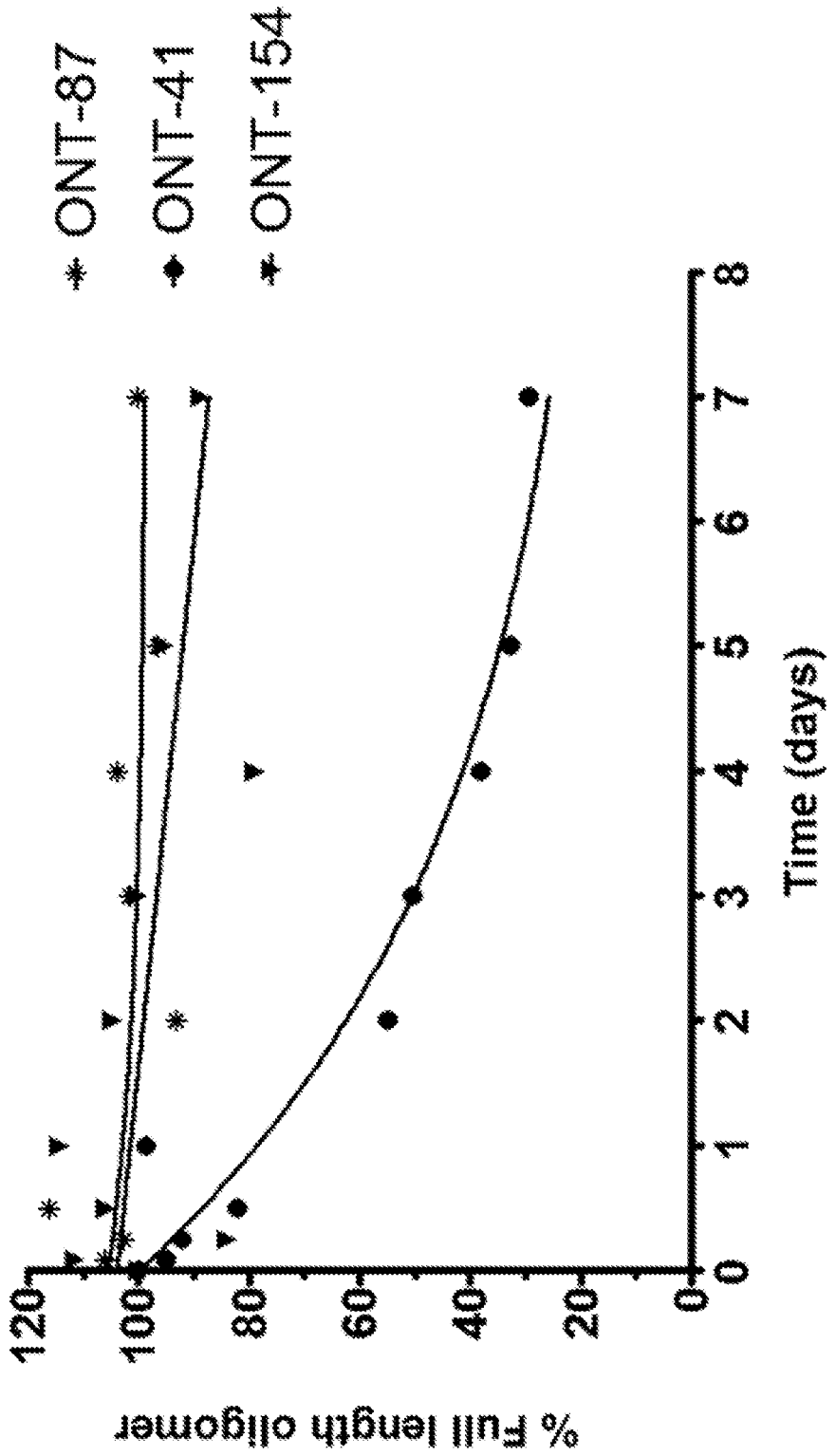

ONT-87
ONT-41
ONT-154
% Full length oligomer
120
100
80
60
40
20
0
0
1
2
3
4
5
6
7
8
Time (days)

FIG. 1

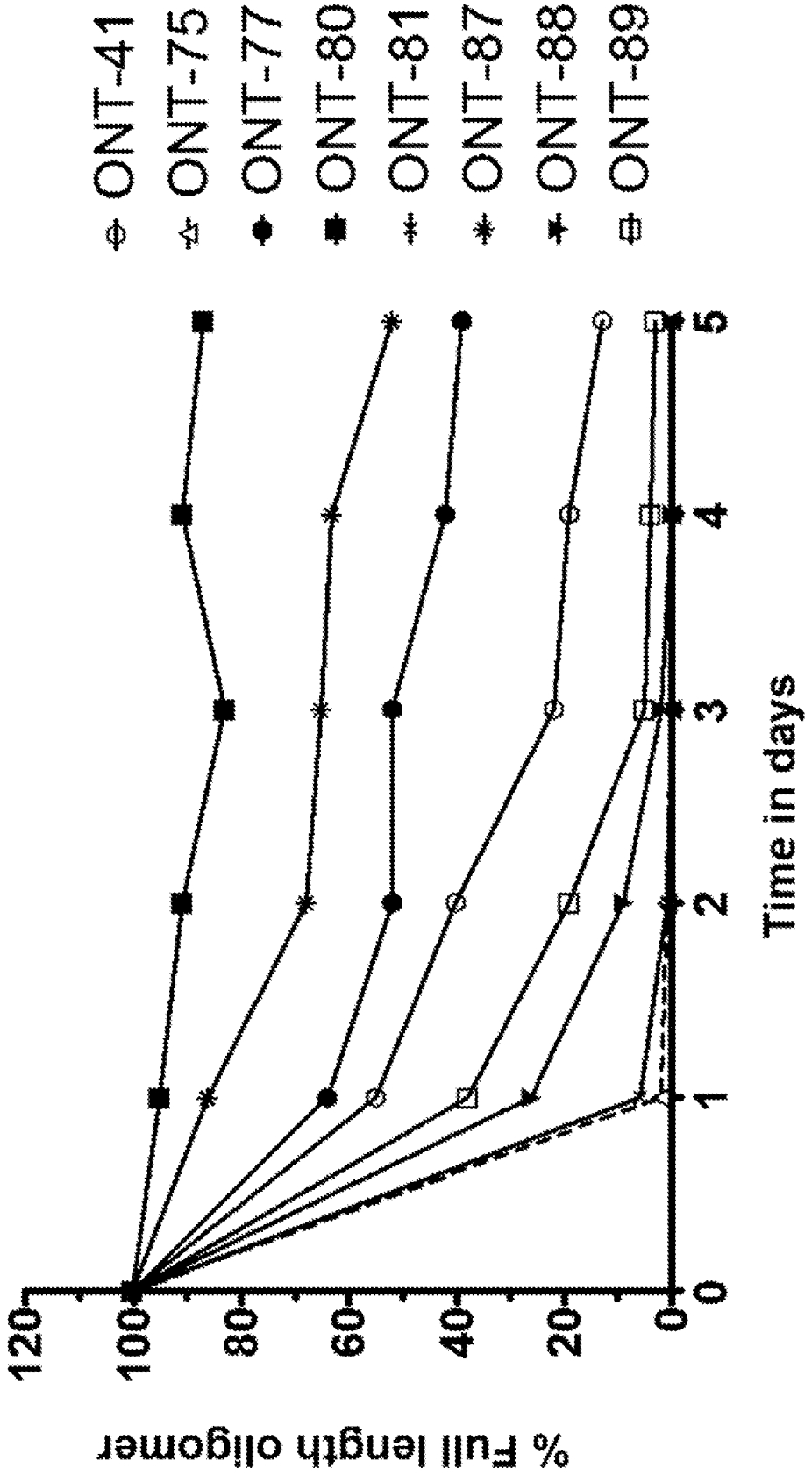

ONT-41
ONT-75
ONT-77
ONT-80
ONT-81
ONT-87
ONT-88
ONT-89
% Full length oligomer
120
100
80
60
40
20
0
0
1
2
3
4
5
Time in days

FIG. 2

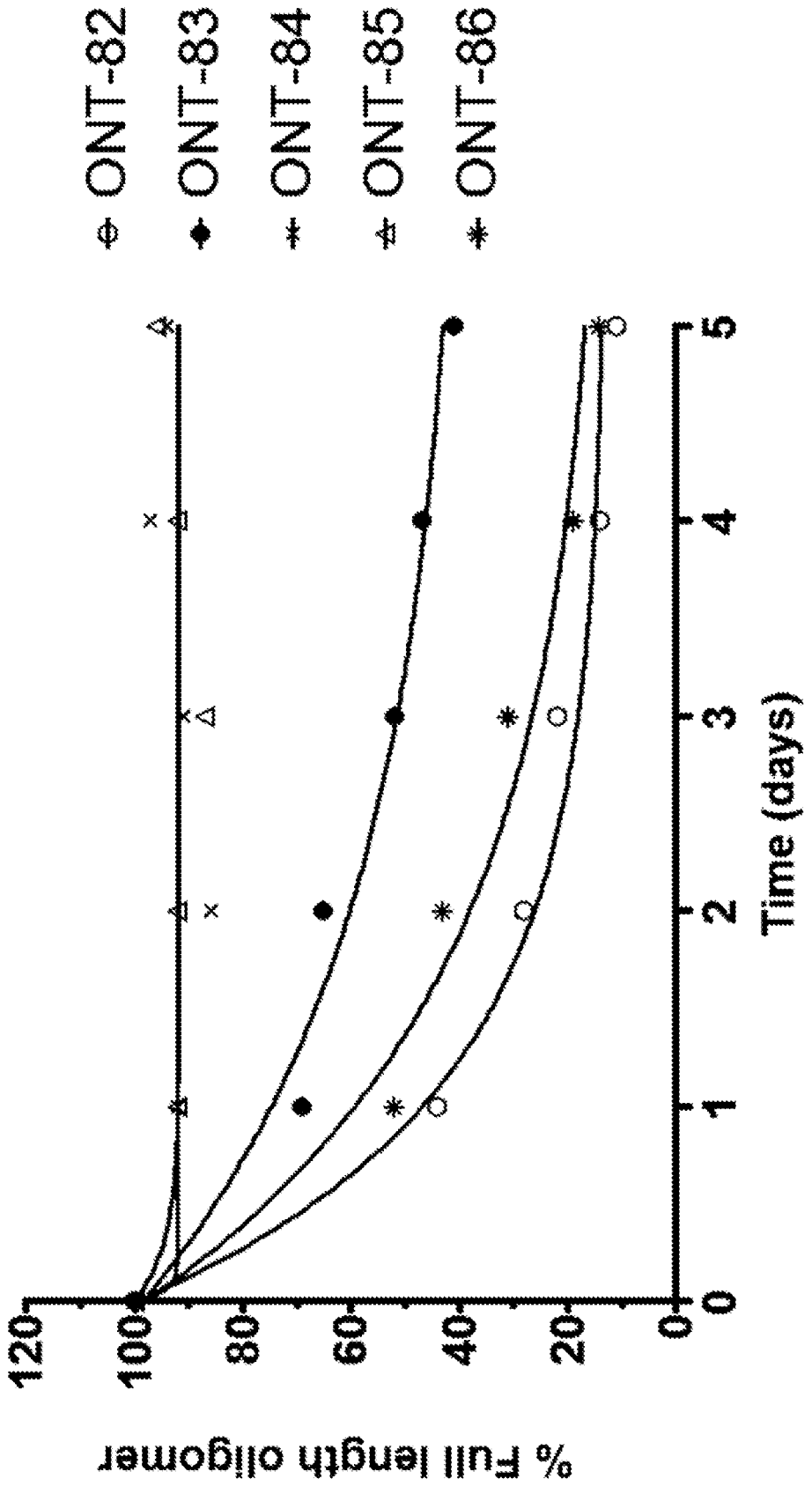

ONT-82
ONT-83
ONT-84
ONT-85
ONT-86
% Full length oligomer
120
100
80
60
40
20
0
0
1
2
3
4
5
Time (days)

FIG. 3

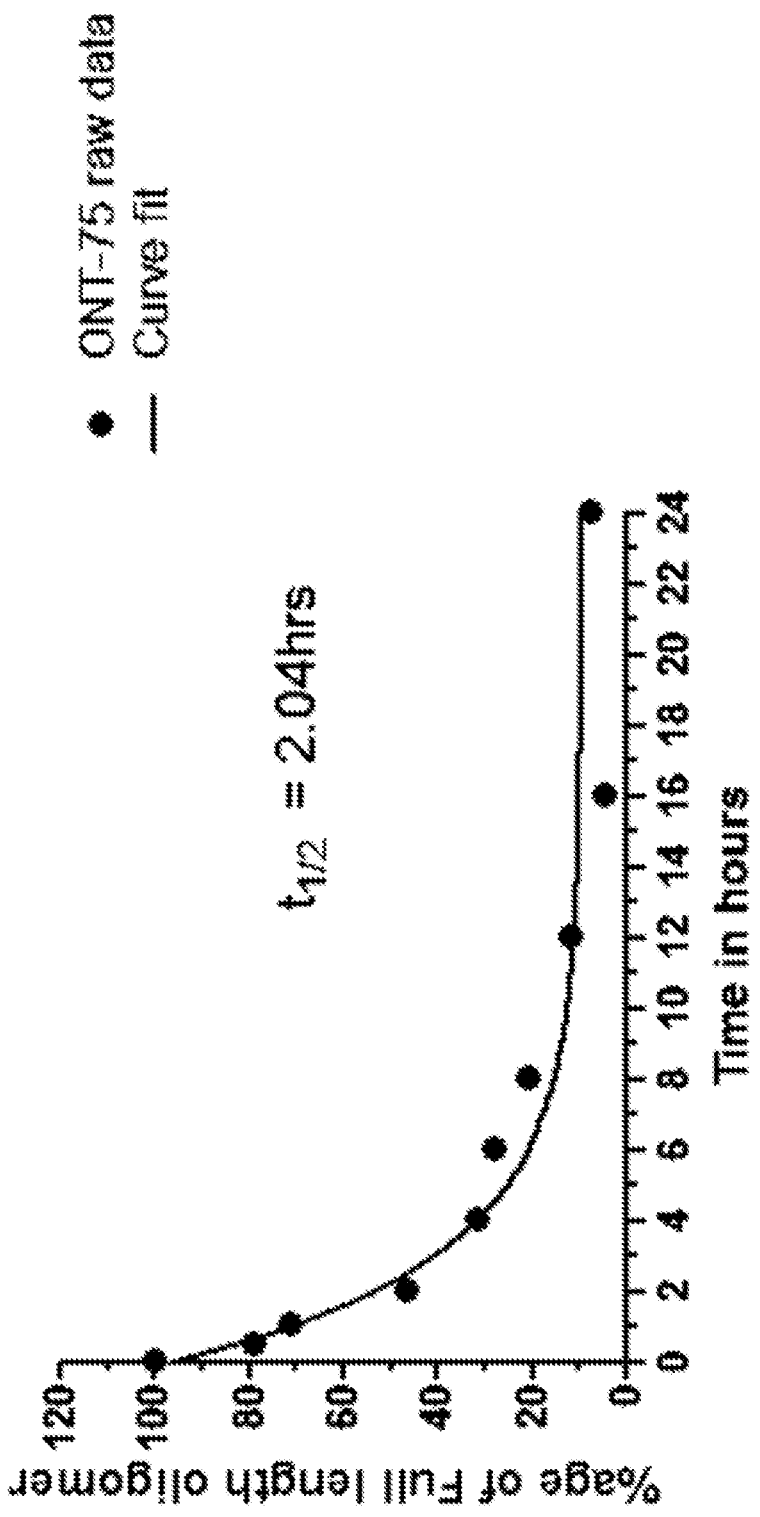

ONT-75 raw data
Curve fit
$t_{1/2}$ = 2.04hrs
%age of Full length oligomer
120
100
80
60
40
20
0
0
2
4
6
8
10
12
14
16
18
20
22
24
Time in hours

FIG. 4

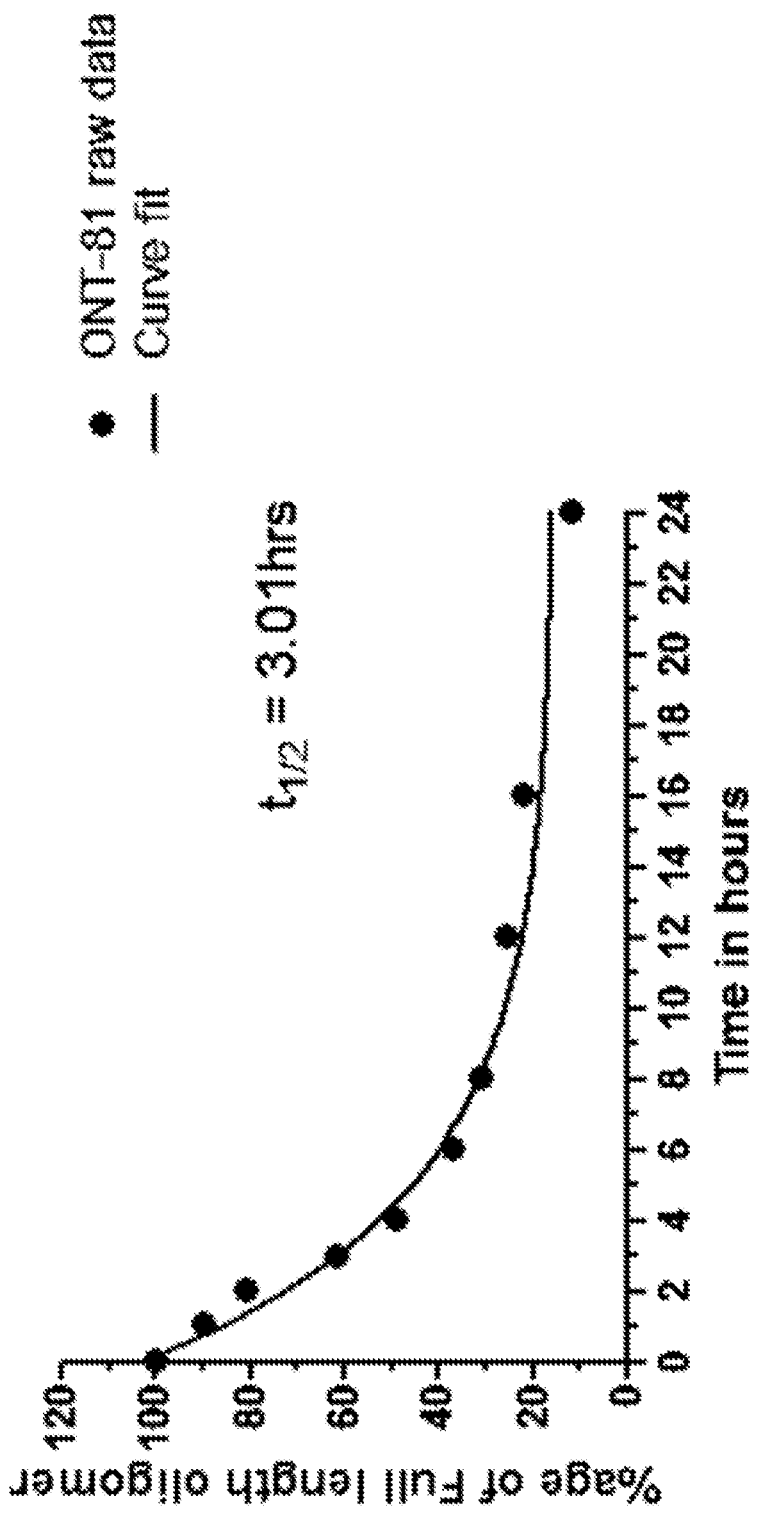

ONT-81 raw data
Curve fit
$t_{1/2}$ = 3.01hrs
%age of Full length oligomer
120
100
80
60
40
20
0
0 2 4 6 8 10 12 14 16 18 20 22 24
Time in hours

FIG. 5

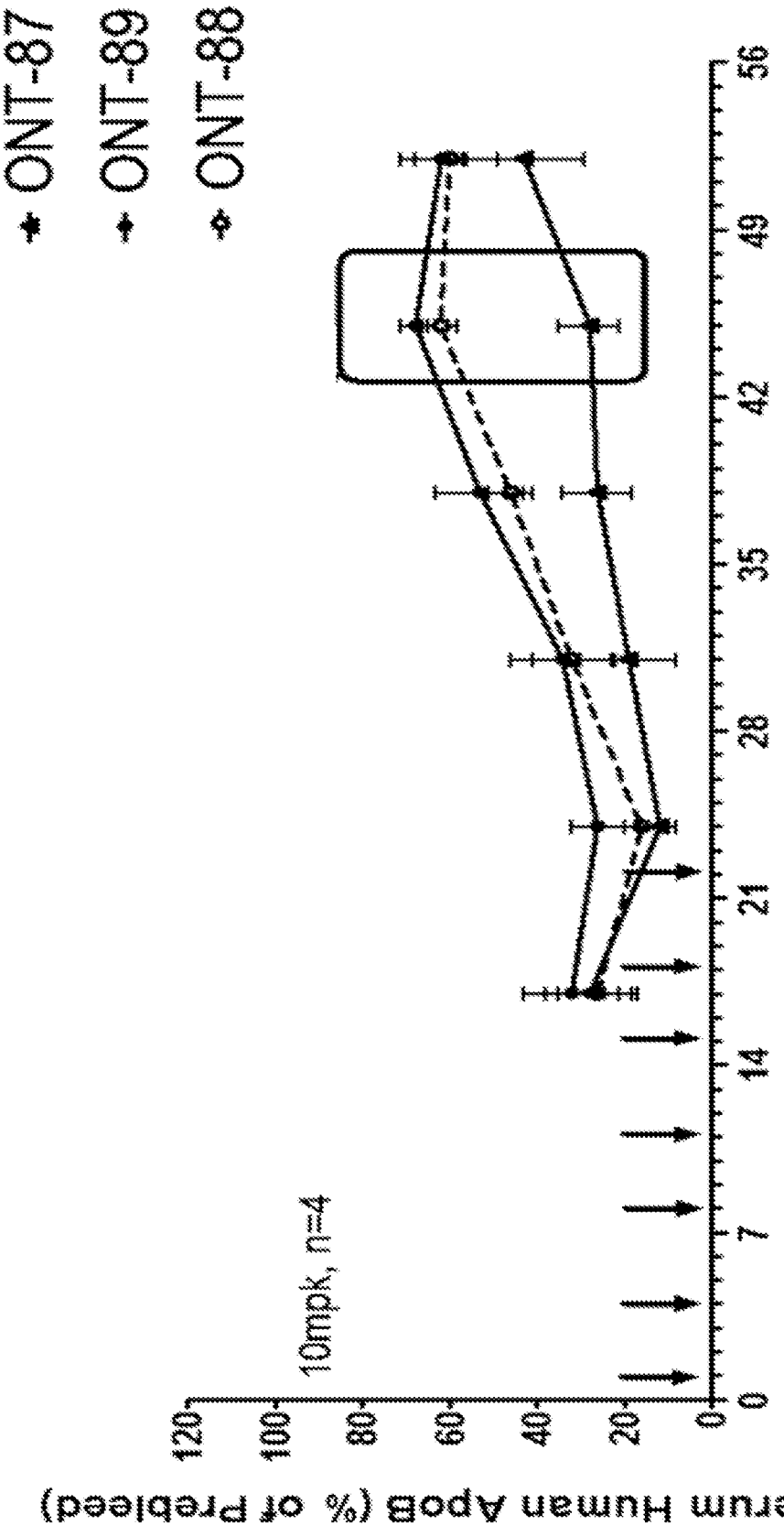

ONT-87
ONT-89
ONT-88
10mpk, n=4
Serum Human ApoB (% of Prebleed)
120
100
80
60
40
20
0
0
7
14
21
28
35
42
49
56
Day

FIG. 6

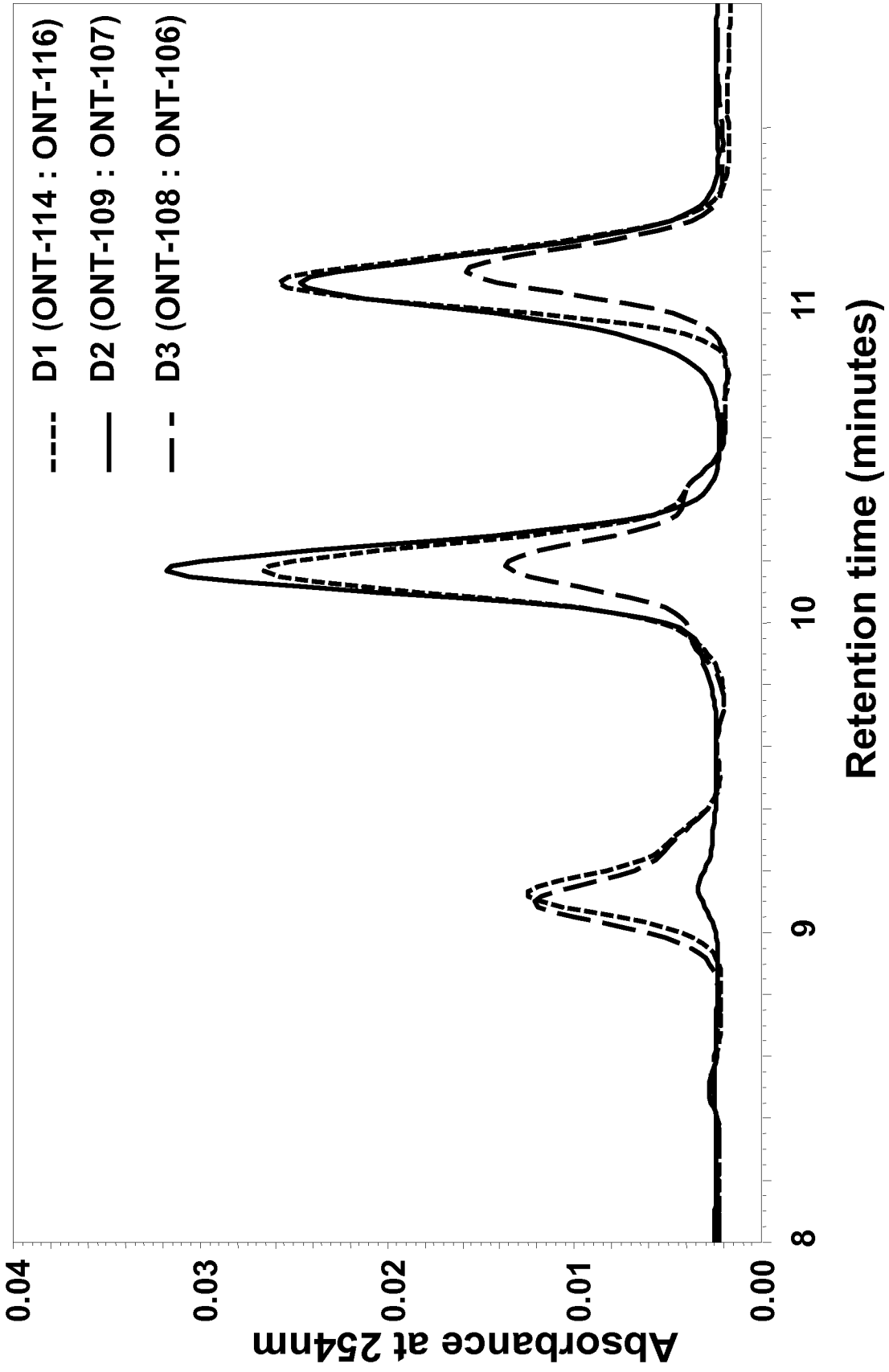

D1 (ONT-114 : ONT-116)
D2 (ONT-109 : ONT-107)
D3 (ONT-108 : ONT-106)
Absorbance at 254nm
0.04
0.03
0.02
0.01
0.00
8
9
10
11
Retention time (minutes)

FIG. 7

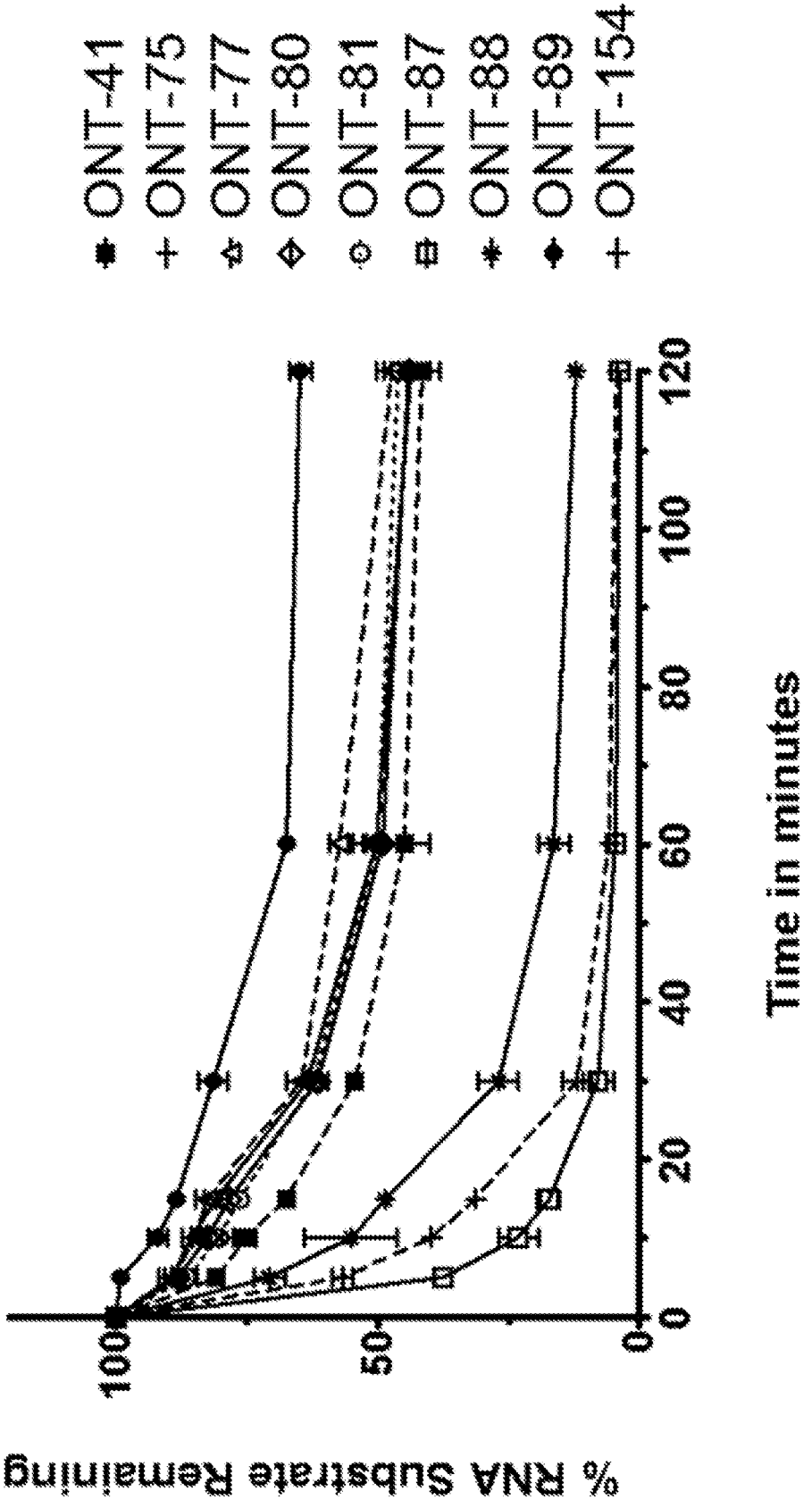
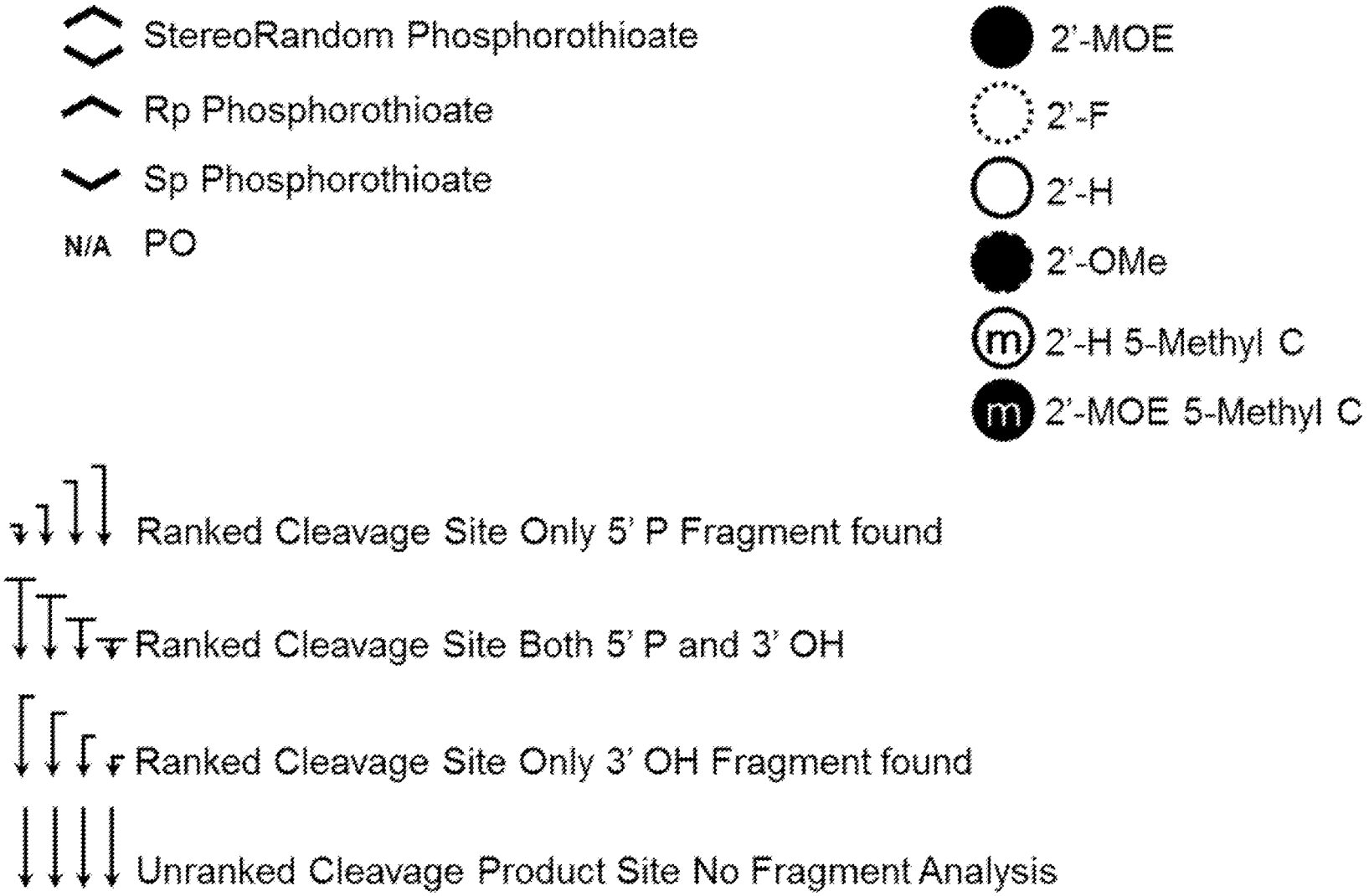
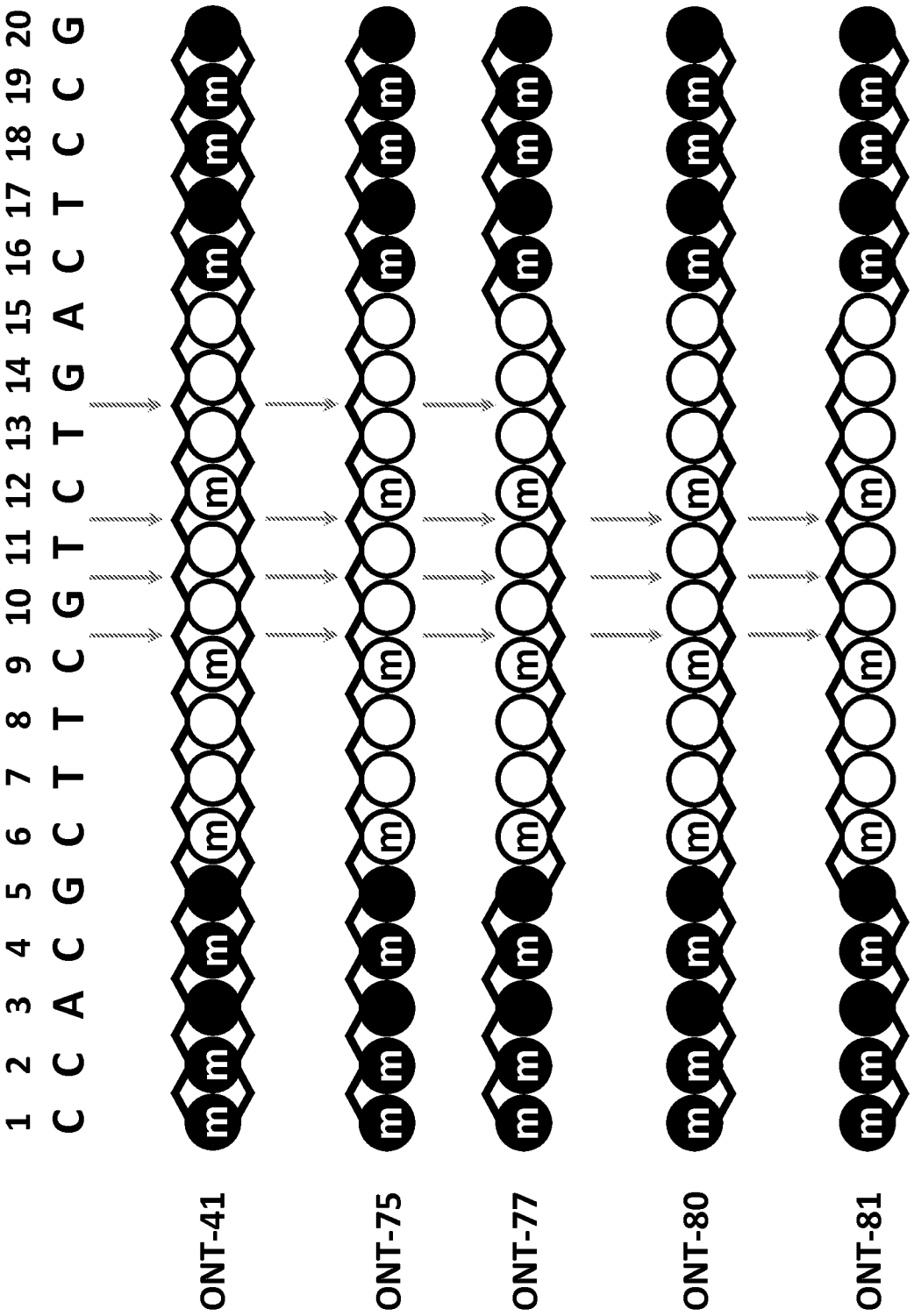

ONT-41
ONT-75
ONT-77
ONT-80
ONT-81
ONT-87
ONT-88
ONT-89
ONT-154
% RNA Substrate Remaining
100
50
0
0
20
40
60
80
100
120
Time in minutes

FIG. 8


StereoRandom Phosphorothioate
Rp Phosphorothioate
Sp Phosphorothioate
N/A PO
2'-MOE
2'-F
2'-H
2'-OMe
m 2'-H 5-Methyl C
m 2'-MOE 5-Methyl C
Ranked Cleavage Site Only 5' P Fragment found
Ranked Cleavage Site Both 5' P and 3' OH
Ranked Cleavage Site Only 3' OH Fragment found
Unranked Cleavage Product Site No Fragment Analysis

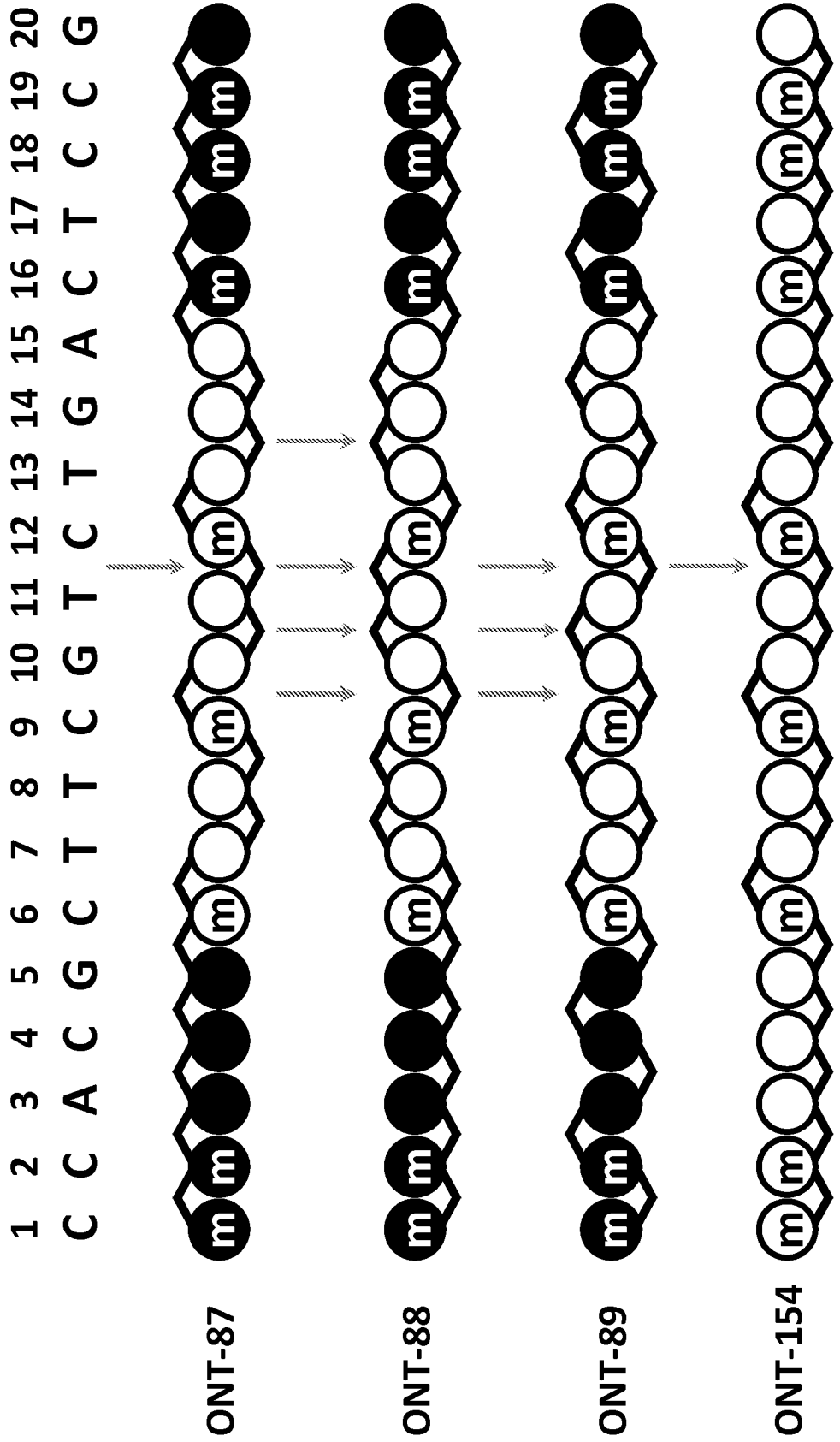
(PANEL A)

FIG. 9



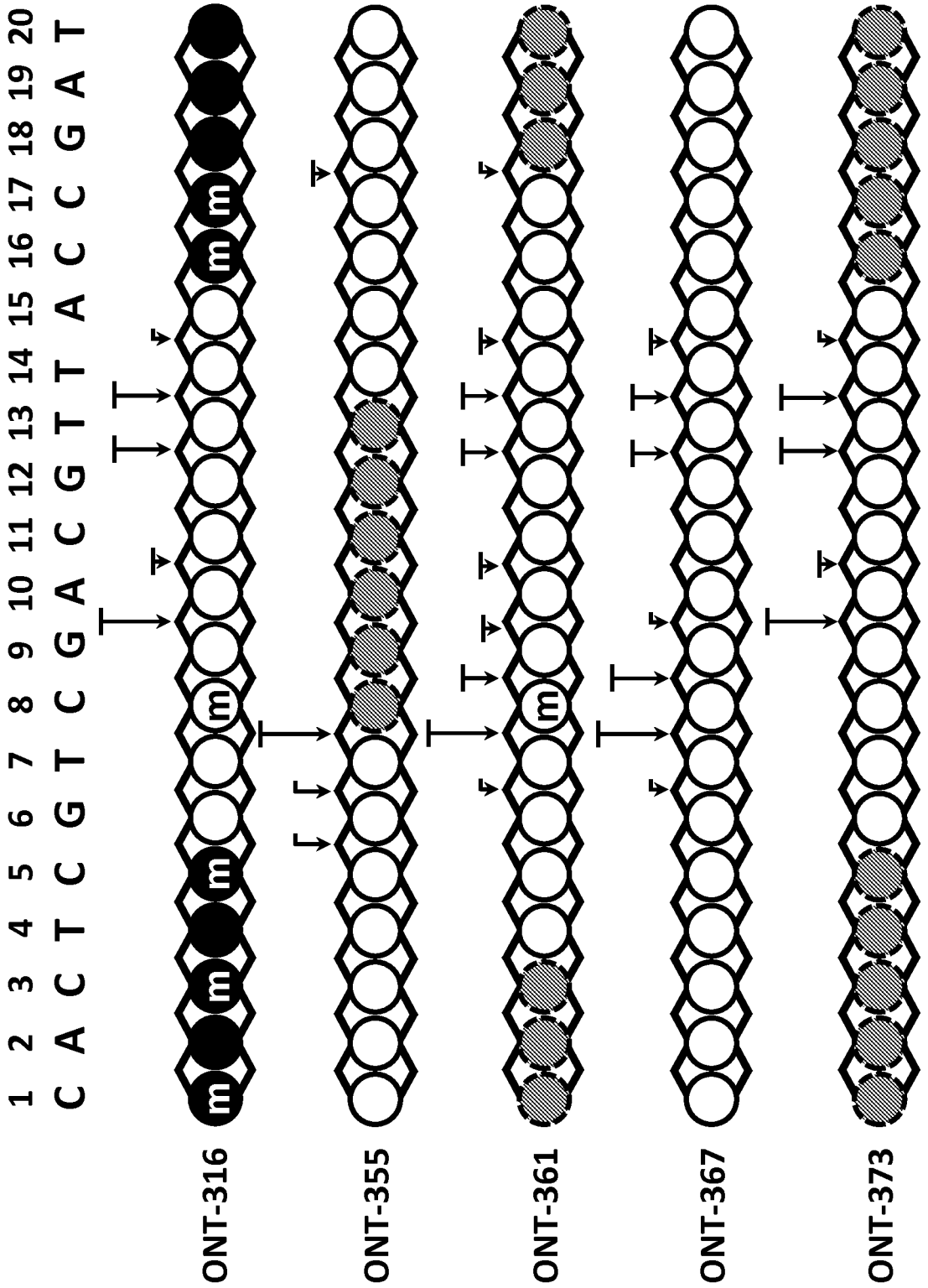
(PANEL B)

FIG. 9 (CONTINUED)



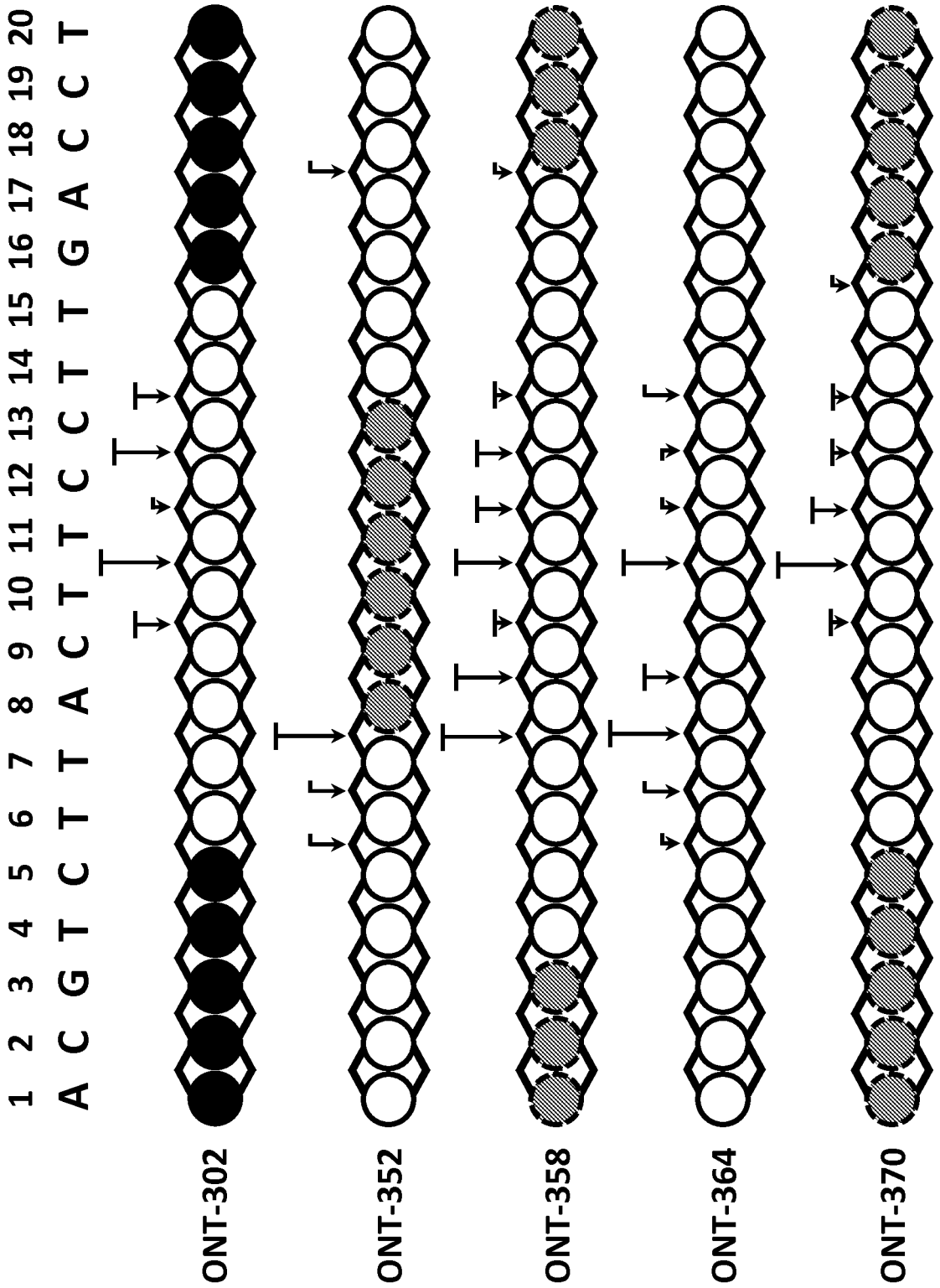
(PANEL C)

FIG. 9 (CONTINUED)



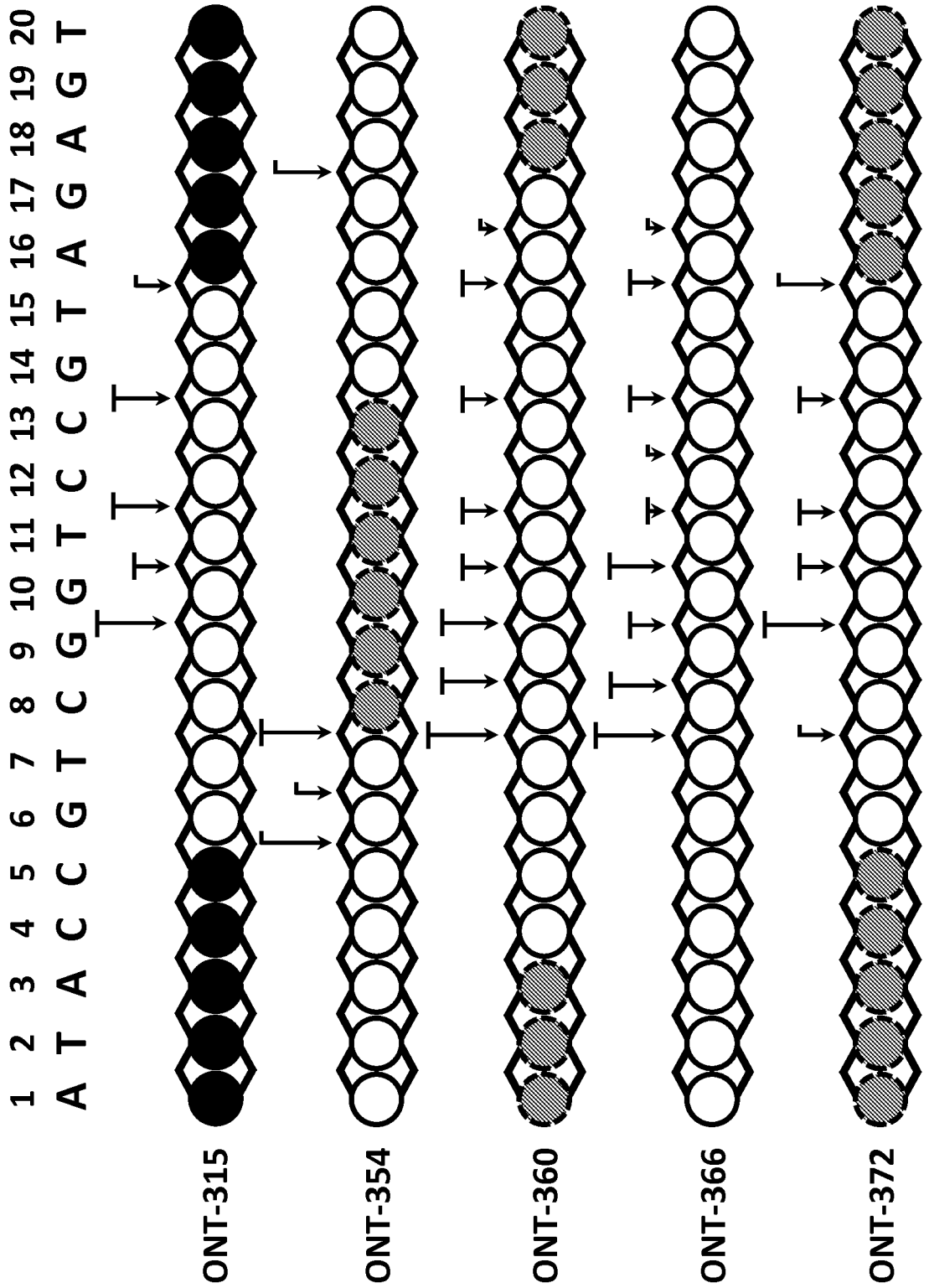
(PANEL A)

FIG. 10



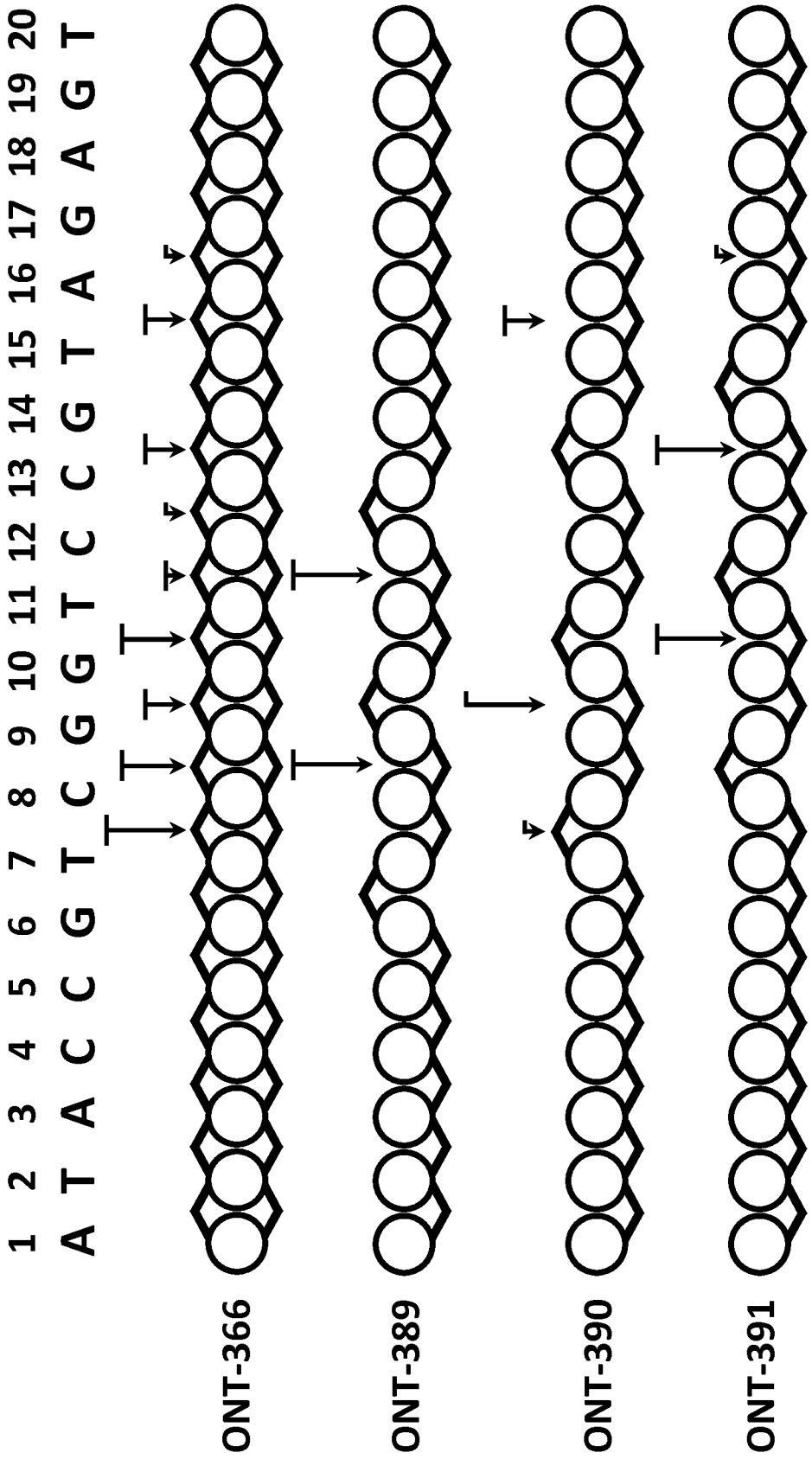
(PANEL B)

FIG. 10 (CONTINUED)



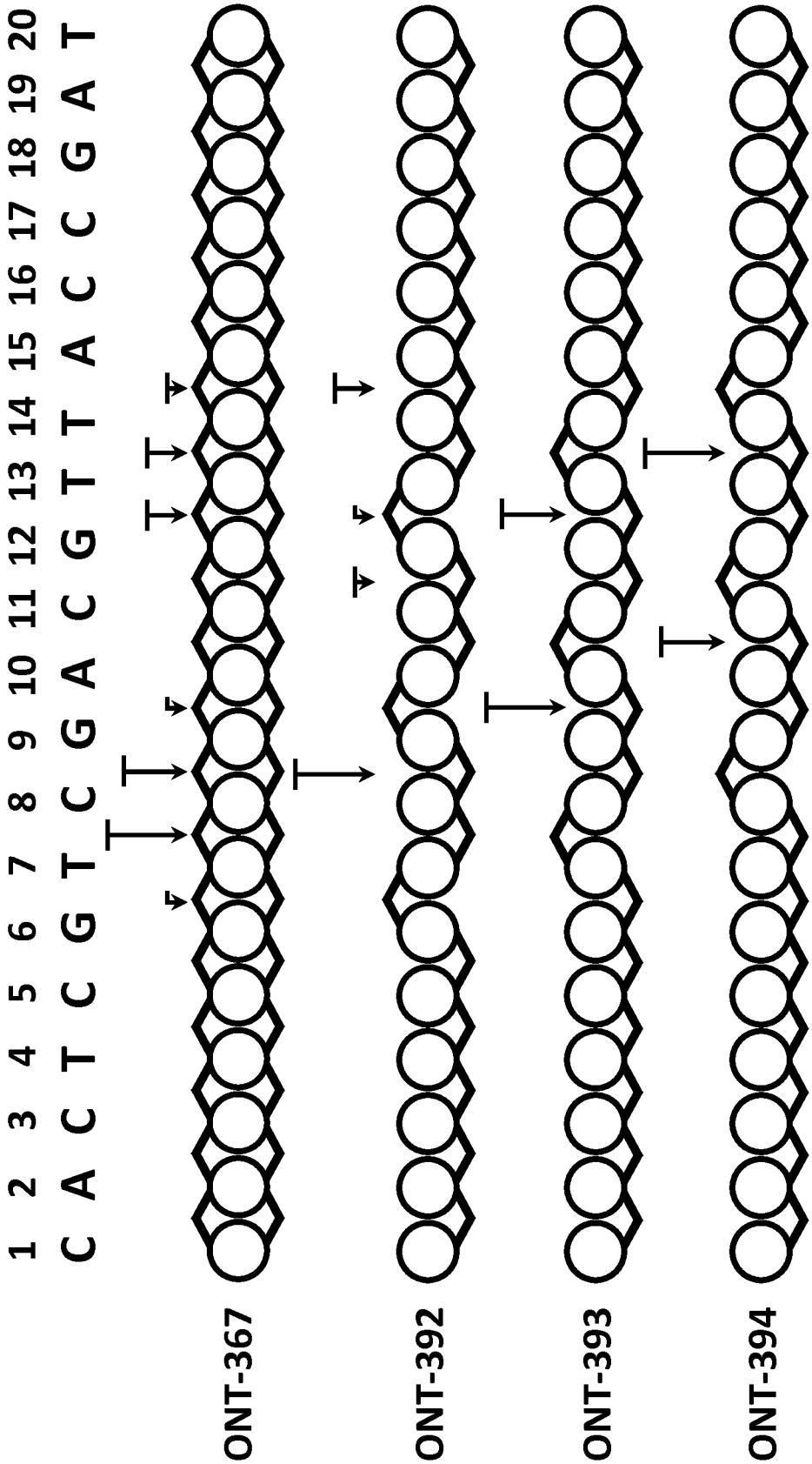
(PANEL C)

FIG. 10 (CONTINUED)



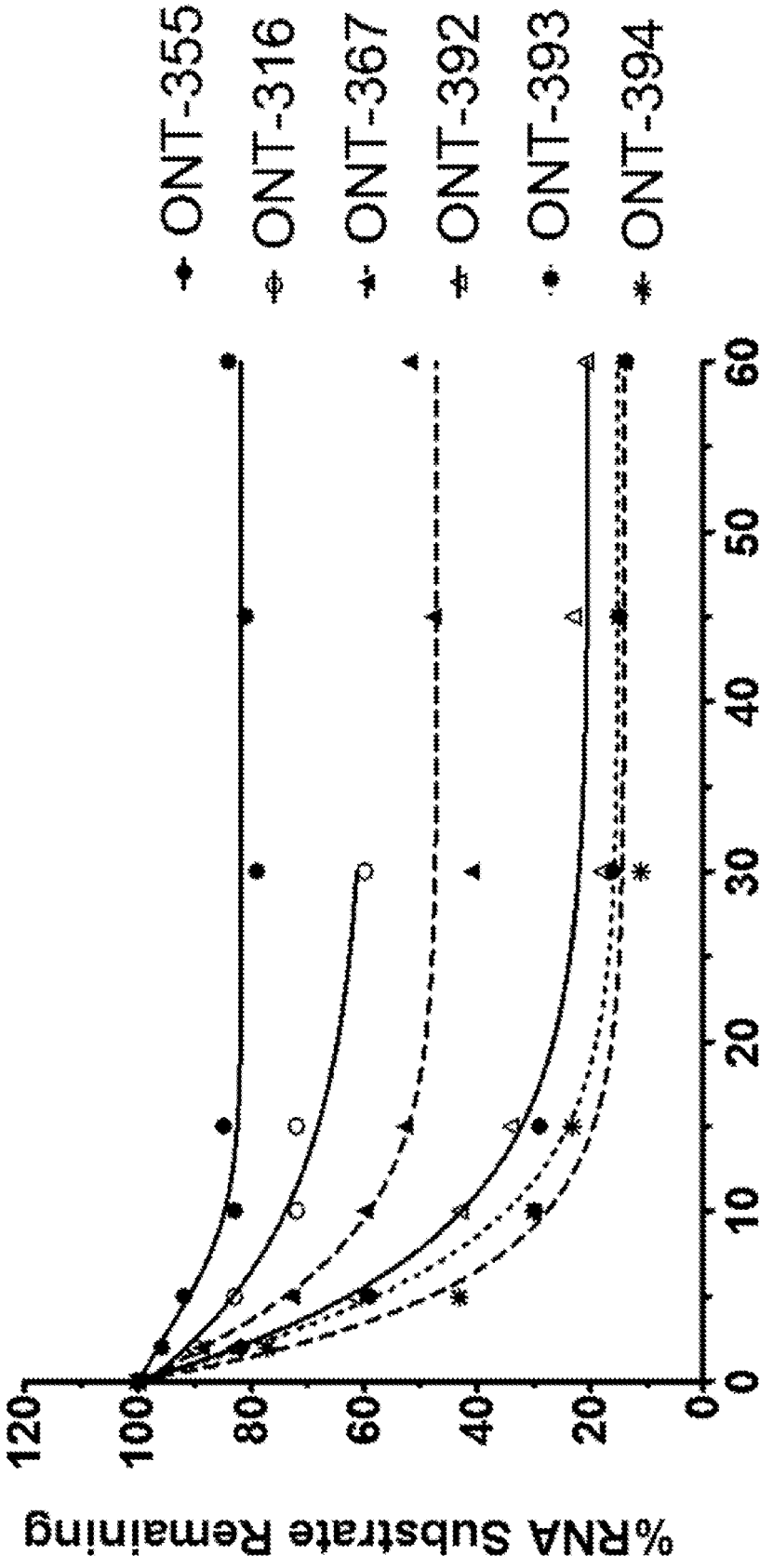
(PANEL A)

FIG. 11



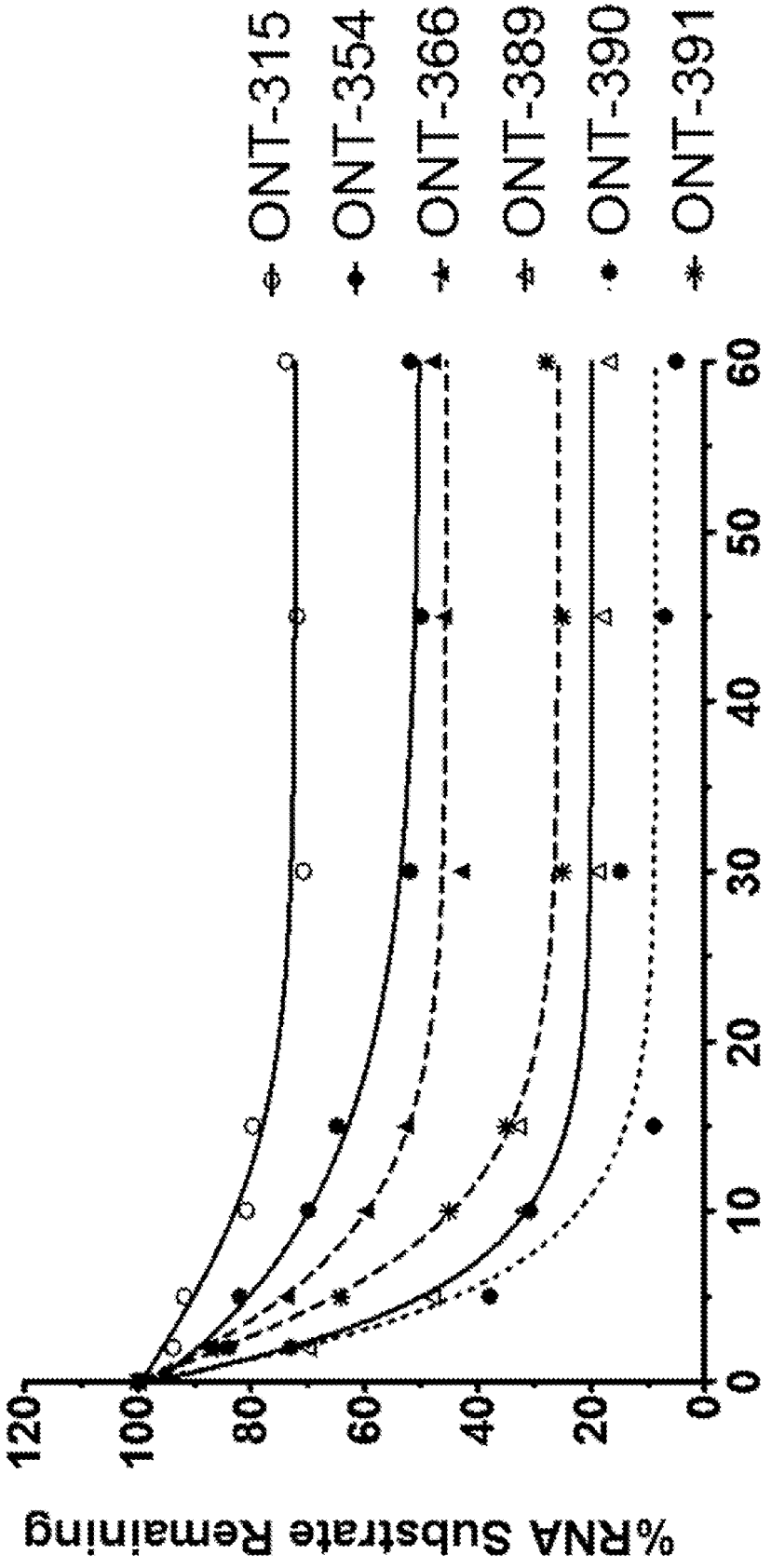
(PANEL B)

FIG. 11 (CONTINUED)



(PANEL A)

FIG. 12



(PANEL B)

FIG. 12 (CONTINUED)

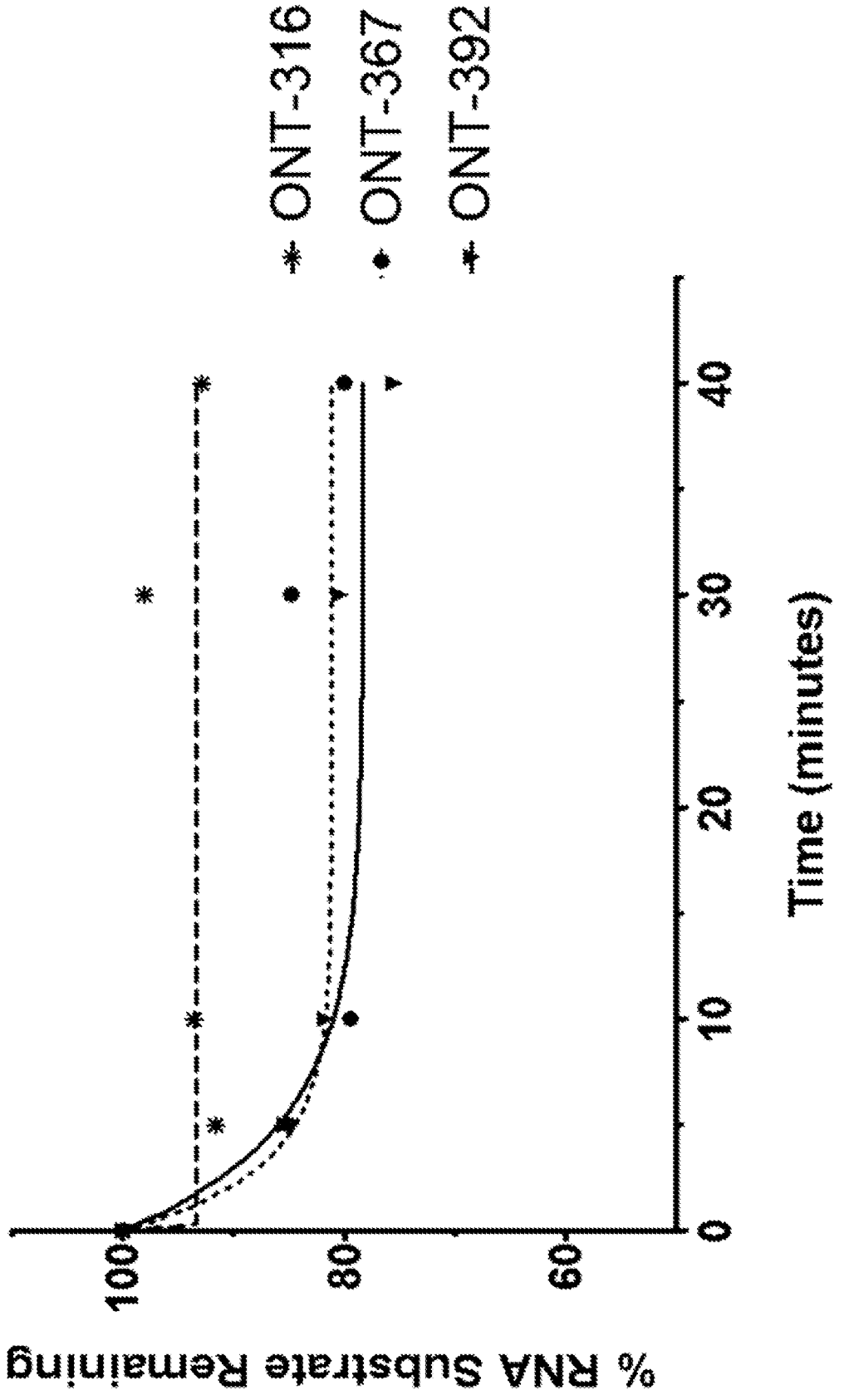

ONT-316
ONT-367
ONT-392
% RNA Substrate Remaining
100
80
60
0
10
20
30
40
Time (minutes)

FIG. 13

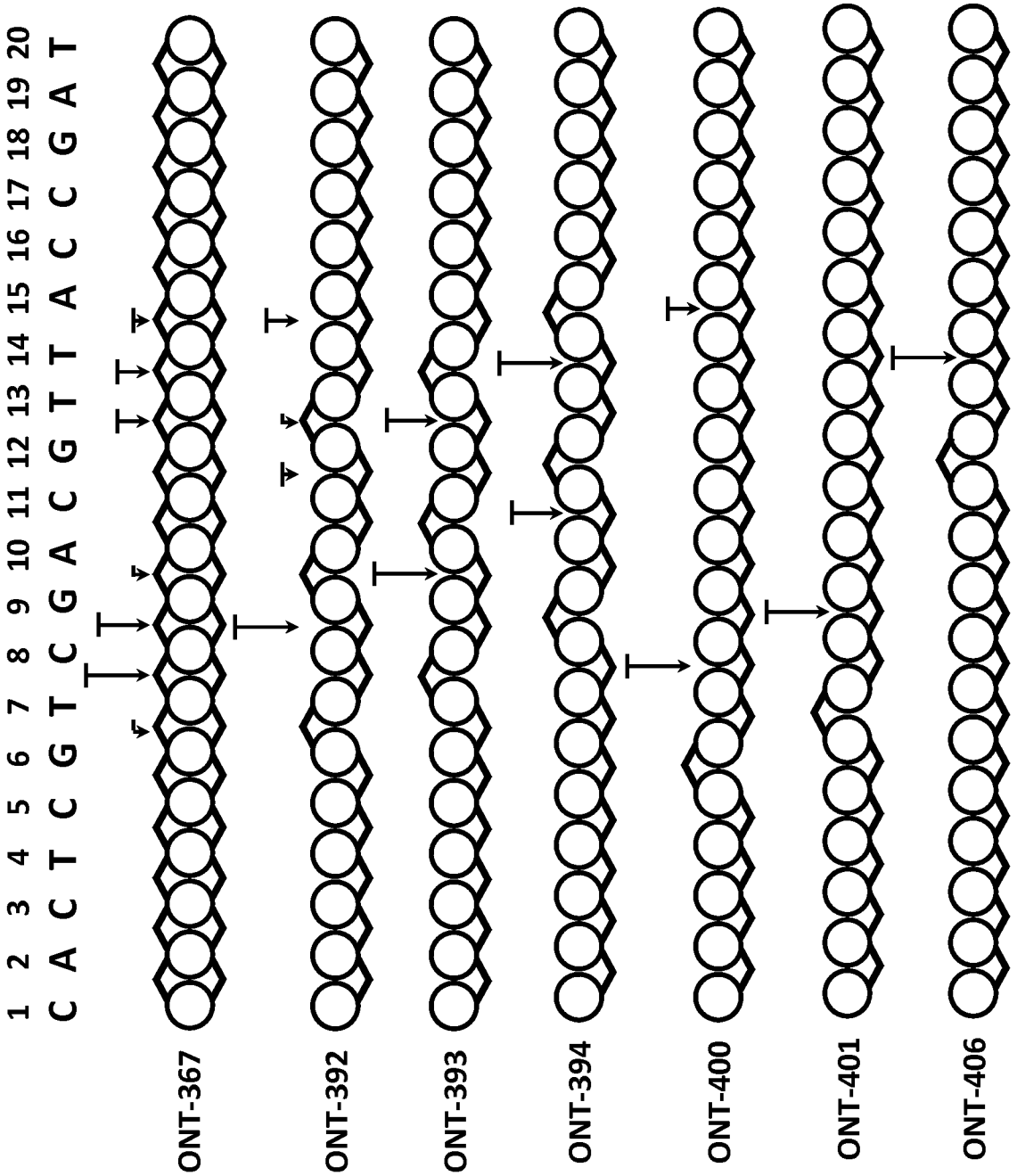

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
C A C T C G T C G A C G T T A C C G A T
ONT-367
ONT-392
ONT-393
ONT-394
ONT-400
ONT-401
ONT-406

FIG. 14

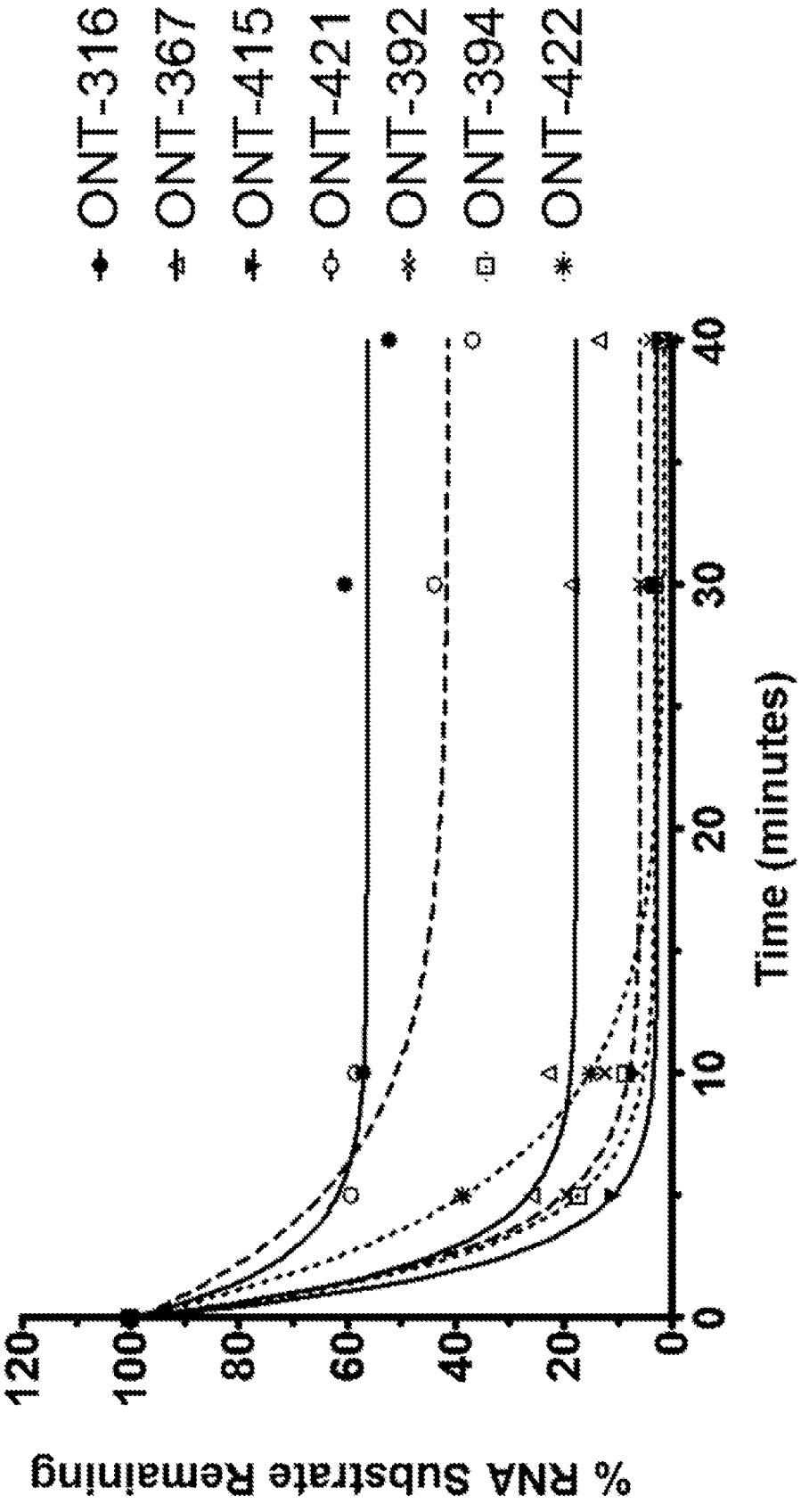

ONT-316
ONT-367
ONT-415
ONT-421
ONT-392
ONT-394
ONT-422
% RNA Substrate Remaining
120
100
80
60
40
20
0
0
10
20
30
40
Time (minutes)

FIG. 15

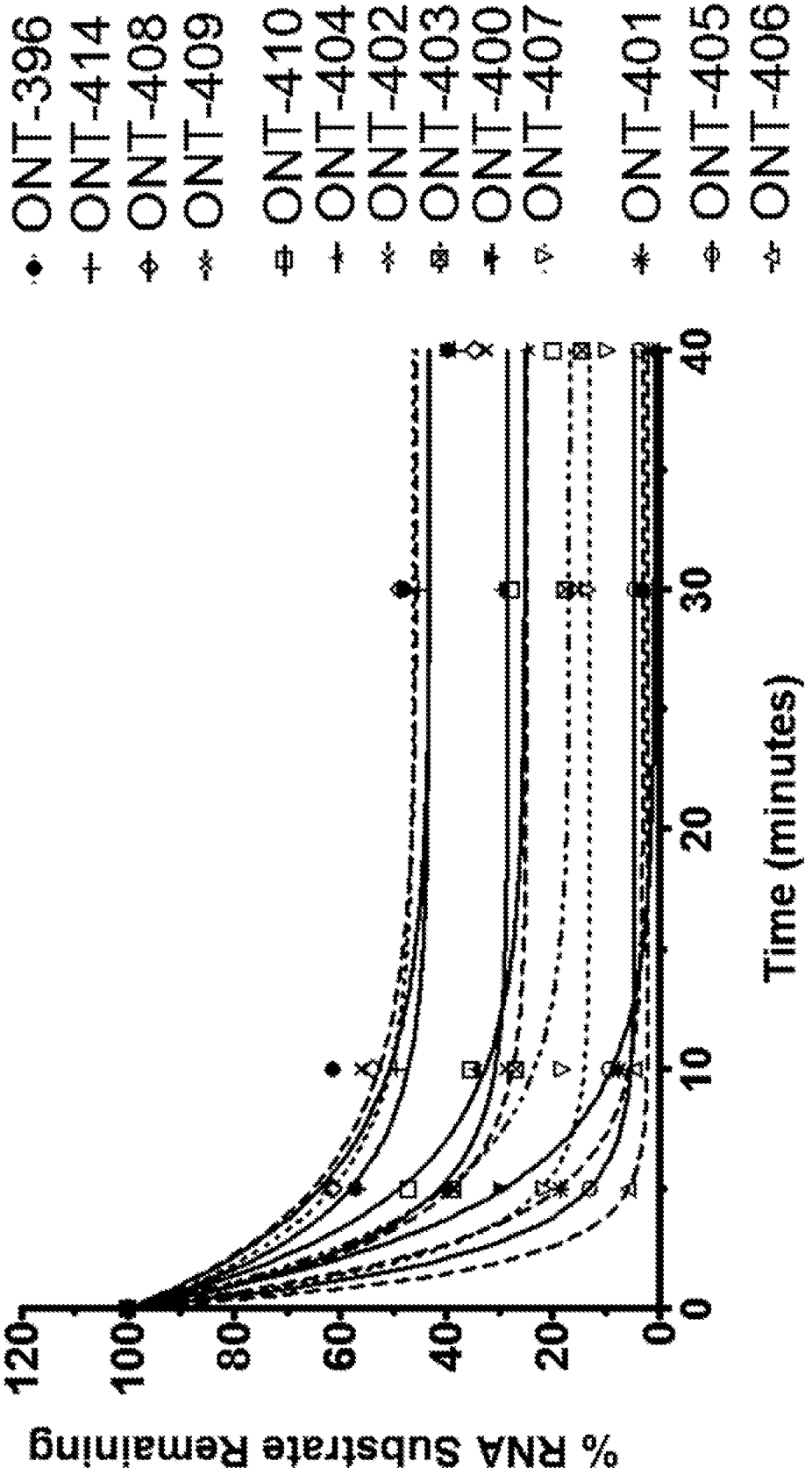

ONT-396
ONT-414
ONT-408
ONT-409
ONT-410
ONT-404
ONT-402
ONT-403
ONT-400
ONT-407
ONT-401
ONT-405
ONT-406
% RNA Substrate Remaining
120
100
80
60
40
20
0
0
10
20
30
40
Time (minutes)

FIG. 16

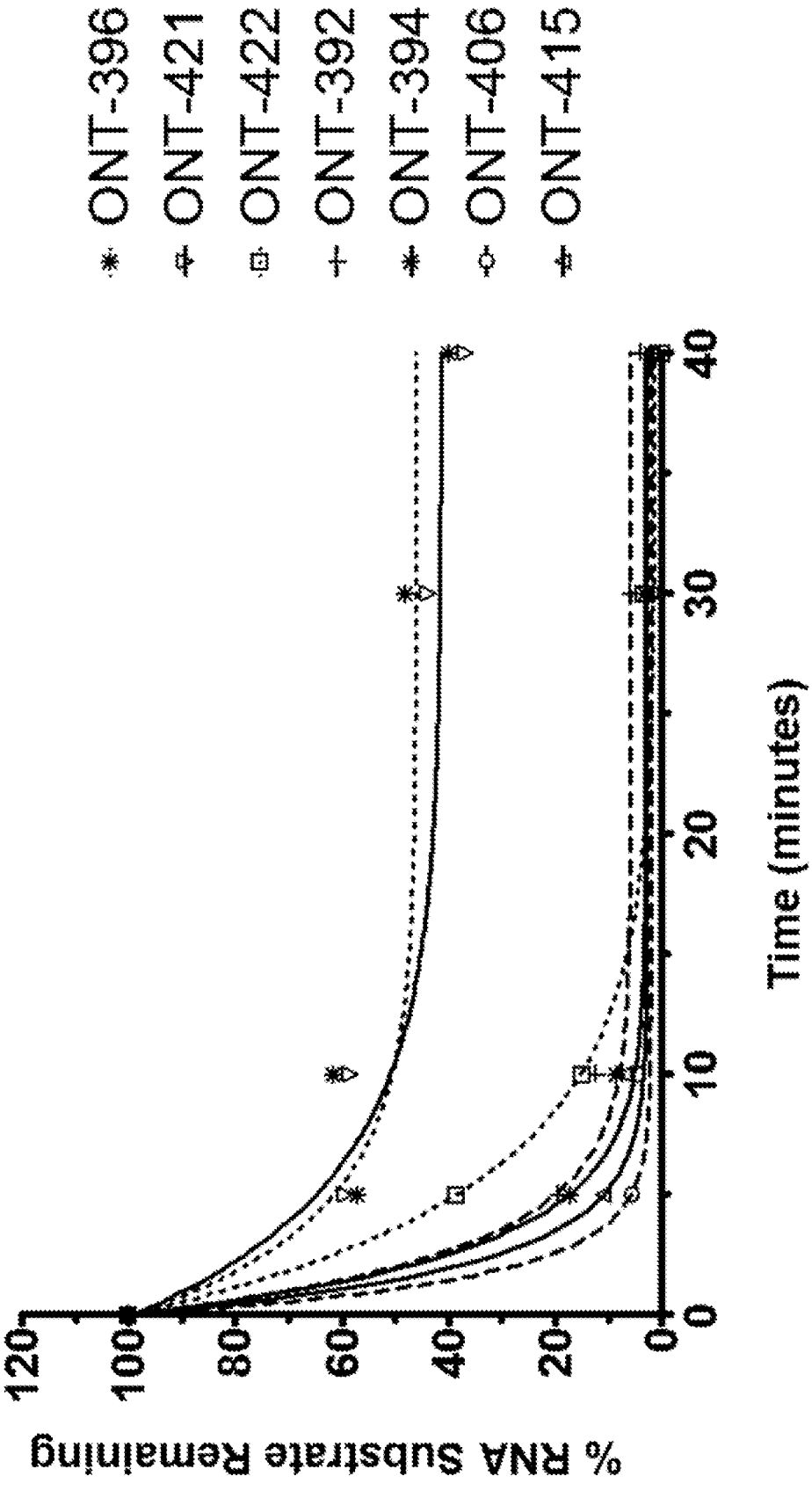

ONT-396
ONT-421
ONT-422
ONT-392
ONT-394
ONT-406
ONT-415
% RNA Substrate Remaining
120
100
80
60
40
20
0
0
10
20
30
40
Time (minutes)

FIG. 17

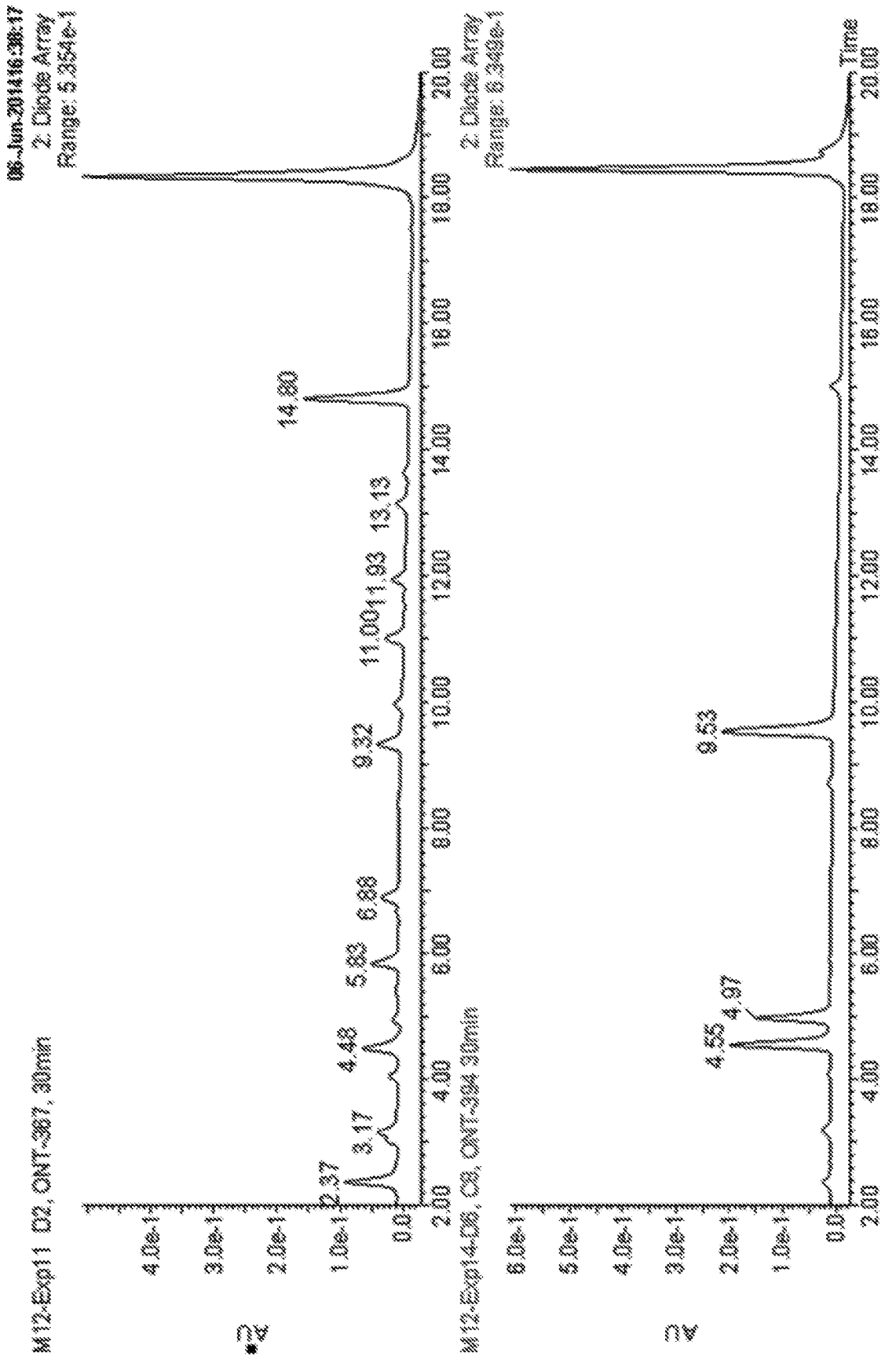

06-Jun-2014 16:38:17
2: Diode Array
Range: 5.354e-1
M12-Exp11 D2, CNT-367, 30min
2.37
3.17
4.48
5.83
6.88
9.32
11.00
11.93
13.13
14.80
2: Diode Array
Range: 6.349e-1
M12-Exp14-D2, CB, CNT-394 30min
4.55
4.97
9.53
Time

FIG. 18

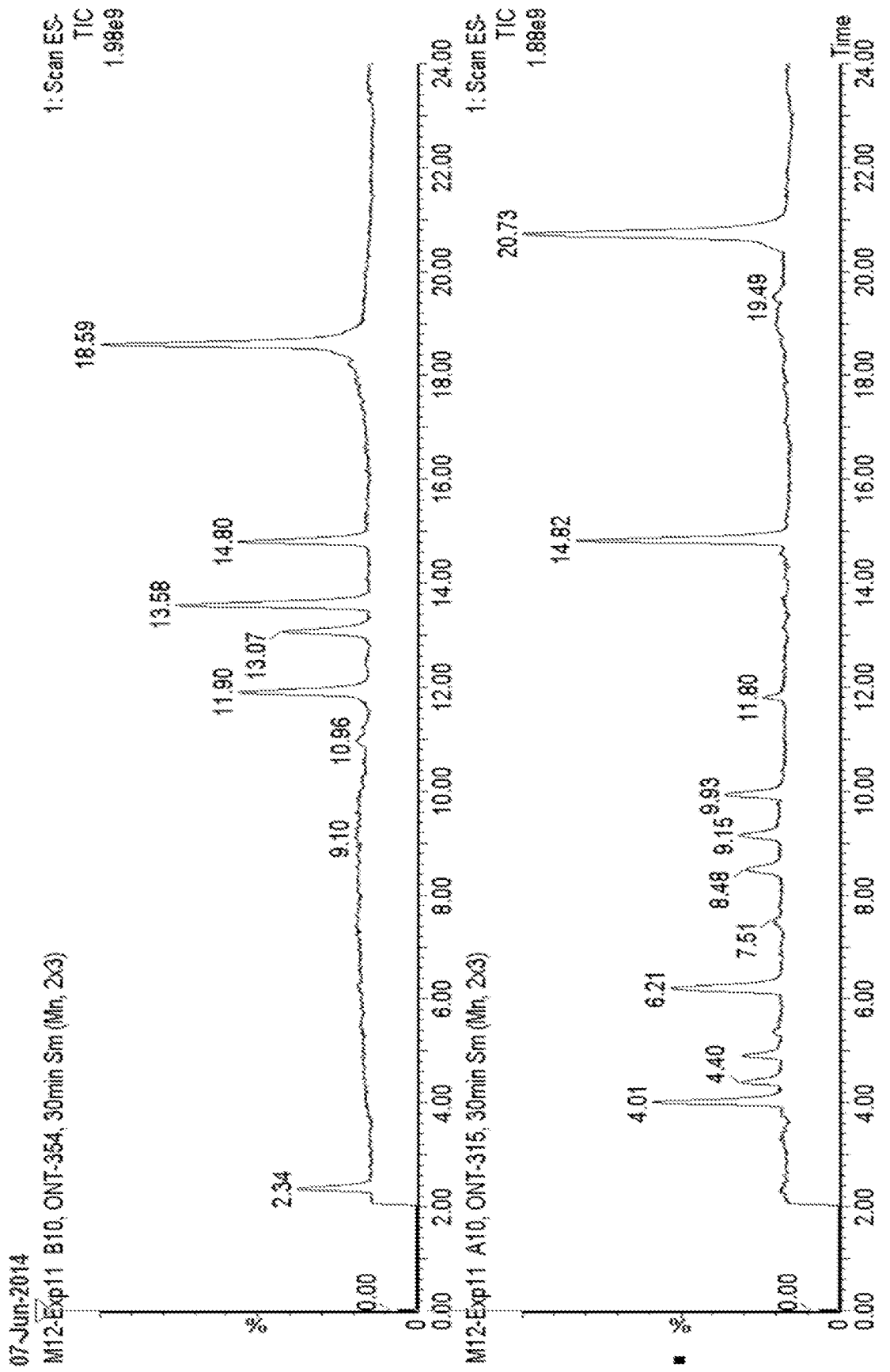

07-Jun-2014
M12-Exp11 B10, ONT-354, 30min Sm (Mn, 2x3)
1: Scan ES-
TIC
1.98e9
18.59
14.80
13.58
13.07
11.90
10.96
9.10
2.34
M12-Exp11 A10, ONT-315, 30min Sm (Mn, 2x3)
1: Scan ES-
TIC
1.88e9
20.73
19.49
14.82
11.80
9.93
9.15
8.48
7.51
6.21
4.40
4.01
%
Time

FIG. 19

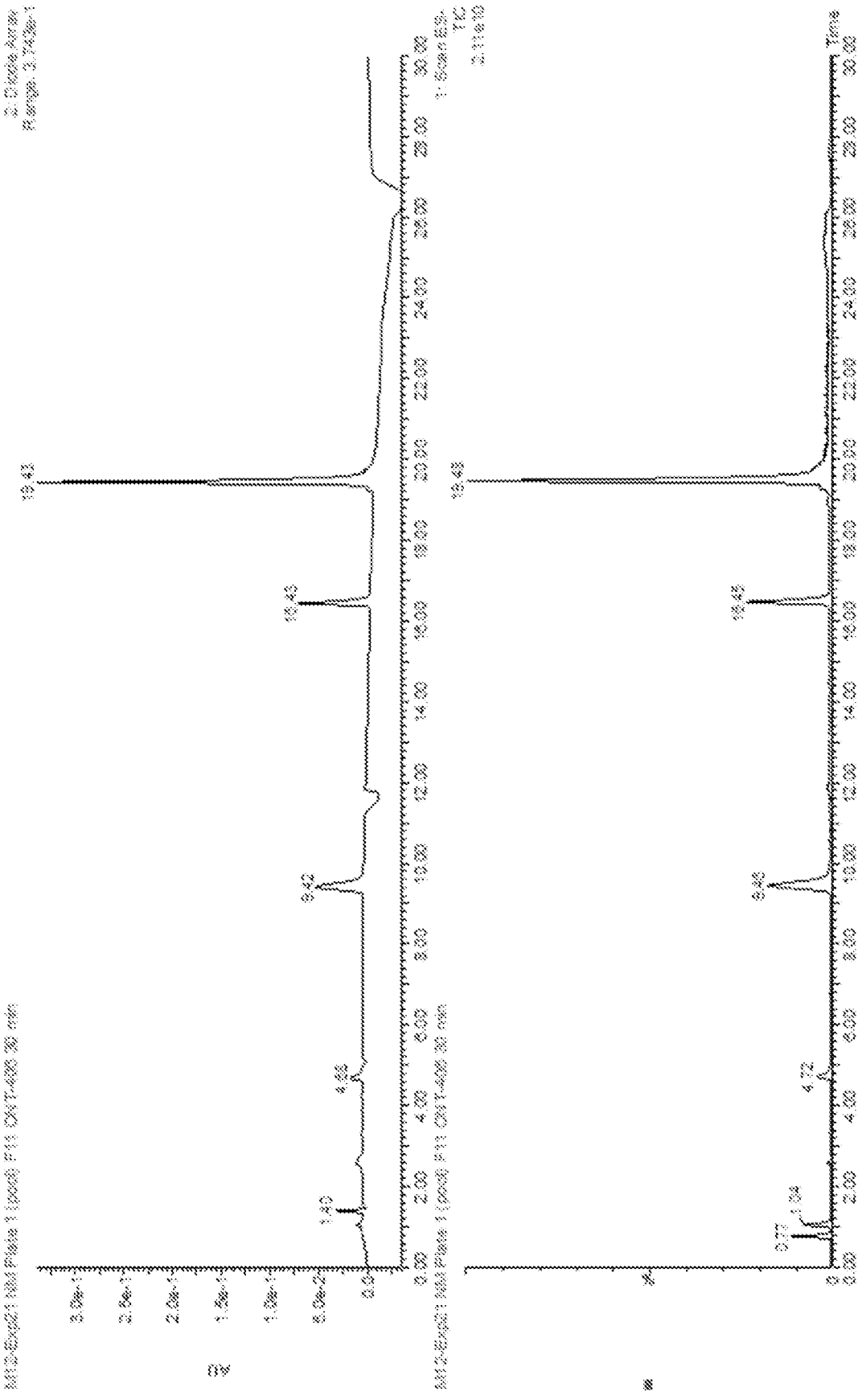

M12-Exp21 NM Plate 1 (rack) F11 OVT-400 30 min
2: Diode Array
Range: 3.743e-1
19.43
18.43
9.42
4.46
1.40
M12-Exp21 NM Plate 1 (rack) F11 OVT-400 30 min
TIC
1: Scan ES+
2.11e10
19.43
18.43
9.42
4.72
1.34
0.77
Time

FIG. 20

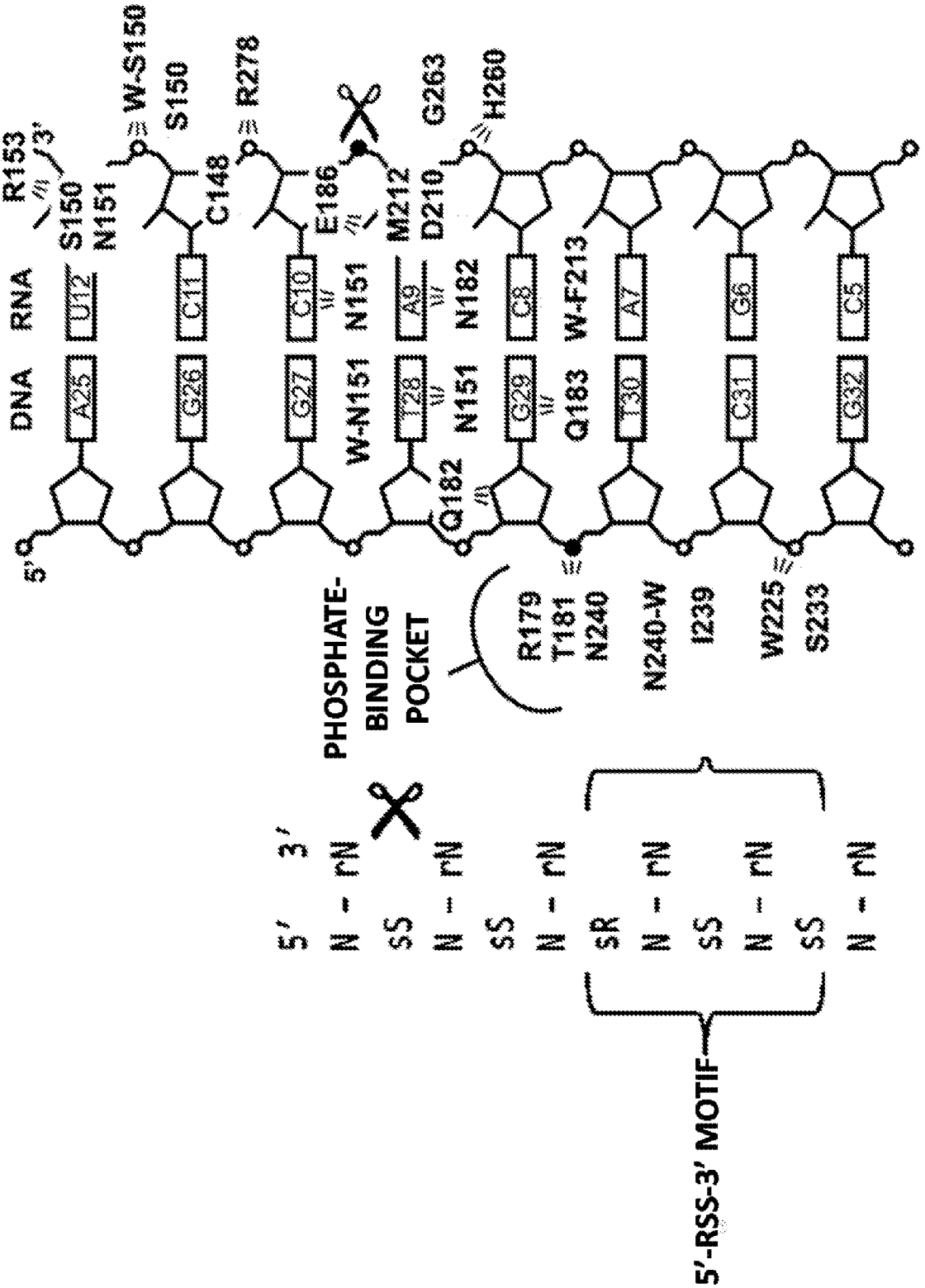
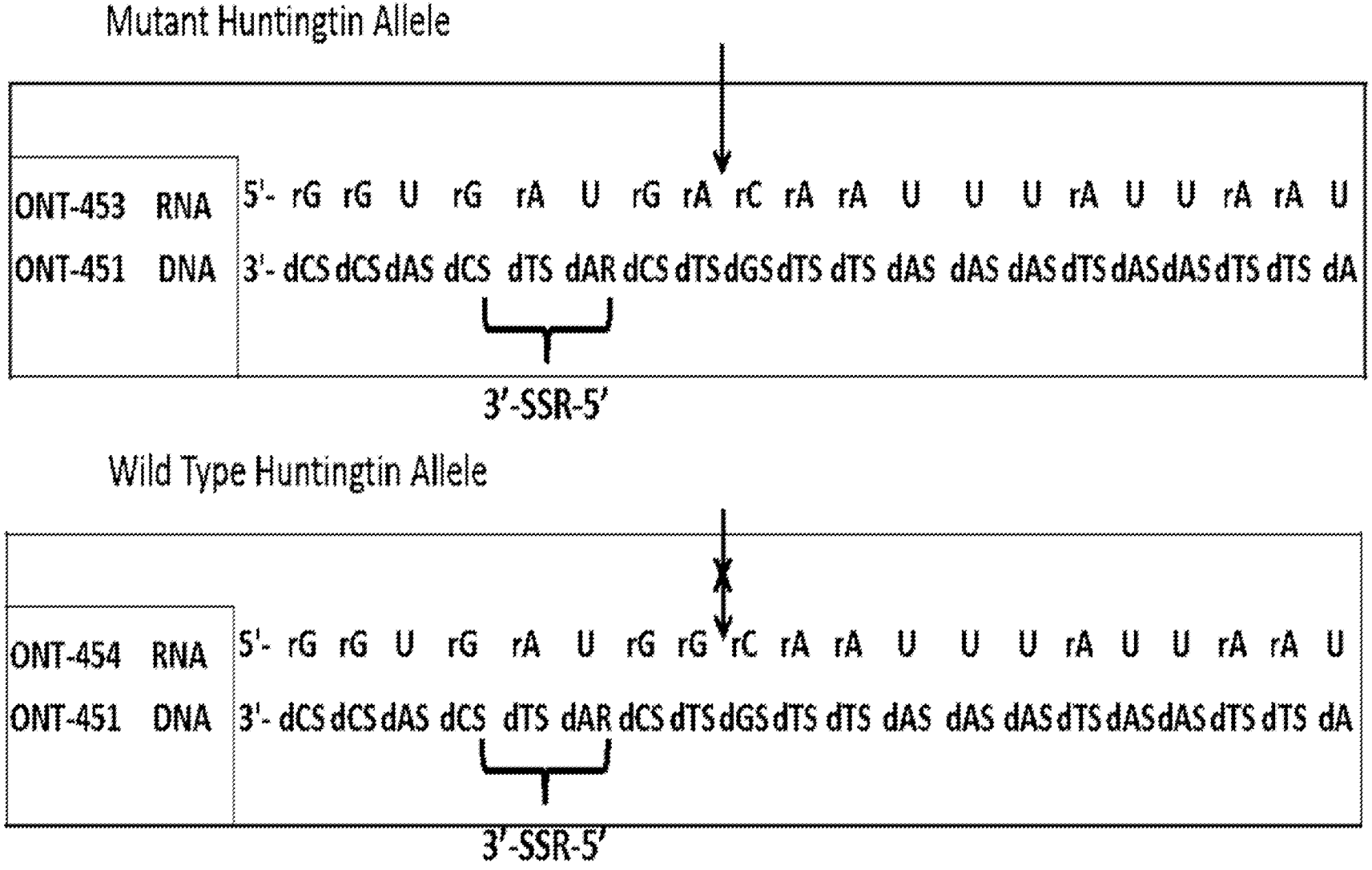
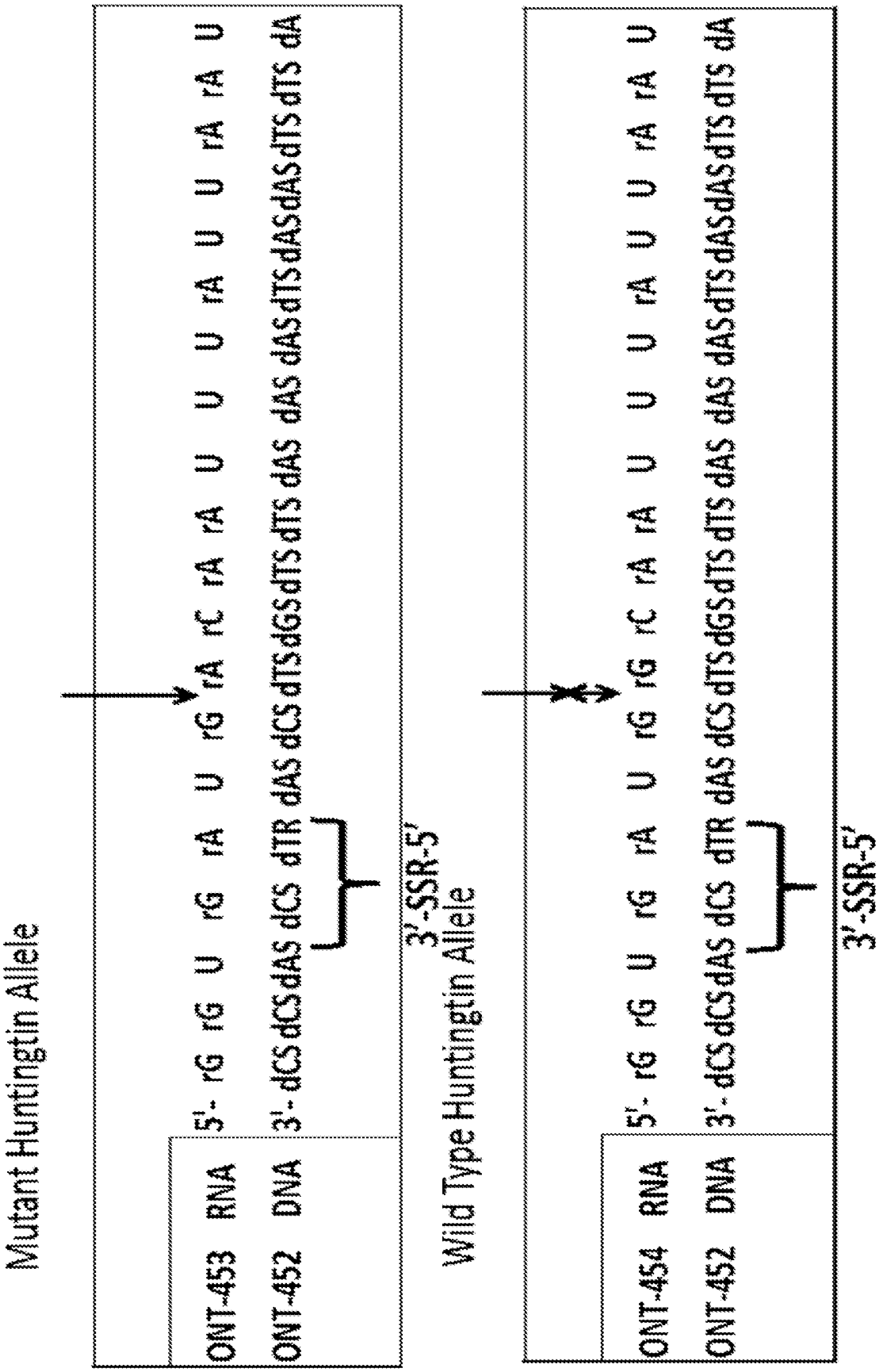

DNA
RNA
A25
U12
G26
C11
G27
C10
T28
A9
G29
C8
T30
A7
C31
G6
G32
C5
5'
3'
R153
S150
N151
W-S150
S150
C148
R278
E186
M212
D210
G263
H260
W-N151
N151
N182
Q182
N151
Q183
W-F213
PHOSPHATE-BINDING POCKET
R179
T181
N240
N240-W
I239
W225
S233
5'-RSS-3' MOTIF

FIG. 21



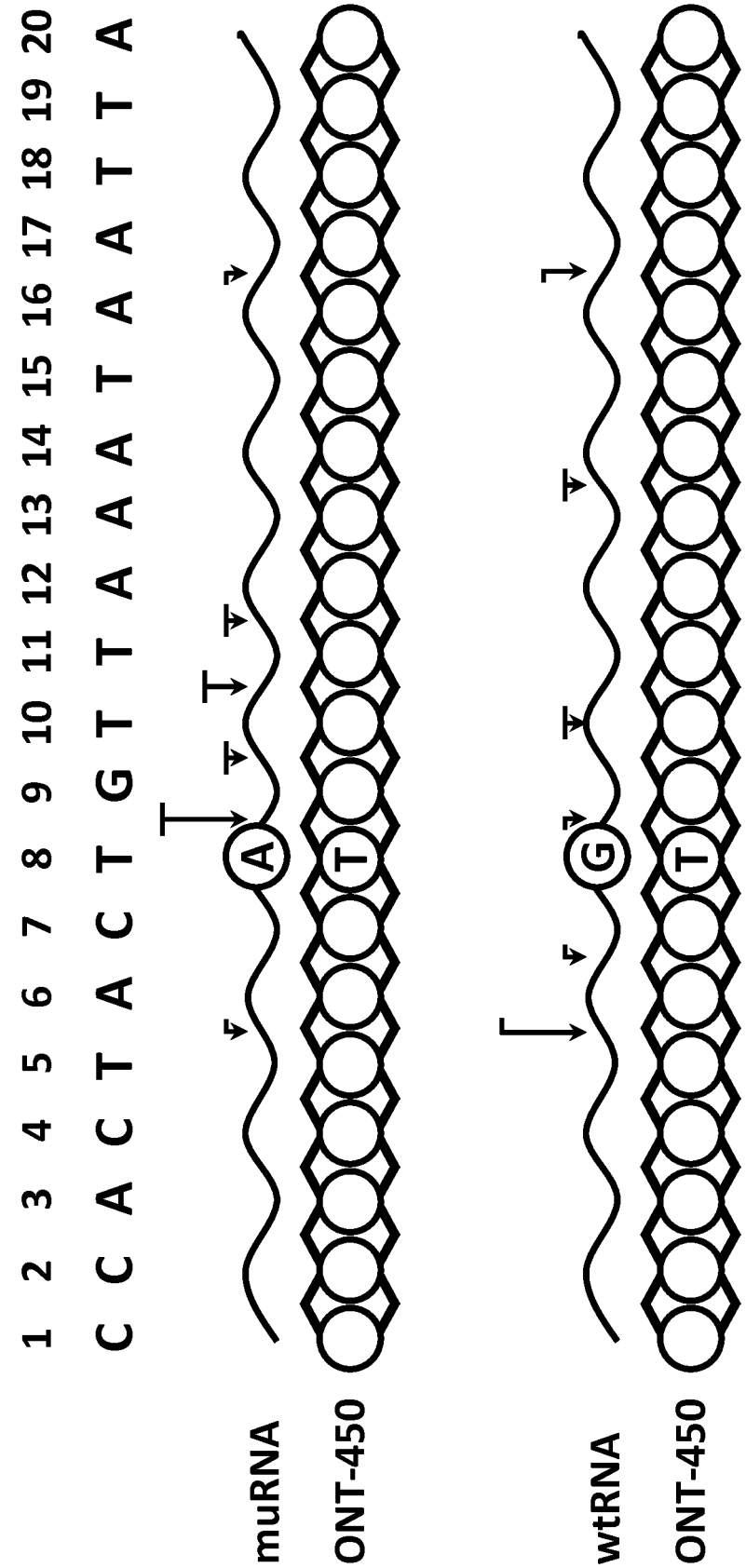
(PANEL A)

FIG. 22



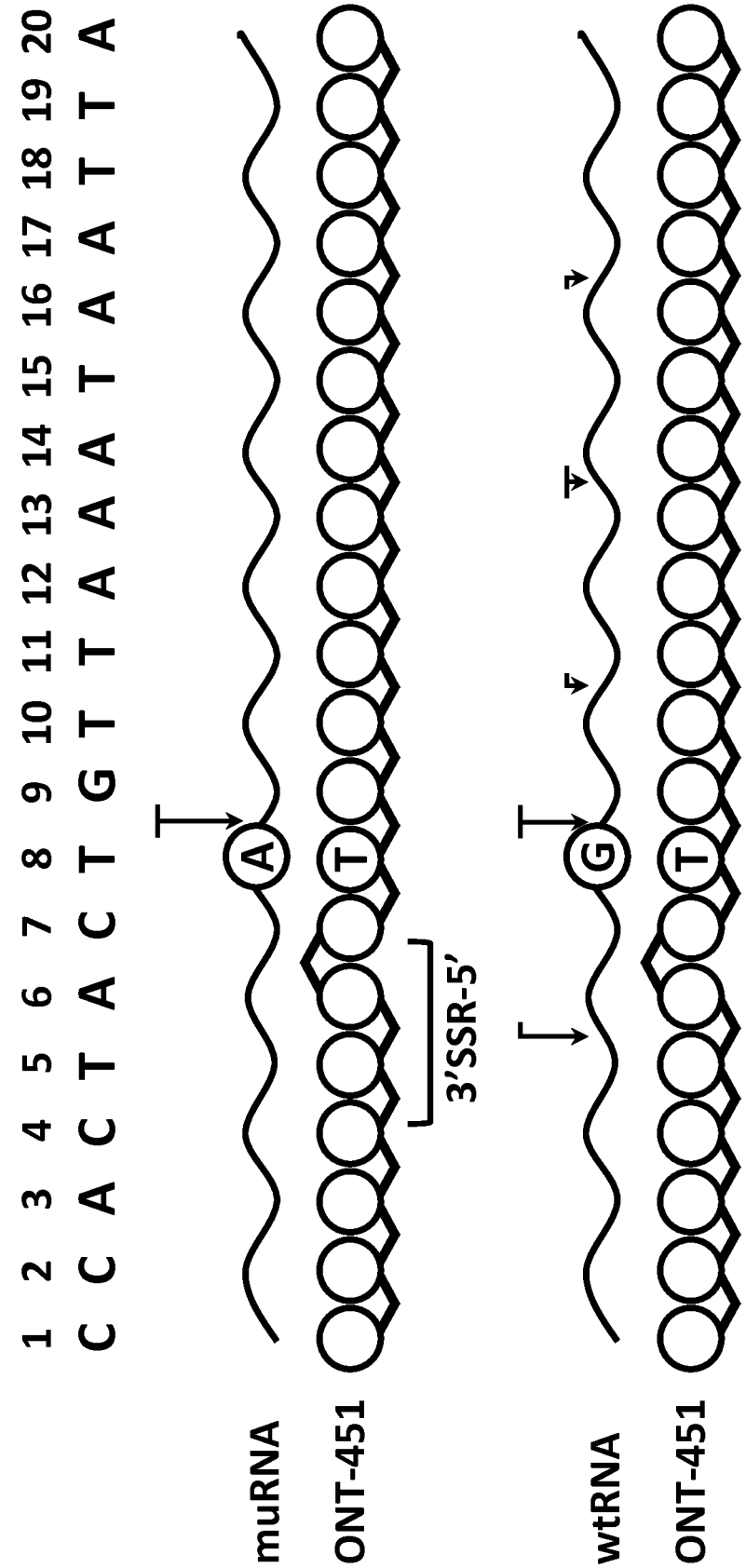
(PANEL B)

FIG. 22 (CONTINUED)



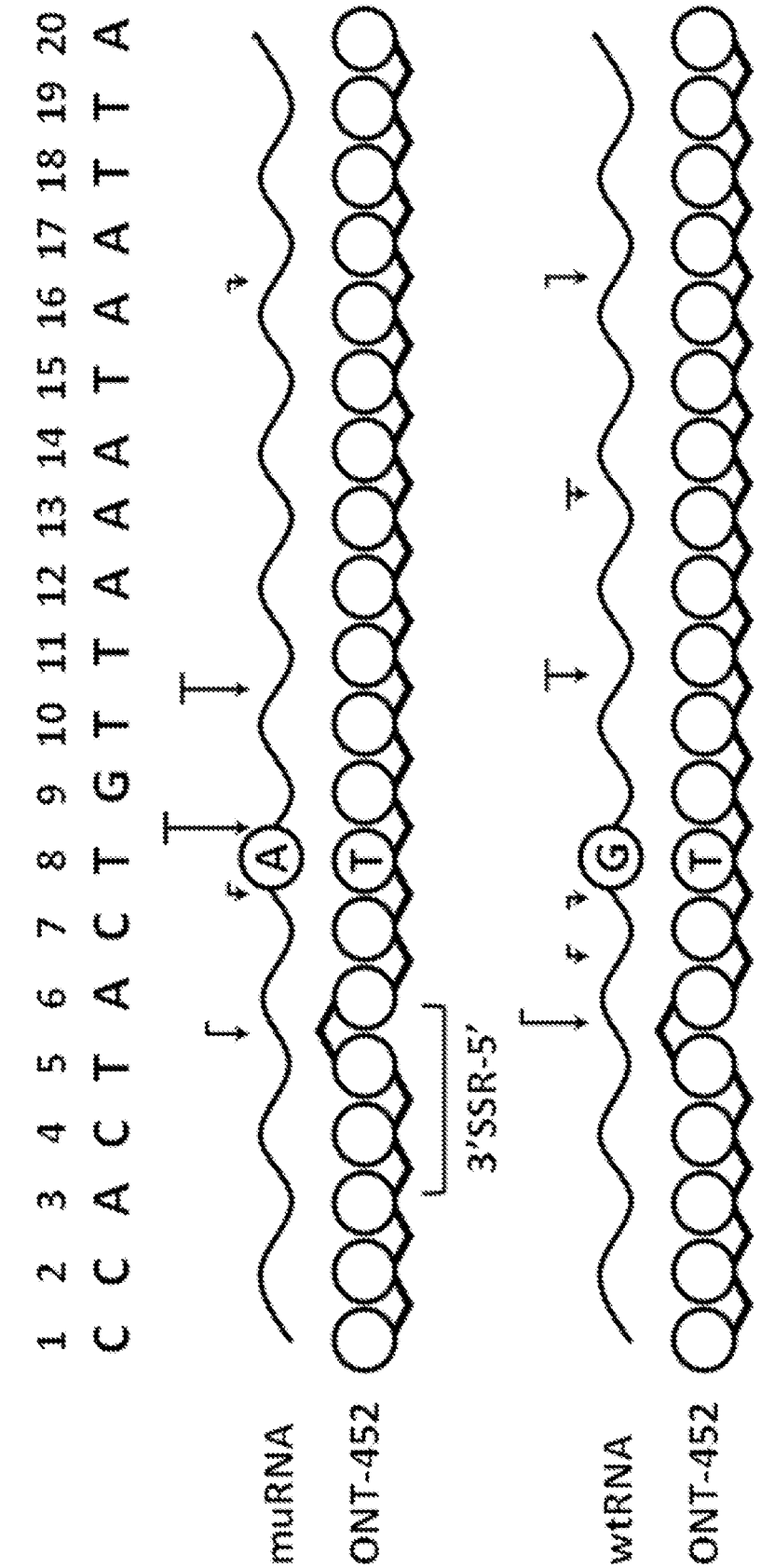
(PANEL C)

FIG. 22 (CONTINUED)



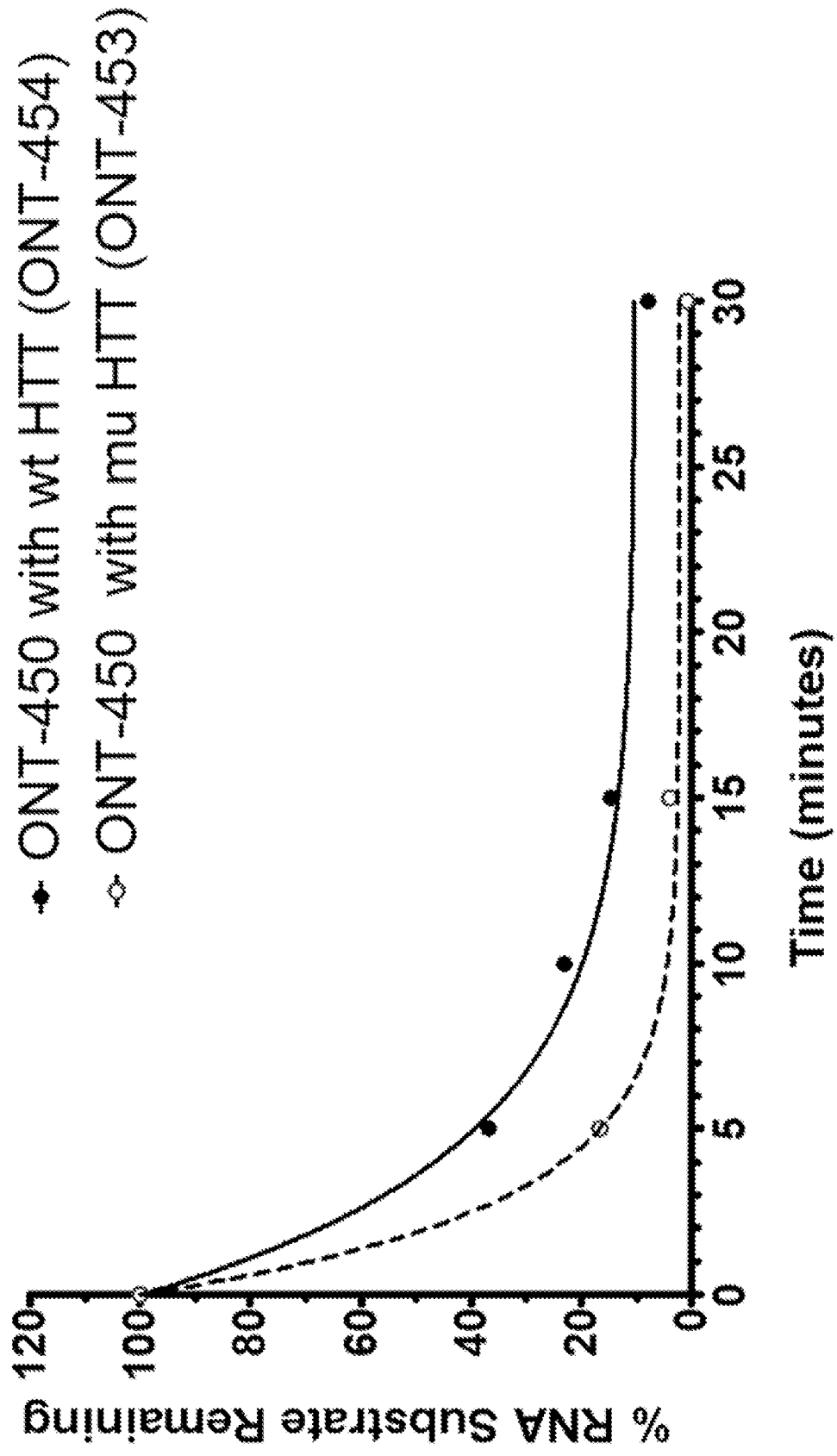
(PANEL D)

FIG. 22 (CONTINUED)



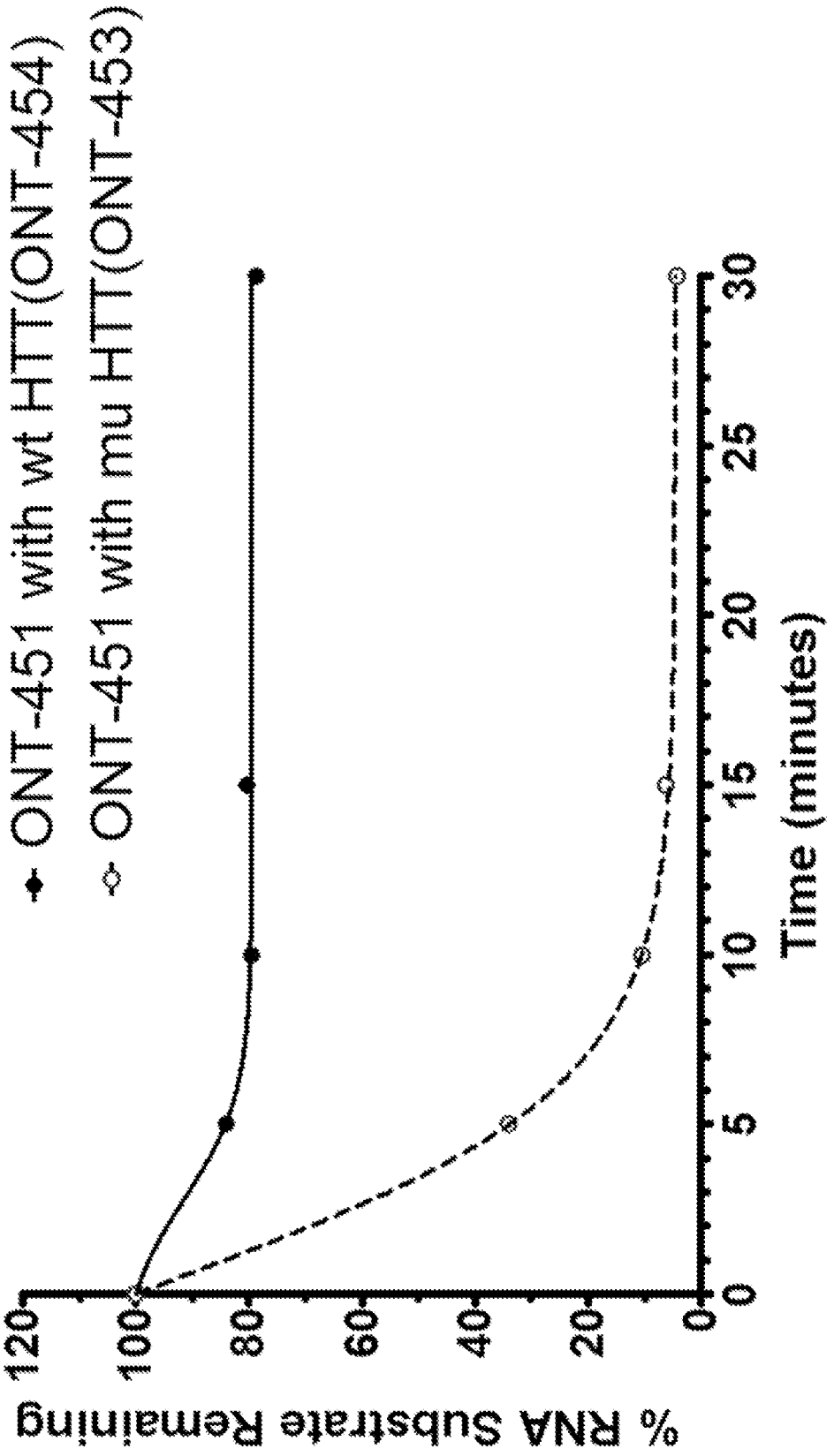
(PANEL E)

FIG. 22 (CONTINUED)



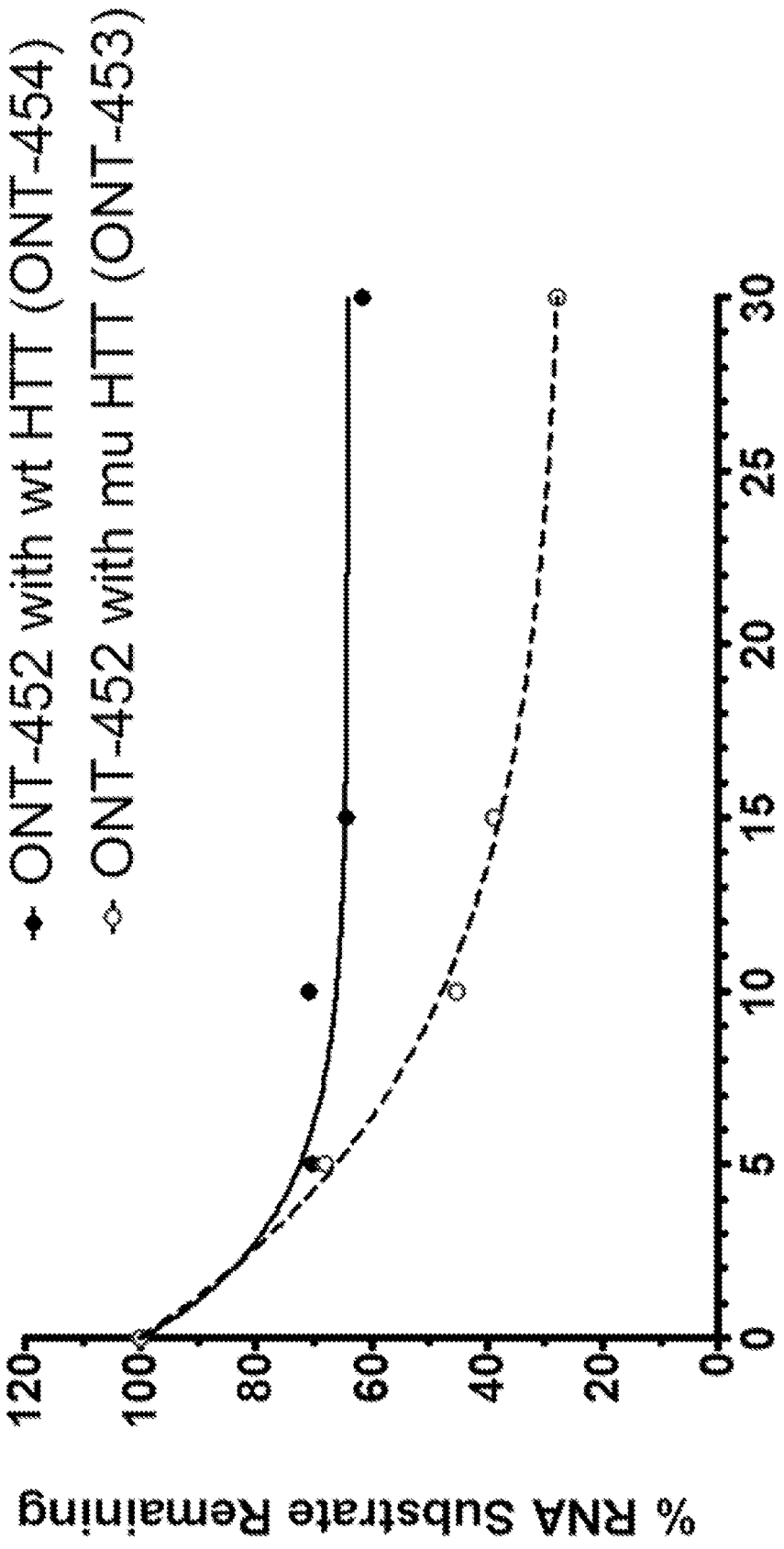
(PANEL F)

FIG. 22 (CONTINUED)



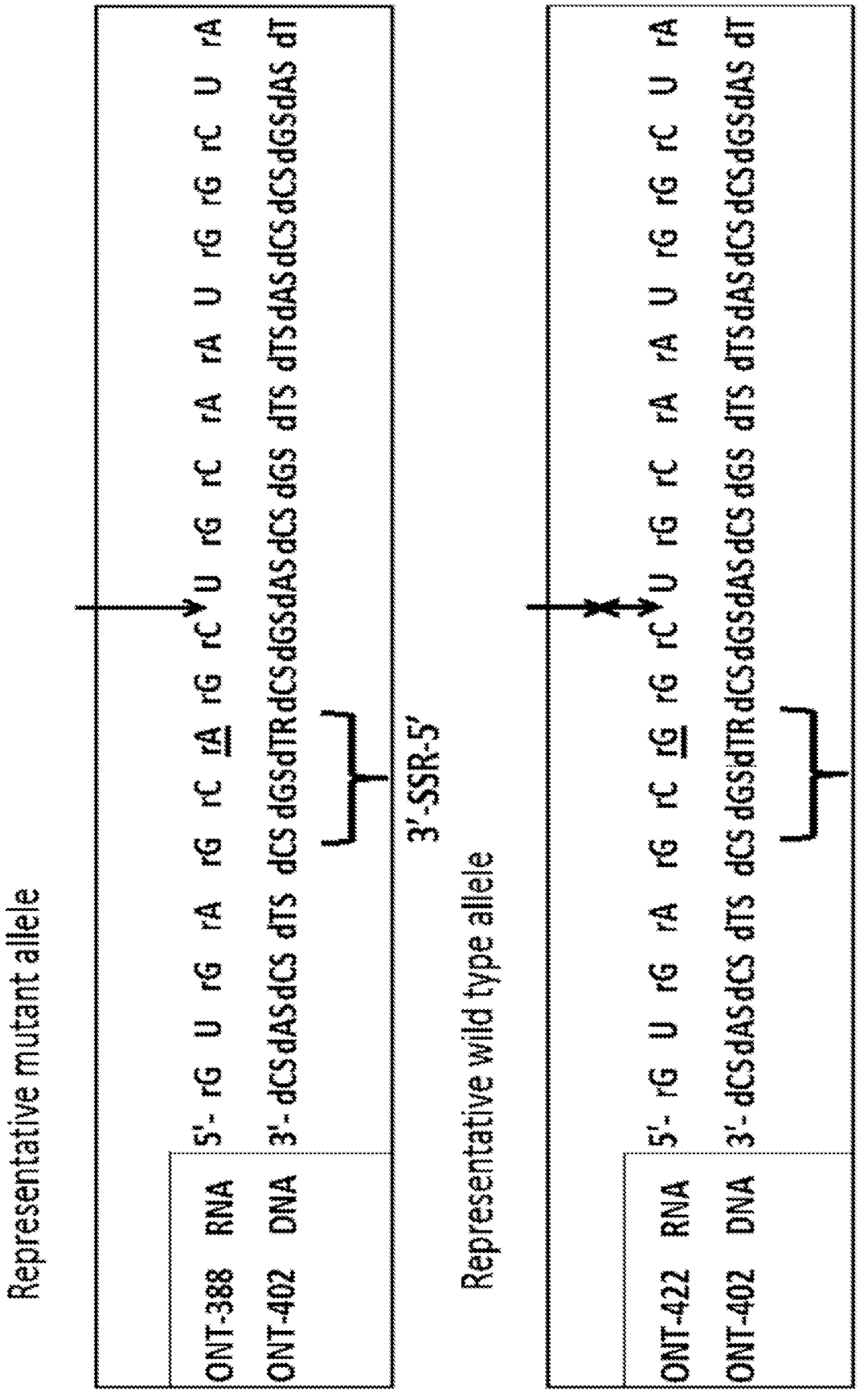
(PANEL G)

FIG. 22 (CONTINUED)

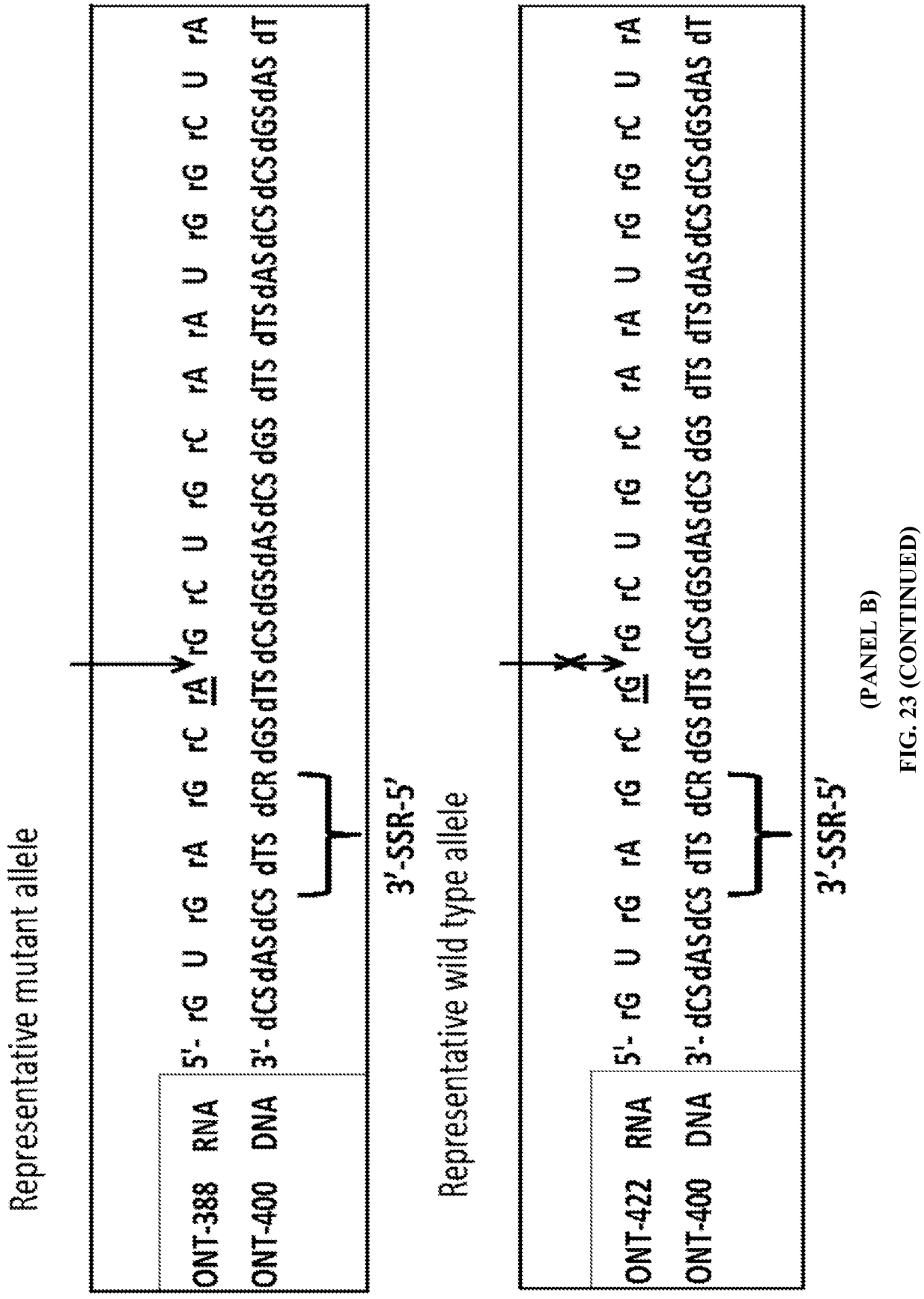


(PANEL H)

FIG. 22 (CONTINUED)

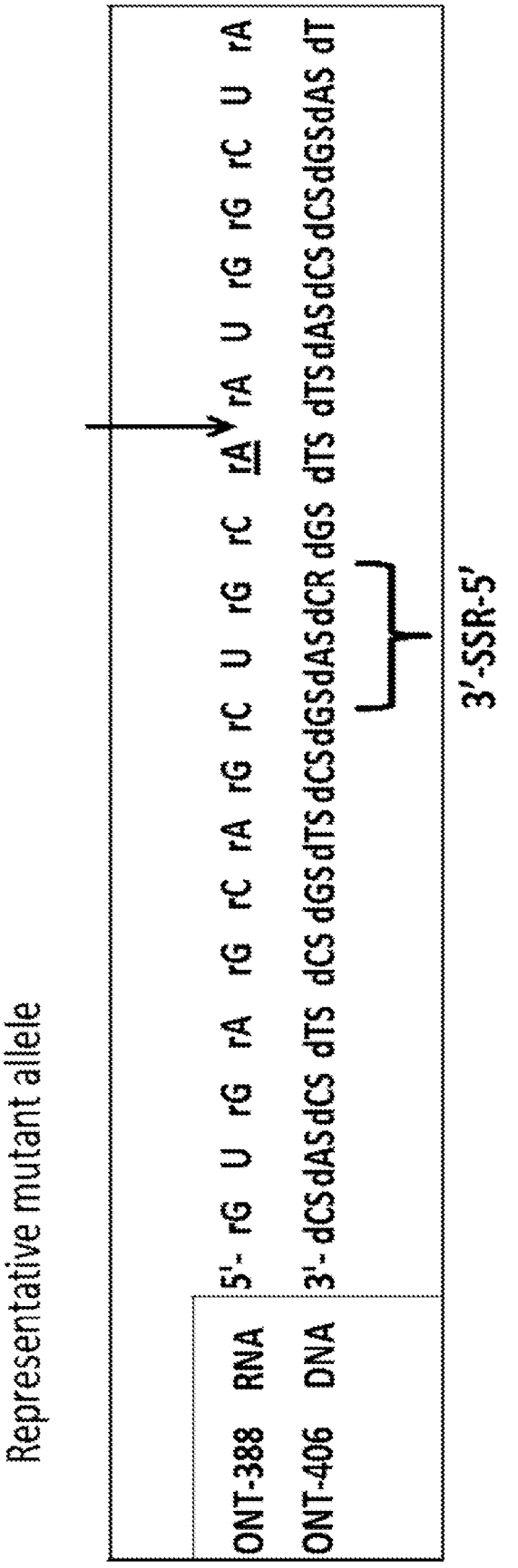


(PANEL A)
FIG. 23



(PANEL B)

FIG. 23 (CONTINUED)



(PANEL C)

FIG. 23 (CONTINUED)

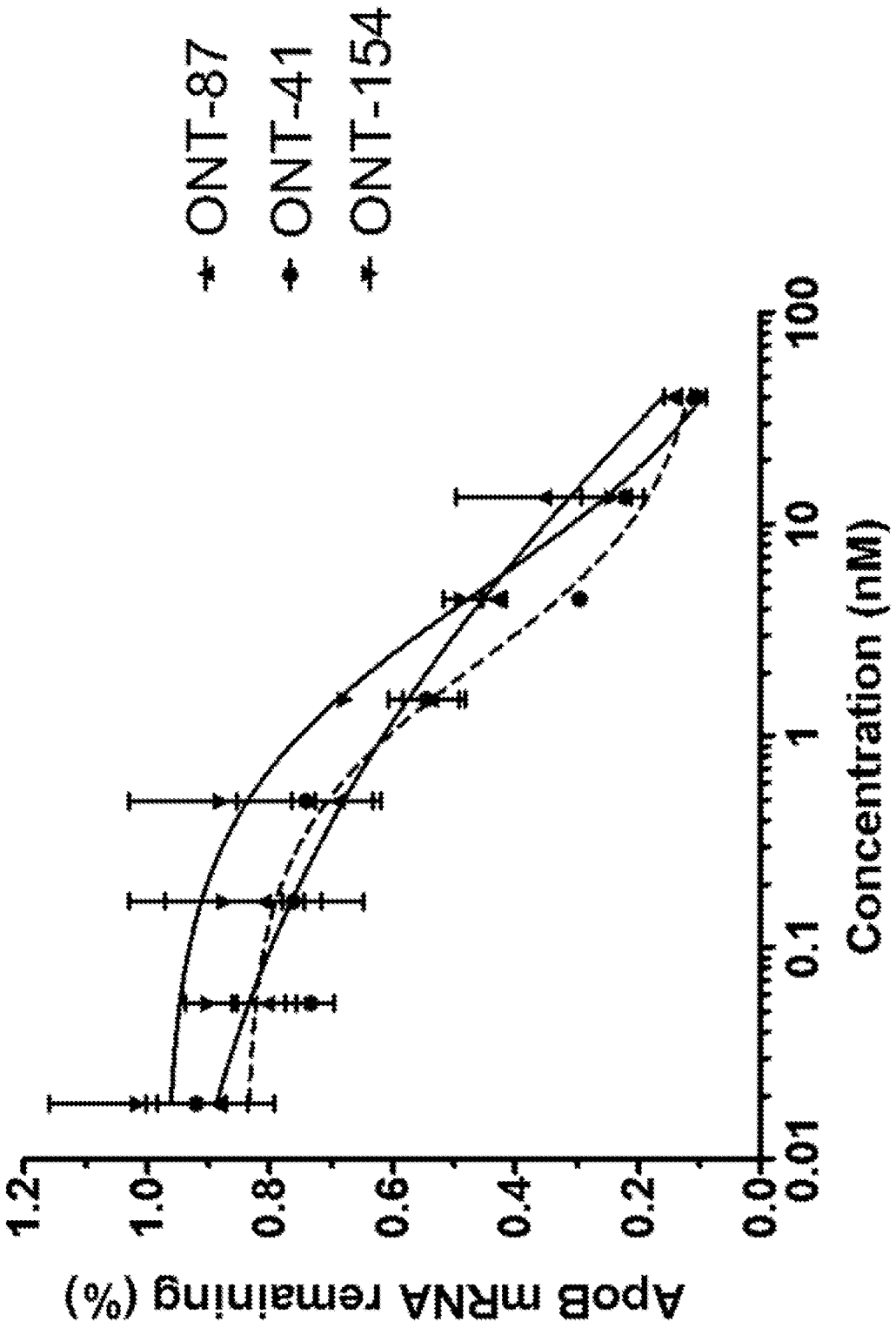
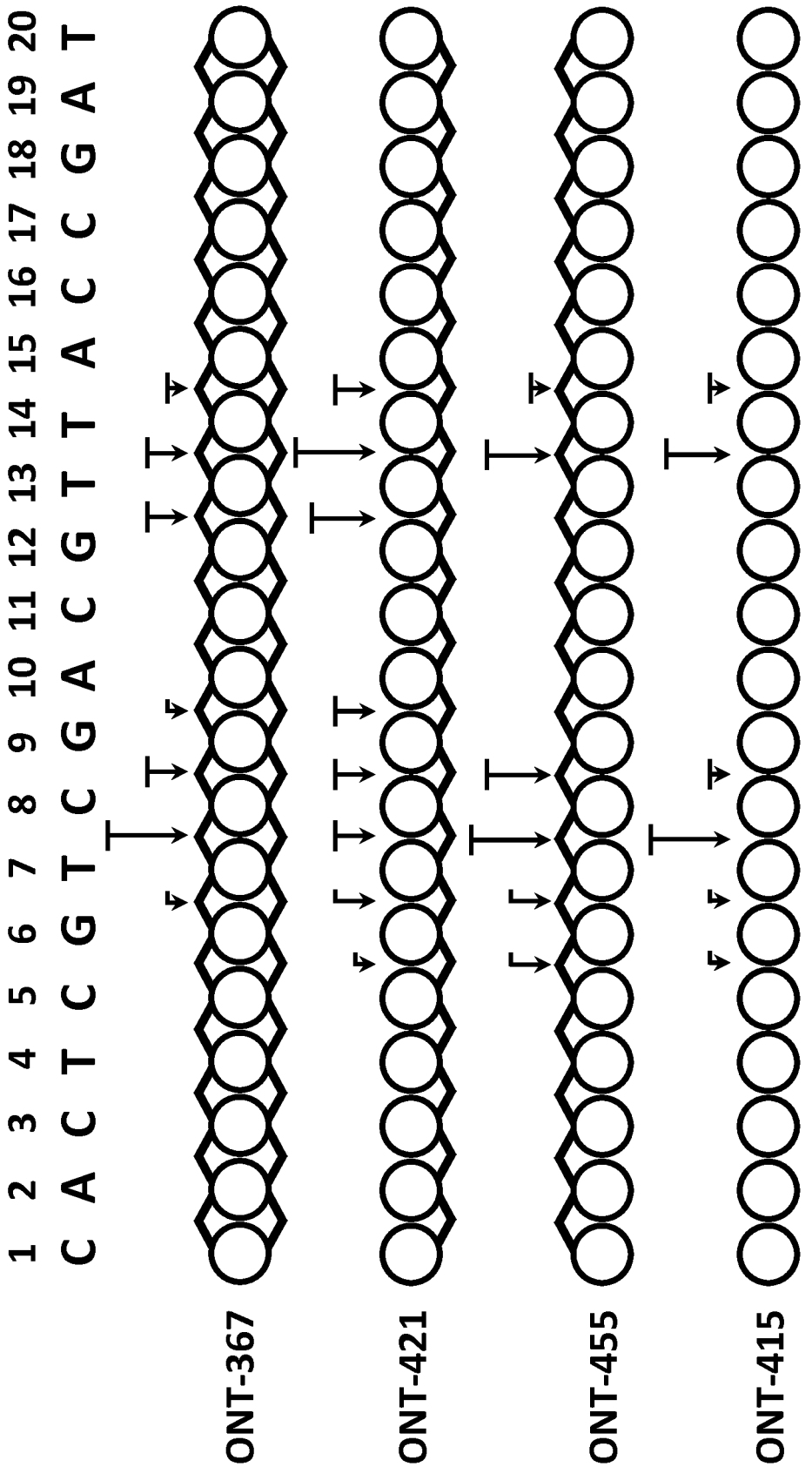
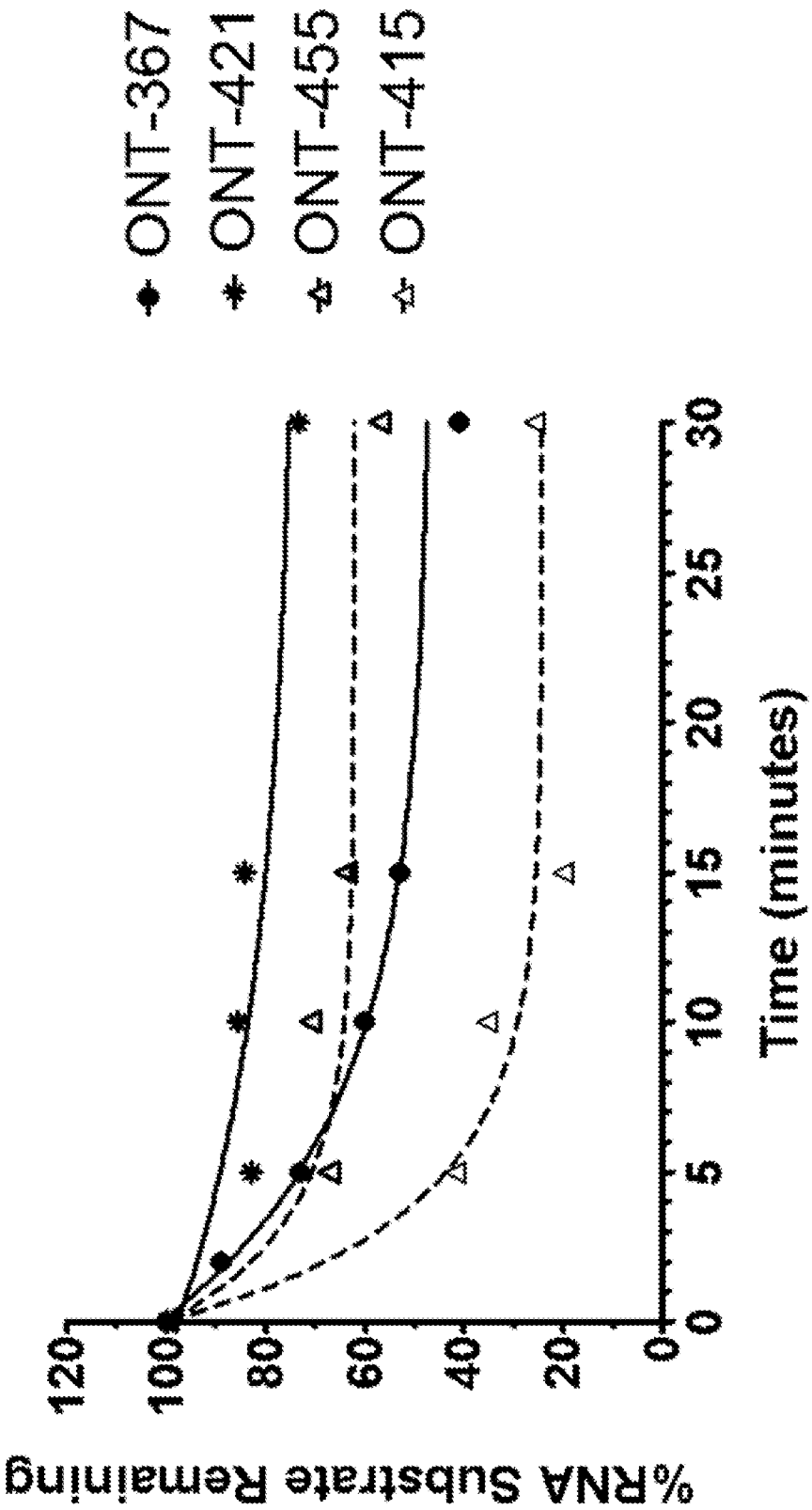

ApoB mRNA remaining (%)
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0.01
0.1
1
10
100
Concentration (nM)
ONT-87
ONT-41
ONT-154

FIG. 24



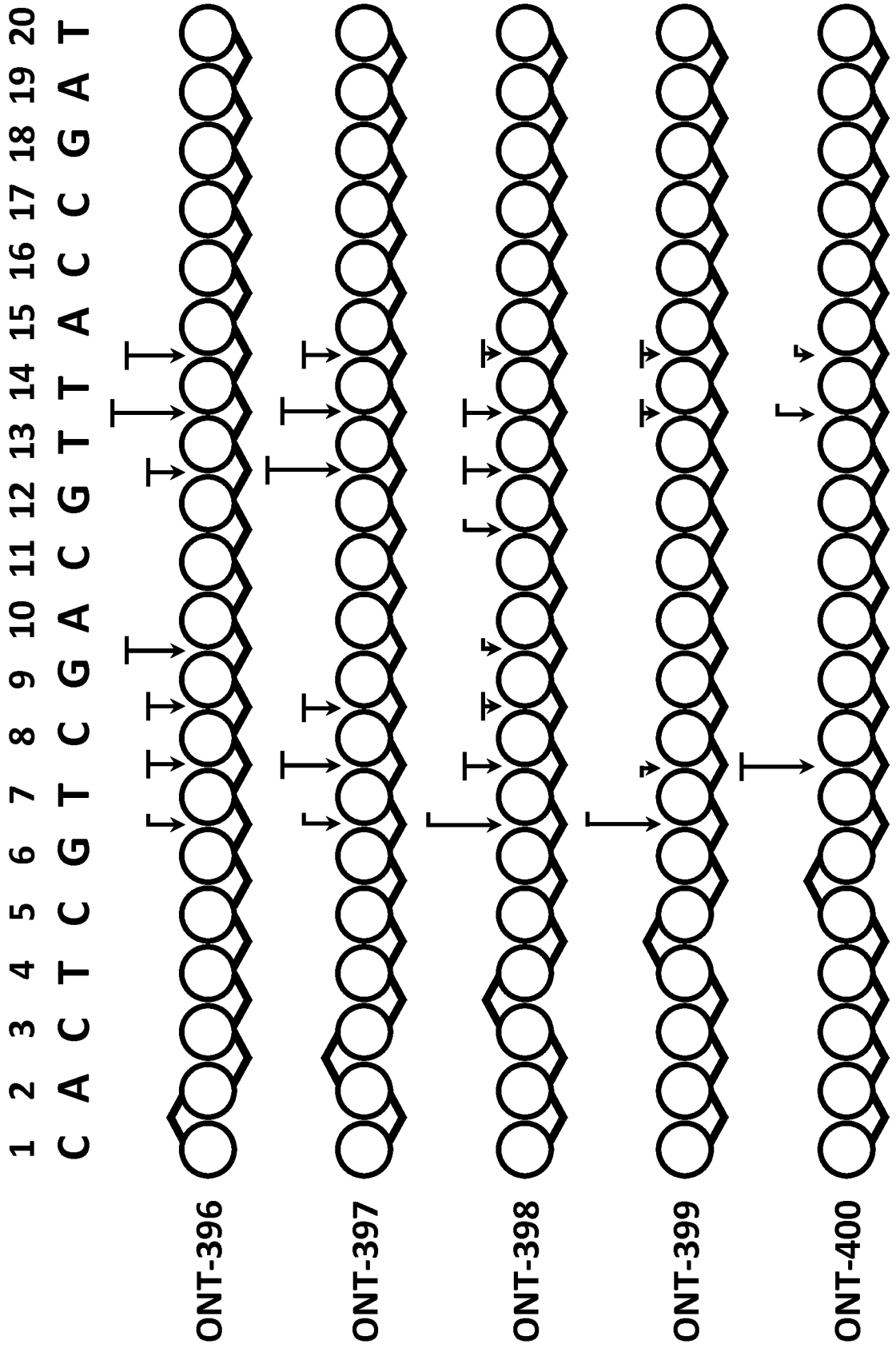
(PANEL A)

FIG. 25



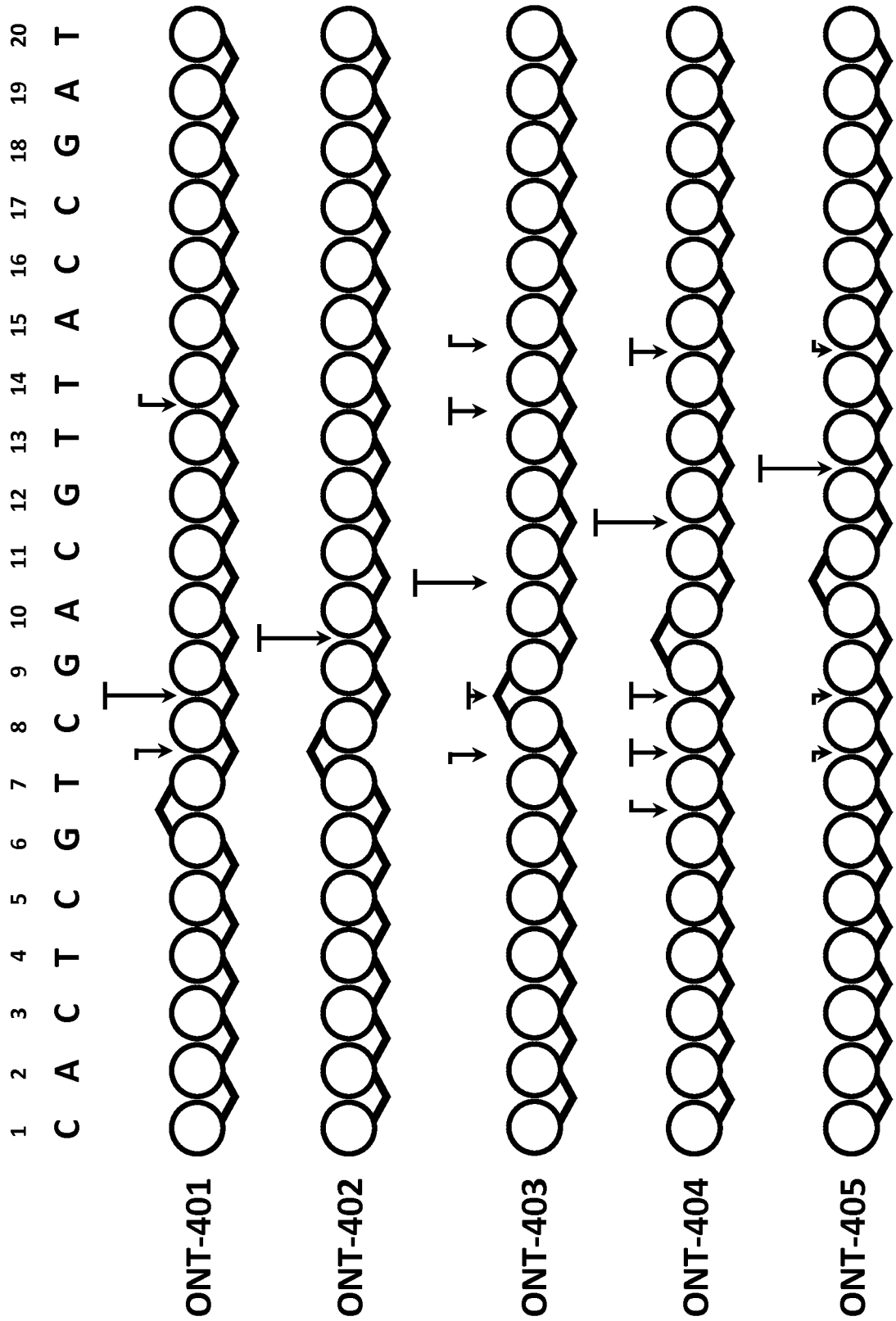
(PANEL B)

FIG. 25 (CONTINUED)



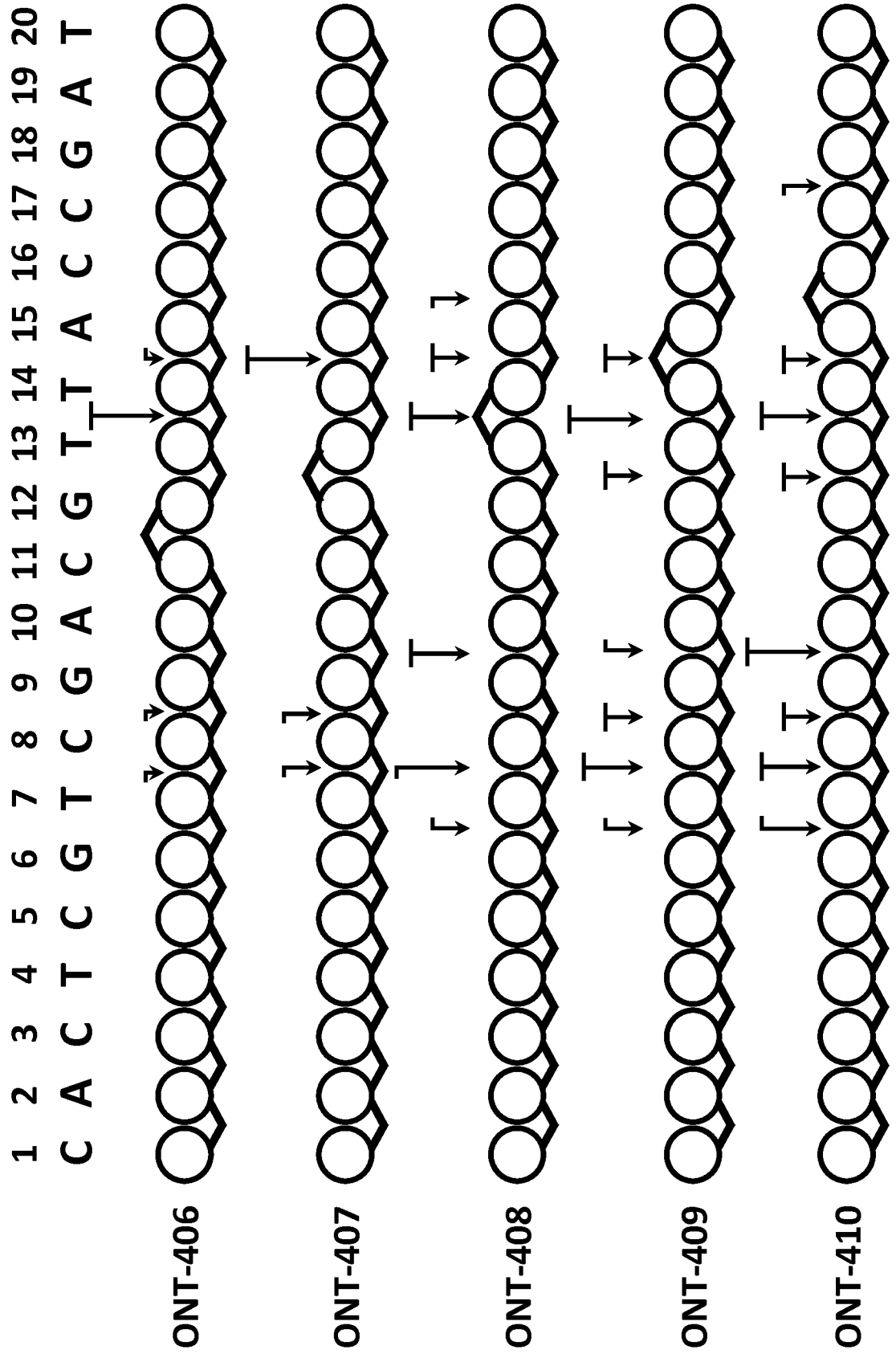
(PANEL A)

FIG. 26



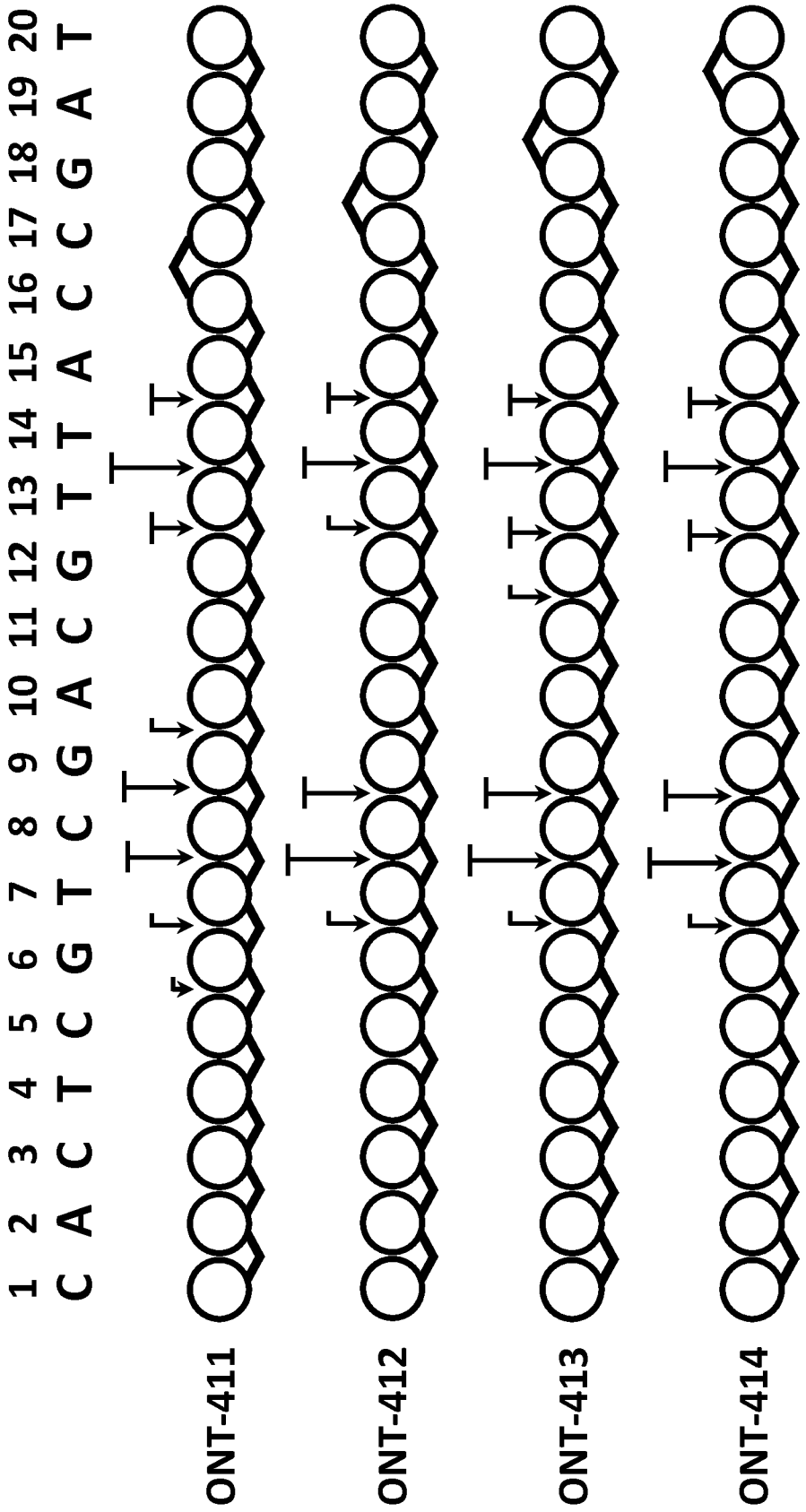
(PANEL B)

FIG. 26 (CONTINUED)



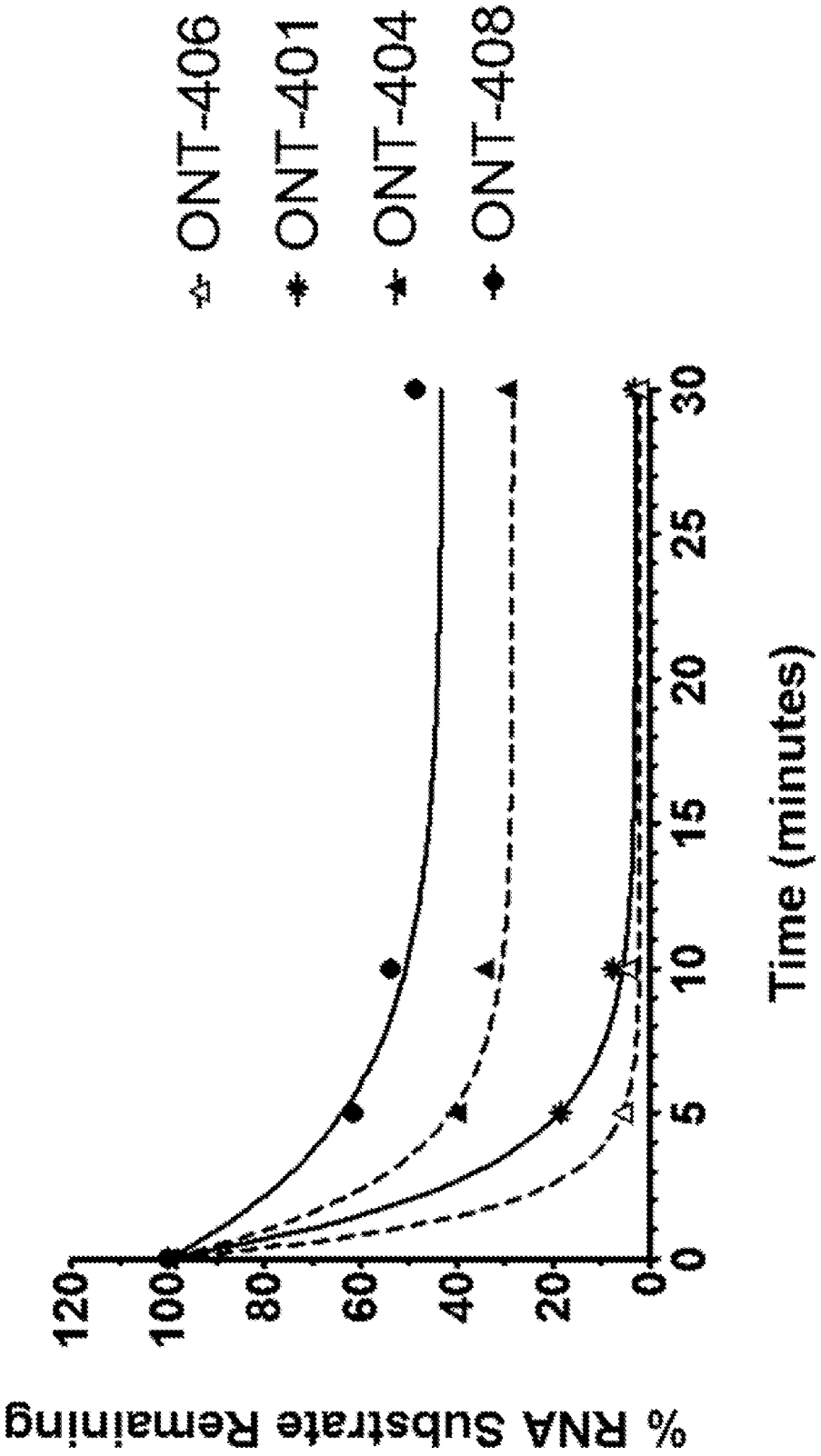
(PANEL C)

FIG. 26 (CONTINUED)



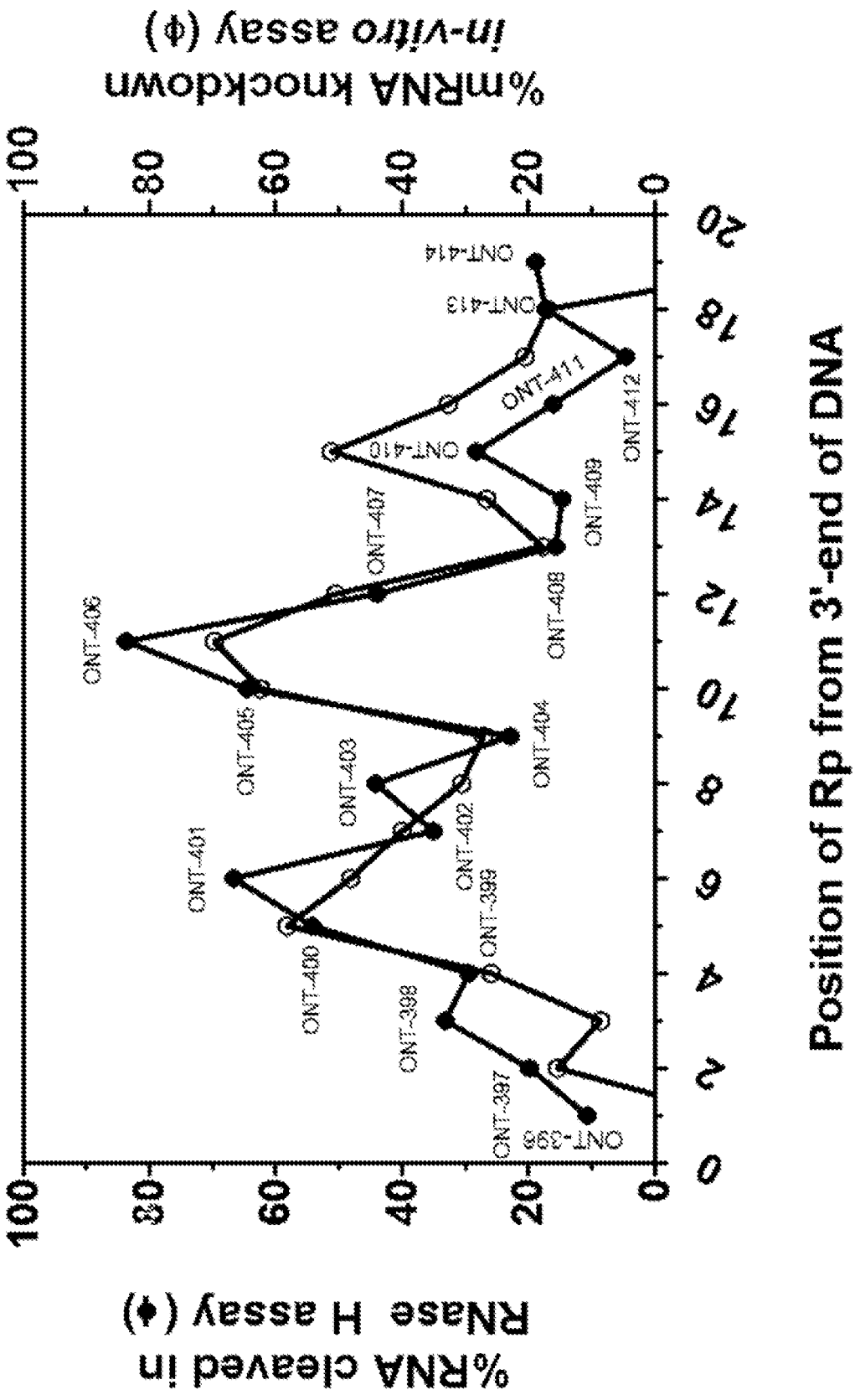
(PANEL D)

FIG. 26 (CONTINUED)



(PANEL A)

FIG. 27



(PANEL B)

FIG. 27 (CONTINUED)

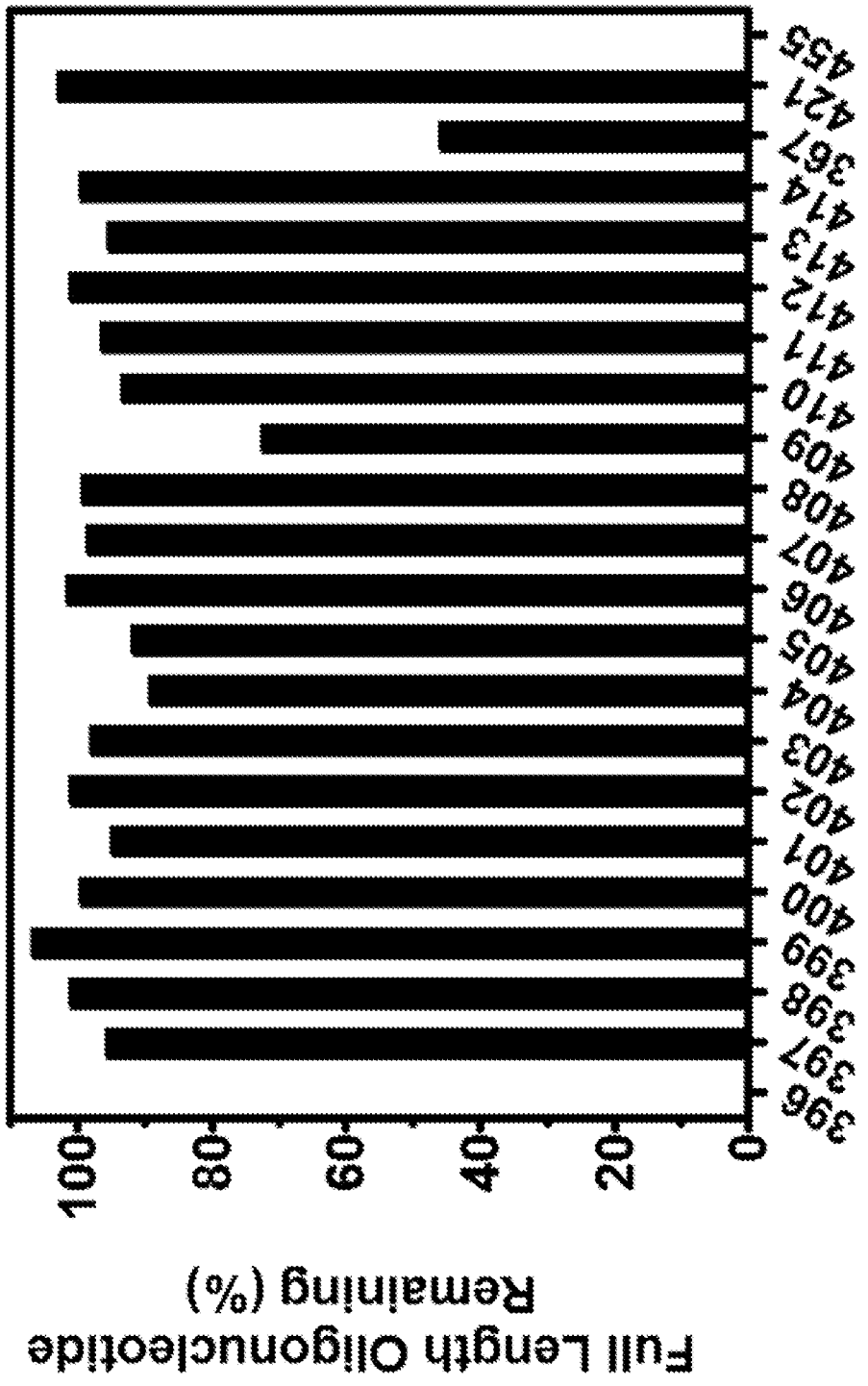
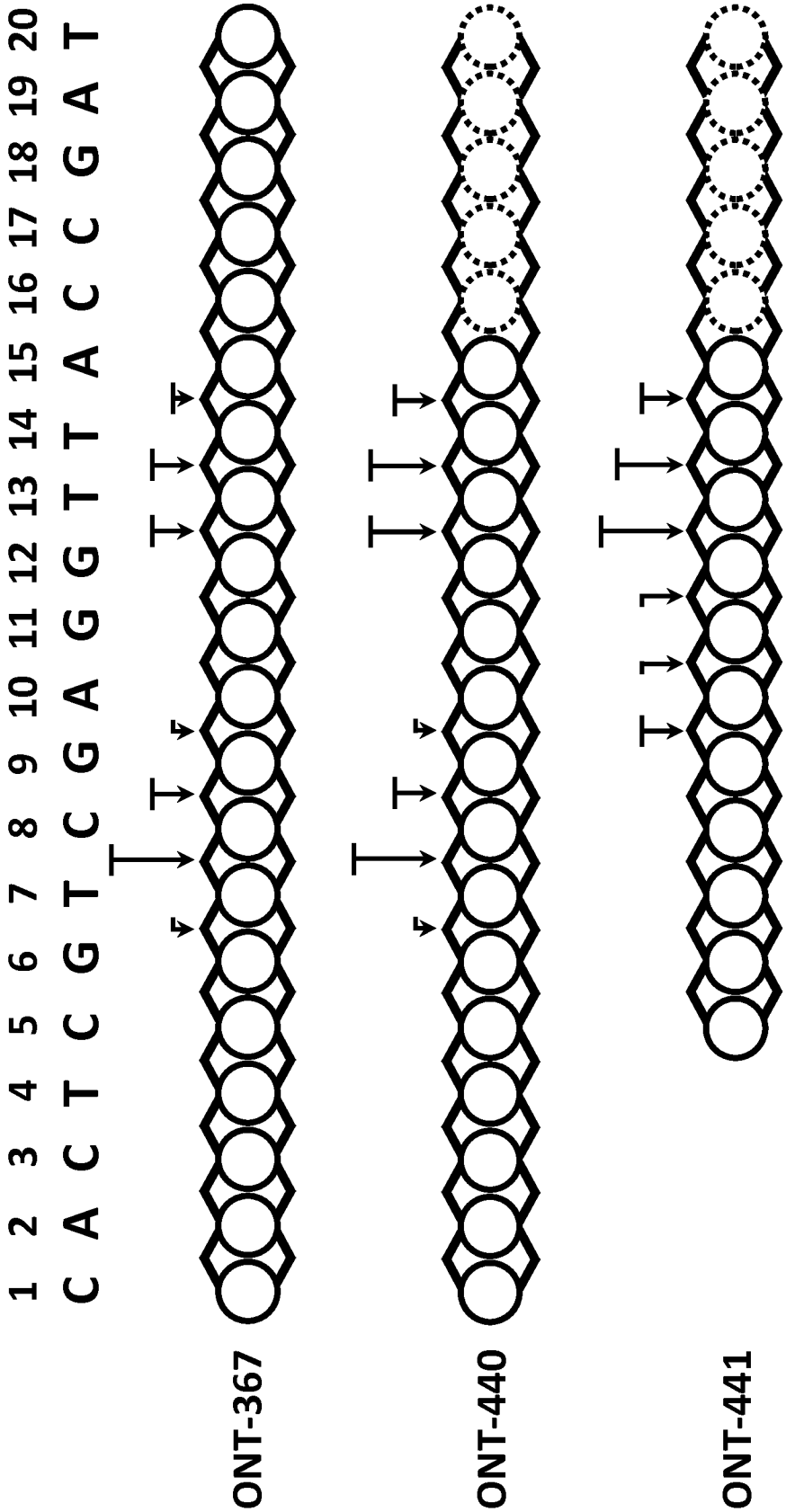
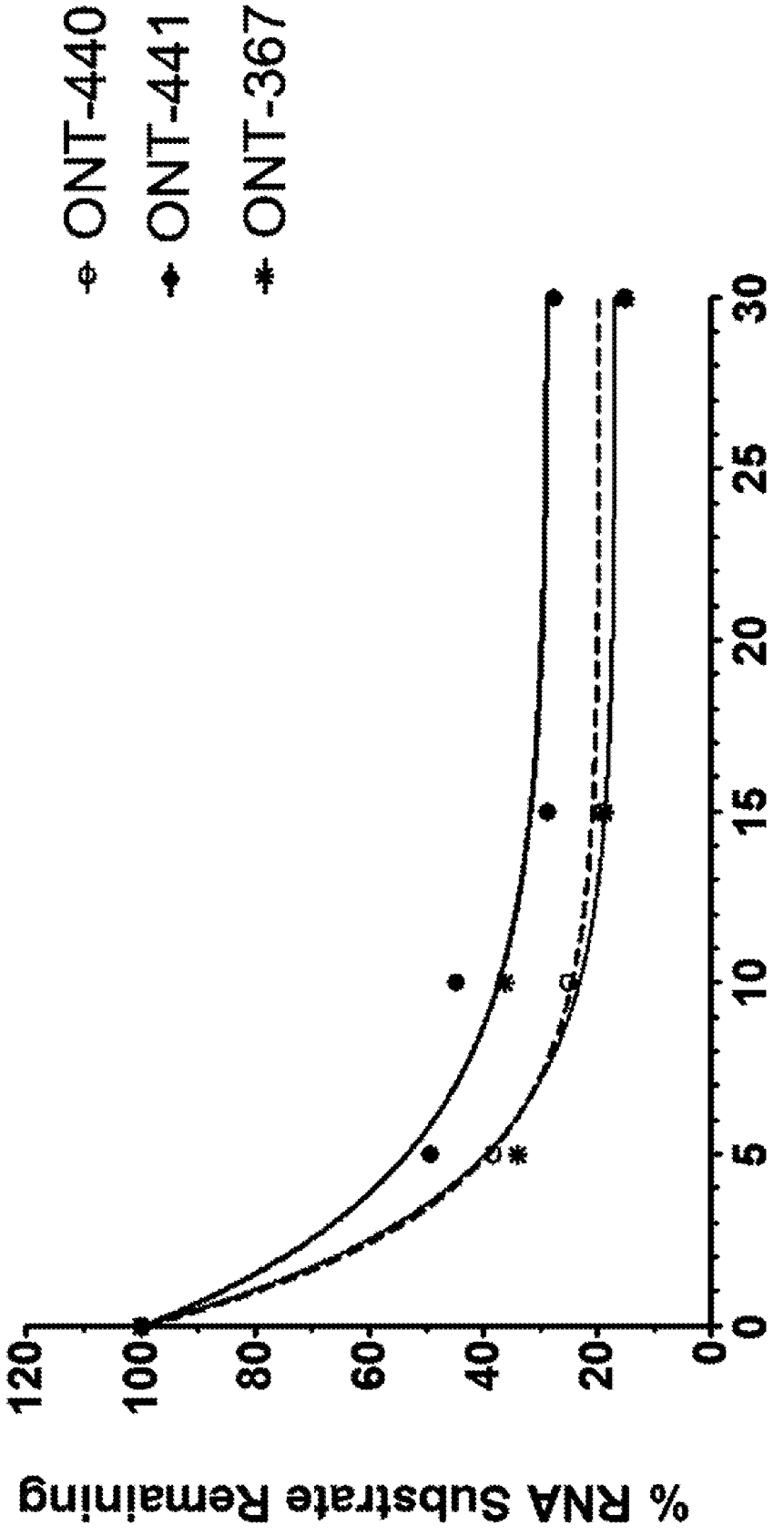

Full Length Oligonucleotide
Remaining (%)
100
80
60
40
20
0
396
397
398
399
400
401
402
403
404
405
406
407
408
409
410
411
412
413
414
367
421
455

FIG. 28



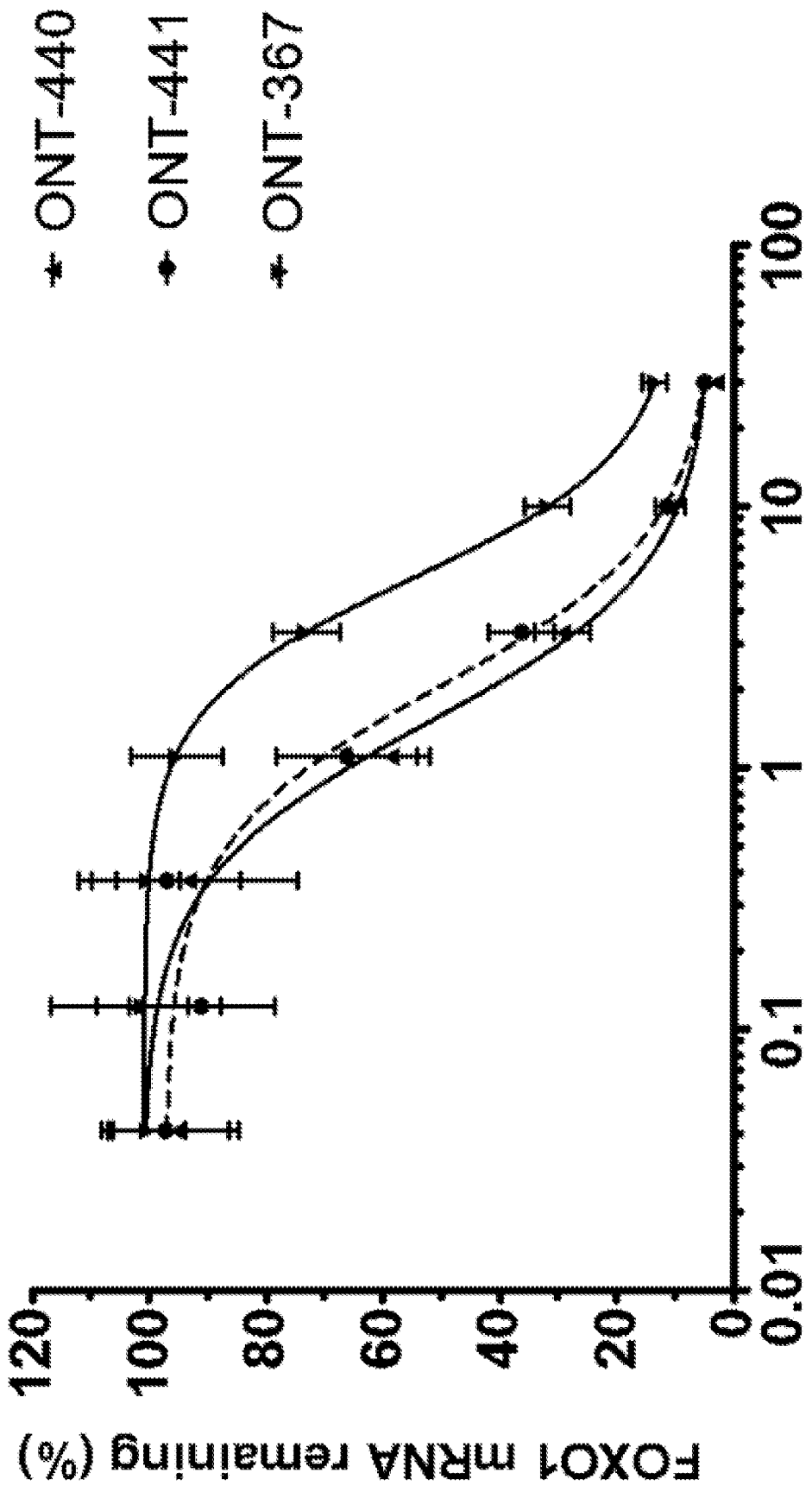
(PANEL A)

FIG. 29



(PANEL B)

FIG. 29 (CONTINUED)



(PANEL C)

FIG. 29 (CONTINUED)

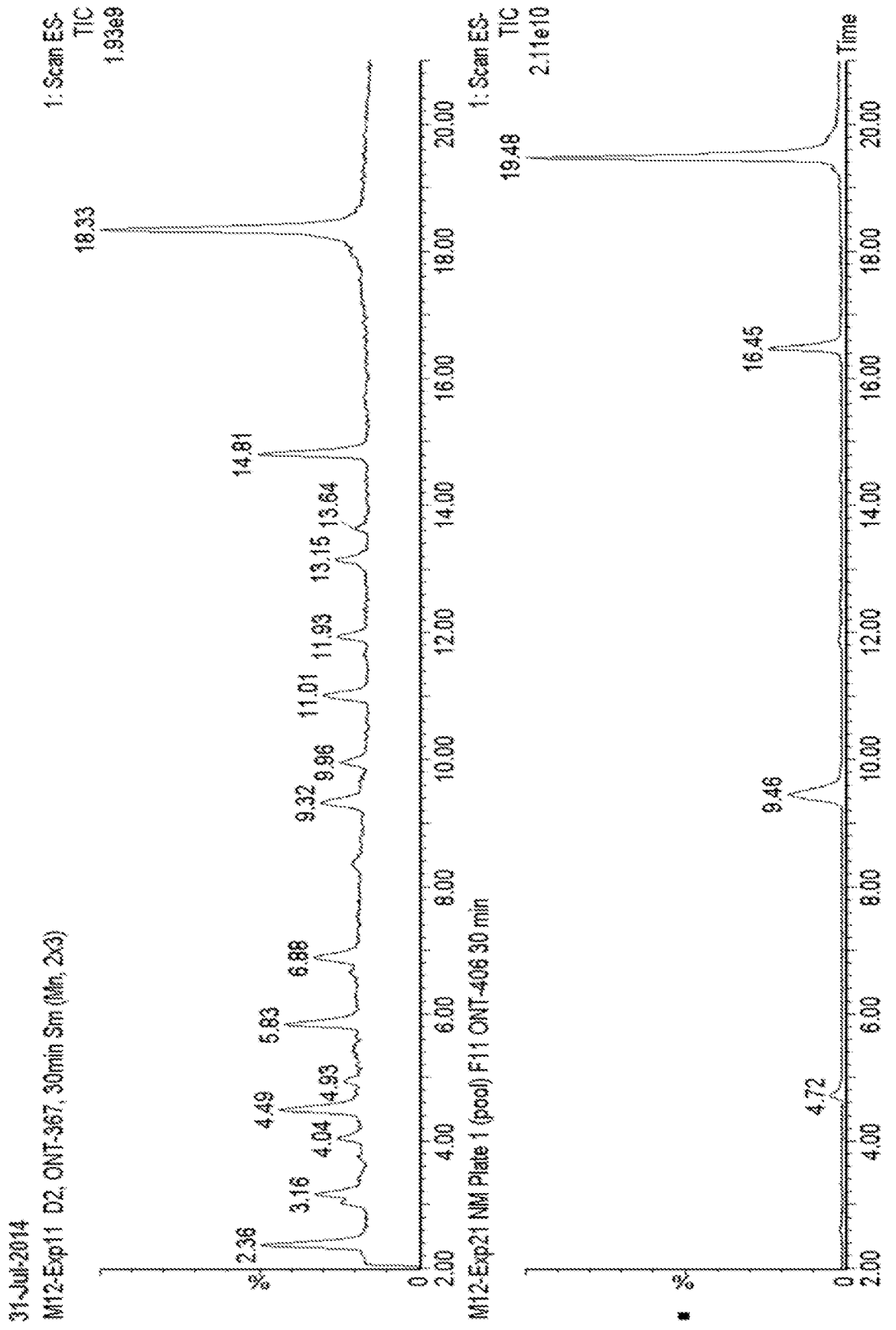

31-Jul-2014
M12-Exp11 D2, ONT-367, 30min Sm (Mn, 2x3)
1: Scan ES-
TIC
1.93e9
18.33
14.81
13.84
13.15
11.93
11.01
9.96
9.32
6.88
5.83
4.93
4.49
4.04
3.16
2.36
%
0
2.00
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
20.00
M12-Exp21 NM Plate 1 (pool) F11 ONT-406 30 min
1: Scan ES-
TIC
2.11e10
19.48
16.45
9.46
4.72
%
0
2.00
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
20.00
Time

FIG. 30