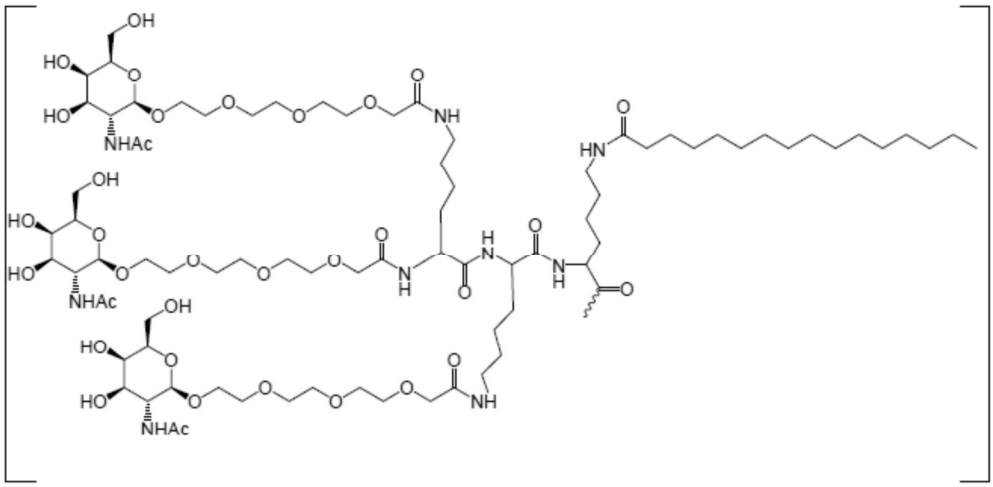
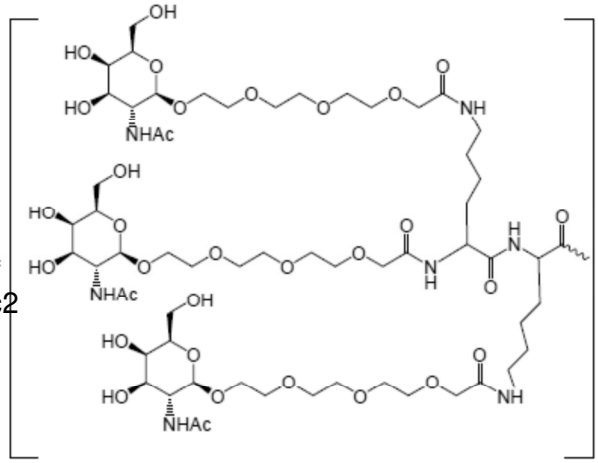
FIGURES

Figure 1

Conj 1–



Conj 2=
GalNAc2



Conj 3=

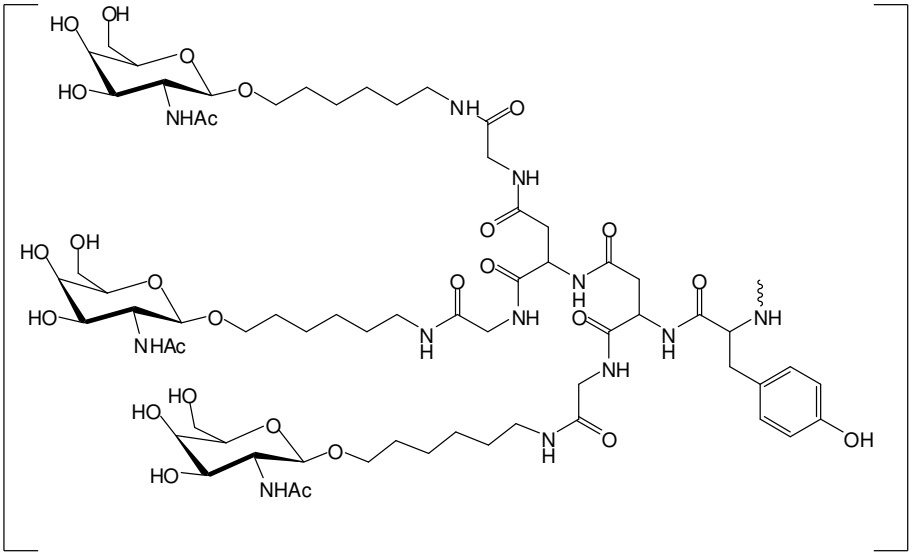
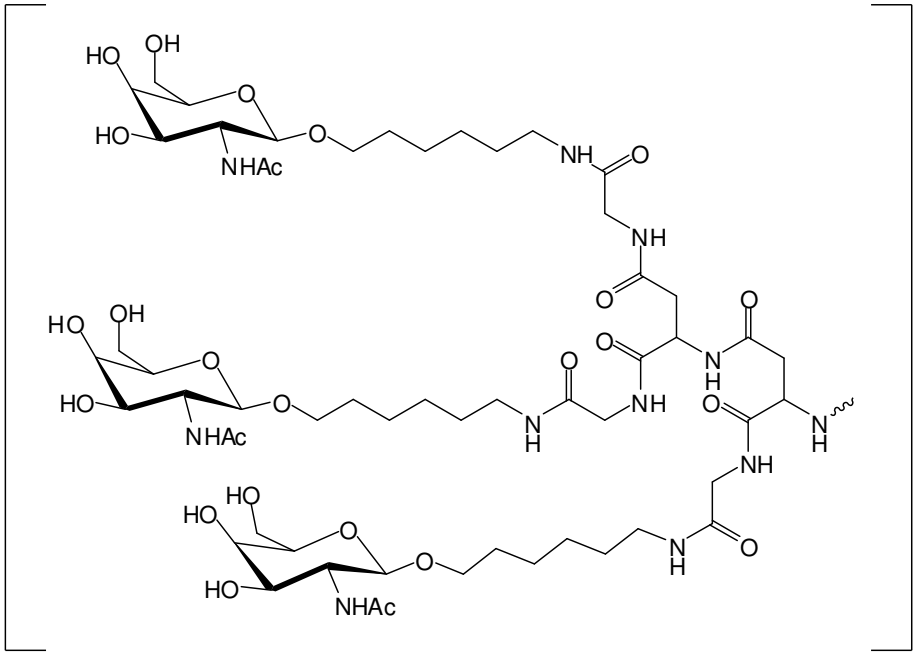


Figure 1 (cont)

Conj 4=



Conj 4a=

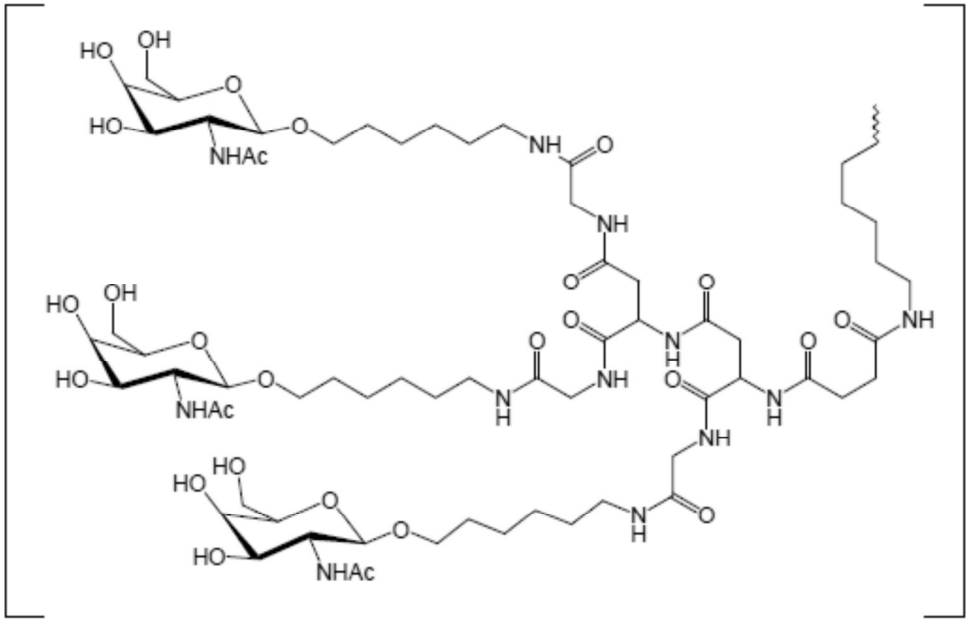
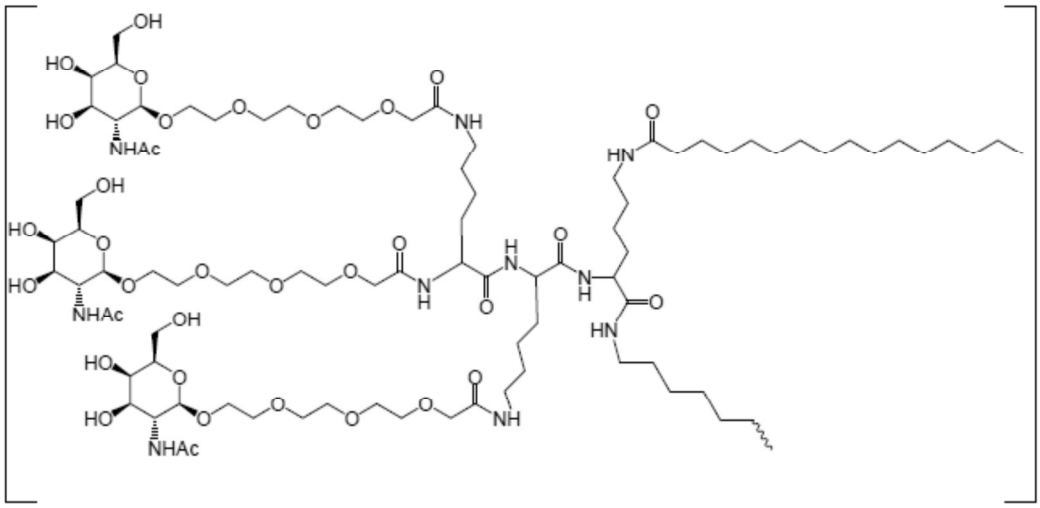
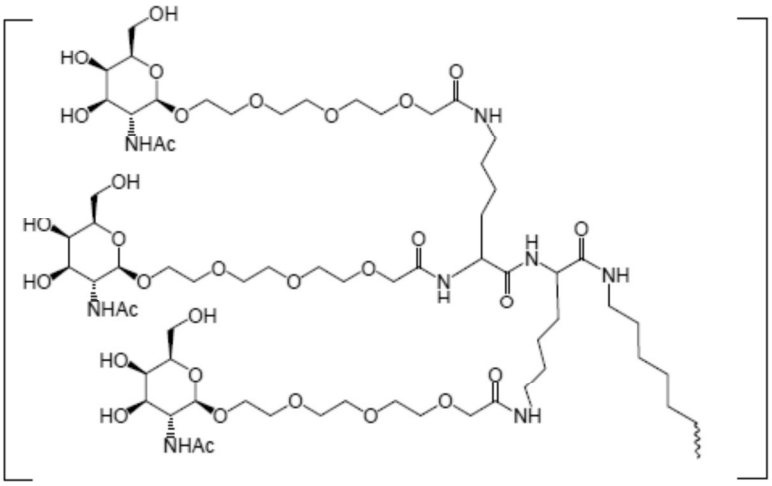


Figure 1 (cont)

Conj 1a=



Conj 2a=



Conj 3a=

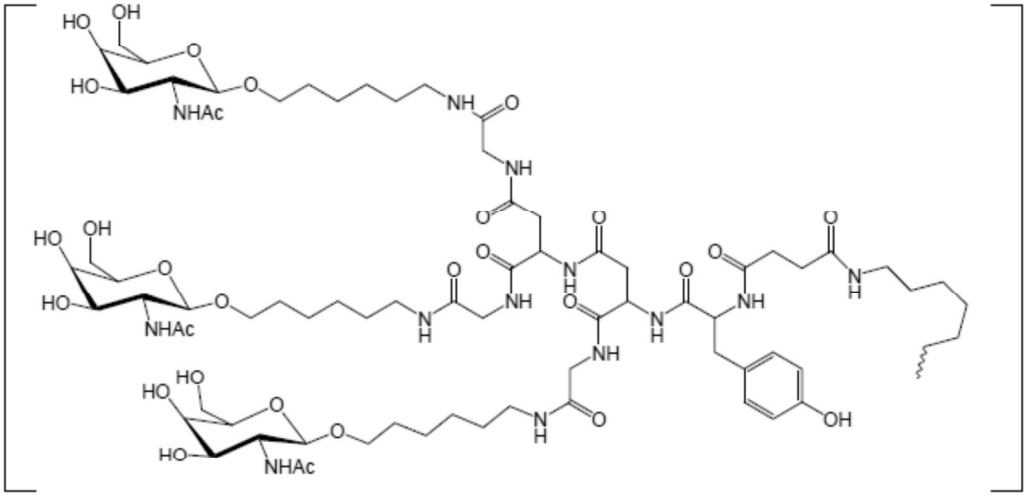
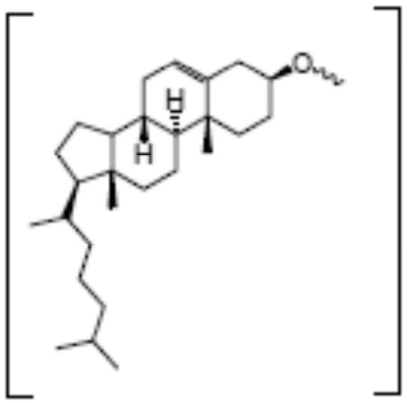
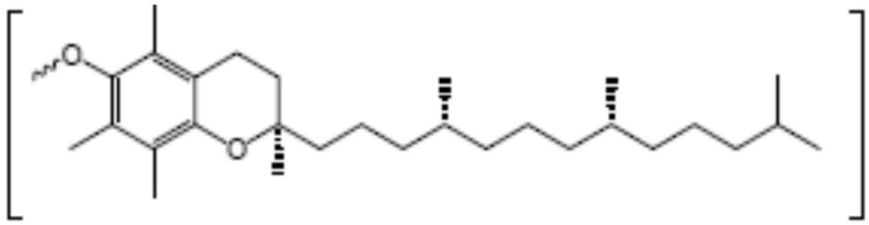


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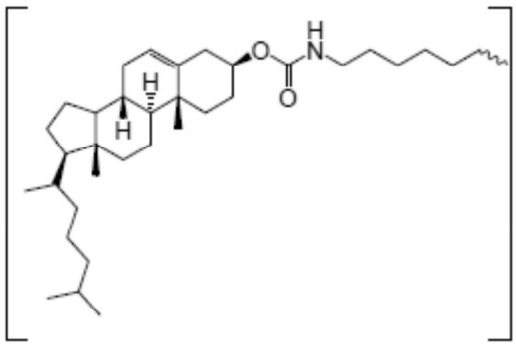
Conj 5=



Conj 6=



Conj 5a=
Chol-C6



Conj 6a=

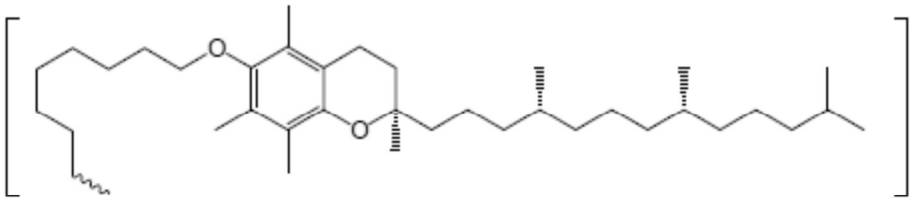


Figure 3

5'-$T^L_sG^L_s{}^{Me}C^L_sT_sA_sC_sA_sA_sA_sA_sC_s{}^{Me}C^L_s{}^{Me}C^L_sA^L$-3'
SEQ ID 1

5'- $A^L_sA^L_s$ $T^L_sG_sC_sT_sA_sC_sA_sA_sA_sA_s{}^{Me}C^L_s{}^{Me}C^L_s{}^{Me}C^L_sA^L$-3'
SEQ ID 2

5'-$A^L_sA^L_sT^L_sG_sC_sT_sA_sC_sA_sA_sA_sA_sC_s{}^{Me}C^L_s{}^{Me}C^L_sA^L$-3'
SEQ ID 3

5'-$G^L_s{}^{Me}C^L_sT_sG_sT_sG_sT_sG_sA_sG_sC_sT_sT_sG^L_sG^L$-3'
SEQ ID 4

5'-$T^L_sG^L_sC_sT_sG_sT_sG_sT_sG_sA_sG_sC_sT_sT^L_sG^L_sG^L$-3'
SEQ ID 5

5'-$T^L_sG^L_s{}^{Me}C^L_sT_sG_sT_sG_sT_sG_sA_sG_sC_sT_sT^L_sG^L_sG^L$-3'
SEQ ID 6

5'-$T^L_s{}^{Me}C^L_s{}^{Me}C^L_sT_sG_sG_sT_sC_sT_sG_sT_sG_sT_sT^L_s{}^{Me}C^L_s{}^{Me}C^L$-3'
SEQ ID 7

5'-$T^L_s{}^{Me}C^L_s{}^{Me}C^L_sT_sG_sG_sT_sC_sT_sG_sT_sG_sT_sT_s{}^{Me}C^L_s{}^{Me}C^L$-3'
SEQ ID 8

Figure 4

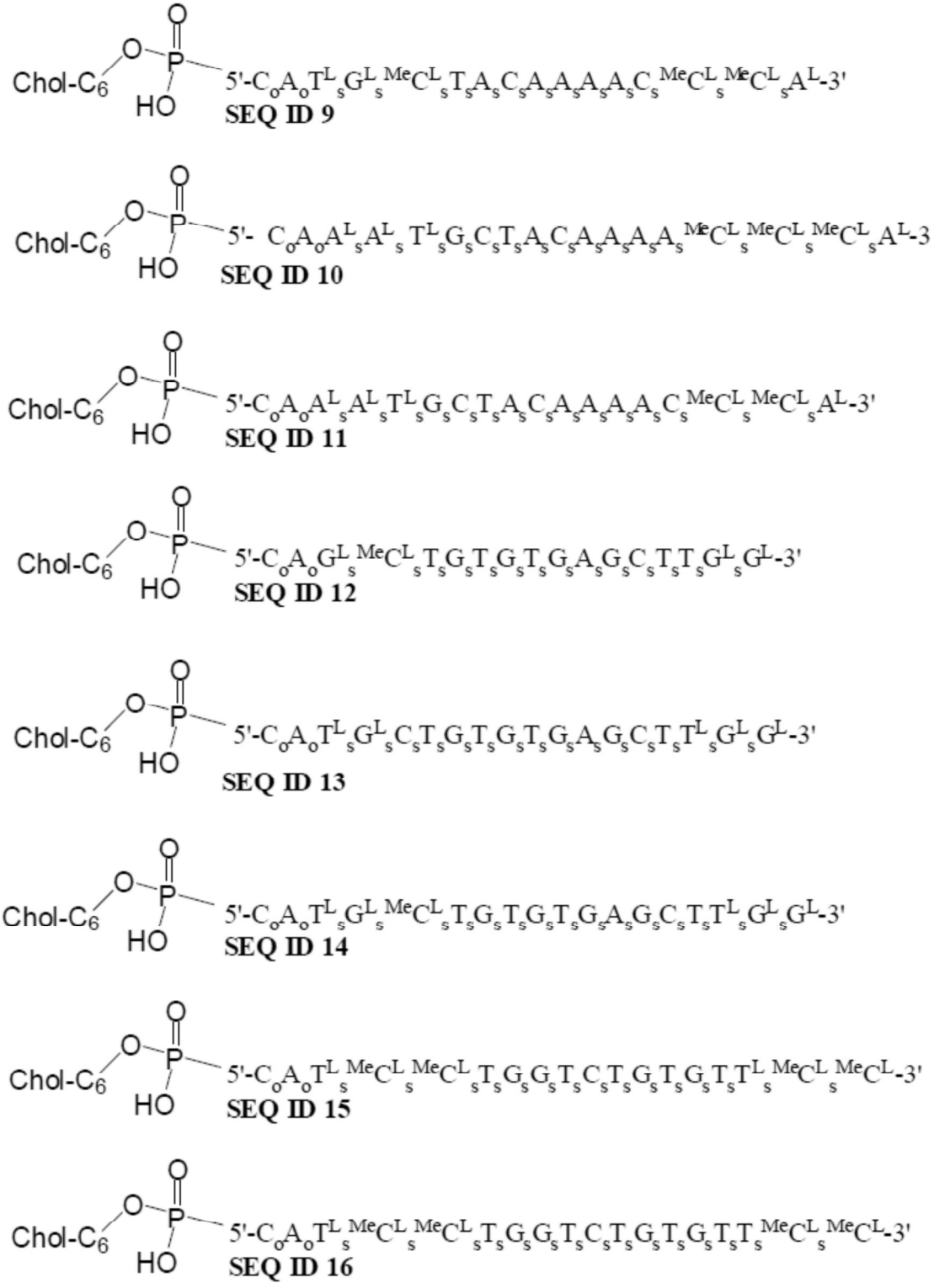
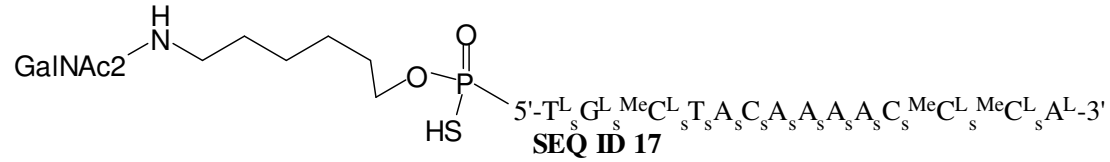
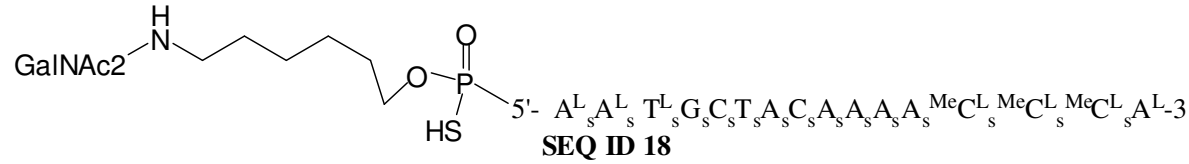

Chol-C6
HO
5'-CoAoTLsGLsMeCLsTsAsCsAsAsAsAsCsMeCLsMeCLsALs-3'
SEQ ID 9
Chol-C6
HO
5'- CoAoALsALs TLsGsCsTsAsCsAsAsAsAsMeCLsMeCLsMeCLsALs-3
SEQ ID 10
Chol-C6
HO
5'-CoAoALsALsTLsGsCsTsAsCsAsAsAsAsCsMeCLsMeCLsALs-3'
SEQ ID 11
Chol-C6
HO
5'-CoAoGLsMeCLsTsGsTsGsTsGsAsGsCsTsTsGLsGLs-3'
SEQ ID 12
Chol-C6
HO
5'-CoAoTLsGLsCsTsGsTsGsTsGsAsGsCsTsTLsGLsGLs-3'
SEQ ID 13
Chol-C6
HO
5'-CoAoTLsGLsMeCLsTsGsTsGsTsGsAsGsCsTsTLsGLsGLs-3'
SEQ ID 14
Chol-C6
HO
5'-CoAoTLsMeCLsMeCLsTsGsGsTsCsTsGsTsGsTsTLsMeCLsMeCLs-3'
SEQ ID 15
Chol-C6
HO
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SEQ ID 16

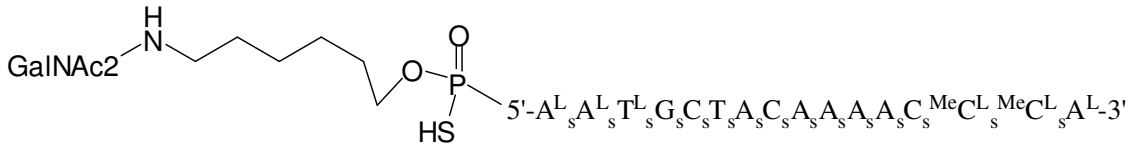
Figure 5



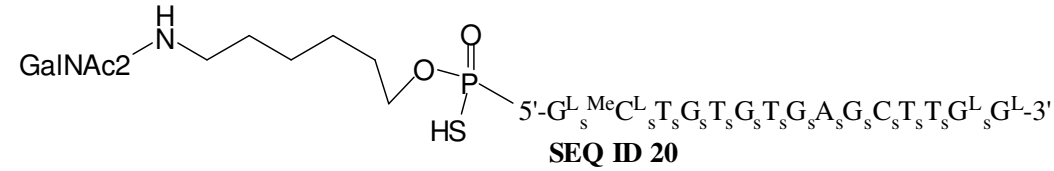
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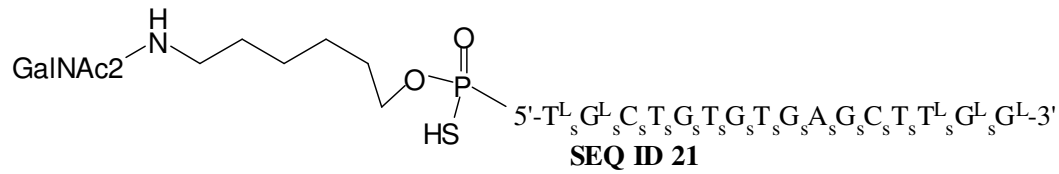
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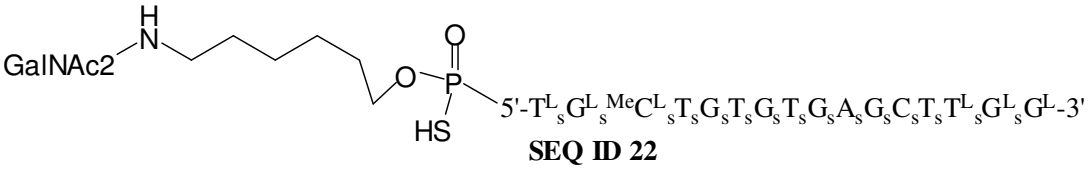
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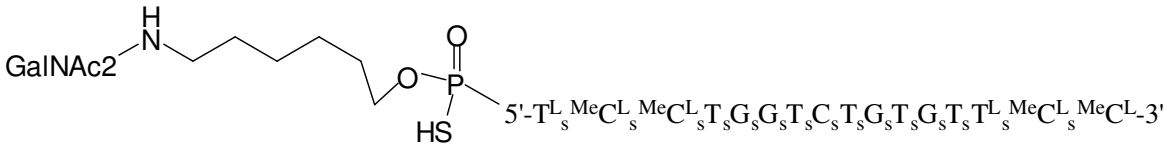
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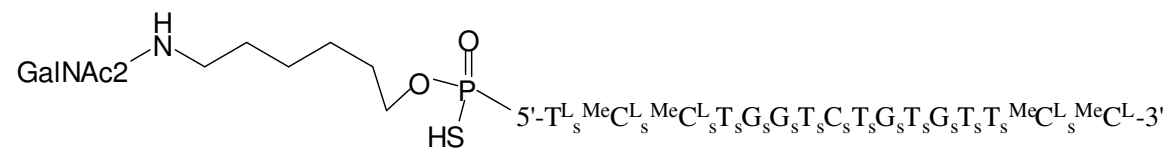
SEQ ID 21



SEQ ID 22



SEQ ID 23



SEQ ID 24

Figure 5A

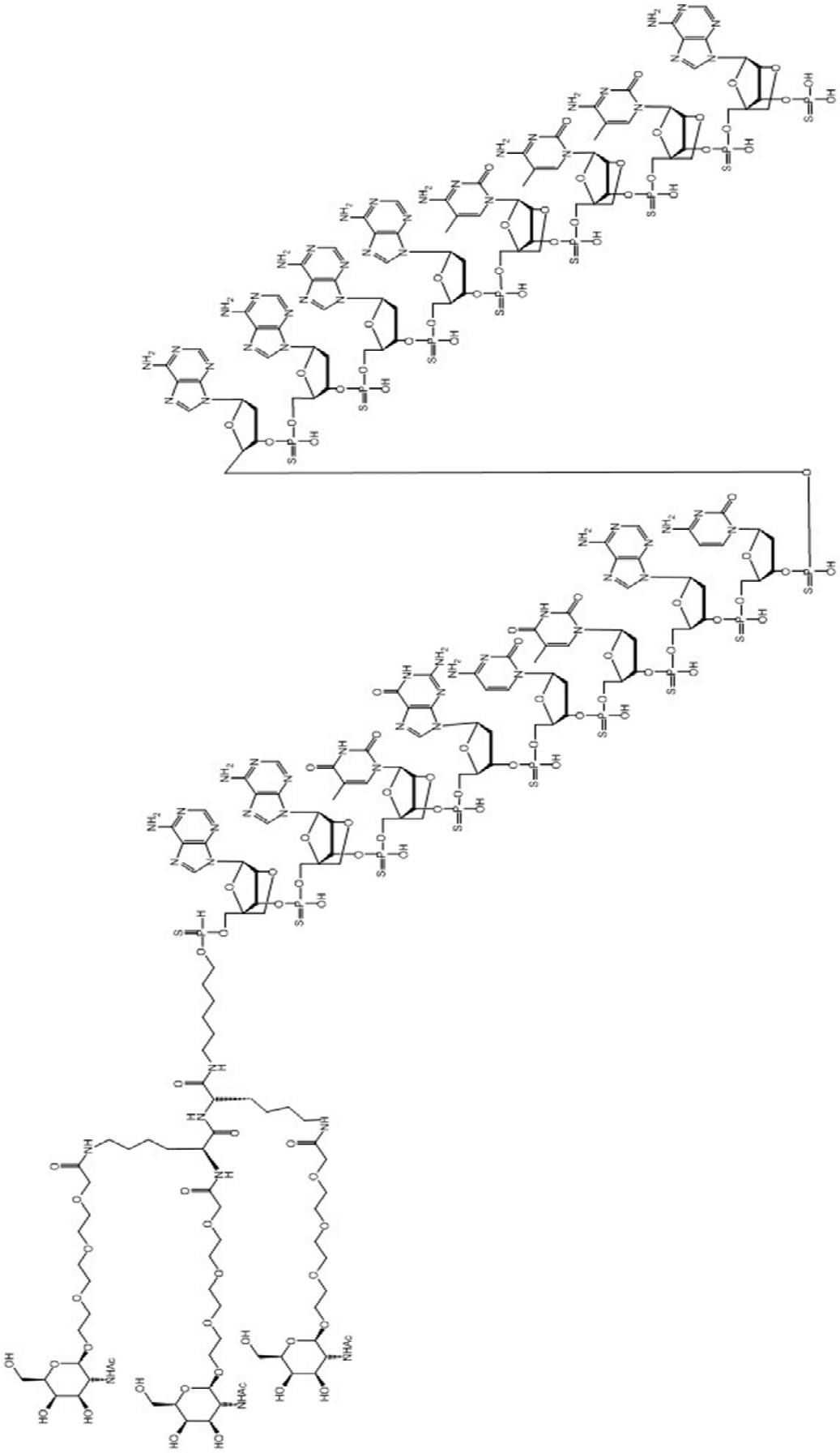


Figure 5B

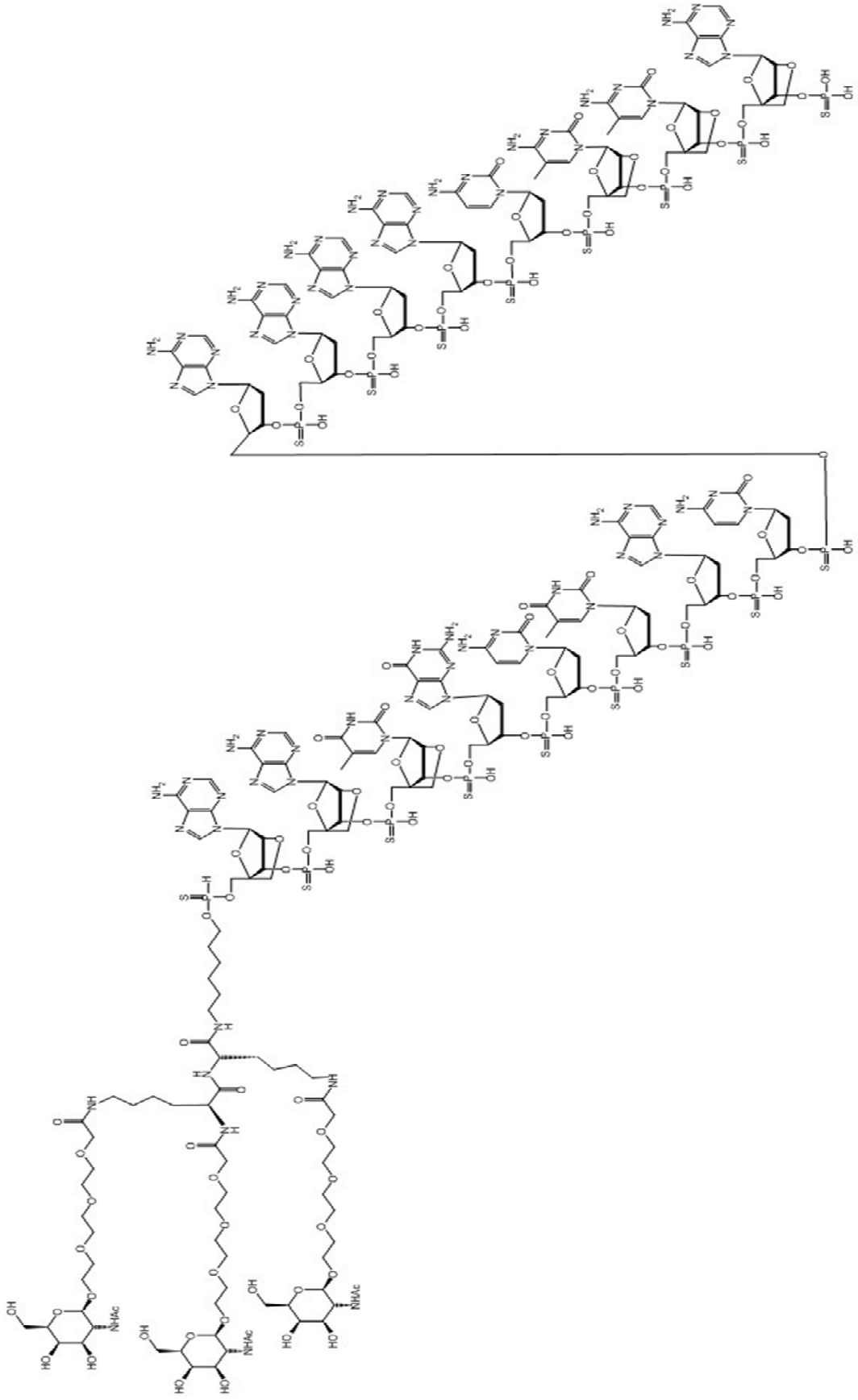


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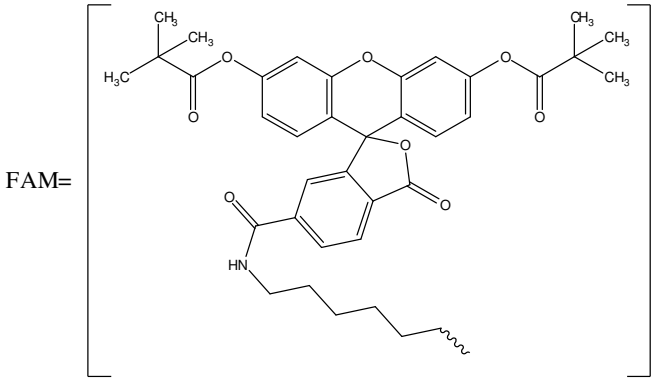


Figure 7

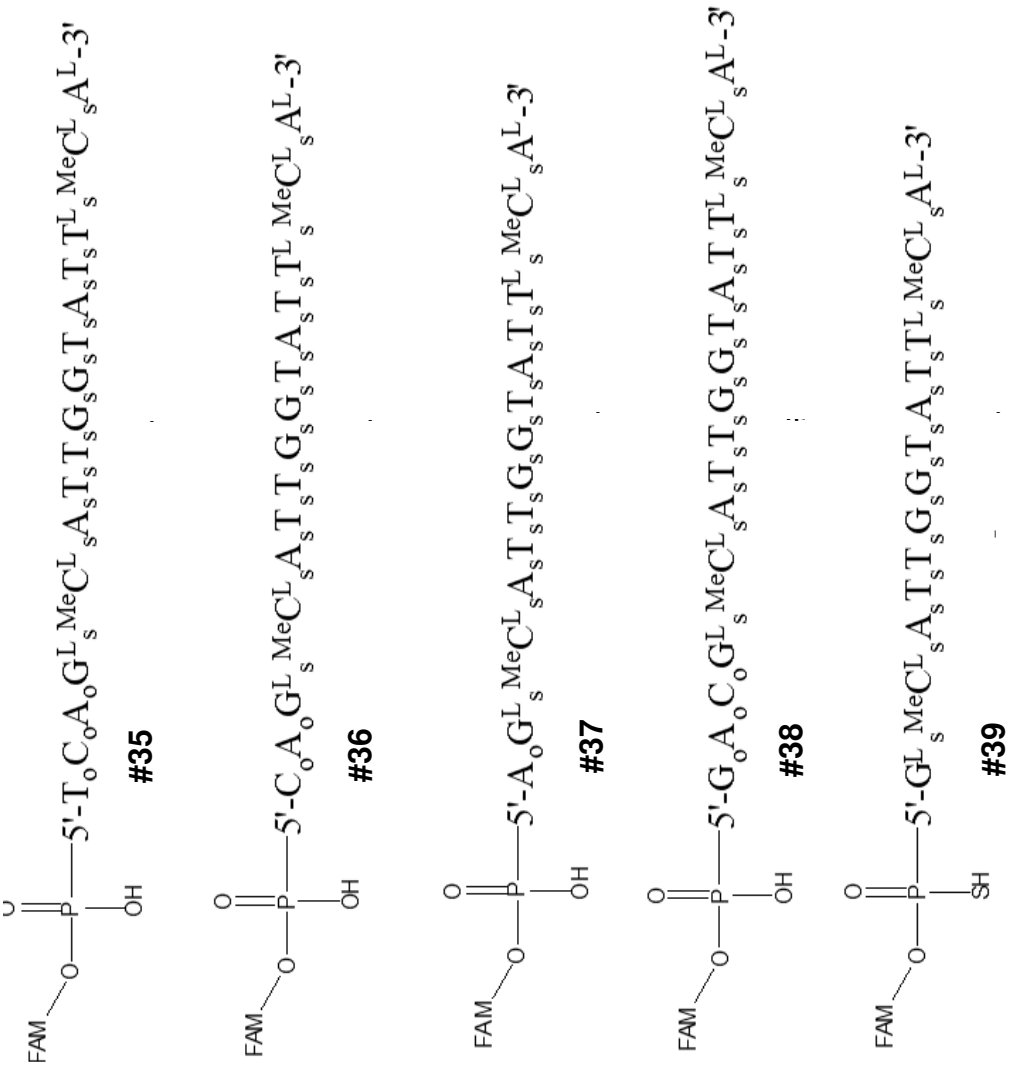


Figure 8

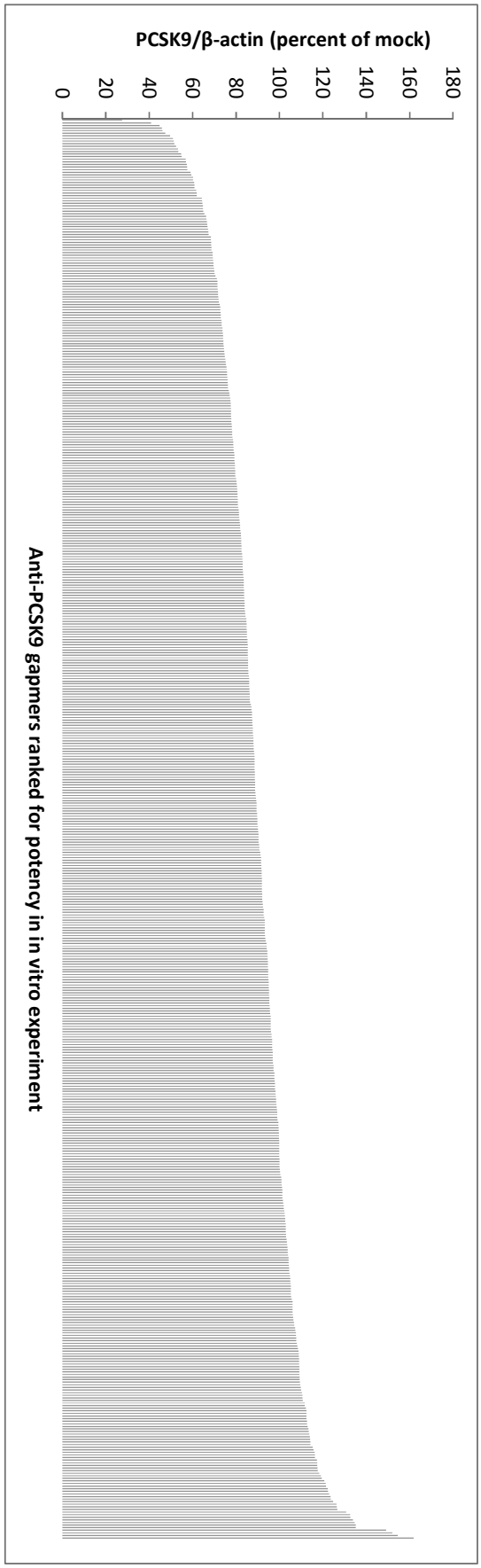

PCSK9/β-actin (percent of mock)
0
20
40
60
80
100
120
140
160
180
Anti-PCSK9 gapmers ranked for potency in in vitro experiment

Figure 9

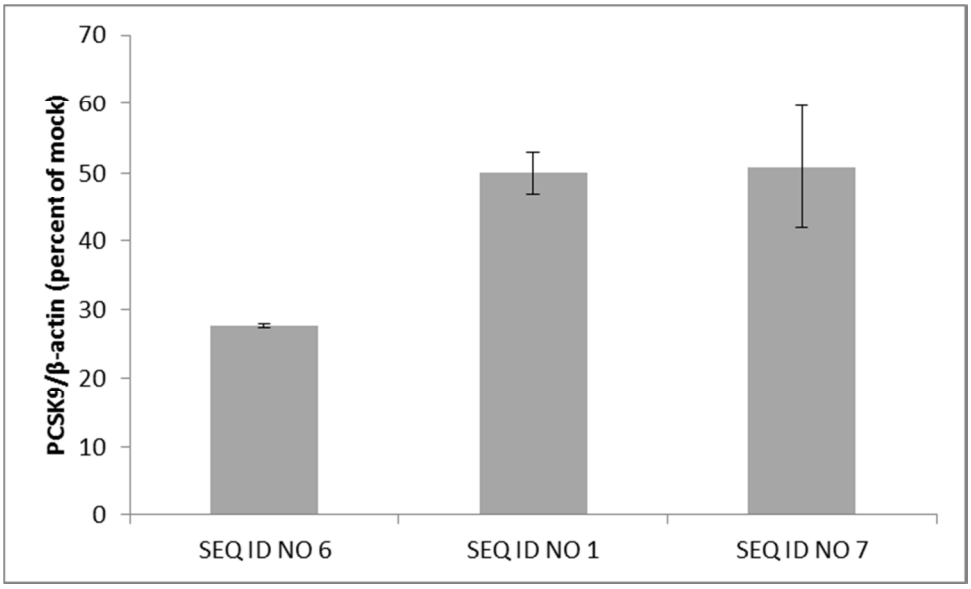

70
60
50
40
30
20
10
0
PCSK9/β-actin (percent of mock)
SEQ ID NO 6
SEQ ID NO 1
SEQ ID NO 7

Figure 10

Figure 11

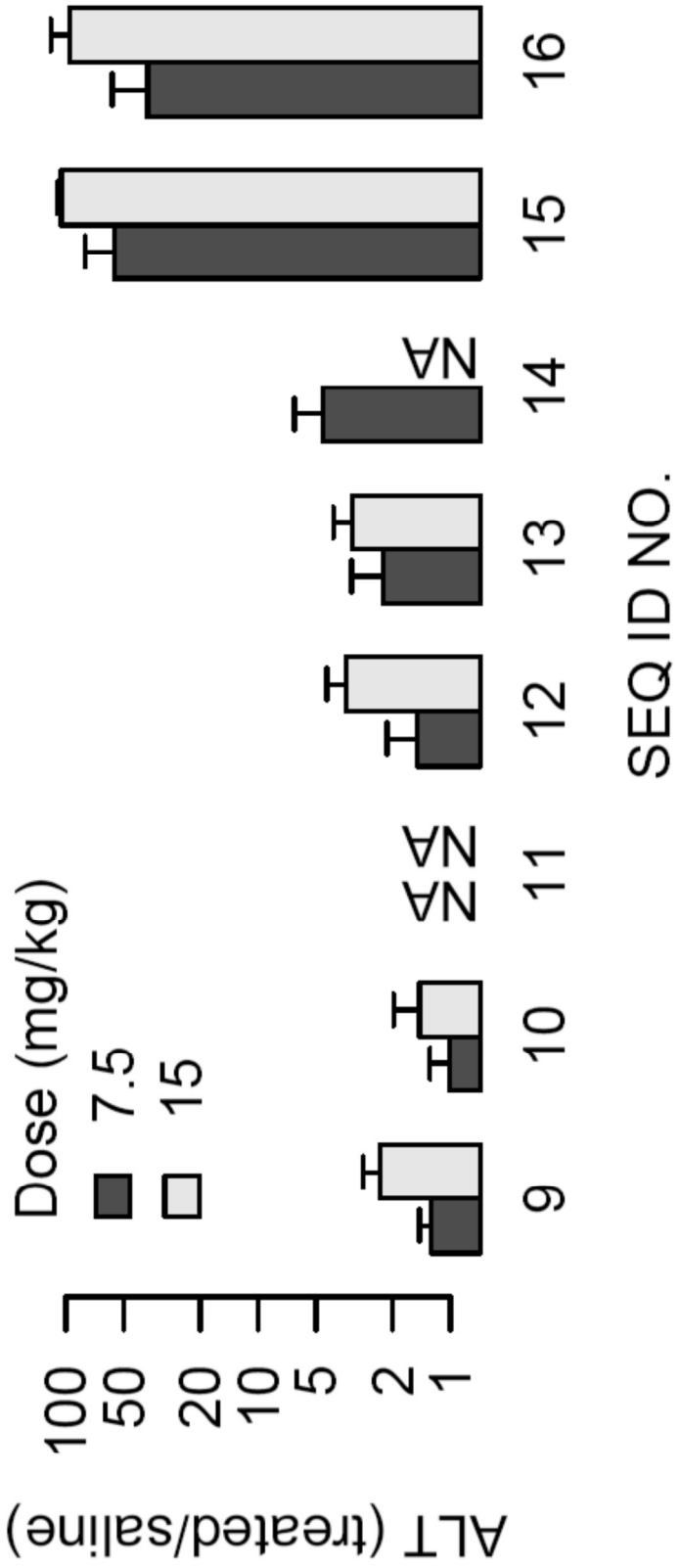

ALT (treated/saline)
100
50
20
10
5
2
1
Dose (mg/kg)
7.5
15
9
10
NA
NA
11
12
13
14
15
16
SEQ ID NO.

Figure 12

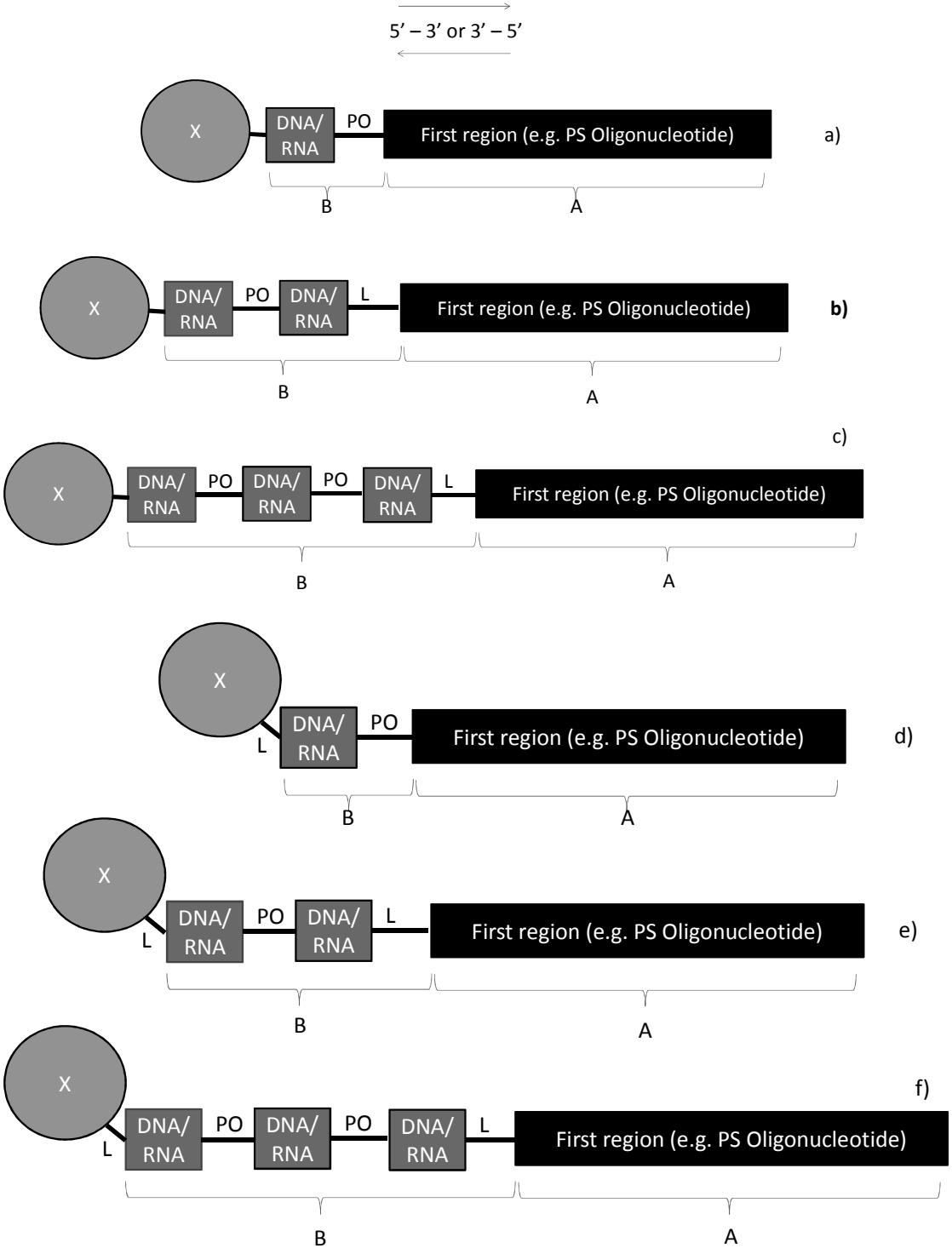

5' – 3' or 3' – 5'
X
DNA/ RNA
PO
First region (e.g. PS Oligonucleotide)
a)
B
A
X
DNA/ RNA
PO
DNA/ RNA
L
First region (e.g. PS Oligonucleotide)
b)
B
A
c)
X
DNA/ RNA
PO
DNA/ RNA
PO
DNA/ RNA
L
First region (e.g. PS Oligonucleotide)
B
A
X
L
DNA/ RNA
PO
First region (e.g. PS Oligonucleotide)
d)
B
A
X
L
DNA/ RNA
PO
DNA/ RNA
L
First region (e.g. PS Oligonucleotide)
e)
B
A
X
L
DNA/ RNA
PO
DNA/ RNA
PO
DNA/ RNA
L
First region (e.g. PS Oligonucleotide)
f)
B
A

Figure 13

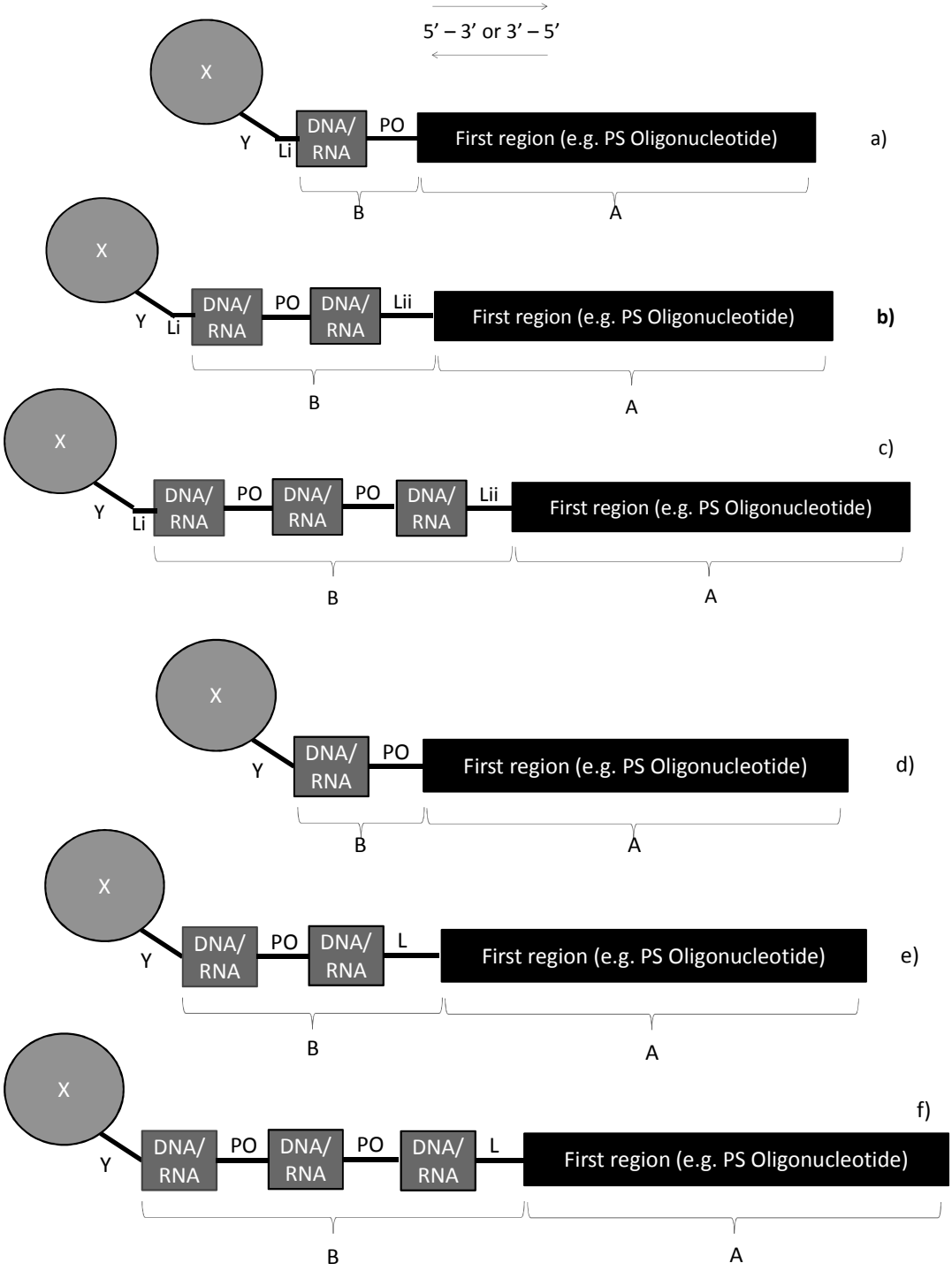
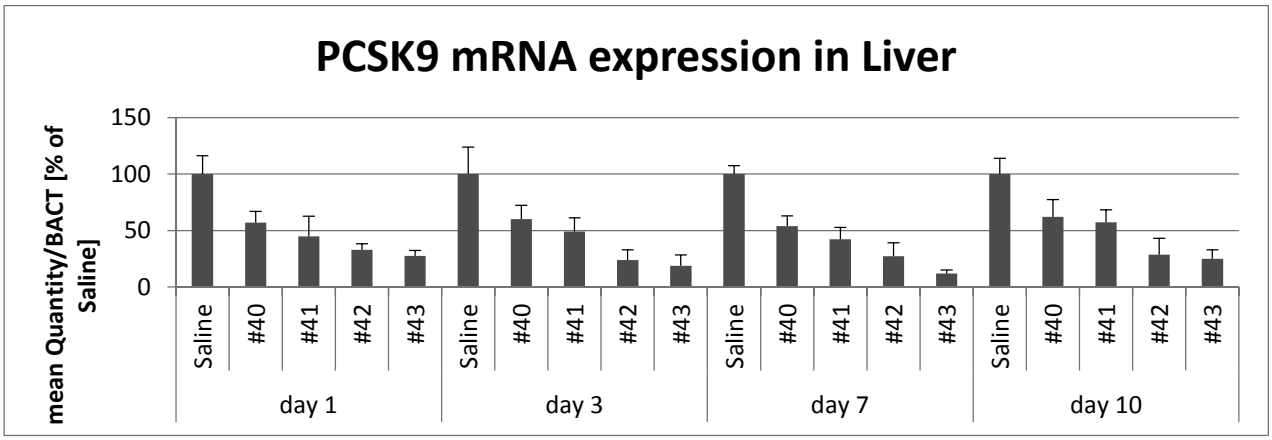

5' – 3' or 3' – 5'
X
Y
Li
DNA/ RNA
PO
First region (e.g. PS Oligonucleotide)
a)
B
A
X
Y
Li
DNA/ RNA
PO
DNA/ RNA
Lii
First region (e.g. PS Oligonucleotide)
b)
B
A
X
Y
Li
DNA/ RNA
PO
DNA/ RNA
PO
DNA/ RNA
Lii
First region (e.g. PS Oligonucleotide)
c)
B
A
X
Y
DNA/ RNA
PO
First region (e.g. PS Oligonucleotide)
d)
B
A
X
Y
DNA/ RNA
PO
DNA/ RNA
L
First region (e.g. PS Oligonucleotide)
e)
B
A
X
Y
DNA/ RNA
PO
DNA/ RNA
PO
DNA/ RNA
L
First region (e.g. PS Oligonucleotide)
f)
B
A

Figure 14

A


PCSK9 mRNA expression in Liver
mean Quantity/BACT [% of Saline]
150
100
50
0
Saline
#40
#41
#42
#43
day 1
day 3
day 7
day 10

B

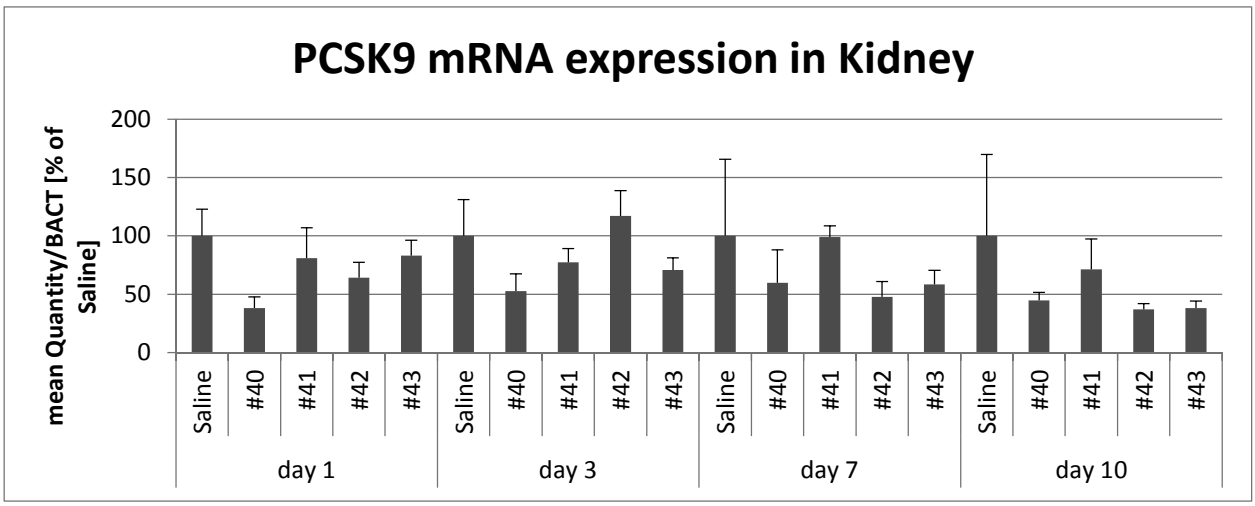

PCSK9 mRNA expression in Kidney
mean Quantity/BACT [% of Saline]
200
150
100
50
0
Saline
#40
#41
#42
#43
day 1
day 3
day 7
day 10

Figure 15

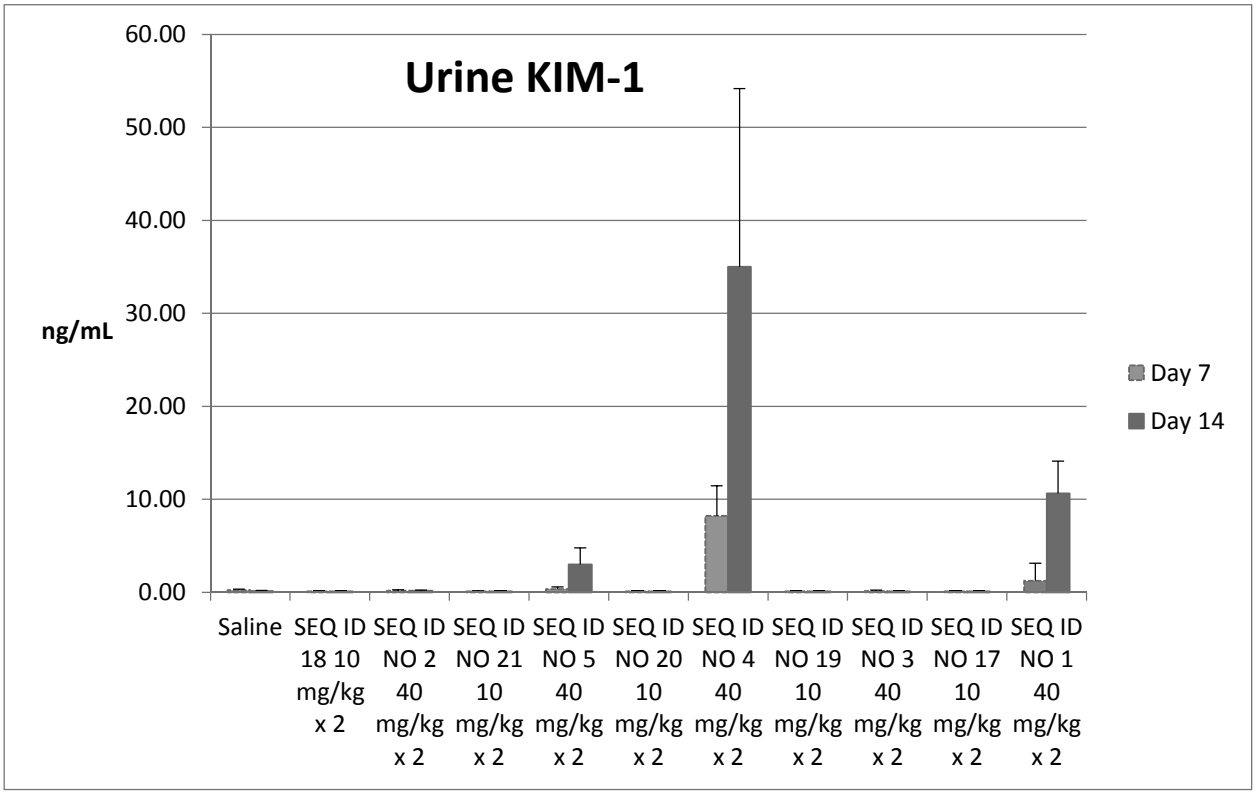


Figure 16

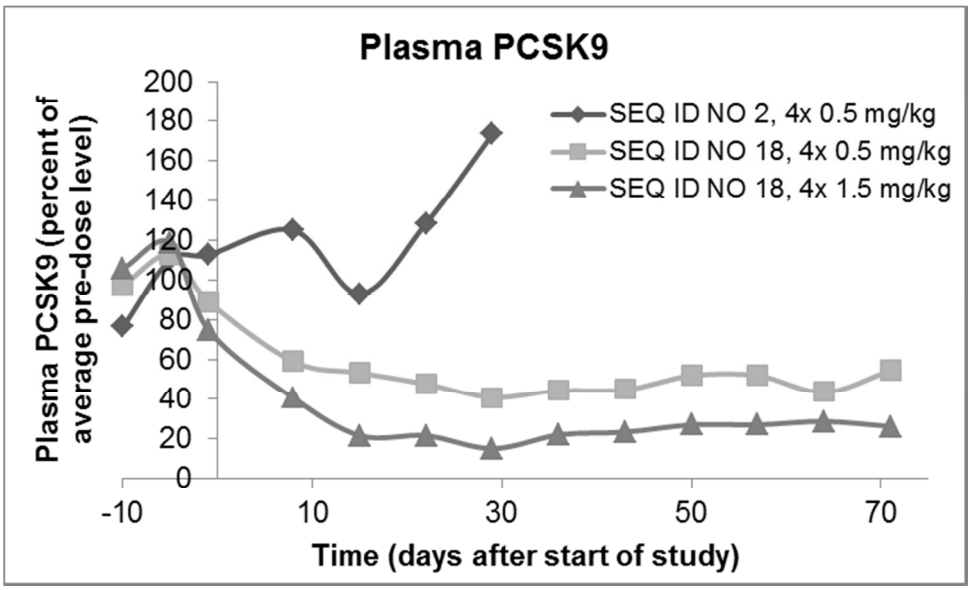


Figure 16 (cont)

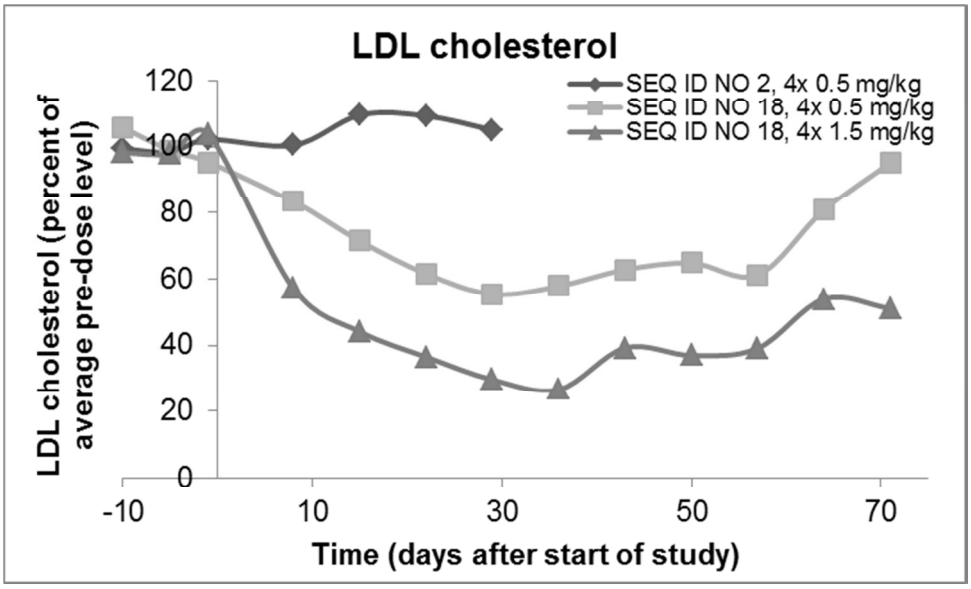


Figure 17

