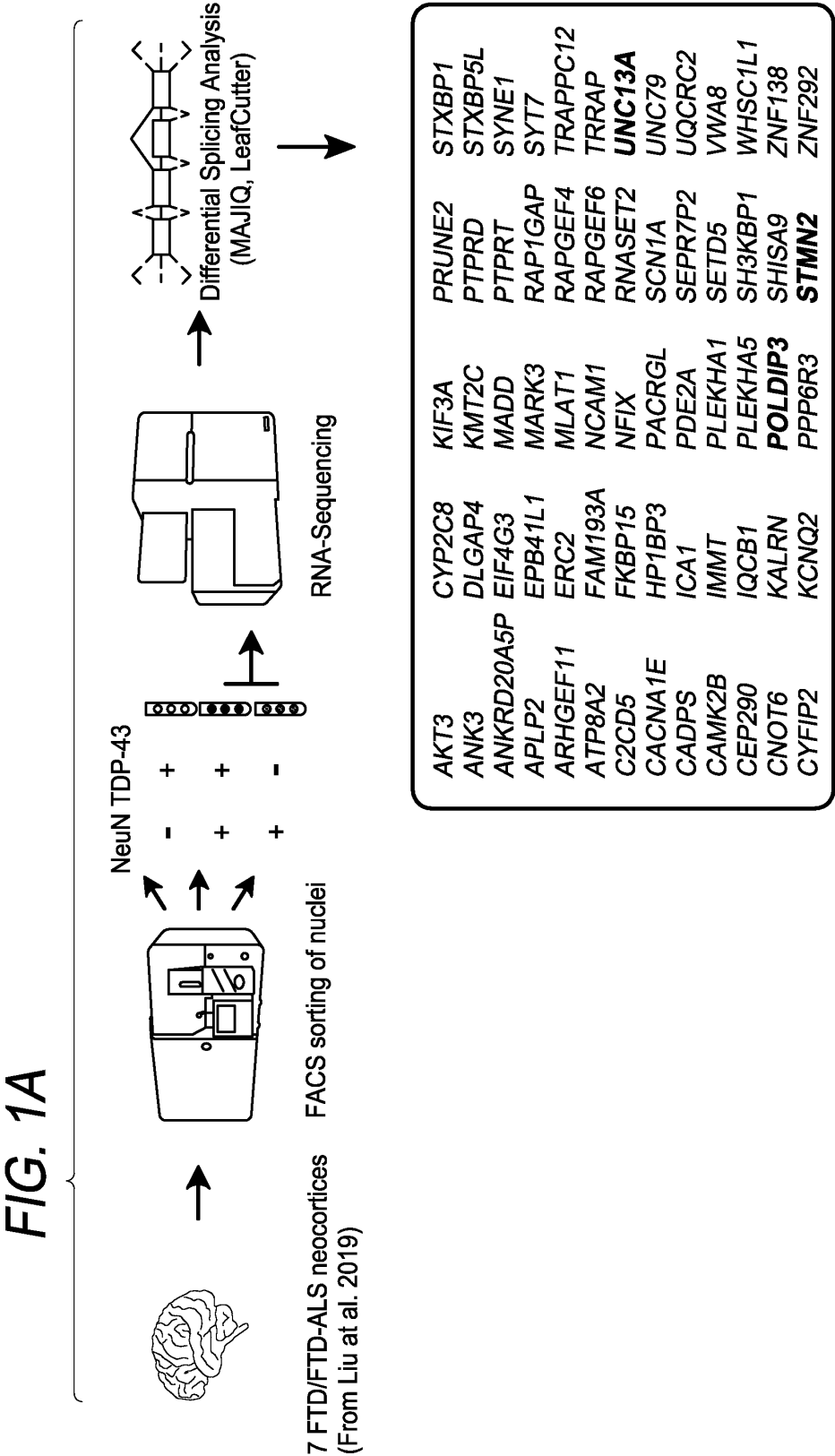




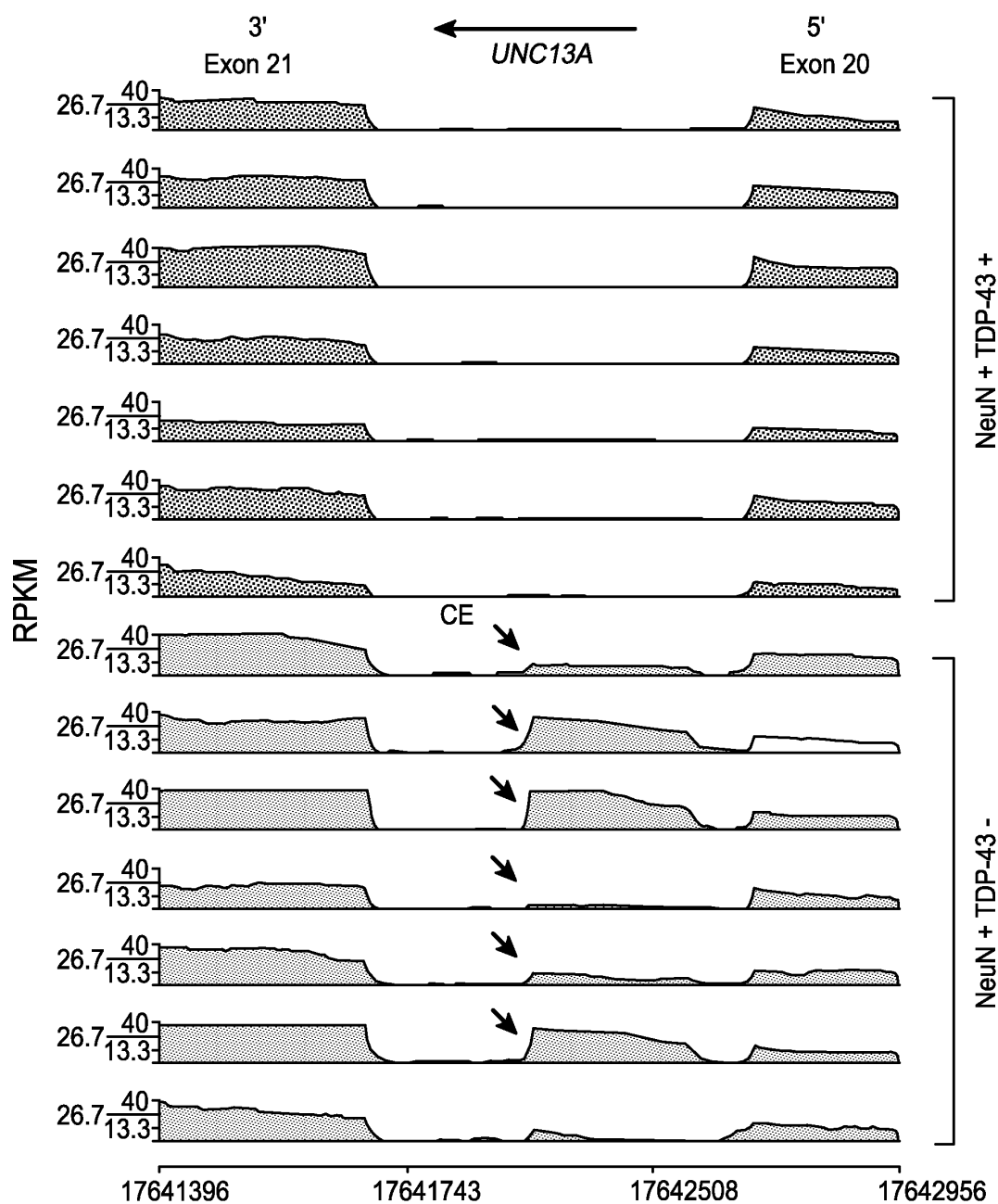


FIG. 1C

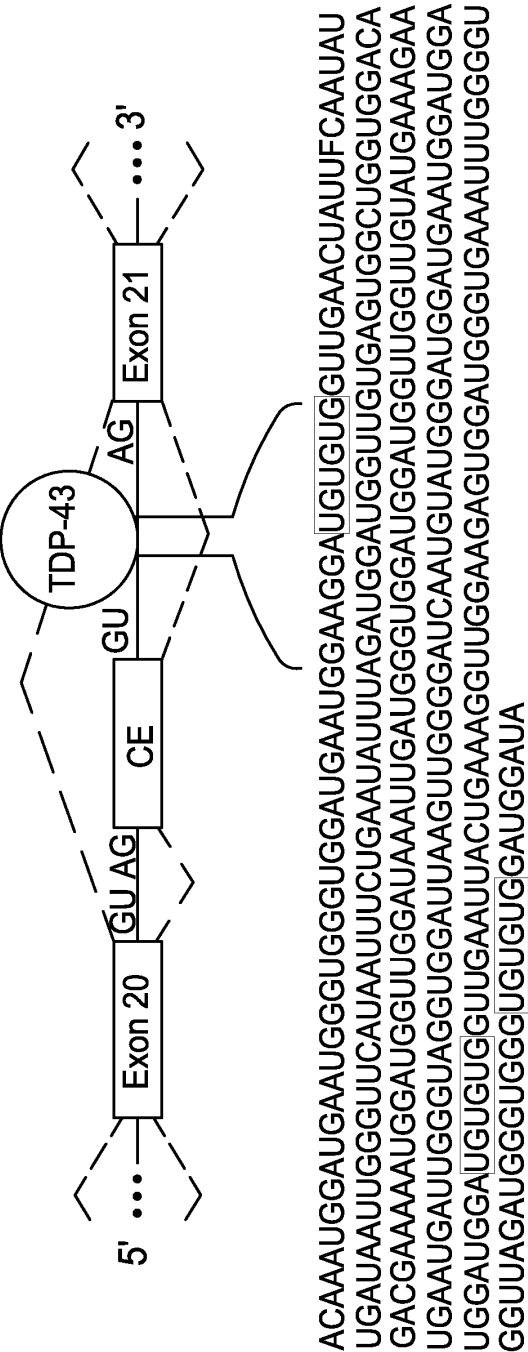


FIG. 1D

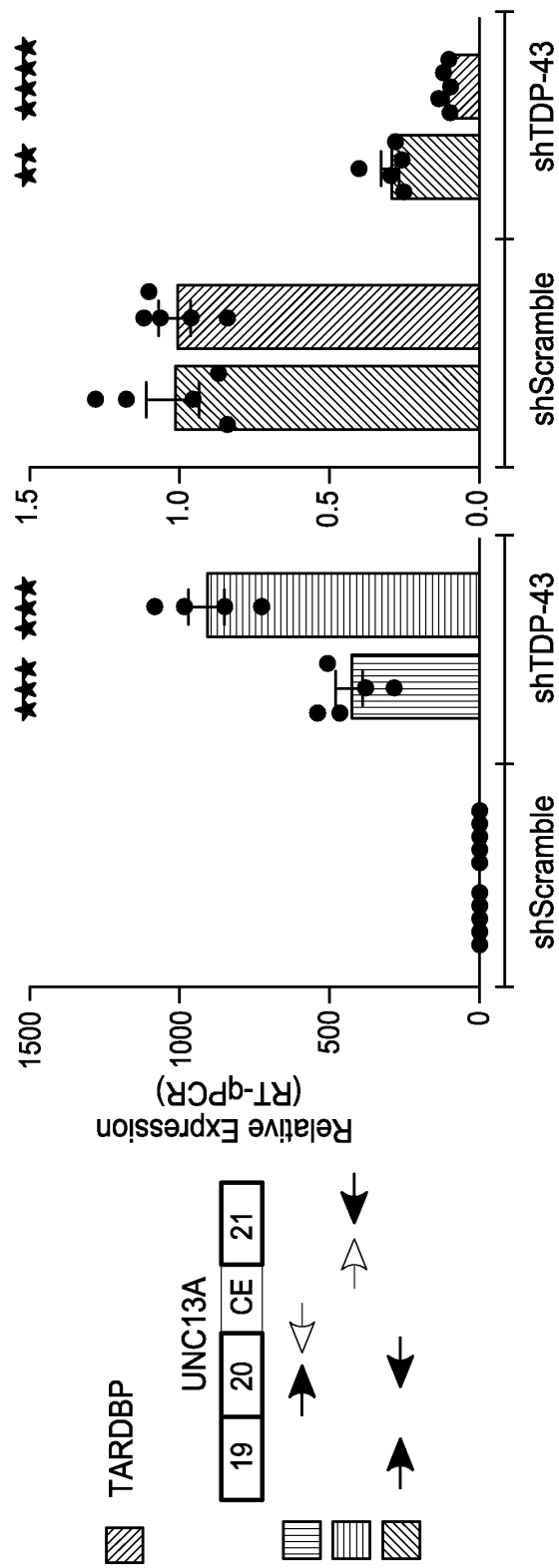


FIG. 1E

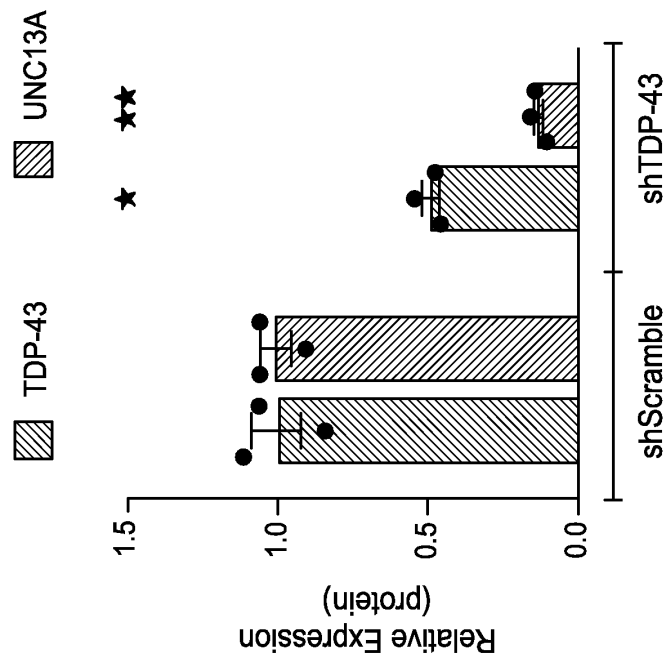


FIG. 1G

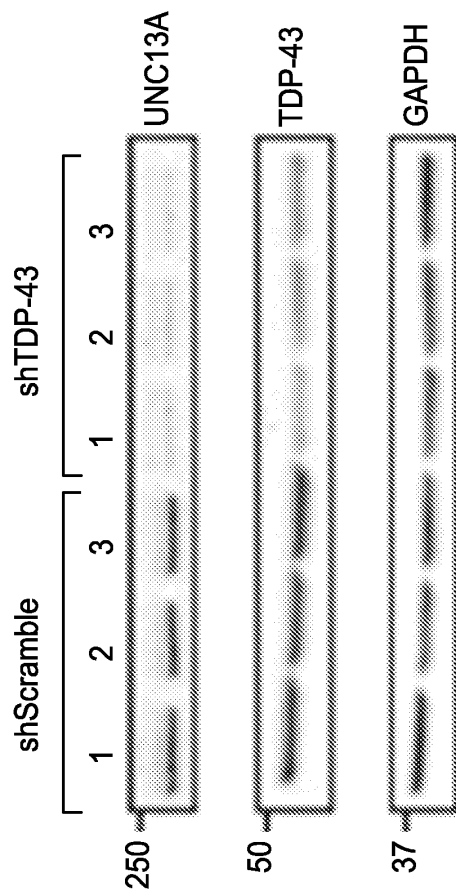


FIG. 1F

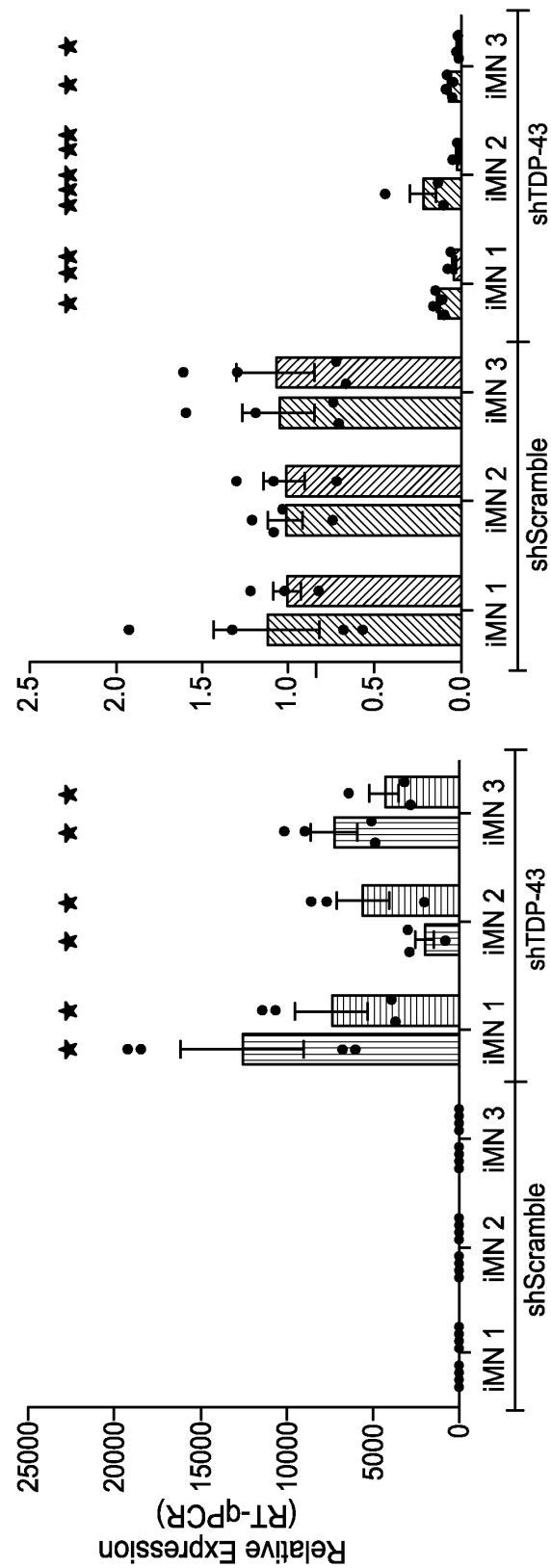


FIG. 1H

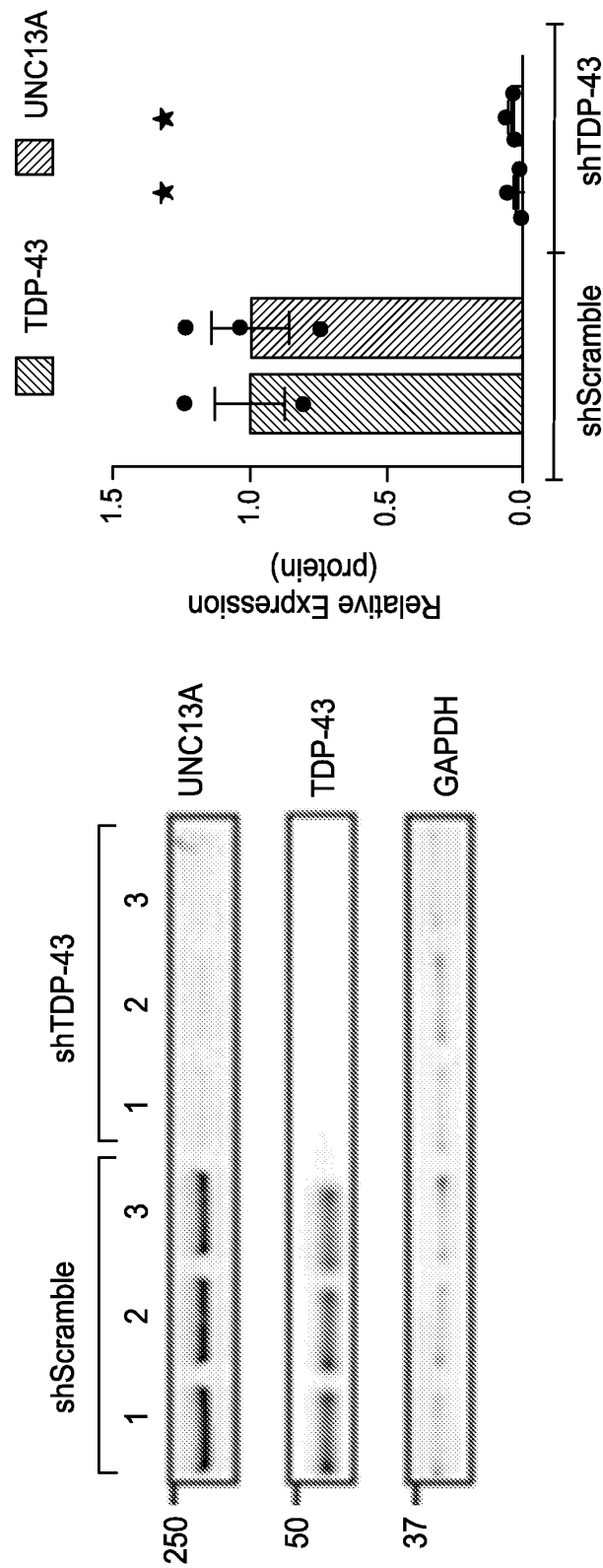


FIG. 11

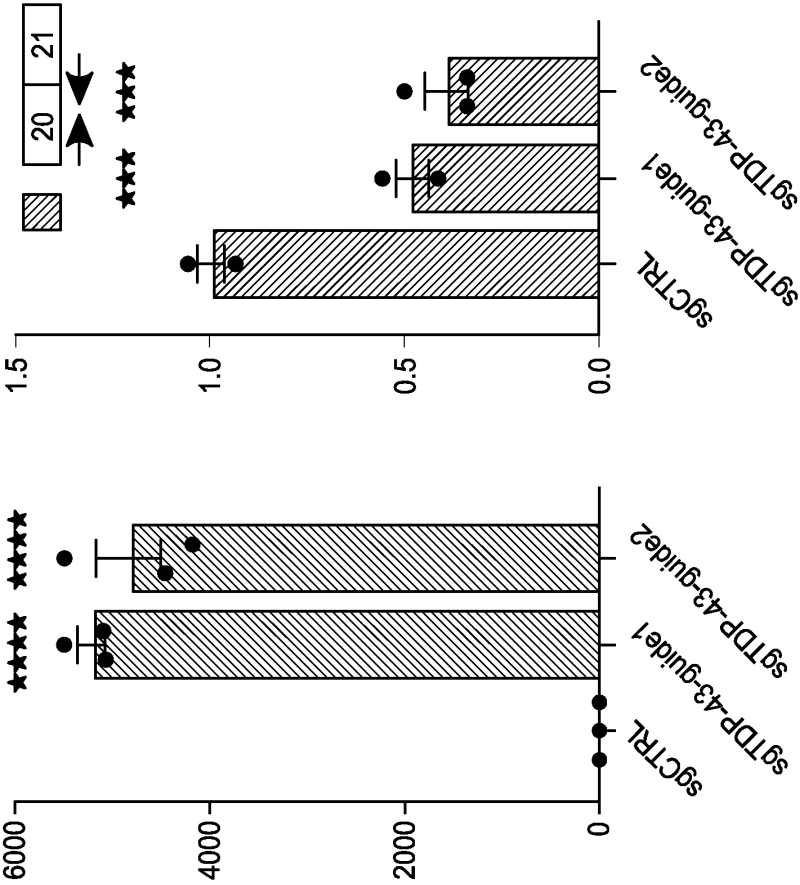


FIG. 1J

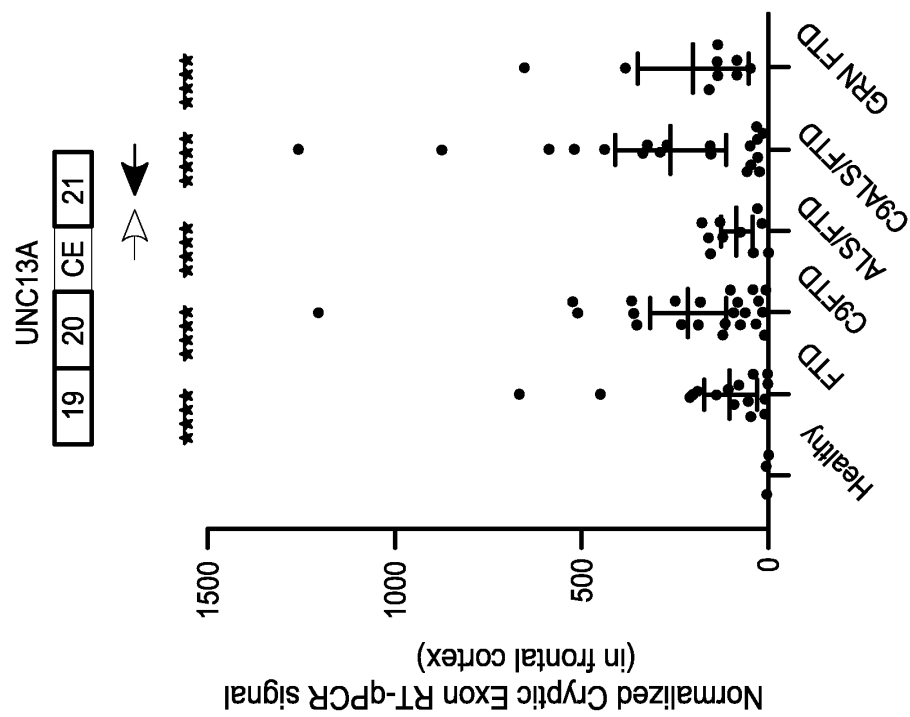


FIG. 2A

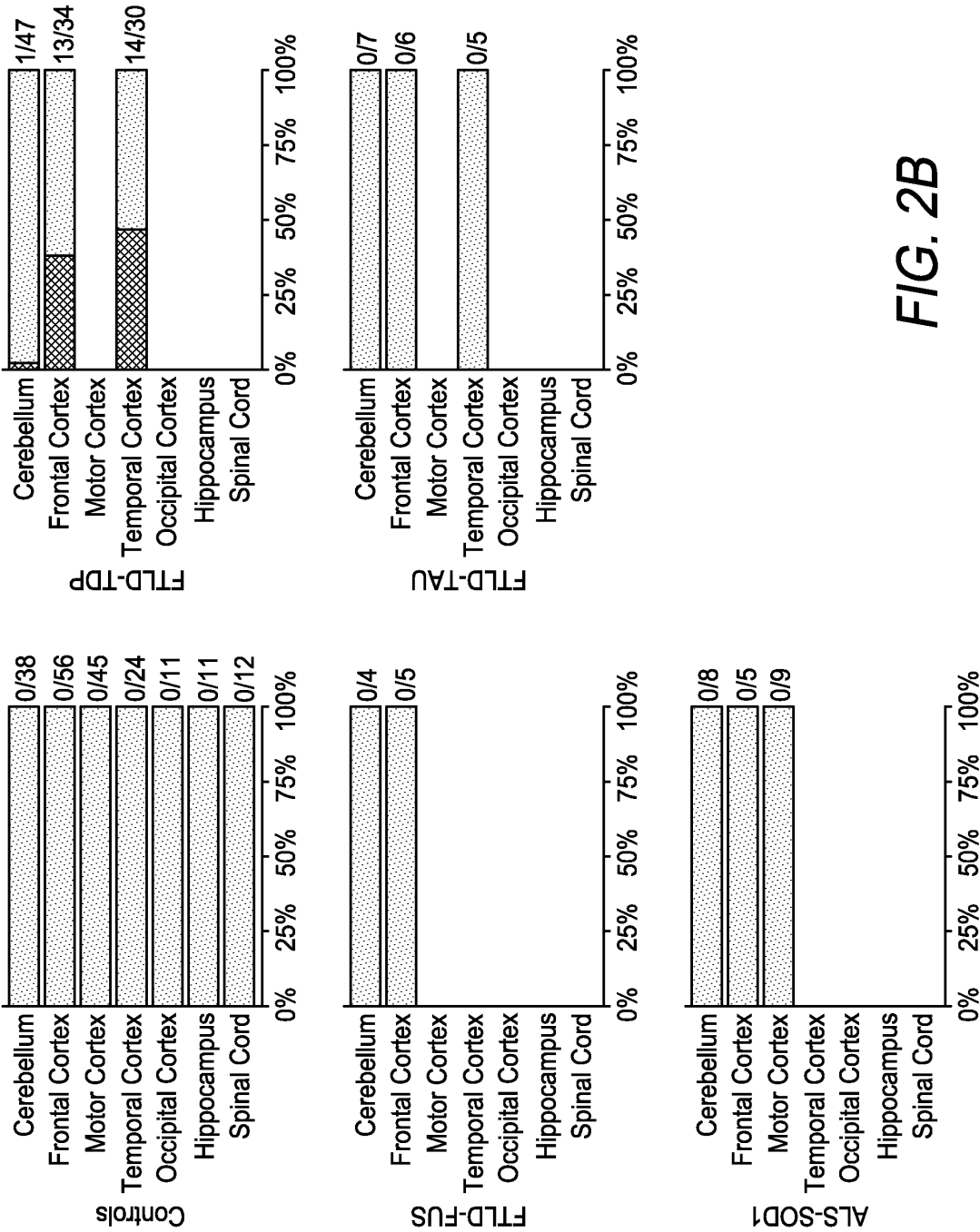


FIG. 2B

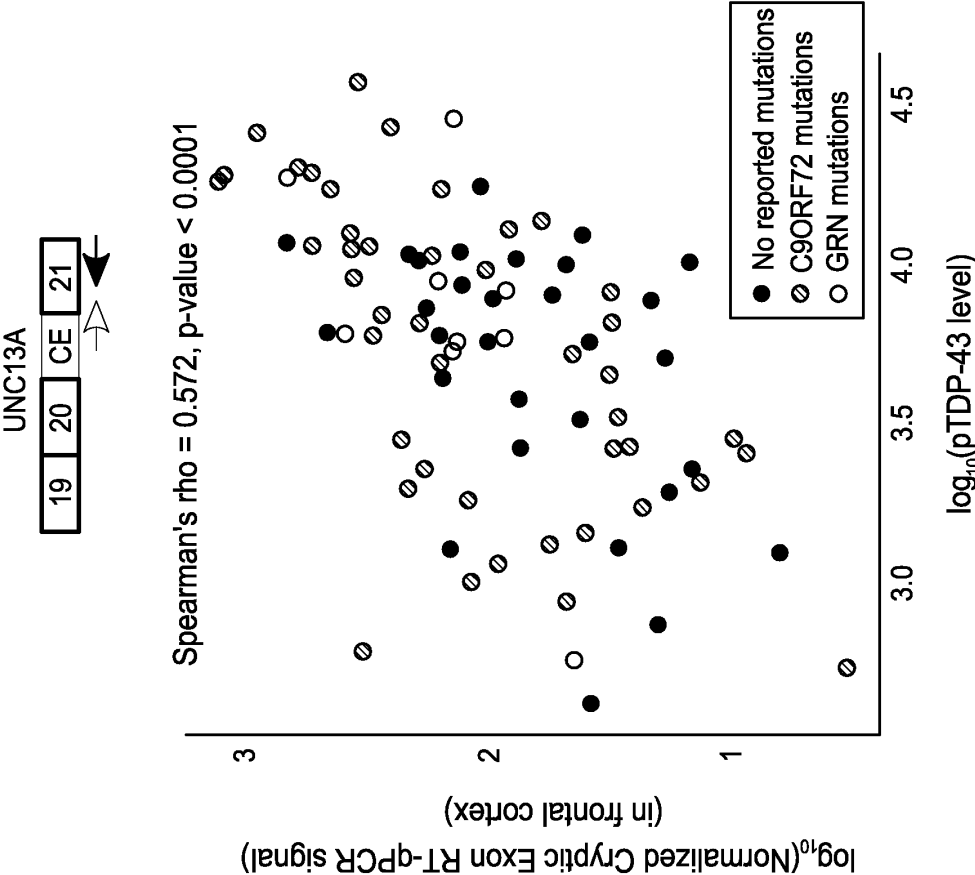
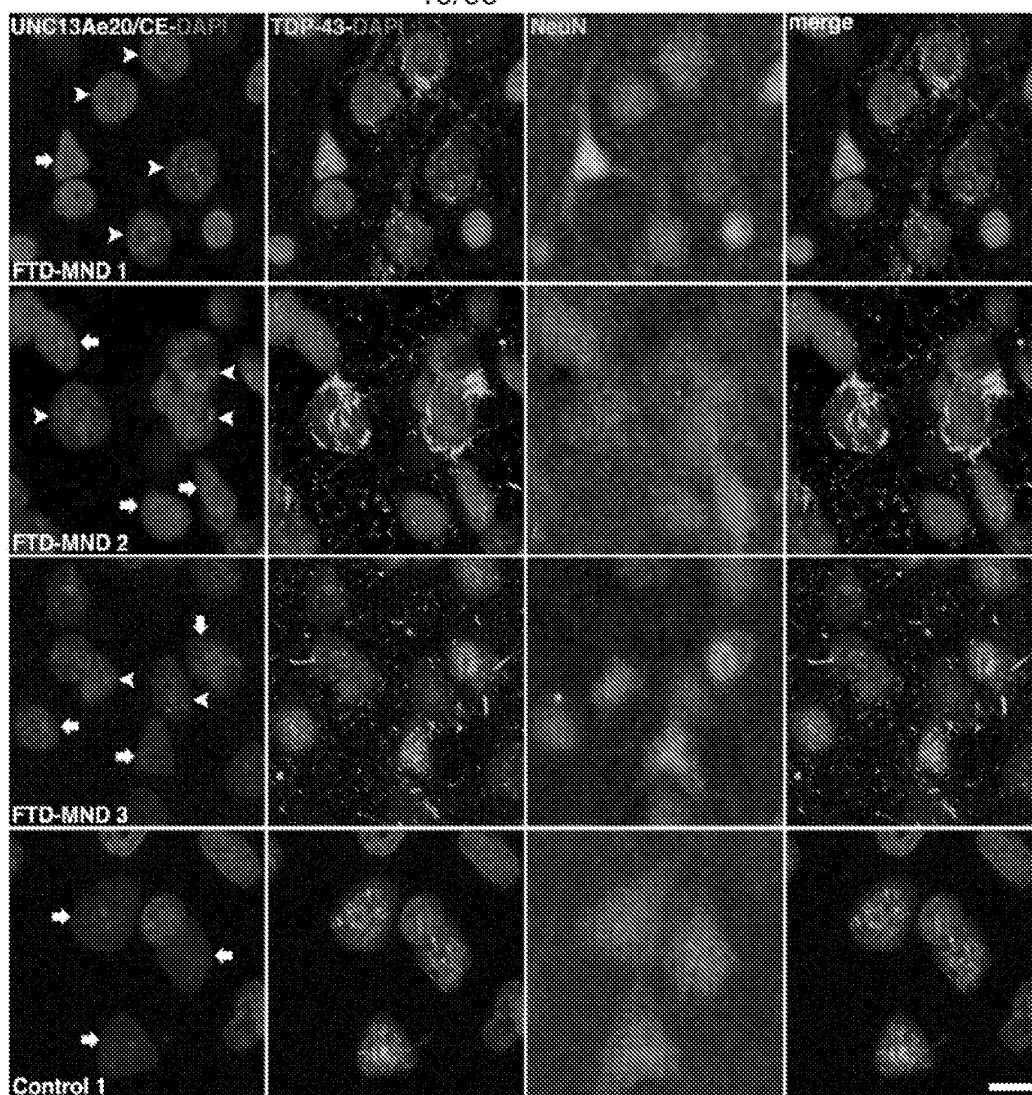
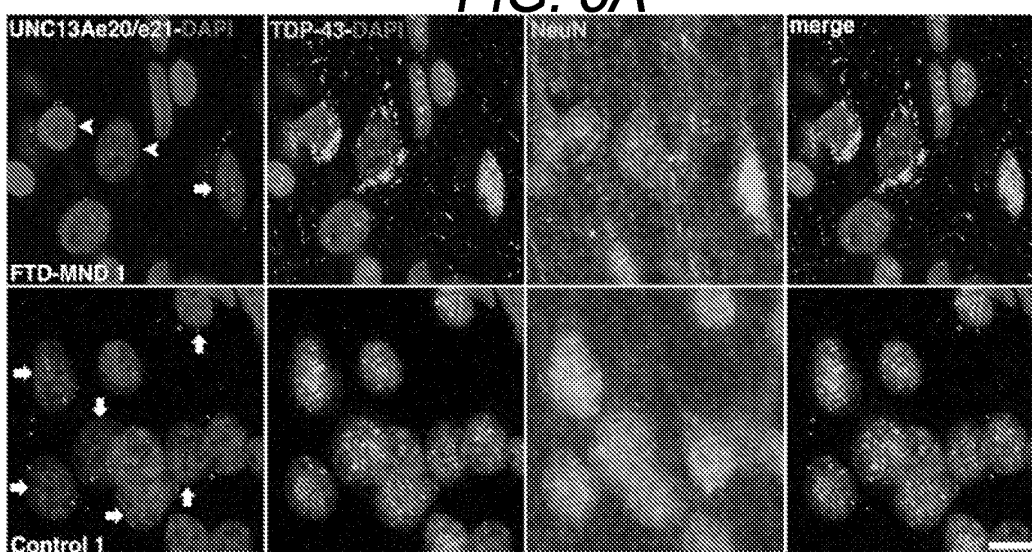


FIG. 2C

Datasets	Sample size	Spearman's rank correlation ρ	P-value
All patients	86	0.572	<0.0001
No reported mutations	30	0.478	0.0082
C9ORF72 mutations	47	0.622	<0.0001
GRN mutations	9	0.617	0.08573
FTD patients	55	0.513	<0.0001
ALS/FTD patients	31	0.666	<0.0001

FIG. 2D

*FIG. 3A**FIG. 3B*

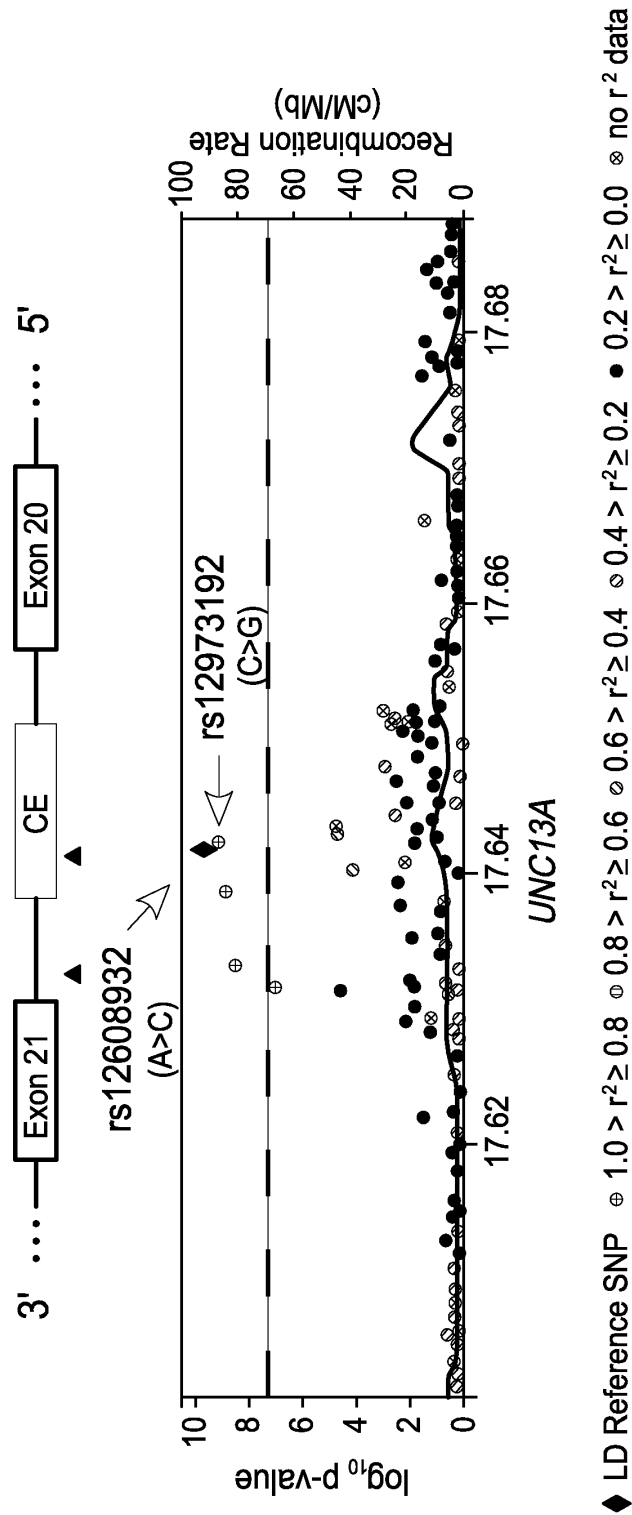


FIG. 4A

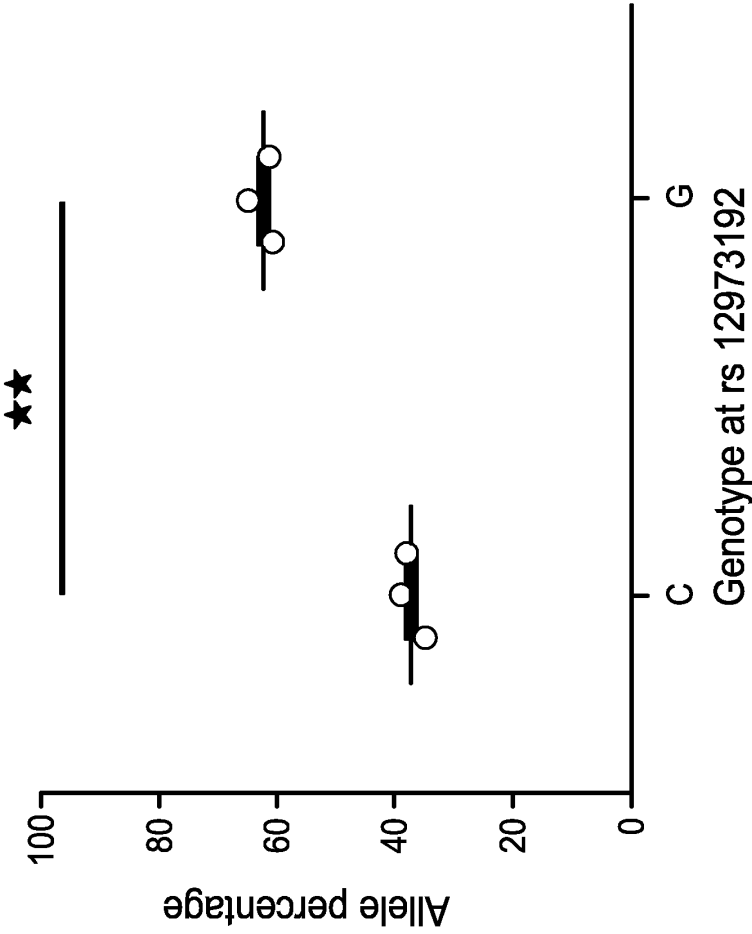


FIG. 4B

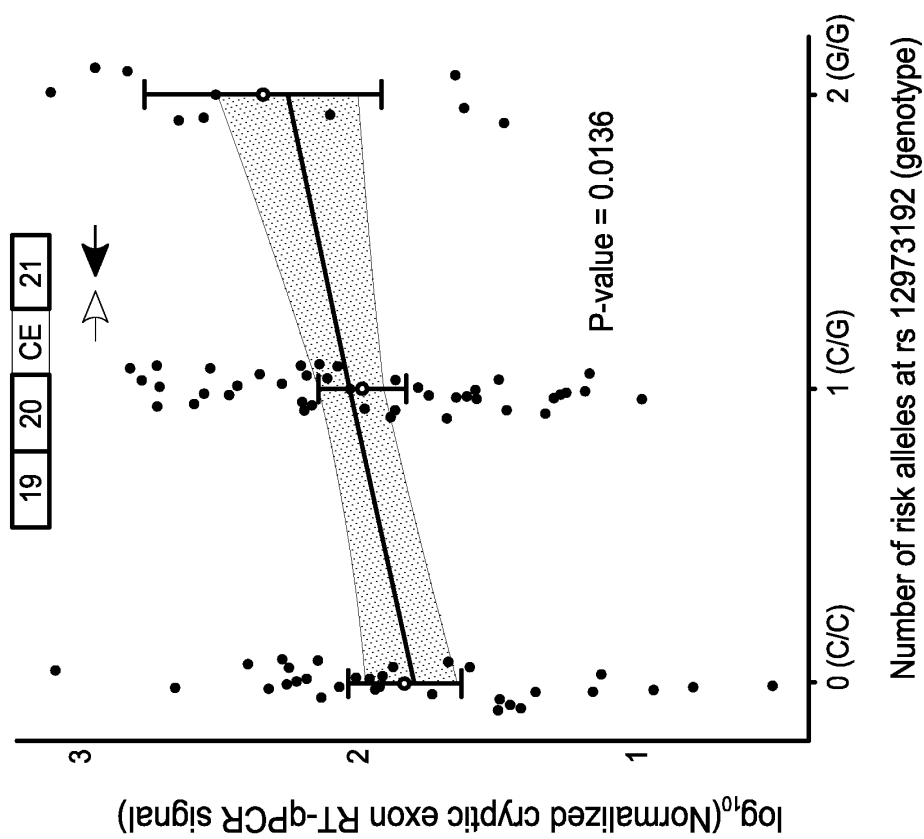


FIG. 4C

Model	Coefficients	Standard error	t value	P-value
Intercept	-0.565	0.415	-1.361	0.177411
Number of risk alleles at rs12973192	0.217	0.080	2.726	0.007922
log10 (pTDP-43)	0.594	0.110	5.414	<0.0001
Male	-0.201	0.101	-1.989	0.050183
C9ORF72 mutations	0.285	0.108	2.635	0.010116
GRN mutations	0.281	0.172	1.635	0.106087
FTD	0.129	0.110	1.174	0.243799
Adjusted R-squared: 0.3616				

FIG. 4D

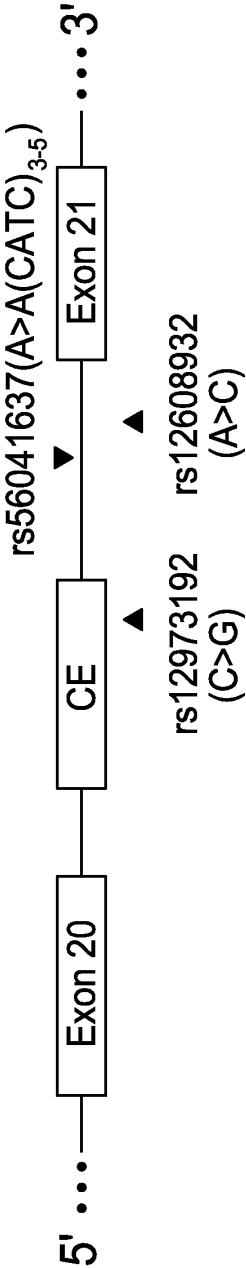


FIG. 4E

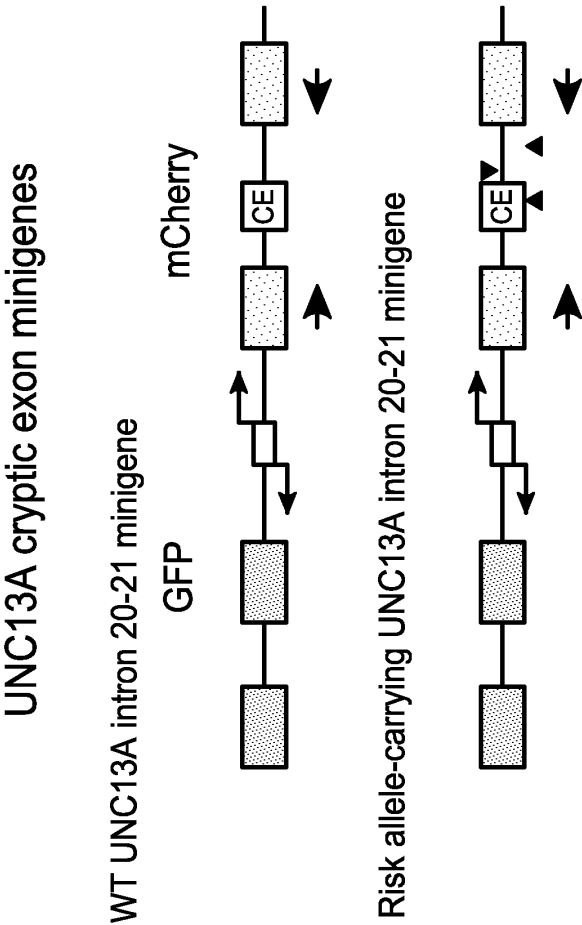


FIG. 4F

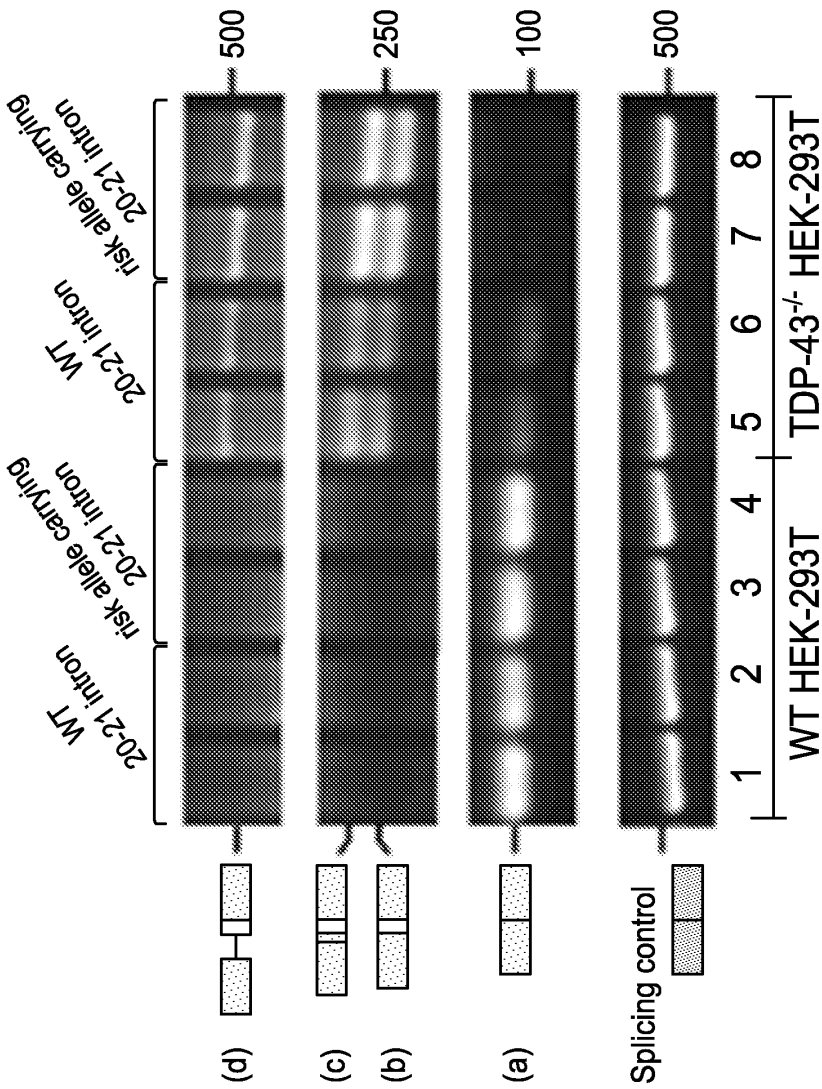


FIG. 4G

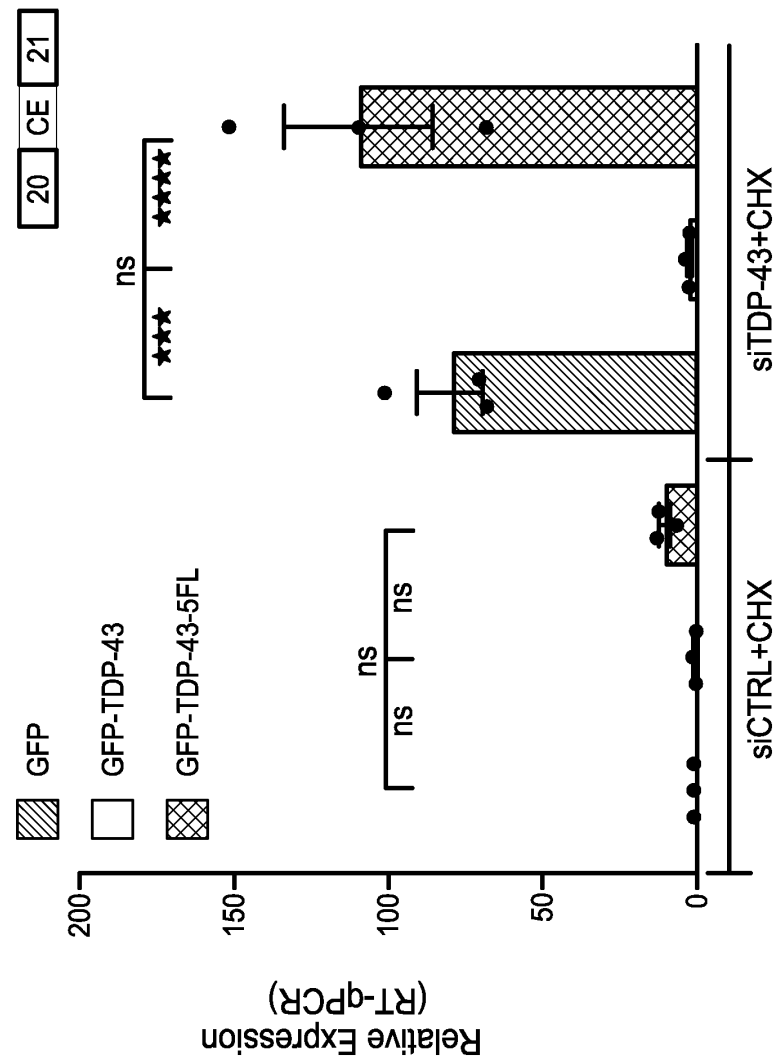


FIG. 4H

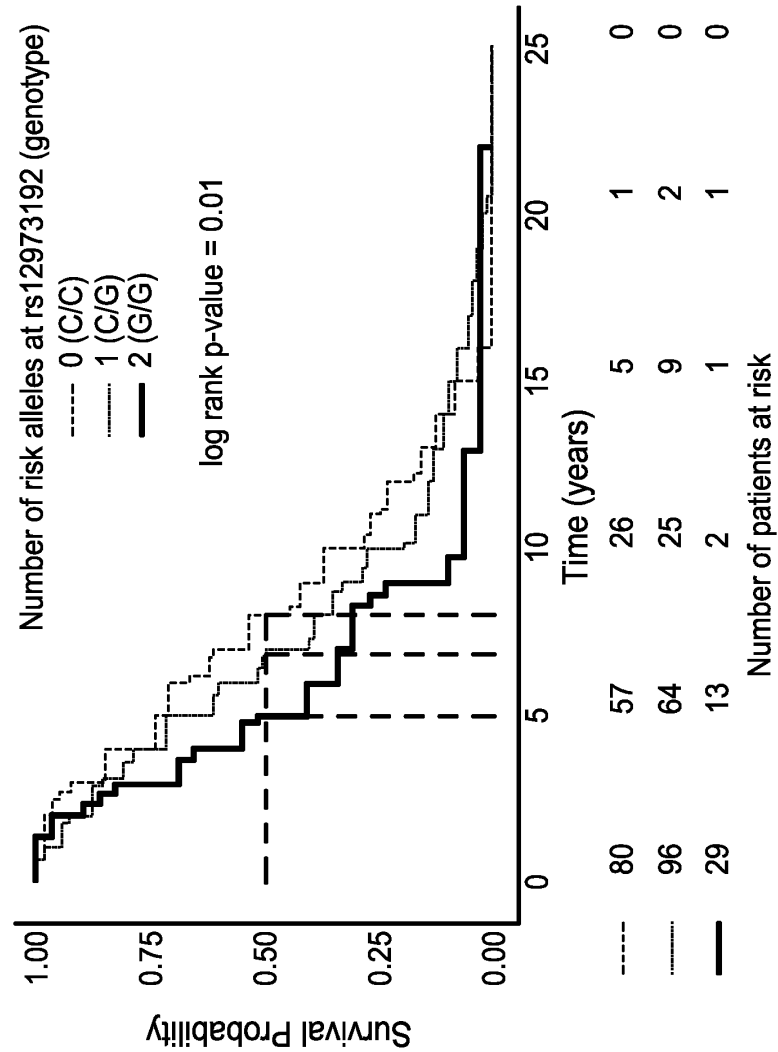


FIG. 4I

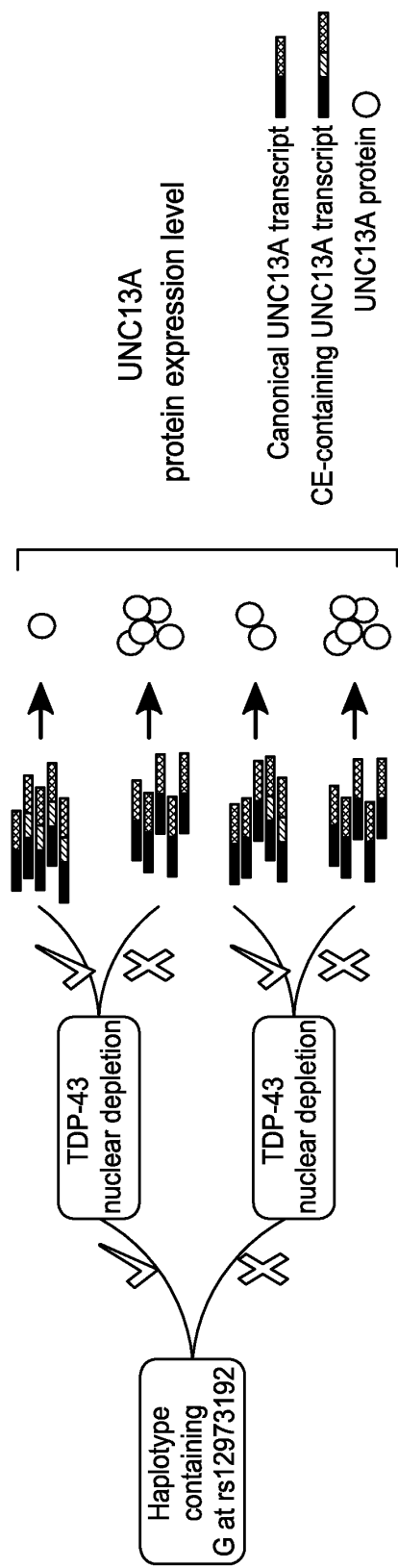
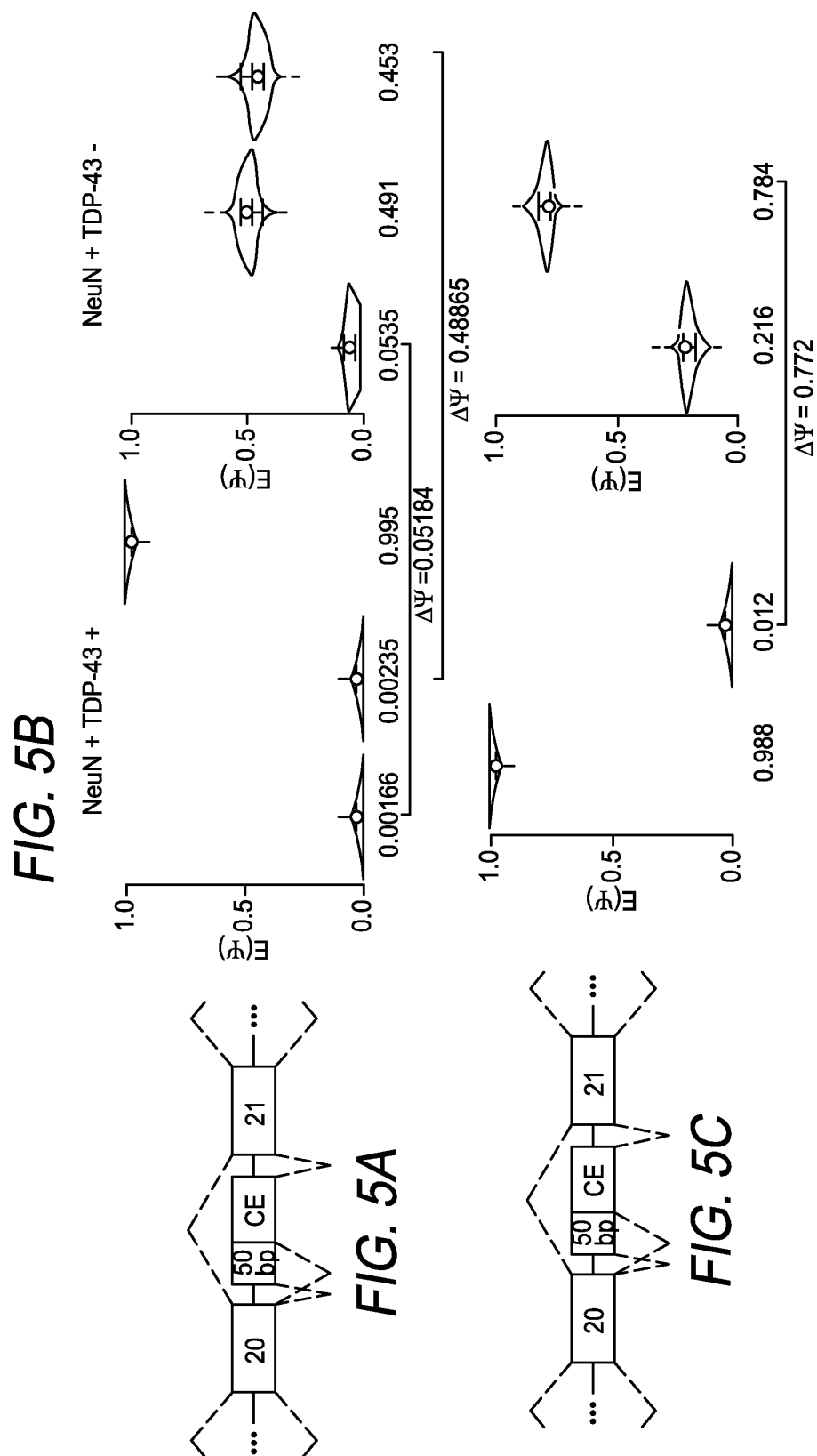


FIG. 4J



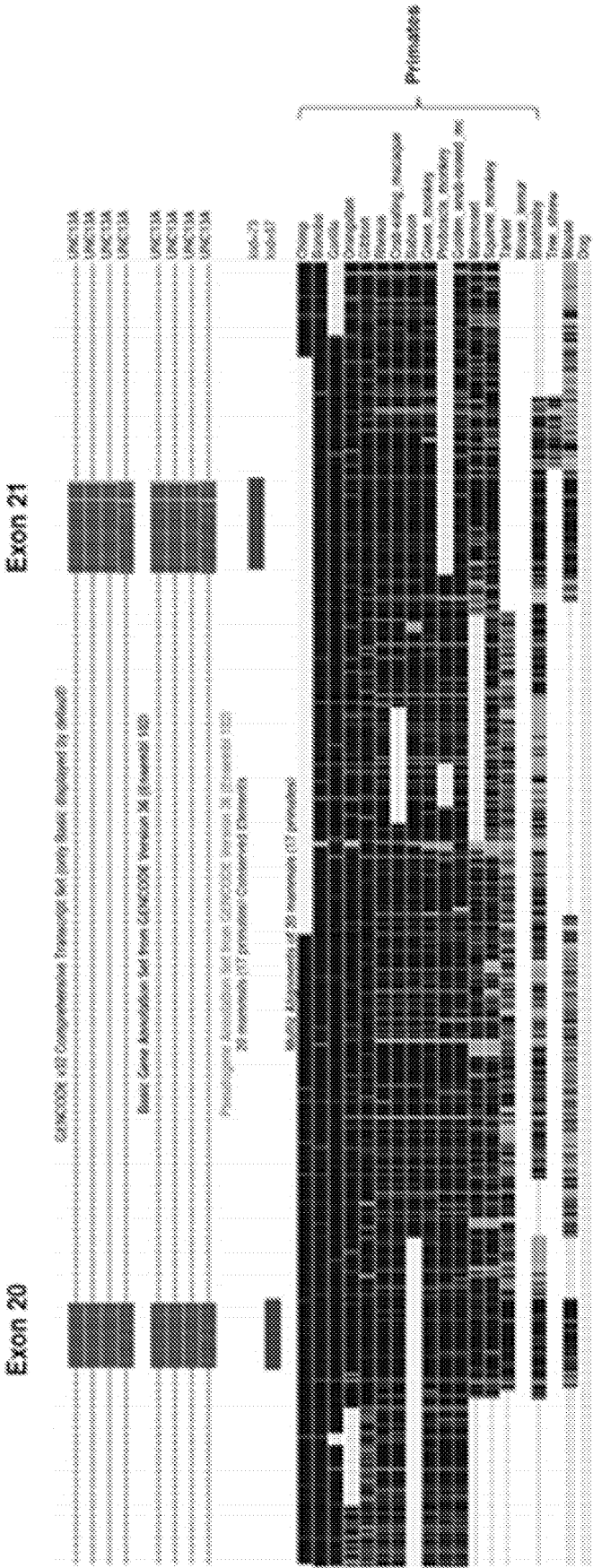
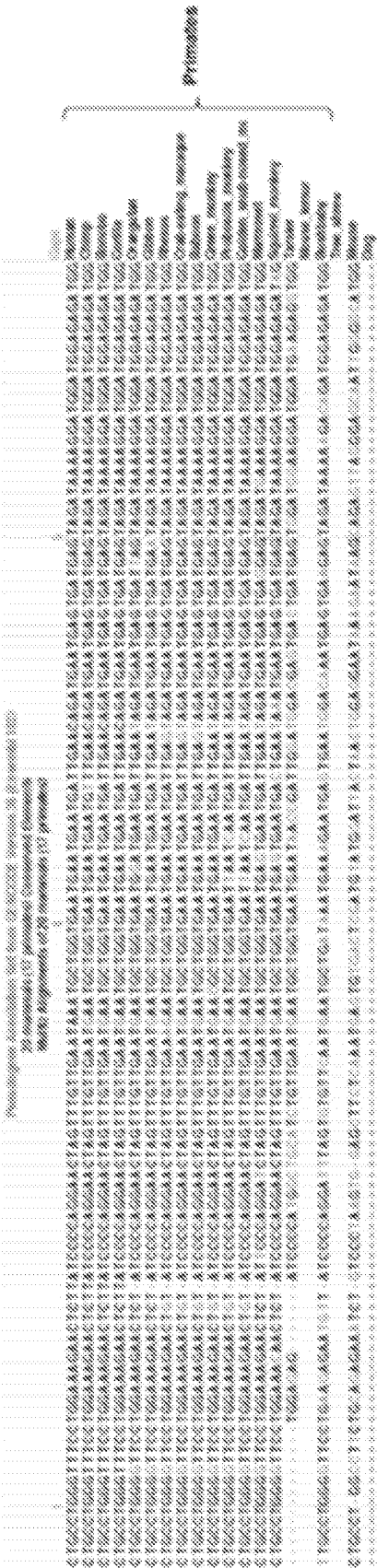


FIG. 6A

FIG. 6B



Cryptic Exon

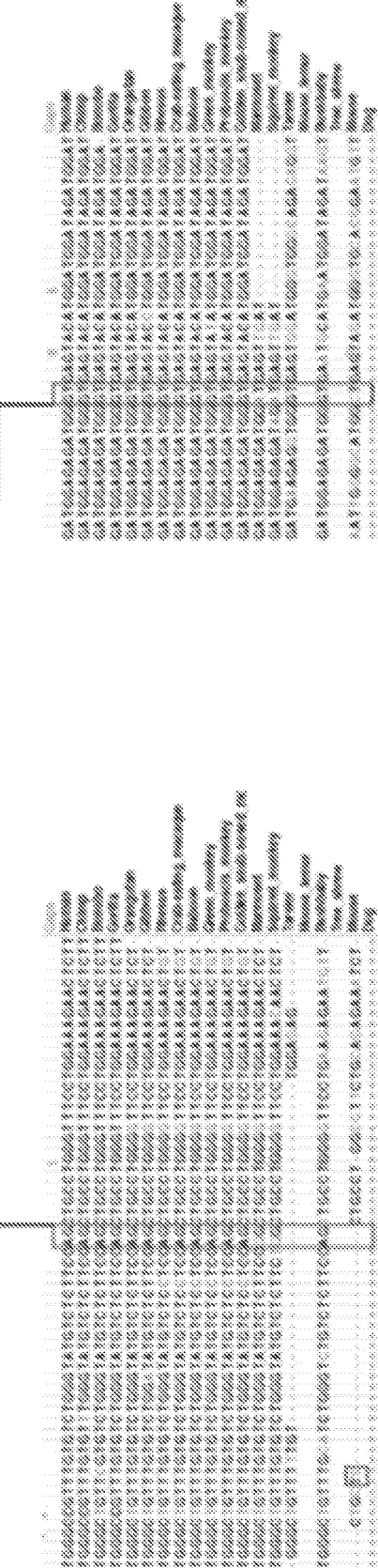


FIG. 6D

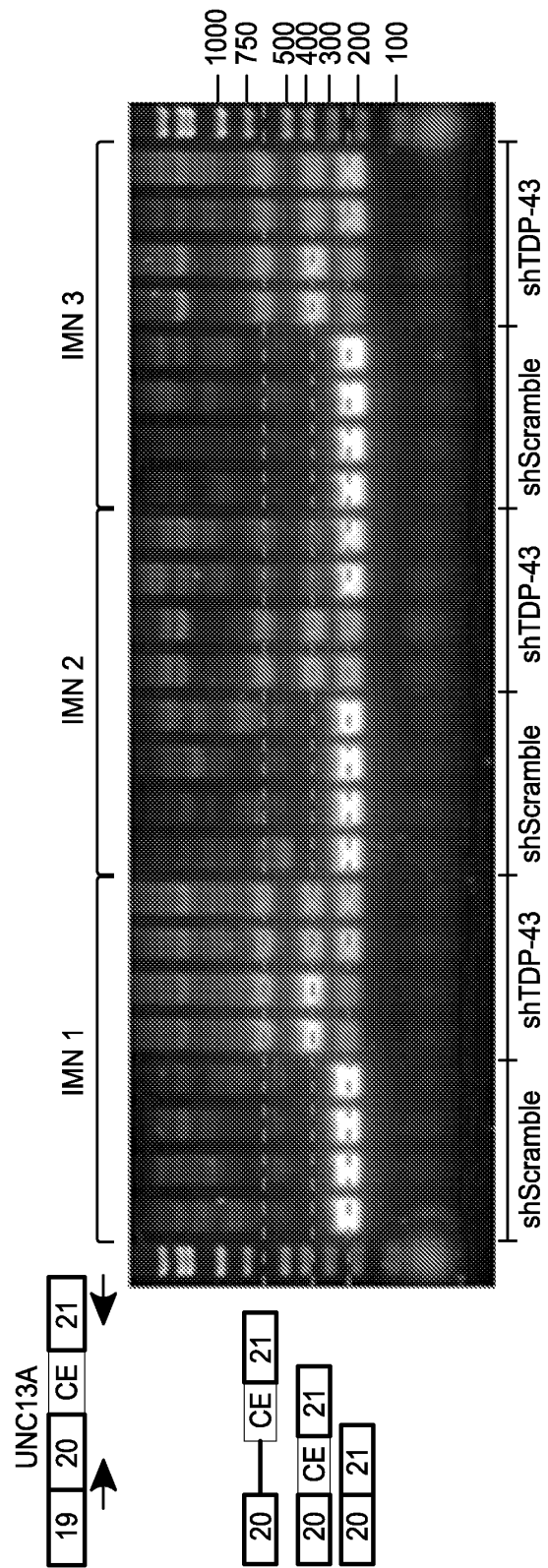


FIG. 7A

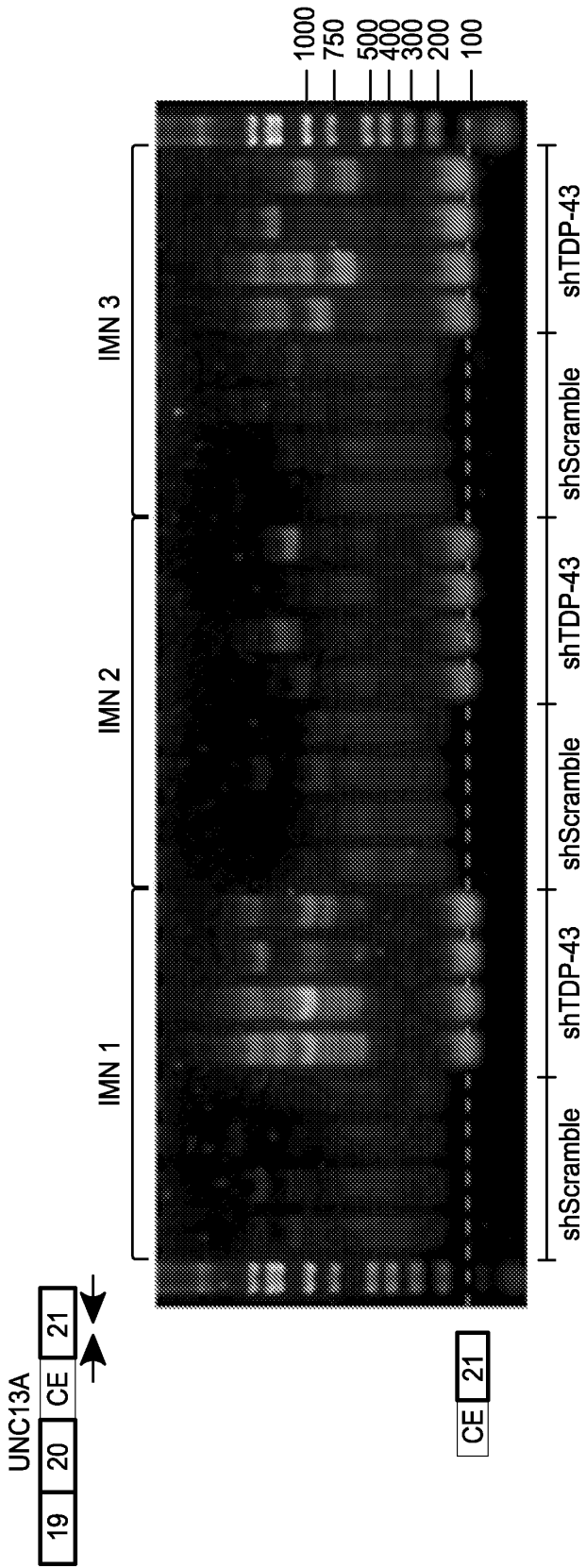


FIG. 7B

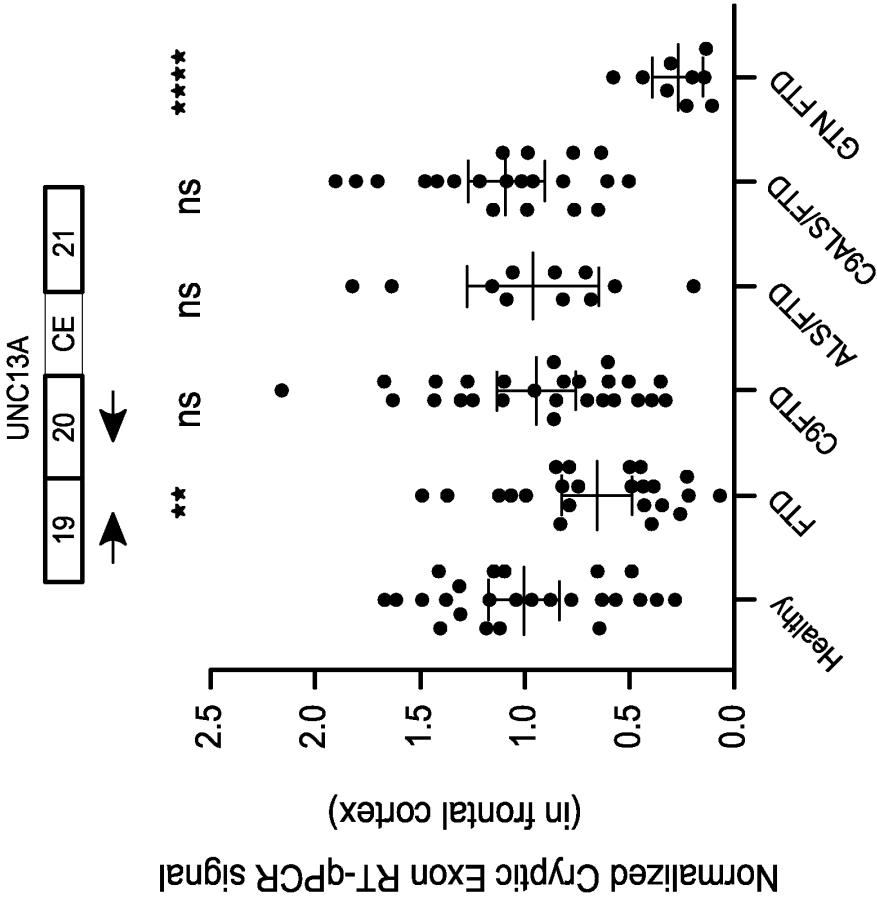


FIG. 8

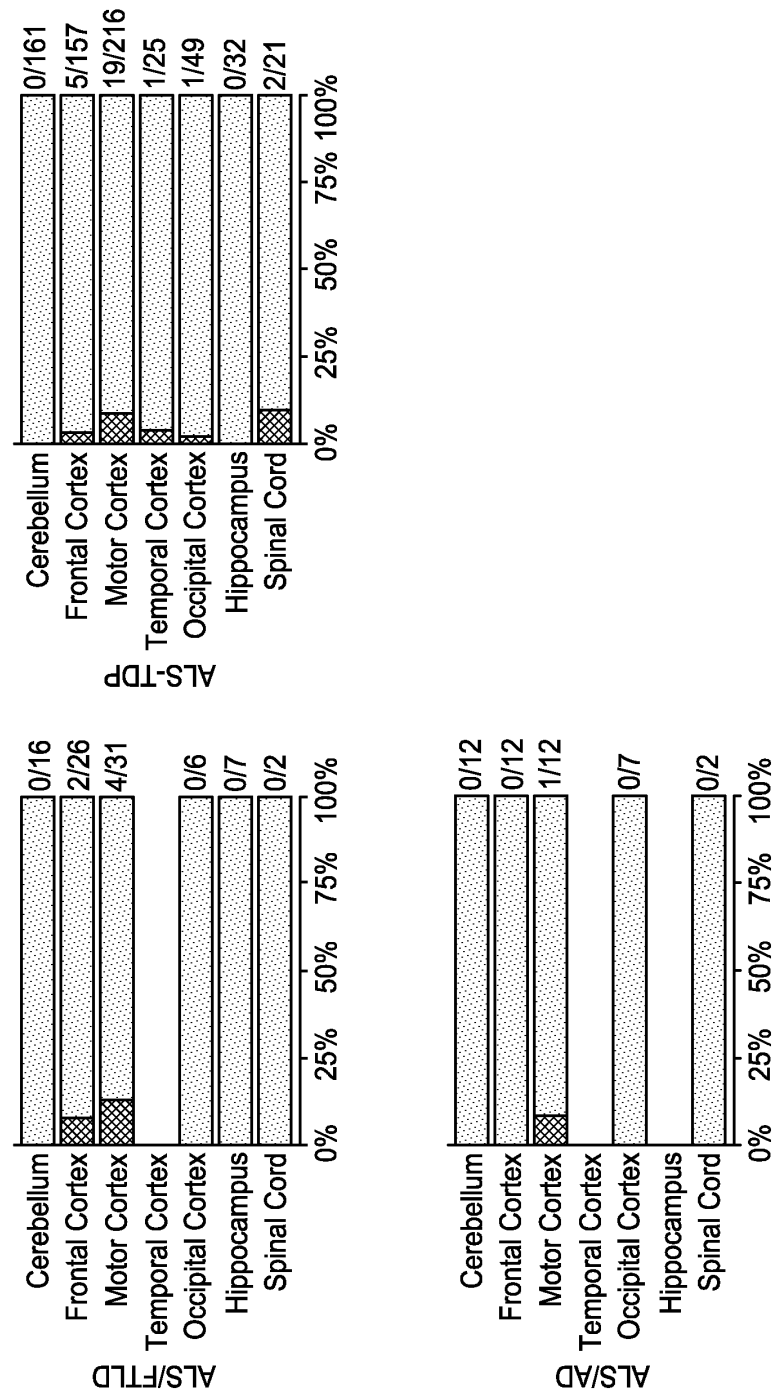


FIG. 9

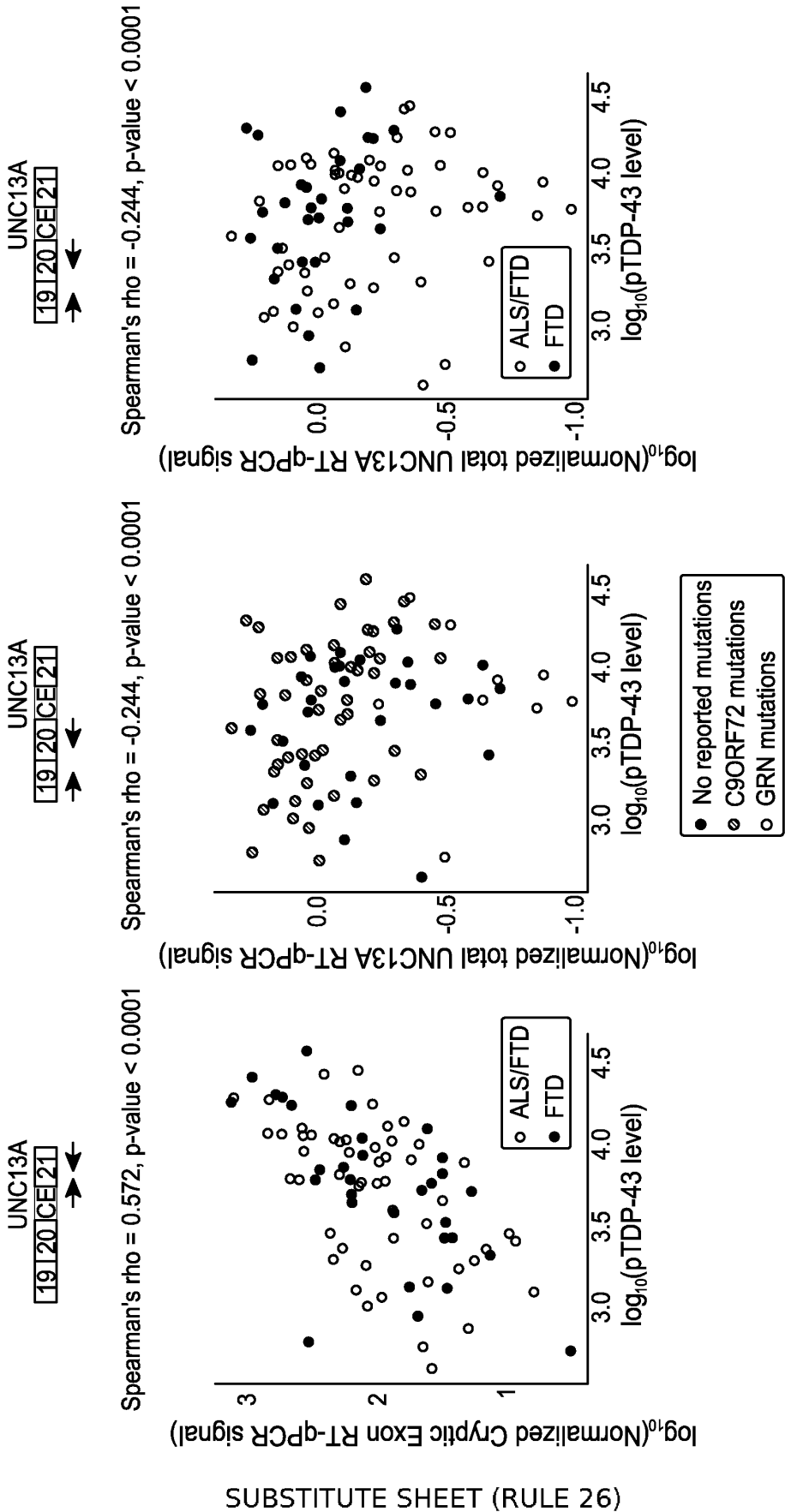


FIG. 10C

FIG. 10B

FIG. 10A

Datasets	Sample size	Spearman's rank correlation rho	P-value
All patients	86	-0.244	0.0236
No reported mutations	30	-0.142	0.4534
C9ORF72 mutations	47	-0.338	0.0208
GRN mutations	9	0.0333	0.9484
FTD patients	55	-0.188	0.1691
ALS/FTD patients	31	-0.299	0.1027

FIG. 10D

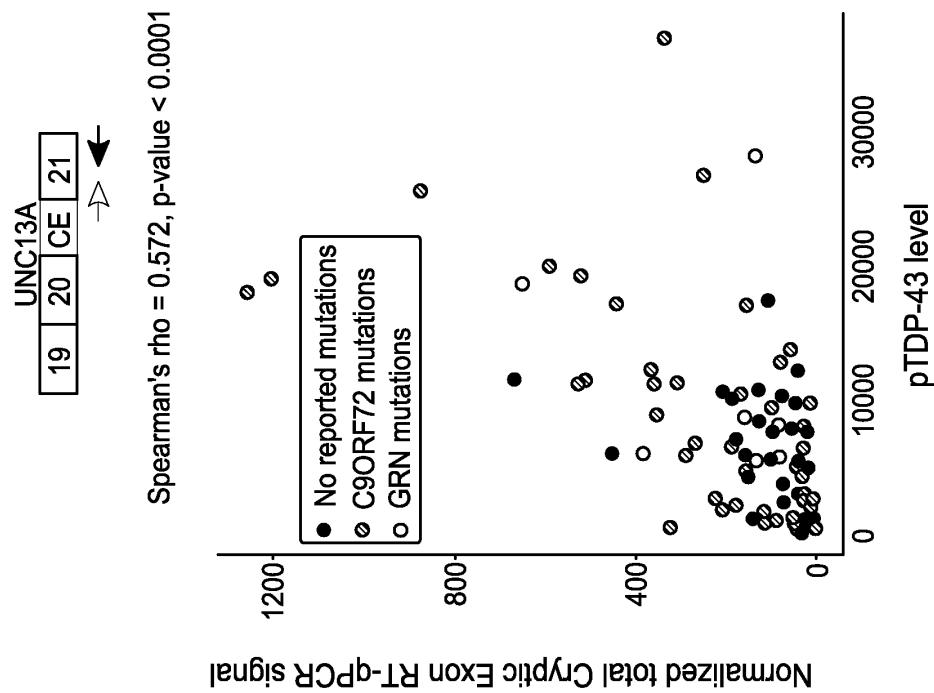


FIG. 10E

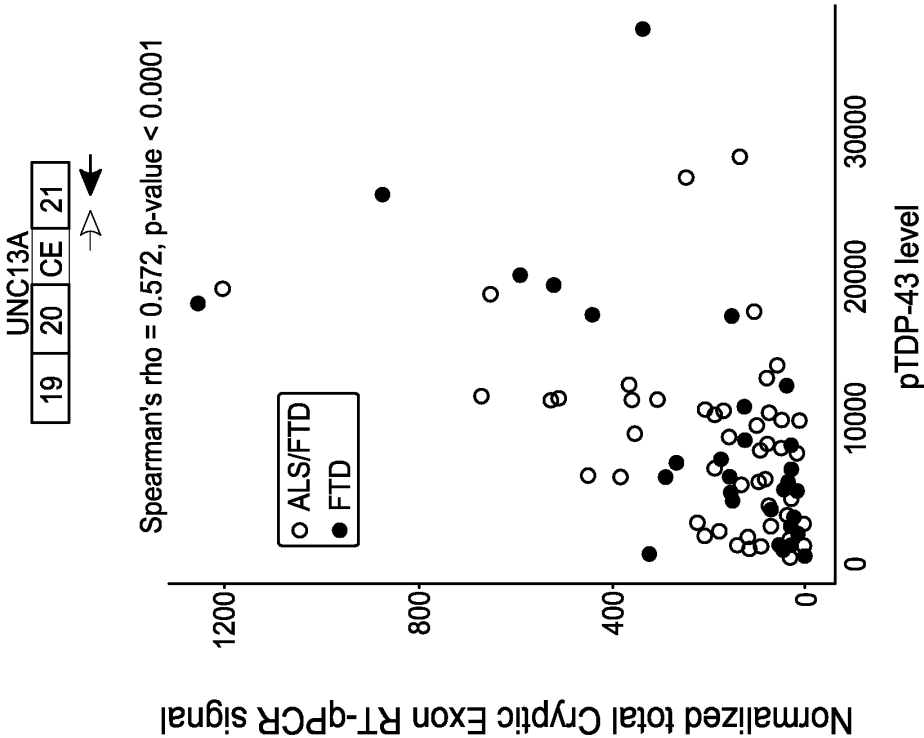


FIG. 10F

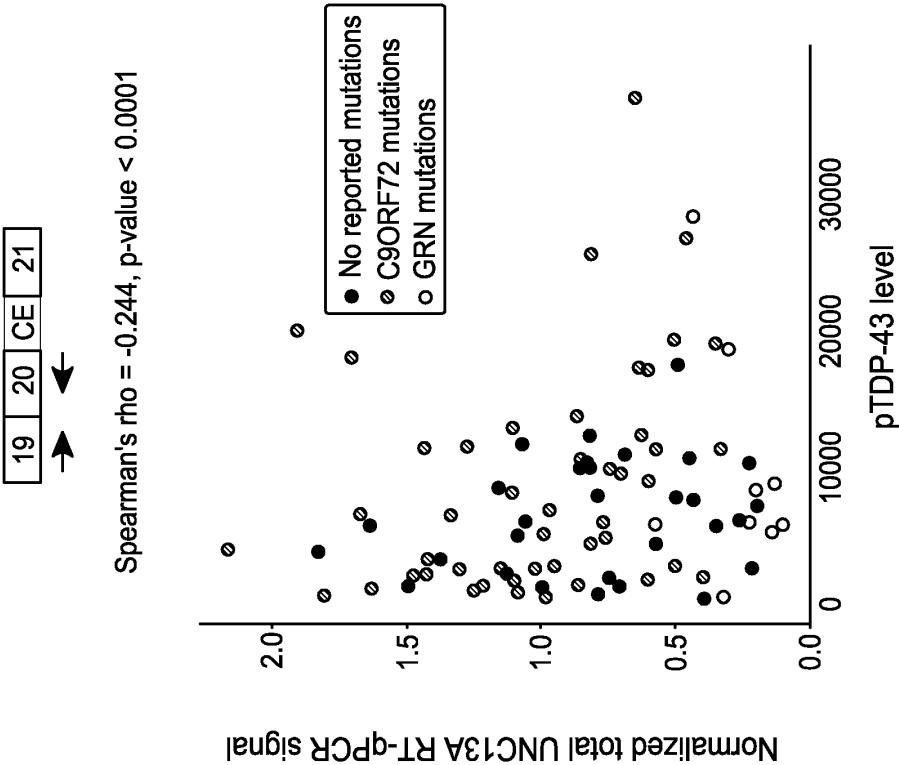


FIG. 10G

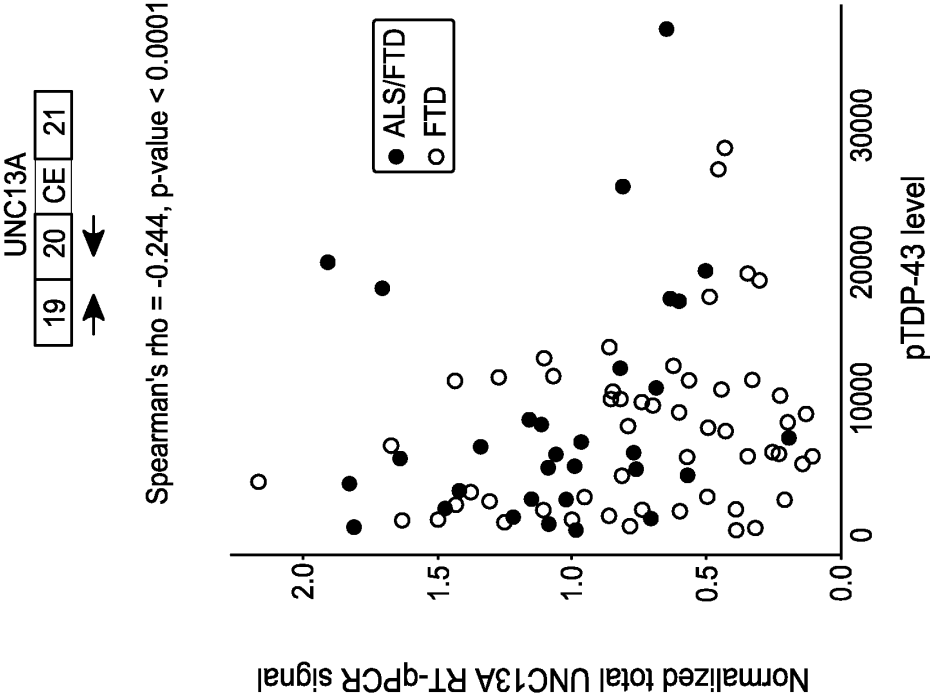


FIG. 10H

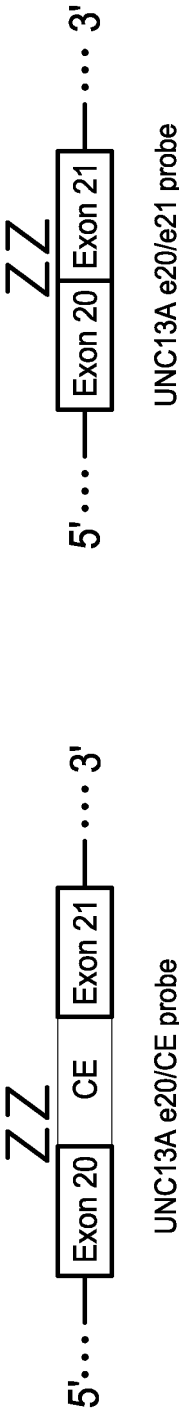
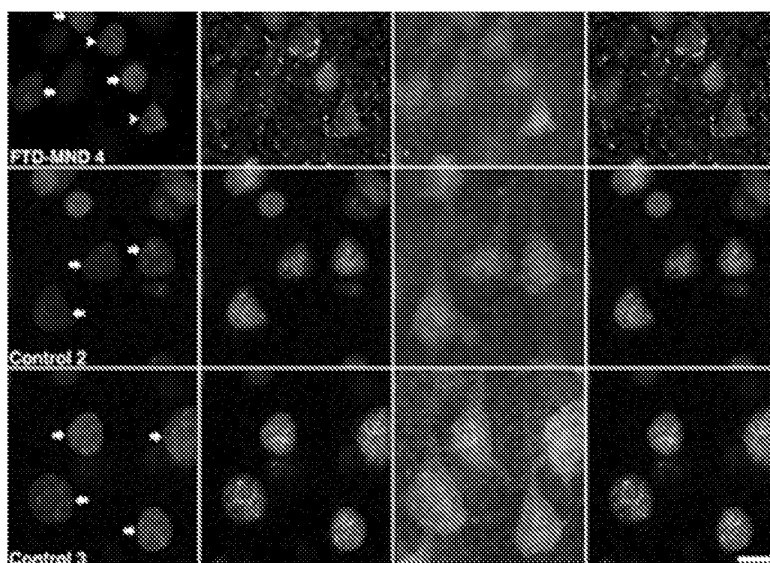
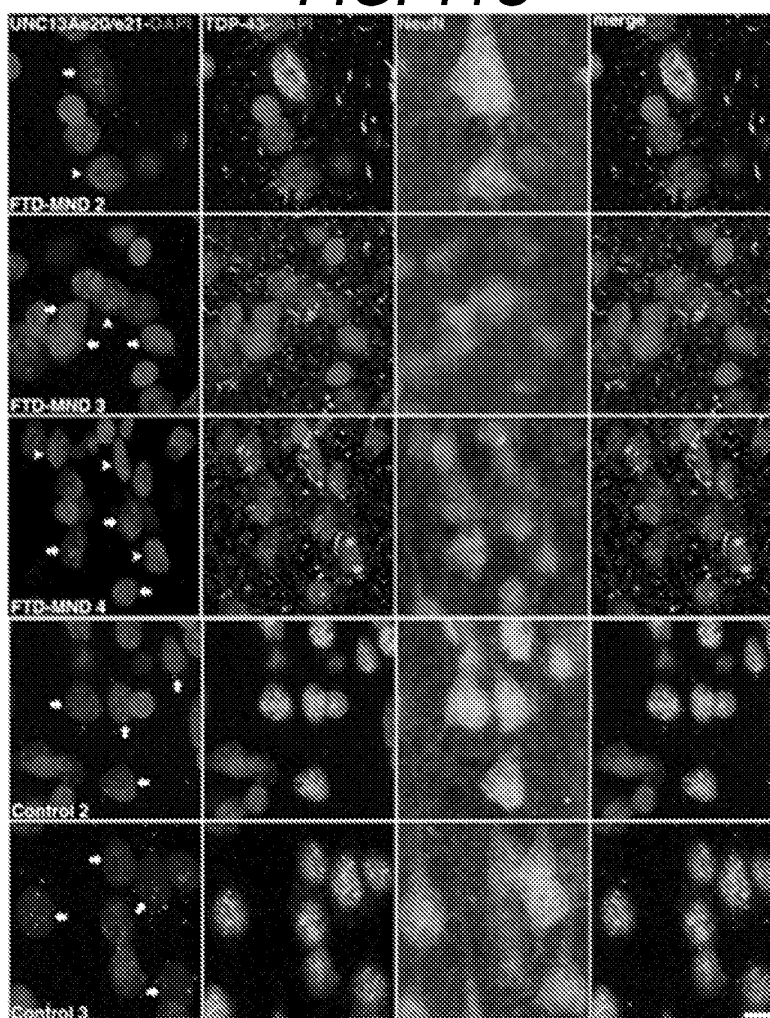


FIG. 11A

FIG. 11B

**FIG. 11C****FIG. 11D**

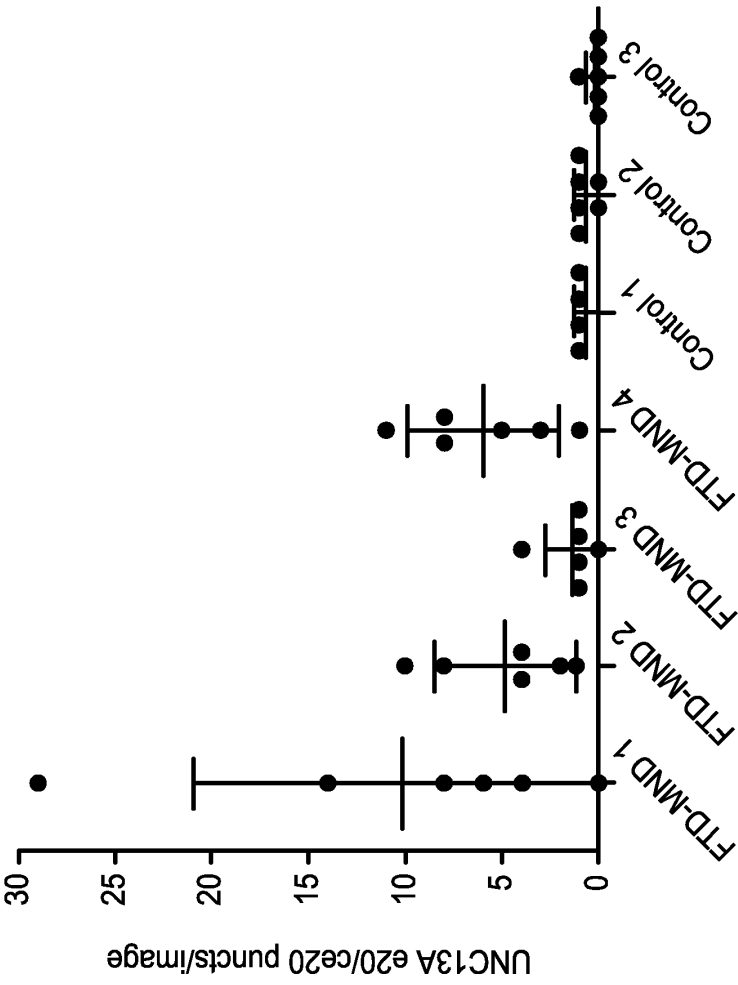


FIG. 11E

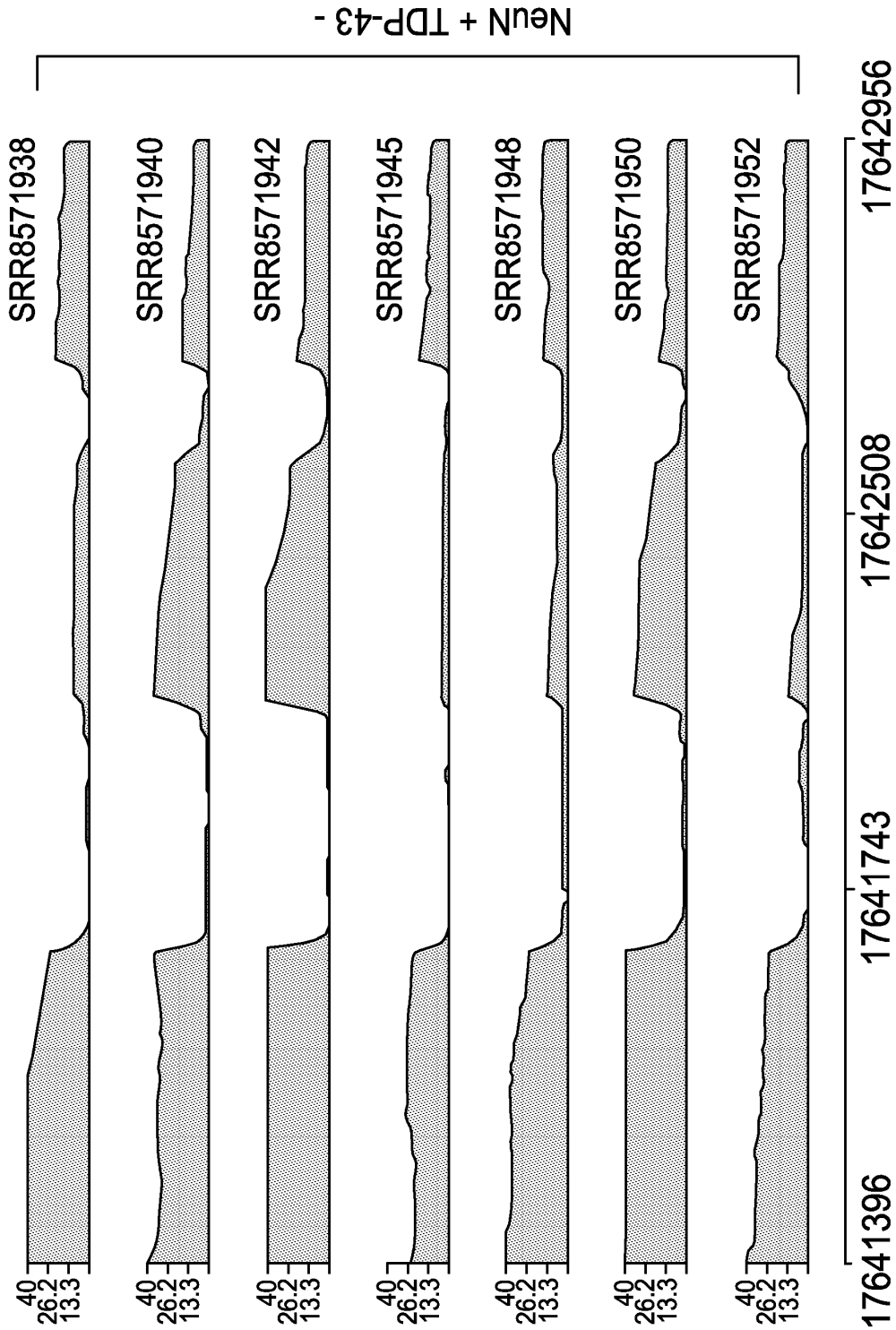


FIG. 12A

Sample Name	Nuclear TDP-43 staining	rs12973192 (C > G)	20-CE Ψ	CE-21 Ψ
SRR8571938	—	C/C	0.213	0.411
SRR8571940	—	G/G	0.891	0.984
SRR8571942	—	G/G	0.940	0.996
SRR8571945	—	G/G	0.102	0.200
SRR8571948	—	C/C	0.234	0.656
SRR8571950	—	C/G	0.787	0.949
SRR8571952	—	C/C	0.258	0.718

FIG. 12B

Sample Name	C allele%	Average within sample %	G allele%	Average within sample %	Exact binomial test p-value
iMN1 replicate 1	41	39.0	59	61.00	0.089
iMN1 replicate 2	37		63		0.012
iMN3 replicate 1	37	38.0	62	61.50	0.015
iMN3 replicate 2	39		61		0.035
SRR8571950	35	35	65	65	0.004

FIG. 12C

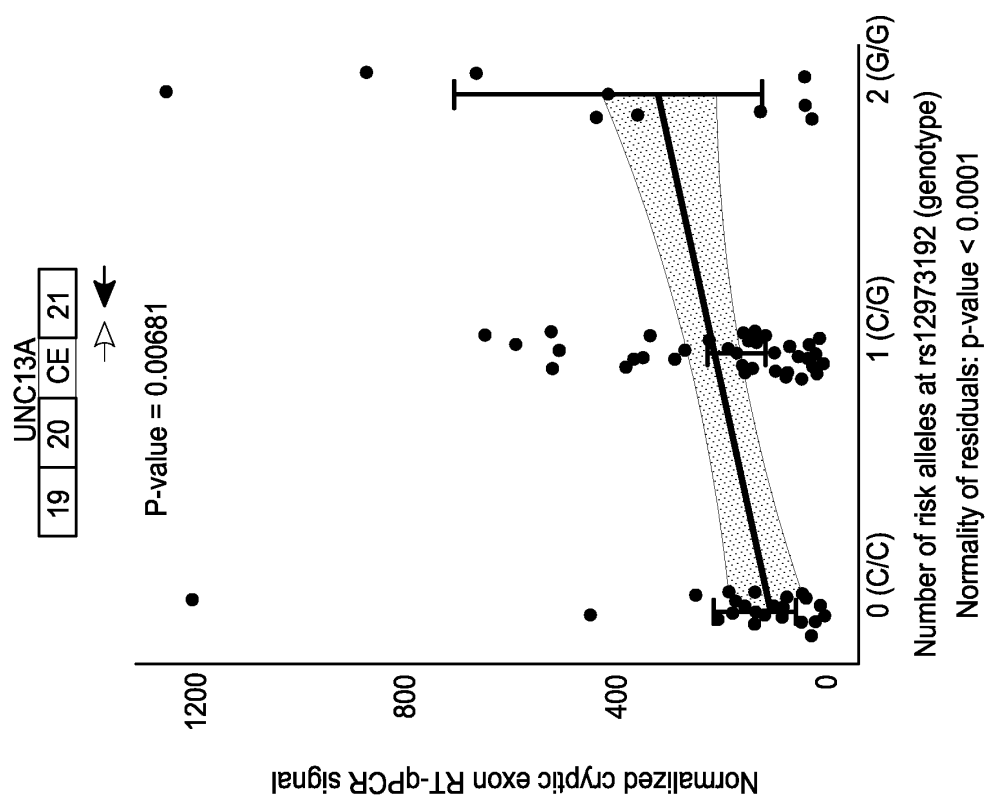


FIG. 13A

UNC13A

19

20

CE

21

↗

↘

Model	Coefficients	Standard error	t value	P-value
Intercept	-65.074	61.206	61.206	0.290972
Number of risk alleles at rs12973192	95.314	35.304	35.304	0.008504
pTDP-43	0.015	0.003	0.003	<0.0001
Male	-94.819	44.807	44.807	0.037523
C9ORF72 mutations	126.050	48.184	48.184	0.010678
GRN mutations	44.420	75.954	75.954	0.560351
FTD	50.416	48.267	48.267	0.293475
Adjusted R-squared: 0.3457				

Normality of residuals: p-value < 0.0001

FIG. 13B

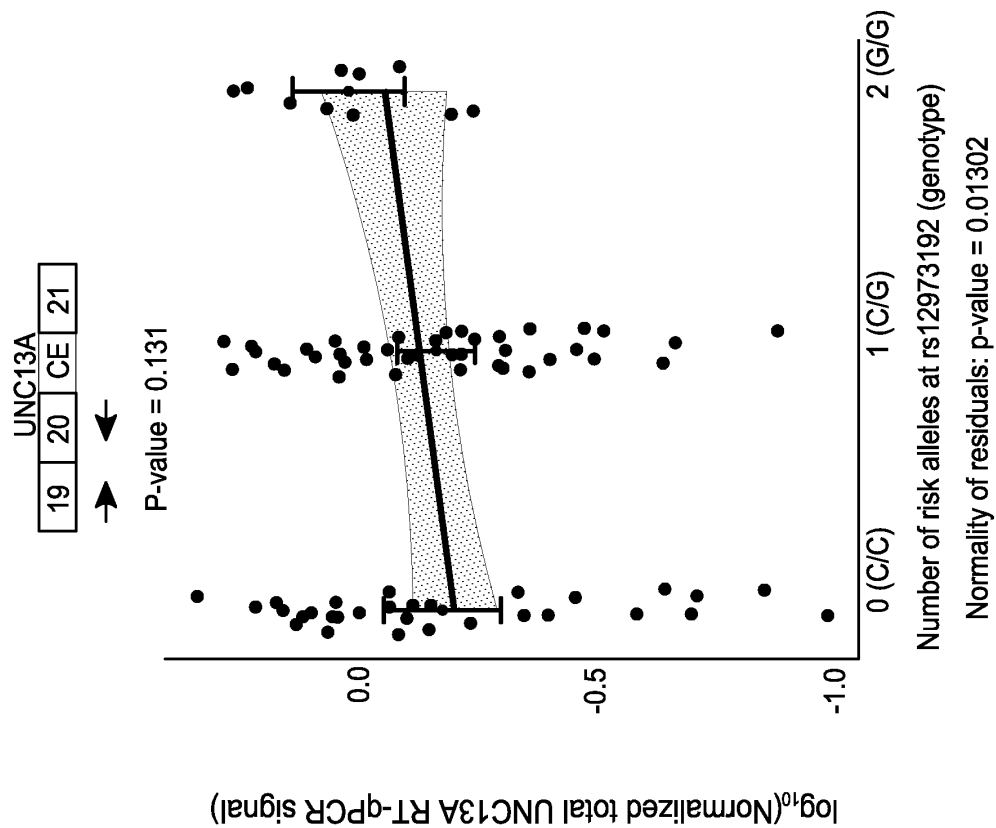


FIG. 13C

UNC13A

19	20	CE	21
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→ ←

Model	Coefficients	Standard error	t value	P-value
Intercept	0.308	0.201	0.201	0.130685
Number of risk alleles at rs12973192	0.031	0.039	0.039	0.423996
log10 (pTDP-43)	-0.126	0.053	0.053	0.020532
Male	0.111	0.049	0.049	0.027042
C9ORF72 mutations	0.092	0.052	0.052	0.083159
GRN mutations	-0.395	0.083	0.083	<0.0001
FTD	-0.119	0.053	0.053	0.028927
Adjusted R-squared: 0.4505				

Normality of residuals: p-value = 0.8814

FIG. 13D

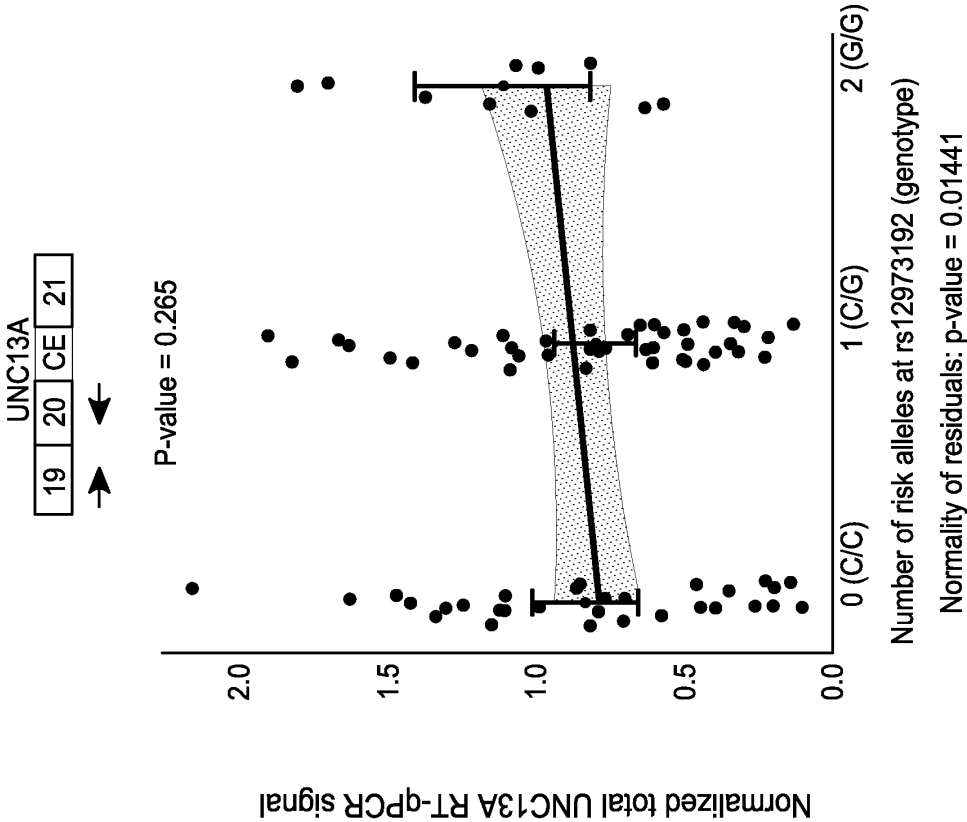


FIG. 13E

UNC13A

19

20

CE

21

→

←

Model	Coefficients	Standard error	t value	P-value
Intercept	0.956	0.122	7.806	-0.0001
Number of risk alleles at rs12973192	0.033	0.071	0.453	0.644681
pTDP-43	-0.00001513	0.00000623	-2.429	0.017420
Male	0.182	0.090	2.033	0.045503
C9ORF72 mutations	0.166	0.096	1.723	0.085808
GRN mutations	-0.385	0.152	-2.532	0.013350
FTD	-0.232	0.097	-2.409	0.018373
Adjusted R-squared: 0.3135				

Normality of residuals: p-value < 0.0001

FIG. 13F

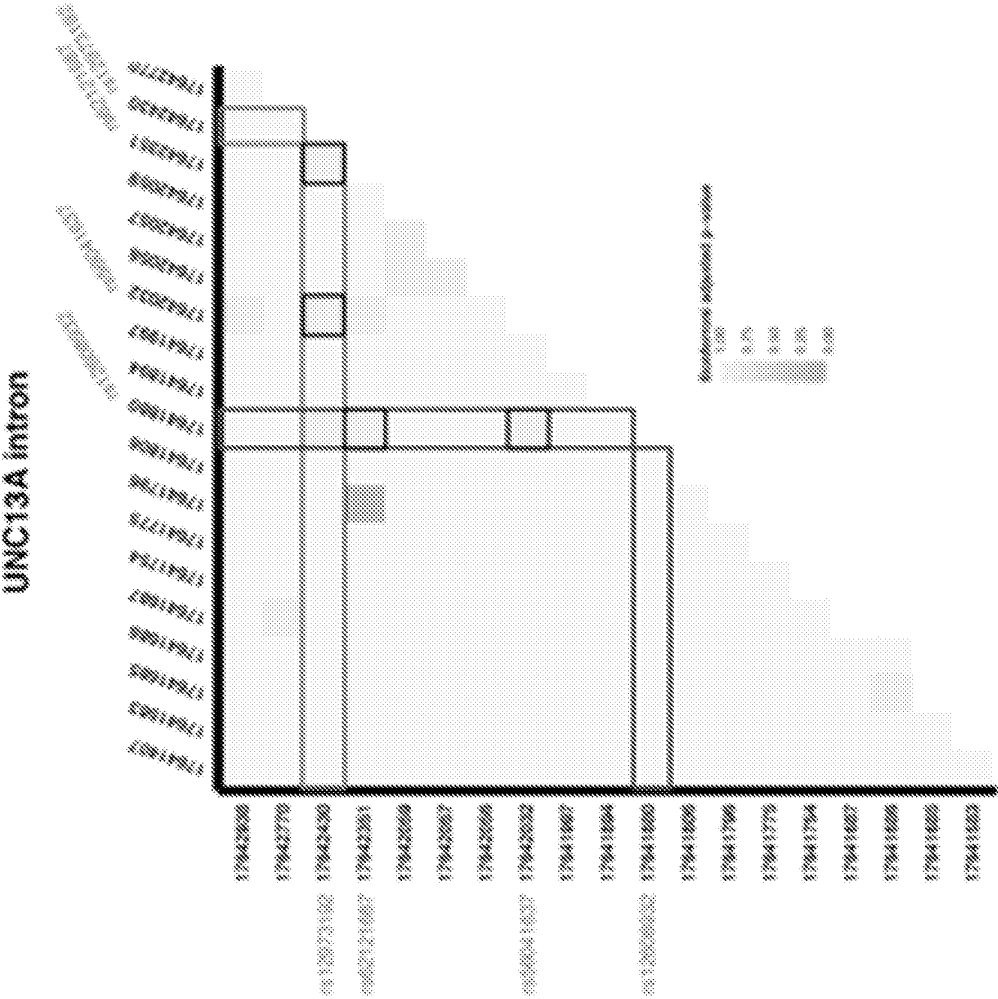


FIG. 14

Factor	Hazard ratio	95% confidence interval	p-value
Number of risk alleles	1.341	1.0627-1.660	0.00717
<i>C9ORF72</i> mutations	1.778	1.2428-2.544	0.00163
No mutations in <i>GRN</i>	1.325	0.3228-5.438	0.69622
<i>GRN</i> mutations	1.668	1.0952-2.540	0.01715
Mutation undetermined	1.100	0.6503-1.860	0.72266
Age at onset	1.006	0.9895-1.022	0.48876
Male	1.077	0.8098-1.432	0.61140

FIG. 15A

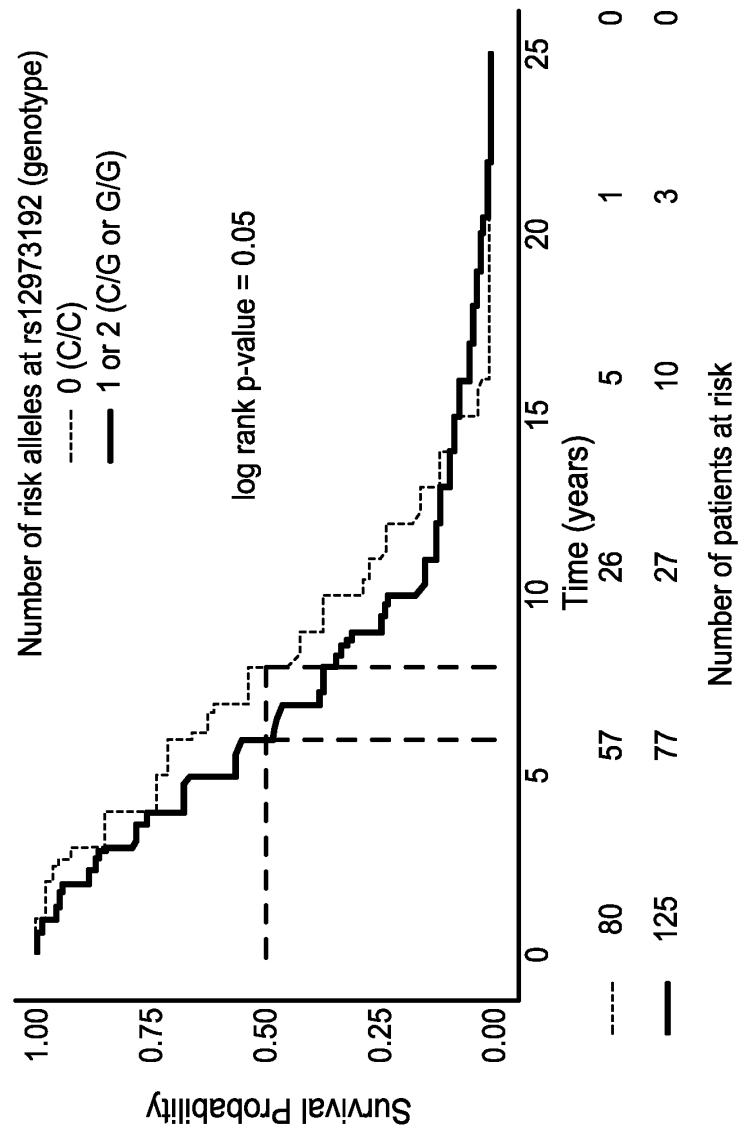


FIG. 15B

Factor	Hazard ratio	95% confidence interval	p-value
Number of risk alleles	1.345	1.0001-1.809	0.04992
<i>C9ORF72</i> mutations	1.745	1.2195-2.497	0.00232
No mutations in <i>GRN</i>	1.269	0.3085-5.223	0.74115
<i>GRN</i> mutations	1.646	1.0805-2.509	0.02034
Mutation undetermined	1.076	0.6340-1.826	0.78649
Age at onset	1.005	0.9889-1.022	0.53231
Male	1.056	0.7927-1.407	0.70927

FIG. 15C

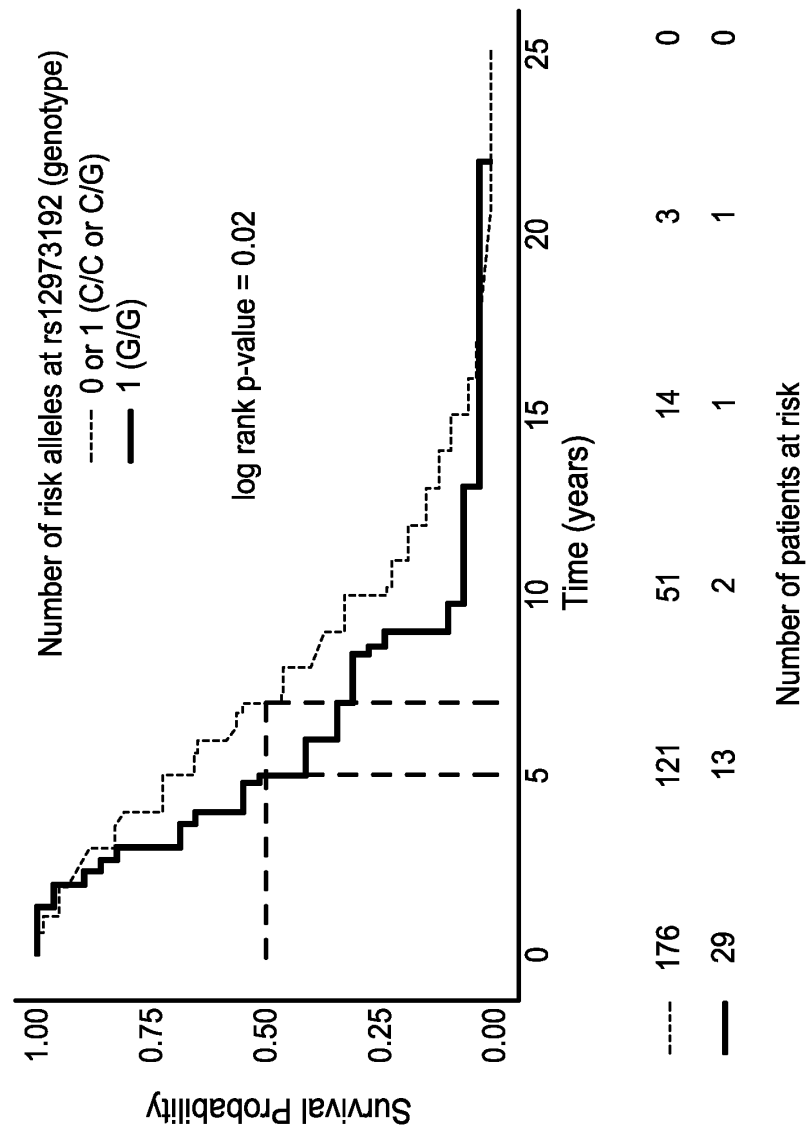


FIG. 15D

Factor	Hazard ratio	95% confidence interval	p-value
Number of risk alleles	1.699	1.1360-2.542	0.01001
<i>C9ORF72</i> mutations	1.682	1.1837-2.391	0.00373
No mutations in <i>GRN</i>	1.518	0.3693-6.241	0.56262
<i>GRN</i> mutations	1.629	1.0720-2.476	0.02229
Mutation undetermined	1.172	0.6927-1.982	0.55443
Age at onset	1.008	0.9393-1.022	0.50441
Male	1.129	0.8479-1.502	0.40696

FIG. 15E

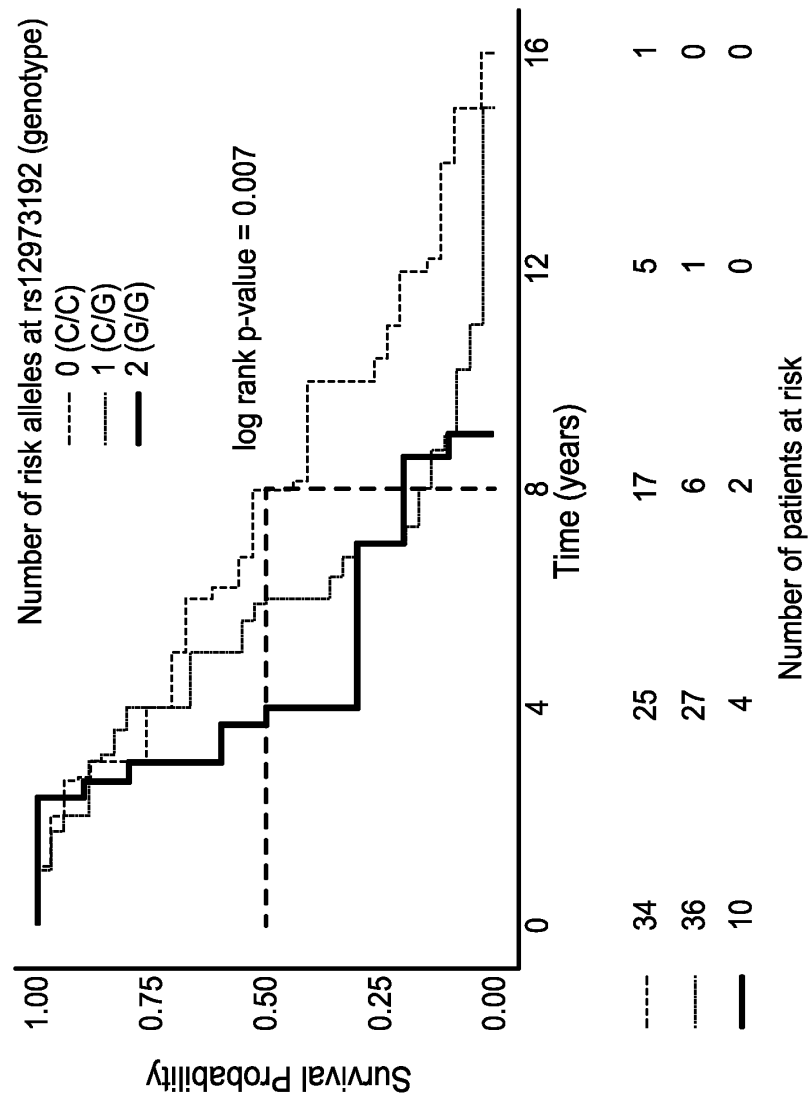


FIG. 16A

Factor	Hazard ratio	95% confidence interval	p-value
Number of risk alleles	1.936	1.3510-2.776	0.00032
GRN mutations	0.854	0.5365-1.359	0.50583
Age at onset	0.992	0.9659-1.019	0.55761
Male	0.679	0.4202-1.097	0.11380

FIG. 16B

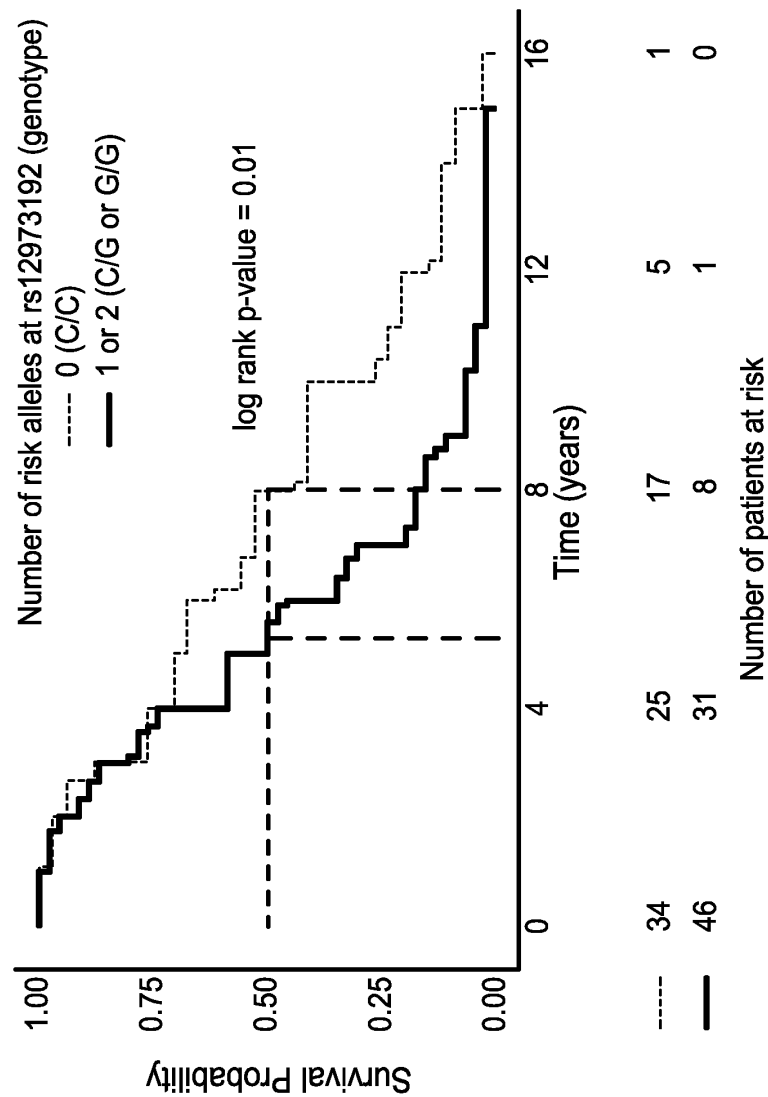


FIG. 16C

Factor	Hazard ratio	95% confidence interval	p-value
Number of risk alleles	2.479	0.4686 - 4.183	0.00068
GRN mutations	0.831	0.5214 - 1.324	0.43623
Age at onset	0.991	0.9651 - 1.018	0.51346
Male	0.665	0.4105 - 1.078	0.09813

FIG. 16D

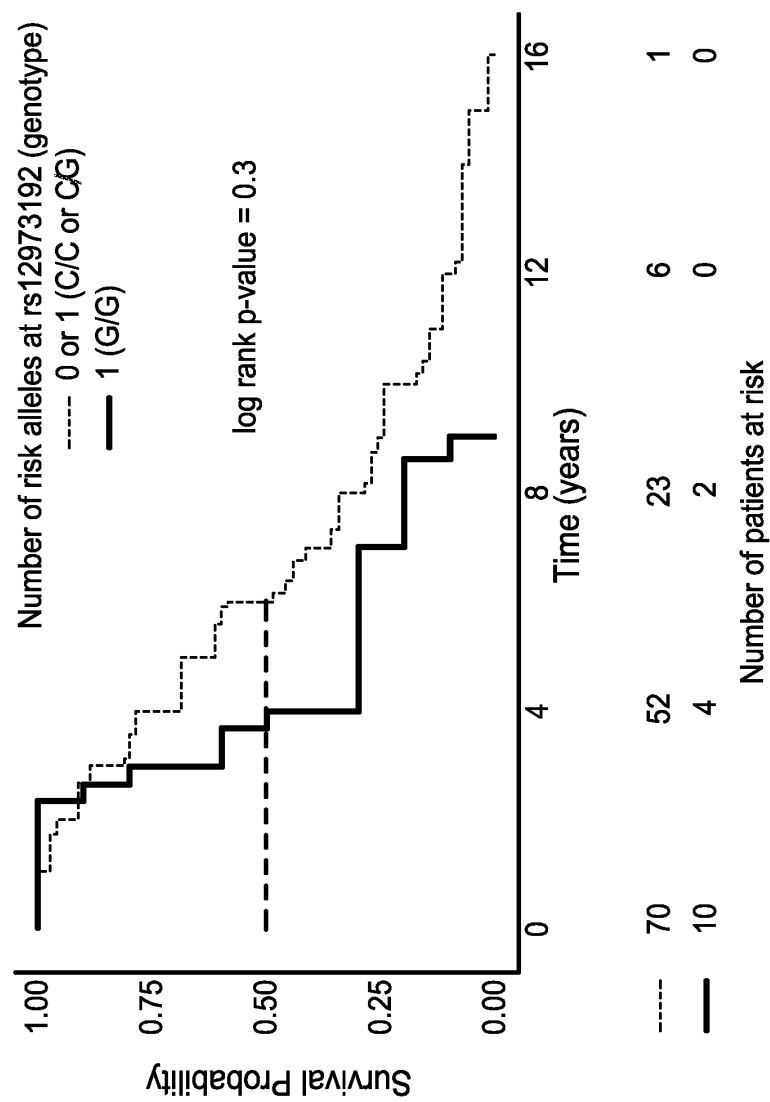


FIG. 16E

Factor	Hazard ratio	95% confidence interval	p-value
Number of risk alleles	2.079	1.0415-4.149	0.03800
GRN mutations	0.923	0.5813-1.466	0.73500
Age at onset	0.991	0.9650-1.018	0.50700
Male	0.835	0.5279-1.322	0.44200

FIG. 16F

FIG. 17



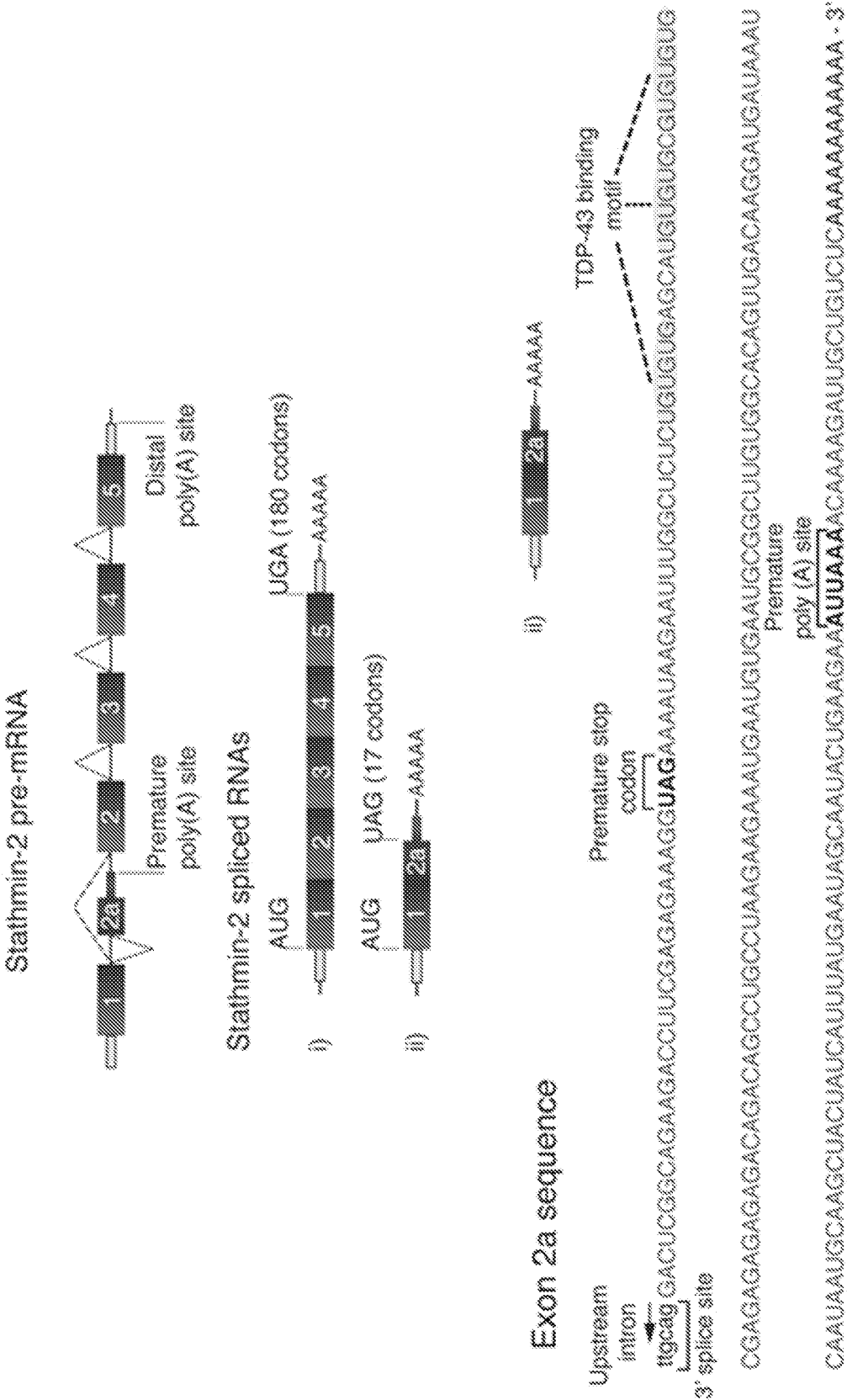


FIG. 18

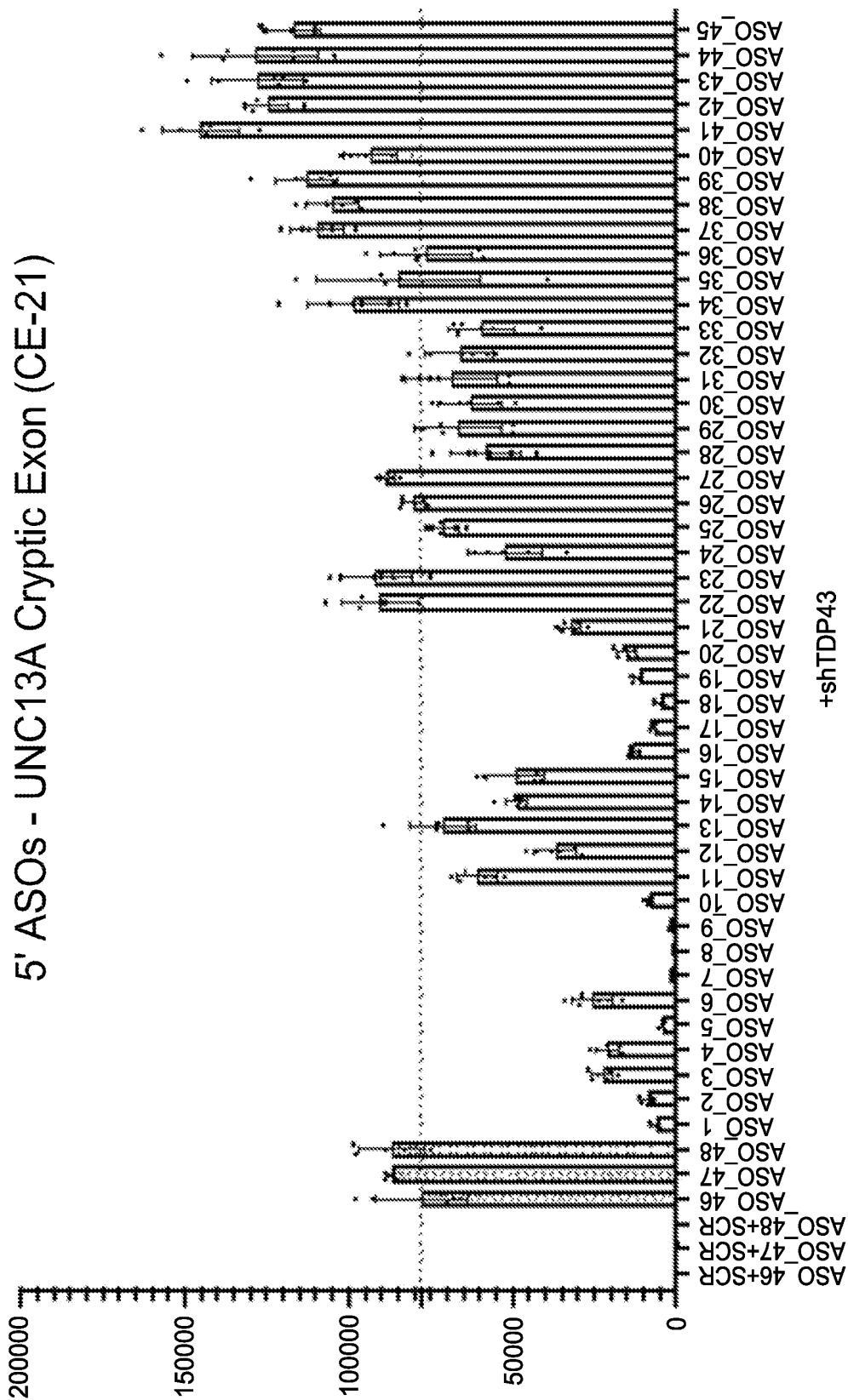


FIG. 19A

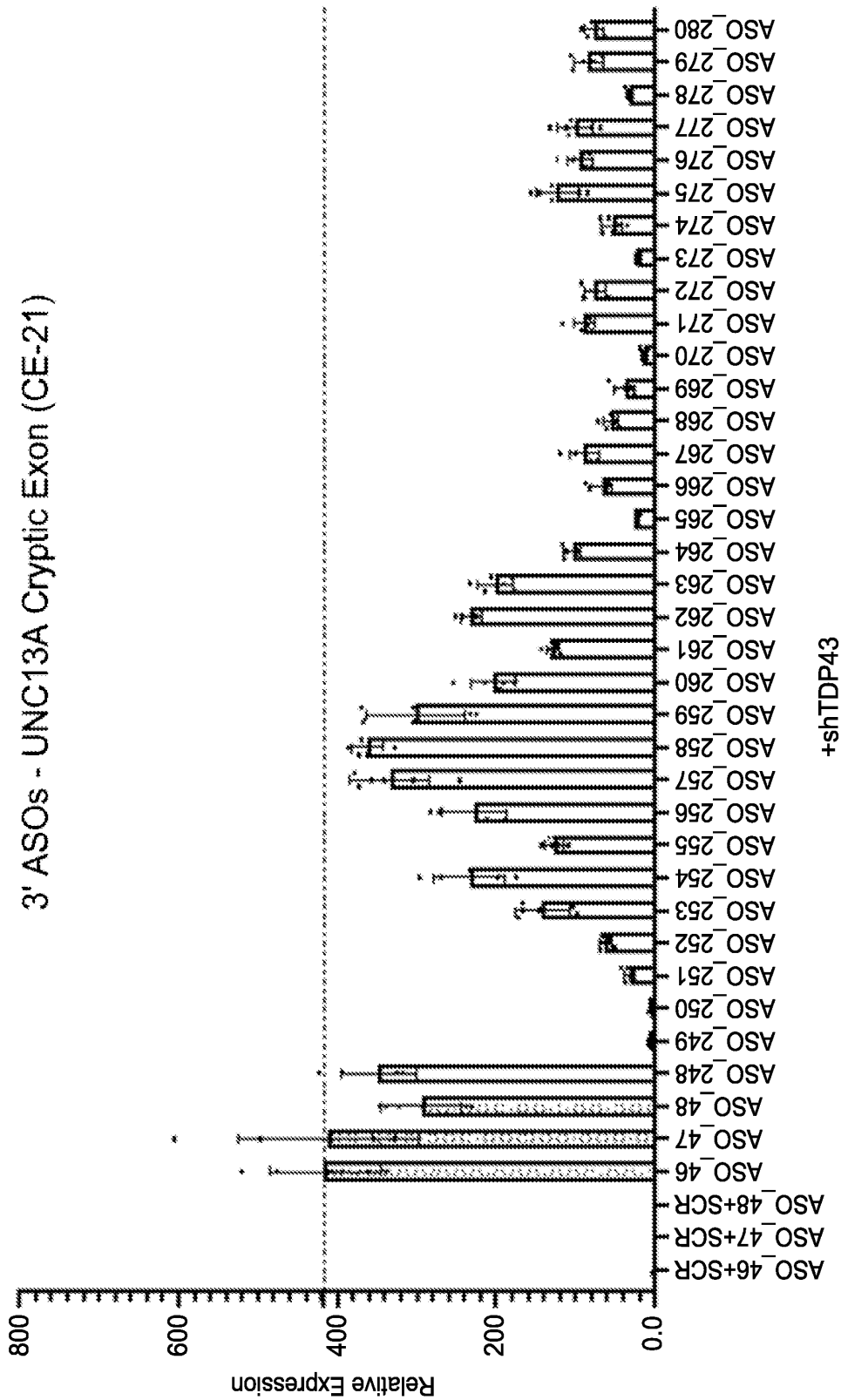


FIG. 19B

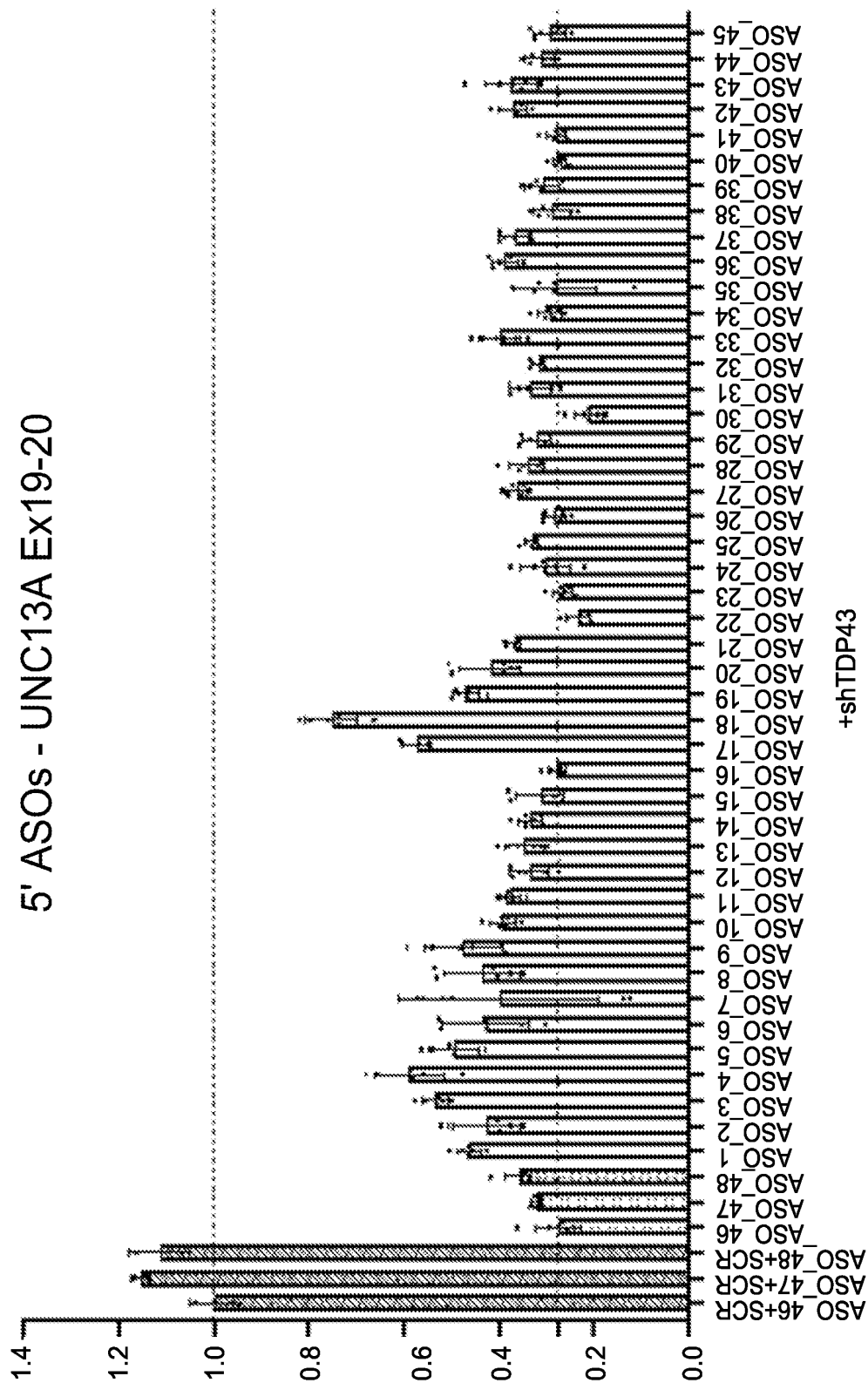


FIG. 19C

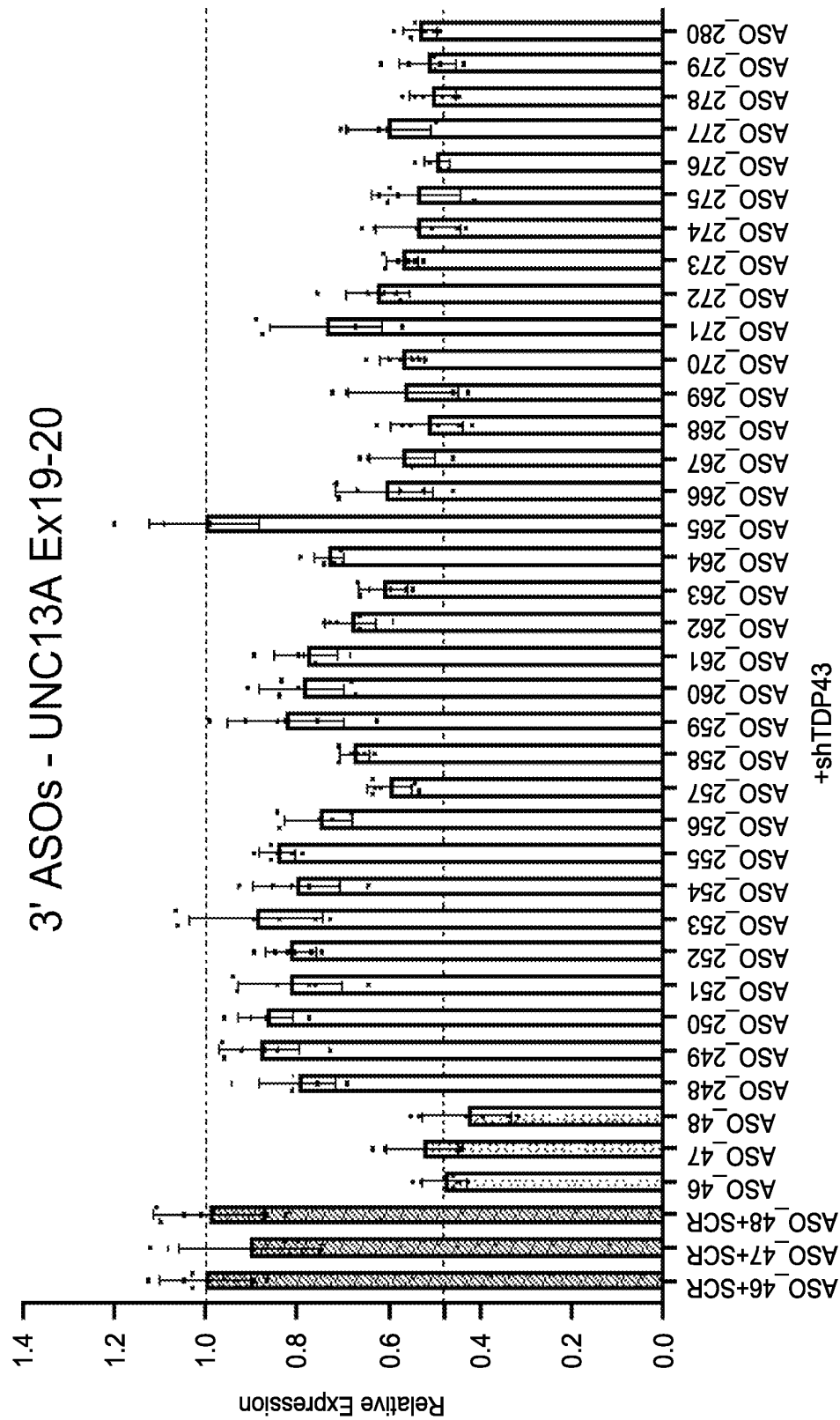


FIG. 19D