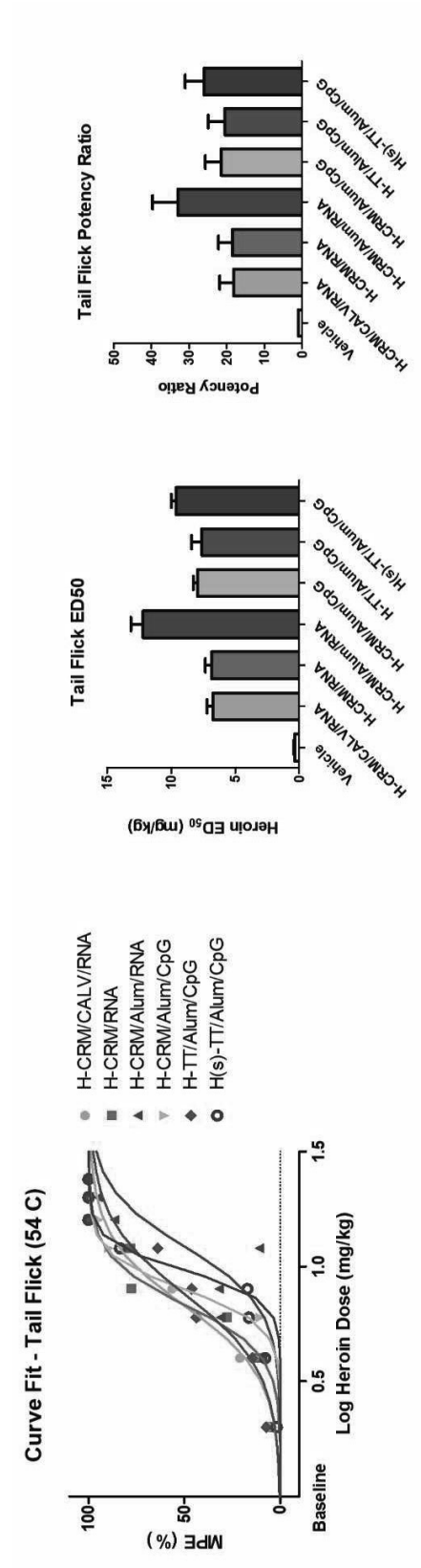
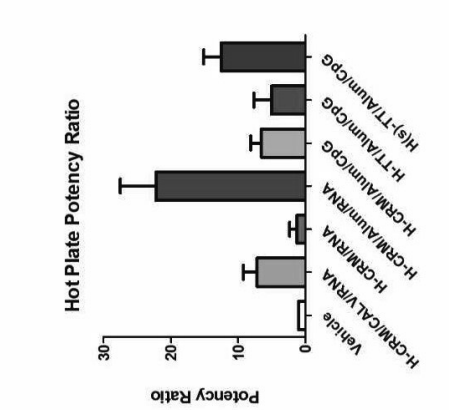

Curve Fit - Tail Flick (54 C)
H-CRM/CALV/RNA
H-CRM/RNA
H-CRM/Alum/RNA
H-CRM/Alum/CpG
H-TT/Alum/CpG
H(s)-TT/Alum/CpG
MPE (%)
Log Heroin Dose (mg/kg)
Baseline
Tail Flick ED50
Heroin ED50 (mg/kg)
Tail Flick Potency Ratio
Potency Ratio
Vehicle
H-CRM/CALV/RNA
H-CRM/RNA
H-CRM/Alum/RNA
H-CRM/Alum/CpG
H-TT/Alum/CpG
H(s)-TT/Alum/CpG

Fig. 1


Hot Plate Potency Ratio
Potency Ratio
30
20
10
0
Vehicle
H-CRM/CALV/RNA
H-CRM/RNA
H-CRM/Alum/RNA
H-CRM/Alum/CpG
H-TT/Alum/CpG
H(s)-TT/Alum/CpG

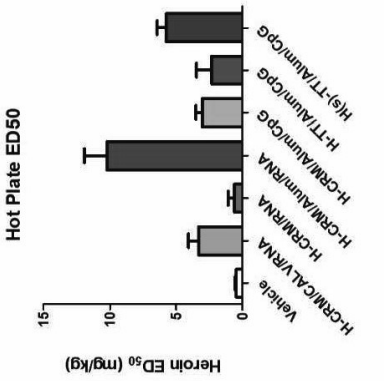

Hot Plate ED50
Heroin ED50 (mg/kg)
15
10
5
0
Vehicle
H-CRM/CALV/RNA
H-CRM/RNA
H-CRM/Alum/RNA
H-CRM/Alum/CpG
H-TT/Alum/CpG
H(s)-TT/Alum/CpG

Fig 2

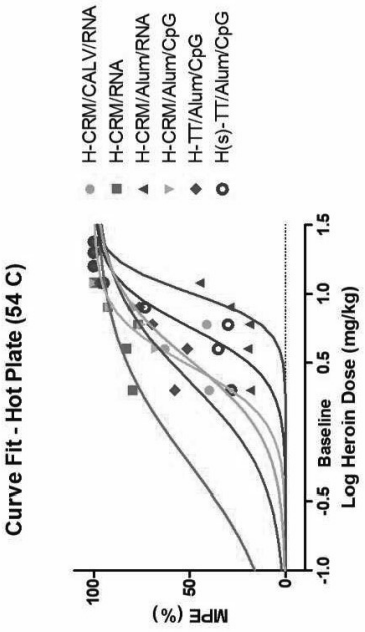
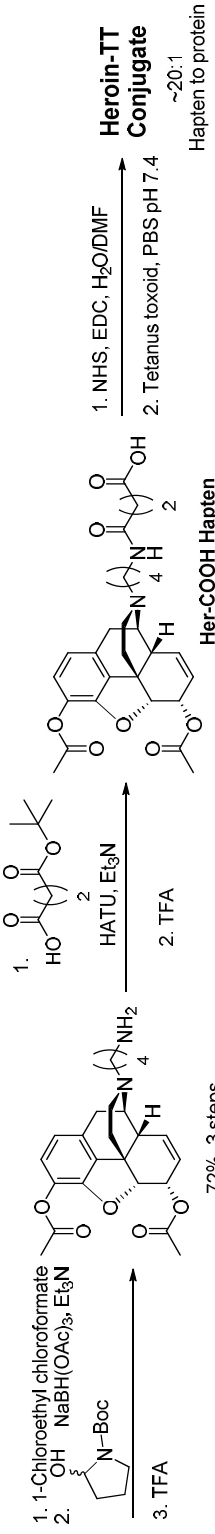

Curve Fit - Hot Plate (54 C)
H-CRM/CALV/RNA
H-CRM/RNA
H-CRM/Alum/RNA
H-CRM/Alum/CpG
H-TT/Alum/CpG
H(s)-TT/Alum/CpG
MPE (%)
100
50
0
-1.0
-0.5
Baseline
0.5
1.0
1.5
Log Heroin Dose (mg/kg)

Fig. 3


Heroin
1. 1-Chloroethyl chloroformate
2. NaBH(OAc)3, Et3N
3. TFA
72%, 3 steps
1.
HATU, Et3N
2. TFA
Her-COOH Hapten
80%, 2 steps
1. NHS, EDC, H2O/DMF
2. Tetanus toxoid, PBS pH 7.4
Heroin-TT Conjugate
~20:1
Hapten to protein

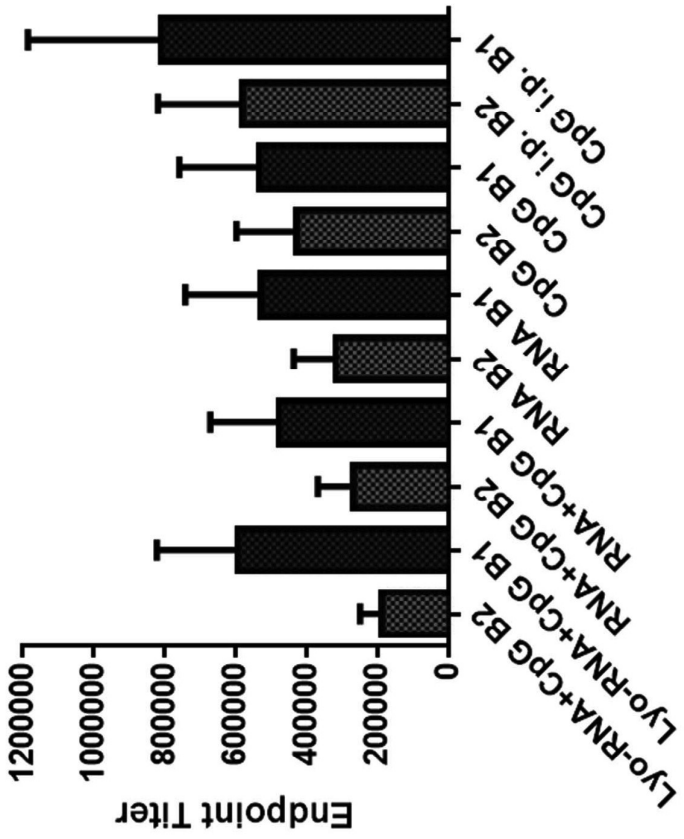

Endpoint Titer
1200000
1000000
800000
600000
400000
200000
0
Lyo-RNA+CpG B2
Lyo-RNA+CpG B1
RNA+CpG B2
RNA+CpG B1
RNA B2
RNA B1
CpG B2
CpG B1
CpG i.p. B2
CpG i.p. B1

Fig. 4

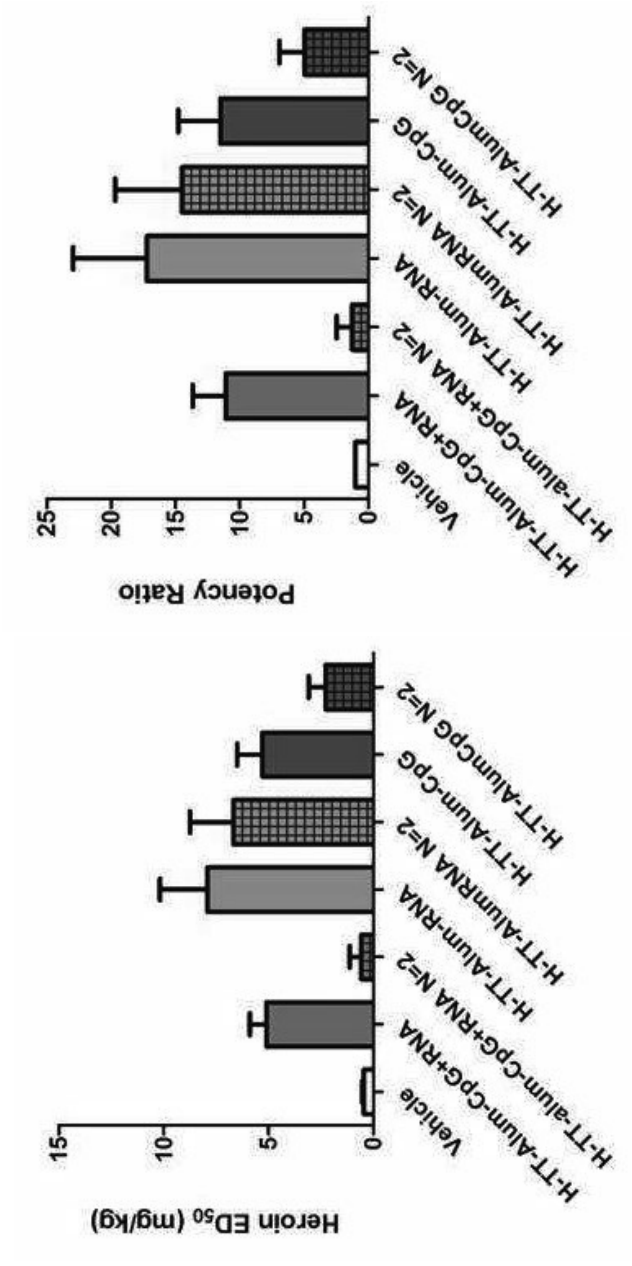

Potency Ratio
0
5
10
15
20
25
Vehicle
H-TT-Alum-CpG+RNA
H-TT-alum-CpG+RNA N=2
H-TT-Alum-RNA
H-TT-AlumRNA N=2
H-TT-Alum-CpG
H-TT-AlumCpG N=2
Heroin ED50 (mg/kg)
0
5
10
15
Vehicle
H-TT-Alum-CpG+RNA
H-TT-alum-CpG+RNA N=2
H-TT-Alum-RNA
H-TT-AlumRNA N=2
H-TT-Alum-CpG
H-TT-AlumCpG N=2

Fig. 5

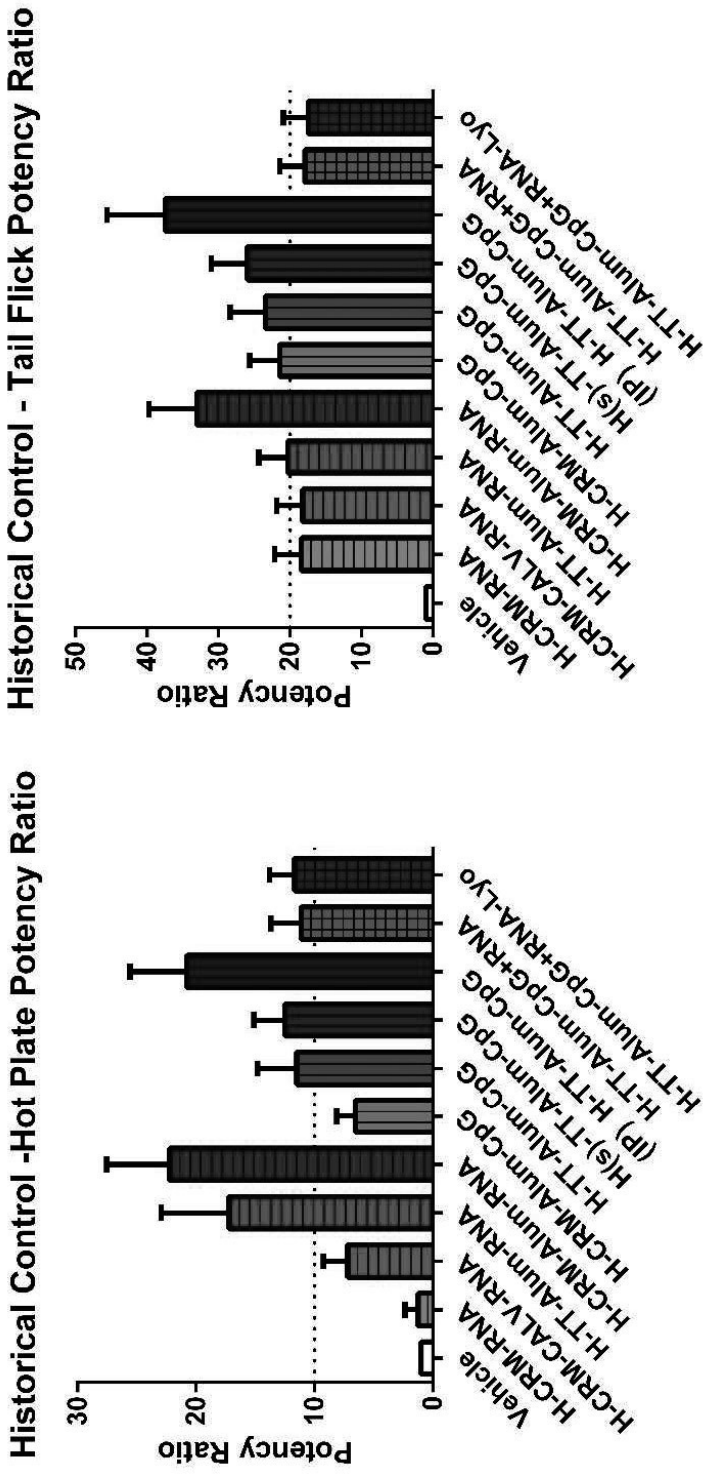

Historical Control -Hot Plate Potency Ratio
Potency Ratio
0
10
20
30
Vehicle
H-CRM-RNA
H-CRM-CALV-RNA
H-TT-Alum-RNA
H-CRM-Alum-RNA
H-TT-Alum-CpG
H(s)-TT-Alum-CpG (IP)
H-CRM-Alum-CpG
H-TT-Alum-CpG+RNA
H-TT-Alum-CpG+RNA-Lyo
Historical Control - Tail Flick Potency Ratio
Potency Ratio
0
10
20
30
40
50
Vehicle
H-CRM-RNA
H-CRM-CALV-RNA
H-TT-Alum-RNA
H-CRM-Alum-RNA
H-TT-Alum-CpG
H(s)-TT-Alum-CpG (IP)
H-CRM-Alum-CpG
H-TT-Alum-CpG+RNA
H-TT-Alum-CpG+RNA-Lyo

Fig. 6

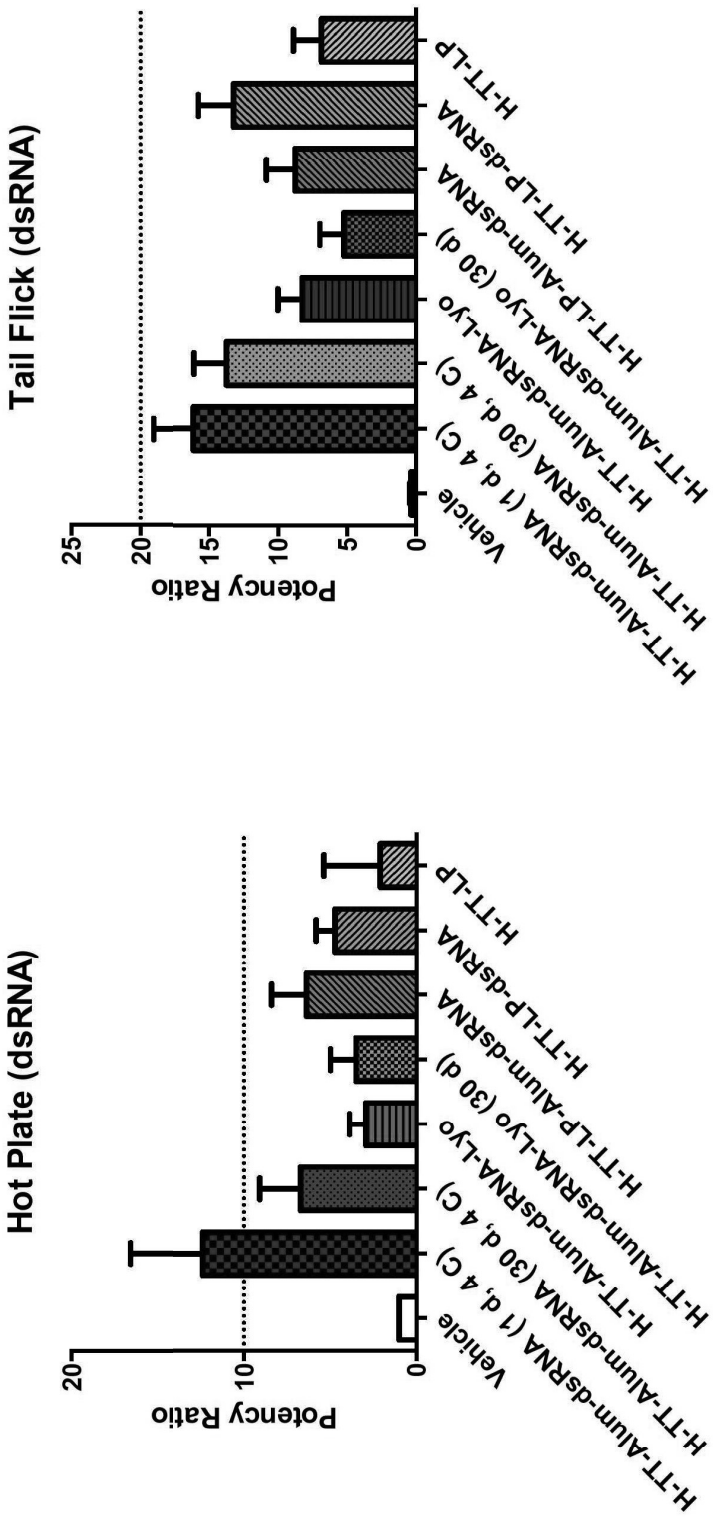

Tail Flick (dsRNA)
Potency Ratio
0
5
10
15
20
25
Vehicle
H-TT-Alum-dsRNA (1 d, 4 C)
H-TT-Alum-dsRNA (30 d, 4 C)
H-TT-Alum-dsRNA-Lyo
H-TT-Alum-dsRNA-Lyo (30 d)
H-TT-LP-Alum-dsRNA
H-TT-LP-dsRNA
H-TT-LP
Hot Plate (dsRNA)
Potency Ratio
0
10
20
Vehicle
H-TT-Alum-dsRNA (1 d, 4 C)
H-TT-Alum-dsRNA (30 d, 4 C)
H-TT-Alum-dsRNA-Lyo
H-TT-Alum-dsRNA-Lyo (30 d)
H-TT-LP-Alum-dsRNA
H-TT-LP-dsRNA
H-TT-LP

Fig. 7

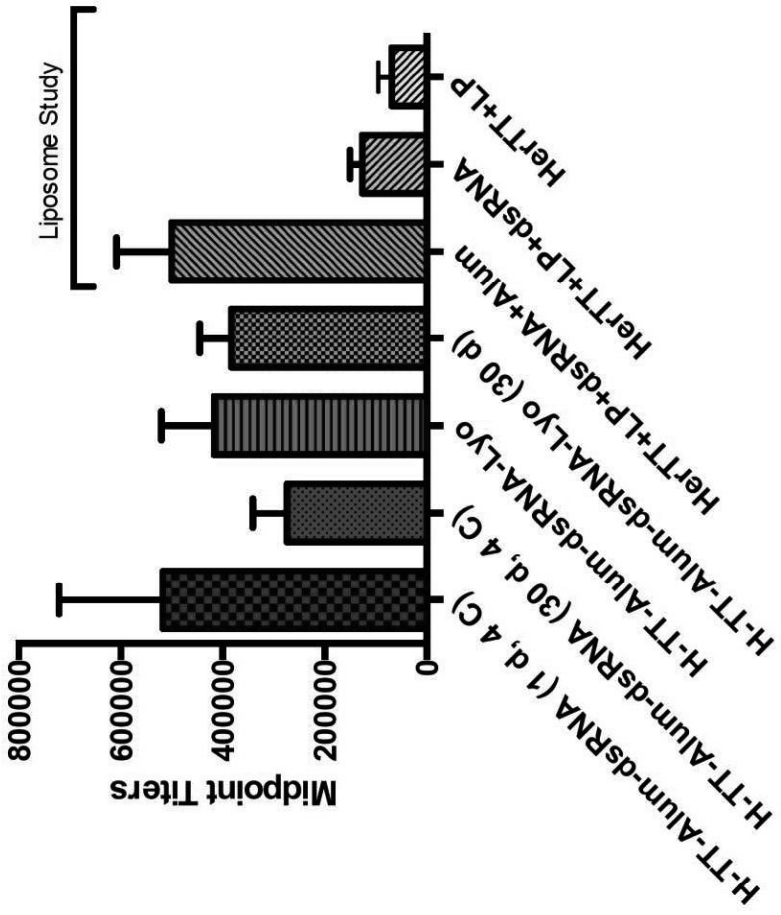

Liposome Study
Midpoint Titers
800000
600000
400000
200000
0
H-TT-Alum-dsRNA (1 d, 4 C)
H-TT-Alum-dsRNA (30 d, 4 C)
H-TT-Alum-dsRNA-Lyo
H-TT-Alum-dsRNA-Lyo (30 d)
HerTT+LP+dsRNA+Alum
HerTT+LP+dsRNA
HerTT+LP

Fig. 8

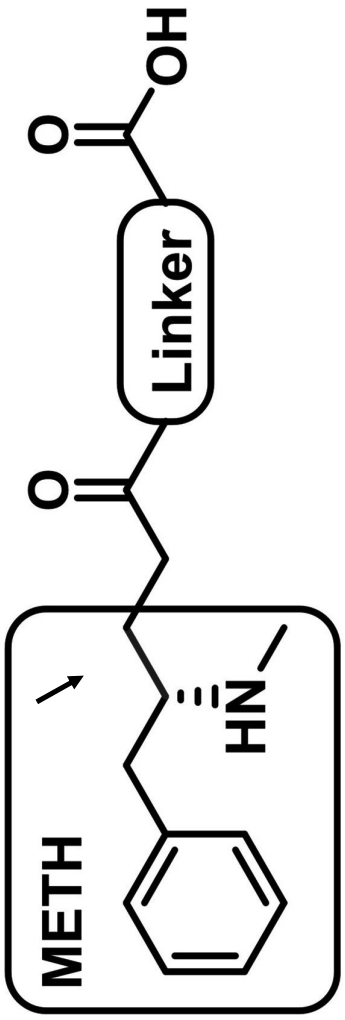
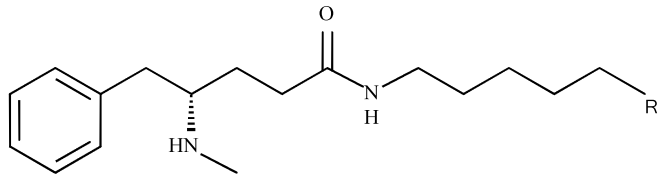


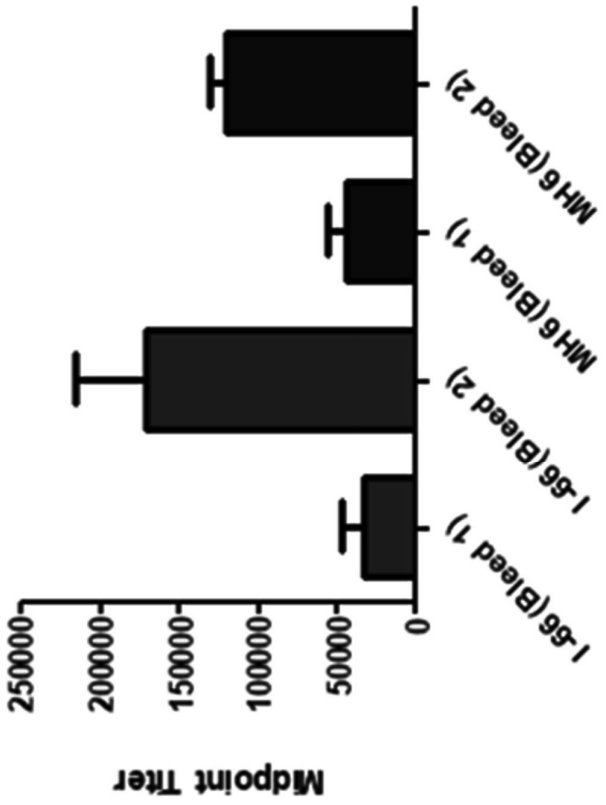
Fig. 9

Fig. 10



R is preferably a maleimide, an alkyl halide, an aryl halide, an alpha-haloacyl, an activated aryl, a pyridyl disulfide, a carbonyl, a carboxyl, a thiol, a thioester, disulfide, a N-hydroxy-succinimide, or a cyclic thiolactone

FIG. 11


Midpoint Titer
250000
200000
150000
100000
50000
0
I-66 (Bleed 1)
I-66 (Bleed 2)
MH6 (Bleed 1)
MH6 (Bleed 2)