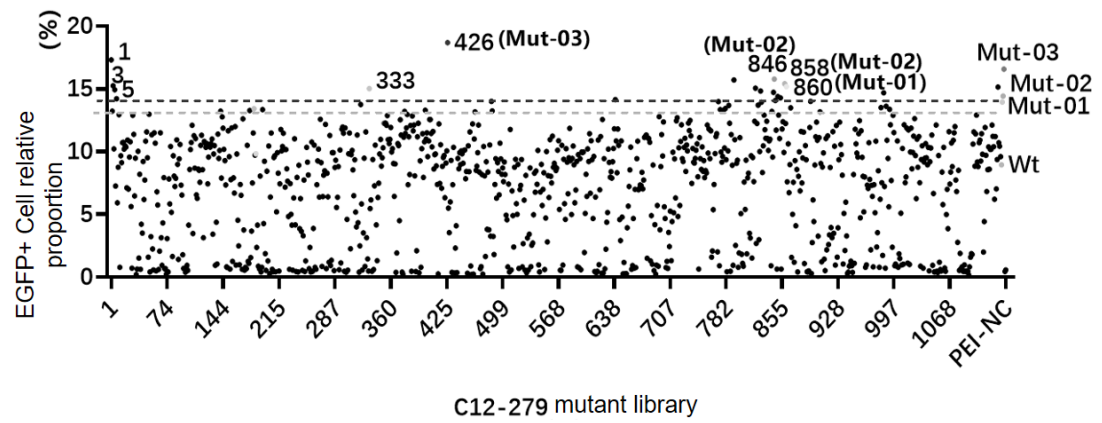


FIG. 17

**FIG. 18**

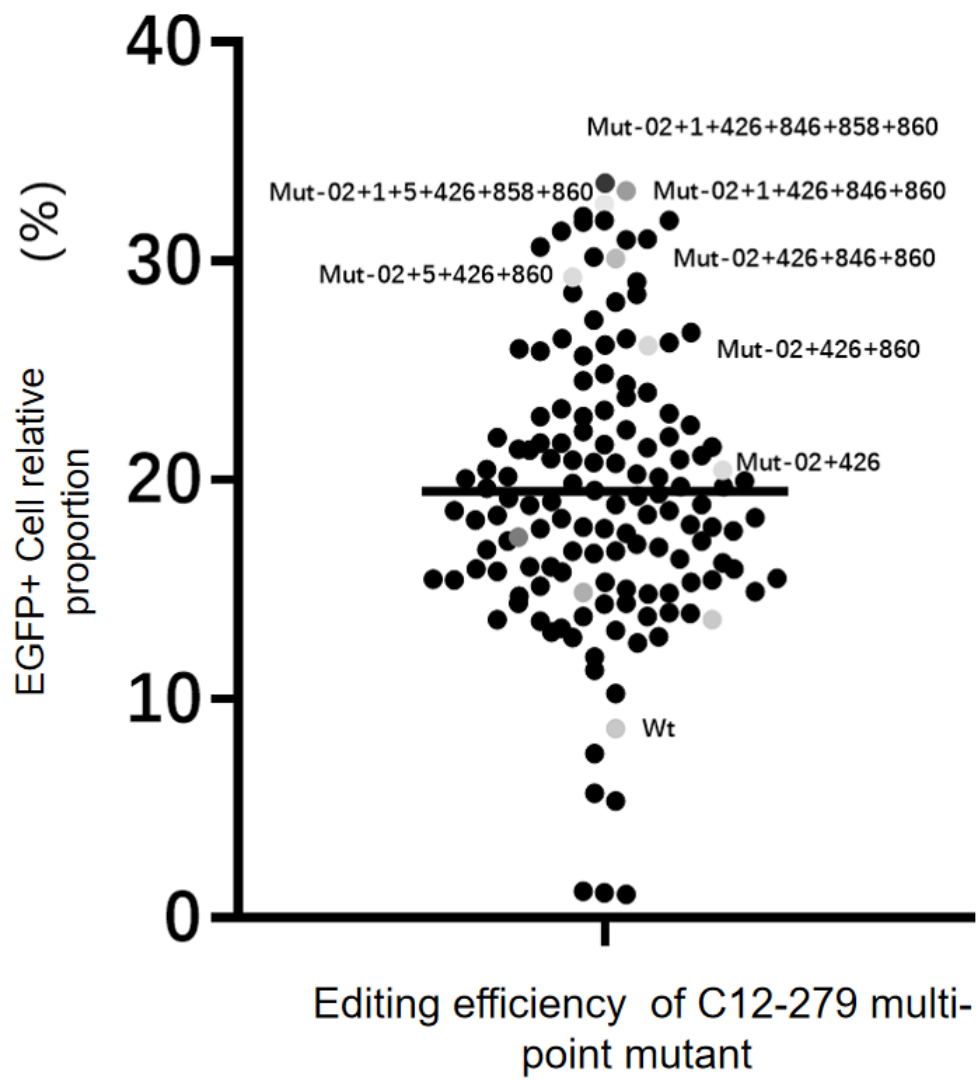
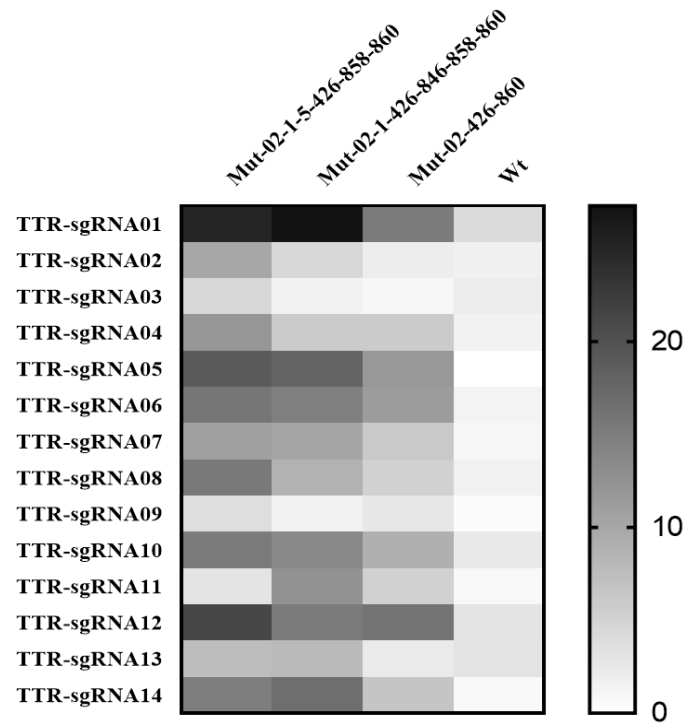
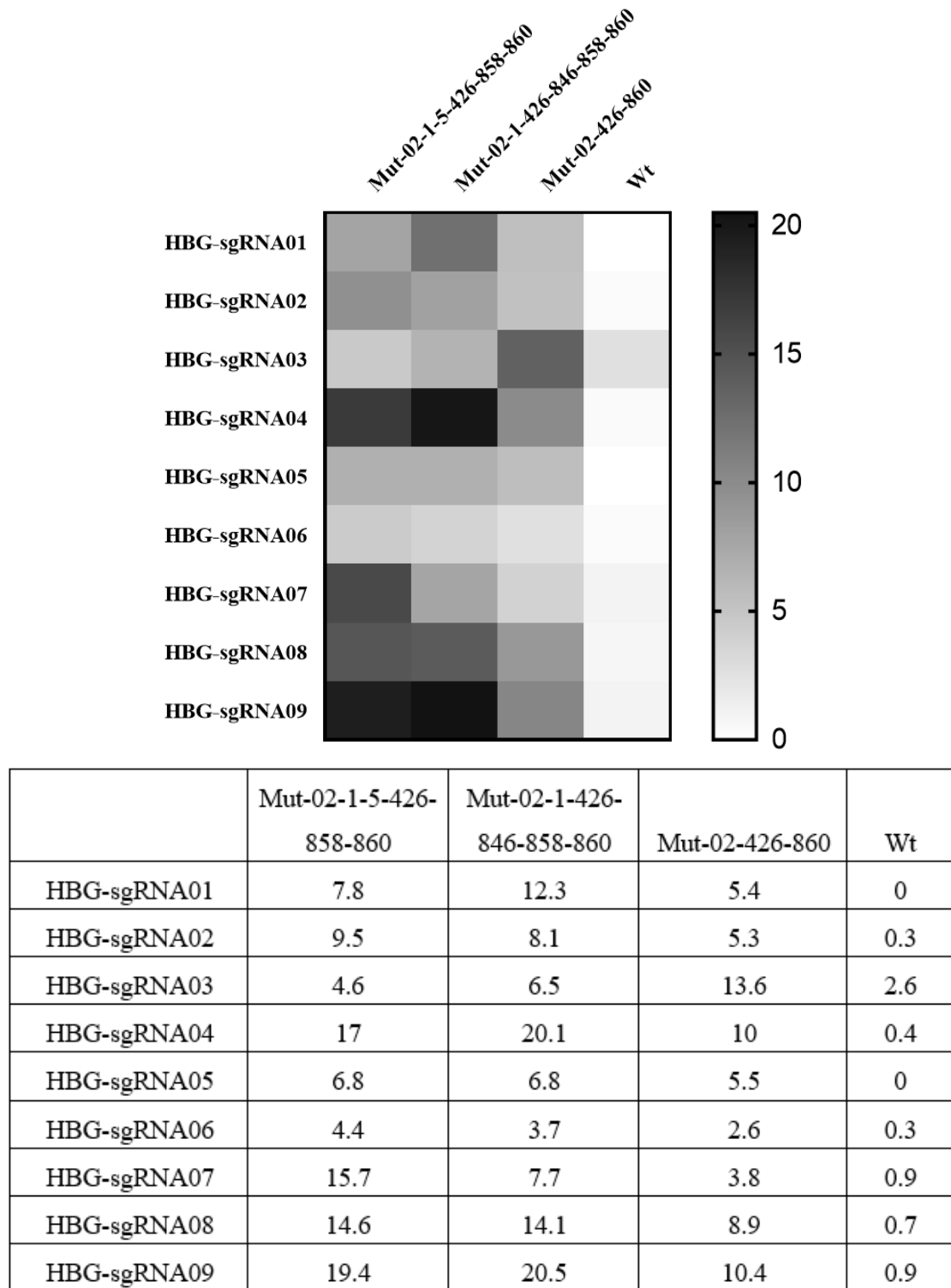


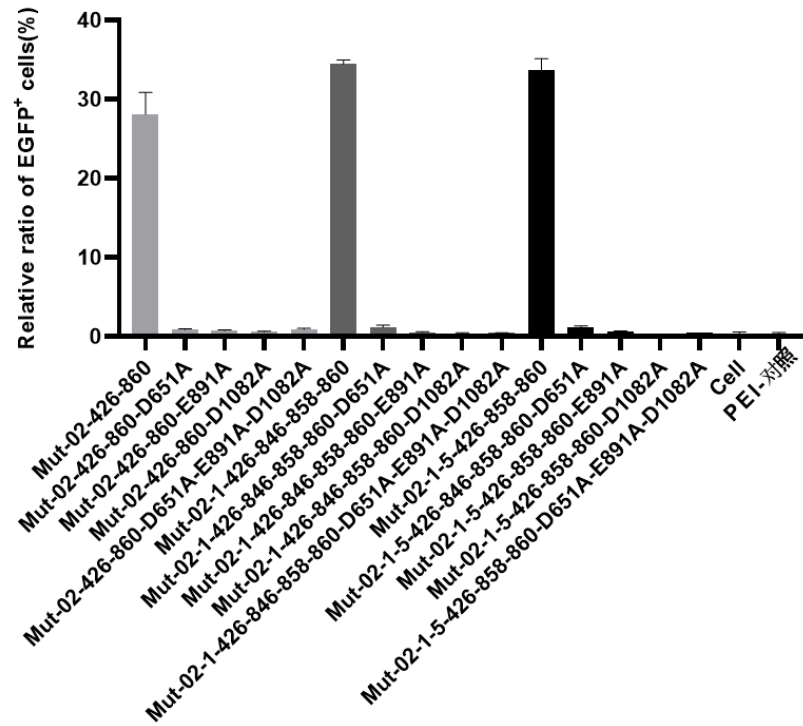
FIG. 19



	Mut-02-1-5-426-858-860	Mut-02-1-426-846-858-860	Mut-02-426-860	Wt
TTR-sgRNA01	25	27.3	15.1	4
TTR-sgRNA02	10	4.6	2	1.7
TTR-sgRNA03	4.5	1.3	0.8	2.1
TTR-sgRNA04	12	5.8	5.8	1.3
TTR-sgRNA05	18.9	17.7	11.8	0
TTR-sgRNA06	15.7	14.5	11.3	1.2
TTR-sgRNA07	10.9	10.3	6.2	0.8
TTR-sgRNA08	15.4	8.7	5.2	1.5
TTR-sgRNA09	3.7	1.5	2.6	0.4
TTR-sgRNA10	15.1	13.6	9.1	2.4
TTR-sgRNA11	3	12.5	5.2	0.7
TTR-sgRNA12	21.1	15.2	15.9	3.1
TTR-sgRNA13	7.5	7.9	2.3	3.2
TTR-sgRNA14	14.7	16.7	6.6	0.7

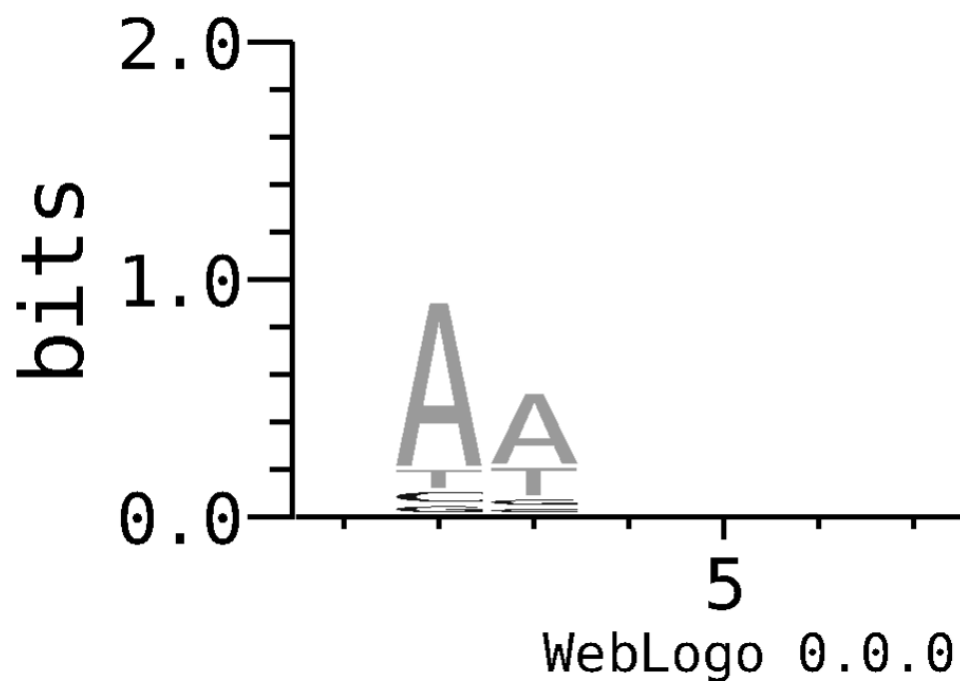
FIG. 20A

**FIG. 20B**



Grouping	Editing efficiency(%)
Mut-02-426-860	28.09
Mut-02-426-860-D651A	0.87
Mut-02-426-860-E891A	0.73
Mut-02-426-860-D1082A	0.56
Mut-02-426-860-D651A-E891A-D1082A	0.89
Mut-02-1-426-846-858-860	34.40
Mut-02-1-426-846-858-860-D651A	1.14
Mut-02-1-426-846-858-860-E891A	0.51
Mut-02-1-426-846-858-860-D1082A	0.35
Mut-02-1-426-846-858-860-D651A-E891A-D1082A	0.41
Mut-02-1-5-426-858-860	33.69
Mut-02-1-5-426-846-858-860-D651A	1.11
Mut-02-1-5-426-858-860-E891A	0.54
Mut-02-1-5-426-858-860-D1082A	0.38
Mut-02-1-5-426-858-860-D651A-E891A-D1082A	0.45
Cell	0.35
PEI-Control	0.35

FIG. 21



index	1	2	3	4	5	6	7
C	22	6	6	27	25	26	25
A	28	77	60	23	20	23	25
T	24	10	25	19	29	23	24
G	24	4	7	28	24	26	25

FIG. 23

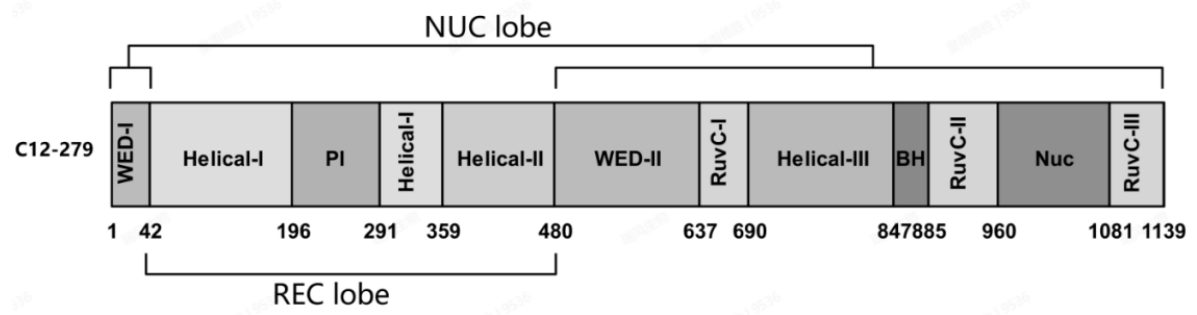


FIG. 24