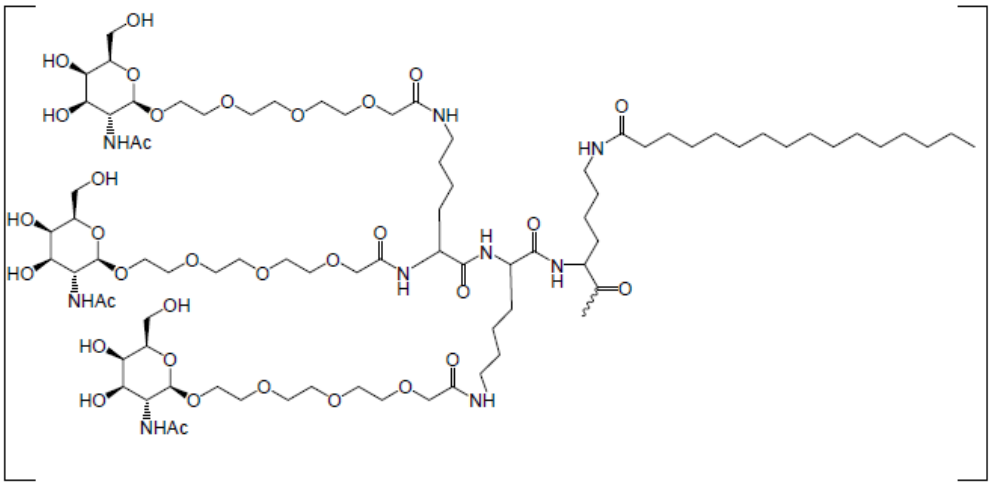
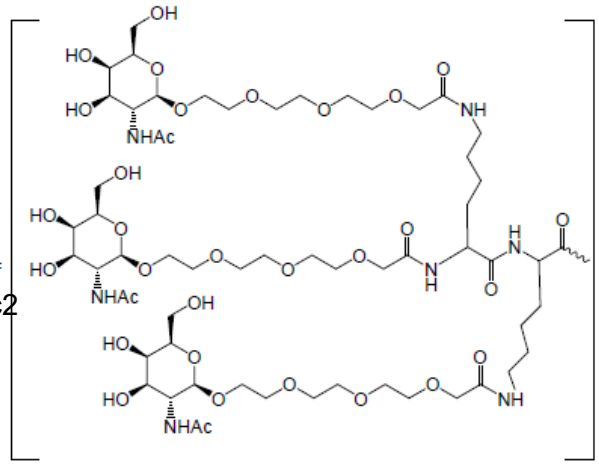
FIGURES

Figure 1

Conj 1=



Conj 2=
GalNAc2



Conj 3=

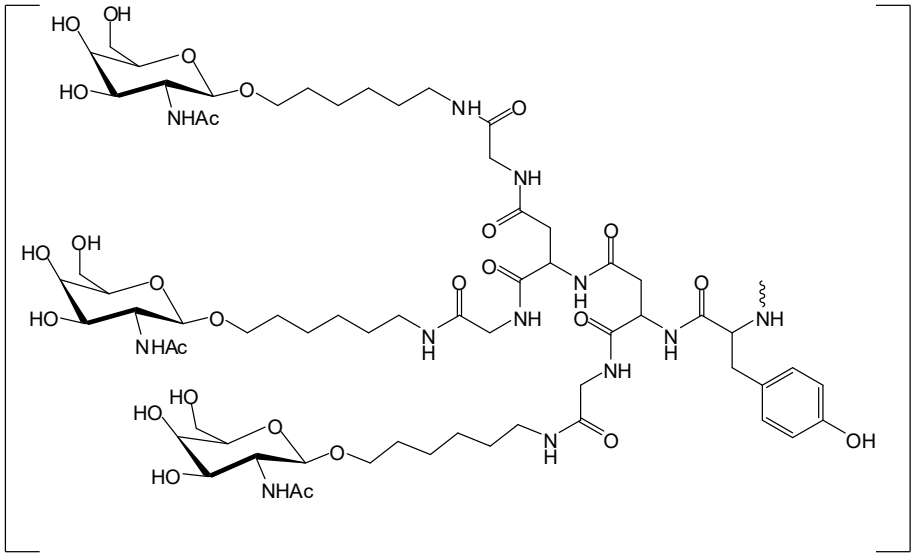
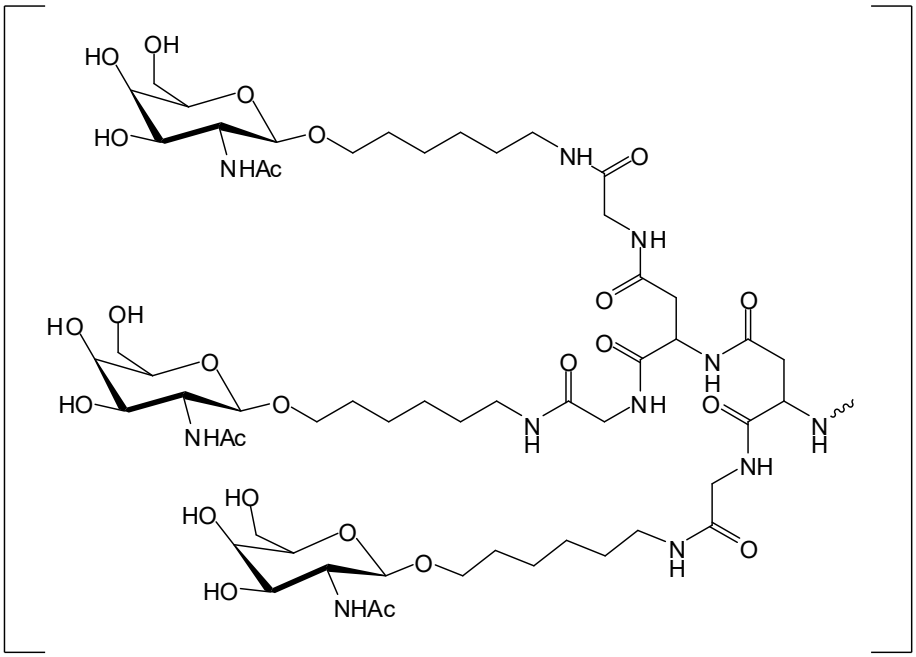


Figure 1 (cont)

Conj 4=



Conj 4a=

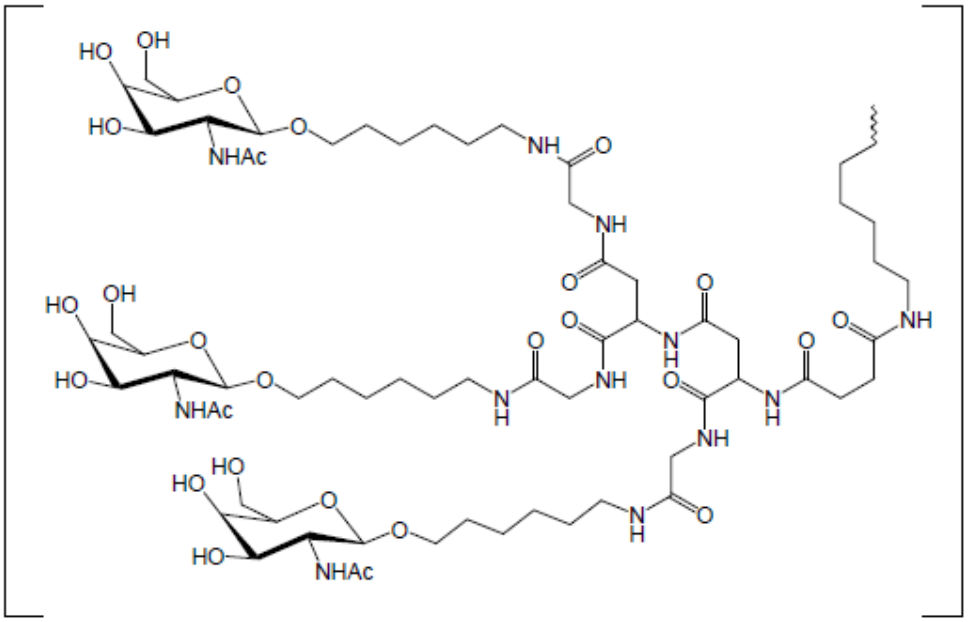
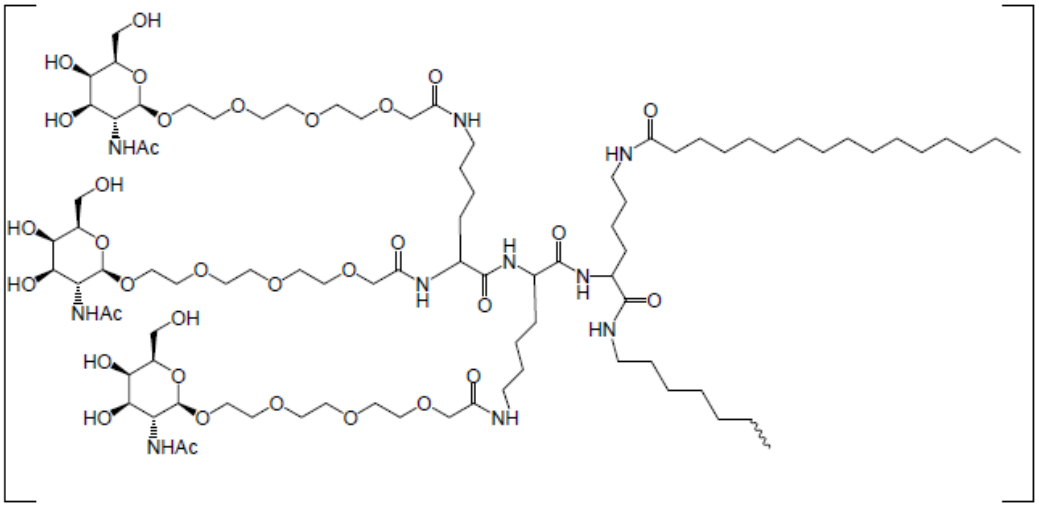
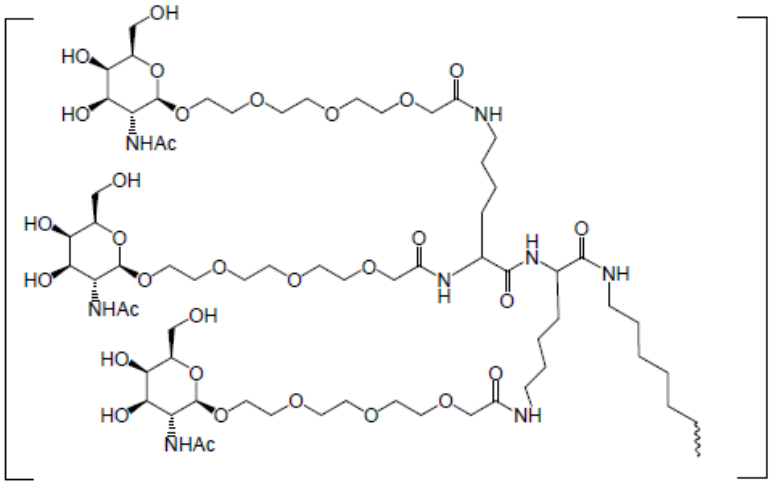


Figure 1 (cont)

Conj 1a=



Conj 2a=



Conj 3a=

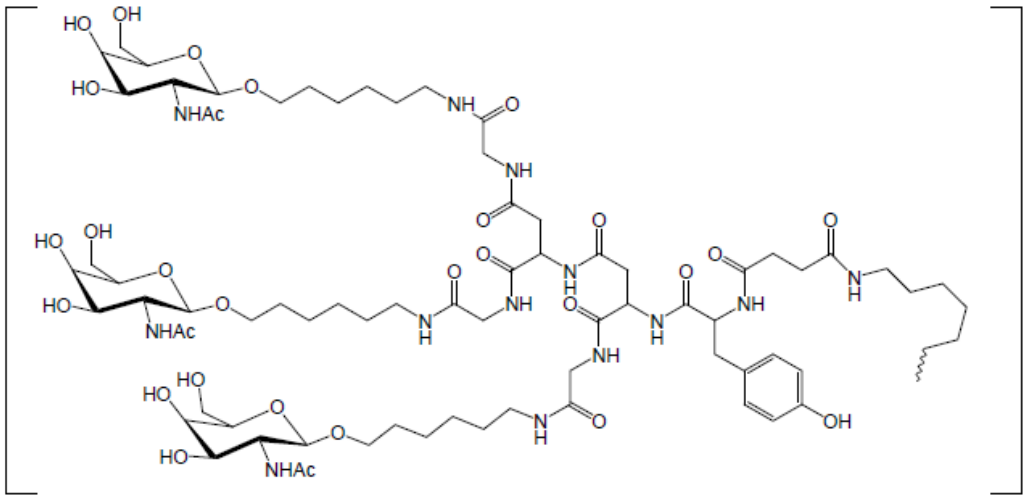
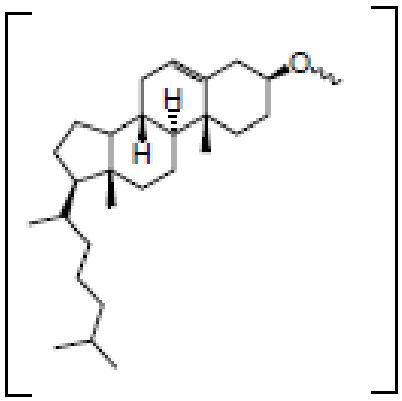
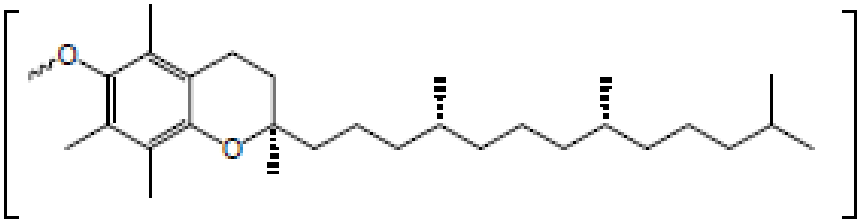


Figure 2

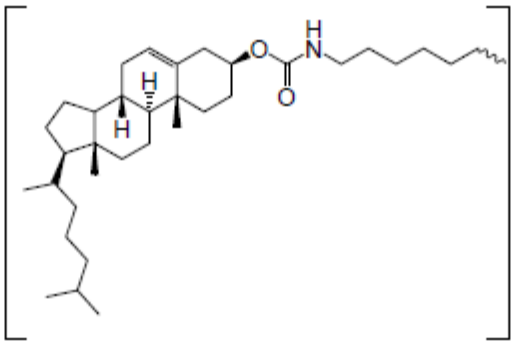
Conj 5=



Conj 6=



Conj 5a=
Chol-C6



Conj 6a=

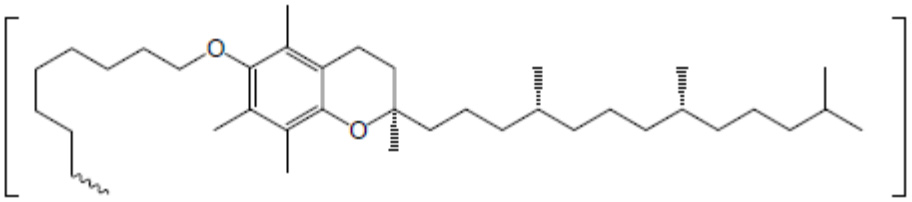
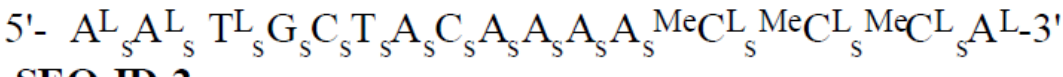


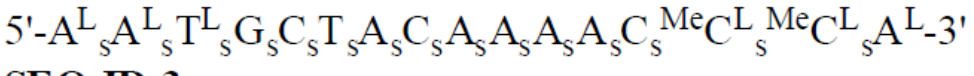
Figure 3



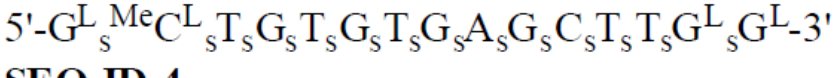
SEQ ID 1



SEQ ID 2



SEQ ID 3



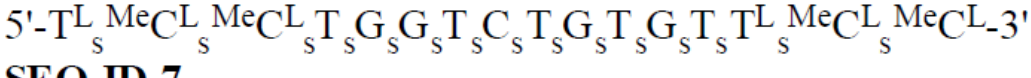
SEQ ID 4



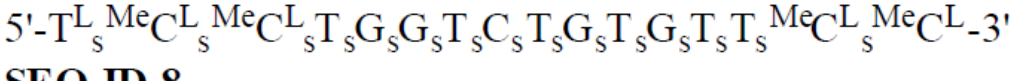
SEQ ID 5



SEQ ID 6



SEQ ID 7



SEQ ID 8

Figure 4

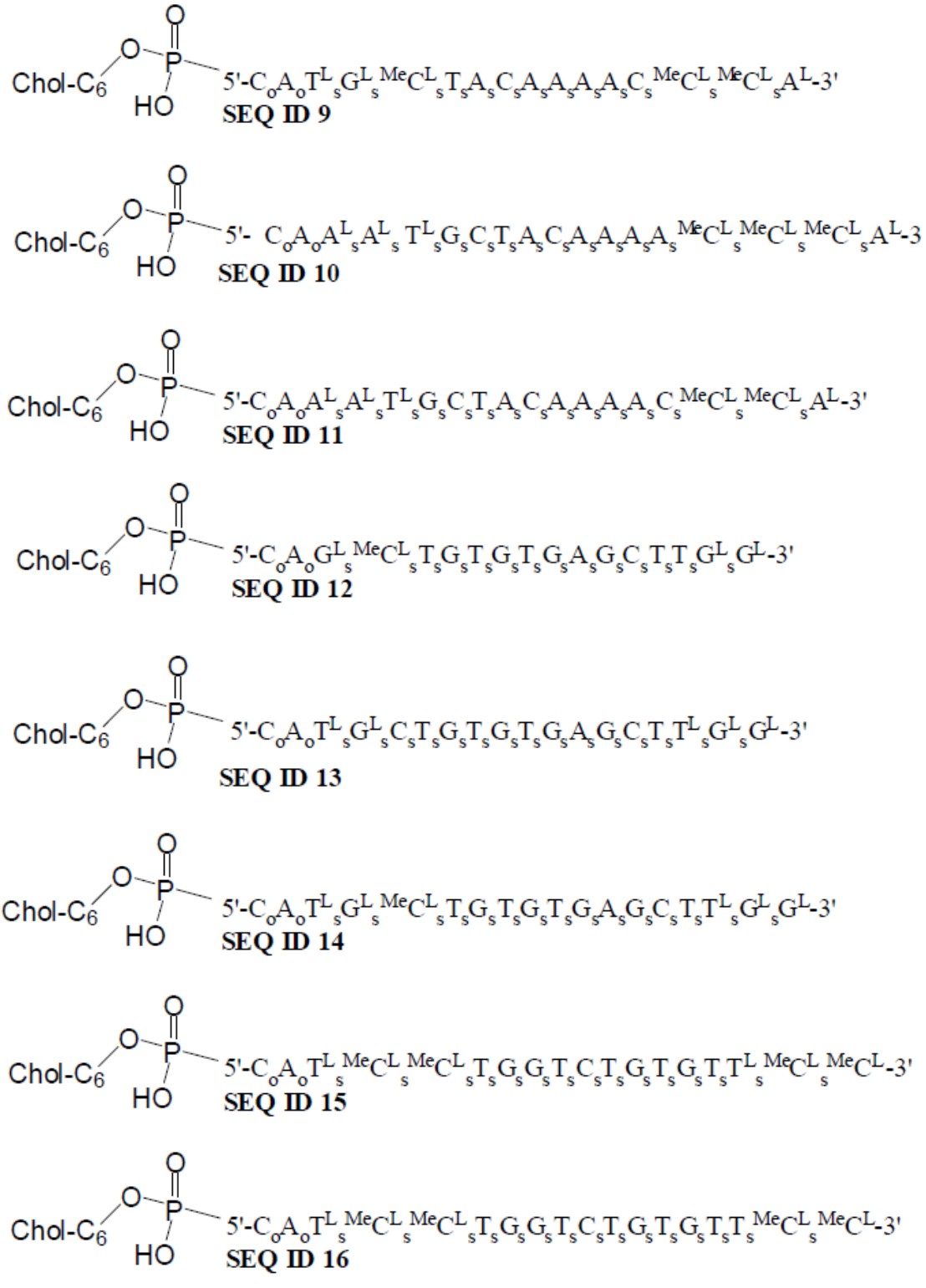
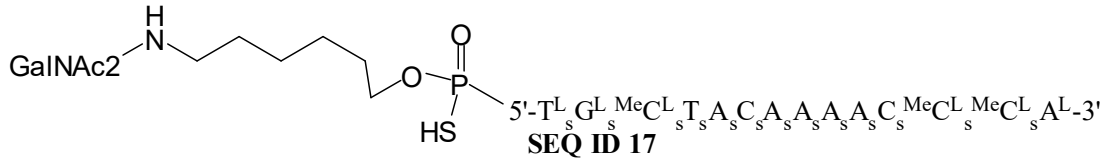

Chol-C6
HO
5'-CoAoTLsGLsMeCLsTsAsCsAsAsAsAsCsMeCLsMeCLsALs-3'
SEQ ID 9
Chol-C6
HO
5'- CoAoALsALs TLsGsCsTsAsCsAsAsAsAsMeCLsMeCLsMeCLsALs-3
SEQ ID 10
Chol-C6
HO
5'-CoAoALsALsTLsGsCsTsAsCsAsAsAsAsCsMeCLsMeCLsALs-3'
SEQ ID 11
Chol-C6
HO
5'-CoAoGLsMeCLsTsGsTsGsTsGsAsGsCsTsTsGLsGLs-3'
SEQ ID 12
Chol-C6
HO
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
5'-CoAoTLsMeCLsMeCLsTsGsGsTsCsTsGsTsGsTsTsMeCLsMeCLs-3'
SEQ ID 16

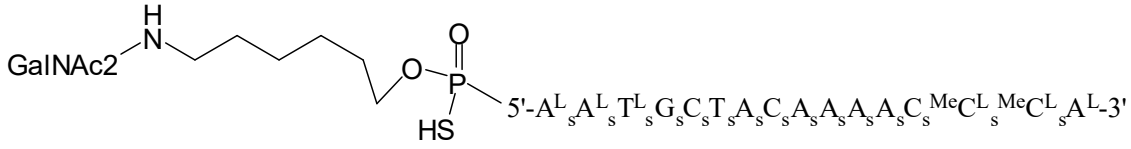
Figure 5



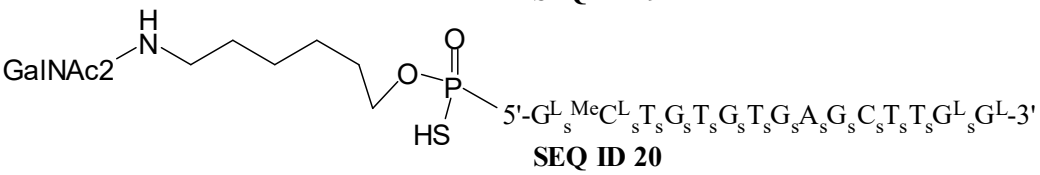
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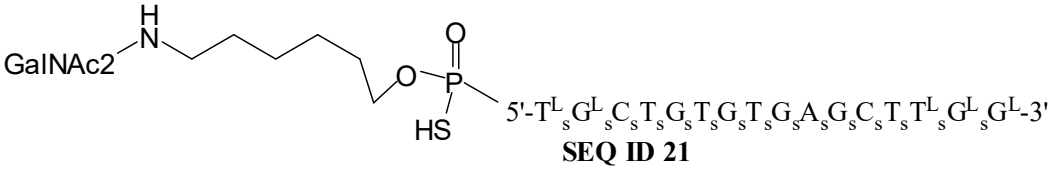
SEQ ID 18



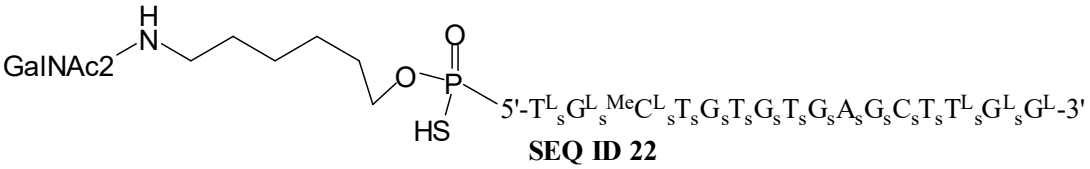
SEQ ID 19



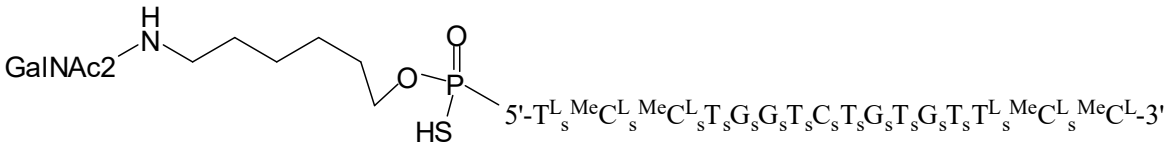
SEQ ID 20



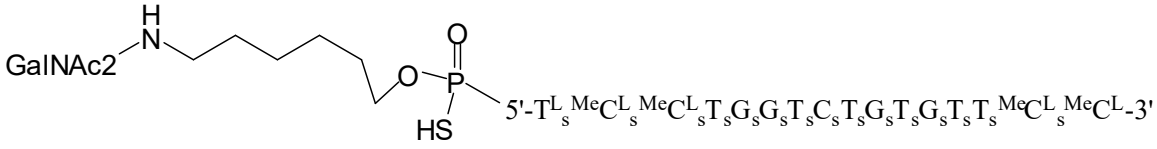
SEQ ID 21



SEQ ID 22



SEQ ID 23



SEQ ID 24

Figure 5A

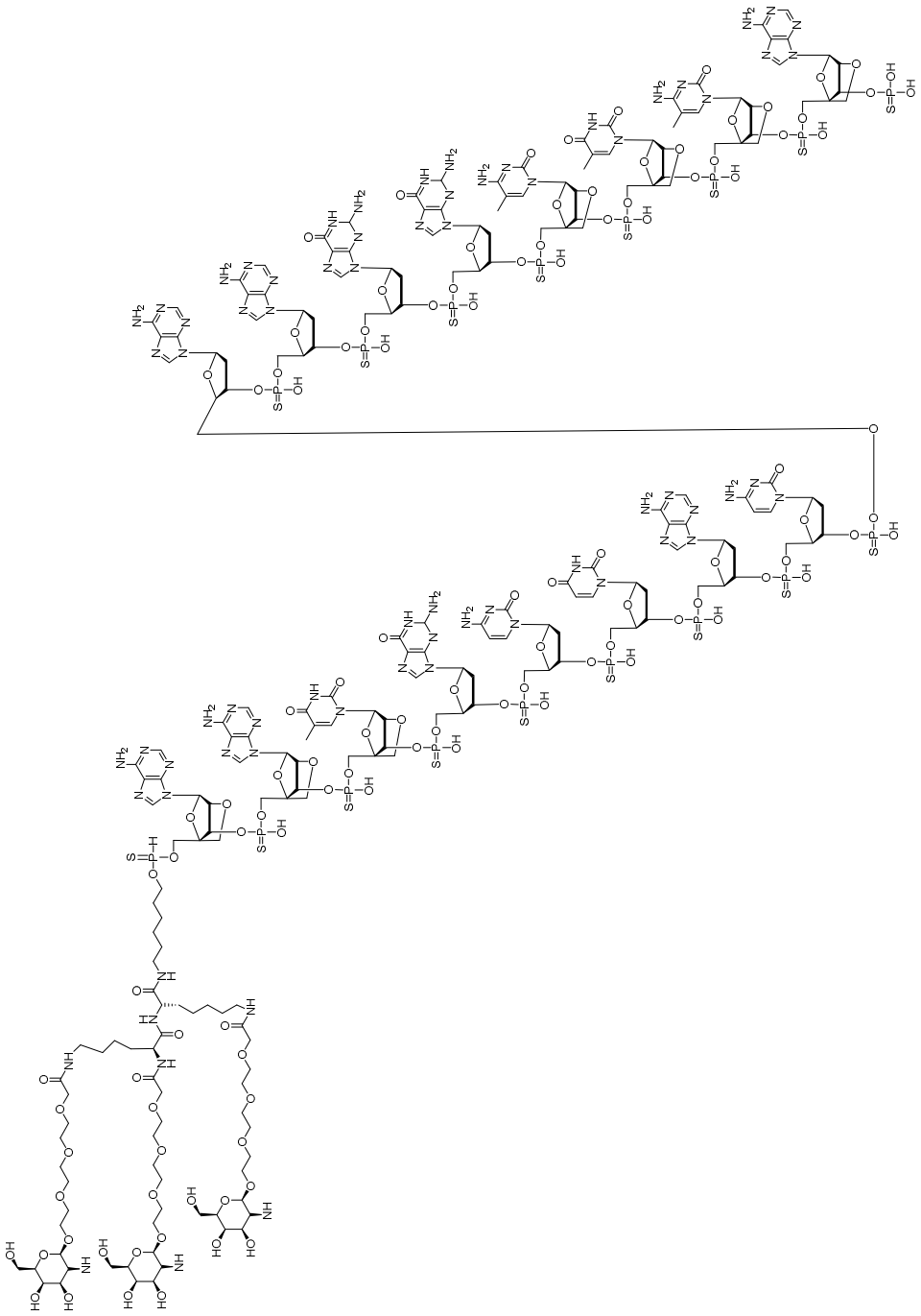


Figure 5B

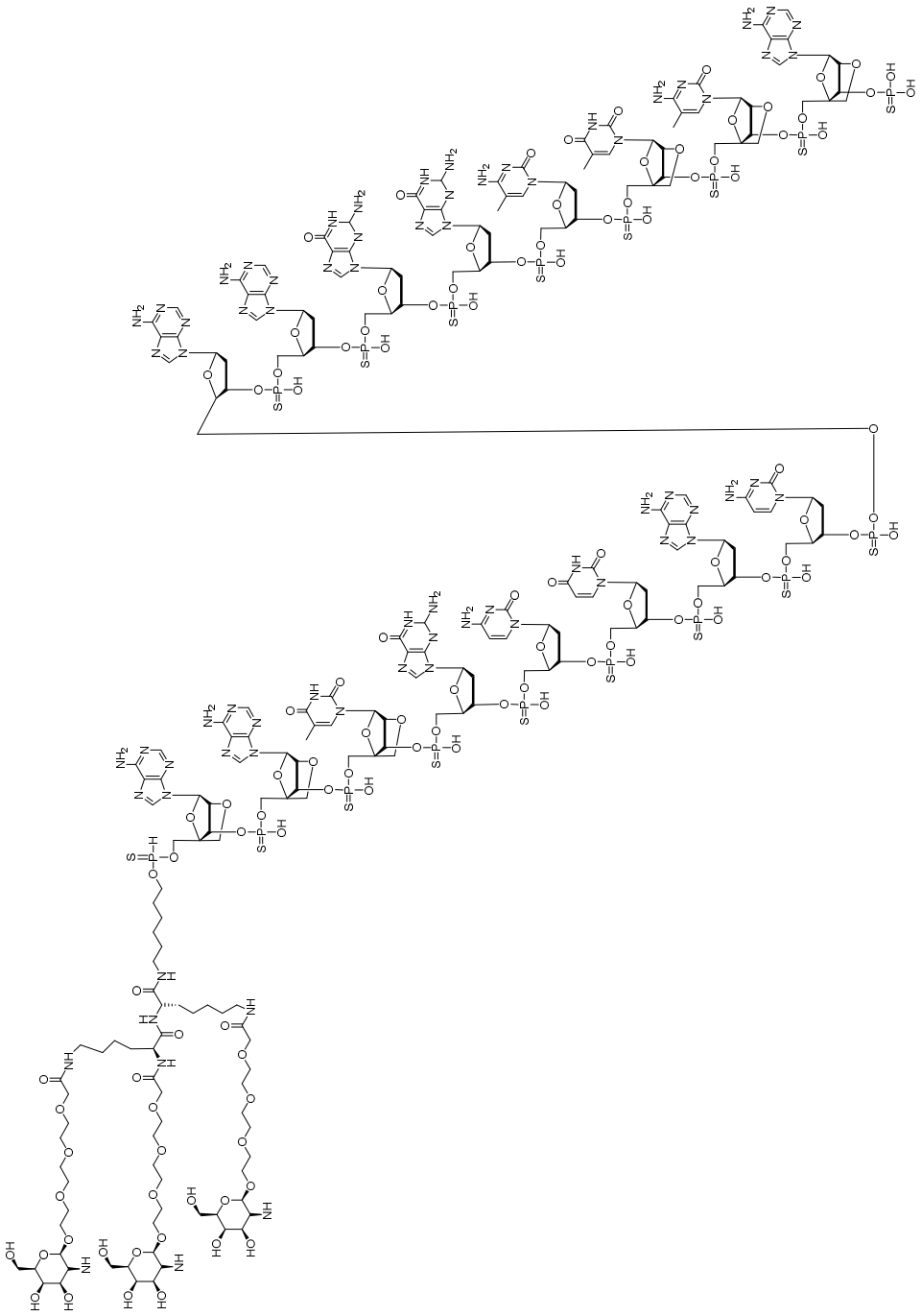


Figure 6

FAM=

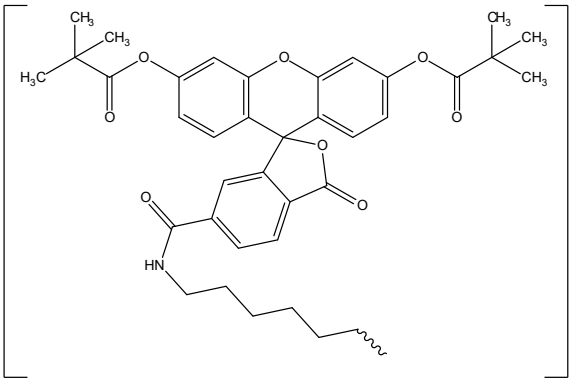


Figure 7

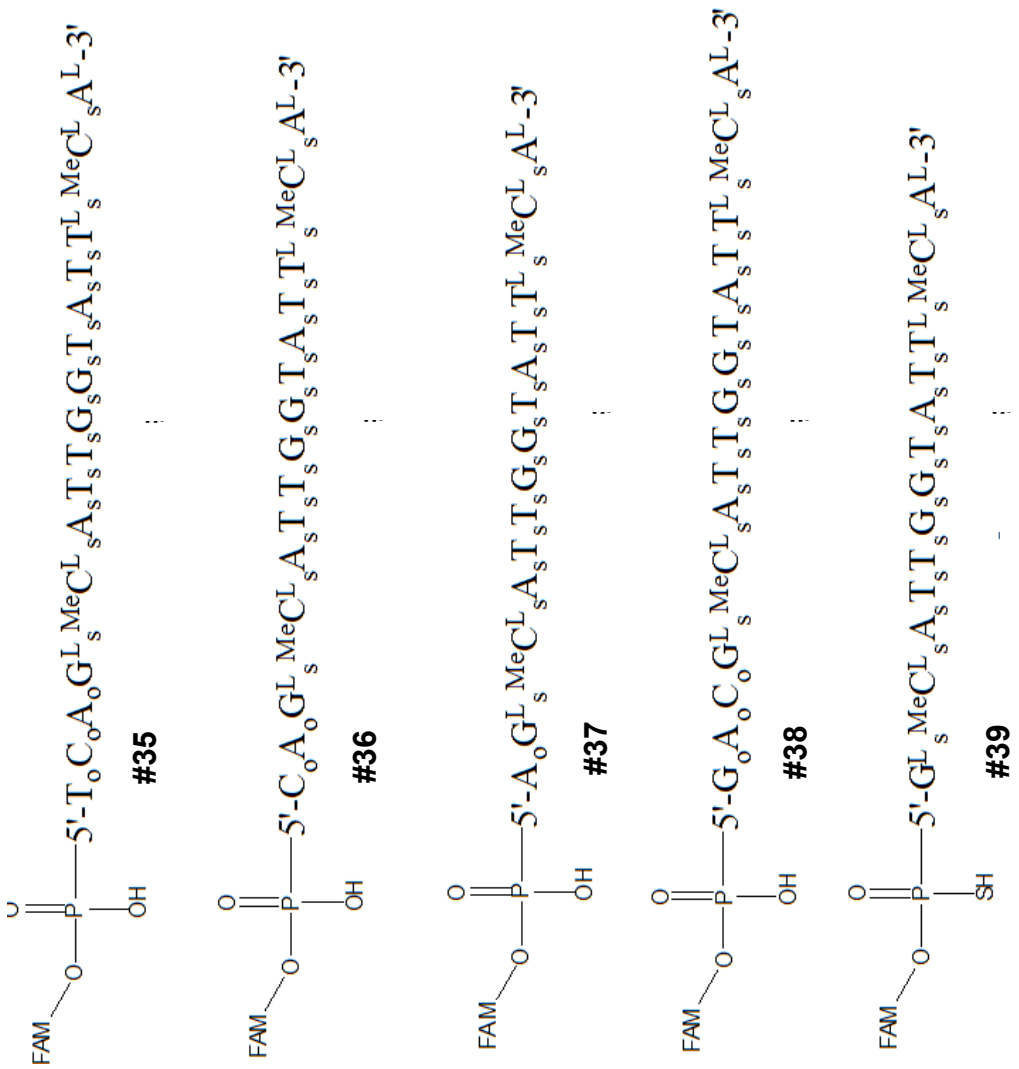


Figure 8

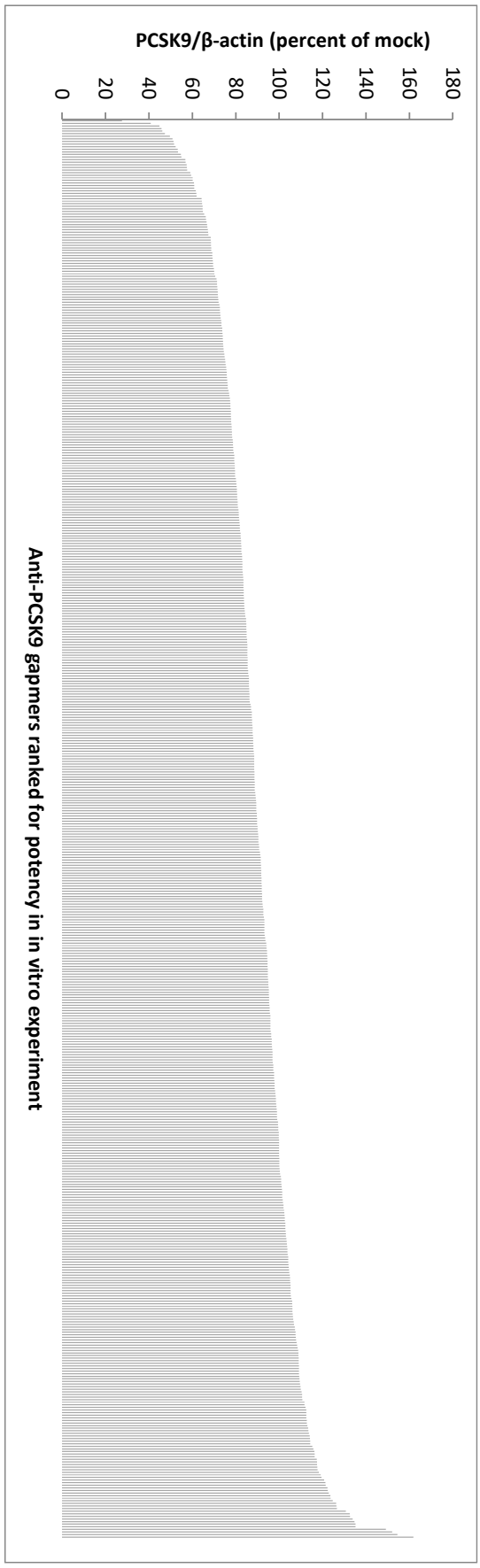

PCSK9/β-actin (percent of mock)
0
20
40
60
80
100
120
140
160
180
Anti-PCSK9 gapmers ranked for potency in in vitro experiment

Figure 9

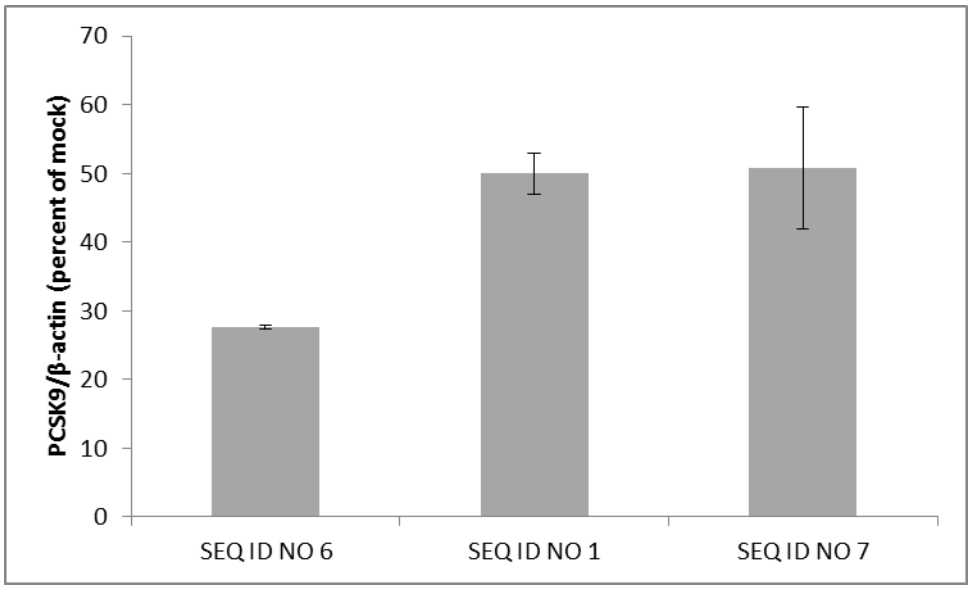

70
60
50
40
30
20
10
0
PCSK9/β-actin (percent of mock)
SEQ ID NO 6
SEQ ID NO 1
SEQ ID NO 7

Figure 10

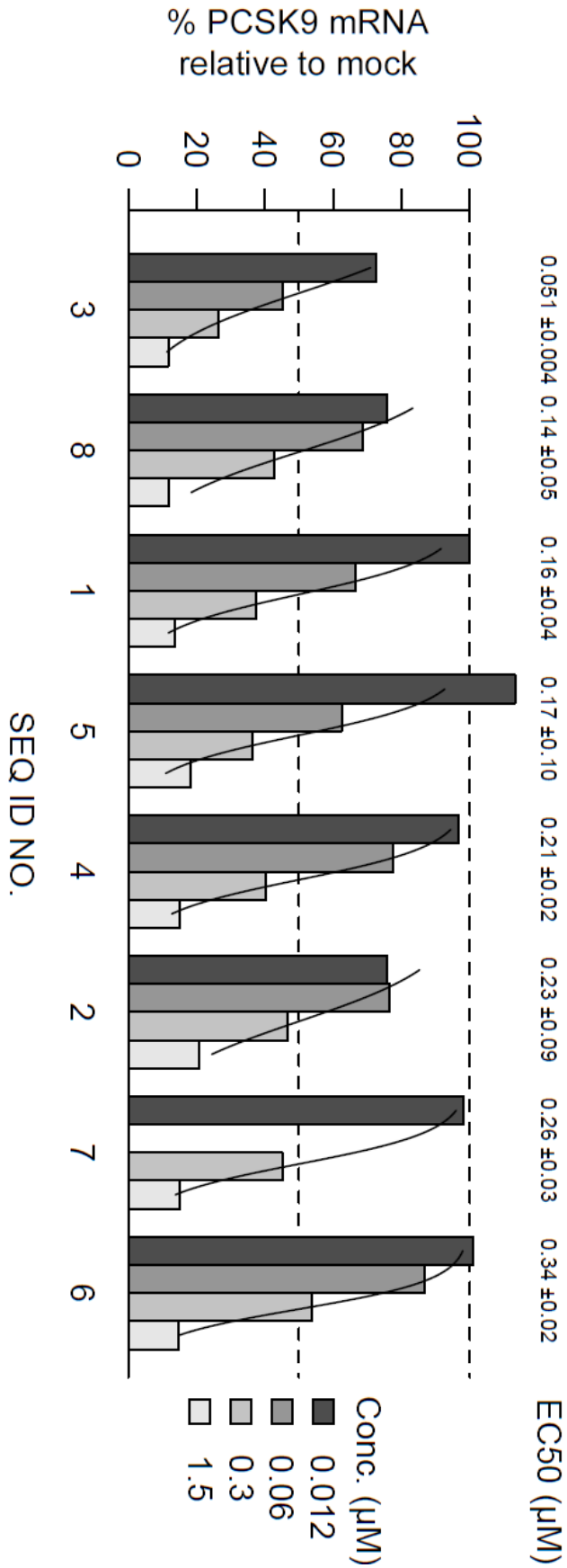

% PCSK9 mRNA
relative to mock
0
20
40
60
80
100
SEQ ID NO.
3
8
1
5
4
2
7
6
0.051 ±0.004
0.14 ±0.05
0.16 ±0.04
0.17 ±0.10
0.21 ±0.02
0.23 ±0.09
0.26 ±0.03
0.34 ±0.02
EC50 (µM)
Conc. (µM)
0.012
0.06
0.3
1.5

Figure 11

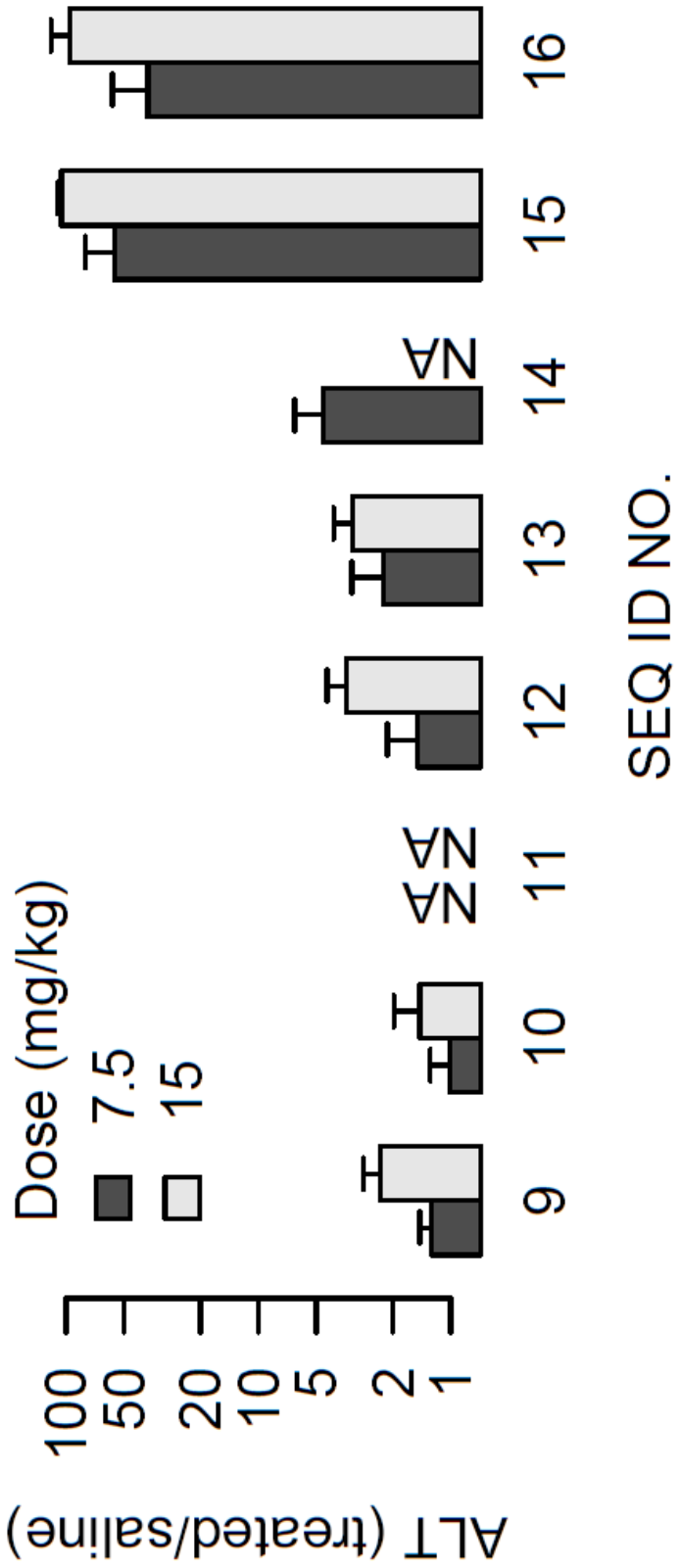

ALT (treated/saline)
100
50
20
10
5
2
1
Dose (mg/kg)
7.5
15
9
10
NA
NA
11
12
13
14
15
16
SEQ ID NO.

Figure 12

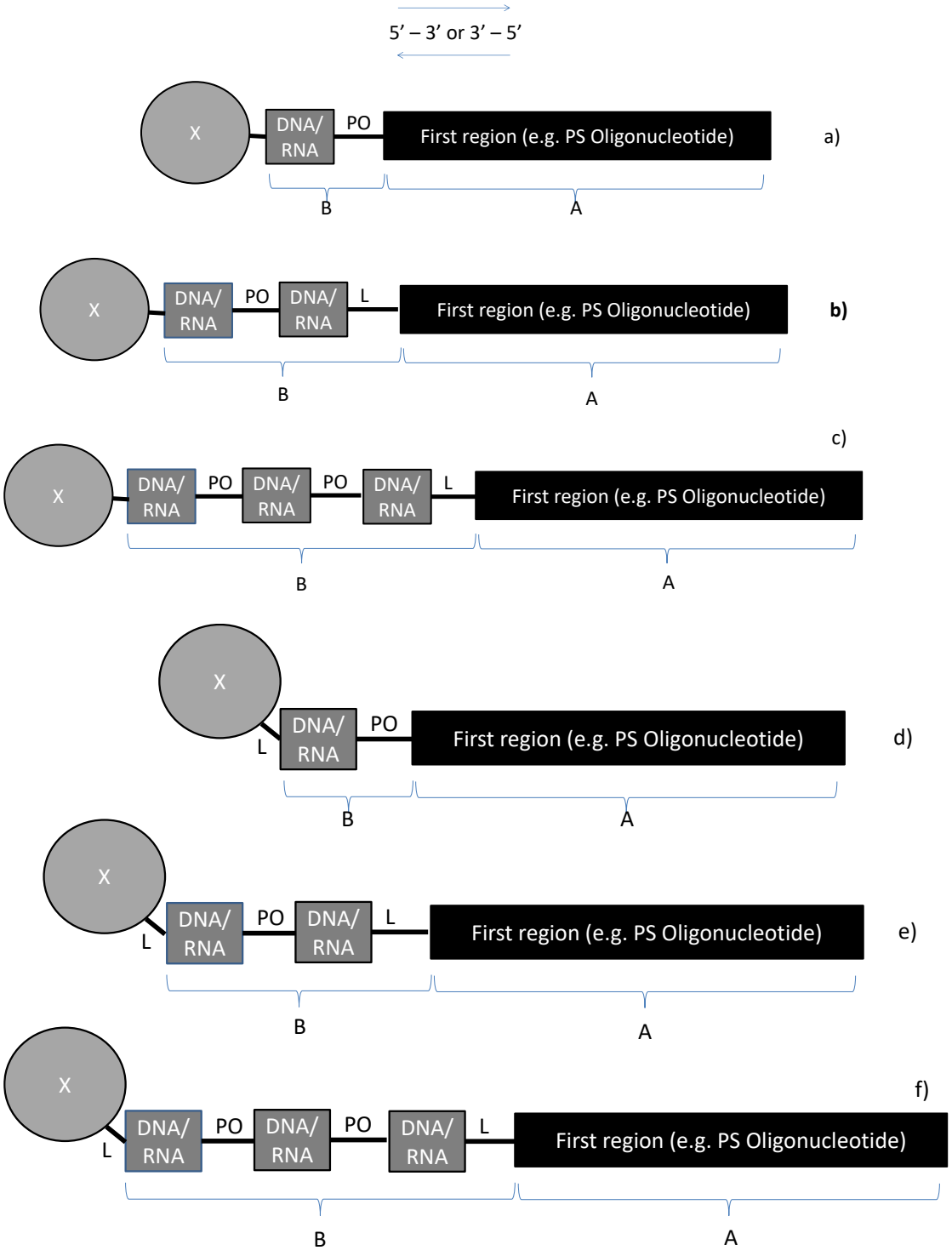

5' – 3' or 3' – 5'
X
DNA/ RNA
PO
First region (e.g. PS Oligonucleotide)
a)
B
A
X
DNA/ RNA
PO
DNA/ RNA
L
First region (e.g. PS Oligonucleotide)
b)
B
A
c)
X
DNA/ RNA
PO
DNA/ RNA
PO
DNA/ RNA
L
First region (e.g. PS Oligonucleotide)
B
A
X
L
DNA/ RNA
PO
First region (e.g. PS Oligonucleotide)
d)
B
A
X
L
DNA/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

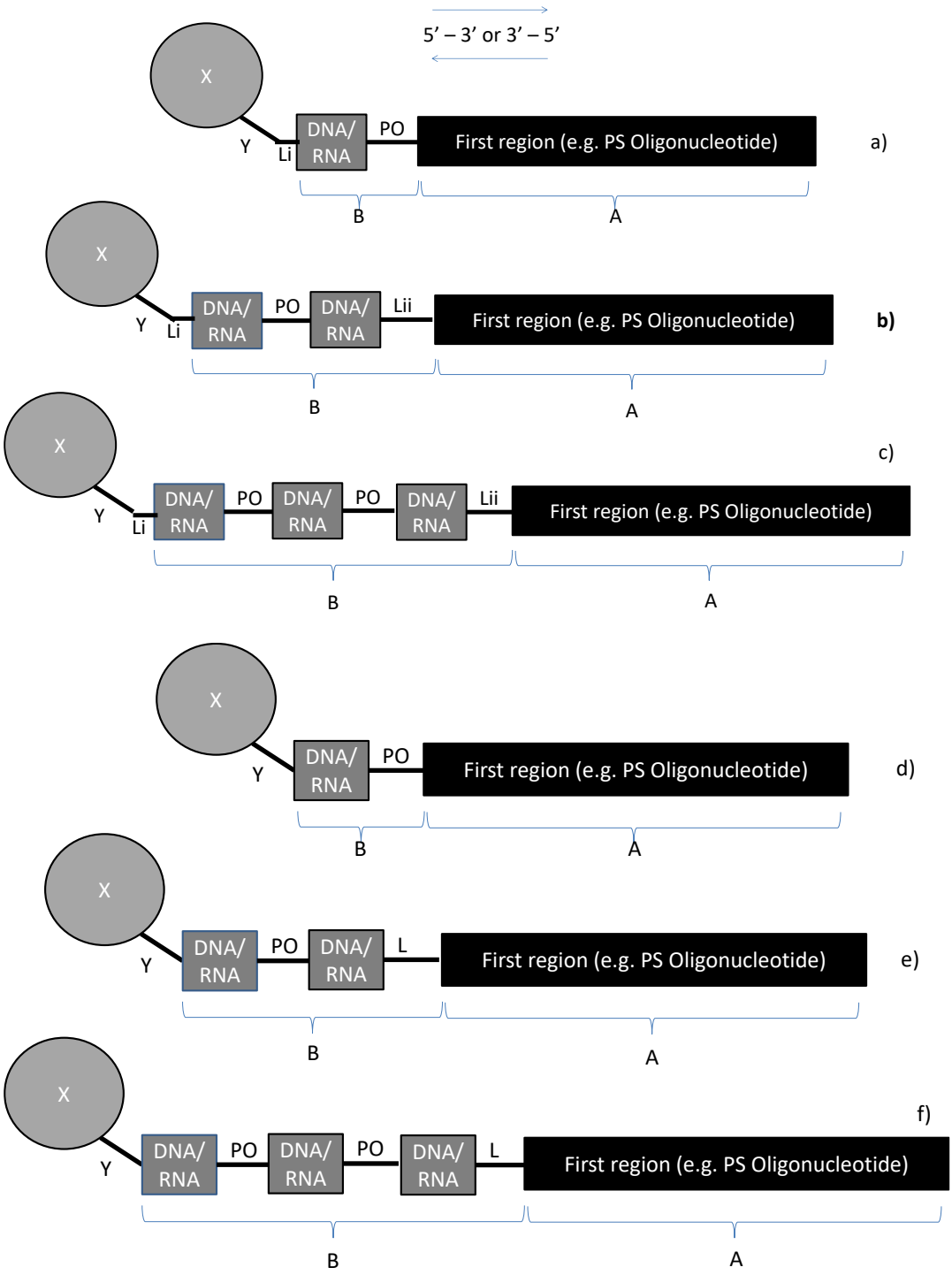
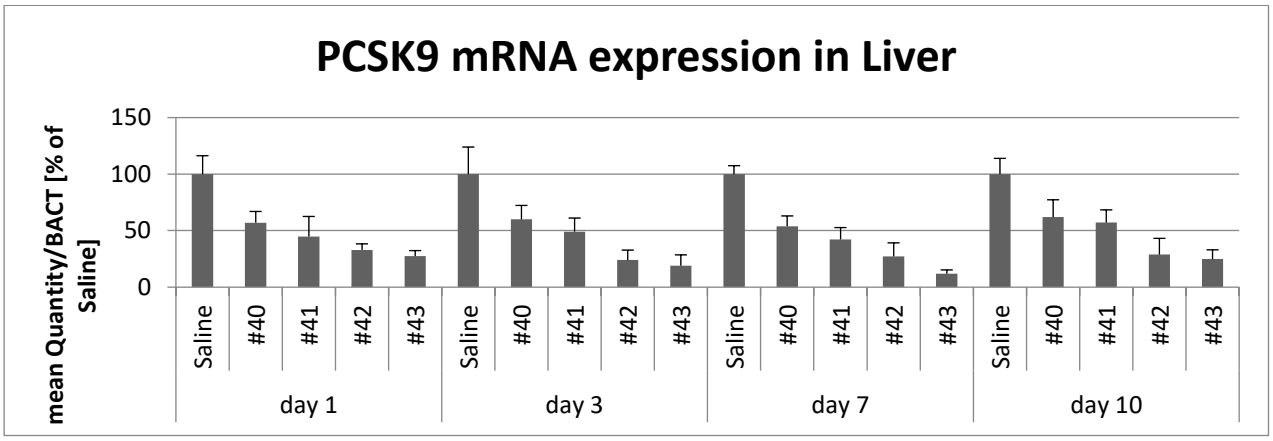

5' – 3' or 3' – 5'
X
Y
Li
DNA/ RNA
PO
First region (e.g. PS Oligonucleotide)
a)
B
A
X
Y
Li
DNA/ RNA
PO
DNA/ RNA
Lii
First region (e.g. PS Oligonucleotide)
b)
B
A
X
Y
Li
DNA/ RNA
PO
DNA/ RNA
PO
DNA/ RNA
Lii
First region (e.g. PS Oligonucleotide)
c)
B
A
X
Y
DNA/ RNA
PO
First region (e.g. PS Oligonucleotide)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

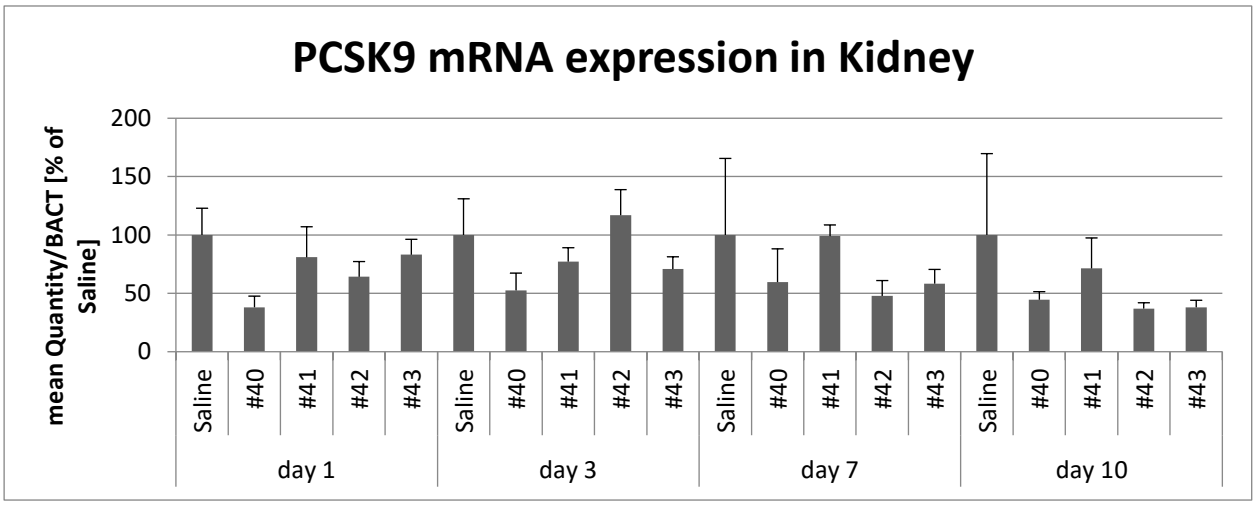

PCSK9 mRNA expression in Kidney
mean Quantity/BACT [% of Saline]
200
150
100
50
0
Saline
#40
#41
#42
#43
day 1
day 3
day 7
day 10

Figure 15

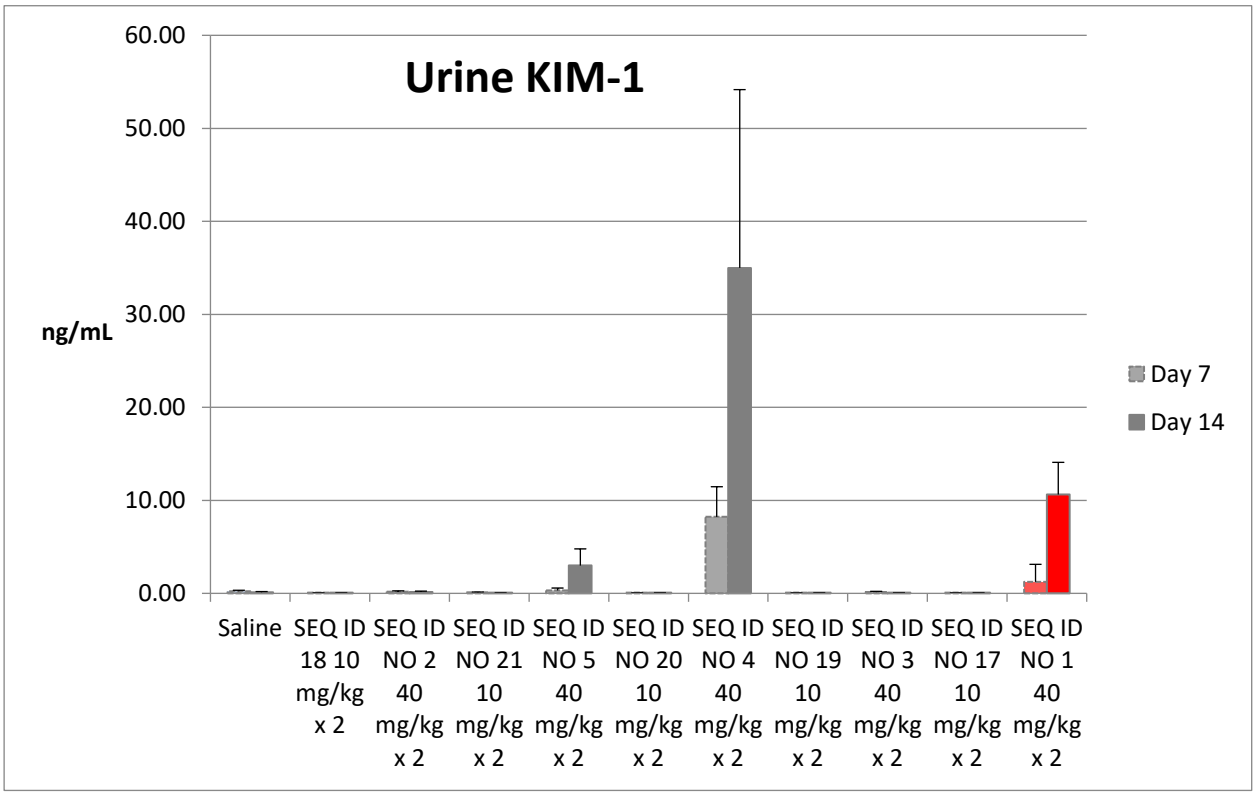


Figure 16

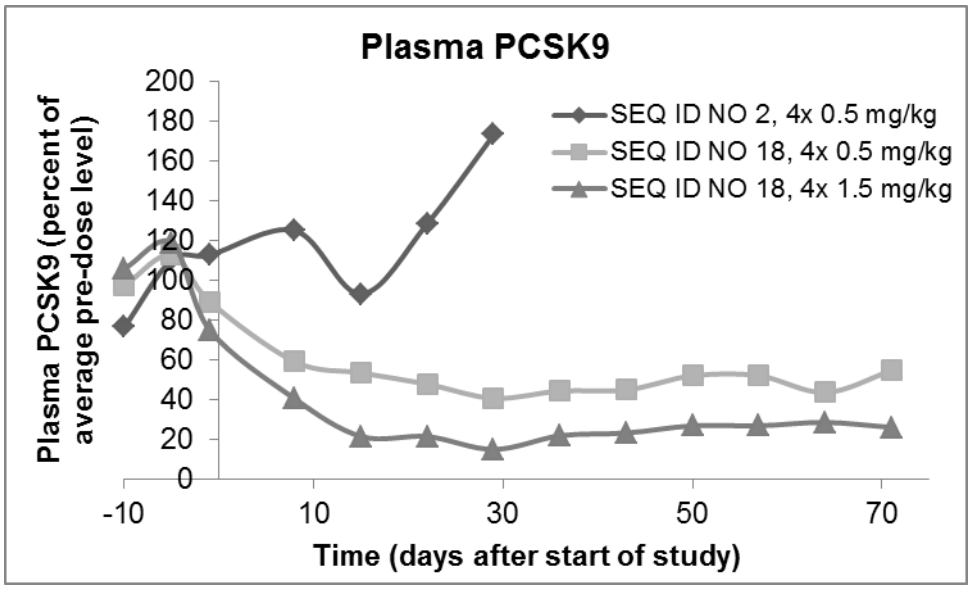


Figure 16 (cont)

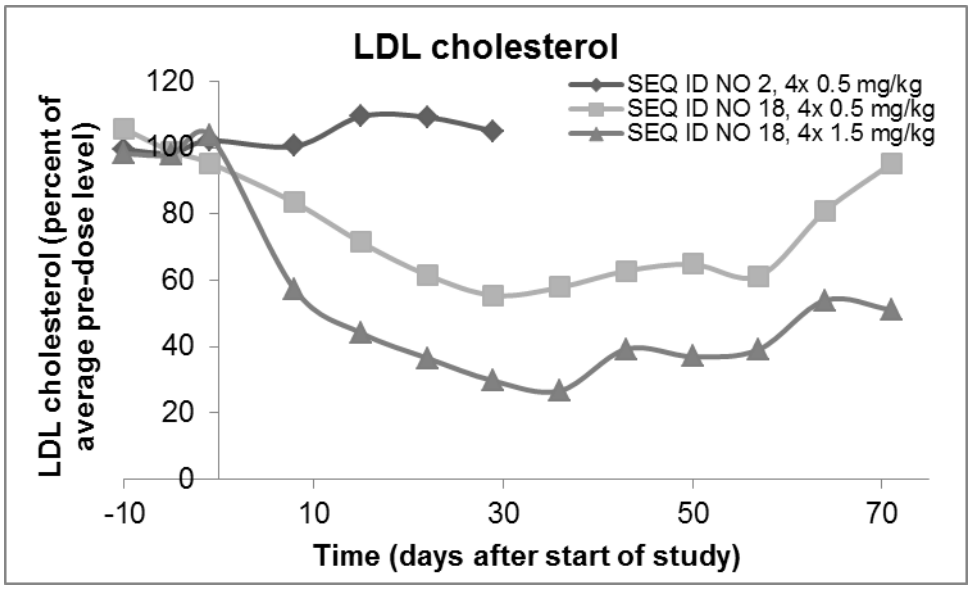


Figure 17

