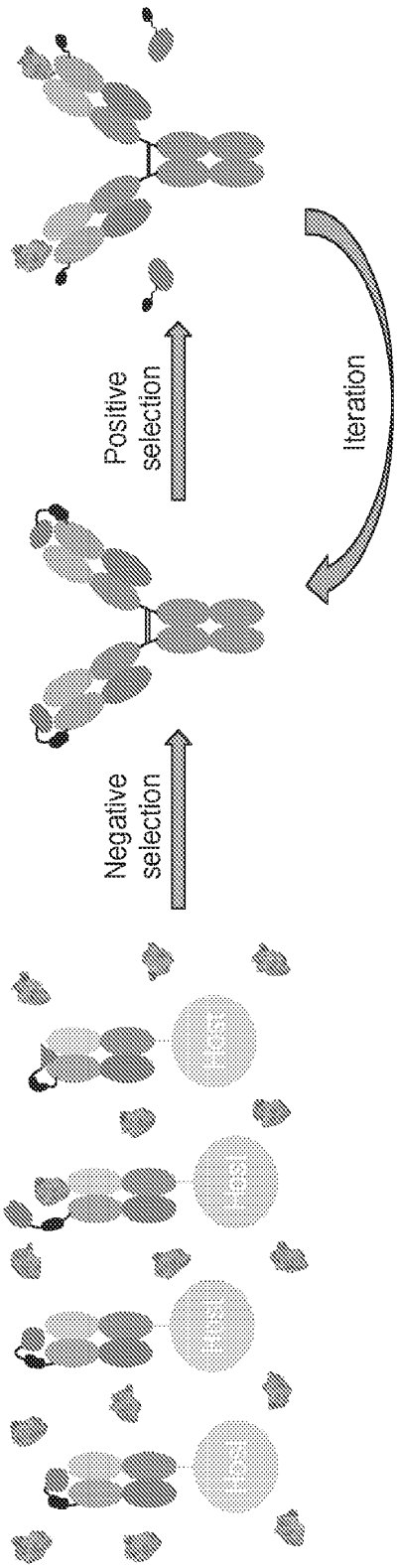
Positive selection
Iteration
Negative selection
Target
Target
Target
Target

FIG. 1

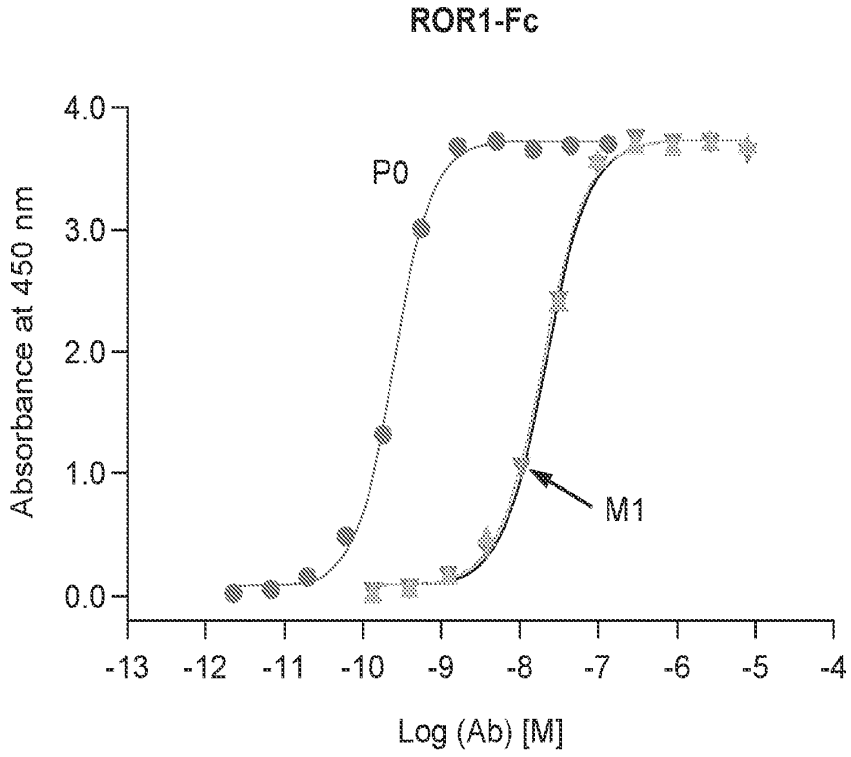
ROR1-Fc
Absorbance at 450 nm
4.0
3.0
2.0
1.0
0.0
P0
M1
-13
-12
-11
-10
-9
-8
-7
-6
-5
-4
Log (Ab) [M]

FIG. 2A

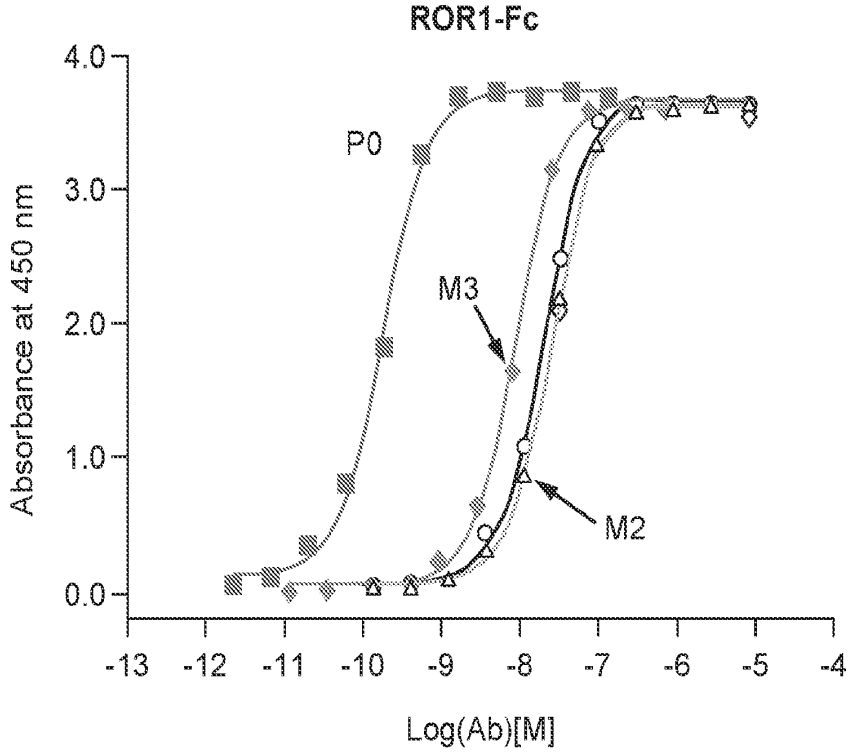
ROR1-Fc
Absorbance at 450 nm
4.0
3.0
2.0
1.0
0.0
P0
M3
M2
-13
-12
-11
-10
-9
-8
-7
-6
-5
-4
Log(Ab)[M]

FIG. 2B

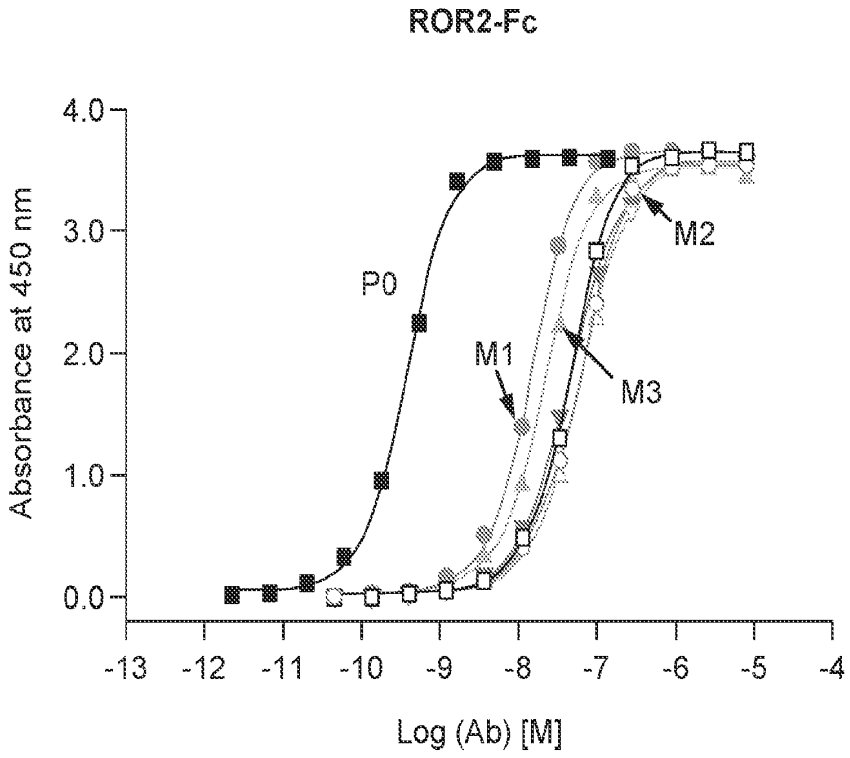
ROR2-Fc
Absorbance at 450 nm
4.0
3.0
2.0
1.0
0.0
P0
M1
M2
M3
-13
-12
-11
-10
-9
-8
-7
-6
-5
-4
Log (Ab) [M]

FIG. 2C

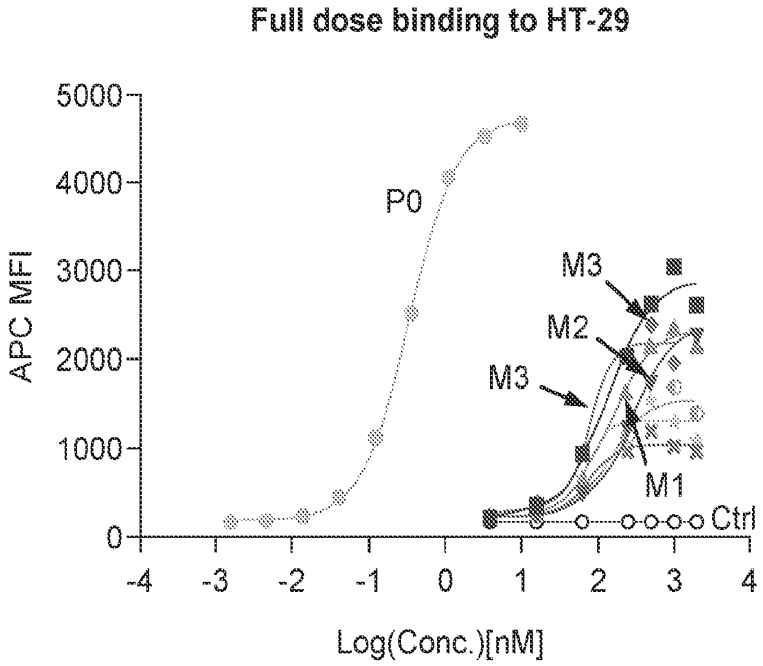
Full dose binding to HT-29
APC MFI
5000
4000
3000
2000
1000
0
P0
M3
M2
M3
M1
Ctrl
-4
-3
-2
-1
0
1
2
3
4
Log(Conc.)[nM]

FIG. 2D

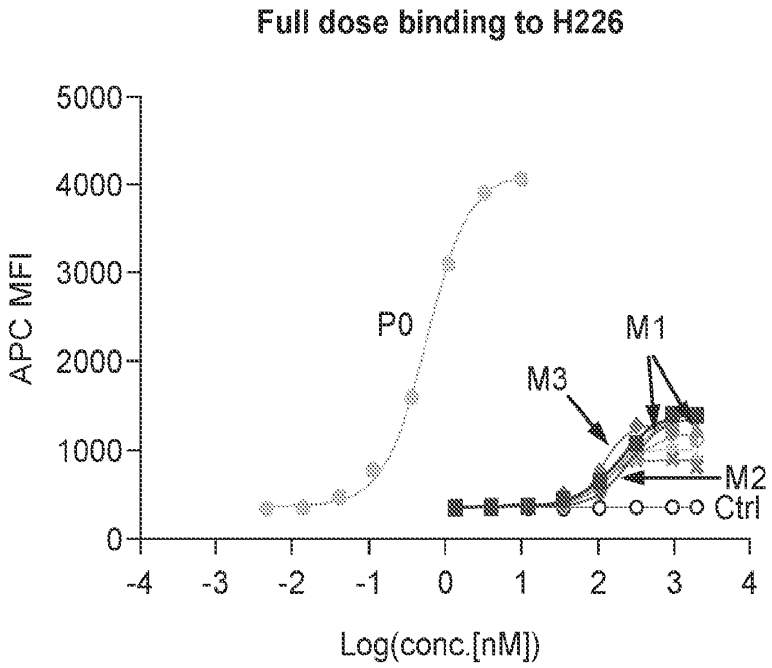
Full dose binding to H226
APC MFI
5000
4000
3000
2000
1000
0
-4
-3
-2
-1
0
1
2
3
4
Log(conc.[nM])
P0
M1
M3
M2
Ctrl

FIG. 2E

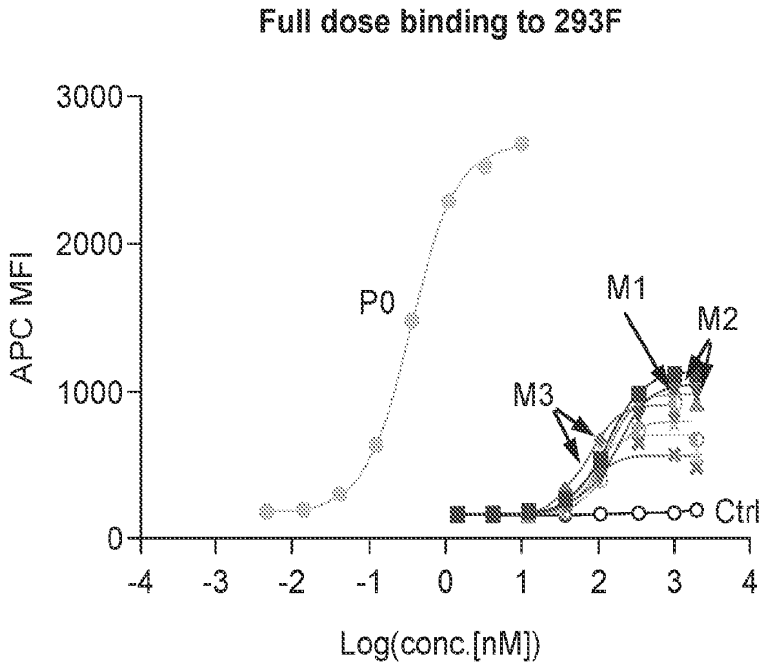
Full dose binding to 293F
APC MFI
3000
2000
1000
0
-4
-3
-2
-1
0
1
2
3
4
Log(conc.[nM])
P0
M1
M2
M3
Ctrl

FIG. 2F

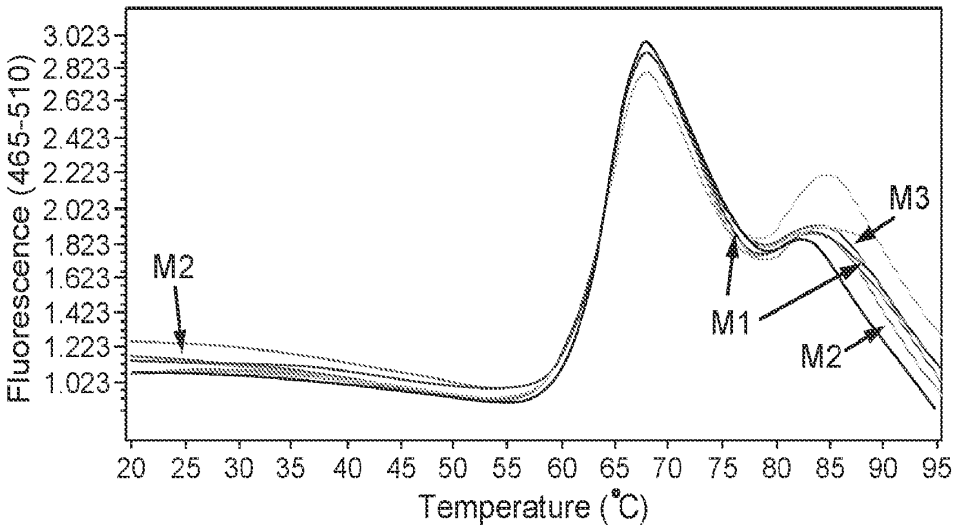
Fluorescence (465-510)
3.023
2.823
2.623
2.423
2.223
2.023
1.823
1.623
1.423
1.223
1.023
M2
M3
M1
M2
20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95
Temperature (°C)

FIG. 3A

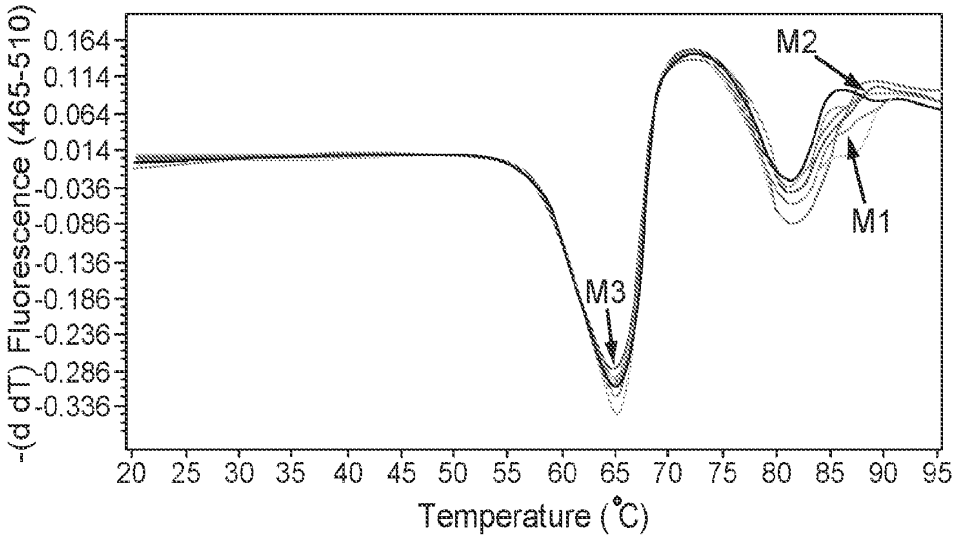
-(d dT) Fluorescence (465-510)
0.164
0.114
0.064
0.014
-0.036
-0.086
-0.136
-0.186
-0.236
-0.286
-0.336
M2
M1
M3
20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95
Temperature (°C)

FIG. 3B

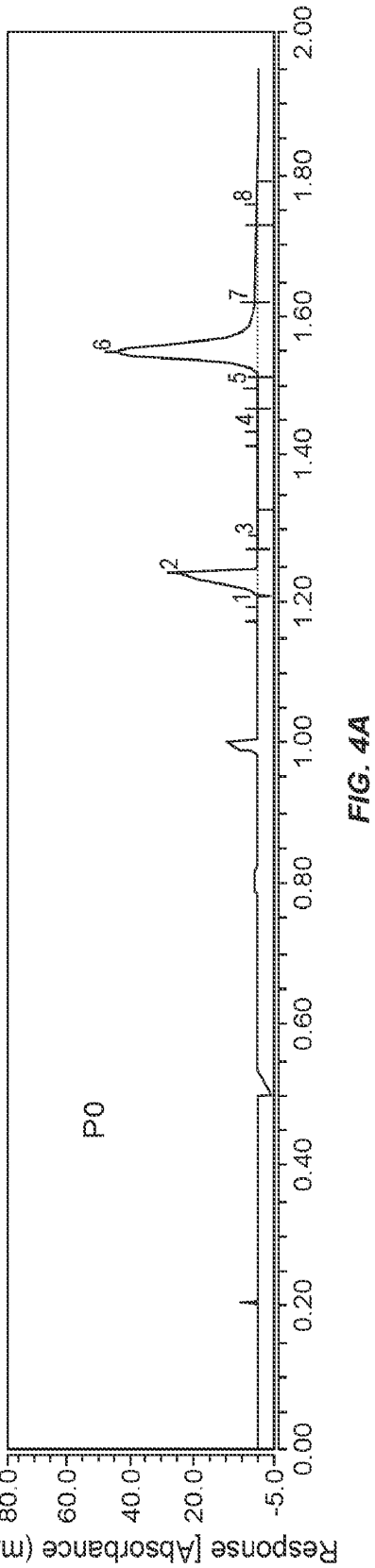
P0
Response [Absorbance (mAU)]
80.0
60.0
40.0
20.0
-5.0
0.00
0.20
0.40
0.60
0.80
1.00
1.20
1.40
1.60
1.80
2.00
1
2
3
4
5
6
7
8

FIG. 4A

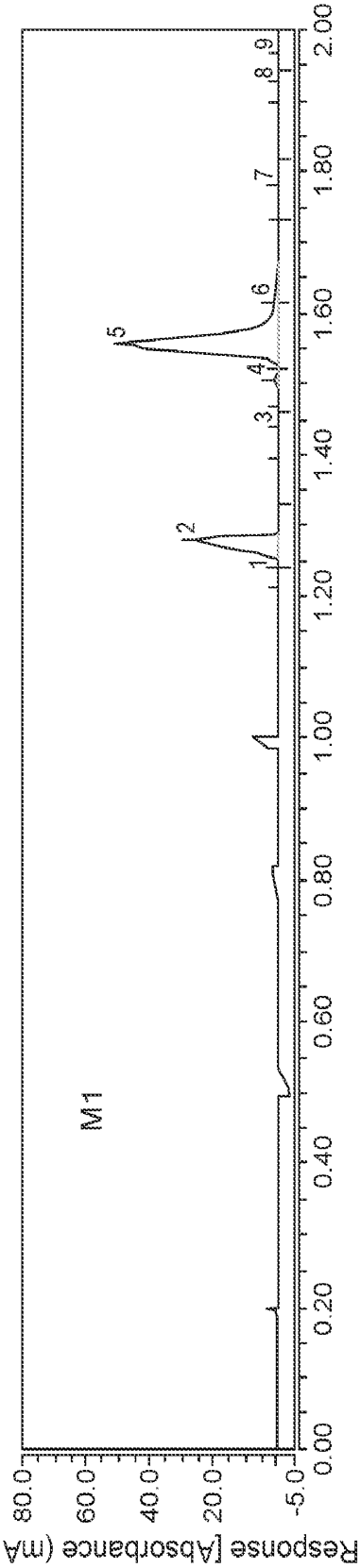
M1
Response [Absorbance (mAU)]
80.0
60.0
40.0
20.0
-5.0
0.00
0.20
0.40
0.60
0.80
1.00
1.20
1.40
1.60
1.80
2.00
1
2
3
4
5
6
7
8
9

FIG. 4B

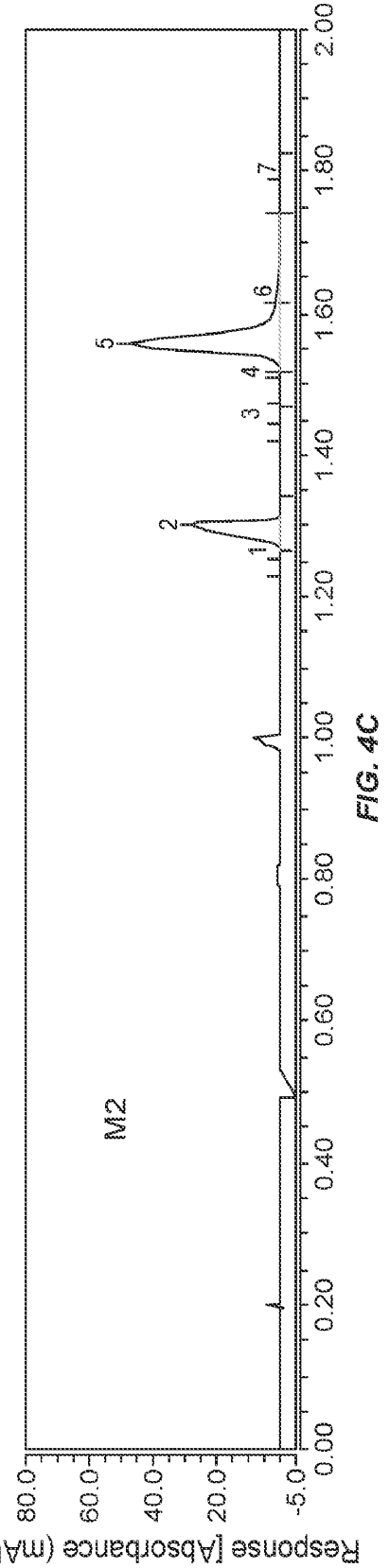
M2
Response [Absorbance (mAU)]
80.0
60.0
40.0
20.0
-5.0
0.00
0.20
0.40
0.60
0.80
1.00
1.20
1.40
1.60
1.80
2.00
1
2
3
4
5
6
7

FIG. 4C

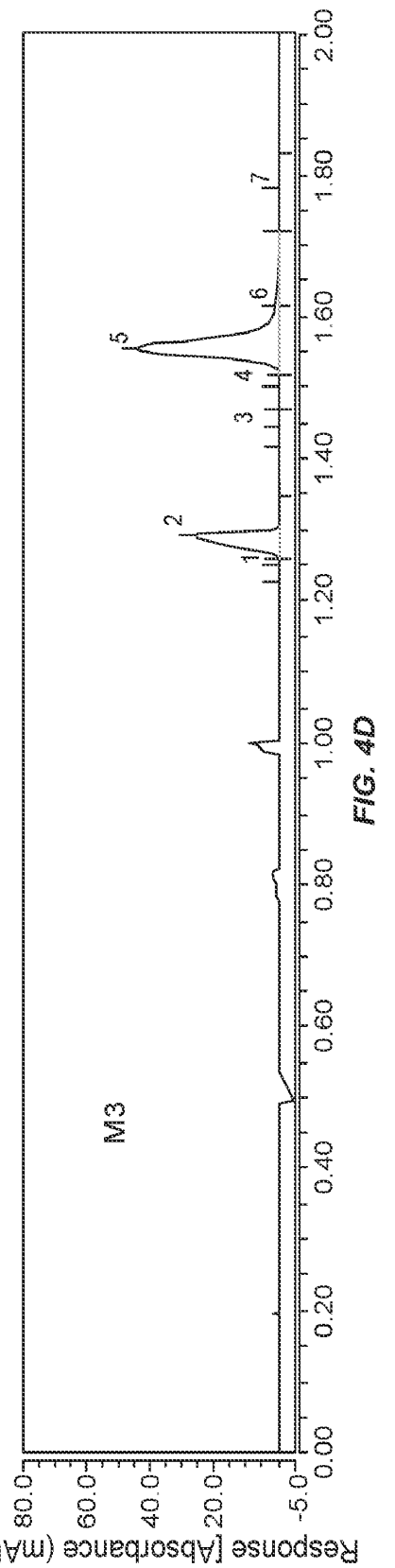
M3
Response [Absorbance (mAU)]
80.0
60.0
40.0
20.0
-5.0
0.00
0.20
0.40
0.60
0.80
1.00
1.20
1.40
1.60
1.80
2.00
1
2
3
4
5
6
7

FIG. 4D

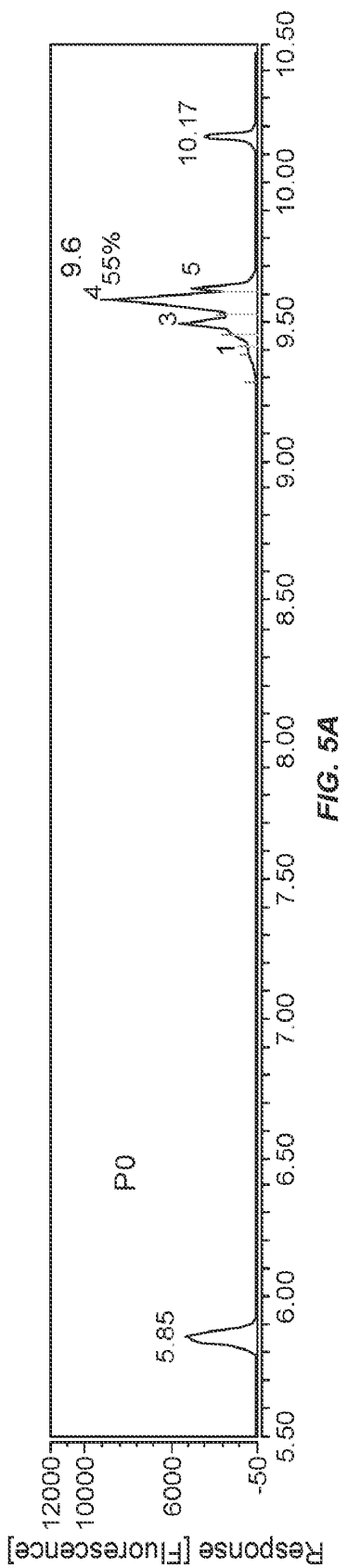
P0
5.85
9.6
55%
10.17
1
3
4
5
Response [Fluorescence]
12000
10000
6000
-50
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
9.50
10.00
10.50

FIG. 5A

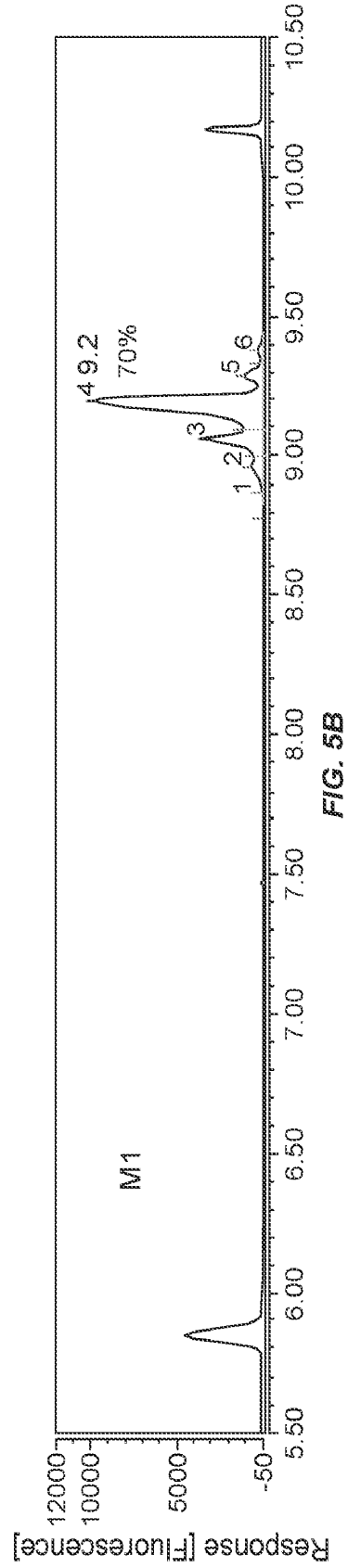
M1
9.2
70%
1
2
3
4
5
6
Response [Fluorescence]
12000
10000
5000
-50
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
9.50
10.00
10.50

FIG. 5B

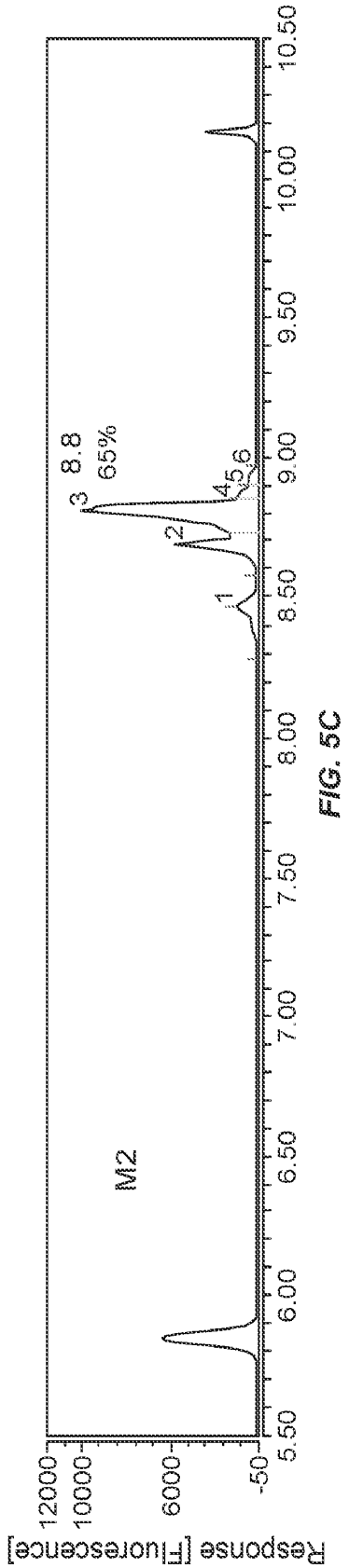
M2
8.8
65%
1
2
3
4
5
6
Response [Fluorescence]
12000
10000
6000
-50
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
9.50
10.00
10.50

FIG. 5C

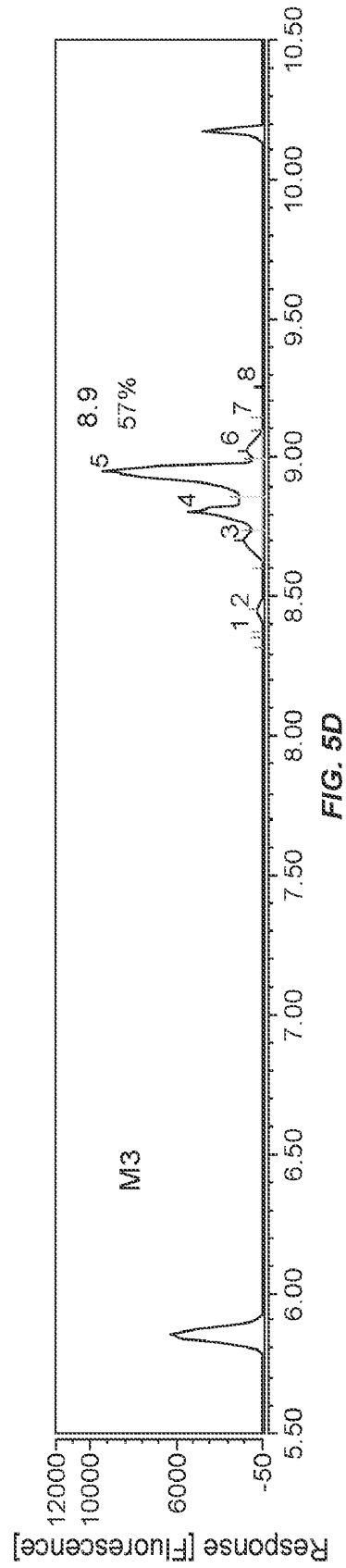
M3
8.9
57%
1
2
3
4
5
6
7
8
Response [Fluorescence]
12000
10000
6000
-50
5.50
6.00
6.50
7.00
7.50
8.00
8.50
9.00
9.50
10.00
10.50

FIG. 5D

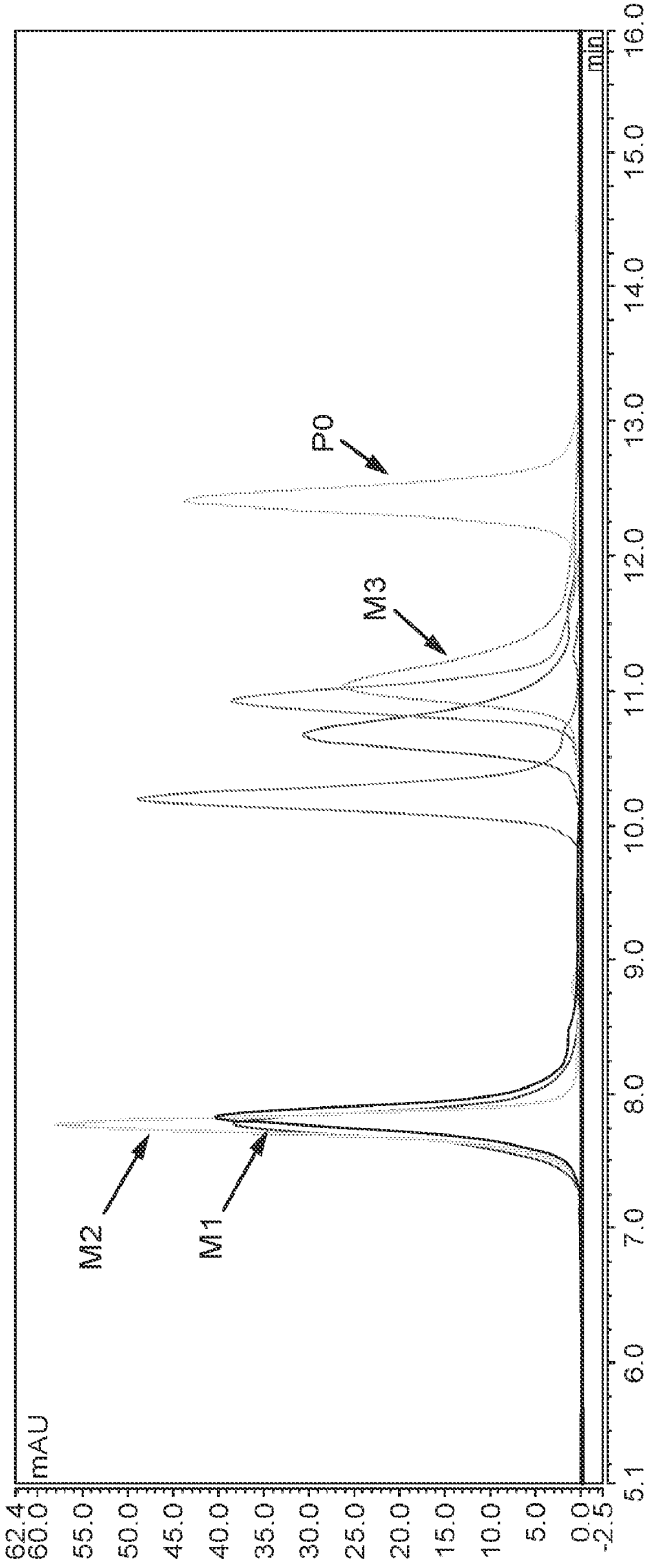
mAU
62.4
60.0
55.0
50.0
45.0
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
-2.5
min
5.1
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
15.0
16.0
M2
M1
M3
P0

FIG. 6

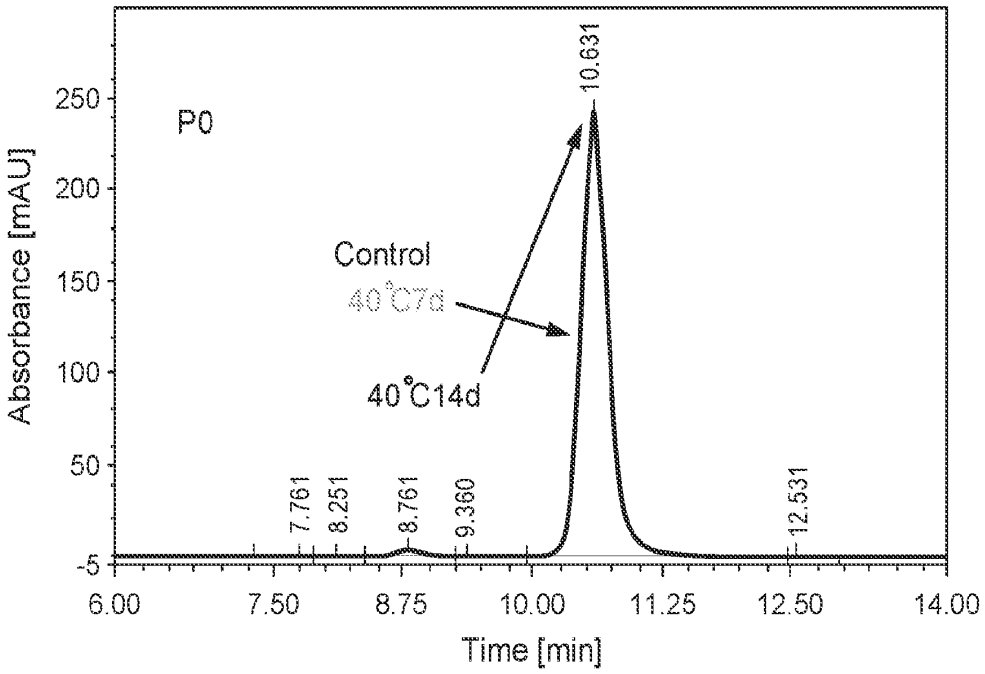
P0
Control
40°C7d
40°C14d
10.631
7.761
8.251
8.761
9.360
12.531
Absorbance [mAU]
Time [min]
250
200
150
100
50
-5
6.00
7.50
8.75
10.00
11.25
12.50
14.00

FIG. 7A

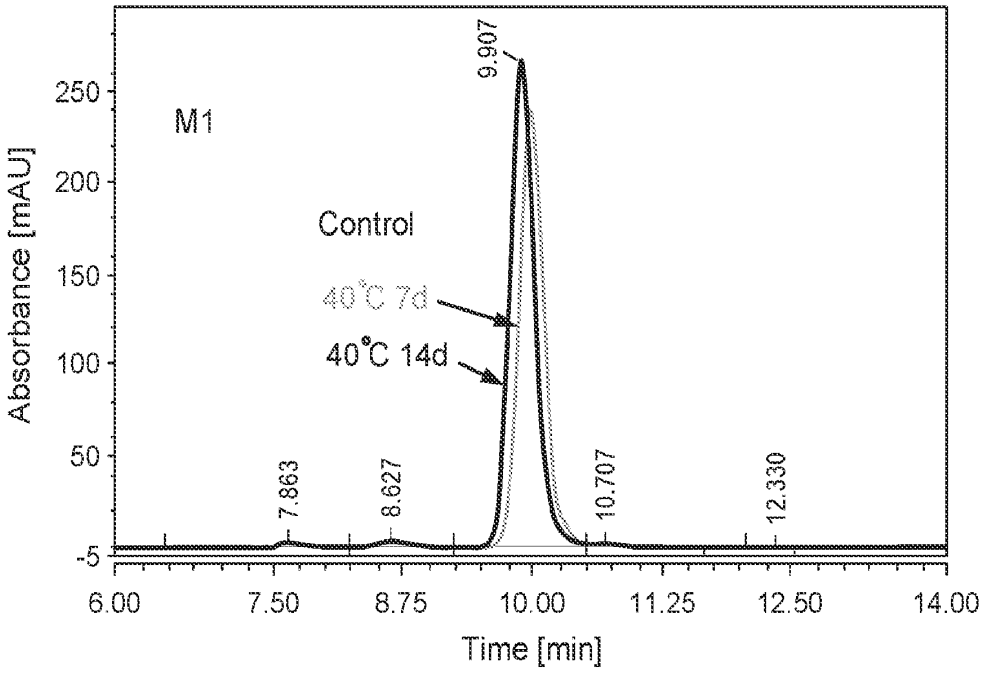
M1
Control
40°C 7d
40°C 14d
9.907
7.863
8.627
10.707
12.330
Absorbance [mAU]
Time [min]
250
200
150
100
50
-5
6.00
7.50
8.75
10.00
11.25
12.50
14.00

FIG. 7B

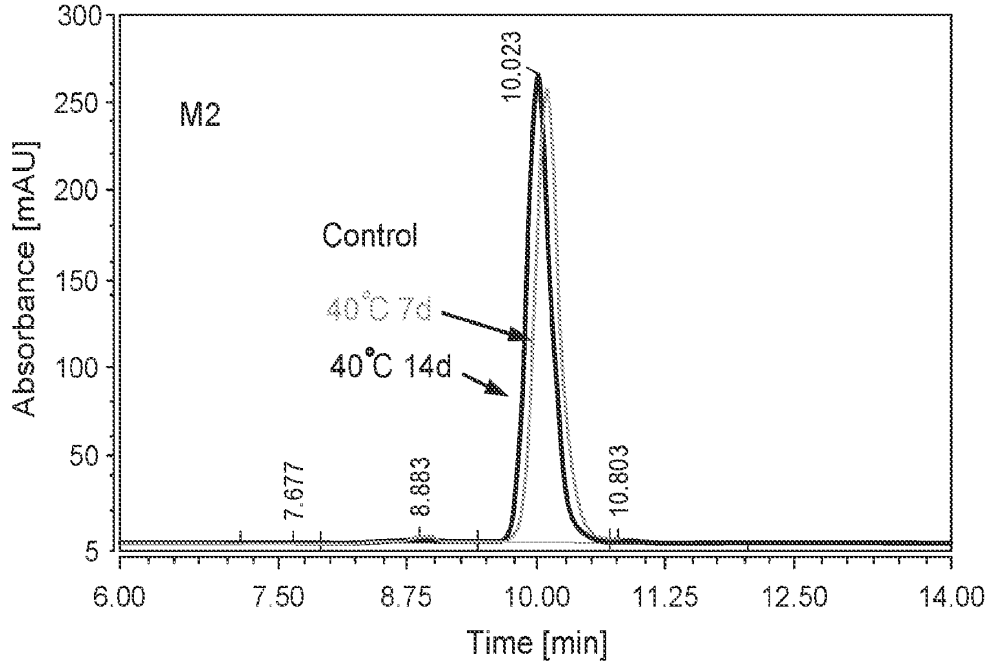
M2
Control
40°C 7d
40°C 14d
10.023
7.677
8.883
10.803
Absorbance [mAU]
Time [min]
300
250
200
150
100
50
5
6.00
7.50
8.75
10.00
11.25
12.50
14.00

FIG. 7C

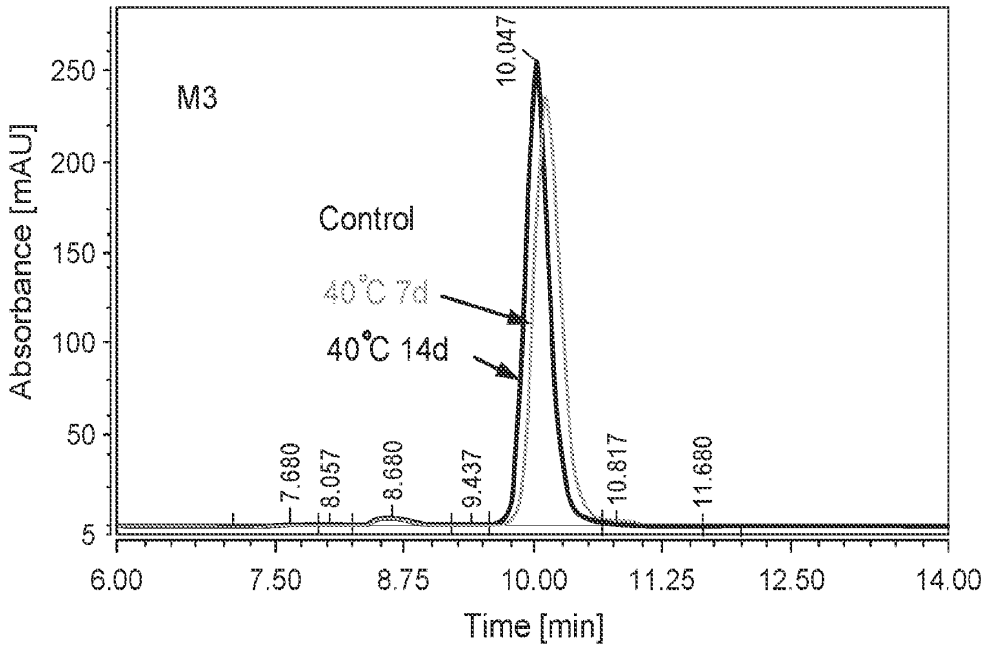
M3
Control
40°C 7d
40°C 14d
10.047
7.680
8.057
8.680
9.437
10.817
11.680
Absorbance [mAU]
Time [min]
250
200
150
100
50
5
6.00
7.50
8.75
10.00
11.25
12.50
14.00

FIG. 7D

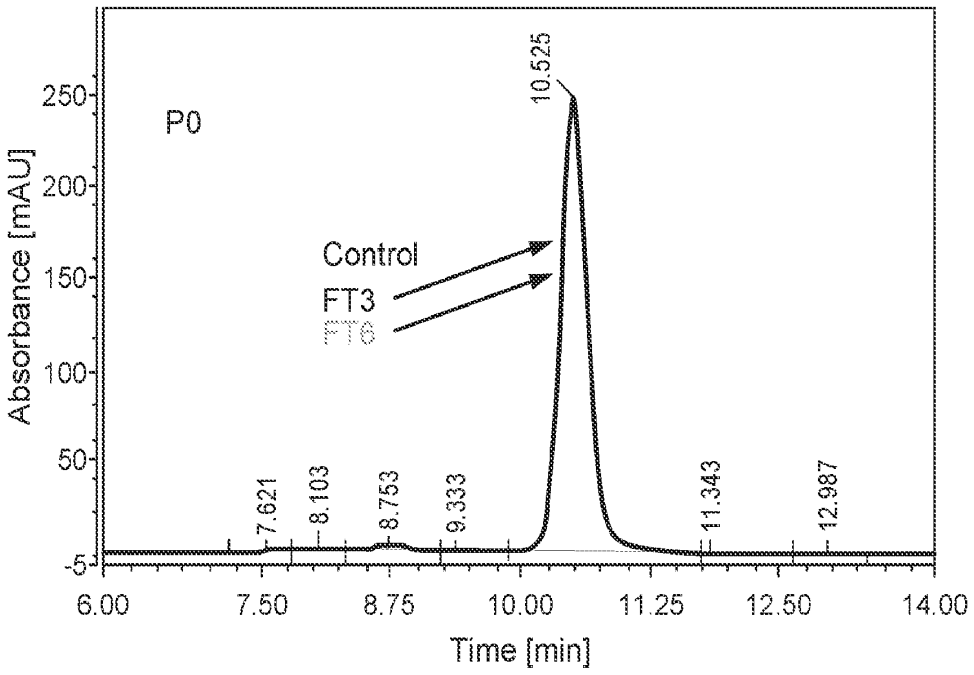
P0
Control
FT3
FT6
Absorbance [mAU]
Time [min]
250
200
150
100
50
-5
6.00
7.50
8.75
10.00
11.25
12.50
14.00
7.621
8.103
8.753
9.333
10.525
11.343
12.987

FIG. 8A

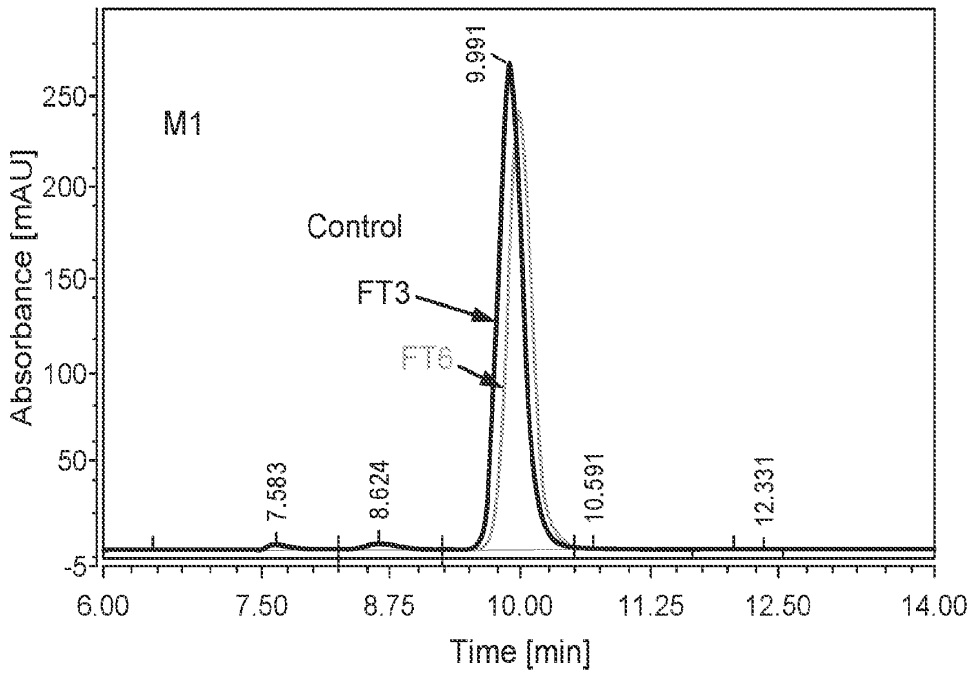
M1
Control
FT3
FT6
Absorbance [mAU]
Time [min]
250
200
150
100
50
-5
6.00
7.50
8.75
10.00
11.25
12.50
14.00
7.583
8.624
9.991
10.591
12.331

FIG. 8B

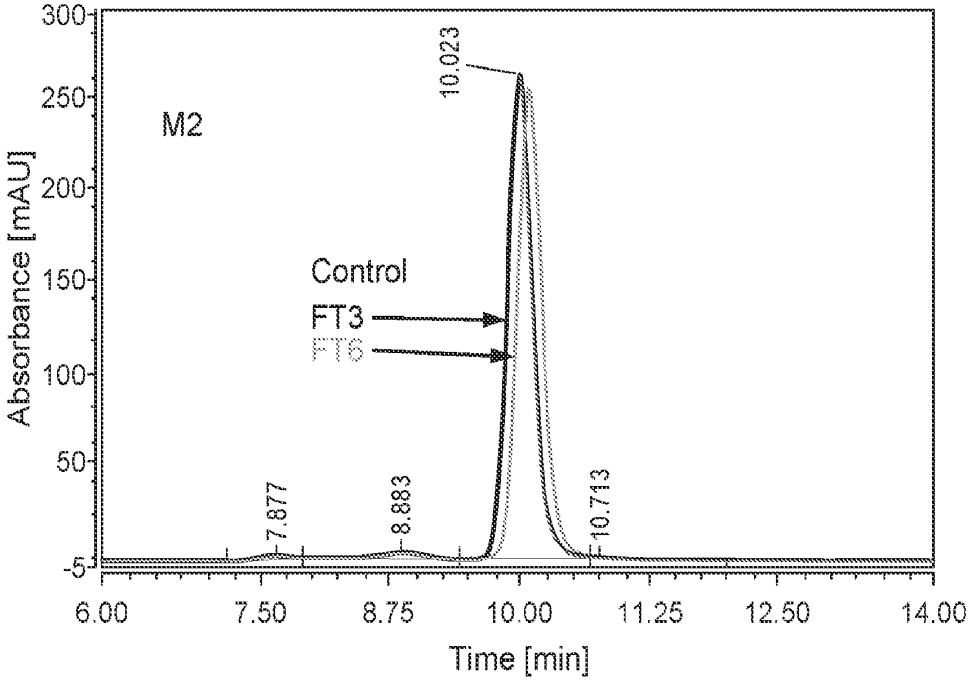
M2
Control
FT3
FT6
10.023
7.877
8.883
10.713
Absorbance [mAU]
Time [min]
300
250
200
150
100
50
-5
6.00
7.50
8.75
10.00
11.25
12.50
14.00

FIG. 8C

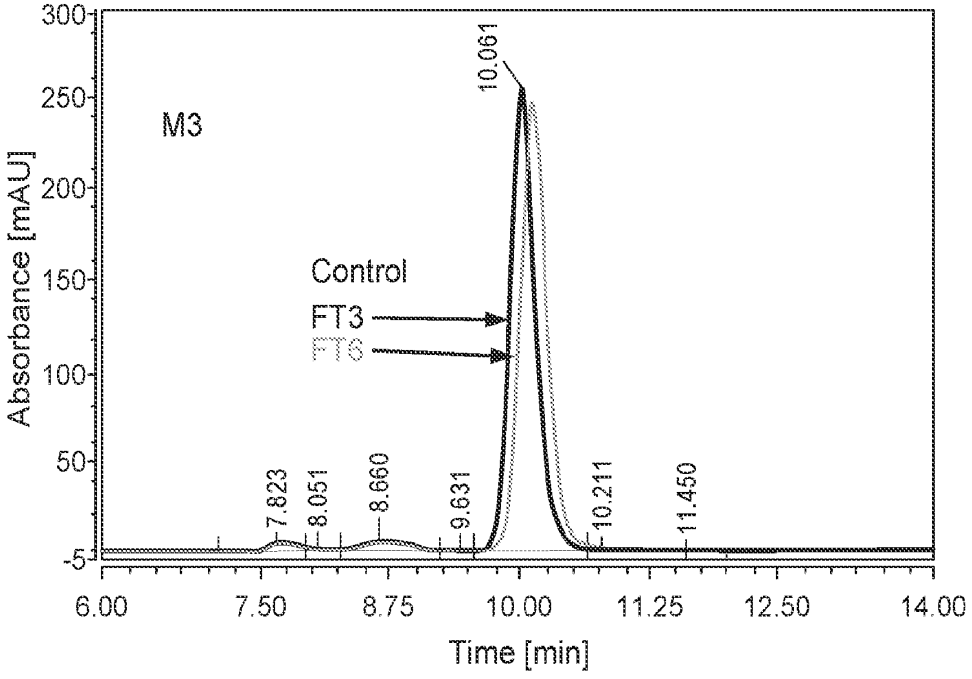
M3
Control
FT3
FT6
10.061
7.823
8.051
8.660
9.631
10.211
11.450
Absorbance [mAU]
Time [min]
300
250
200
150
100
50
-5
6.00
7.50
8.75
10.00
11.25
12.50
14.00

FIG. 8D

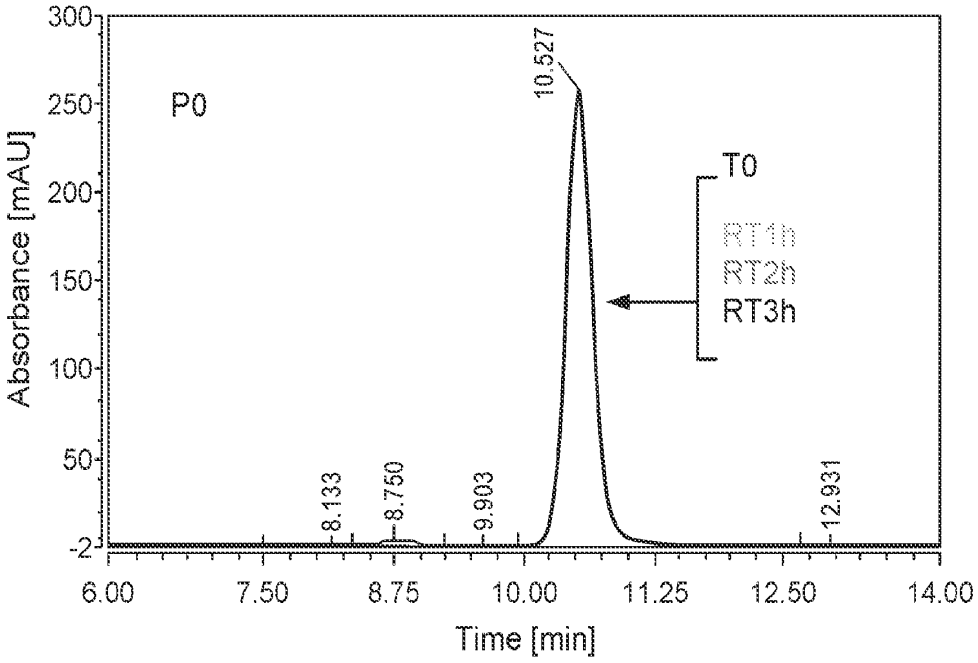
P0
10.527
T0
RT1h
RT2h
RT3h
8.133
8.750
9.903
12.931
Absorbance [mAU]
300
250
200
150
100
50
-2
6.00
7.50
8.75
10.00
11.25
12.50
14.00
Time [min]

FIG. 9A

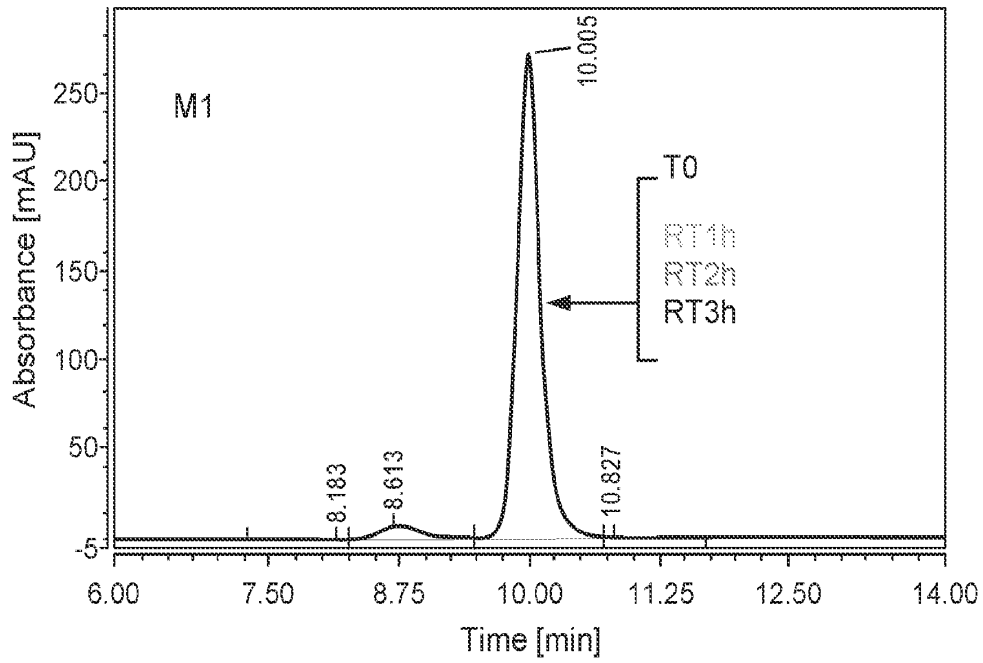
M1
10.005
T0
RT1h
RT2h
RT3h
8.183
8.613
10.827
Absorbance [mAU]
250
200
150
100
50
-5
6.00
7.50
8.75
10.00
11.25
12.50
14.00
Time [min]

FIG. 9B

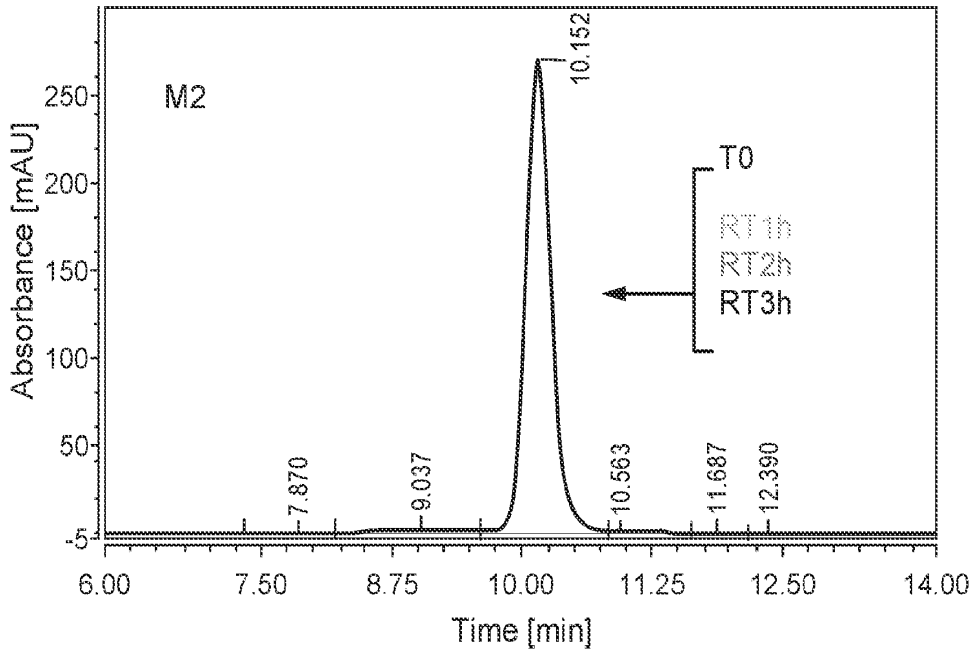
M2
10.152
T0
RT1h
RT2h
RT3h
7.870
9.037
10.563
11.687
12.390
Absorbance [mAU]
250
200
150
100
50
-5
6.00
7.50
8.75
10.00
11.25
12.50
14.00
Time [min]

FIG. 9C

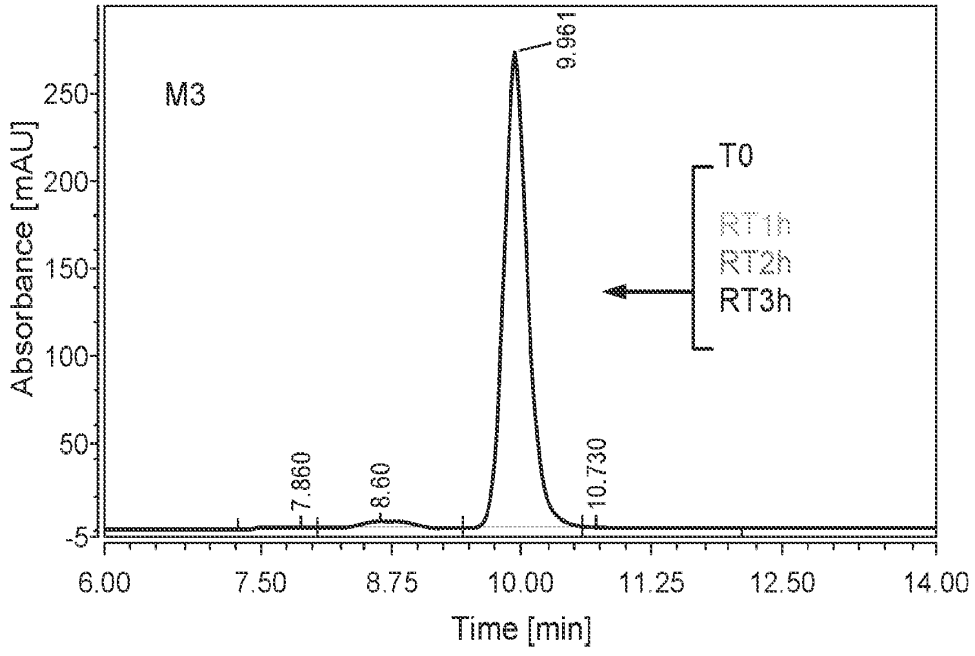
M3
9.961
T0
RT1h
RT2h
RT3h
7.860
8.60
10.730
Absorbance [mAU]
250
200
150
100
50
-5
6.00
7.50
8.75
10.00
11.25
12.50
14.00
Time [min]

FIG. 9D

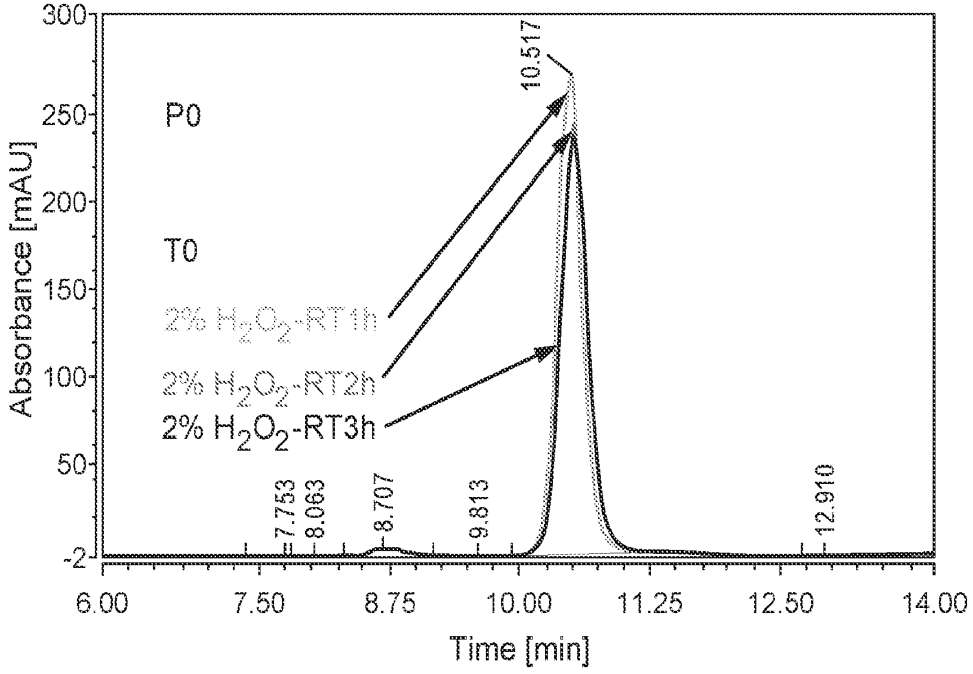

FIG. 10A

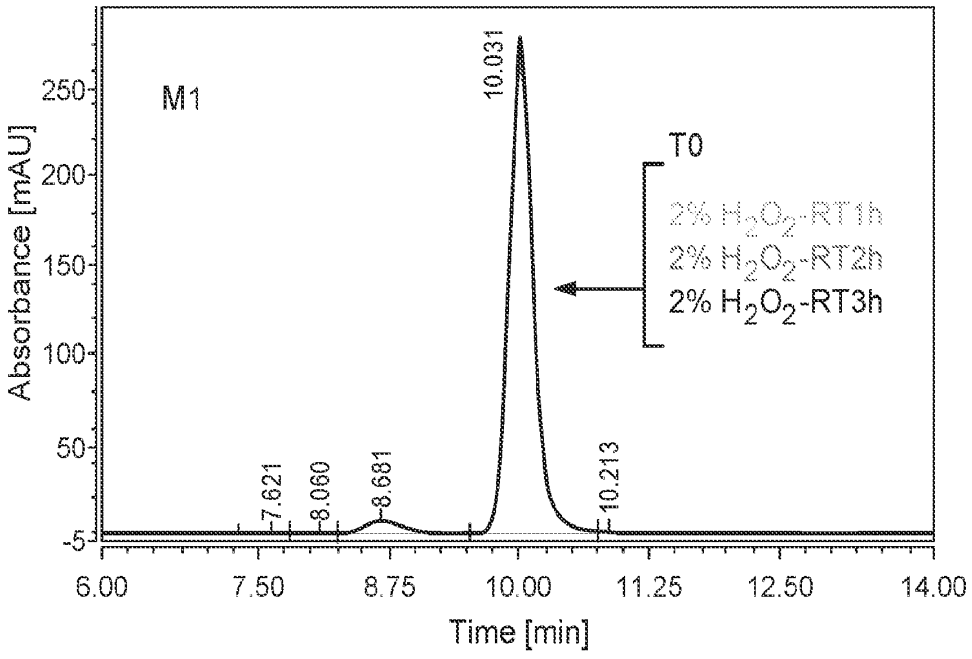

FIG. 10B

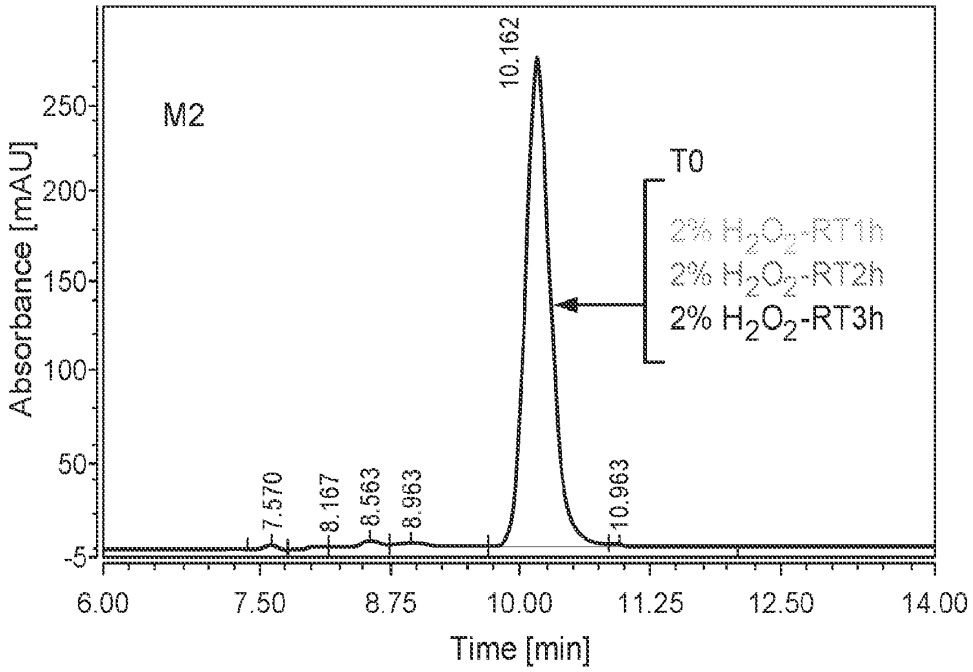

FIG. 10C

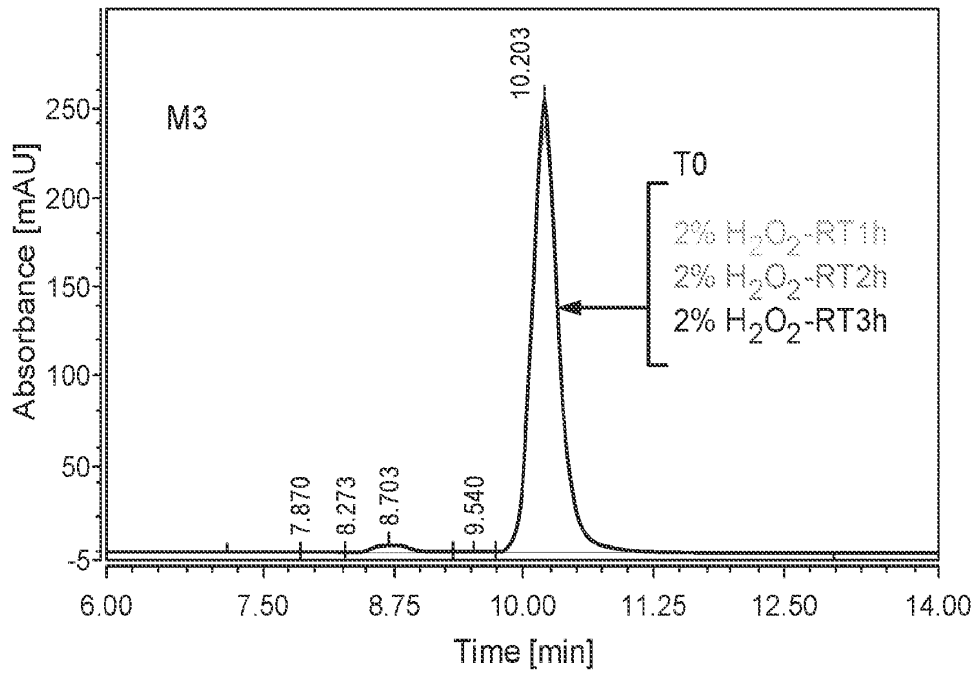

FIG. 10D

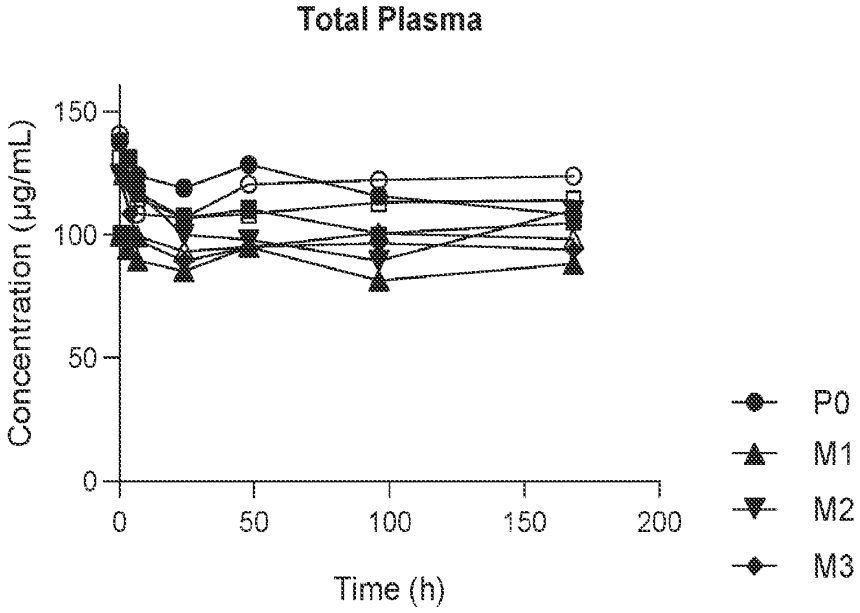

FIG. 11A

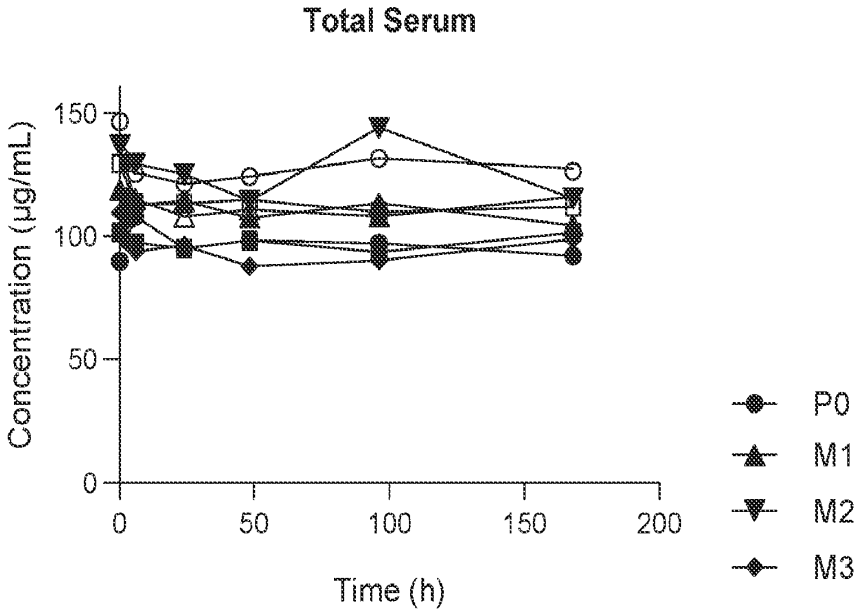

FIG. 11B

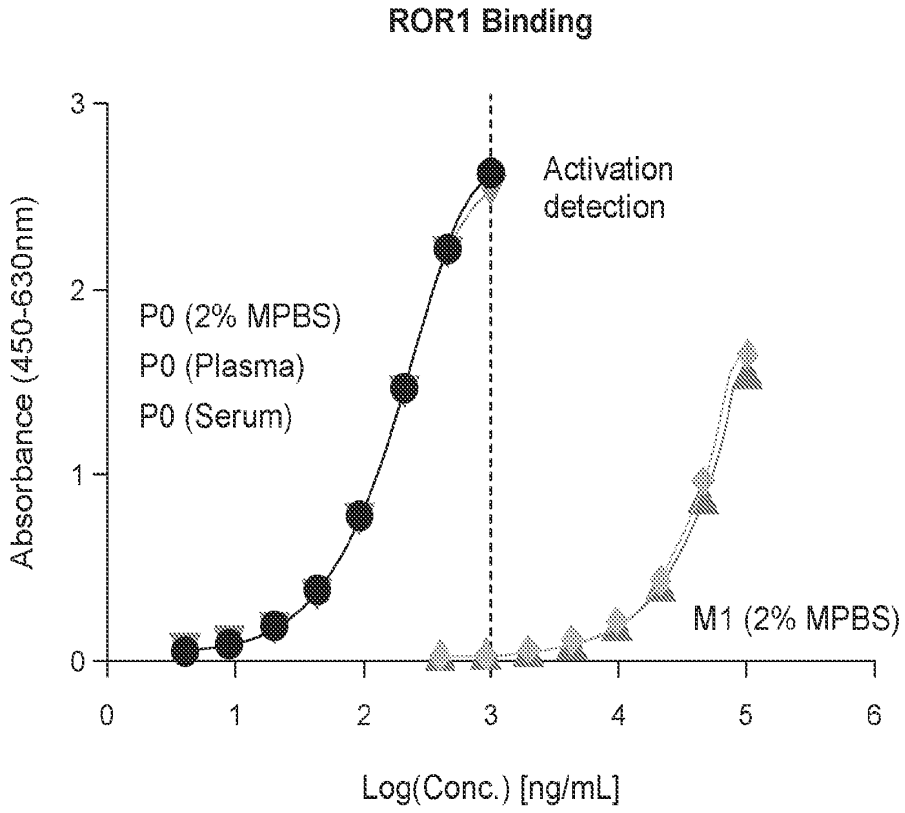
ROR1 Binding
Absorbance (450-630nm)
Log(Conc.) [ng/mL]
Activation detection
P0 (2% MPBS)
P0 (Plasma)
P0 (Serum)
M1 (2% MPBS)
0
1
2
3
4
5
6

FIG. 11C

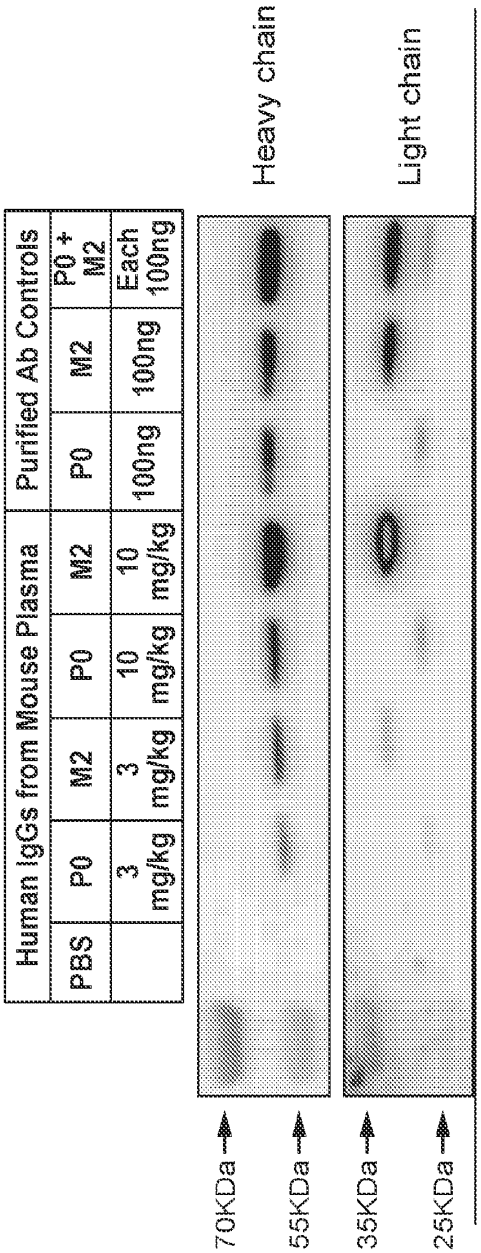
Human IgGs from Mouse Plasma
PBS
P0
3 mg/kg
M2
3 mg/kg
P0
10 mg/kg
M2
10 mg/kg
Purified Ab Controls
P0
100ng
M2
100ng
P0 + M2
Each 100ng
Heavy chain
Light chain
70KDa
55KDa
35KDa
25KDa

FIG. 12

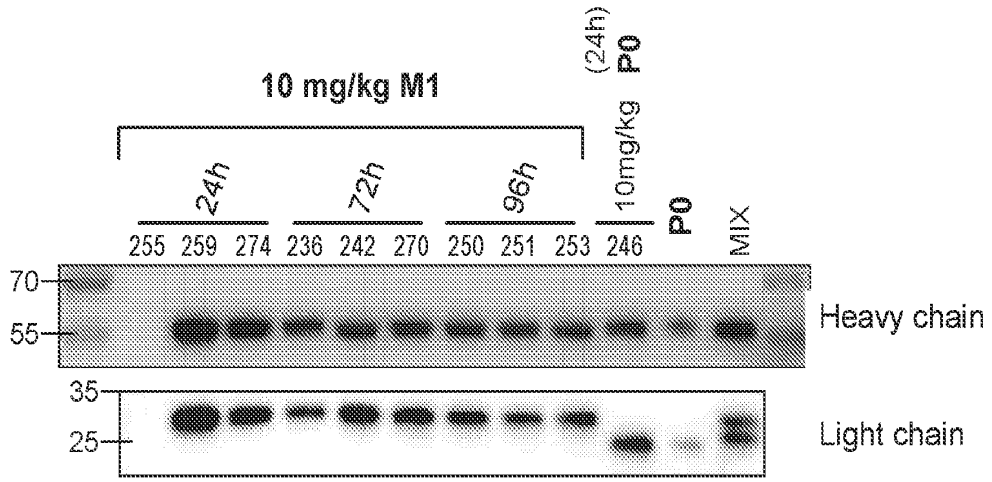

FIG. 13A

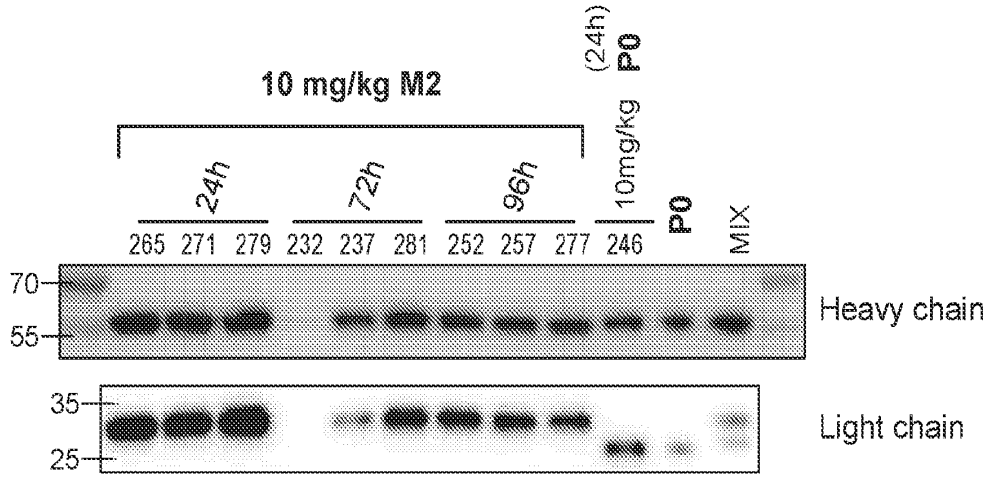

FIG. 13B

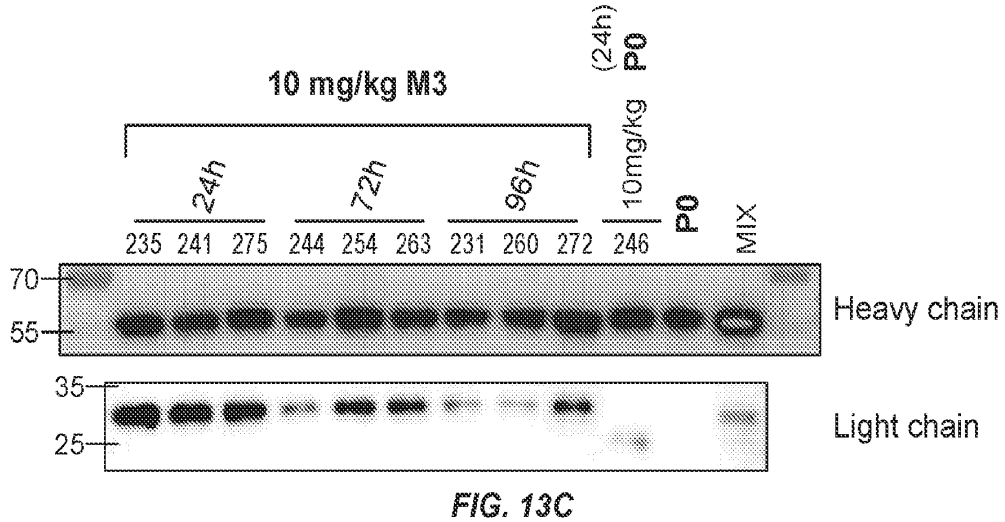

FIG. 13C

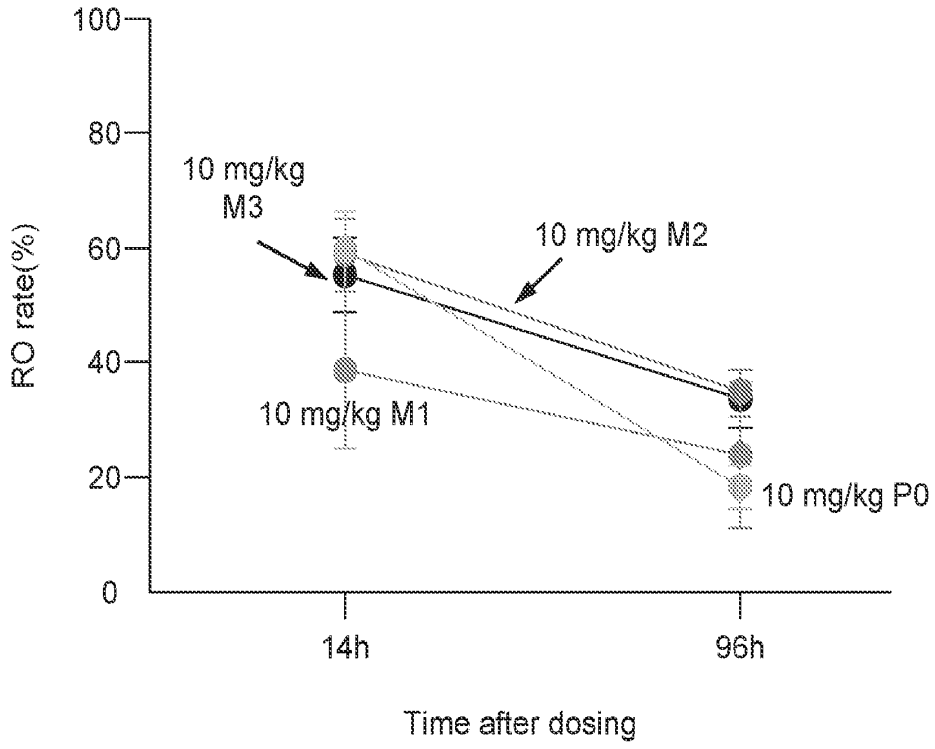
100
80
60
40
20
0
RO rate(%)
10 mg/kg
M3
10 mg/kg M2
10 mg/kg M1
10 mg/kg P0
14h
96h
Time after dosing

FIG. 14

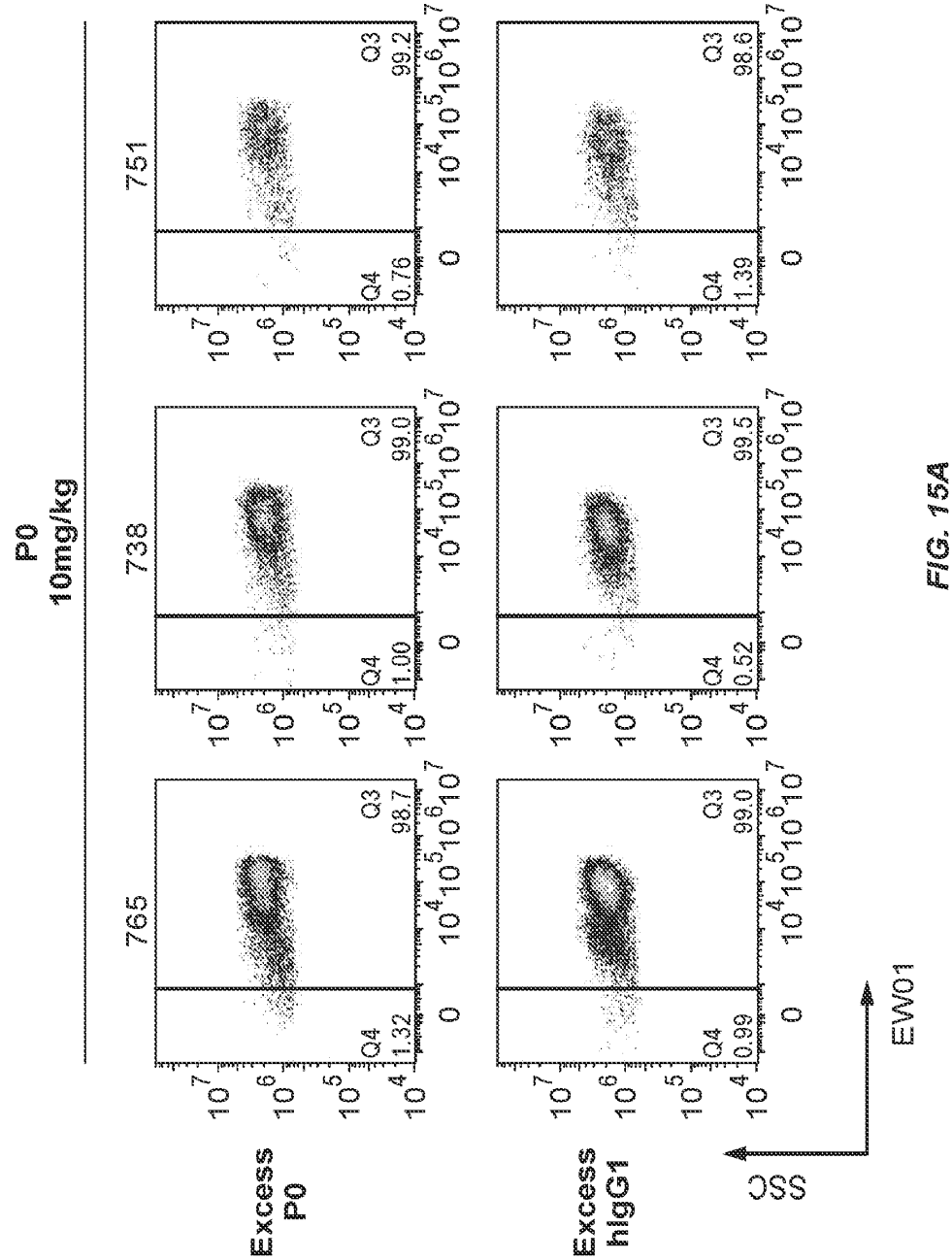
P0
10mg/kg
765
738
751
Excess P0
Excess hIgG1
SSC
EW01
Q3
Q4
98.7
1.32
99.0
1.00
99.2
0.76
99.0
0.99
99.5
0.52
98.6
1.39

FIG. 15A

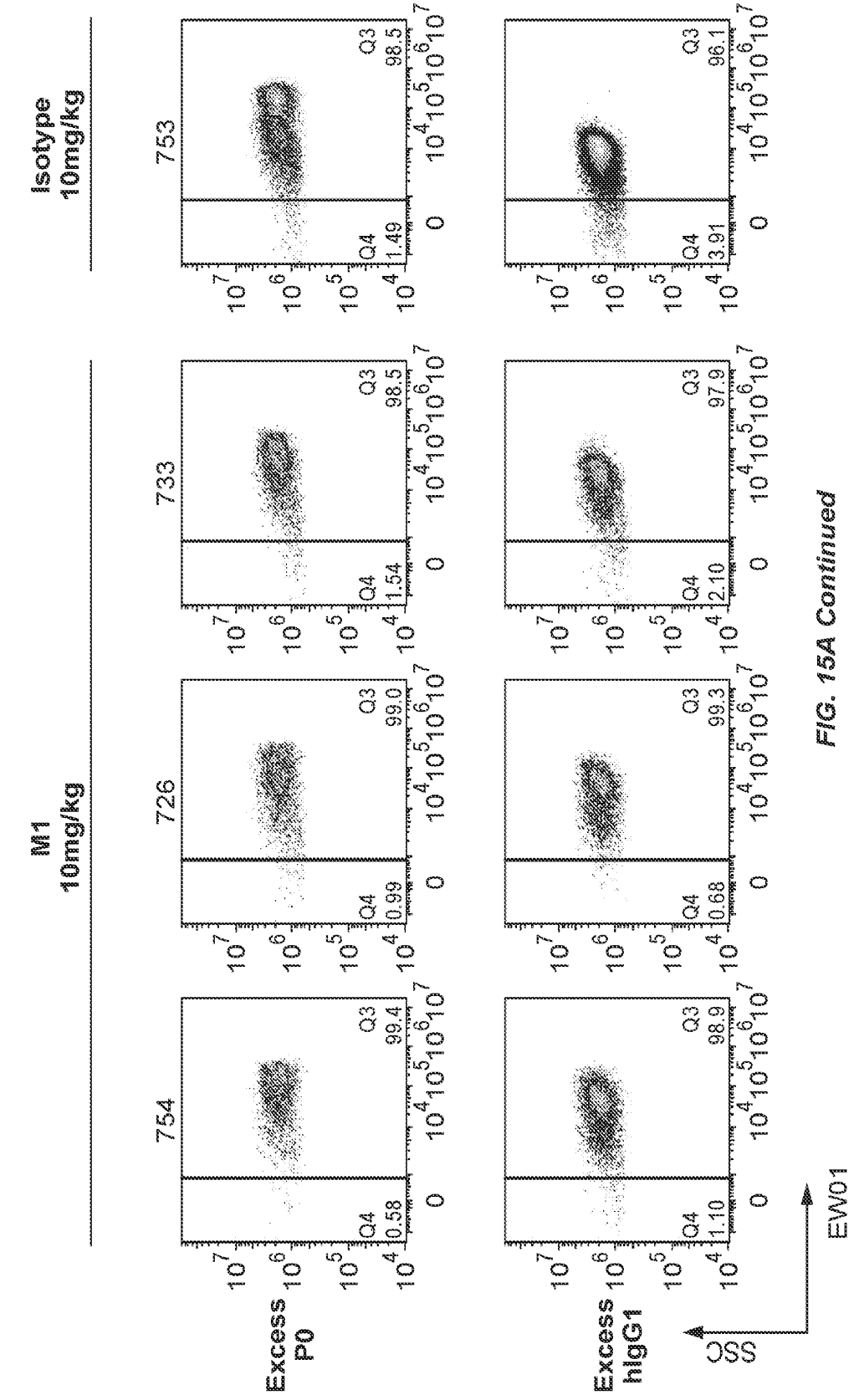

FIG. 15A Continued

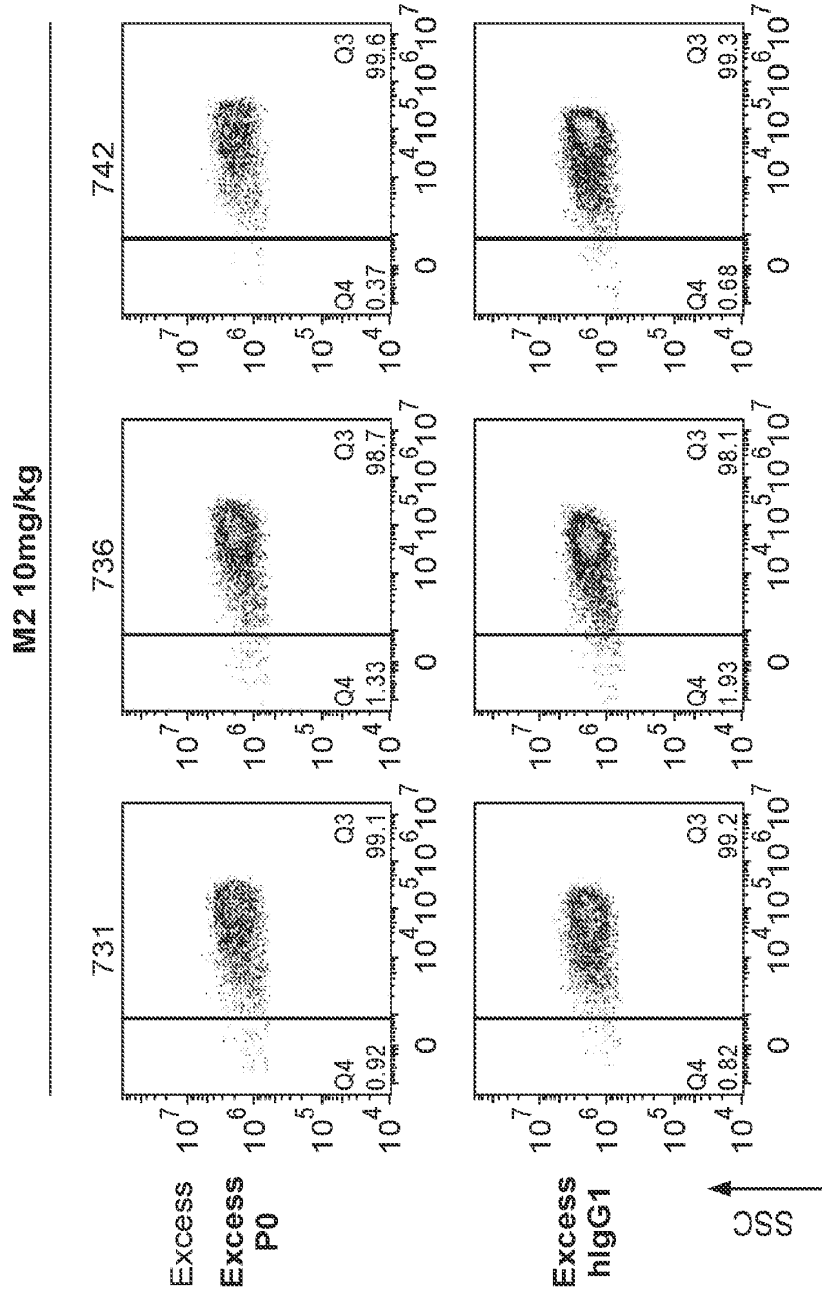
M2 10mg/kg
731
736
742
Excess
Excess P0
Excess hIgG1
SSC
EW01
Q4
Q3
0.92
99.1
1.33
98.7
0.37
99.6
0.82
99.2
1.93
98.1
0.68
99.3

FIG. 15B

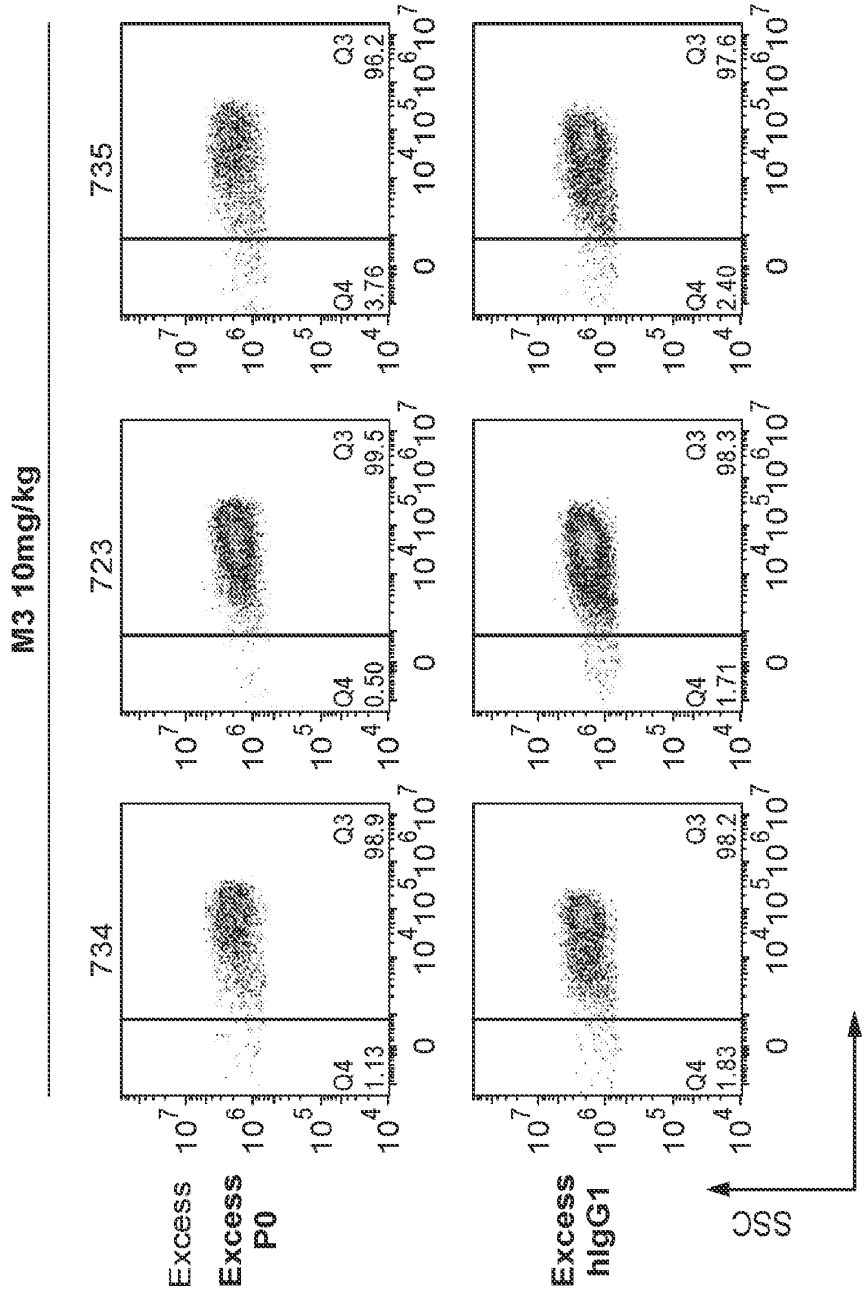

FIG. 15B Continued

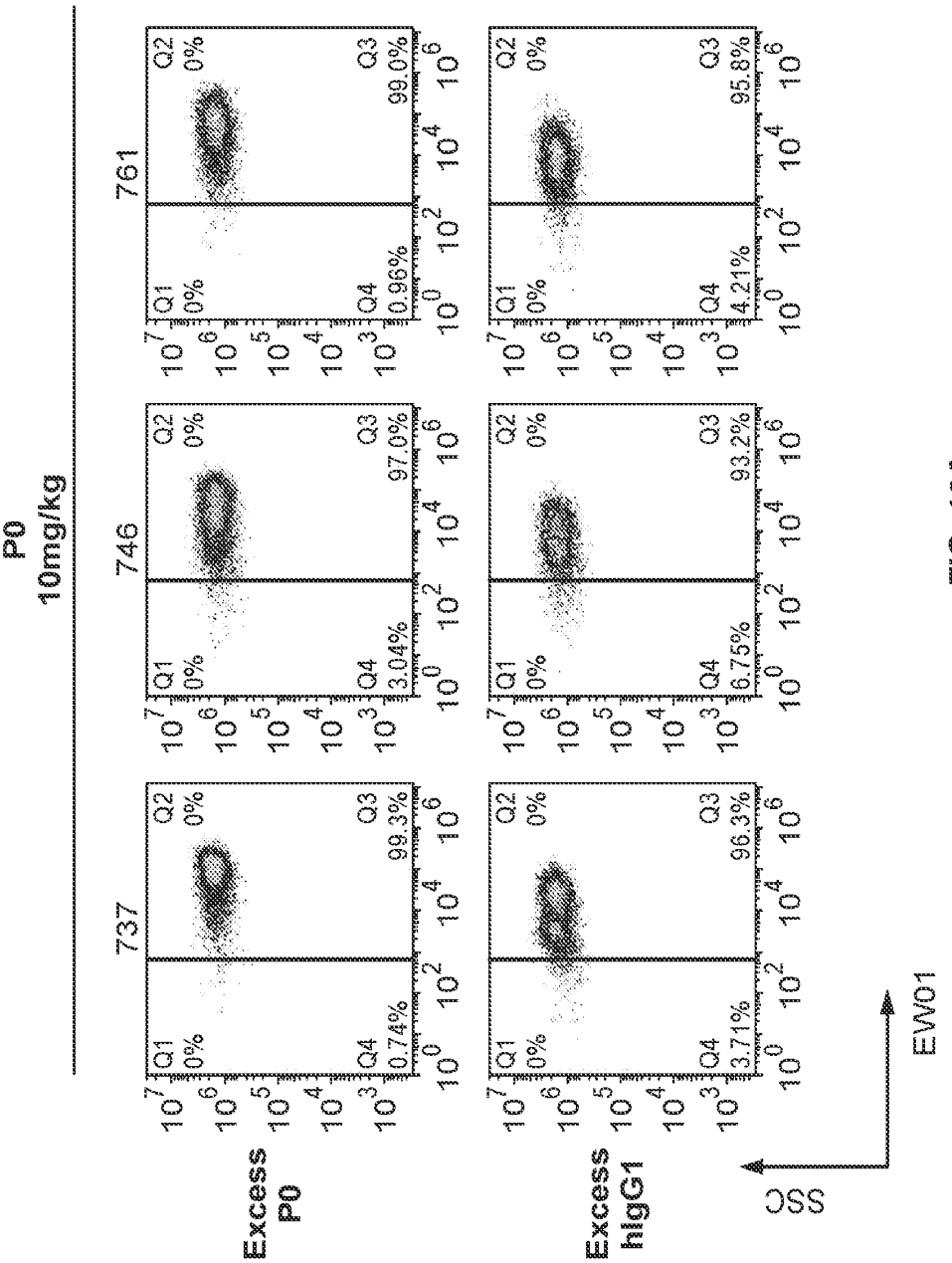
P0
10mg/kg
737
746
761
Excess P0
Excess hIgG1
Q1 0%
Q2 0%
Q3 99.3%
Q4 0.74%
Q3 97.0%
Q4 3.04%
Q3 99.0%
Q4 0.96%
Q3 96.3%
Q4 3.71%
Q3 93.2%
Q4 6.75%
Q3 95.8%
Q4 4.21%
SSC
EW01

FIG. 16A

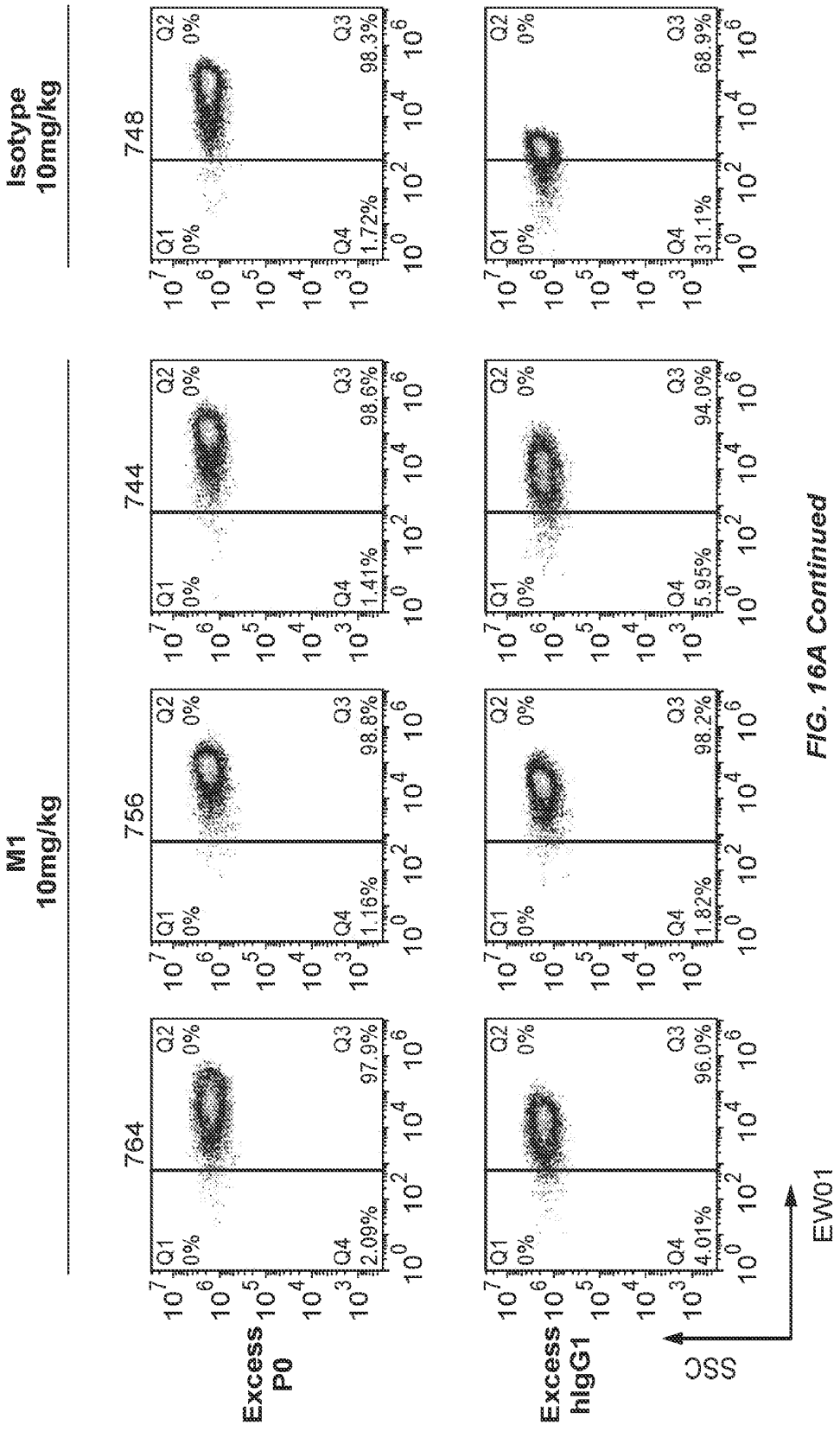

FIG. 16A Continued

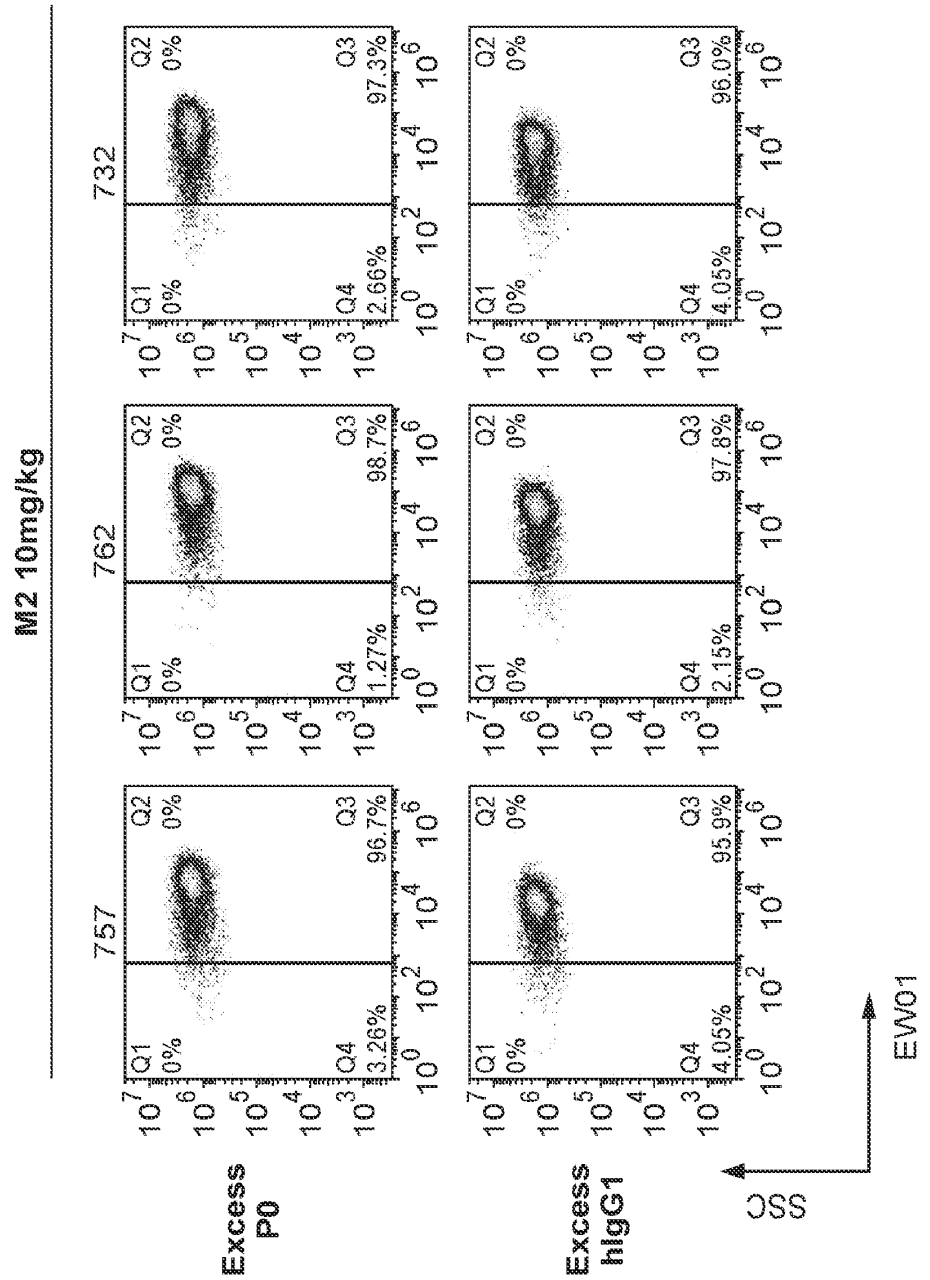
M2 10mg/kg
757
762
732
Excess P0
Excess hIgG1
Q1 0%
Q2 0%
Q3 96.7%
Q4 3.26%
Q3 98.7%
Q4 1.27%
Q3 97.3%
Q4 2.66%
Q3 95.9%
Q4 4.05%
Q3 97.8%
Q4 2.15%
Q3 96.0%
Q4 4.05%
SSC
FW01

FIG. 16B

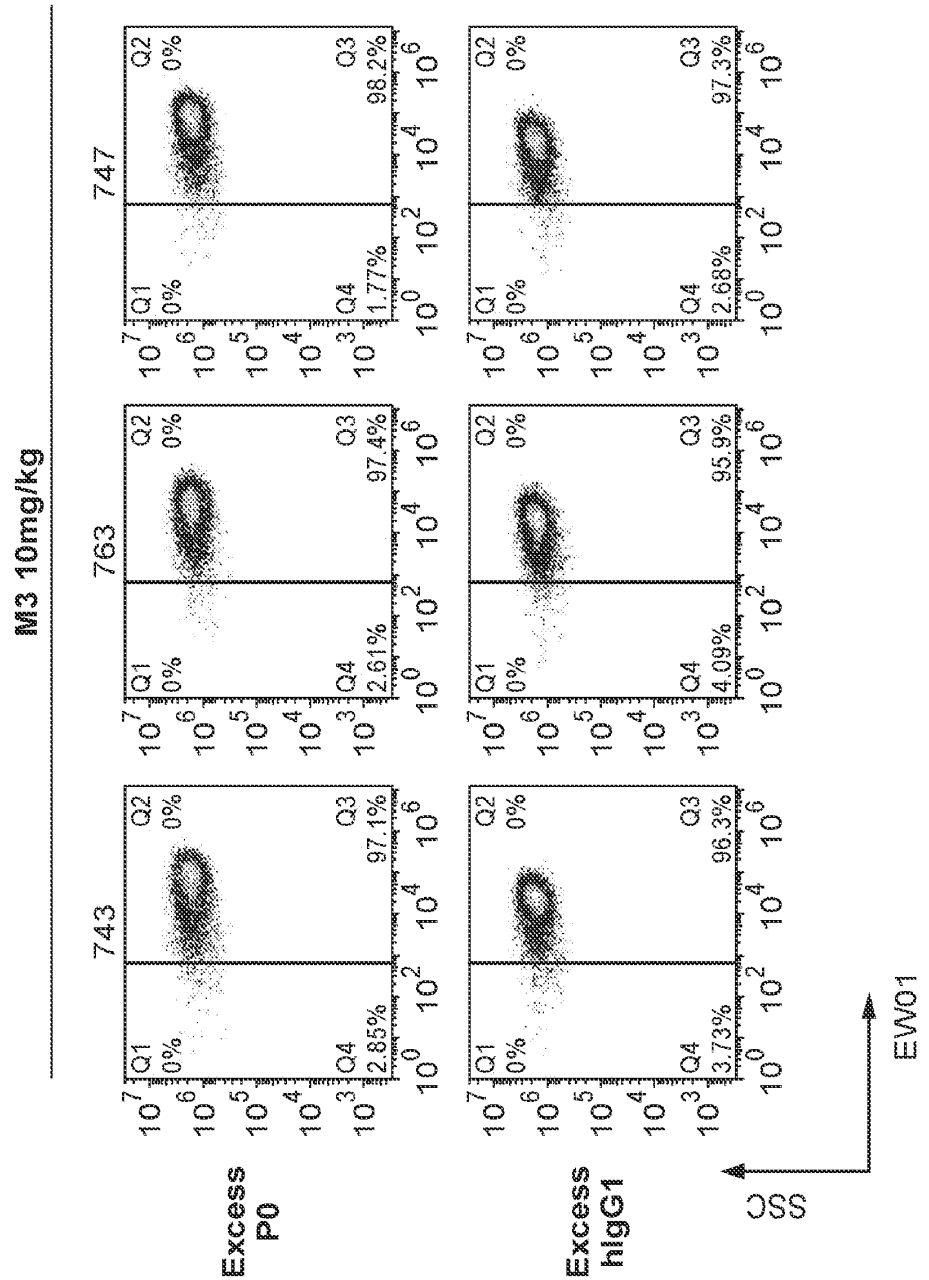

FIG. 16B Continued

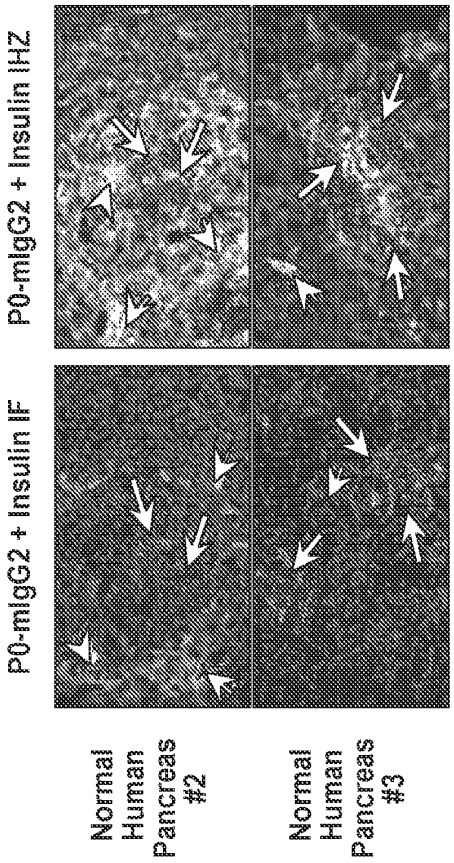
P0-mIgG2 + Insulin IF
P0-mIgG2 + Insulin IHZ
Normal Human Pancreas #2
Normal Human Pancreas #3

FIG. 17

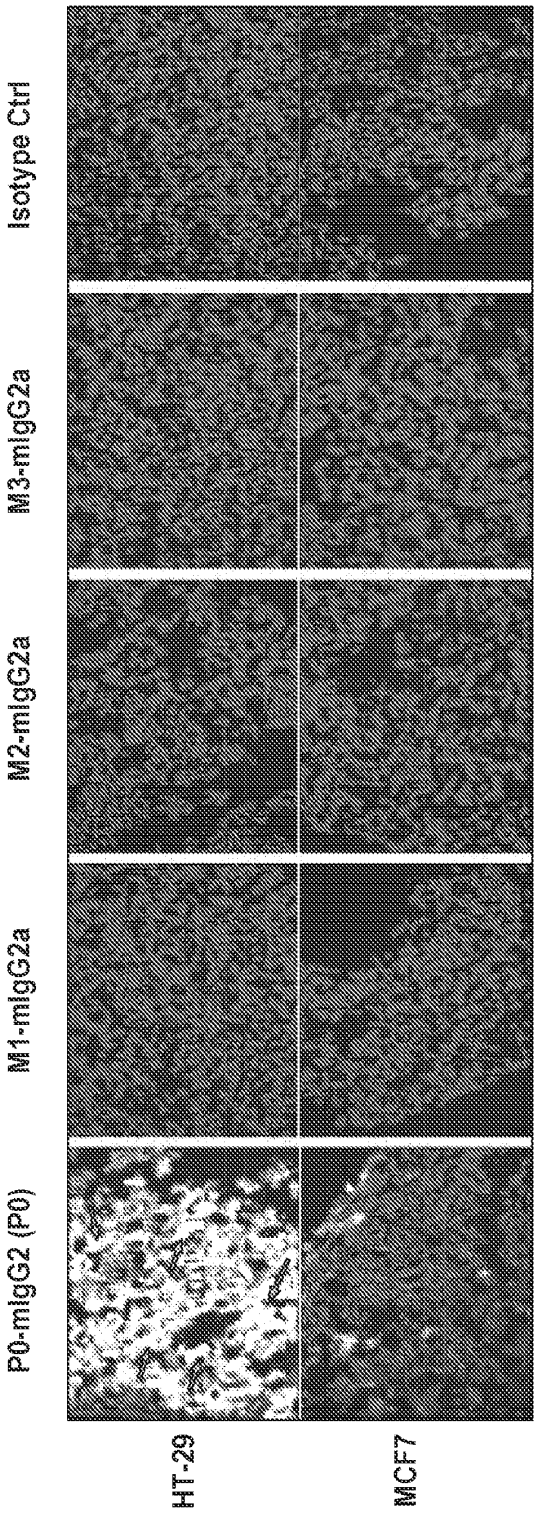
P0-mIgG2 (P0)
M1-mIgG2a
M2-mIgG2a
M3-mIgG2a
Isotype Ctrl
HT-29
MCF7

FIG. 18A

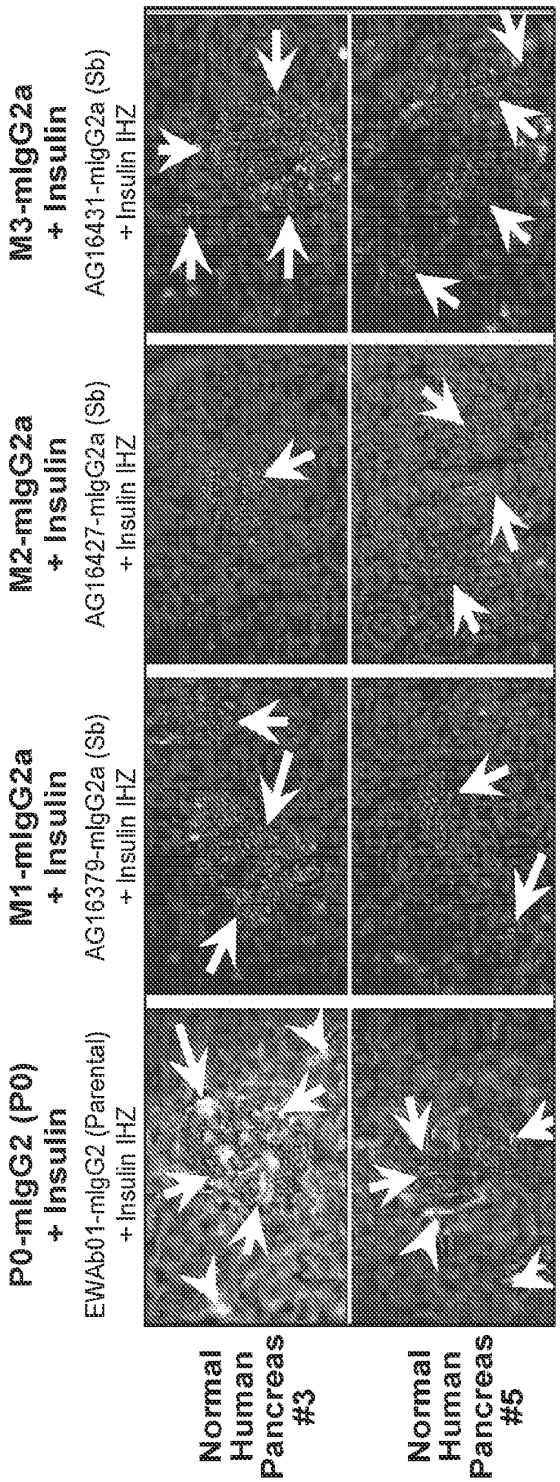
P0-mIgG2 (P0)
+ Insulin
EWAb01-mIgG2 (Parental)
+ Insulin IHZ
M1-mIgG2a
+ Insulin
AG16379-mIgG2a (Sb)
+ Insulin IHZ
M2-mIgG2a
+ Insulin
AG16427-mIgG2a (Sb)
+ Insulin IHZ
M3-mIgG2a
+ Insulin
AG16431-mIgG2a (Sb)
+ Insulin IHZ
Normal Human Pancreas #3
Normal Human Pancreas #5

FIG. 18B

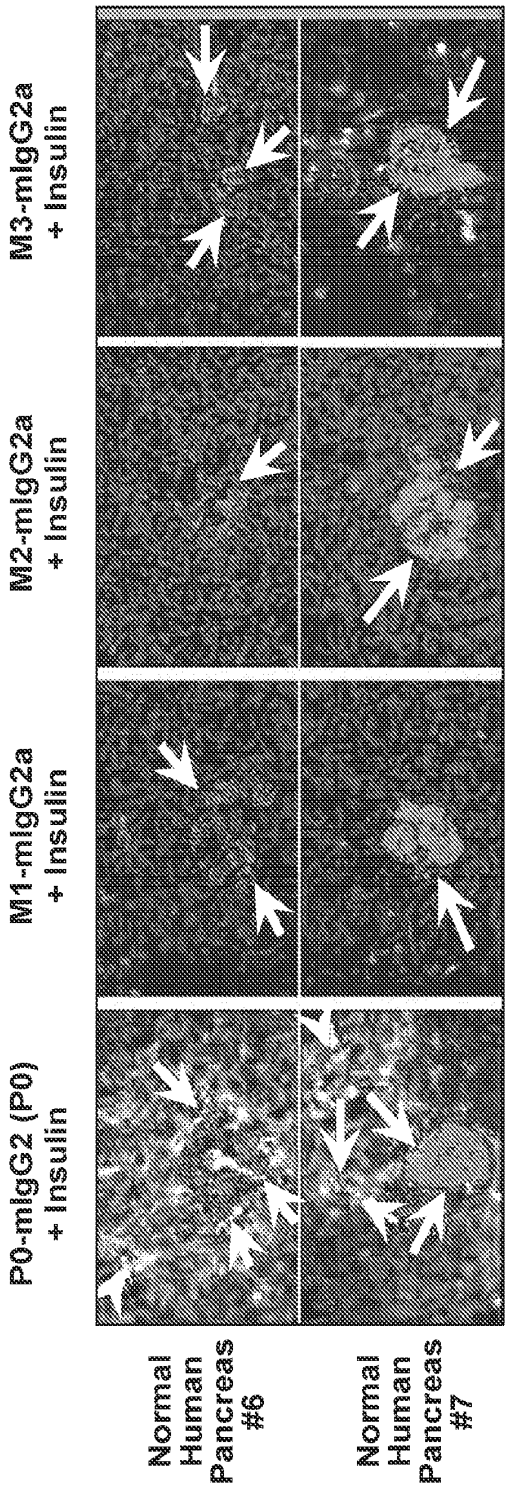
P0-mIgG2 (P0)
+ Insulin
M1-mIgG2a
+ Insulin
M2-mIgG2a
+ Insulin
M3-mIgG2a
+ Insulin
Normal Human Pancreas #6
Normal Human Pancreas #7

FIG. 18C

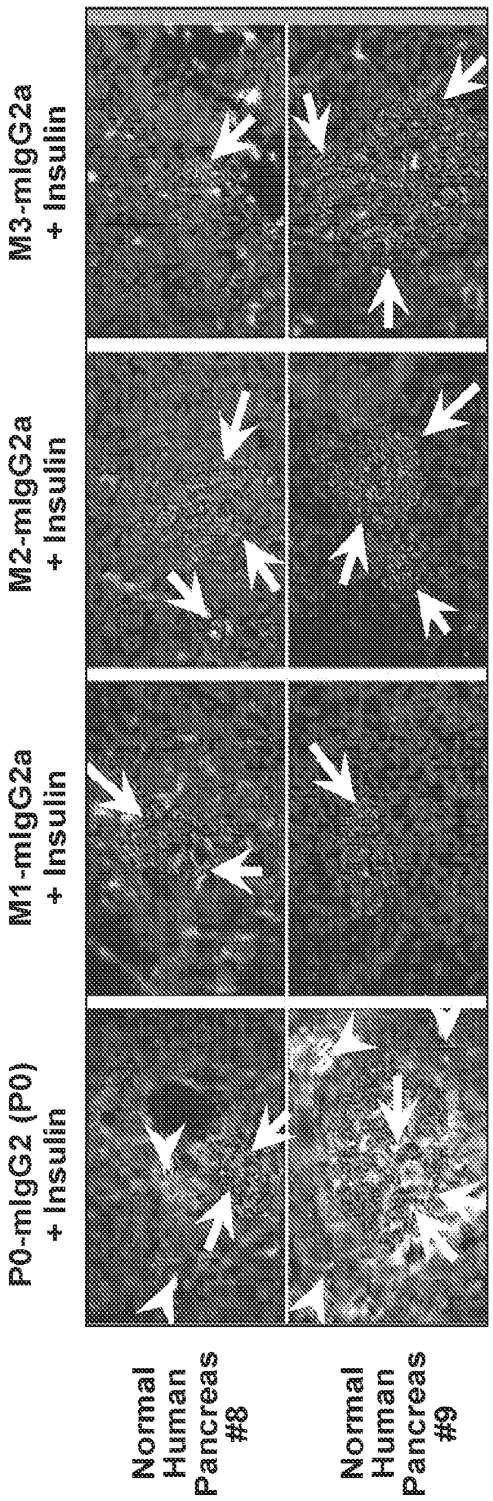
P0-mIgG2 (P0)
+ Insulin
M1-mIgG2a
+ Insulin
M2-mIgG2a
+ Insulin
M3-mIgG2a
+ Insulin
Normal
Human
Pancreas
#8
Normal
Human
Pancreas
#9

FIG. 18D