【FIG 1/37】

【FIG 1a】

sgRNAs	Direction	Mismatch 0	Mismatch 1	Mismatch 2	Indel ratio(%)
sgRNA_TATA_Sp#1	-	1	0	1	32.80
sgRNA_TATA_Sp#2	+	1	0	0	42.00
sgRNA_TATA_Sp#3	+	1	0	0	25.20
sgRNA_TATA_Sp#4	+	1	0	2	59.10
sgRNA_TATA_Sp#5	+	1	0	0	16.20
sgRNA_TATA_Sp#6	+	1	0	1	30.30
sgRNA_TATA_Sp#7	-	1	0	1	53.80
sgRNA_TATA_Sp#8	+	1	0	0	7.30
sgRNA_TATA_Sp#9	-	1	0	1	26.90
sgRNA_TATA_Sp#10	-	1	0	1	15.90
sgRNA_TATA_Sp#11	-	1	0	2	24.20
sgRNA_TATA_Sp#12	-	1	0	2	38.20
sgRNA_TATA_Sp#13	-	1	0	0	6.90
sgRNA_TATA_Sp#14	+	1	0	1	62.00
sgRNA_TATA_Sp#15	+	1	0	1	54.60
sgRNA_TATA_Sp#16	-	1	0	1	32.50

【FIG 1b】

sgRNAs	Direction	Mismatch 0	Mismatch 1	Mismatch 2	Indel ratio(%)
sgRNA_Enh_Sp#1	-	1	0	1	66.30
sgRNA_Enh_Sp#2	-	1	0	0	18.80
sgRNA_Enh_Sp#3	-	1	0	1	24.40
sgRNA_Enh_Sp#4	-	1	0	0	44.00
sgRNA_Enh_Sp#5	-	1	0	2	41.30
sgRNA_Enh_Sp#6	+	1	0	1	8.60
sgRNA_Enh_Sp#10	-	1	0	2	19.30
sgRNA_Enh_Sp#11	-	1	0	2	21.90
sgRNA_Enh_Sp#12	-	1	0	2	2.50
sgRNA_Enh_Sp#13	-	1	0	1	12.80
sgRNA_Enh_Sp#14	-	1	0	1	11.40
sgRNA_Enh_Sp#15	+	1	0	1	21.80
sgRNA_Enh_Sp#16	+	1	0	1	47.40

【FIG 2/37】

【FIG 2a】

sgRNAs	Direction	Mismatch 0	Mismatch 1	Mismatch 2	Indel ratio(%)
sgRNA_TATA_Cj#1	+	1	0	0	0.35
sgRNA_TATA_Cj#2	+	1	0	0	0.07
sgRNA_TATA_Cj#3	+	1	0	0	0.04
sgRNA_TATA_Cj#4	+	1	0	1	3.80
sgRNA_TATA_Cj#5	+	1	0	0	36.10
sgRNA_TATA_Cj#6	-	1	0	0	0.02
sgRNA_TATA_Cj#7	+	1	0	0	0.02
sgRNA_TATA_Cj#8	-	1	0	0	0.06
sgRNA_TATA_Cj#9	-	1	0	0	0.15
sgRNA_TATA_Cj#10	-	1	0	0	13.10
sgRNA_TATA_Cj#11	-	1	0	0	0.12

【FIG 3/37】

【FIG 2b】

sgRNAs	Direction	Mismatch 0	Mismatch 1	Mismatch 2	Indel ratio(%)
sgRNA_Enh_Cj#1	+	1	0	0	16.70
sgRNA_Enh_Cj#2	+	1	0	0	0.07
sgRNA_Enh_Cj#3	-	1	0	0	0
sgRNA_Enh_Cj#4	+	1	0	0	1.18
sgRNA_Enh_Cj#5	-	1	0	0	0.03
sgRNA_Enh_Cj#6	-	1	0	0	0.05
sgRNA_Enh_Cj#7	-	1	0	0	0.09
sgRNA_Enh_Cj#8	+	1	0	0	0.28
sgRNA_Enh_Cj#9	-	1	0	0	41.40
sgRNA_Enh_Cj#10	+	1	0	0	0.45
sgRNA_Enh_Cj#11	-	1	0	0	0.55
sgRNA_Enh_Cj#12	+	1	0	0	2.83
sgRNA_Enh_Cj#13	+	1	0	0	0.03

【FIG 5/37】

【FIG 3】

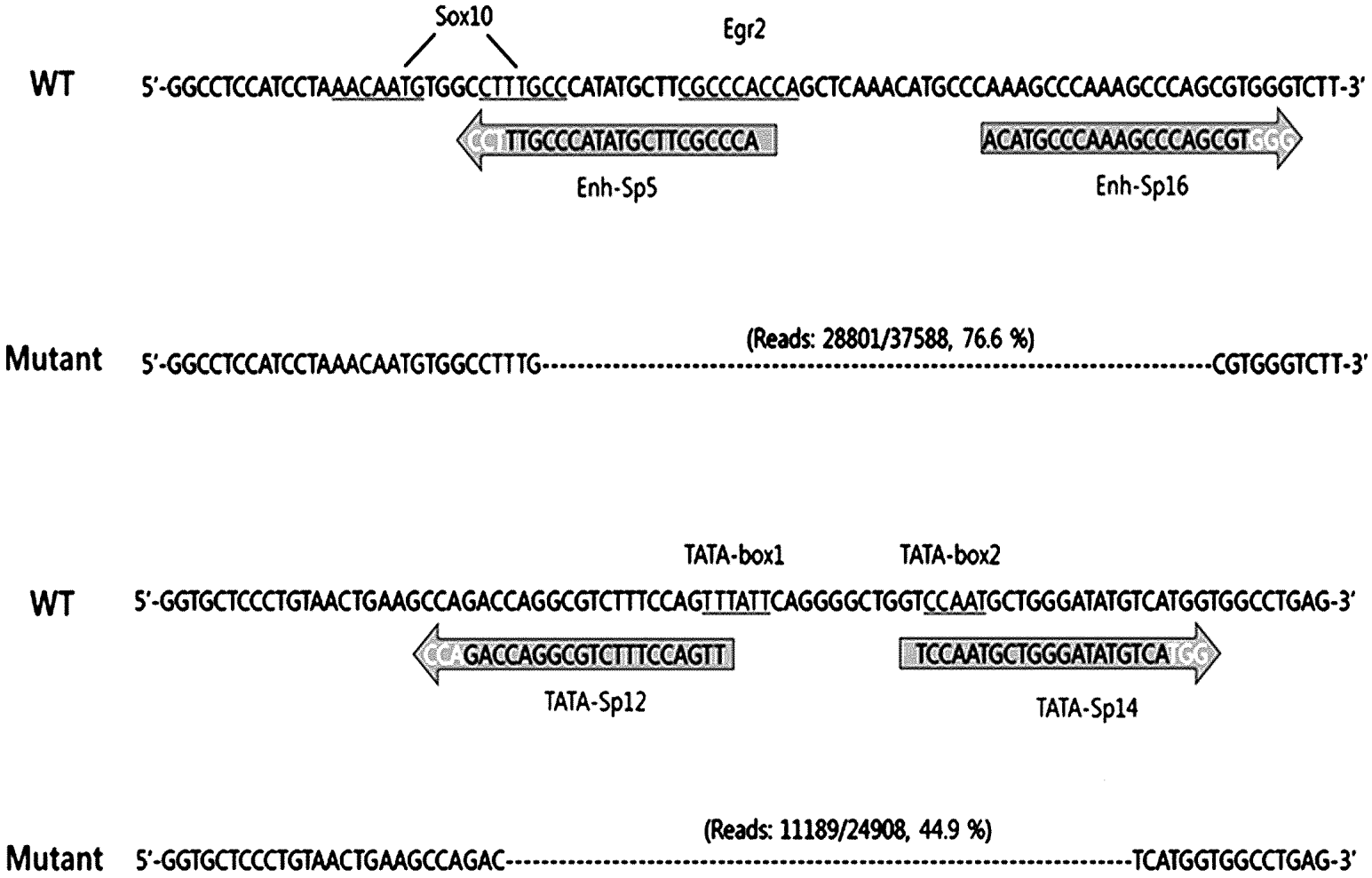
Name	sgRNAs	More than minimum frequency	Insertions	Deletions	Indel ratio(%)
TATA WT		26730	28	70	0.40
TATA-1	sgRNA_TATA_Sp#15	30466	3110	6357	31.10
TATA-2	sgRNA_TATA_Sp#12	9286	0	6929	74.60
	sgRNA_TATA_Sp#14	5651	118	4972	90.10
Enh WT		27917	0	11	0.00
Enh-3	sgRNA_Enh_Sp#1	32148	8744	10126	58.70
Enh-4	sgRNA_Enh_Sp#5	37486	23	30928	82.60
	sgRNA_Enh_Sp#16	37277	69	35000	94.10
Enh-5	sgRNA_Enh_Sp#1	30576	2782	14544	56.70
	sgRNA_Enh_Sp#4	30399	217	11894	39.80
CDS-SP1 WT		35424	0	40	0.10
CDS-SP1	sgRNA_CDS_Sp#1	32206	4613	9077	42.50
CDS-SP3 WT		21997	0	0	0.00
CDS-SP3	sgRNA_CDS_Sp#3	27511	3441	11877	55.70

【FIG 4】

sgRNAs	CDS-SP1		CDS-SP3	
	Reads	Ratio	Reads	Ratio
Total indels	13690	1	15312	1
3N±1, 3N±2	10063	0.74	12795	0.84
3N±0	3627	0.26	2517	0.16

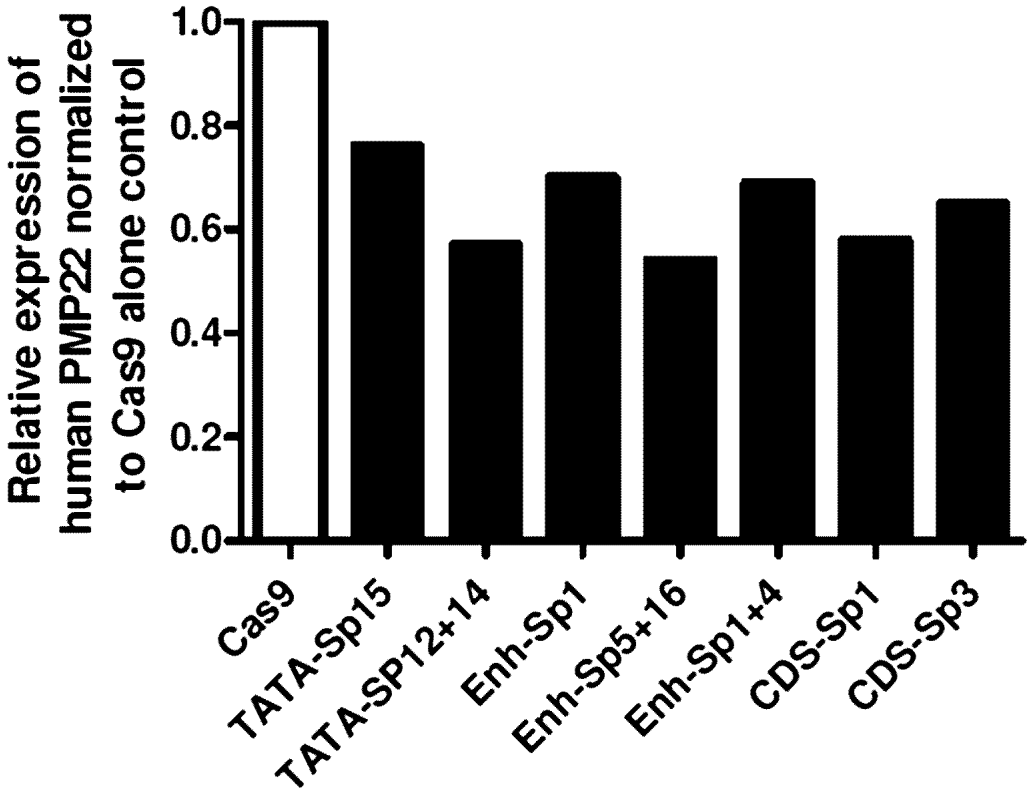
【FIG 6/37】

【FIG 5】


Sox10
Egr2
WT
5'-GGCCTCCATCCTAAACAATGTGGCCTTTGCCCATATGCTTCGCCCACCAGCTCAAACATGCCCAAAGCCCAAAGCCCAGCGTGGGTCTT-3'
TTGCCCATATGCTTCGCCCA
ACATGCCCAAAGCCCAGCGT
Enh-Sp5
Enh-Sp16
(Reads: 28801/37588, 76.6 %)
Mutant
5'-GGCCTCCATCCTAAACAATGTGGCCTTTG----------CGTGGGTCTT-3'
TATA-box1
TATA-box2
WT
5'-GGTGCTCCCTGTAACTGAAGCCAGACCAGGCGTCTTTCCAGTTTATTCAGGGGCTGGTCCAATGCTGGGATATGTCATGGTGGCCTGAG-3'
GACCAGGCGTCTTTCCAGTT
TCCAATGCTGGGATATGTCA
TATA-Sp12
TATA-Sp14
(Reads: 11189/24908, 44.9 %)
Mutant
5'-GGTGCTCCCTGTAACTGAAGCCAGAC----------TCATGGTGGCCTGAG-3'

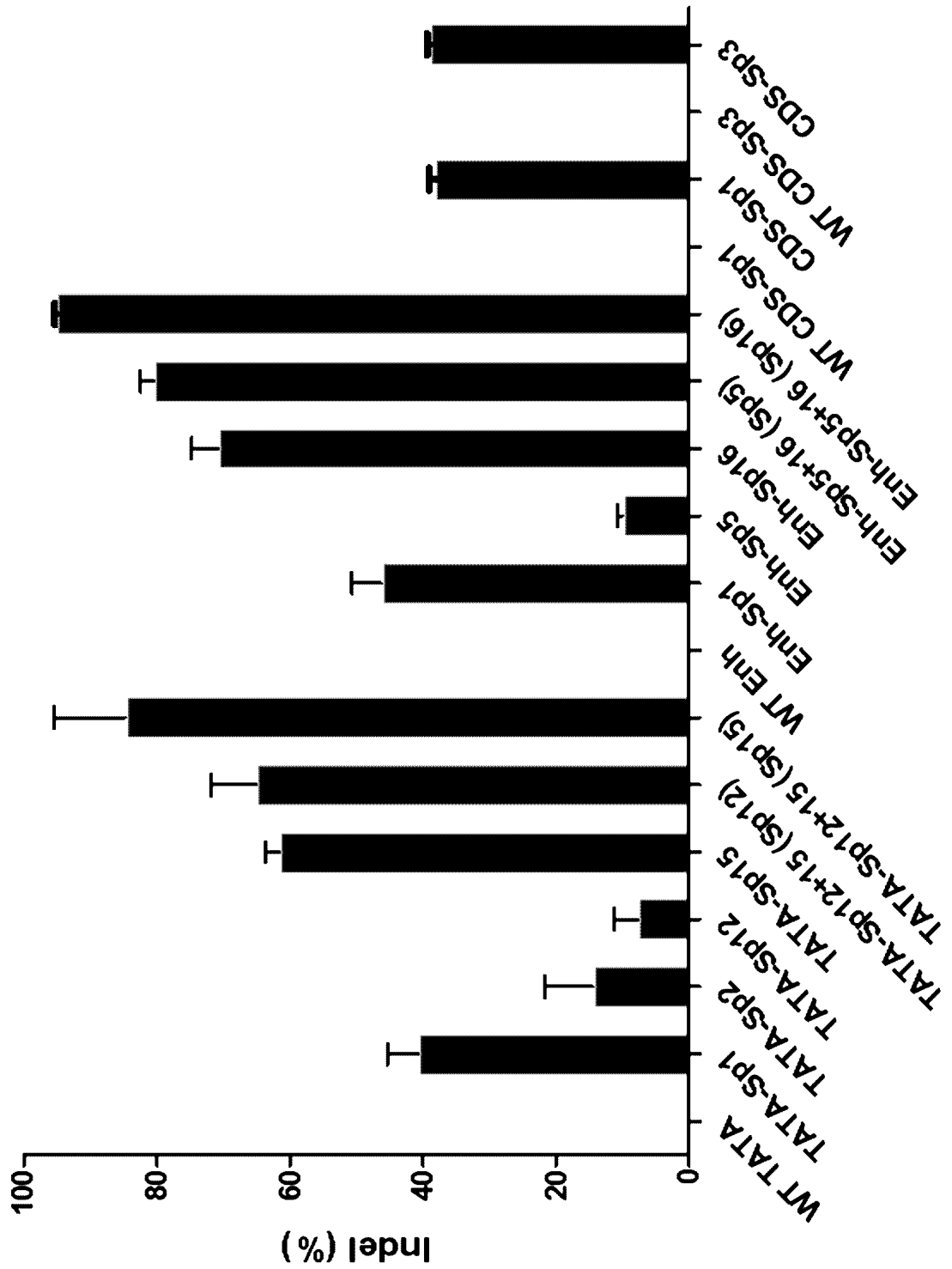
【FIG 7/37】

【FIG 6】


Relative expression of human PMP22 normalized to Cas9 alone control
1.0
0.8
0.6
0.4
0.2
0.0
Cas9
TATA-Sp15
TATA-SP12+14
Enh-Sp1
Enh-Sp5+16
Enh-Sp1+4
CDS-Sp1
CDS-Sp3

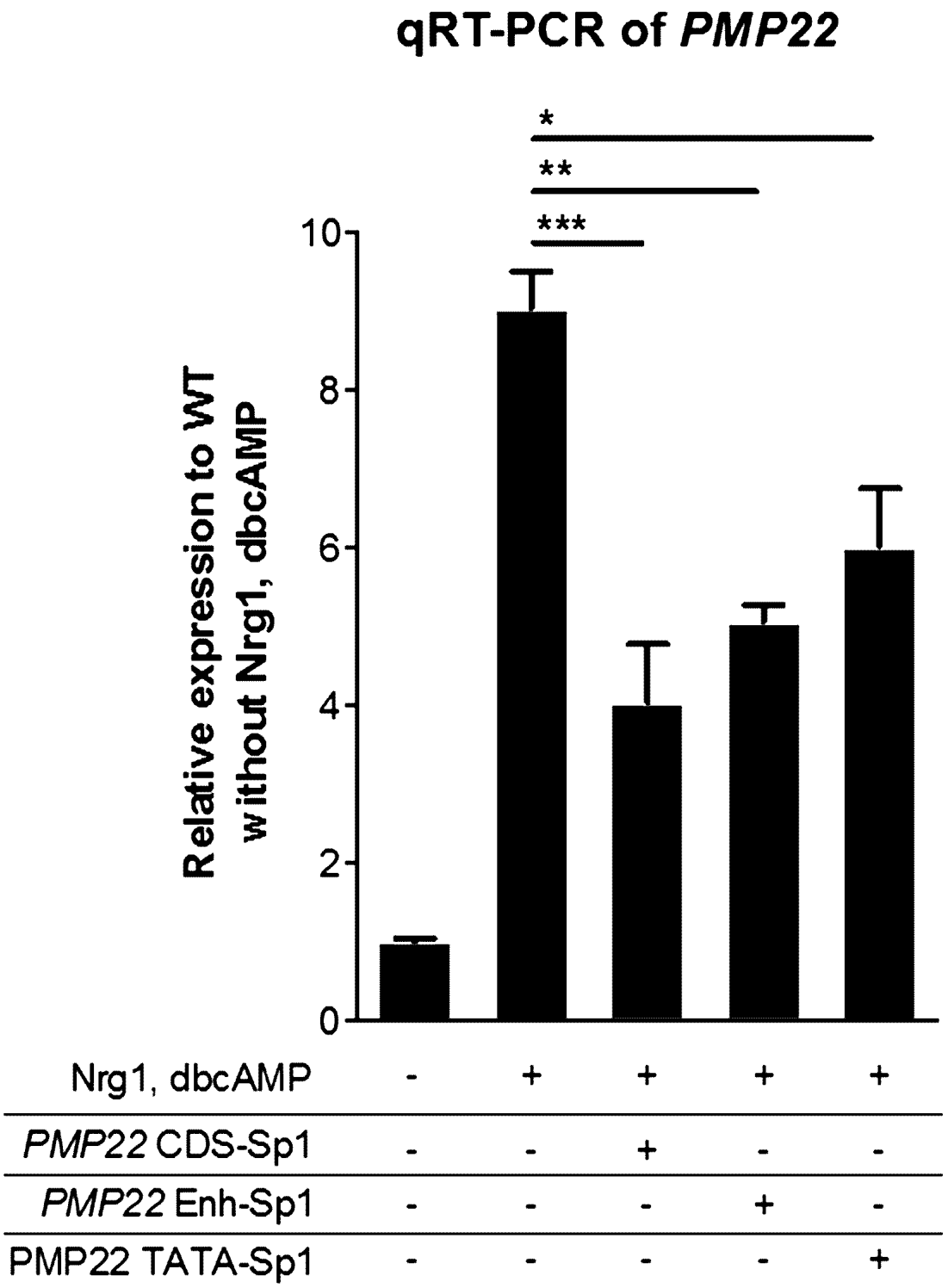
【FIG 8/37】

【FIG 7a】



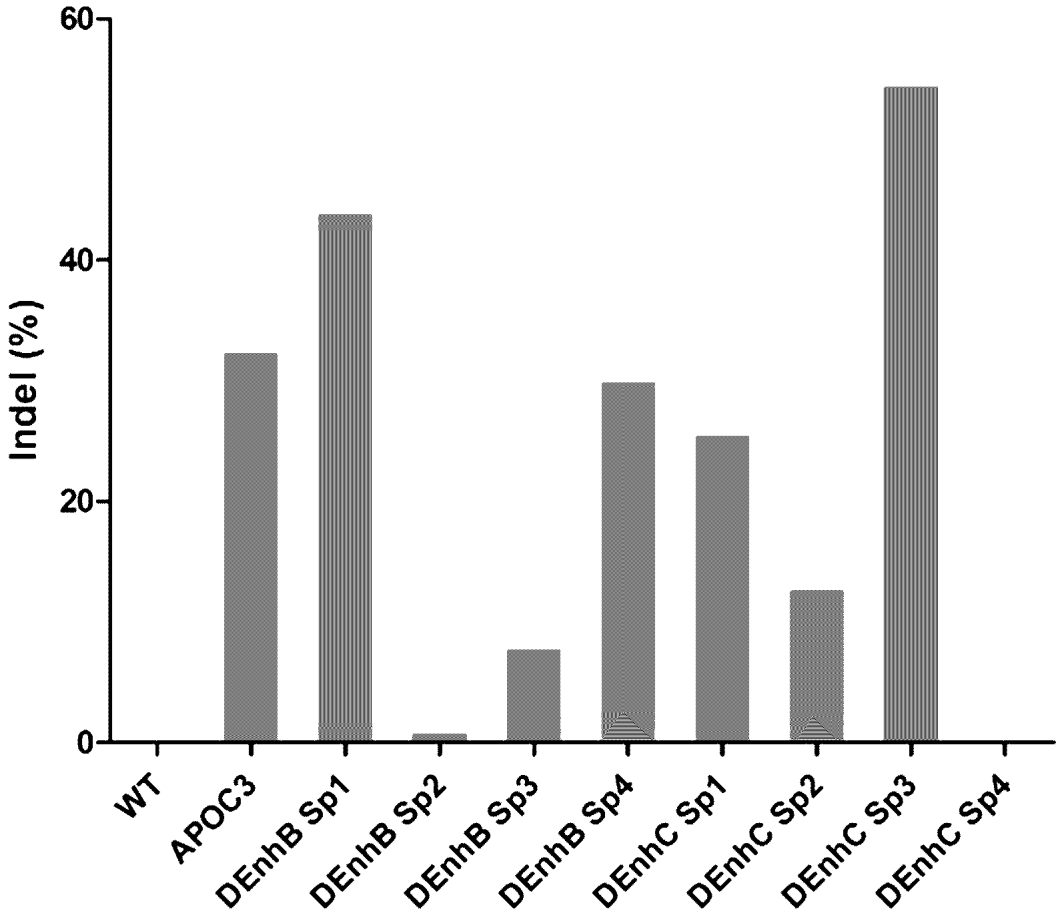
【FIG 9/37】

【FIG 7b】



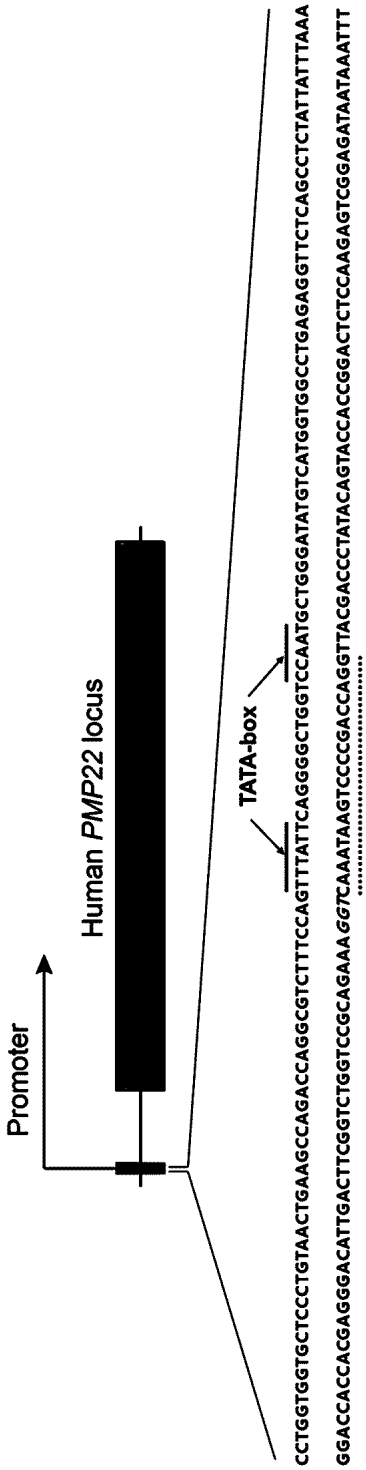
【FIG 10/37】

【FIG 7c】



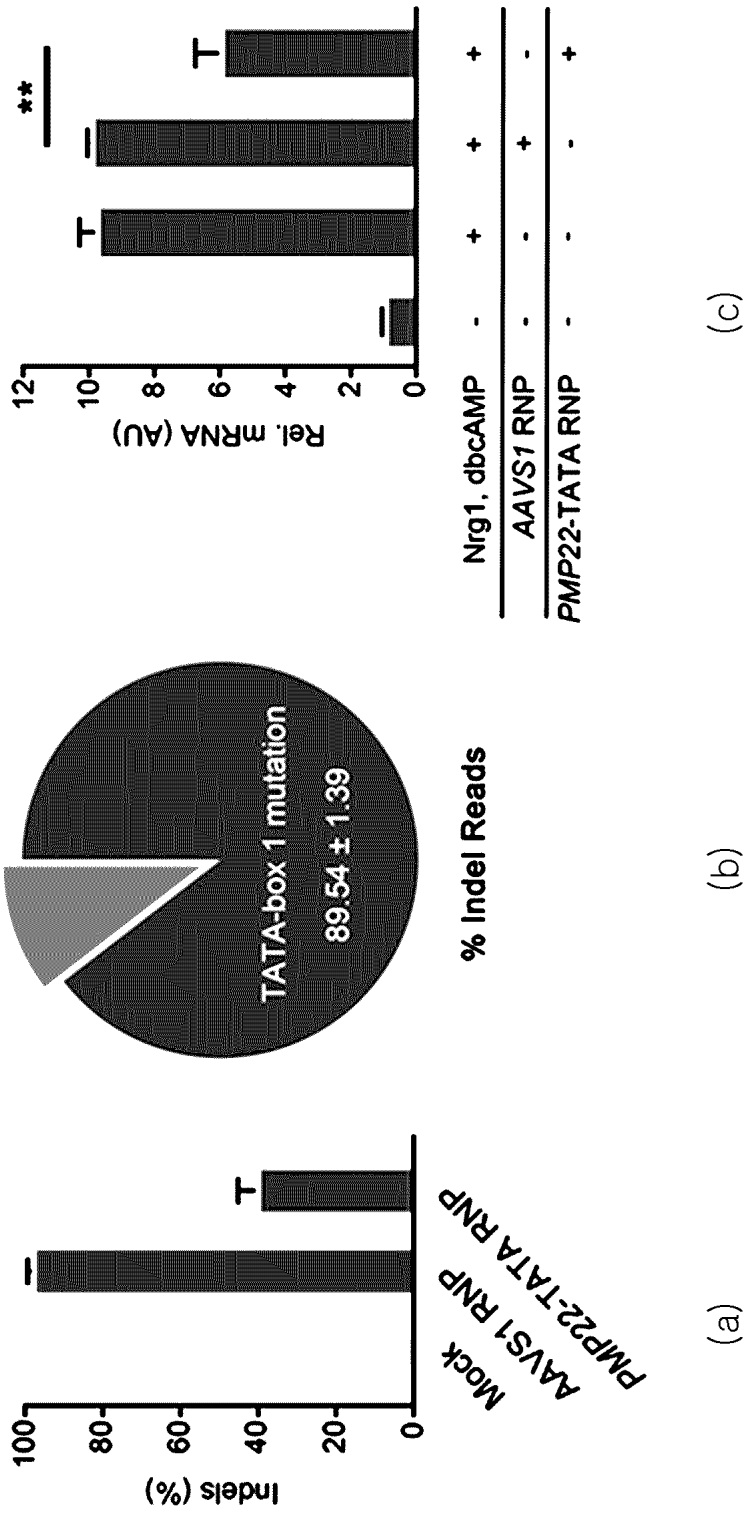
【FIG 11/37】

【FIG 8a】



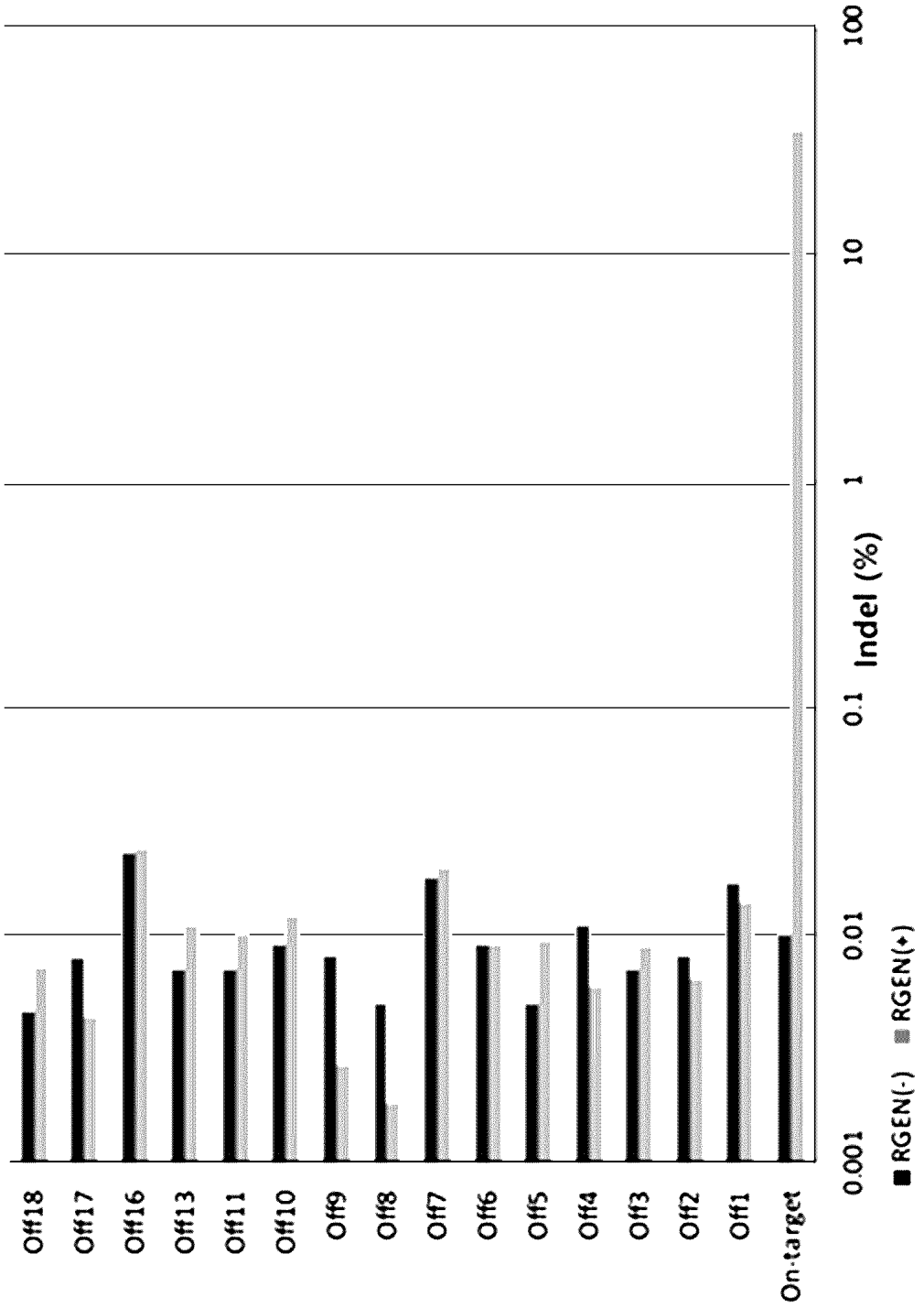
【FIG 12/37】

【FIG 8b】



【FIG 13/37】

【FIG 9a】



【FIG 14/37】

【FIG 9b】

Indel	Local Sequence	Frequency (%)
WT	ACTGAAGCCAGACCAGGCGTCTTTCCAG**TTTATT**CAGGGGCTGG *TCC*AATGCTGGGATATGTCATGGTGGCCTGAGAGGTTCTCAGCCTC	
-1	ACTGAAGCCAGACCAGGCGTCTTTCCAG-TTATTCAGGGGCTGGTCCAATGCTGGGATATGTCATGGCGGCCTGAGAGGTTCTCAGCCTC	14.00
-2	ACTGAAGCCAGACCAGGCGTCTTTCCAGTT--TTCAGGGGCTGGTCCAATGCTGGGATATGTCATGGTGGCCTGAGAGGTTCTCAGCCTC	8.86
+1	ACTGAAGCCAGACCAGGCGTCTTTCCAGTTTTATTCAGGGGCTGGTCCAATGCTGGGATATGTCATGGCGGCCTGAGAGGTTCTCAGCCTC	3.84
-3	ACTGAAGCCAGACCAGGCGTCTTTCCAGT---TTCAGGGGCTGGTCCAATGCTGGGATATGTCATGGCGGCCTGAGAGGTTCTCAGCCTC	3.53
-4	ACTGAAGCCAGACCAGGCGTCTTTCCAG----TTCAGGGGCTGGTCCAATGCTGGGATATGTCATGGCGGCCTGAGAGGTTCTCAGCCTC	2.81

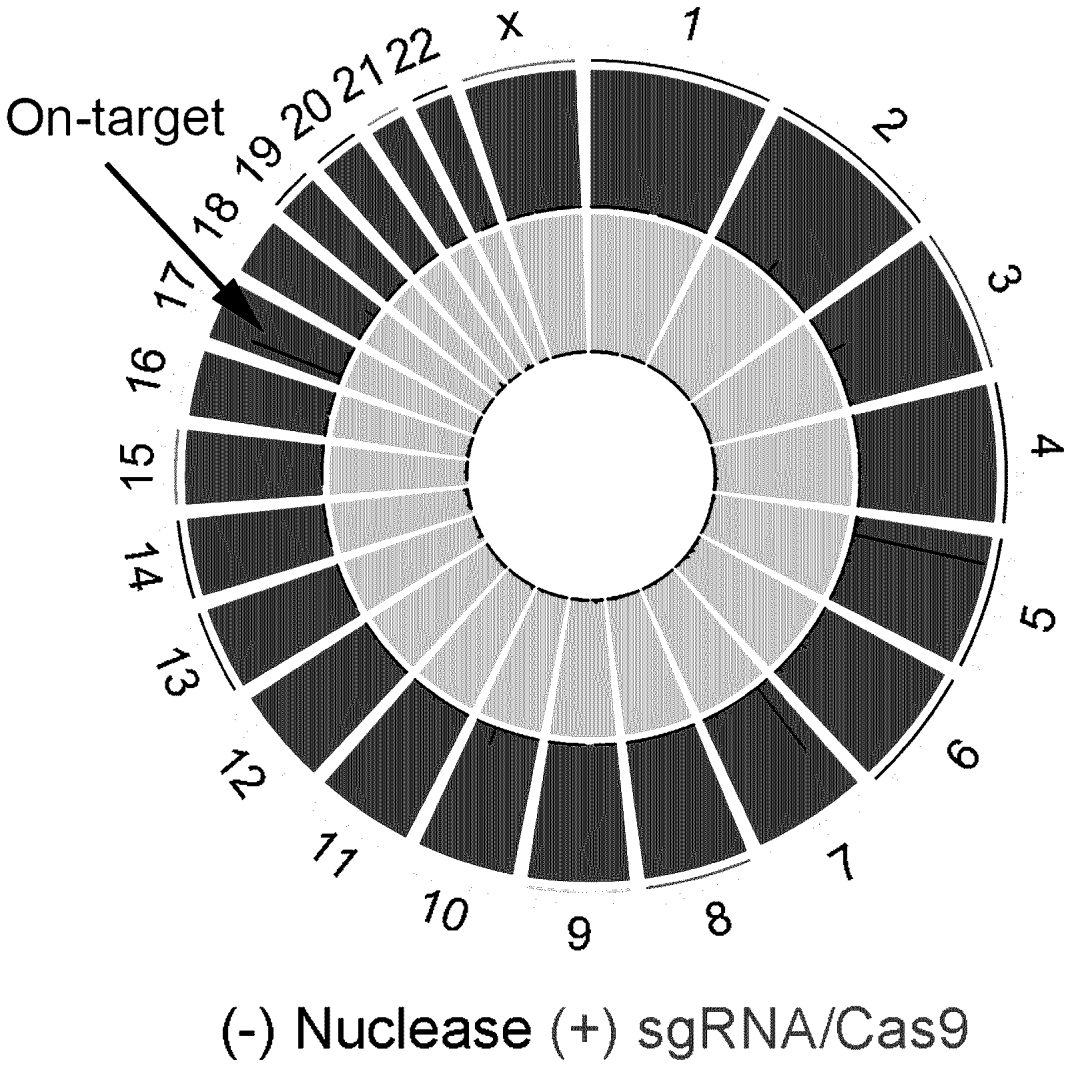
【FIG 15/37】

【FIG 9c】

	Location	Position	Target sequence (5' to 3')	Gene
On-target	chr17	15265347	GGACCAGCCCCTGAATAAAC*TGG*	hPMP22-TATA
Off1	chr5	135488419	GGACCAGCCaCaGAATAAAC*AAG*	Intergenic
Off2	chr8	140735957	tGACCAGtCCaTGAATAAAC*CAG*	PTK2 (Intron)
Off3	chr12	14124312	GGACCAGaCaCTGAATAtAC*CAG*	Intergenic
Off4	chr4	97775621	GGACCAGCCaCaGAATAAAt*TGG*	STPG2 (Intron)
Off5	chr5	26531145	GGAtCAGCCCCaGAATAAAt*TAG*	Intergenic
Off6	chr1	41780482	GGAgCAtCCCCaGAATAAAC*CAG*	HIVEP3 (Intron)
Off7	chr1	157564675	GGAtCAGCgtCTGAATAAAC*AAG*	Intergenic
Off8	chr13	20254256	aGACCAGCCCCaGAAcAAAC*AAG*	Intergenic
Off9	chr15	100401183	GtACgAGCCCCTGAATAAAt*AGG*	CERS3 (Exon)
Off10	chr6	26006396	GGACCAaaCaCTGAATAAAC*CAG*	Intergenic
Off11	chr20	10136908	GcACCAGCCaCTGAATtAAC*AAG*	SNAP25 (Intron)
Off12	chrX	7525146	GtACCAGCCaCTGAAaAAAC*AGG*	Intergenic
Off13	chr18	1972251	GaACCAGCCCCTGAtTAgAC*CAG*	Intergenic
Off14	chr18	77536261	GtACCAGCCaCTGAAaAAAC*AGG*	Intergenic
Off15	chr11	30065750	GtACCAGCCCCTGcAaAAAC*AGG*	Intergenic
Off16	chr11	30579429	GcACCAGgCCtTGAATAAAC*AAG*	MPP2D2 (Intron)
Off17	chr11	35726323	GGcCCAGCCaCTGAgTAAAC*TAG*	TRIM44 (Intron)
Off18	chr11	112468286	GGAattGCCCCTGAATAAAC*AAG*	RP11-65M17.3 (Intron)

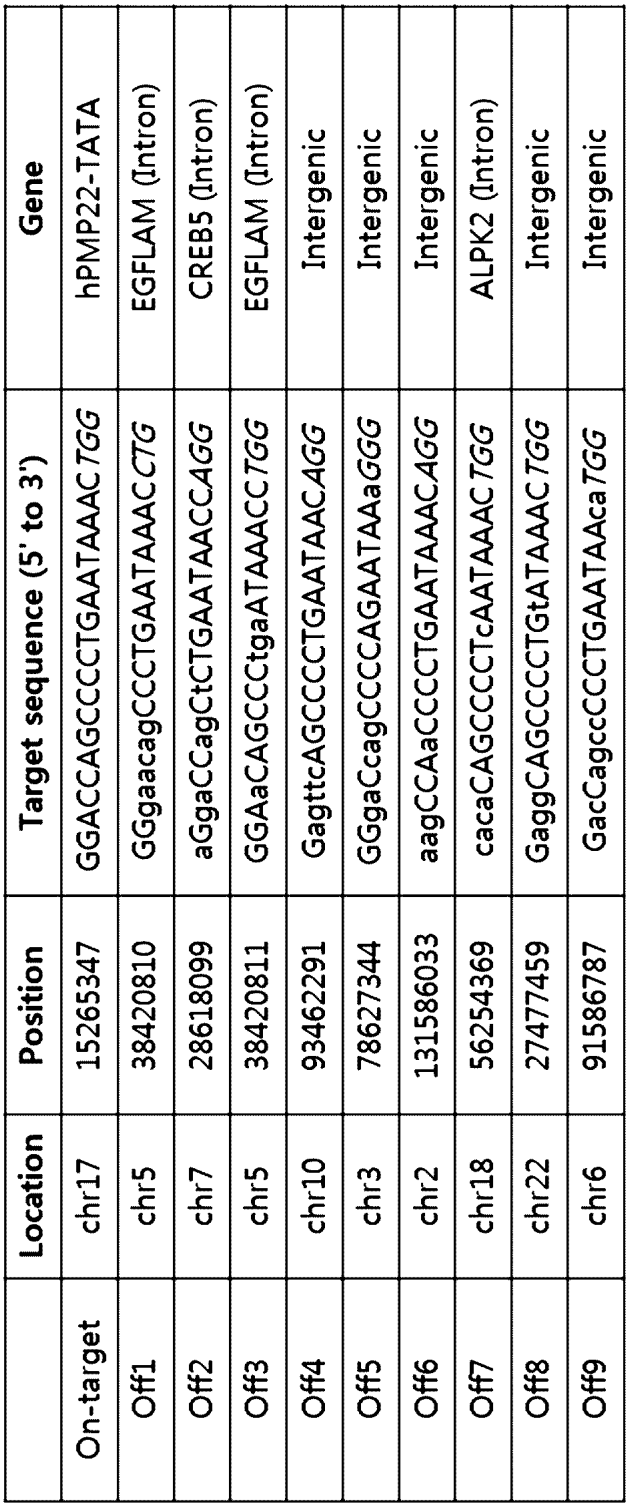
【FIG 16/37】

【FIG 10a】



【FIG 17/37】

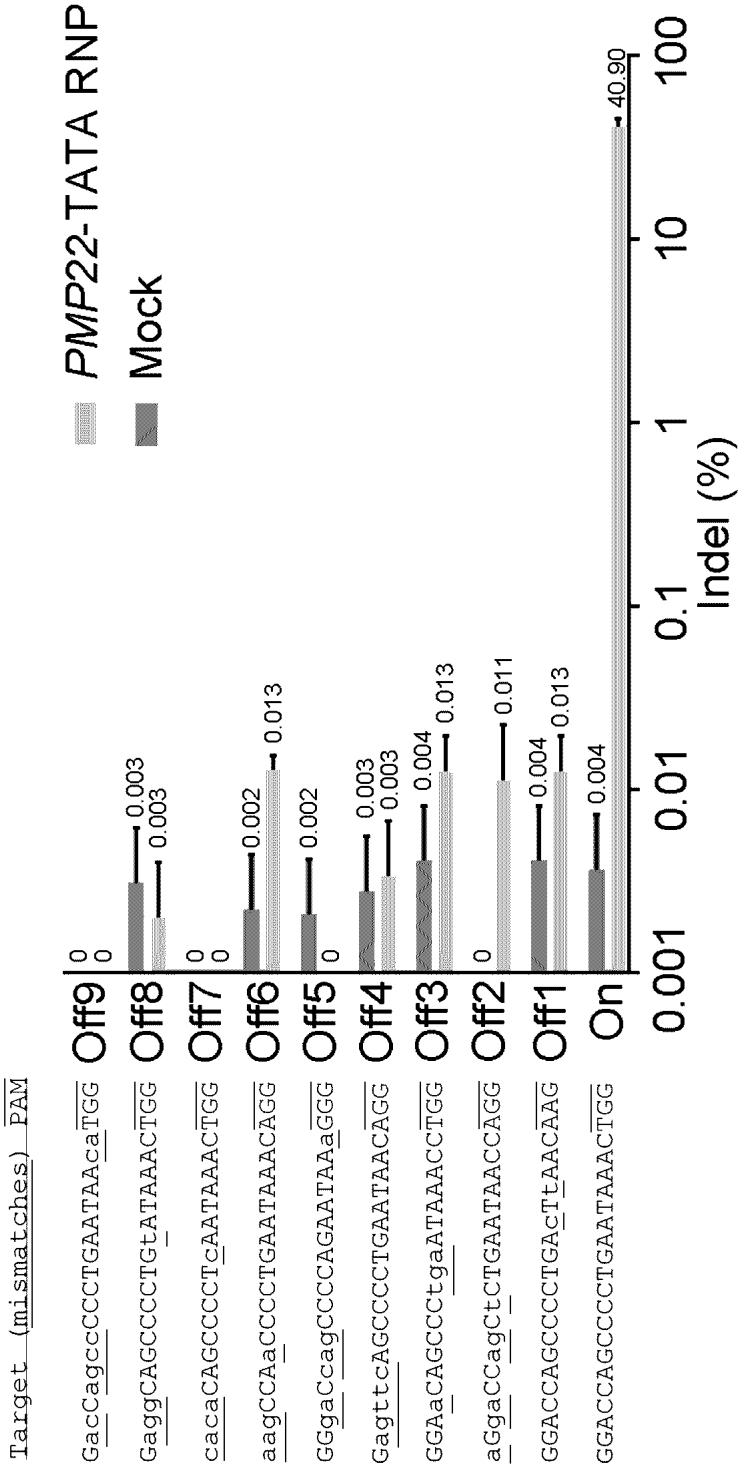
【FIG 10b】



	Location	Position	Target sequence (5' to 3')	Gene
On-target	chr17	15265347	GGACCAGCCCCCTGAATAAAC*TGG*	hPMP22-TATA
Off1	chr5	38420810	GGgaacagCCCTGAATAAAC*CTG*	EGFLAM (Intron)
Off2	chr7	28618099	aGgaCCagCtCTGAATAACC*AGG*	CREB5 (Intron)
Off3	chr5	38420811	GGAaCAGCCCtgaATAAACC*TGG*	EGFLAM (Intron)
Off4	chr10	93462291	GagttcAGCCCCCTGAATAAC*AGG*	Intergenic
Off5	chr3	78627344	GGgaCcagCCCCAGAATAAa*GGG*	Intergenic
Off6	chr2	131586033	aagCCAaCCCCTGAATAAAC*AGG*	Intergenic
Off7	chr18	56254369	cacaCAGCCCCCTcAATAAAC*TGG*	ALPK2 (Intron)
Off8	chr22	27477459	GaggCAGCCCCCTGtATAAAC*TGG*	Intergenic
Off9	chr6	91586787	GacCagccCCCTGAATAAca*TGG*	Intergenic

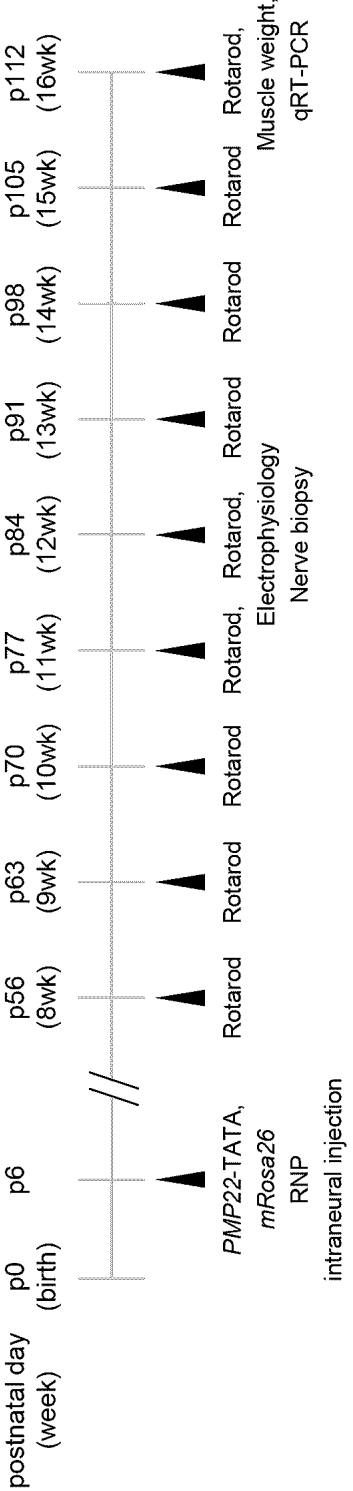
【FIG 18/37】

【FIG 10c】



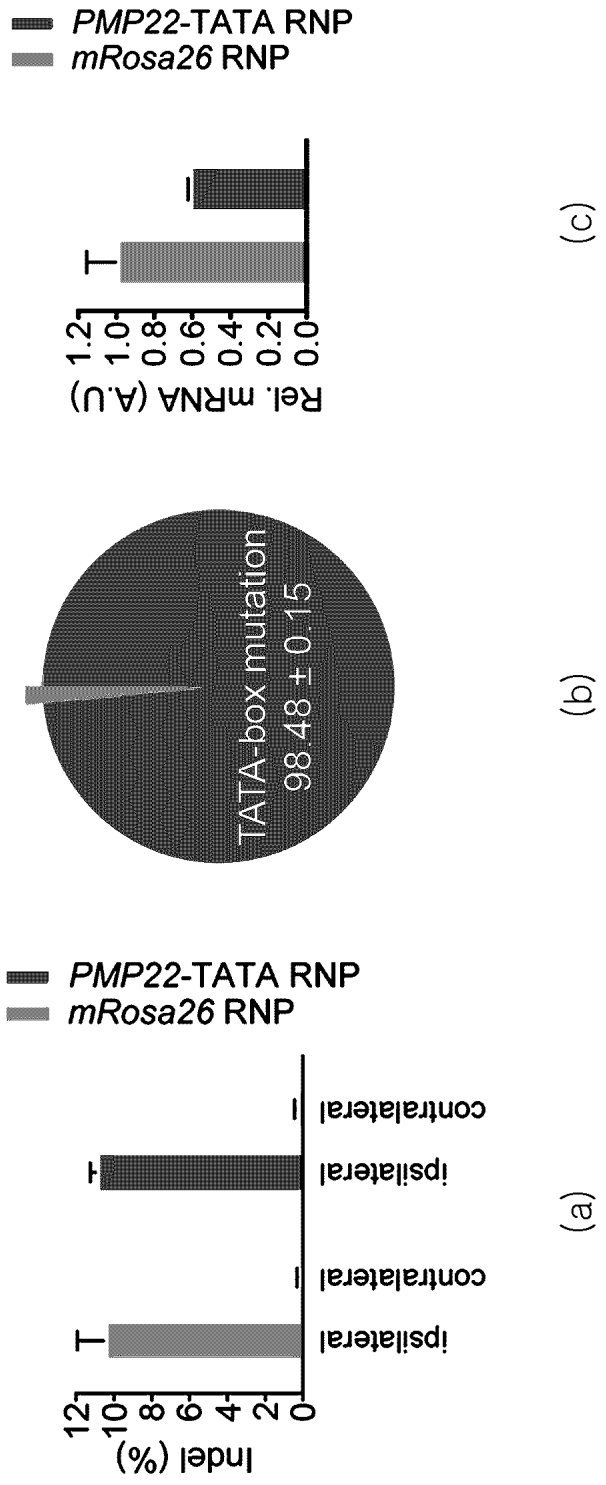
【FIG 19/37】

【FIG 11】



【FIG 20/37】

【FIG 12】



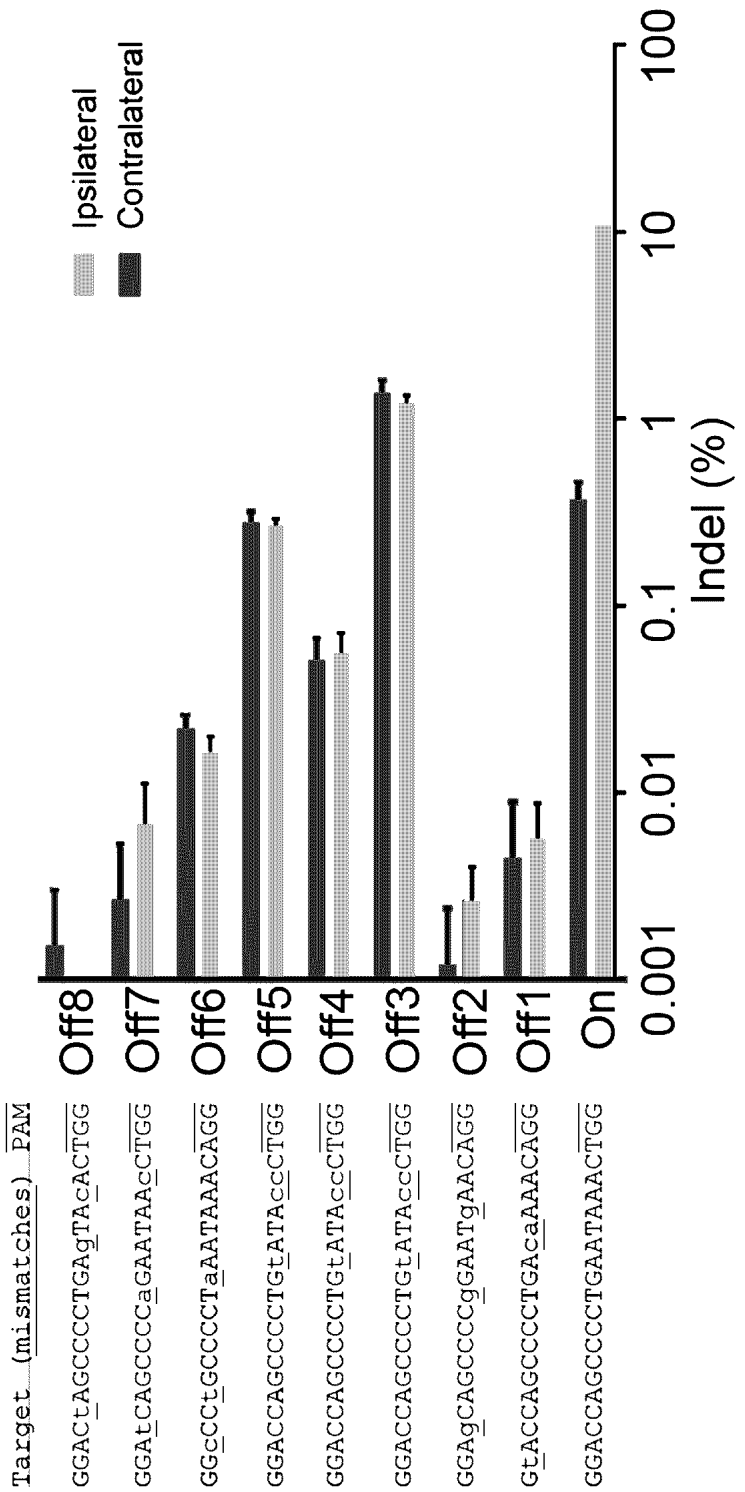
【FIG 21/37】

【FIG 13a】

	Location	Position	Target sequence (5' to 3')	Gene
On-target	chr17	15265347	GGACCAGCCCCTGAATAAAC*TGG*	hPMP22-TATA
Off1	chr12	118558427	GtACCAGCCCCTGAcaAAAC*AGG*	Intergenic
Off2	chr1	74579514	GGAgCAGCCCCgGAATgAAC*AGG*	Zfp142 (Exon)
Off3	chr13	50187695	GGACCAGCCCCTGtATAccC*TGG*	Intergenic
Off4	chr13	50319559	GGACCAGCCCCTGtATAccC*TGG*	Intergenic
Off5	chr13	50623450	GGACCAGCCCCTGtATAccC*TGG*	Intergenic
Off6	chr2	29191358	GGcCCtGCCCCTaAATAAAC*AGG*	Intergenic
Off7	chr9	102823783	GGAtCAGCCCCaGAATAAcC*TGG*	Intergenic
Off8	chrX	101405421	GGACtAGCCCCTGAgTAcAC*TGG*	Zmym3 (Exon)

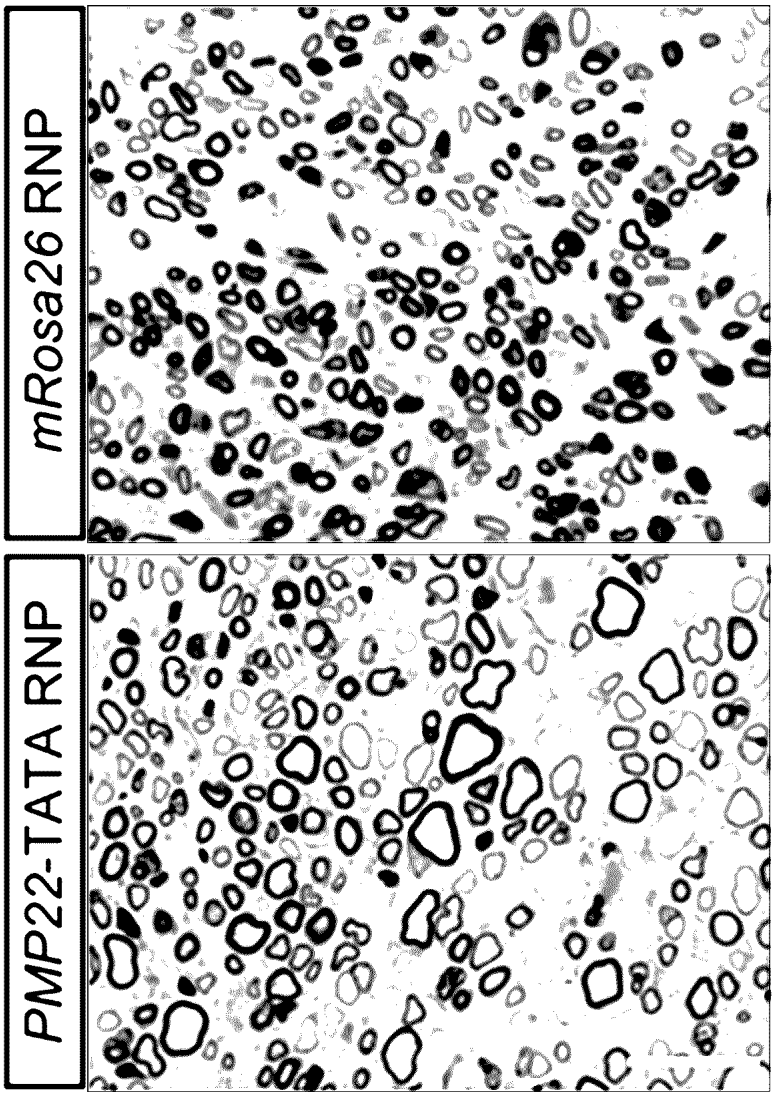
【FIG 22/37】

【FIG 13b】



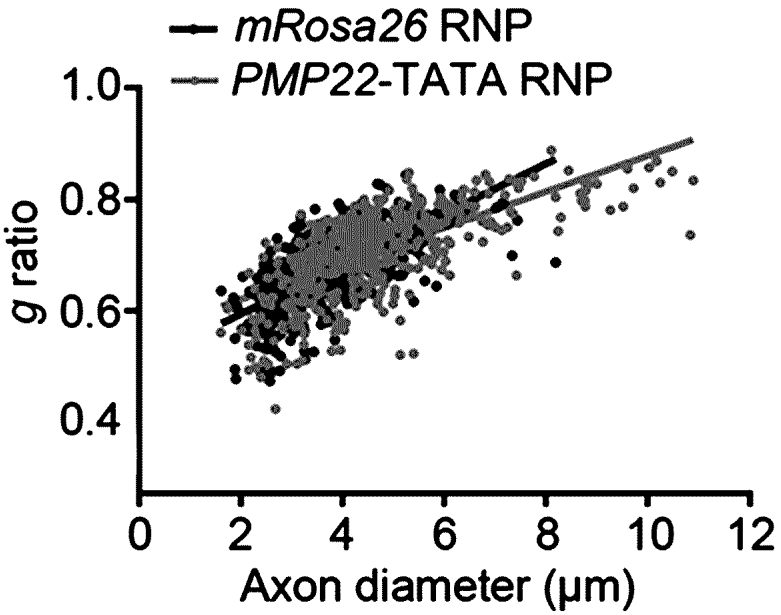
【FIG 23/37】

【FIG 14a】

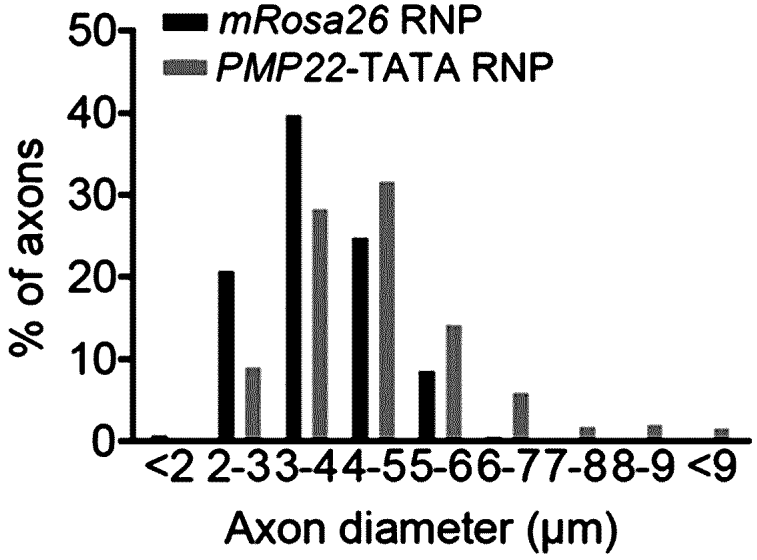


【FIG 24/37】

【FIG 14b】



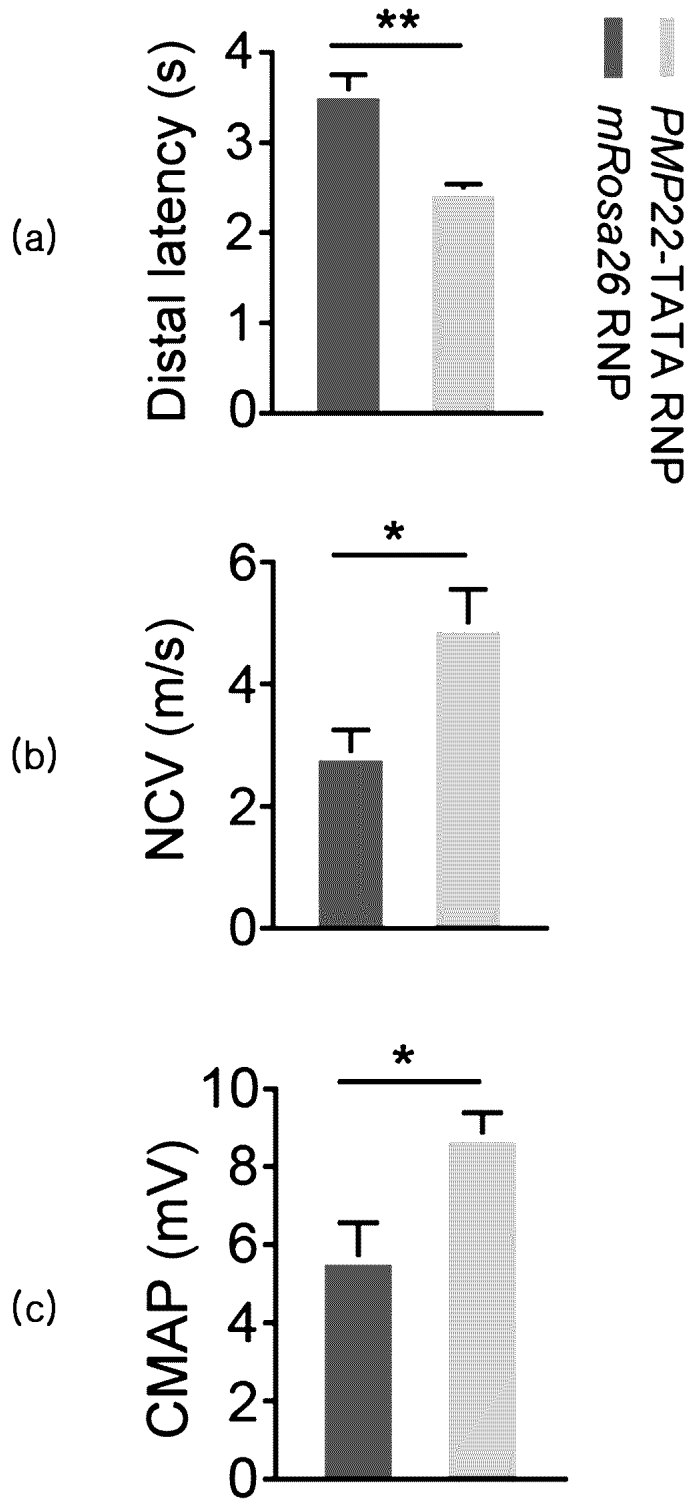
(a)



(b)

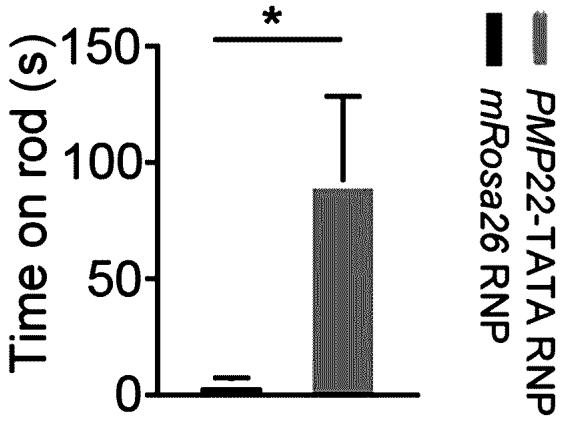
【FIG 25/37】

【FIG 15】

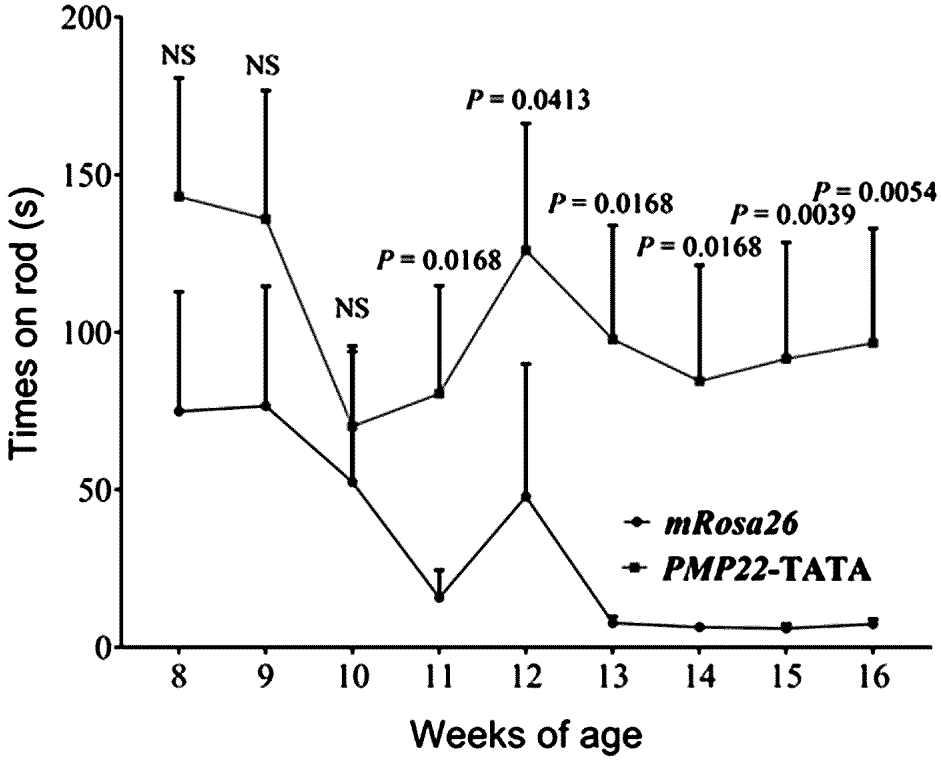


【FIG 26/37】

【FIG 16a】



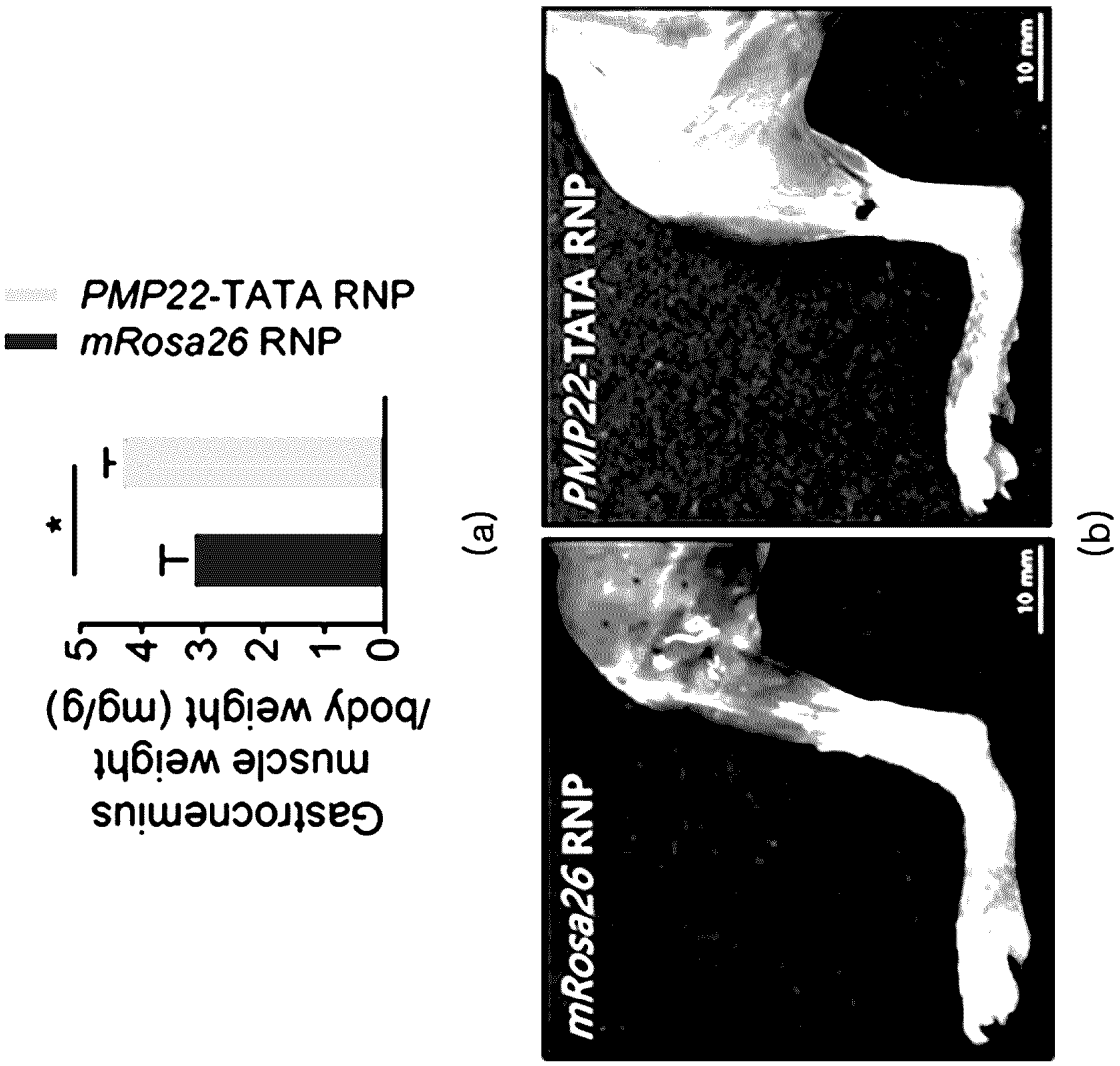
(a)



(b)

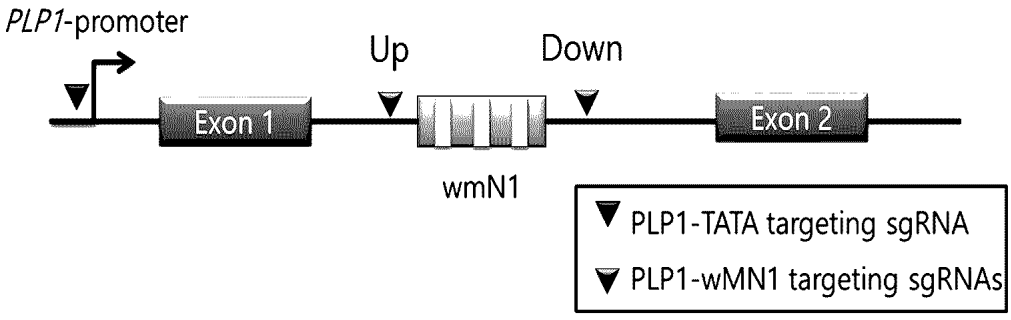
【FIG 27/37】

【FIG 16b】



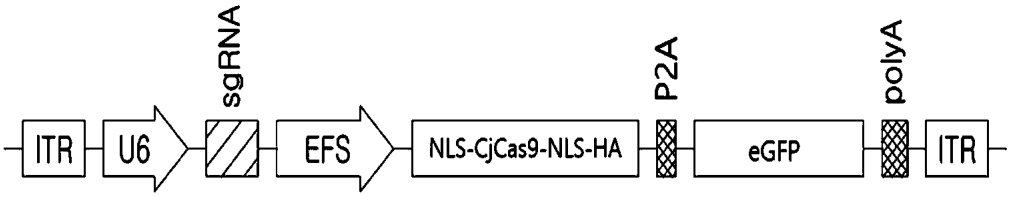
【FIG 28/37】

【FIG 17】



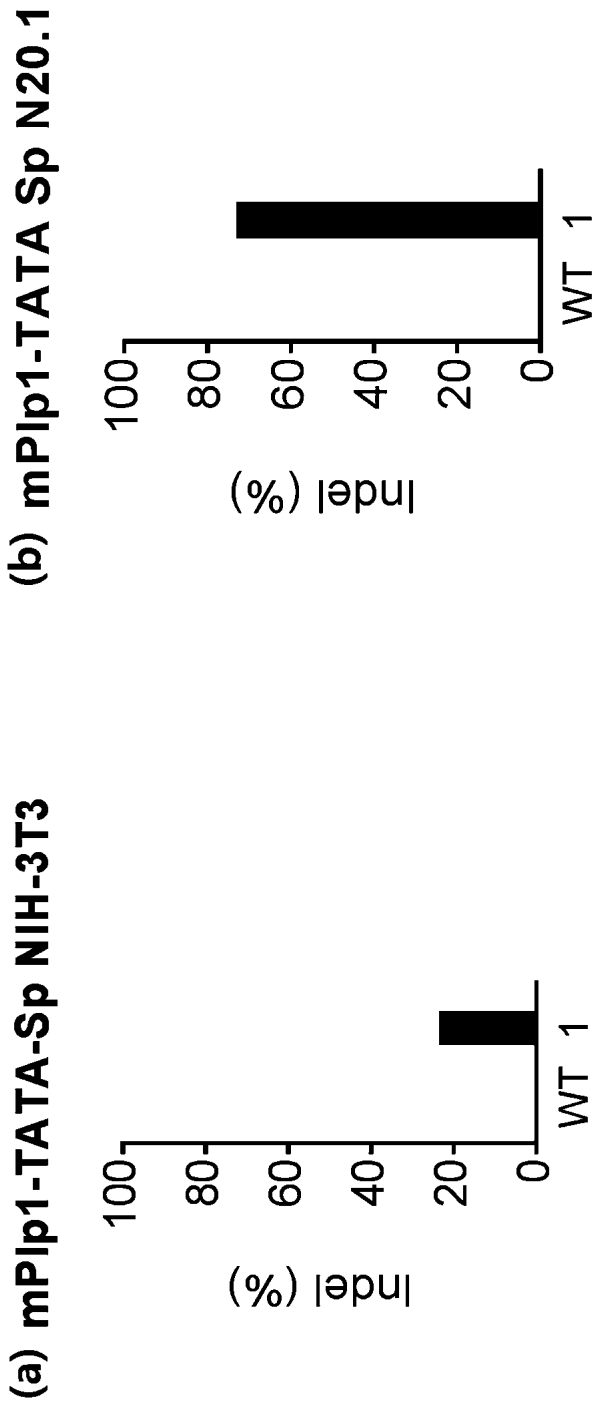
【FIG 29/37】

【FIG 18】



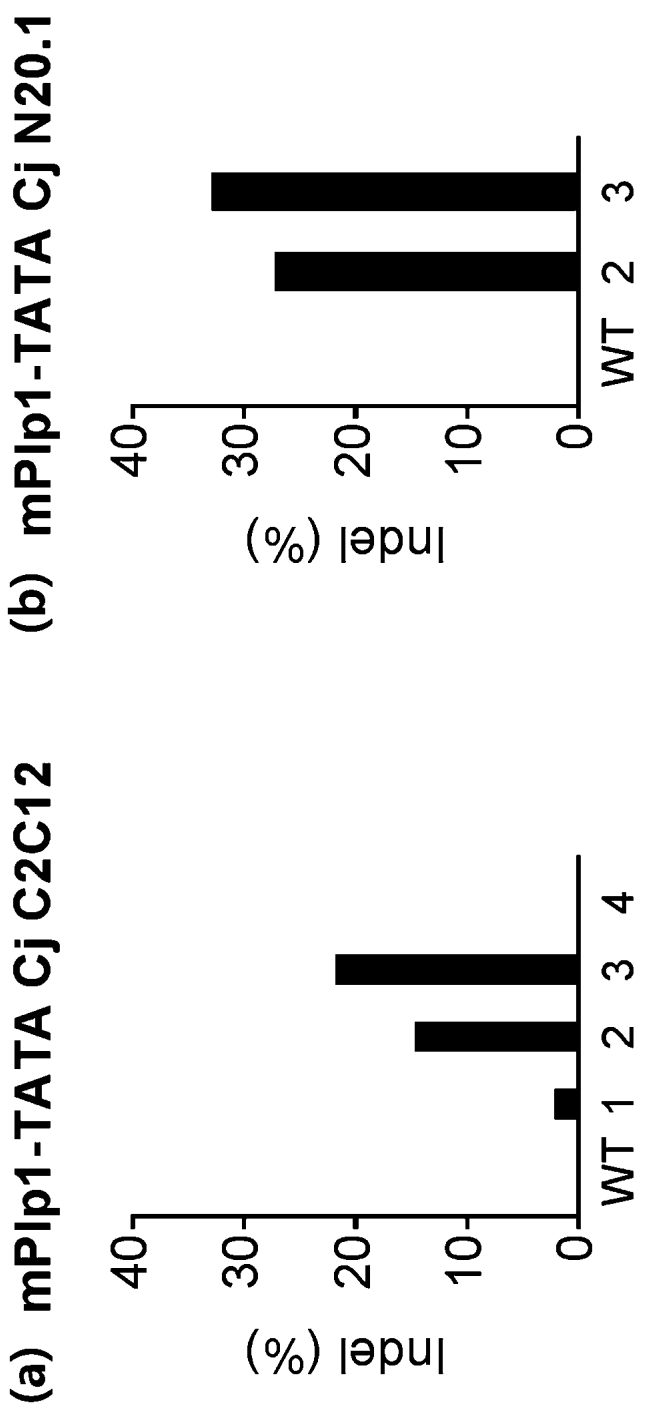
【FIG 30/37】

【FIG 19】



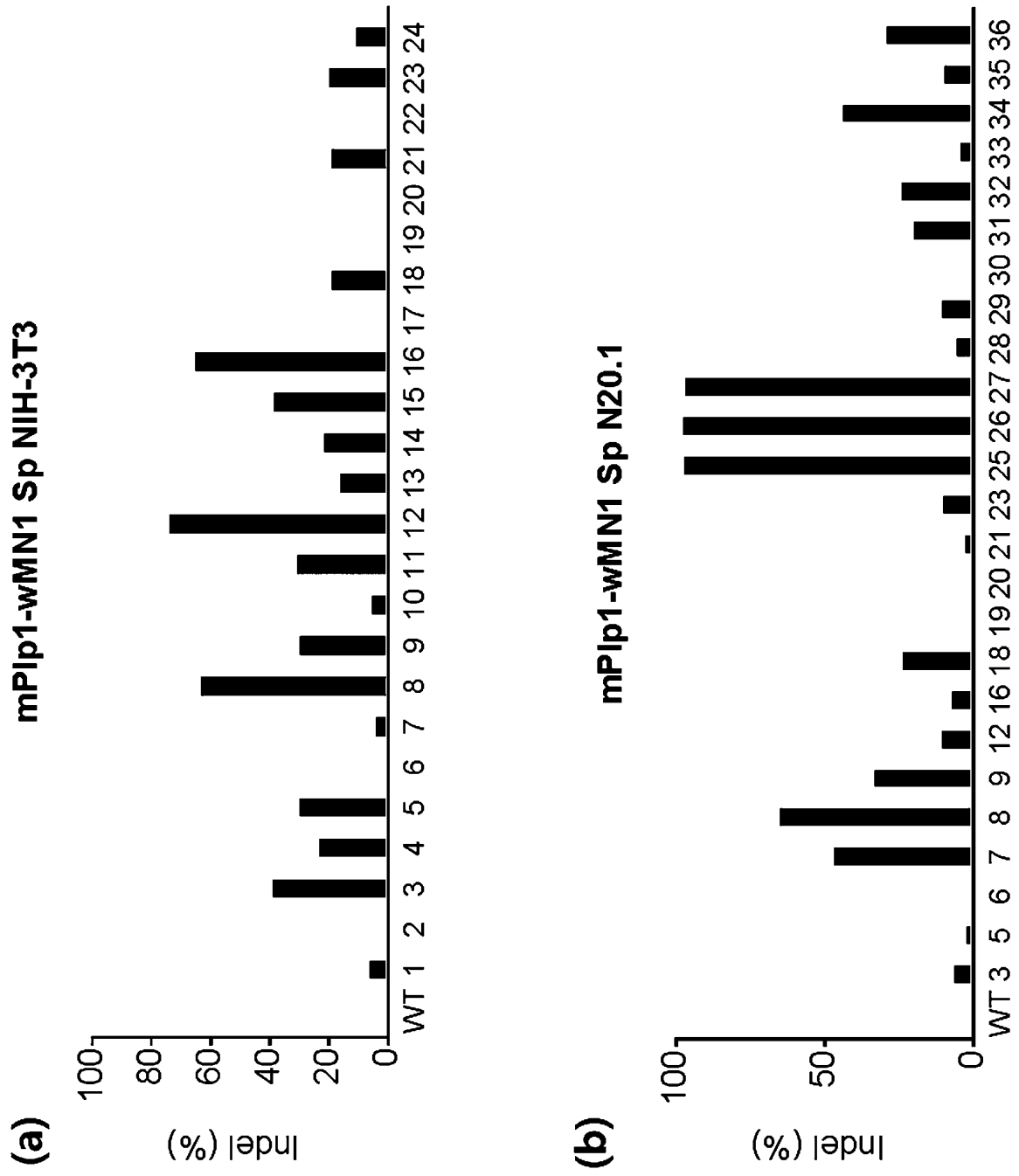
【FIG 31/37】

【FIG 20】



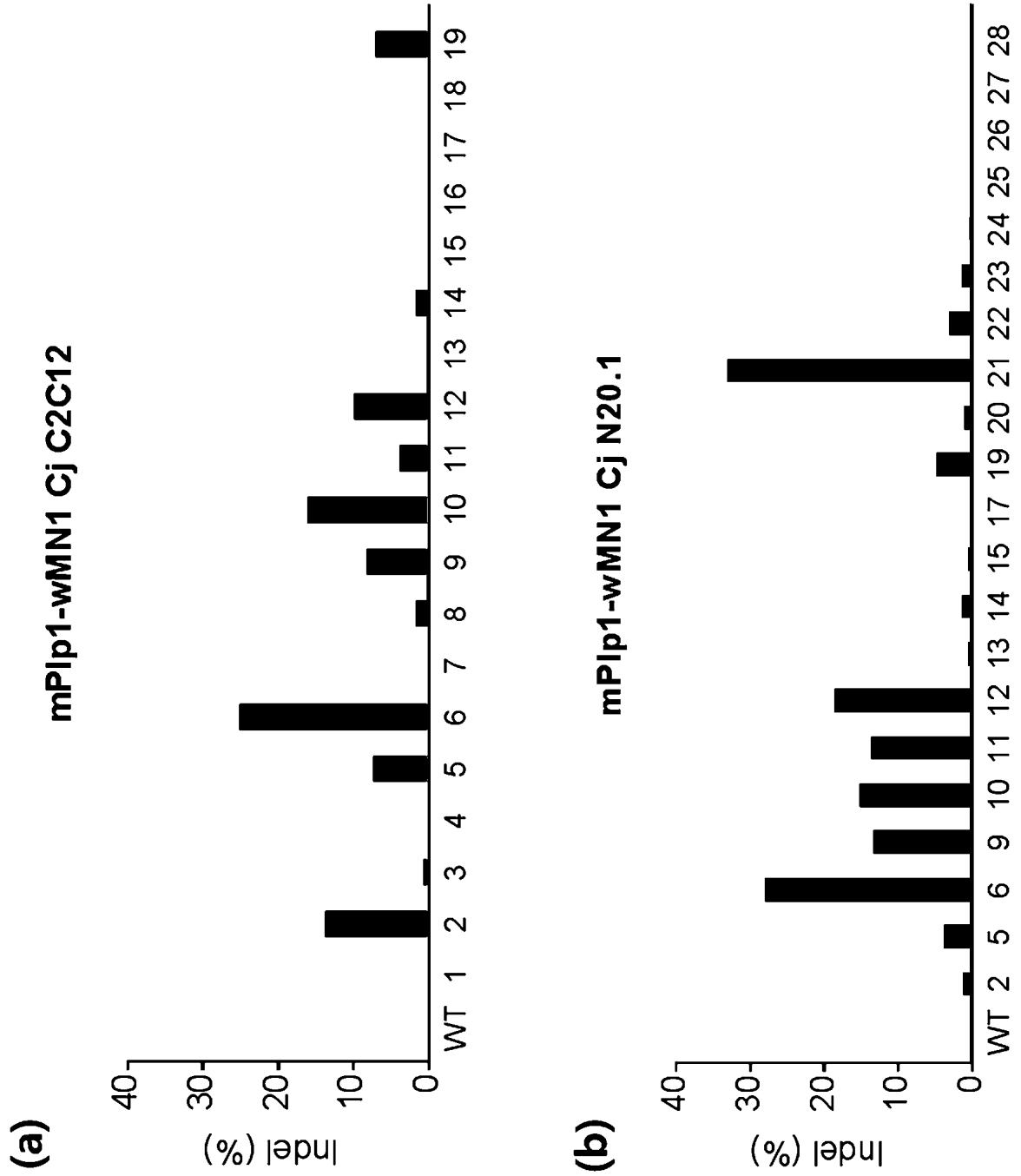
【FIG 32/37】

【FIG 21】



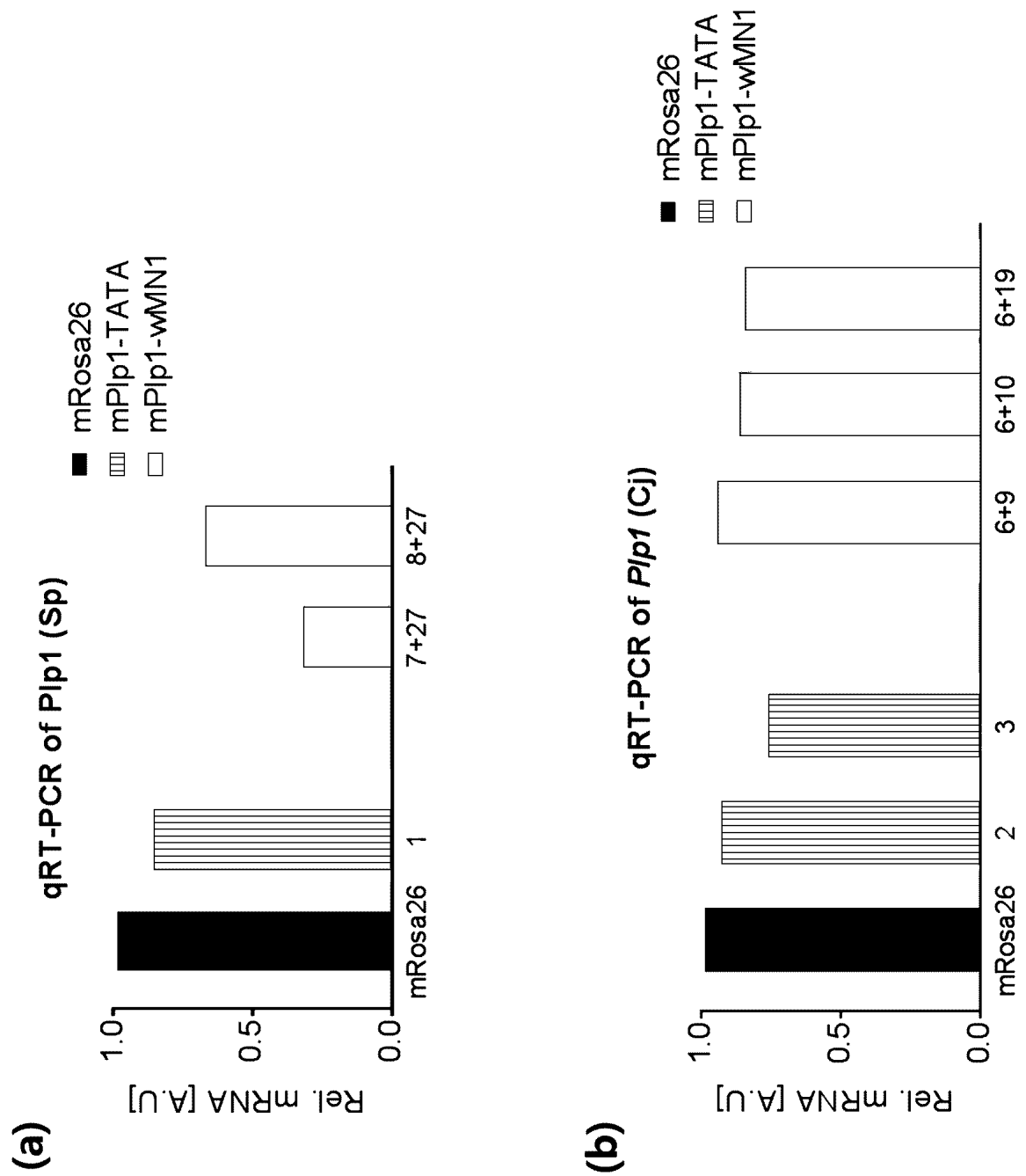
【FIG 33/37】

【FIG 22】



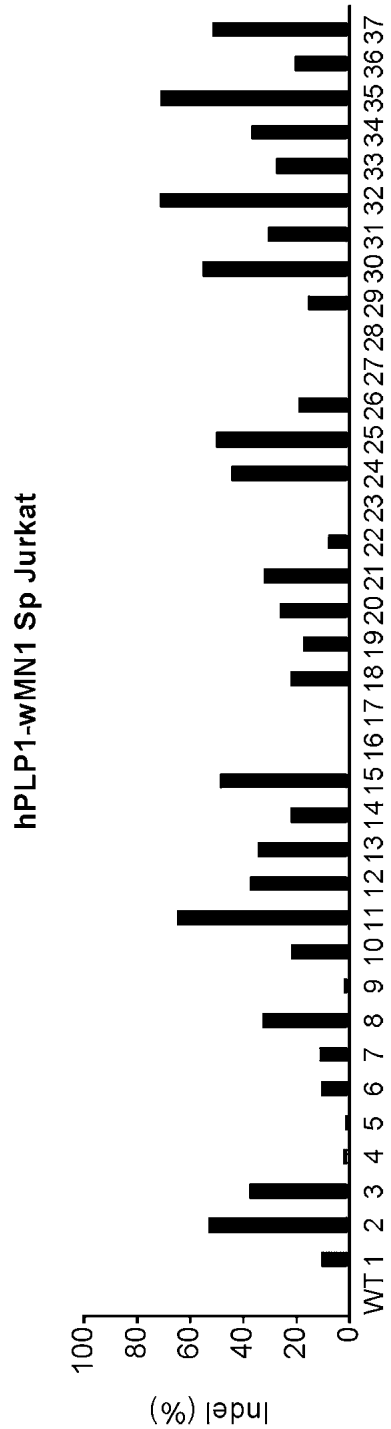
【FIG 34/37】

【FIG 23】



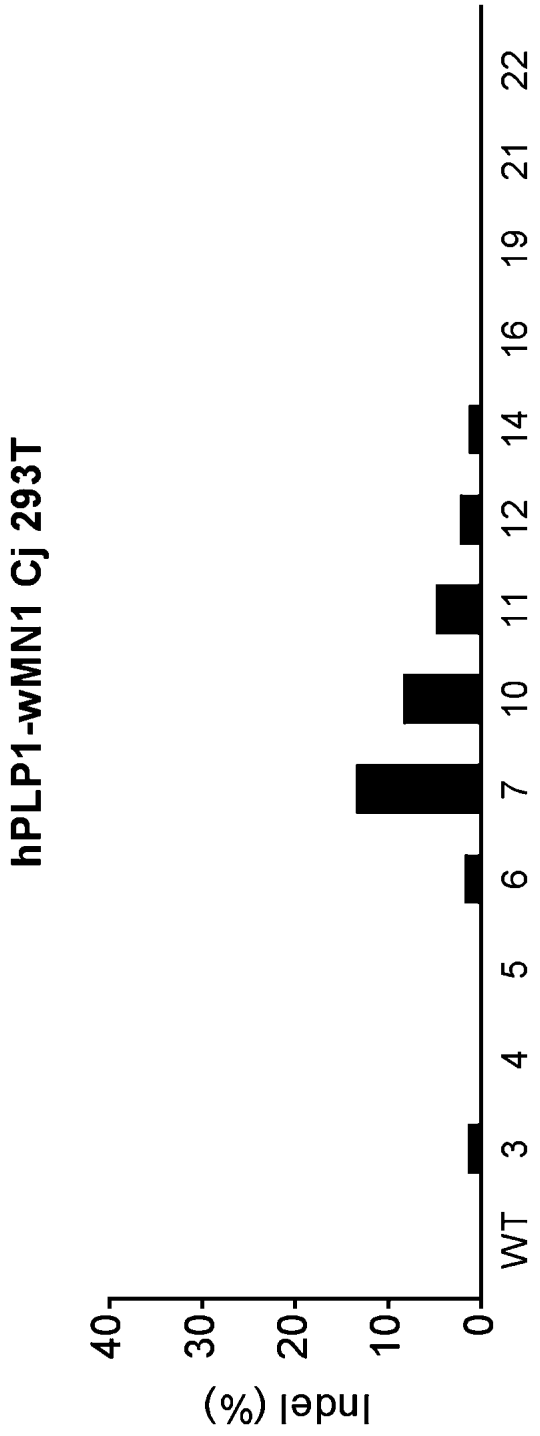
【FIG 35/37】

【FIG 24】



【FIG 36/37】

【FIG 25】



【FIG 37/37】