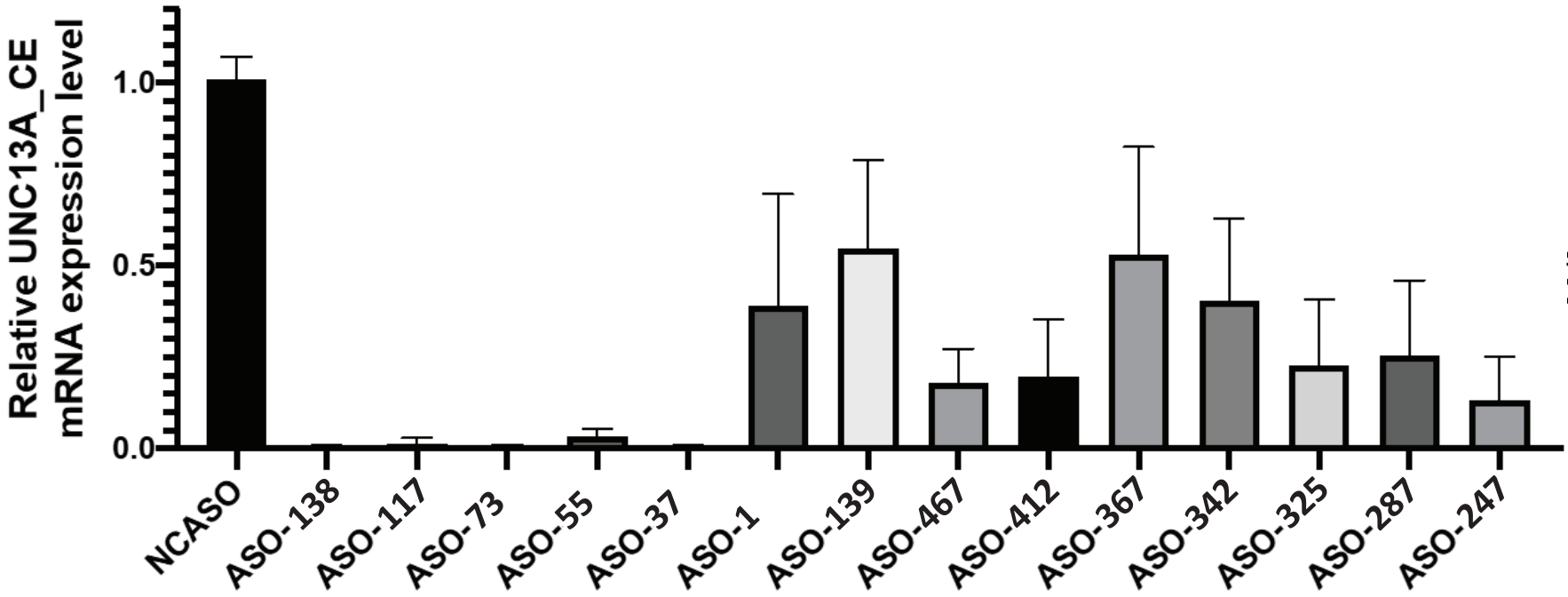

Relative UNC13A_CE
mRNA expression level
1.0
0.5
0.0
NCASO
ASO-138
ASO-117
ASO-73
ASO-55
ASO-37
ASO-1
ASO-139
ASO-467
ASO-412
ASO-367
ASO-342
ASO-325
ASO-287
ASO-247

FIG. 1

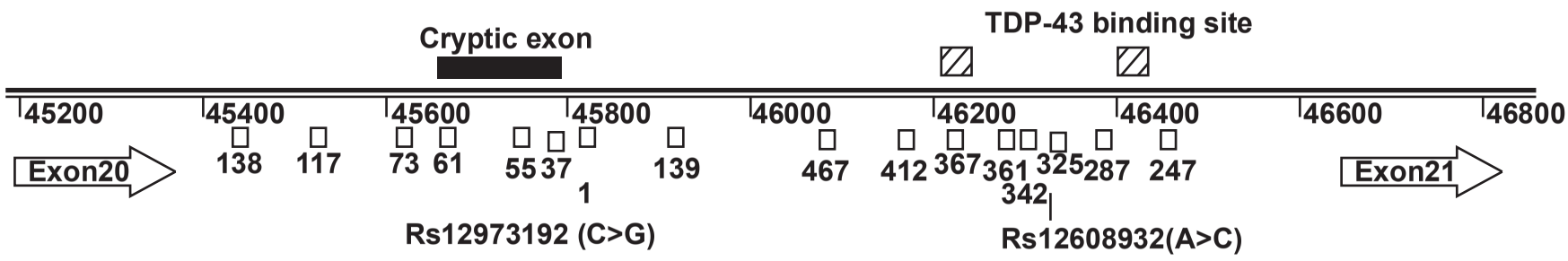

Cryptic exon
TDP-43 binding site
45200
45400
45600
45800
46000
46200
46400
46600
46800
Exon20
Exon21
138
117
73
61
55
37
1
139
467
412
367
361
342
325
287
247
Rs12973192 (C>G)
Rs12608932(A>C)

FIG. 2

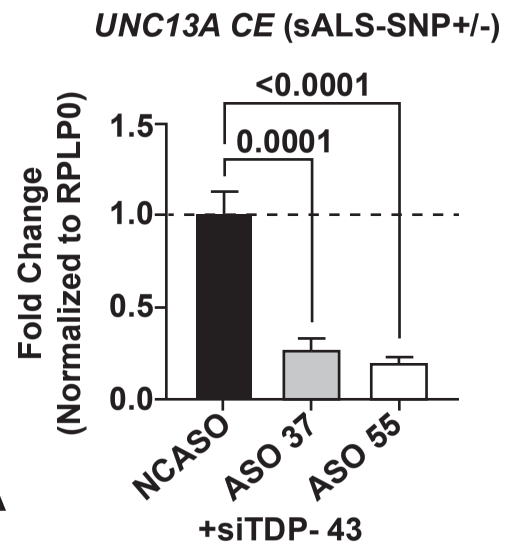


FIG. 3A

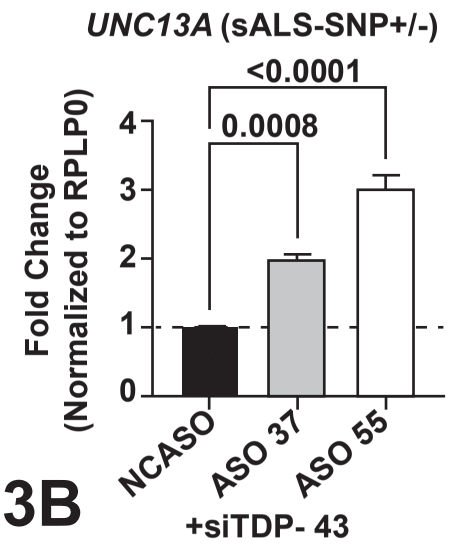


FIG. 3B

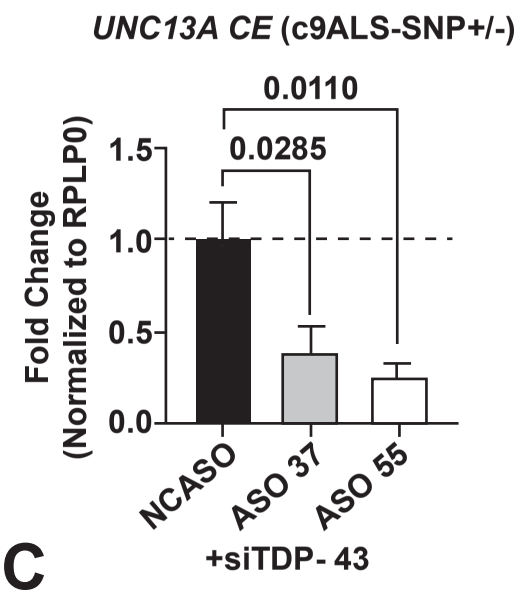


FIG. 3C

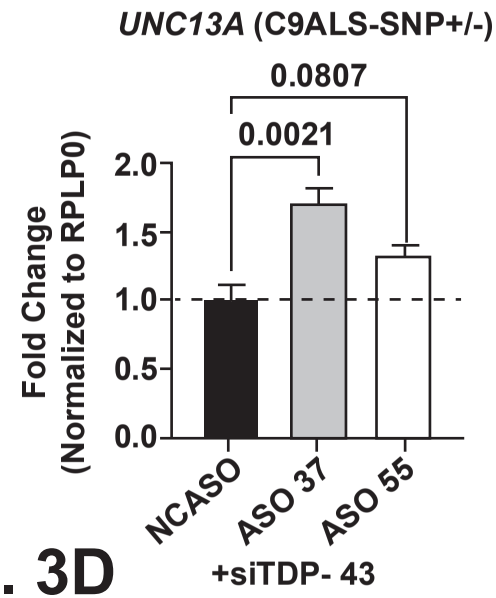


FIG. 3D

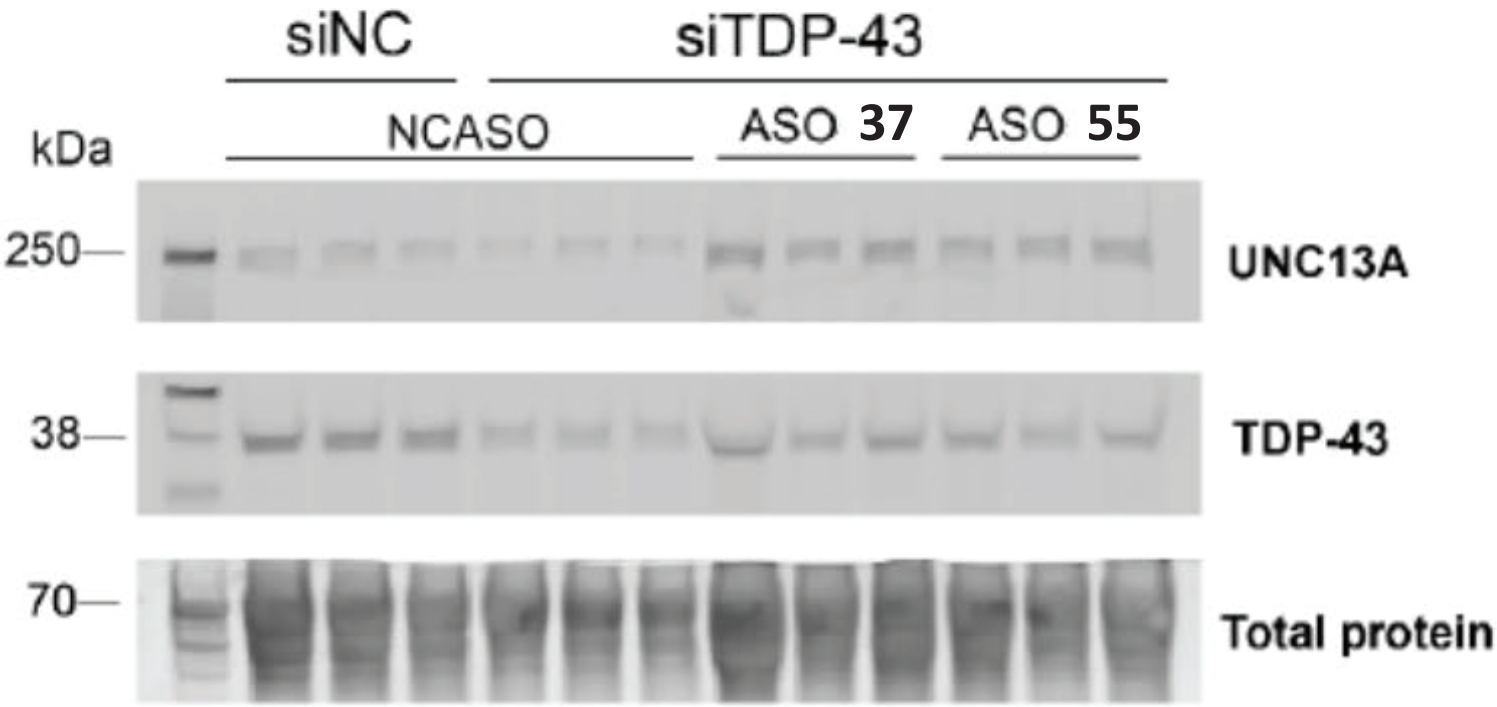

siNC
siTDP-43
kDa
NCASO
ASO 37
ASO 55
250
UNC13A
38
TDP-43
70
Total protein

FIG. 3E

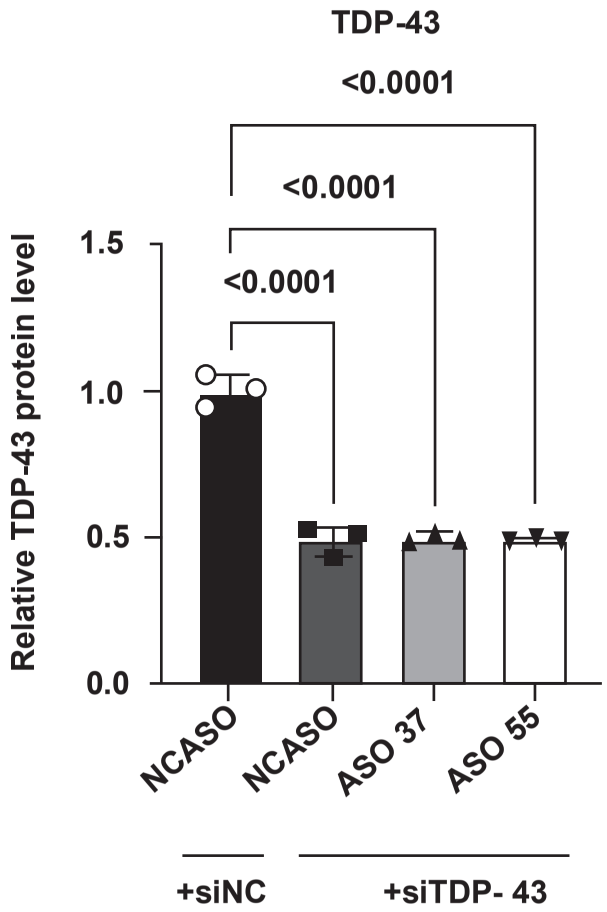

TDP-43
<0.0001
<0.0001
<0.0001
Relative TDP-43 protein level
1.5
1.0
0.5
0.0
NCASO
NCASO
ASO 37
ASO 55
+siNC
+siTDP- 43

FIG. 3F

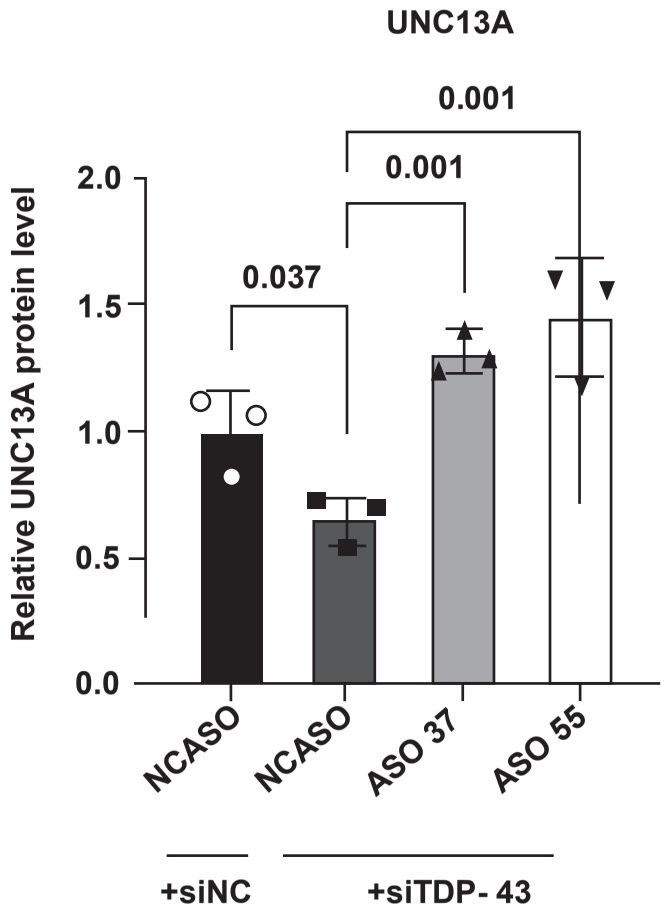

UNC13A
0.001
0.001
0.037
Relative UNC13A protein level
2.0
1.5
1.0
0.5
0.0
NCASO
NCASO
ASO 37
ASO 55
+siNC
+siTDP- 43

FIG. 3G

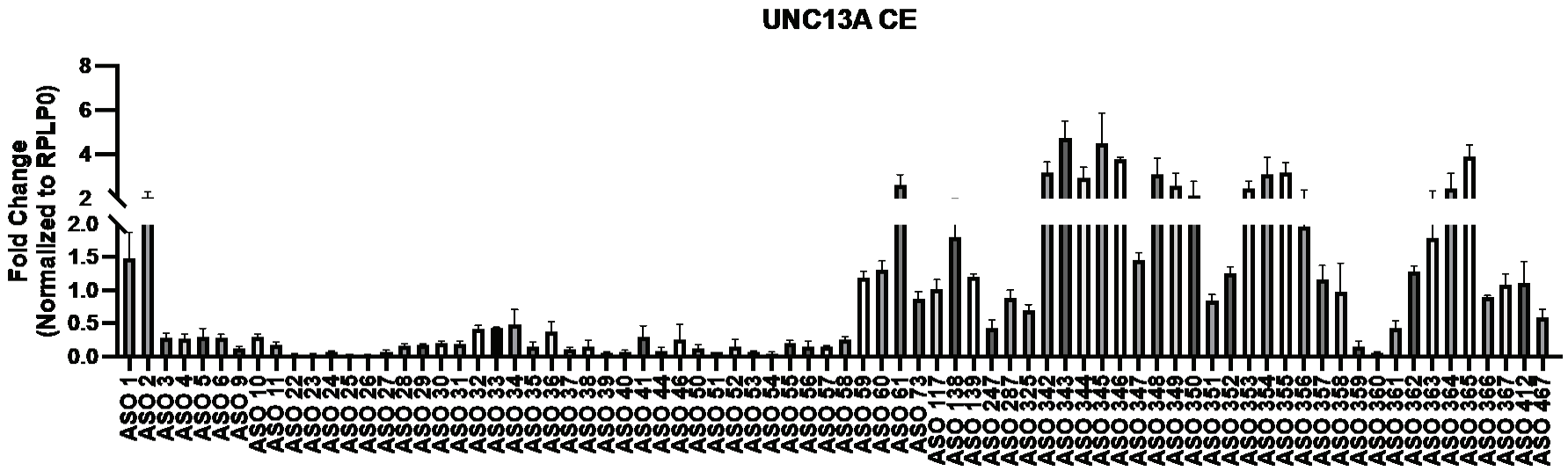

UNC13A CE
Fold Change
(Normalized to RPLP0)
8
6
4
2
2.0
1.5
1.0
0.5
0.0
1
2
3
4
5
6
9
10
11
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
44
46
50
51
52
53
54
55
56
57
58
59
60
61
73
117
138
139
247
287
325
342
343
344
345
346
347
348
349
350
351
352
353
354
355
356
357
358
359
360
361
362
363
364
365
366
367
412
467

FIG. 4A

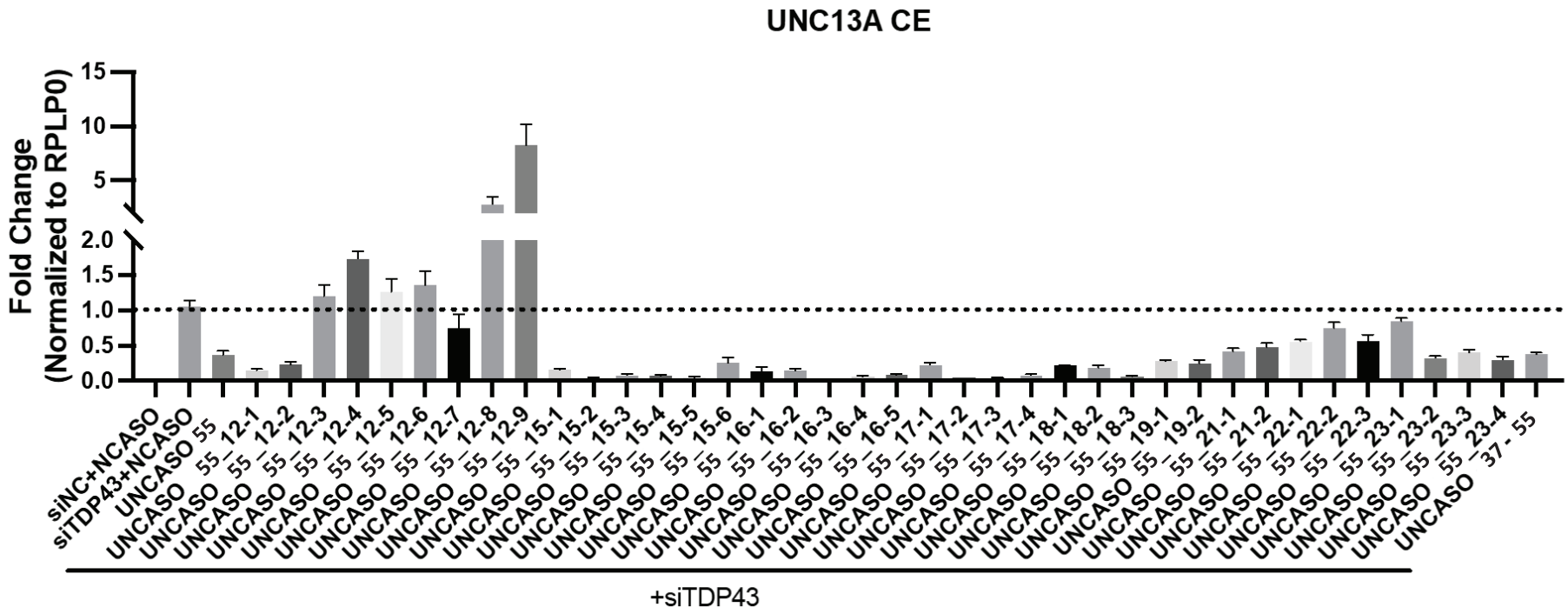

UNC13A CE
Fold Change
(Normalized to RPLP0)
15
10
5
2.0
1.5
1.0
0.5
0.0
siNC+NCASO
siTDP43+NCASO
UNCASO 55
UNCASO 55_12-1
UNCASO 55_12-2
UNCASO 55_12-3
UNCASO 55_12-4
UNCASO 55_12-5
UNCASO 55_12-6
UNCASO 55_12-7
UNCASO 55_12-8
UNCASO 55_12-9
UNCASO 55_15-1
UNCASO 55_15-2
UNCASO 55_15-3
UNCASO 55_15-4
UNCASO 55_15-5
UNCASO 55_15-6
UNCASO 55_16-1
UNCASO 55_16-2
UNCASO 55_16-3
UNCASO 55_16-4
UNCASO 55_16-5
UNCASO 55_17-1
UNCASO 55_17-2
UNCASO 55_17-3
UNCASO 55_17-4
UNCASO 55_18-1
UNCASO 55_18-2
UNCASO 55_18-3
UNCASO 55_19-1
UNCASO 55_19-2
UNCASO 55_21-1
UNCASO 55_21-2
UNCASO 55_22-1
UNCASO 55_22-2
UNCASO 55_22-3
UNCASO 55_23-1
UNCASO 55_23-2
UNCASO 55_23-3
UNCASO 55_23-4
UNCASO 37 - 55
+siTDP43

FIG. 4B

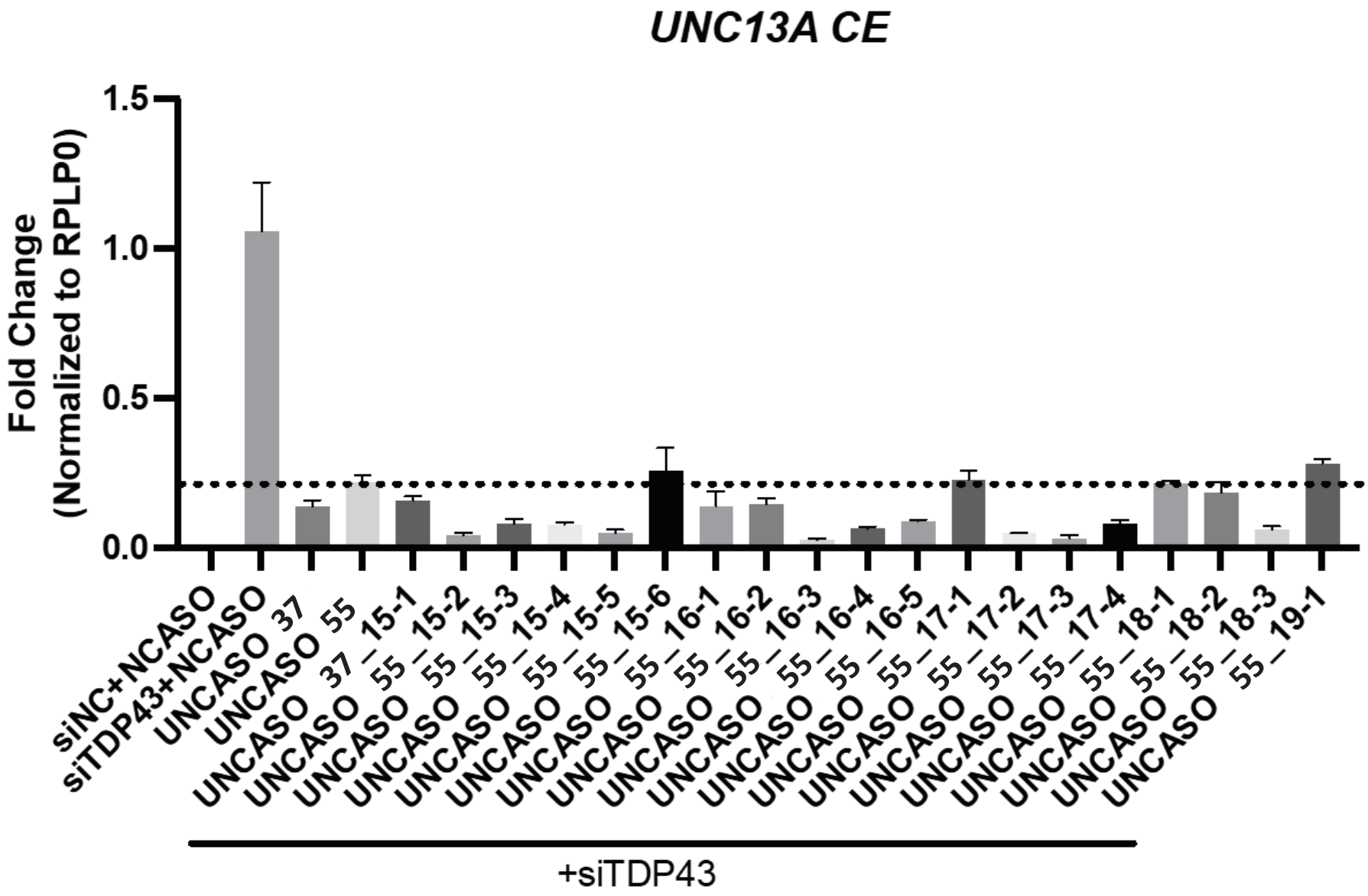

UNC13A CE
Fold Change
(Normalized to RPLP0)
1.5
1.0
0.5
0.0
siNC+NCASO
siTDP43+NCASO
UNCASO 37
UNCASO 55
UNCASO 37 / 15-1
UNCASO 55 / 15-2
UNCASO 55 / 15-3
UNCASO 55 / 15-4
UNCASO 55 / 15-5
UNCASO 55 / 15-6
UNCASO 55 / 16-1
UNCASO 55 / 16-2
UNCASO 55 / 16-3
UNCASO 55 / 16-4
UNCASO 55 / 16-5
UNCASO 55 / 17-1
UNCASO 55 / 17-2
UNCASO 55 / 17-3
UNCASO 55 / 17-4
UNCASO 55 / 18-1
UNCASO 55 / 18-2
UNCASO 55 / 18-3
UNCASO 55 / 19-1
+siTDP43

FIG. 4C

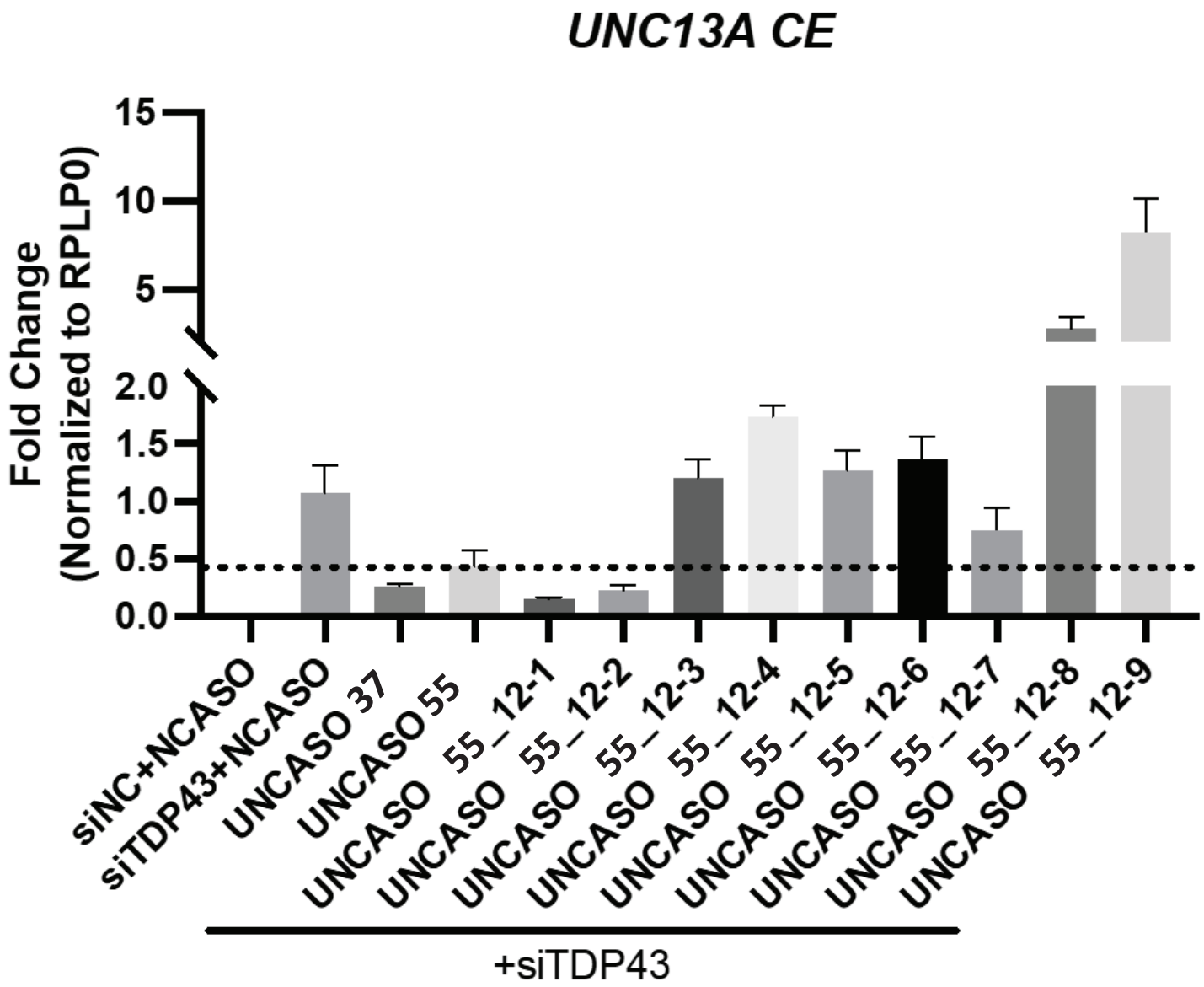
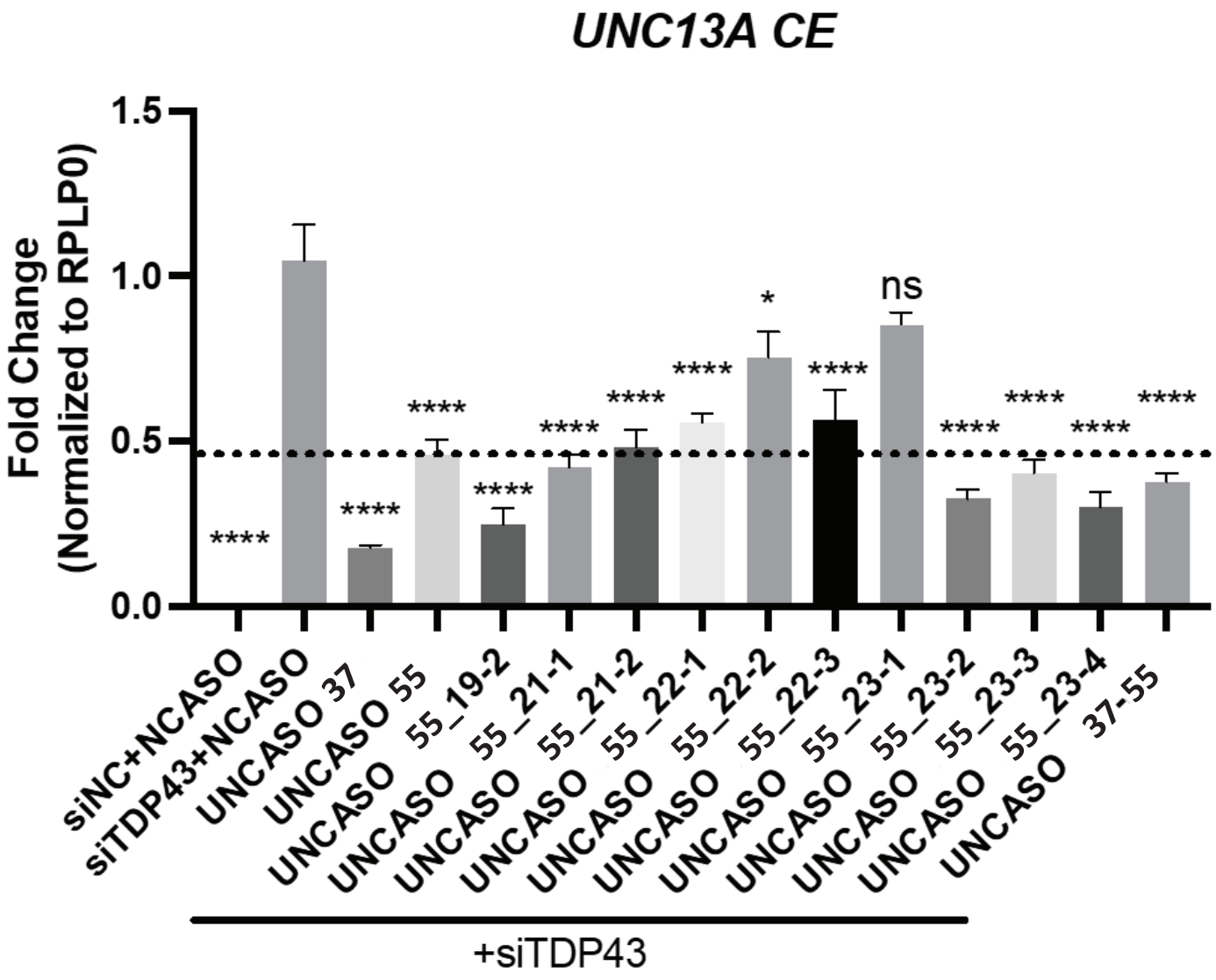
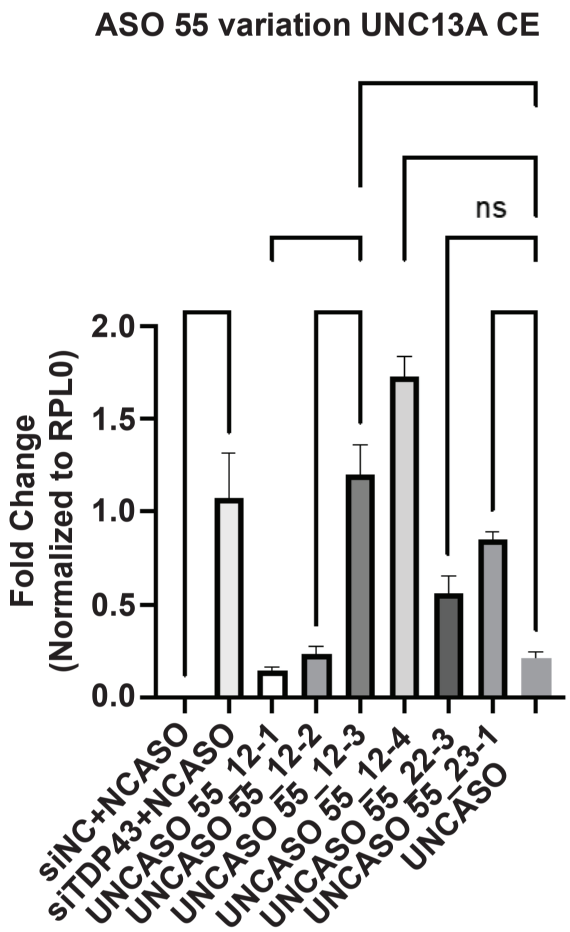

UNC13A CE
Fold Change
(Normalized to RPLP0)
15
10
5
2.0
1.5
1.0
0.5
0.0
siNC+NCASO
siTDP43+NCASO
UNCASO 37
UNCASO 55
UNCASO 55_12-1
UNCASO 55_12-2
UNCASO 55_12-3
UNCASO 55_12-4
UNCASO 55_12-5
UNCASO 55_12-6
UNCASO 55_12-7
UNCASO 55_12-8
UNCASO 55_12-9
+siTDP43

FIG. 4D



****P<0.0001, *<0.05, ns:non specific

FIG. 4E



ID	Sequence
hUNC13A-ASO55_12-1	TCATTCATCTGT
hUNC13A-ASO55_12-2	CTCATTCATCTG
hUNC13A-ASO55_12-3	ACTCATTCATCT
hUNC13A-ASO55_12-4	CACTCATTCATC
hUNC13A-ASO55	CTCATCACTCATTCATCTGT
hUNC13A-ASO55_22-3	TACTCATCACTCATTCATCTGT
hUNC13A-ASO55_23-1	ACTCATCACTCATTCATCTGTTC

FIG. 4F