

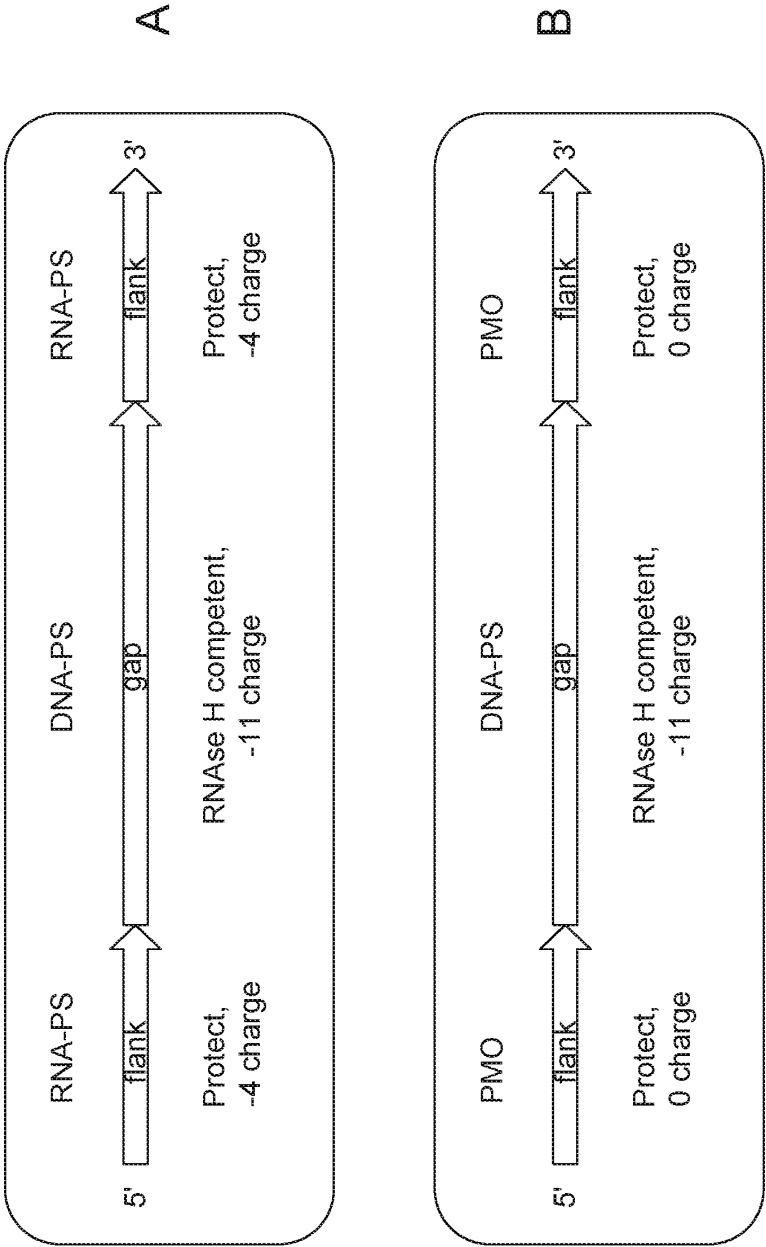
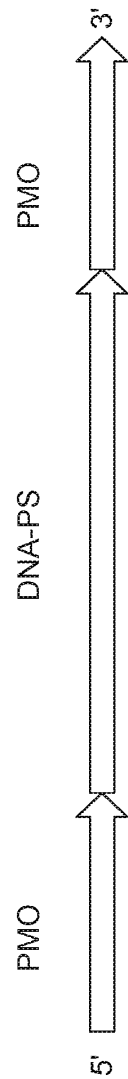


Figure 1



	PMO-ASO Mixed backbone	PMO Neutral backbone	ASO(PS) Negatively charged backbone
Charge	1-18	0	19
Toxicity	low to moderate	low	high
RNA binding activity	Expect high	high	high
Mechanism activity	Steric block, RNAse H	Steric block	Steric block, RNAse H
In vivo delivery	Free uptake	Requires assistance	Free uptake

Figure 2

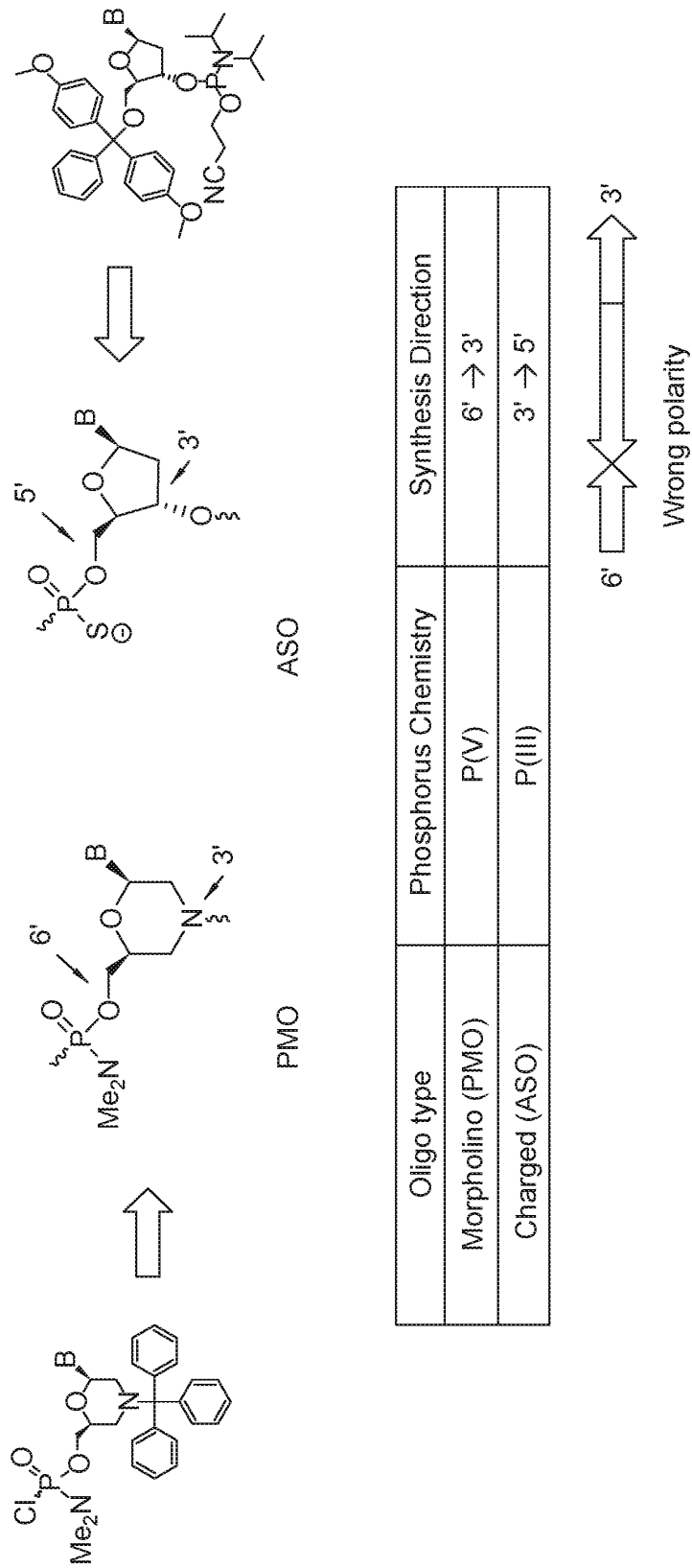
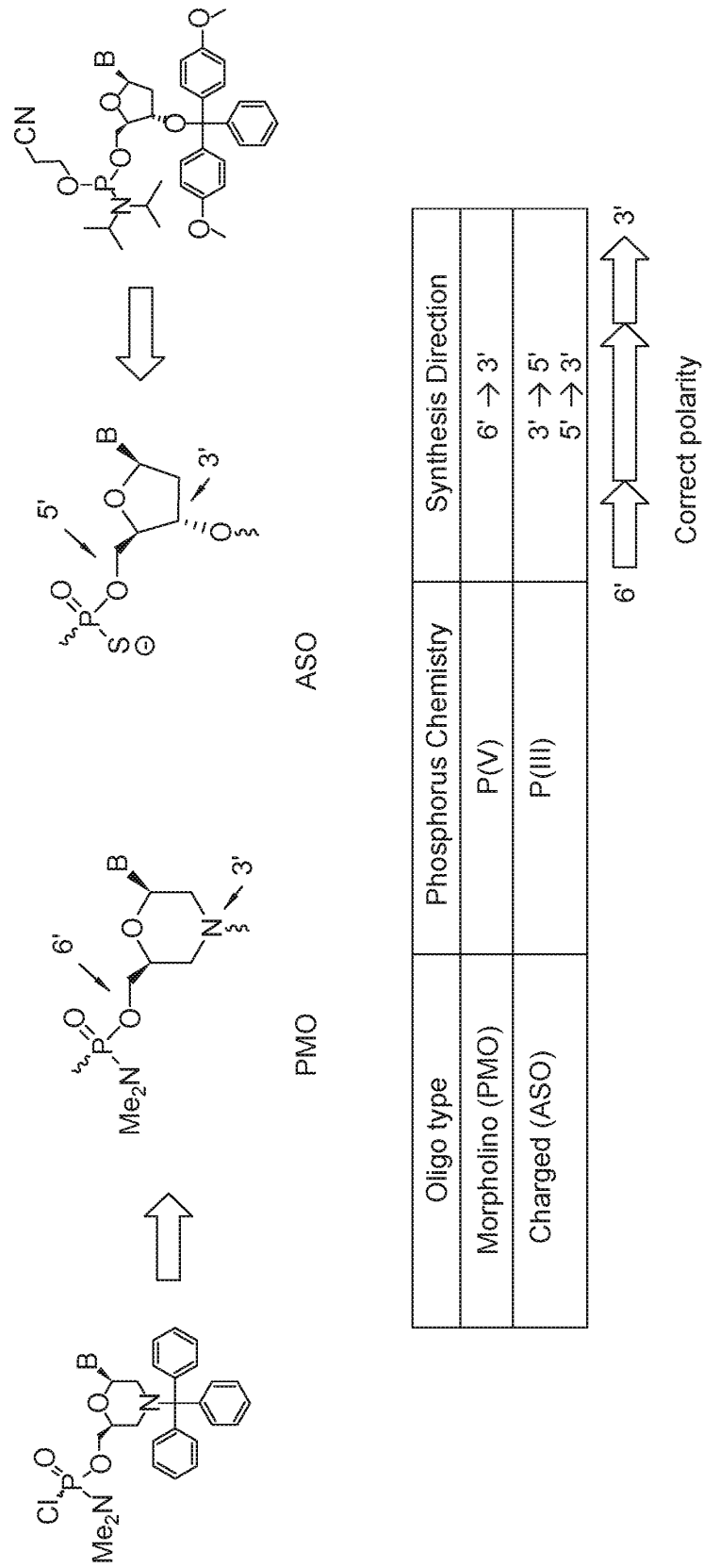


Figure 3



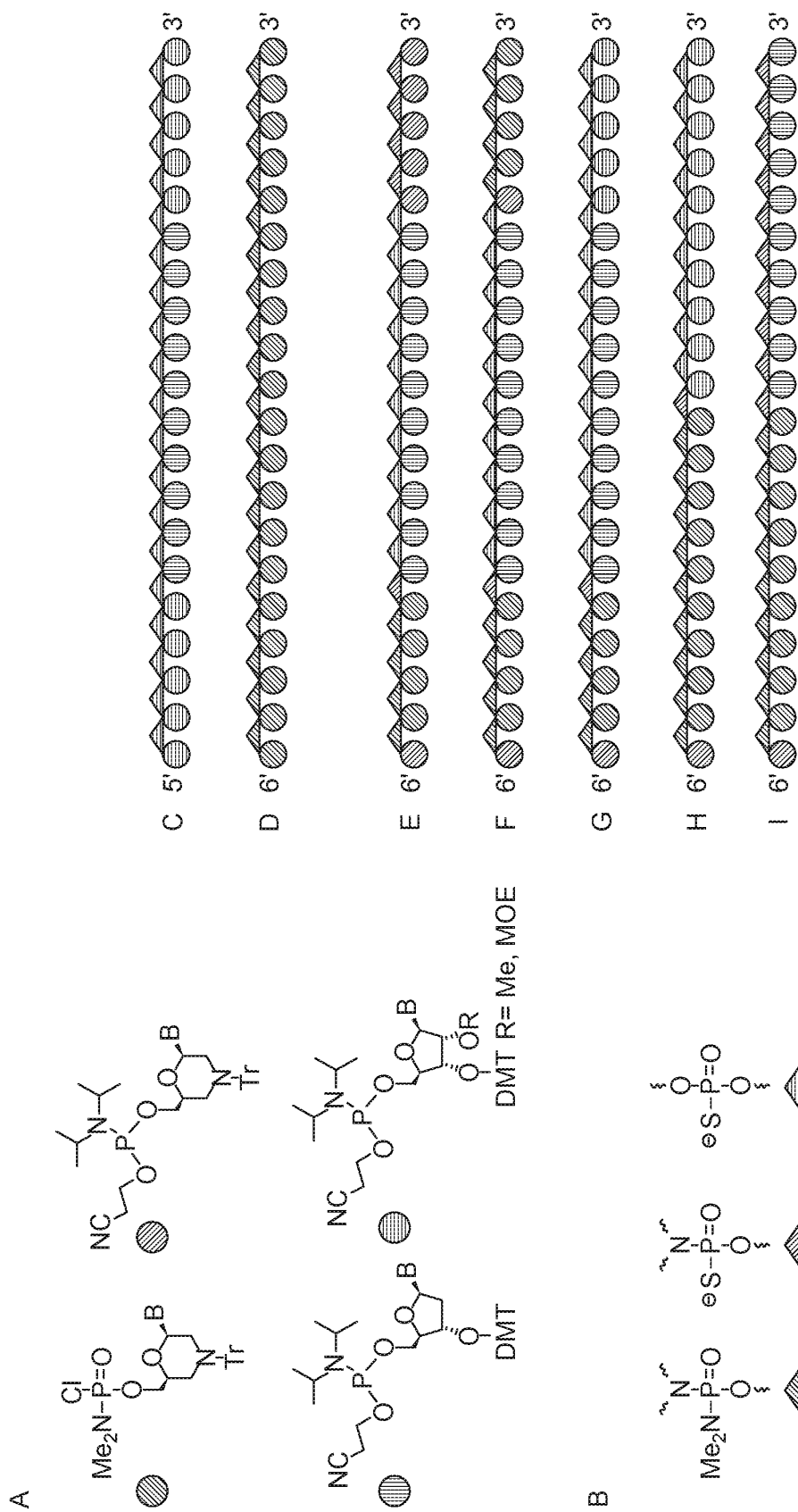
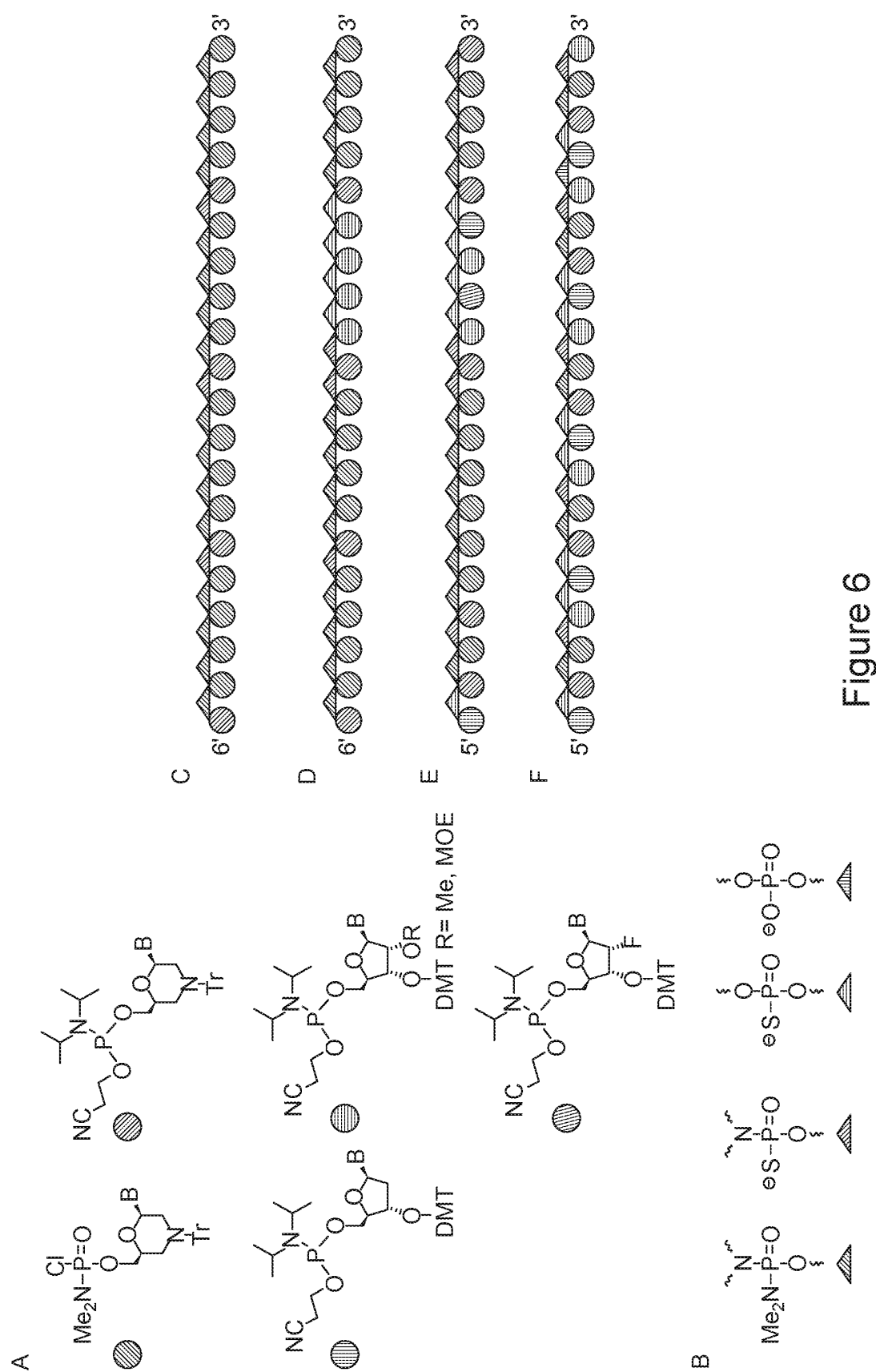


Figure 5



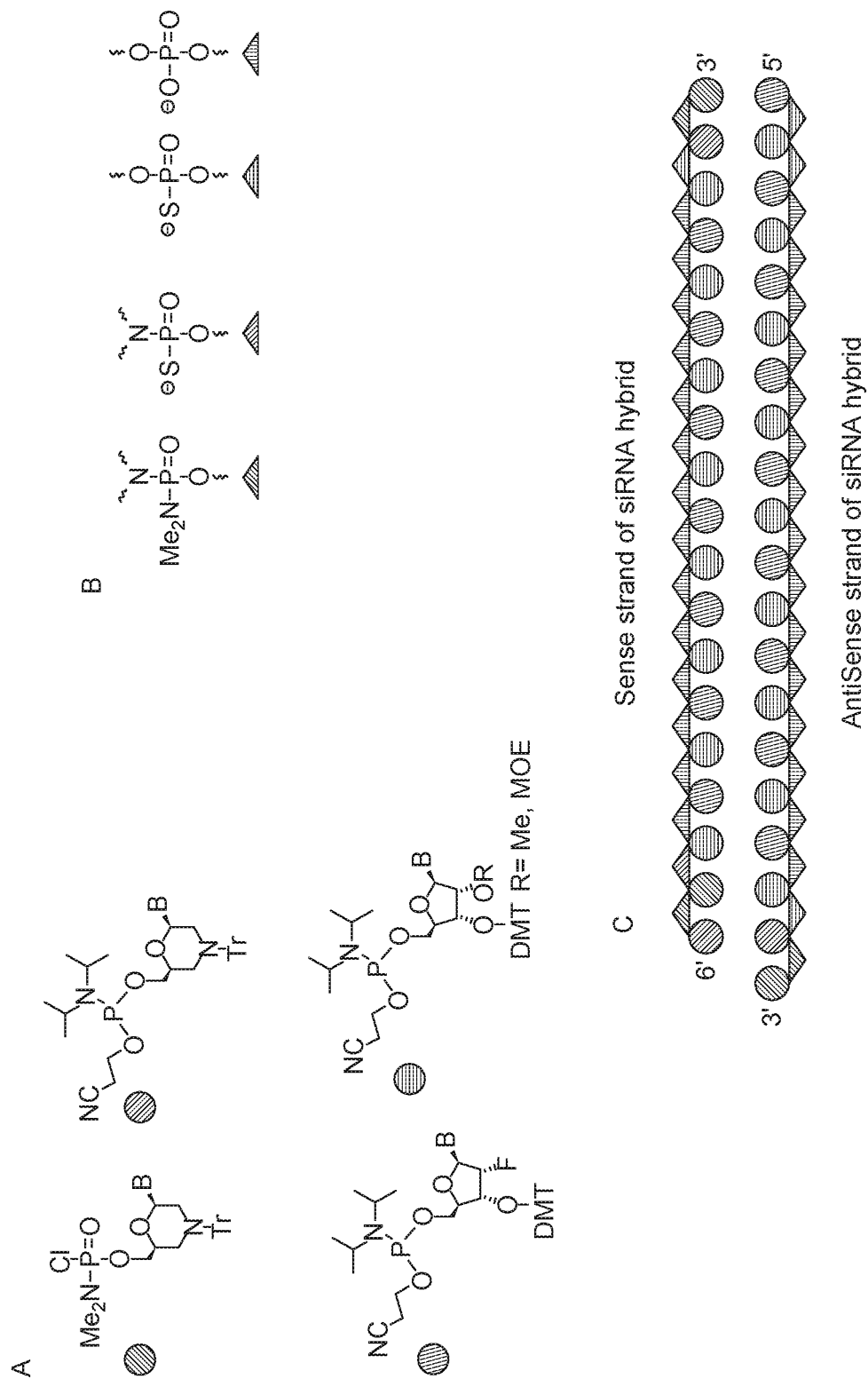


Figure 7

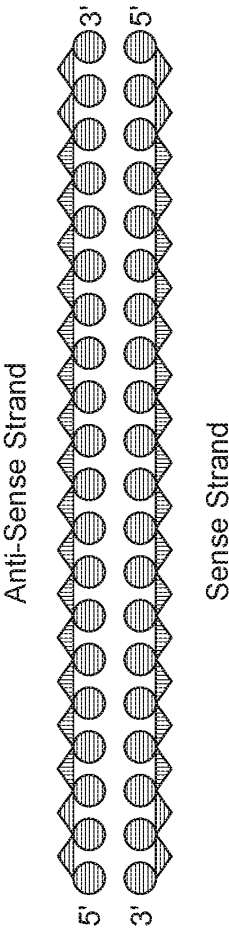


Figure 8

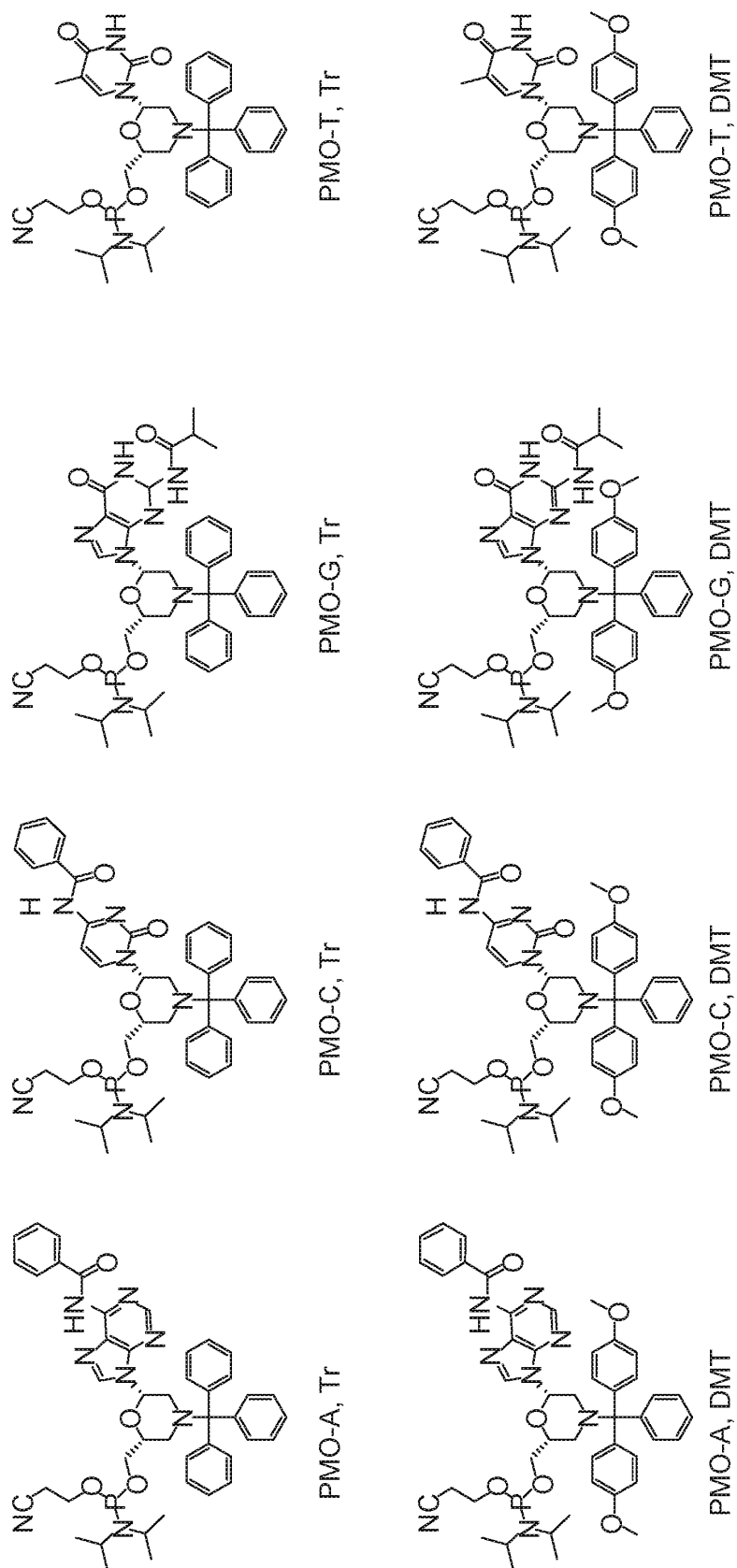
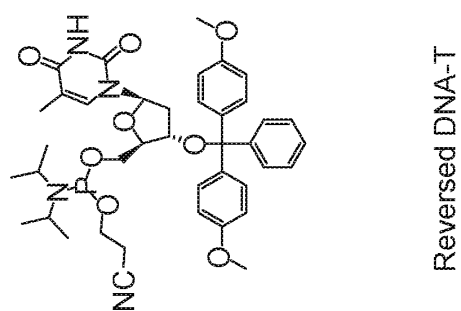
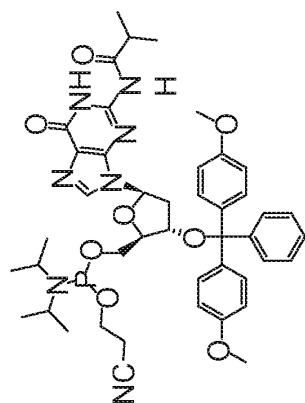


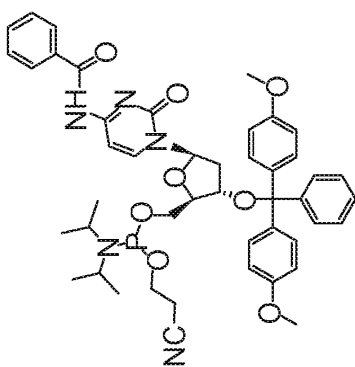
Figure 10



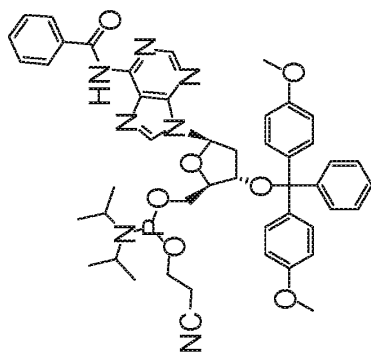
Reversed DNA-T



Reversed DNA-G



Reversed DNA-C



Reversed DNA-A

Figure 11

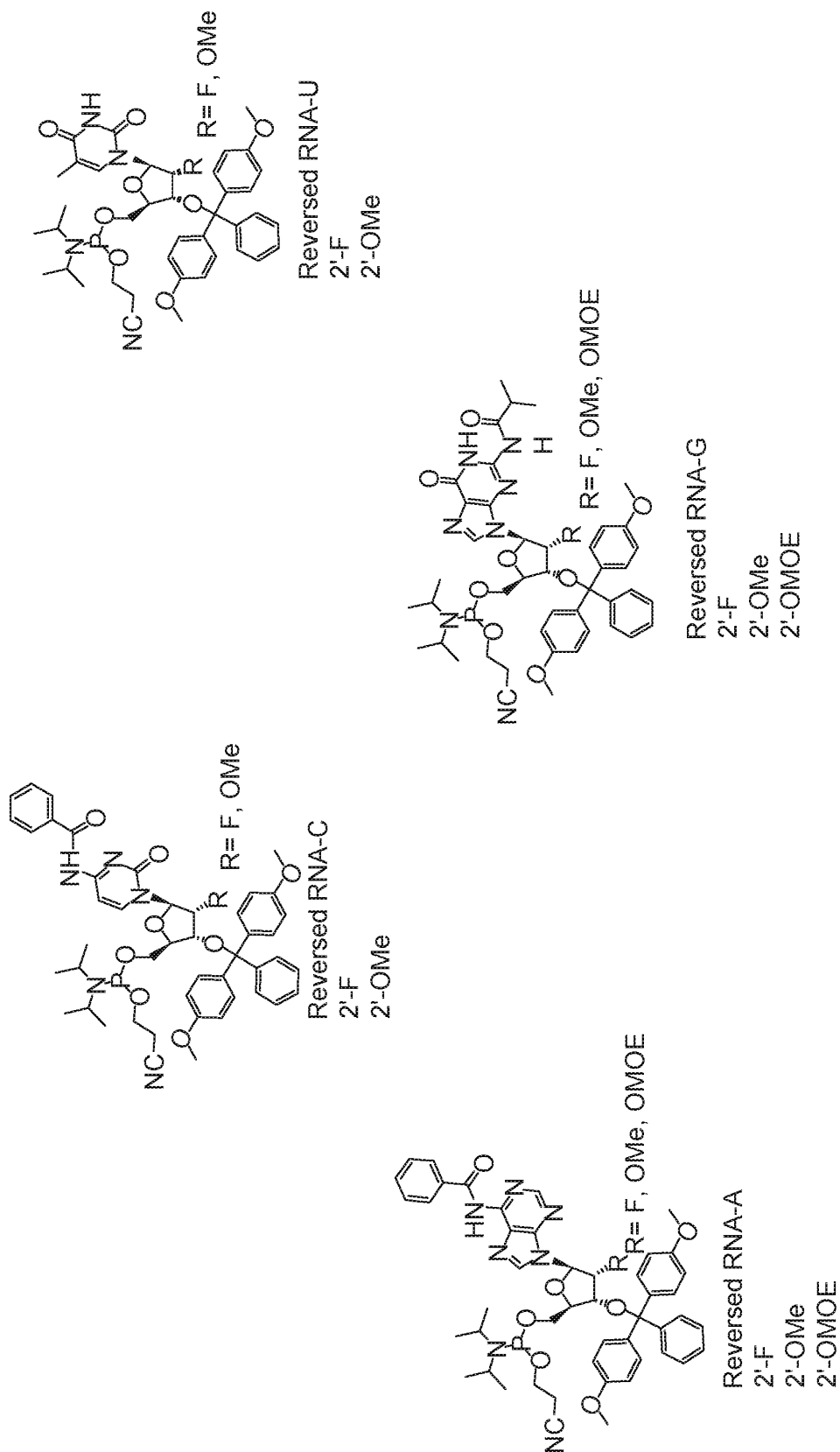


Figure 12

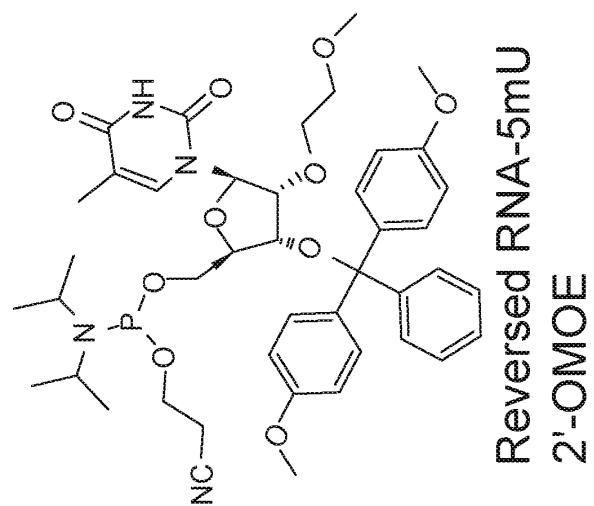
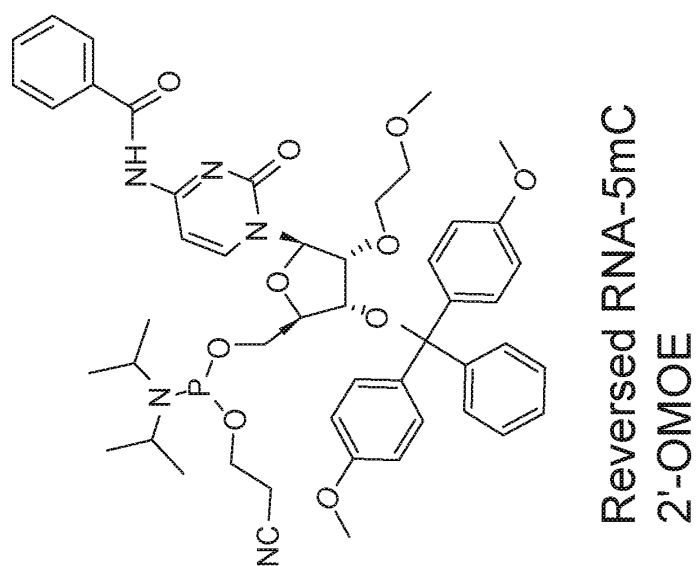


Figure 13

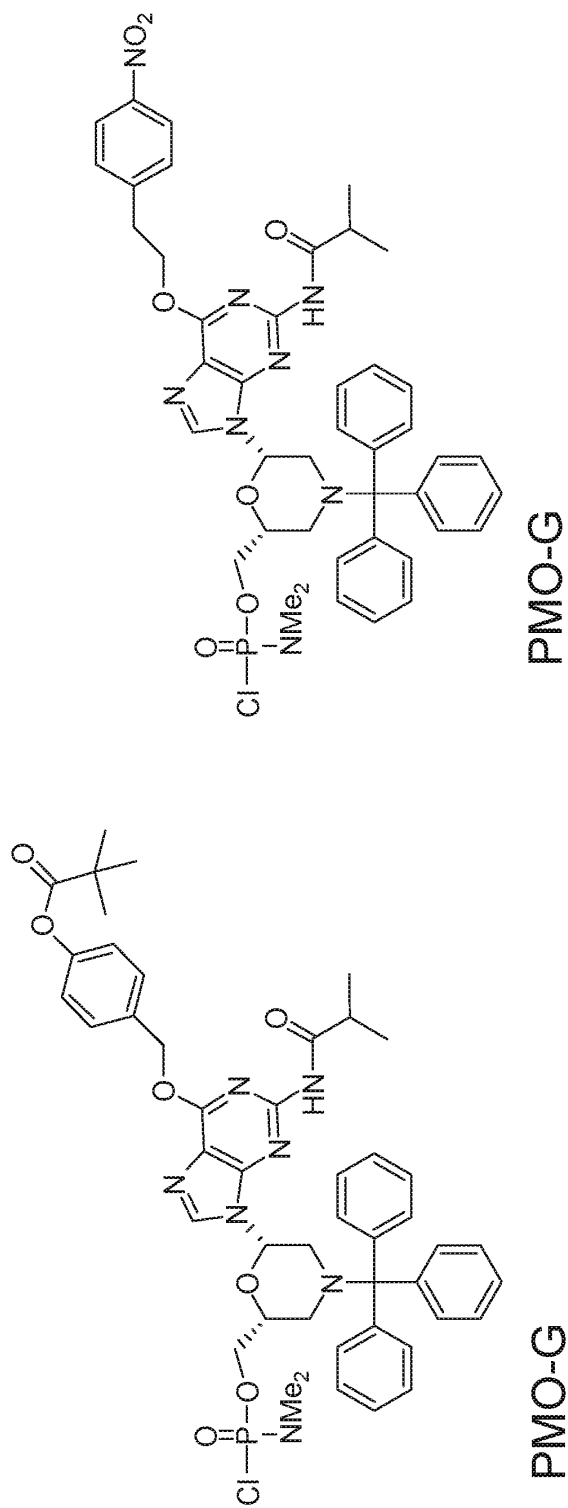


Figure 14

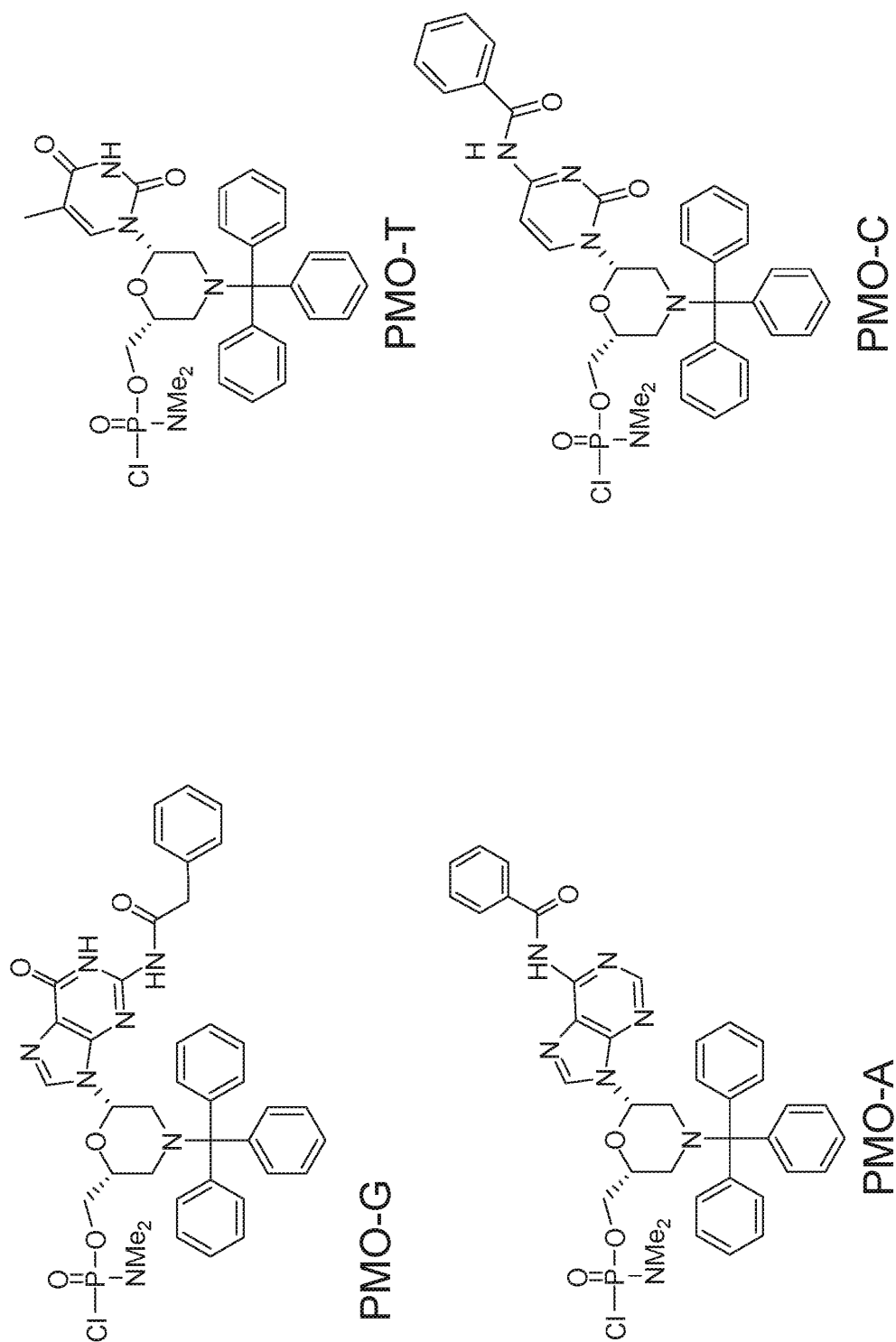


Figure 15

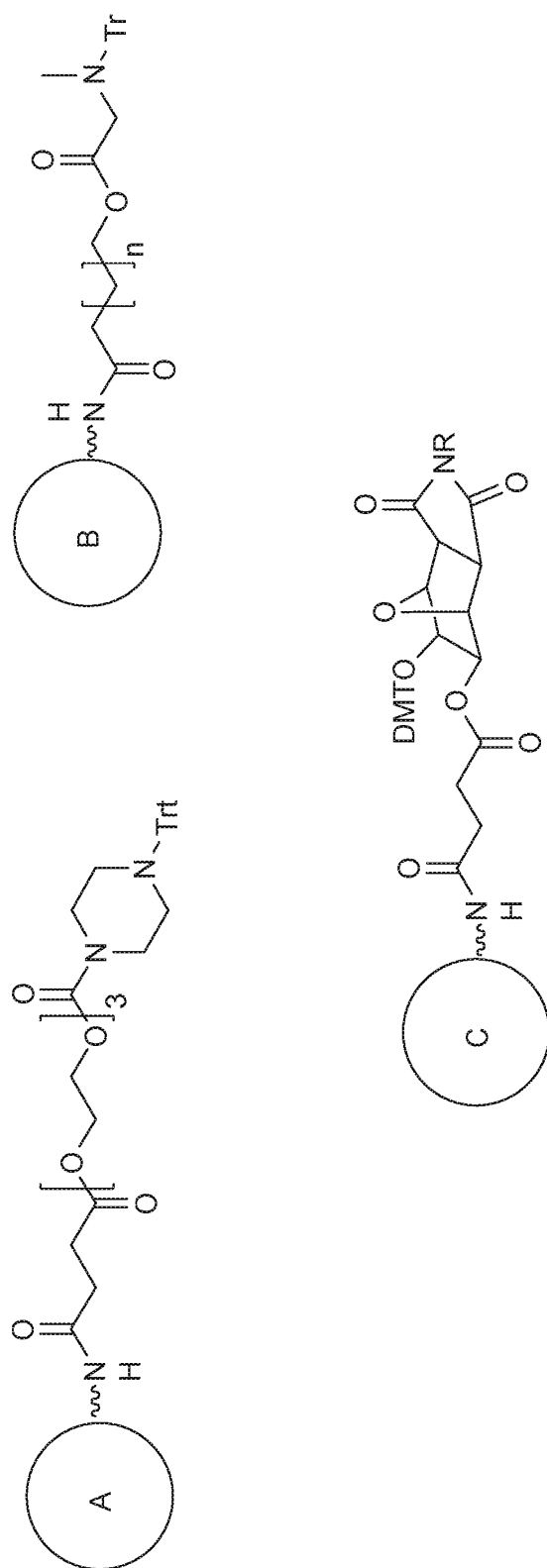


Figure 16

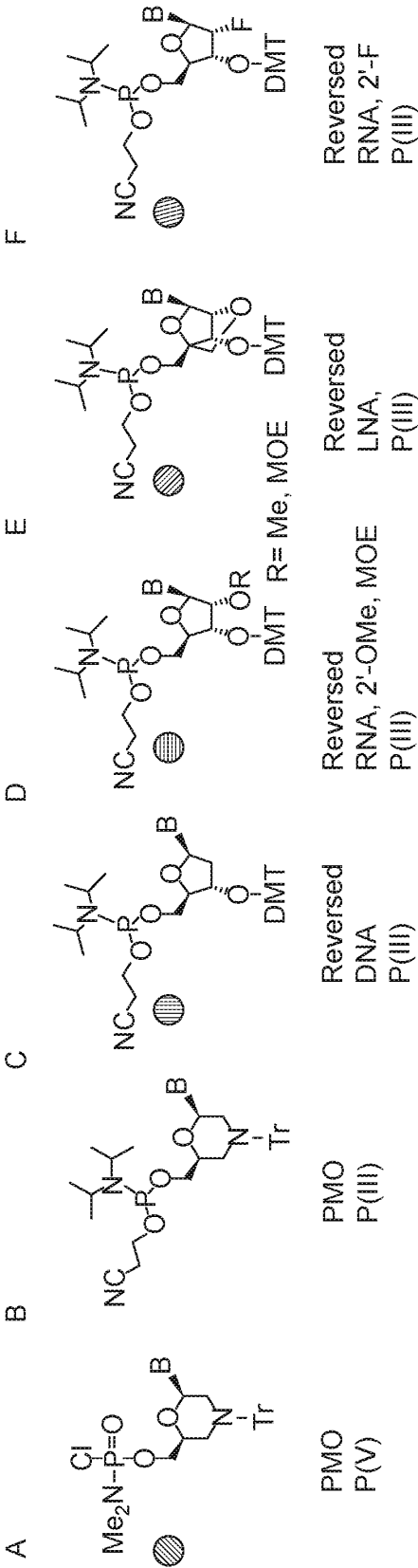


Figure 17

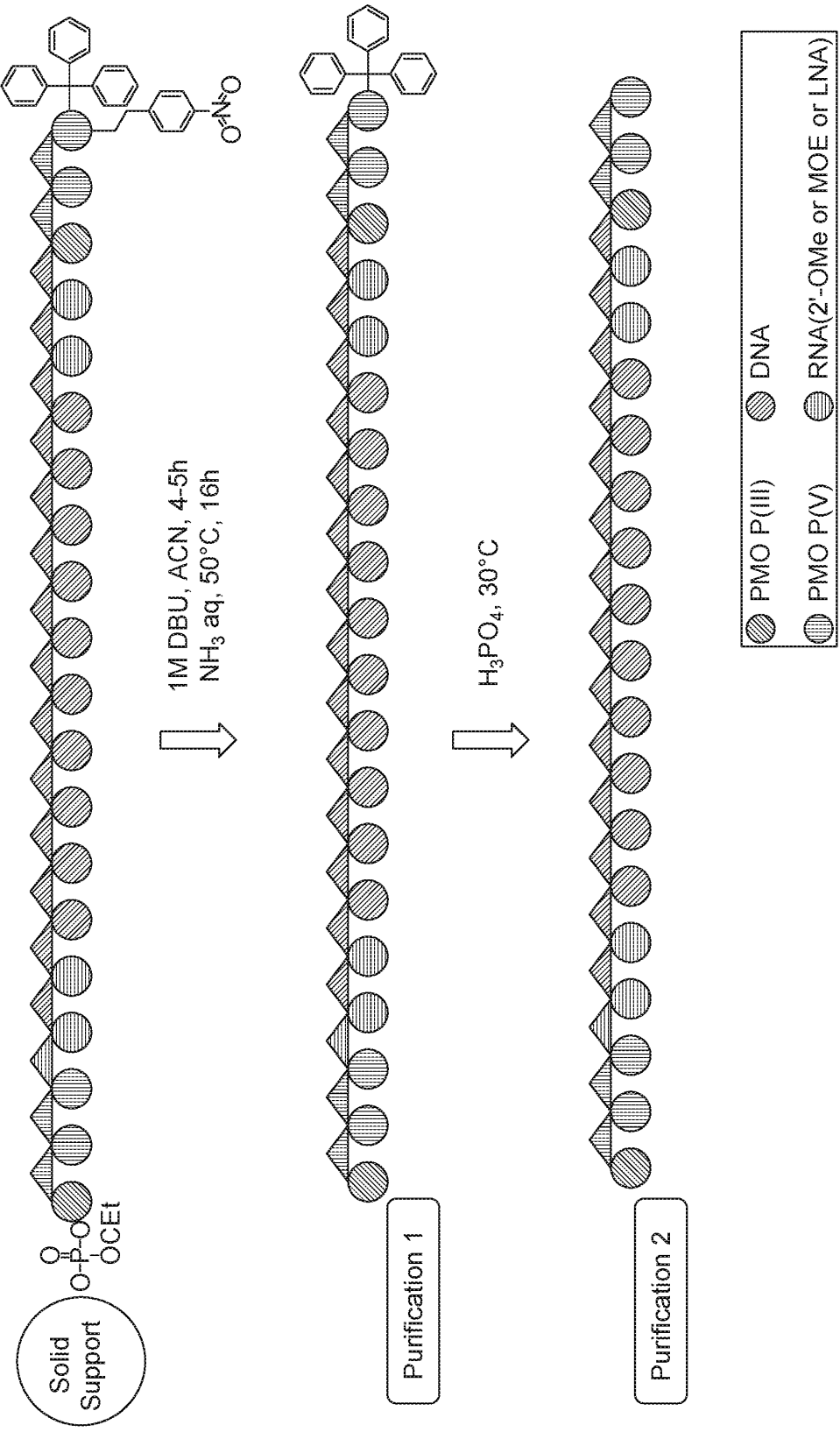
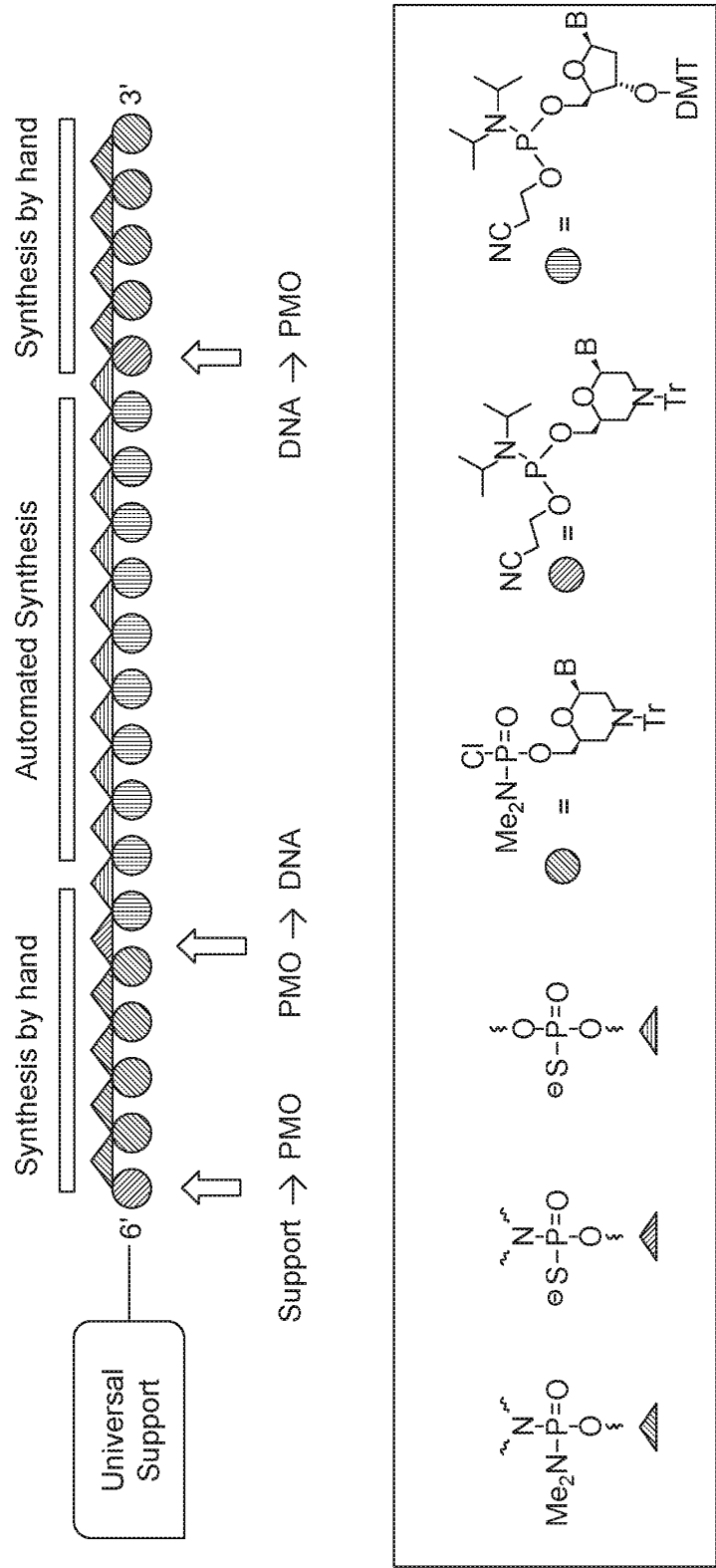


Figure 18



- PMO, DNA monomers
- 3 types of internucleotidic linkages

Figure 19

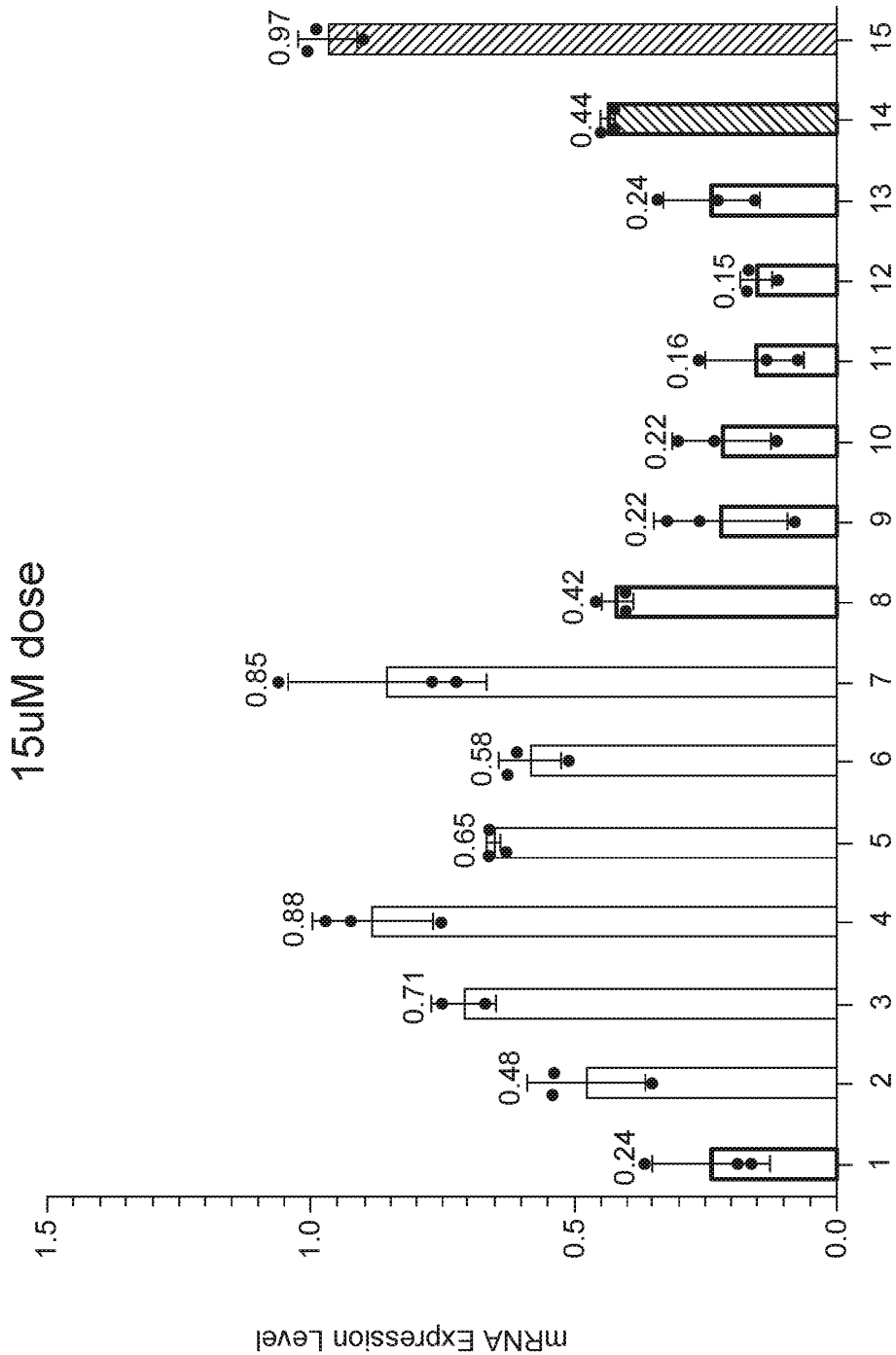


Figure 20

20mer ASO/PMO Hybrid 15uM Dose

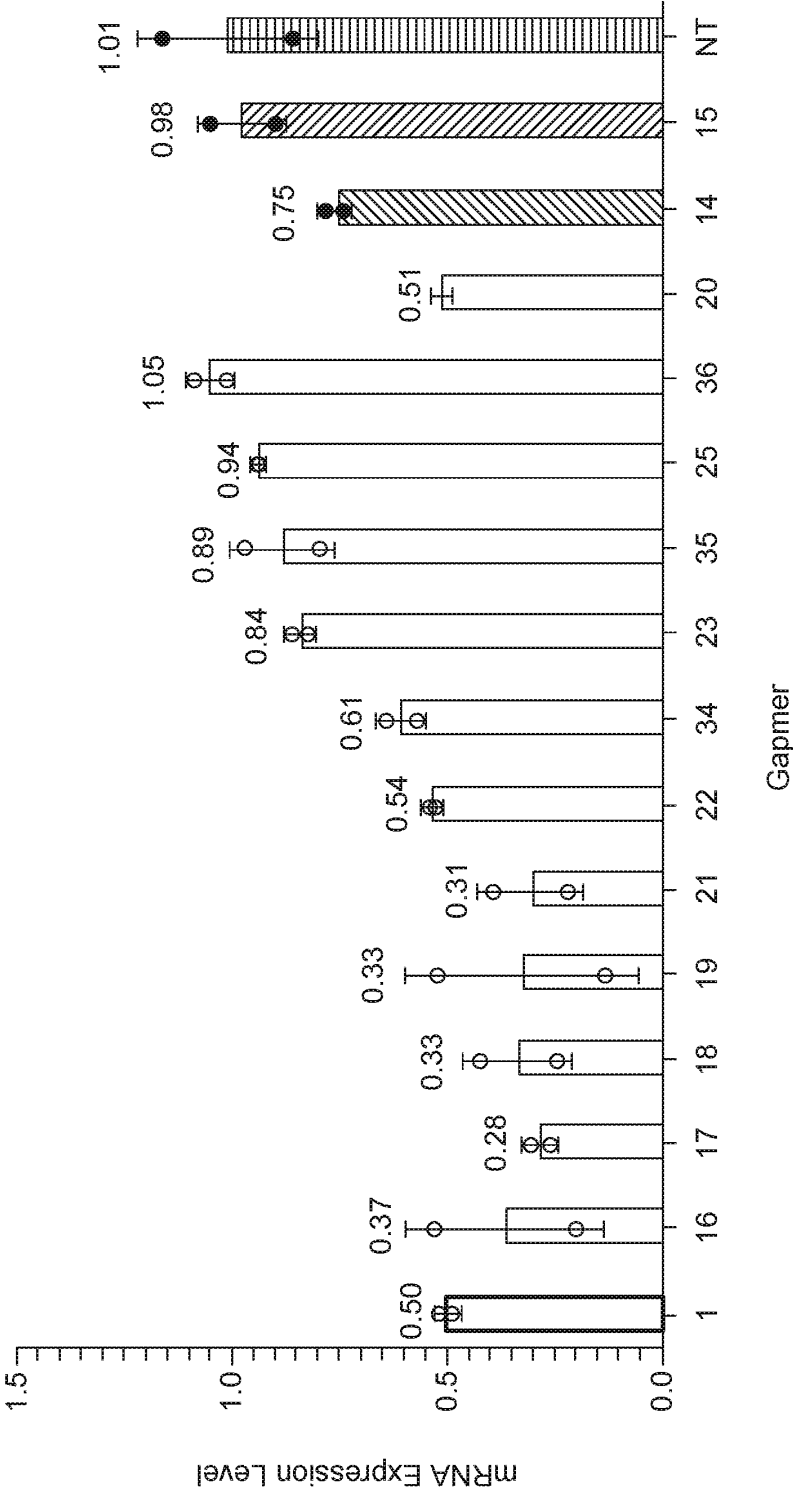


Figure 21

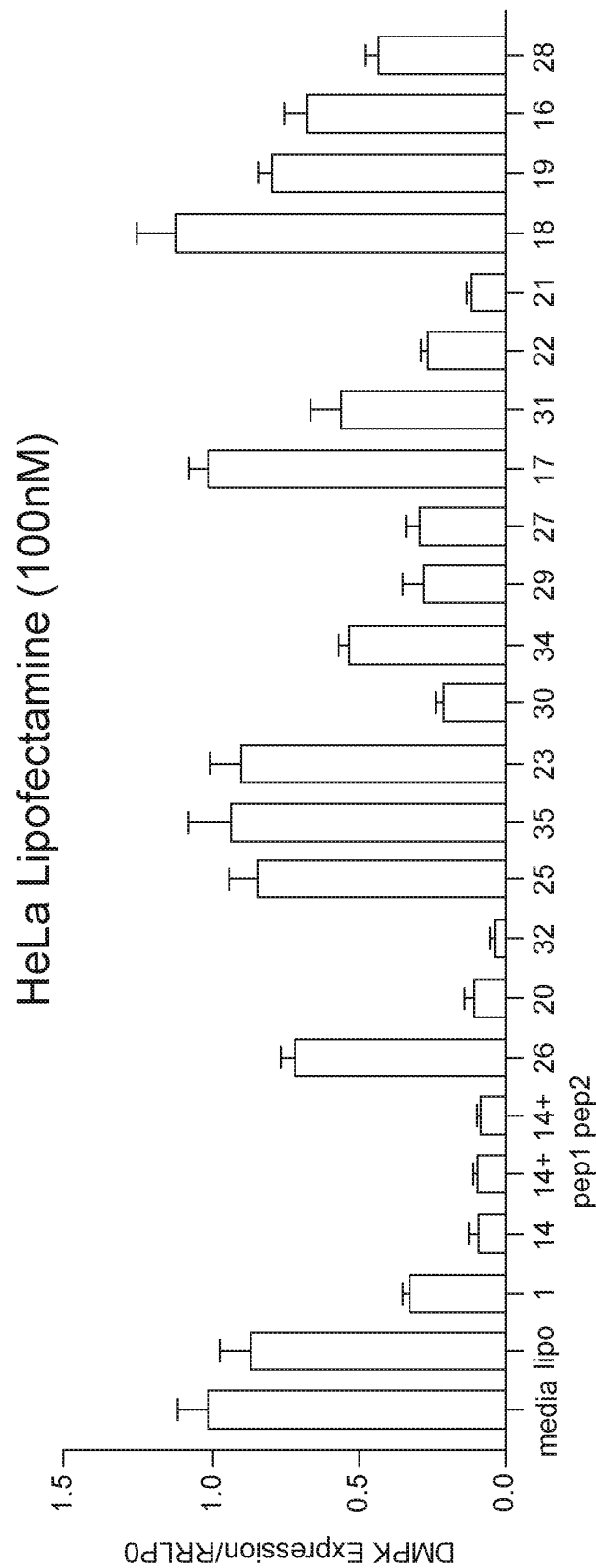


Figure 22

HeLa Lipofectamine (100nM)

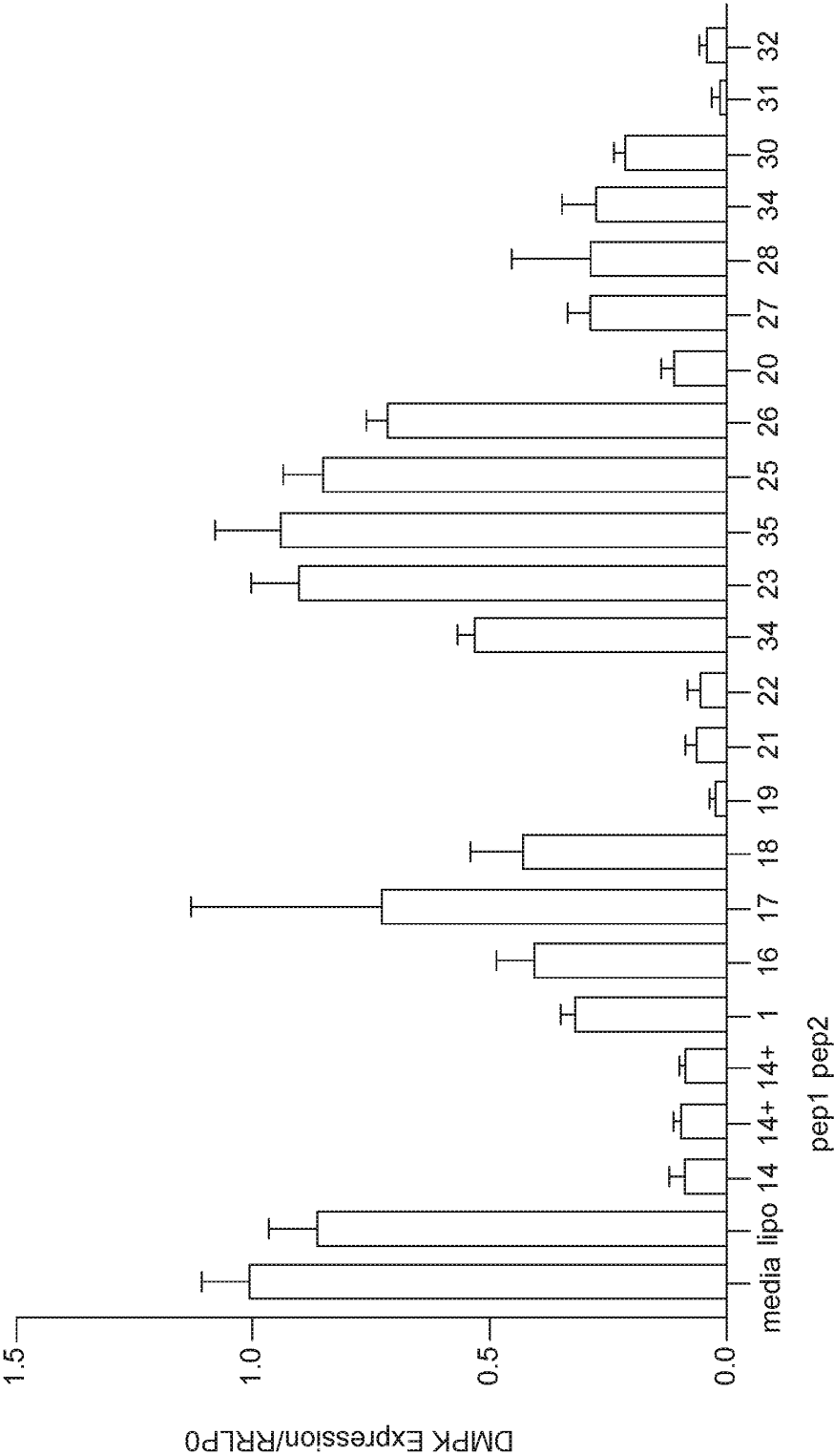


Figure 23



Figure 24

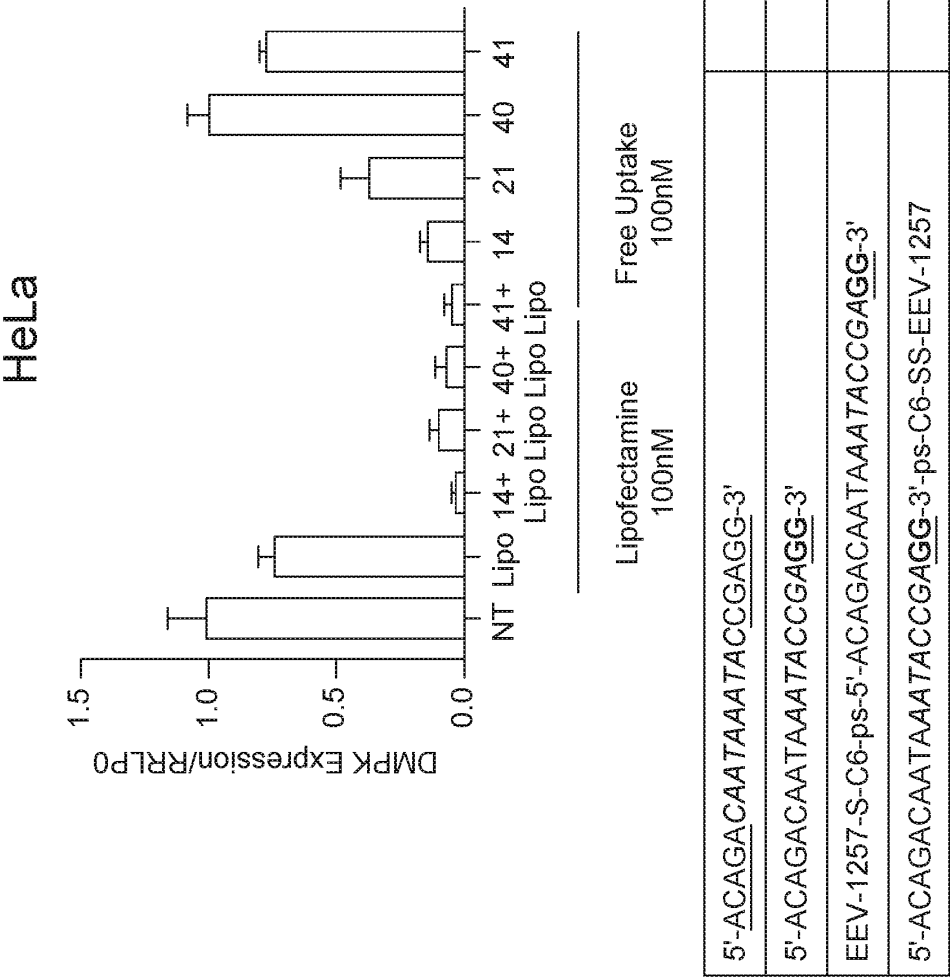
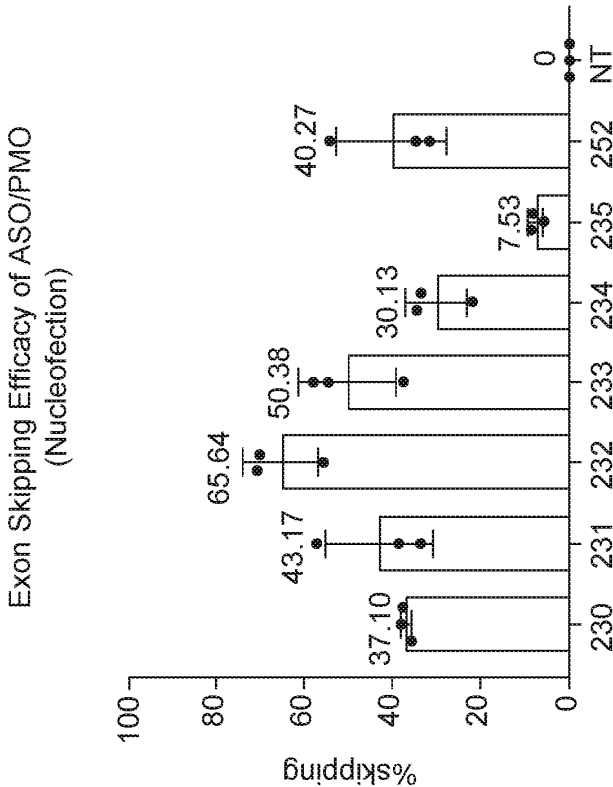
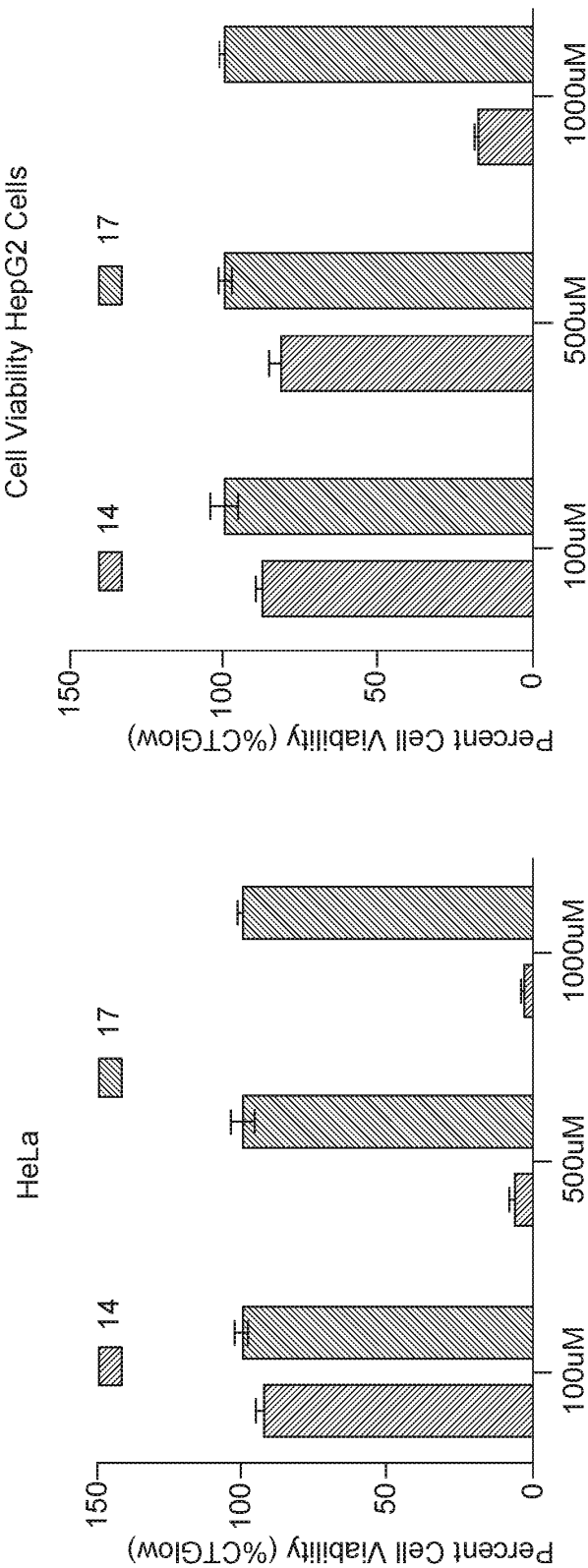


Figure 25



5'-GCUAUUACCUUAACCCAG-3'	48
5'-GCTAUUACCUUAACCCAG-3'	49
5'-GCTATTACCUUAACCCAG-3'	50
5'-GCTATTACCUUAACCCAG-3'	51
5'-GCTATTACCTTAACCCAG-3'	52
5'-GCTATTACCTTAACCCAG-3'	53
5'-GCTATTACCTTAACCCAG-3'	54

Figure 26



5'-ACAGACAA TAAATACCGAGG-3'	14
5'-ACAGACAA TAAATACCGAGG-3'	17
6'-ACAGACAA TAAATACCGAGG-3'	55

Figure 27

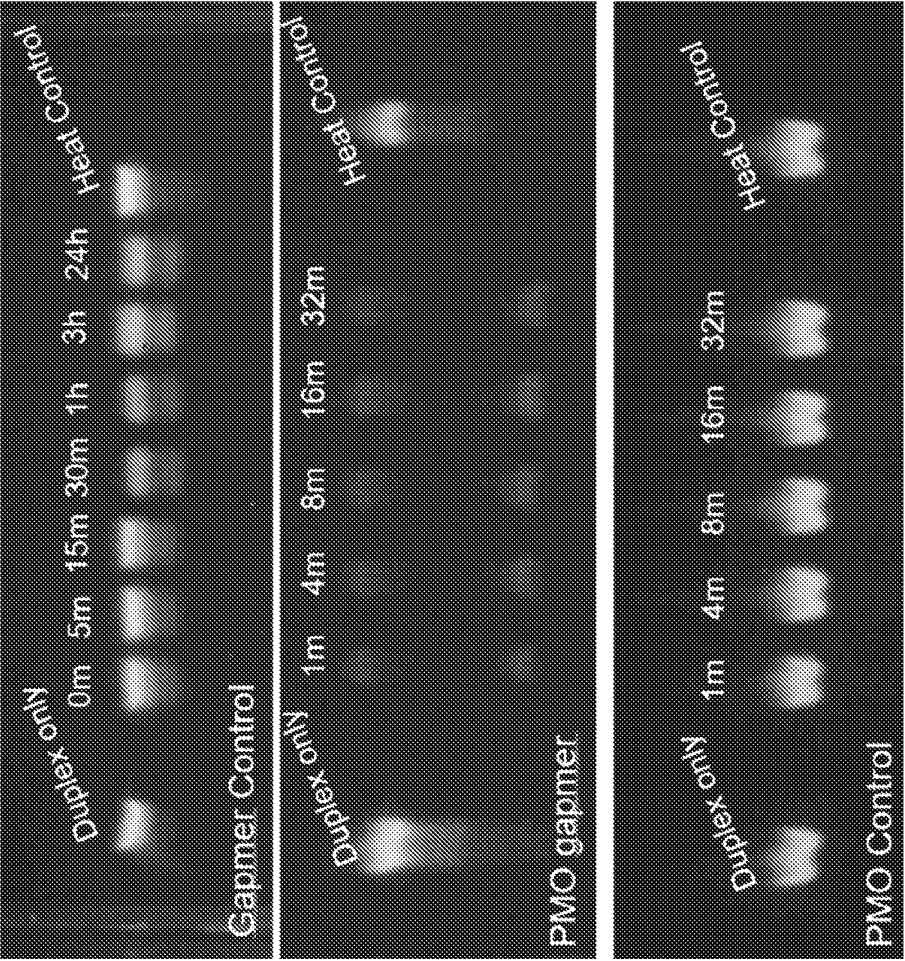
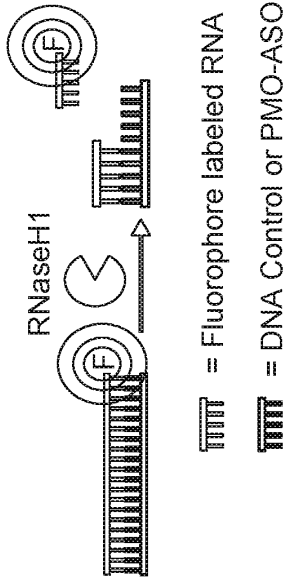


Figure 28



5'- <u>ACAGACAA</u> TAAATACCGAGG-3'	Gapmer control
5'-ACAGACAA <u>TAAATACCGAGG</u> -3'	PMO gapmer
5'-ACAGACAAATAAATACCGAGG-3'	PMO control

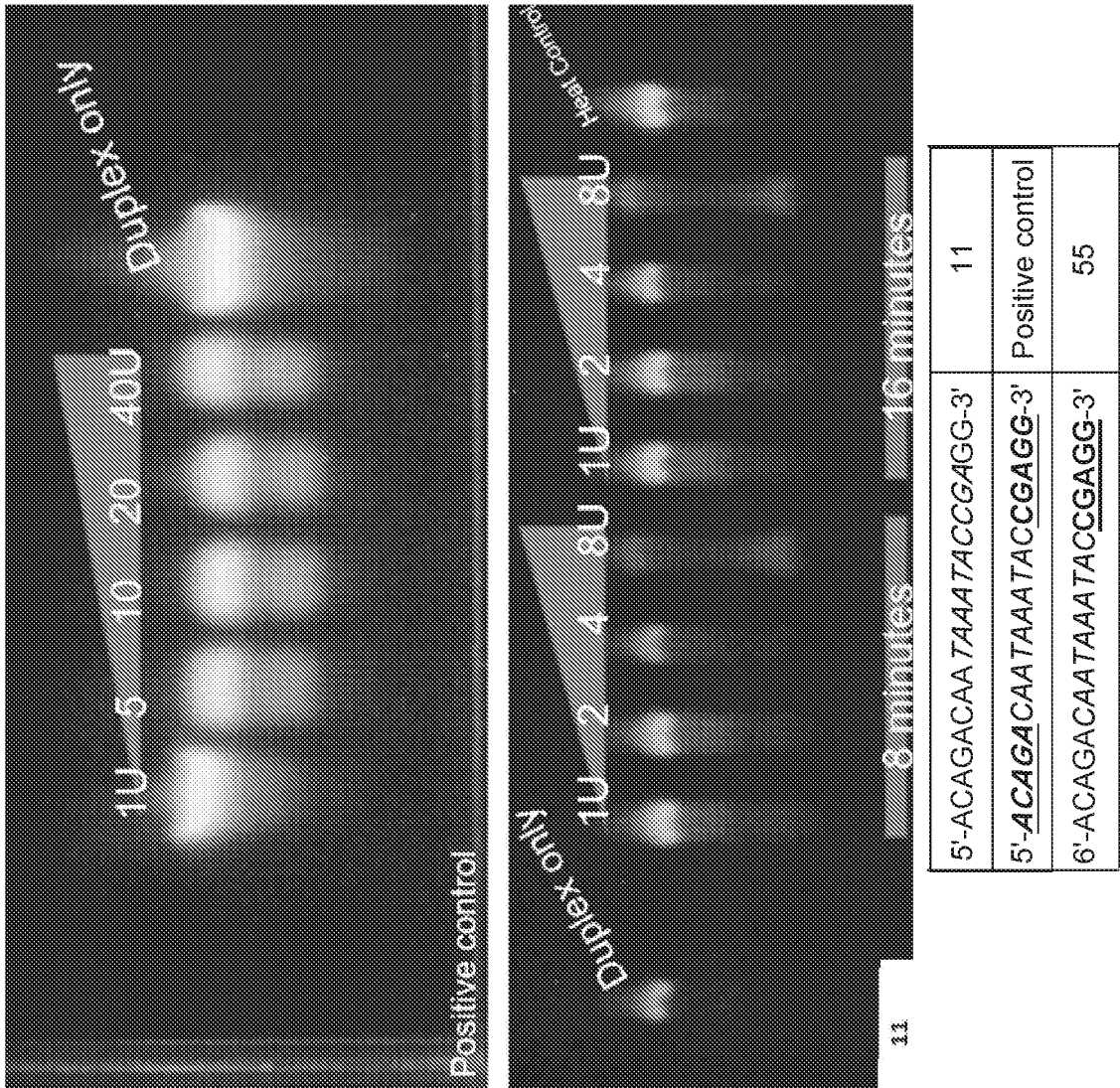


Figure 29

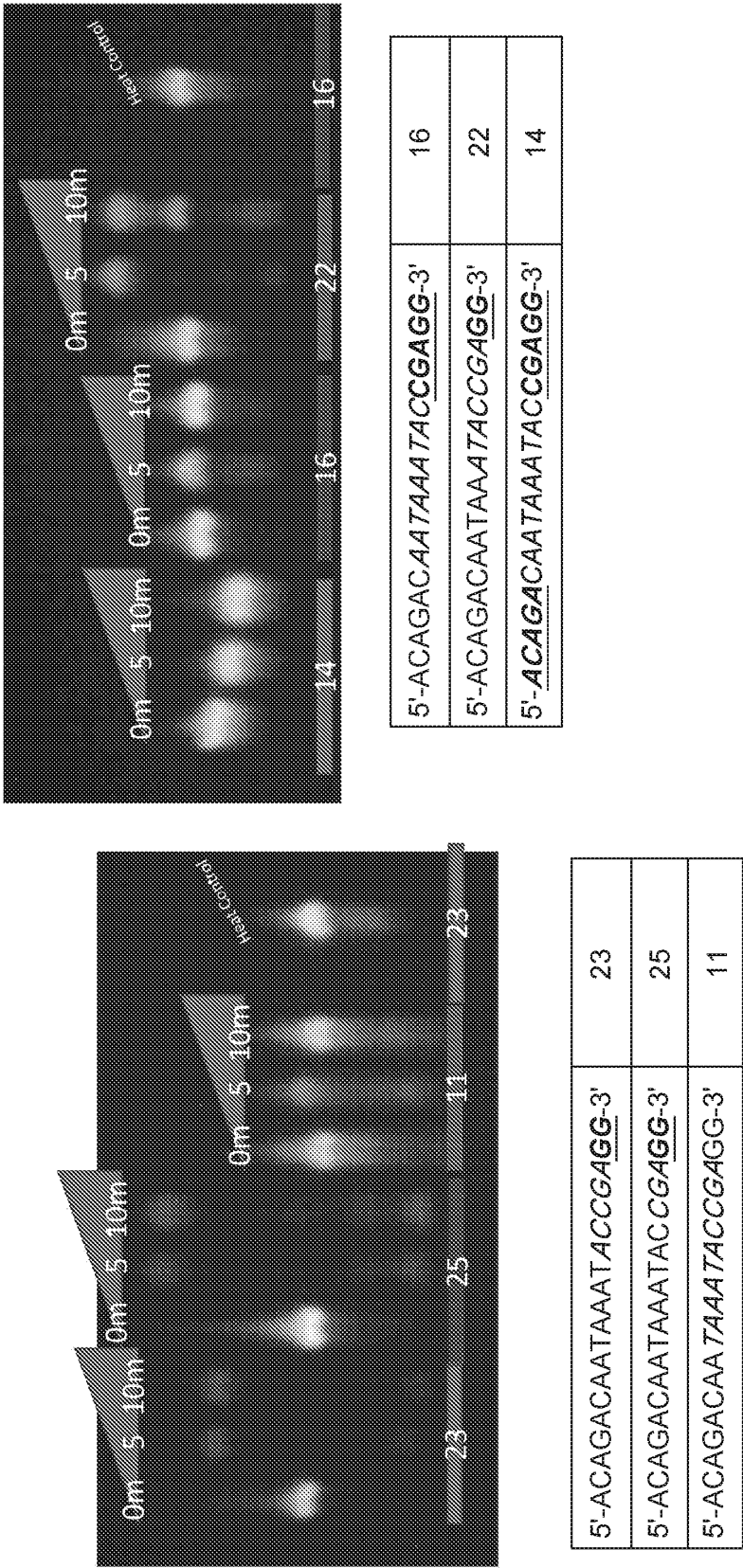


Figure 30

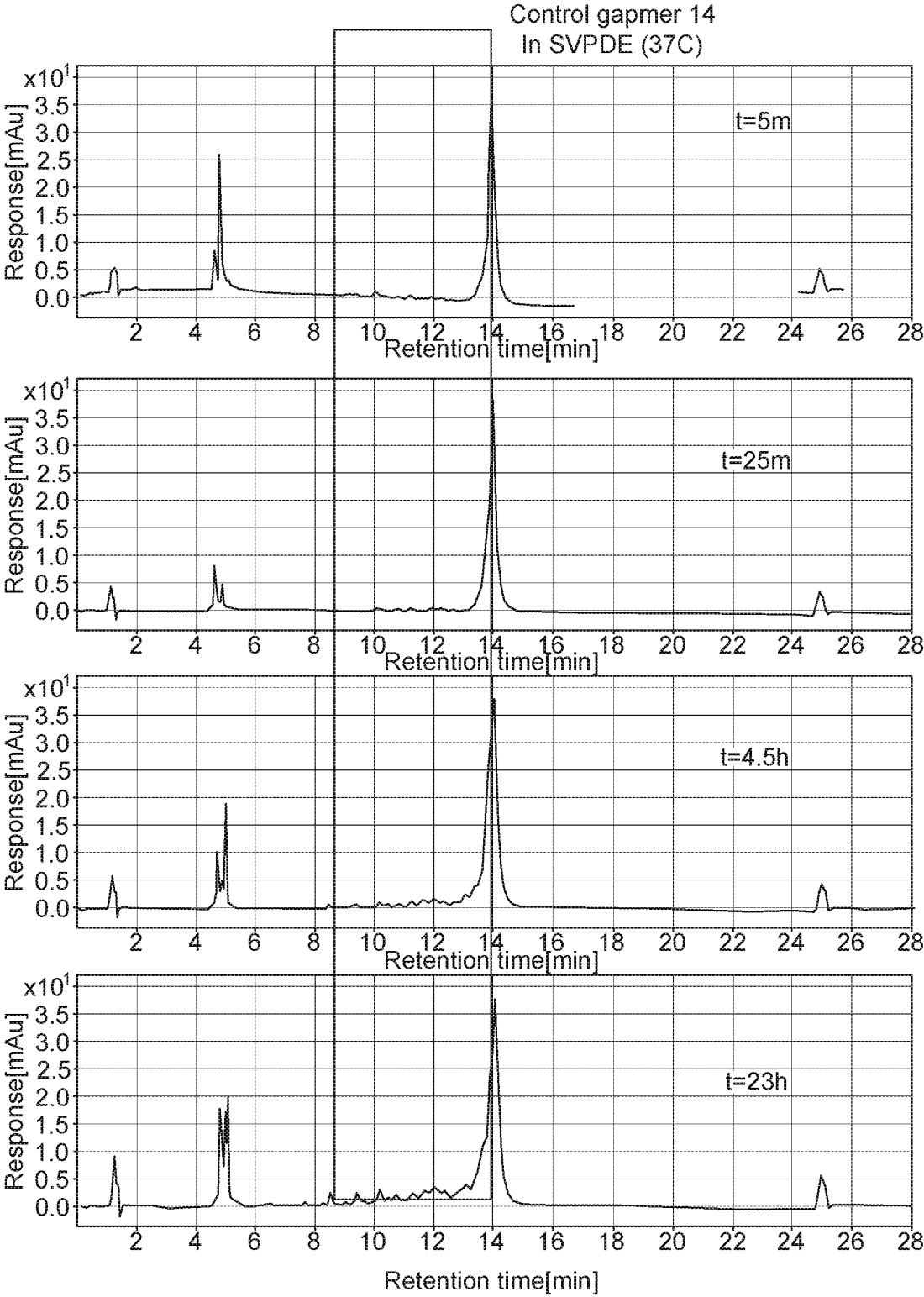


Figure 31

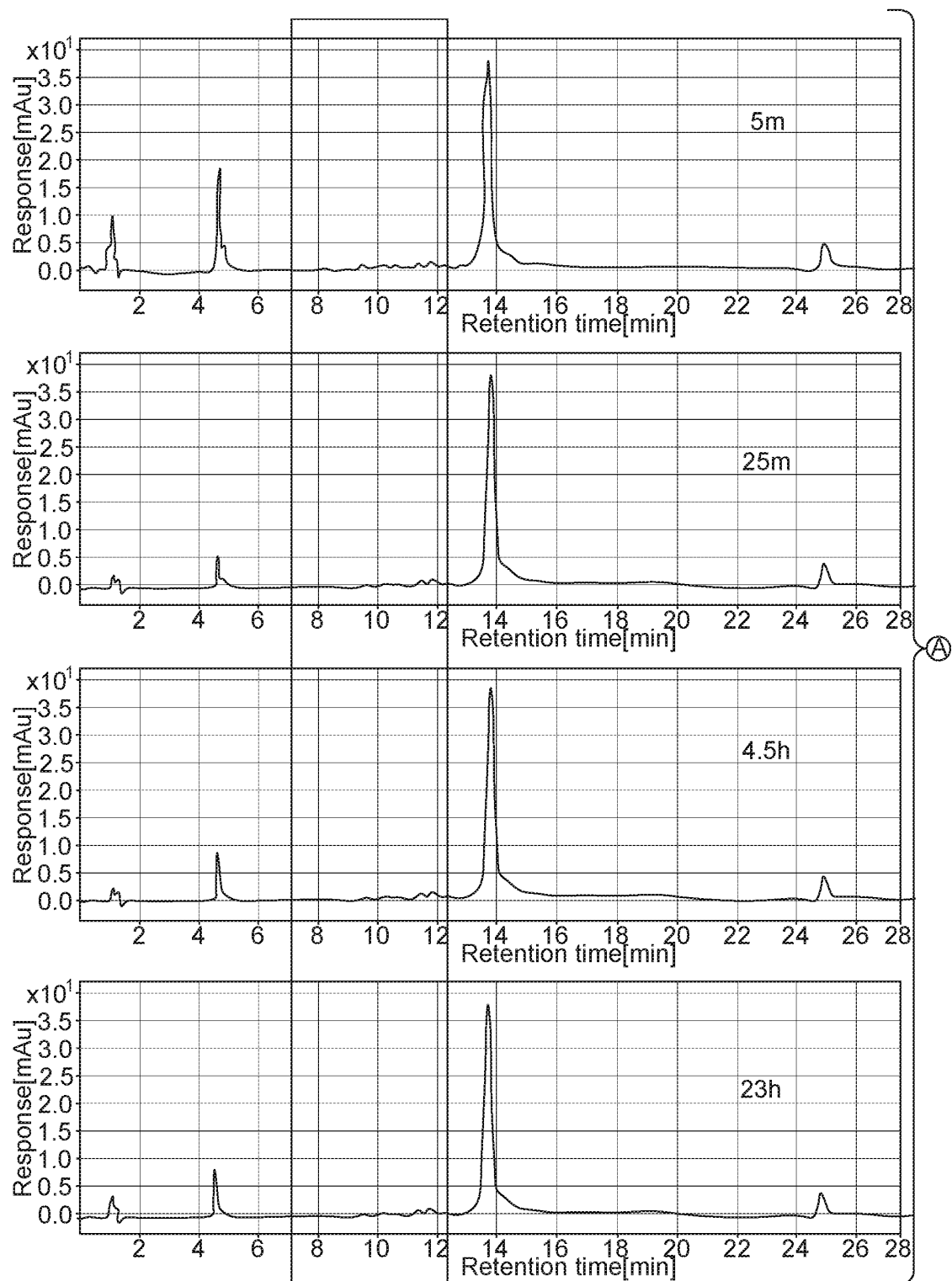
3 ASO-PMO Hybrid
In SVPDE (37C)

Figure 32

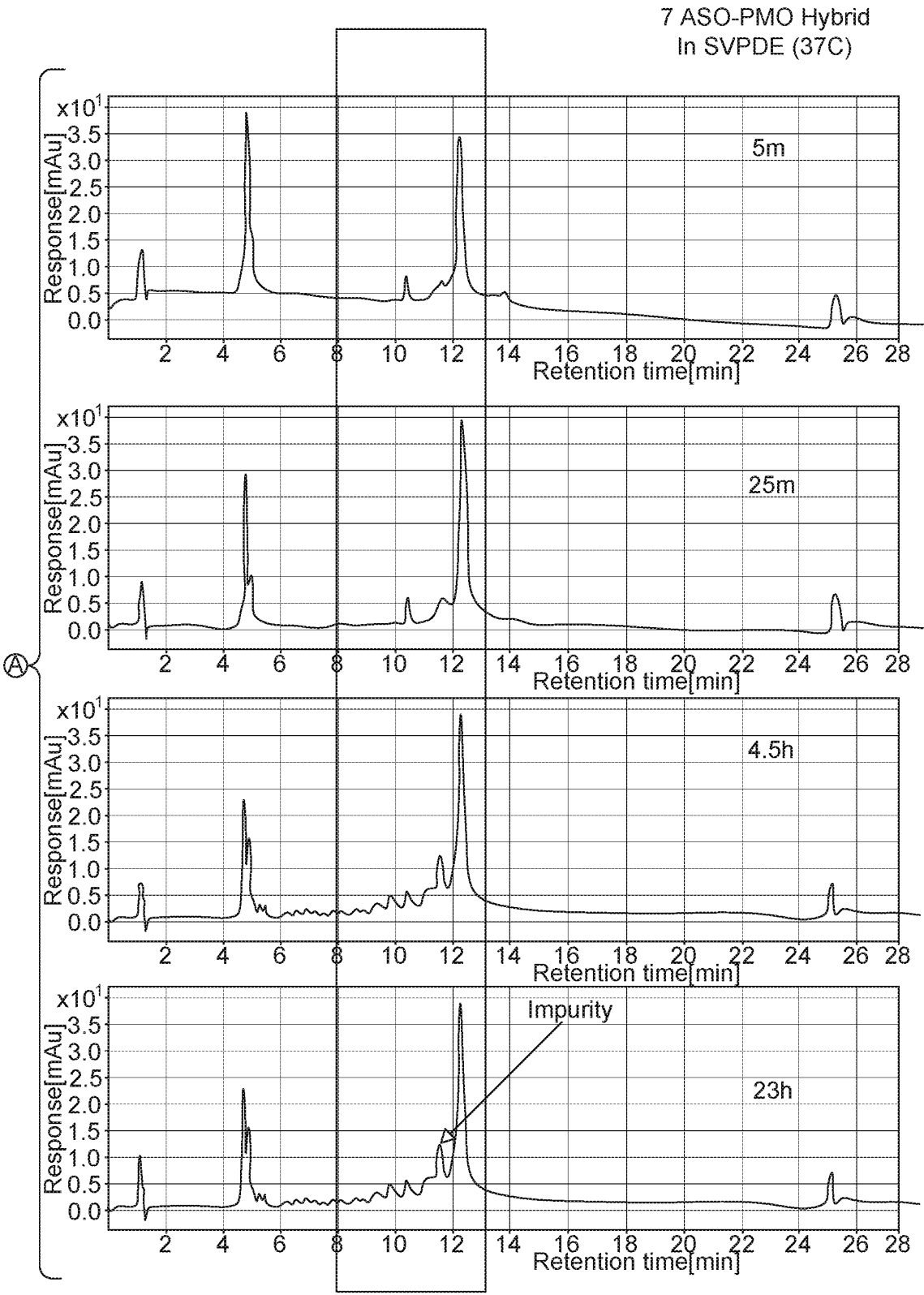


Figure 32(Continued)

A (PS Control) in SVPDE (37C)

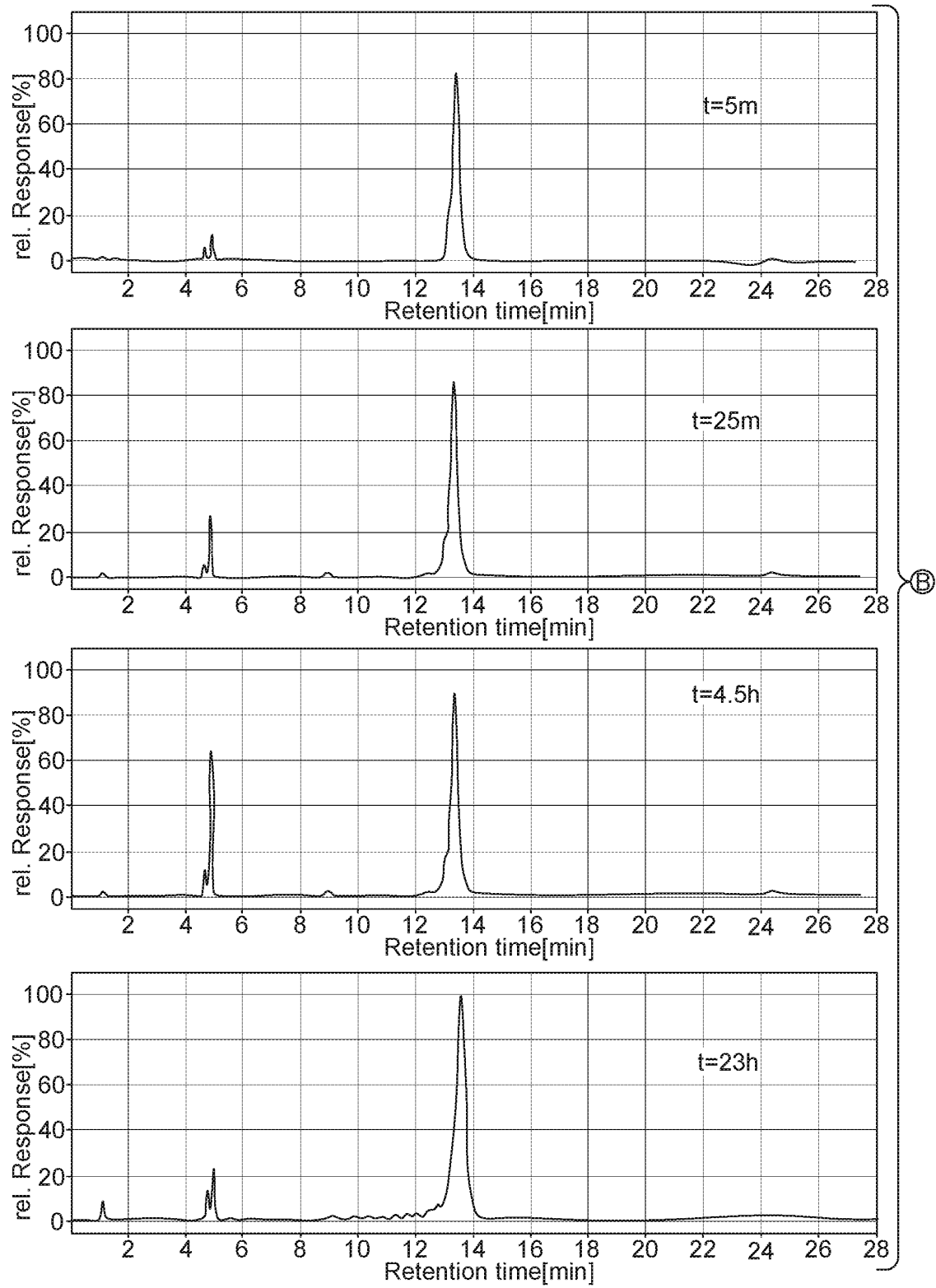


Figure 33

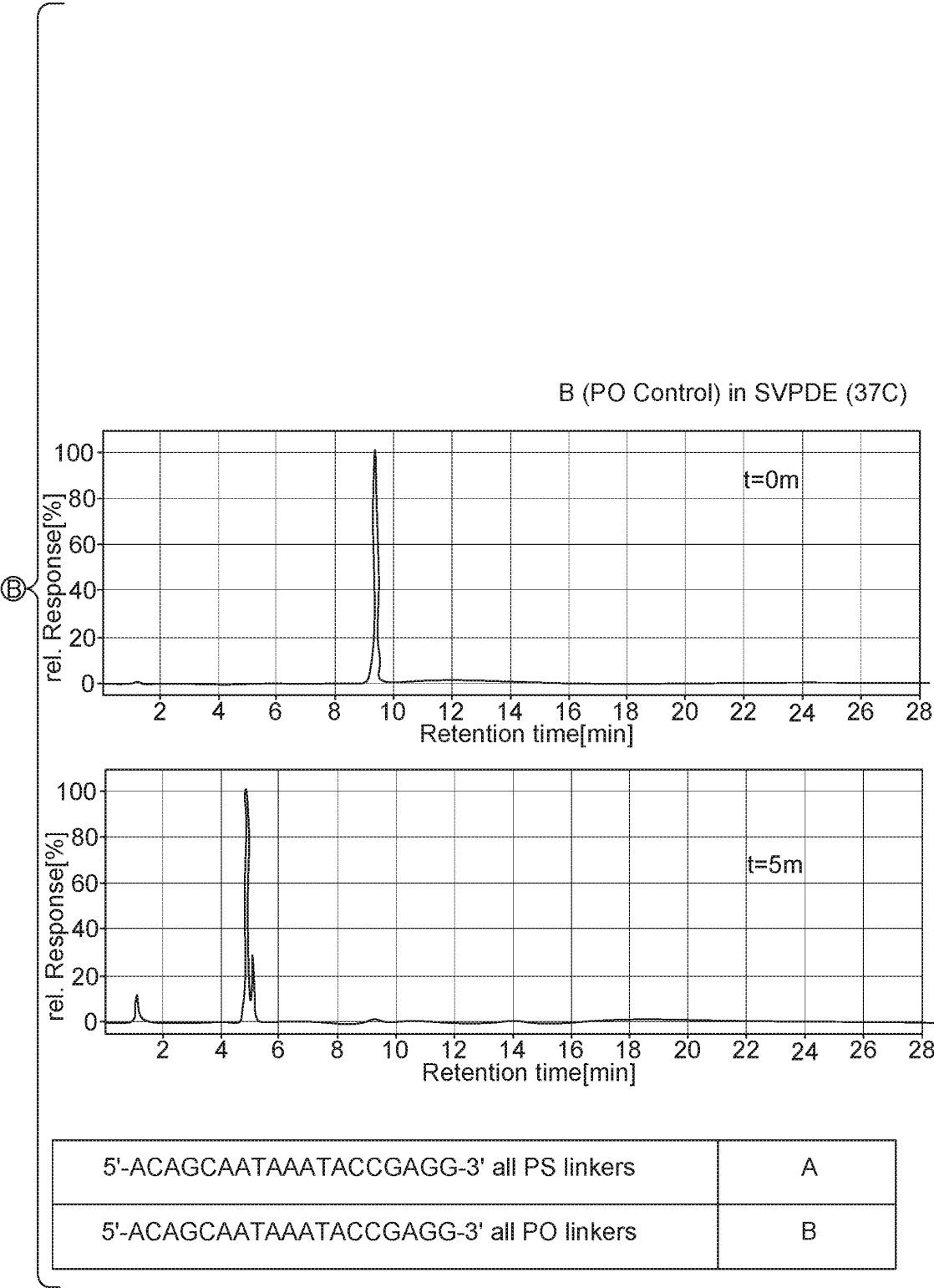


Figure 33(Continued)

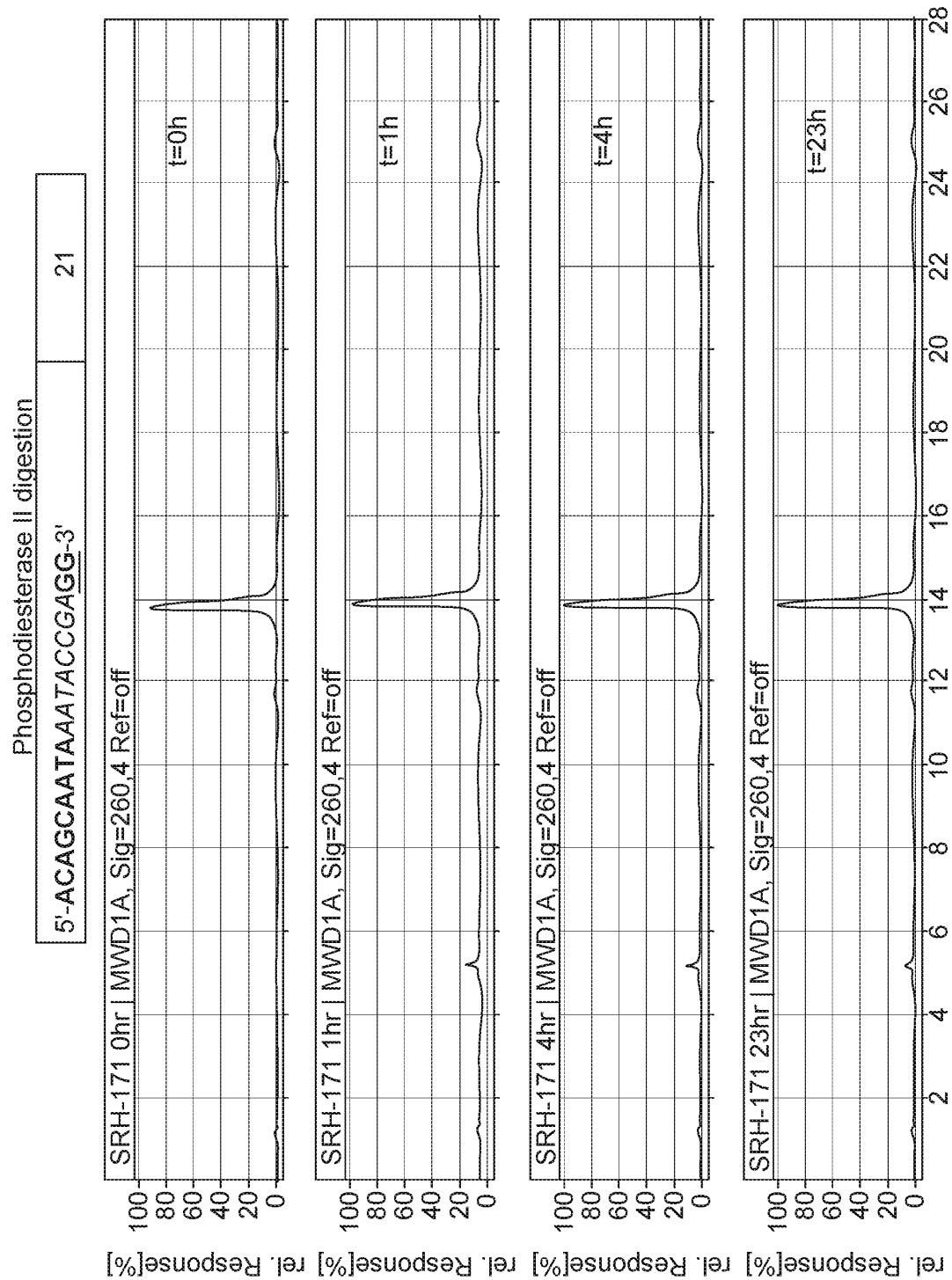


Figure 34

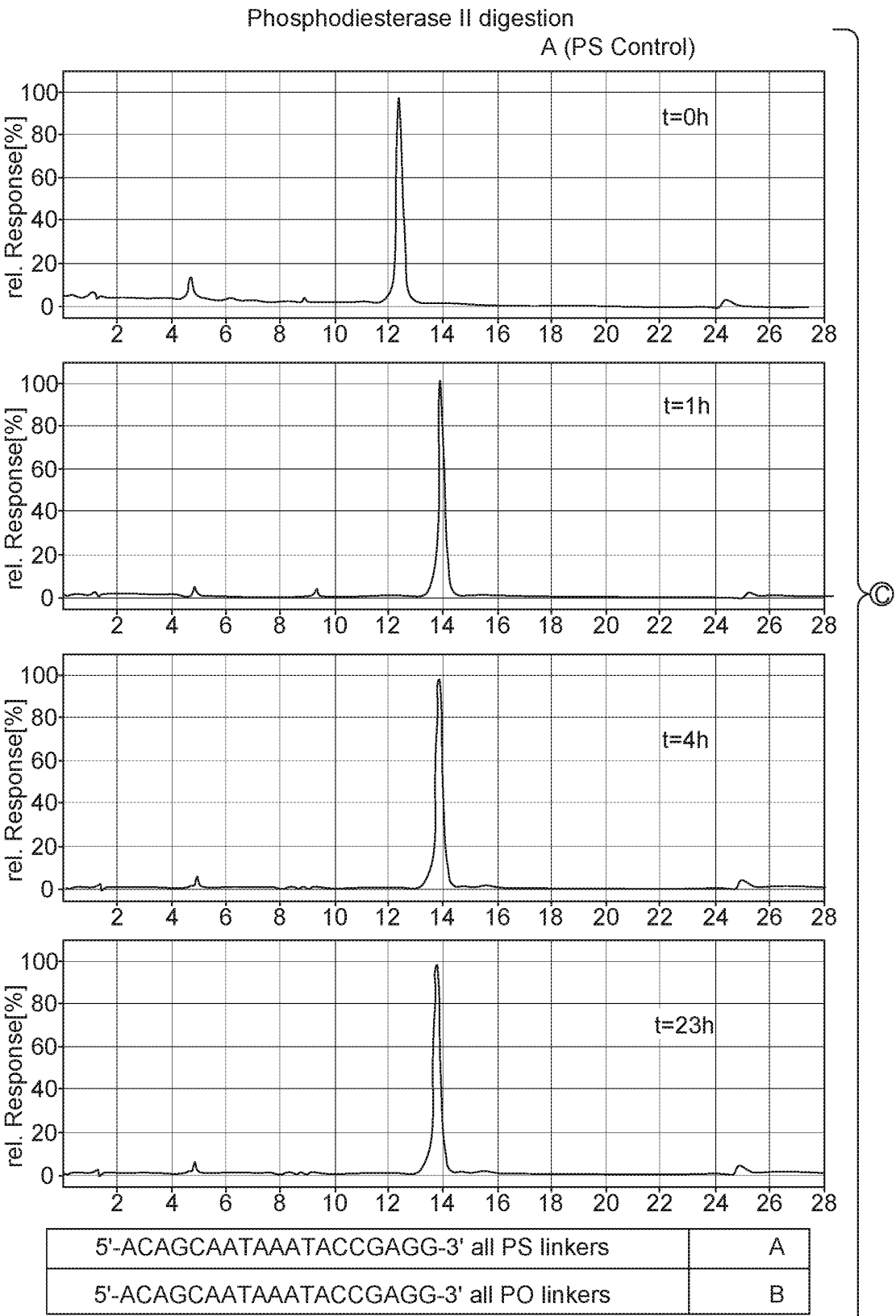


Figure 35

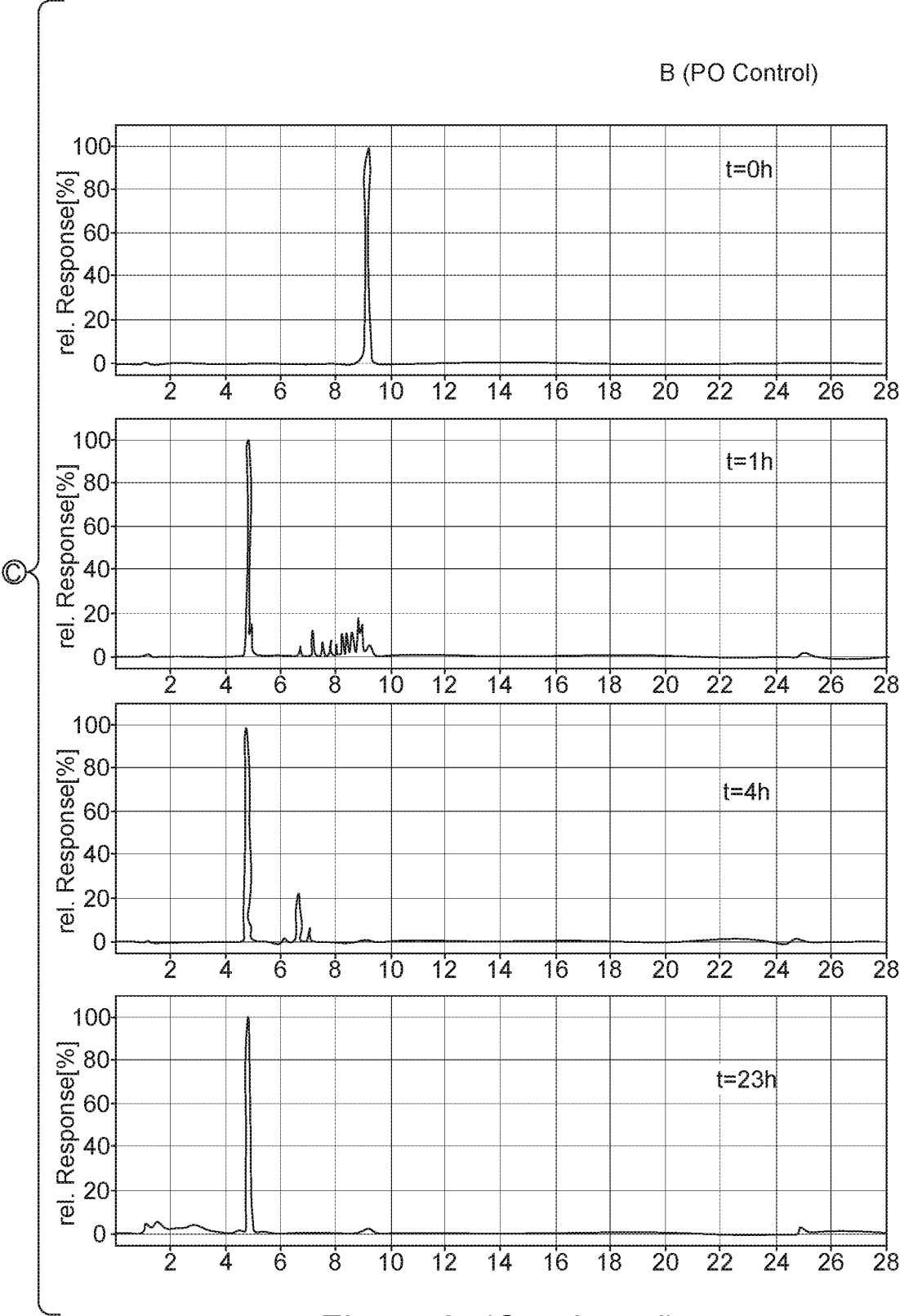


Figure 35(Continued)

US Patent No. 11,479,772

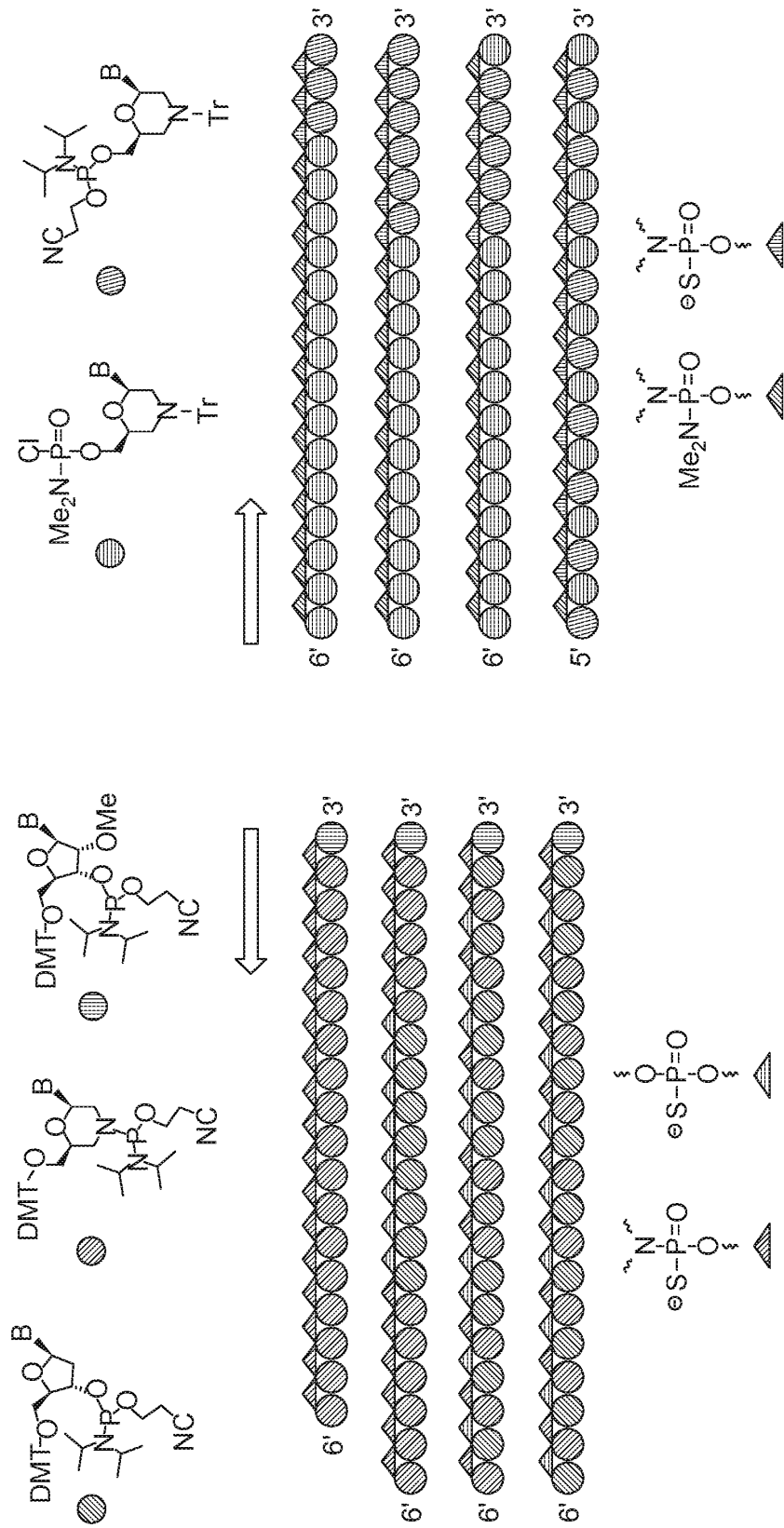


Figure 36

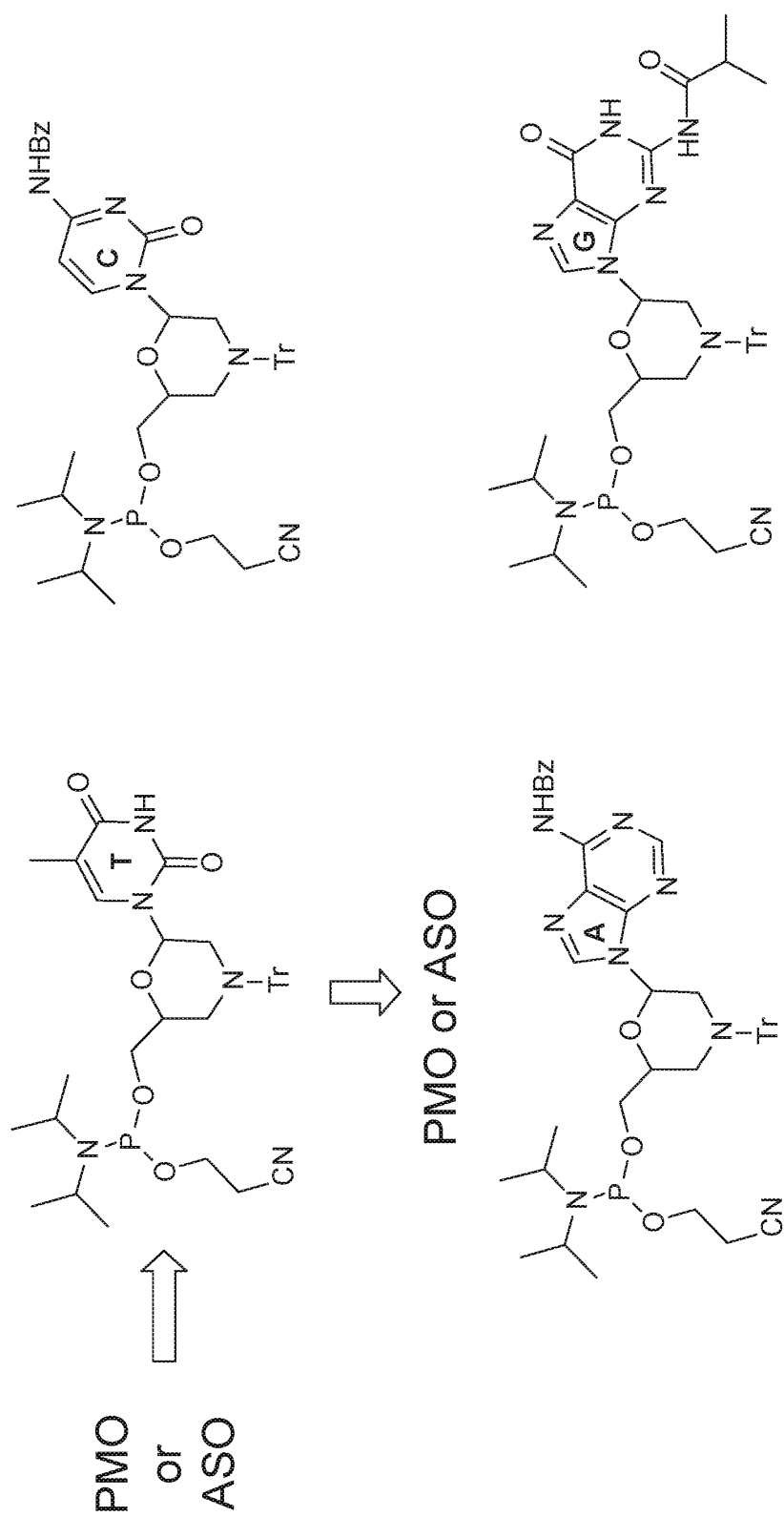
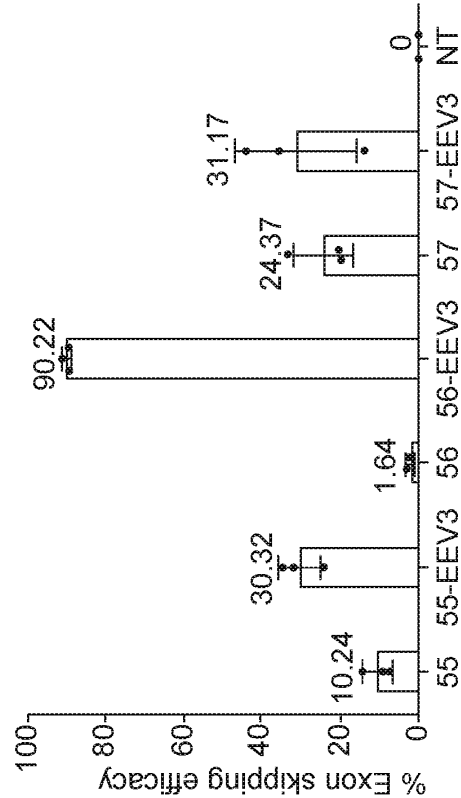


Figure 37



Sample ID	sequence
55	5'-GCTATTACCTTAACCCAG-3'
55-EEV3	5'-GCTATTACCTTAACCCAG-3'-1120
56	5'-GCTATTACCTTAACCCAG-3'
56-EEV3	5'-GCTATTACCTTAACCCAG-3'-1120
57	5'-GCTATTACCTTAACCCAG-3'
57-EEV3	5'-GCTATTACCTTAACCCAG-3'-1120

Black refers to charged PMO

Black color is regular PMO

Figure 38