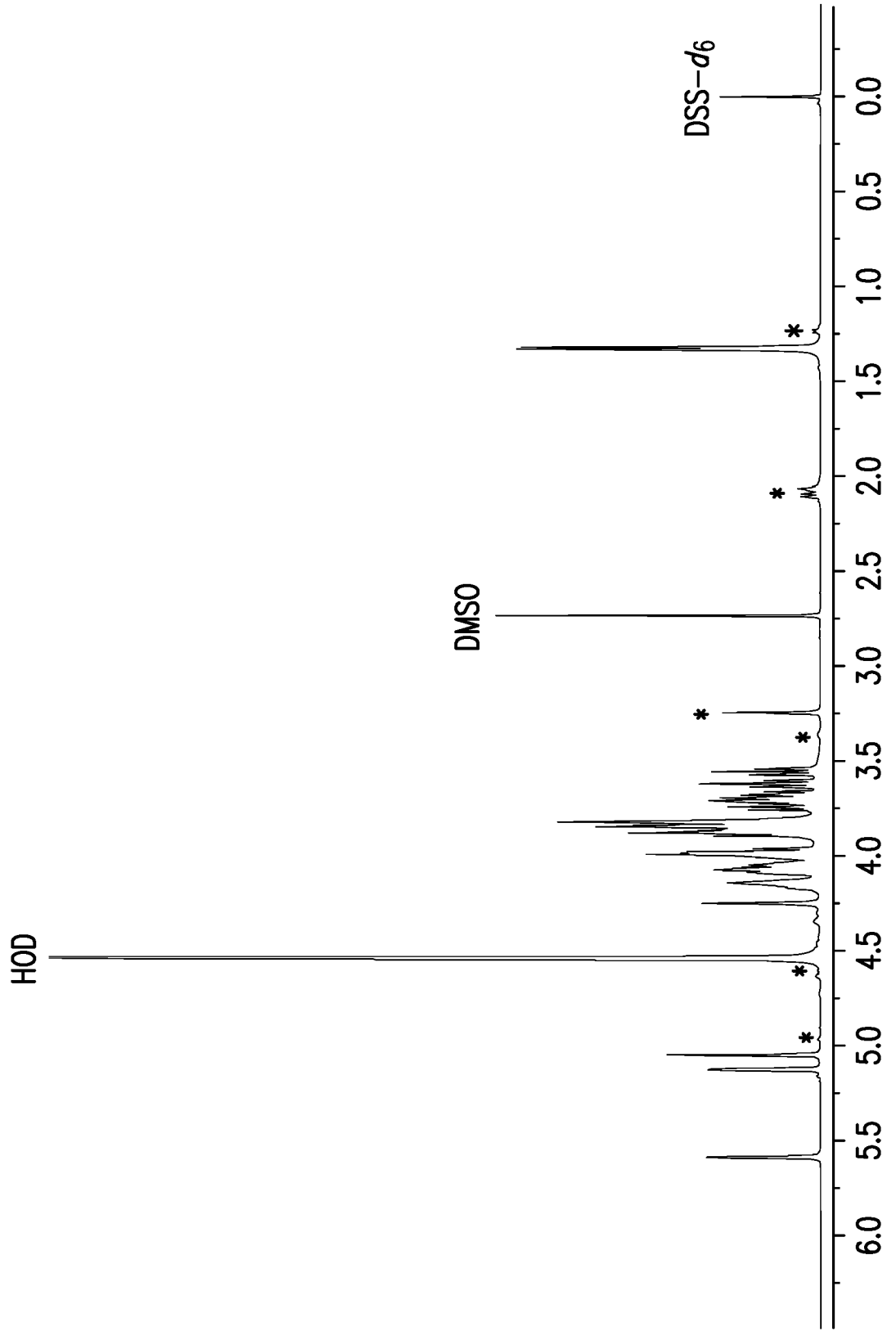


FIG. 1

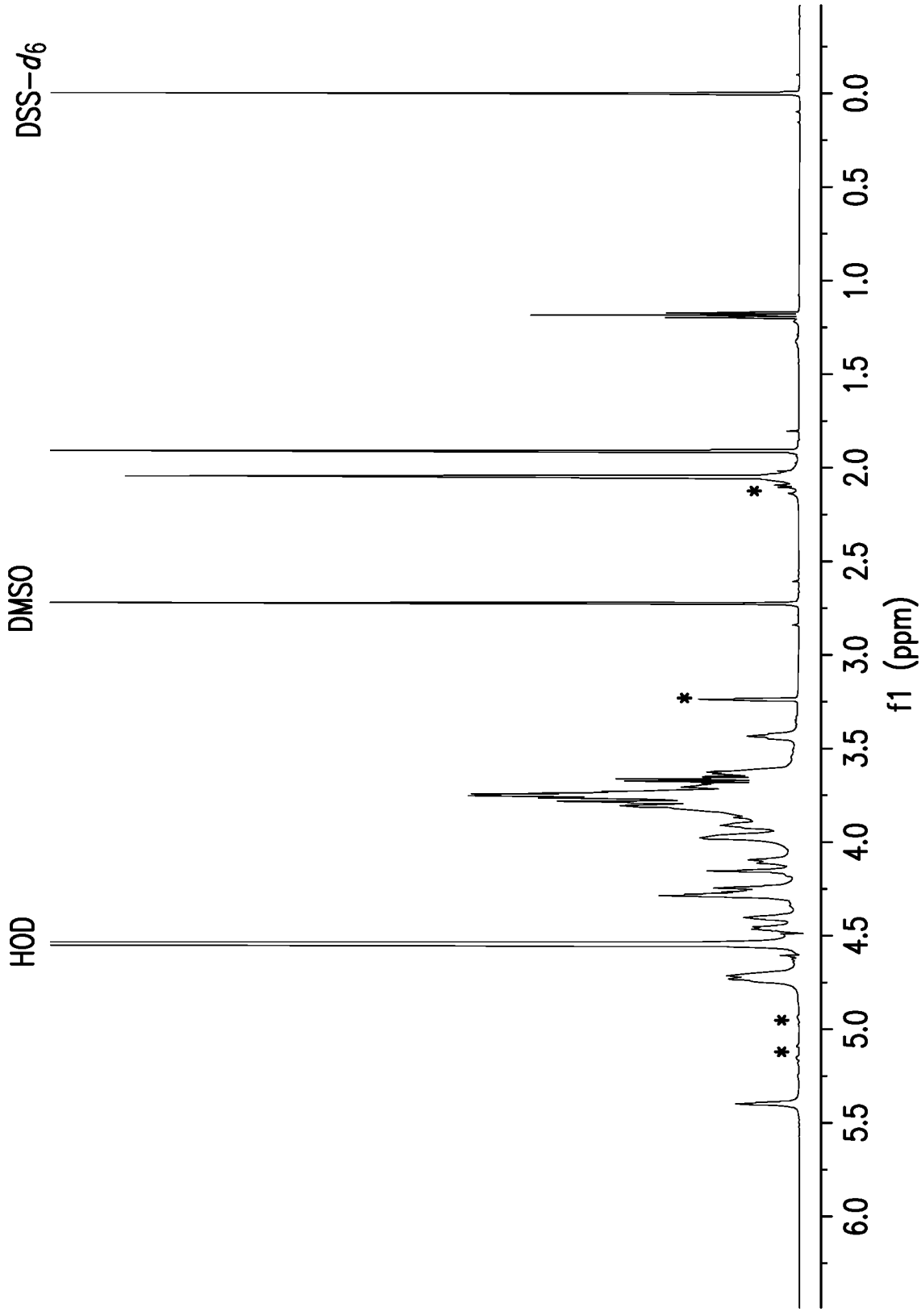


FIG.2

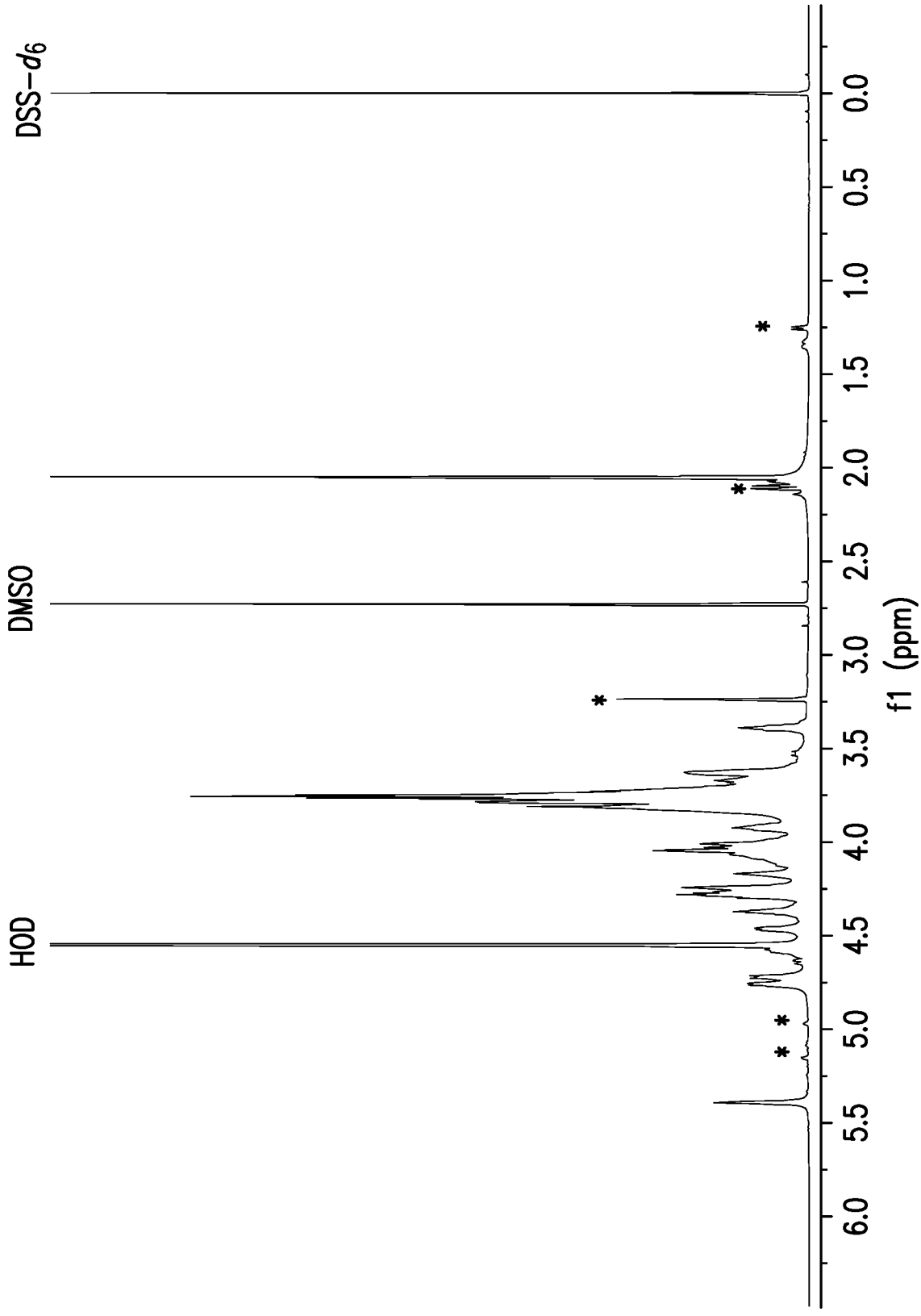


FIG.3

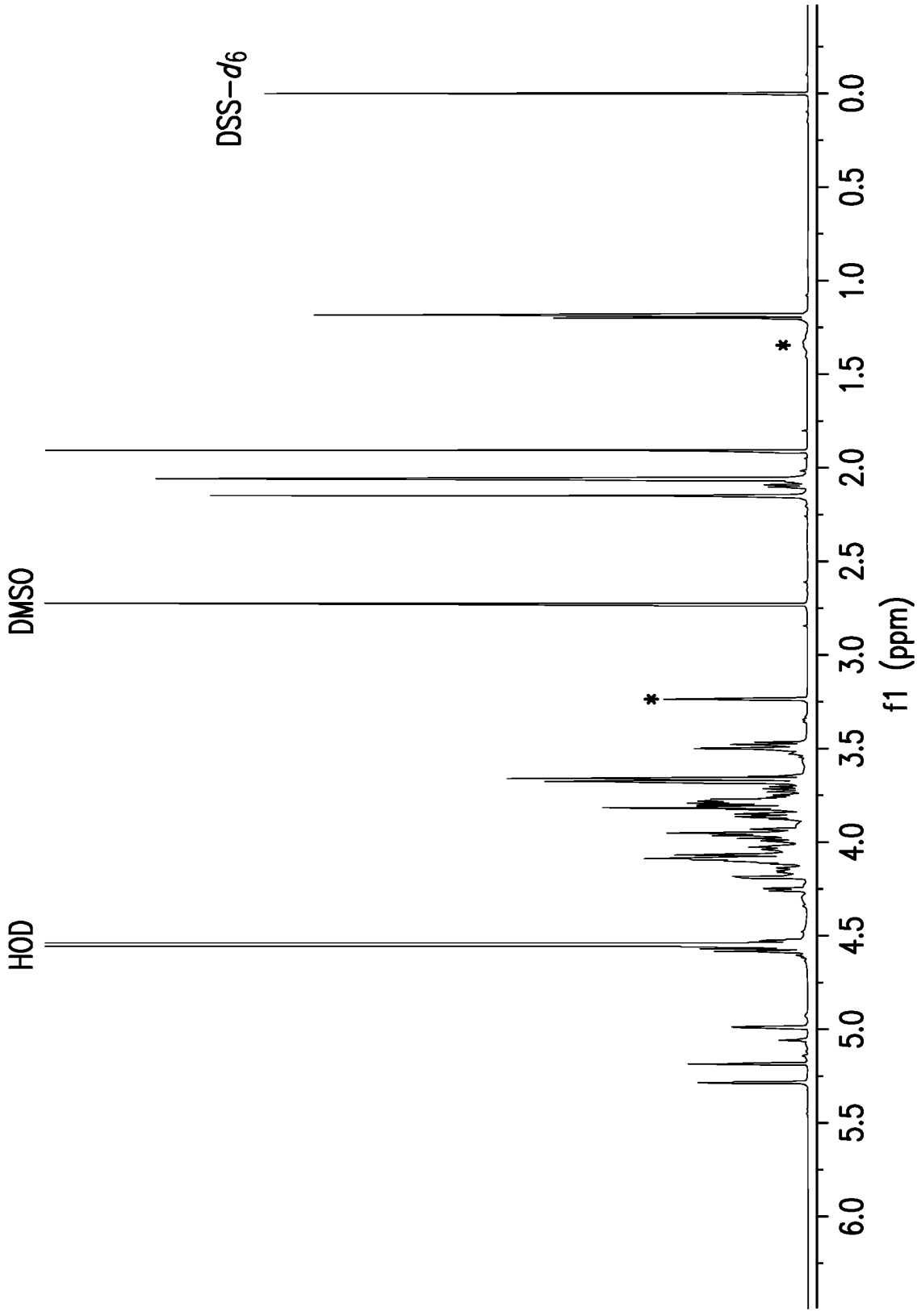


FIG.4

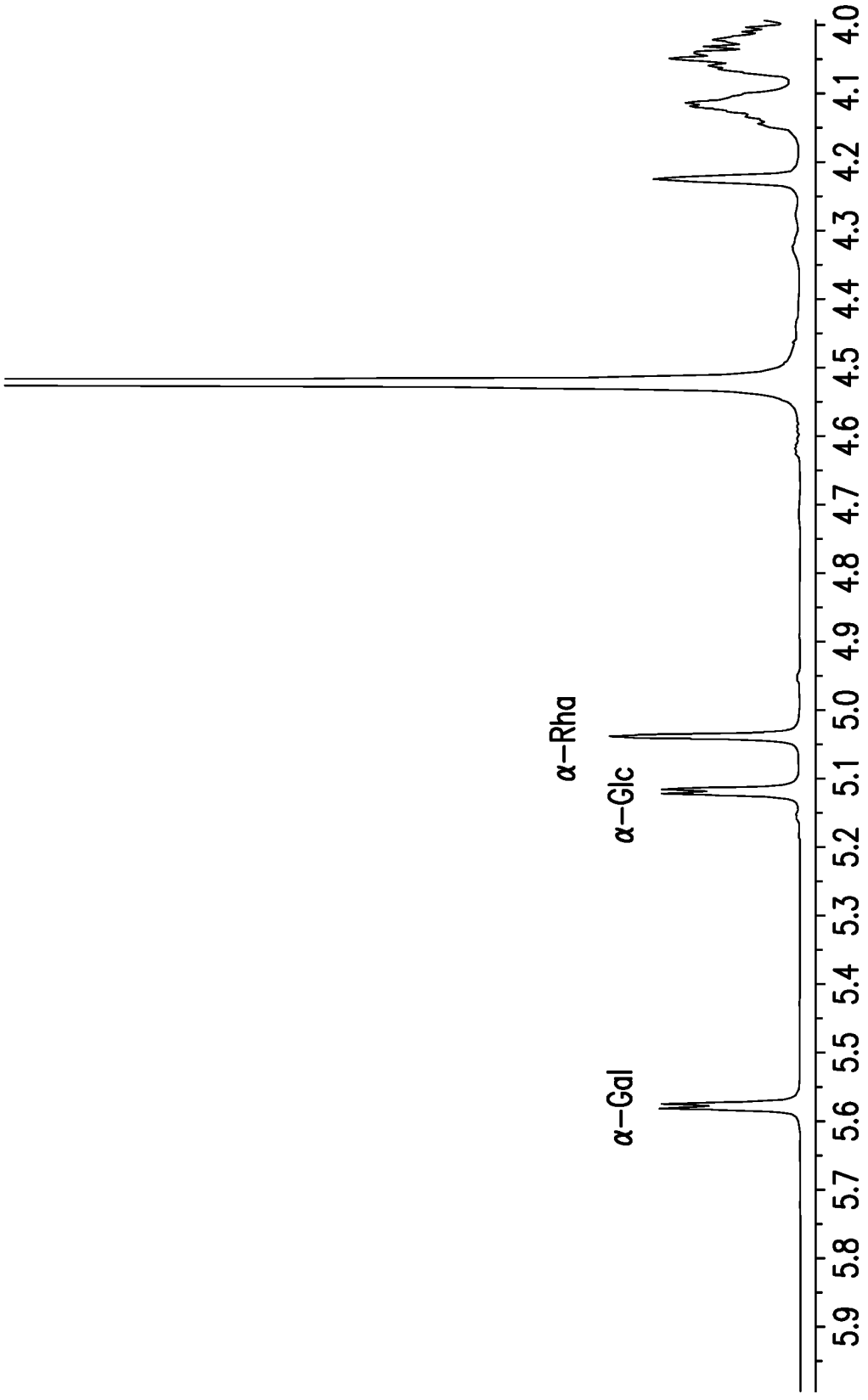

α−Rha
α−Glc
α−Gal
5.9 5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0
f1 (ppm)

FIG.5

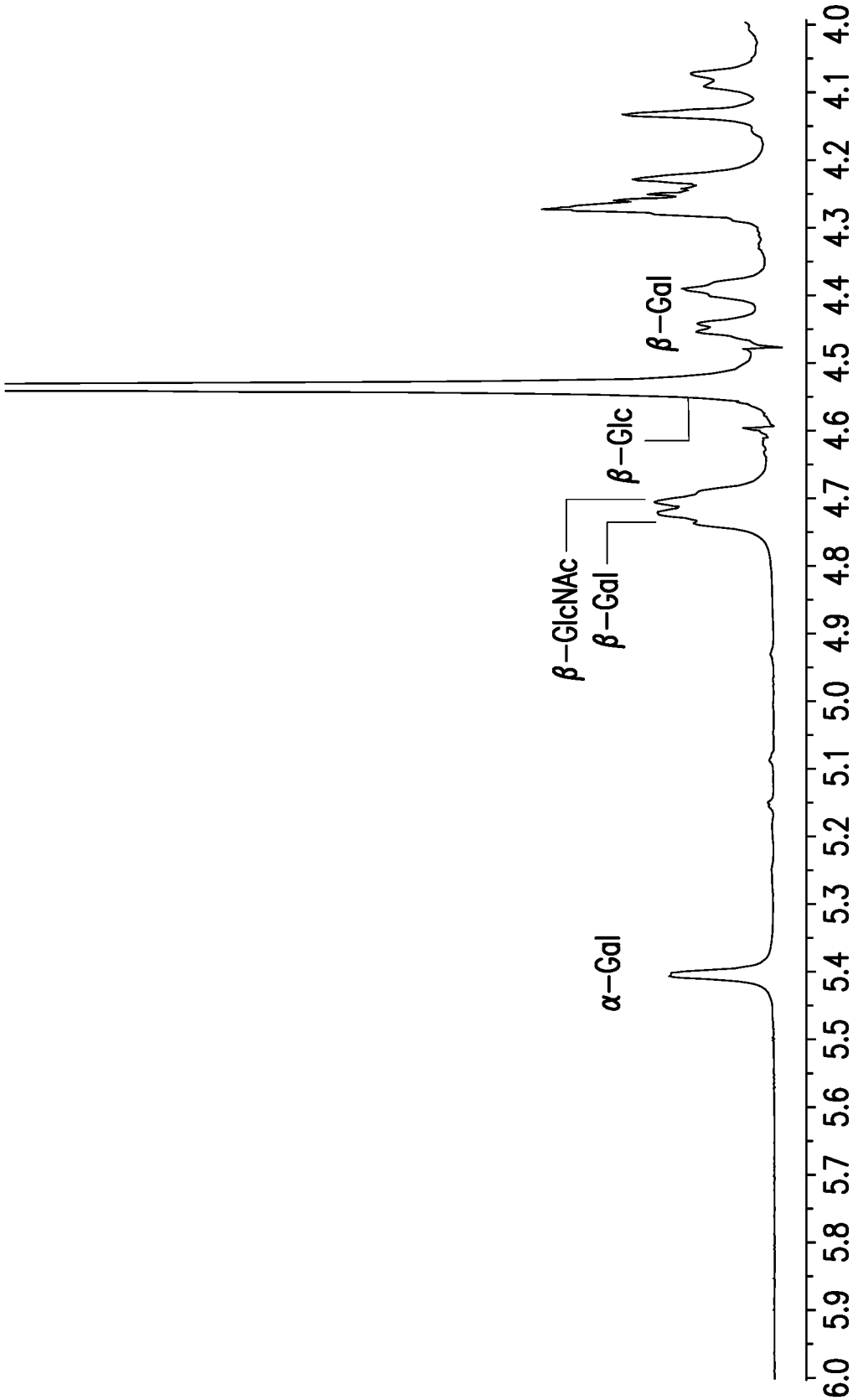

β–Gal
β–Glc
β–GlcNAc
β–Gal
α–Gal
6.0 5.9 5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0
f1 (ppm)

FIG.6

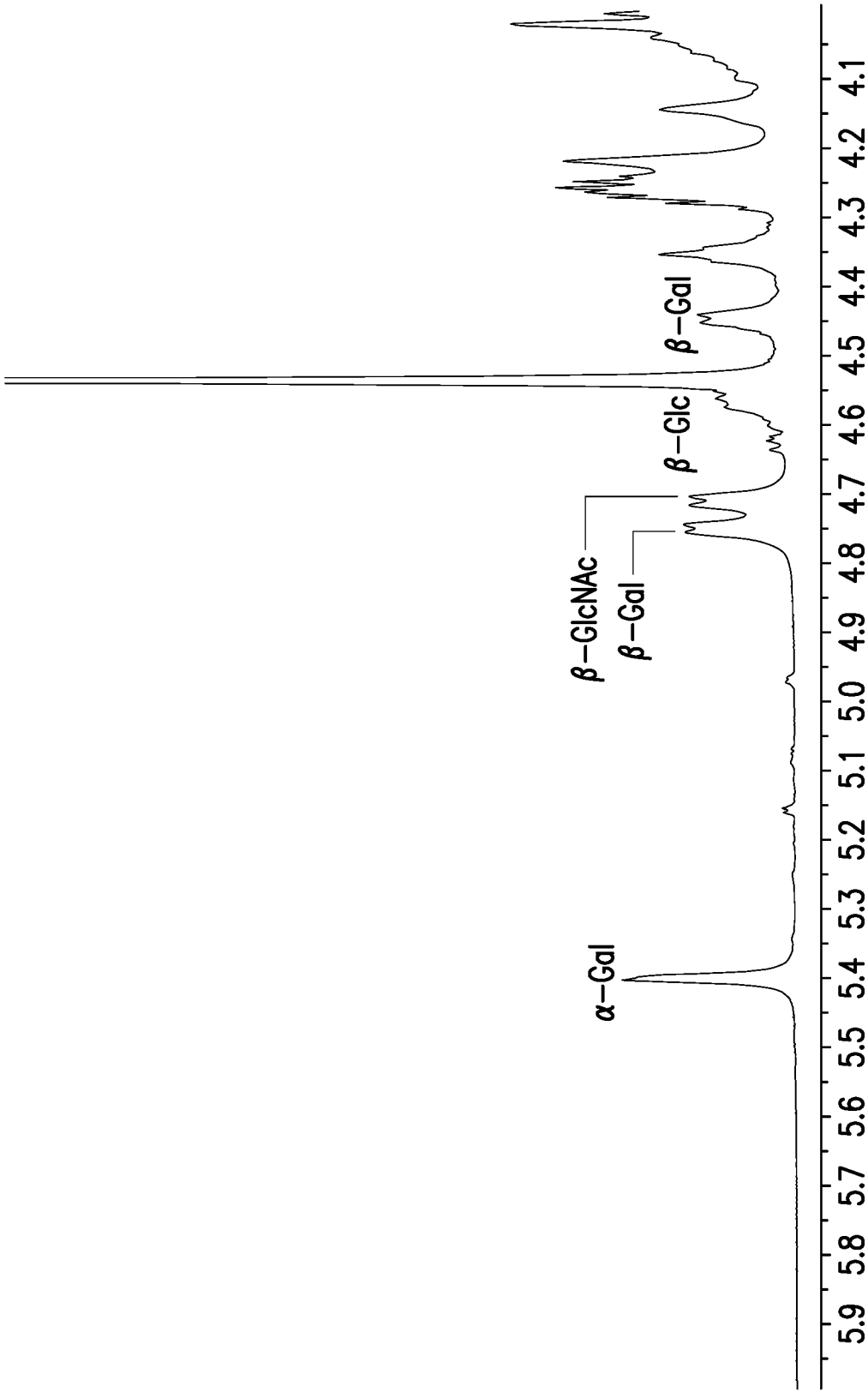

α–Gal
β–GlcNAc
β–Gal
β–Glc
β–Gal
5.9 5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1
f1 (ppm)

FIG. 7

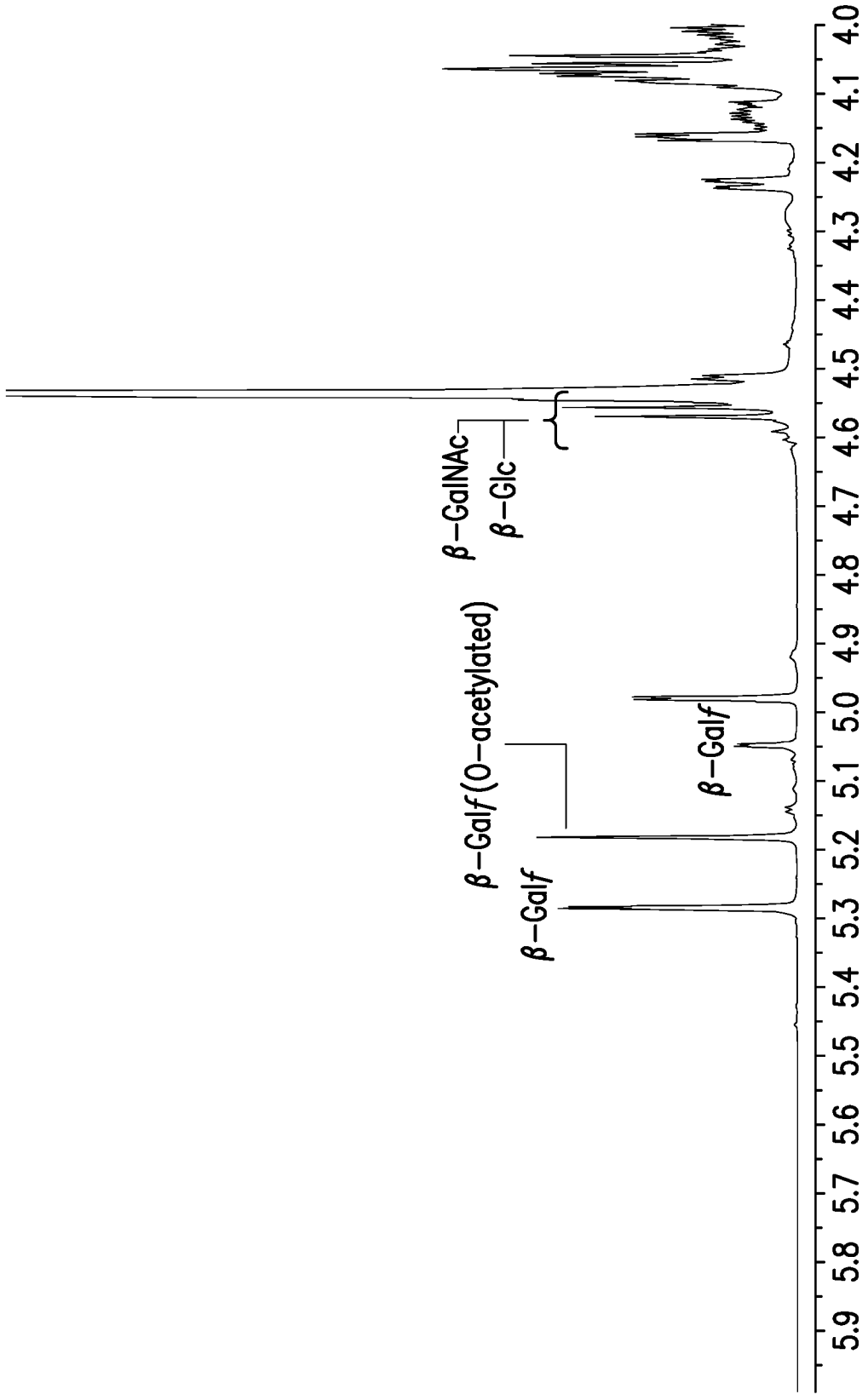

β-GalNAc
β-Glc
β-Galf(O-acetylated)
β-Galf
β-Galf
5.9 5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0
f1 (ppm)

FIG.8

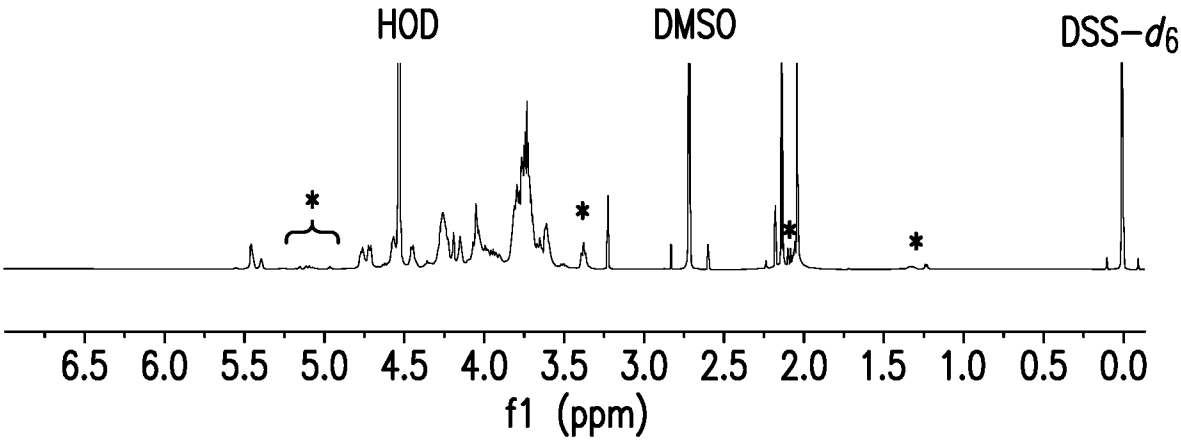


FIG.9A

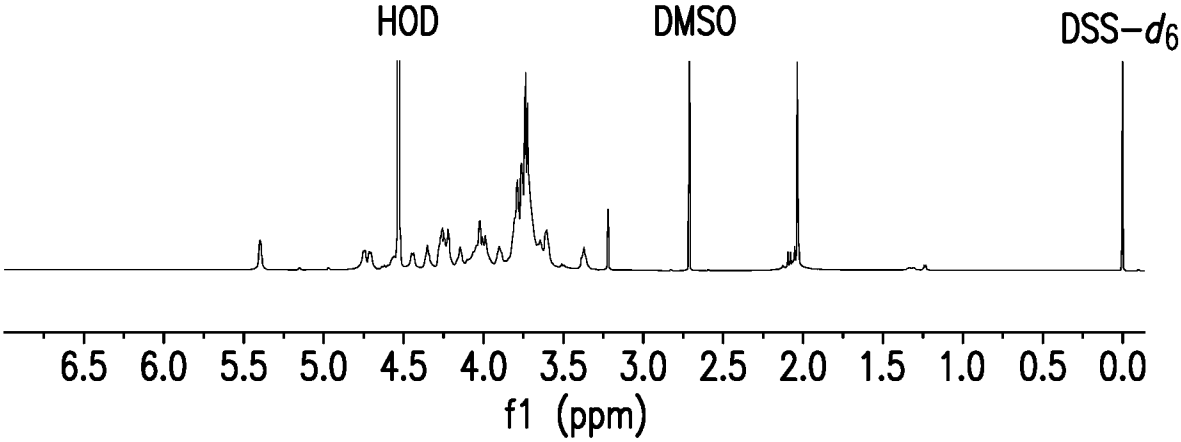


FIG.9B

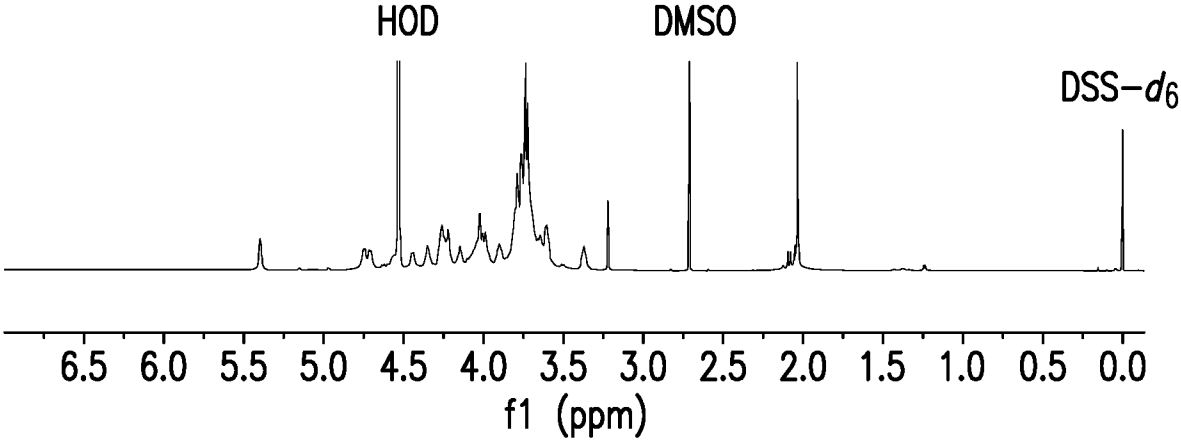


FIG.9C

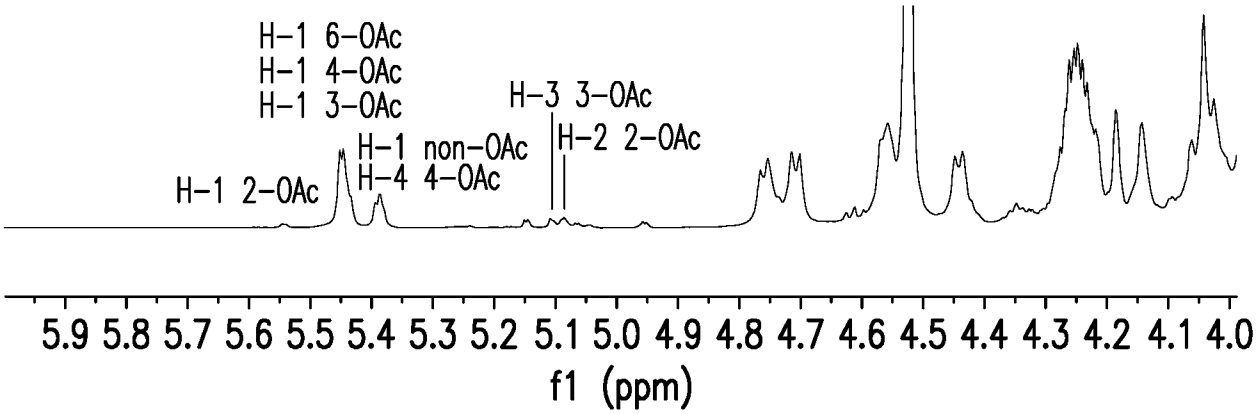


FIG.10A

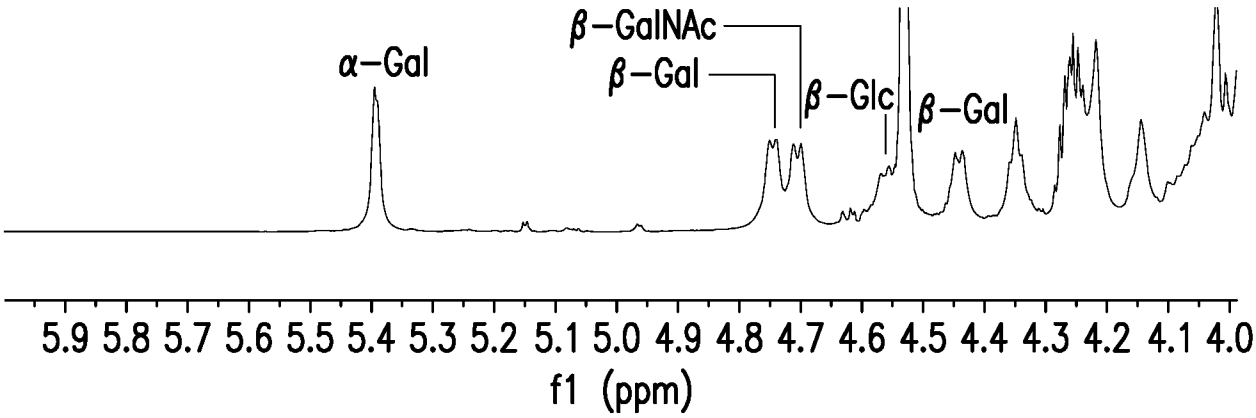


FIG.10B

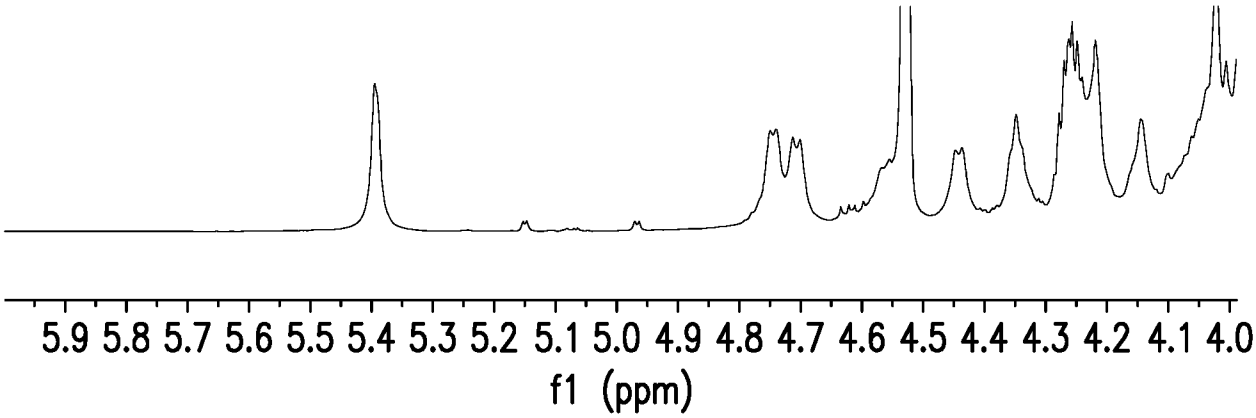


FIG.10C

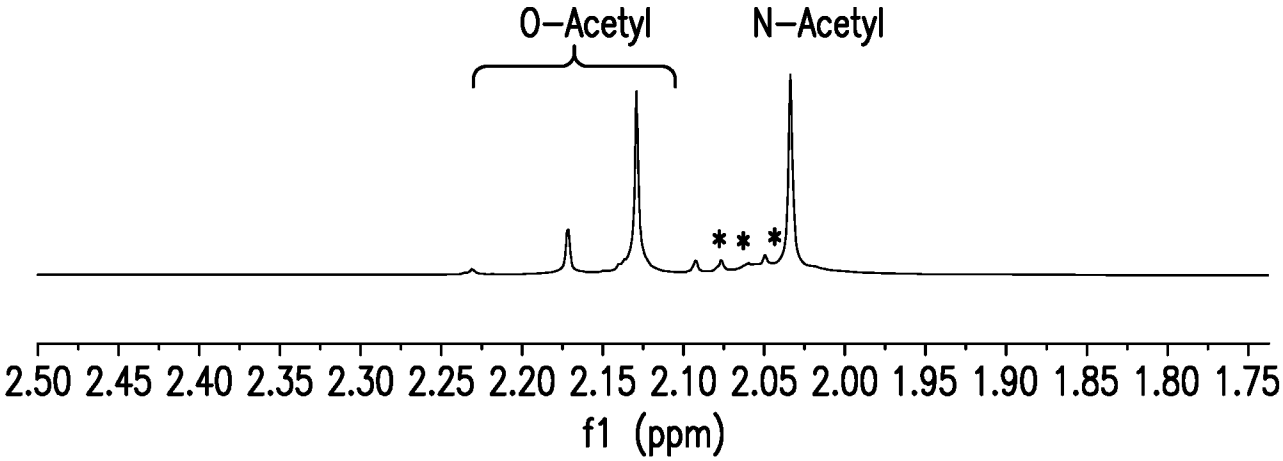


FIG.10D

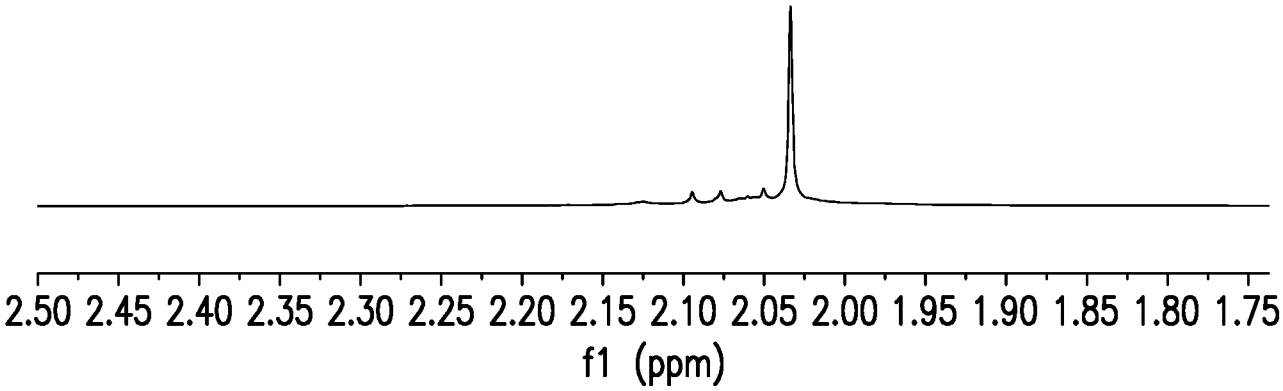


FIG.10E

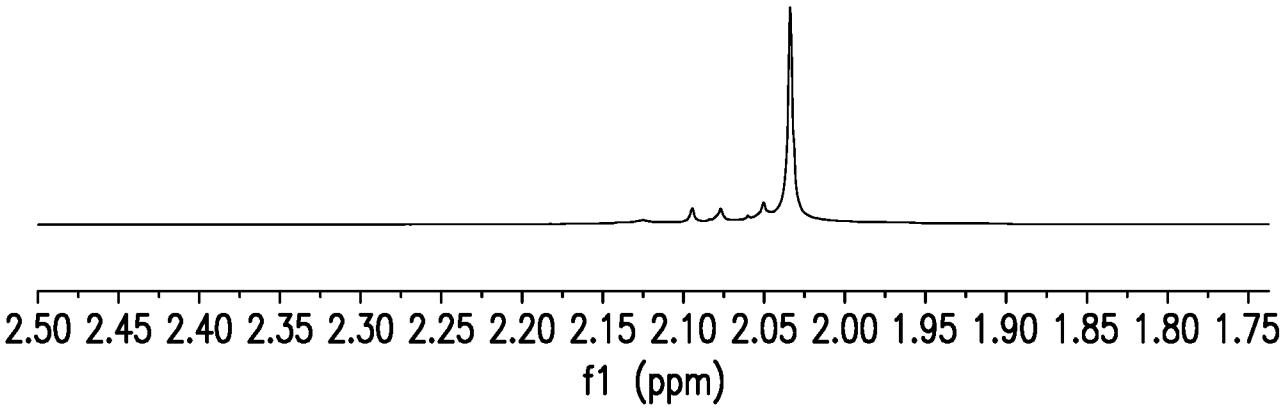


FIG.10F

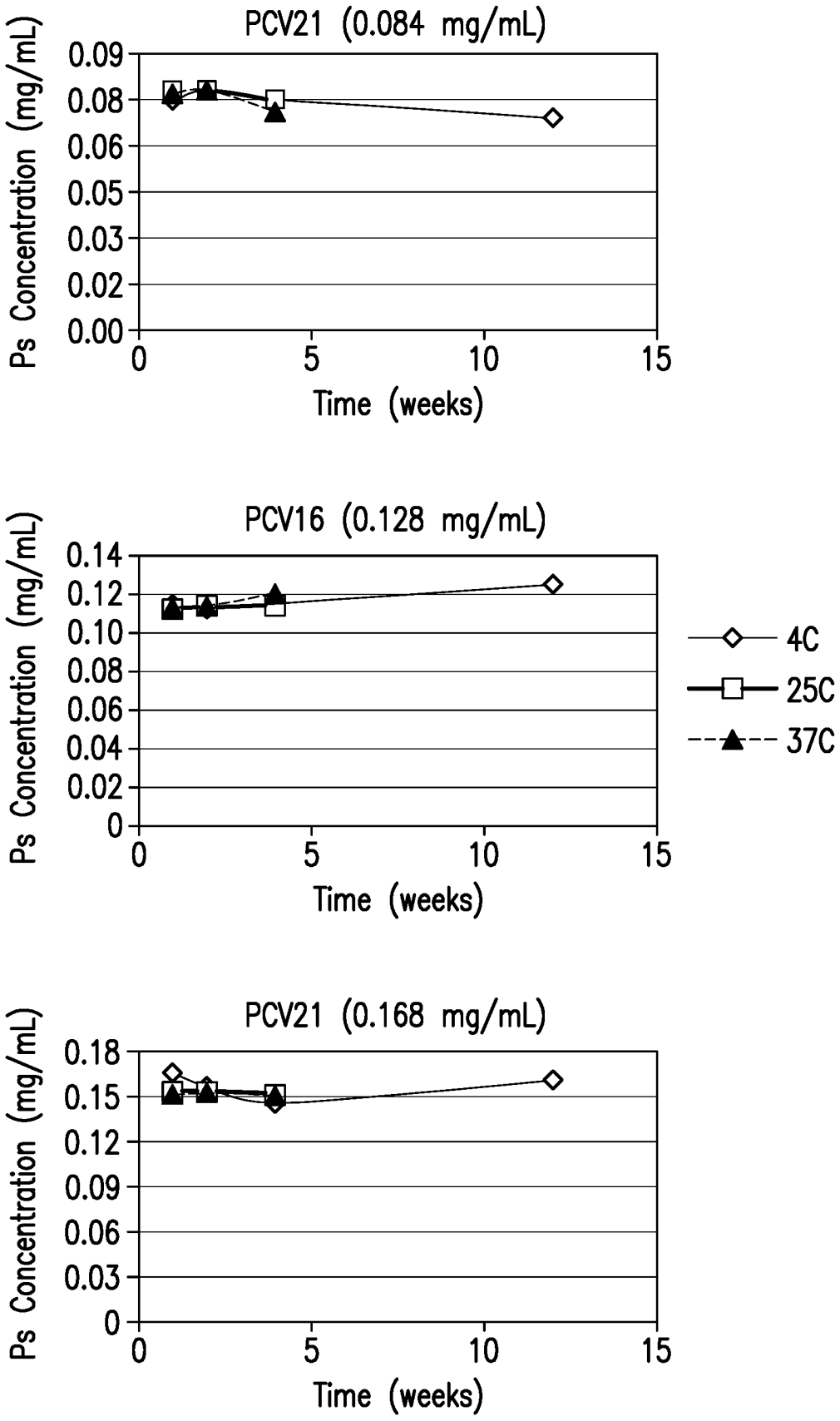

PCV21 (0.084 mg/mL)
Ps Concentration (mg/mL)
0.09
0.08
0.06
0.05
0.03
0.02
0.00
0
5
10
15
Time (weeks)
PCV16 (0.128 mg/mL)
Ps Concentration (mg/mL)
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0
Time (weeks)
4C
25C
37C
PCV21 (0.168 mg/mL)
Ps Concentration (mg/mL)
0.18
0.15
0.12
0.09
0.06
0.03
0
Time (weeks)

FIG.11

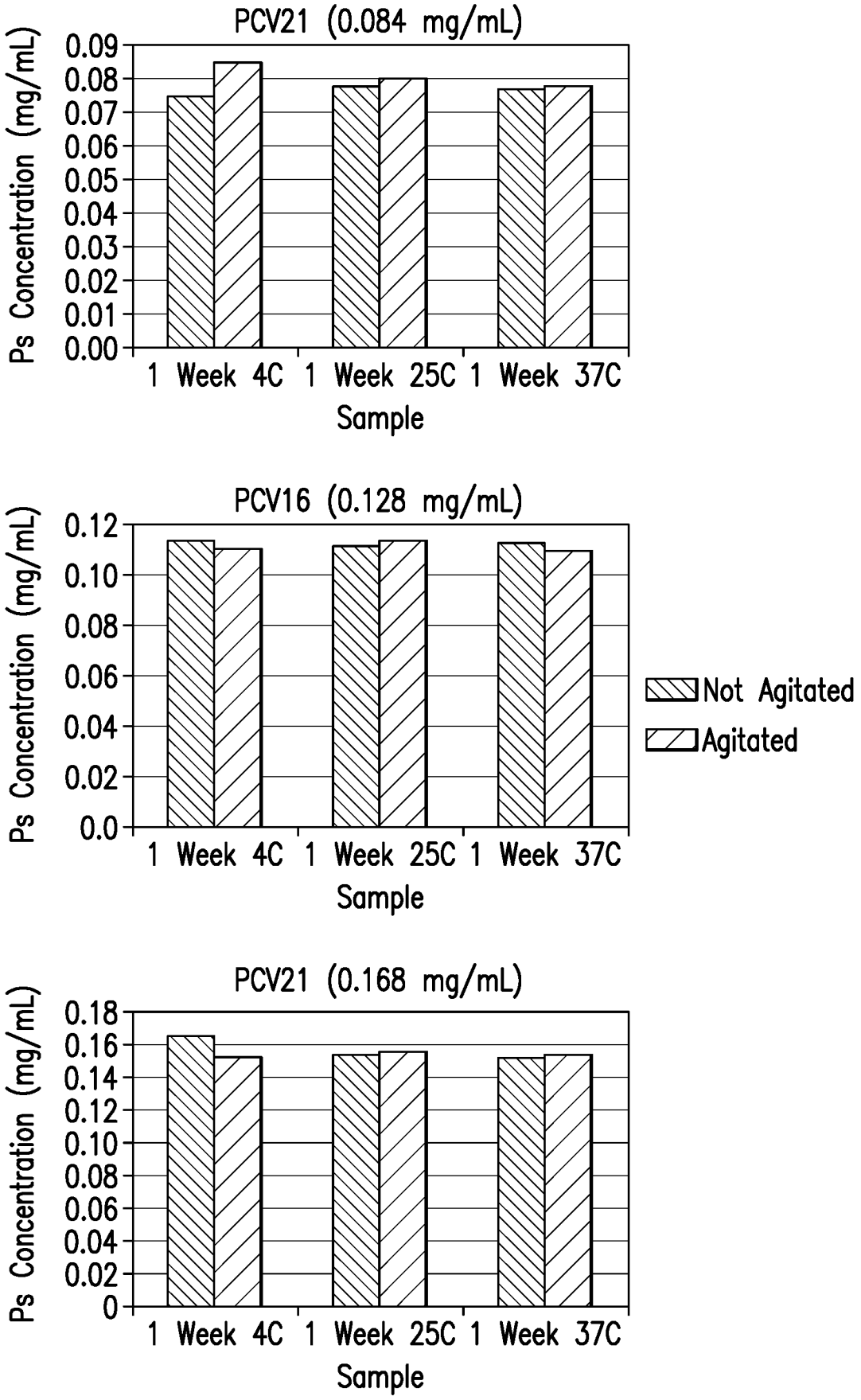

PCV21 (0.084 mg/mL)
Ps Concentration (mg/mL)
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
1 Week 4C
1 Week 25C
1 Week 37C
Sample
PCV16 (0.128 mg/mL)
Ps Concentration (mg/mL)
0.12
0.10
0.08
0.06
0.04
0.02
0.0
1 Week 4C
1 Week 25C
1 Week 37C
Sample
Not Agitated
Agitated
PCV21 (0.168 mg/mL)
Ps Concentration (mg/mL)
0.18
0.16
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0
1 Week 4C
1 Week 25C
1 Week 37C
Sample

FIG.12

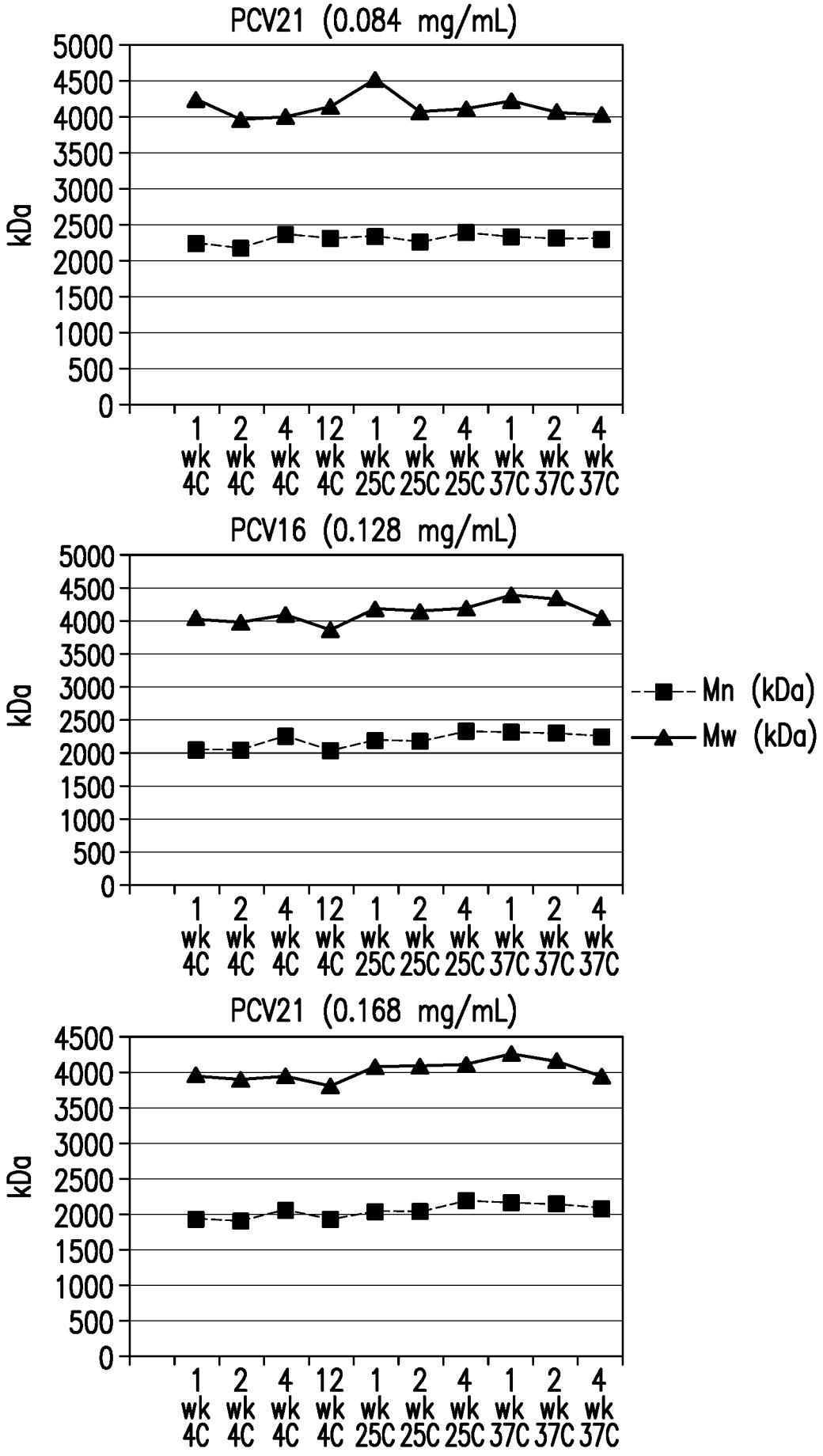

PCV21 (0.084 mg/mL)
kDa
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
1 wk 4C
2 wk 4C
4 wk 4C
12 wk 4C
1 wk 25C
2 wk 25C
4 wk 25C
1 wk 37C
2 wk 37C
4 wk 37C
PCV16 (0.128 mg/mL)
Mn (kDa)
Mw (kDa)
PCV21 (0.168 mg/mL)

FIG.13

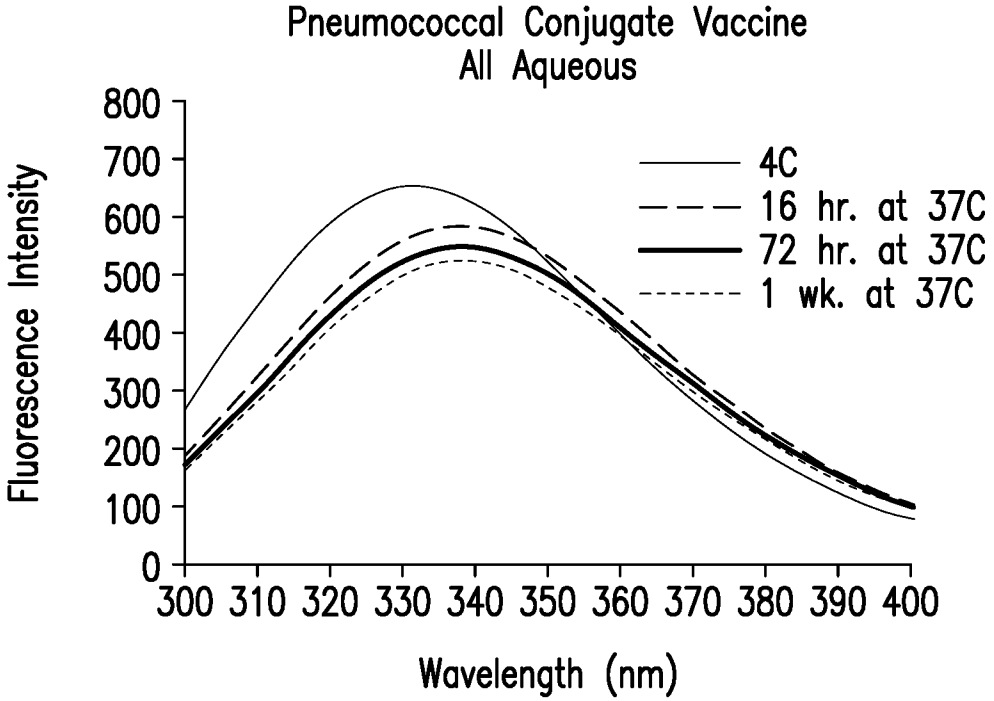


FIG.14A

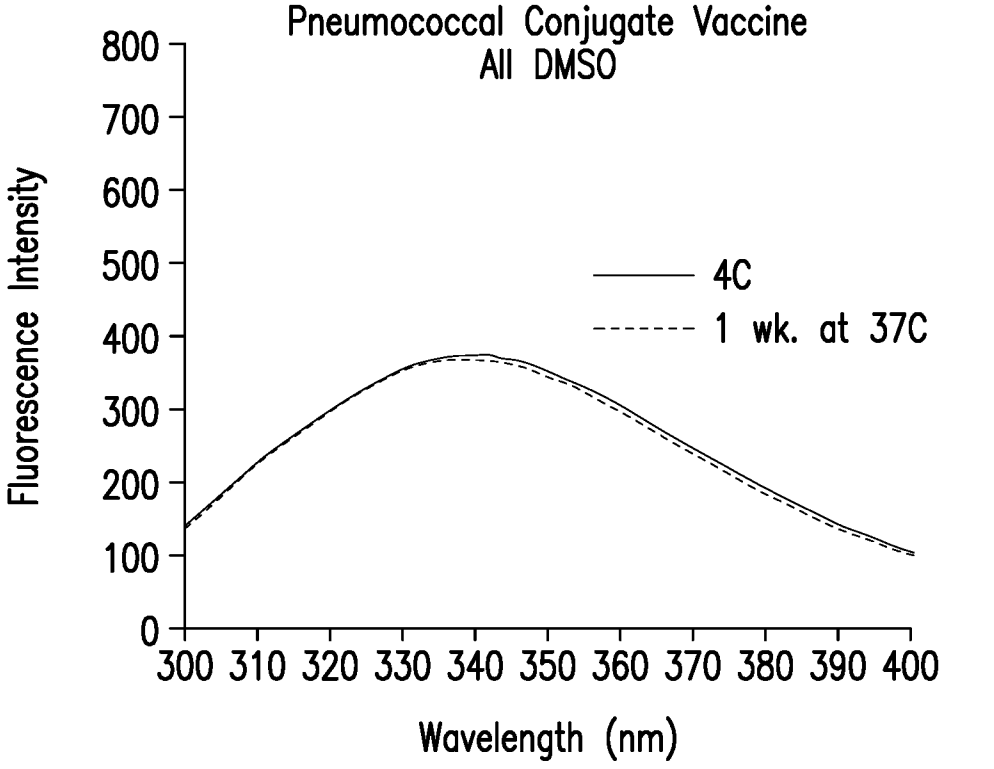


FIG.14B

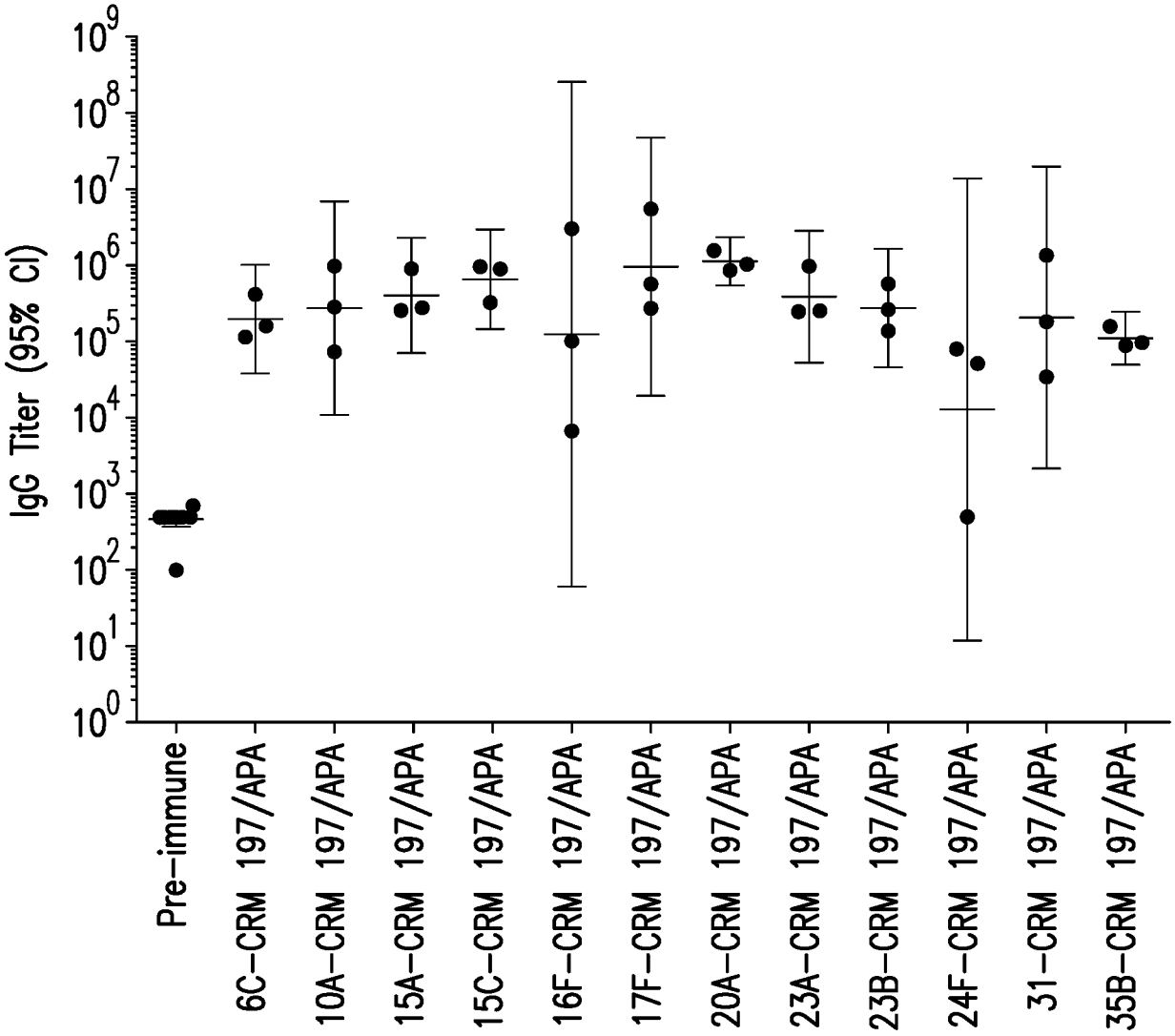

IgG Titer (95% CI)
10^9
10^8
10^7
10^6
10^5
10^4
10^3
10^2
10^1
10^0
Pre-immune
6C-CRM 197/APA
10A-CRM 197/APA
15A-CRM 197/APA
15C-CRM 197/APA
16F-CRM 197/APA
17F-CRM 197/APA
20A-CRM 197/APA
23A-CRM 197/APA
23B-CRM 197/APA
24F-CRM 197/APA
31-CRM 197/APA
35B-CRM 197/APA

FIG.15

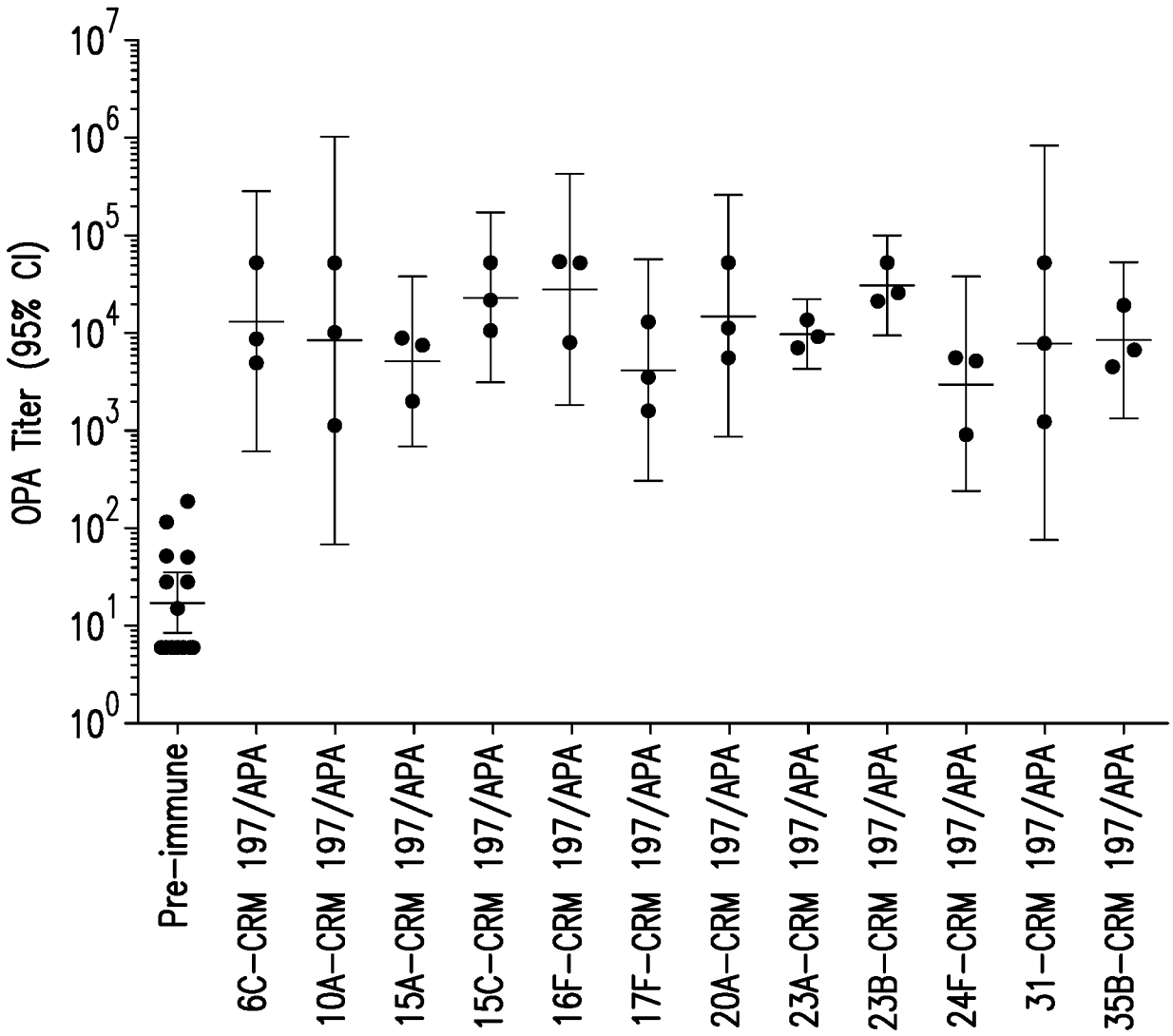

OPA Titer (95% CI)
10^0
10^1
10^2
10^3
10^4
10^5
10^6
10^7
Pre−immune
6C−CRM 197/APA
10A−CRM 197/APA
15A−CRM 197/APA
15C−CRM 197/APA
16F−CRM 197/APA
17F−CRM 197/APA
20A−CRM 197/APA
23A−CRM 197/APA
23B−CRM 197/APA
24F−CRM 197/APA
31−CRM 197/APA
35B−CRM 197/APA

FIG.16

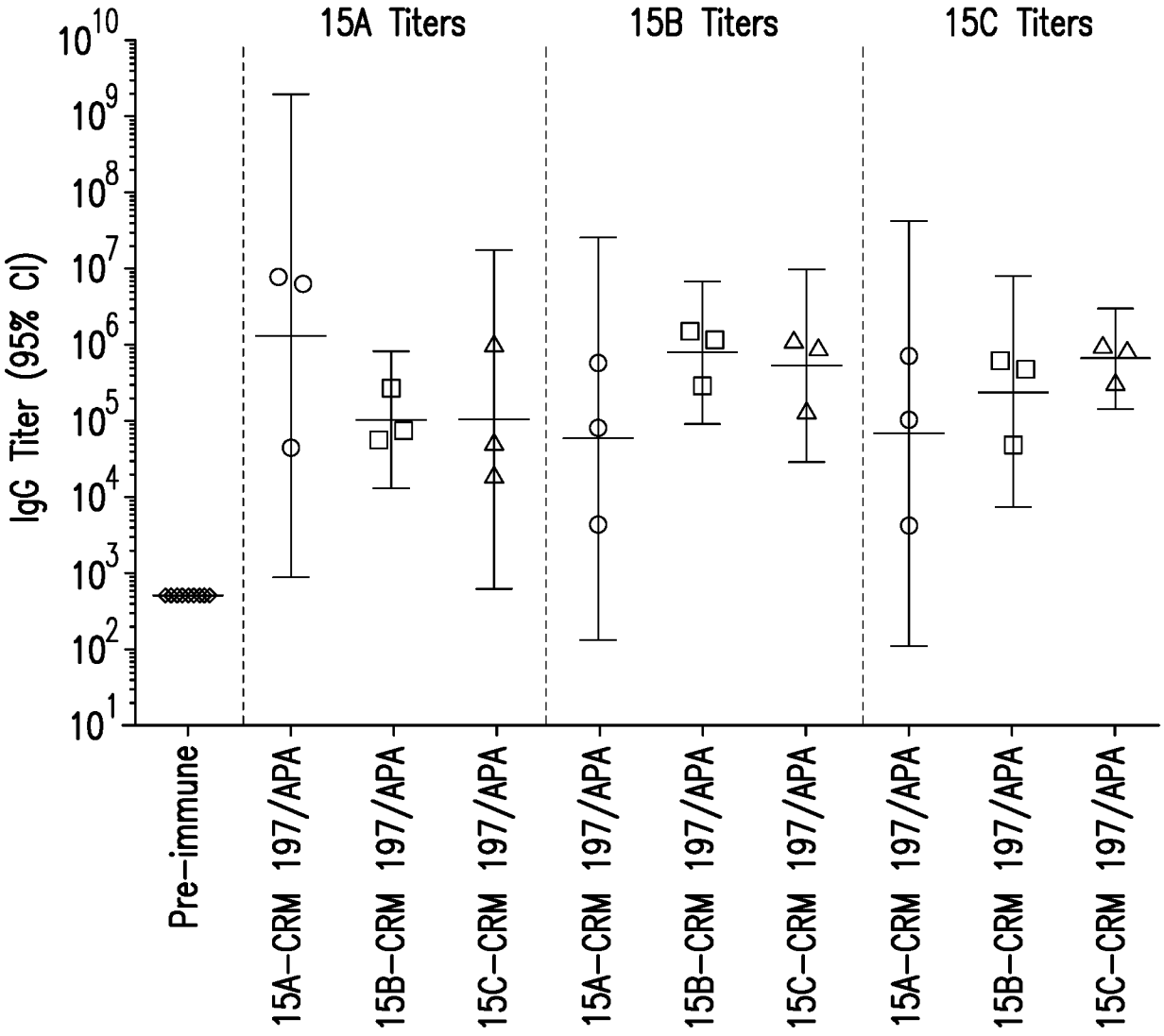

15A Titers
15B Titers
15C Titers
IgG Titer (95% CI)
10^{10}
10^{9}
10^{8}
10^{7}
10^{6}
10^{5}
10^{4}
10^{3}
10^{2}
10^{1}
Pre-immune
15A-CRM 197/APA
15B-CRM 197/APA
15C-CRM 197/APA
15A-CRM 197/APA
15B-CRM 197/APA
15C-CRM 197/APA
15A-CRM 197/APA
15B-CRM 197/APA
15C-CRM 197/APA

FIG.17

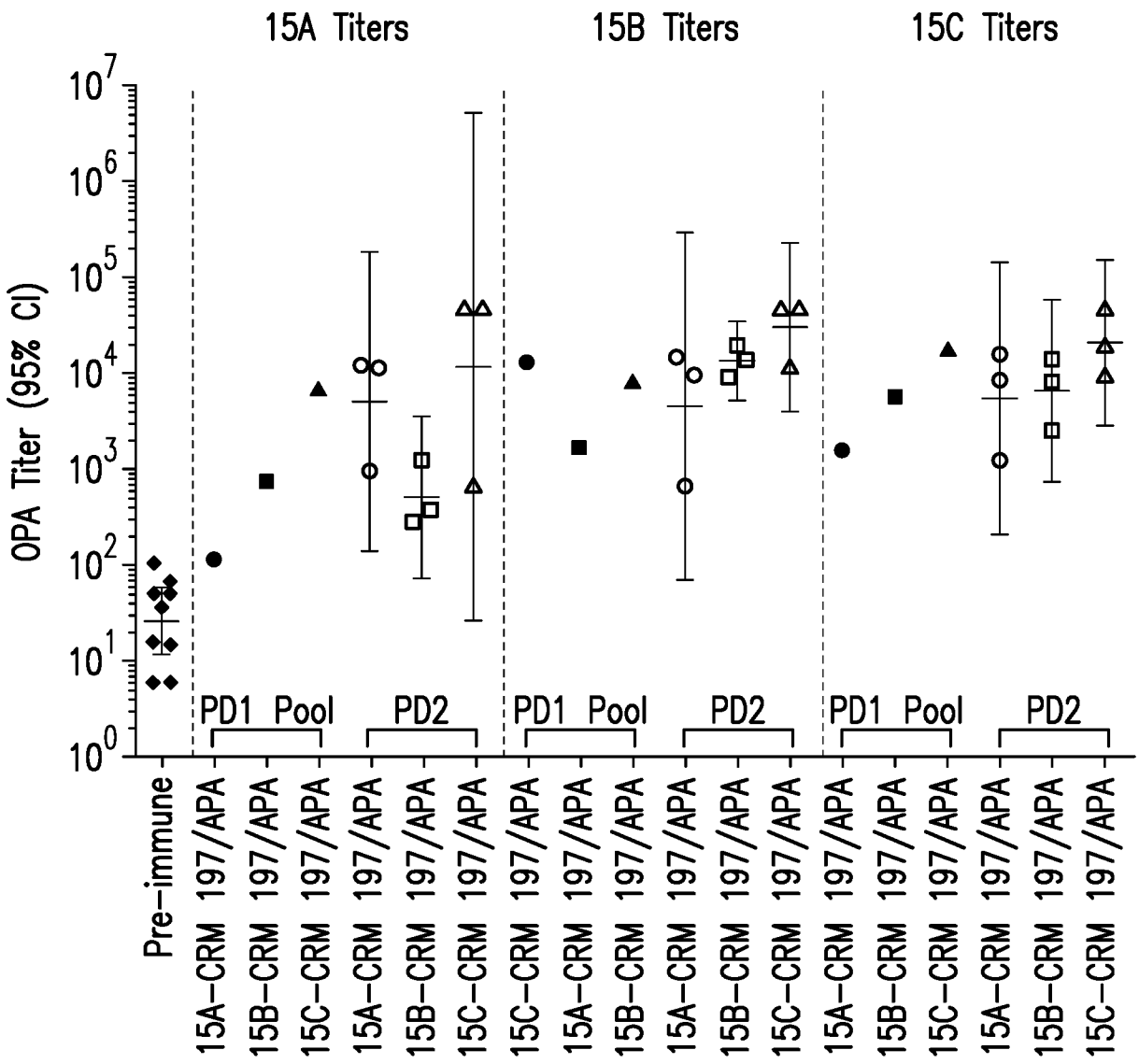

15A Titers
15B Titers
15C Titers
OPA Titer (95% CI)
10^7
10^6
10^5
10^4
10^3
10^2
10^1
10^0
PD1 Pool
PD2
Pre-immune
15A-CRM 197/APA
15B-CRM 197/APA
15C-CRM 197/APA

FIG.18

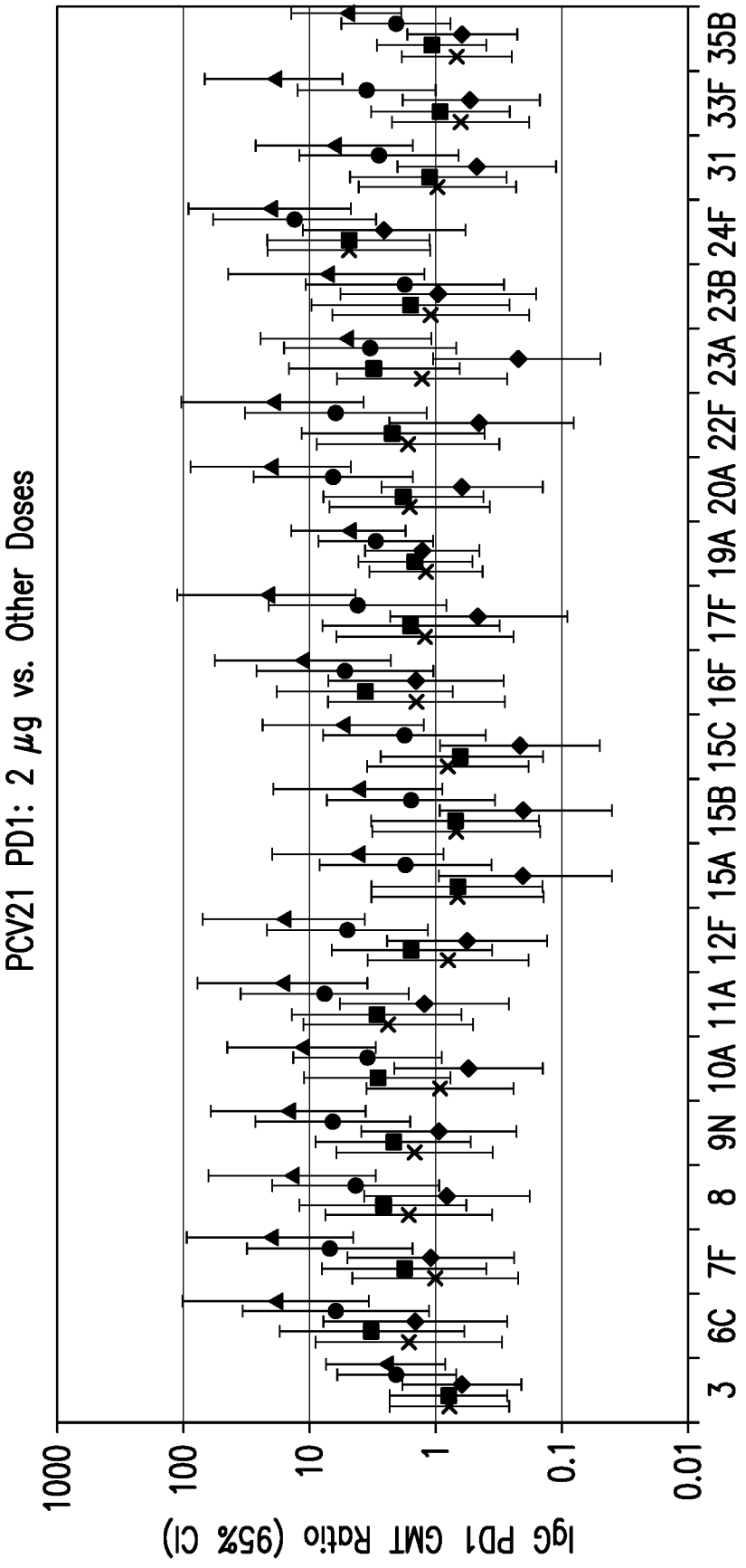

PCV21 PD1: 2 μg vs. Other Doses
lgG PD1 GMT Ratio (95% CI)
1000
100
10
1
0.1
0.01
3 6C 7F 8 9N 10A 11A 12F 15A 15B 15C 16F 17F 19A 20A 22F 23A 23B 24F 31 33F 35B
Pn Type
× 2 μg vs. 4 μg
■ 2 μg vs. 1 μg
◆ 2 μg vs. 0.4 μg
● 2 μg vs. 0.08 μg
▲ 2 μg vs. 0.016 μg

FIG.19A

Serotype	2 μg v. 4 μg	2 μg v. 1 μg	2 μg v. 0.4 μg	2 μg v. 0.08 μg	2 μg v. 0.016 μg
3	0.78 (0.26, 2.3)	0.79 (0.27, 2.3)	0.62 (0.21, 1.84)	2.1 (0.7, 6.1)	2.5 (0.85, 7.5)
6C	1.64 (0.3, 8.9)	3.2 (0.6, 18)	1.44 (0.27, 7.8)	6.3 (1.15, 34)	19 (3.5, 102)
7F	1.01 (0.22, 4.6)	1.76 (0.39, 8)	1.11 (0.24, 5.1)	6.9 (1.52, 32)	21 (4.5, 94)
8	1.64 (0.36, 7.5)	2.6 (0.57, 12)	0.81 (0.18, 3.7)	4.3 (0.94, 20)	14 (3, 63)
9N	1.46 (0.35, 6)	2.1 (0.52, 8.9)	0.94 (0.23, 3.9)	6.5 (1.58, 27)	15 (3.5, 60)
10A	0.92 (0.24, 3.5)	2.9 (0.75, 11)	0.55 (0.14, 2.1)	3.5 (0.9, 13)	12 (3, 44)
11A	2.4 (0.51, 11)	2.9 (0.62, 14)	1.21 (0.26, 5.7)	7.5 (1.61, 35)	16 (3.5, 77)
12F	0.79 (0.18, 3.5)	1.54 (0.35, 6.7)	0.55 (0.13, 2.4)	5 (1.14, 22)	16 (3.7, 70)
15A	0.68 (0.14, 3.3)	0.67 (0.14, 3.2)	0.2 (0.041, 0.95)	1.73 (0.36, 8.3)	4.1 (0.86, 20)
15B	0.68 (0.15, 3.1)	0.7 (0.15, 3.3)	0.2 (0.043, 0.93)	1.57 (0.34, 7.3)	4.2 (0.89, 19)
15C	0.81 (0.18, 3.5)	0.63 (0.14, 2.8)	0.21 (0.49, 0.93)	1.77 (0.4, 7.7)	5.4 (1.24, 24)
16F	1.42 (0.28, 7.1)	3.7 (0.73, 18)	1.43 (0.29, 7.2)	5.3 (1.05, 29)	11 (2.3, 57)
17F	1.22 (0.24, 6.2)	1.58 (0.31, 8.1)	0.46 (0.09, 2.3)	4.2 (0.82, 21)	22 (4.3, 112)
19A	1.19 (0.42, 3.4)	1.45 (0.51, 4.1)	1.29 (0.45, 3.7)	3 (1.05, 8.5)	5 (1.74, 14)
20A	1.59 (0.37, 6.9)	1.82 (0.42, 7.9)	0.62 (0.14, 2.7)	6.5 (1.52, 28)	20 (4.7, 88)
22F	1.65 (0.31, 8.8)	2.2 (0.41, 12)	0.45 (0.084, 2.4)	6.2 (1.17, 33)	20 (3.7, 105)
23A	1.27 (0.27, 6)	3.1 (0.65, 15)	0.22 (0.046, 1.04)	3.3 (0.7, 16)	5.1 (1.08, 25)
23B	1.09 (0.18, 6.7)	1.59 (0.26, 9.7)	0.95 (0.16, 5.8)	1.8 (0.29, 11)	7.4 (1.21, 45)
24F	4.9 (1.1, 21)	4.9 (1.11, 22)	2.6 (0.58, 11)	13 (3, 59)	21 (4.7, 92)
31	0.96 (0.23, 4.1)	1.13 (0.27, 4.8)	0.47 (0.11, 2)	2.1 (0.66, 12)	6.4 (1.51, 27)
33F	0.64 (0.18, 2.2)	0.92 (0.26, 3.3)	0.53 (0.15, 1.85)	3.6 (1.03, 13)	19 (5.5, 68)
35B	0.69 (0.25, 1.87)	1.08 (0.4, 2.9)	0.63 (0.23, 1.69)	2.1 (0.77, 5.6)	5.1 (1.9, 14)

FIG.19B

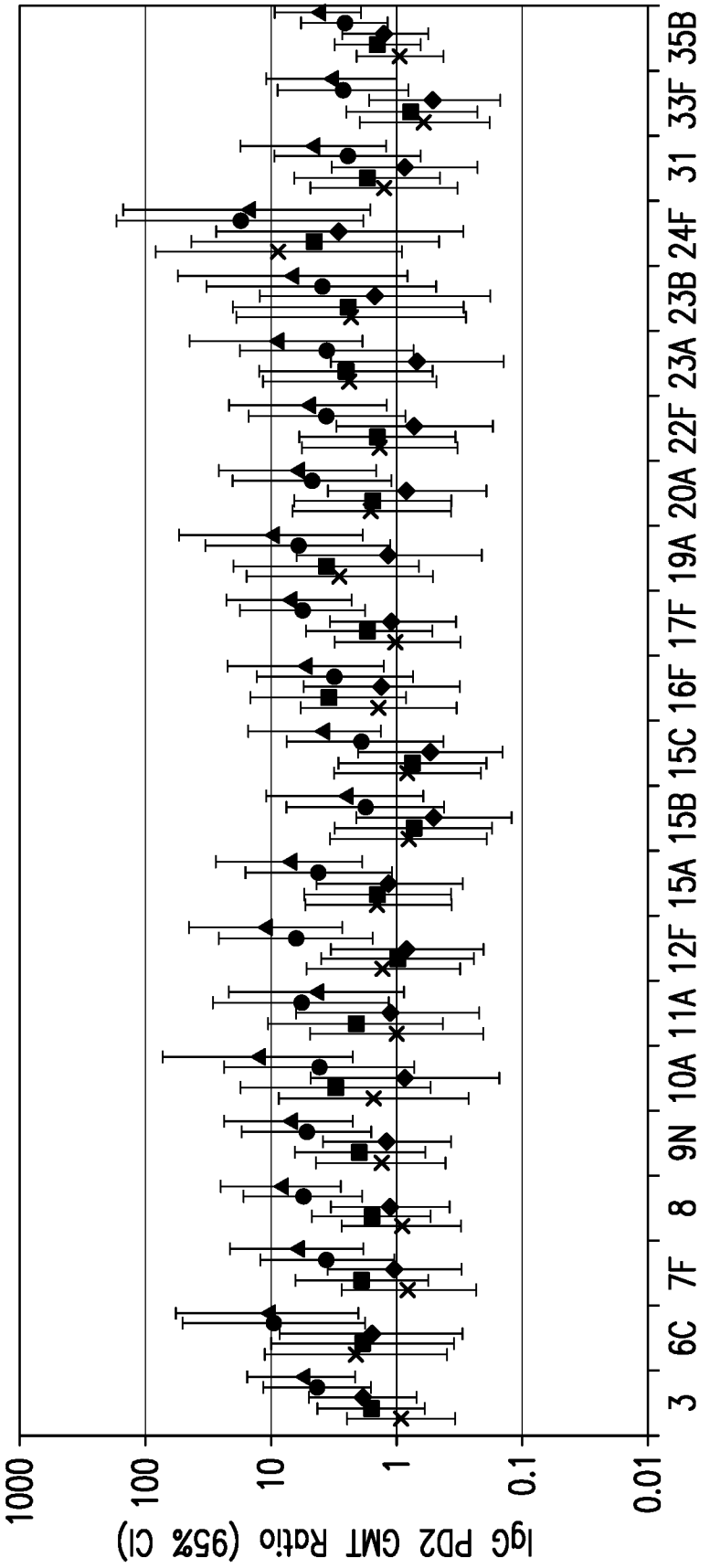

1000
100
10
1
0.1
0.01
lgG PD2 GMT Ratio (95% CI)
3 6C 7F 8 9N 10A 11A 12F 15A 15B 15C 16F 17F 19A 20A 22F 23A 23B 24F 31 33F 35B
Pn Type
× 2 μg vs. 4 μg
■ 2 μg vs. 1 μg
◆ 2 μg vs. 0.4 μg
● 2 μg vs. 0.08 μg
▲ 2 μg vs. 0.016 μg

FIG.20A

Serotype	2 μg v. 4 μg	2 μg v. 1 μg	2 μg v. 0.4 μg	2 μg v. 0.08 μg	2 μg v. 0.016 μg
3	0.91 (0.34, 2.5)	1.58 (0.59, 4.3)	1.86 (0.69, 5.0)	4.3 (1.59, 12.0)	5.7 (2.1, 15.0)
6C	2.1 (0.39, 11.0)	1.87(0.35, 10)	1.6 (0.3, 8.6)	9.6 (1.79, 51)	11 (1.98, 56)
7F	0.8 (0.23, 2.7)	1.88 (0.55, 6.4)	1.03 (0.3, 3.5)	3.6 (1.05, 12)	6.2 (1.83, 21)
8	0.9 (0.3, 2.7)	1.57 (0.53, 4.7)	1.1 (0.37, 3.3)	5.5 (1.84, 17)	8.3 (2.8, 25)
9N	1.31 (0.4, 4.3)	1.92 (0.58, 6.3)	1.17 (0.36, 3.8)	5.1 (1.56, 17)	7.1 (2.2, 23)
10A	1.49 (0.26, 8.6)	3 (0.53, 17)	0.84 (0.15, 4.8)	4.1 (0.71, 23)	13 (2.2, 72)
11A	0.98 (0.2, 4.9)	2.1 (0.42, 10)	1.09 (0.22, 5.4)	5.7 (1.15, 29)	4.3 (0.86, 22)
12F	1.28 (0.31, 5.2)	0.96 (0.24, 3.9)	0.8 (0.2, 3.3)	6.3 (1.53, 26)	11 (2.7, 45)
15A	1.39 (0.36, 5.3)	1.39 (0.36, 5.3)	1.12 (0.29, 4.3)	4.1 (1.06, 16)	7.1 (1.85, 27)
15B	0.79 (0.19, 3.3)	0.72 (0.17, 3)	0.49 (0.12, 2.1)	1.75 (0.41, 7.4)	2.5 (0.6, 11)
15C	0.81 (0.21, 3.1)	0.74 (0.19, 2.9)	0.53 (0.14, 2)	1.92 (0.5, 7.4)	3.9 (1.03, 15)
16F	1.37 (0.33, 5.8)	3.5 (0.83, 15)	1.31 (0.31, 5.5)	3.1 (0.73, 13)	5.2 (1.24, 22)
17F	0.99 (0.31, 3.1)	1.65 (0.52, 5.2)	1.06 (0.33, 3.4)	5.6 (1.76, 18)	7.1 (2.3, 23)
19A	2.8 (0.51, 16)	3.6 (0.65, 20)	1.13 (0.21, 6.2)	6.1 (1.0, 33)	9.8 (1.78, 54)
20A	1.59 (0.37, 6.8)	1.53 (0.36, 6.5)	0.83 (0.19, 3.5)	4.7 (1.1, 20)	6.2 (1.45, 26)
22F	1.34 (0.32, 5.7)	1.42 (0.34, 6)	0.72 (0.17, 3)	3.6 (0.84, 15)	5.1 (1.2, 21)
23A	2.4 (0.48, 12)	2.5 (0.51, 12)	0.67 (0.14, 3.3)	3.6 (0.74, 18)	9.1 (1.84, 45)
23B	2.3 (0.28, 19)	2.4 (0.29, 20)	1.49 (0.18, 12)	4 (0.48, 33)	6.8 (0.82, 56)
24F	8.6 (0.9, 83)	4.5 (0.46, 43)	2.9 (0.3, 28)	18 (1.85, 172)	16 (1.61, 150)
31	1.26 (0.33, 4.8)	1.17 (0.45, 6.5)	0.86 (0.23, 3.3)	2.5 (0.64, 9.4)	4.7 (1.22, 18)
33F	0.6 (0.18, 1.97)	0.77 (0.23, 2.5)	0.5 (0.15, 1.65)	2.7 (0.81, 8.9)	3.4 (1.02, 11)
35B	0.94 (0.43, 2.1)	1.41 (0.64, 3.1)	1.24 (0.56, 2.8)	2.6 (1.18, 5.8)	4.3 (1.94, 9.6)

FIG.20B

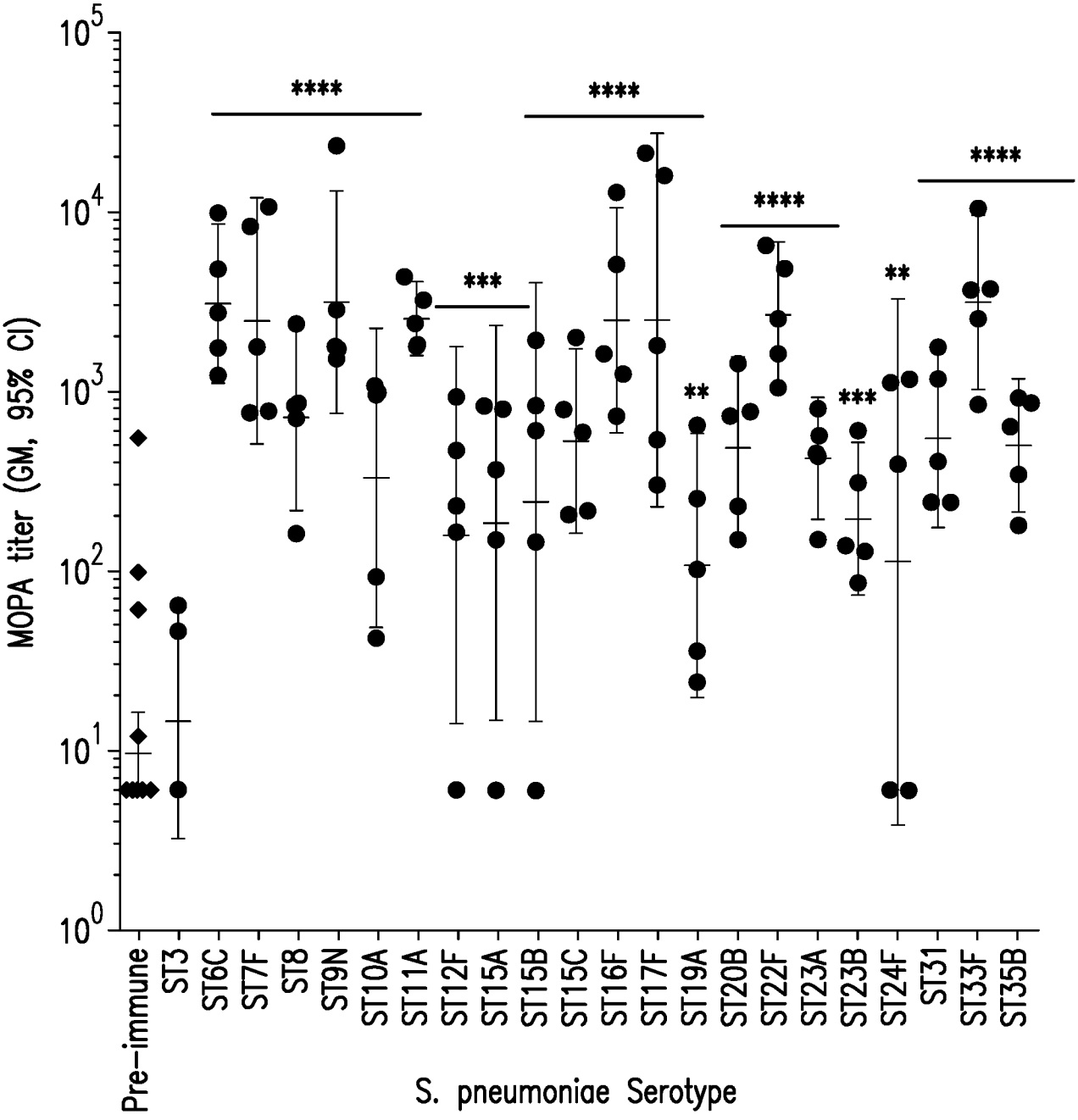

MOPA titer (GM, 95% CI)
10^0
10^1
10^2
10^3
10^4
10^5
****
****
***
****
**
***
**
****
Pre-immune
ST3
ST6C
ST7F
ST8
ST9N
ST10A
ST11A
ST12F
ST15A
ST15B
ST15C
ST16F
ST17F
ST19A
ST20B
ST22F
ST23A
ST23B
ST24F
ST31
ST33F
ST35B
S. pneumoniae Serotype

FIG.21A

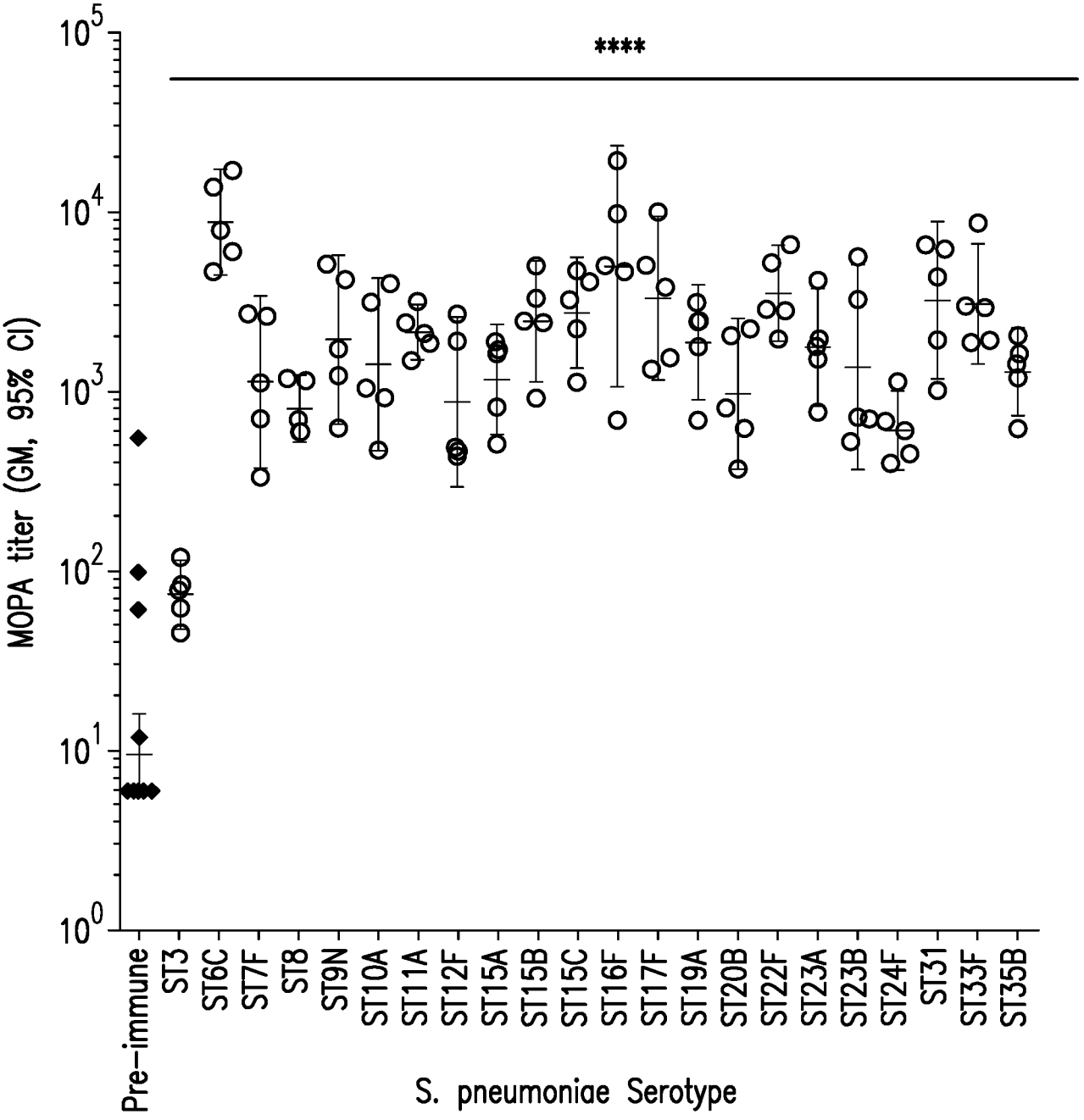

****
MOPA titer (GM, 95% CI)
10^0
10^1
10^2
10^3
10^4
10^5
Pre-immune
ST3
ST6C
ST7F
ST8
ST9N
ST10A
ST11A
ST12F
ST15A
ST15B
ST15C
ST16F
ST17F
ST19A
ST20B
ST22F
ST23A
ST23B
ST24F
ST31
ST33F
ST35B
S. pneumoniae Serotype

FIG.21B

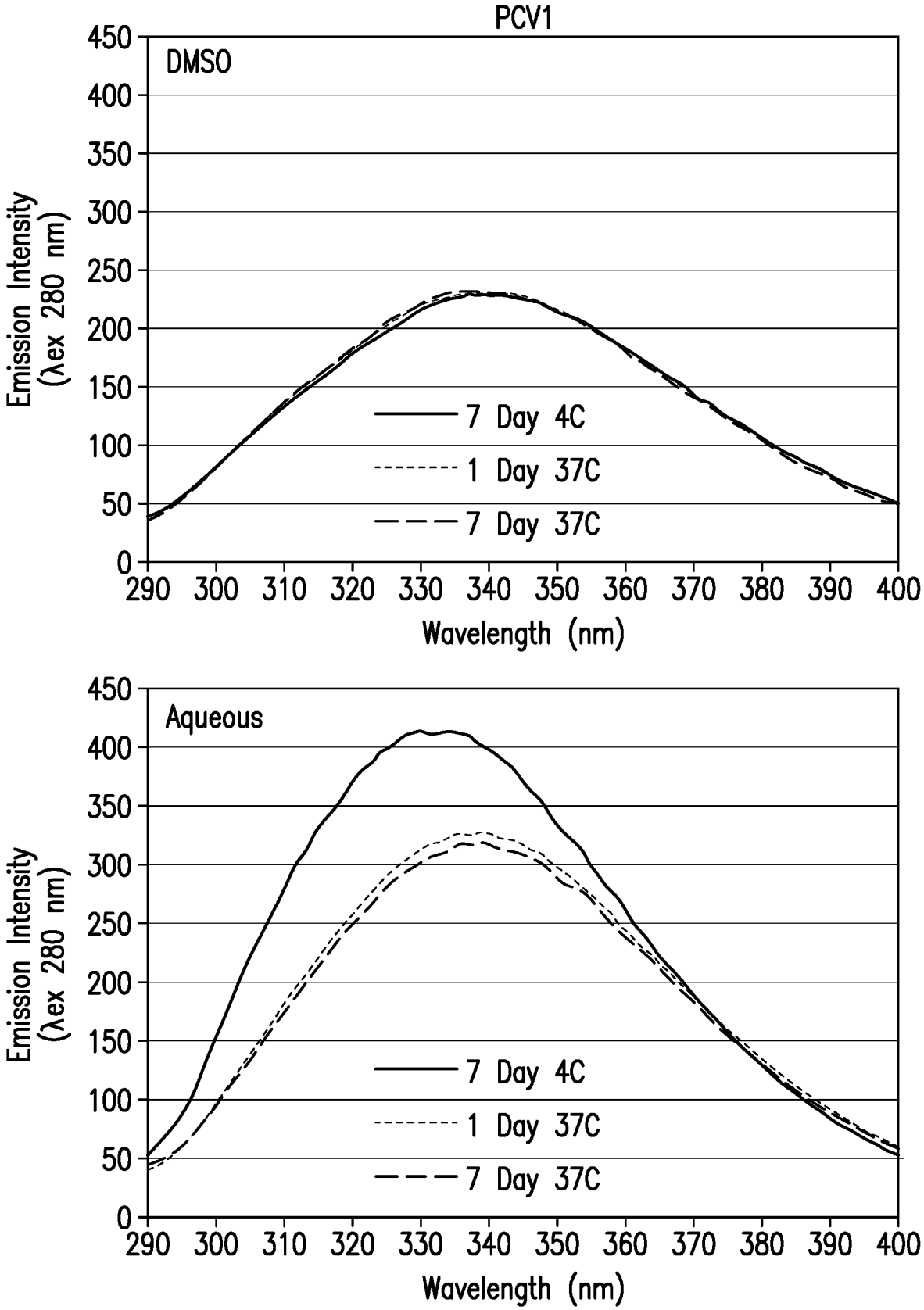

PCV1
DMSO
Emission Intensity (λex 280 nm)
450
400
350
300
250
200
150
100
50
0
290 300 310 320 330 340 350 360 370 380 390 400
Wavelength (nm)
7 Day 4C
1 Day 37C
7 Day 37C
Aqueous
Emission Intensity (λex 280 nm)
450
400
350
300
250
200
150
100
50
0
290 300 310 320 330 340 350 360 370 380 390 400
Wavelength (nm)
7 Day 4C
1 Day 37C
7 Day 37C

FIG.22A

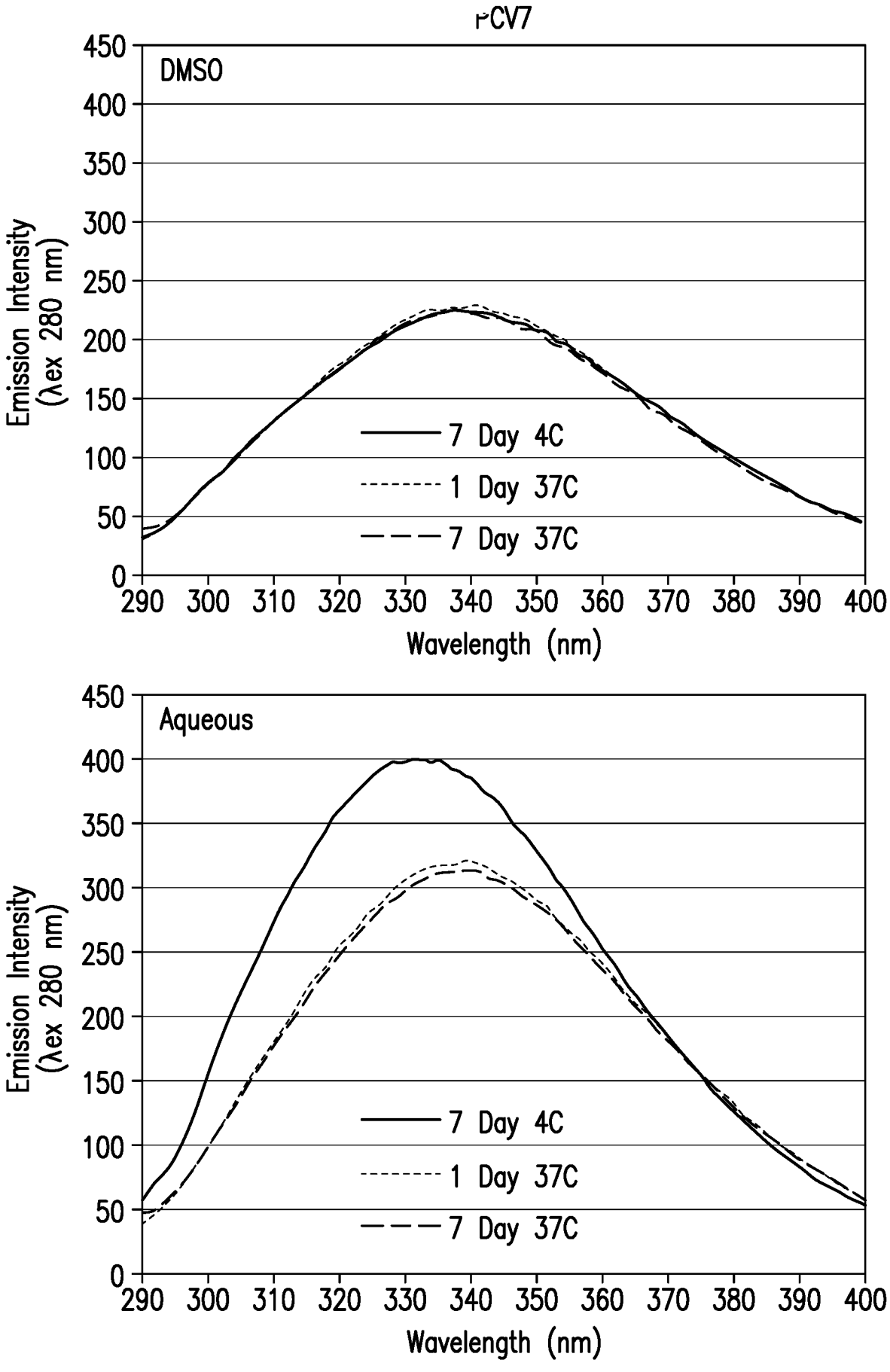

PCV7
DMSO
Emission Intensity (λex 280 nm)
450
400
350
300
250
200
150
100
50
0
290 300 310 320 330 340 350 360 370 380 390 400
Wavelength (nm)
7 Day 4C
1 Day 37C
7 Day 37C
Aqueous
Emission Intensity (λex 280 nm)
450
400
350
300
250
200
150
100
50
0
290 300 310 320 330 340 350 360 370 380 390 400
Wavelength (nm)
7 Day 4C
1 Day 37C
7 Day 37C

FIG.22B

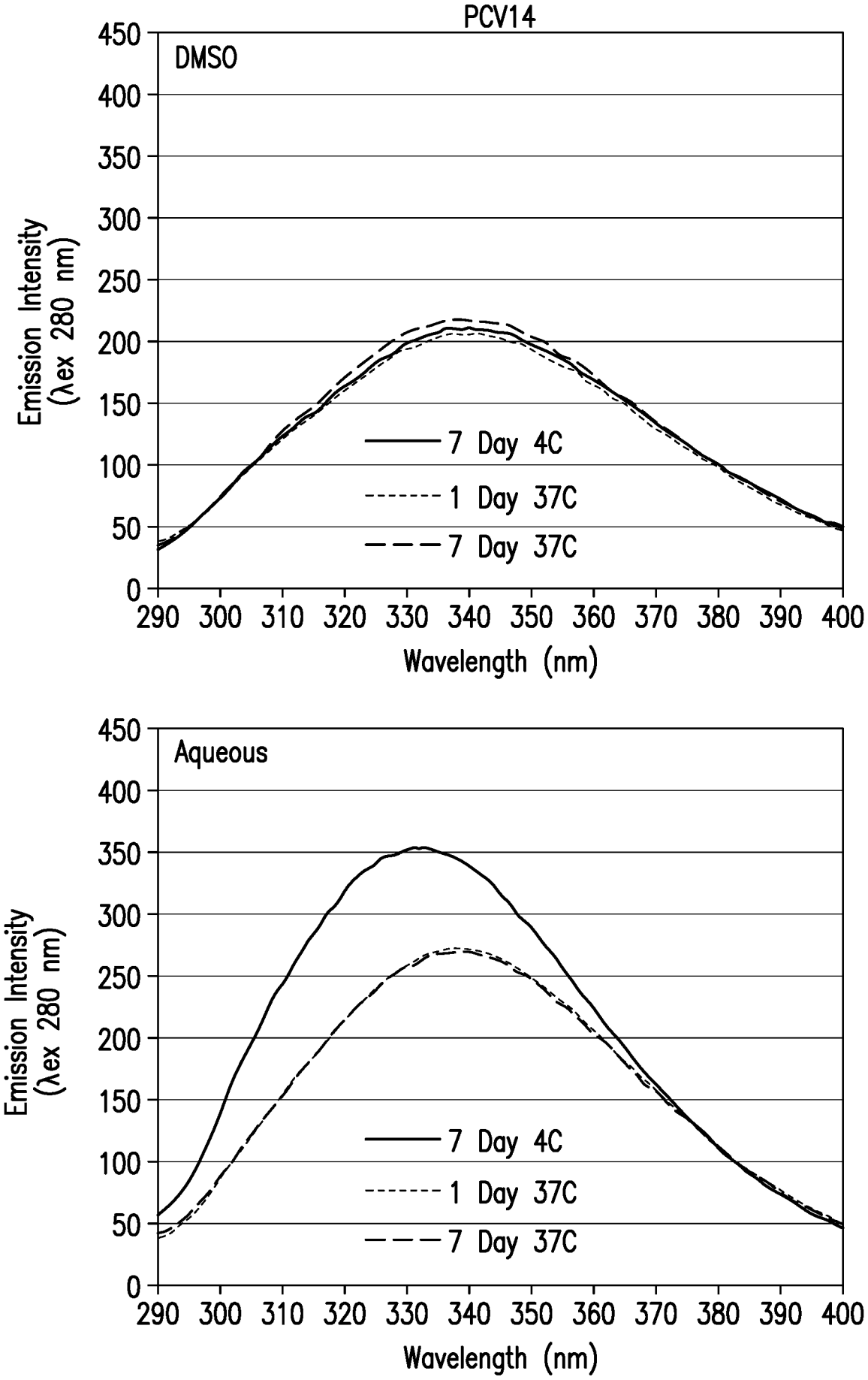

PCV14
DMSO
Emission Intensity (λex 280 nm)
450
400
350
300
250
200
150
100
50
0
7 Day 4C
1 Day 37C
7 Day 37C
290 300 310 320 330 340 350 360 370 380 390 400
Wavelength (nm)
Aqueous
Emission Intensity (λex 280 nm)
450
400
350
300
250
200
150
100
50
0
7 Day 4C
1 Day 37C
7 Day 37C
290 300 310 320 330 340 350 360 370 380 390 400
Wavelength (nm)

FIG.22C

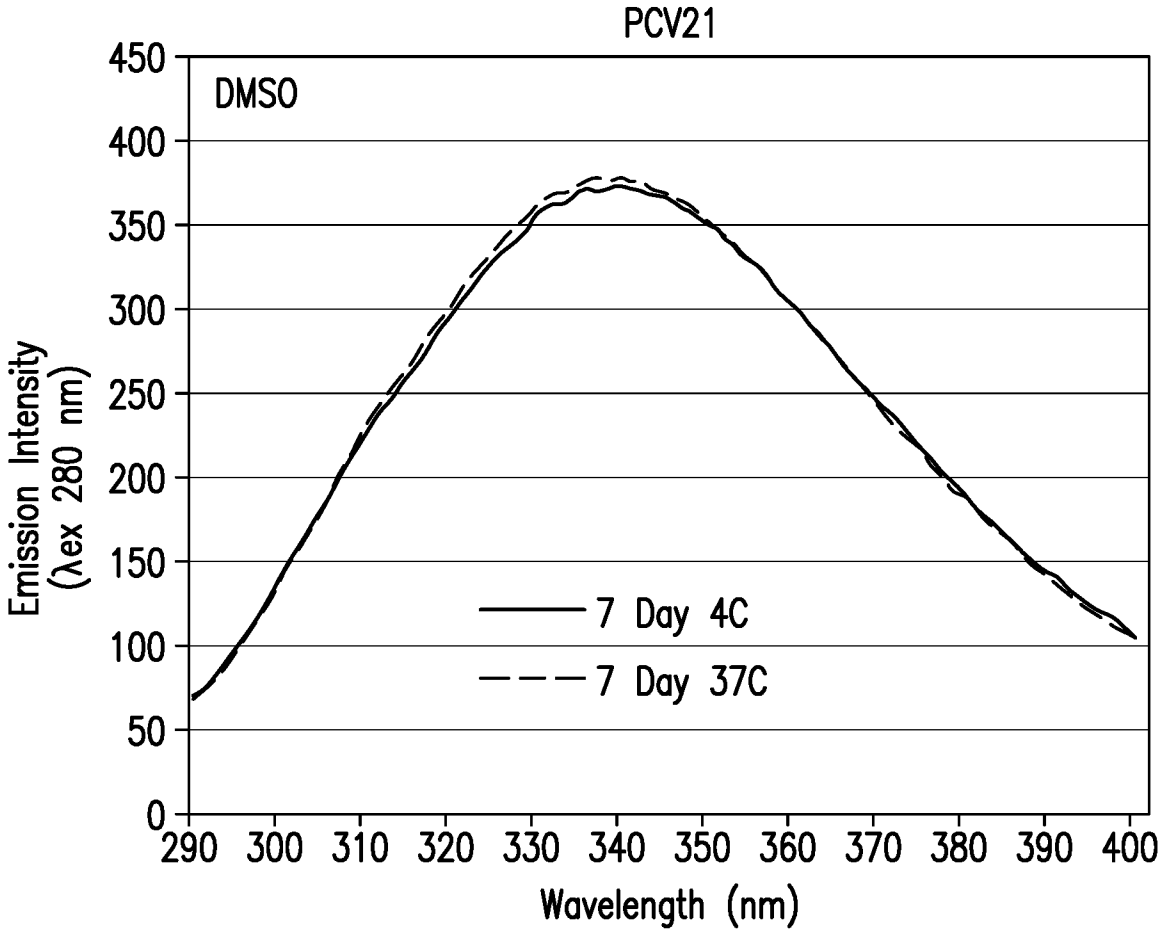

PCV21
DMSO
Emission Intensity
(λex 280 nm)
450
400
350
300
250
200
150
100
50
0
290
300
310
320
330
340
350
360
370
380
390
400
Wavelength (nm)
7 Day 4C
7 Day 37C

FIG.22D

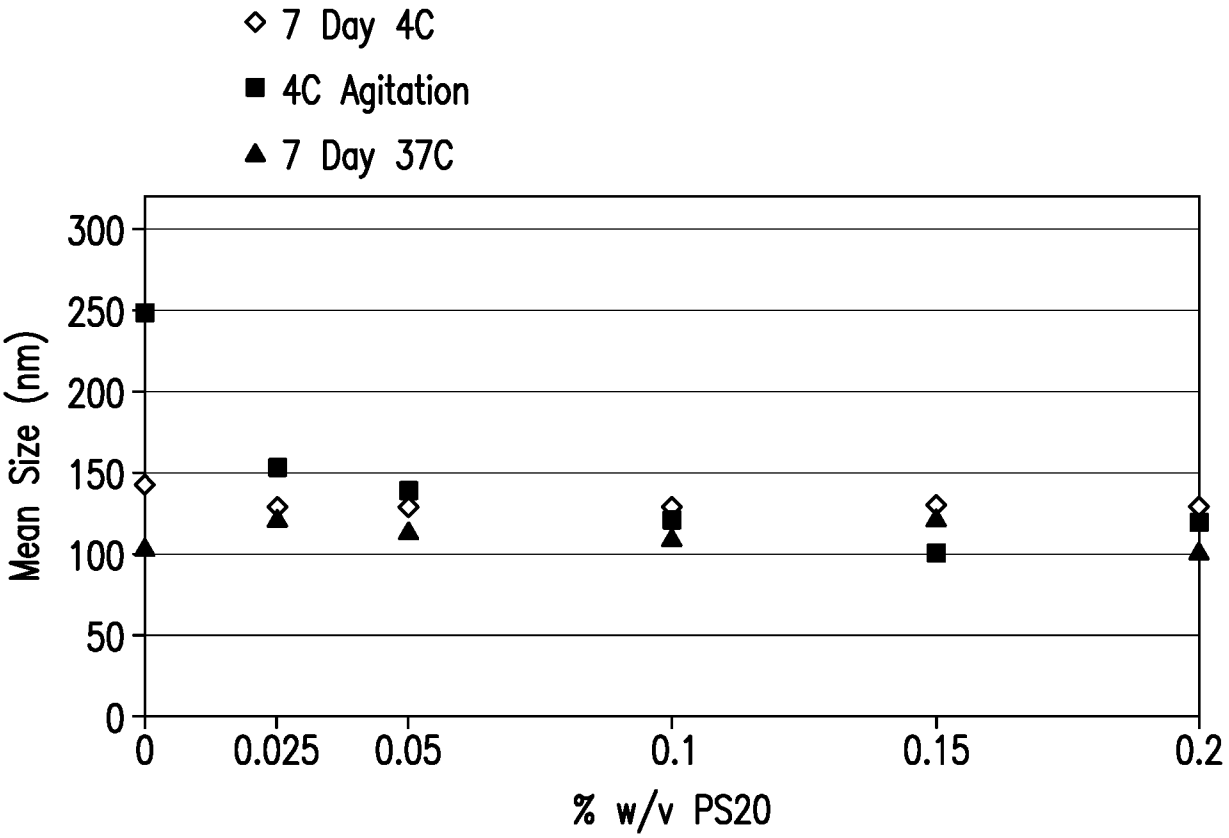

7 Day 4C
4C Agitation
7 Day 37C
Mean Size (nm)
300
250
200
150
100
50
0
0
0.025
0.05
0.1
0.15
0.2
% w/v PS20

FIG.23

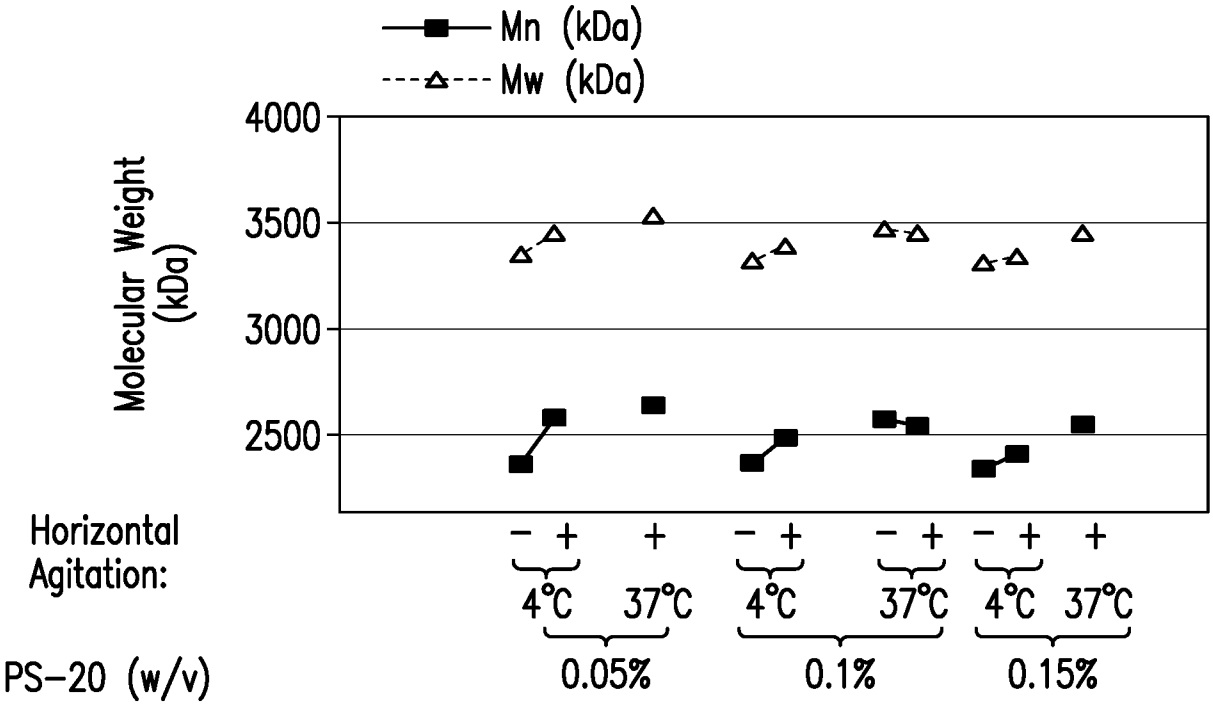

Mn (kDa)
Mw (kDa)
Molecular Weight (kDa)
4000
3500
3000
2500
Horizontal Agitation:
− + + − + − + − + +
4°C 37°C 4°C 37°C 4°C 37°C
PS−20 (w/v)
0.05%
0.1%
0.15%

FIG.24

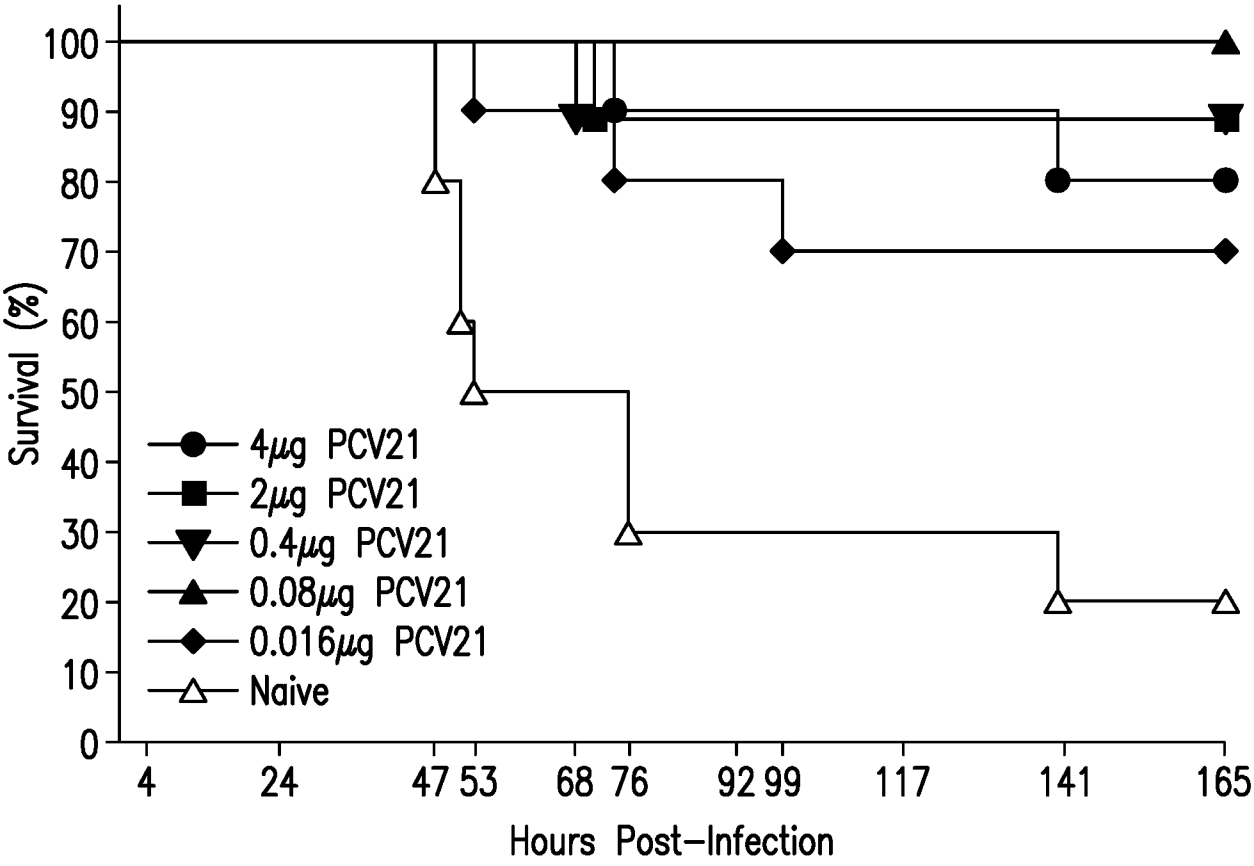

100
90
80
70
60
50
40
30
20
10
0
Survival (%)
4μg PCV21
2μg PCV21
0.4μg PCV21
0.08μg PCV21
0.016μg PCV21
Naive
4
24
47 53
68 76
92 99
117
141
165
Hours Post-Infection

FIG.25

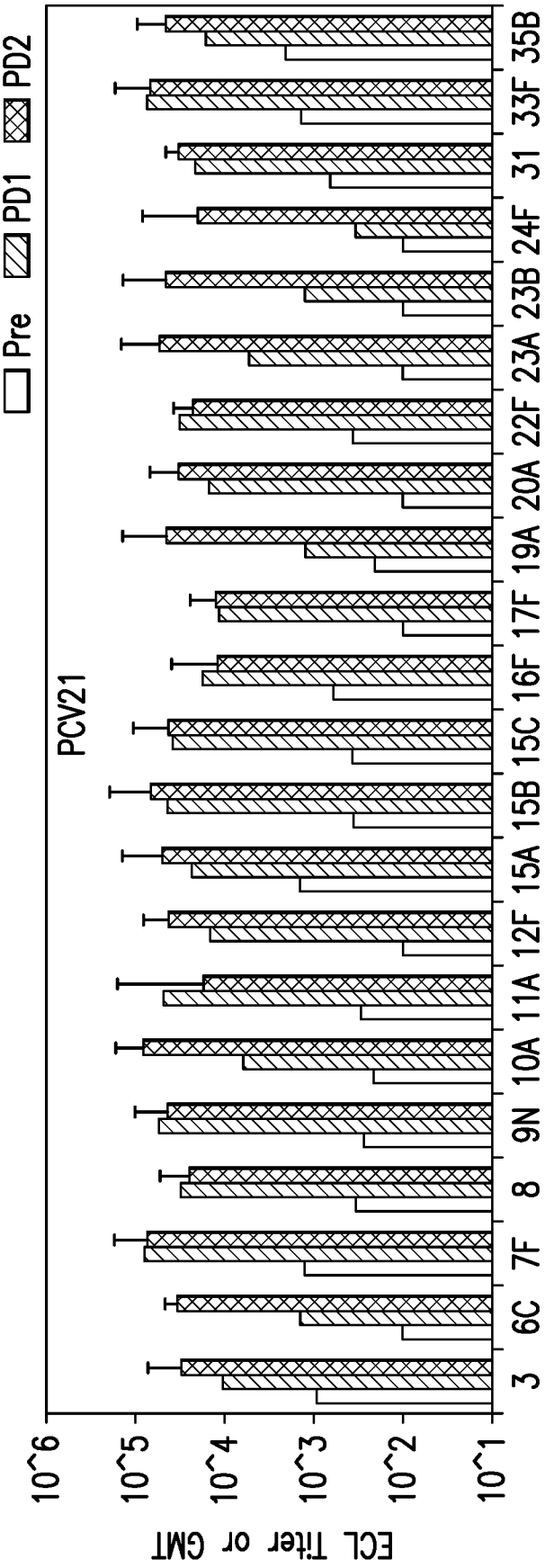

Pre
PD1
PD2
PCV21
ECL Titer or GMT
10^6
10^5
10^4
10^3
10^2
10^1
3
6C
7F
8
9N
10A
11A
12F
15A
15B
15C
16F
17F
19A
20A
22F
23A
23B
24F
31
33F
35B
Serotype

FIG.26A

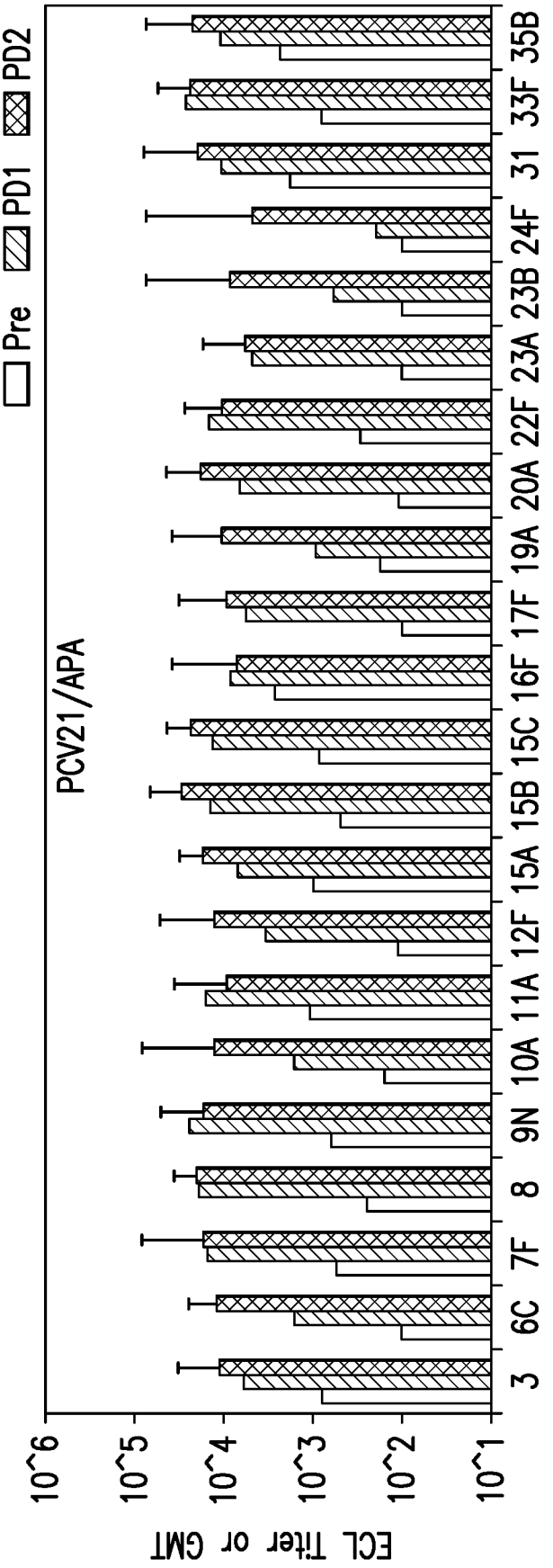

Pre
PD1
PD2
PCV21/APA
ECL Titer or GMT
10^6
10^5
10^4
10^3
10^2
10^1
3
6C
7F
8
9N
10A
11A
12F
15A
15B
15C
16F
17F
19A
20A
22F
23A
23B
24F
31
33F
35B
Serotype

FIG.26B

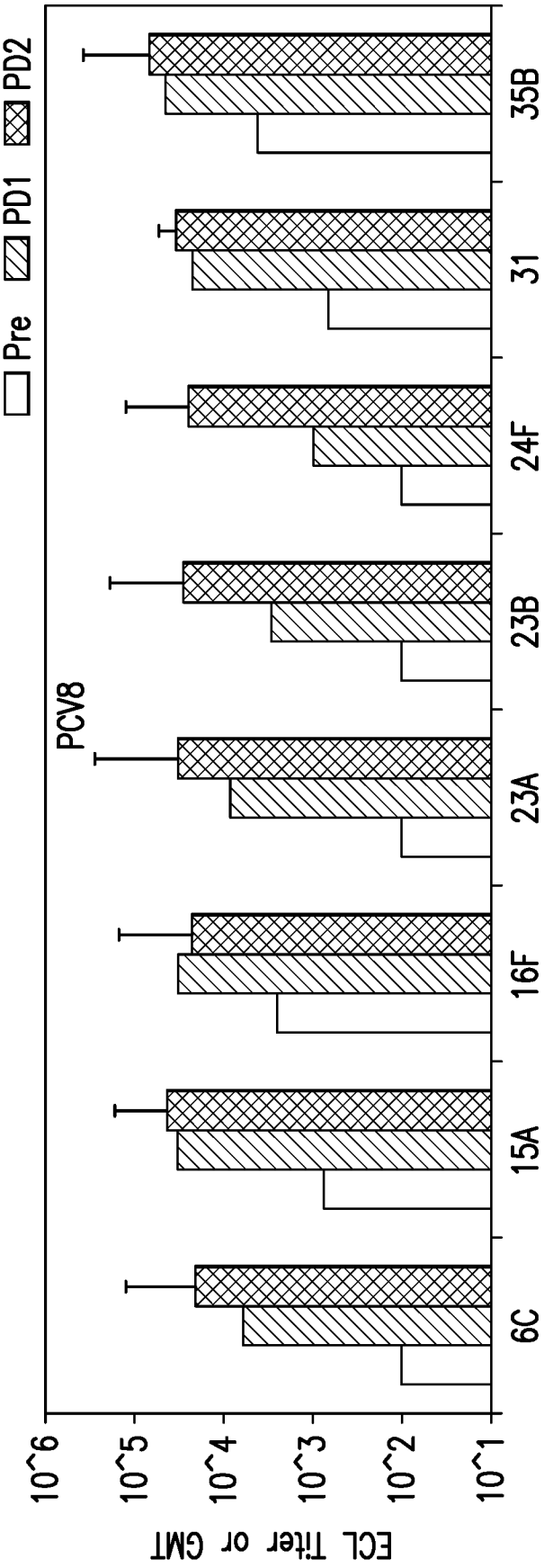

Pre
PD1
PD2
PCV8
6C
15A
16F
23A
23B
24F
31
35B
Serotype
ECL Titer or GMT
10^1
10^2
10^3
10^4
10^5
10^6

FIG.27A

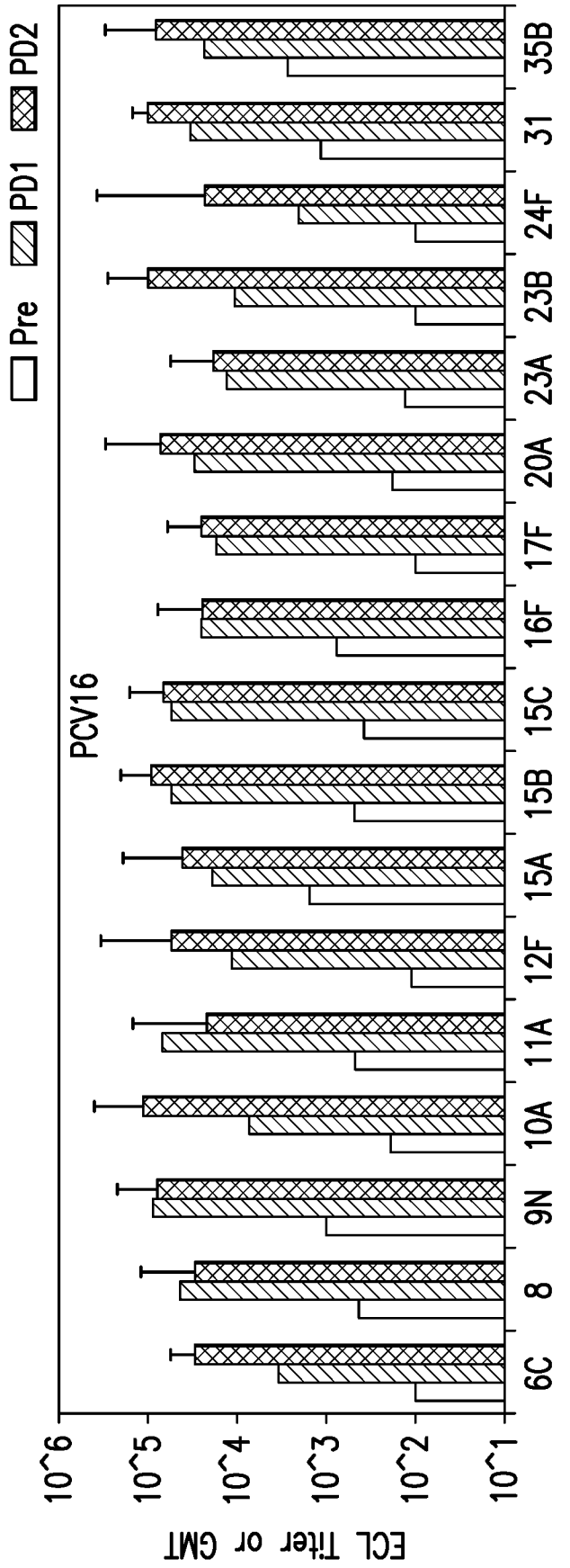

Pre
PD1
PD2
PCV16
ECL Titer or GMT
10^6
10^5
10^4
10^3
10^2
10^1
6C
8
9N
10A
11A
12F
15A
15B
15C
16F
17F
20A
23A
23B
24F
31
35B
Serotype

FIG.27B

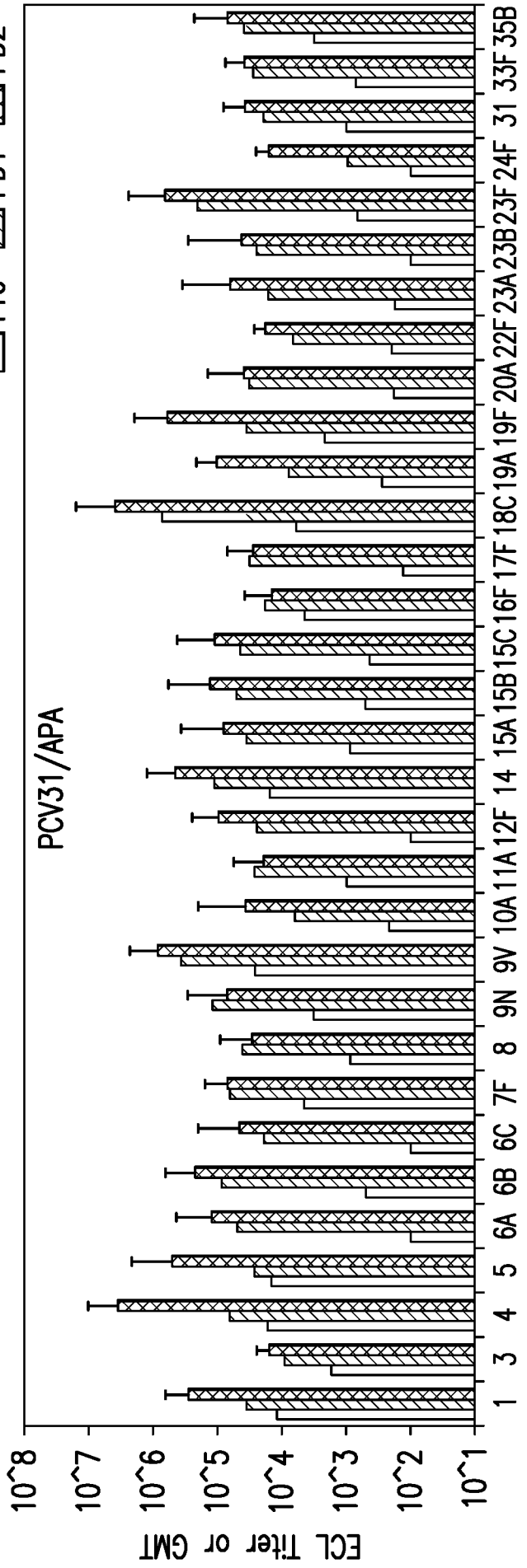

Pre
PD1
PD2
PCV31/APA
ECL Titer or GMT
10^8
10^7
10^6
10^5
10^4
10^3
10^2
10^1
1
3
4
5
6A
6B
6C
7F
8
9N
9V
10A
11A
12F
14
15A
15B
15C
16F
17F
18C
19A
19F
20A
22F
23A
23B
23F
24F
31
33F
35B
Serotype

FIG.27C

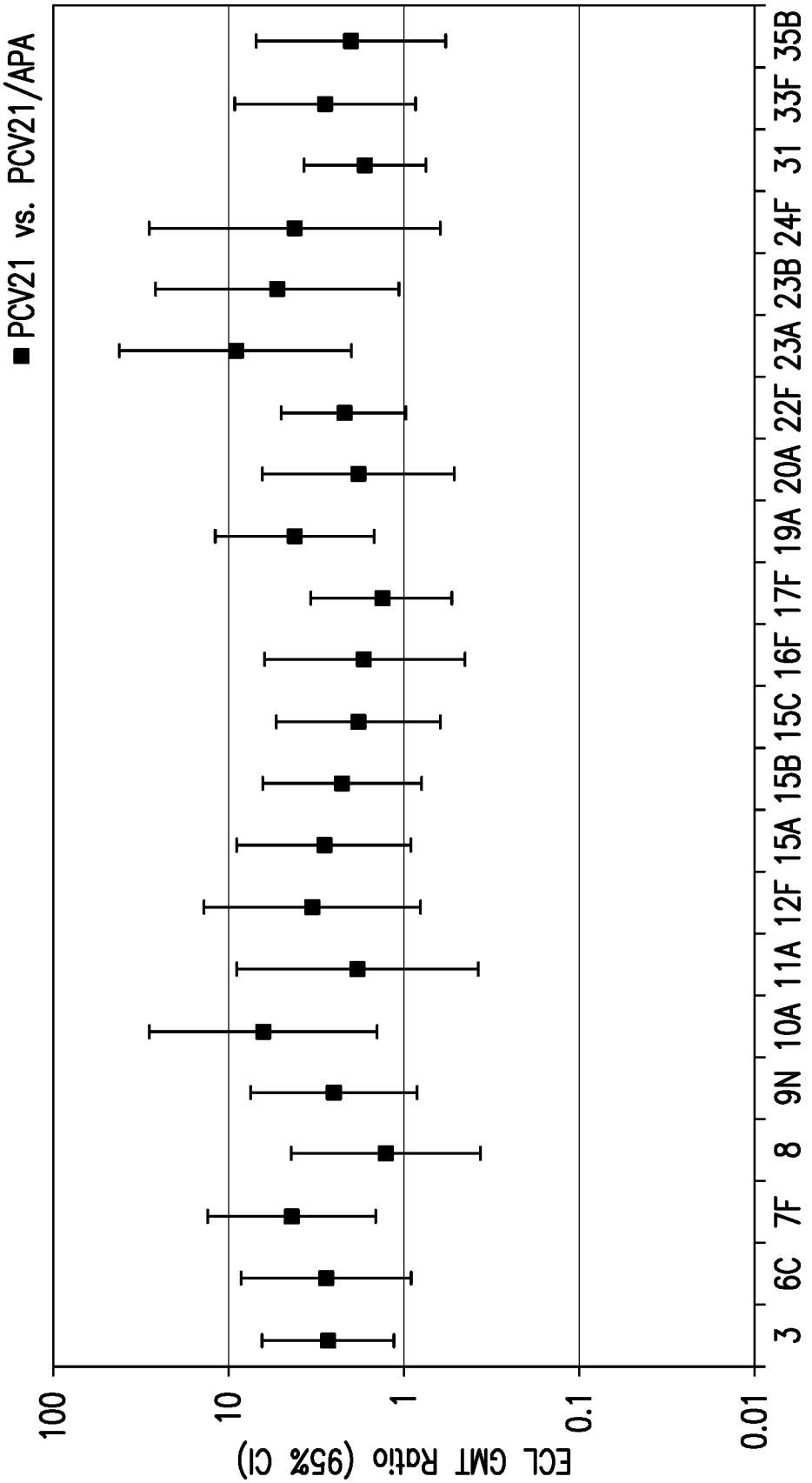

PCV21 vs. PCV21/APA
ECL GMT Ratio (95% CI)
100
10
1
0.1
0.01
3 6C 7F 8 9N 10A 11A 12F 15A 15B 15C 16F 17F 19A 20A 22F 23A 23B 24F 31 33F 35B
Serotype

FIG.28

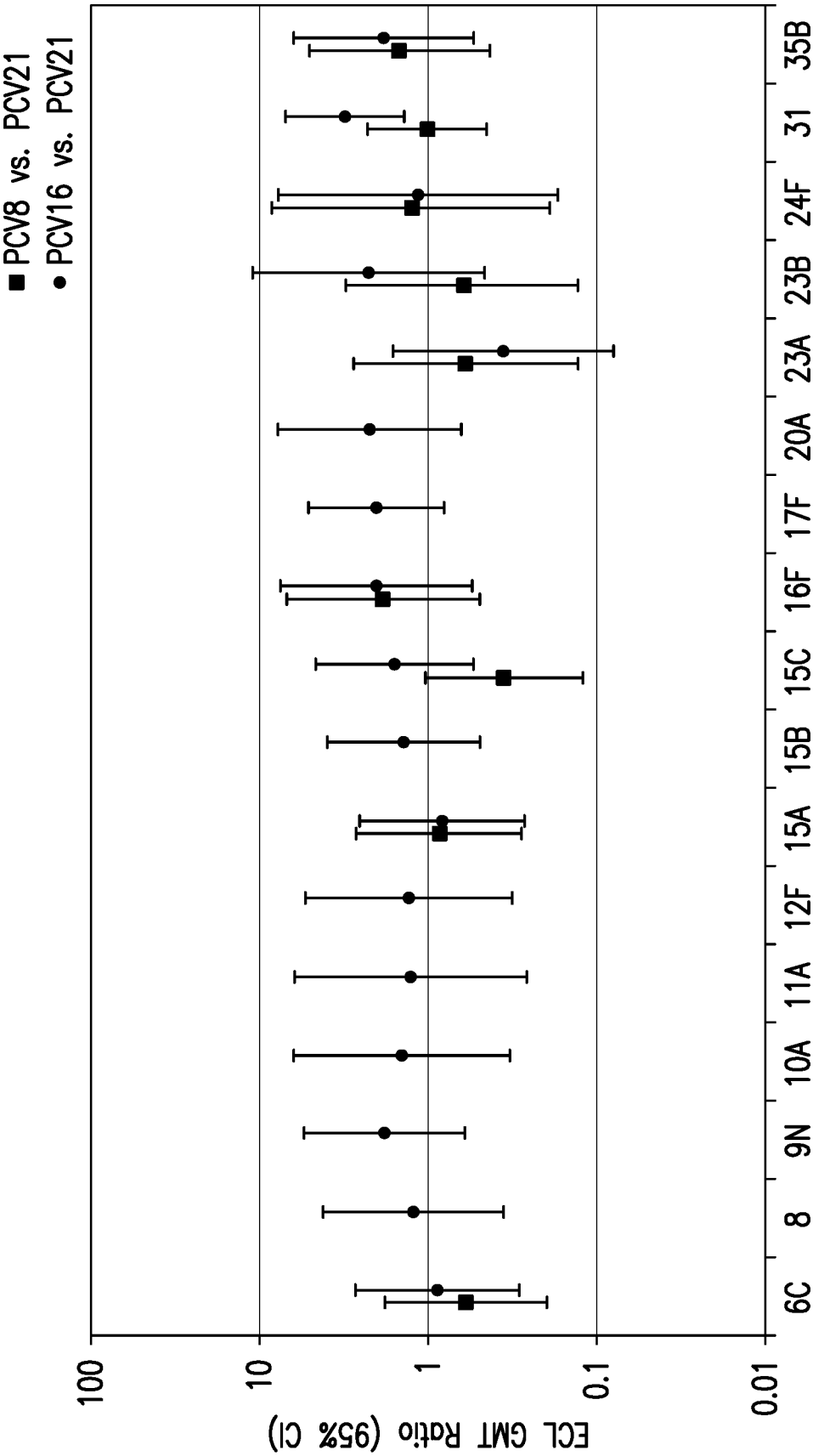

■ PCV8 vs. PCV21
● PCV16 vs. PCV21
ECL GMT Ratio (95% CI)
100
10
1
0.1
0.01
6C
8
9N
10A
11A
12F
15A
15B
15C
16F
17F
20A
23A
23B
24F
31
35B
Serotype

FIG.29

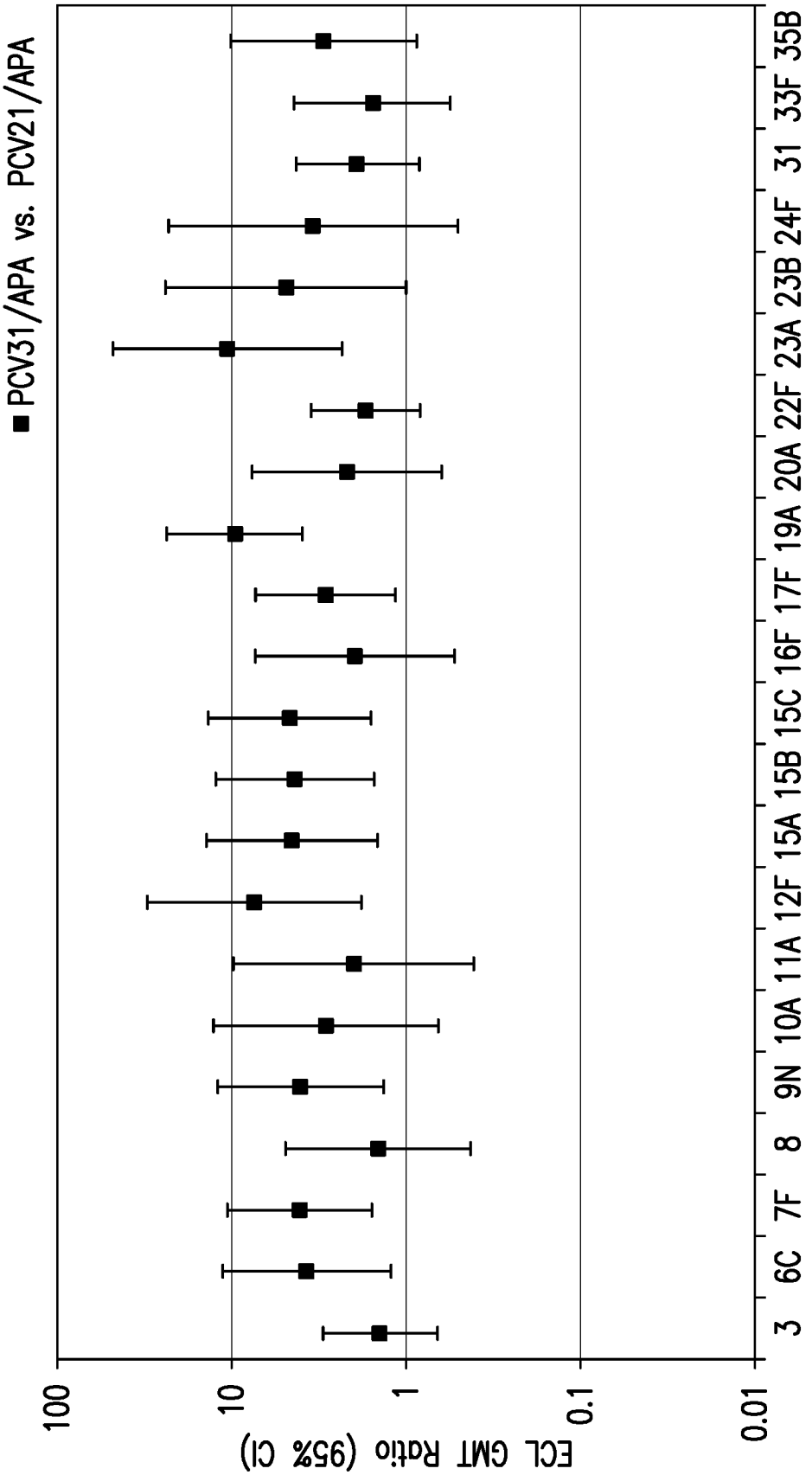

PCV31/APA vs. PCV21/APA
ECL GMT Ratio (95% CI)
100
10
1
0.1
0.01
3 6C 7F 8 9N 10A 11A 12F 15A 15B 15C 16F 17F 19A 20A 22F 23A 23B 24F 31 33F 35B
Serotype

FIG.3O

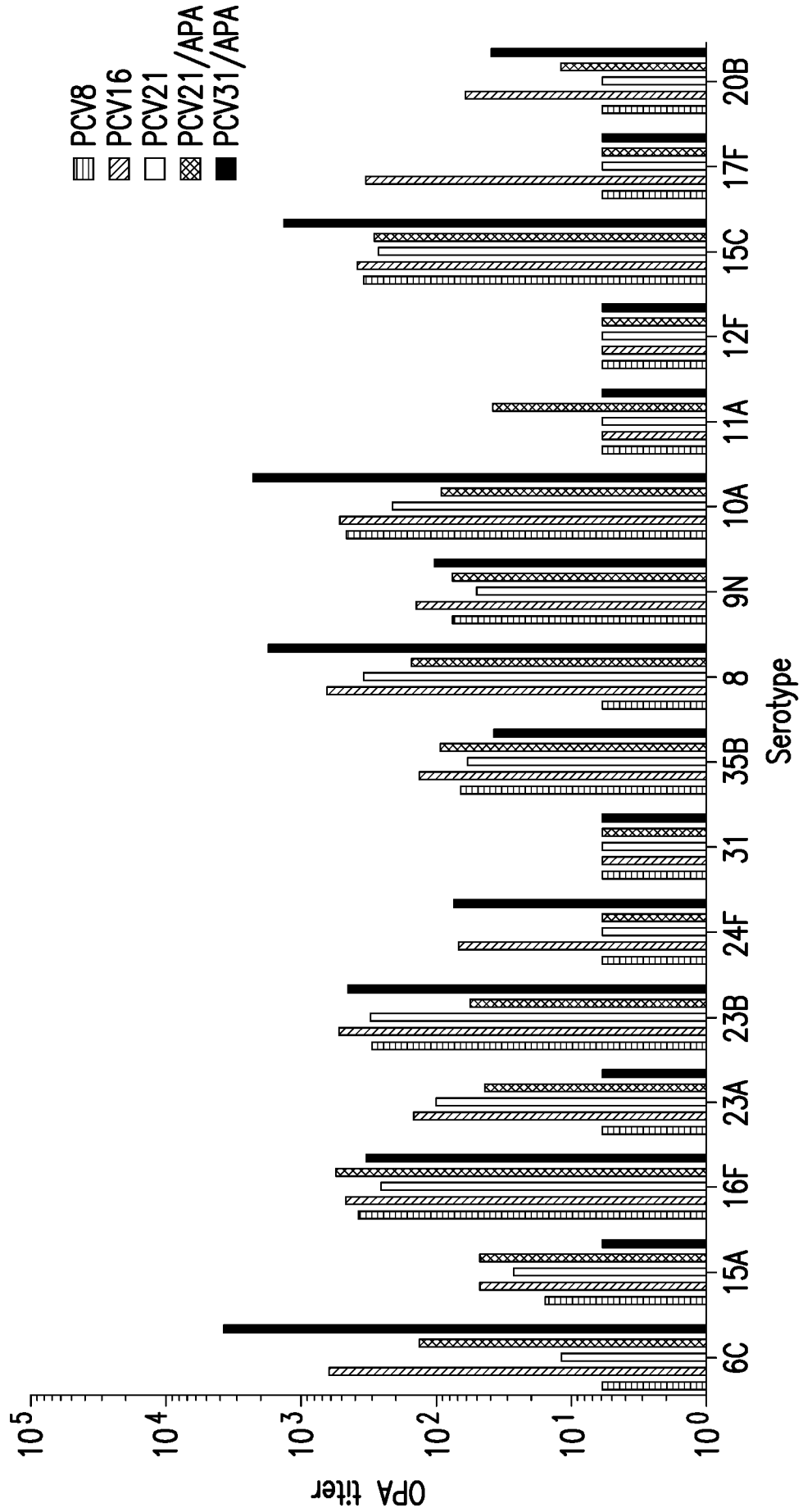

PCV8
PCV16
PCV21
PCV21/APA
PCV31/APA
OPA titer
10^0
10^1
10^2
10^3
10^4
10^5
6C
15A
16F
23A
23B
24F
31
35B
8
9N
10A
11A
12F
15C
17F
20B
Serotype

FIG.31A

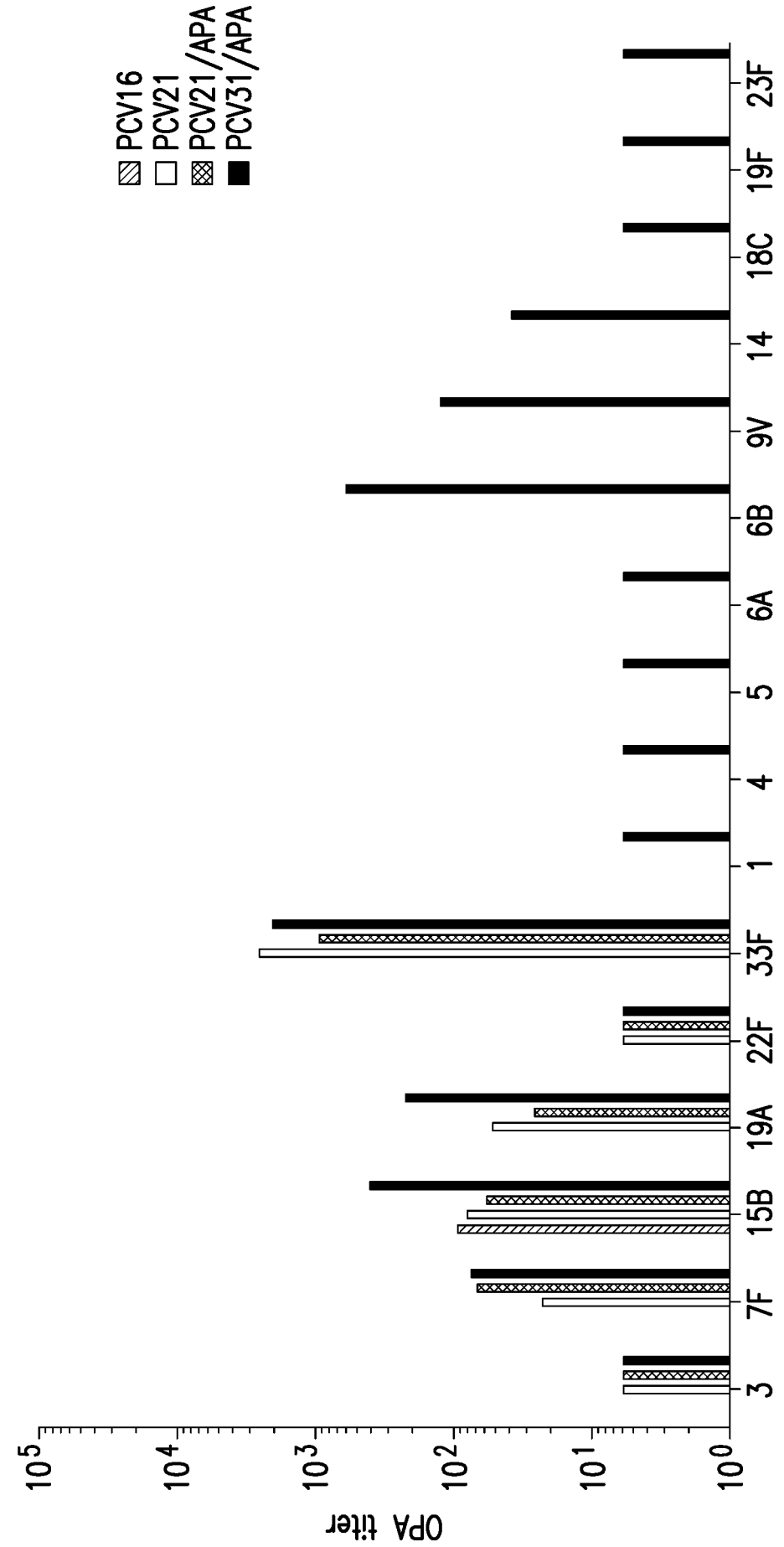

PCV16
PCV21
PCV21/APA
PCV31/APA
OPA titer
10^0
10^1
10^2
10^3
10^4
10^5
3
7F
15B
19A
22F
33F
1
4
5
6A
6B
9V
14
18C
19F
23F
Serotype

FIG.31B

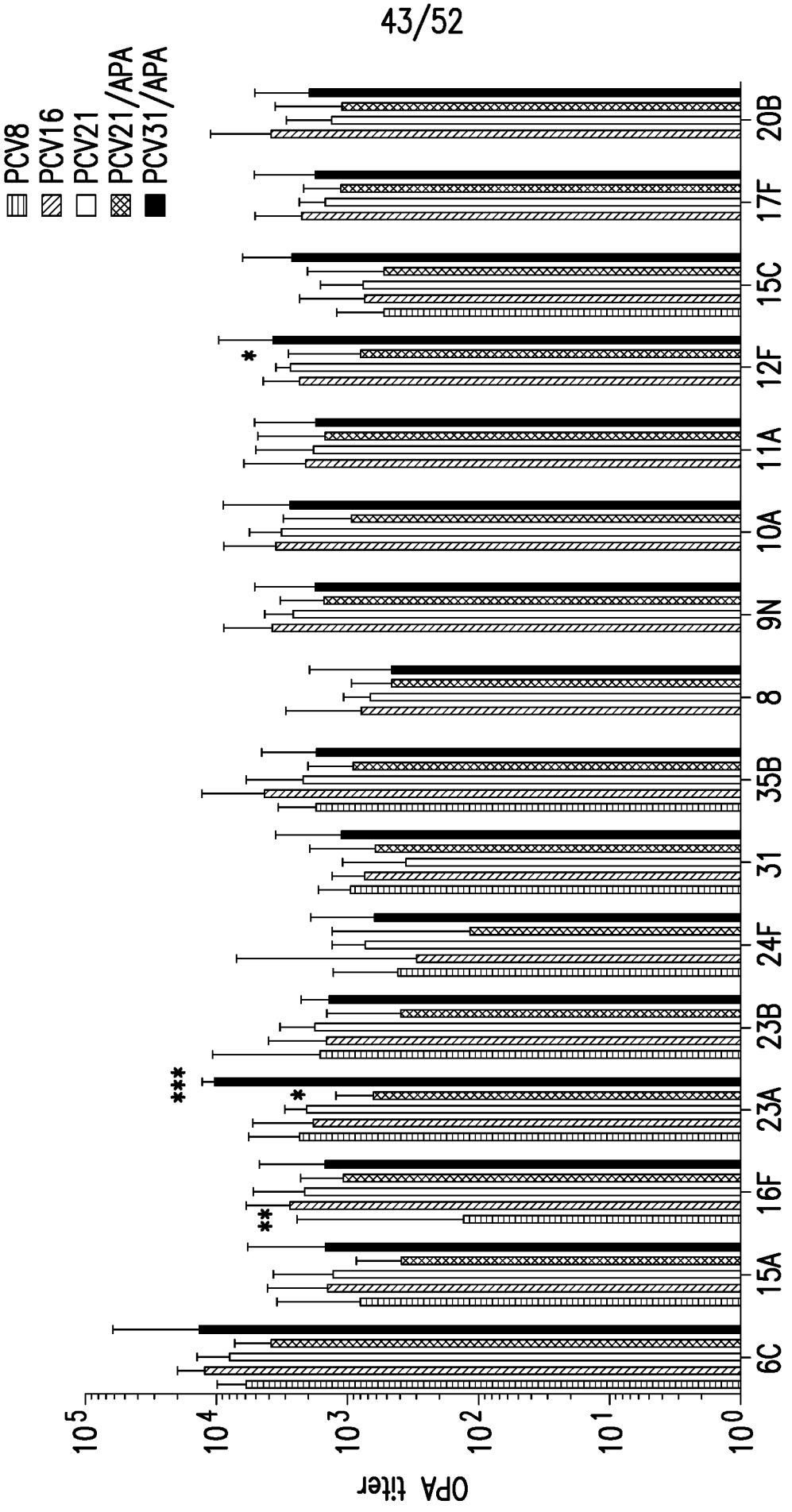

PCV8
PCV16
PCV21
PCV21/APA
PCV31/APA
OPA titer
10^5
10^4
10^3
10^2
10^1
10^0
6C
15A
16F
23A
23B
24F
31
35B
8
9N
10A
11A
12F
15C
17F
20B
Serotype
***
**
*
*

FIG.31C

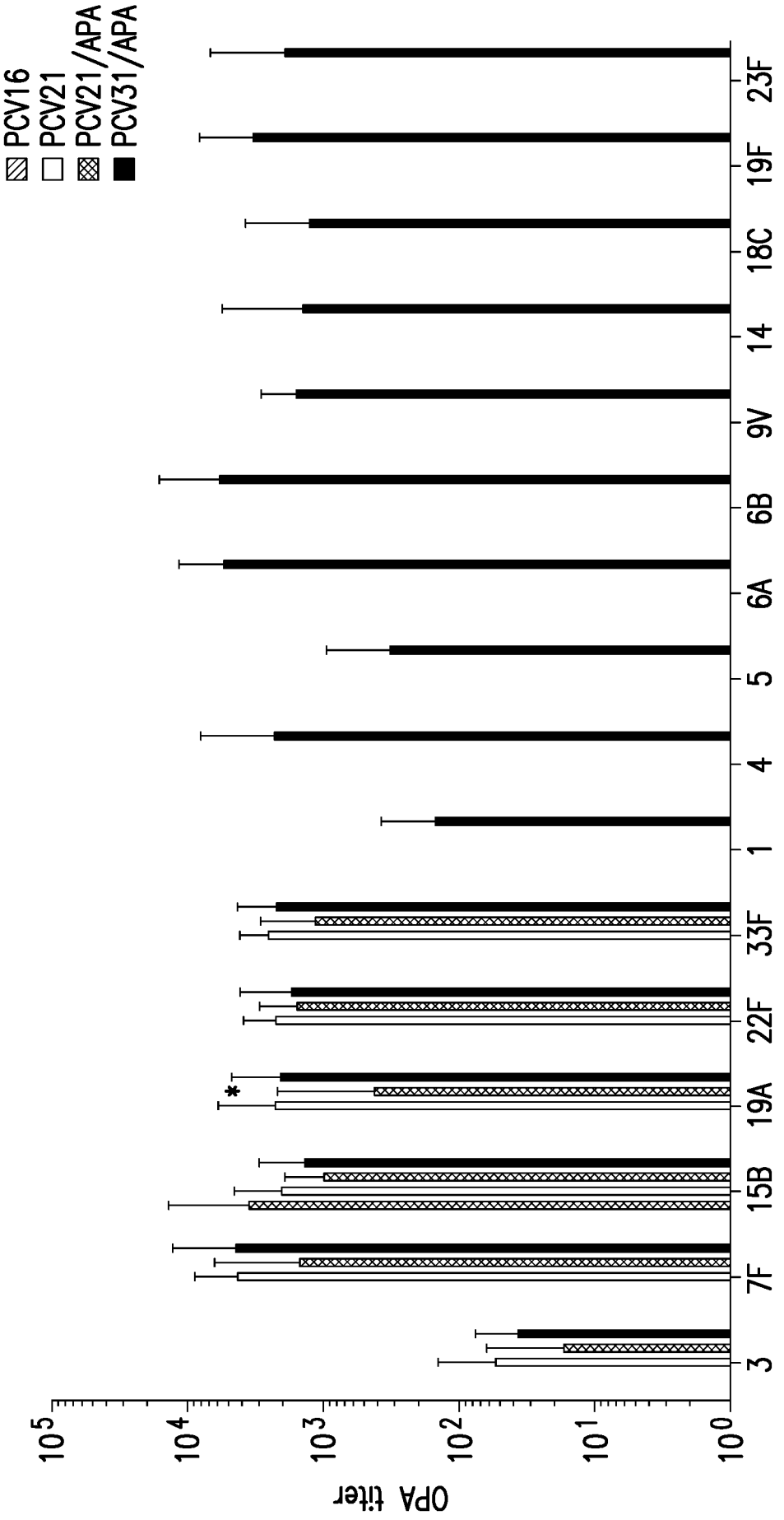

PCV16
PCV21
PCV21/APA
PCV31/APA
OPA titer
10^0
10^1
10^2
10^3
10^4
10^5
3
7F
15B
19A
22F
33F
1
4
5
6A
6B
9V
14
18C
19F
23F
Serotype
*

FIG.31D

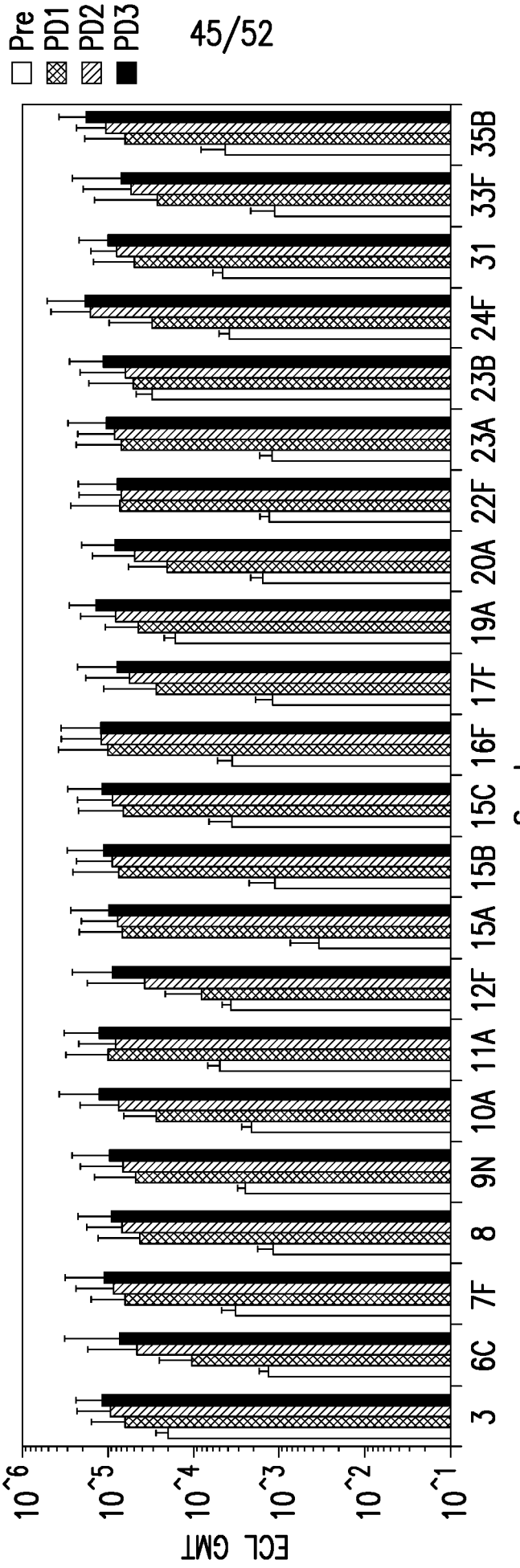

Pre
PD1
PD2
PD3
ECL GMT
10^6
10^5
10^4
10^3
10^2
10^1
3
6C
7F
8
9N
10A
11A
12F
15A
15B
15C
16F
17F
19A
20A
22F
23A
23B
24F
31
33F
35B
Serotype

FIG.32

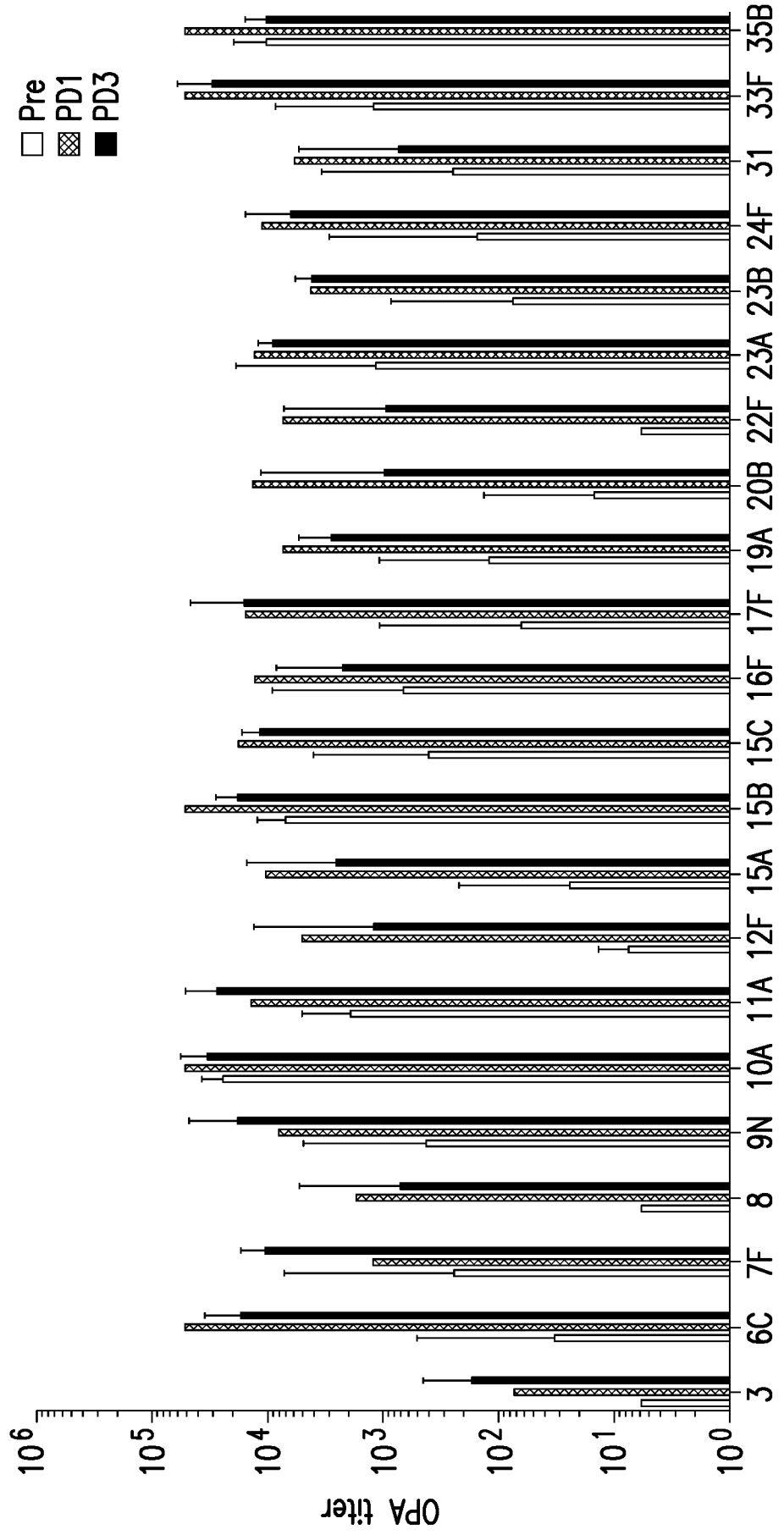

Pre
PD1
PD3
OPA titer
10^0
10^1
10^2
10^3
10^4
10^5
10^6
3
6C
7F
8
9N
10A
11A
12F
15A
15B
15C
16F
17F
19A
20B
22F
23A
23B
24F
31
33F
35B
Serotype

FIG.33

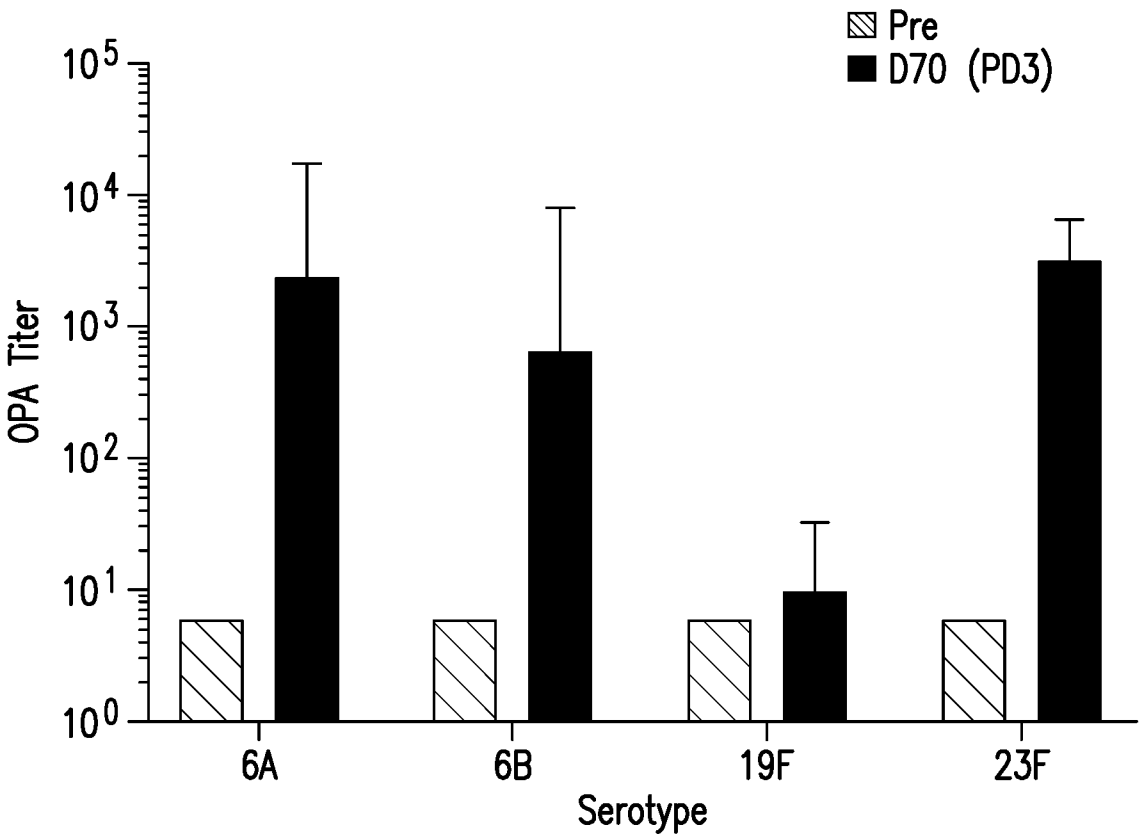

Pre
D70 (PD3)
OPA Titer
10^5
10^4
10^3
10^2
10^1
10^0
6A
6B
19F
23F
Serotype

FIG.34

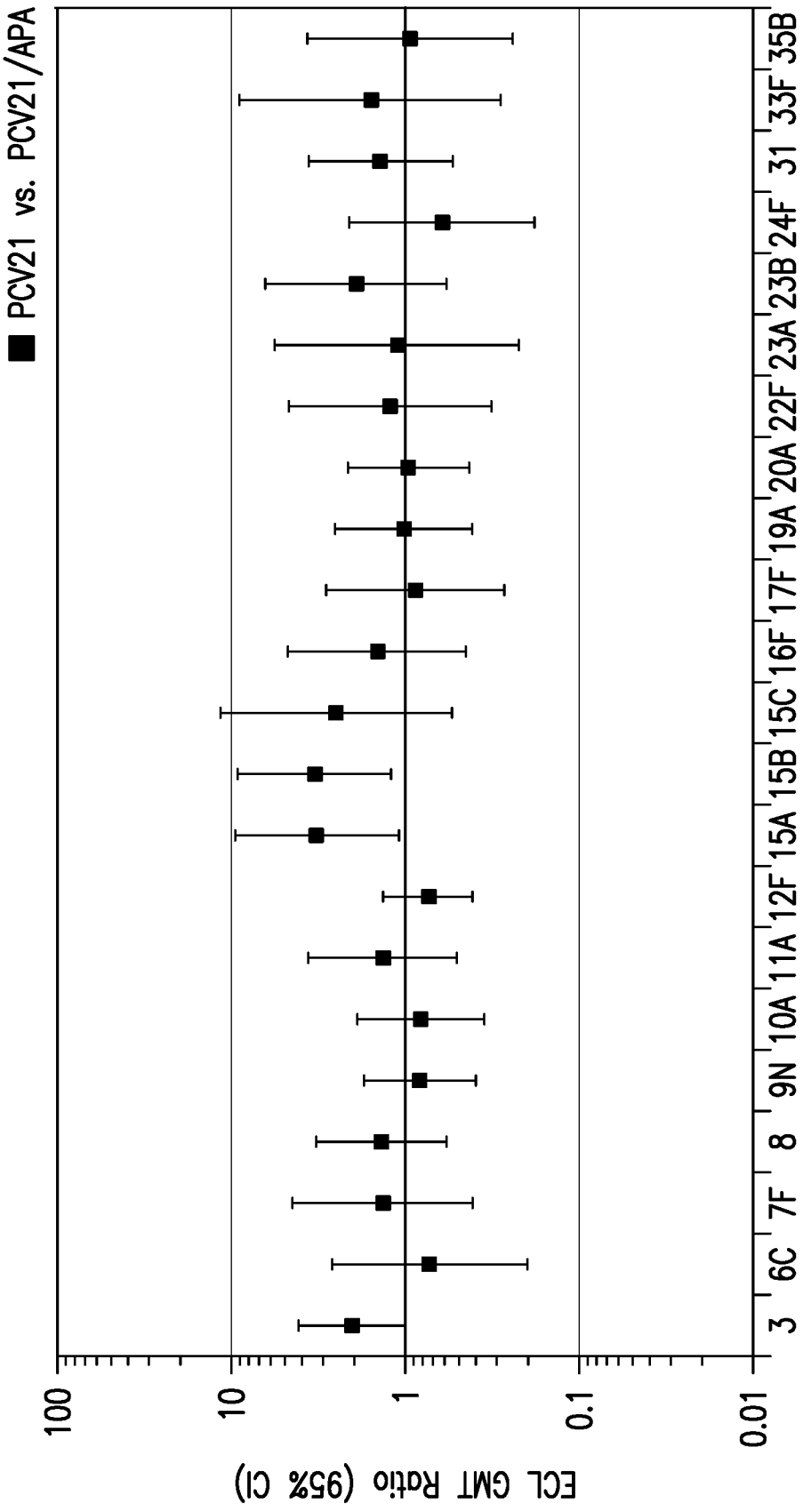

PCV21 vs. PCV21/APA
ECL GMT Ratio (95% CI)
100
10
1
0.1
0.01
3
6C
7F
8
9N
10A
11A
12F
15A
15B
15C
16F
17F
19A
20A
22F
23A
23B
24F
31
33F
35B
Serotype

FIG.35

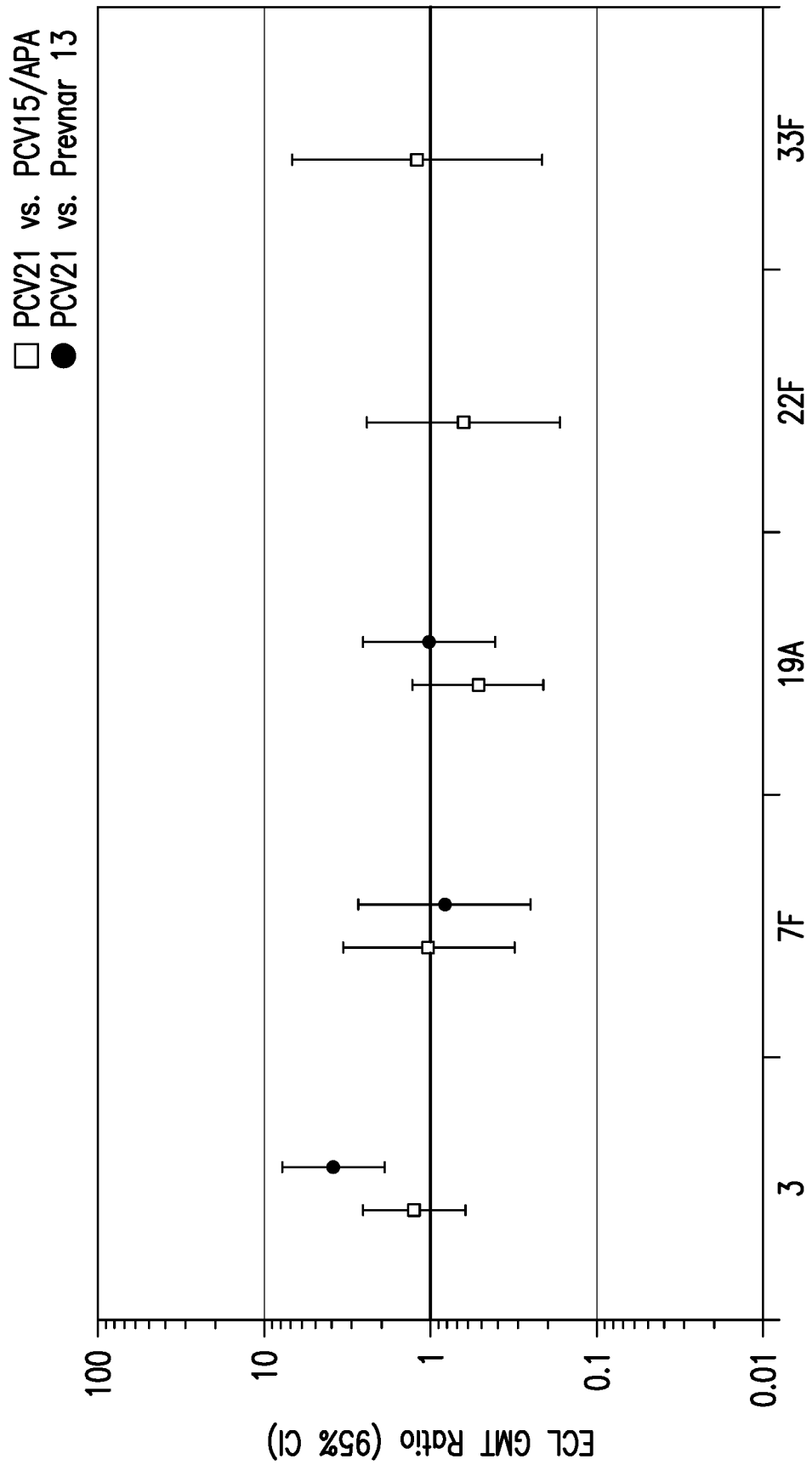

□ PCV21 vs. PCV15/APA
● PCV21 vs. Prevnar 13
ECL GMT Ratio (95% CI)
100
10
1
0.1
0.01
3
7F
19A
22F
33F
Serotype

FIG.36

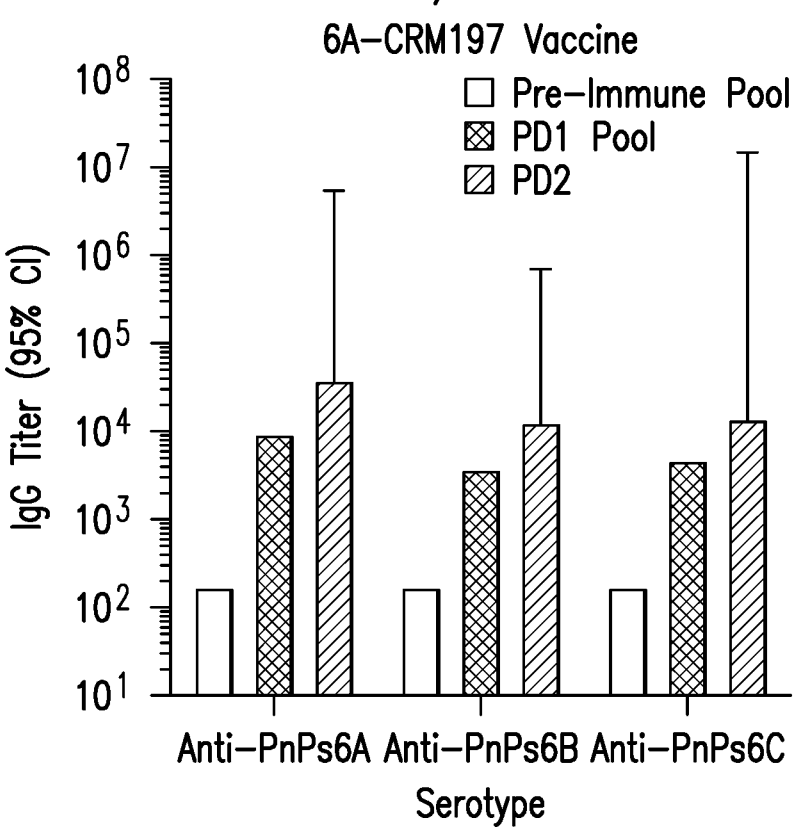


FIG.37A

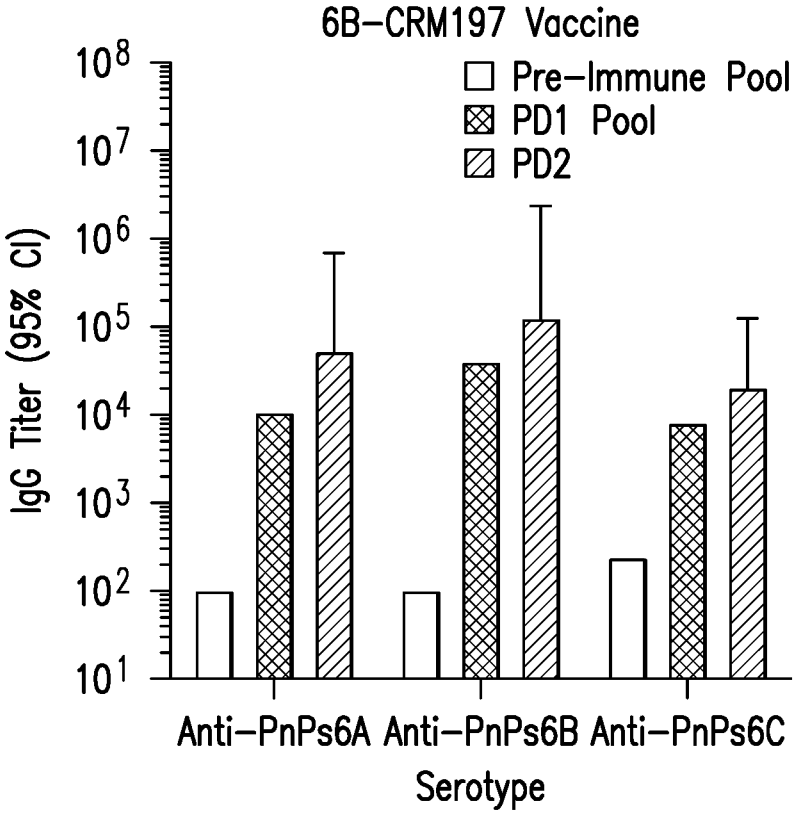


FIG.37B

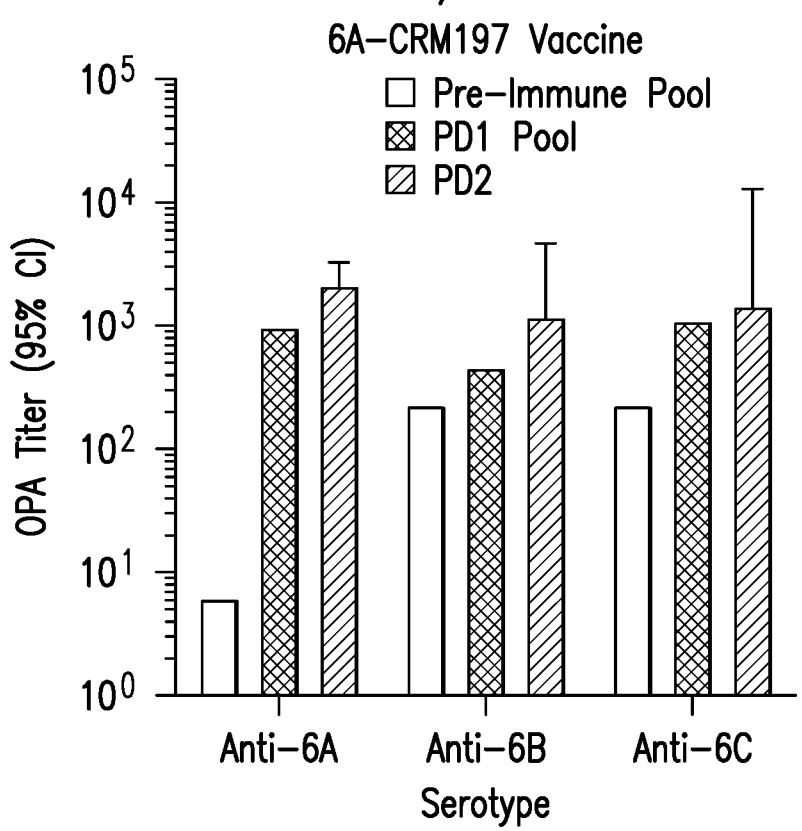


FIG.38A

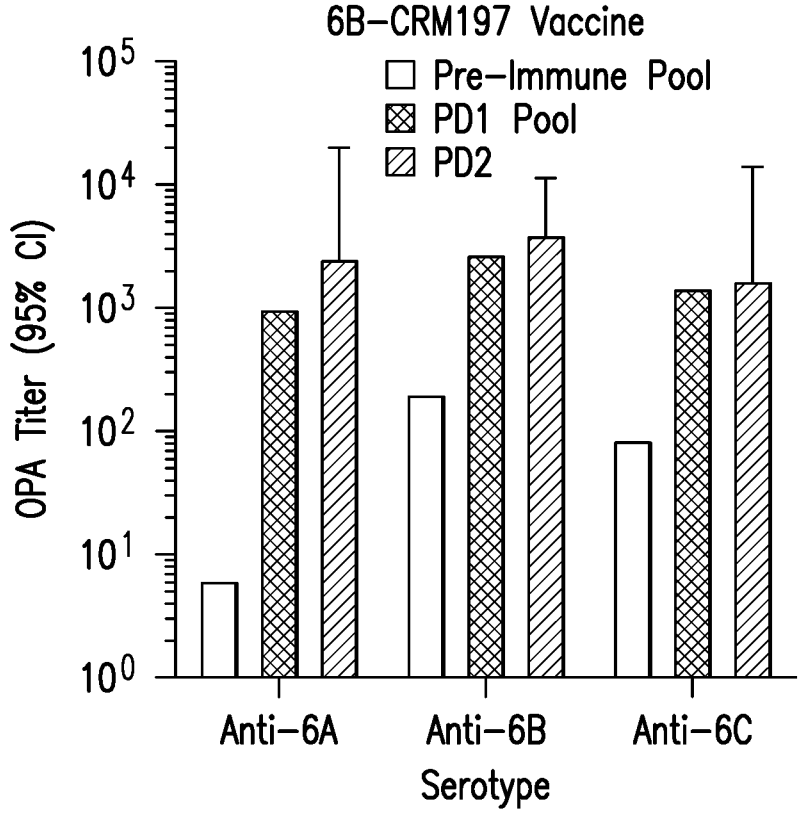


FIG.38B

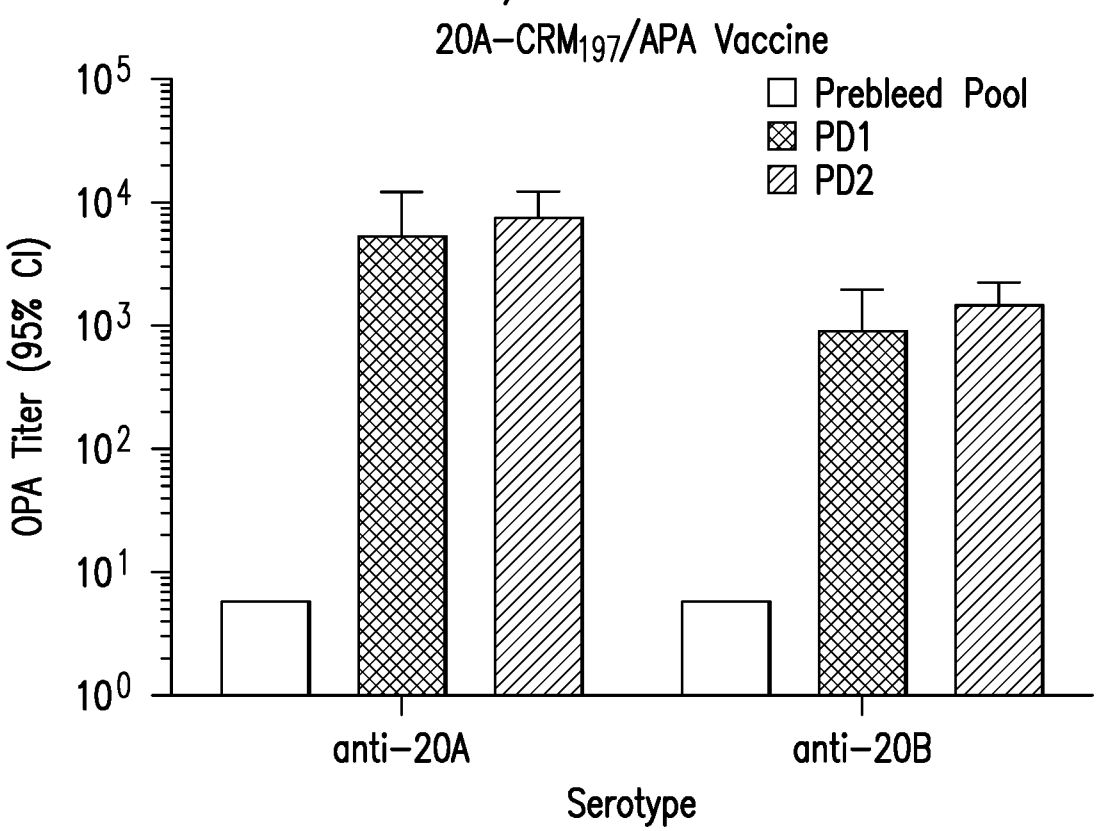


FIG.39A

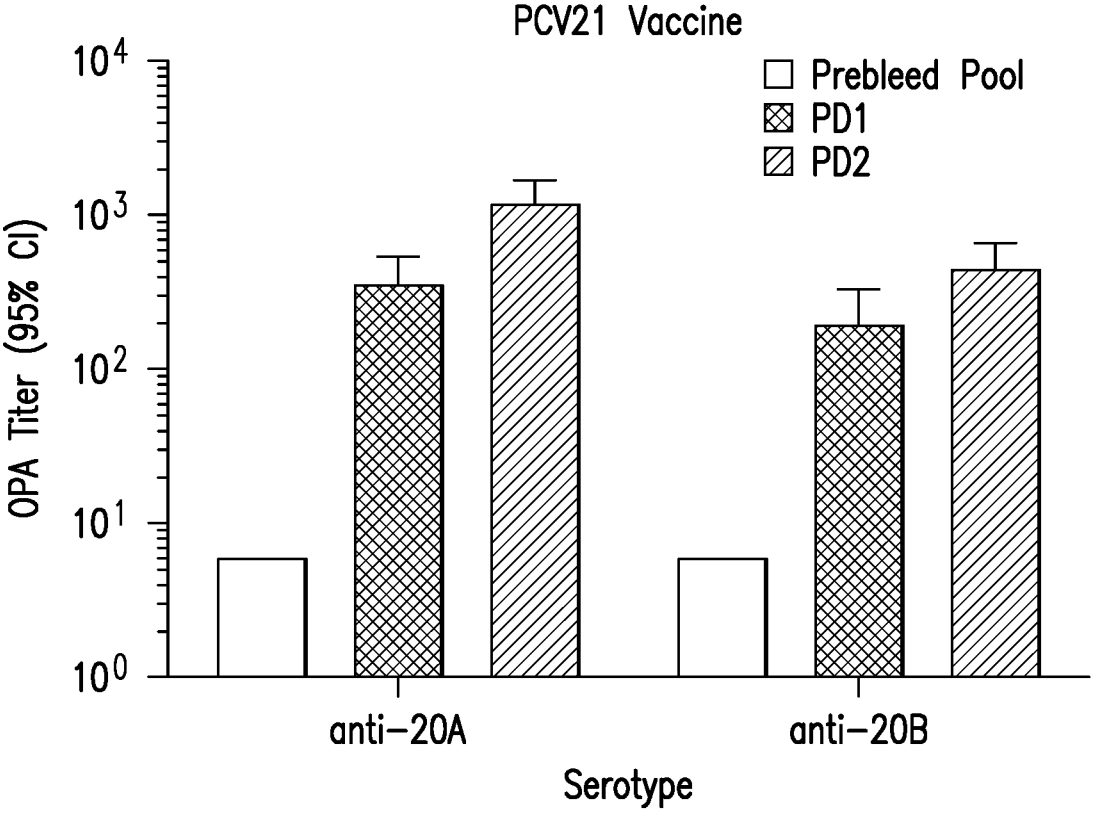


FIG.39B