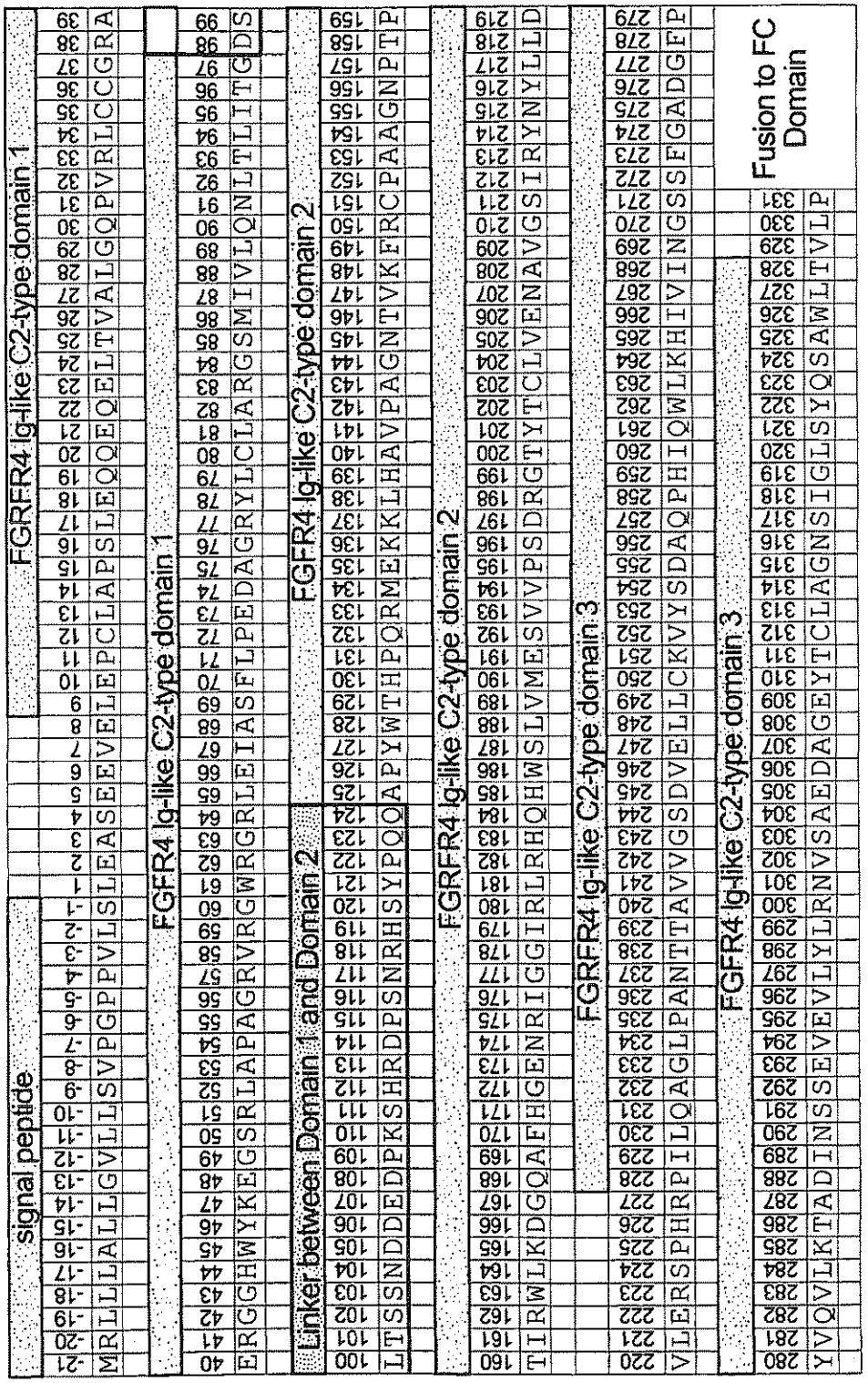
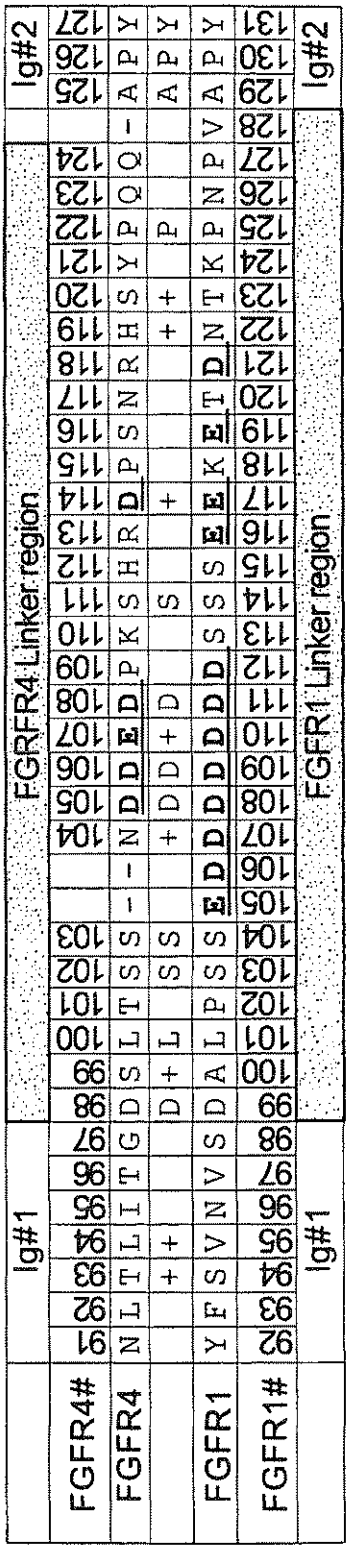

signal peptide
FGFR4 Ig-like C2-type domain 1
FGFR4 Ig-like C2-type domain 1
Linker between Domain 1 and Domain 2
FGFR4 Ig-like C2-type domain 2
FGFR4 Ig-like C2-type domain 2
FGFR4 Ig-like C2-type domain 3
FGFR4 Ig-like C2-type domain 3
Fusion to FC Domain

FIG. 1


Ig#1
FGRFR4 Linker region
Ig#2
FGFR4#
FGFR4
FGFR1
FGFR1#
Ig#1
FGFR1 Linker region
Ig#2

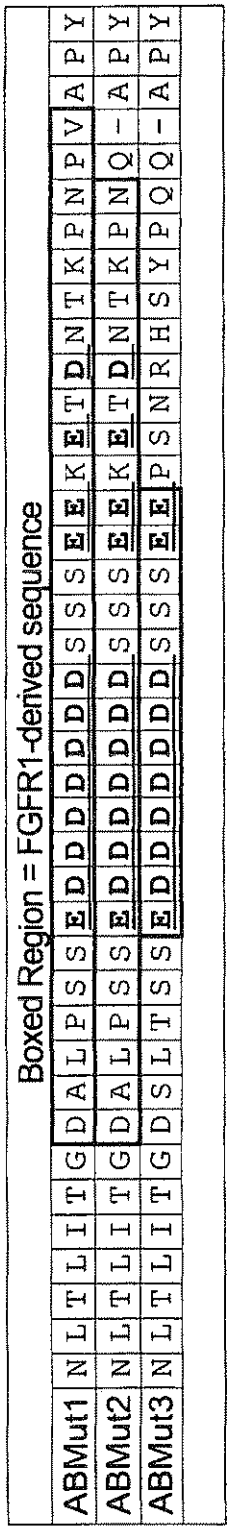

Boxed Region = FGFR1-derived sequence
ABMut1
ABMut2
ABMut3

FIG. 2

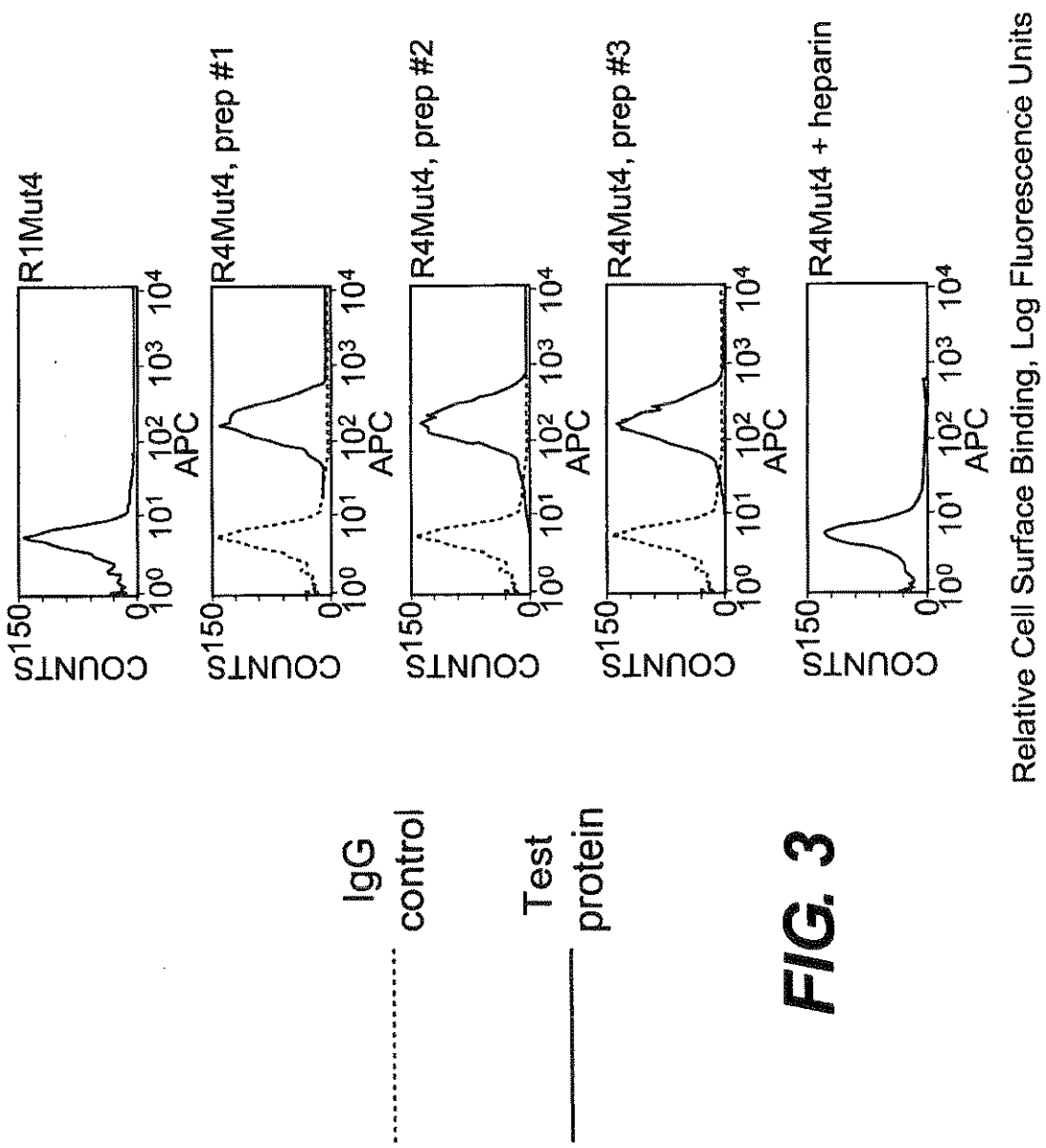

R1Mut4
R4Mut4, prep #1
R4Mut4, prep #2
R4Mut4, prep #3
R4Mut4 + heparin
COUNTS
150
0
APC
10^0 10^1 10^2 10^3 10^4
IgG control
Test protein
Relative Cell Surface Binding, Log Fluorescence Units

FIG. 3

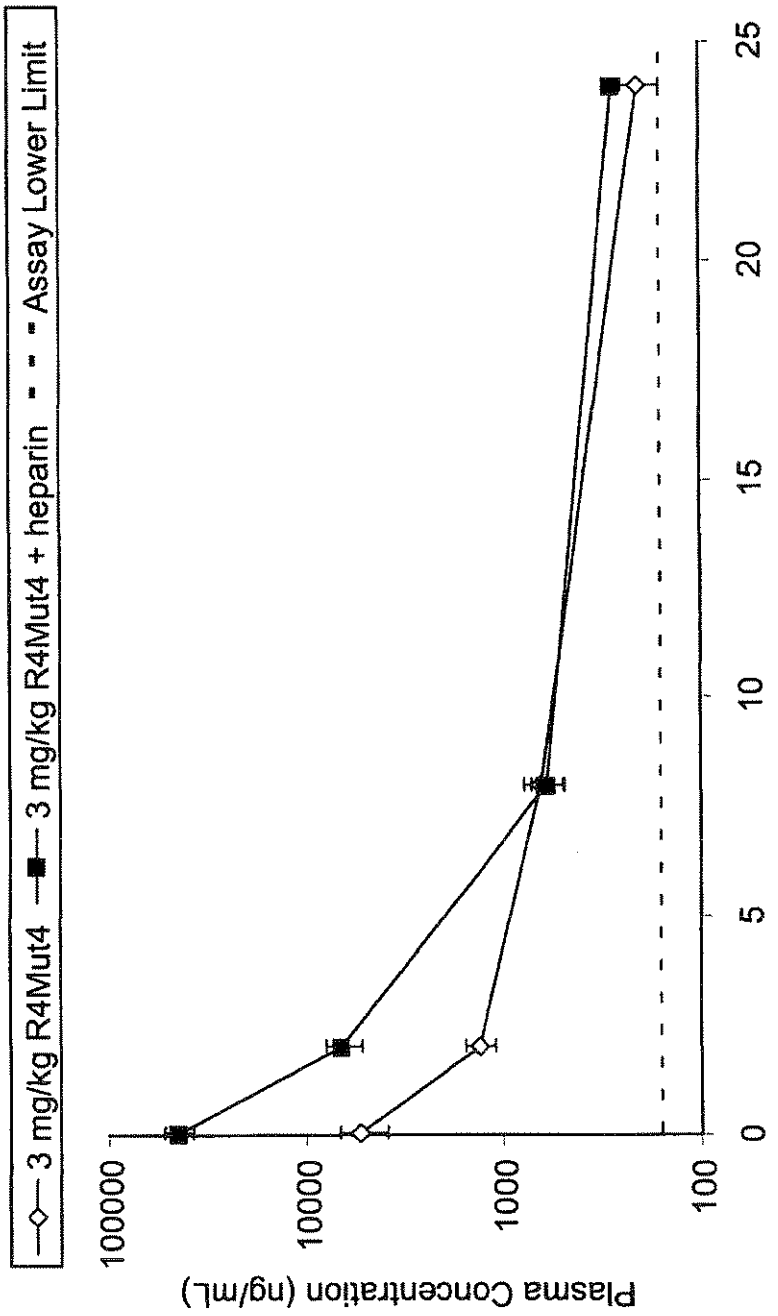

3 mg/kg R4Mut4
3 mg/kg R4Mut4 + heparin
Assay Lower Limit
Plasma Concentration (ng/mL)
100000
10000
1000
100
0
5
10
15
20
25
Time (h)

FIG. 4

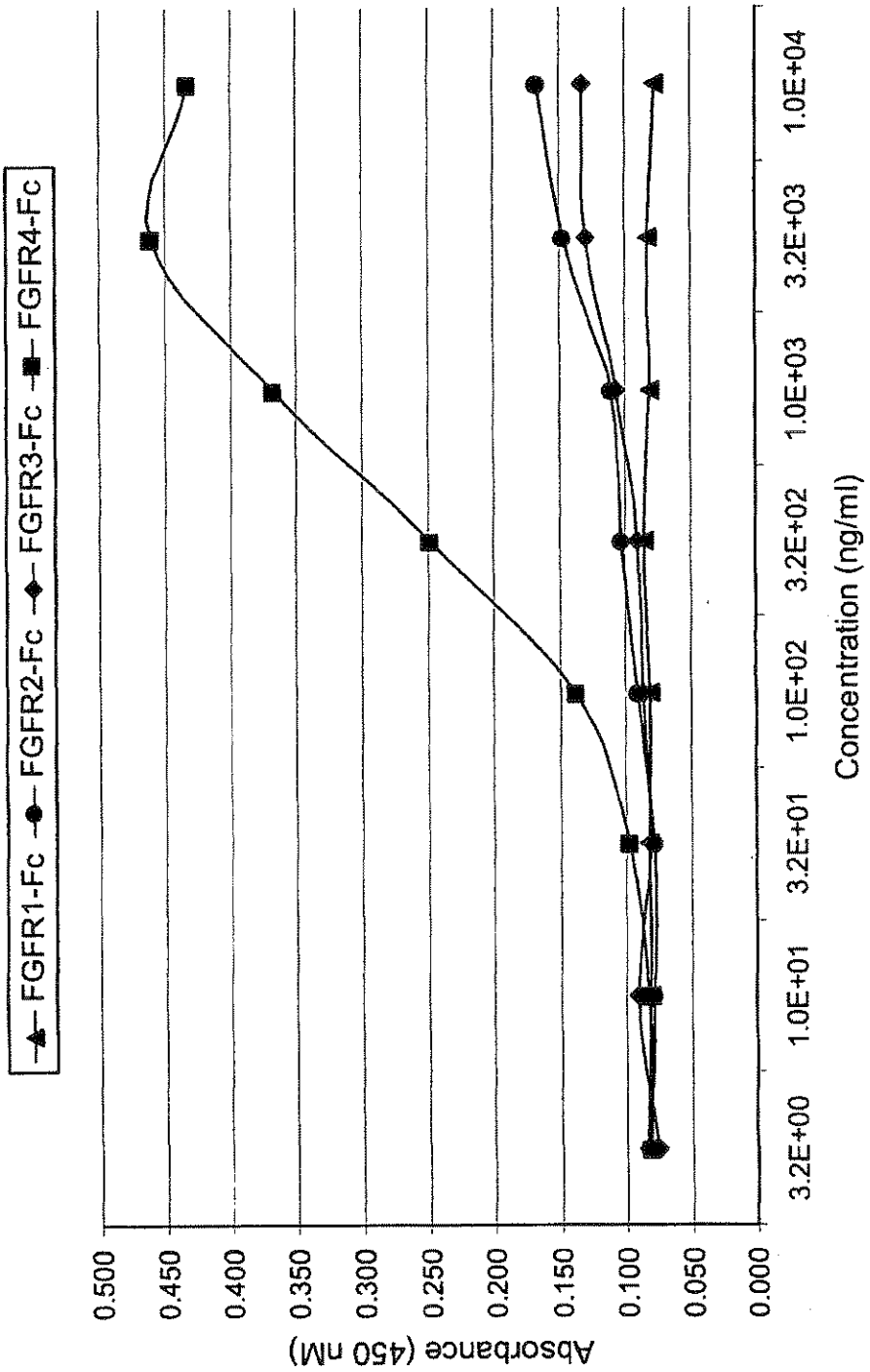

FGFR1-Fc
FGFR2-Fc
FGFR3-Fc
FGFR4-Fc
Absorbance (450 nM)
0.500
0.450
0.400
0.350
0.300
0.250
0.200
0.150
0.100
0.050
0.000
3.2E+00
1.0E+01
3.2E+01
1.0E+02
3.2E+02
1.0E+03
3.2E+03
1.0E+04
Concentration (ng/ml)

FIG. 5

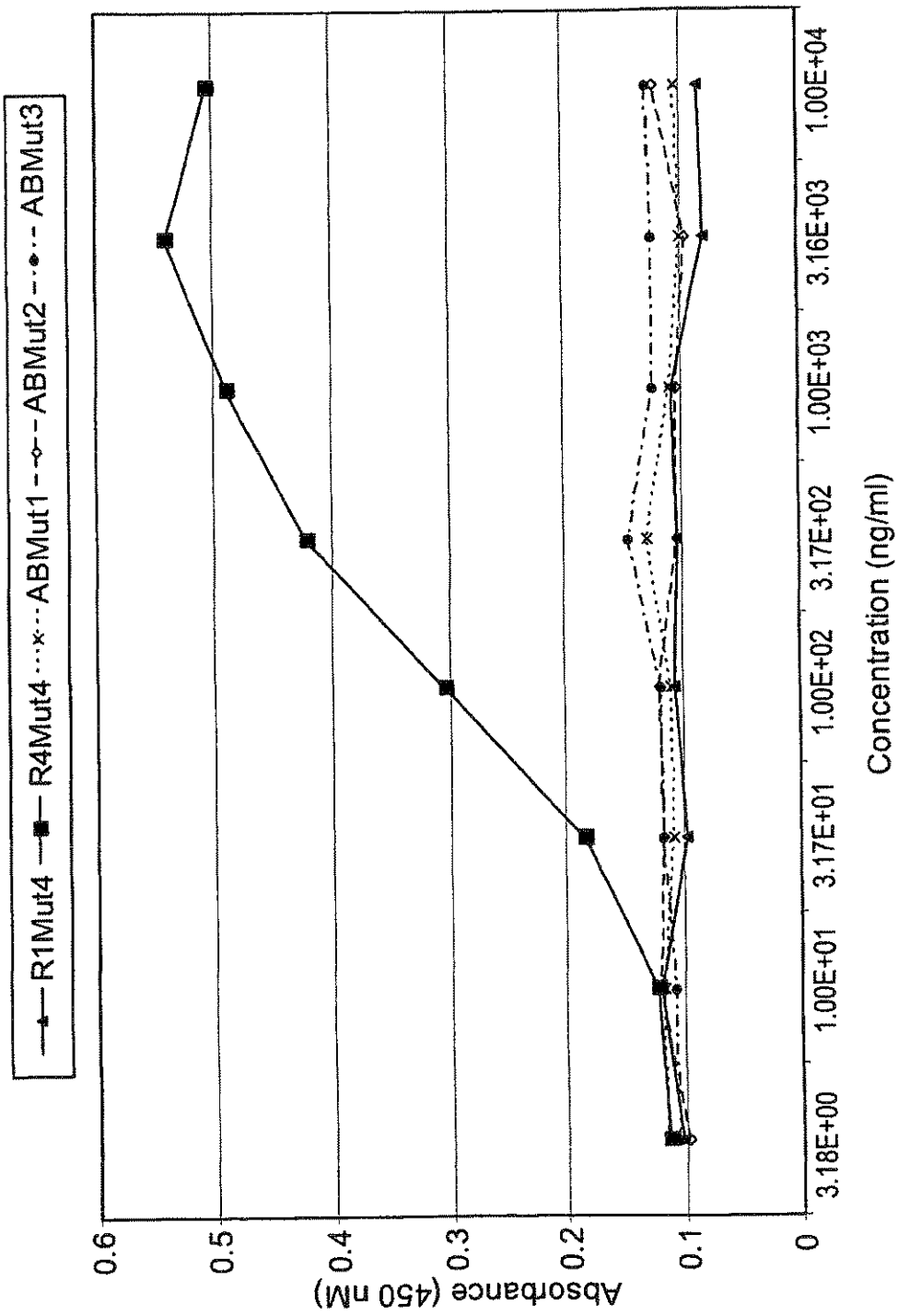

R1Mut4
R4Mut4
ABMut1
ABMut2
ABMut3
Absorbance (450 nM)
0
0.1
0.2
0.3
0.4
0.5
0.6
3.18E+00
1.00E+01
3.17E+01
1.00E+02
3.17E+02
1.00E+03
3.16E+03
1.00E+04
Concentration (ng/ml)

FIG. 6

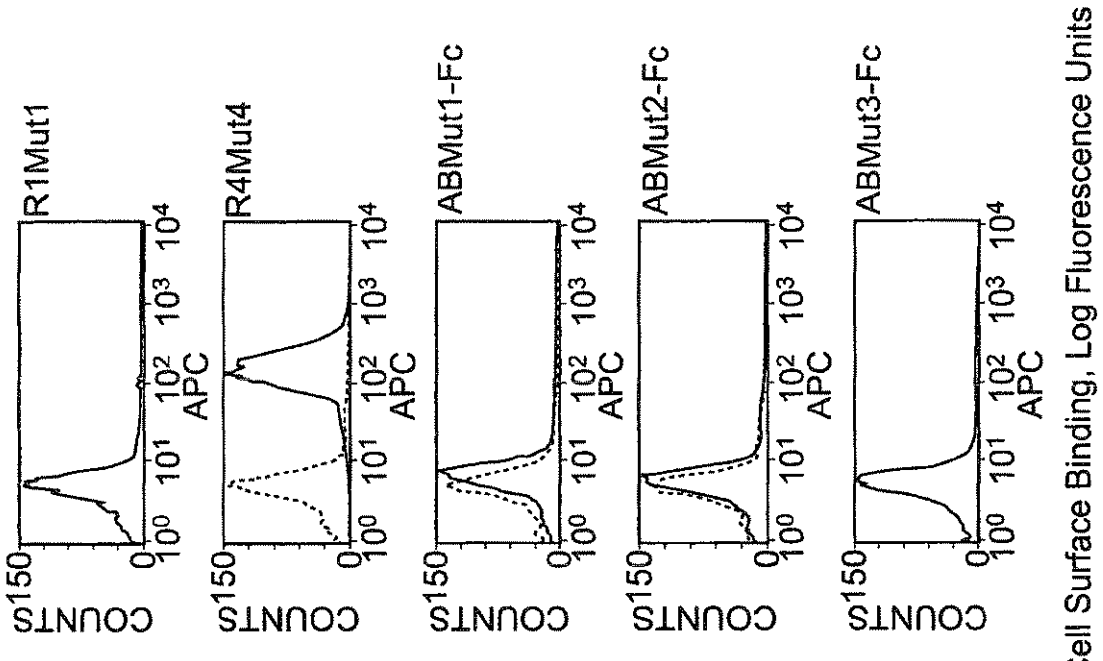

R1Mut1
R4Mut4
ABMut1-Fc
ABMut2-Fc
ABMut3-Fc
COUNTS
150
0
10^0 10^1 10^2 10^3 10^4
APC
IgG control
Test protein
Relative Cell Surface Binding, Log Fluorescence Units

FIG. 7

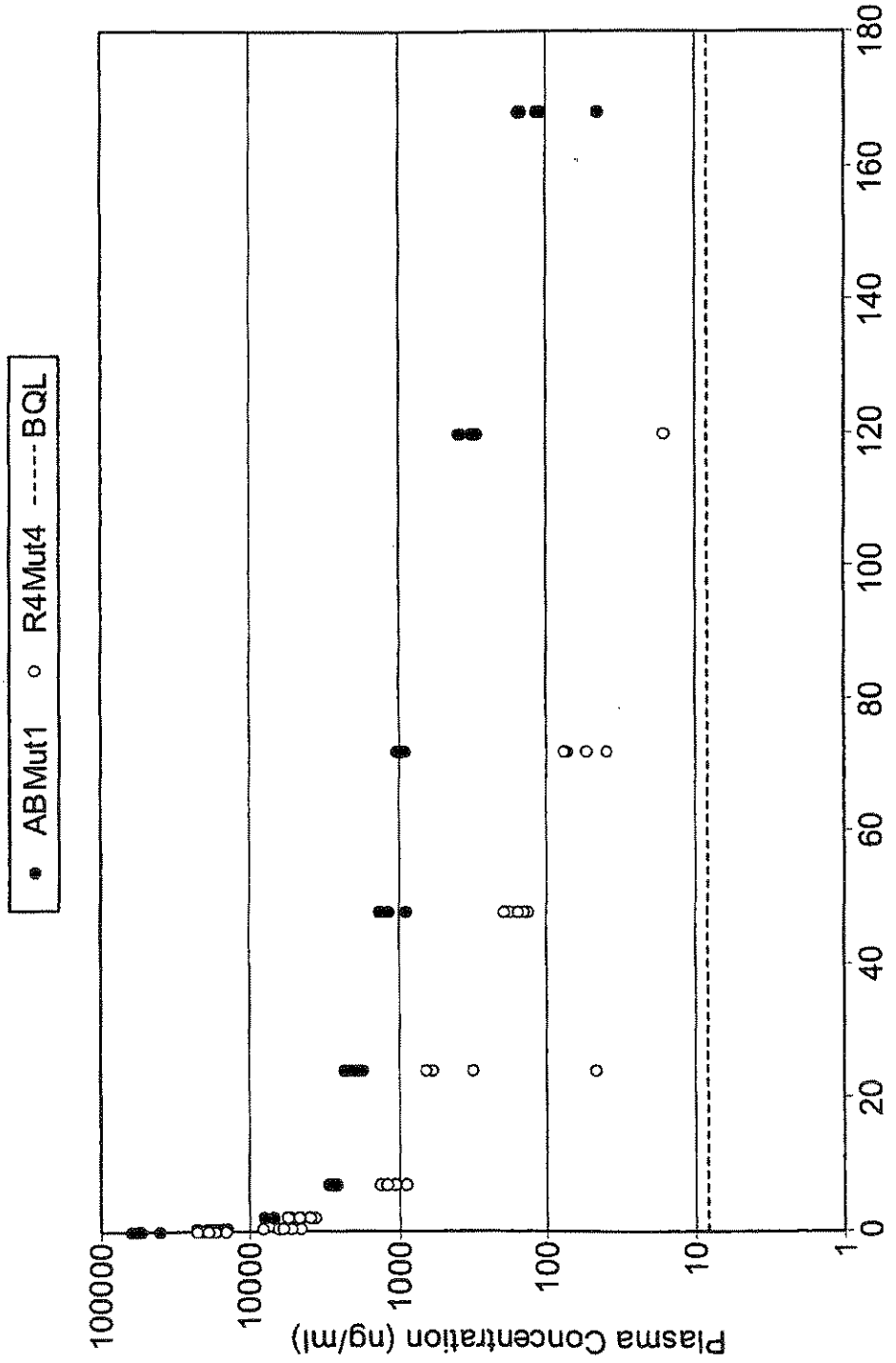

ABMut1
R4Mut4
BQL
Plasma Concentration (ng/ml)
100000
10000
1000
100
10
1
0
20
40
60
80
100
120
140
160
180
Time (hr)

FIG. 8

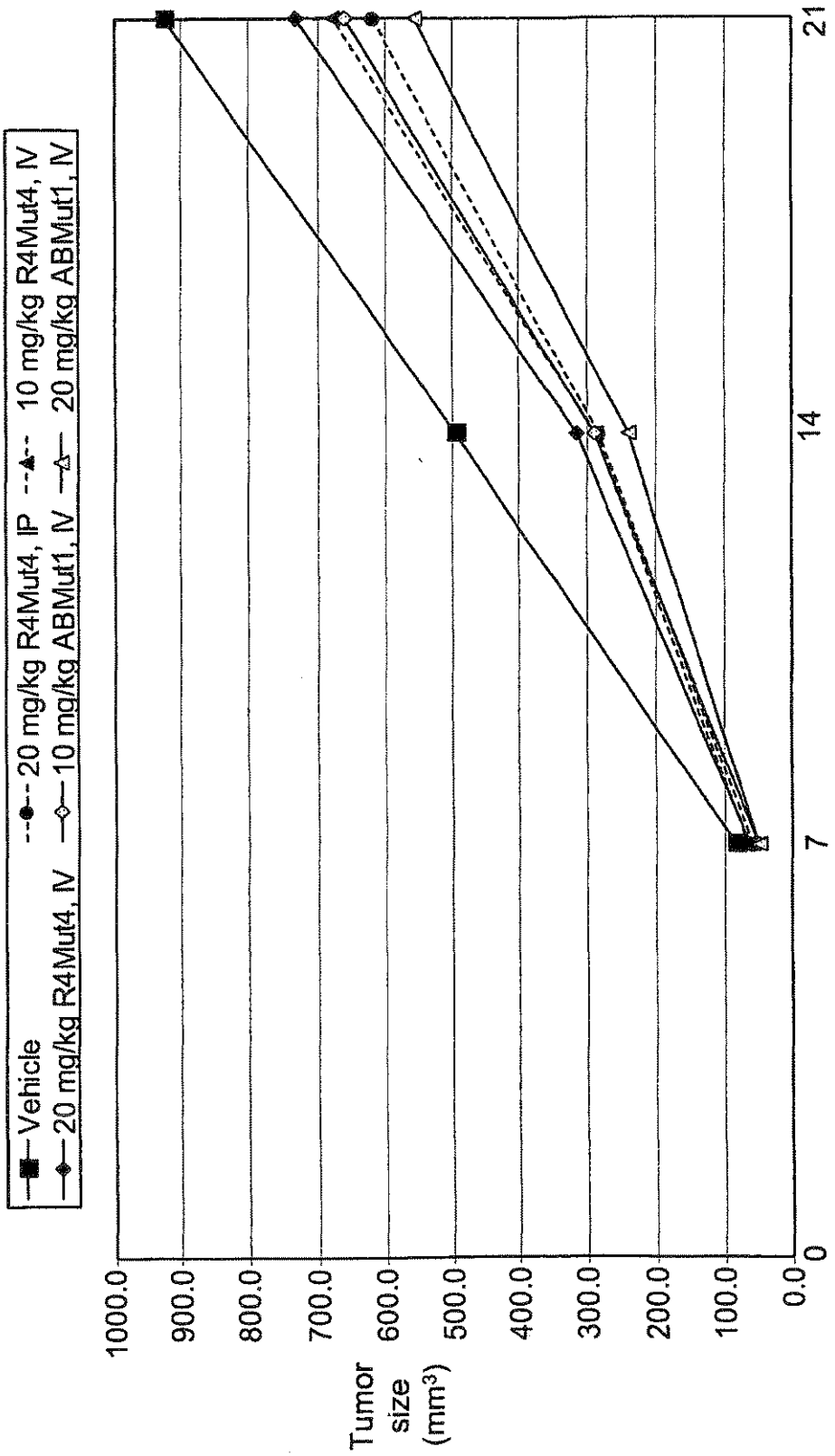

Vehicle
20 mg/kg R4Mut4, IV
20 mg/kg R4Mut4, IP
10 mg/kg ABMut1, IV
10 mg/kg R4Mut4, IV
20 mg/kg ABMut1, IV
1000.0
900.0
800.0
700.0
600.0
500.0
400.0
300.0
200.0
100.0
0.0
Tumor size (mm³)
0
7
14
21
Days following tumor inoculation

FIG. 9

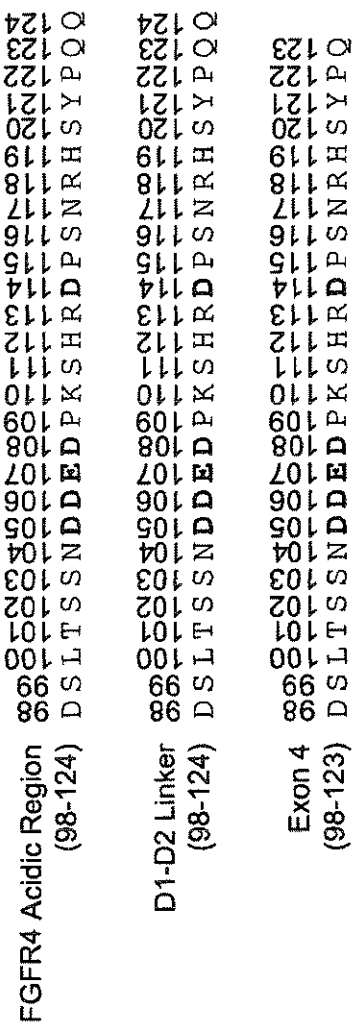

FGFR4 Acidic Region (98-124)
D S L T S S N D D E D P K S H R D P S N R H S Y P Q Q
98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124
D1-D2 Linker (98-124)
D S L T S S N D D E D P K S H R D P S N R H S Y P Q Q
98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124
Exon 4 (98-123)
D S L T S S N D D E D P K S H R D P S N R H S Y P Q
98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123
Long Acid Box (104-118)
N D D E D P K S H R D P S N R
104 105 106 107 108 109 110 111 112 113 114 115 116 117 118
Acid Box Region (98...105-113...124)
D D E D P K S H R
105 106 107 108 109 110 111 112 113
Acid Box (105-113)
D D E D P K S H R
105 106 107 108 109 110 111 112 113
Short Acid Box (105-108)
D D E D
105 106 107 108

FIG. 10

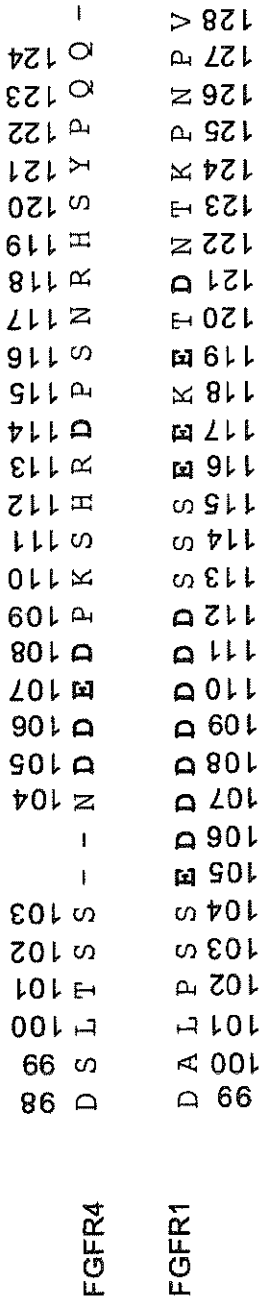

FGFR4
FGFR1
D S L T S S - - N D D E D P K S H R D P S N R H S Y P Q Q -
D A L P S S E D D D D D D D D D S S S S S E E K E T D N T K P N P V
98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124 125 126 127 128

FIG. 11A

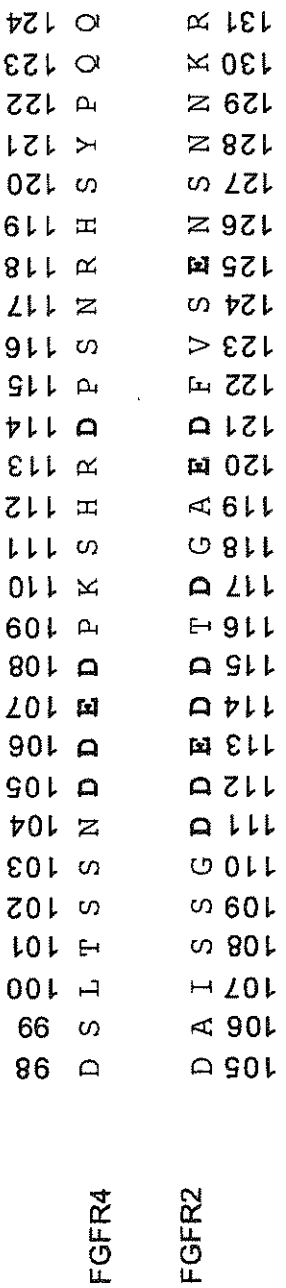

FGFR2
D A I S S G D D D E D D T D G A E D F V S E N S N N K R
105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124 125 126 127 128 129 130 131
FGFR4
D S L T S S N D D E D D P K S H R D P S N R H S Y P Q Q
98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124

FIG. 11B

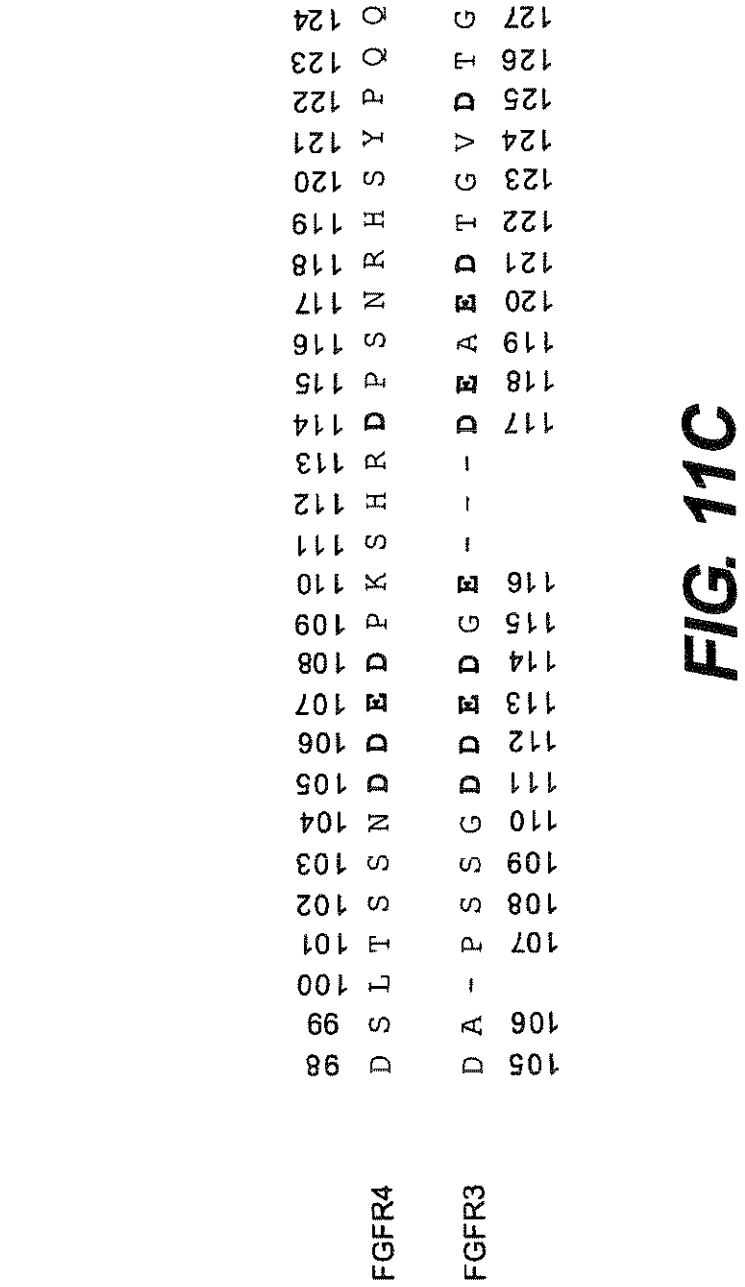

FGFR4
FGFR3
D S L T S S N D D E D D P K S H R D P S N R H S Y P Q Q
D A - P S S G D D E D D G E - - - D E A E D T G V D T G
98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124
105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124 125 126 127

FIG. 11C

FGFR2		FGFR1	
D	105	D	99
A	106	A	100
I	107	L	101
S	108	P	102
S	109	S	103
G	110	S	104
D	111	E	105
D	112	D	106
E	113	D	107
D	114	D	108
D	115	D	109
T	116	D	110
D	117	D	111
G	118	D	112
A	119	S	113
E	120	S	114
D	121	S	115
F	122	E	116
V	123	E	117
S	124	K	118
E	125	E	119
N	126	T	120
S	127	D	121
N	128	N	122
N	129	T	123
K	130	K	124
R	131	P	125
-		N	126
-		P	127
-		V	128

FIG. 11D

FGFR3		FGFR1	
D	105	D	99
A	106	A	100
-		L	101
P	107	P	102
S	108	S	103
S	109	S	104
G	110	E	105
D	111	D	106
D	112	D	107
E	113	D	108
D	114	D	109
G	115	D	110
E	116	D	111
D	117	D	112
-		S	113
-		S	114
-		S	115
-		E	116
-		E	117
-		K	118
E	118	E	119
A	119	T	120
E	120	D	121
D	121	N	122
T	122	T	123
G	123	K	124
V	124	P	125
D	125	N	126
T	126	P	127
G	127	V	128

FIG. 11E

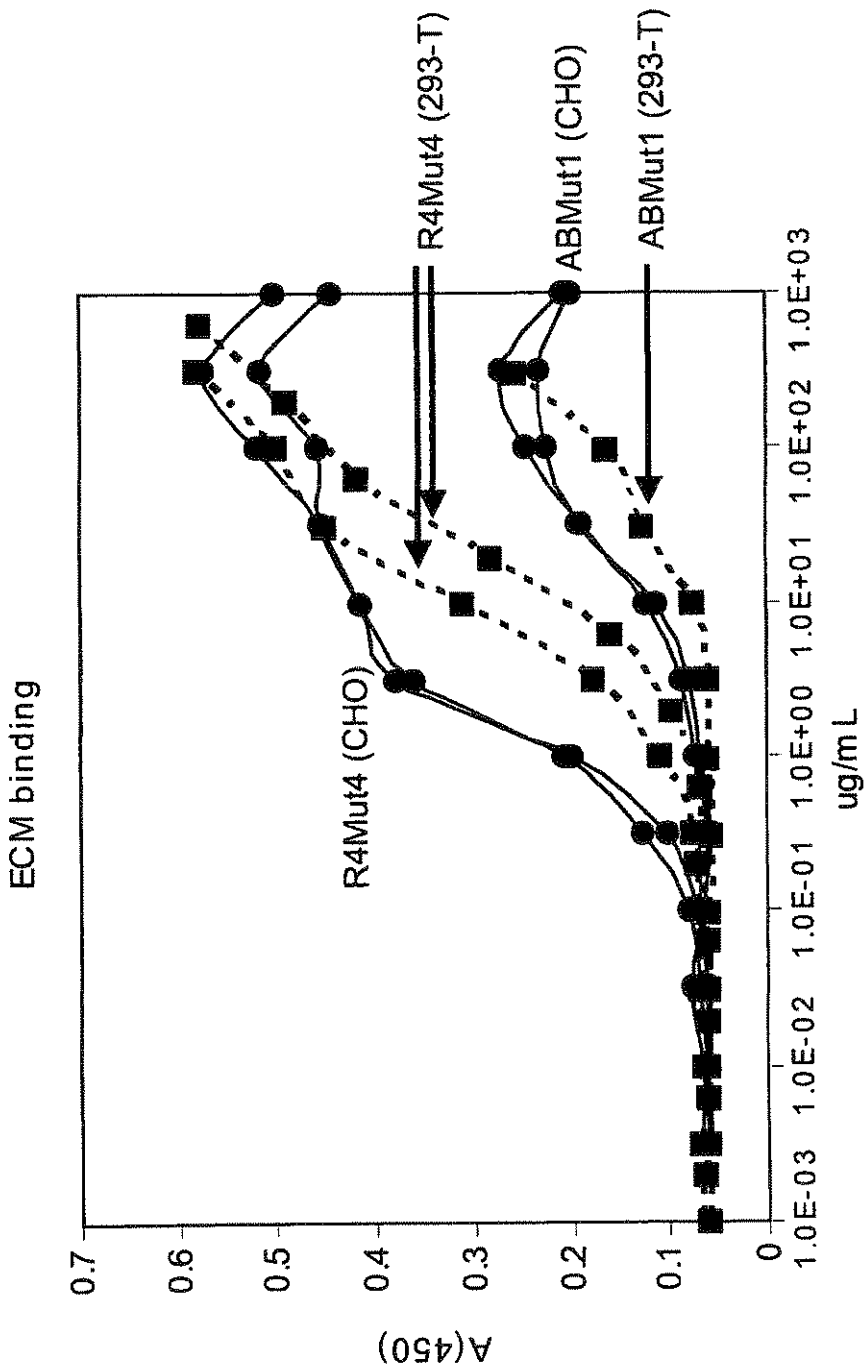

ECM binding
A(450)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
1.0E-03
1.0E-02
1.0E-01
1.0E+00
1.0E+01
1.0E+02
1.0E+03
ug/mL
R4Mut4 (293-T)
ABMut1 (CHO)
ABMut1 (293-T)
R4Mut4 (CHO)

FIG. 12

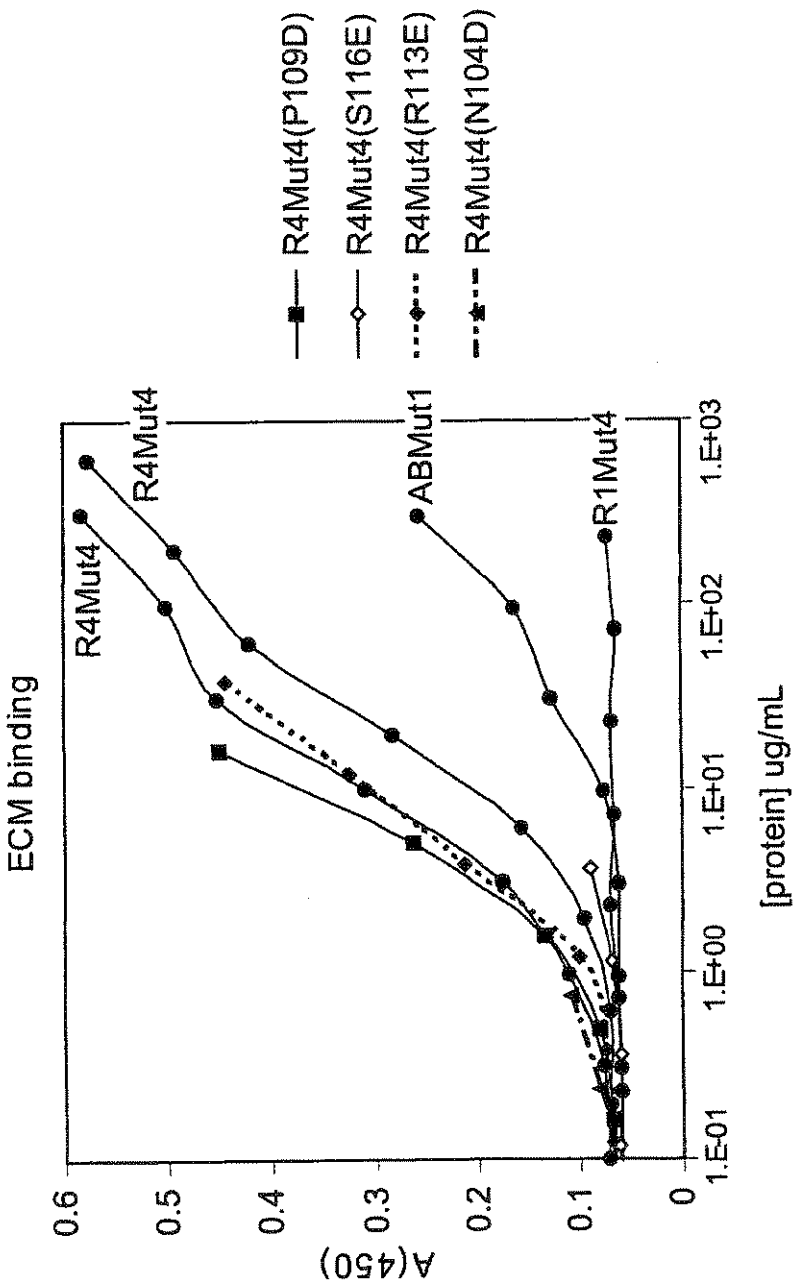

R4Mut4(P109D)
R4Mut4(S116E)
R4Mut4(R113E)
R4Mut4(N104D)
R4Mut4
R4Mut4
ABMut1
R1Mut4
ECM binding
A(450)
0.6
0.5
0.4
0.3
0.2
0.1
0
1.E-01
1.E+00
1.E+01
1.E+02
1.E+03
[protein] ug/mL

FIG. 13

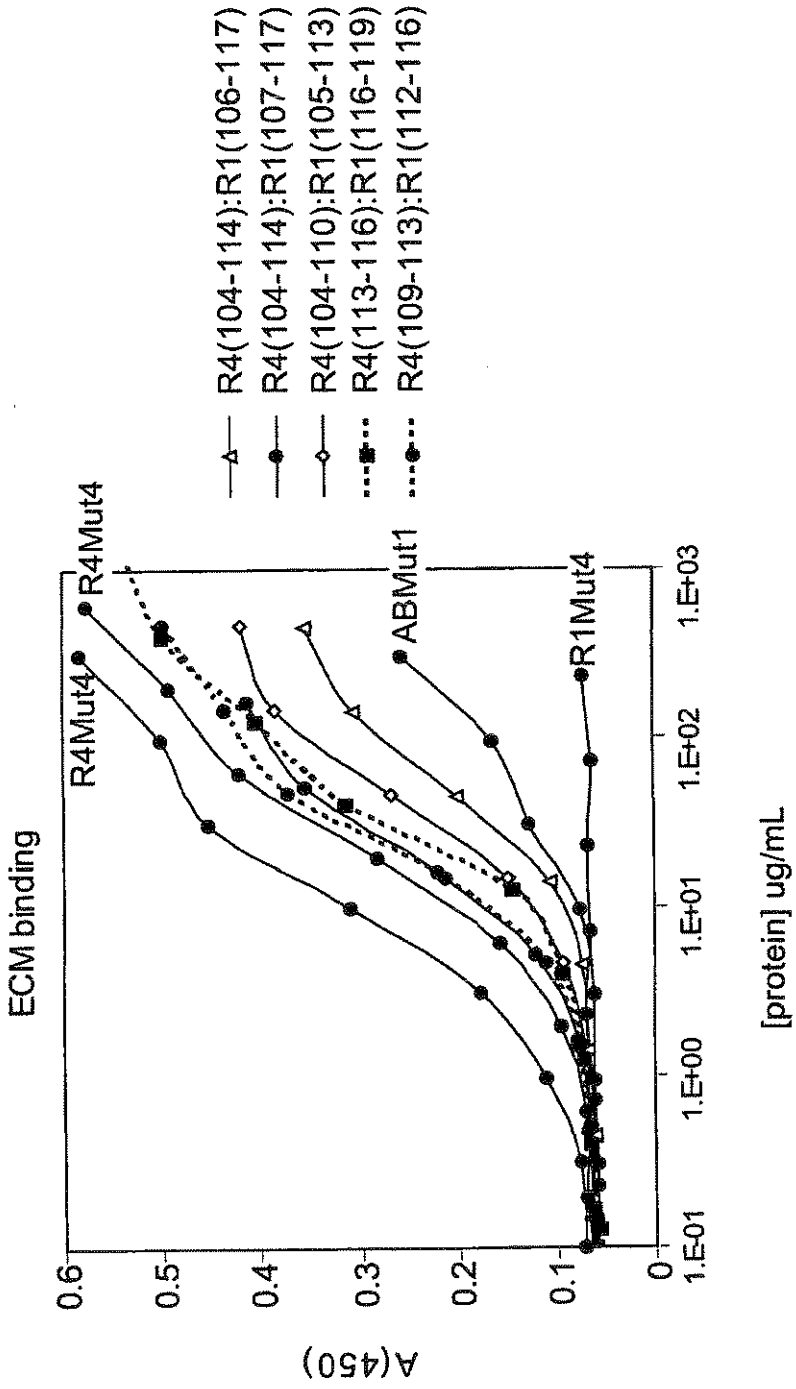

R4(104-114):R1(106-117)
R4(104-114):R1(107-117)
R4(104-110):R1(105-113)
R4(113-116):R1(116-119)
R4(109-113):R1(112-116)
R4Mut4
R4Mut4
ABMut1
R1Mut4
ECM binding
A(450)
0.6
0.5
0.4
0.3
0.2
0.1
0
1.E-01
1.E+00
1.E+01
1.E+02
1.E+03
[protein] ug/mL

FIG. 14

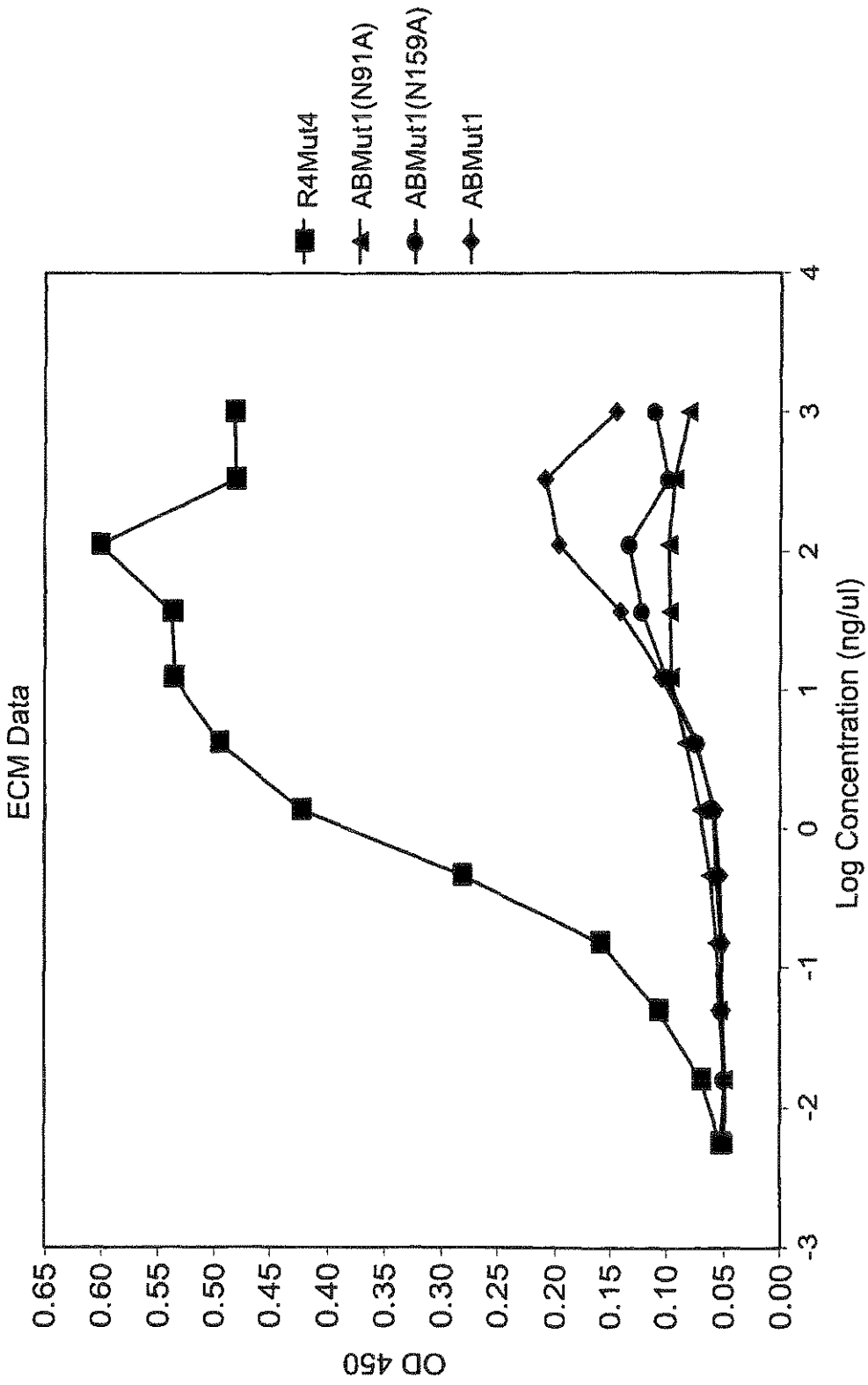

ECM Data
R4Mut4
ABMut1(N91A)
ABMut1(N159A)
ABMut1
OD 450
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
-3
-2
-1
0
1
2
3
4
Log Concentration (ng/ul)

FIG. 15

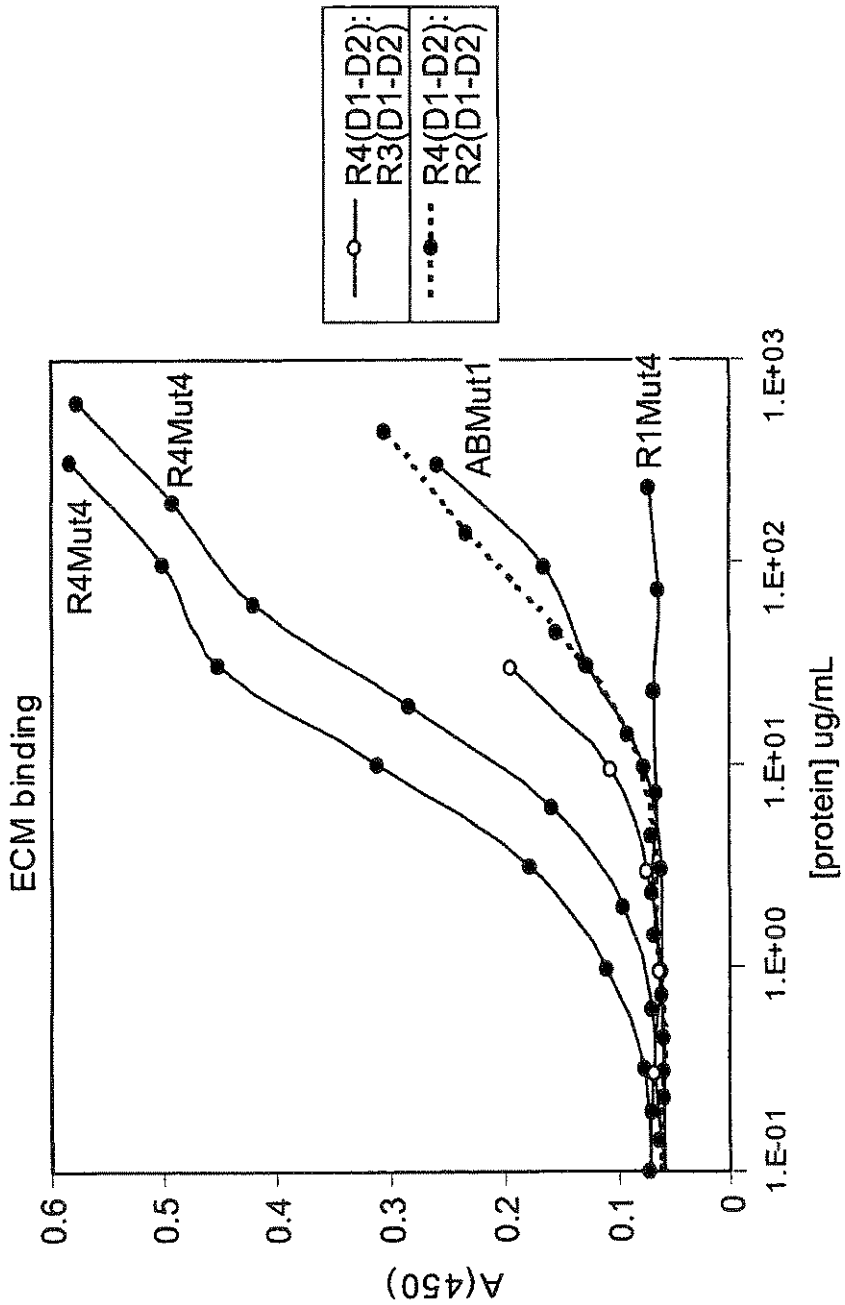

R4(D1-D2): R3(D1-D2)
R4(D1-D2): R2(D1-D2)
ECM binding
A(450)
0.6
0.5
0.4
0.3
0.2
0.1
0
1.E-01
1.E+00
1.E+01
1.E+02
1.E+03
[protein] ug/mL
R4Mut4
R4Mut4
ABMut1
R1Mut4

FIG. 16

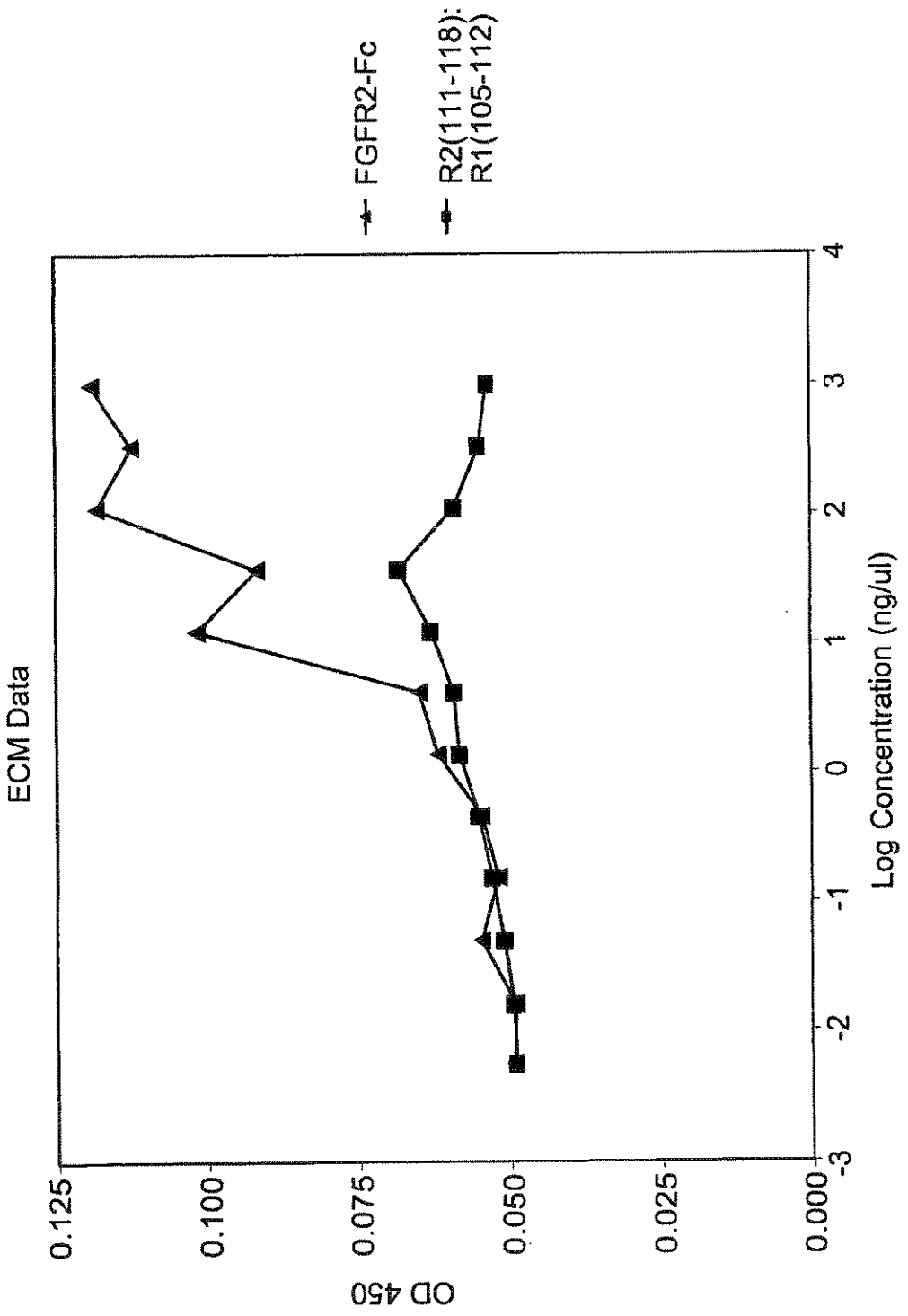

FGFR2-Fc
R2(111-118):
R1(105-112)
ECM Data
OD 450
0.125
0.100
0.075
0.050
0.025
0.000
-3
-2
-1
0
1
2
3
4
Log Concentration (ng/ul)

FIG. 17A

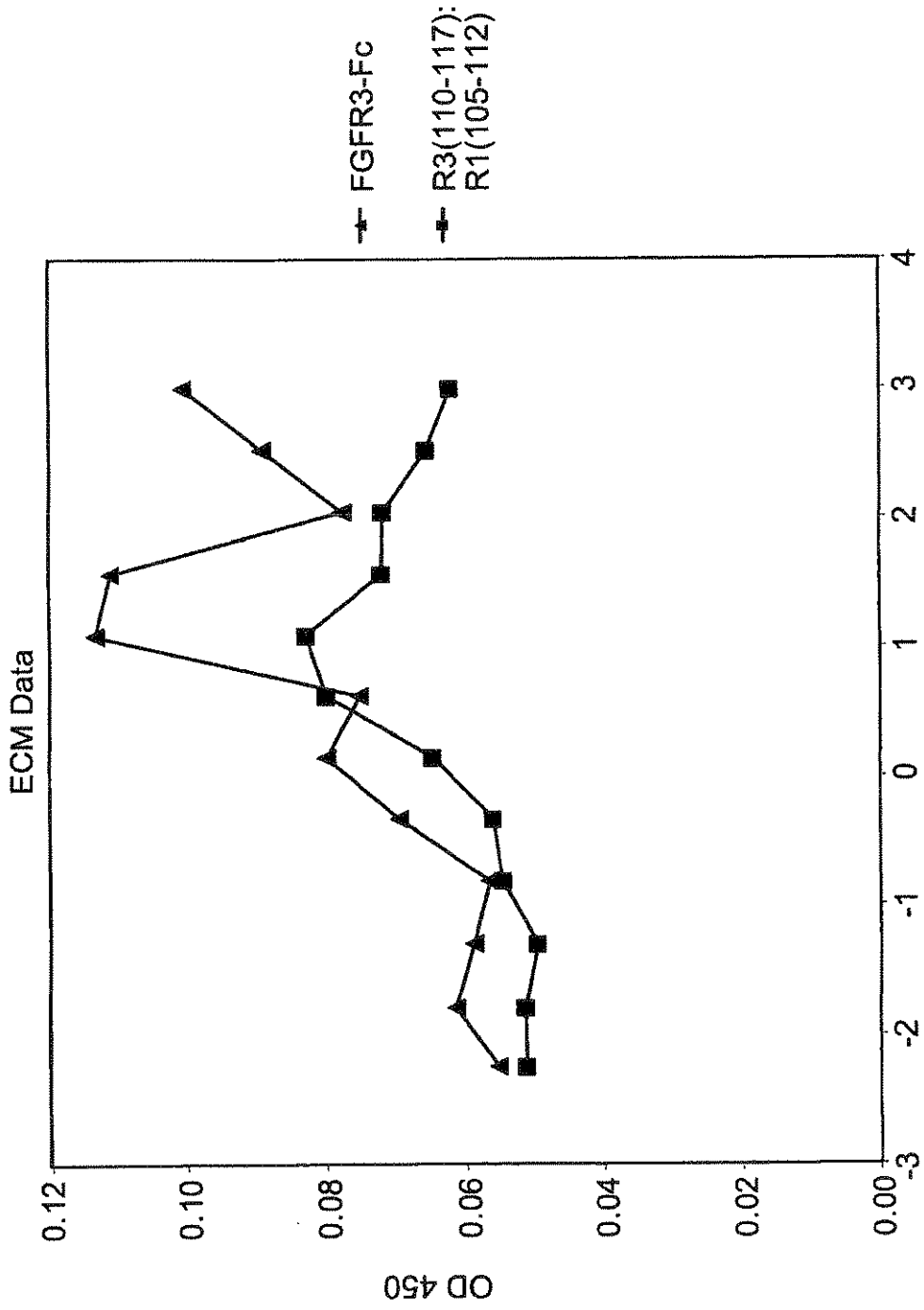

FGFR3-Fc
R3(110-117): R1(105-112)
ECM Data
OD 450
0.12
0.10
0.08
0.06
0.04
0.02
0.00
-3
-2
-1
0
1
2
3
4
Log Concentration (ng/ul)

FIG. 17B