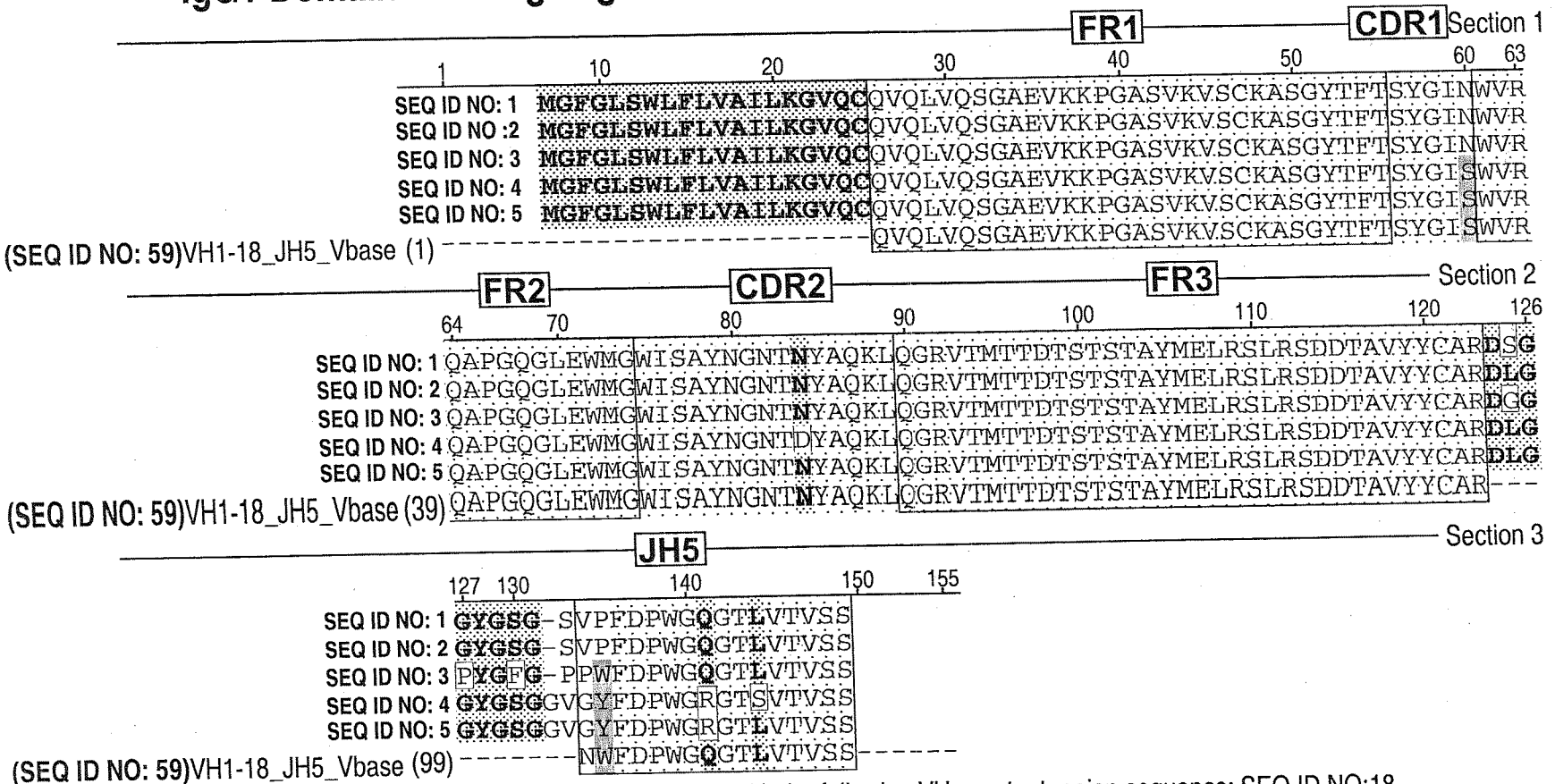
IgG1 Domain ID using alignment with a Vbase database VH region



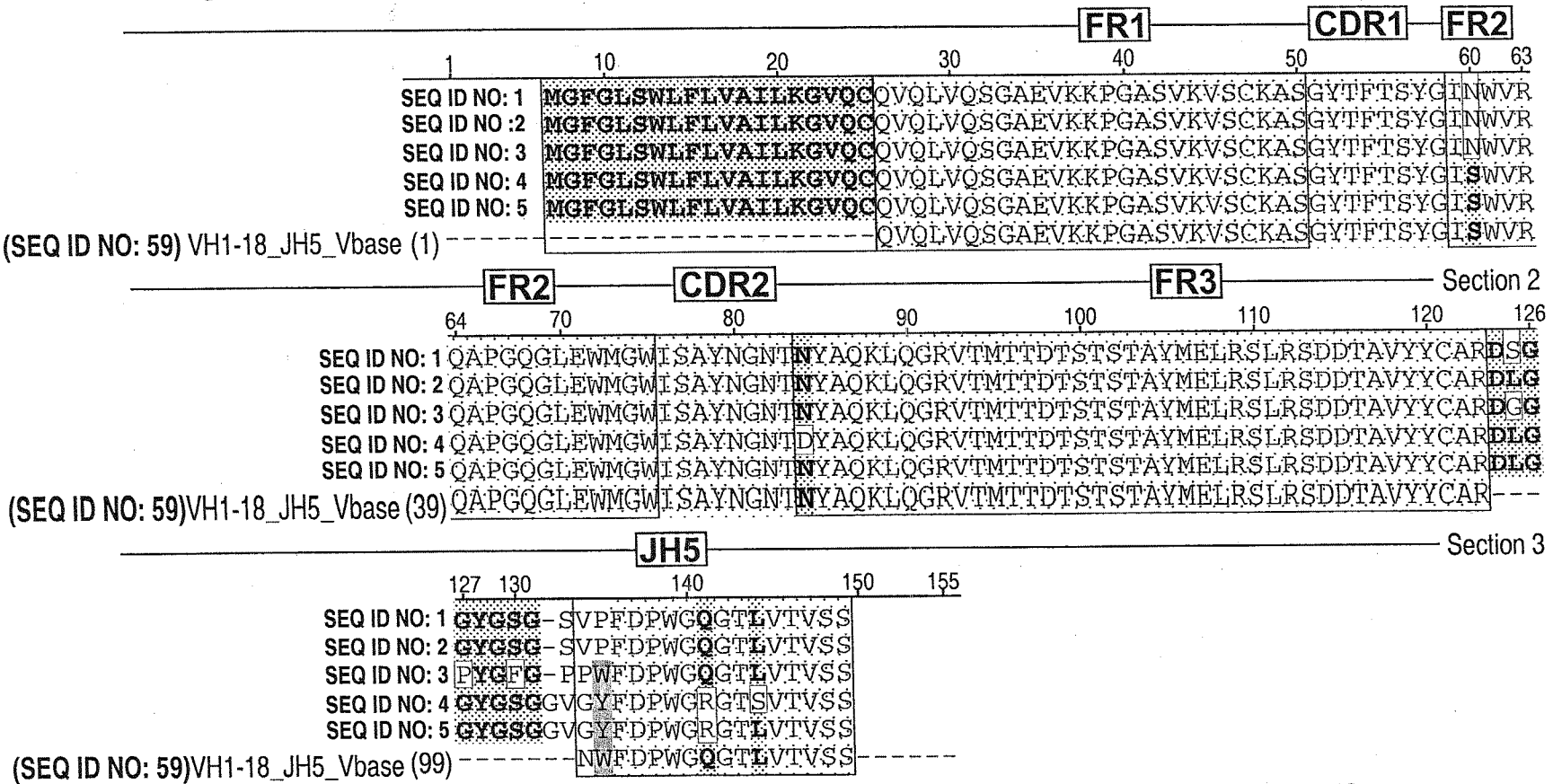
Immediately following the JH sequence SS, all VH sequences end with the following VH constant region sequence: SEQ ID NO:18
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS
NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ
YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSTCLVKGFYPSDIAVEWESNG
QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Numbers above sequences are offset by +6, so that the glycine labeled 10 is properly amino acid number 4

Amino acids numbers 1 -20 for each of SEQ ID NO1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, and SEQ ID NO:5 are MGFGLSWLFLVAILKGVQCQ **(SEQ ID NO: 60)**

Fig. 1

IgG1 Domain ID using alignment with an IMGT database VH region

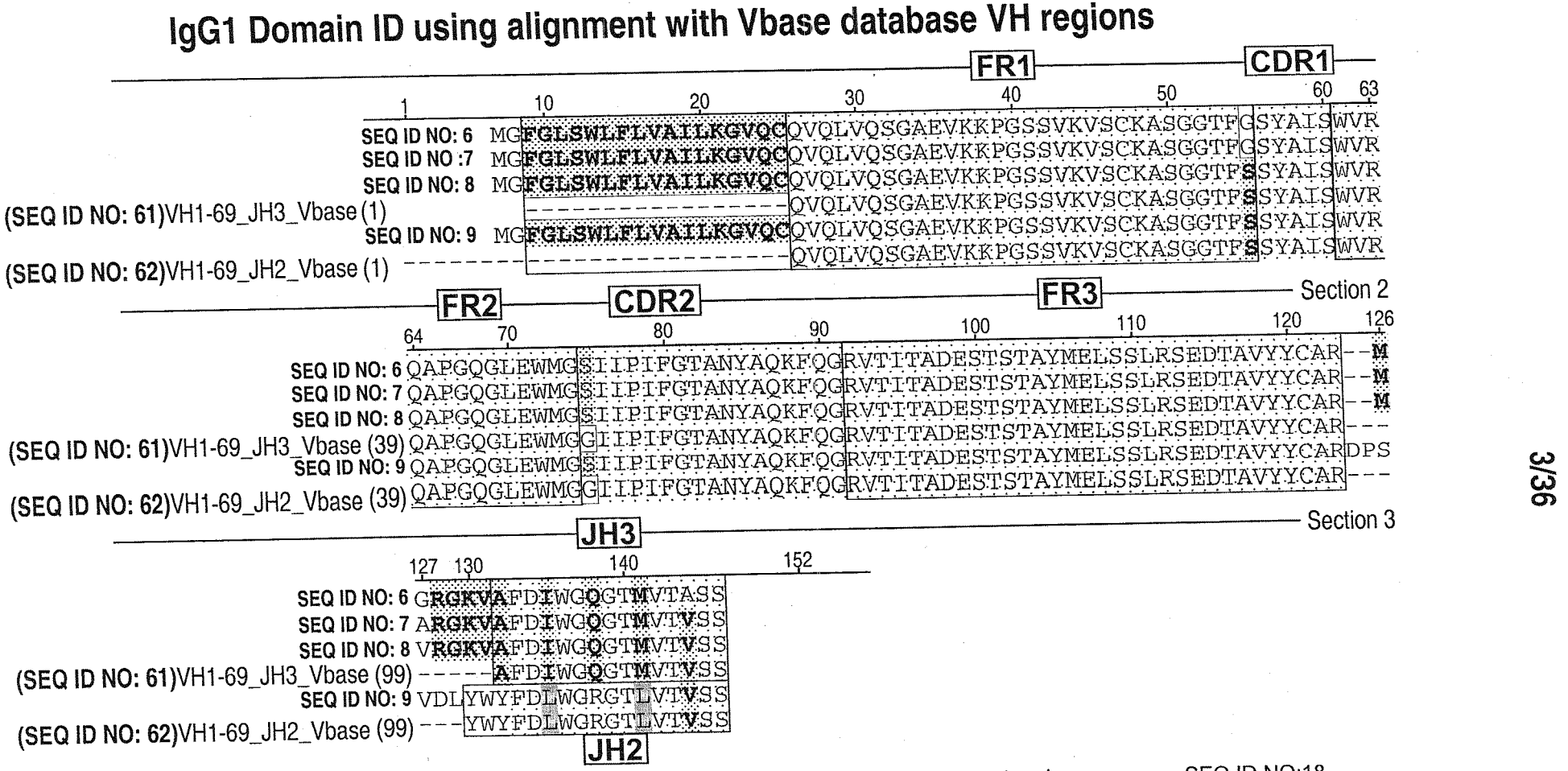


Immediately following the JH sequence SS, all VH sequences end with the following VH constant region sequence: SEQ ID NO:18
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS
NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ
YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSTCLVKGFYPSDIAVEWESNG
QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Numbers above sequences are offset by +6, so that the glycine labeled 10 is properly amino acid number 4

Amino acids numbers 1 -20 for each of SEQ ID NO1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, and SEQ ID NO:5 are MGFGLSWLFLVAILKGVQCQ**(SEQ ID NO: 60)**

Fig. 2



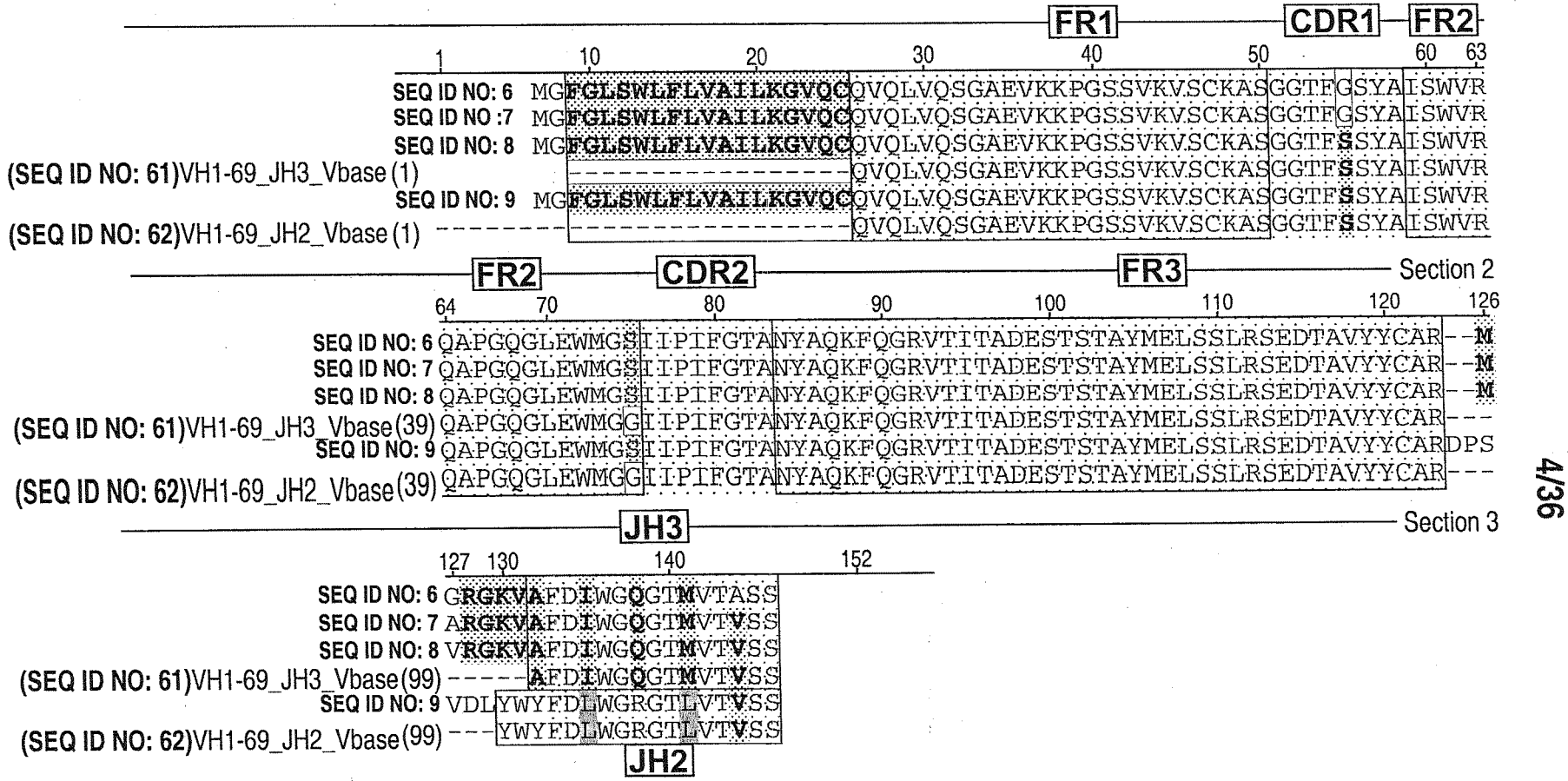
Immediately following the JH sequence SS, all VH sequences end with the following VH constant region sequence: SEQ ID NO:18
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVE
PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW
LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVD
KSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Numbers above sequences are offset by +6, so that the glycine labeled 10 is properly amino acid number 4

Amino acids numbers 1 -20 for each of SEQ ID NO6, SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9 are MGFGLSWLFLVAILKGVQCQ **(SEQ ID NO: 60)**

Fig. 3

IgG1 Domain ID using alignment with IMGT database VH regions

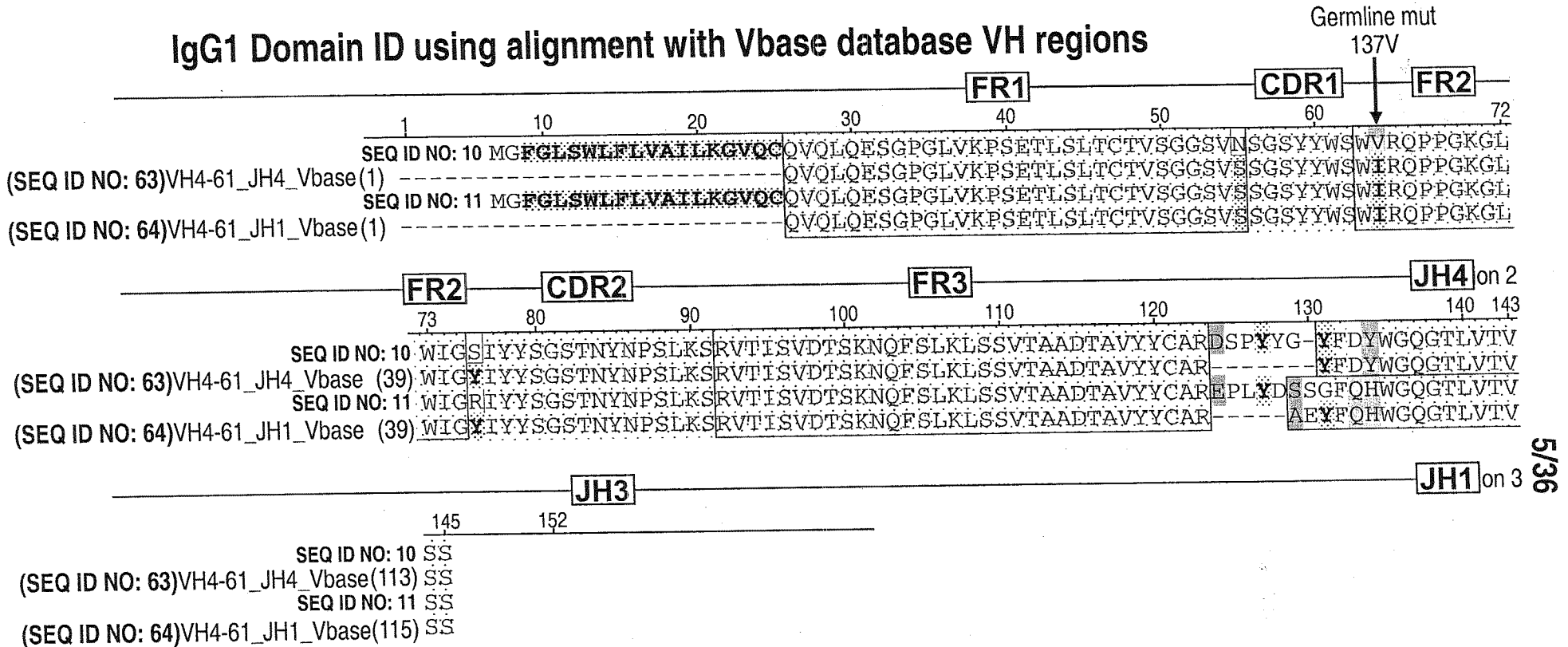


Immediately following the JH sequence SS, all VH sequences end with the following VH constant region sequence: SEQ ID NO:18
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCD
KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV
MHEALHNHYTQKSLSLSPGK

Numbers above sequences are offset by +6, so that the glycine labeled 10 is properly amino acid number 4

Amino acids numbers 1 -20 for each of SEQ ID NO6, SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9 are MGFGLSWLFLVAILKGVQCQ **(SEQ ID NO: 60)**

Fig. 4



Immediately following the sequence SS C-terminal to the JH region, all VH sequences end with the following VH constant region sequence:

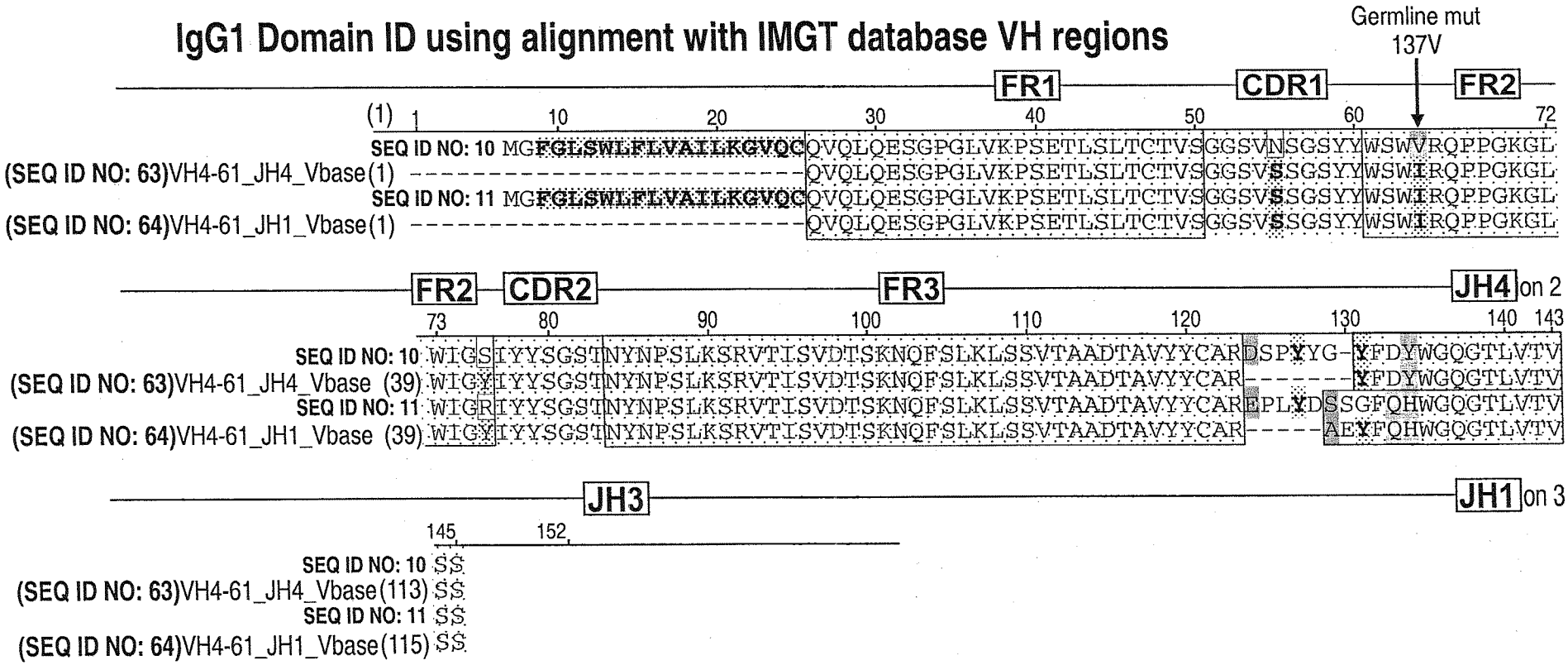
SEQ ID NO:18

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKV
EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD
WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Numbers above sequences are offset by +6, so that the glycine labeled 10 is properly amino acid number 4

Amino acids numbers 1 -20 for each of SEQ ID NO 10 and SEQ ID NO:11 are MGFGLSWLFLVAILKGVQCQ **(SEQ ID NO: 60)**

Fig. 5



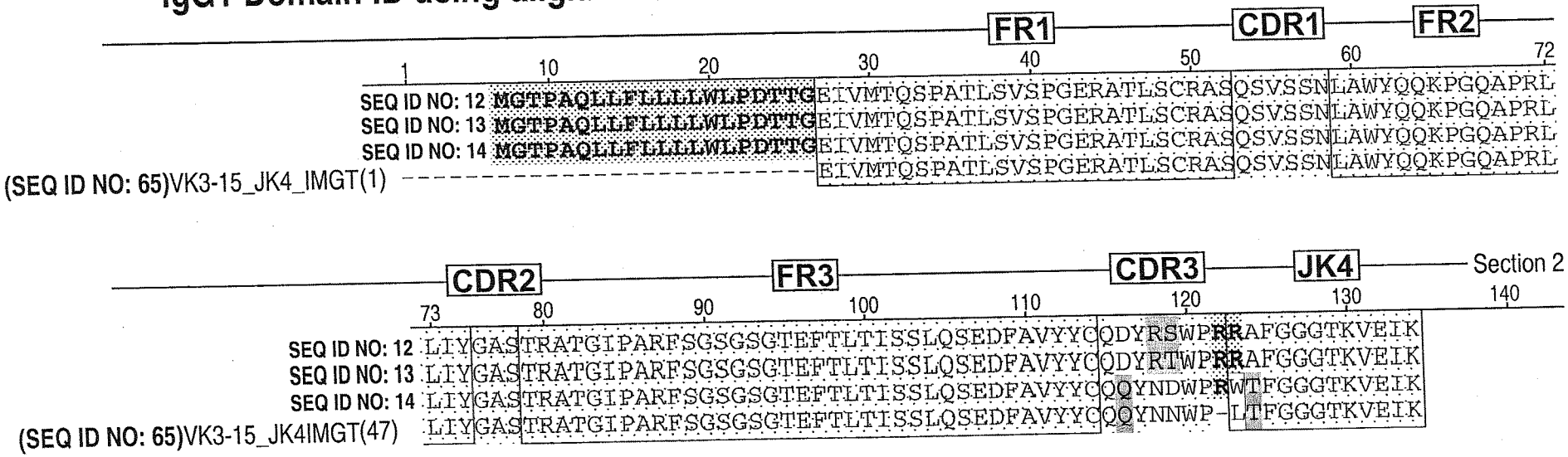
Immediately following the sequence SS C-terminal to the JH region, all VH sequences end with the following VH constant region sequence:
SEQ ID NO:18
ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP
KSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR
WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Numbers above sequences are offset by +6, so that the glycine labeled 10 is properly amino acid number 4

Amino acids numbers 1 -20 for each of SEQ ID NO 10 and SEQ ID NO:11 are MGFGLSWLFLVAILKGVQCQ **(SEQ ID NO: 60)**

Fig. 6

IgG1 Domain ID using alignment with an IMGT database VK region



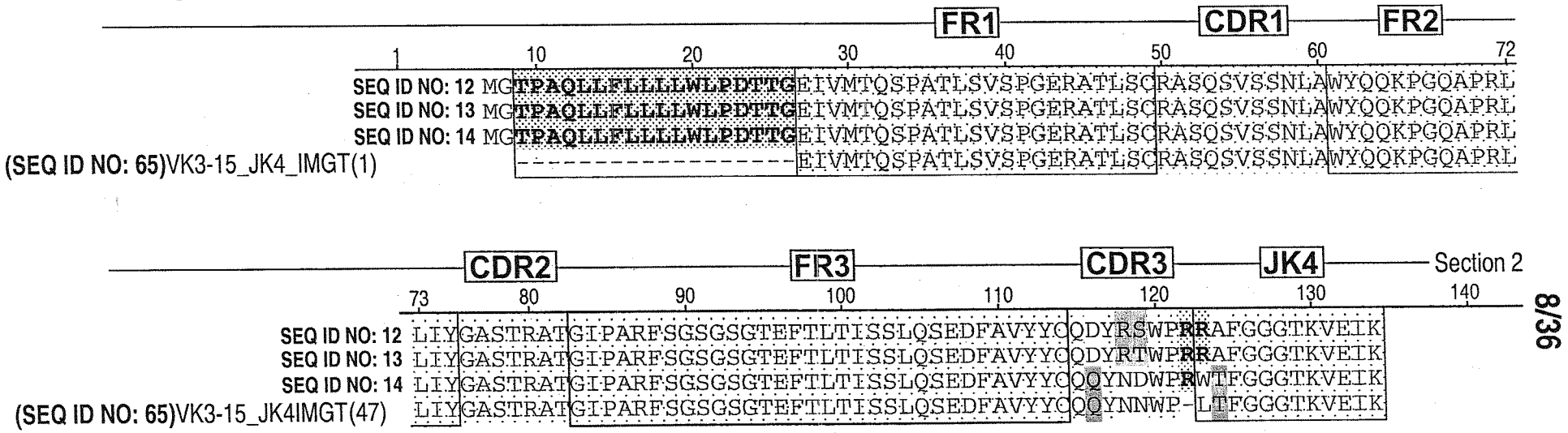
Immediately following the JK sequence EIK, all VK sequences end with the following VK constant region sequence: SEQ ID NO:66
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYAC
EVTHQGLSSPVTKSFNRGEC

Numbers above sequences are offset by +6, so that the proline labeled 10 is properly amino acid number 4

Amino acids numbers 1 -20 for each of SEQ ID NO 12, SEQ ID NO:13, and SEQ ID NO:14 are MGTPAQLLFLLLLWLPDTTG **(SEQ ID NO: 67)**

Fig. 7

IgG1 Domain ID using alignment with a Vbase database VK region



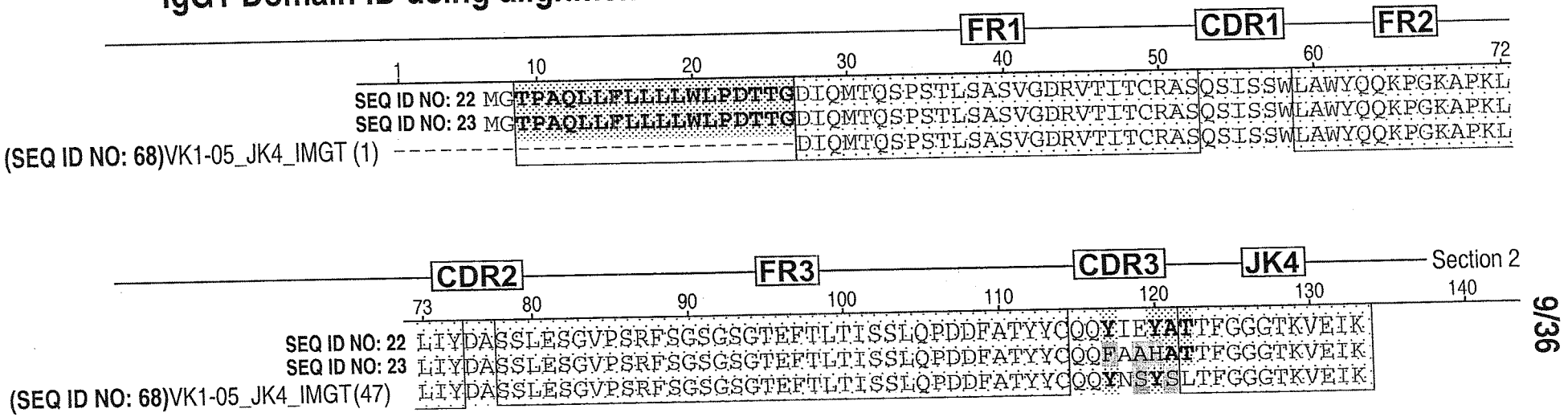
Immediately following the JK sequence EIK, all VK sequences end with the following VK constant region sequence: SEQ ID NO:66
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEV
THQGLSSPVTKSFNRGEC

Numbers above sequences are offset by +6, so that the proline labeled 10 is properly amino acid number 4

Amino acids numbers 1 -20 for each of SEQ ID NO 12, SEQ ID NO:13, and SEQ ID NO:14 are MGTPAQLLFLLLLWLPDTTG **(SEQ ID NO: 67)**

Fig. 8

IgG1 Domain ID using alignment with an IMGT database VK region



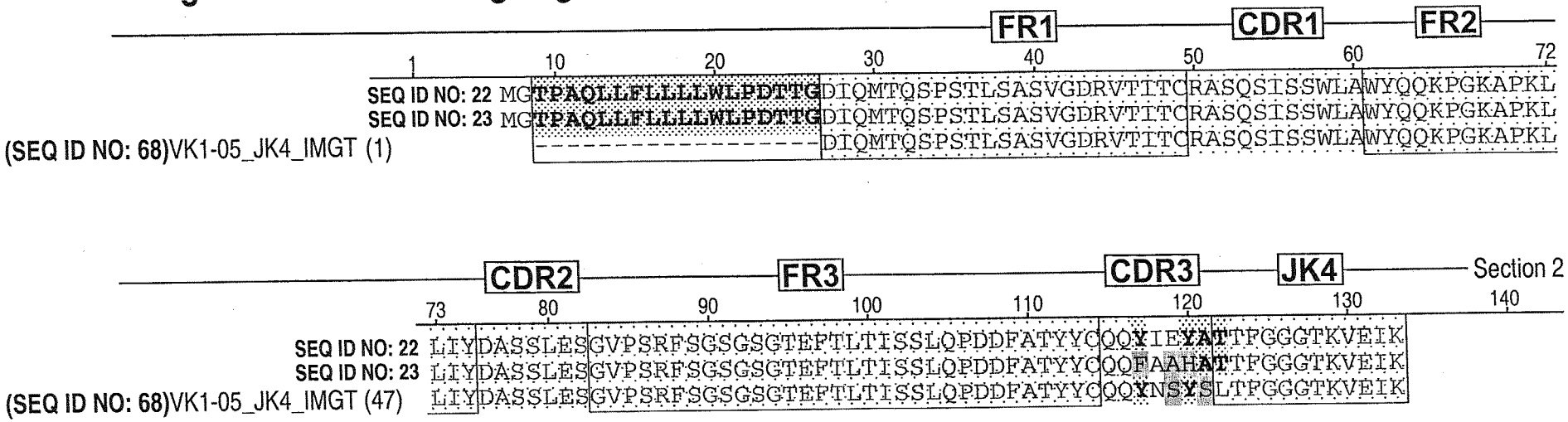
Immediately following the JK sequence EIK, all VK sequences end with the following VK constant region sequence: SEQ ID NO:66
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEV
THQGLSSPVTKSFNRGEC

Numbers above sequences are offset by +6, so that the proline labeled 10 is properly amino acid number 4

Amino acids numbers 1 -20 for each of SEQ ID NO 20 and SEQ ID NO:22 are MGTPAQLLFLLLLWLPDTTG **(SEQ ID NO: 67)**

Fig. 9

IgG1 Domain ID using alignment with a Vbase database VK region



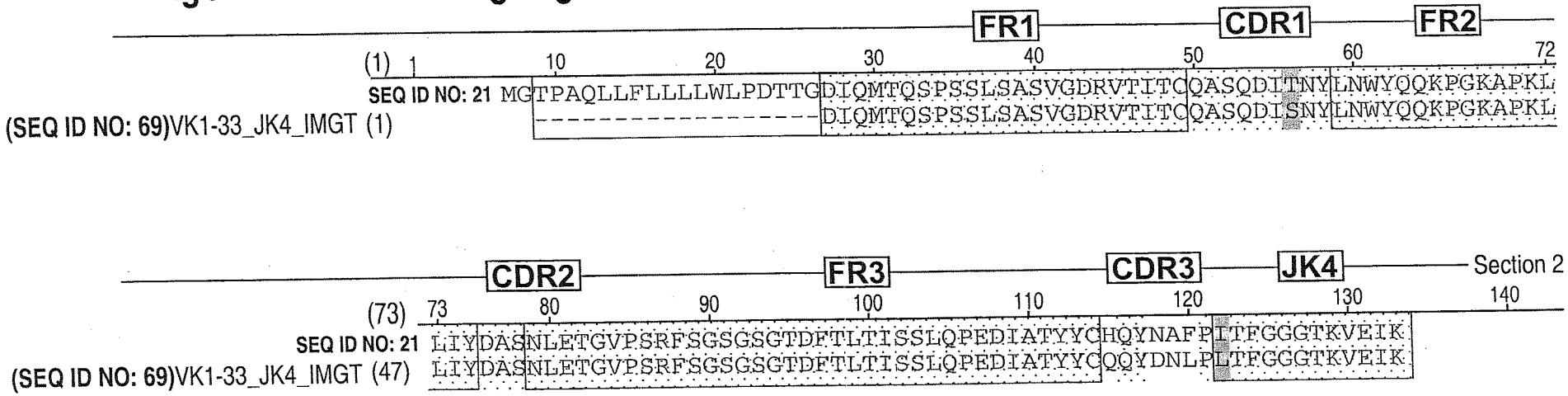
Immediately following the JK sequence EIK, all VK sequences end with the following VK constant region sequence: SEQ ID NO:66
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACE
VTHQGLSSPVTKSFNRGEC

Numbers above sequences are offset by +6, so that the proline labeled 10 is properly amino acid number 4

Amino acids numbers 1 -20 for each of SEQ ID NO 20 and SEQ ID NO:22 are MGTPAQLLFLLLLWLPDTTG **(SEQ ID NO: 67)**

Fig. 10

IgG1 Domain ID using alignment with an IMGT database VK region



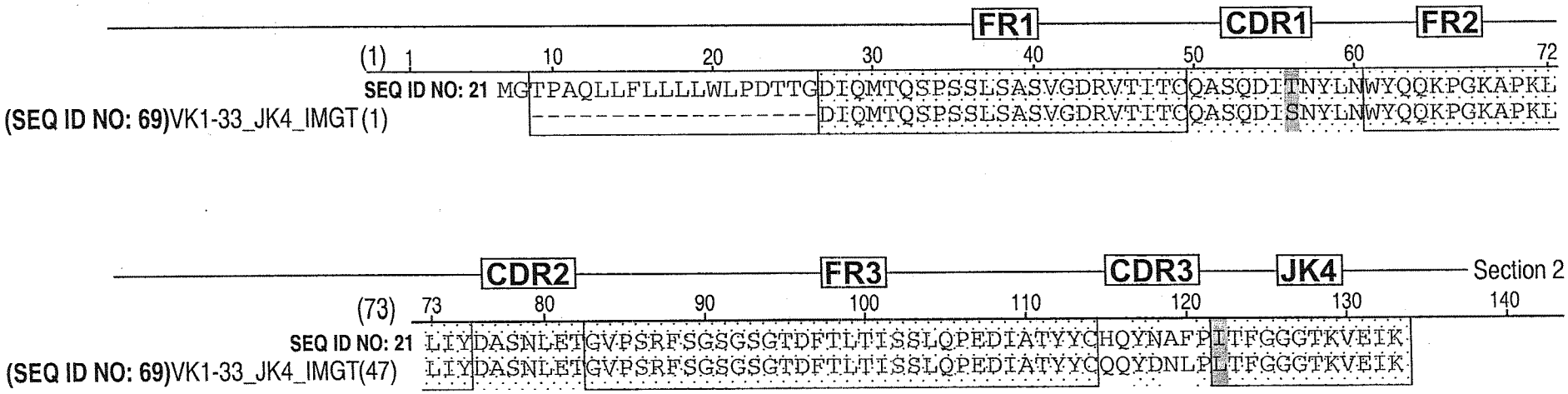
Immediately following the JK sequence EIK, all VK sequences end with the following VK constant region sequence: SEQ ID NO:66
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACE
VTHQGLSSPVTKSFNRGEC

Numbers above sequences are offset by +6, so that the proline labeled 10 is properly amino acid number 4

Amino acids numbers 1 -20 for SEQ ID NO: 21 are MGTPAQLLFLLLLWLPDTTG **(SEQ ID NO: 67)**

Fig. 11

IgG1 Domain ID using alignment with a Vbase database VK region



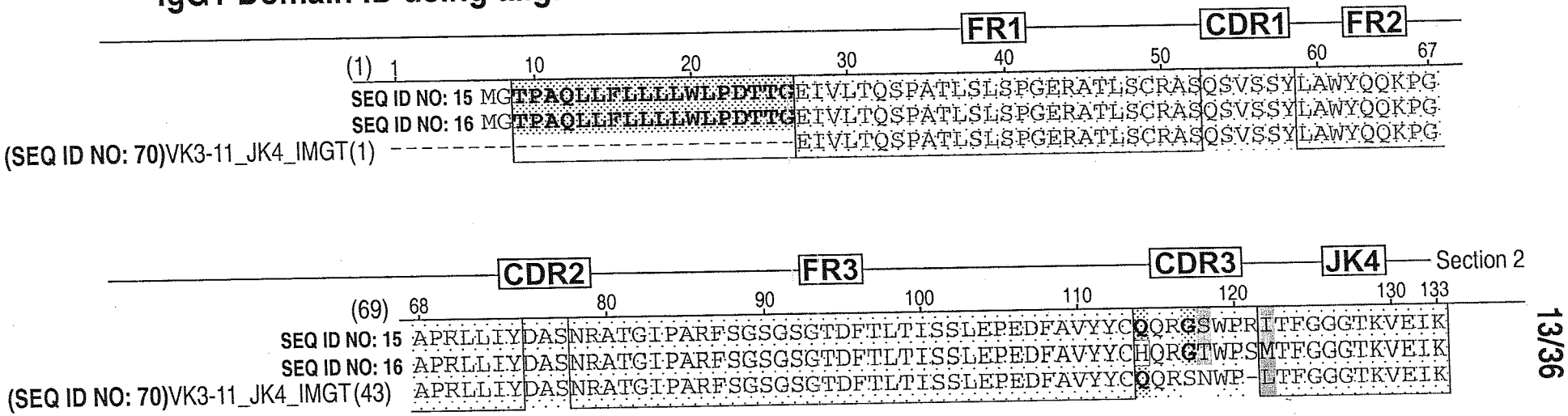
Immediately following the JK sequence EIK, all VK sequences end with the following VK constant region sequence: SEQ ID NO:66
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYAC
EVTHQGLSSPVTKSFNRGEC

Numbers above sequences are offset by +6, so that the proline labeled 10 is properly amino acid number 4

Amino acids numbers 1 -20 for SEQ ID NO: 21 are MGTPAQLLFLLLLWLPDTTG **(SEQ ID NO: 67)**

Fig. 12

IgG1 Domain ID using alignment with an IMGT database VK region



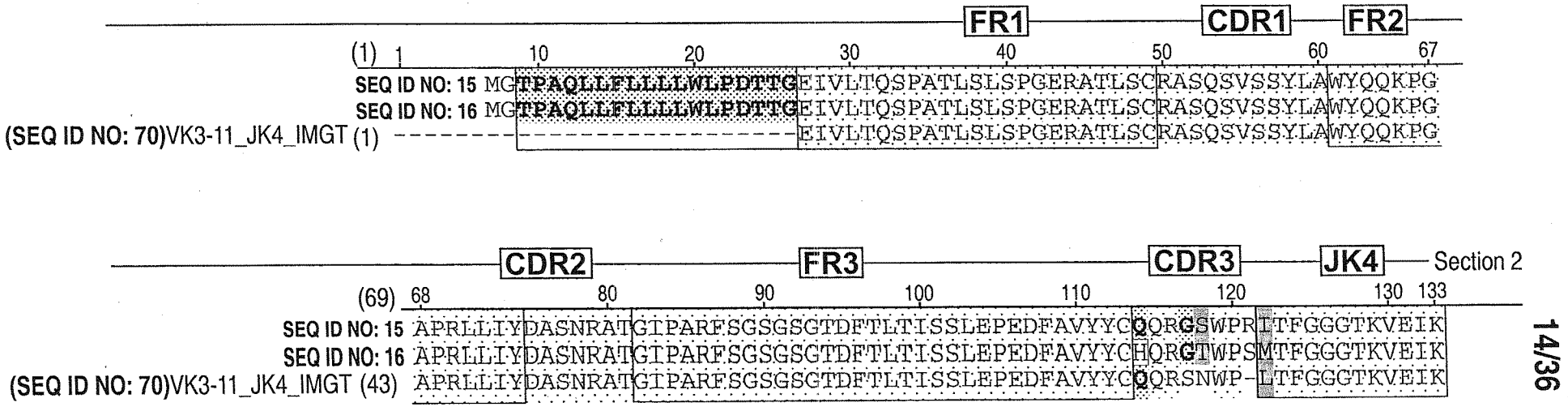
Immediately following the JK sequence EIK, all VK sequences end with the following VK constant region sequence: SEQ ID NO:66
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACE
VTHQGLSSPVTKSFNRGEC

Numbers above sequences are offset by +6, so that the proline labeled 10 is properly amino acid number 4

Amino acids numbers 1 -20 for EACH OF SEQ ID NO: 15 and SEQ ID NO: 16 are MGTPAQLLFLLLLWLPDTTG **(SEQ ID NO: 67)**

Fig. 13

IgG1 Domain ID using alignment with a Vbase database VK region



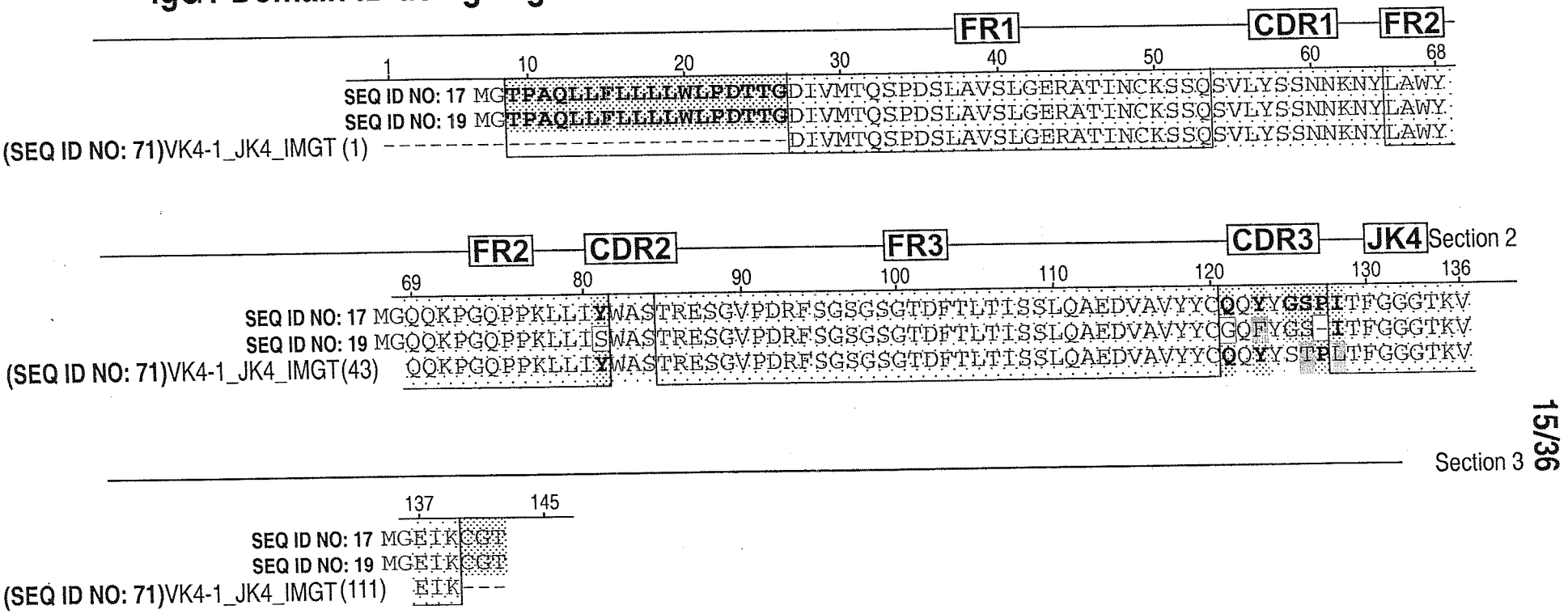
Immediately following the JK sequence EIK, all VK sequences end with the following VK constant region sequence: SEQ ID NO:66
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACE
VTHQGLSSPVTKSFNRGEC

Numbers above sequences are offset by +6, so that the proline labeled 10 is properly amino acid number 4

Amino acids numbers 1 -20 for EACH OF SEQ ID NO: 15 and SEQ ID NO: 16 are MGTPAQLLFLLLLWLPDTTG **(SEQ ID NO: 67)**

Fig. 14

IgG1 Domain ID using alignment with an IMGT database VK region



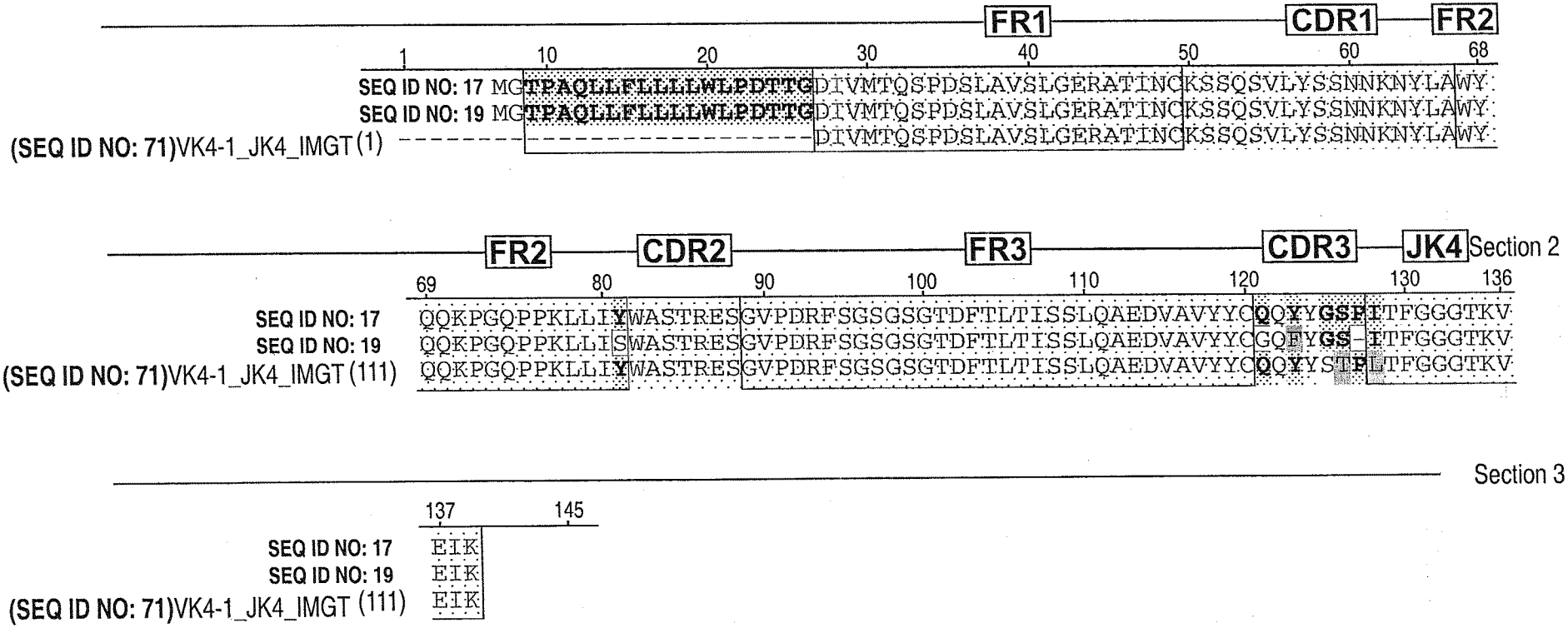
Immediately following the JK sequence EIK, all VK sequences end with the following VK constant region sequence: SEQ ID NO:66
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACE
VTHQGLSSPVTKSFNRGEC

Numbers above sequences are offset by +6, so that the proline labeled 10 is properly amino acid number 4

Amino acids numbers 1 -20 for EACH OF SEQ ID NO: 17 and SEQ ID NO: 19 are MGTPAQLLFLLLLWLPDTTG **(SEQ ID NO: 67)**

Fig. 15

IgG1 Domain ID using alignment with a Vbase database VK region



Immediately following the JK sequence EIK, all VK sequences end with the following VK constant region sequence: SEQ ID NO:66
RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACE
VTHQGLSSPVTKSFNRGEC

Numbers above sequences are offset by +6, so that the proline labeled 10 is properly amino acid number 4

Amino acids numbers 1 -20 for EACH OF SEQ ID NO: 17 and SEQ ID NO: 19 are MGTPAQLLFLLLLWLPDTT**(SEQ ID NO: 67)**

Fig. 16

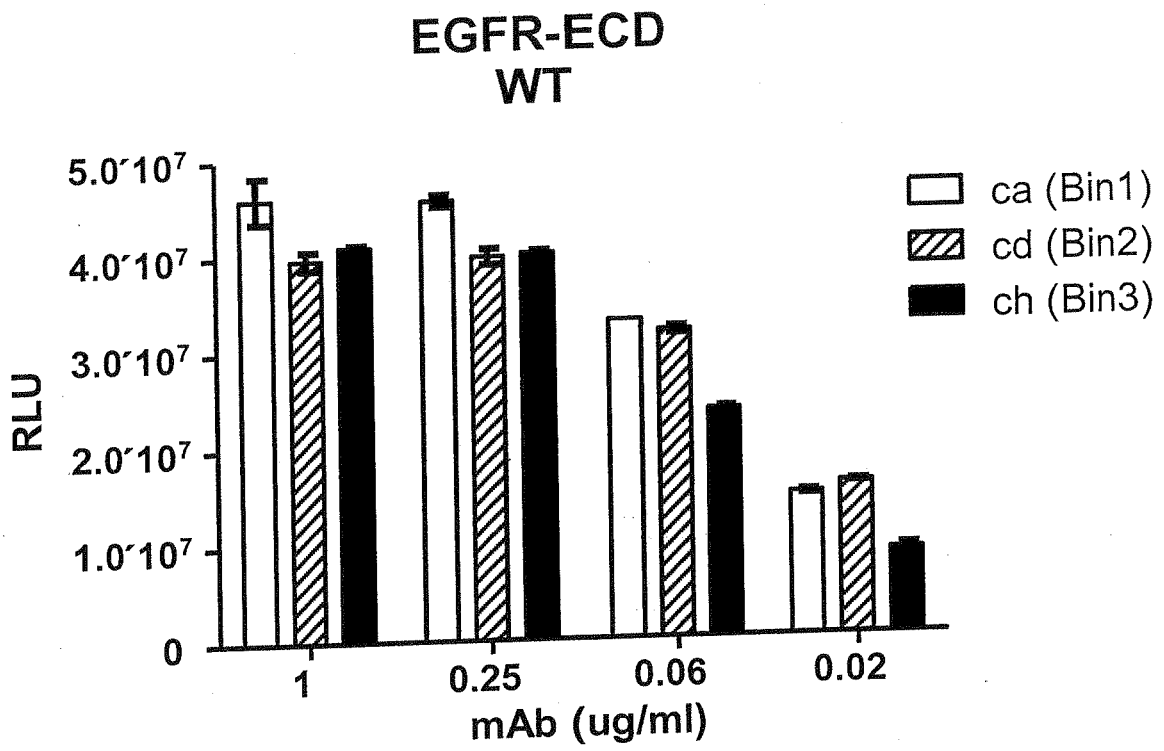


Fig. 17A

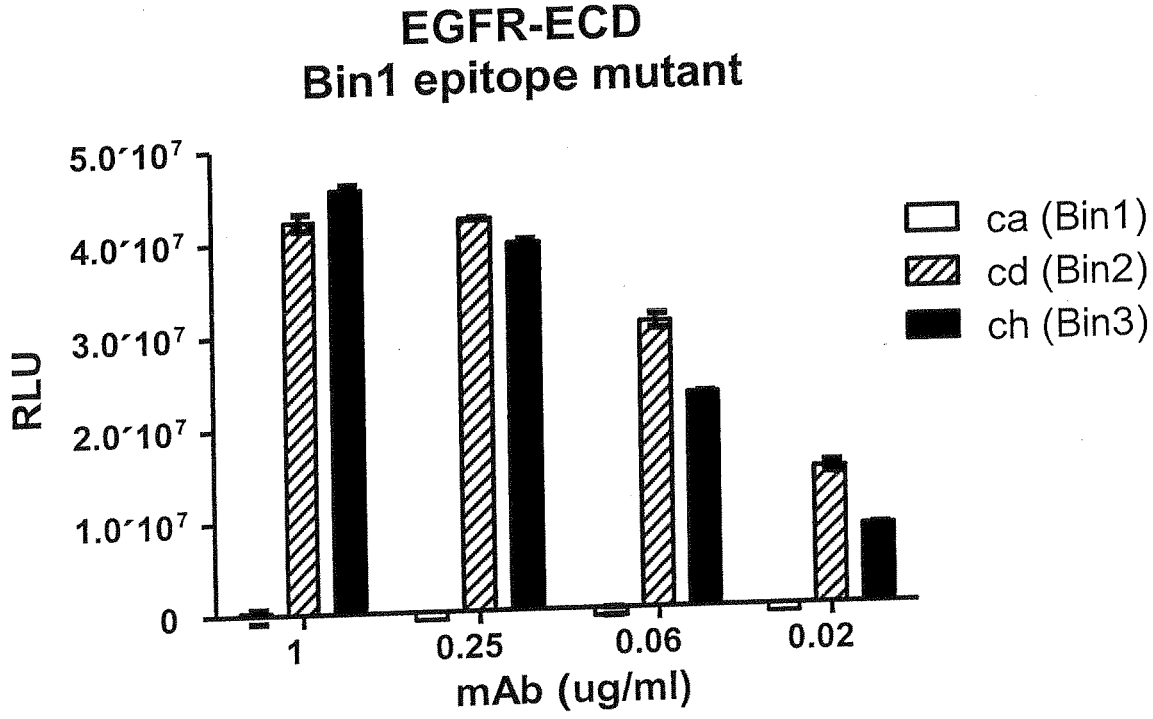


Fig. 17B

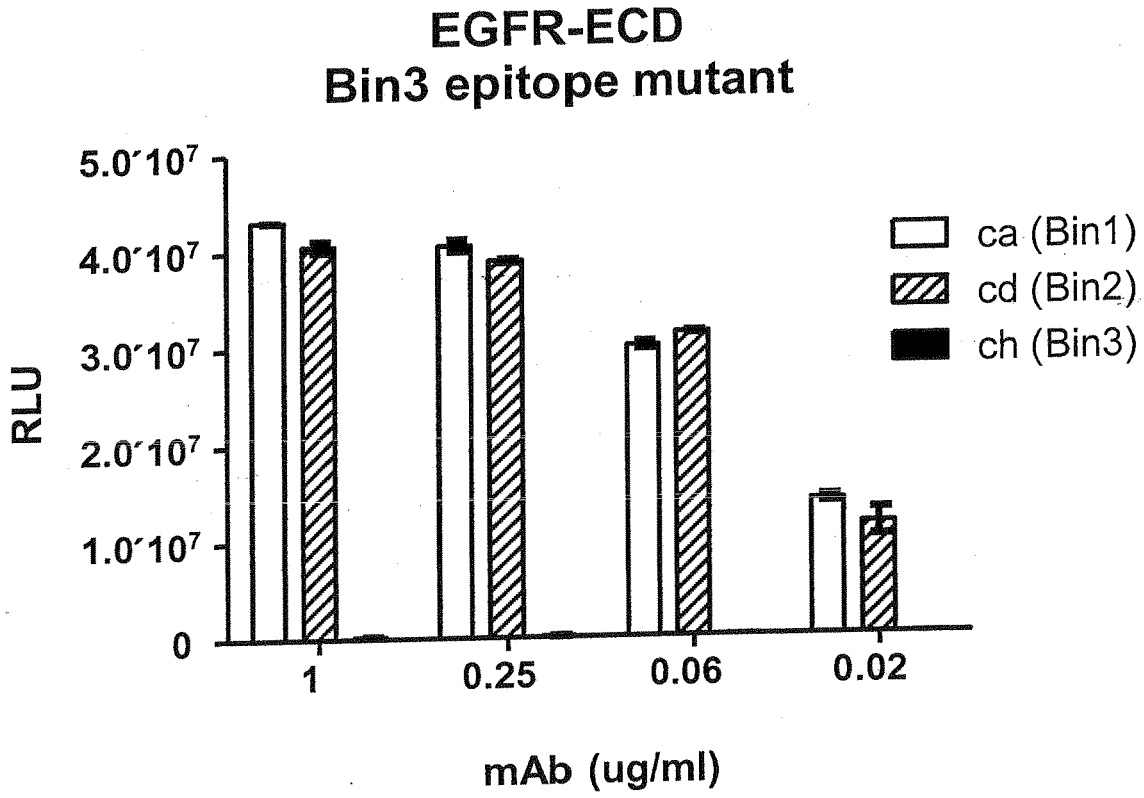

EGFR-ECD
Bin3 epitope mutant
RLU
5.0´10⁷
4.0´10⁷
3.0´10⁷
2.0´10⁷
1.0´10⁷
0
1
0.25
0.06
0.02
mAb (ug/ml)
ca (Bin1)
cd (Bin2)
ch (Bin3)

Fig. 17C

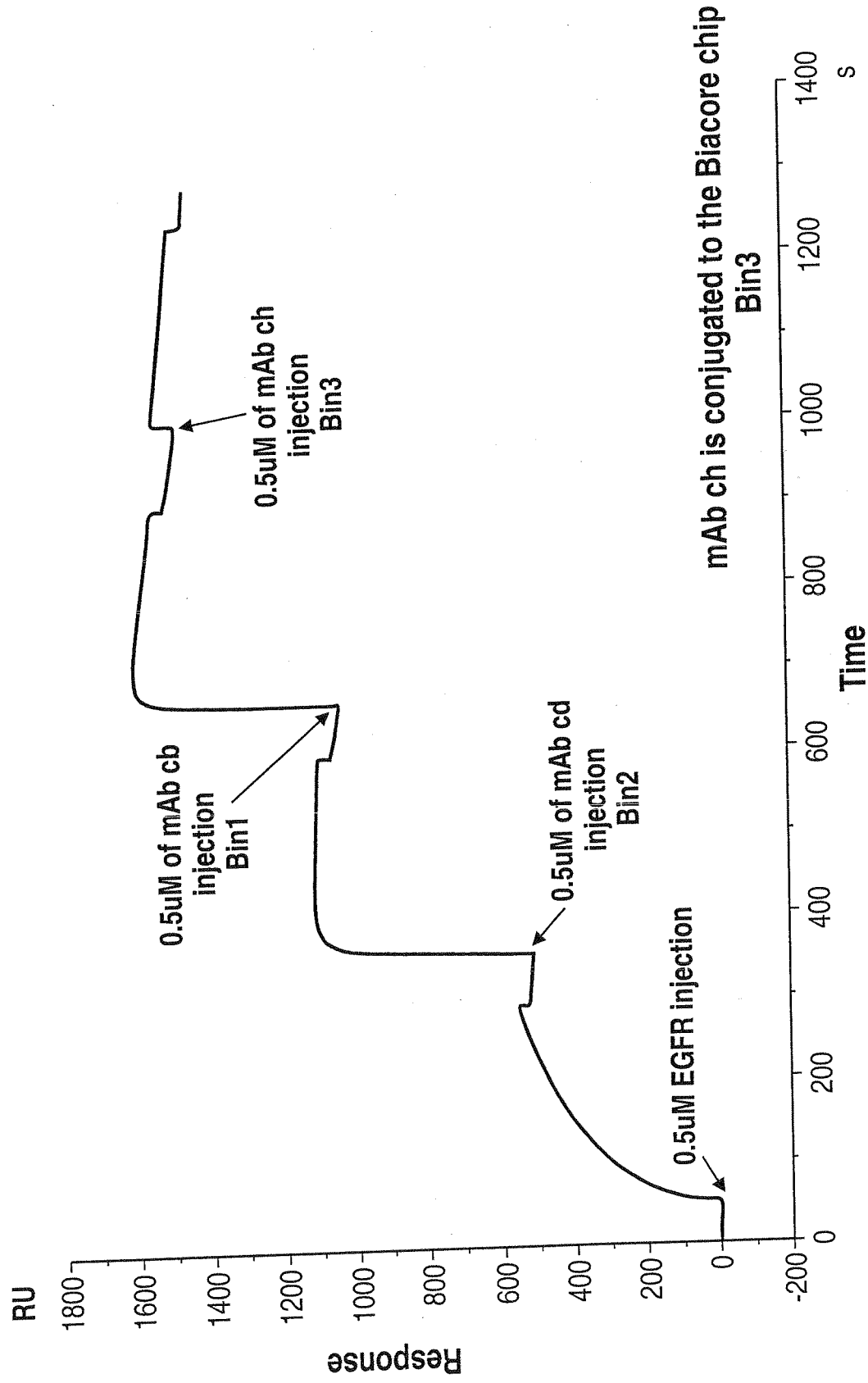
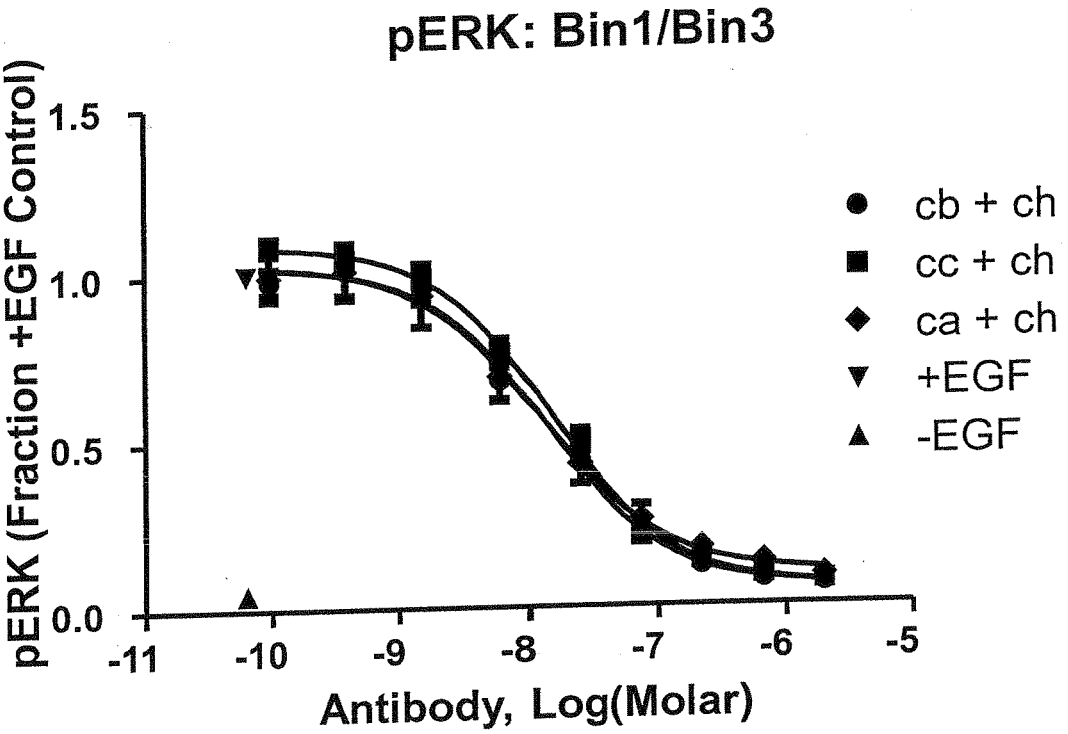
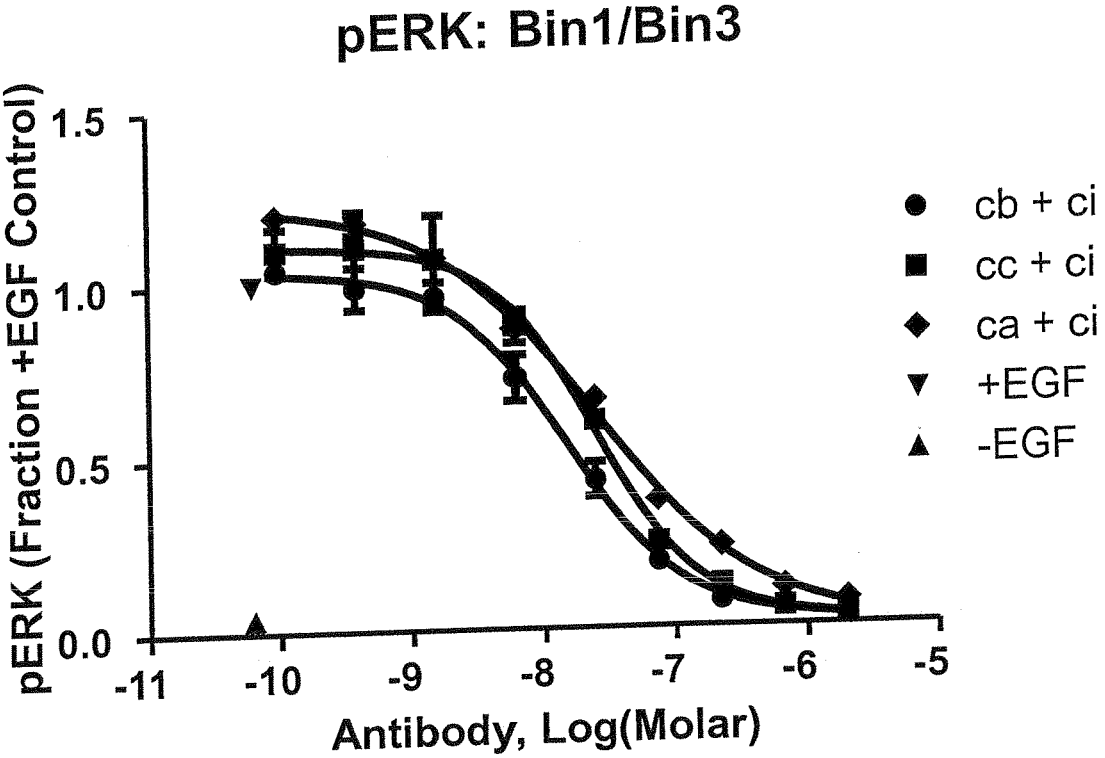

RU
1800
1600
1400
1200
1000
800
600
400
200
0
-200
Response
0
200
400
600
800
1000
1200
1400
s
Time
0.5uM EGFR injection
0.5uM of mAb cd injection Bin2
0.5uM of mAb cb injection Bin1
0.5uM of mAb ch injection Bin3
mAb ch is conjugated to the Biacore chip Bin3

Fig. 17D



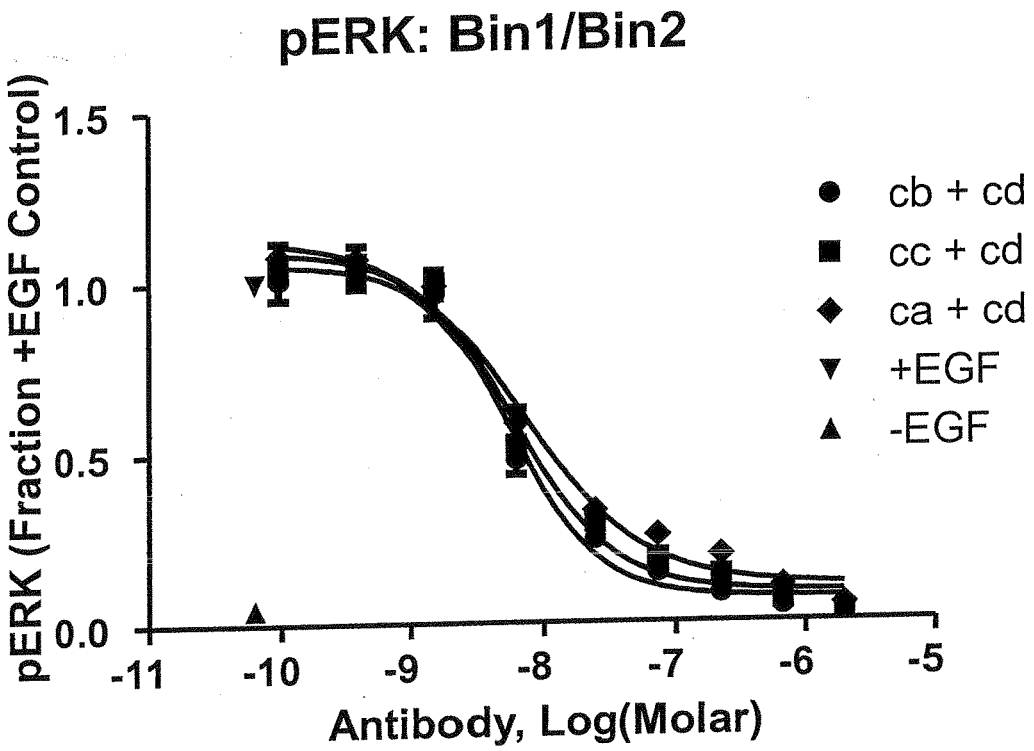
	Bottom	IC50	IC90
cb + ch	0.057	1.405e-008	1.426e-007
cc + ch	0.057	1.531e-008	1.591e-007
ca + ch	0.097	1.268e-008	1.429e-007

Fig. 18A



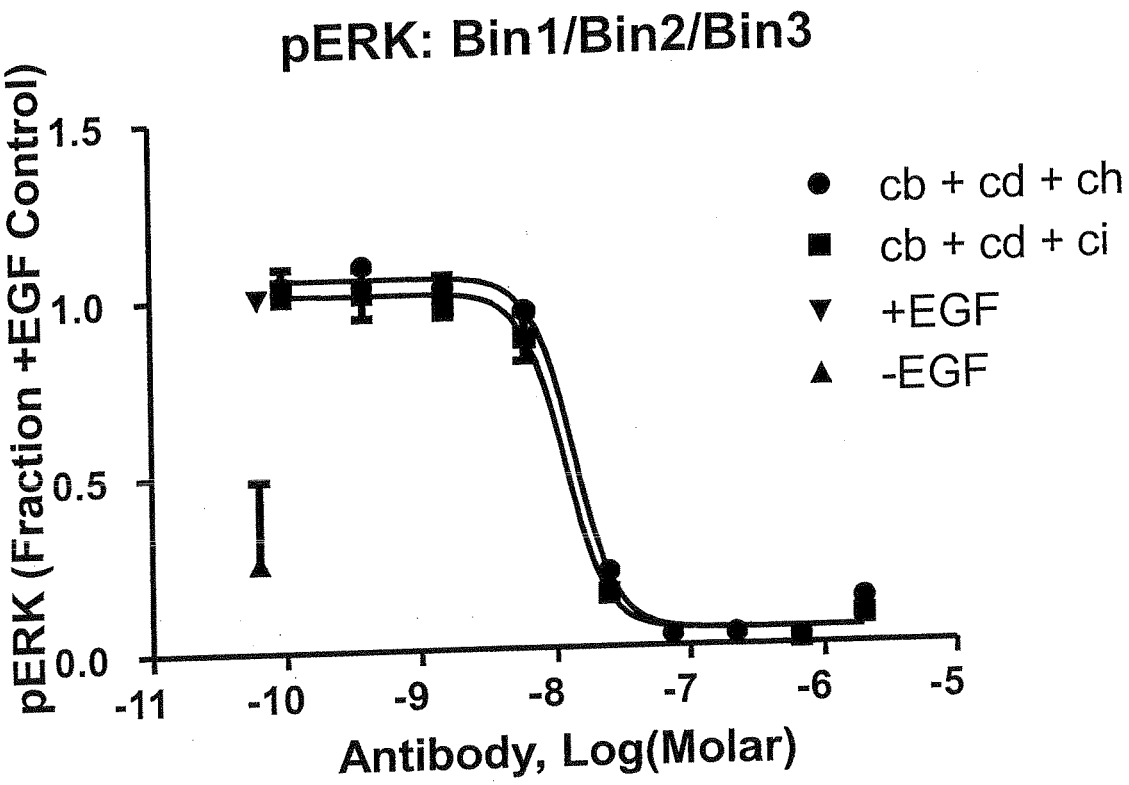
	Bottom	IC50	IC90
cb + ci	0.021	1.528e-008	1.416e-007
cc + ci	0.023	2.487e-008	1.841e-007
ca + ci	0.006	2.504e-008	5.916e-007

Fig. 18B



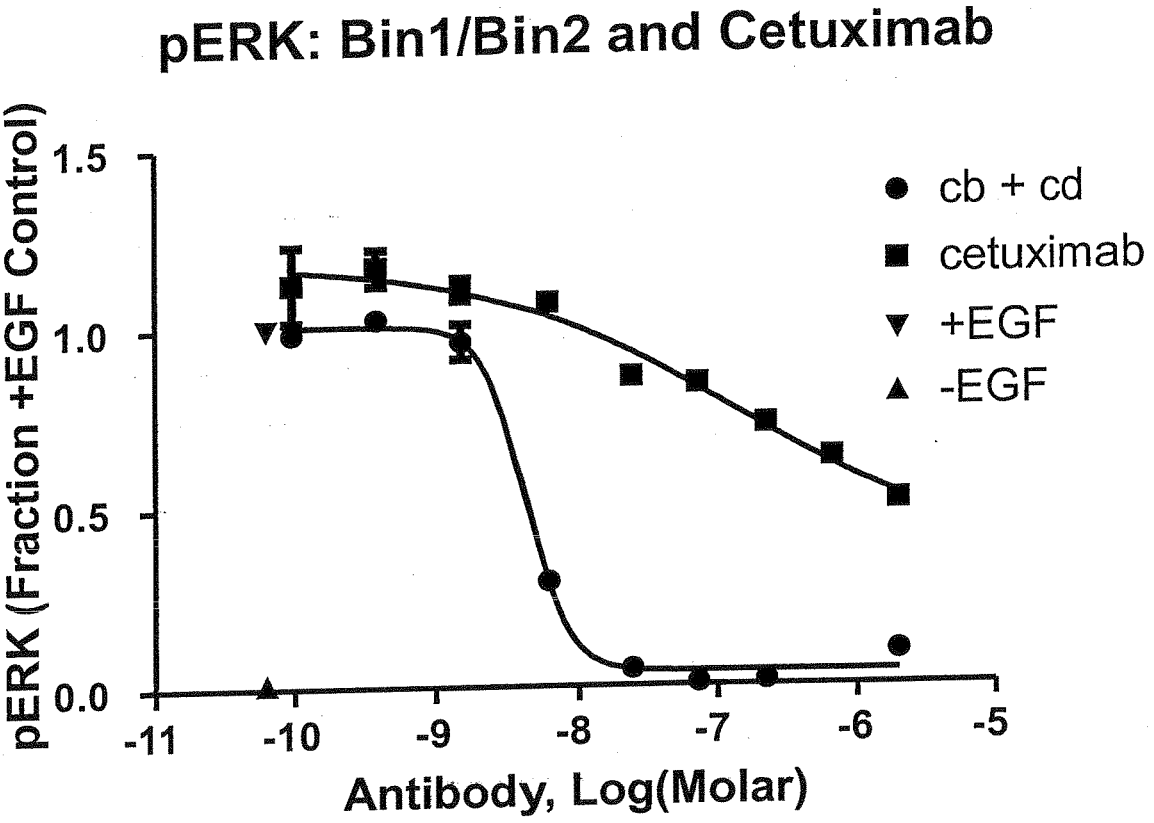
	Bottom	IC50	IC90
cb + cd	0.070	5.765e-009	3.089e-008
cc + cd	0.086	6.047e-009	4.077e-008
ca + cd	0.105	6.825e-009	7.013e-008

Fig. 18C



	Bottom	IC50	IC90
cb + cd + ch	0.048	1.379e-008	3.020e-008
cb + cd + ci	0.048	1.179e-008	2.543e-008

Fig. 19A



	Bottom	IC50	IC90
cb + cd	0.039	4.358e-009	9.165e-009
Cetuximab	0.351	1.337e-007	1.296e-005

Fig. 19B

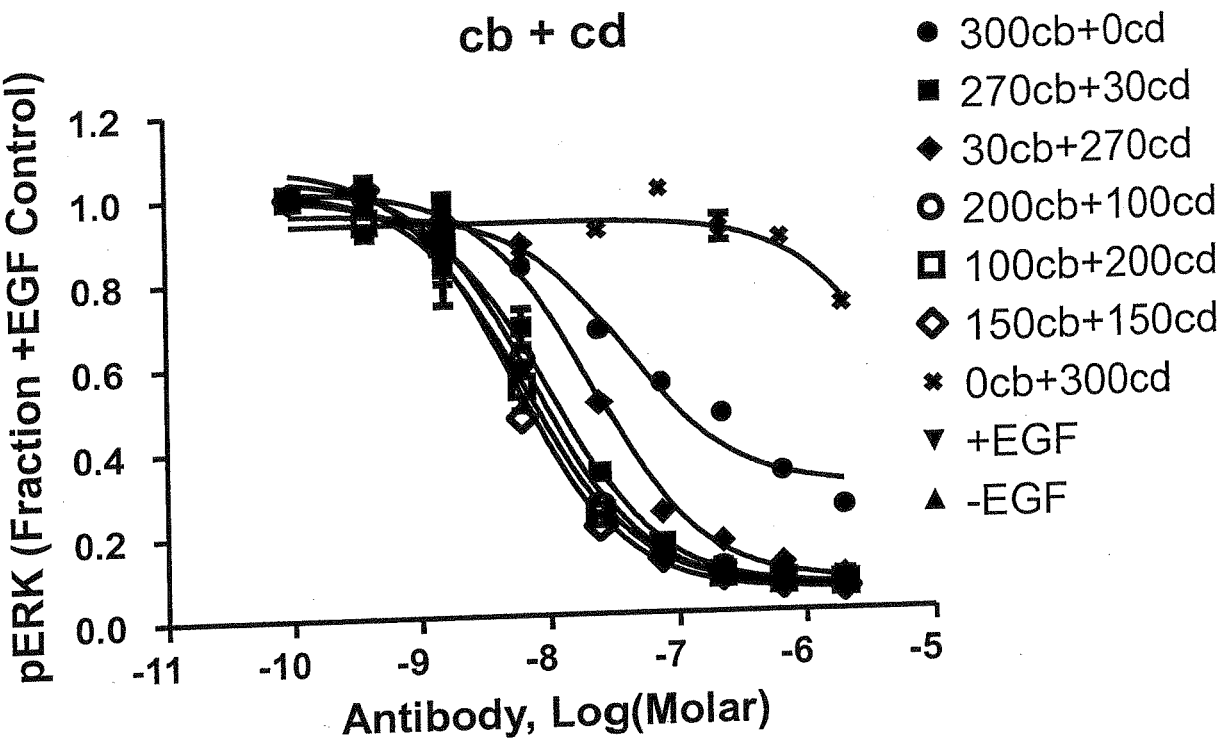


Fig. 20A

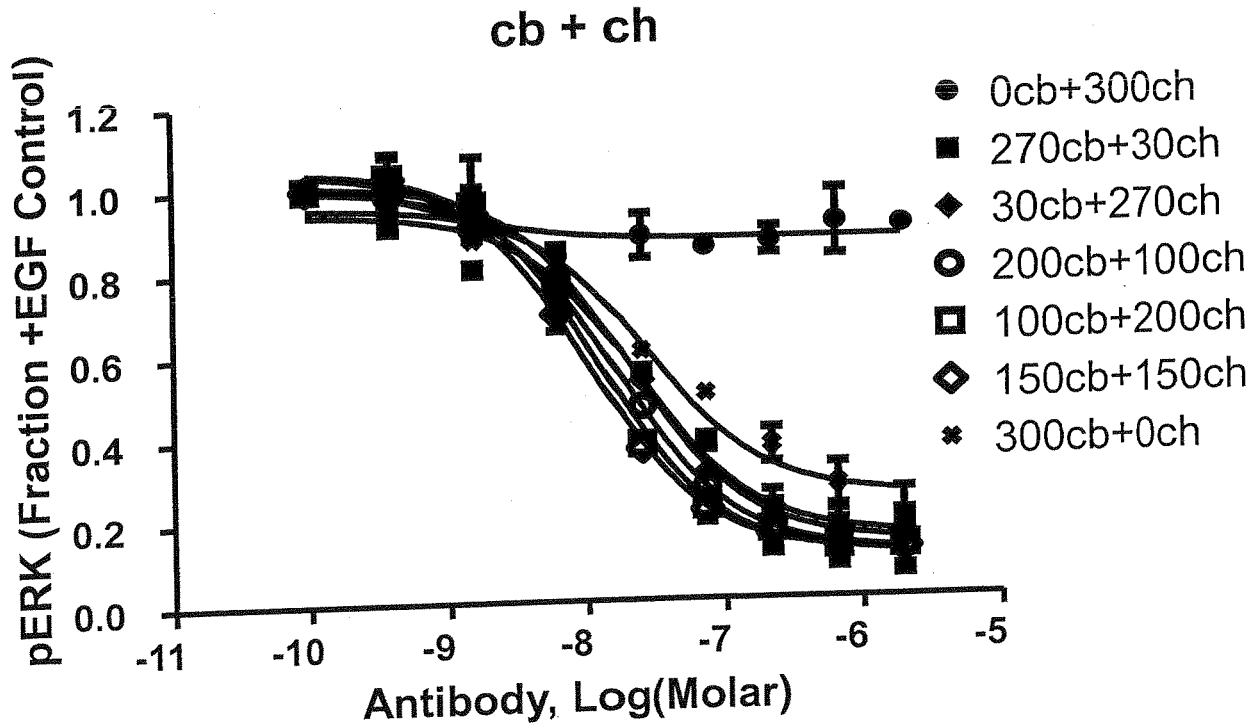


Fig. 20B

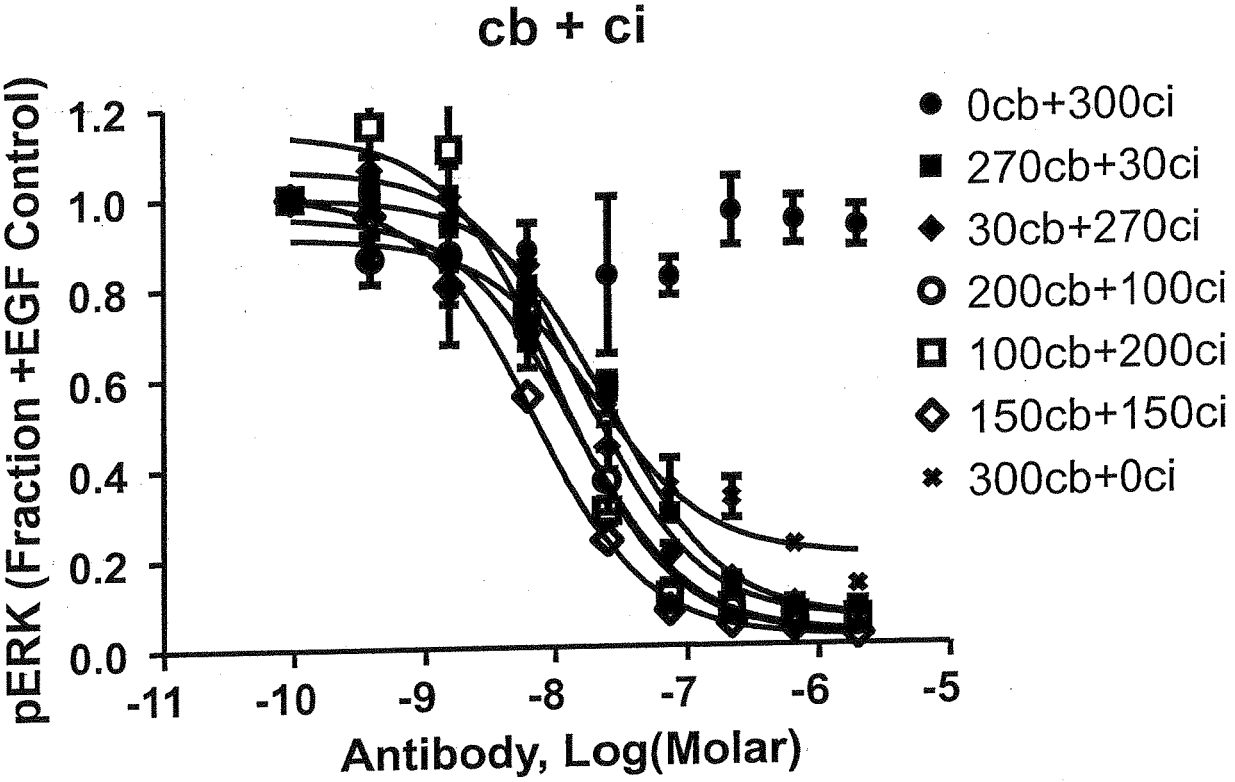


Fig. 20C

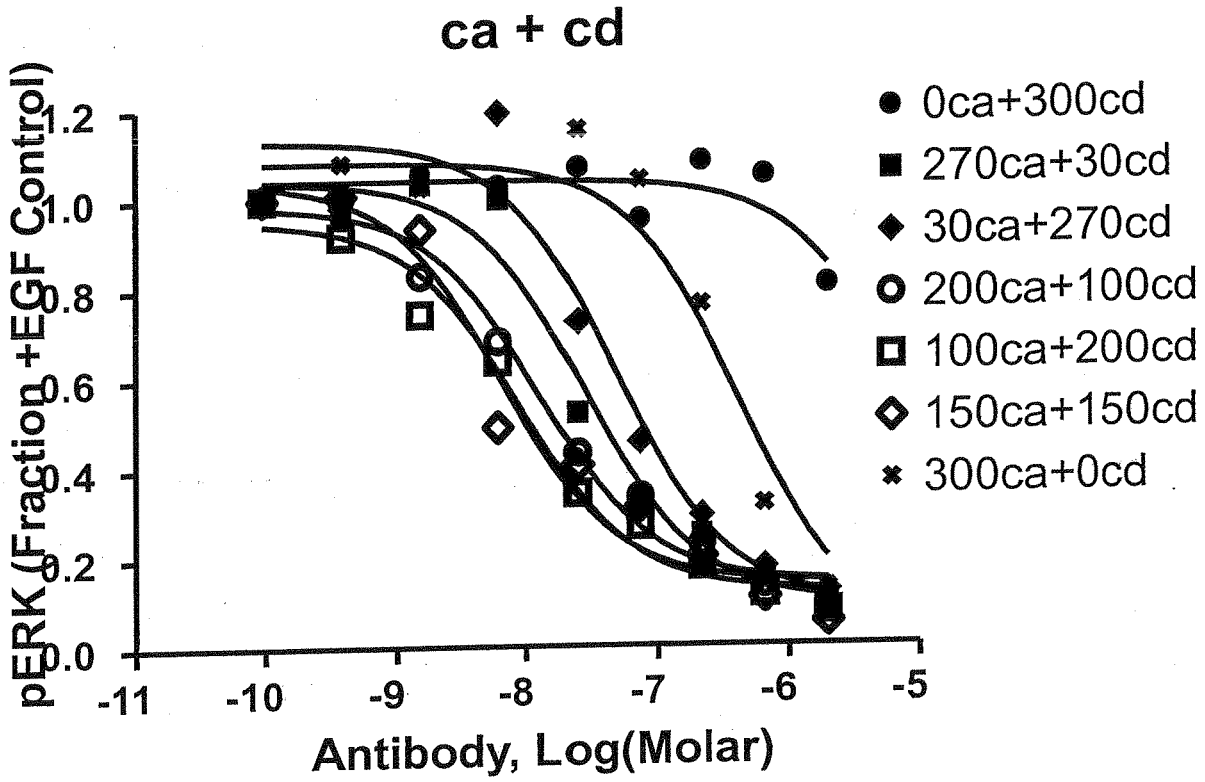


Fig. 20D

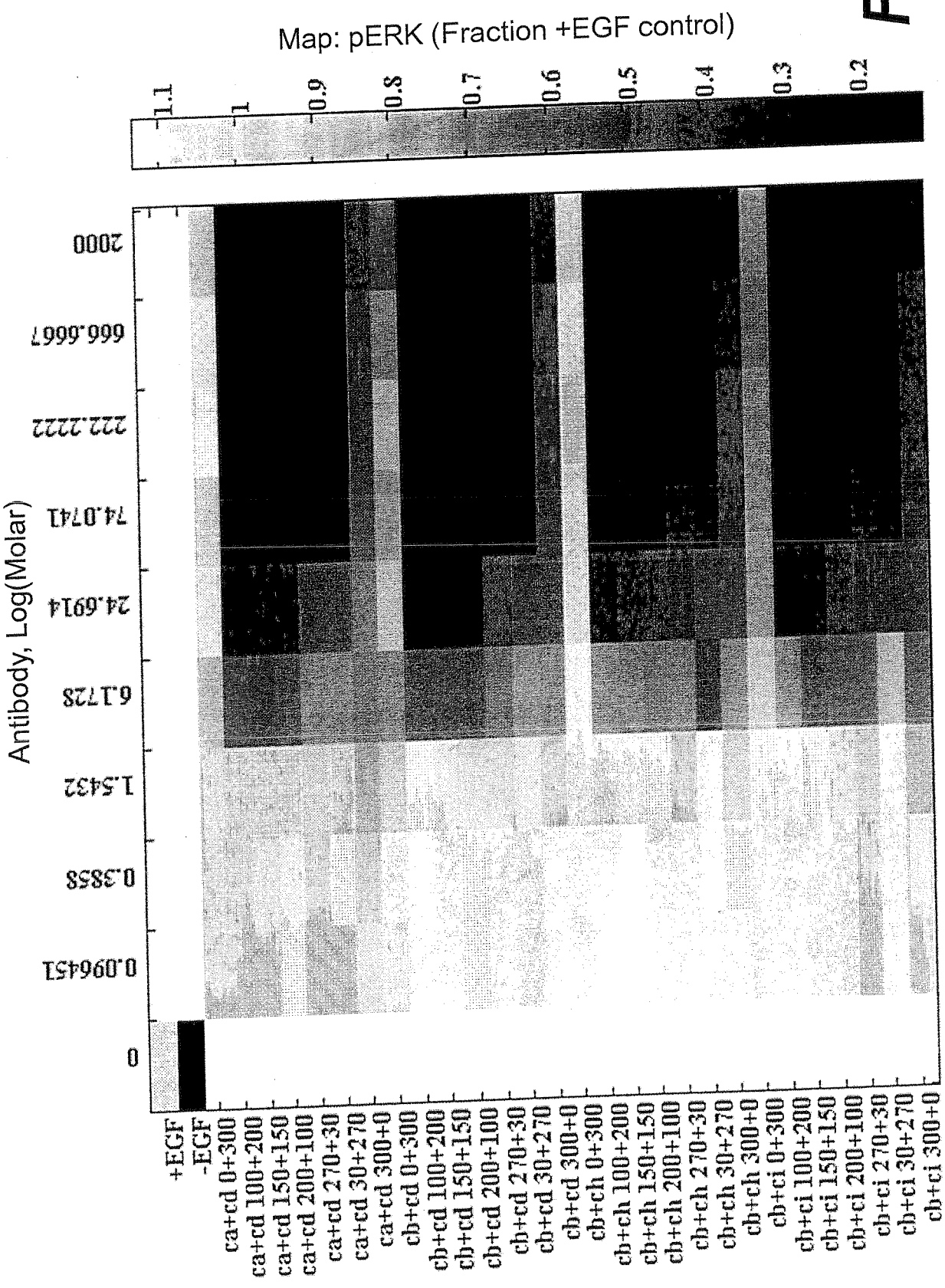

Map: pERK (Fraction +EGF control)
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
Antibody, Log(Molar)
2000
666.6667
222.2222
74.0741
24.6914
6.1728
1.5432
0.3858
0.096451
0
+EGF
-EGF
ca+cd 0+300
ca+cd 100+200
ca+cd 150+150
ca+cd 200+100
ca+cd 270+30
ca+cd 30+270
ca+cd 300+0
cb+cd 0+300
cb+cd 100+200
cb+cd 150+150
cb+cd 200+100
cb+cd 270+30
cb+cd 30+270
cb+cd 300+0
cb+ch 0+300
cb+ch 100+200
cb+ch 150+150
cb+ch 200+100
cb+ch 270+30
cb+ch 30+270
cb+ch 300+0
cb+ci 0+300
cb+ci 100+200
cb+ci 150+150
cb+ci 200+100
cb+ci 270+30
cb+ci 30+270
cb+ci 300+0

Fig. 21

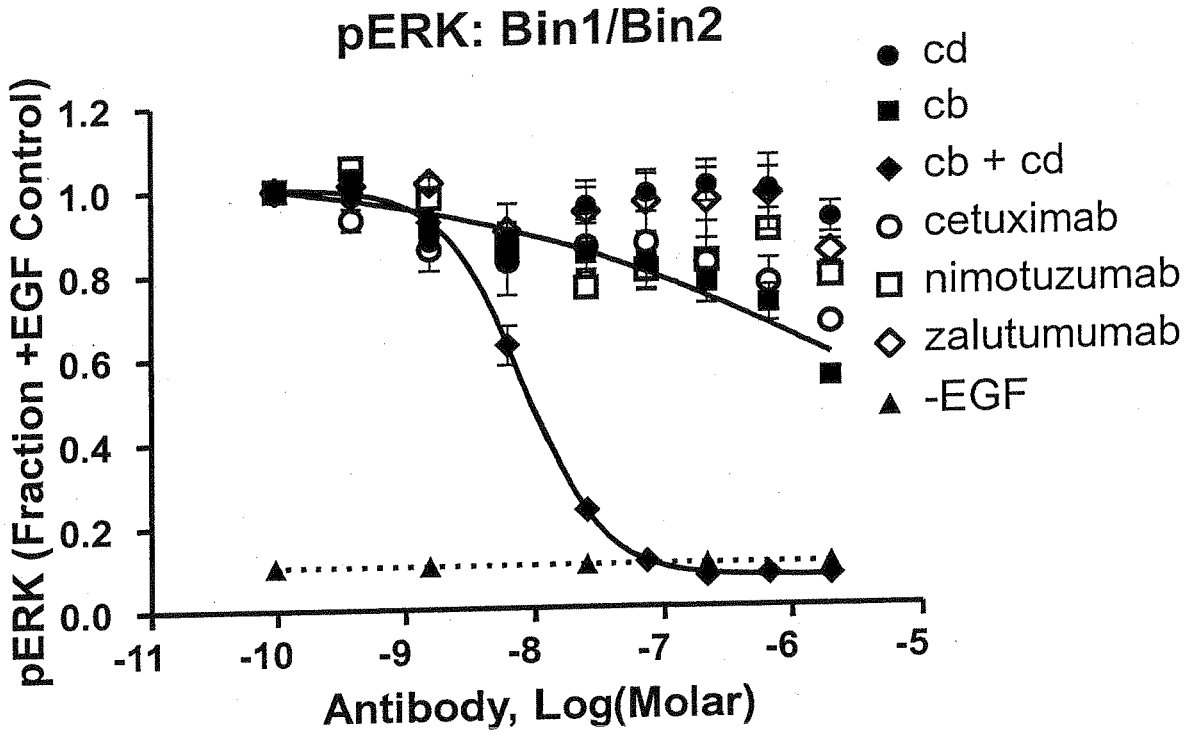


Fig. 22A

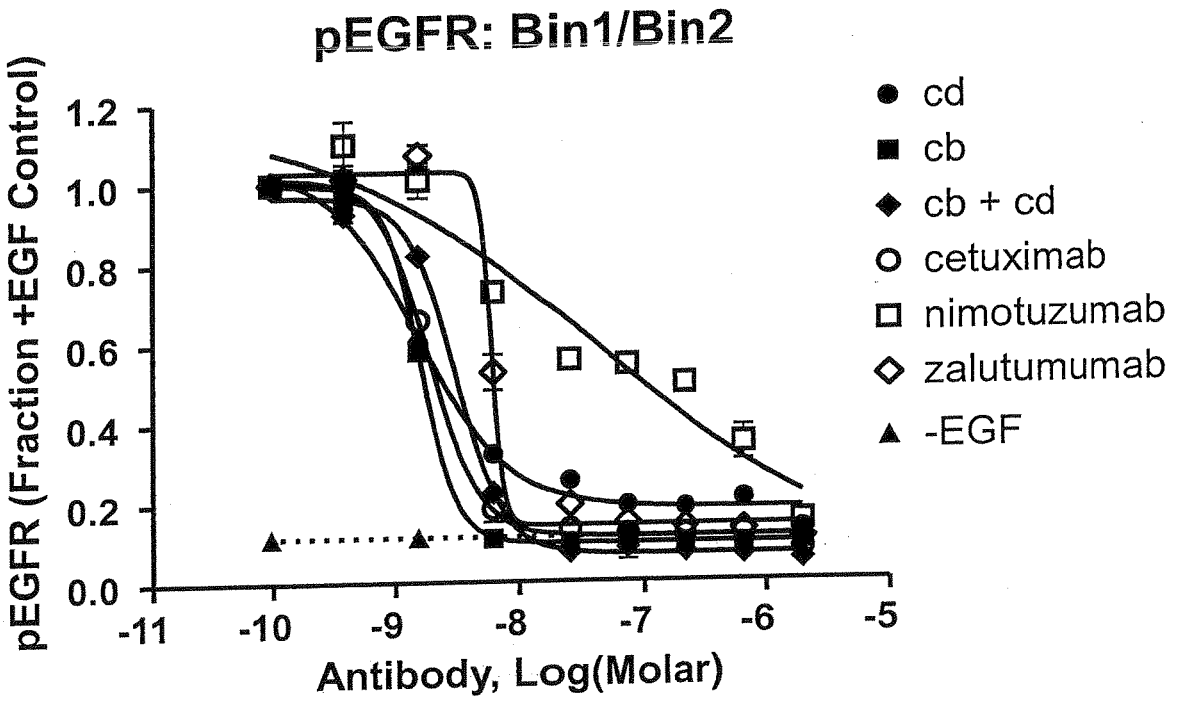


Fig. 22B

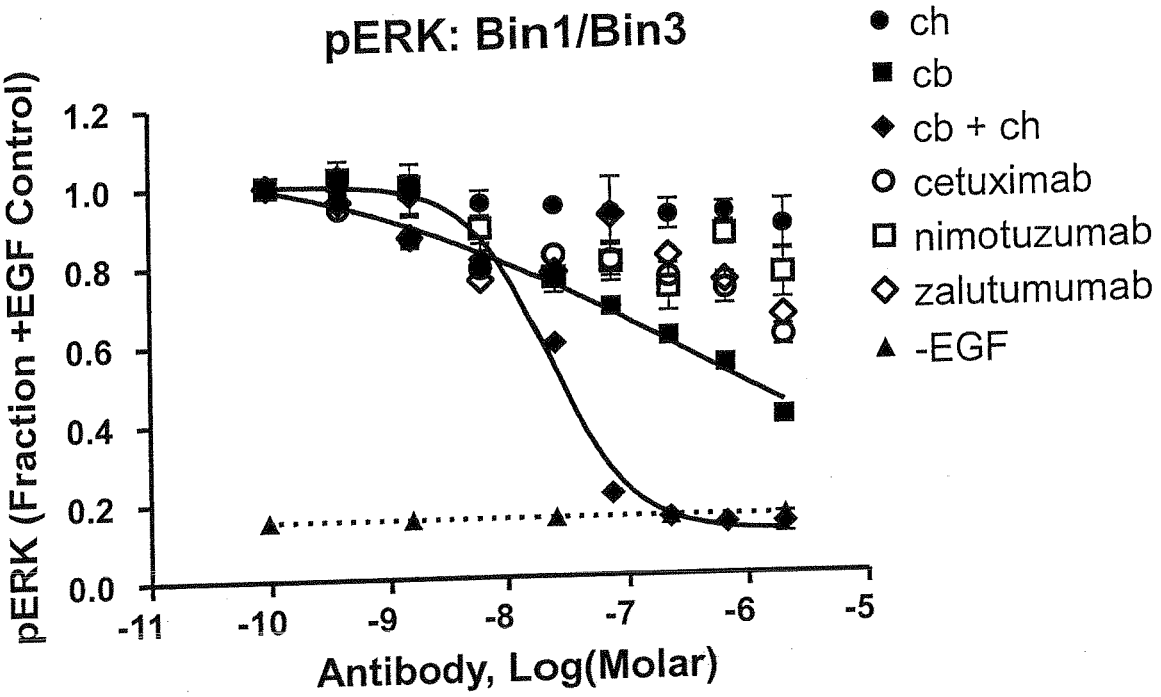

pERK: Bin1/Bin3
pERK (Fraction +EGF Control)
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-11
-10
-9
-8
-7
-6
-5
Antibody, Log(Molar)
ch
cb
cb + ch
cetuximab
nimotuzumab
zalutumumab
-EGF

Fig. 22C

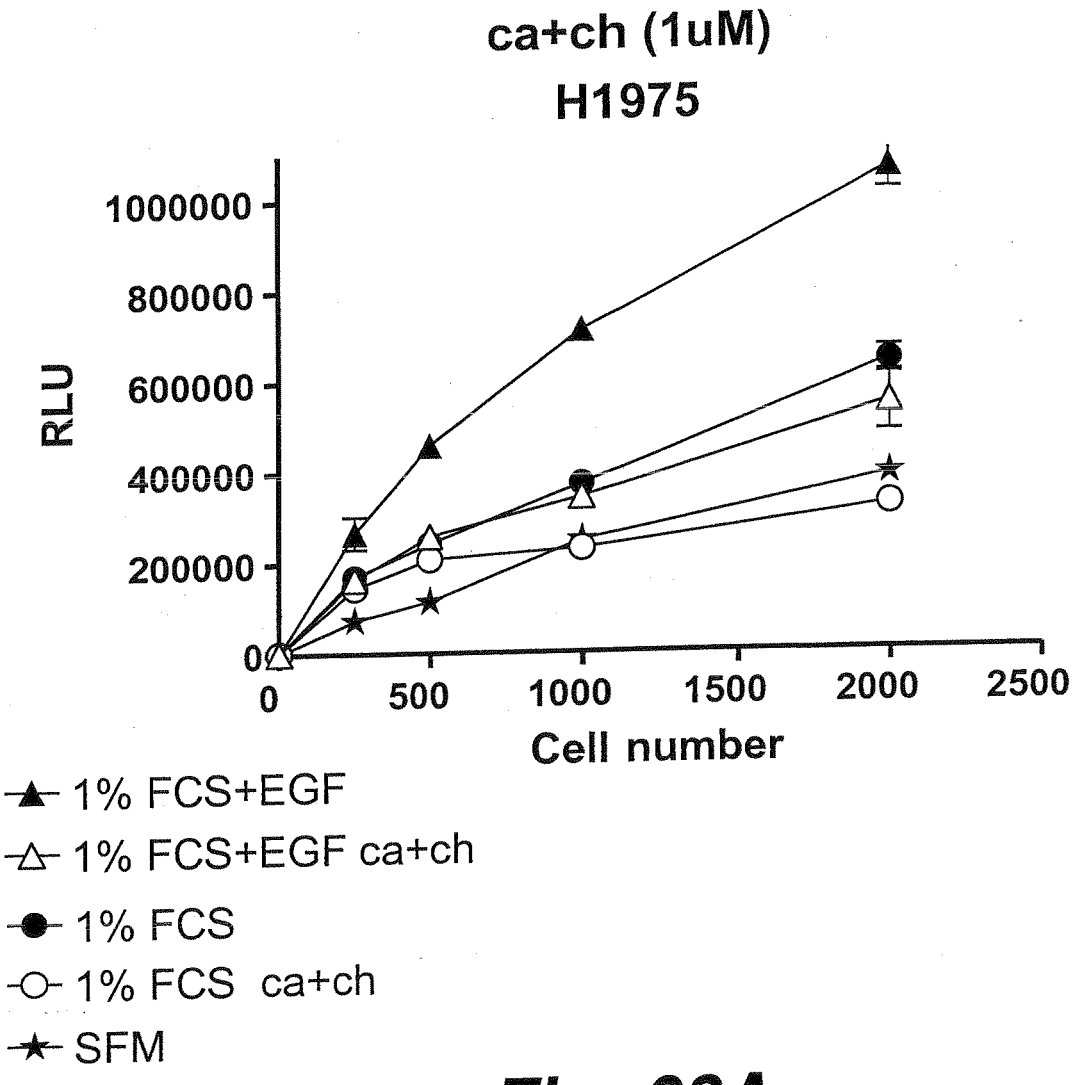

ca+ch (1uM)
H1975
RLU
1000000
800000
600000
400000
200000
0
0
500
1000
1500
2000
2500
Cell number
1% FCS+EGF
1% FCS+EGF ca+ch
1% FCS
1% FCS ca+ch
SFM

Fig. 23A

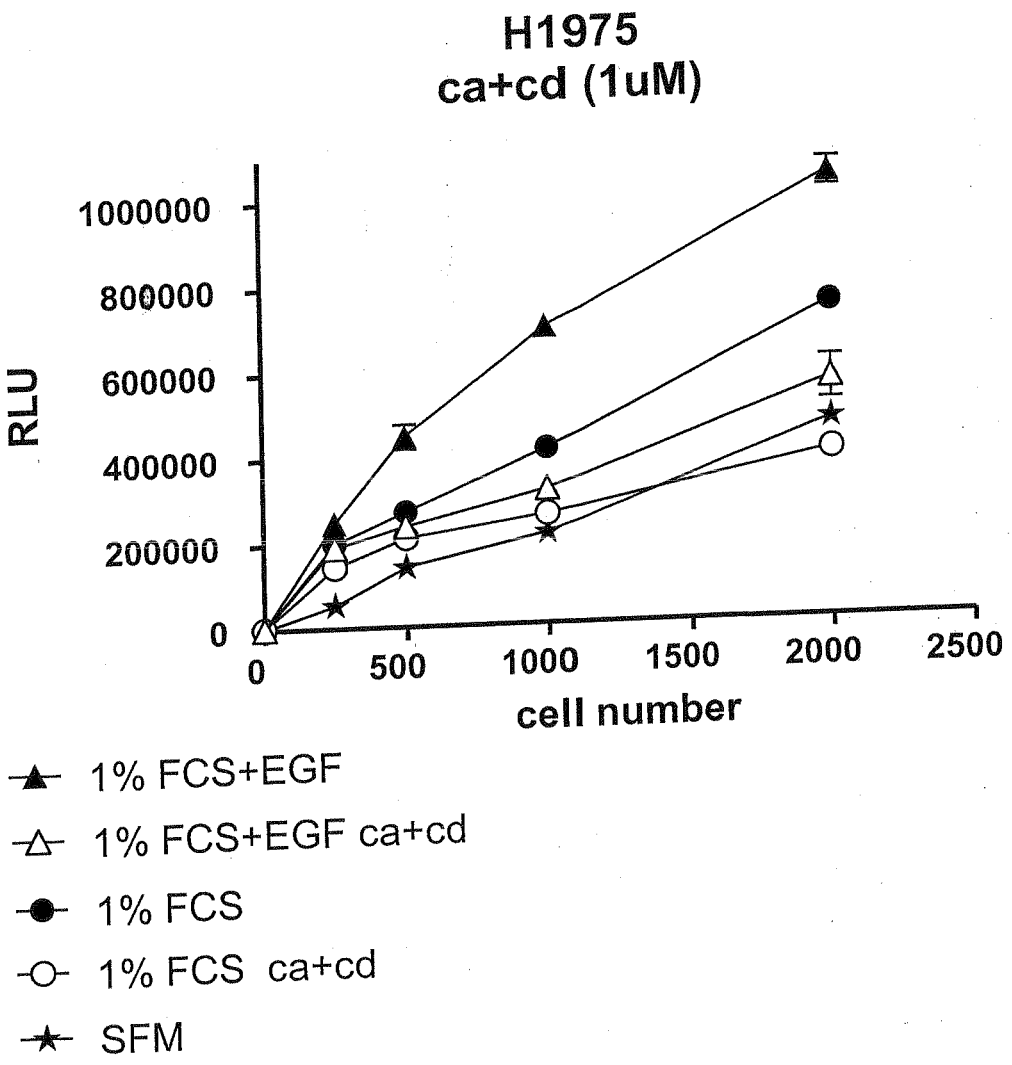

H1975
ca+cd (1uM)
RLU
1000000
800000
600000
400000
200000
0
0
500
1000
1500
2000
2500
cell number
1% FCS+EGF
1% FCS+EGF ca+cd
1% FCS
1% FCS ca+cd
SFM

Fig. 23B

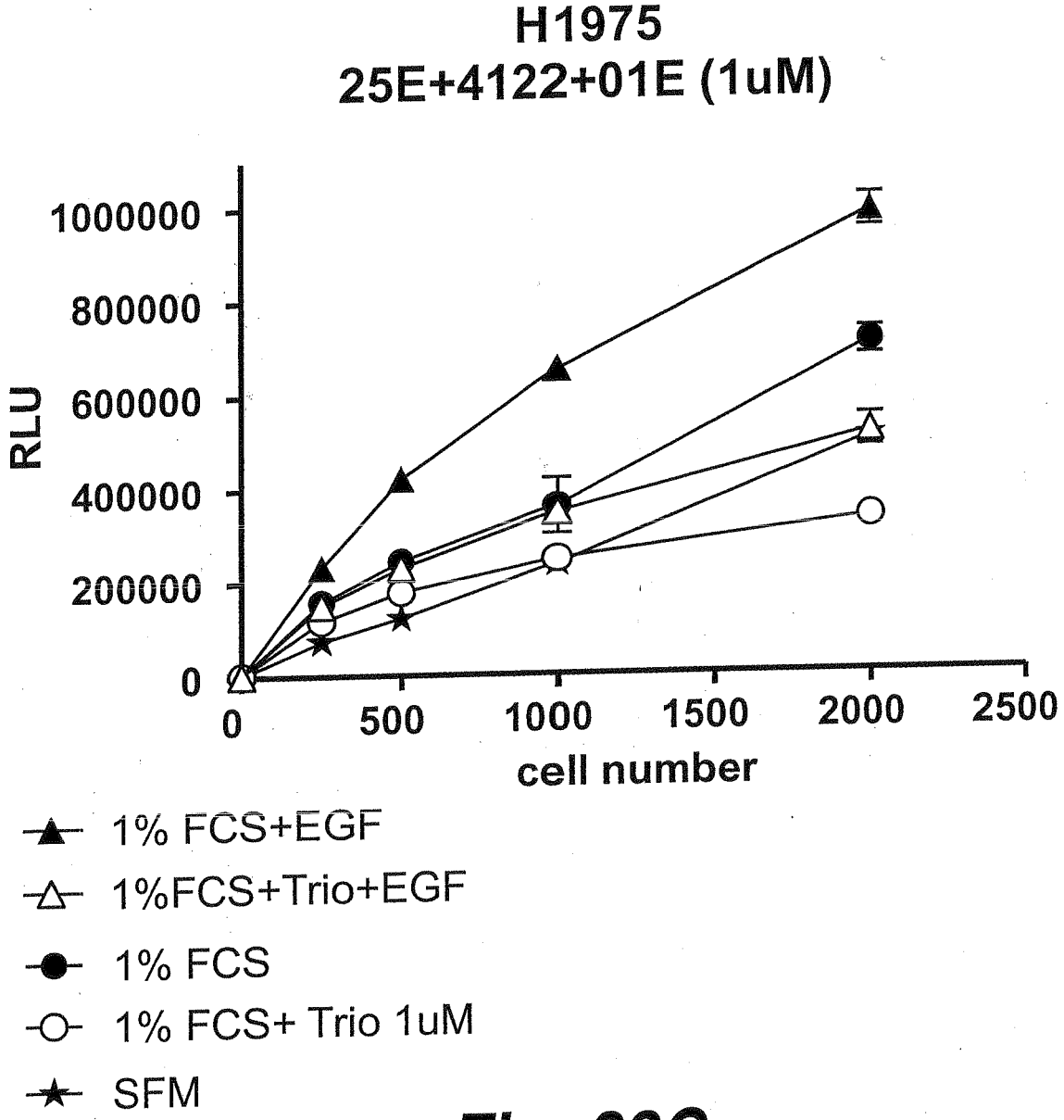

H1975
25E+4122+01E (1uM)
RLU
1000000
800000
600000
400000
200000
0
0
500
1000
1500
2000
2500
cell number
1% FCS+EGF
1%FCS+Trio+EGF
1% FCS
1% FCS+ Trio 1uM
SFM

Fig. 23C

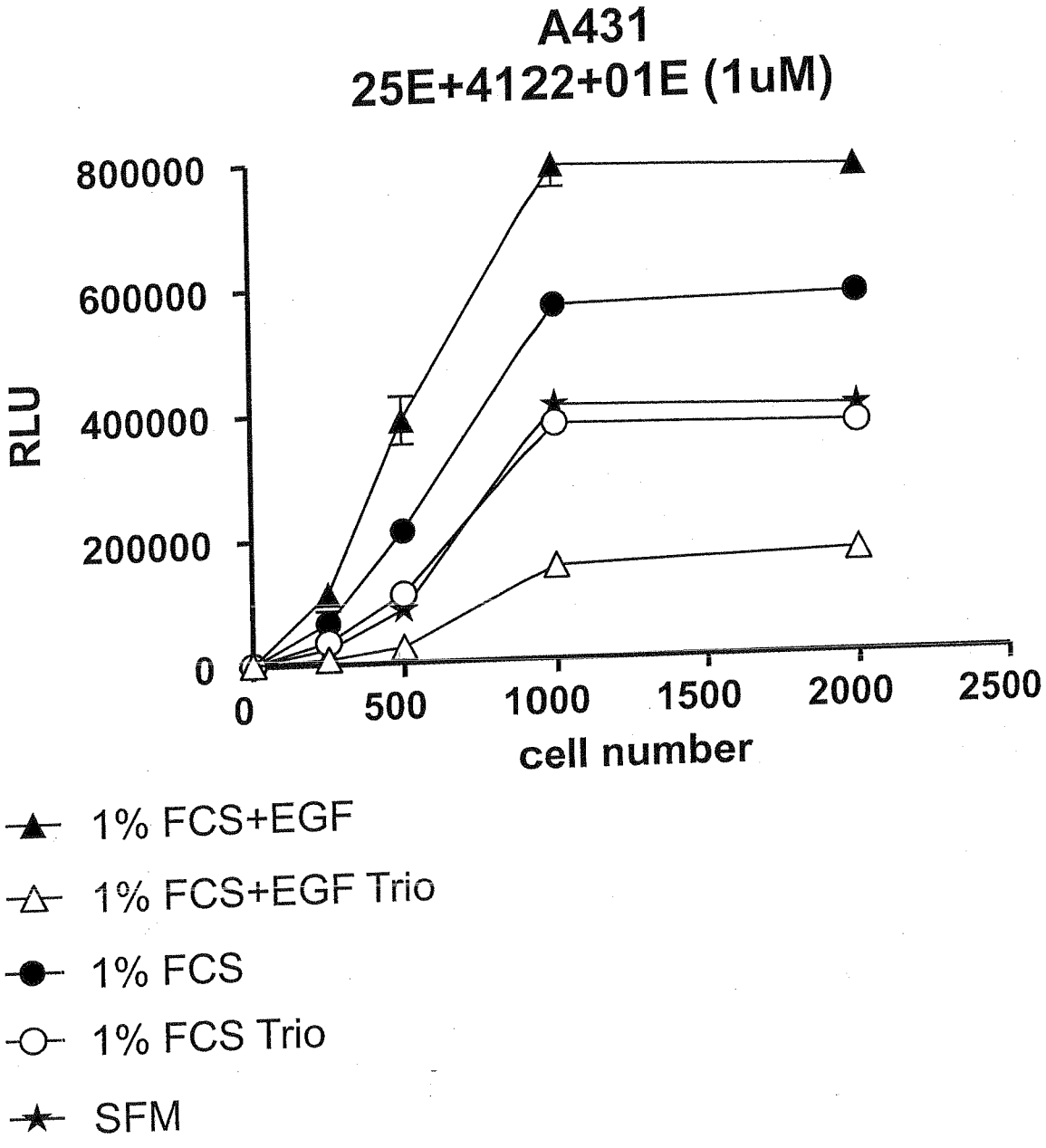

A431
25E+4122+01E (1uM)
800000
600000
400000
200000
0
RLU
0
500
1000
1500
2000
2500
cell number
1% FCS+EGF
1% FCS+EGF Trio
1% FCS
1% FCS Trio
SFM

Fig. 23D

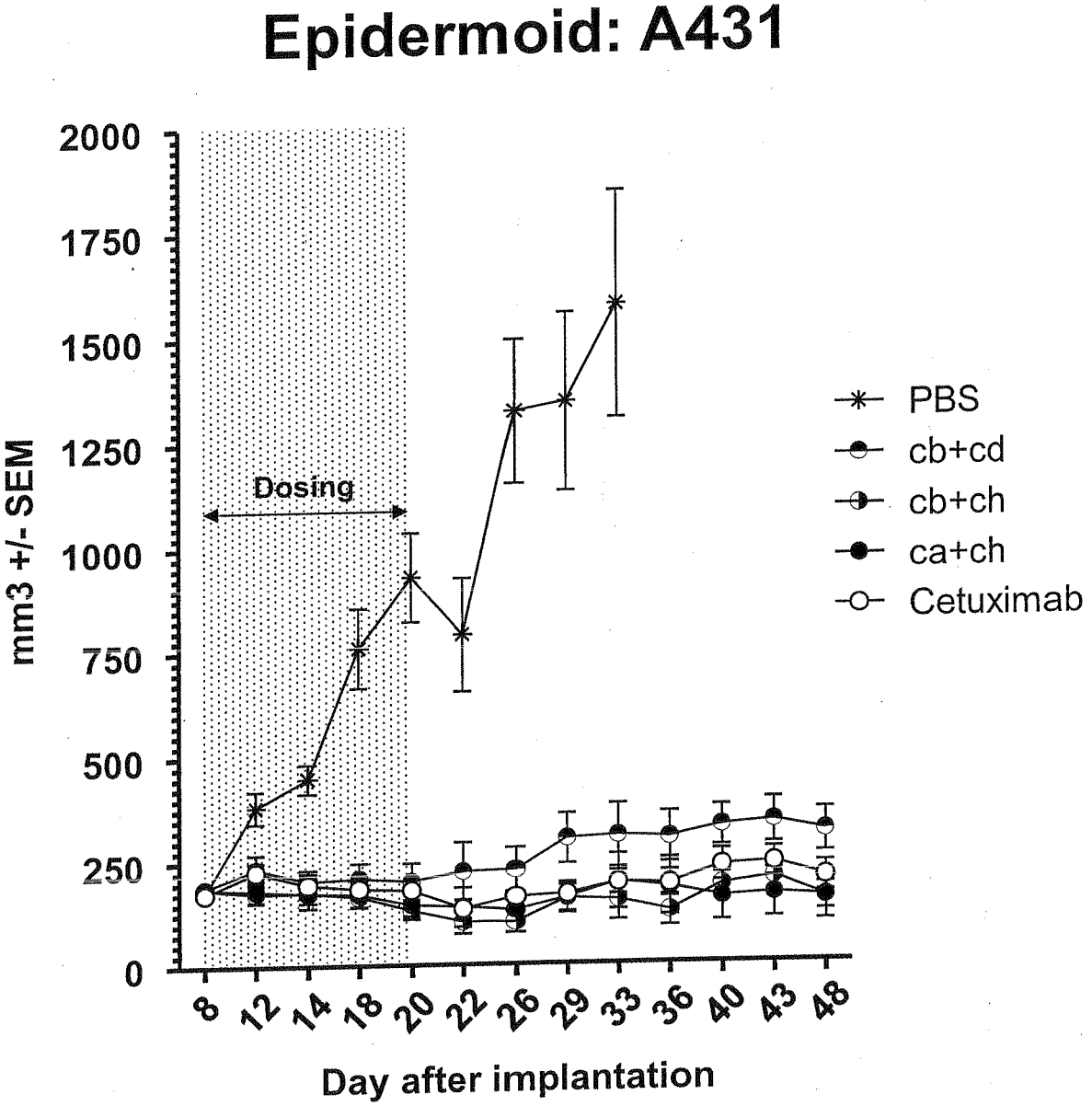

Epidermoid: A431
2000
1750
1500
1250
1000
750
500
250
0
mm3 +/- SEM
Dosing
8
12
14
18
20
22
26
29
33
36
40
43
48
Day after implantation
PBS
cb+cd
cb+ch
ca+ch
Cetuximab

Fig. 24A

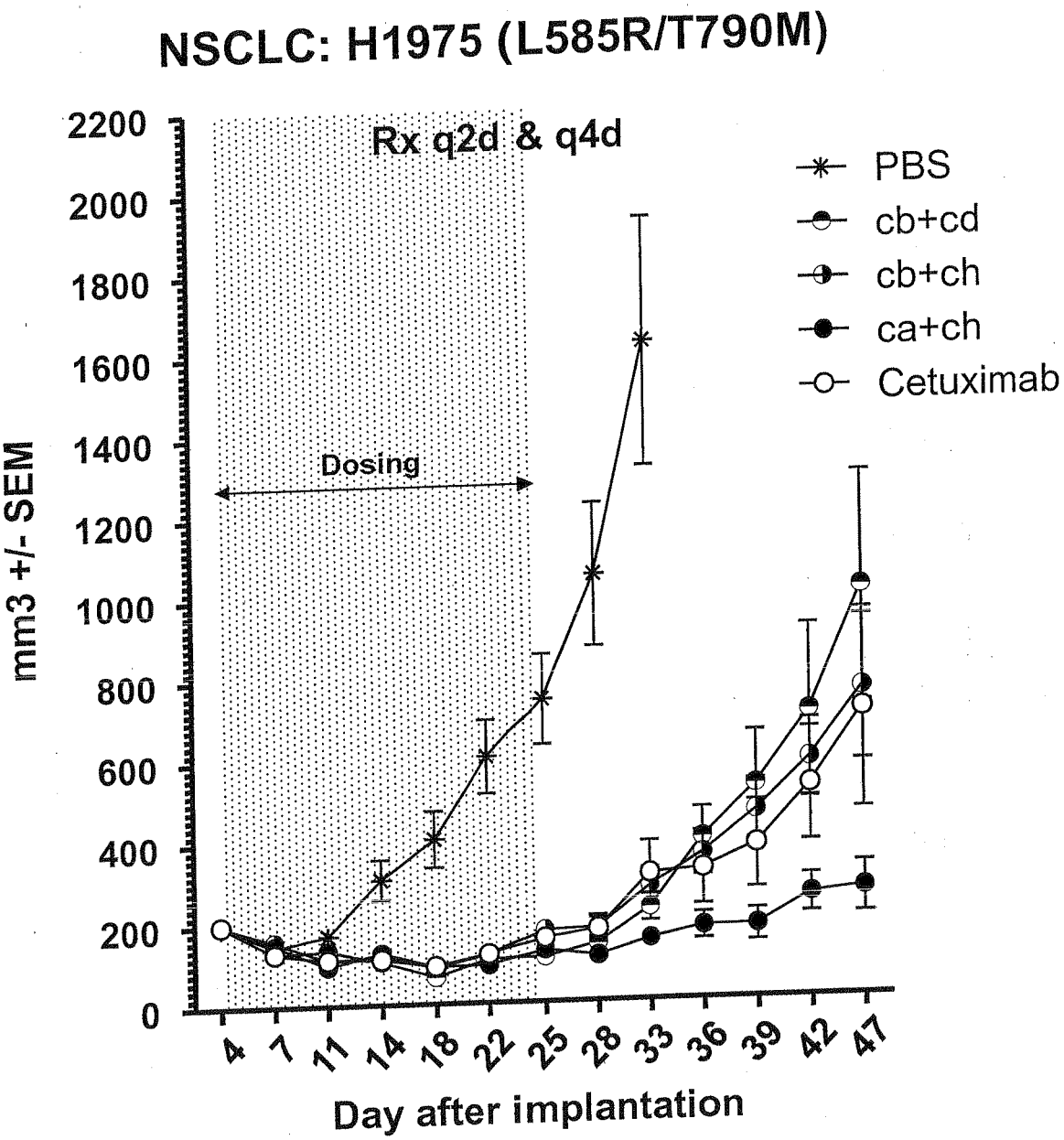

NSCLC: H1975 (L585R/T790M)
Rx q2d & q4d
Dosing
PBS
cb+cd
cb+ch
ca+ch
Cetuximab
mm3 +/- SEM
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
4
7
11
14
18
22
25
28
33
36
39
42
47
Day after implantation

Fig. 24B

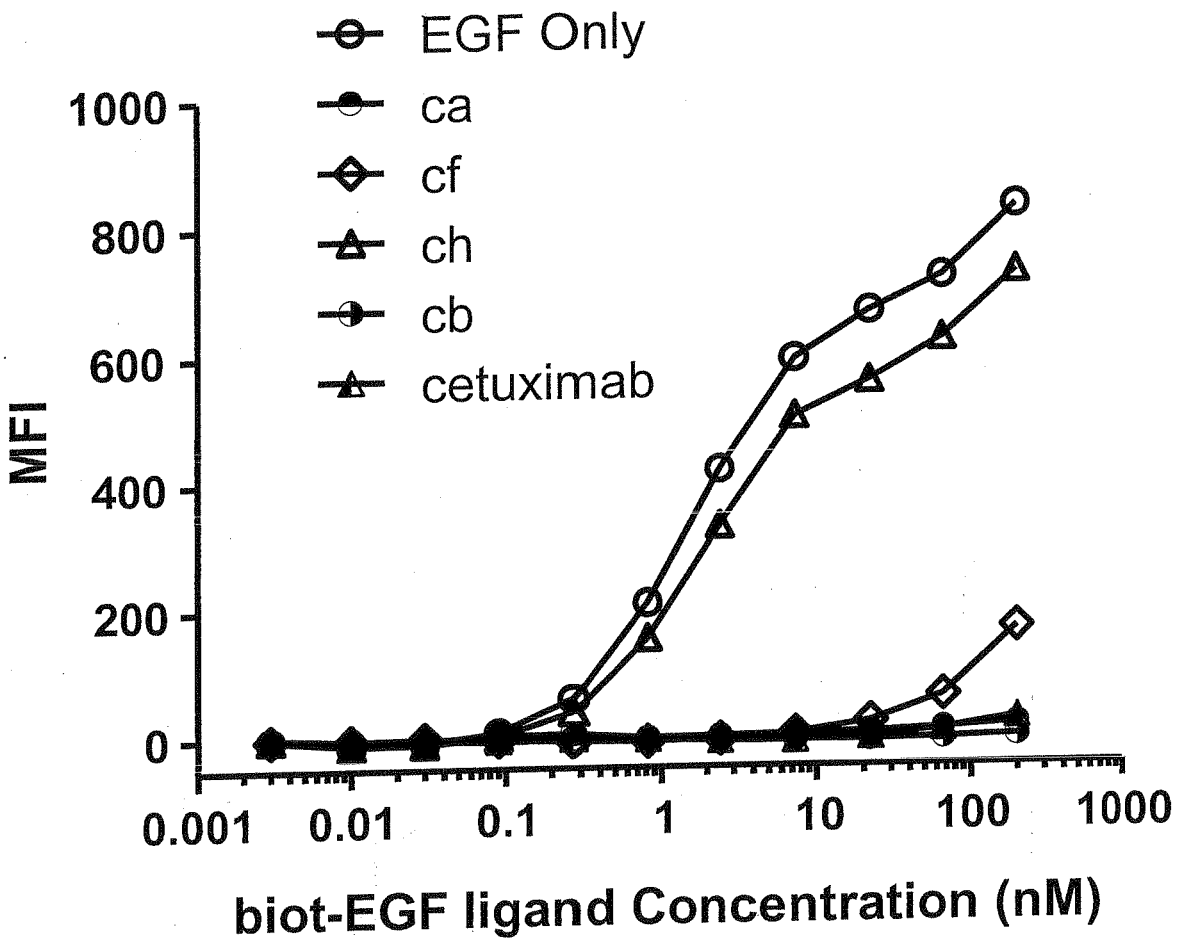

EGF Only
ca
cf
ch
cb
cetuximab
MFI
1000
800
600
400
200
0
0.001
0.01
0.1
1
10
100
1000
biot-EGF ligand Concentration (nM)

Fig. 25