Figure 1

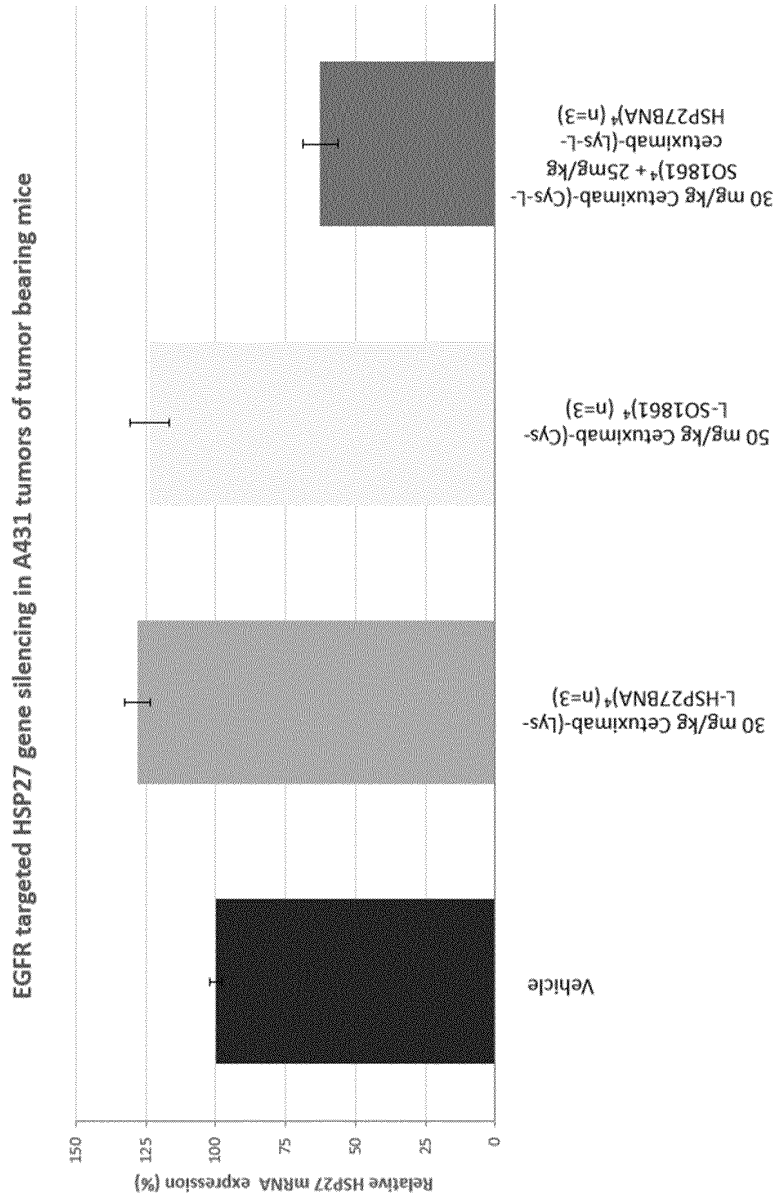

EGFR targeted HSP27 gene silencing in A431 tumors of tumor bearing mice
Relative HSP27 mRNA expression (%)
150
125
100
75
50
25
0
Vehicle
30 mg/kg Cetuximab-(Lys-L-HSP27BNA)4 (n=3)
50 mg/kg Cetuximab-(Cys-L-SO1861)4 (n=3)
30 mg/kg Cetuximab-(Cys-L-SO1861)4 + 25mg/kg cetuximab-(Lys-L-HSP27BNA)4 (n=3)

Figure 2

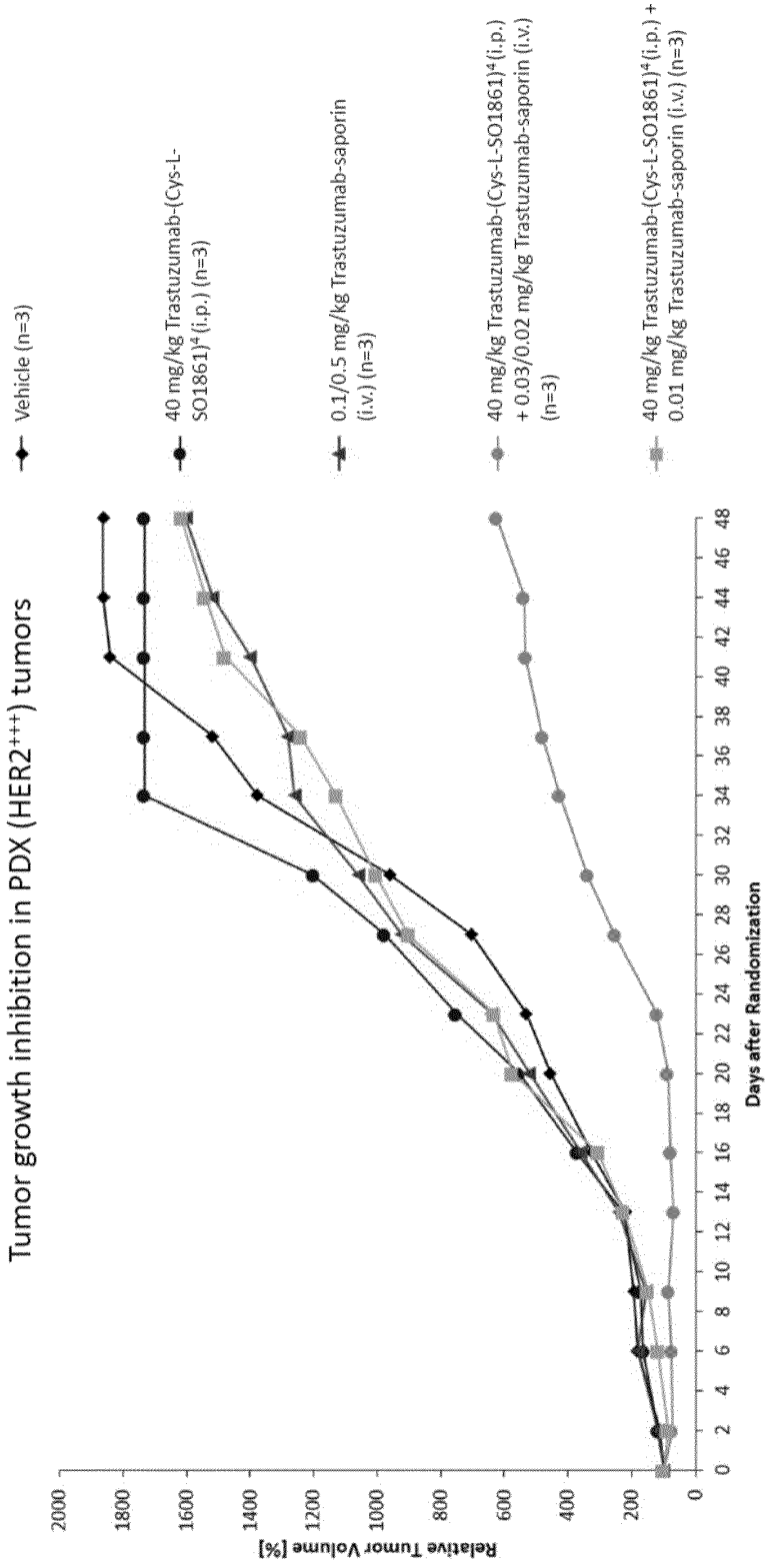

Tumor growth inhibition in PDX (HER2+++) tumors
Vehicle (n=3)
40 mg/kg Trastuzumab-(Cys-L-SO1861)4 (i.p.) (n=3)
0.1/0.5 mg/kg Trastuzumab-saporin (i.v.) (n=3)
40 mg/kg Trastuzumab-(Cys-L-SO1861)4 (i.p.) + 0.03/0.02 mg/kg Trastuzumab-saporin (i.v.) (n=3)
40 mg/kg Trastuzumab-(Cys-L-SO1861)4 (i.p.) + 0.01 mg/kg Trastuzumab-saporin (i.v.) (n=3)
Relative Tumor Volume [%]
Days after Randomization

Figure 3

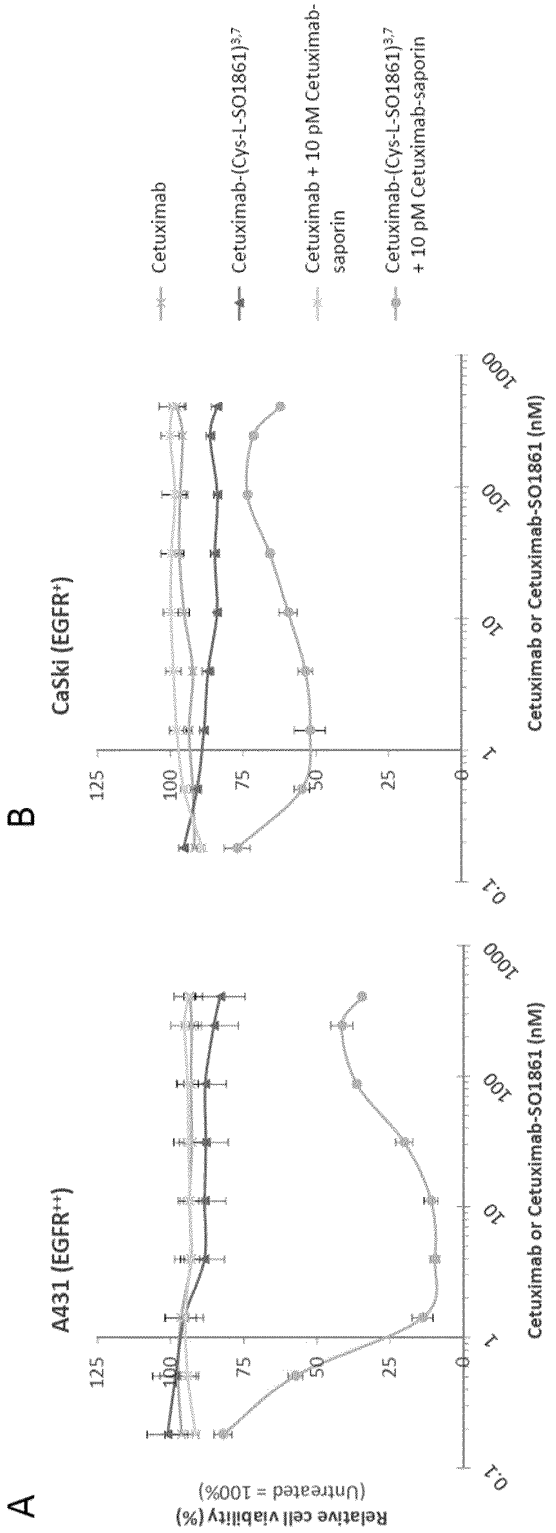

A
A431 (EGFR++)
B
CaSki (EGFR+)
Relative cell viability (%)
(Untreated = 100%)
125
100
75
50
25
0
0.1
1
10
100
1000
Cetuximab or Cetuximab-SO1861 (nM)
Cetuximab
Cetuximab-(Cys-L-SO1861)3,7
Cetuximab + 10 pM Cetuximab-saporin
Cetuximab-(Cys-L-SO1861)3,7 + 10 pM Cetuximab-saporin

Figure 3

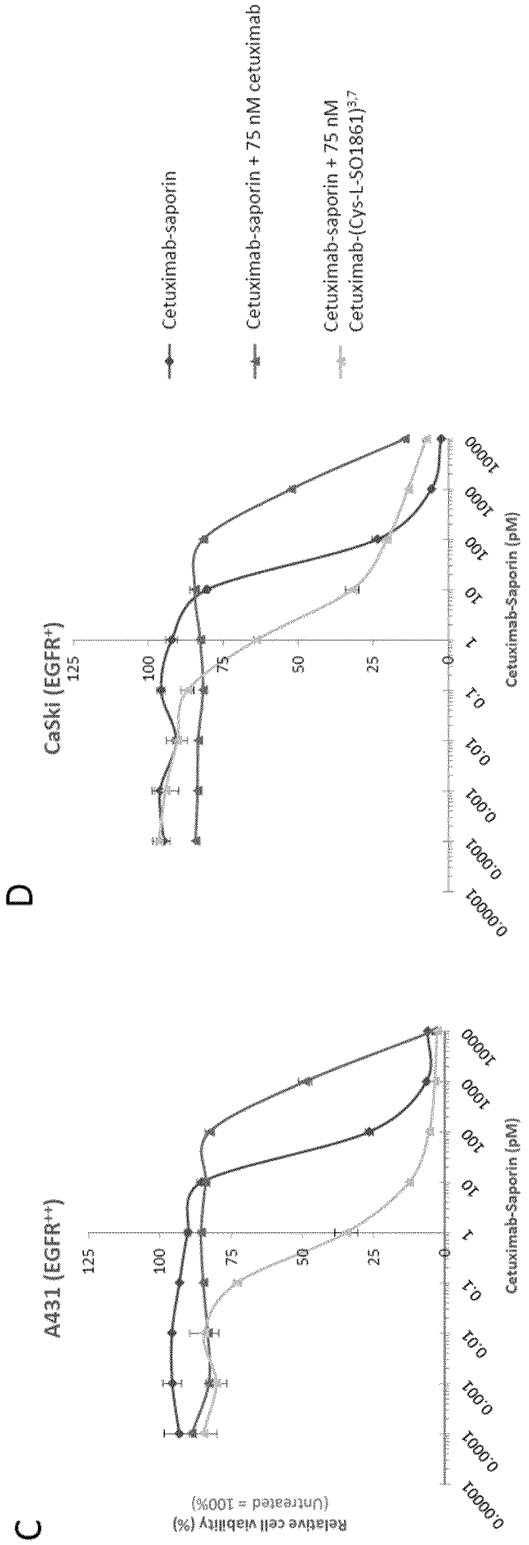

Cetuximab-saporin
Cetuximab-saporin + 75 nM cetuximab
Cetuximab-saporin + 75 nM Cetuximab-(Cys-L-SO1861)3,7
D
CaSki (EGFR+)
C
A431 (EGFR++)
Relative cell viability (%)
(Untreated = 100%)
Cetuximab-Saporin (pM)
125
100
75
50
25
0
0,00001
0,0001
0,001
0,01
0,1
1
10
100
1000
10000

Figure 4

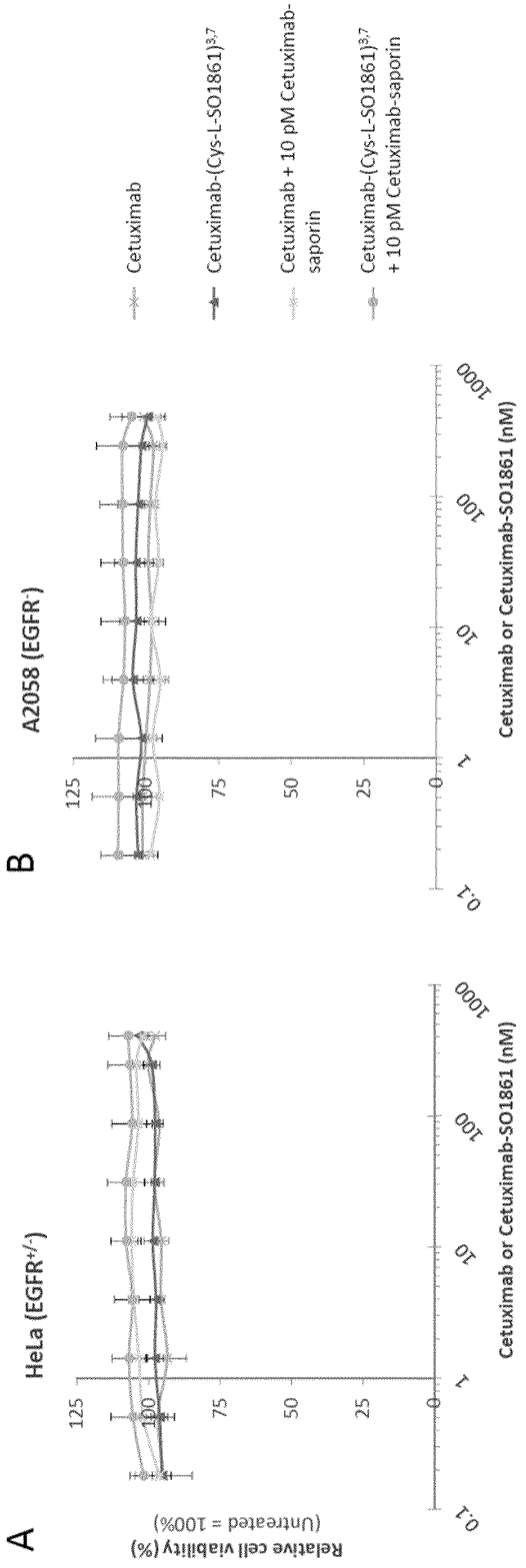

A
HeLa (EGFR+/-)
Relative cell viability (%)
(Untreated = 100%)
125
100
75
50
25
0
0,1
1
10
100
1000
Cetuximab or Cetuximab-SO1861 (nM)
B
A2058 (EGFR-)
Cetuximab
Cetuximab-(Cys-L-SO1861)3.7
Cetuximab + 10 pM Cetuximab-saporin
Cetuximab-(Cys-L-SO1861)3.7 + 10 pM Cetuximab-saporin

Figure 4

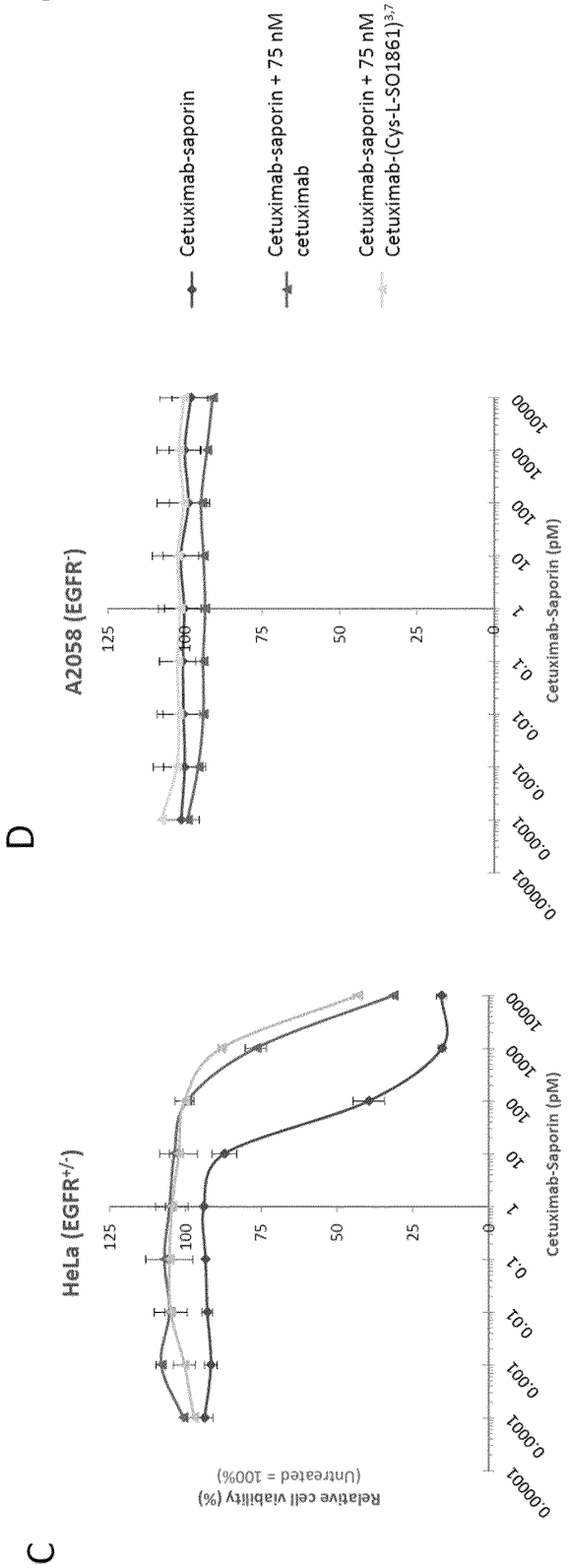

C
D
Cetuximab-saporin
Cetuximab-saporin + 75 nM cetuximab
Cetuximab-saporin + 75 nM Cetuximab-(Cys-L-SO1861)3,7
HeLa (EGFR+/-)
A2058 (EGFR-)
Relative cell viability (%)
(Untreated = 100%)
125
100
75
50
25
0
Cetuximab-Saporin (pM)
0,00001
0,0001
0,001
0,01
0,1
1
10
100
1000
10000

Figure 5

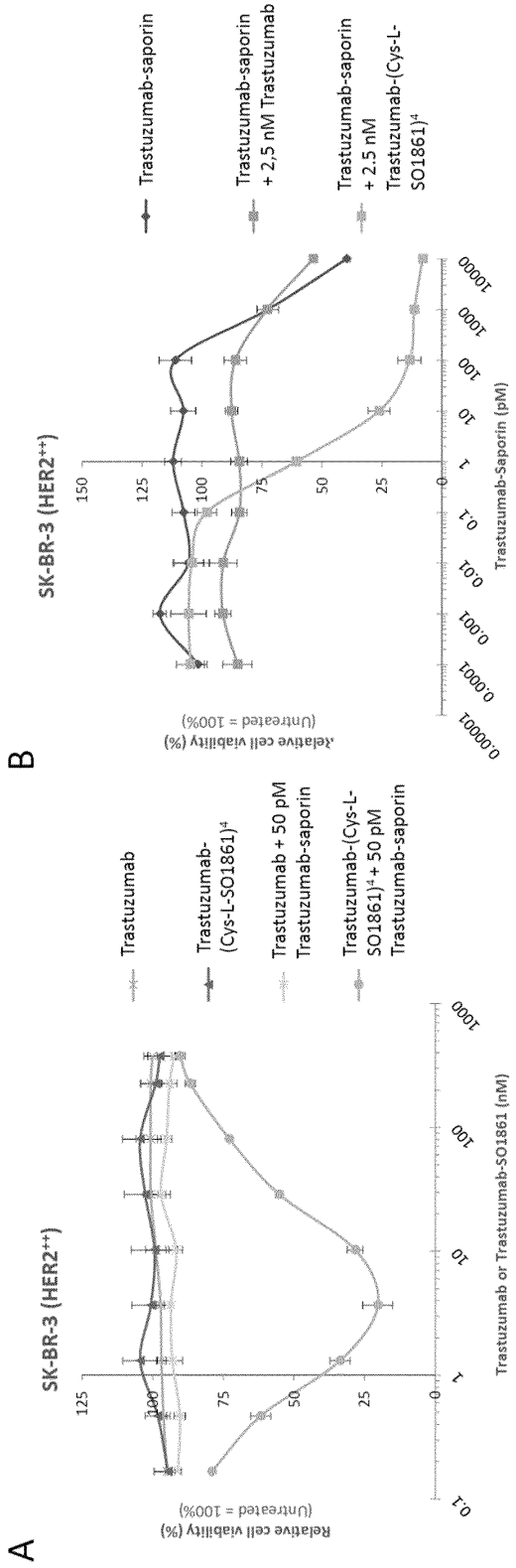

A
SK-BR-3 (HER2++)
Relative cell viability (%)
(Untreated = 100%)
Trastuzumab or Trastuzumab-SO1861 (nM)
Trastuzumab
Trastuzumab-(Cys-L-SO1861)4
Trastuzumab + 50 pM Trastuzumab-saporin
Trastuzumab-(Cys-L-SO1861)4 + 50 pM Trastuzumab-saporin
B
SK-BR-3 (HER2++)
Relative cell viability (%)
(Untreated = 100%)
Trastuzumab-Saporin (pM)
Trastuzumab-saporin
Trastuzumab-saporin + 2.5 nM Trastuzumab
Trastuzumab-saporin + 2.5 nM Trastuzumab-(Cys-L-SO1861)4

Figure 6

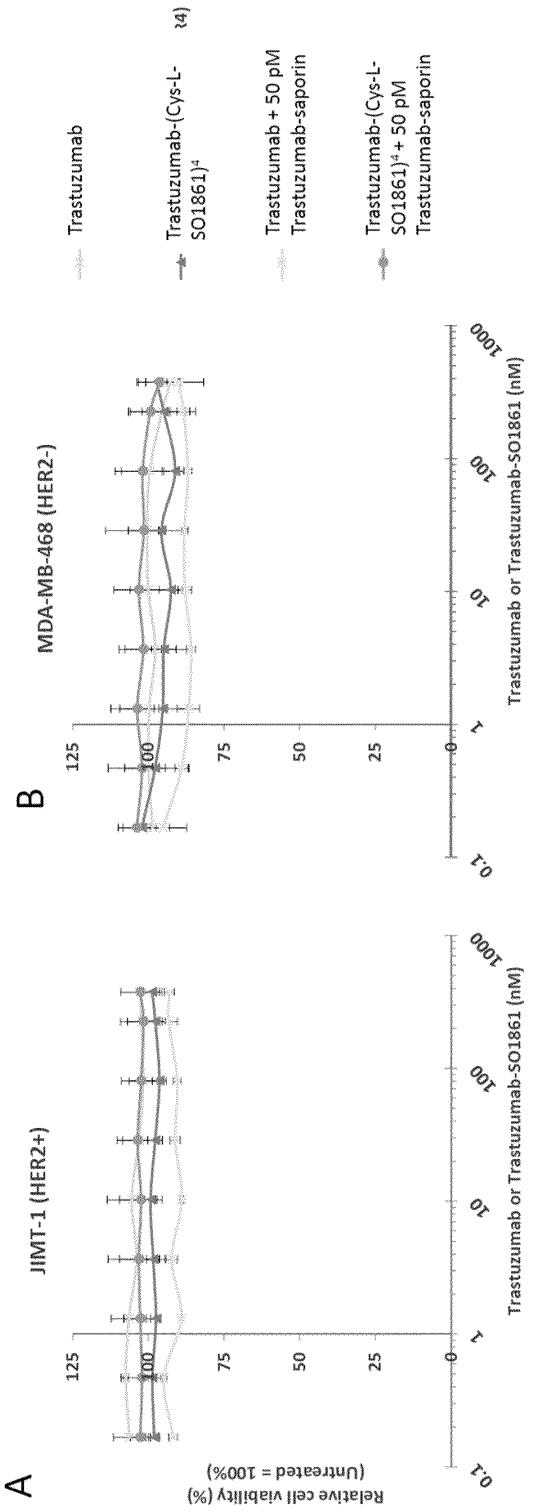

A
JIMT-1 (HER2+)
Relative cell viability (%)
(Untreated = 100%)
125
100
75
50
25
0
0,1
1
10
100
1000
Trastuzumab or Trastuzumab-SO1861 (nM)
B
MDA-MB-468 (HER2-)
Trastuzumab
Trastuzumab-(Cys-L-SO1861)4
Trastuzumab + 50 pM Trastuzumab-saporin
Trastuzumab-(Cys-L-SO1861)4 + 50 pM Trastuzumab-saporin

Figure 6

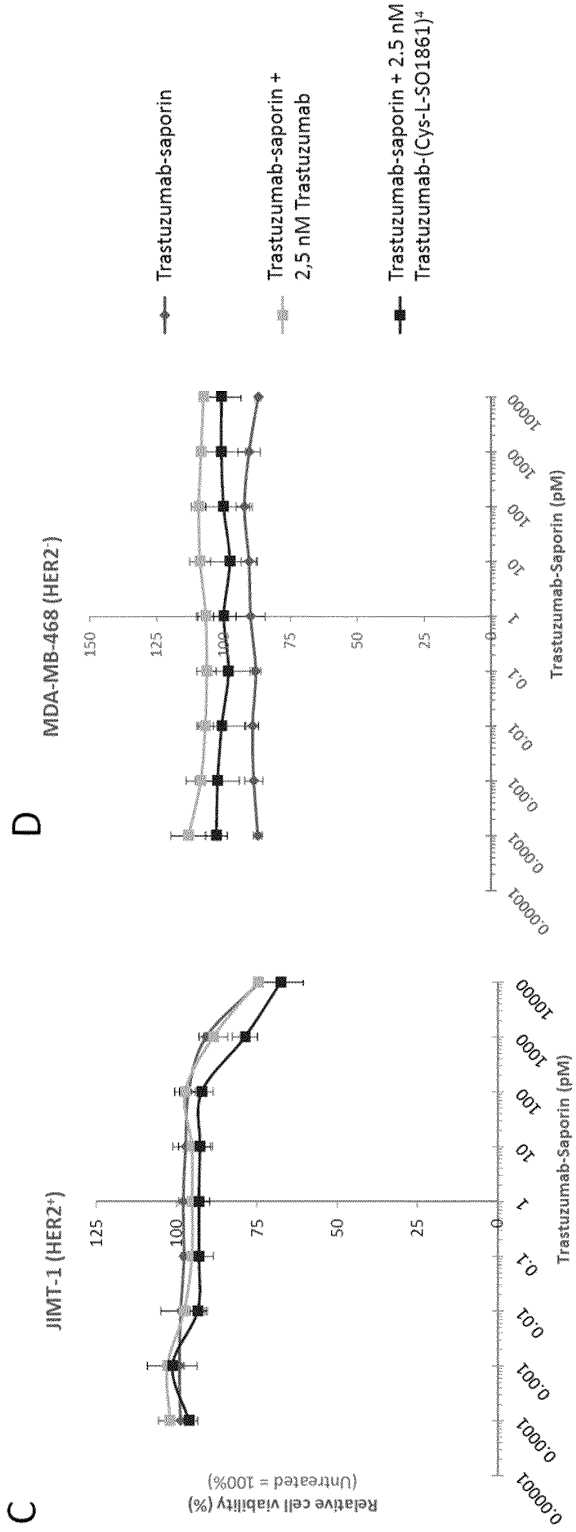

C
JIMT-1 (HER2+)
Relative cell viability (%)
(Untreated = 100%)
125
100
75
50
25
0
0,00001
0,0001
0,001
0,01
0,1
1
10
100
1000
10000
Trastuzumab-Saporin (pM)
D
MDA-MB-468 (HER2-)
150
125
100
75
50
25
0
0,00001
0,0001
0,001
0,01
0,1
1
10
100
1000
10000
Trastuzumab-Saporin (pM)
Trastuzumab-saporin
Trastuzumab-saporin + 2,5 nM Trastuzumab
Trastuzumab-saporin + 2.5 nM Trastuzumab-(Cys-L-SO1861)4

Figure 8

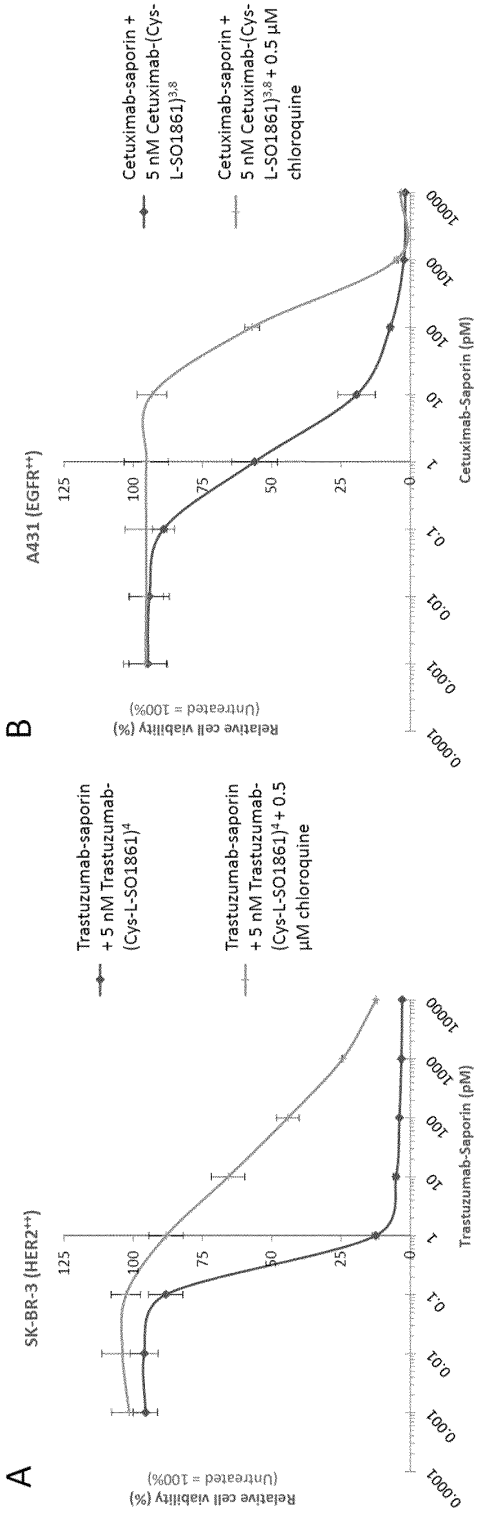

A
SK-BR-3 (HER2++)
Relative cell viability (%)
(Untreated = 100%)
125
100
75
50
25
0
0.0001
0.001
0.01
0.1
1
10
100
1000
10000
Trastuzumab-Saporin (pM)
Trastuzumab-saporin + 5 nM Trastuzumab-(Cys-L-SO1861)4
Trastuzumab-saporin + 5 nM Trastuzumab-(Cys-L-SO1861)4 + 0.5 µM chloroquine
B
A431 (EGFR++)
Relative cell viability (%)
(Untreated = 100%)
Cetuximab-Saporin (pM)
Cetuximab-saporin + 5 nM Cetuximab-(Cys-L-SO1861)3,8
Cetuximab-saporin + 5 nM Cetuximab-(Cys-L-SO1861)3,8 + 0.5 µM chloroquine

Figure 9

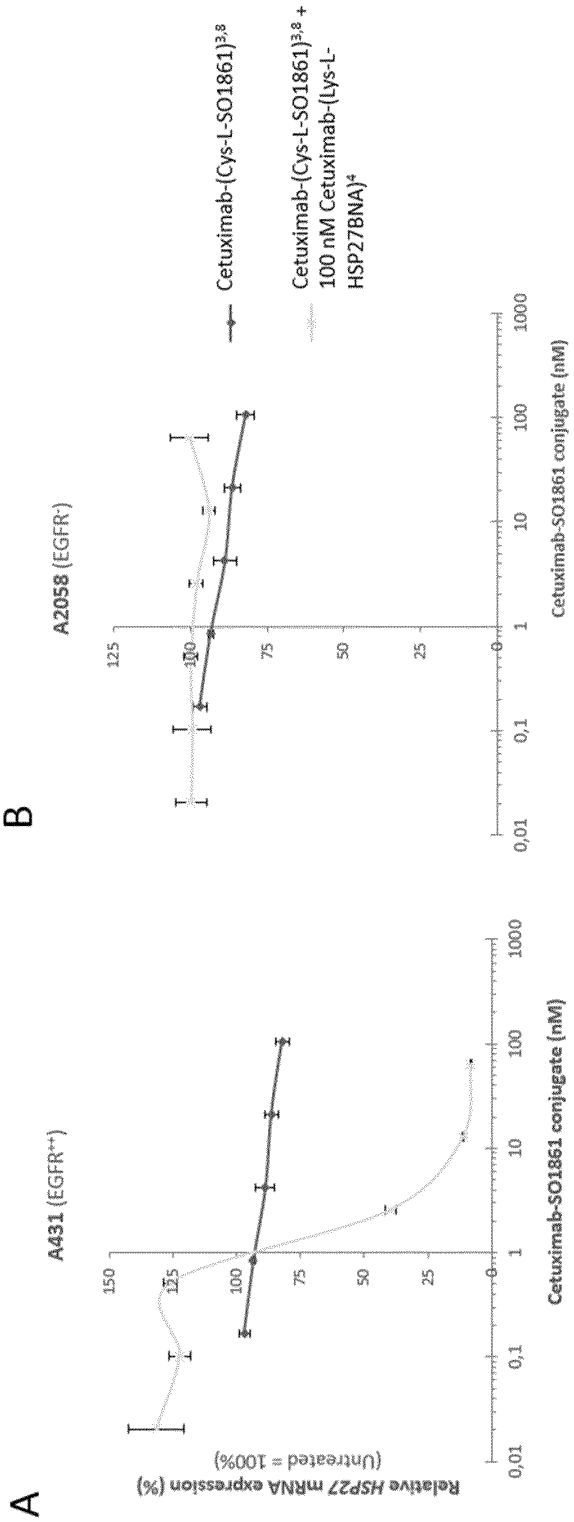

A
A431 (EGFR++)
Relative HSP27 mRNA expression (%)
(Untreated = 100%)
150
125
100
75
50
25
0
0,01
0,1
1
10
100
1000
Cetuximab-SO1861 conjugate (nM)
B
A2058 (EGFR-)
Cetuximab-(Cys-L-SO1861)3,8
Cetuximab-(Cys-L-SO1861)3,8 + 100 nM Cetuximab-(Lys-L-HSP27BNA)4
125
100
75
50
25
0
0,01
0,1
1
10
100
1000
Cetuximab-SO1861 conjugate (nM)

Figure 9

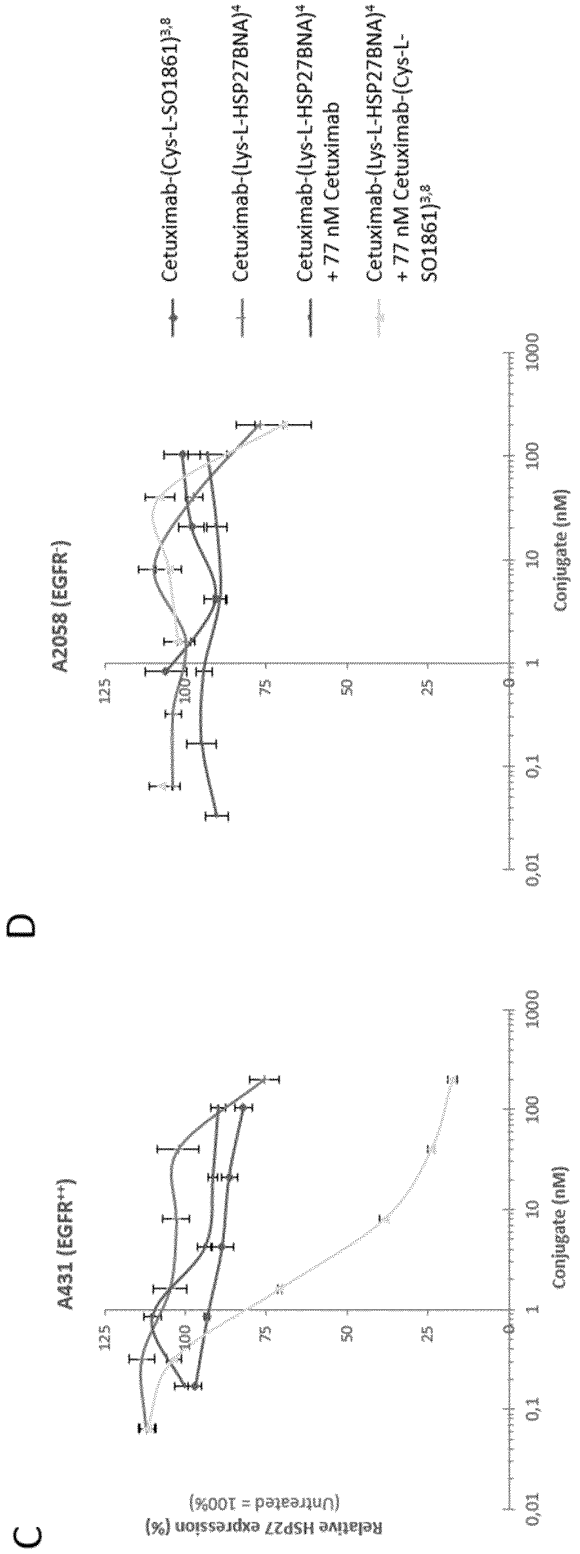

C
A431 (EGFR++)
Relative HSP27 expression (%)
(Untreated = 100%)
125
100
75
50
25
0
0,01
0,1
1
10
100
1000
Conjugate (nM)
D
A2058 (EGFR-)
Cetuximab-(Cys-L-SO1861)3,8
Cetuximab-(Lys-L-HSP27BNA)4
Cetuximab-(Lys-L-HSP27BNA)4 + 77 nM Cetuximab
Cetuximab-(Lys-L-HSP27BNA)4 + 77 nM Cetuximab-(Cys-L-SO1861)3,8

Figure 10

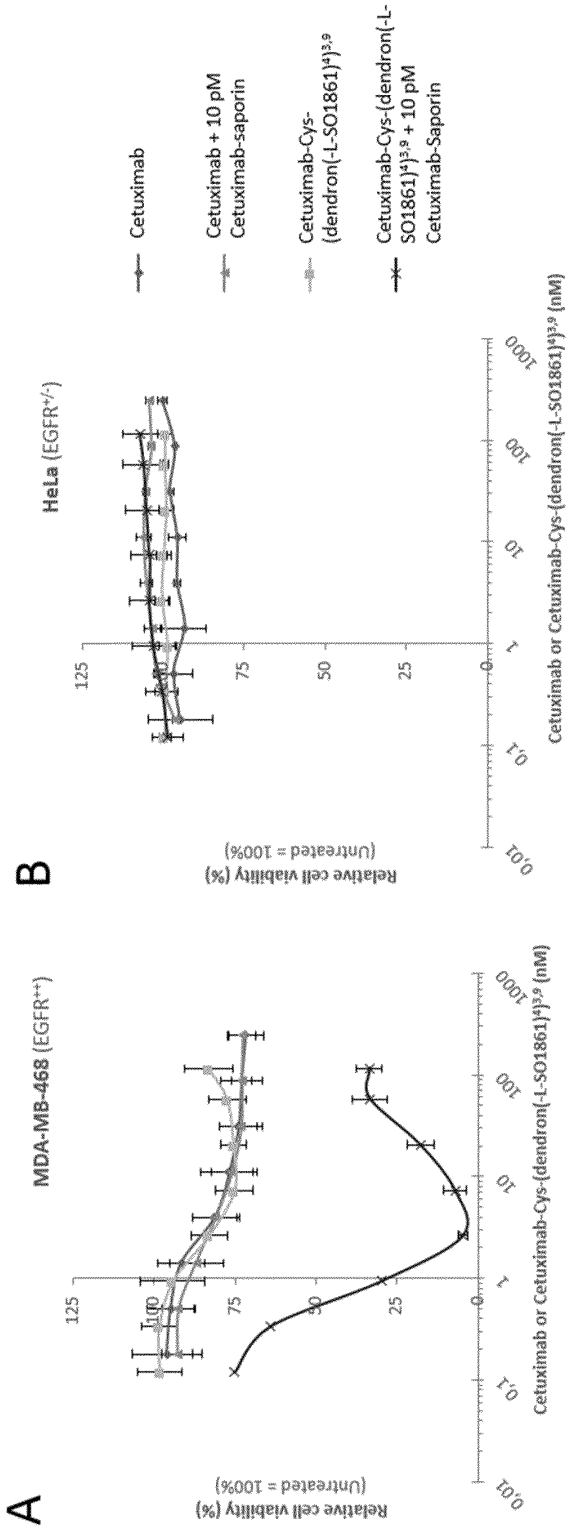

A
MDA-MB-468 (EGFR++)
Relative cell viability (%)
(Untreated = 100%)
125
100
75
50
25
0
0,01
0,1
1
10
100
1000
Cetuximab or Cetuximab-Cys-(dendron(-L-SO1861)4)3,9 (nM)
B
HeLa (EGFR+/-)
Relative cell viability (%)
(Untreated = 100%)
Cetuximab
Cetuximab + 10 pM Cetuximab-saporin
Cetuximab-Cys-(dendron(-L-SO1861)4)3,9
Cetuximab-Cys-(dendron(-L-SO1861)4)3,9 + 10 pM Cetuximab-Saporin
Cetuximab or Cetuximab-Cys-(dendron(-L-SO1861)4)3,9 (nM)

Figure 10

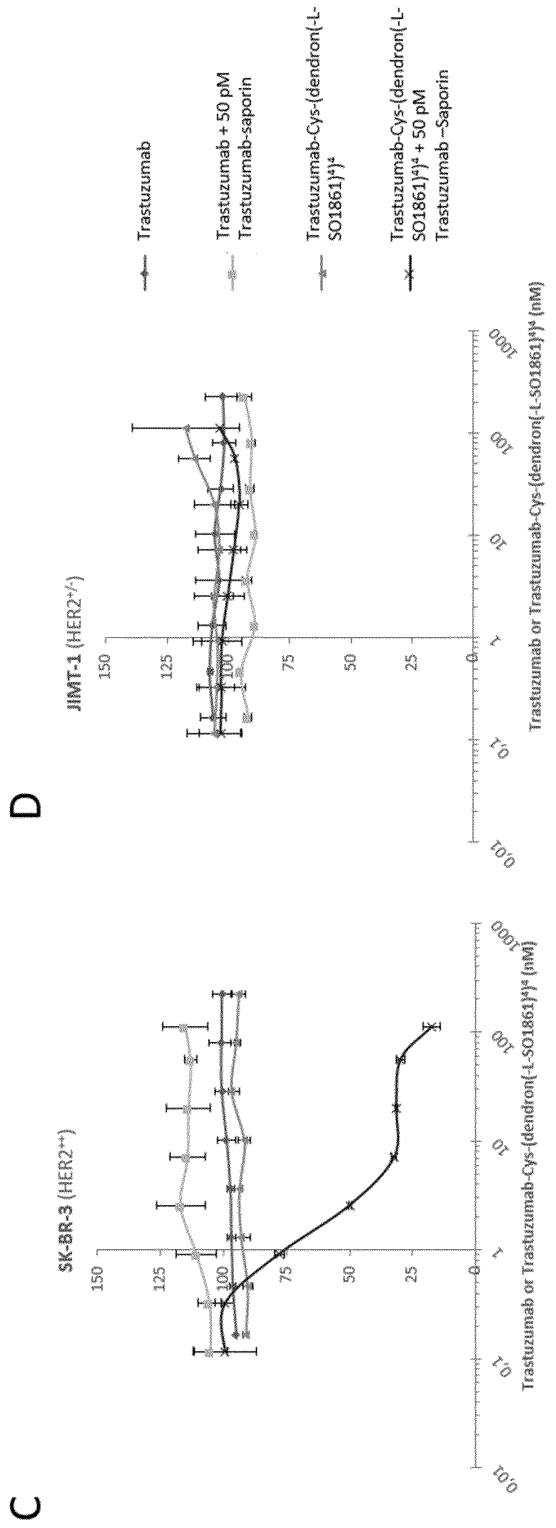

C
SK-BR-3 (HER2++)
D
JIMT-1 (HER2+/-)
Trastuzumab
Trastuzumab + 50 pM Trastuzumab-saporin
Trastuzumab-Cys-(dendron(-L-SO1861)4)4
Trastuzumab-Cys-(dendron(-L-SO1861)4)4 + 50 pM Trastuzumab –Saporin
Trastuzumab or Trastuzumab-Cys-(dendron(-L-SO1861)4)4 (nM)
150
125
100
75
50
25
0
0,01
0,1
1
10
100
1000

Figure 11

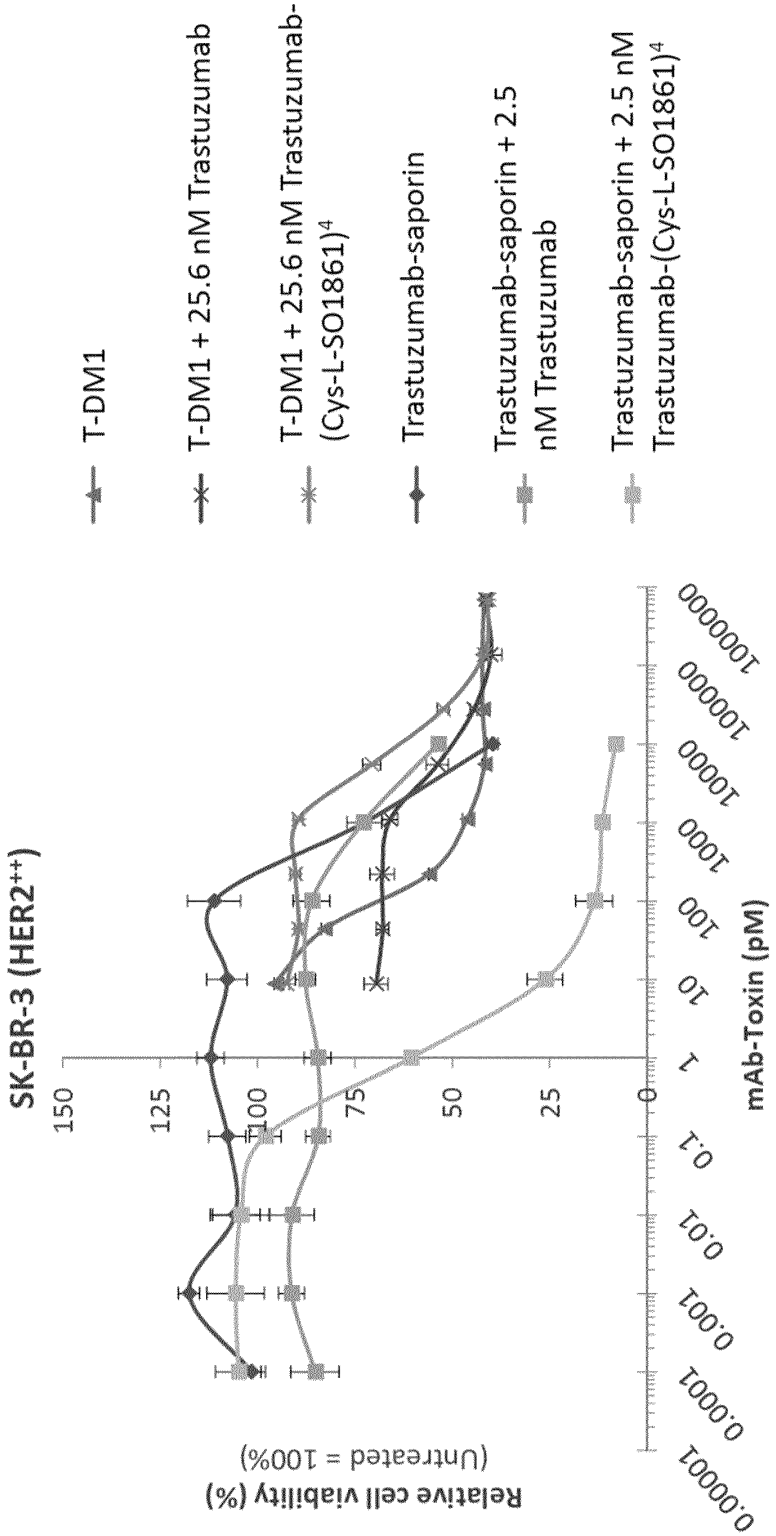

T-DM1
T-DM1 + 25.6 nM Trastuzumab
T-DM1 + 25.6 nM Trastuzumab-(Cys-L-SO1861)4
Trastuzumab-saporin
Trastuzumab-saporin + 2.5 nM Trastuzumab
Trastuzumab-saporin + 2.5 nM Trastuzumab-(Cys-L-SO1861)4
SK-BR-3 (HER2++)
Relative cell viability (%)
(Untreated = 100%)
150
125
100
75
50
25
0
mAb-Toxin (pM)
0.0001
0.001
0.01
0.1
1
10
100
1000
10000
100000
1000000

Figure 12

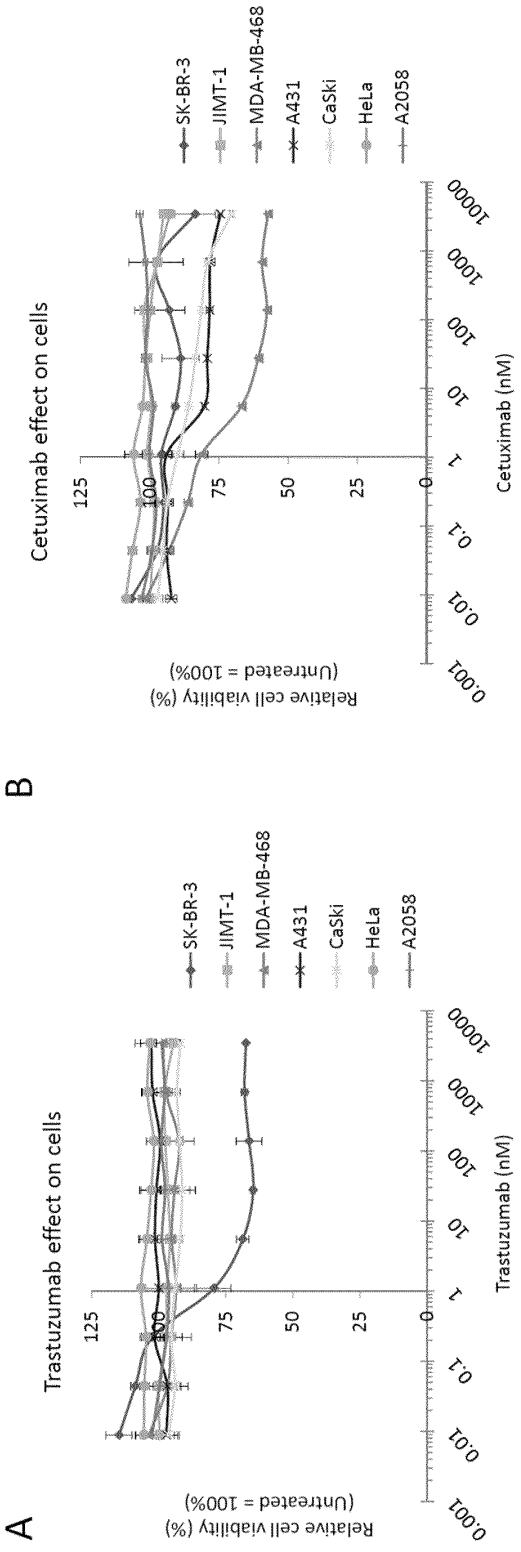

A
Trastuzumab effect on cells
Relative cell viability (%)
(Untreated = 100%)
125
100
75
50
25
0
0.001
0.01
0.1
1
10
100
1000
10000
Trastuzumab (nM)
SK-BR-3
JIMT-1
MDA-MB-468
A431
CaSki
HeLa
A2058
B
Cetuximab effect on cells
Relative cell viability (%)
(Untreated = 100%)
125
100
75
50
25
0
0.001
0.01
0.1
1
10
100
1000
10000
Cetuximab (nM)
SK-BR-3
JIMT-1
MDA-MB-468
A431
CaSki
HeLa
A2058

Figure 12

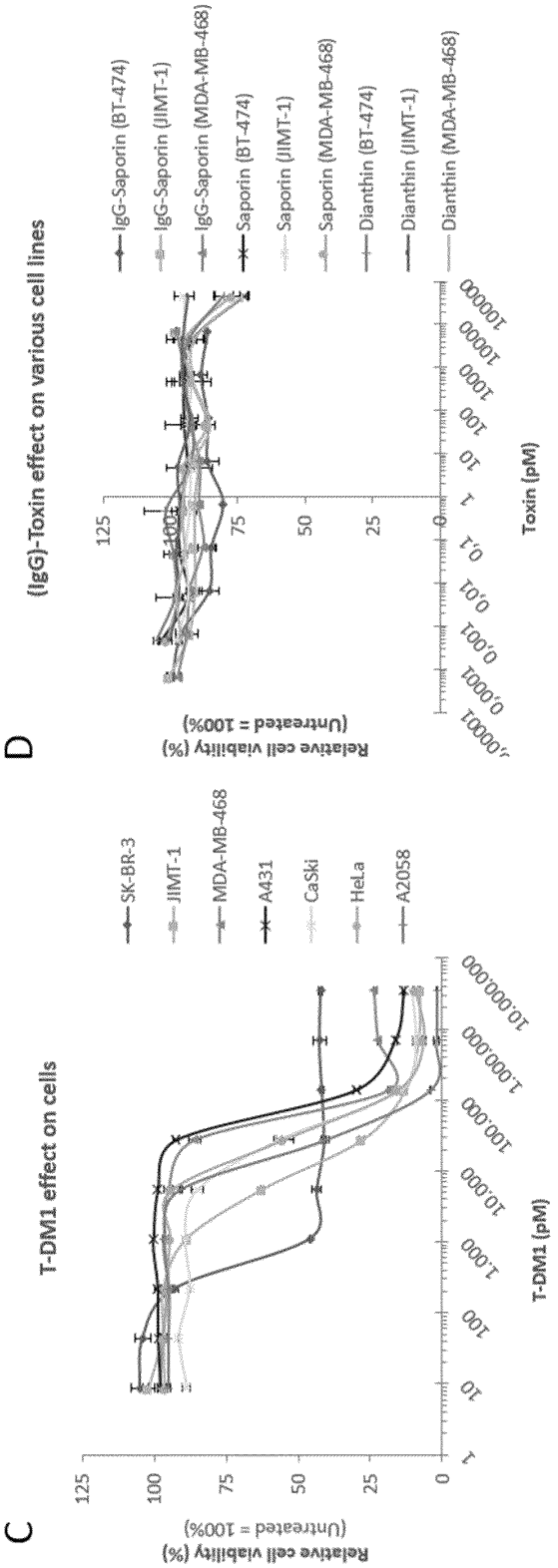

C
T-DM1 effect on cells
Relative cell viability (%)
(Untreated = 100%)
125
100
75
50
25
0
1
10
100
1.000
10.000
100.000
1.000.000
10.000.000
T-DM1 (pM)
SK-BR-3
JIMT-1
MDA-MB-468
A431
CaSki
HeLa
A2058
D
(IgG)-Toxin effect on various cell lines
Relative cell viability (%)
(Untreated = 100%)
125
100
75
50
25
0
0,00001
0,0001
0,001
0,01
0,1
1
10
100
1000
10000
100000
Toxin (pM)
IgG-Saporin (BT-474)
IgG-Saporin (JIMT-1)
IgG-Saporin (MDA-MB-468)
Saporin (BT-474)
Saporin (JIMT-1)
Saporin (MDA-MB-468)
Dianthin (BT-474)
Dianthin (JIMT-1)
Dianthin (MDA-MB-468)

Figure 13

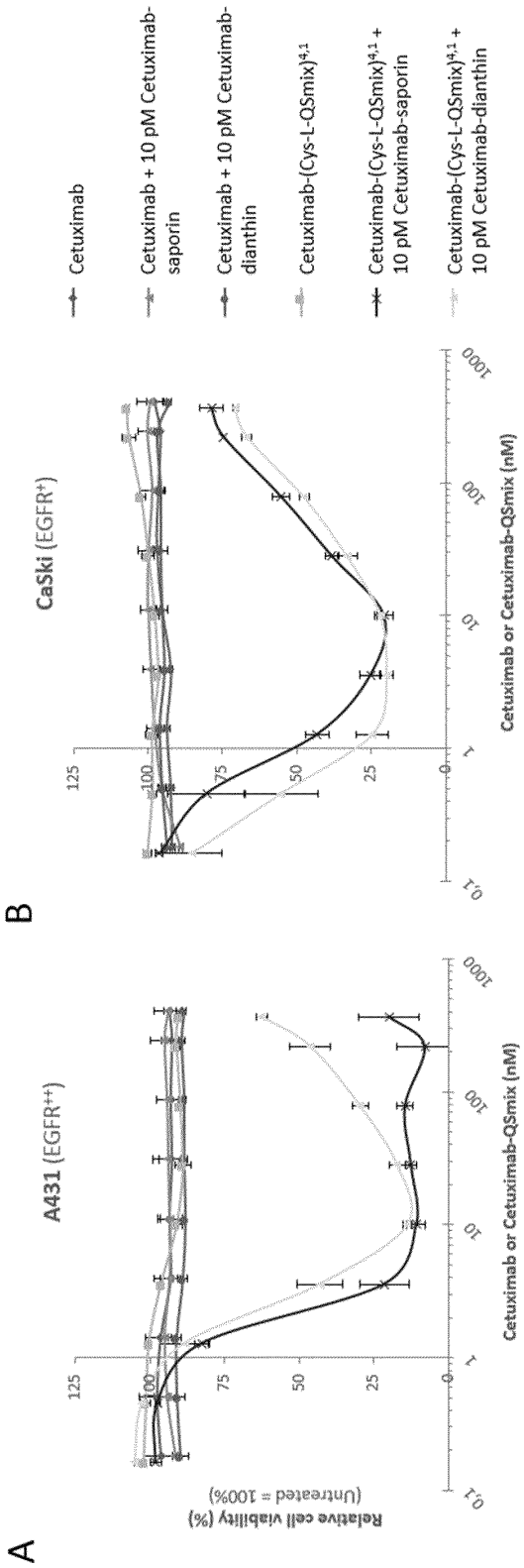

A
B
A431 (EGFR++)
CaSki (EGFR+)
Relative cell viability (%)
(Untreated = 100%)
Cetuximab or Cetuximab-QSmix (nM)
Cetuximab
Cetuximab + 10 pM Cetuximab-saporin
Cetuximab + 10 pM Cetuximab-dianthin
Cetuximab-(Cys-L-QSmix)4:1
Cetuximab-(Cys-L-QSmix)4:1 + 10 pM Cetuximab-saporin
Cetuximab-(Cys-L-QSmix)4:1 + 10 pM Cetuximab-dianthin

Figure 13

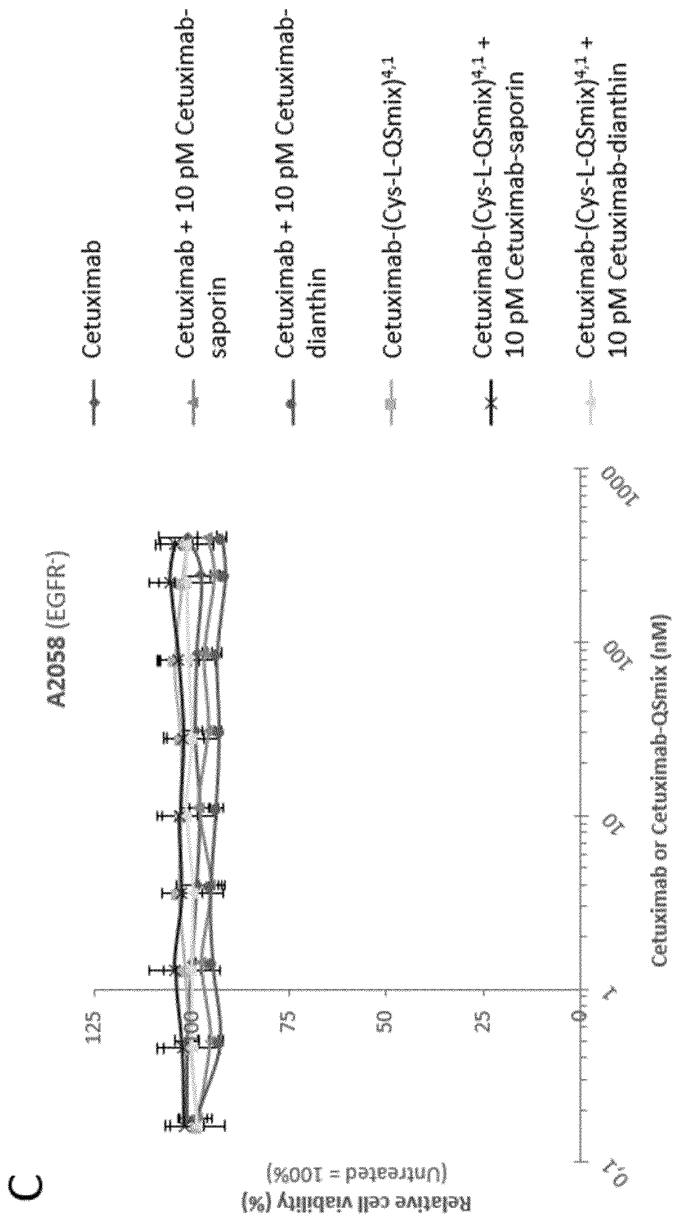

C
A2058 (EGFR-)
Relative cell viability (%)
(Untreated = 100%)
125
100
75
50
25
0
0,1
1
10
100
1000
Cetuximab or Cetuximab-QSmix (nM)
Cetuximab
Cetuximab + 10 pM Cetuximab-saporin
Cetuximab + 10 pM Cetuximab-dianthin
Cetuximab-(Cys-L-QSmix)4,1
Cetuximab-(Cys-L-QSmix)4,1 + 10 pM Cetuximab-saporin
Cetuximab-(Cys-L-QSmix)4,1 + 10 pM Cetuximab-dianthin

Figure 14

L1-(S)n + L1-E concept: mAb1-SO1861 + mAb1-toxin

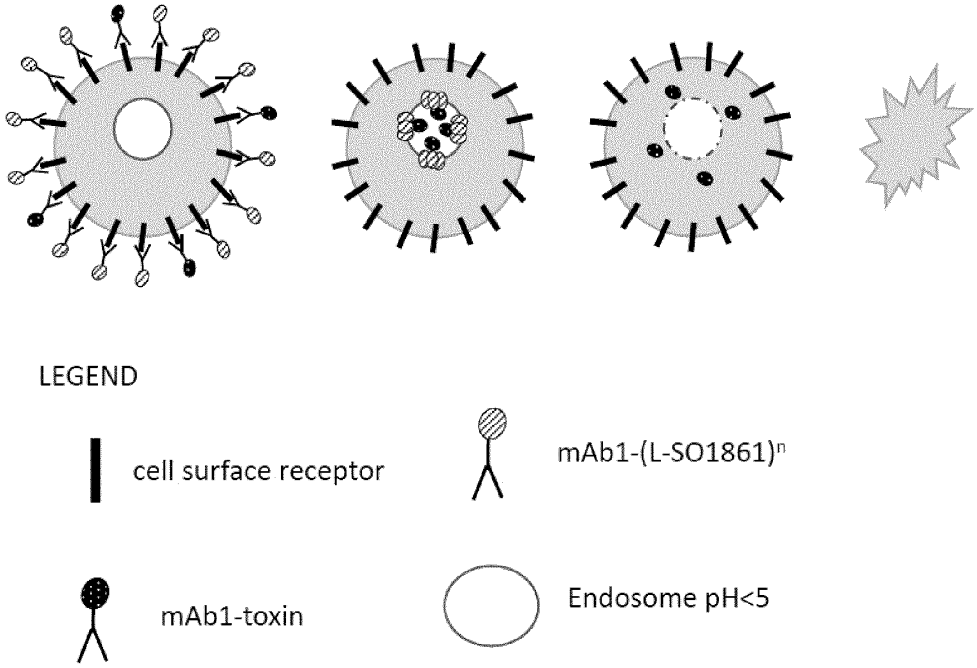


Figure 15

L1-(S)n + L1-E concept: mAb1-SO1861 + mAb1-BNA oligo

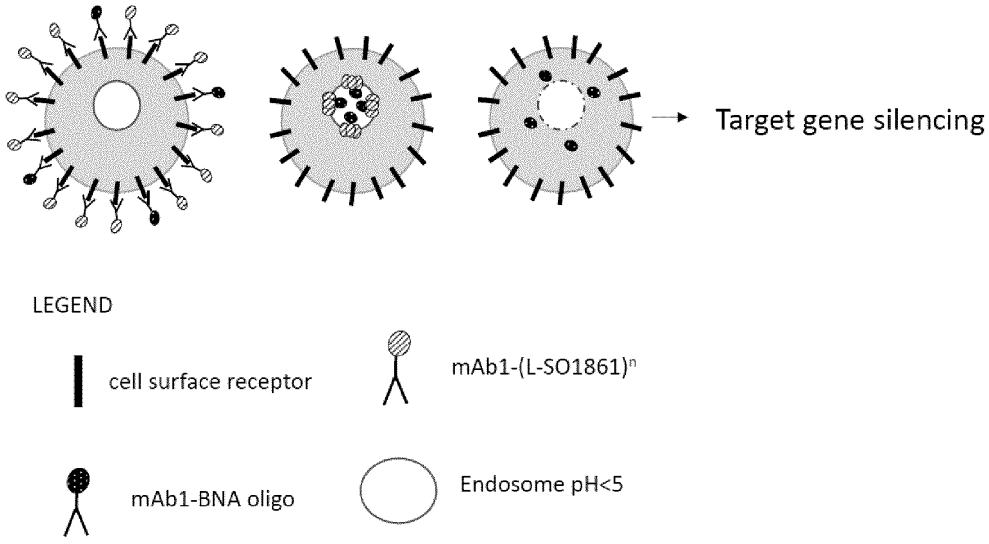


Figure 16

Scaffold-Sn concept: mAb1-(scaffold(-SO1861)^n)^n + mAb1-protein toxin

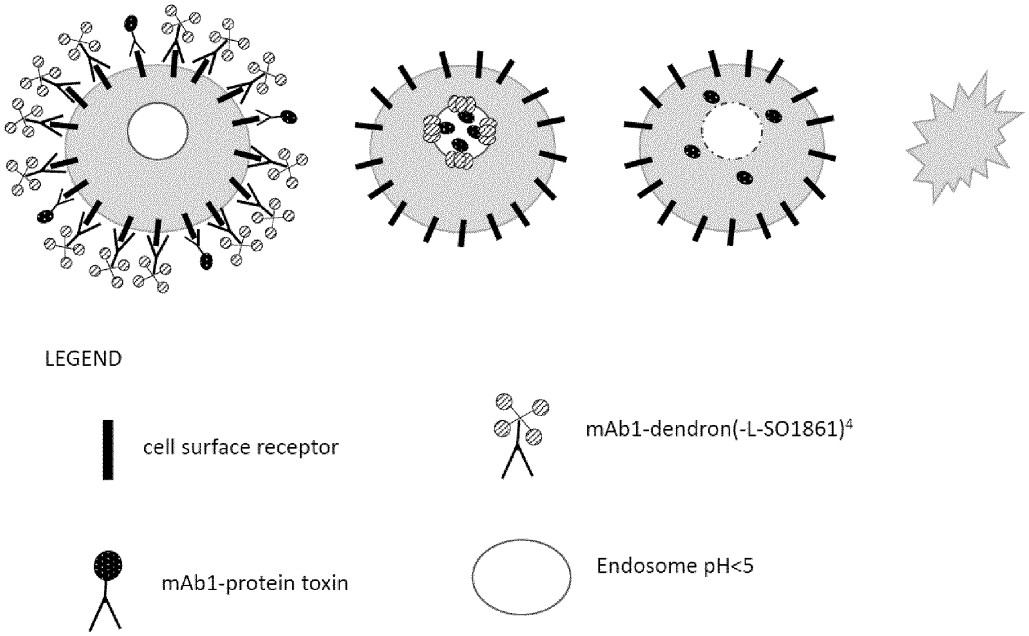


Figure 17

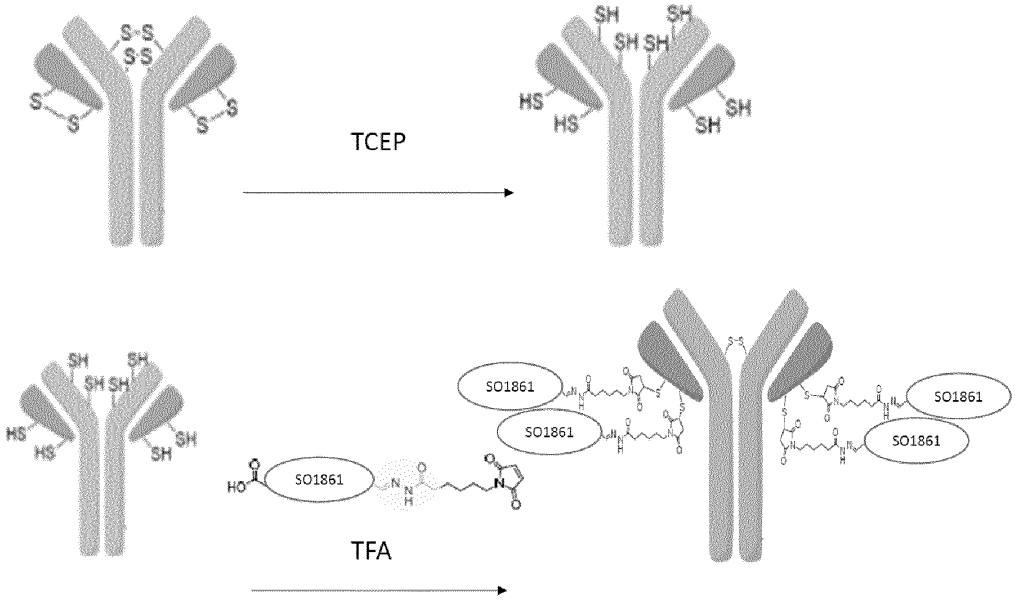


Figure 18

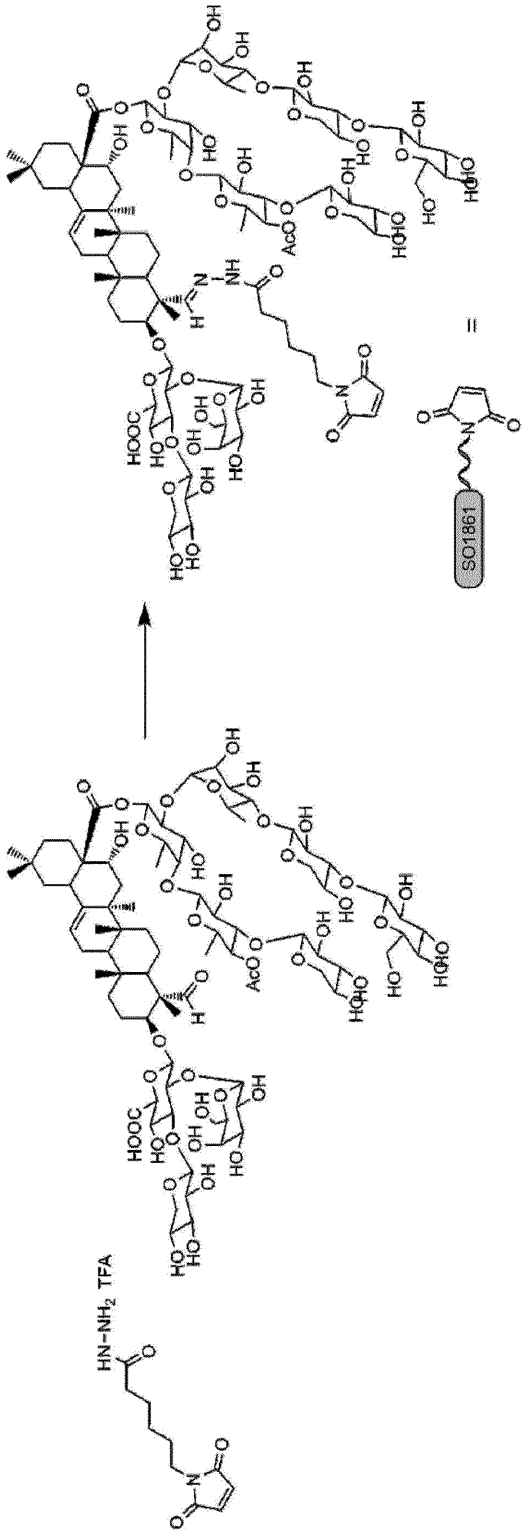


Figure 19

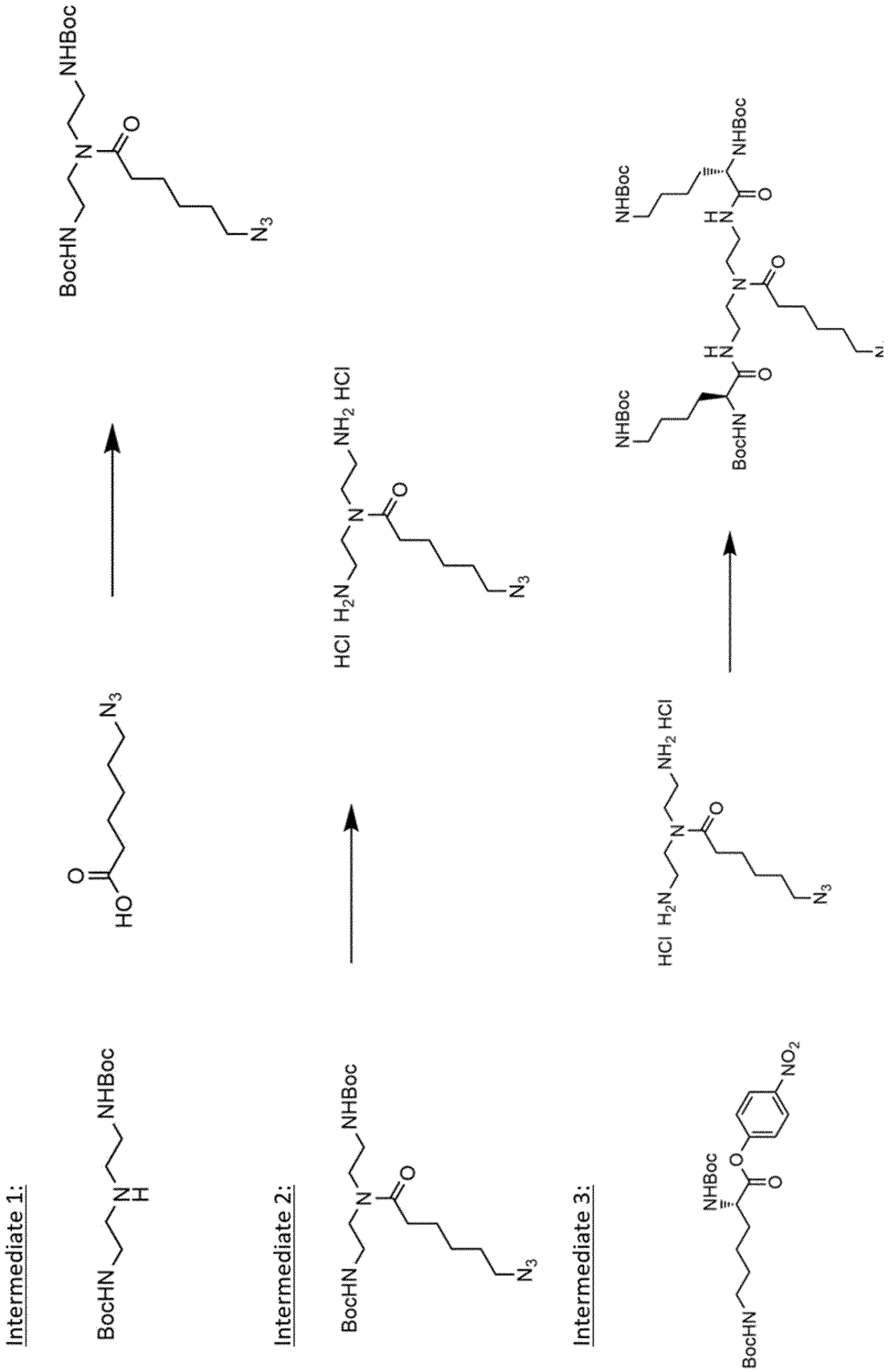

Intermediate 1:
BocHN
NH
NHBoc
HO
O
N3
Intermediate 2:
BocHN
NHBoc
HCl H2N
NH2 HCl
Intermediate 3:
NHBoc
BocHN
NO2
O
NH

Figure 19

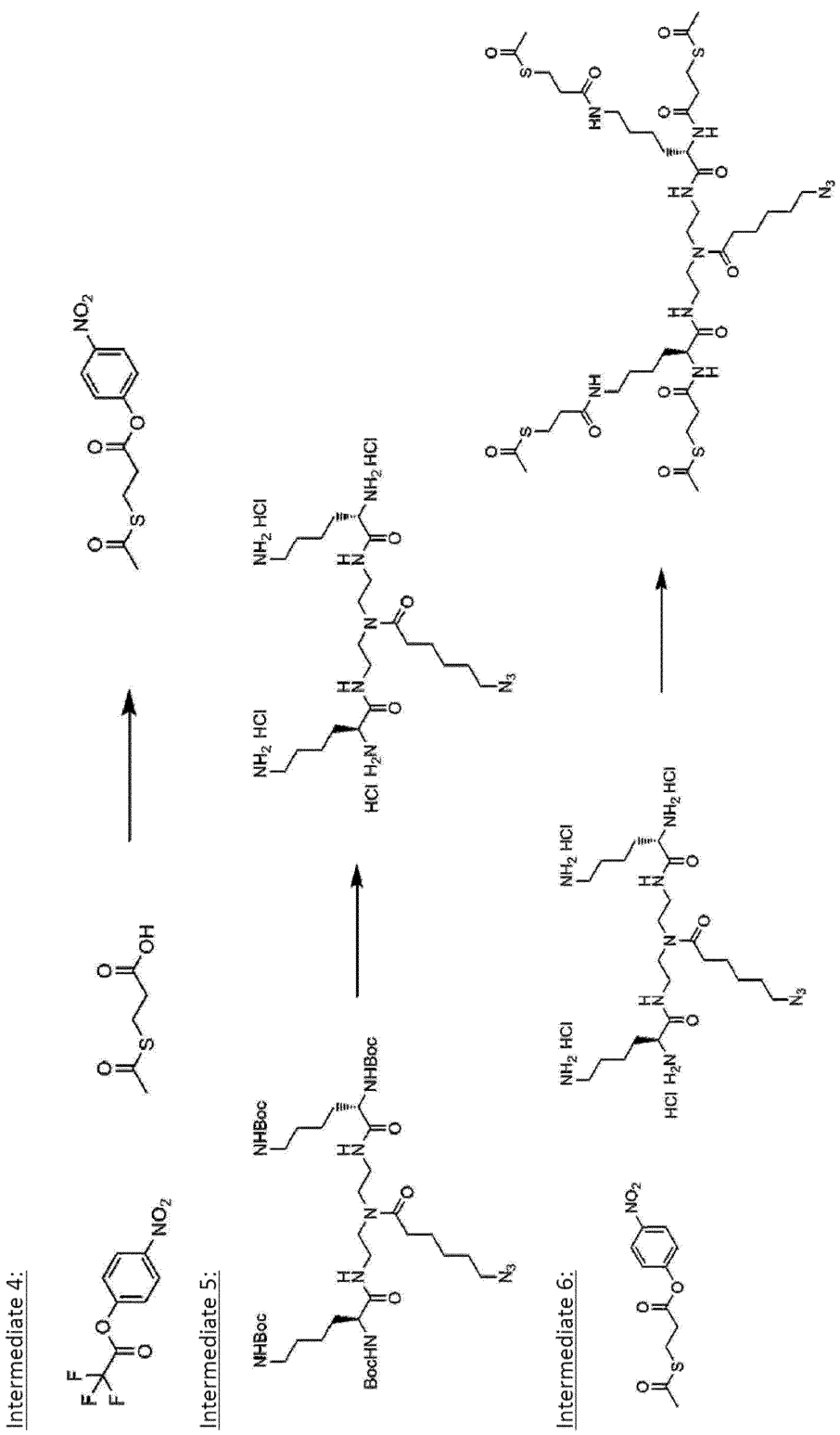


Figure 19

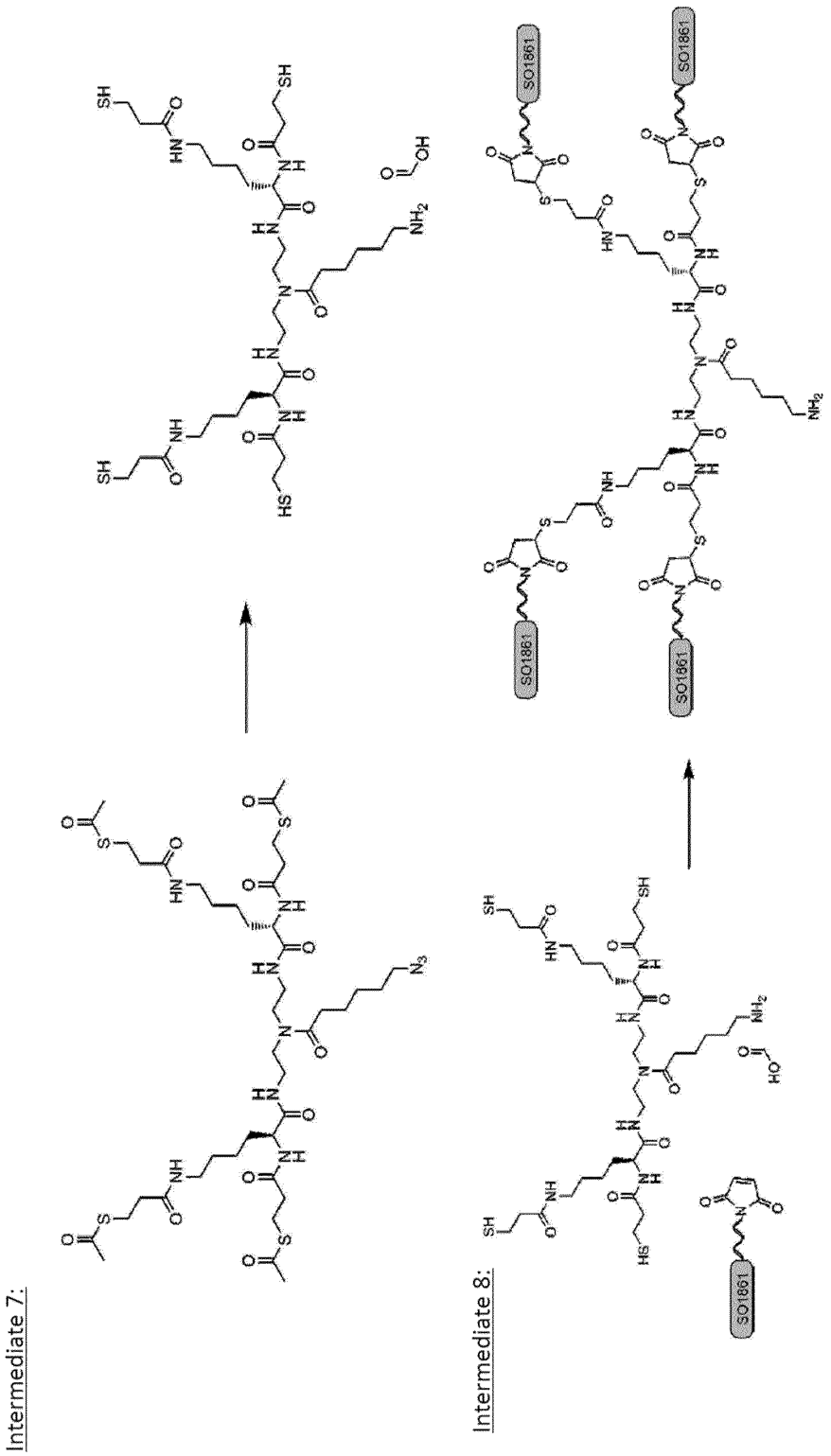
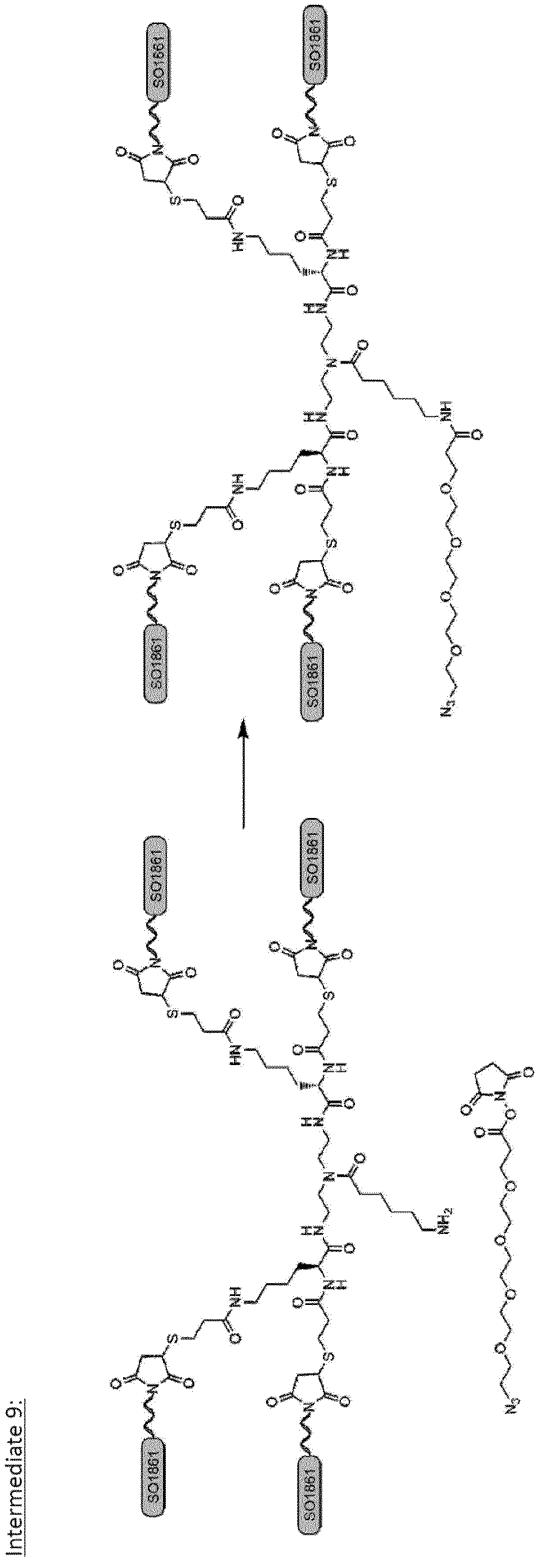
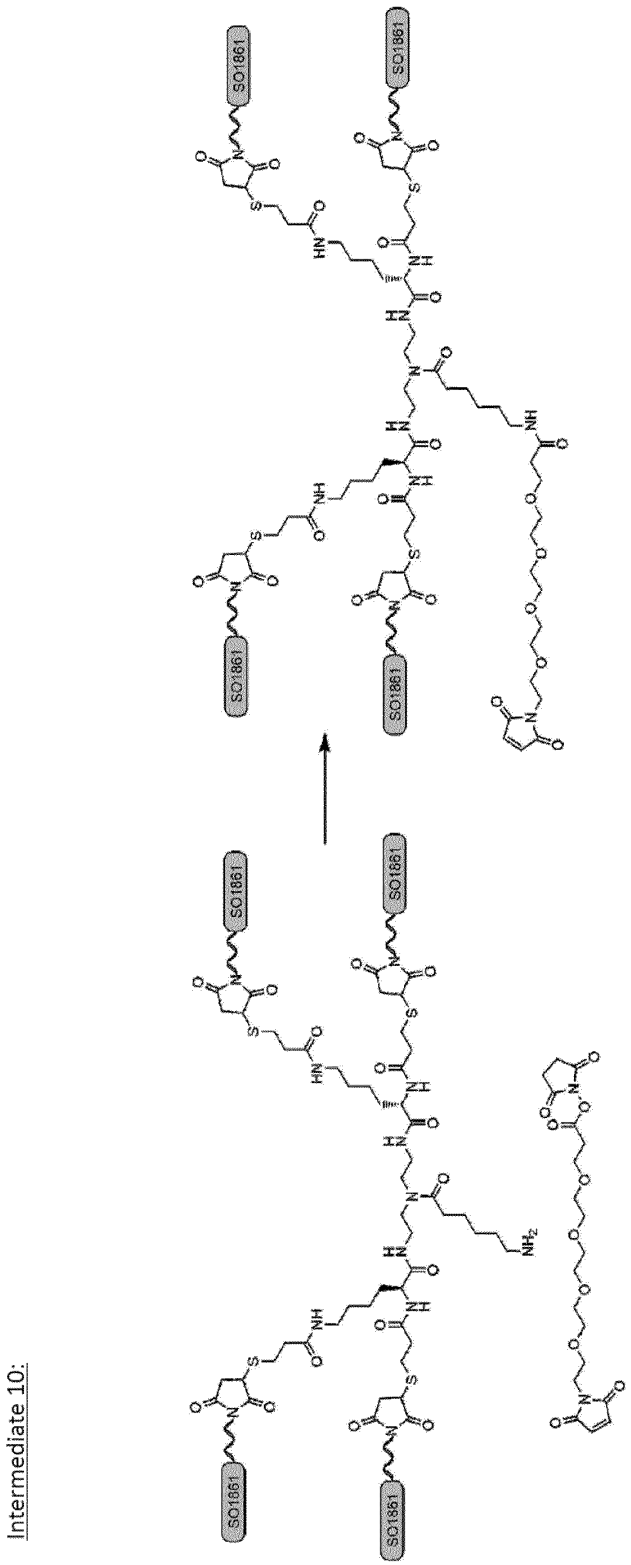


Figure 19



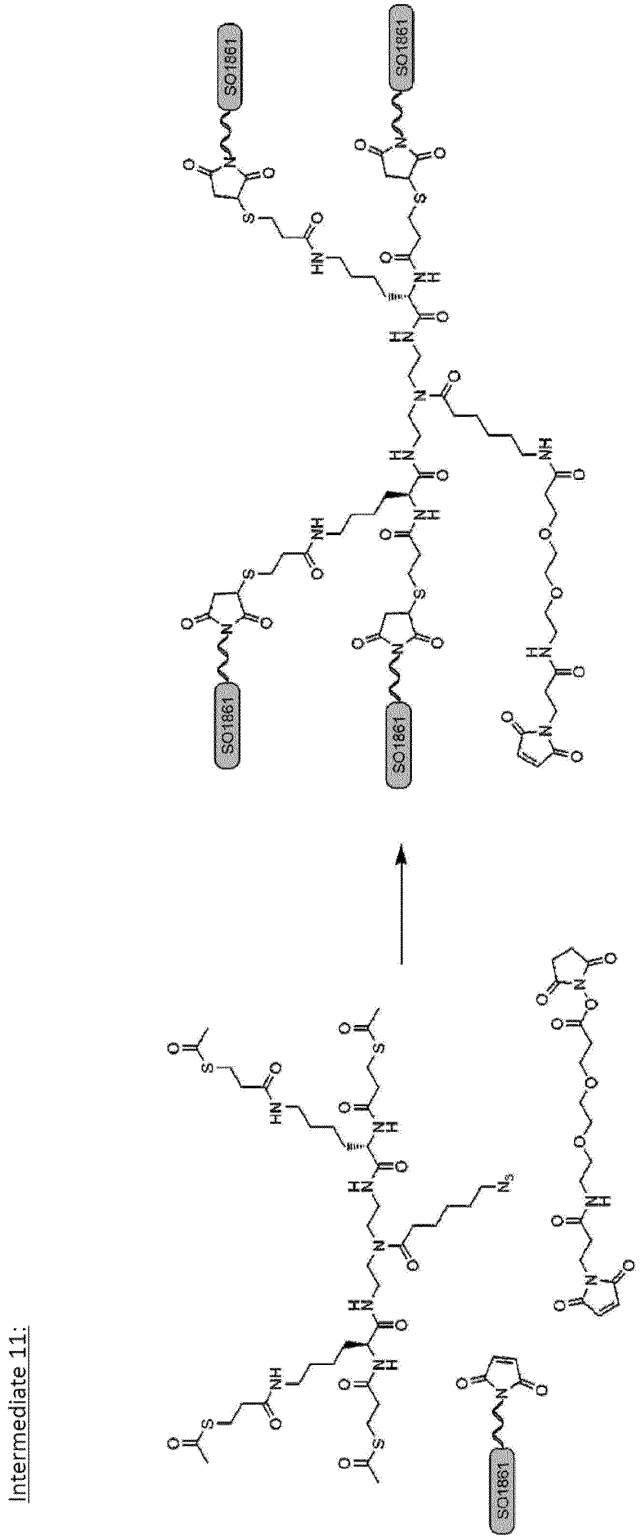
Intermediate 9:

Figure 19



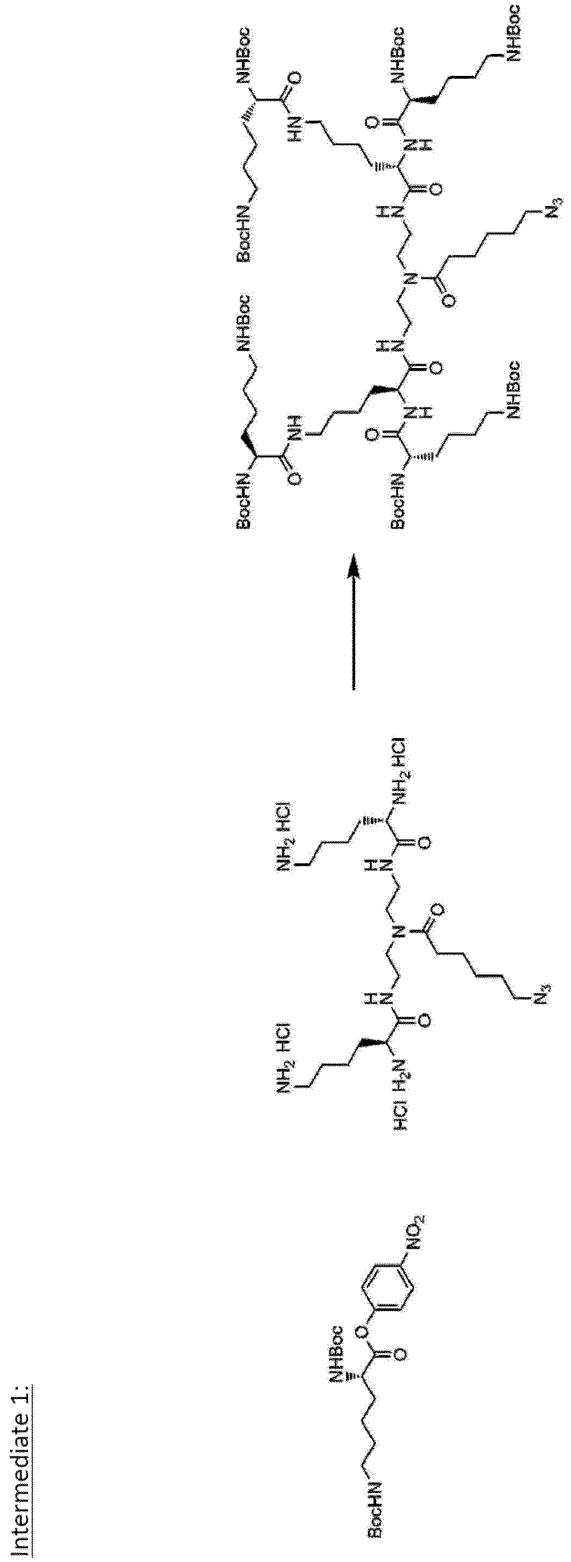
Intermediate 10:

Figure 19



Intermediate 11:

Figure 20



Intermediate 1:

Figure 20

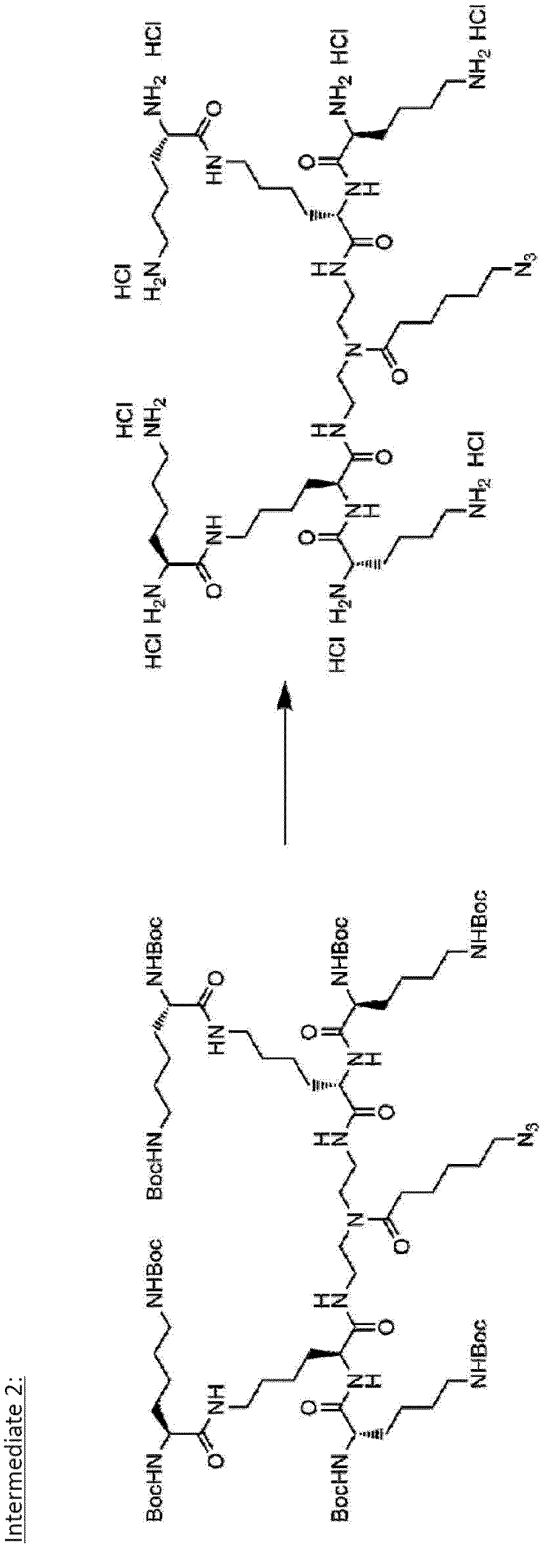


Figure 20

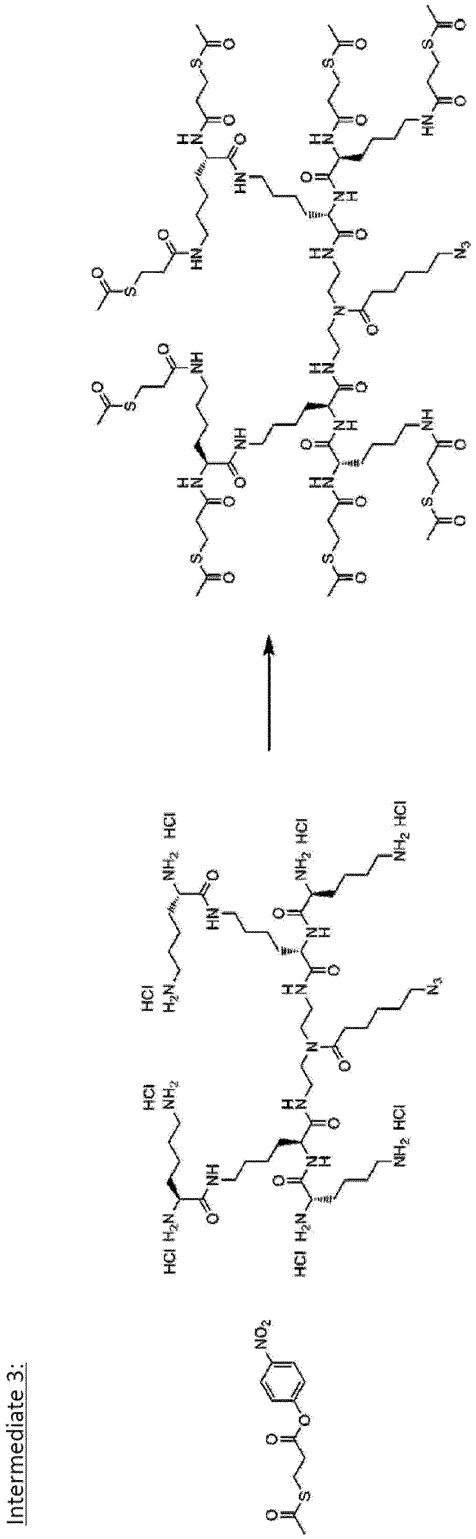


Figure 20

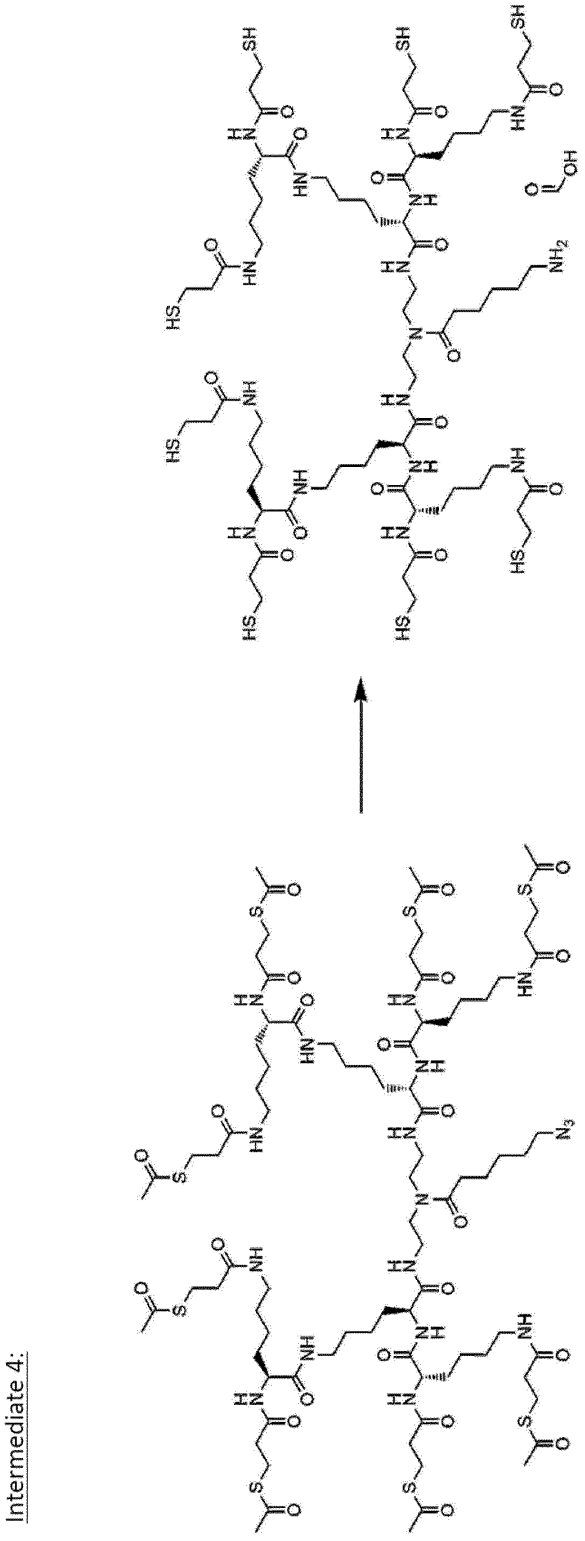


Figure 20

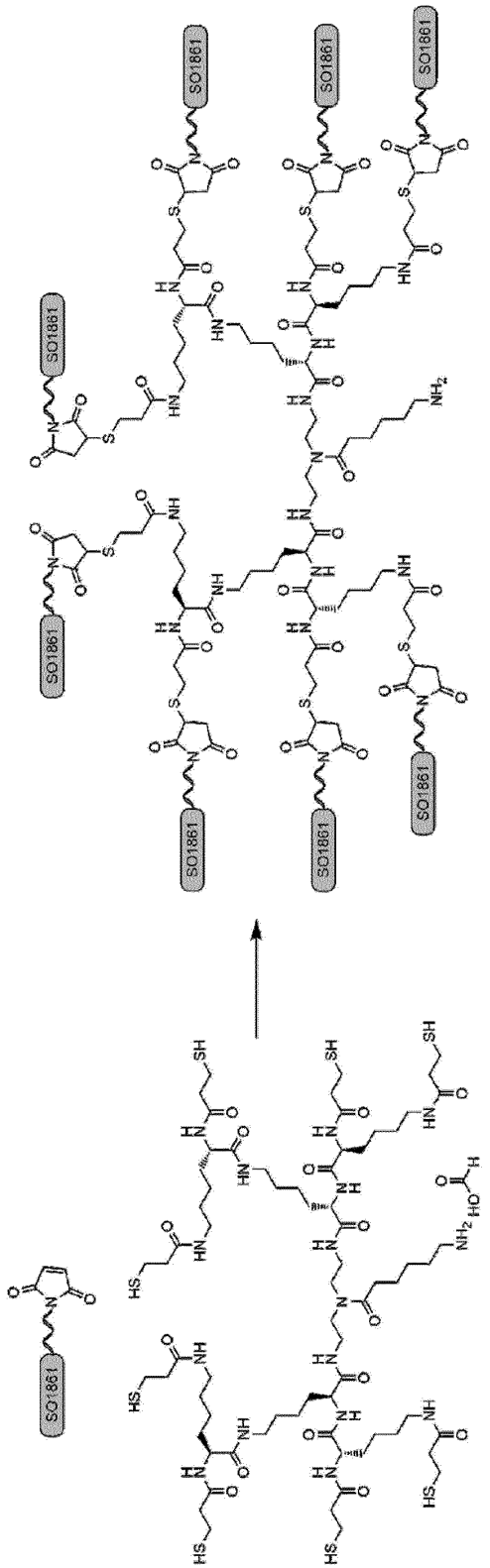


Figure 21

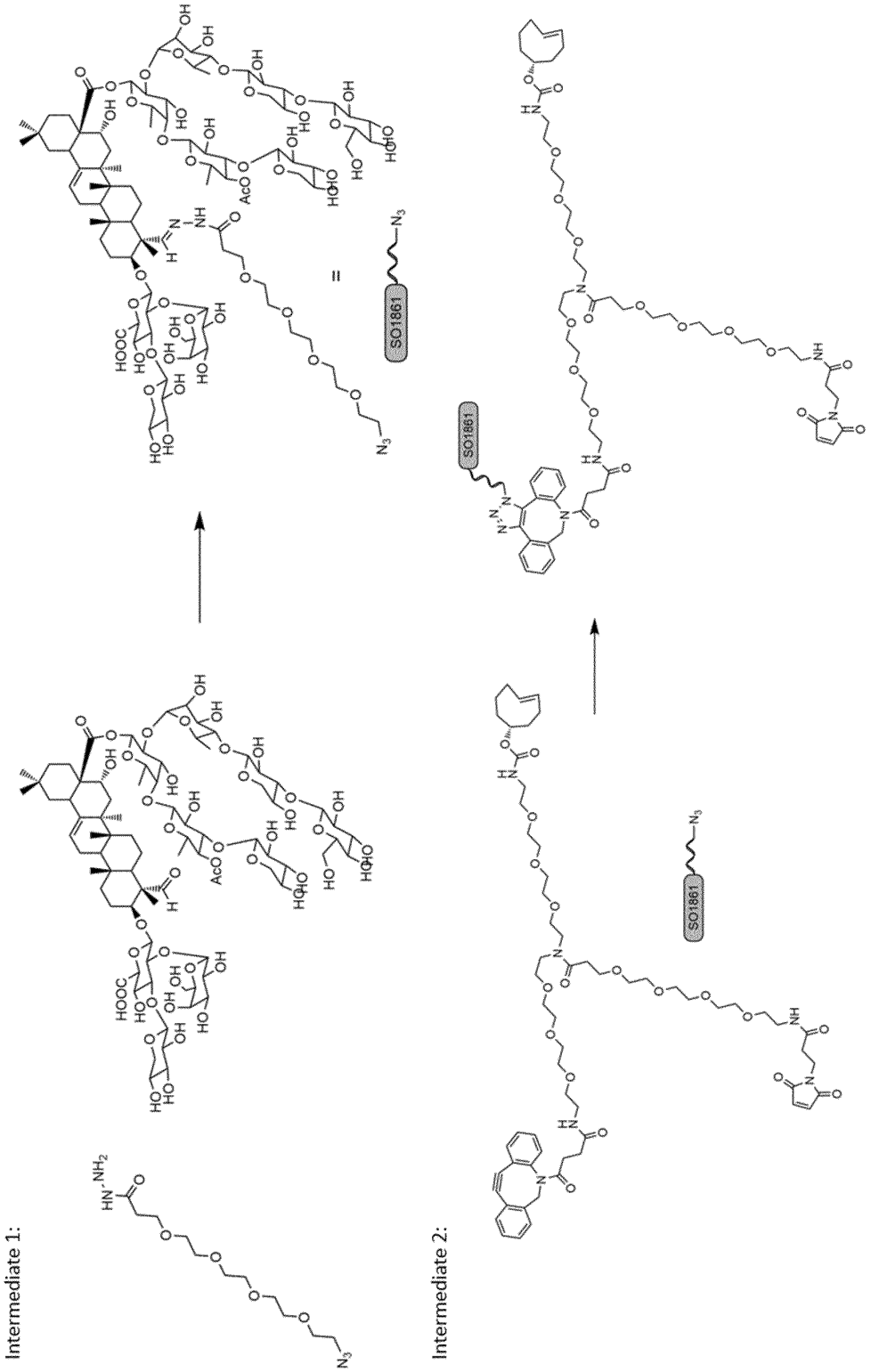


Figure 21

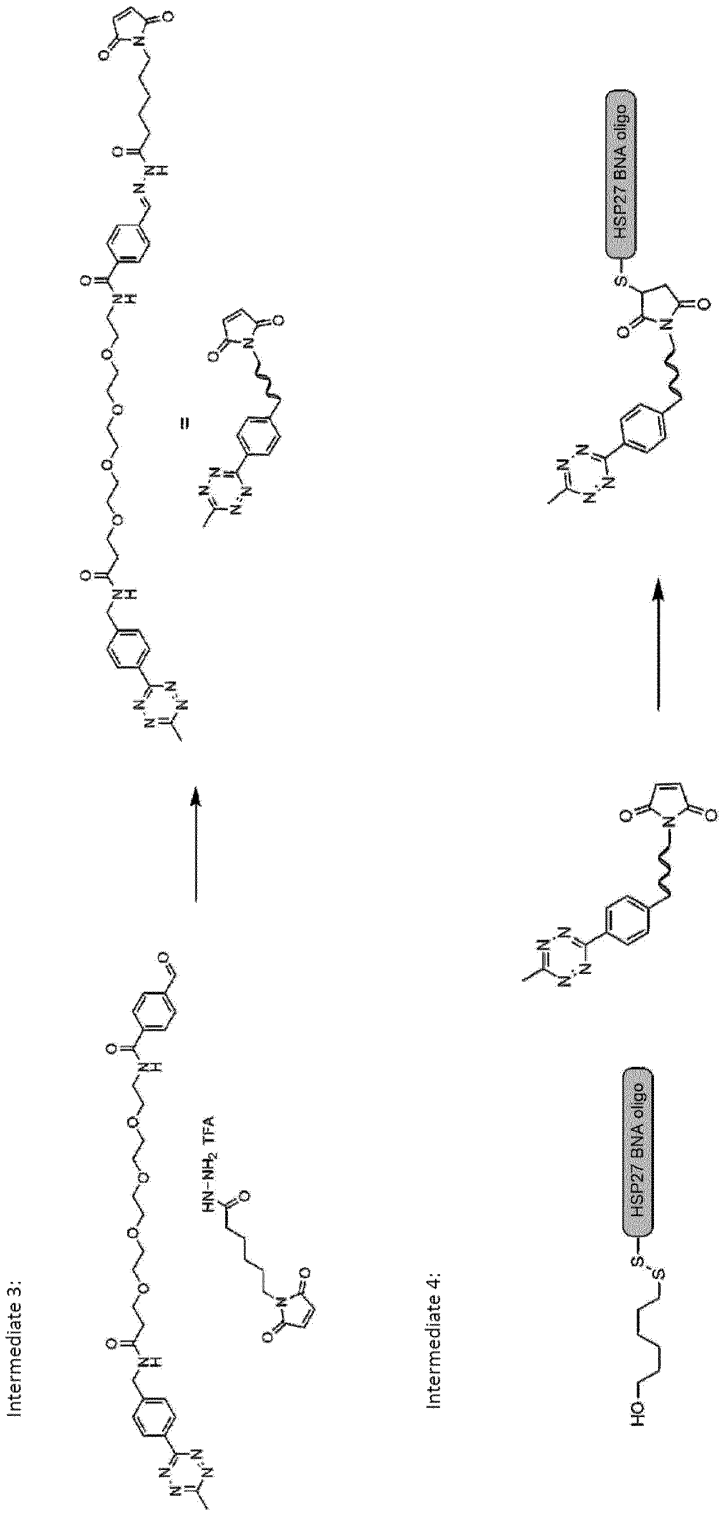
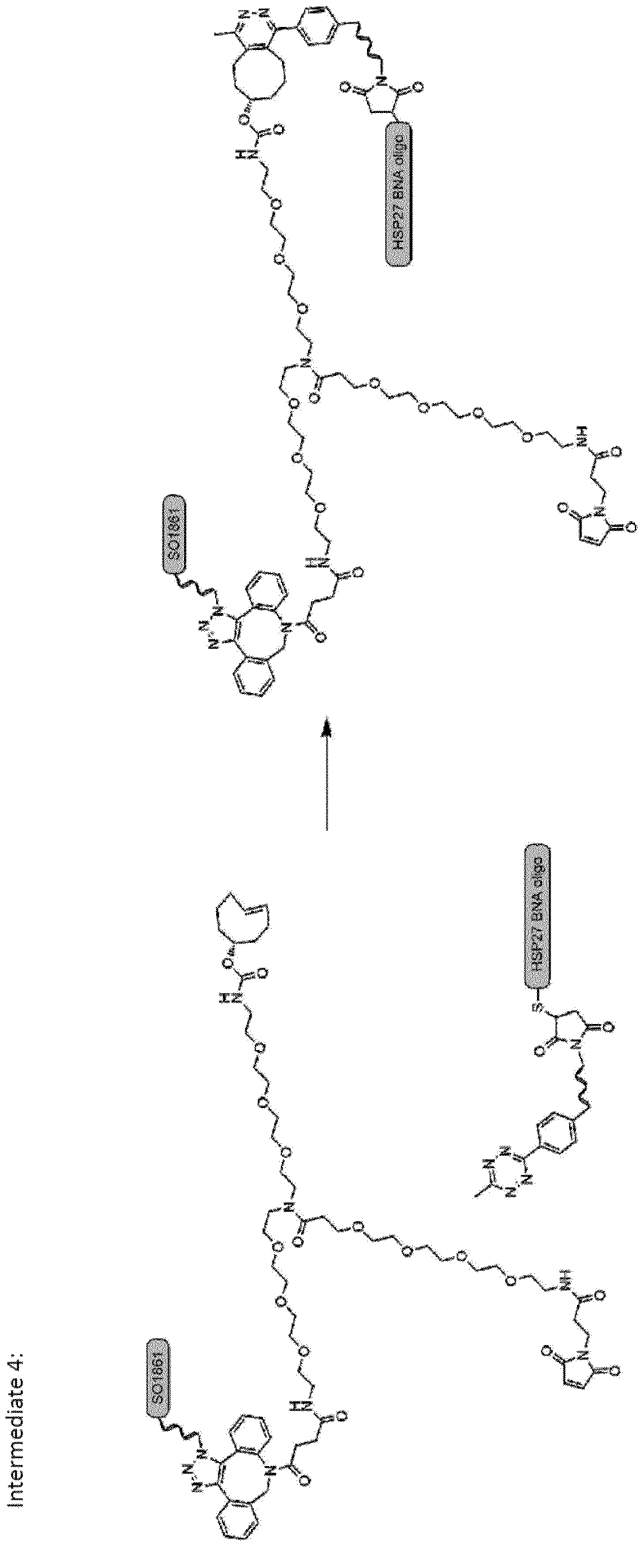

Intermediate 3:
HN-NH2 TFA
=
Intermediate 4:
HSP27 BNA oligo
HSP27 BNA oligo
HO

Figure 21



Intermediate 4:

Figure 22

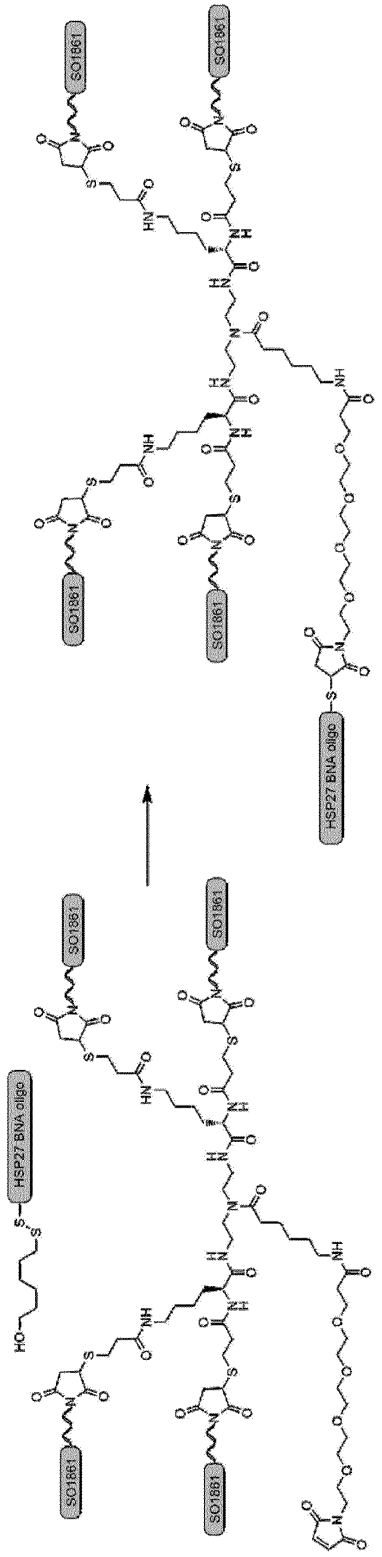


Figure 23

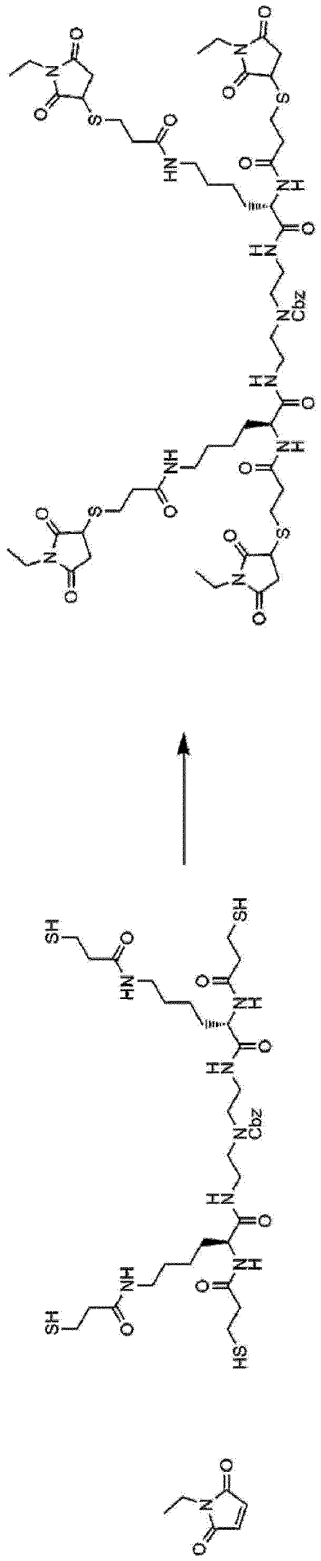


Figure 24

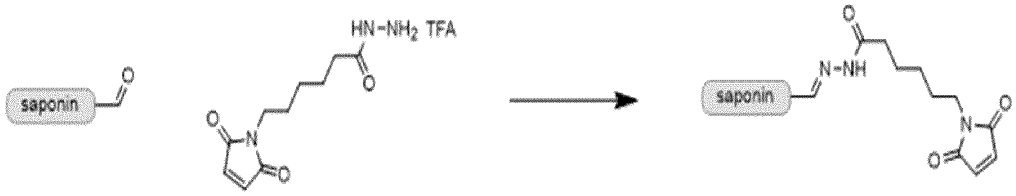


Figure 25

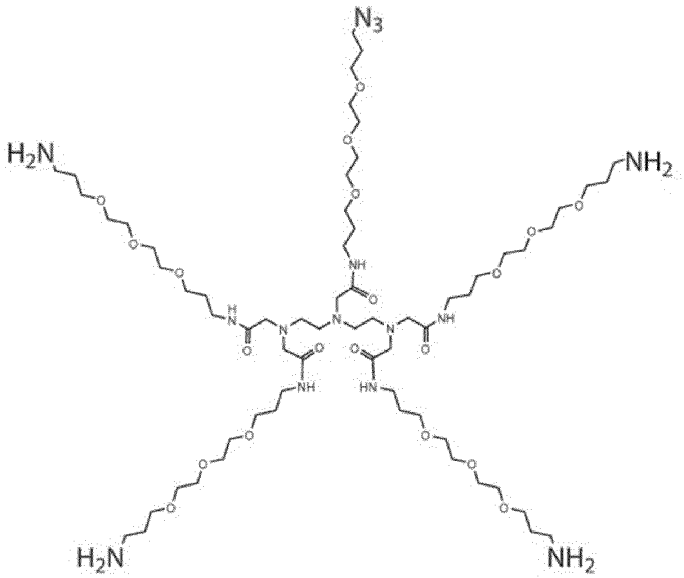


Figure 26

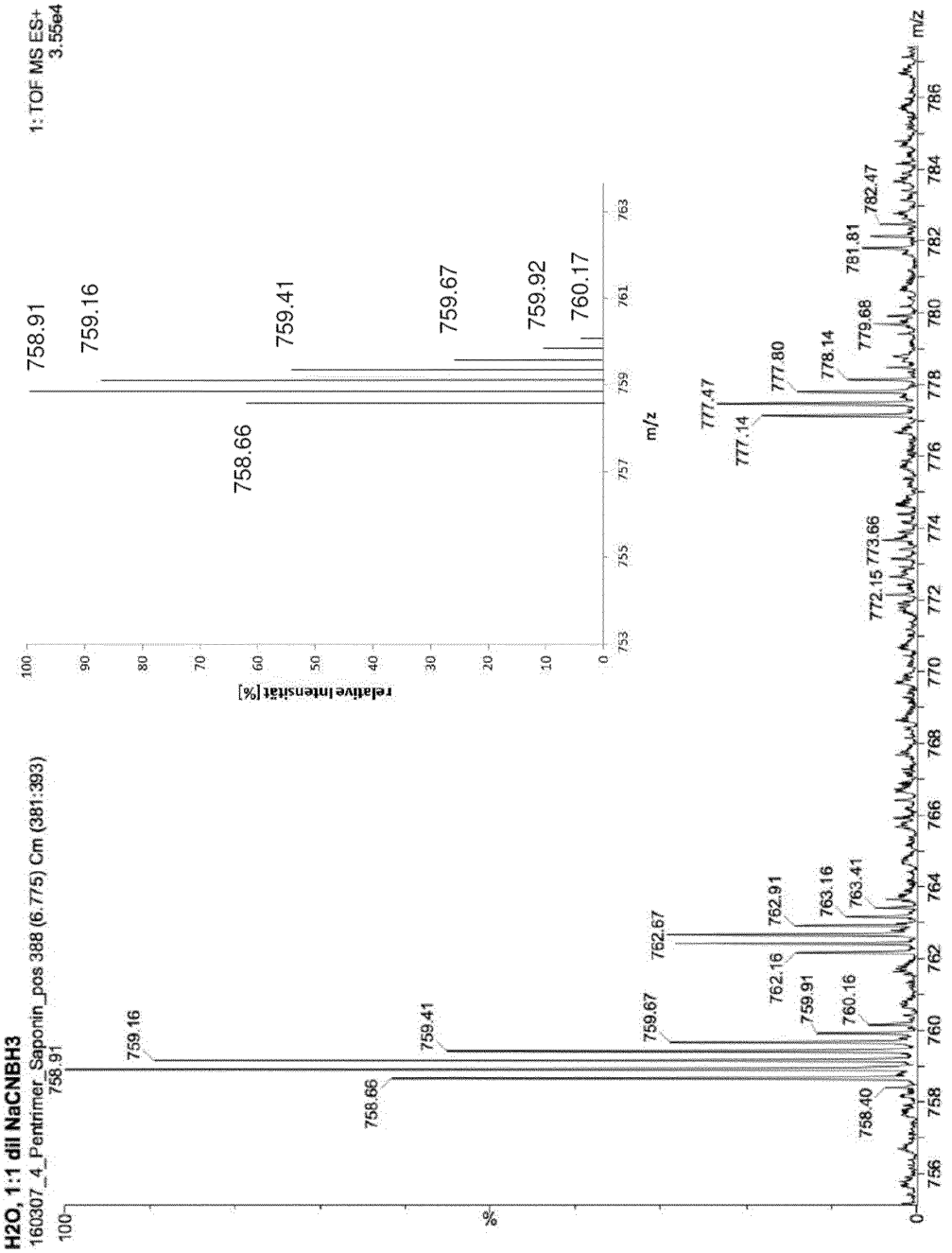

H2O, 1:1 dil NaCNBH3
160307_4_Pentrimer_Saponin_pos 388 (6.775) Cm (381:393)
1: TOF MS ES+
3.55e4
relative Intensität [%]
m/z
%
758.91
759.16
759.41
759.67
759.92
760.17
758.66
762.67
762.91
763.16
763.41
762.16
759.91
760.16
758.40
772.15
773.66
777.47
777.14
777.80
778.14
779.68
781.81
782.47

Figure 27

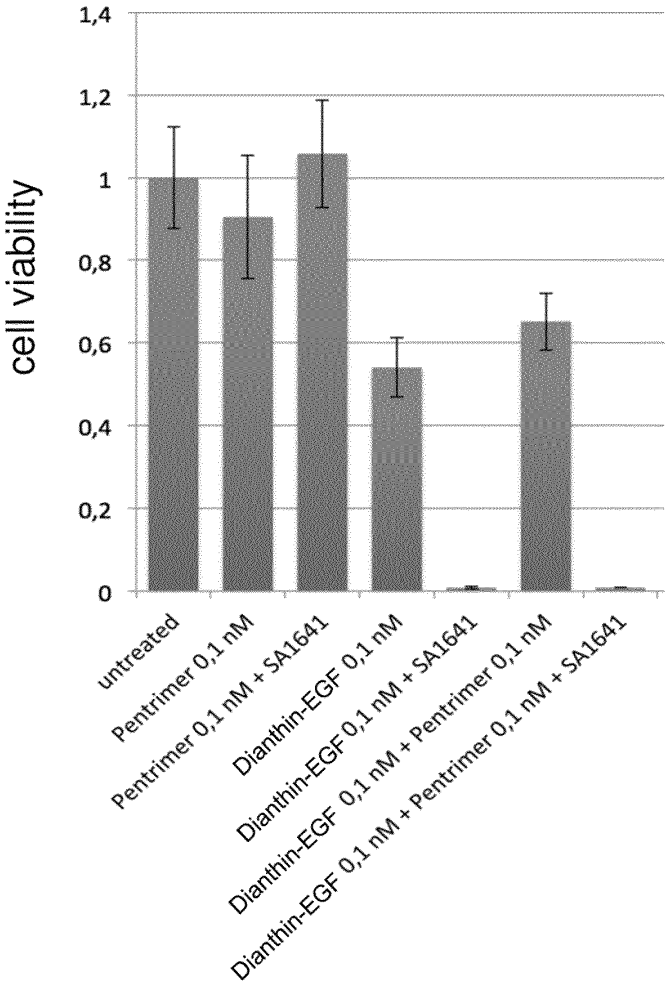

cell viability
1,4
1,2
1
0,8
0,6
0,4
0,2
0
untreated
Pentrimer 0,1 nM
Pentrimer 0,1 nM + SA1641
Dianthin-EGF 0,1 nM
Dianthin-EGF 0,1 nM + SA1641
Dianthin-EGF 0,1 nM + Pentrimer 0,1 nM
Dianthin-EGF 0,1 nM + Pentrimer 0,1 nM + SA1641

Figure 28

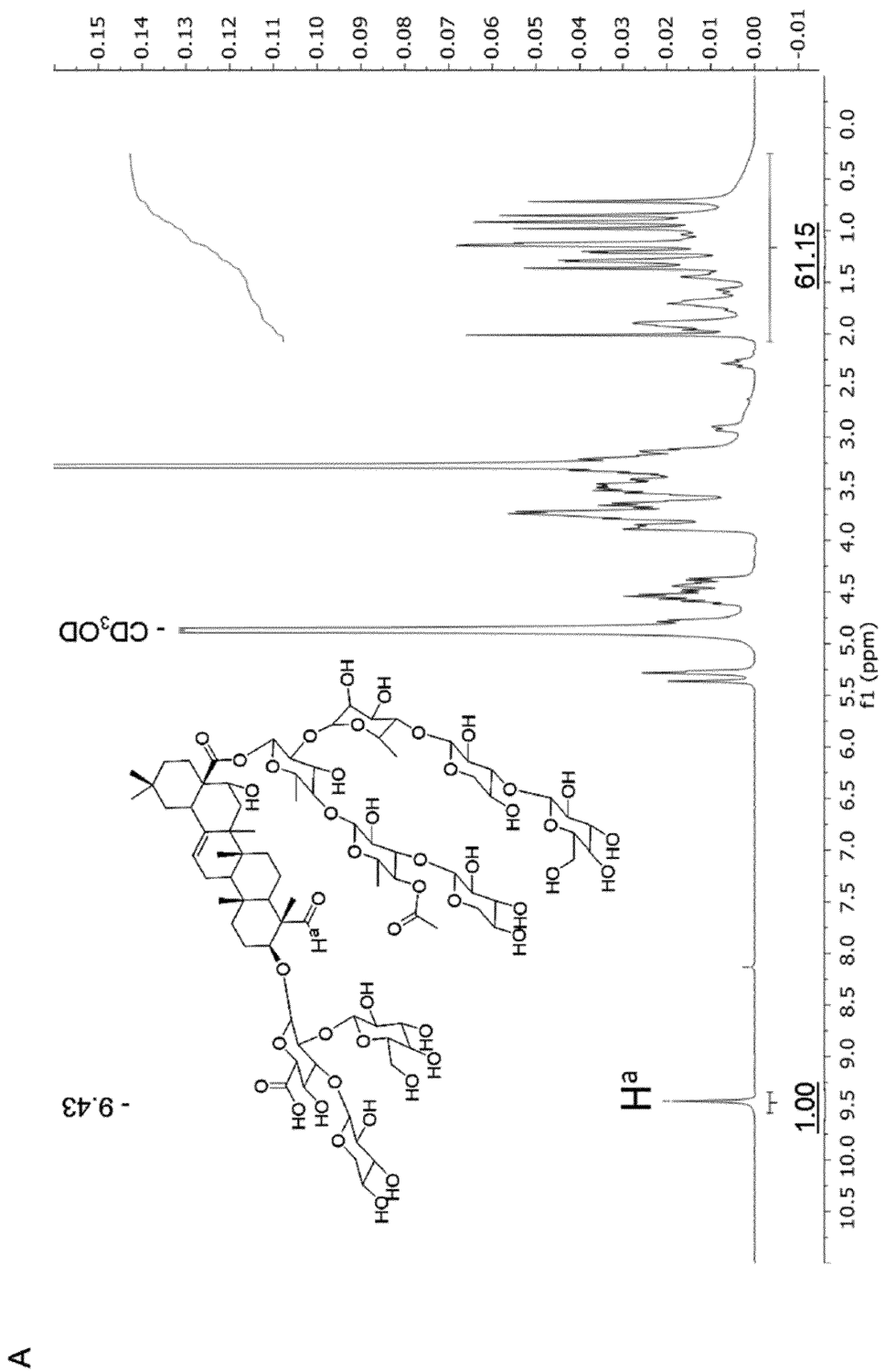


Figure 28

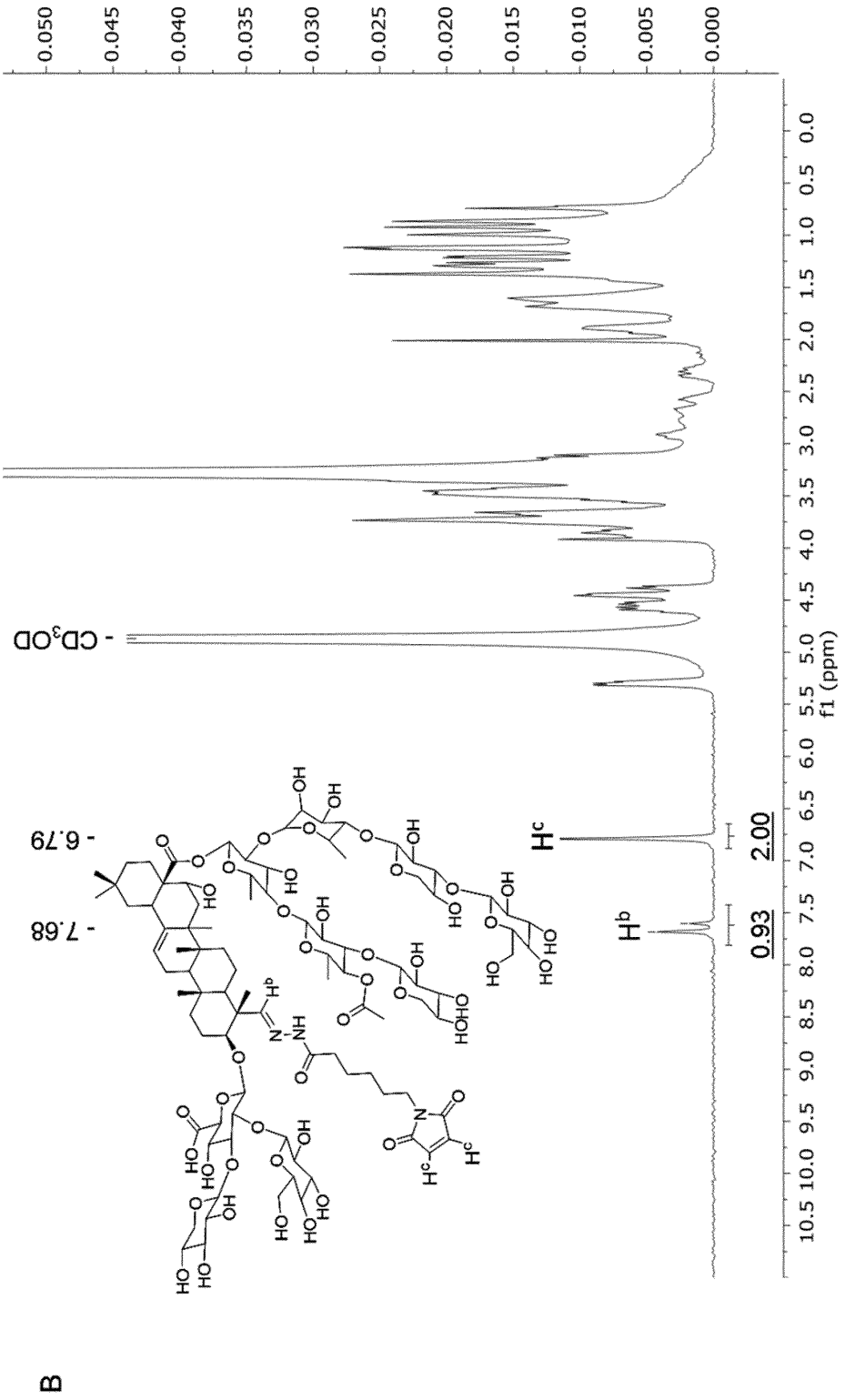


Figure 29

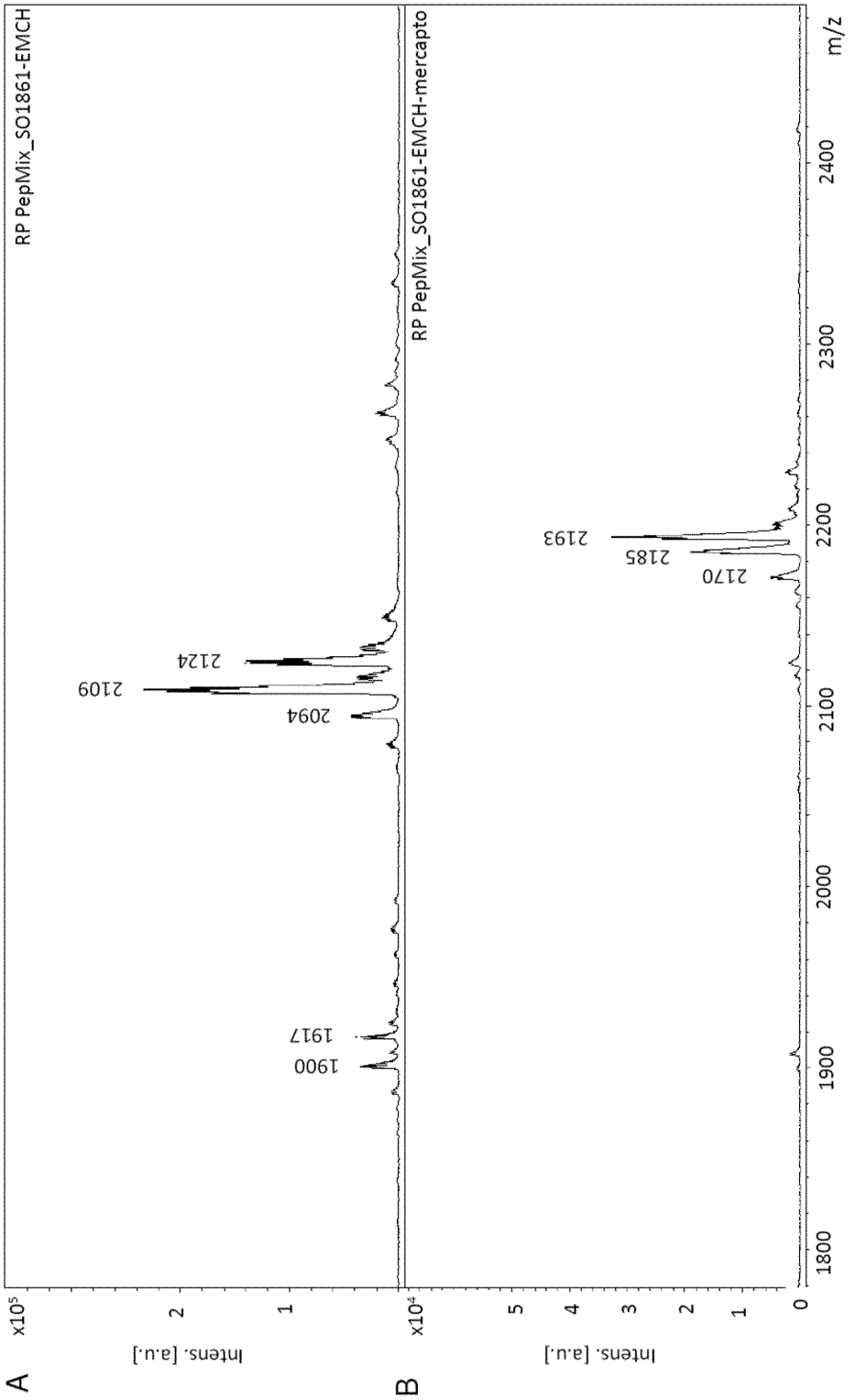

A
B
RP PepMix_SO1861-EMCH
RP PepMix_SO1861-EMCH-mercapto
Intens. [a.u.]
x10⁵
x10⁴
m/z
1800
1900
2000
2100
2200
2300
2400
1900
1917
2094
2109
2124
2170
2185
2193

Figure 30

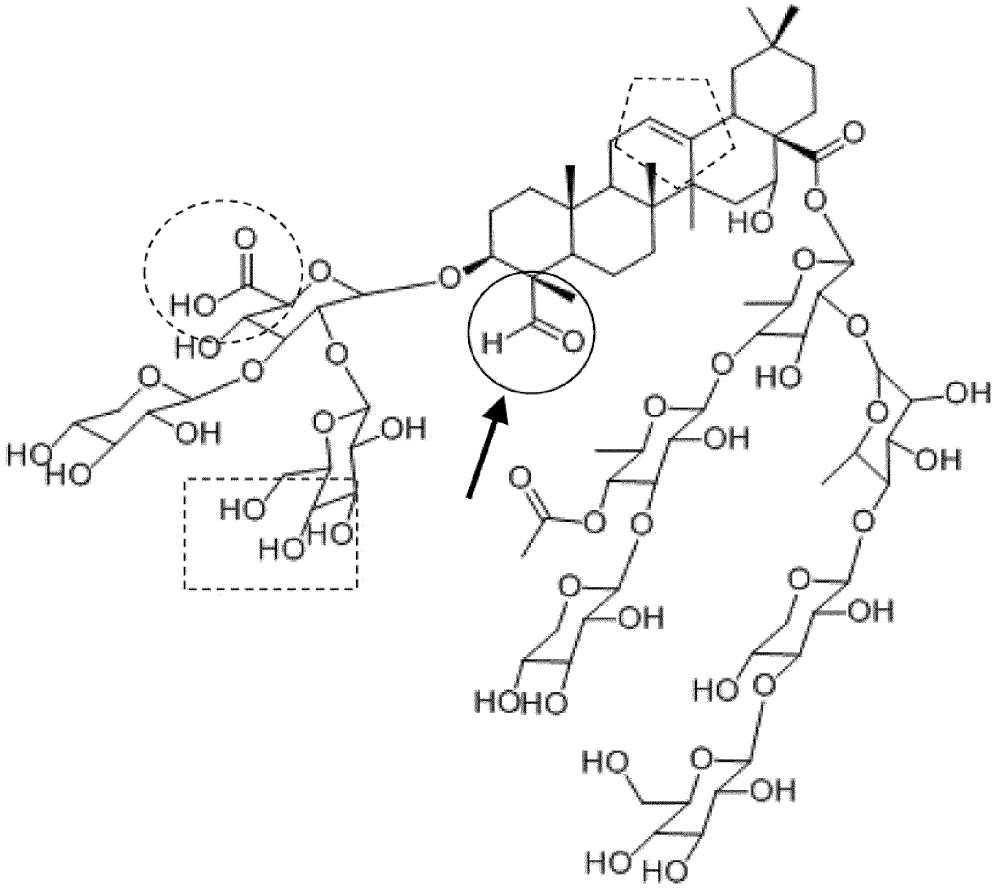


Figure 31

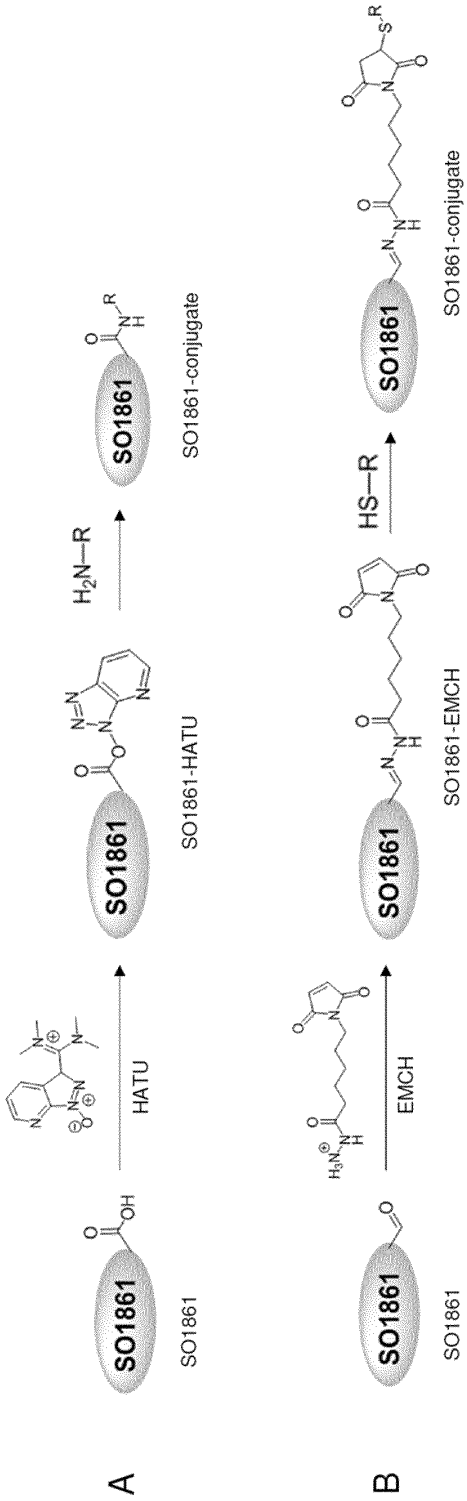

A
SO1861
HATU
SO1861-HATU
H2N—R
SO1861-conjugate
B
SO1861
EMCH
SO1861-EMCH
HS—R
SO1861-conjugate

Figure 32

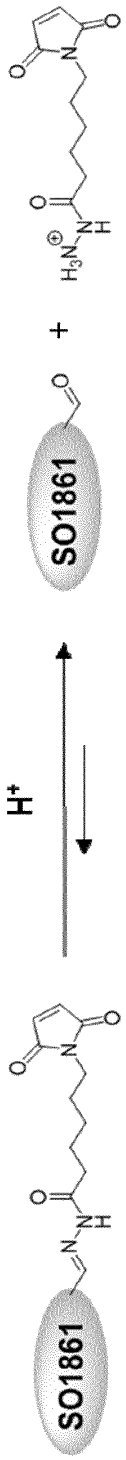
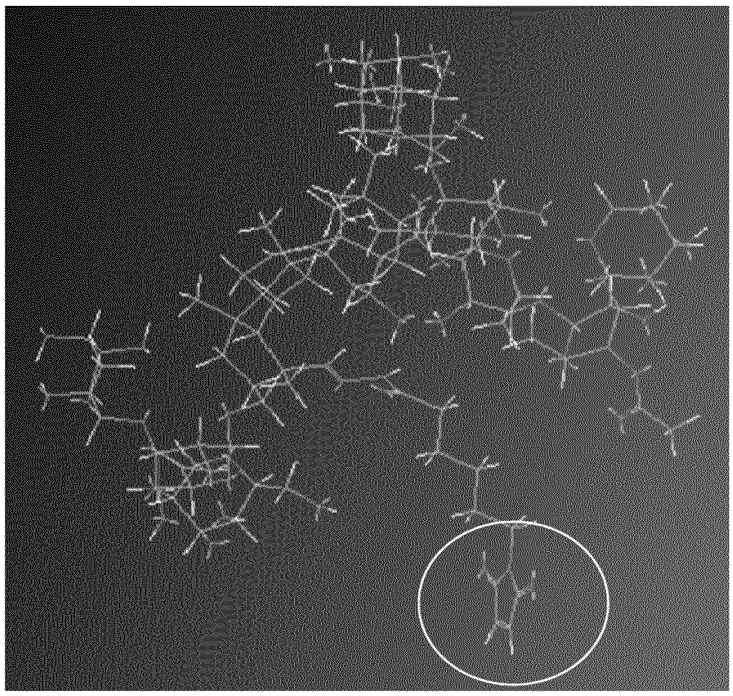
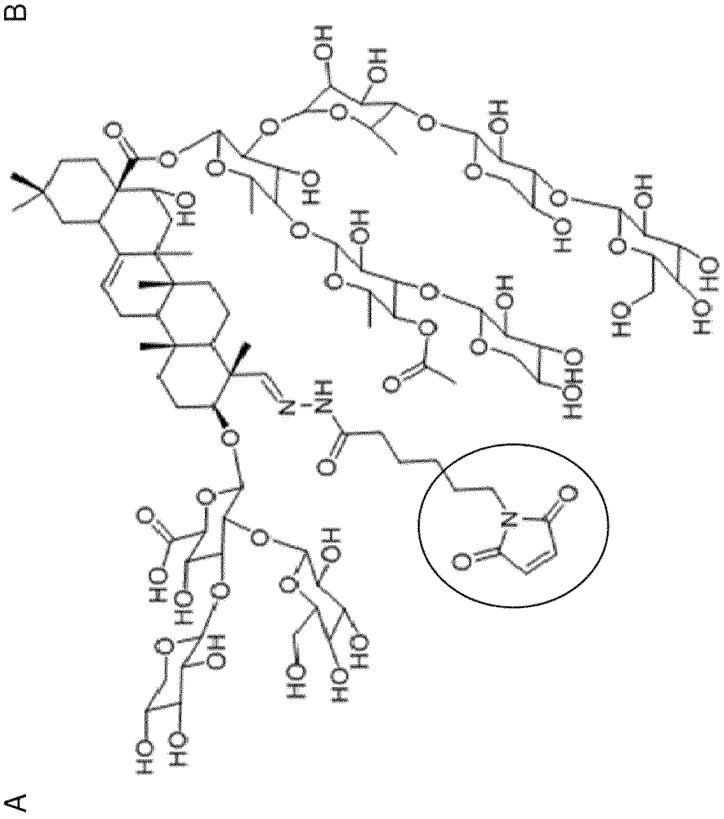


Figure 33



B



A

Figure 34

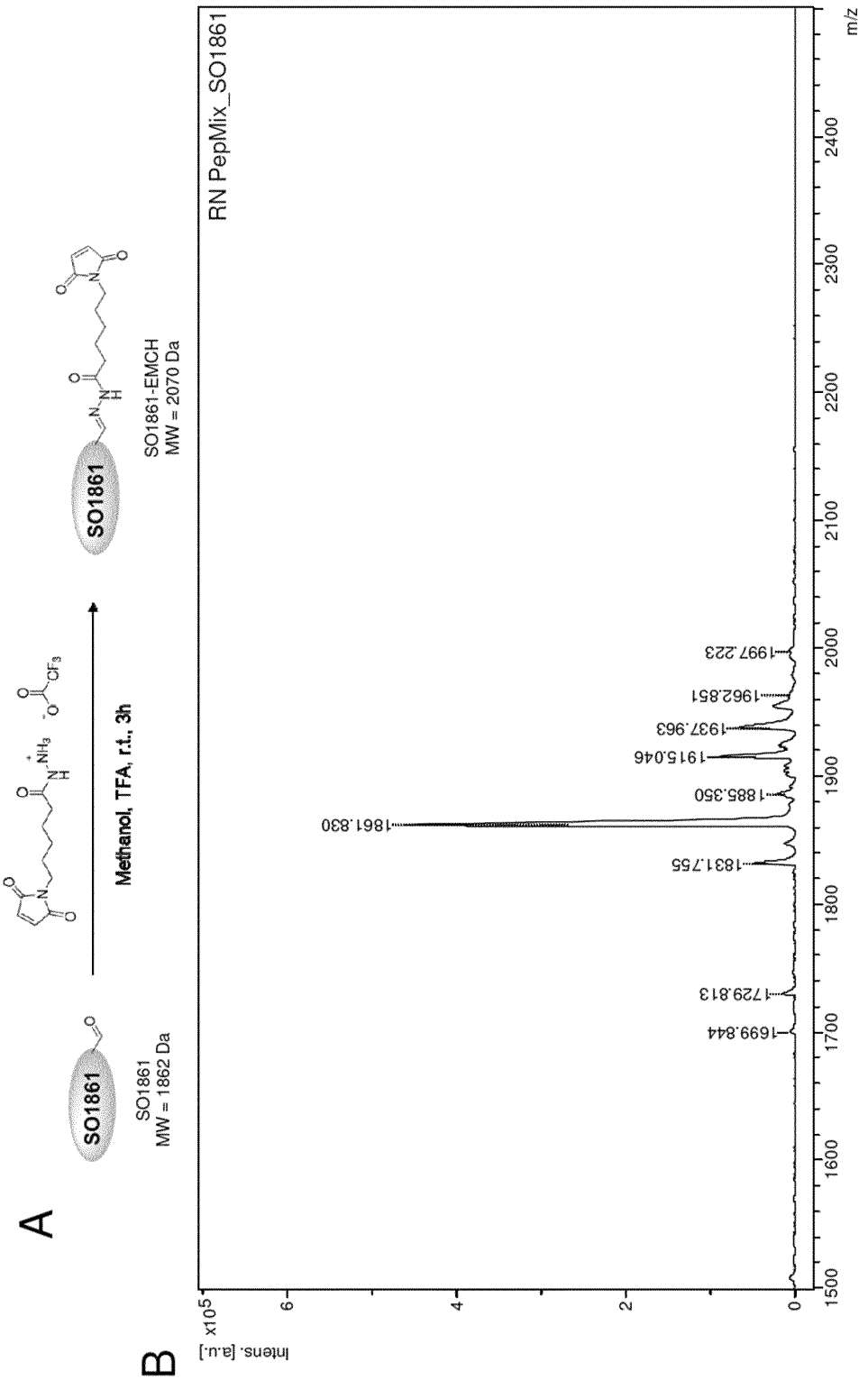

A
SO1861
SO1861
MW = 1862 Da
Methanol, TFA, r.t., 3h
SO1861
SO1861-EMCH
MW = 2070 Da
B
RN PepMix_SO1861
Intens. [a.u.]
x10^5
m/z
1699.844
1729.813
1831.755
1861.830
1885.350
1915.046
1937.963
1962.851
1997.223

Figure 34

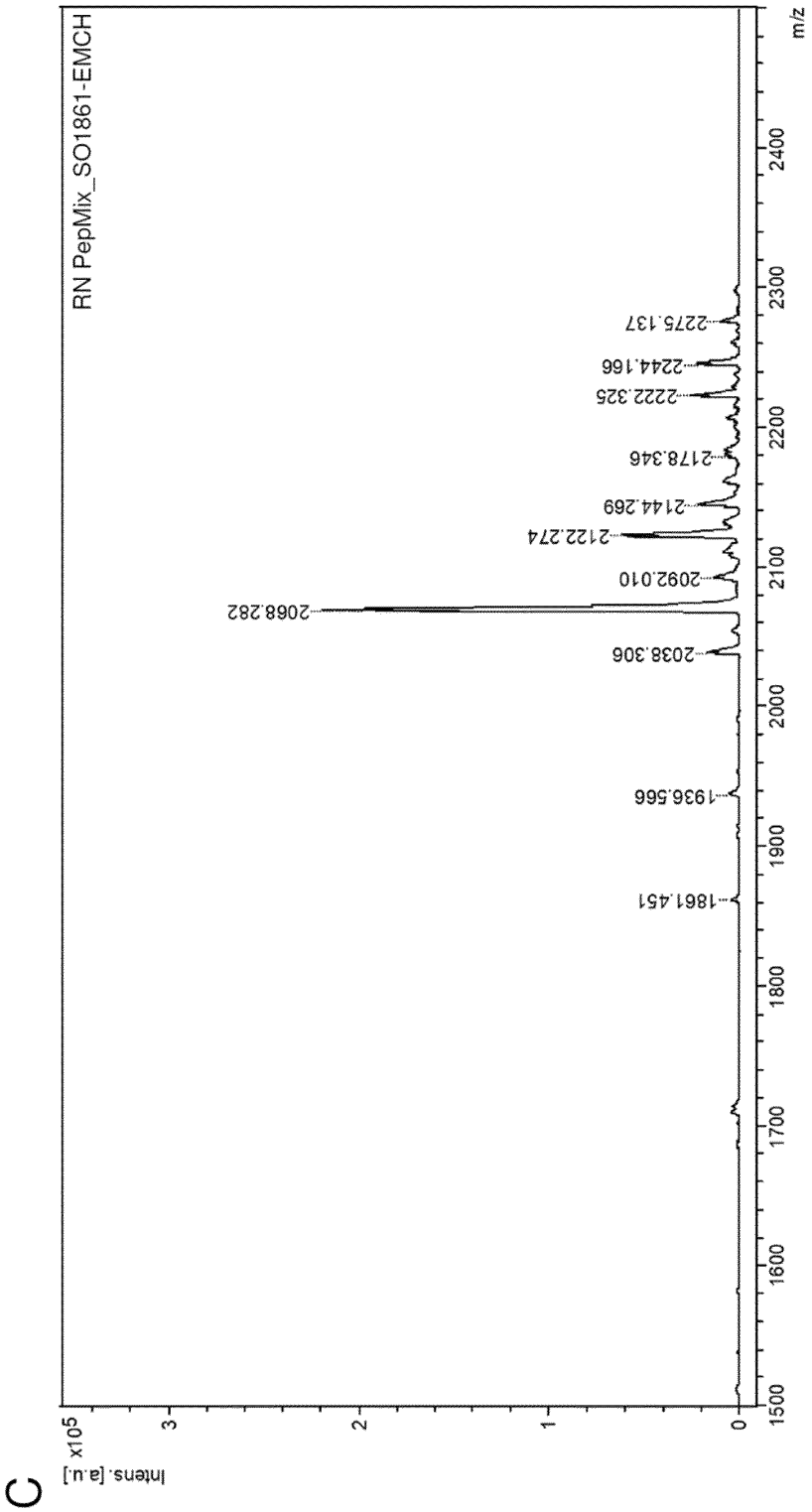

C
RN PepMix_SO1861-EMCH
Intens. [a.u.]
x10^5
3
2
1
0
1500
1600
1700
1800
1900
2000
2100
2200
2300
2400
m/z
1861.451
1936.566
2038.306
2068.282
2092.010
2122.274
2144.269
2178.346
2222.325
2244.166
2275.137

Figure 35

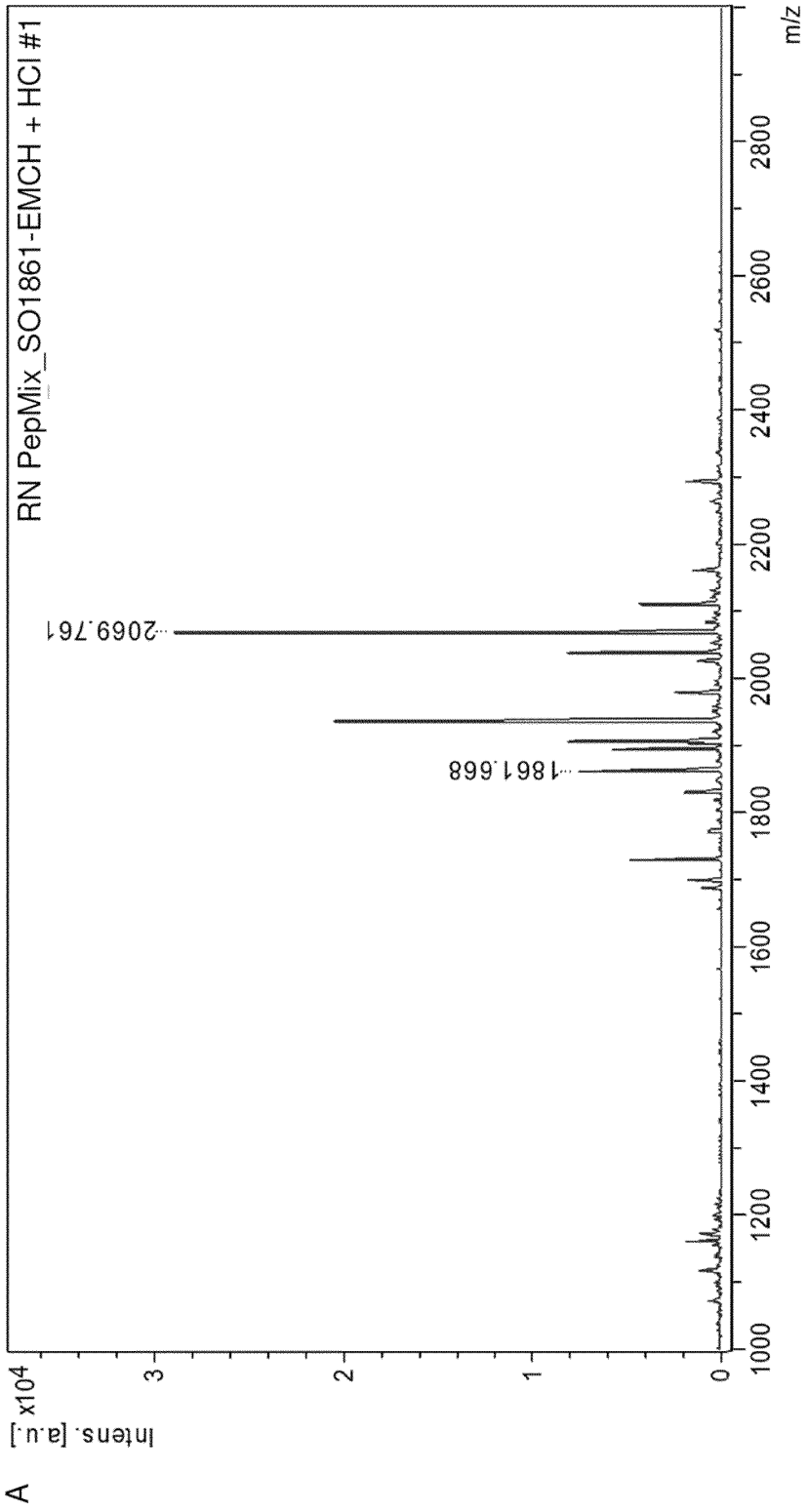

A
Intens. [a.u.]
x10^4
3
2
1
0
1000
1200
1400
1600
1800
2000
2200
2400
2600
2800
m/z
RN PepMix_SO1861-EMCH + HCl #1
2069.761
1861.668

Figure 35

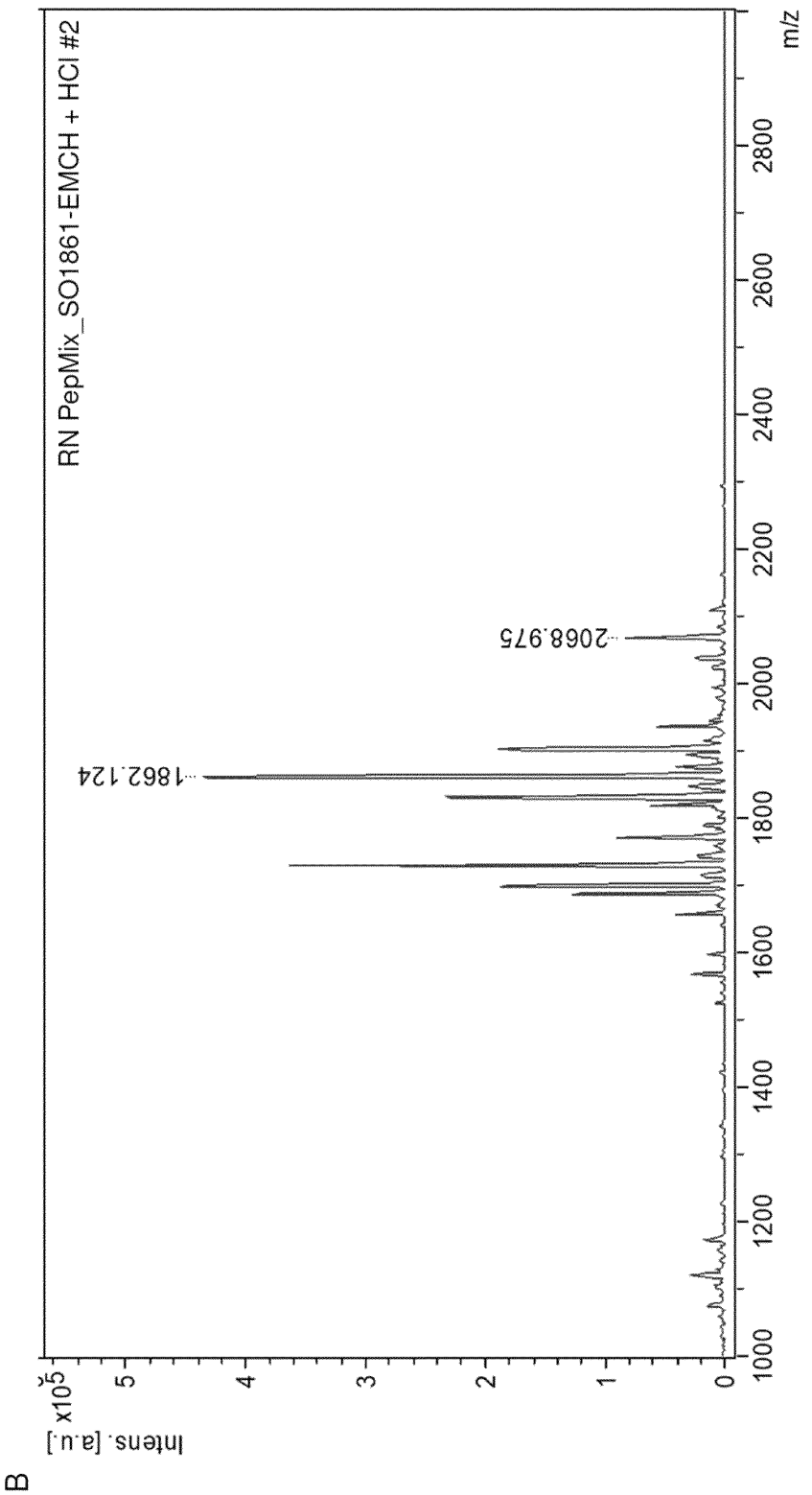

B
RN PepMix_SO1861-EMCH + HCl #2
Intens. [a.u.]
x10^5
5
4
3
2
1
0
1000
1200
1400
1600
1800
2000
2200
2400
2600
2800
m/z
1862.124
2068.975

Figure 36

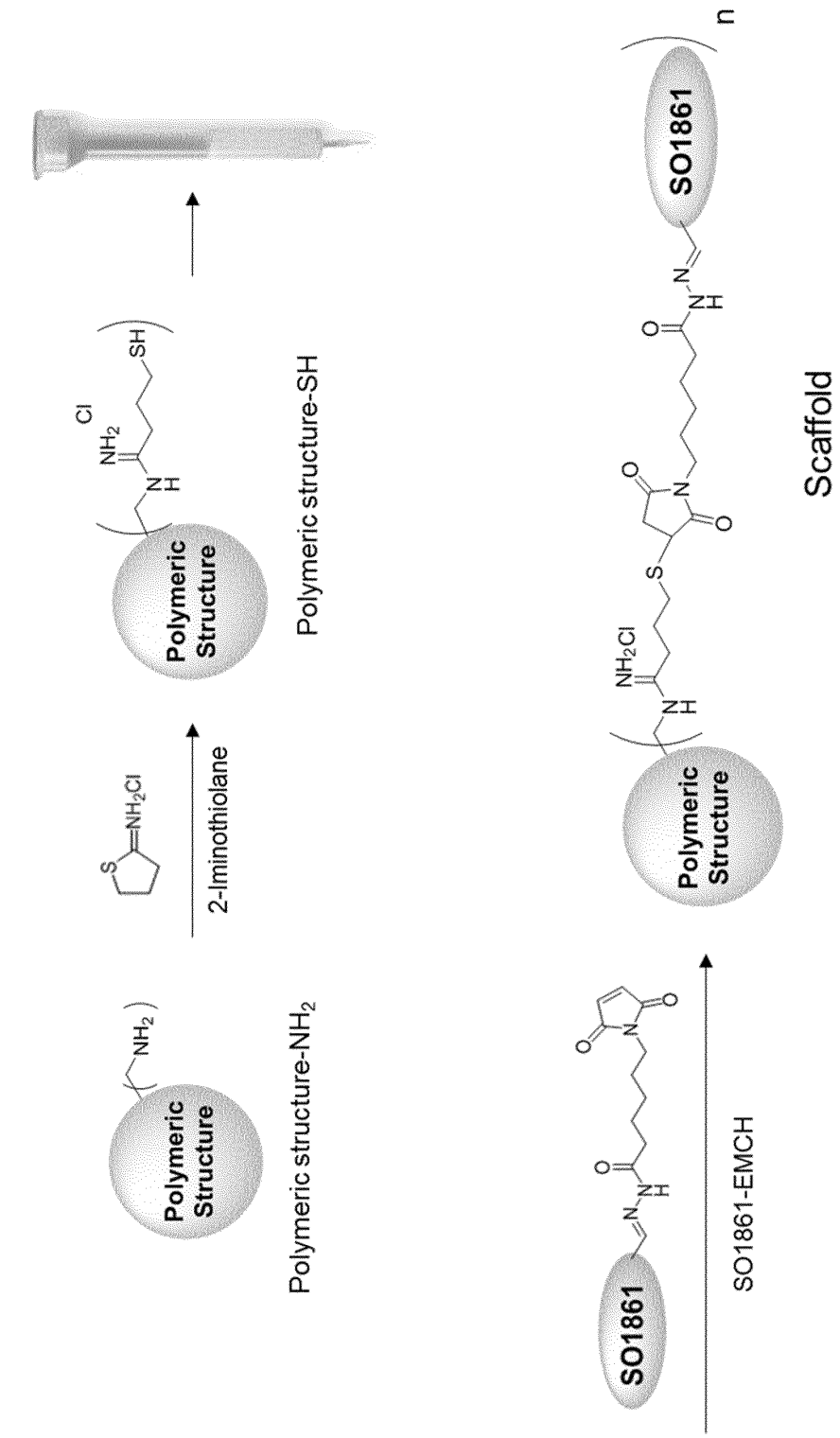

Polymeric Structure
Polymeric structure-NH2
2-Iminothiolane
Polymeric structure-SH
SO1861-EMCH
Scaffold
SO1861
n

Figure 37

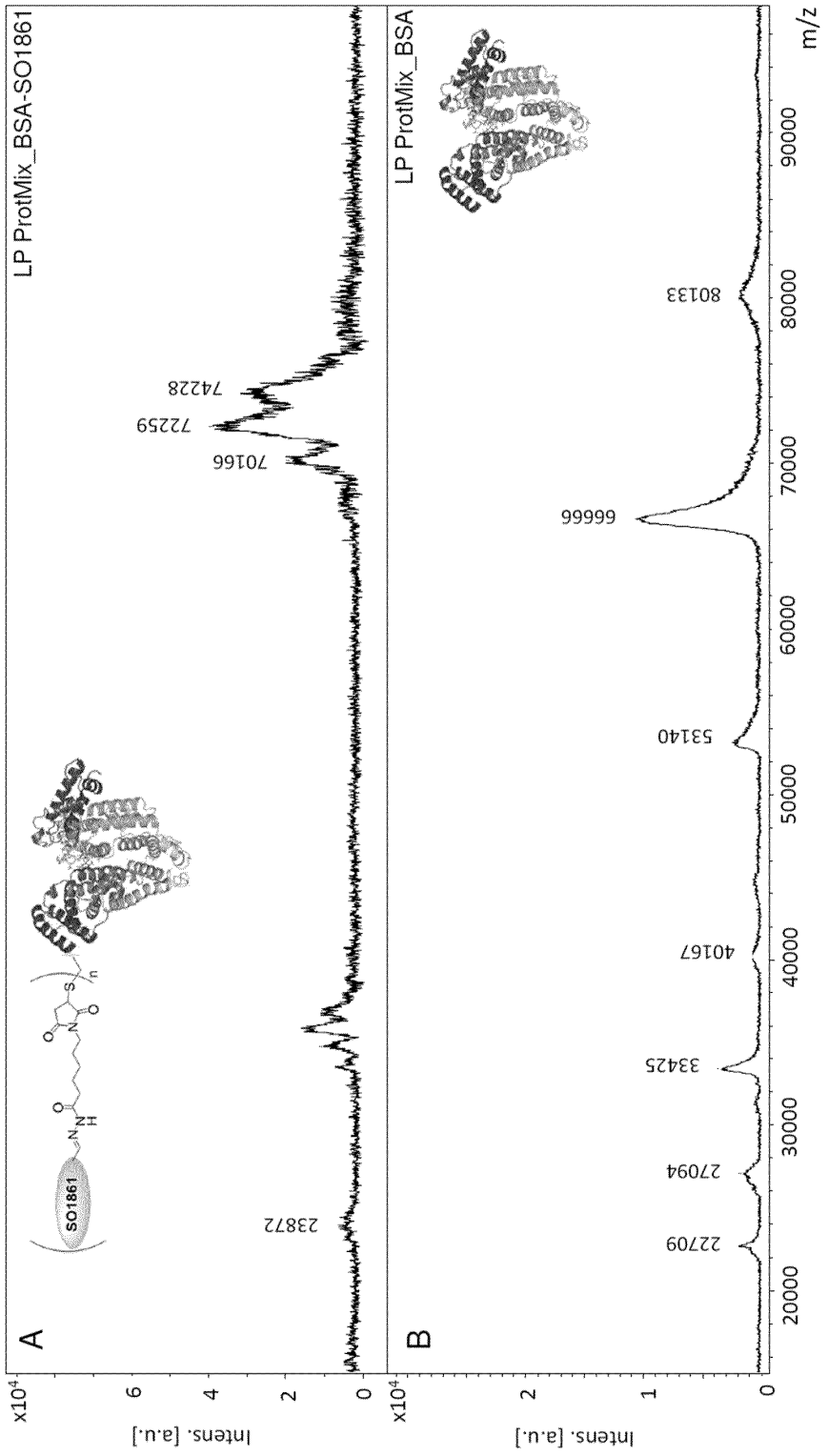

LP ProtMix_BSA-SO1861
A
SO1861
23872
70166
72259
74228
Intens. [a.u.]
x10^4
LP ProtMix_BSA
B
22709
27094
33425
40167
53140
66666
80133
m/z
20000
30000
40000
50000
60000
70000
80000
90000

Figure 38

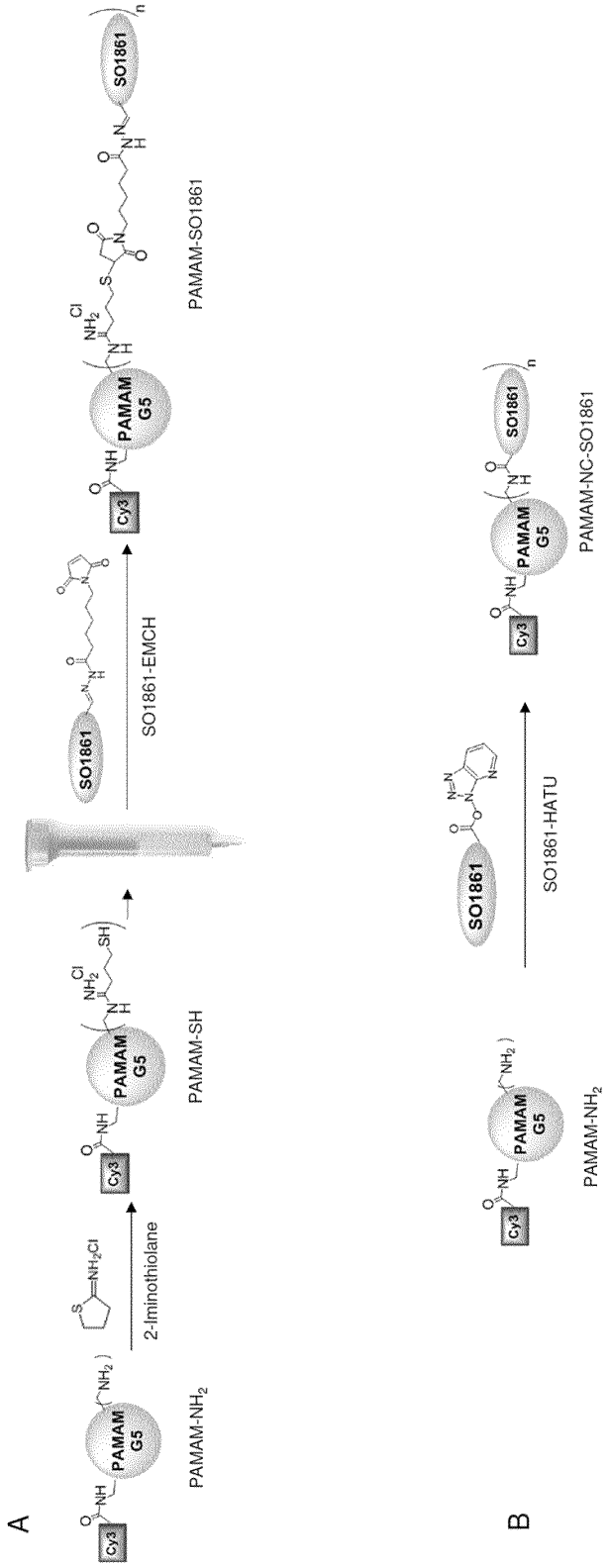

A
Cy3
PAMAM G5
PAMAM-NH2
2-Iminothiolane
PAMAM-SH
SO1861-EMCH
PAMAM-SO1861
B
SO1861-HATU
PAMAM-NC-SO1861

Figure 39

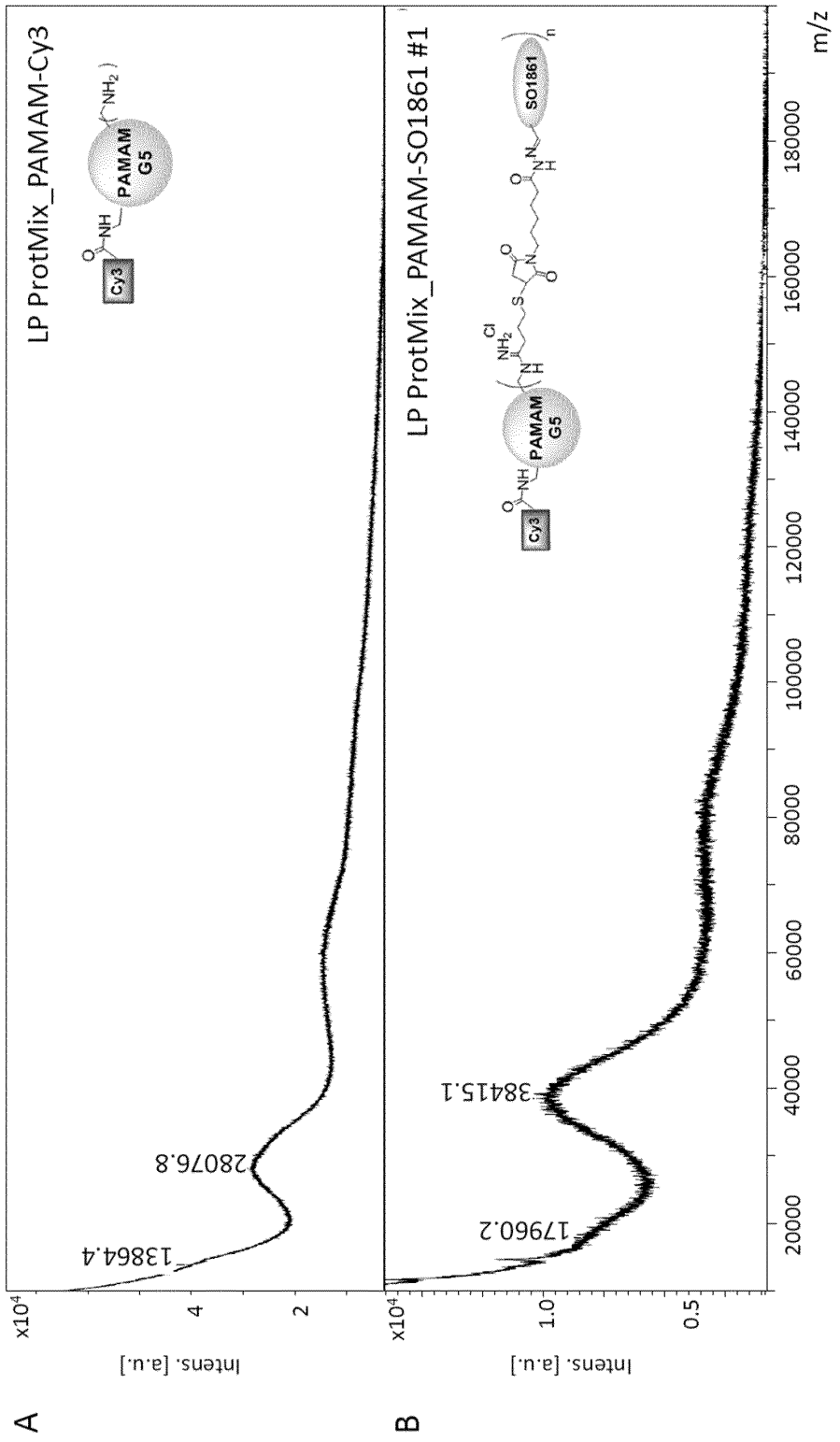

A
LP ProtMix_PAMAM-Cy3
PAMAM G5
Cy3
13864.4
28076.8
Intens. [a.u.]
x10^4
4
2
B
LP ProtMix_PAMAM-SO1861 #1
PAMAM G5
Cy3
SO1861
17960.2
38415.1
Intens. [a.u.]
x10^4
1.0
0.5
20000
40000
60000
80000
100000
120000
140000
160000
180000
m/z

Figure 39

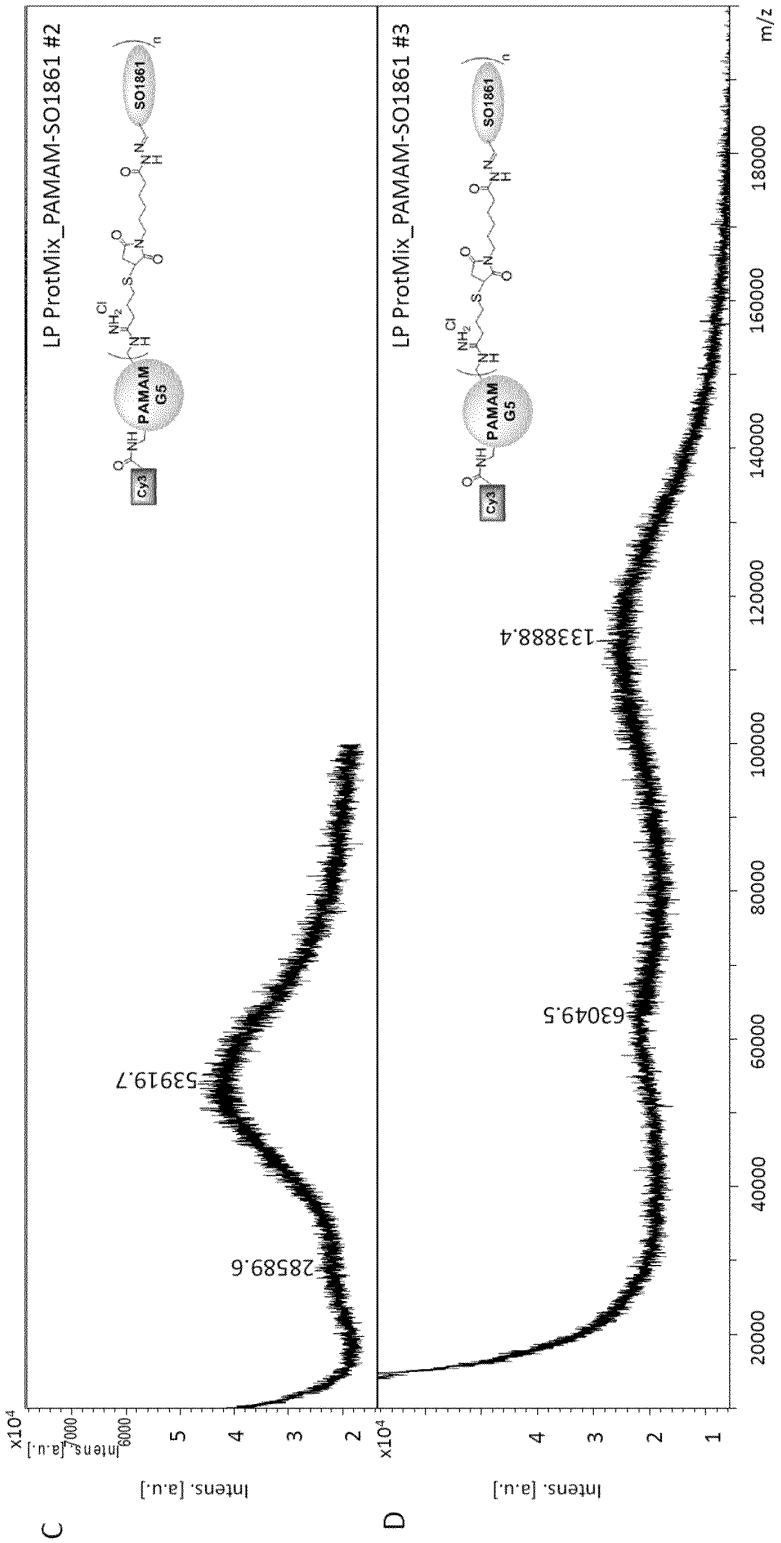

C
D
LP ProtMix_PAMAM-SO1861 #2
LP ProtMix_PAMAM-SO1861 #3
Intens. [a.u.]
x10^4
m/z
20000
40000
60000
80000
100000
120000
140000
160000
180000
28589.6
53919.7
63049.5
133888.4
PAMAM G5
Cy3
SO1861

Figure 40

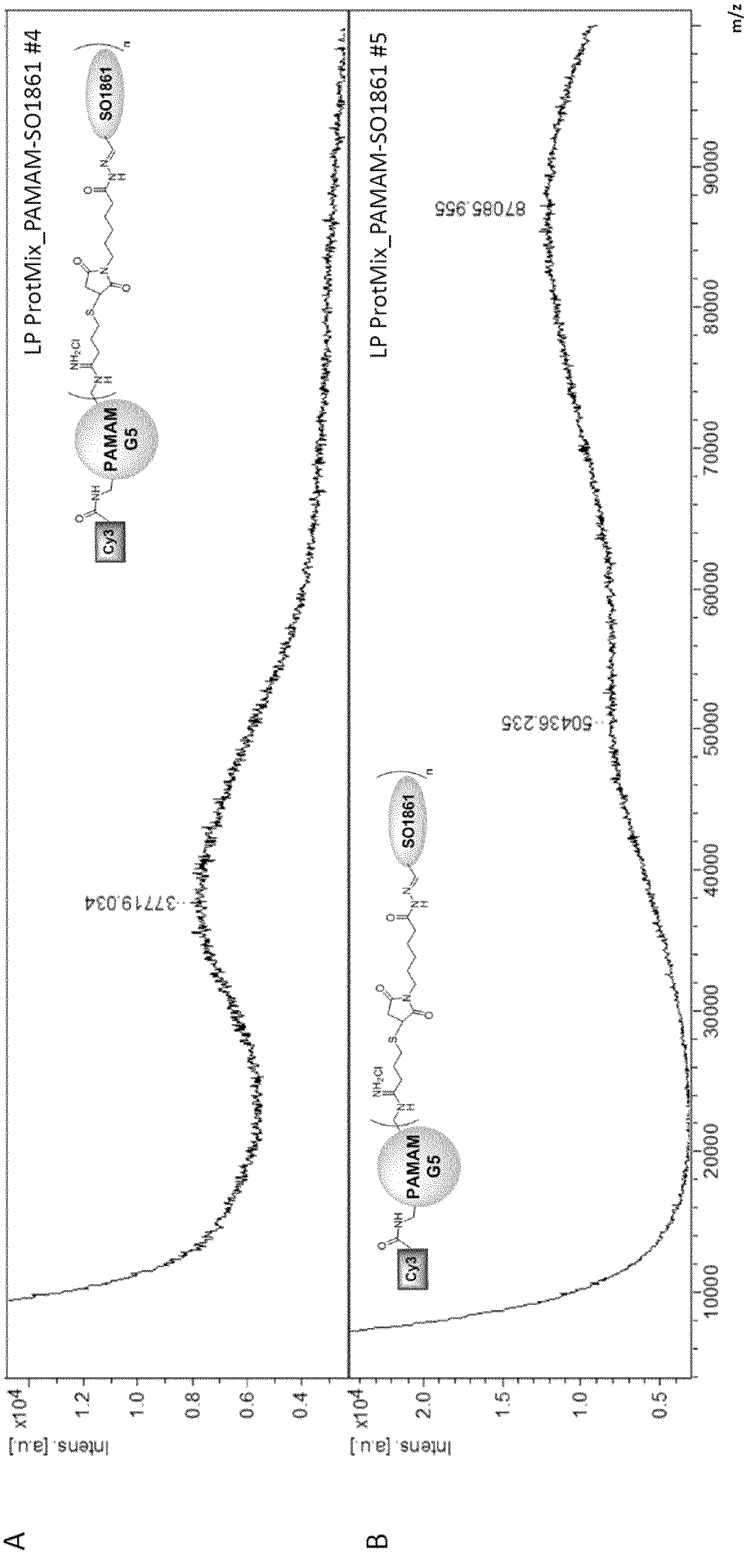

LP ProtMix_PAMAM-SO1861 #4
LP ProtMix_PAMAM-SO1861 #5
37719.034
50436.235
87085.955
Intens. [a.u.]
x10^4
m/z
PAMAM G5
Cy3
SO1861
A
B

Figure 41

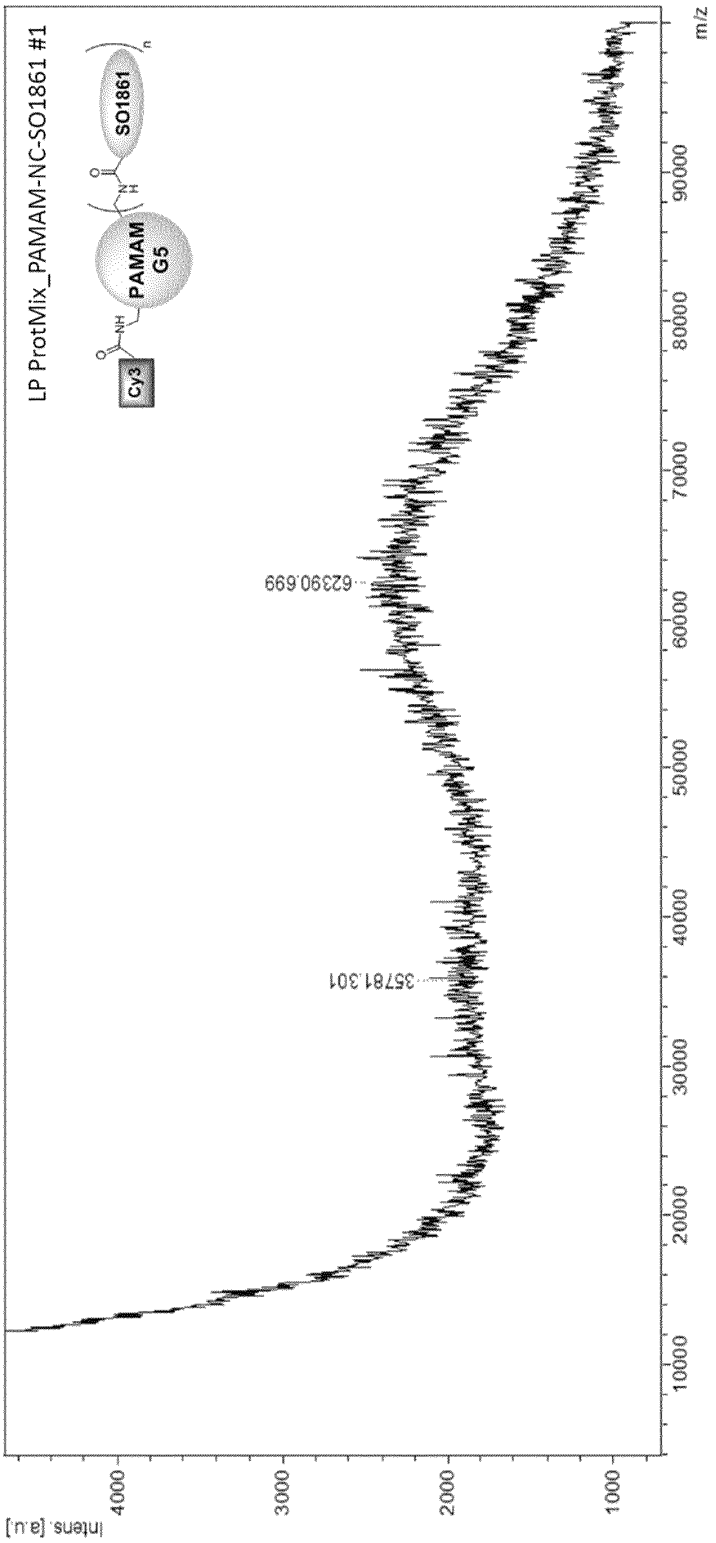

LP ProtMix_PAMAM-NC-SO1861 #1
SO1861
PAMAM G5
Cy3
62390.699
35781.301
Intens. [a.u.]
4000
3000
2000
1000
m/z
10000
20000
30000
40000
50000
60000
70000
80000
90000

Figure 42

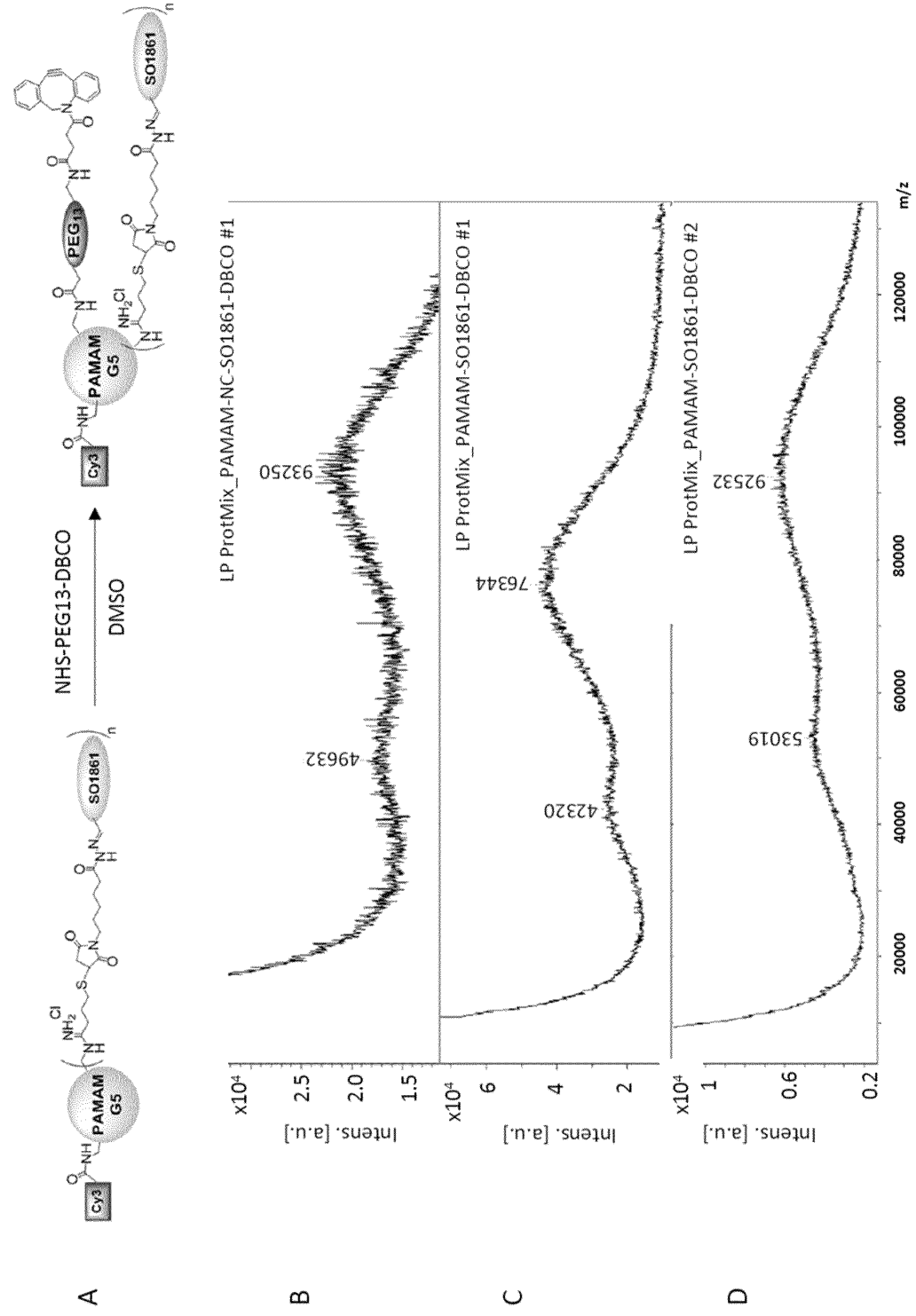

A
NHS-PEG13-DBCO
DMSO
Cy3
PAMAM G5
PEG13
SO1861
B
LP ProtMix_PAMAM-NC-SO1861-DBCO #1
9325O
4963 2
C
LP ProtMix_PAMAM-SO1861-DBCO #1
76344
42320
D
LP ProtMix_PAMAM-SO1861-DBCO #2
92532
53019
Intens. [a.u.]
x10^4
m/z
20000
40000
60000
80000
100000
120000

Figure 43

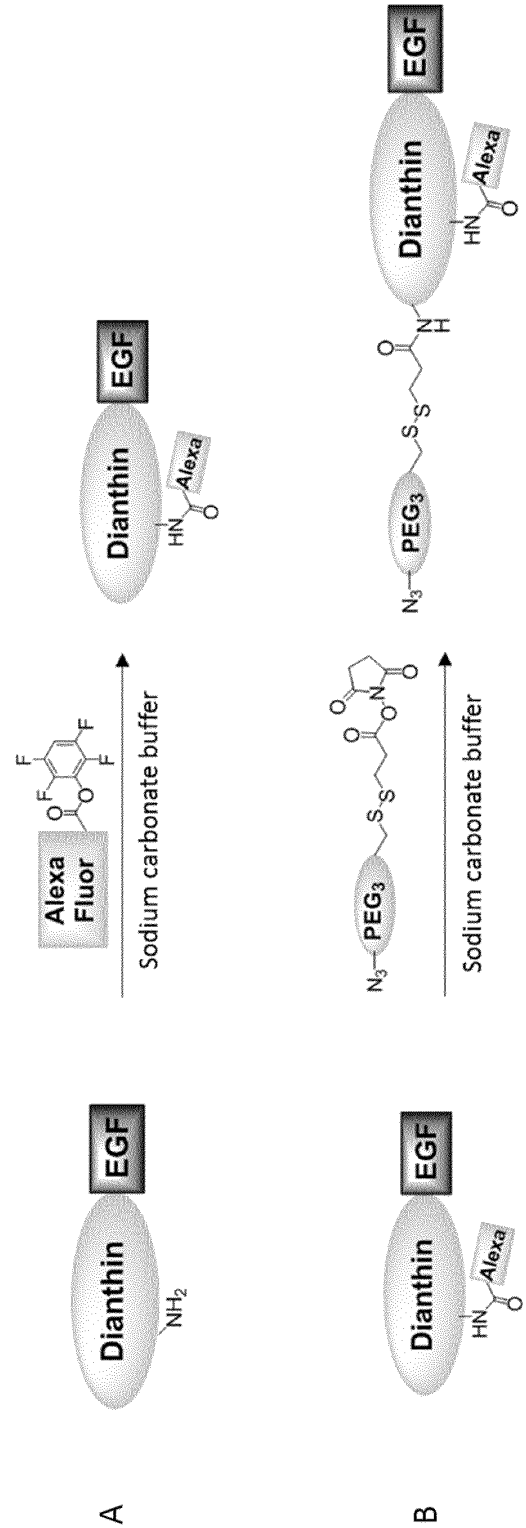

EGF
Dianthin
NH2
Alexa Fluor
Sodium carbonate buffer
EGF
Dianthin
Alexa
HN
O
PEG3
N3
S
S
N
H
A
B

Figure 43

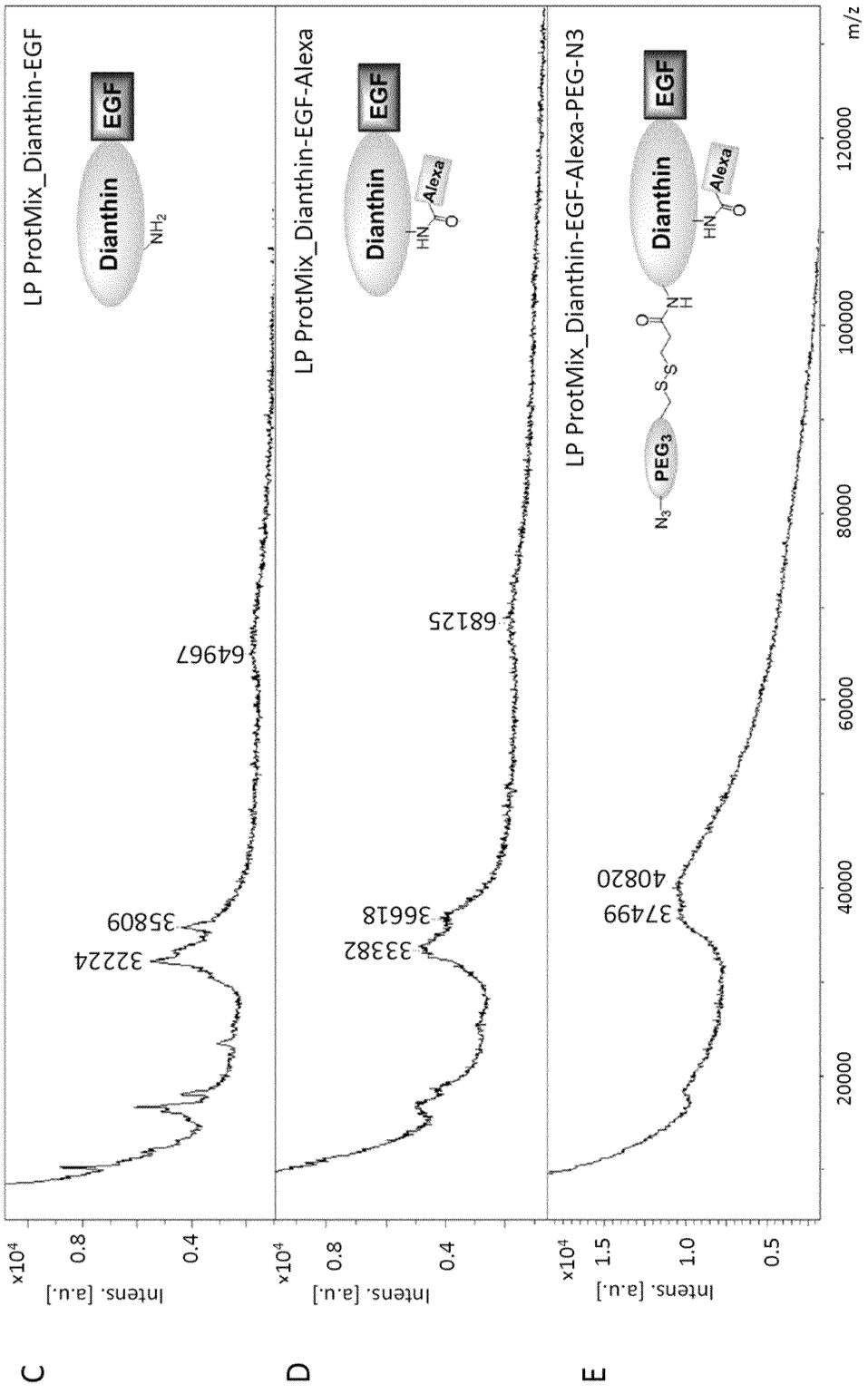

C
D
E
LP ProtMix_Dianthin-EGF
LP ProtMix_Dianthin-EGF-Alexa
LP ProtMix_Dianthin-EGF-Alexa-PEG-N3
EGF
Dianthin
Alexa
PEG3
N3
NH2
HN
O
S
S
64967
35809
32224
68125
36618
33382
40820
37499
Intens. [a.u.]
x10^4
0.4
0.8
0.5
1.0
1.5
20000
40000
60000
80000
100000
120000
m/z

Figure 44

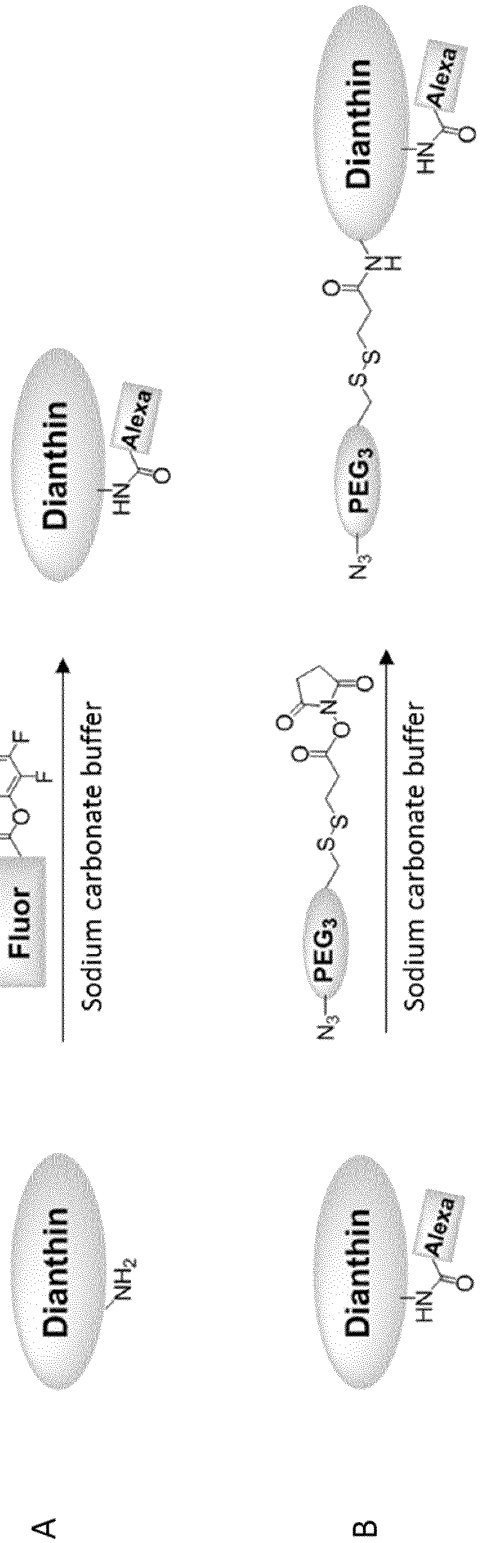

A
Dianthin
NH2
Alexa Fluor
Sodium carbonate buffer
Dianthin
Alexa
HN
B
Dianthin
Alexa
HN
PEG3
N3
Sodium carbonate buffer
Dianthin
Alexa
HN
NH
PEG3
N3

Figure 44

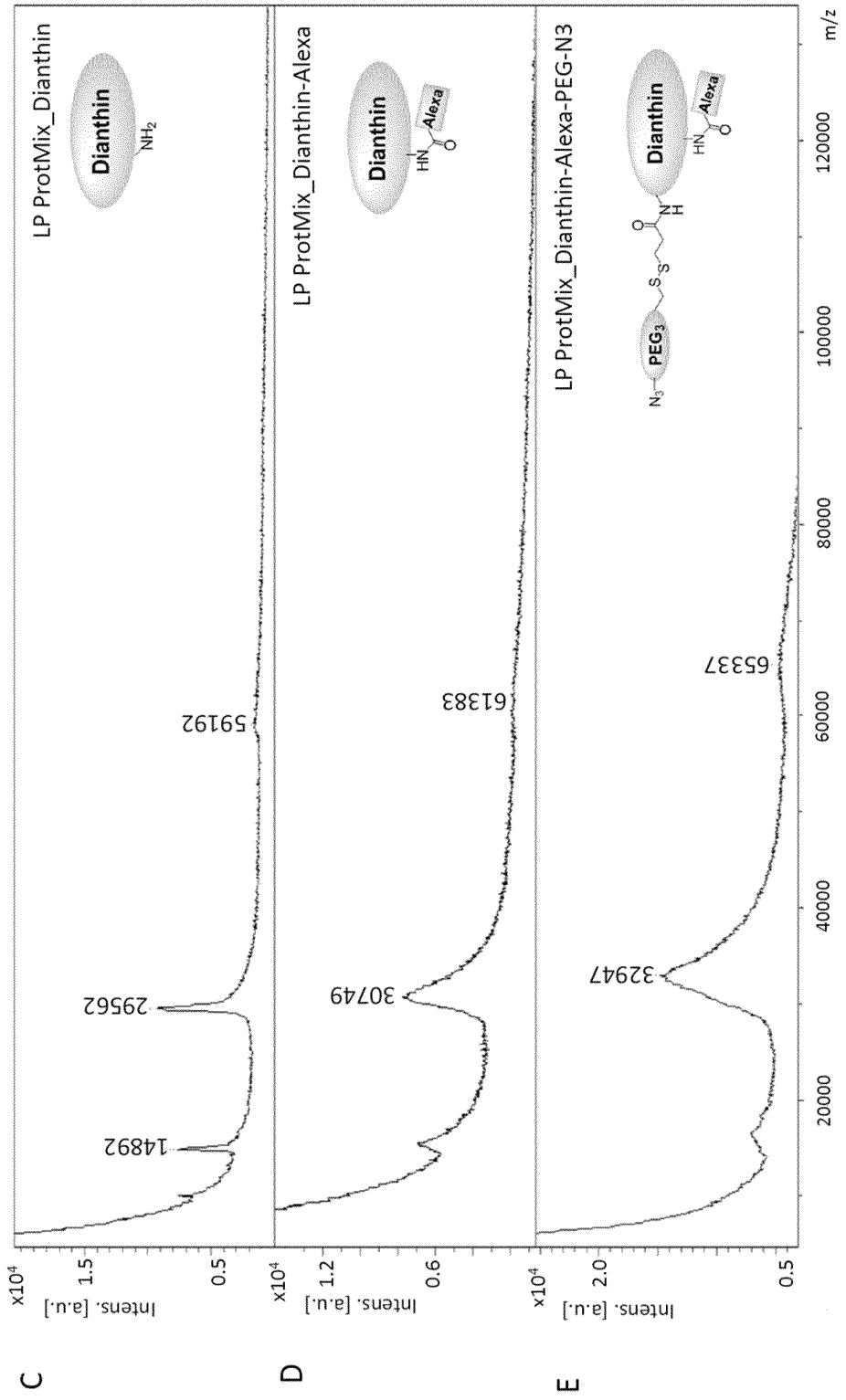

C
LP ProtMix_Dianthin
Dianthin
NH2
14892
29562
59192
Intens. [a.u.]
x10^4
1.5
0.5
D
LP ProtMix_Dianthin-Alexa
Dianthin
Alexa
HN
O
30749
61383
Intens. [a.u.]
x10^4
1.2
0.6
E
LP ProtMix_Dianthin-Alexa-PEG-N3
Dianthin
Alexa
HN
O
N
H
O
S
S
PEG3
N3
32947
65337
Intens. [a.u.]
x10^4
2.0
0.5
20000
40000
60000
80000
100000
120000
m/z

Figure 45

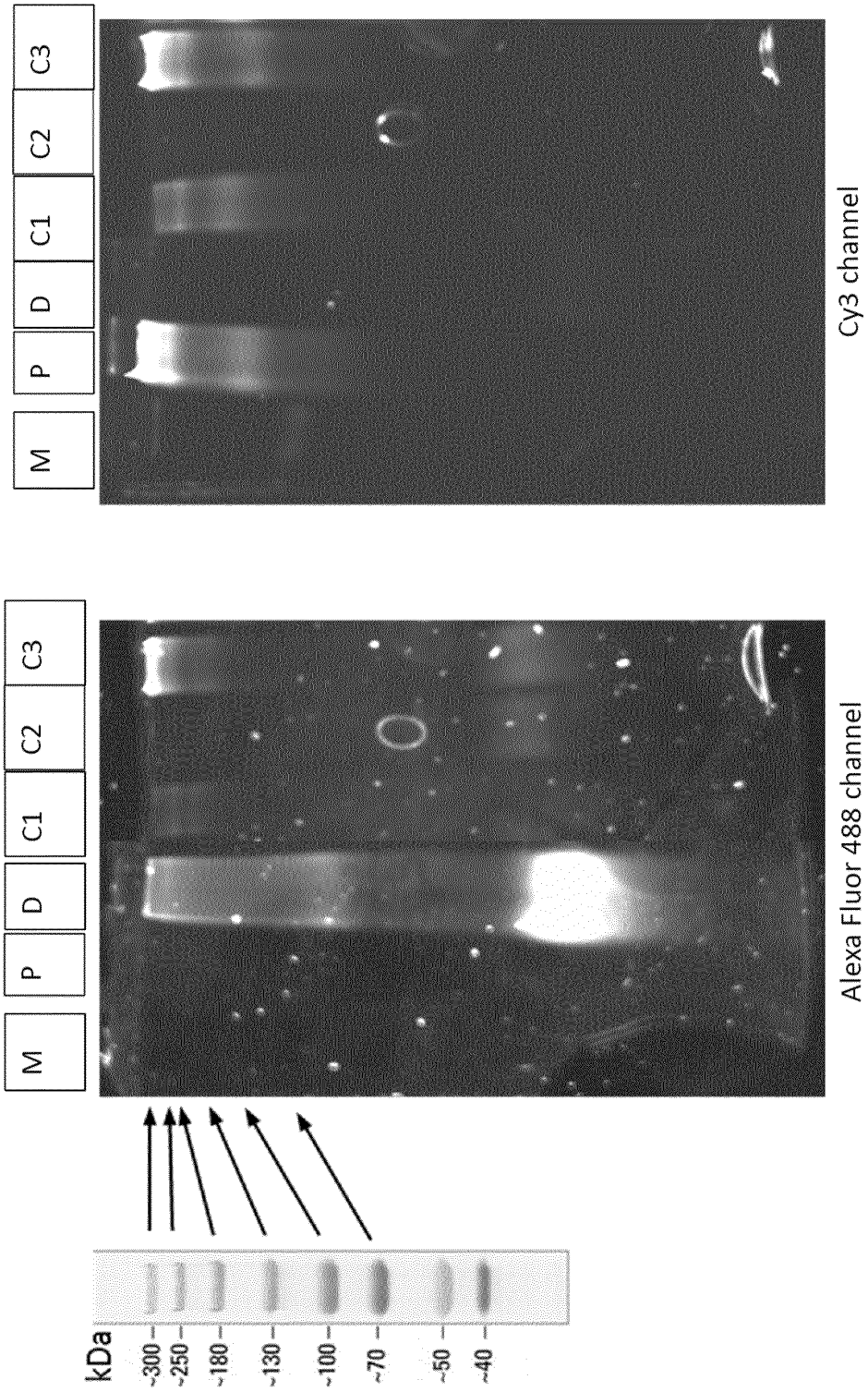

M
P
D
C1
C2
C3
Cy3 channel
M
P
D
C1
C2
C3
Alexa Fluor 488 channel
kDa
~300
~250
~180
~130
~100
~70
~50
~40

Figure 46

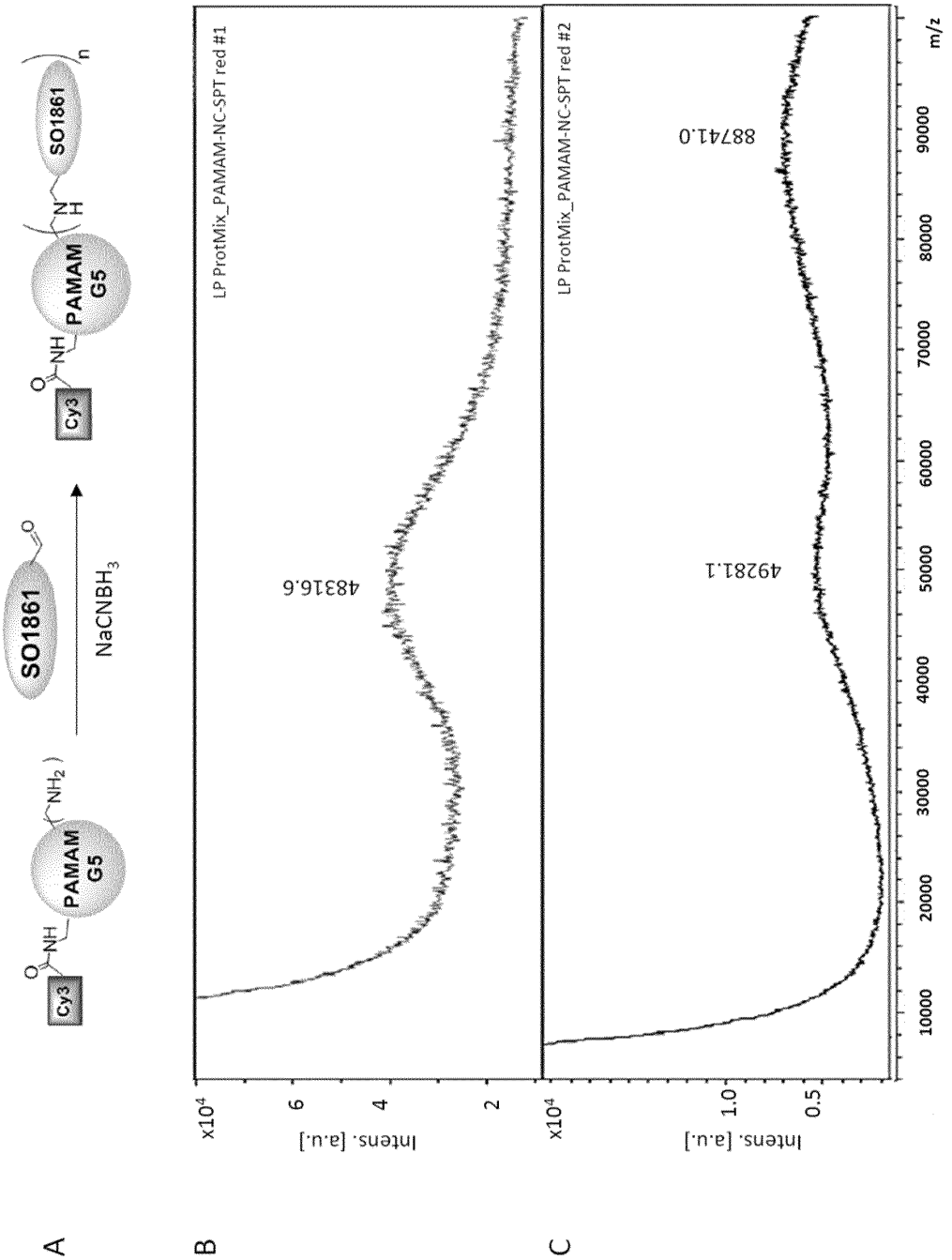

A
B
C
Cy3
PAMAM G5
NH
NH2
SO1861
NaCNBH3
n
LP ProtMix_PAMAM-NC-SPT red #1
48316.6
Intens. [a.u.]
x10^4
LP ProtMix_PAMAM-NC-SPT red #2
49281.1
87741.0
m/z

Figure 47

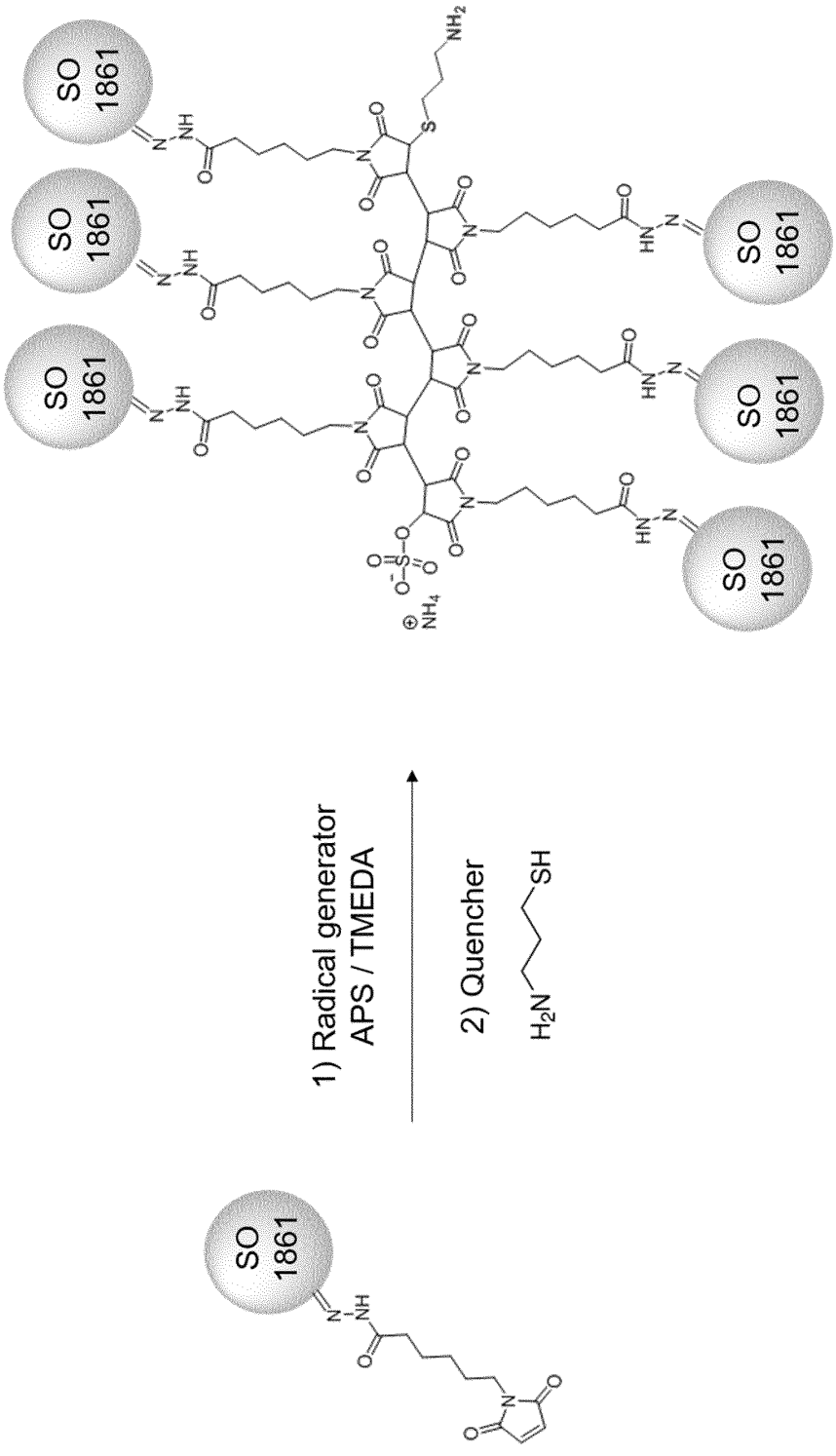


Figure 48

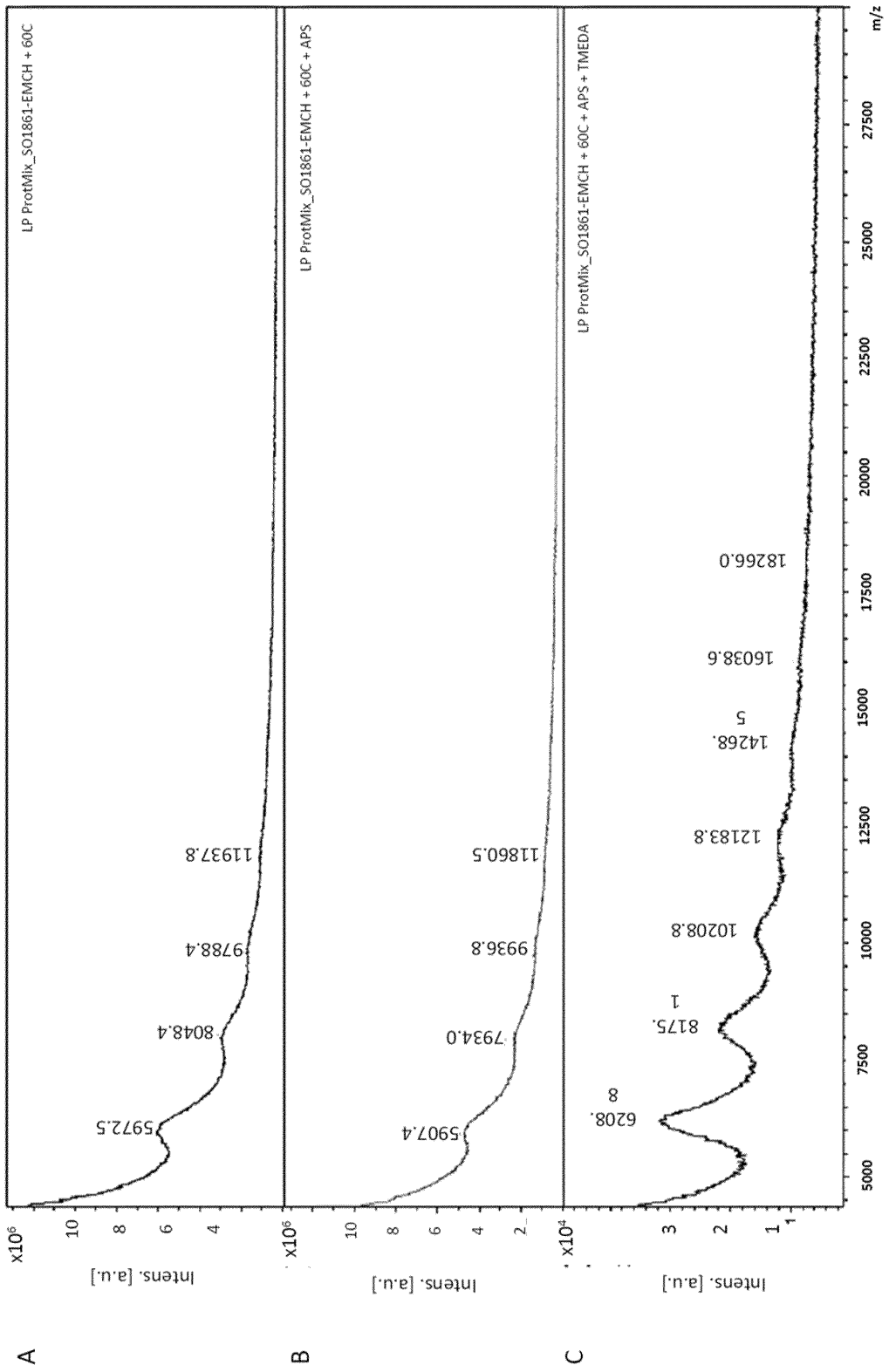

LP ProtMix_SO1861-EMCH + 60C
LP ProtMix_SO1861-EMCH + 60C + APS
LP ProtMix_SO1861-EMCH + 60C + APS + TMEDA
Intens. [a.u.]
m/z
A
B
C
5972.5
8048.4
9788.4
11937.8
5907.4
7934.0
9936.8
11860.5
6208.8
8175.1
10208.8
12183.8
14268.5
16038.6
18266.0

Figure 49

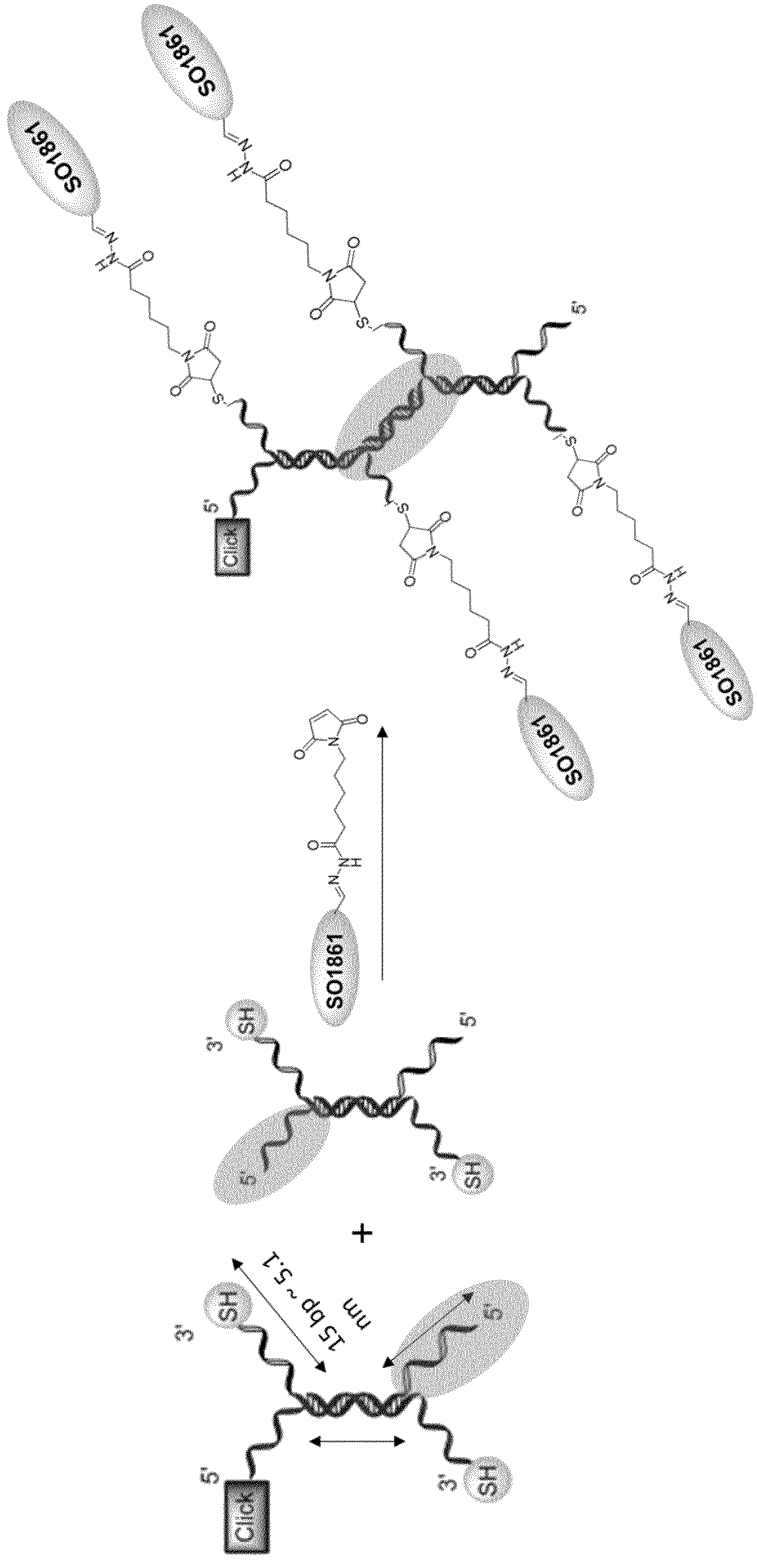

SO1861
SO1861
SO1861
SO1861
SO1861
5'
Click
SO1861
3'
SH
5'
5'
3'
SH
+
3'
SH
15 bp ~ 5,1 nm
5'
5'
Click
3'
SH

Figure 50

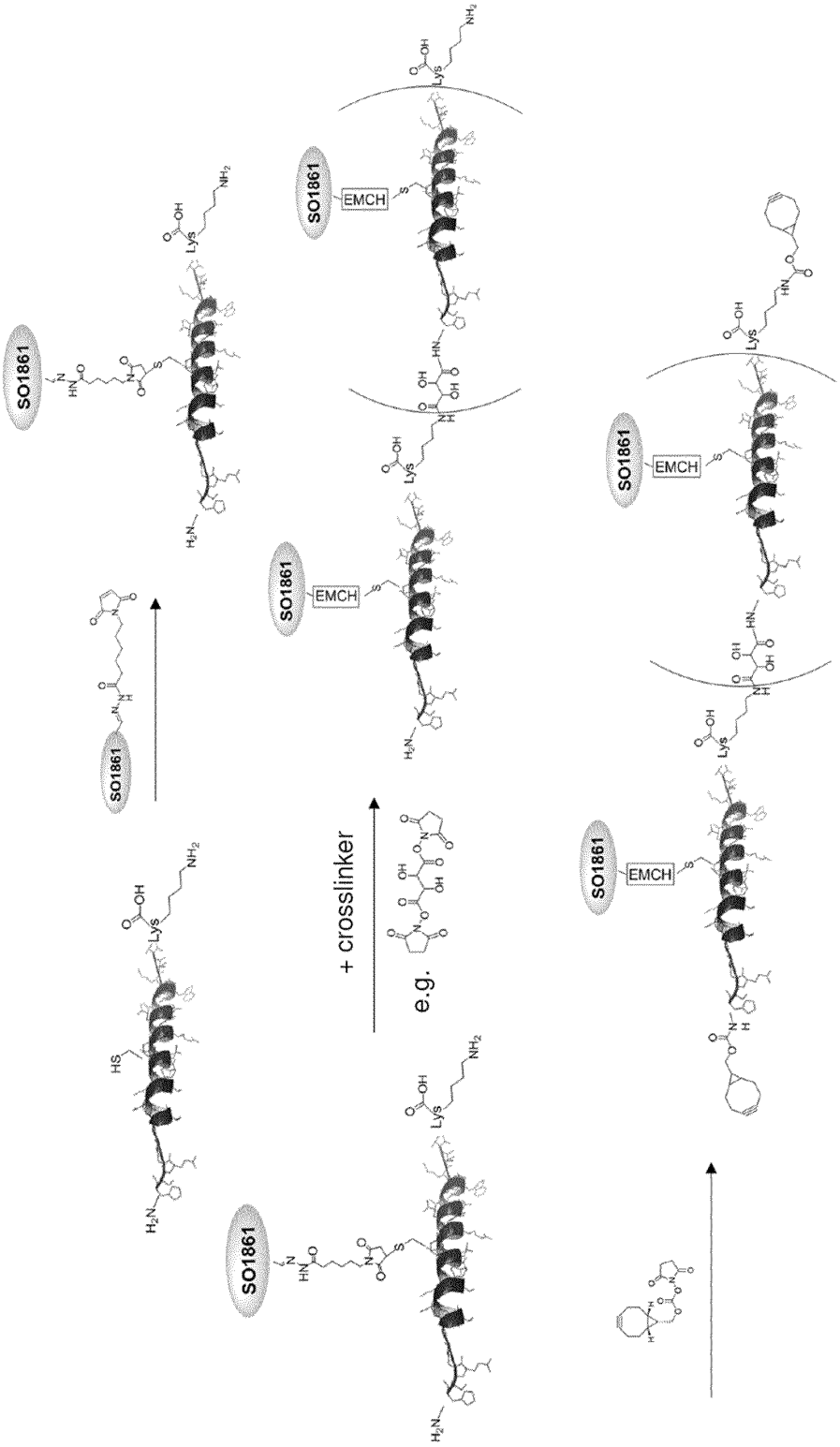


Figure 51

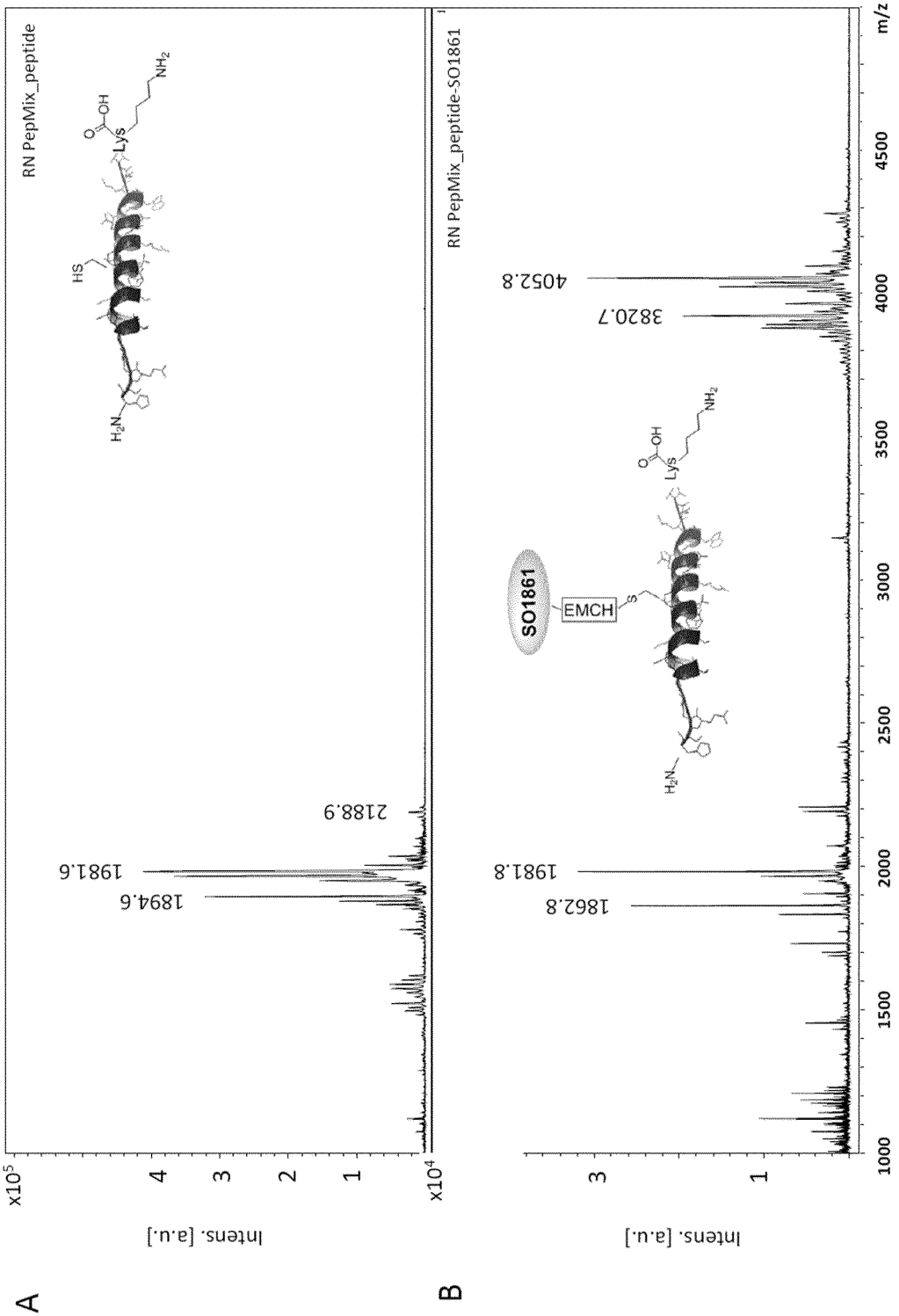

A
RN PepMix_peptide
Intens. [a.u.]
x10^5
4
3
2
1
2188.9
1981.6
1894.6
His
Lys
NH2
OH
O
H2N
B
RN PepMix_peptide-SO1861
Intens. [a.u.]
x10^4
3
1
4052.8
3820.7
1981.8
1862.8
SO1861
EMCH
S
1000
1500
2000
2500
3000
3500
4000
4500
m/z

Figure 52

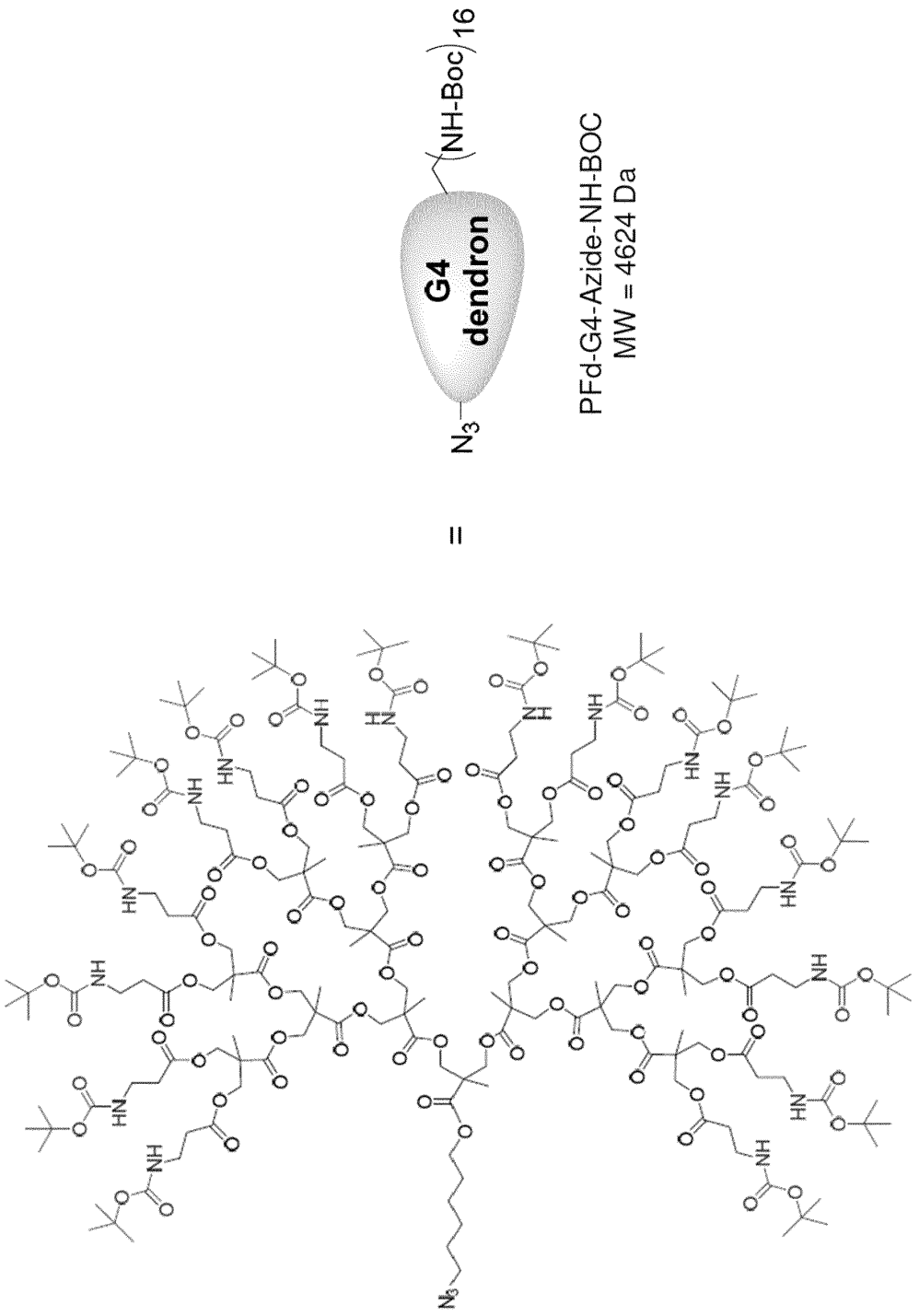


Figure 53

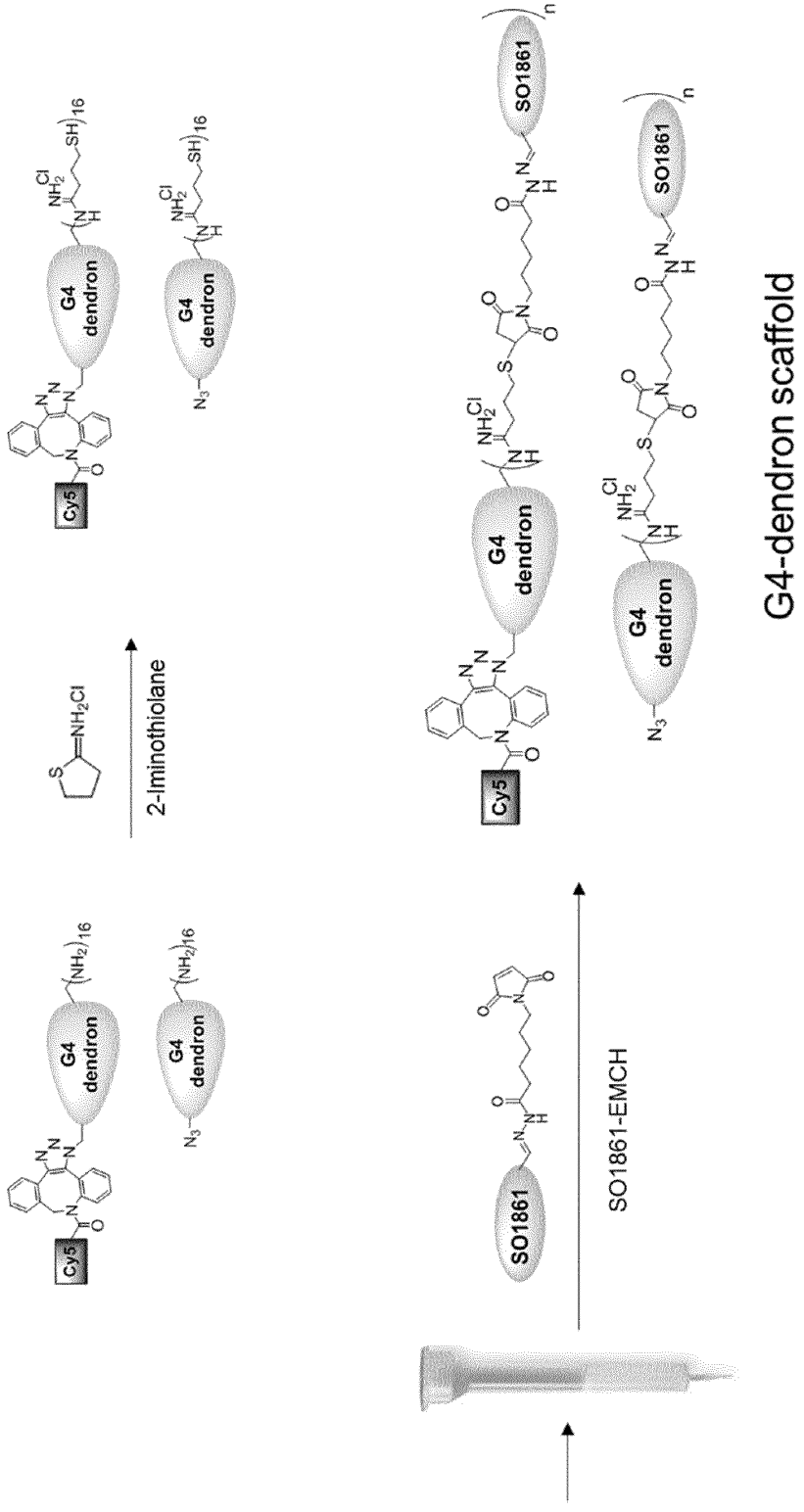

G4 dendron
Cy5
2-Iminothiolane
SO1861
SO1861-EMCH
G4-dendron scaffold

Figure 54

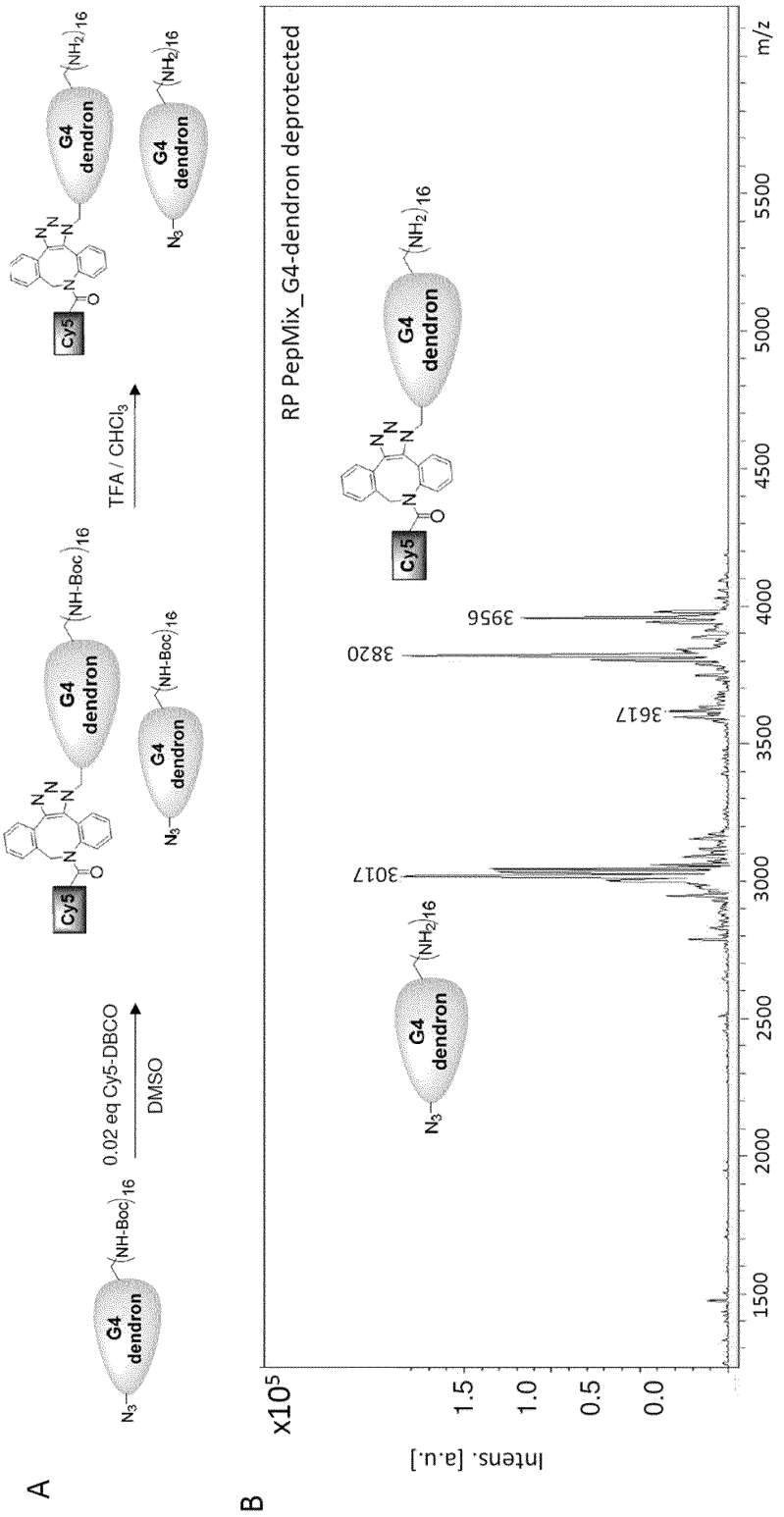

A
B
G4 dendron
(NH-Boc)16
(NH2)16
N3
0.02 eq Cy5-DBCO
DMSO
TFA / CHCl3
Cy5
RP PepMix_G4-dendron deprotected
x10^5
Intens. [a.u.]
m/z
3017
3617
3820
3956

Figure 55

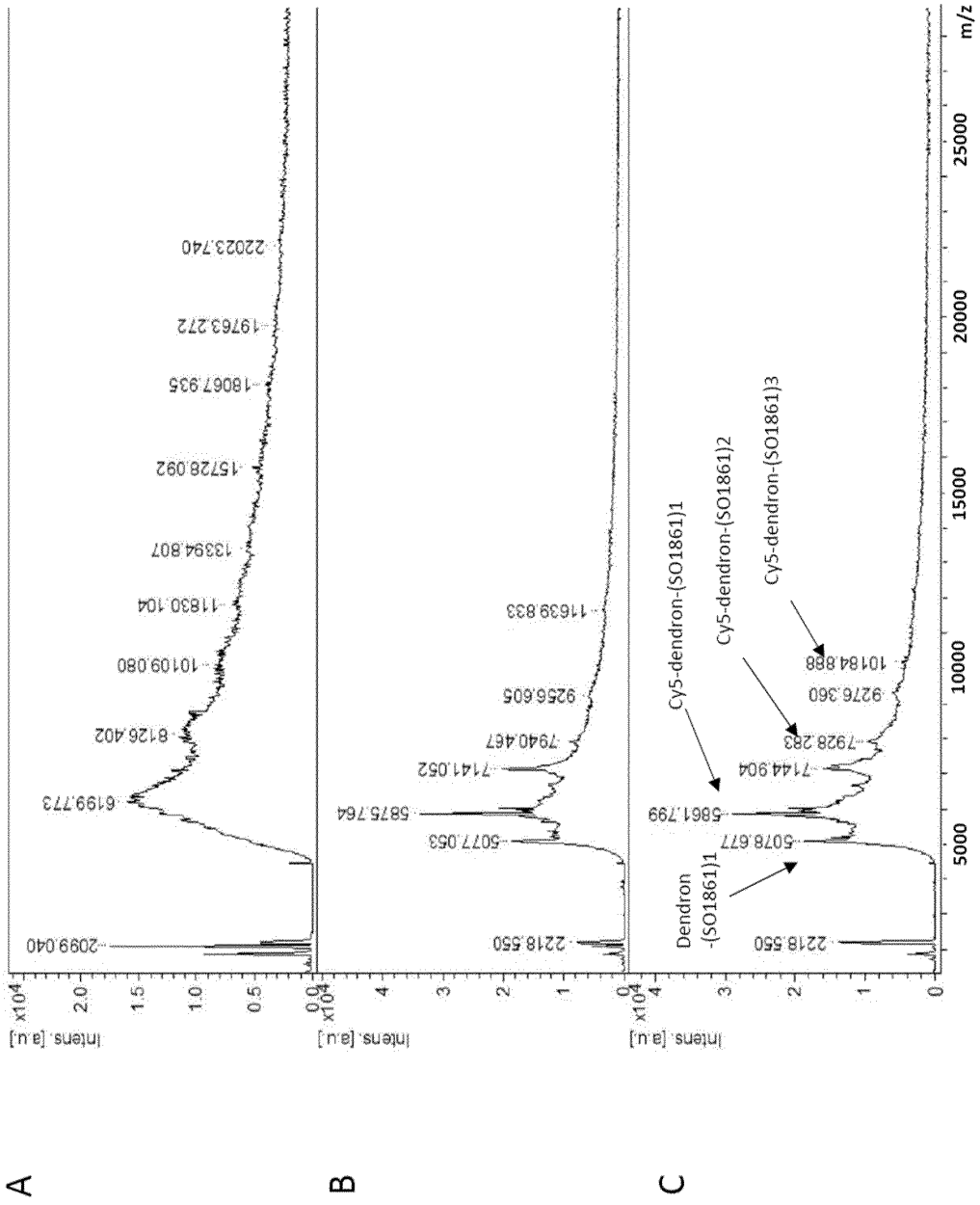

A
B
C
Intens. [a.u.]
x10⁴
m/z
2099.040
6199.773
8126.402
10109.080
11830.104
13394.807
15728.092
18067.935
19763.272
22023.740
2218.550
5077.053
5875.764
7141.052
7940.467
9256.605
11639.833
Dendron -(SO1861)1
Cy5-dendron-(SO1861)1
Cy5-dendron-(SO1861)2
Cy5-dendron-(SO1861)3
5078.677
5861.799
7144.904
7928.283
9276.360
10184.888
0
5000
10000
15000
20000
25000

Figure 56

A

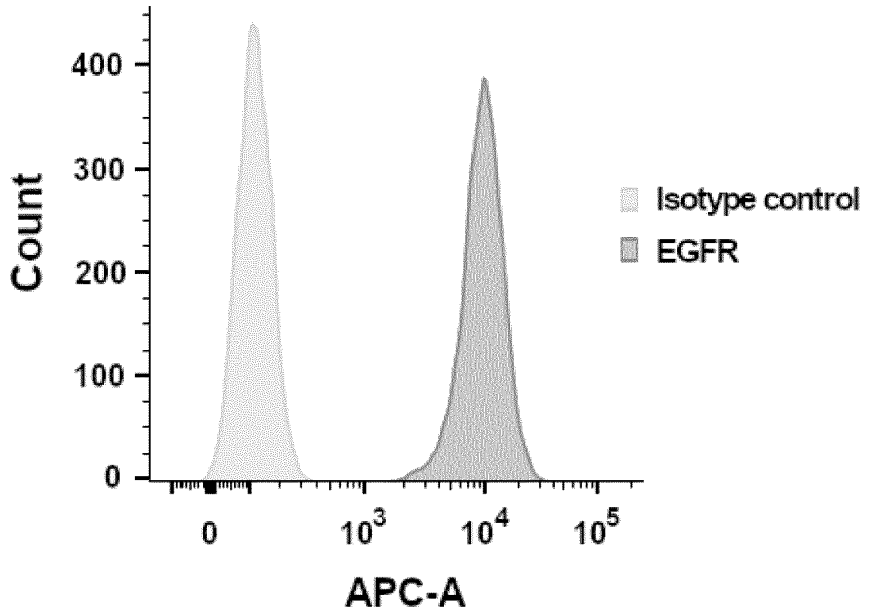


Figure 56

B

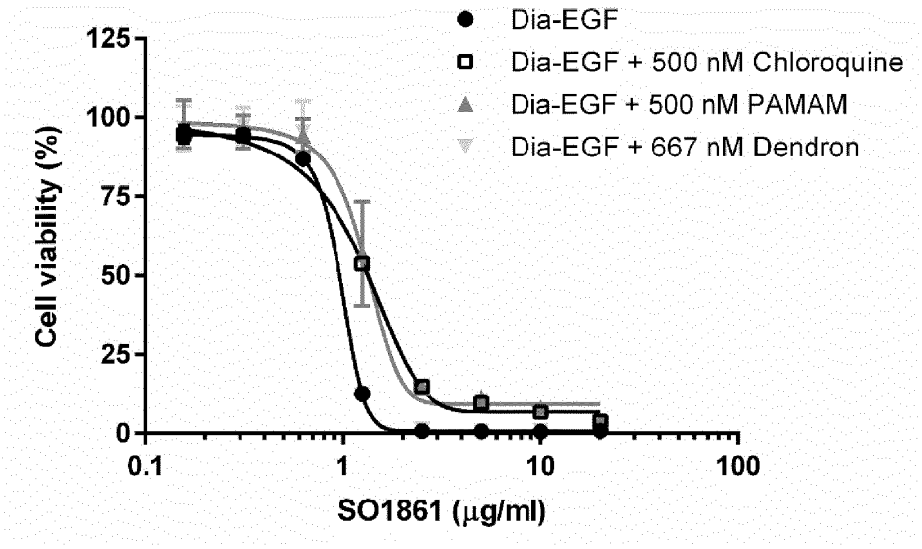


Figure 56

C

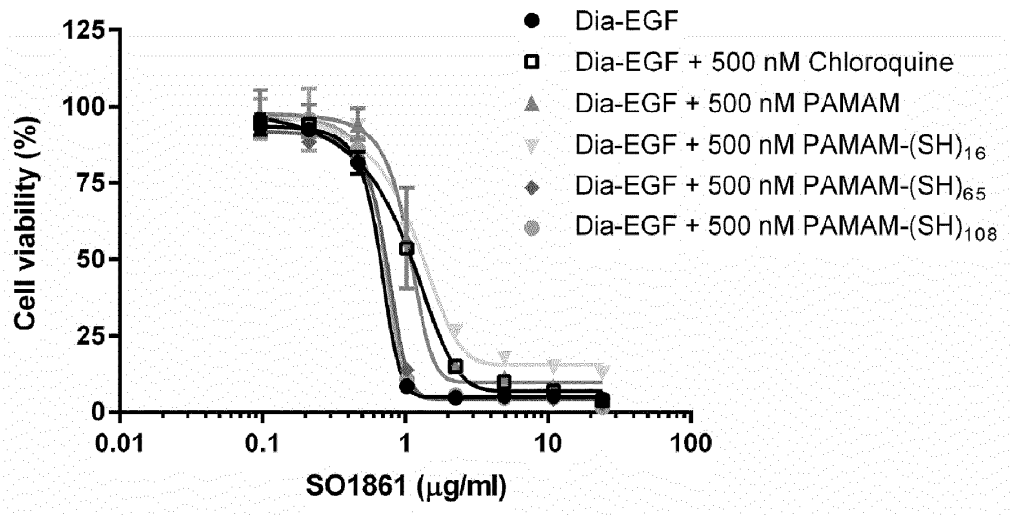


Figure 56

D

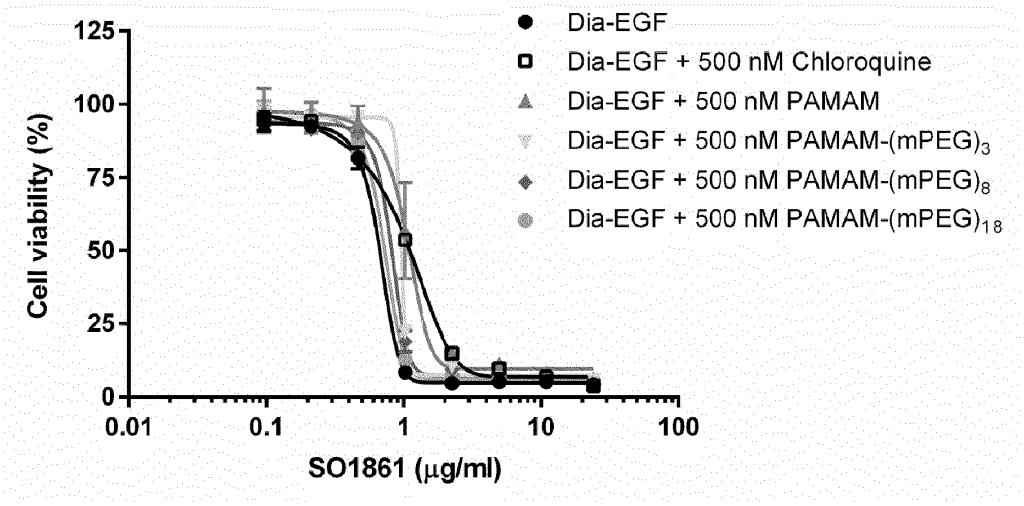


Figure 57

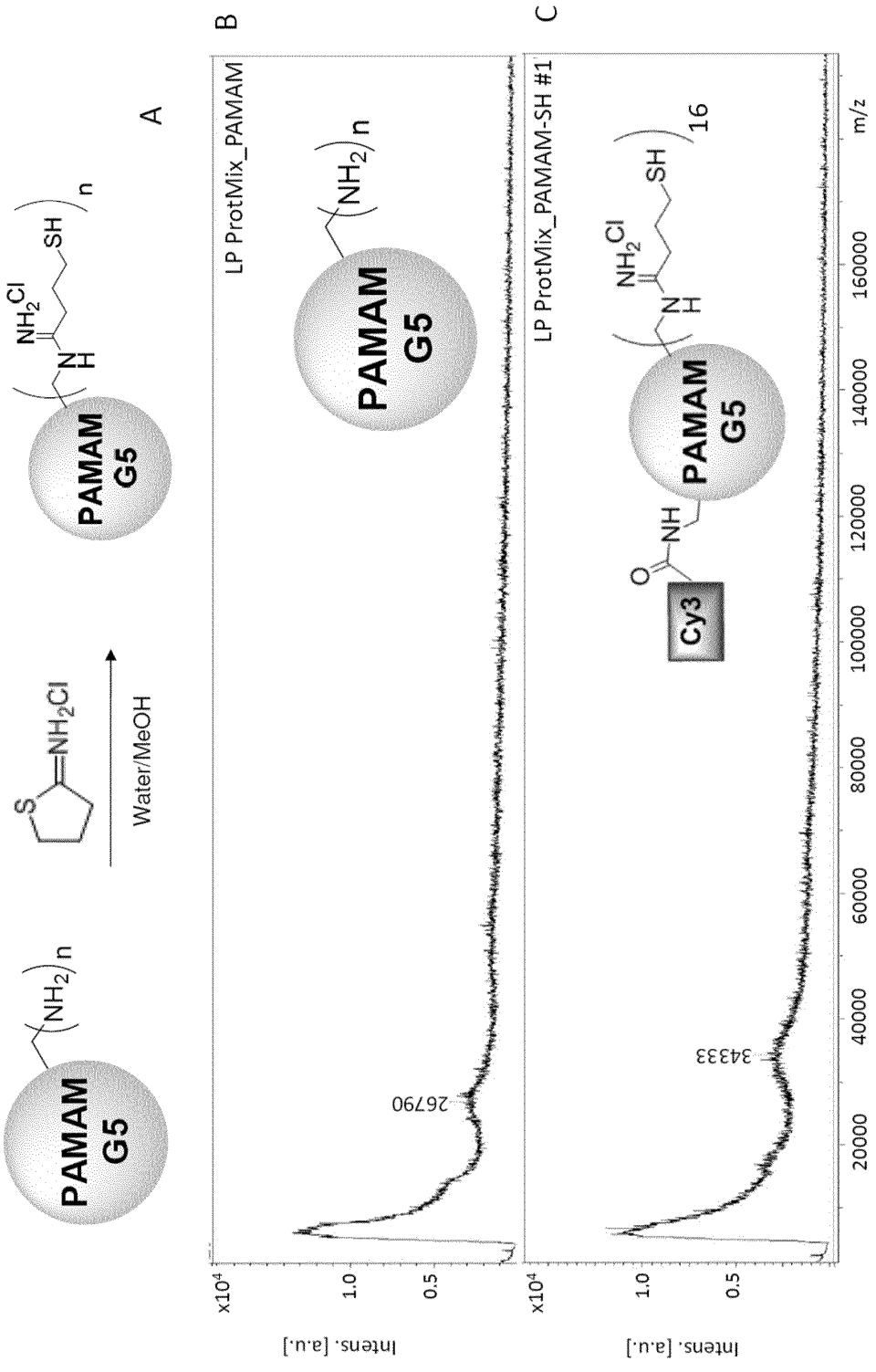

A
PAMAM G5
(NH2)n
Water/MeOH
NH2Cl
S
PAMAM G5
NH2Cl
SH
N
H
n
B
LP ProtMix_PAMAM
PAMAM G5
(NH2)n
26790
x10^4
1.0
0.5
Intens. [a.u.]
C
LP ProtMix_PAMAM-SH #1
PAMAM G5
NH2Cl
SH
16
N
H
NH
O
Cy3
34333
x10^4
1.0
0.5
Intens. [a.u.]
20000
40000
60000
80000
100000
120000
140000
160000
m/z

Figure 57

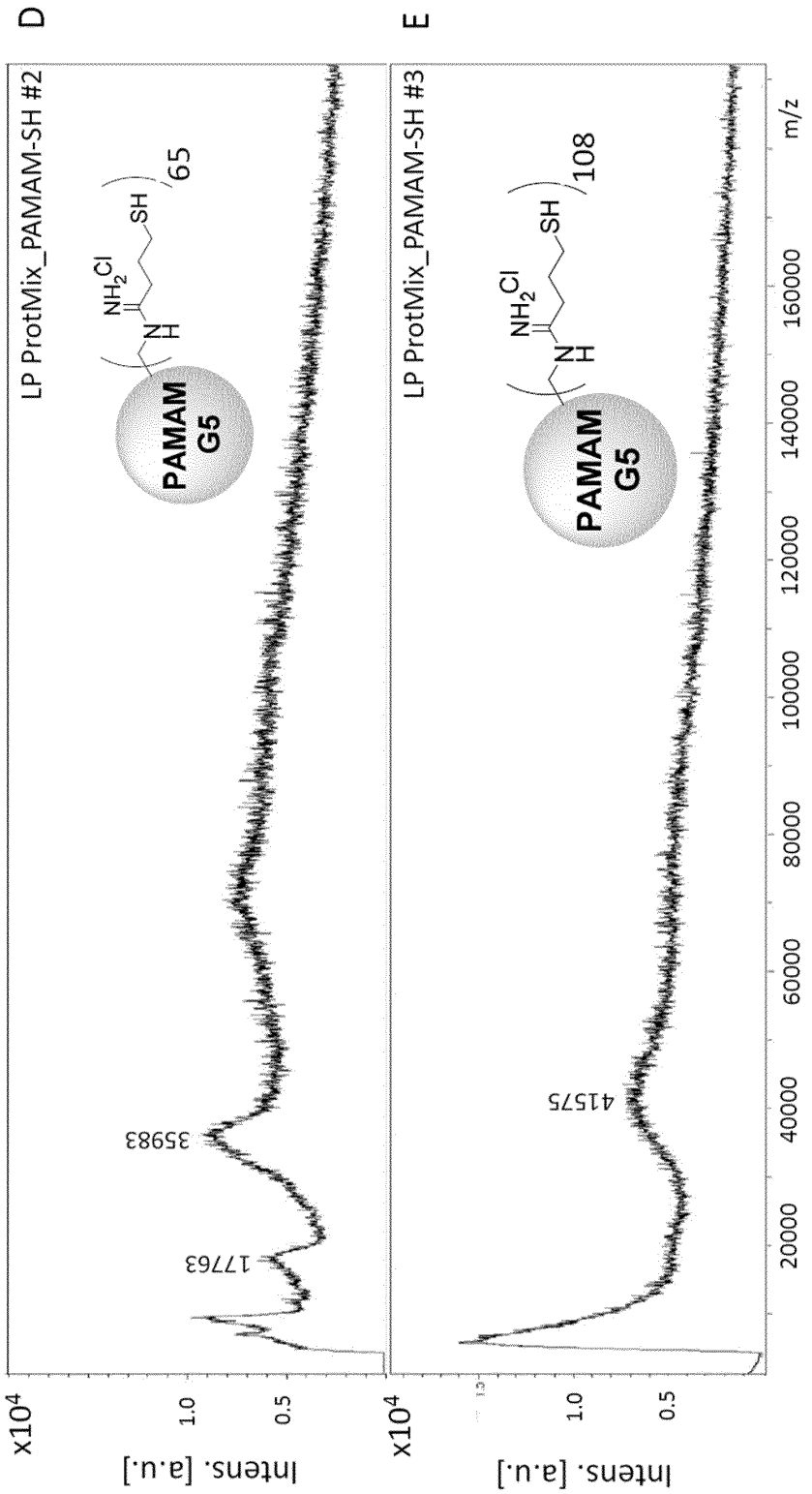

D
LP ProtMix_PAMAM-SH #2
PAMAM G5
65
35983
17763
x10^4
Intens. [a.u.]
E
LP ProtMix_PAMAM-SH #3
PAMAM G5
108
41575
x10^4
Intens. [a.u.]
m/z
20000
40000
60000
80000
100000
120000
140000
160000

Figure 58

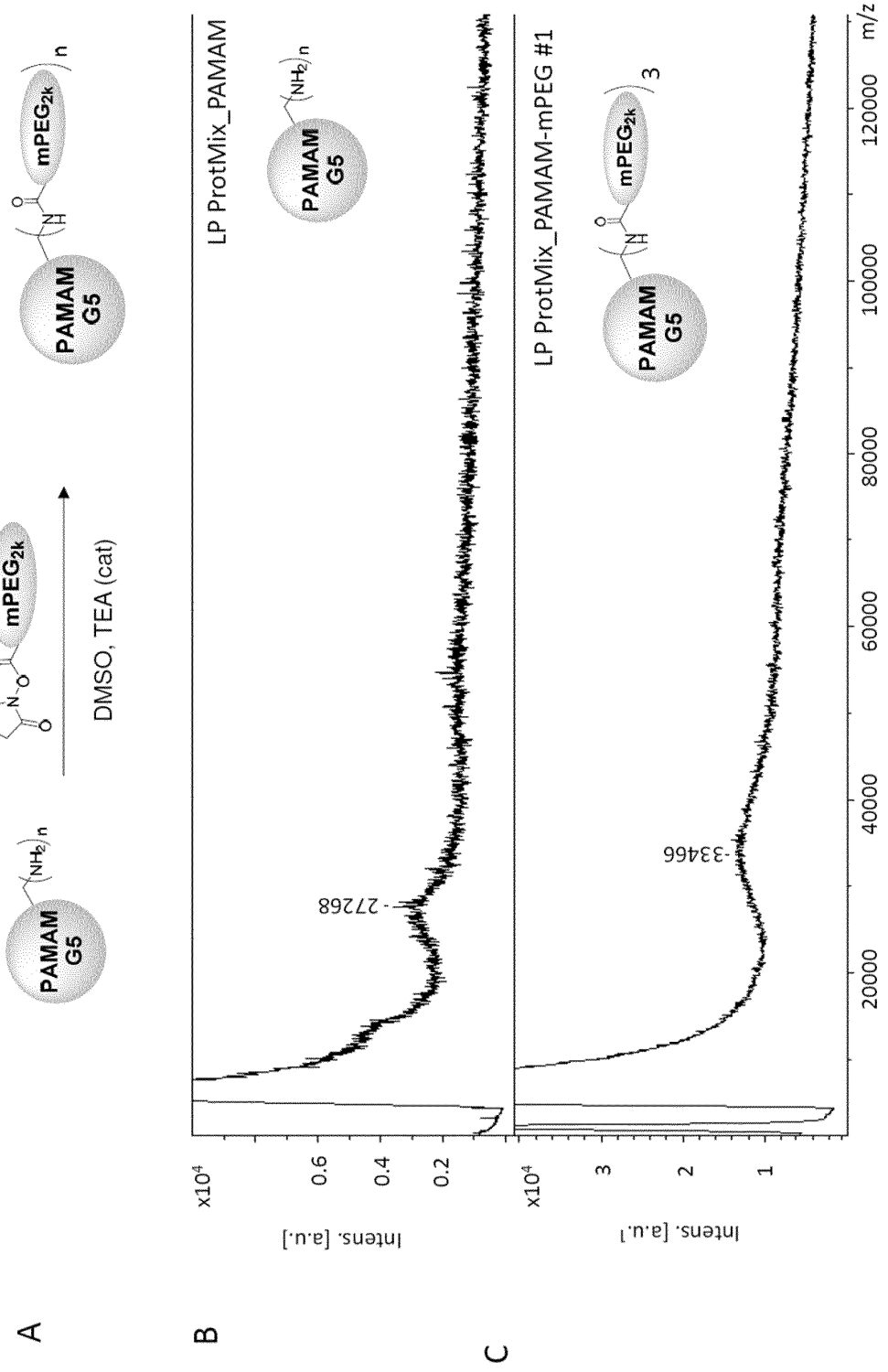

A
PAMAM G5
DMSO, TEA (cat)
mPEG2k
B
LP ProtMix_PAMAM
27268
Intens. [a.u.]
x10^4
C
LP ProtMix_PAMAM-mPEG #1
33466
Intens. [a.u.]
m/z

Figure 58

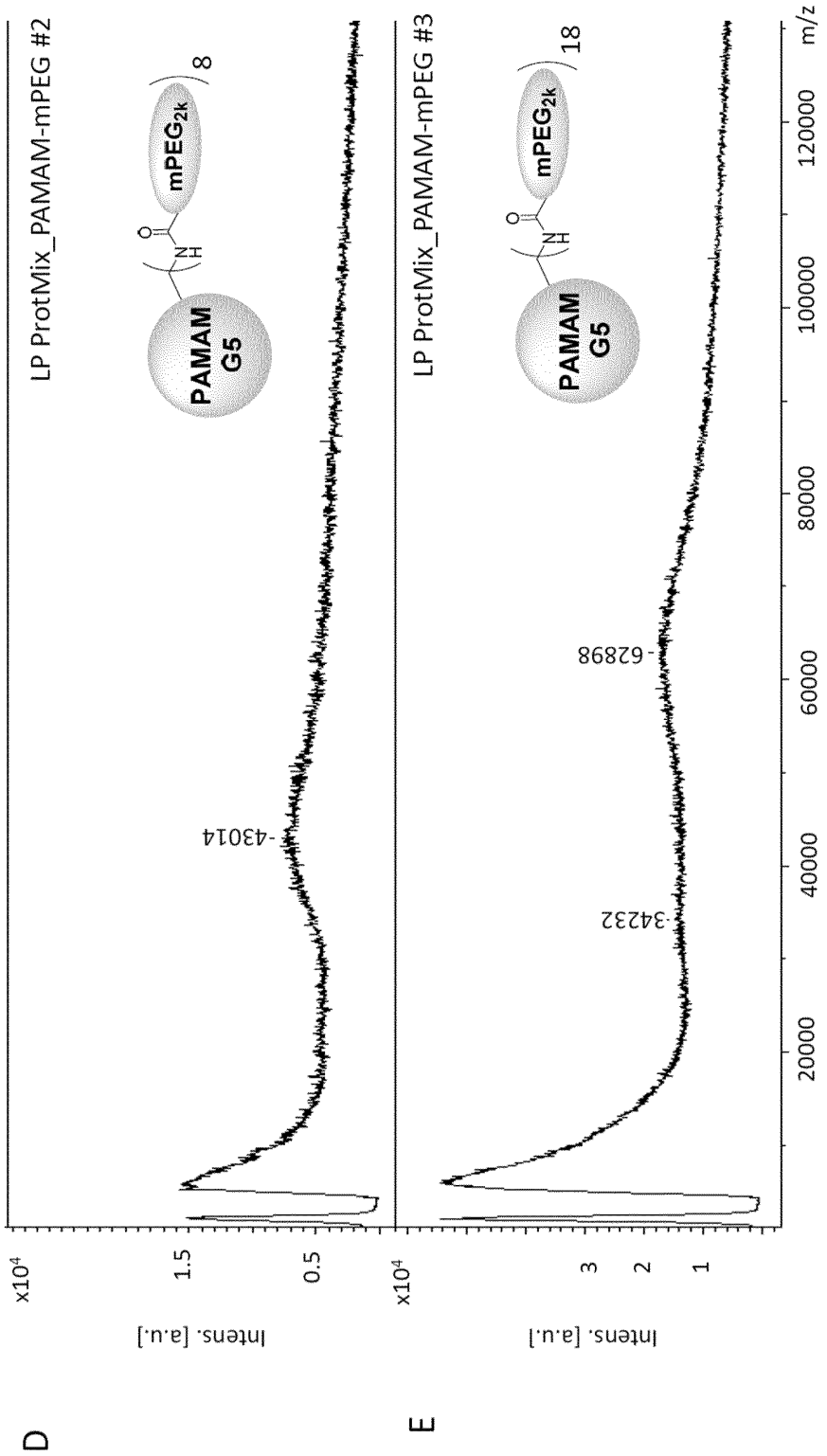

D
LP ProtMix_PAMAM-mPEG #2
PAMAM G5
mPEG2k
8
43014
Intens. [a.u.]
x10^4
1.5
0.5
E
LP ProtMix_PAMAM-mPEG #3
PAMAM G5
mPEG2k
18
62898
34232
Intens. [a.u.]
x10^4
3
2
1
20000
40000
60000
80000
100000
120000
m/z

FIGURE 59

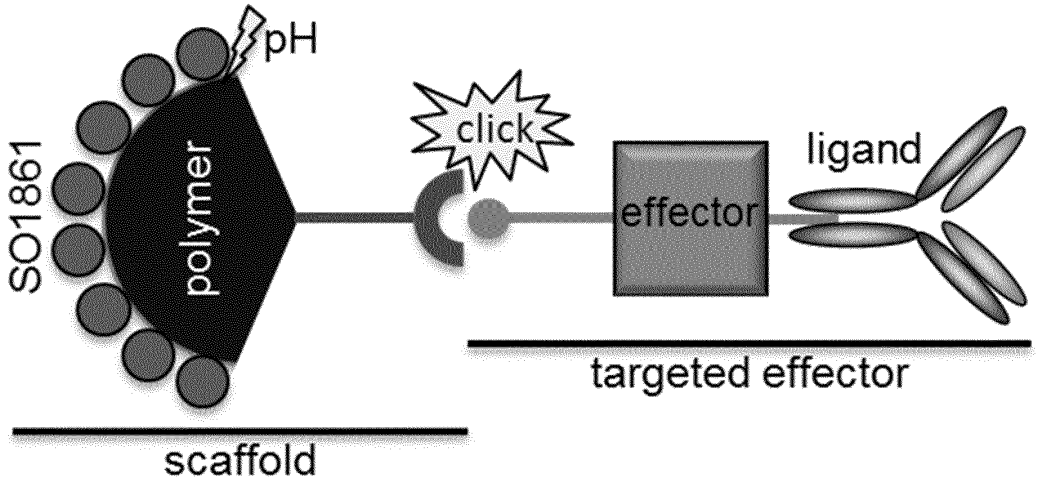


FIGURE 60

