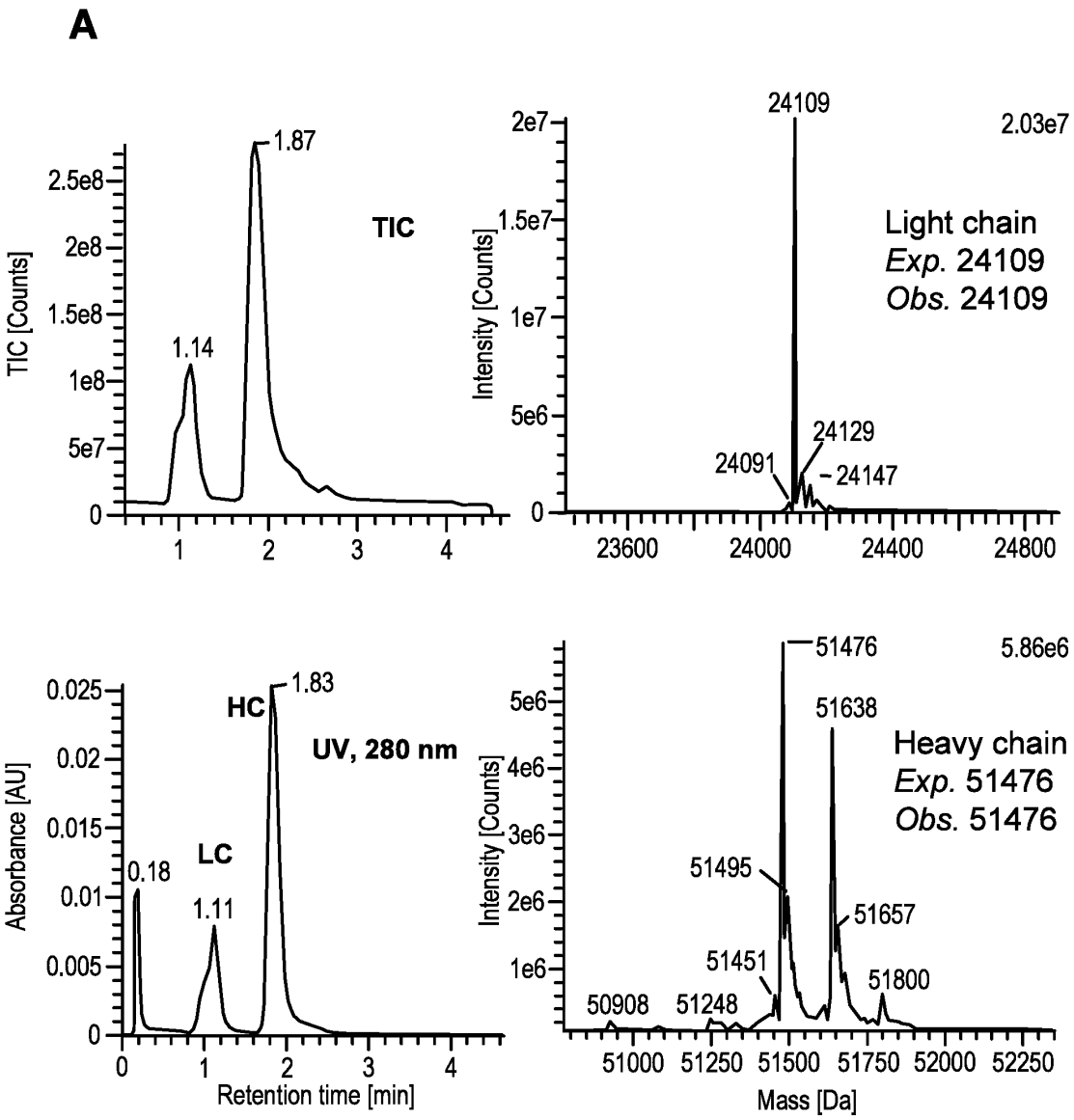

A
TIC
1.87
1.14
TIC [Counts]
2.5e8
2e8
1.5e8
1e8
5e7
0
1
2
3
4
24109
2.03e7
2e7
1.5e7
1e7
5e6
Intensity [Counts]
Light chain
Exp. 24109
Obs. 24109
24129
24091
24147
23600
24000
24400
24800
HC
1.83
UV, 280 nm
LC
0.18
1.11
Absorbance [AU]
0.025
0.02
0.015
0.01
0.005
Retention time [min]
51476
5.86e6
5e6
4e6
3e6
2e6
1e6
51638
Heavy chain
Exp. 51476
Obs. 51476
51495
51657
51451
51800
50908
51248
51000
51250
51500
51750
52000
52250
Mass [Da]

FIG. 1

B

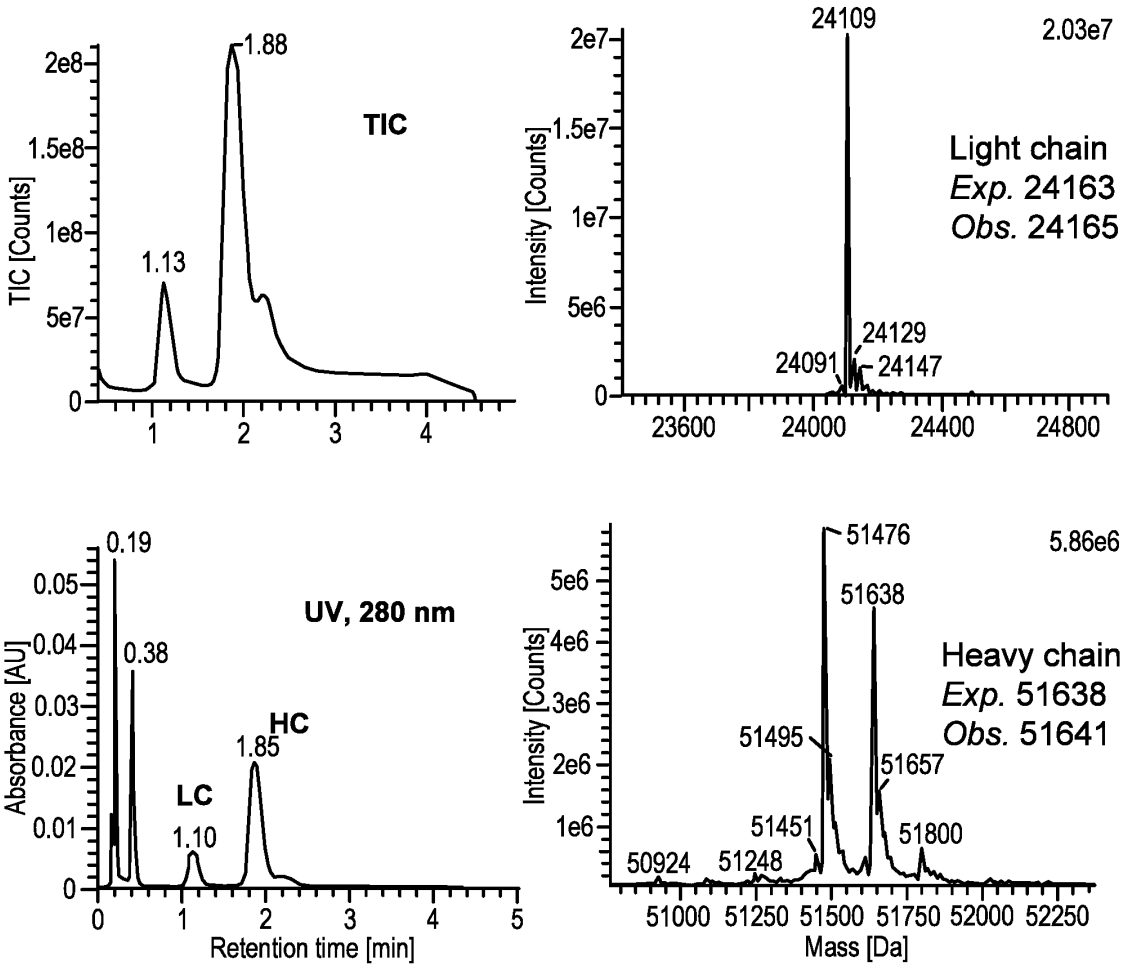

TIC
1.88
1.13
TIC [Counts]
2e8
1.5e8
1e8
5e7
0
1
2
3
4
24109
2.03e7
Light chain
Exp. 24163
Obs. 24165
Intensity [Counts]
2e7
1.5e7
1e7
5e6
24129
24091
24147
23600
24000
24400
24800
UV, 280 nm
0.19
0.38
HC
1.85
LC
1.10
Absorbance [AU]
0.05
0.04
0.03
0.02
0.01
Retention time [min]
51476
5.86e6
51638
Heavy chain
Exp. 51638
Obs. 51641
51495
51657
51451
51800
50924
51248
5e6
4e6
3e6
2e6
1e6
51000
51250
51500
51750
52000
52250
Mass [Da]

FIG. 1

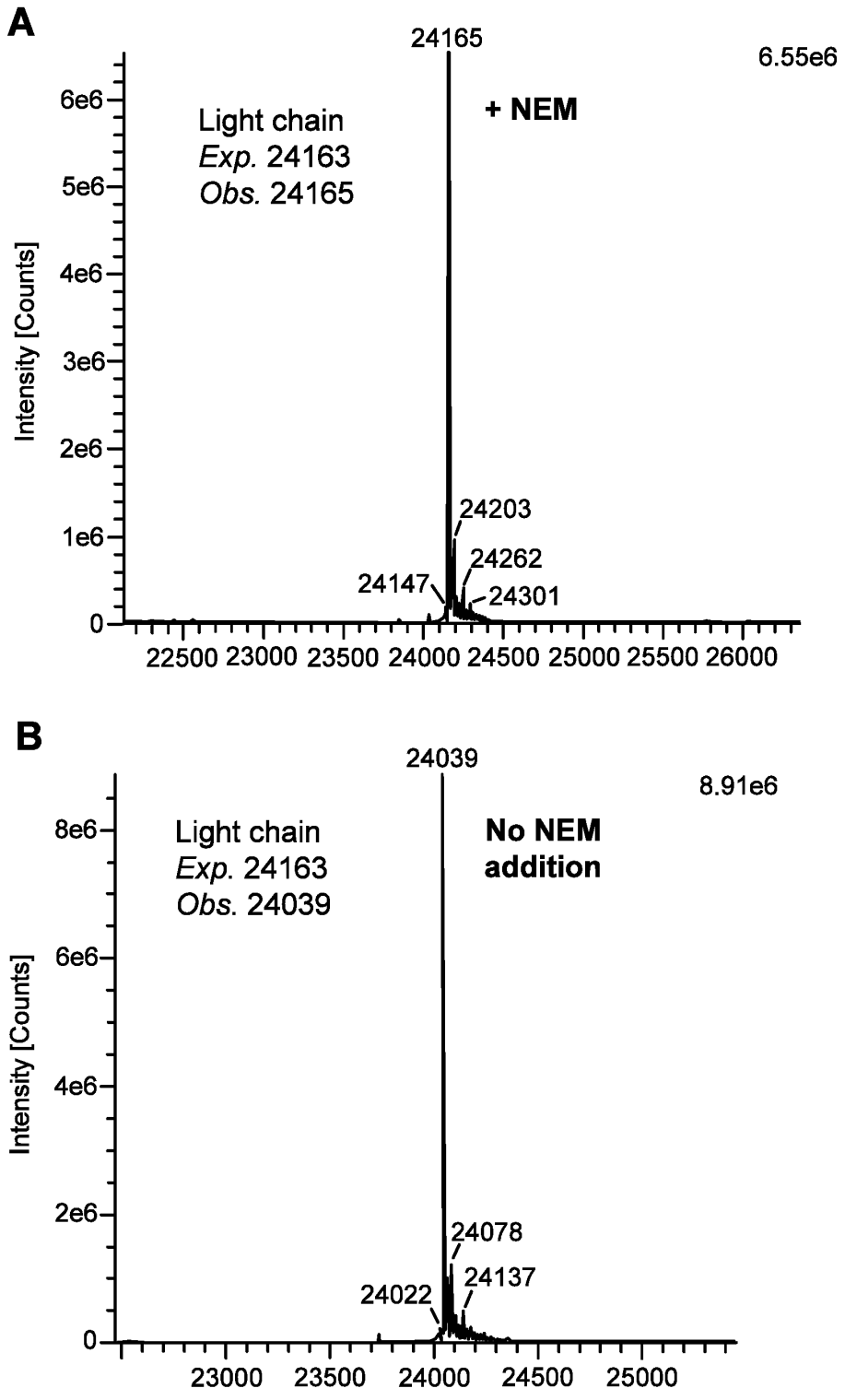

A
24165
6.55e6
+ NEM
Light chain
Exp. 24163
Obs. 24165
Intensity [Counts]
6e6
5e6
4e6
3e6
2e6
1e6
0
24203
24262
24147
24301
22500 23000 23500 24000 24500 25000 25500 26000
B
24039
8.91e6
No NEM addition
Light chain
Exp. 24163
Obs. 24039
Intensity [Counts]
8e6
6e6
4e6
2e6
0
24078
24137
24022
23000 23500 24000 24500 25000

FIG. 2

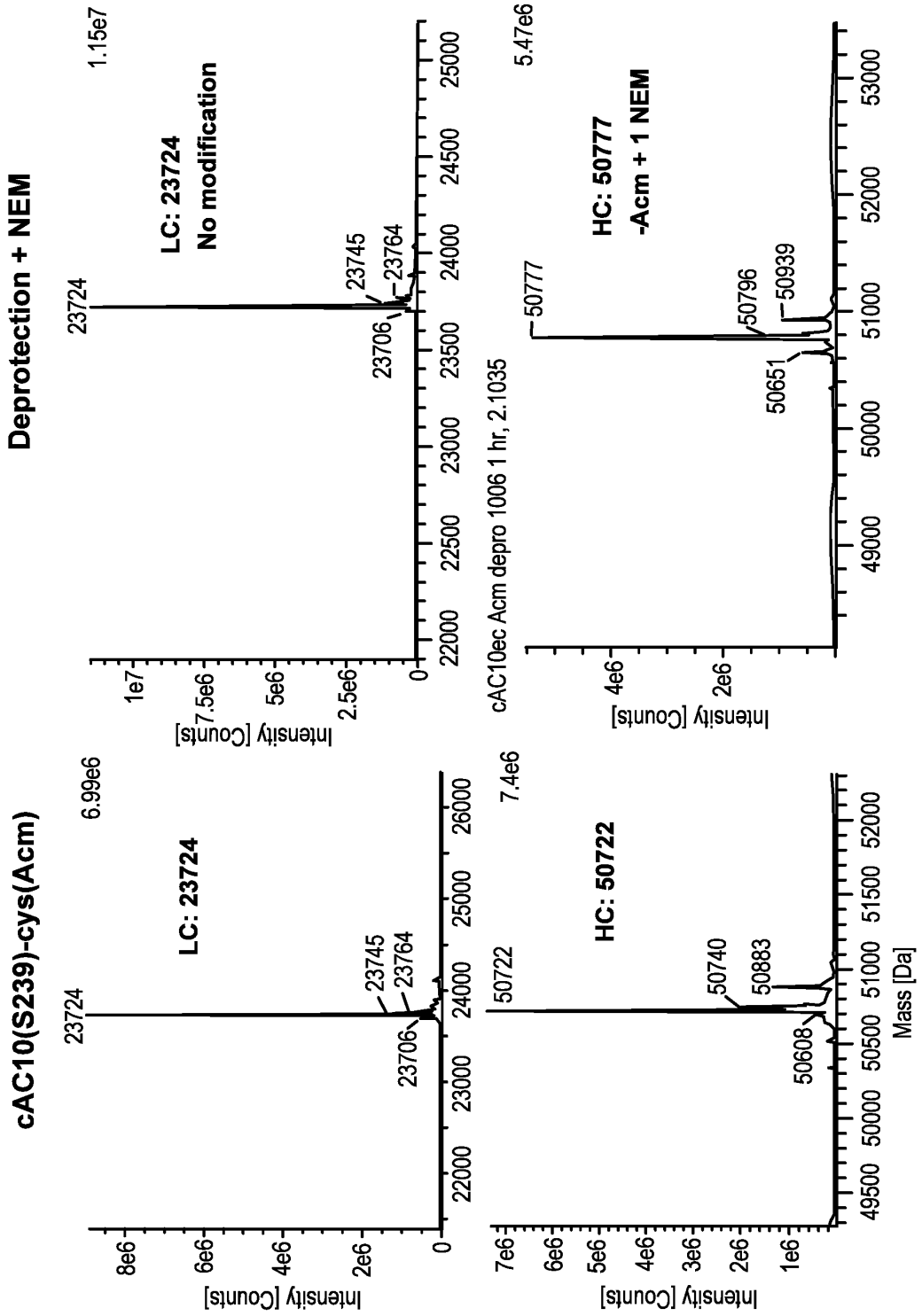

Deprotection + NEM
LC: 23724
No modification
23724
23745
23764
23706
1.15e7
1e7
7.5e6
5e6
2.5e6
0
Intensity [Counts]
22000
22500
23000
23500
24000
24500
25000
cAC10ec Acm depro 1006 1 hr, 2.1035
HC: 50777
-Acm + 1 NEM
50777
50796
50939
50651
5.47e6
4e6
2e6
49000
50000
51000
52000
53000
cAC10(S239)-cys(Acm)
LC: 23724
23724
23745
23764
23706
6.99e6
8e6
6e6
4e6
2e6
0
22000
23000
24000
25000
26000
HC: 50722
50722
50740
50883
50608
7.4e6
7e6
6e6
5e6
4e6
3e6
2e6
1e6
49500
50000
50500
51000
51500
52000
Mass [Da]

FIG. 3

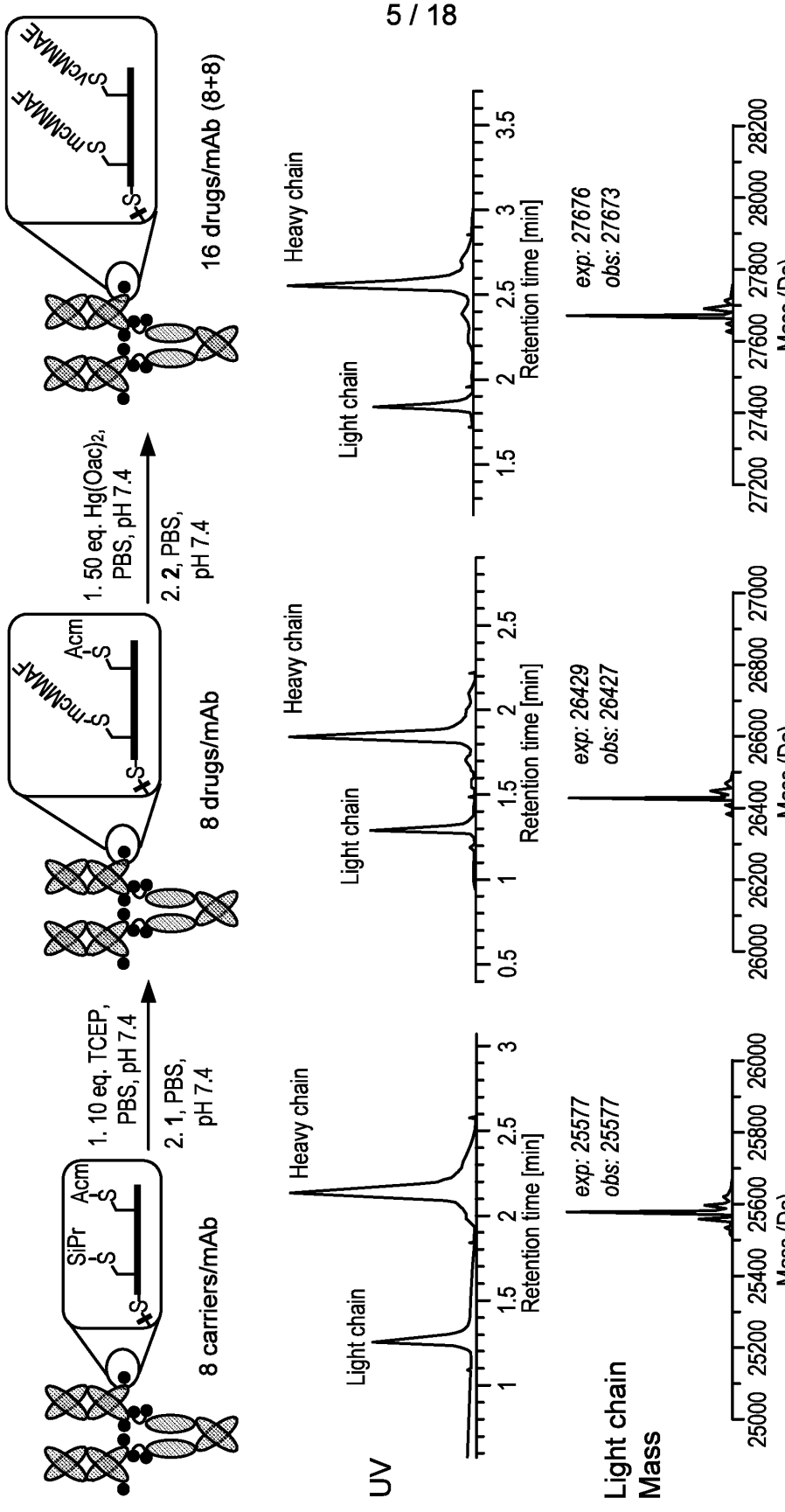

SiPr
Acm
1. 10 eq. TCEP, PBS, pH 7.4
2. 1, PBS, pH 7.4
8 carriers/mAb
Acm
mcMMAF
1. 50 eq. Hg(Oac)2, PBS, pH 7.4
2. 2, PBS, pH 7.4
8 drugs/mAb
mcMMAF
vcMMAE
16 drugs/mAb (8+8)
UV
Light chain
Heavy chain
Retention time [min]
Light Mass
exp: 25577
obs: 25577
exp: 26429
obs: 26427
exp: 27676
obs: 27673
Mass (Da)

FIG. 4

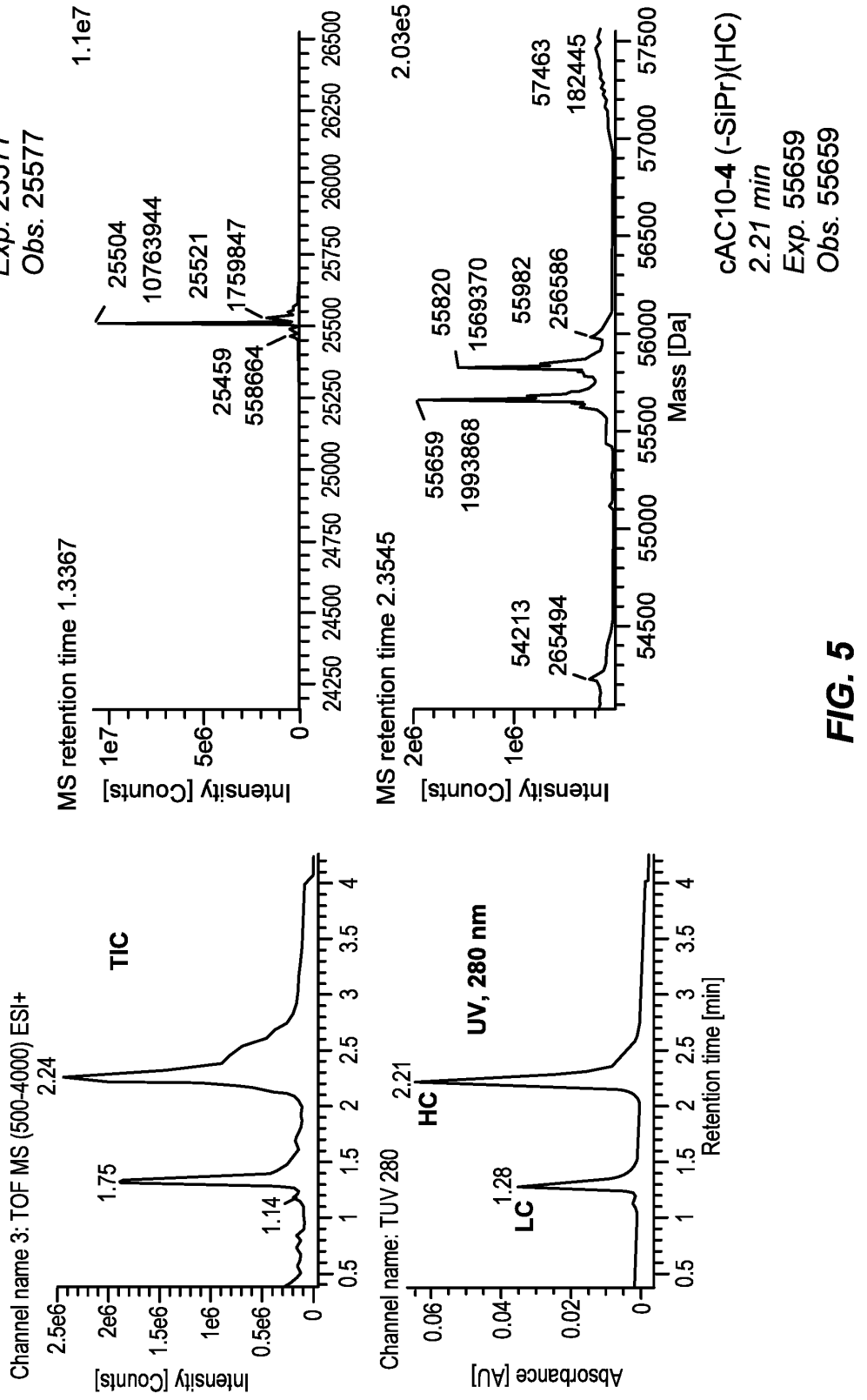
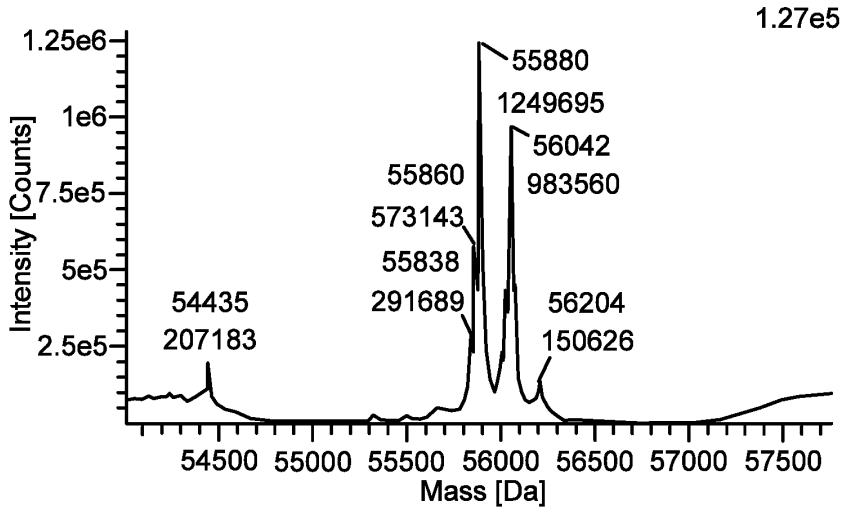

cAC10-4 (-SiPr)(LC)
1.28 min
Exp. 25577
Obs. 25577
MS retention time 1.3367
Intensity [Counts]
1.1e7
1e7
5e6
0
25504
10763944
25521
1759847
25459
558664
24250 24500 24750 25000 25250 25500 25750 26000 26250 26500
Channel name 3: TOF MS (500-4000) ESI+
TIC
Intensity [Counts]
2.5e6
2e6
1.5e6
1e6
0.5e6
0
2.24
1.75
1.14
0.5 1 1.5 2 2.5 3 3.5 4
Channel name: TUV 280
UV, 280 nm
Absorbance [AU]
0.06
0.04
0.02
0
2.21
HC
1.28
LC
0.5 1 1.5 2 2.5 3 3.5 4
Retention time [min]
MS retention time 2.3545
Intensity [Counts]
2.03e5
2e6
1e6
55659
1993868
55820
1569370
55982
256586
57463
182445
54213
265494
54500 55000 55500 56000 56500 57000 57500
Mass [Da]
cAC10-4 (-SiPr)(HC)
2.21 min
Exp. 55659
Obs. 55659

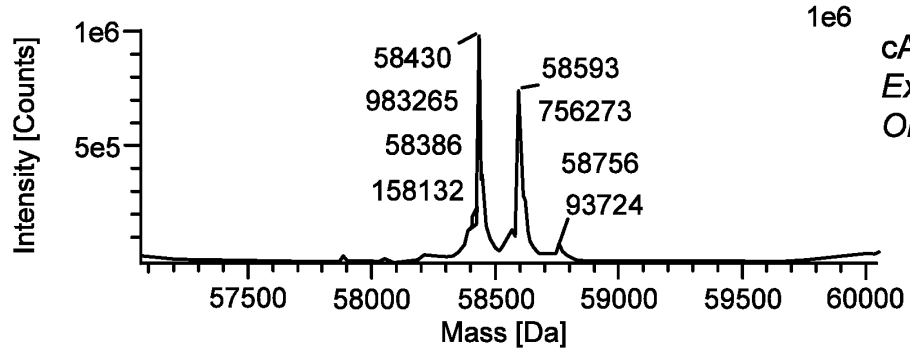
FIG. 5

MS retention time 2.4052



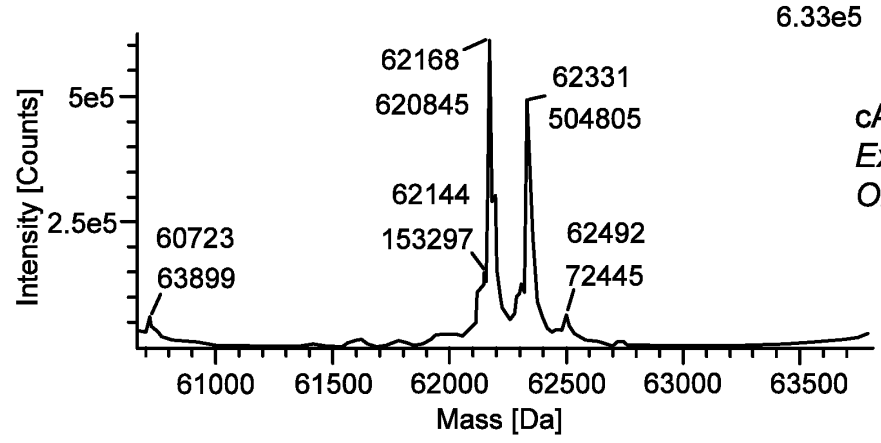
cAC10-**4** (HC)
Exp. 55880
Obs. 55880

MS retention time 1.8918



cAC10-**4-1** (HC)
Exp. 58433
Obs. 58430

MS retention time 2.6052



cAC10-**4-1-3** (HC)
Exp. 62171
Obs. 62168

FIG. 6

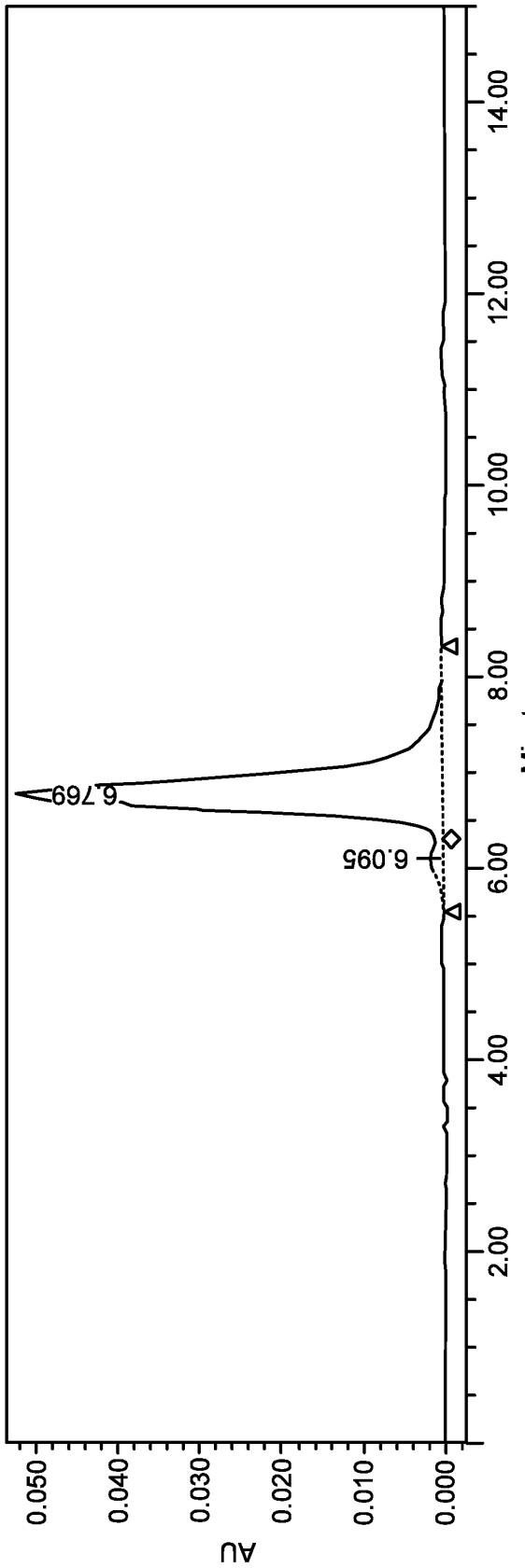

6.769
6.095
0.050
0.040
0.030
0.020
0.010
0.000
AU
2.00
4.00
6.00
8.00
10.00
12.00
14.00
Minutes

FIG. 7

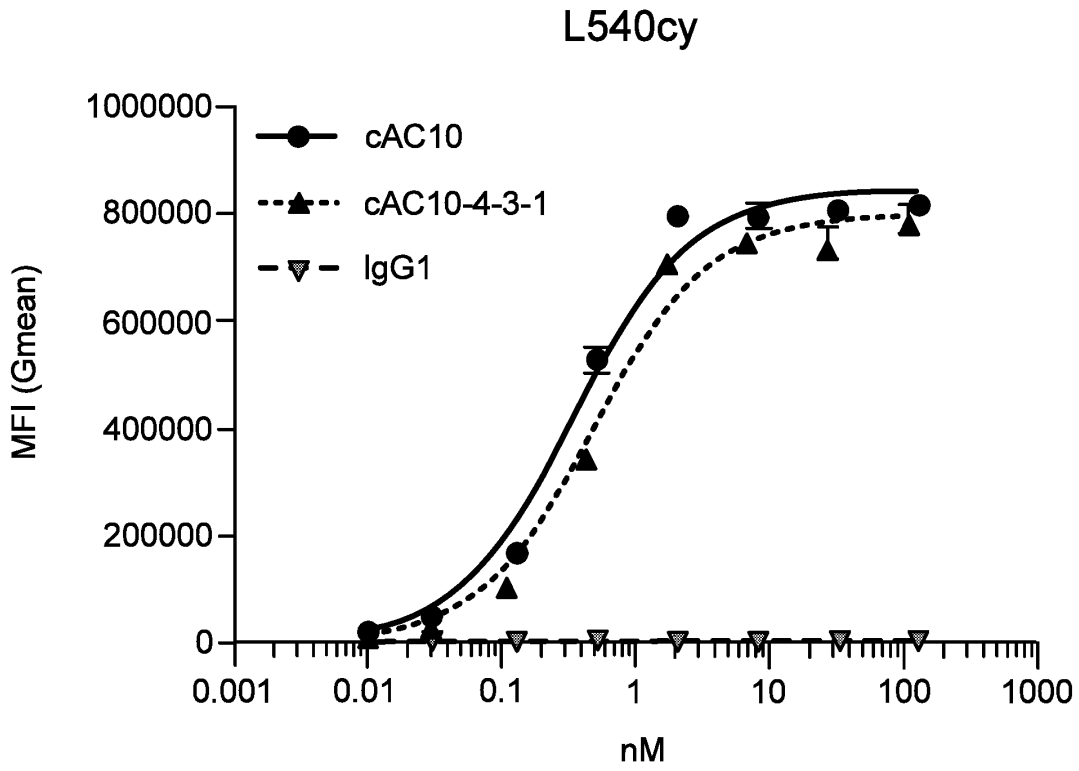
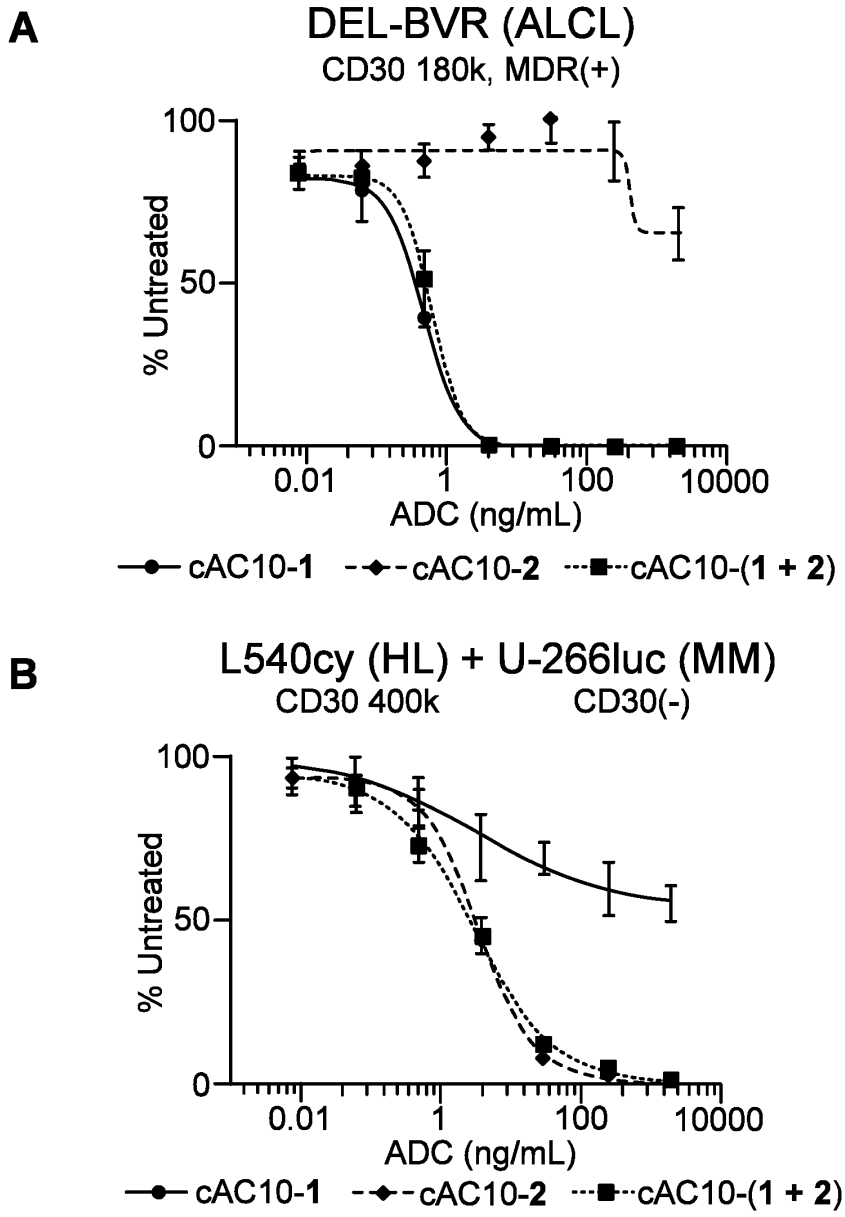

L540cy
1000000
800000
600000
400000
200000
0
MFI (Gmean)
cAC10
cAC10-4-3-1
IgG1
0.001
0.01
0.1
1
10
100
1000
nM

FIG. 8



ADC	**L540cy** CD30(+) MDR(-) HL	**DEL** CD30(+) MDR(-) ALCL	**DEL-BVR** CD30(+) MDR(+) ALCL	**L540cy + U-266luc** Bystander model	**U-266luc** CD30(-) Multiple Myeloma
cAC10-**1**	0.6	0.5	1.0	**>1000**	>1000
cAC10-**2**	2.3	1.4	**>2000**	3.9	>1000
cAC10-(**1+2**)	0.5	0.3	0.8	3.9	>1000

FIG. 9

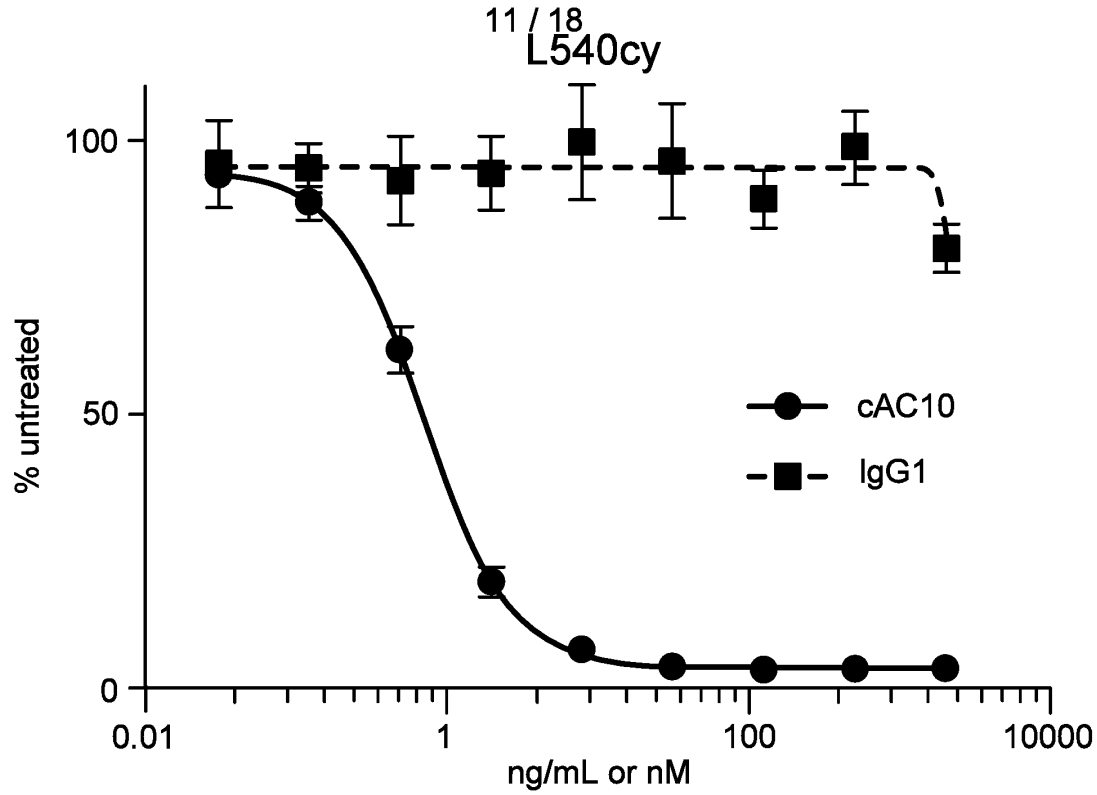

L540cy
100
50
0
% untreated
0.01
1
100
10000
ng/mL or nM
cAC10
IgG1

FIG. 10

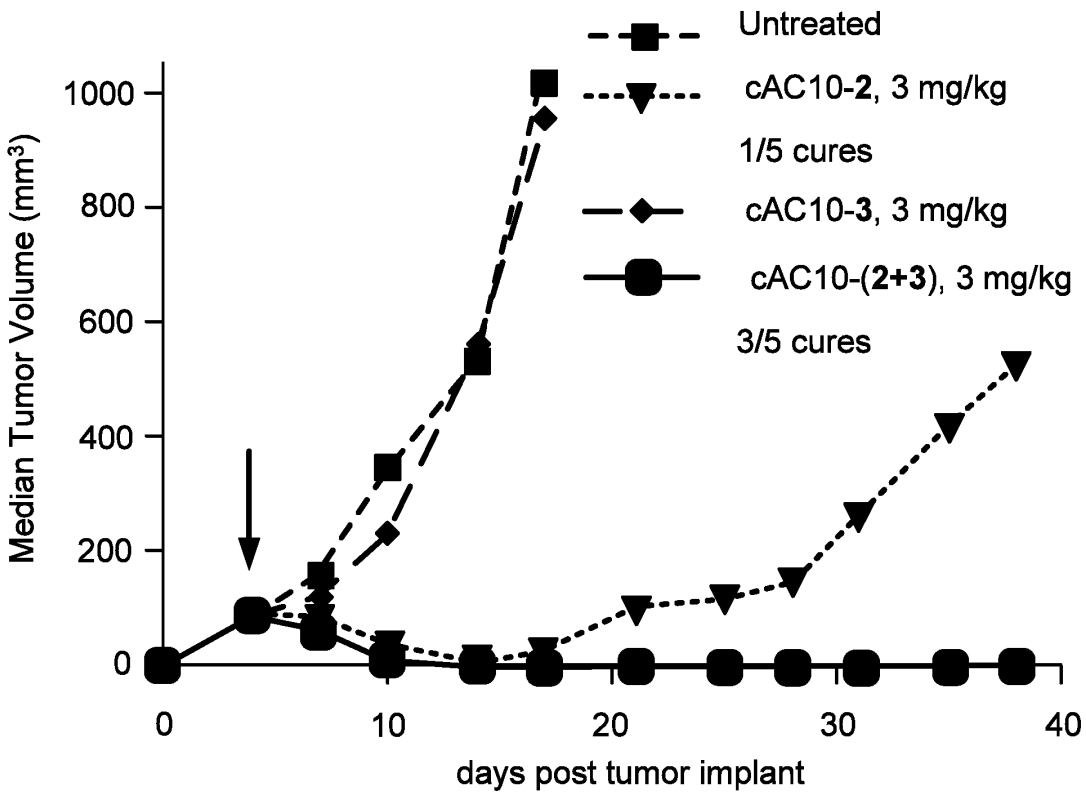

Untreated
cAC10-2, 3 mg/kg
1/5 cures
cAC10-3, 3 mg/kg
cAC10-(2+3), 3 mg/kg
3/5 cures
1000
800
600
400
200
0
Median Tumor Volume (mm3)
0
10
20
30
40
days post tumor implant

FIG. 11

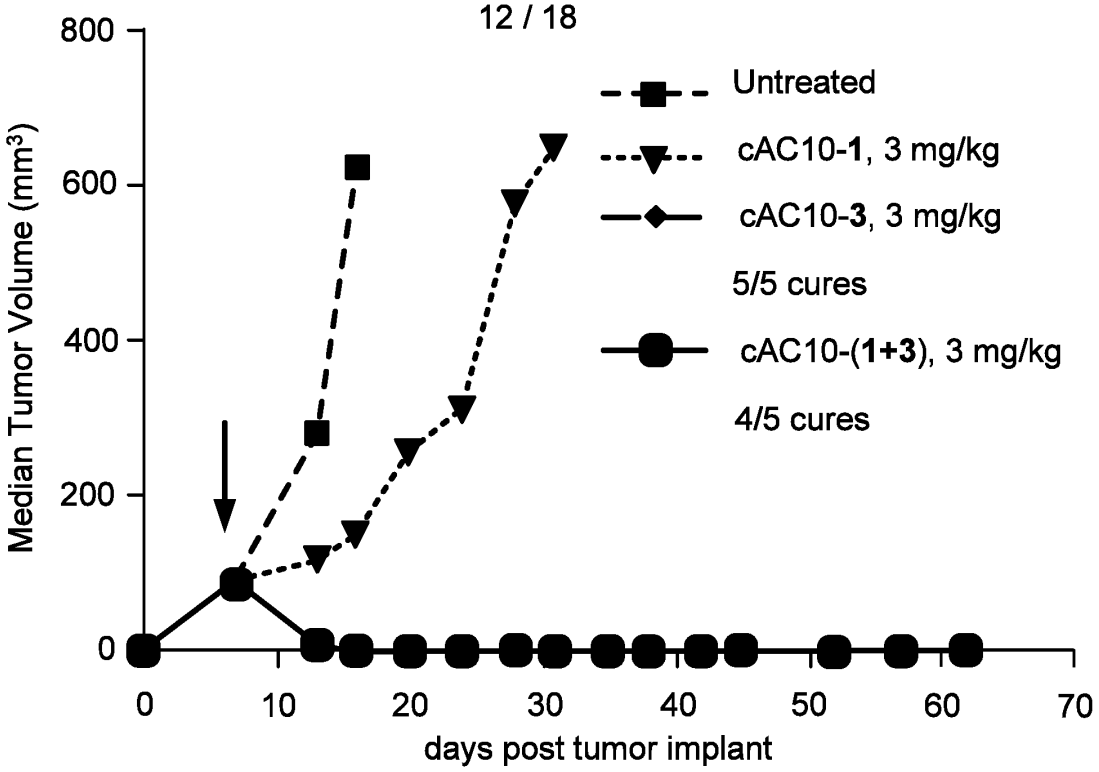

Median Tumor Volume (mm3)
800
600
400
200
0
0
10
20
30
40
50
60
70
days post tumor implant
Untreated
cAC10-1, 3 mg/kg
cAC10-3, 3 mg/kg
5/5 cures
cAC10-(1+3), 3 mg/kg
4/5 cures

FIG. 12

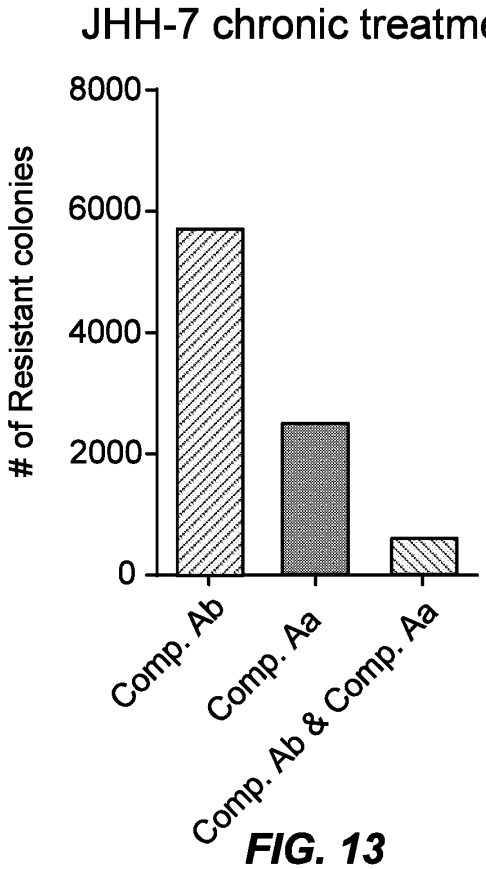

JHH-7 chronic treatment
# of Resistant colonies
8000
6000
4000
2000
0
Comp. Ab
Comp. Aa
Comp. Ab & Comp. Aa

FIG. 13

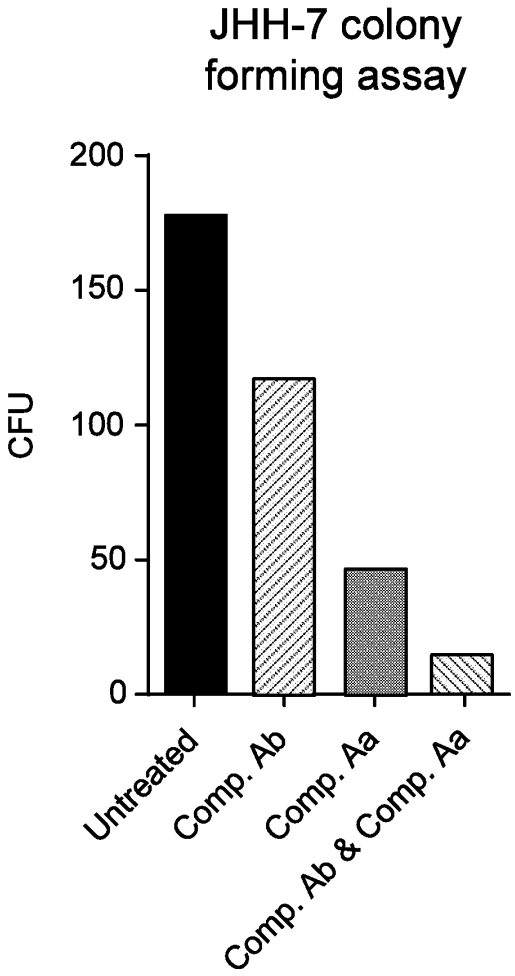

JHH-7 colony forming assay
CFU
200
150
100
50
0
Untreated
Comp. Ab
Comp. Aa
Comp. Ab & Comp. Aa

FIG. 14

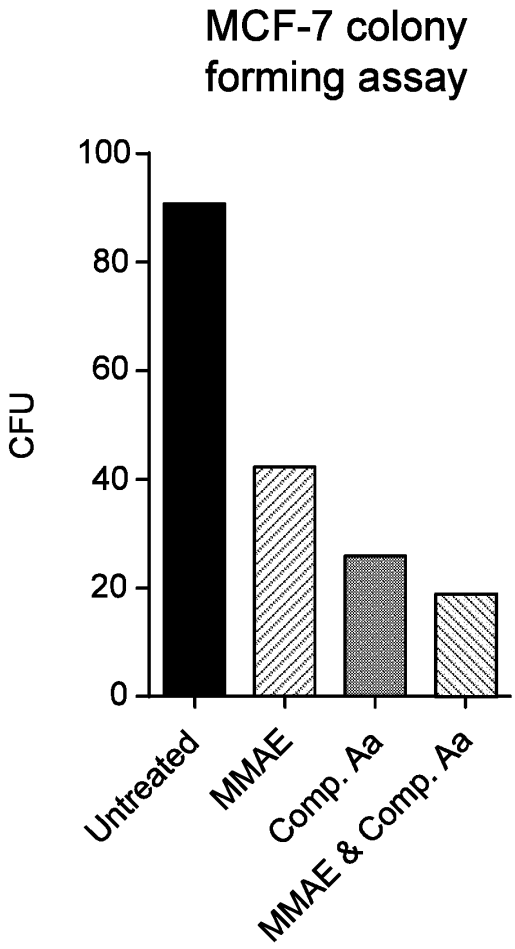

MCF-7 colony forming assay
CFU
100
80
60
40
20
0
Untreated
MMAE
Comp. Aa
MMAE & Comp. Aa

FIG. 15

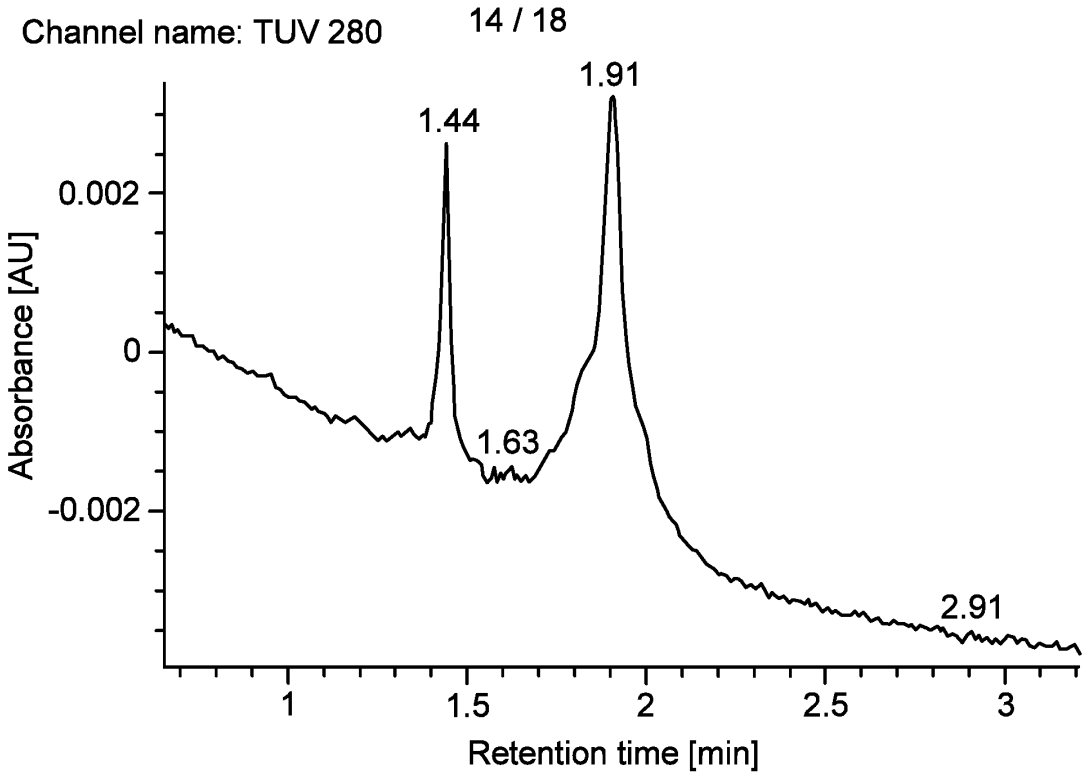


FIG. 16A

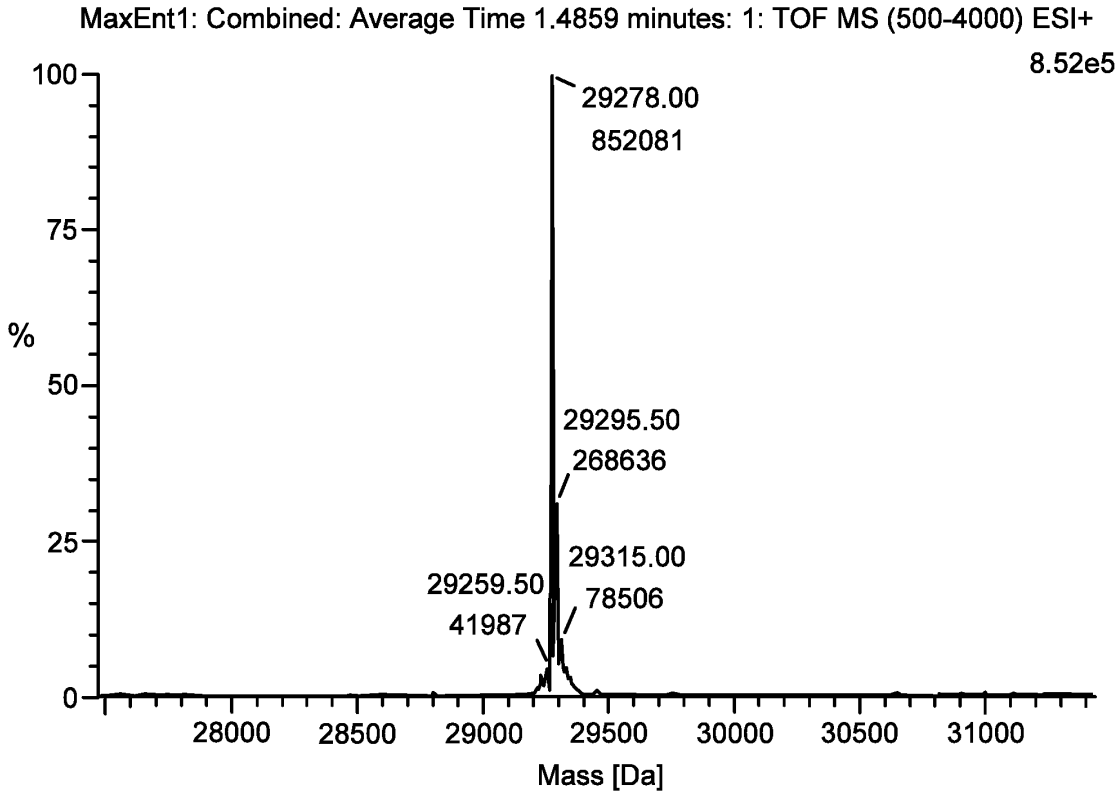


FIG. 16B

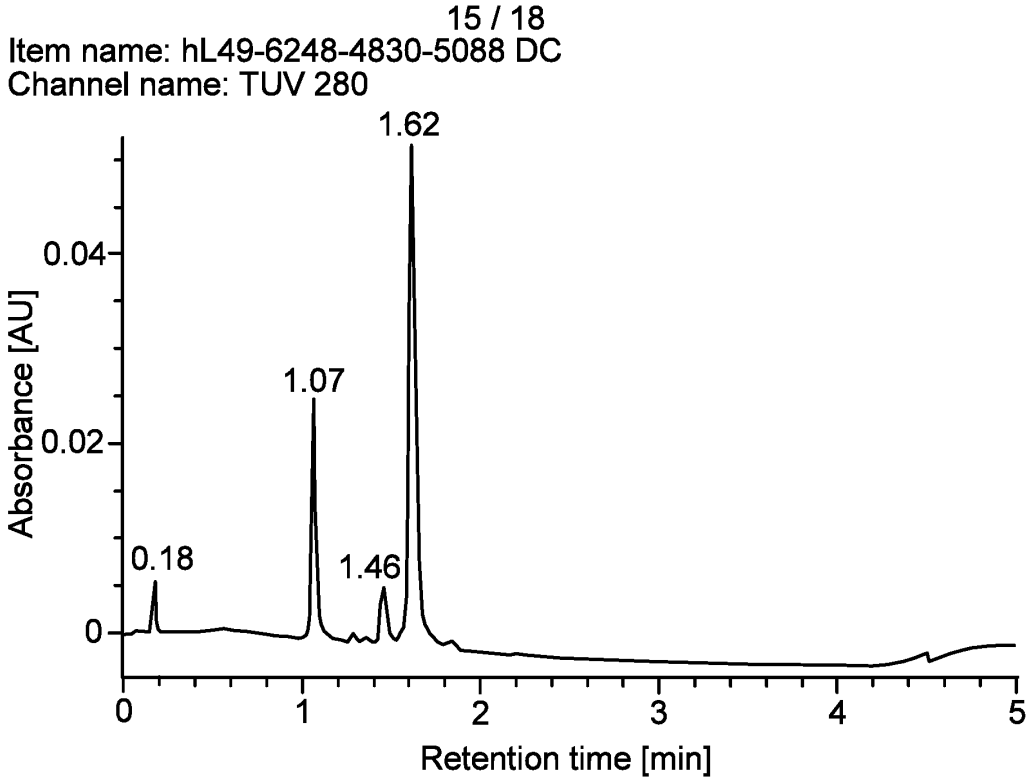


FIG. 17A

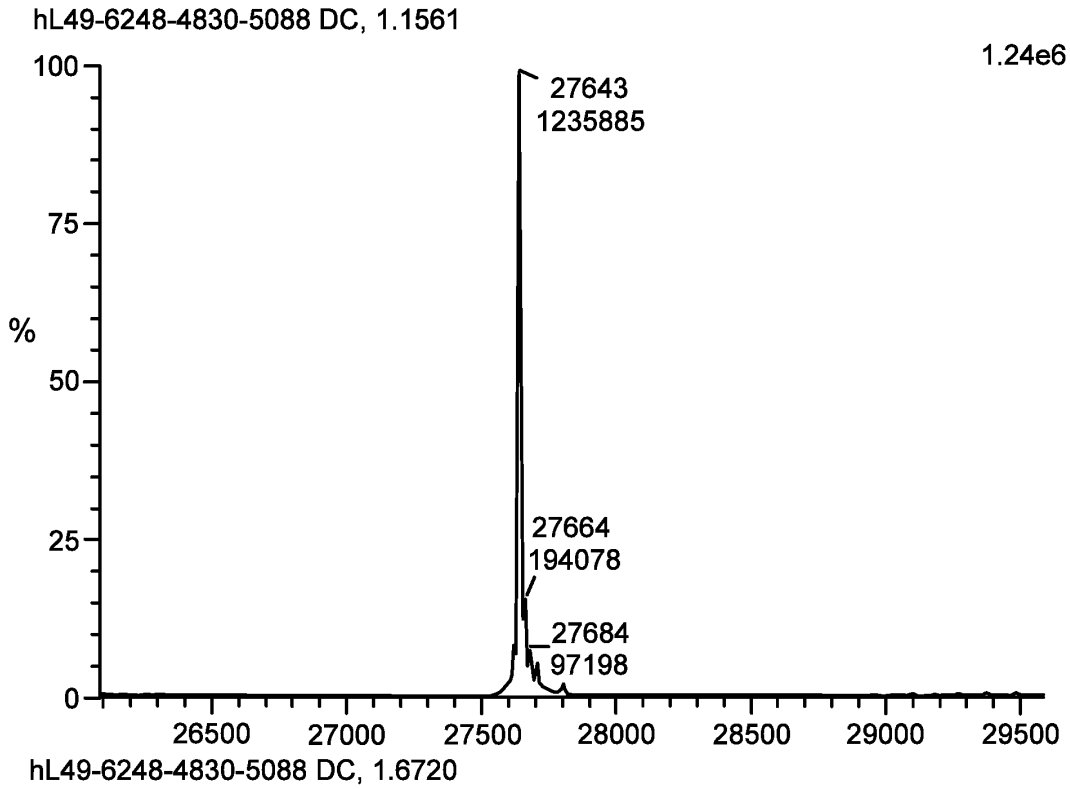


FIG. 17B

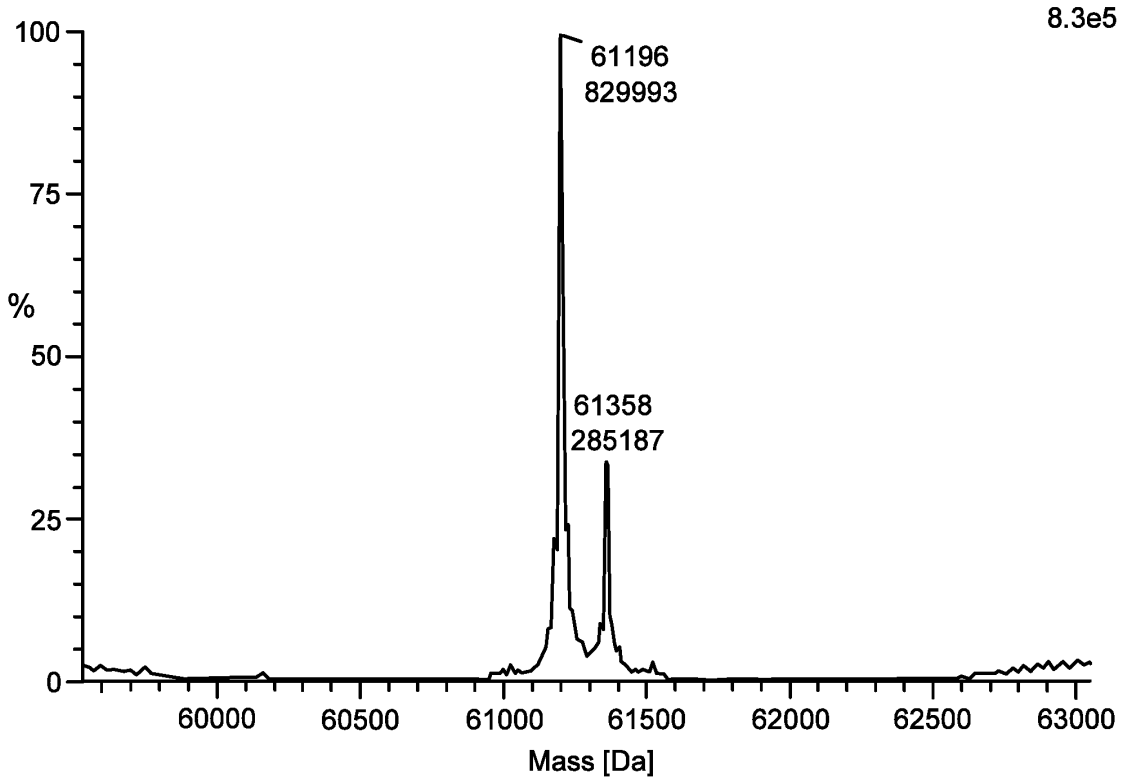

8.3e5
100
75
%
50
25
0
61196
829993
61358
285187
60000
60500
61000
61500
62000
62500
63000
Mass [Da]

FIG. 17C

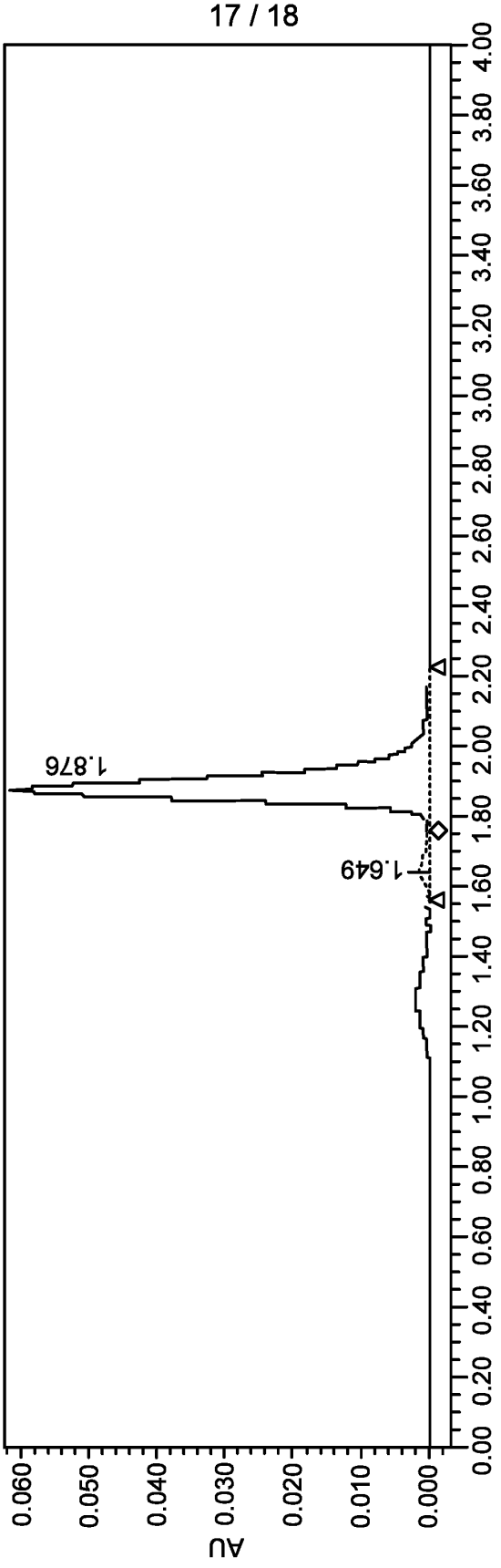

1.876
1.649
AU
0.060
0.050
0.040
0.030
0.020
0.010
0.000
Minutes
0.00
0.20
0.40
0.60
0.80
1.00
1.20
1.40
1.60
1.80
2.00
2.20
2.40
2.60
2.80
3.00
3.20
3.40
3.60
3.80
4.00

FIG. 17D

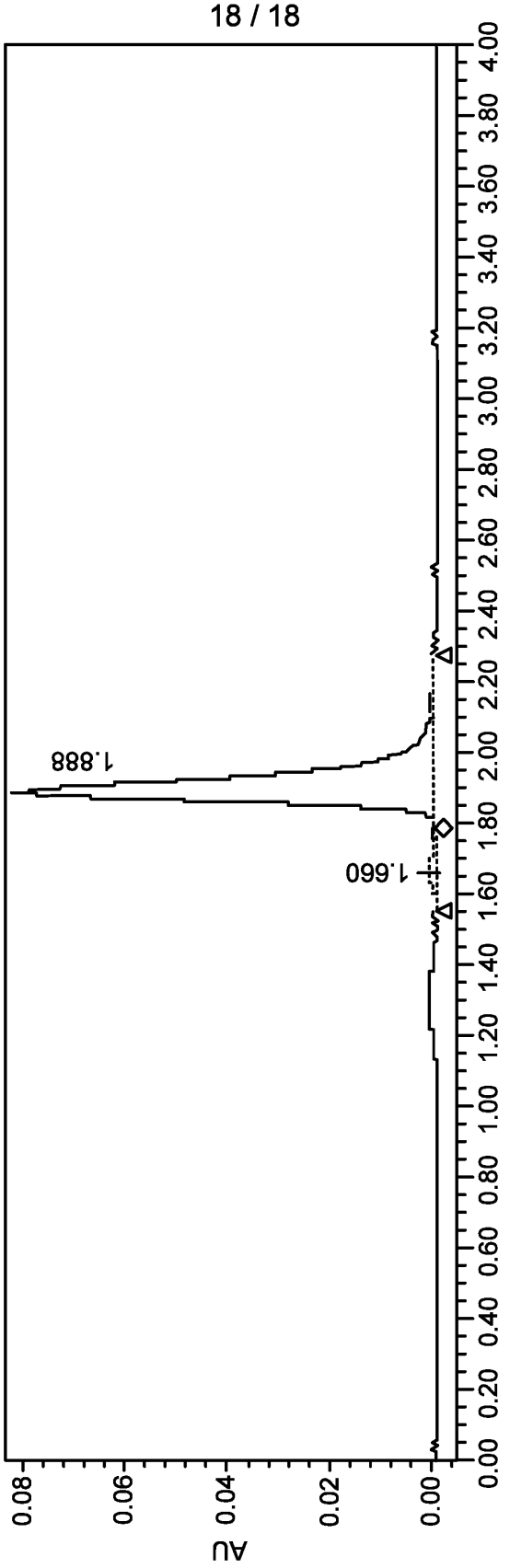

1.888
1.660
Minutes
0.00
0.20
0.40
0.60
0.80
1.00
1.20
1.40
1.60
1.80
2.00
2.20
2.40
2.60
2.80
3.00
3.20
3.40
3.60
3.80
4.00
AU
0.08
0.06
0.04
0.02
0.00

FIG. 17E