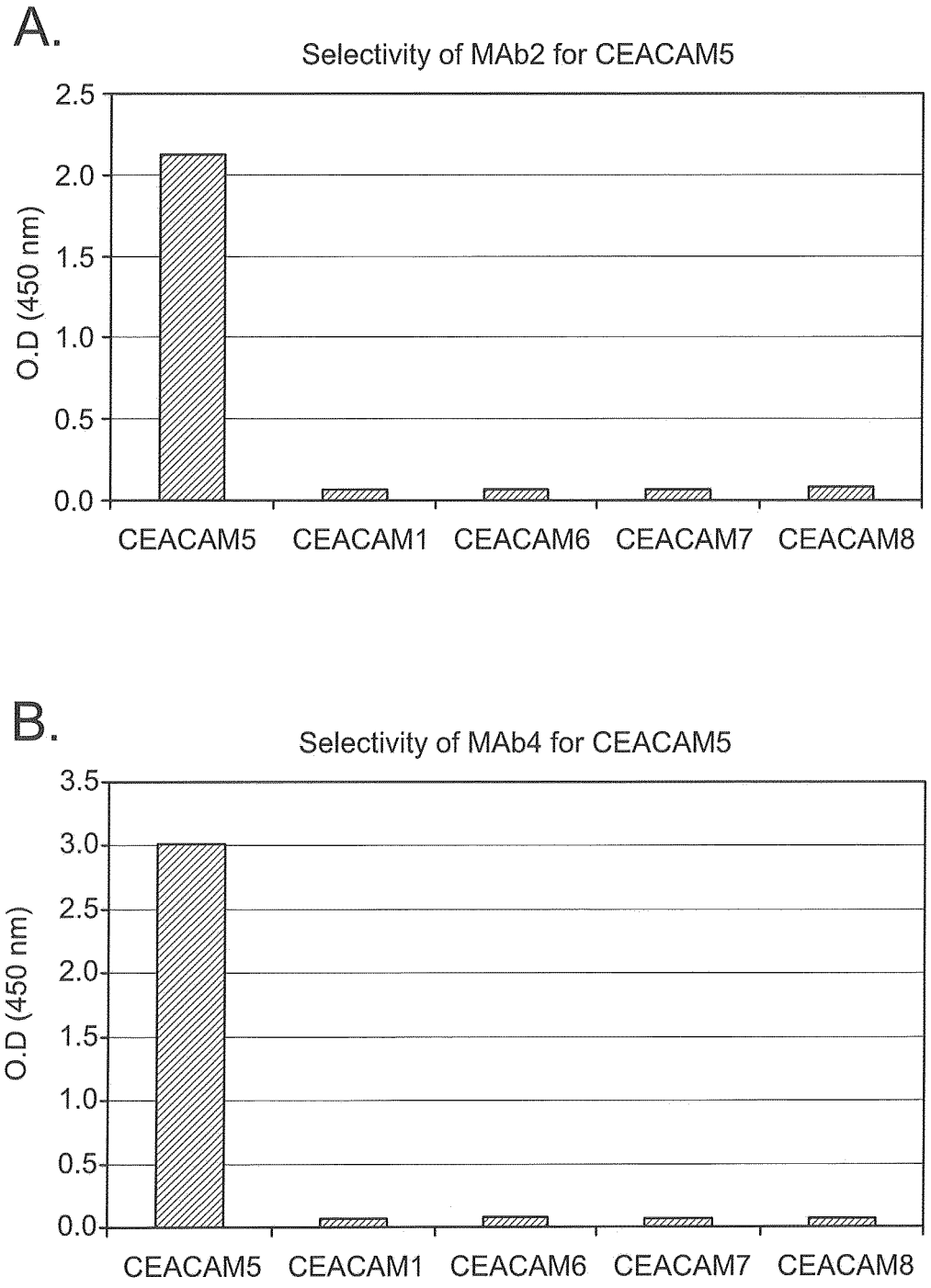
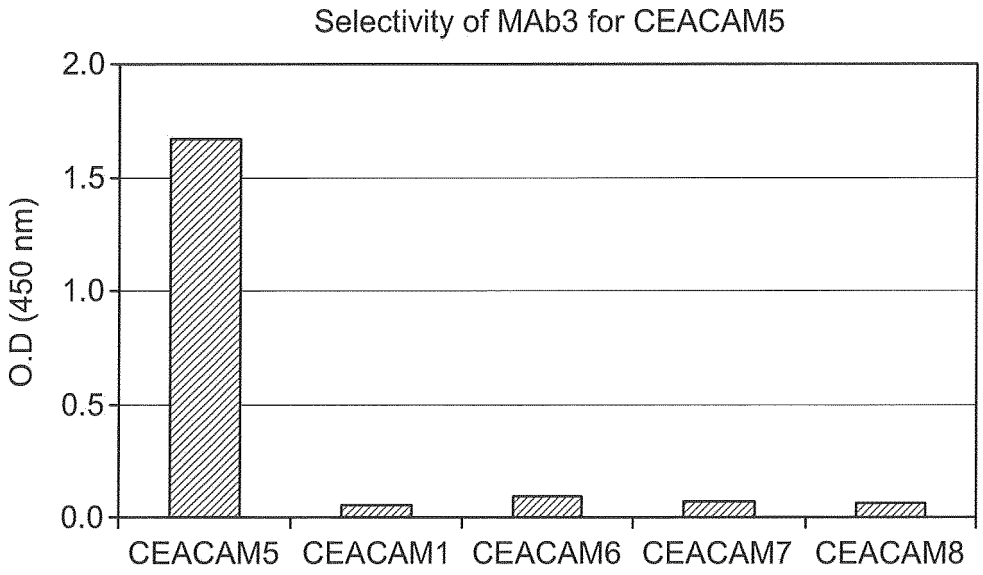


FIG.1 Beginning

C.



D.

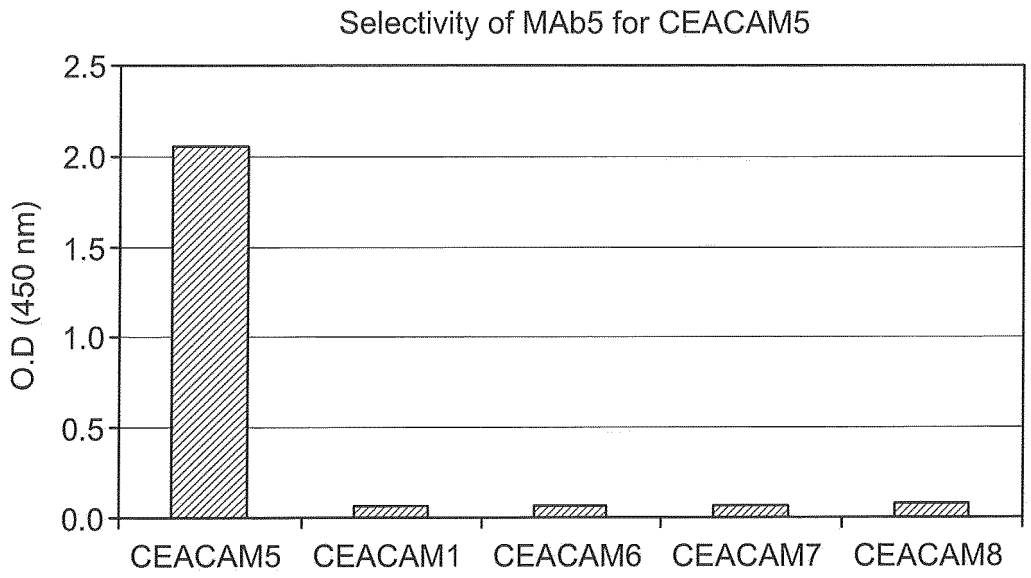


FIG.1 Continuation

E.

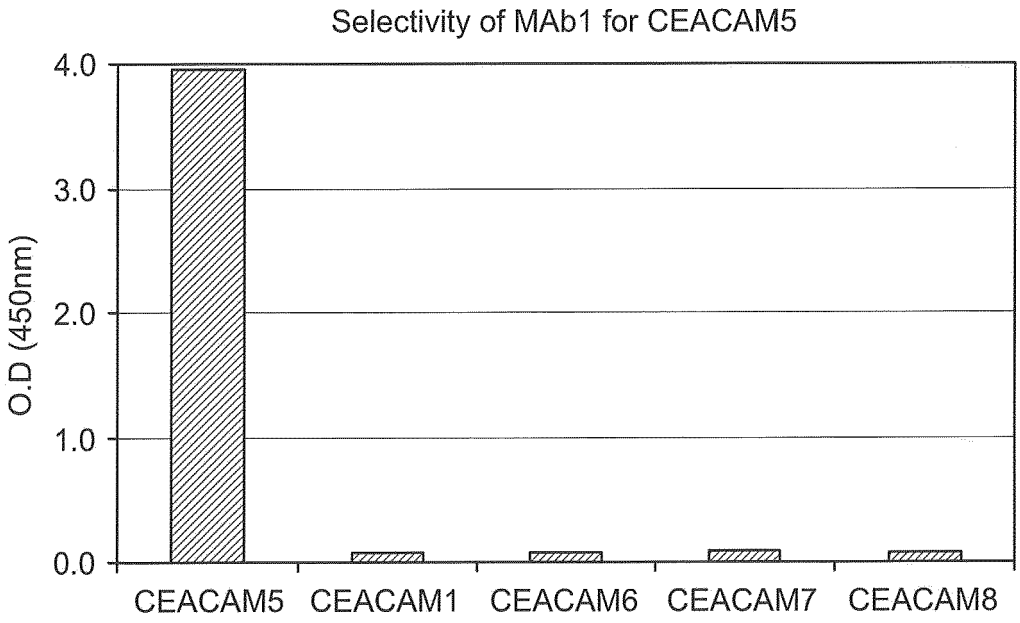

Selectivity of MAb1 for CEACAM5
O.D (450nm)
4.0
3.0
2.0
1.0
0.0
CEACAM5
CEACAM1
CEACAM6
CEACAM7
CEACAM8

FIG.1 End

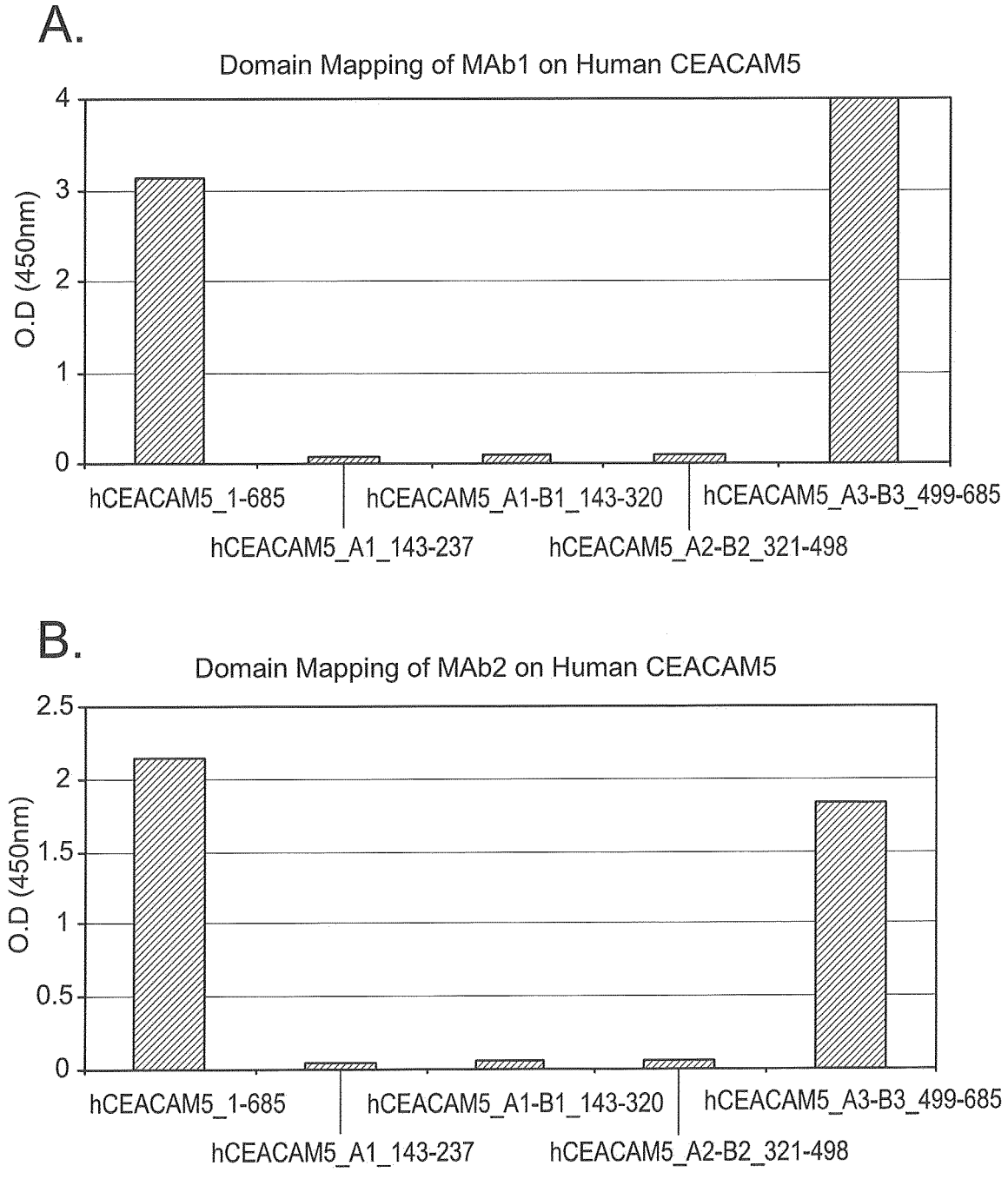


FIG.2 Beginning

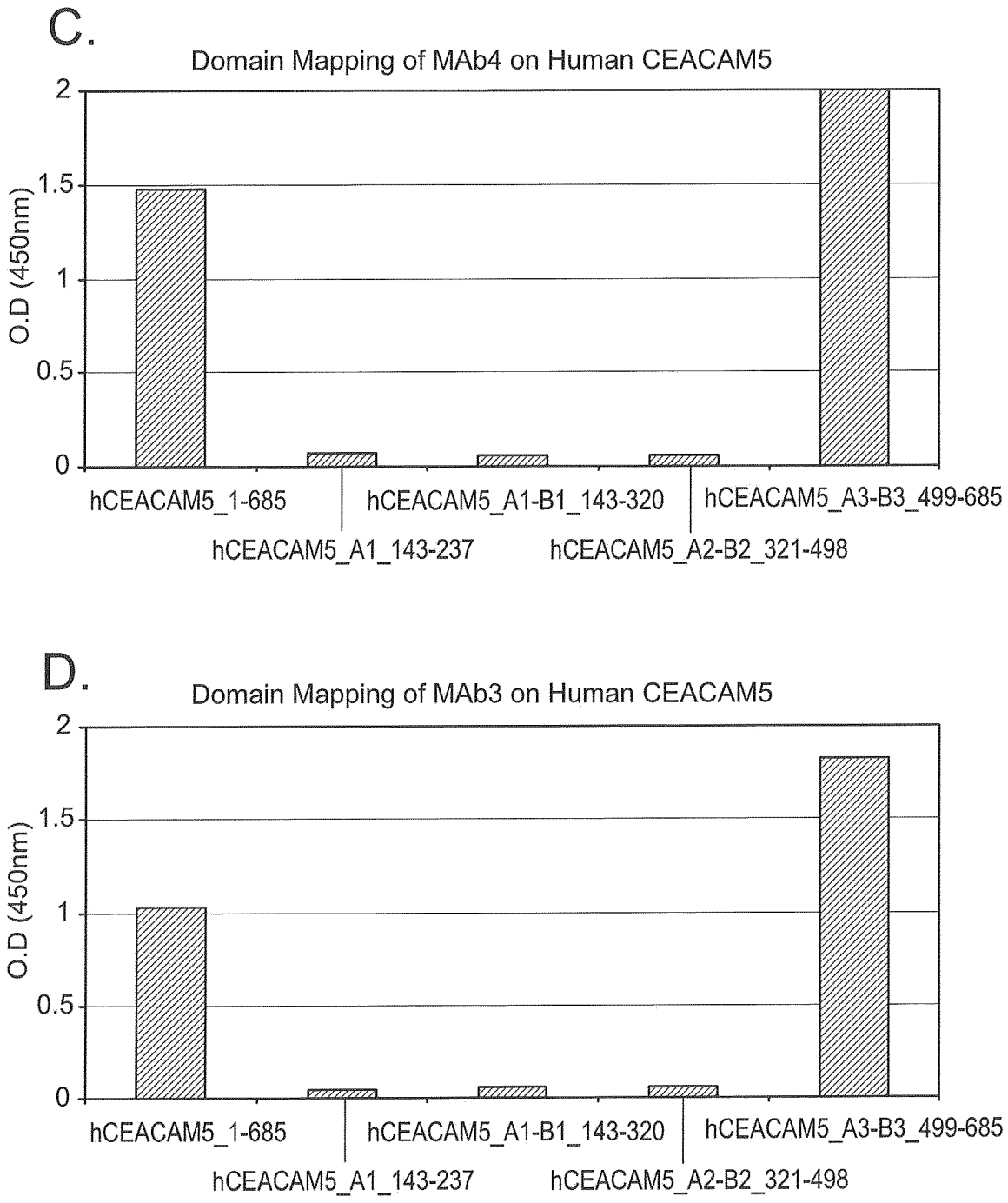


FIG.2 Continuation

E.

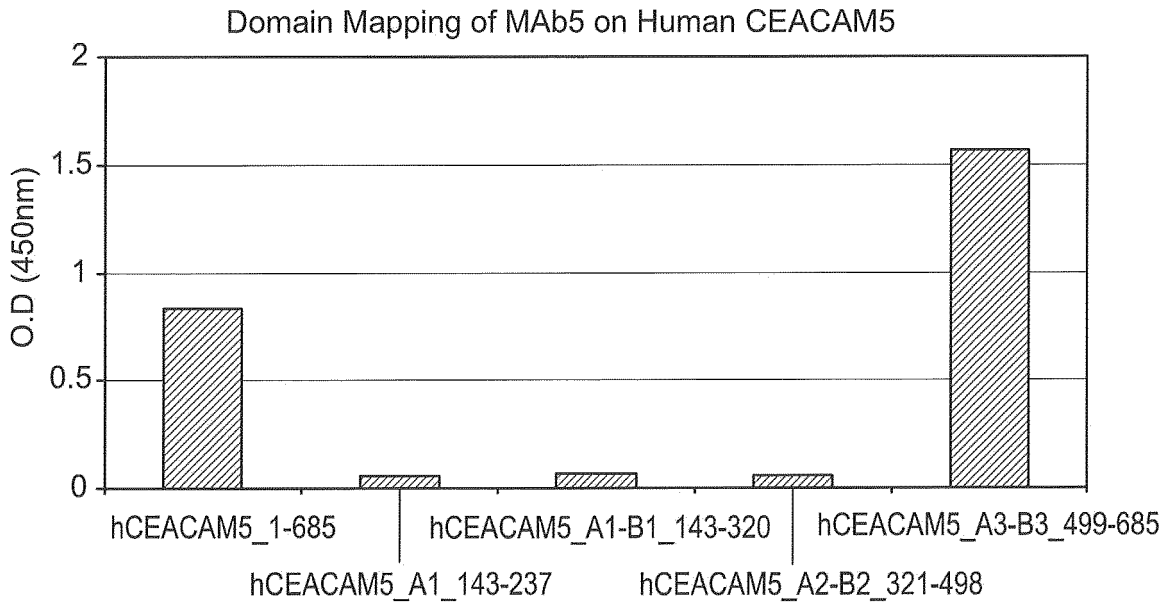

Domain Mapping of MAb5 on Human CEACAM5
O.D (450nm)
2
1.5
1
0.5
0
hCEACAM5_1-685
hCEACAM5_A1_143-237
hCEACAM5_A1-B1_143-320
hCEACAM5_A2-B2_321-498
hCEACAM5_A3-B3_499-685

FIG.2 End

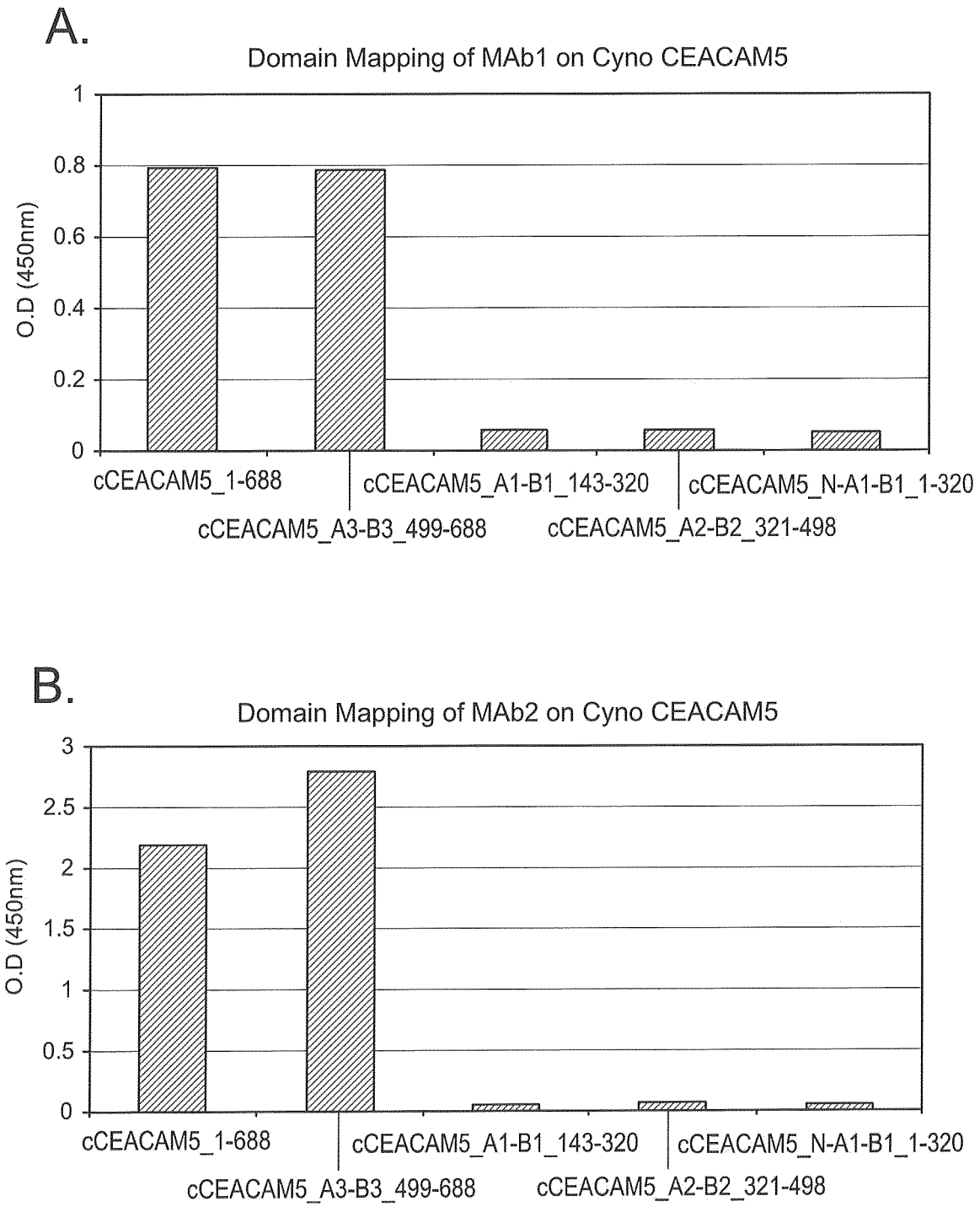
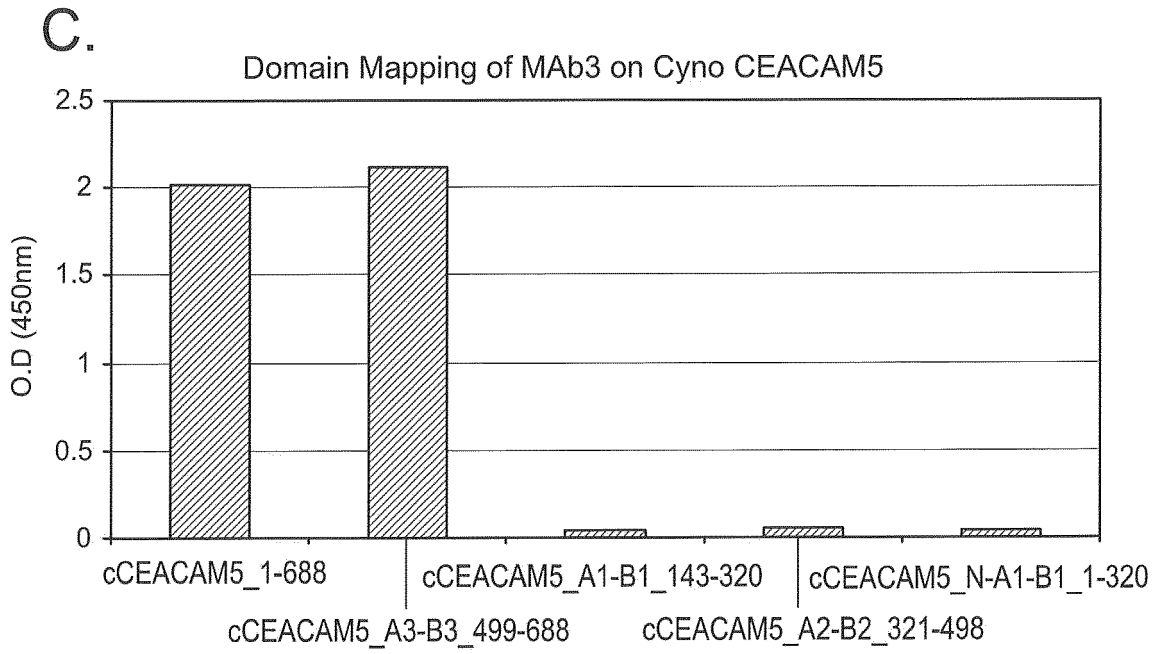


FIG.3 Beginning



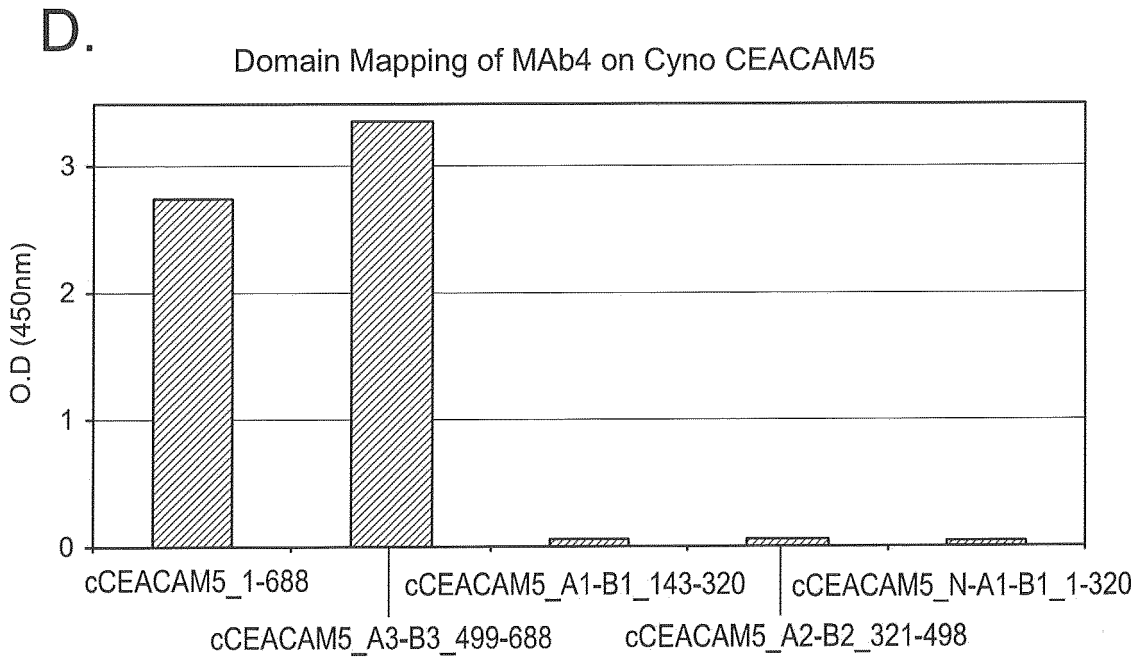


FIG.3 Continuation

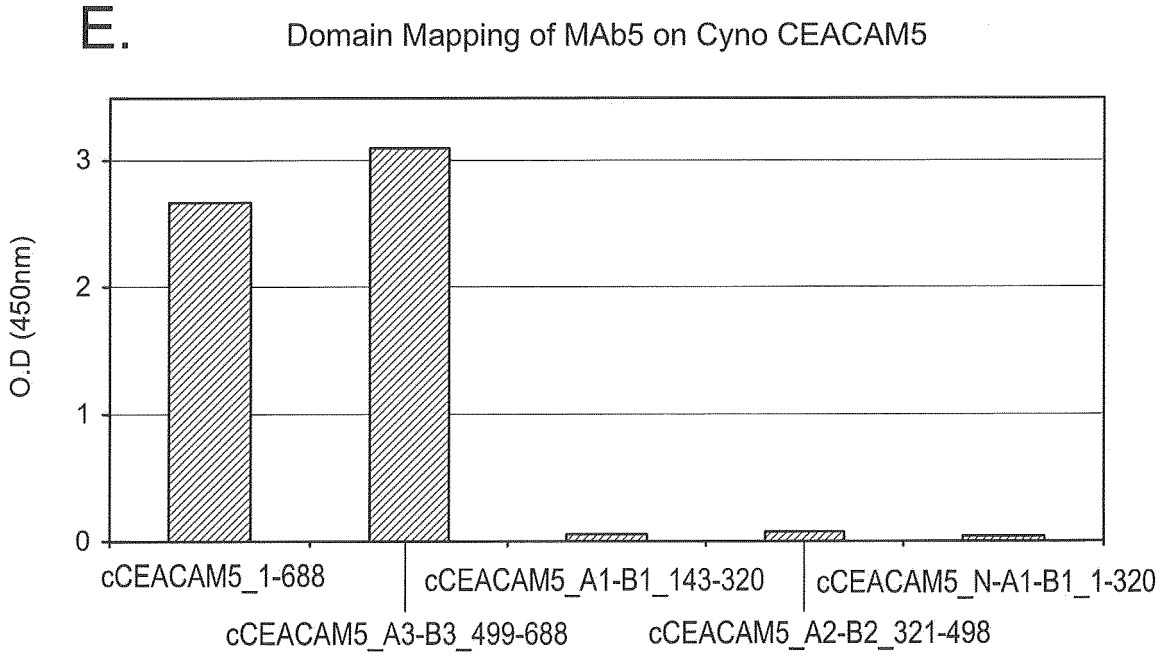

E.
Domain Mapping of MAb5 on Cyno CEACAM5
O.D (450nm)
3
2
1
0
cCEACAM5_1-688
cCEACAM5_A3-B3_499-688
cCEACAM5_A1-B1_143-320
cCEACAM5_A2-B2_321-498
cCEACAM5_N-A1-B1_1-320

FIG.3 End

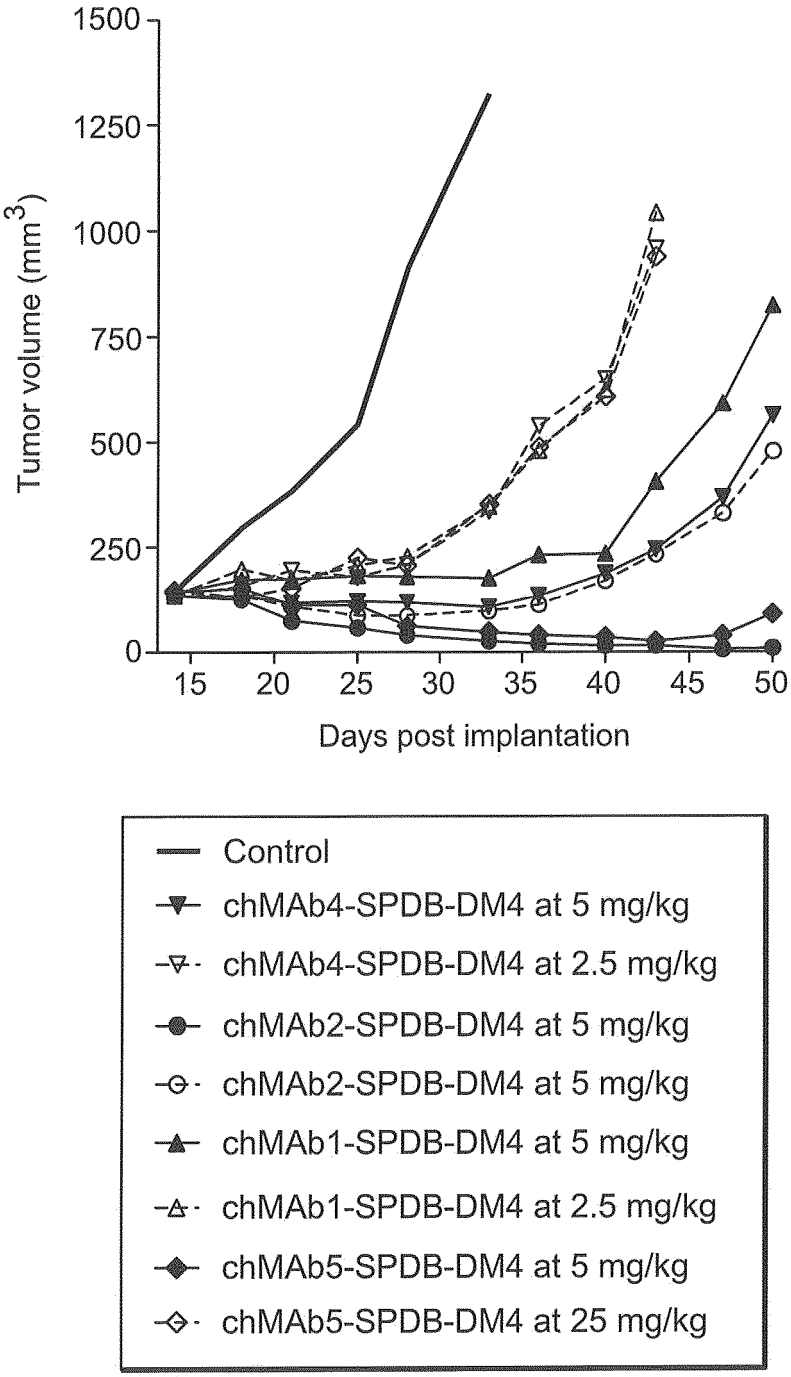

1500
1250
1000
750
500
250
0
Tumor volume (mm3)
15
20
25
30
35
40
45
50
Days post implantation
Control
chMAb4-SPDB-DM4 at 5 mg/kg
chMAb4-SPDB-DM4 at 2.5 mg/kg
chMAb2-SPDB-DM4 at 5 mg/kg
chMAb2-SPDB-DM4 at 5 mg/kg
chMAb1-SPDB-DM4 at 5 mg/kg
chMAb1-SPDB-DM4 at 2.5 mg/kg
chMAb5-SPDB-DM4 at 5 mg/kg
chMAb5-SPDB-DM4 at 25 mg/kg

FIG.4

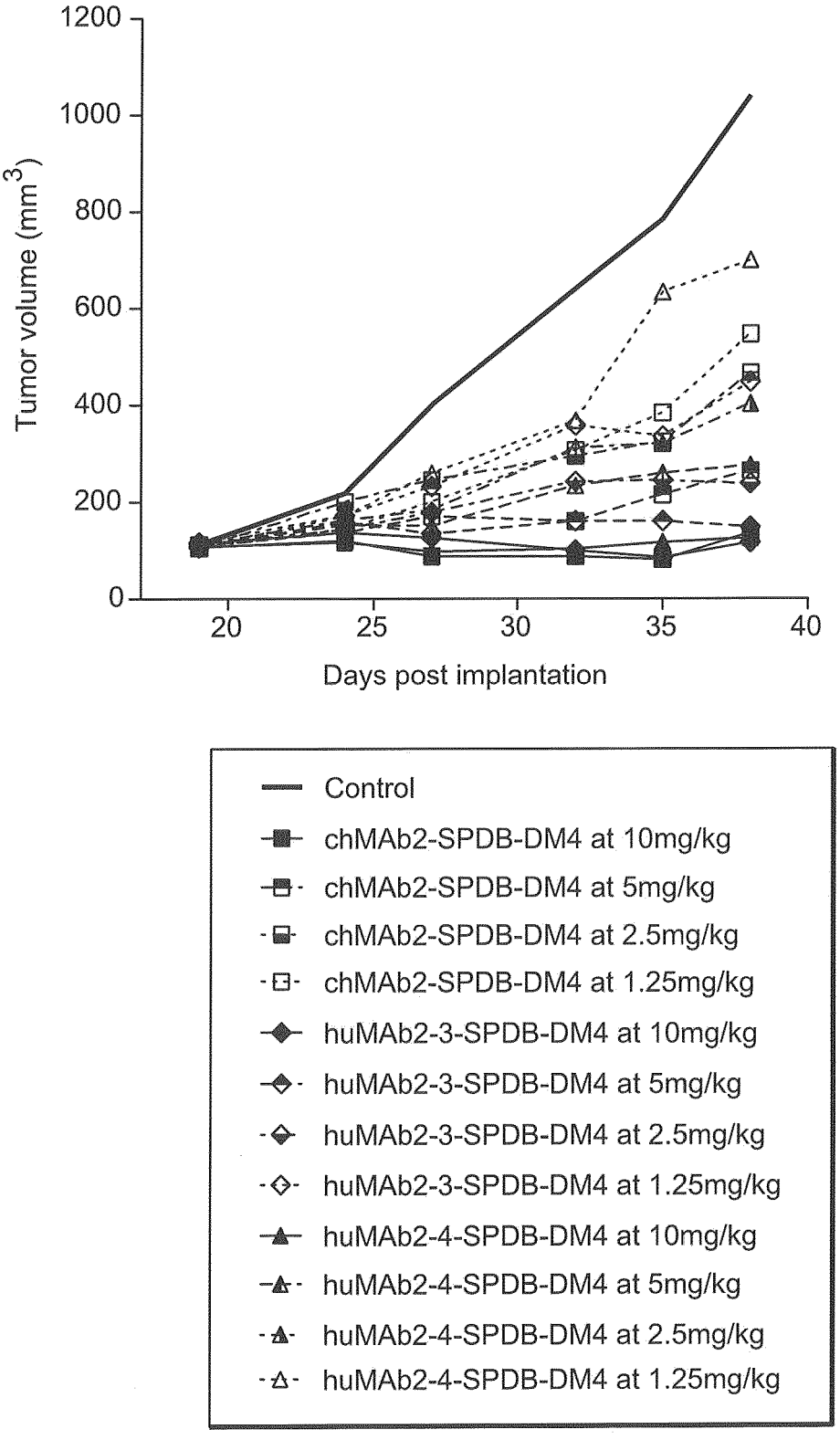

1200
1000
800
600
400
200
0
Tumor volume (mm3)
20
25
30
35
40
Days post implantation
Control
chMAb2-SPDB-DM4 at 10mg/kg
chMAb2-SPDB-DM4 at 5mg/kg
chMAb2-SPDB-DM4 at 2.5mg/kg
chMAb2-SPDB-DM4 at 1.25mg/kg
huMAb2-3-SPDB-DM4 at 10mg/kg
huMAb2-3-SPDB-DM4 at 5mg/kg
huMAb2-3-SPDB-DM4 at 2.5mg/kg
huMAb2-3-SPDB-DM4 at 1.25mg/kg
huMAb2-4-SPDB-DM4 at 10mg/kg
huMAb2-4-SPDB-DM4 at 5mg/kg
huMAb2-4-SPDB-DM4 at 2.5mg/kg
huMAb2-4-SPDB-DM4 at 1.25mg/kg

FIG.5

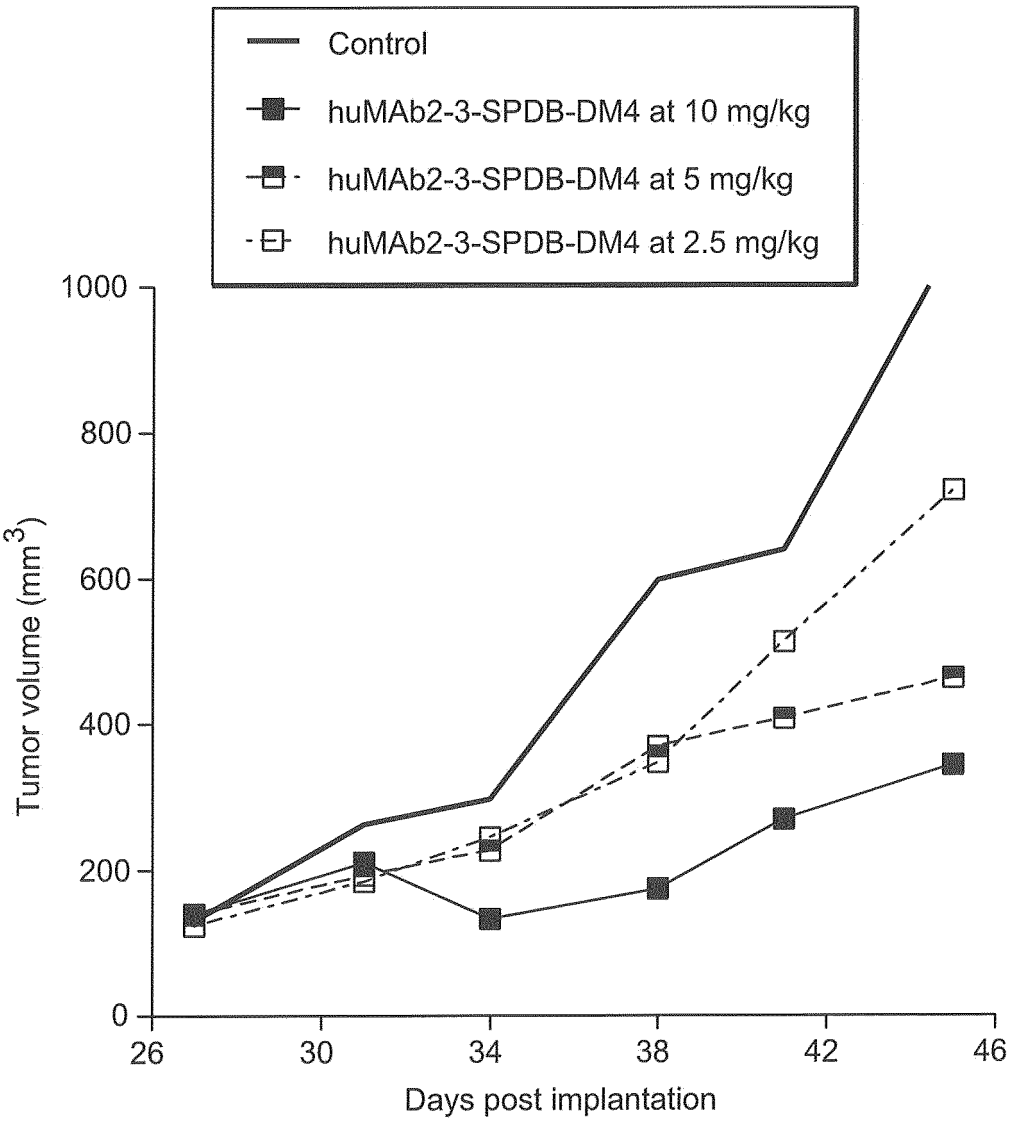

Control
huMAb2-3-SPDB-DM4 at 10 mg/kg
huMAb2-3-SPDB-DM4 at 5 mg/kg
huMAb2-3-SPDB-DM4 at 2.5 mg/kg
Tumor volume (mm3)
1000
800
600
400
200
0
26
30
34
38
42
46
Days post implantation

FIG.6

```
MAb3 VH   (1)  EVKLVESGGGLVKPGGSLTLPCAASGFTFSRYAMSWVRQTPEKRLEWVASISSGG-DTYY
MAb1 VH   (1)  EVMLVESGGGLVKPGGSLKLSCAASGFTFSSYAMSWVRQTPEKRLEWVATISSGGSYIYY
MAb4 VH   (1)  EVQLVESGGGLVKPGGSLKLSCAASGFTFSSYDMSWVRQTPEKRLEWVAFISSYGGRTYY
MAb5 VH   (1)  ELQLVESGGVLVKPGGSLKLSCAASGFAFSSYDMSWVRQTPEKRLEWVTYINSGGGITYY
MAb2 VH   (1)  EVQLQESGGVLVKPGGSLKLSCAASGFVFSSYDMSWVRQTPEKRLEWVAYISSGGGITYF

MAb3 VH   (60) PDSVKGRFTVSRDNARNILFLQMSSLRSEDTGMYYCARVNYYDSSFLDWWGQGTTLTVSS
MAb1 VH   (61) LDSVKGRFTISRDNAKNTLYLQMSSLRSEDTAMYYCARPAYYGNPAMDYWGQGTSVTVSS
MAb4 VH   (61) ADTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMFYCAAHYFGTSGPFAYWGQGTLVTVSE
MAb5 VH   (61) PDTVKGRFTISRDNARNTLYLQMSSLKSEDTAIYYCTAHYFGSSGPFAYWGQGTLVTVSA
MAb2 VH   (61) PDTVQGRFTVSRDNAKNTLYLQMNSLKSEDTAIYYCAAHYFGSSGPFAYWGQGTLVTVSA

MAb3 VH   (1)  DIVMTQSQRFMSTLEGDRVSVTCKASQNVGTNVAWYQQKPGQSPKALIYSASYRYSGVPD
MAb1 VH   (1)  DILMTQSQKFMSTSVGDRVSVTCKASQNVGTNVAWYQQKPGQSPKPLIYSASYRYSGVPD
MAb4 VH   (1)  DIQMTQSPASLSASVGETVTITCRASENIYSYFAWYQQKQGKSPQLLVYNAKILAEGVPS
MAb5 VH   (1)  DIQMTQSPASLSASVGETVTITCRASENIYSYLAWYQQKQGKSPQLLVYNAKTLTEGVPS
MAb2 VH   (1)  DIQMTQSPASLSASVGETVTITCRASENIFSYLAWYQQKQGKSPQLLVYNTKTLAEGVPS

MAb3 VH   (61) RFTGSGSGTDFTLTISNVQSEDLAEYFCQQYNNYPLYTFGGGTKLEIK
MAb1 VH   (61) RFTGSGSGTDFTLTISNVQSEDLAEYFCQQYNSYPLYTFGGGTKLEIK
MAb4 VH   (61) RFSGSGSGTQFSLKINSLQPEDFGTYYCQHHYGIP-FTFGSGTKLELK
MAb5 VH   (61) RFSGSGSGTQFSLKINSLQPEDFGSYYCQHHYGTP-FTFGSGTKLEIK
MAb2 VH   (61) RFSGSGSGTQFSLKINSLQPEDFGSYYCQHHYGTP-FTFGSGTKLEIK
```

FIG.7

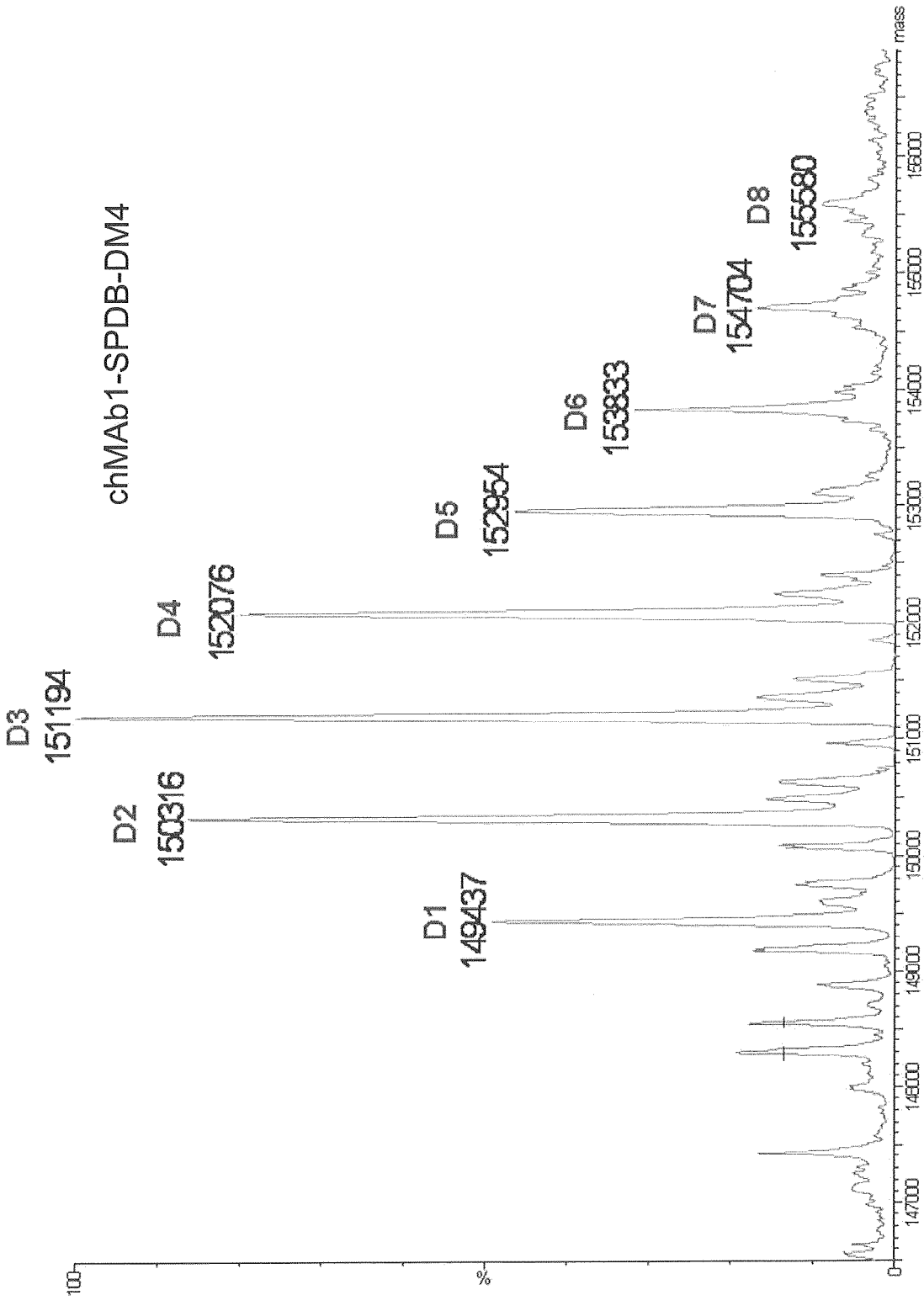

chMAb1-SPDB-DM4
D1
149437
D2
150316
D3
151194
D4
152076
D5
152954
D6
153833
D7
154704
D8
155580
100
%
0
147000
148000
149000
150000
151000
152000
153000
154000
155000
156000
mass

FIG.8

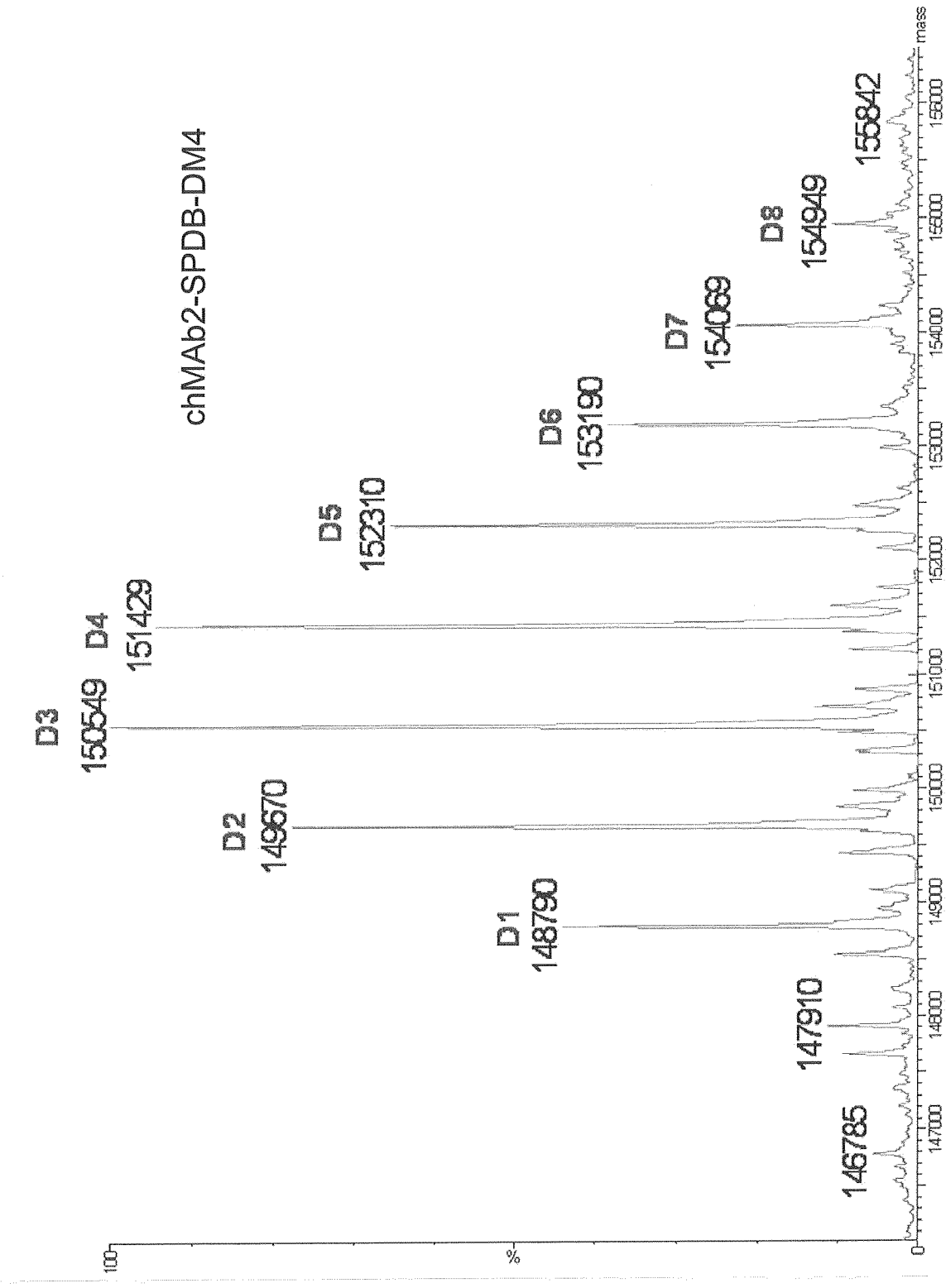

chMAb2-SPDB-DM4
D1
148790
D2
149670
D3
150549
D4
151429
D5
152310
D6
153190
D7
154069
D8
154949
146785
147910
155842
100
%
0
mass
147000
148000
149000
150000
151000
152000
153000
154000
155000
156000

FIG.9

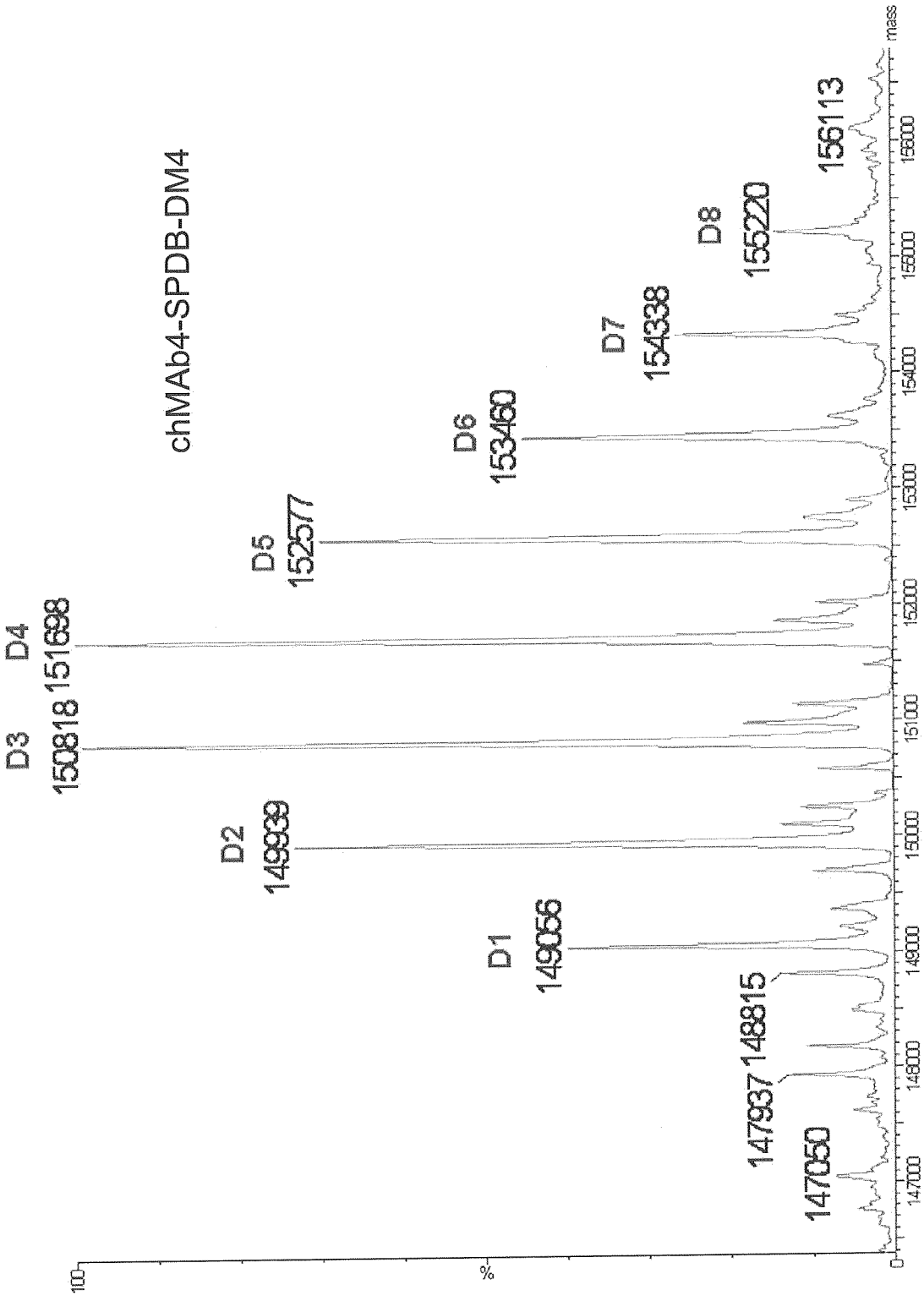

chMAb4-SPDB-DM4
D1
149056
D2
149939
D3
150818
D4
151698
D5
152577
D6
153460
D7
154338
D8
155220
156113
147937
148815
147050
100
%
0
mass
147000
148000
149000
150000
151000
152000
153000
154000
155000
156000

FIG.10

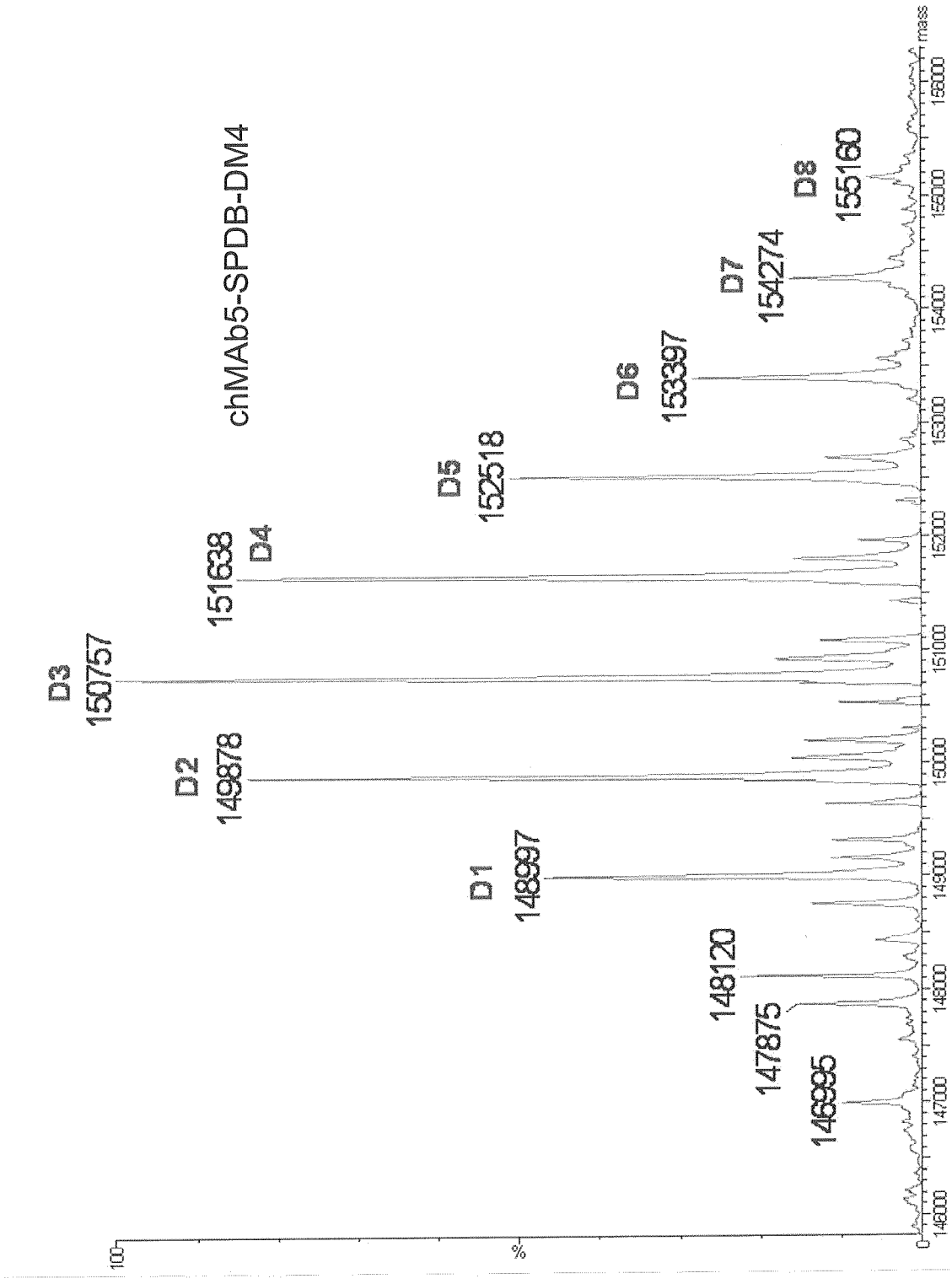

chMAb5-SPDB-DM4
D1
148997
D2
149878
D3
150757
151638
D4
D5
152518
D6
153397
D7
154274
D8
155160
148120
147875
146995
100
%
0
146000
147000
148000
149000
150000
151000
152000
153000
154000
155000
156000
mass

FIG.11

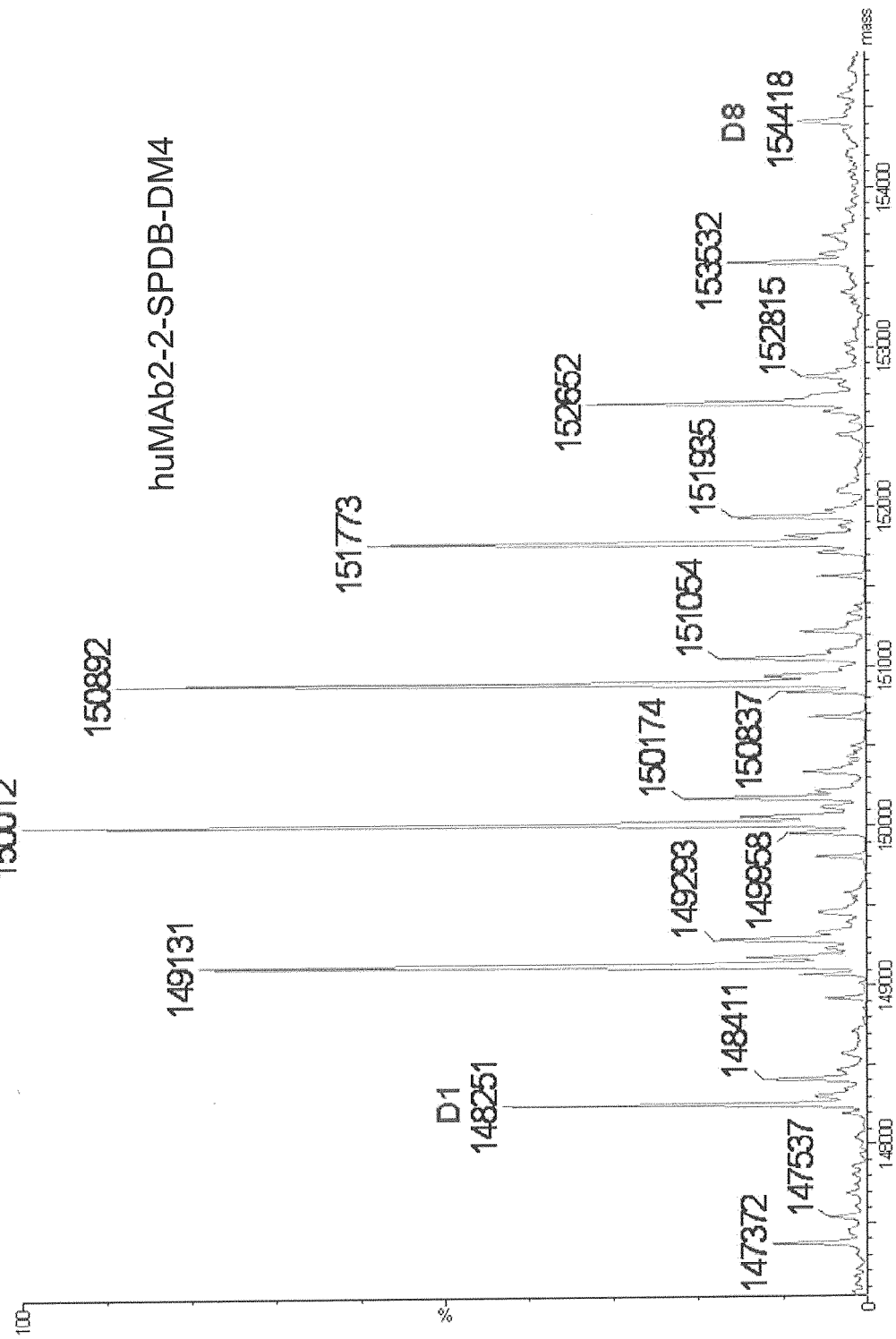

huMAb2-2-SPDB-DM4
100
%
0
147372
147537
D1
148251
148411
149131
149293
149358
150012
150174
150837
150892
151054
151773
151935
152652
152815
153532
D8
154418
mass
148000
149000
150000
151000
152000
153000
154000

FIG.12

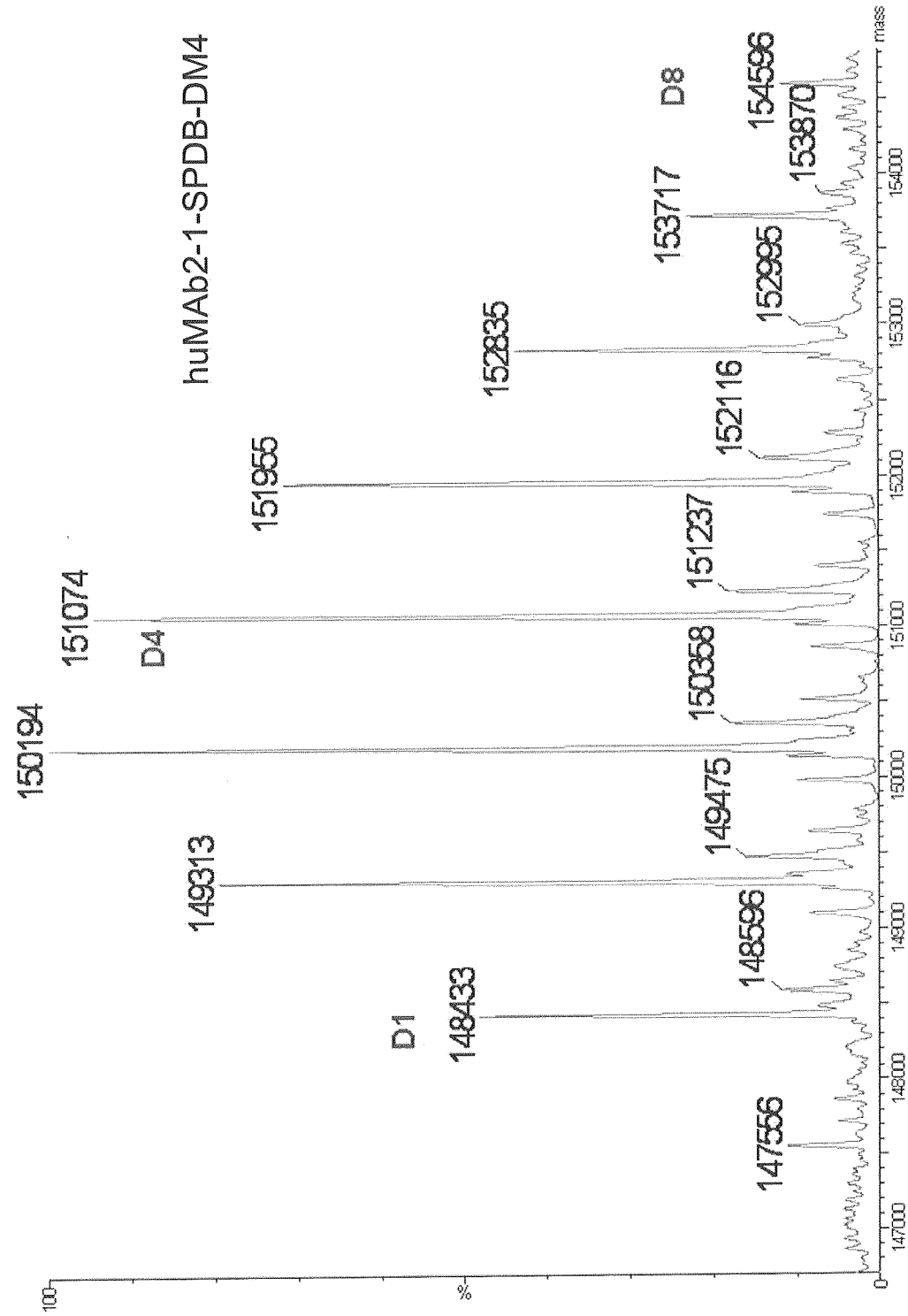

huMAb2-1-SPDB-DM4
D1
D4
D8
147556
148433
148596
149313
149475
150194
150358
151074
151237
151955
152116
152835
152985
153717
153870
154596
100
%
0
147000
148000
149000
150000
151000
152000
153000
154000
mass

FIG.13

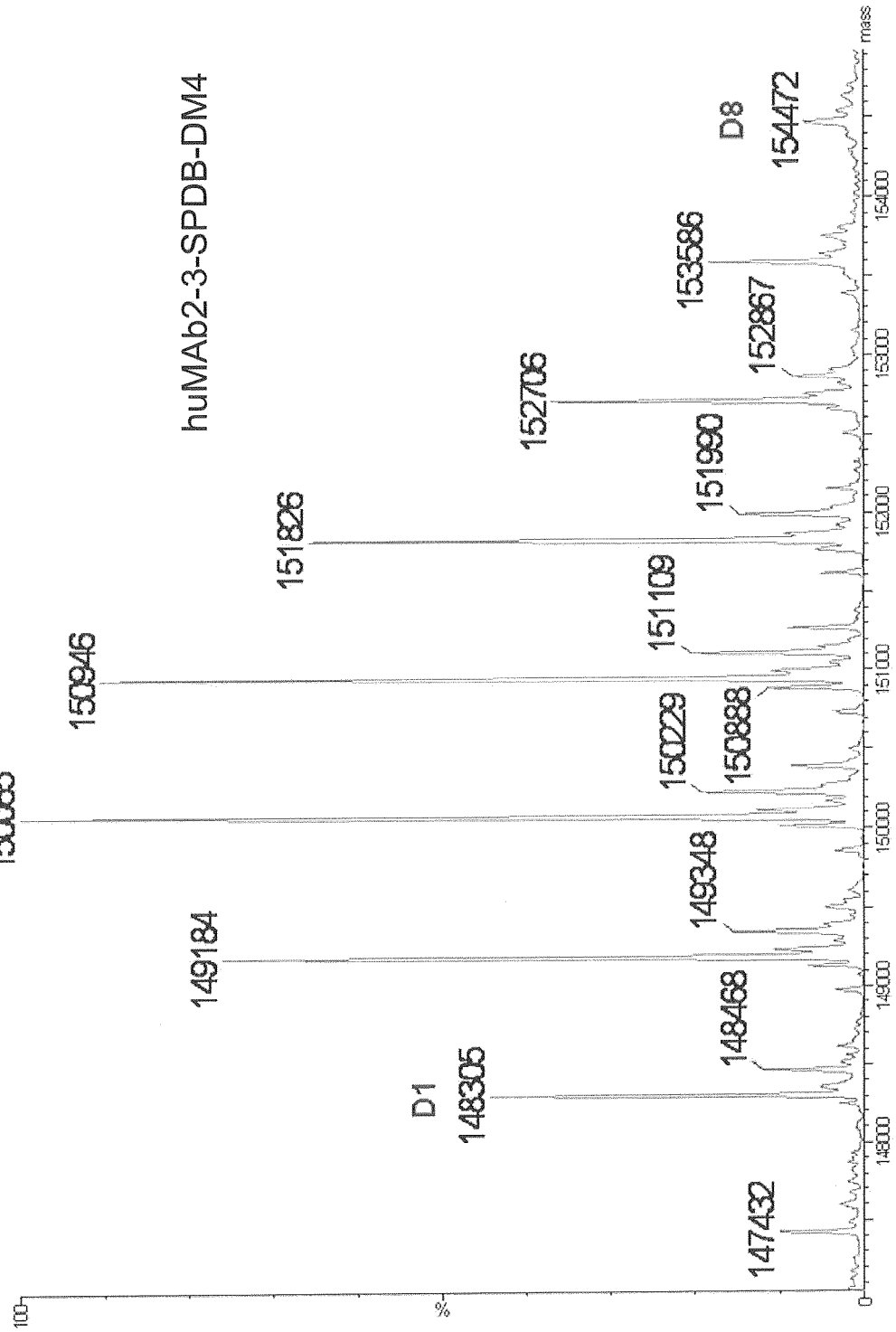

huMAb2-3-SPDB-DM4
100
%
0
147432
148305
D1
148468
149184
149348
150065
150229
150838
150946
151109
151826
151990
152706
152867
153586
154472
D8
mass
148000
149000
150000
151000
152000
153000
154000

FIG.14

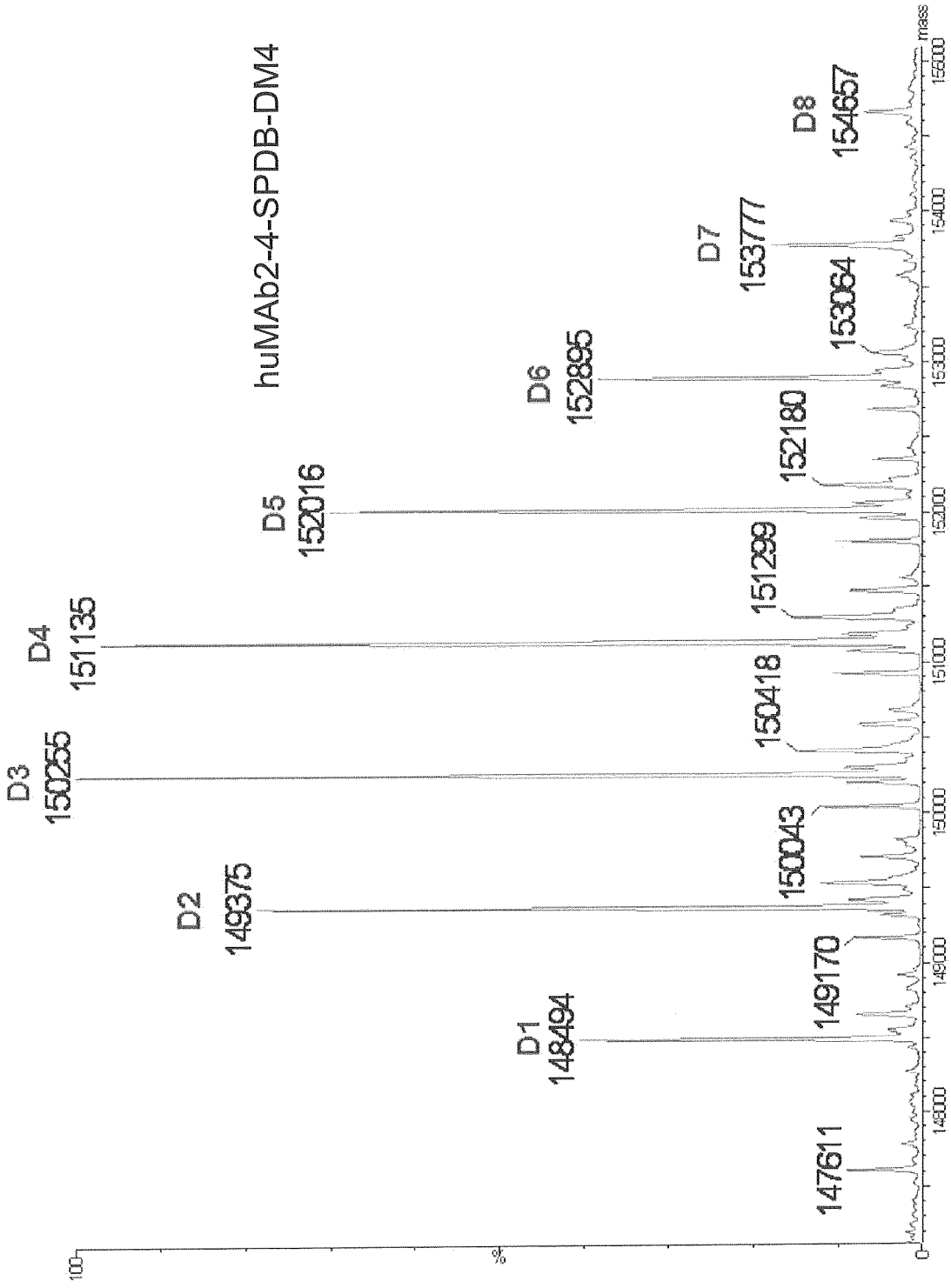

huMAb2-4-SPDB-DM4
D1
148494
D2
149375
D3
150255
D4
151135
D5
152016
D6
152895
D7
153777
D8
154657
147611
149170
150043
150418
151299
152180
153064
100
%
0
mass
148000
149000
150000
151000
152000
153000
154000
155000

FIG.15

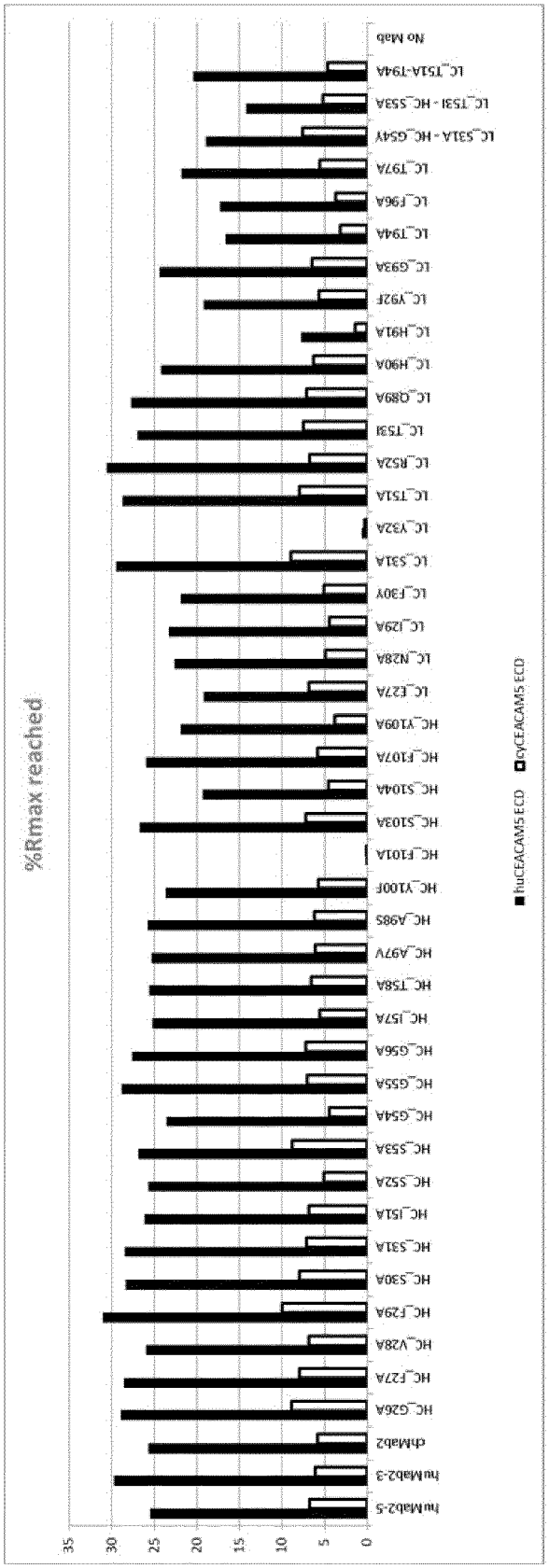

%Rmax reached
huCEACAM5 ECD
cyCEACAM5 ECD
No Mab
LC_T51A-T94A
LC_T51I - HC_S53A
LC_S31A - HC_G54Y
LC_T97A
LC_F96A
LC_T94A
LC_G93A
LC_Y92F
LC_H91A
LC_H90A
LC_Q89A
LC_T53I
LC_R52A
LC_T51A
LC_Y32A
LC_S31A
LC_F30Y
LC_I29A
LC_N28A
LC_E27A
HC_Y109A
HC_F107A
HC_S104A
HC_S103A
HC_F101A
HC_Y100F
HC_A98S
HC_A97V
HC_T58A
HC_I57A
HC_G56A
HC_G55A
HC_G54A
HC_S53A
HC_S52A
HC_I51A
HC_S31A
HC_S30A
HC_F29A
HC_V28A
HC_F27A
HC_G26A
chMab2
huMab2-3
huMab2-5
35
30
25
20
15
10
5
0

FIG.16

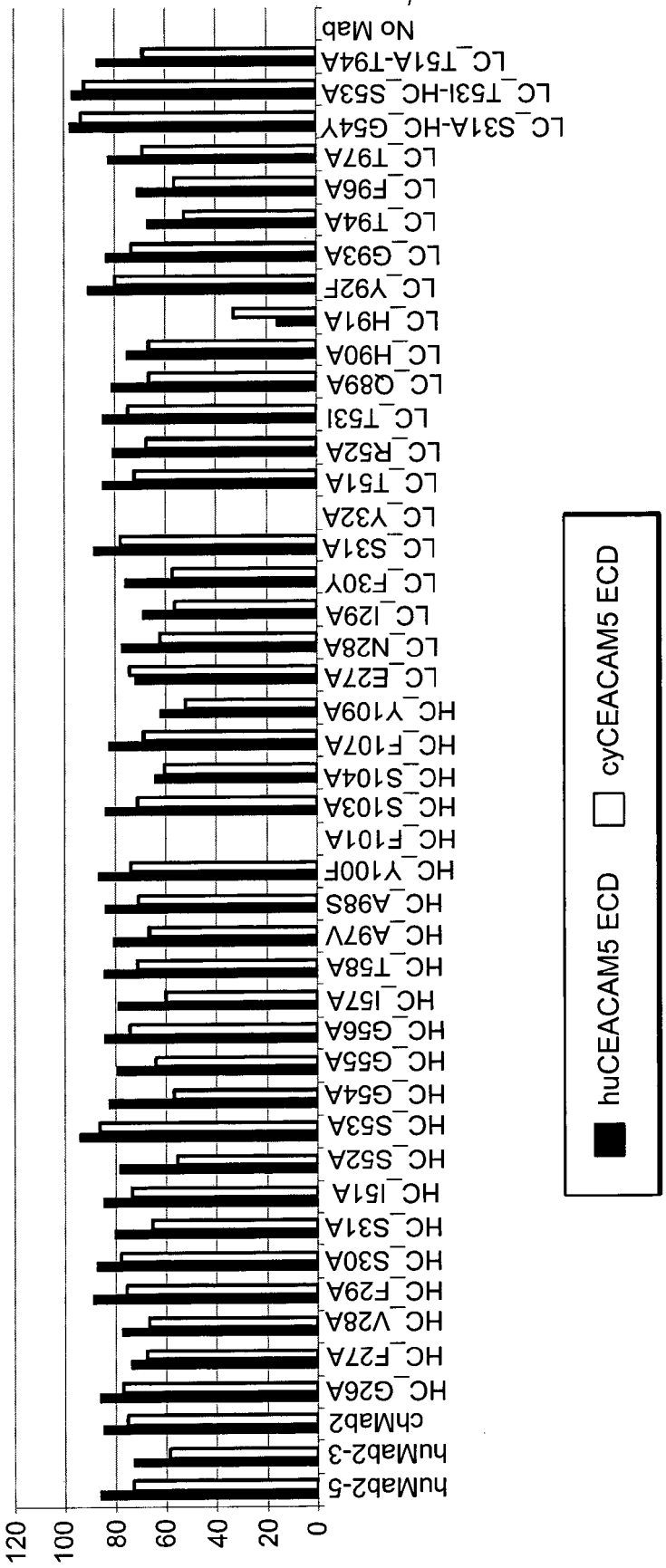

% Remaining signal after 50 seconds
120
100
80
60
40
20
0
huMab2-5
huMab2-3
chMab2
HC_G26A
HC_F27A
HC_V28A
HC_F29A
HC_S30A
HC_S31A
HC_I51A
HC_S52A
HC_S53A
HC_G54A
HC_G55A
HC_G56A
HC_I57A
HC_T58A
HC_A97V
HC_A98S
HC_Y100F
HC_F101A
HC_S103A
HC_S104A
HC_F107A
HC_Y109A
LC_E27A
LC_N28A
LC_I29A
LC_F30Y
LC_S31A
LC_Y32A
LC_T51A
LC_R52A
LC_T531
LC_Q89A
LC_H90A
LC_H91A
LC_Y92F
LC_G93A
LC_T94A
LC_F96A
LC_T97A
LC_S31A-HC_G54Y
LC_T531-HC_S53A
LC_T51A-T94A
No Mab
huCEACAM5 ECD
cyCEACAM5 ECD

FIG.17

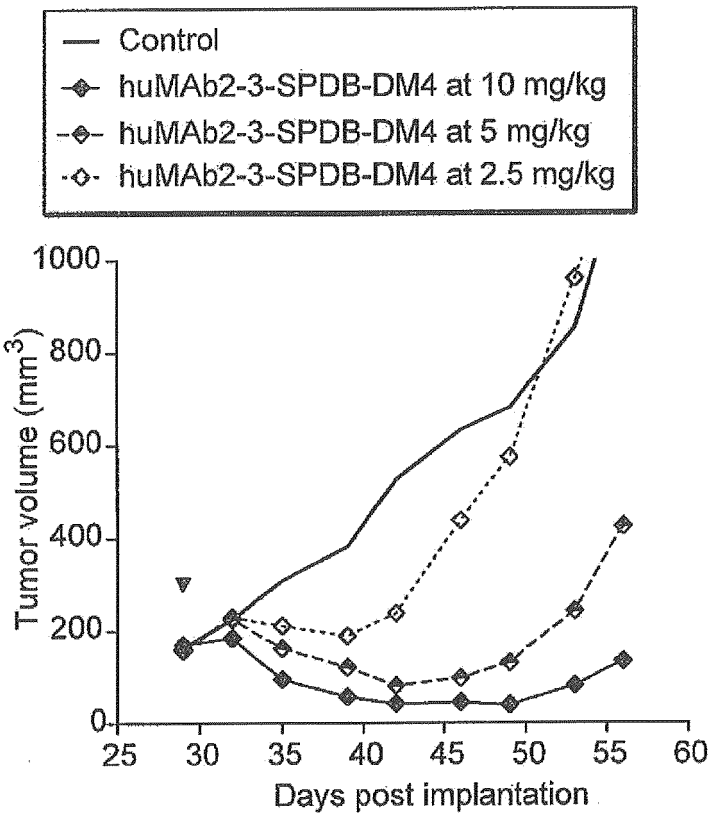

Control
huMAb2-3-SPDB-DM4 at 10 mg/kg
huMAb2-3-SPDB-DM4 at 5 mg/kg
huMAb2-3-SPDB-DM4 at 2.5 mg/kg
Tumor volume (mm3)
1000
800
600
400
200
0
25
30
35
40
45
50
55
60
Days post implantation

FIG.18

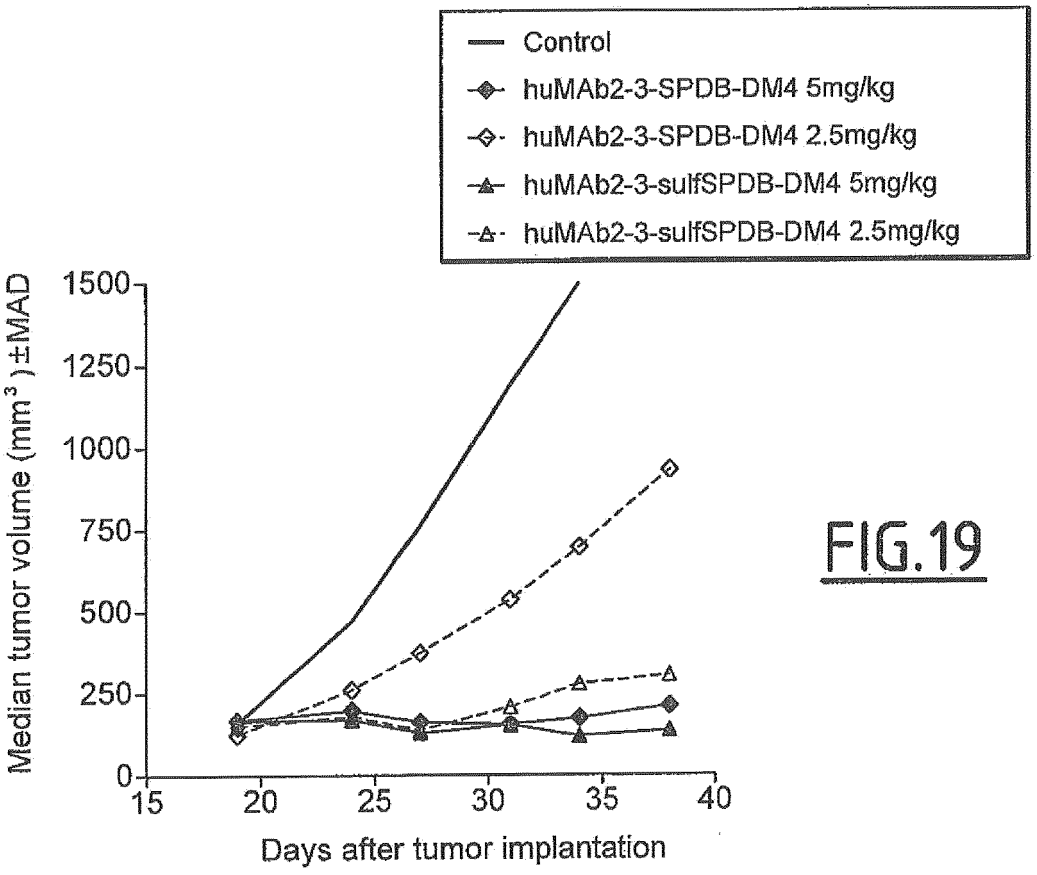

Control
huMAb2-3-SPDB-DM4 5mg/kg
huMAb2-3-SPDB-DM4 2.5mg/kg
huMAb2-3-sulfSPDB-DM4 5mg/kg
huMAb2-3-sulfSPDB-DM4 2.5mg/kg
Median tumor volume (mm3) ±MAD
1500
1250
1000
750
500
250
0
15
20
25
30
35
40
Days after tumor implantation

FIG.19

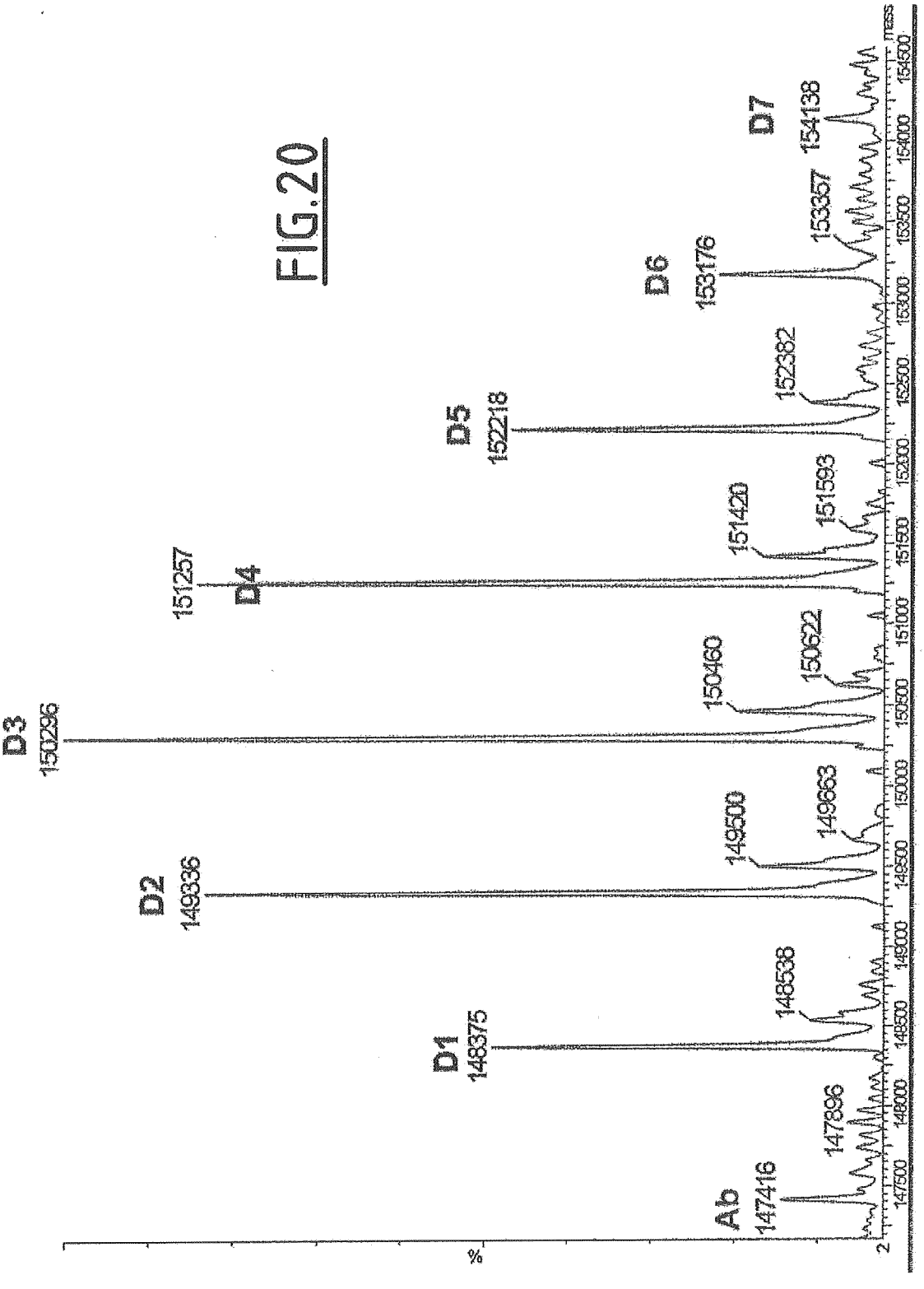

Ab
147416
147896
D1
148375
148538
D2
149336
149500
149663
D3
150296
150460
150622
D4
151257
151420
151593
D5
152218
152382
D6
153176
D7
153357
154138
%
2
mass

FIG.20

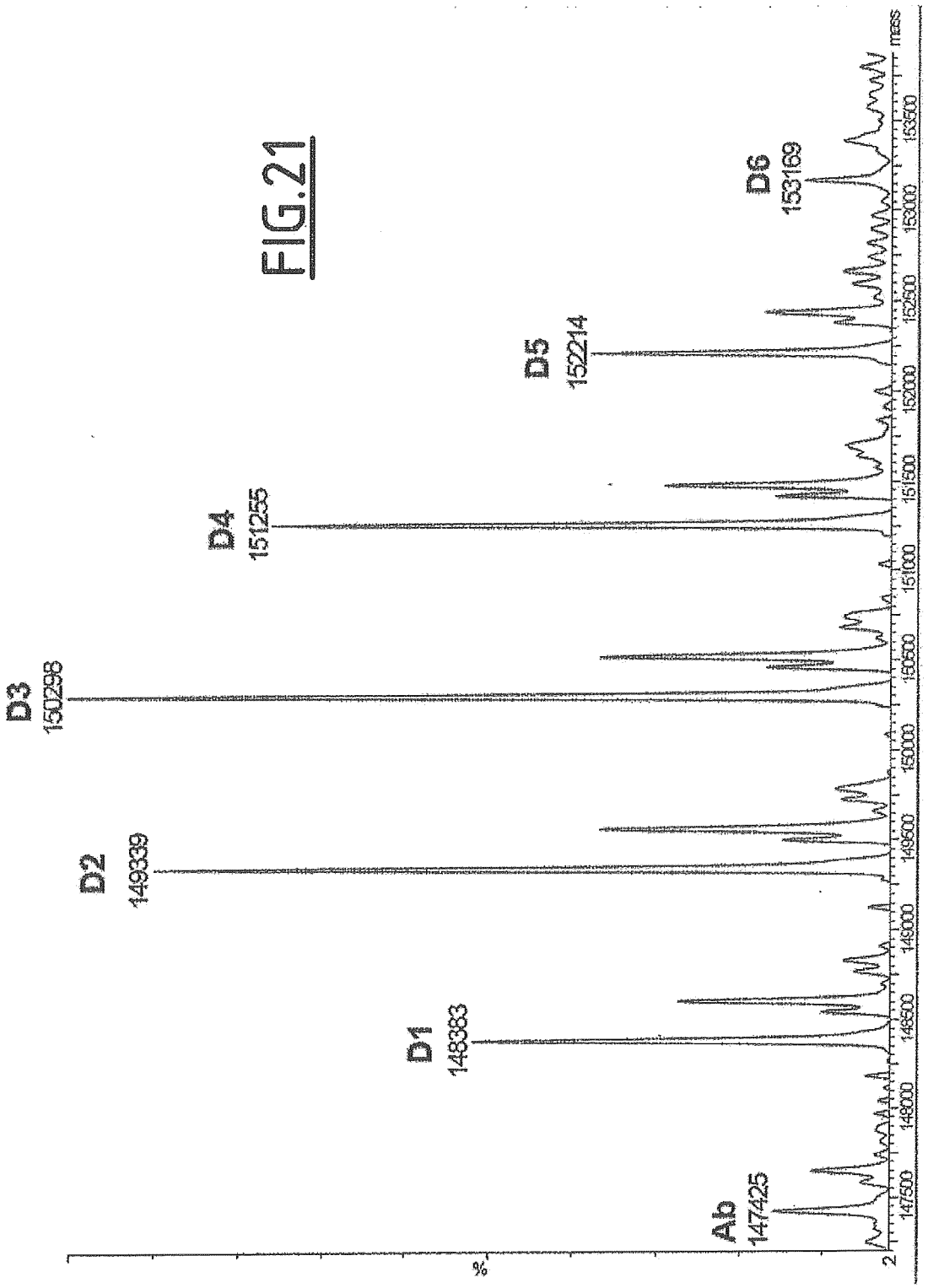

Ab
147425
D1
148383
D2
149339
D3
150298
D4
151255
D5
152214
D6
153169
%
mass

FIG.21

Heavy Chain variable domain alignment

```
Mab2              SEQ ID NO:33  (1) EVQLQESGGVLVKPGGSLKLSCAAS GFVFSSYDMSWVRQTPEKRLEWVAYISSGGGITYF (60)
Mab4              SEQ ID NO:37  (1) EVQLVESGGGLVKPGGSLKLSCAAS GFTFSSYDMSWVRQTPEKRLEWVAFISSYGGRTYY (60)
Mab5              SEQ ID NO:39  (1) ELQLVESGGVLVKPGGSLKLSCAAS GFAFSSYDMSWVRQTPEKRLEWVTYINSGGGITYY (60)
humanized VH1a    SEQ ID NO:5   (1) EVQLQESGPGLVKPGGSLSLSCAAS GFVFSSYDMSWVRQTPERGLEWVAYISSGGGITYA (60)
humanized VH1     SEQ ID NO:51  (1) EVQLQESGPGLVKPGGSLSLSCAAS GFVFSSYDMSWVRQTPERRLEWVAYISSGGGITYF (60)
humanized VHg2    SEQ ID NO:74  (1) EVQLVESGGGLVQPGGSLRLSCAAS GFVFSSYDMSWVRQAPGKGLEWVSYISSGGGLTYY (60)

Mab2              SEQ ID NO:33 (61) PDTVQGRFTVSRDNAKNTLYLQMNSLKSEDTAIYYC AAHYFGSSGPFAYWGQGTLVTVSA (120)
Mab4              SEQ ID NO:37 (61) ADTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMFYC AAHYFGTSGPFAYWGQGTLVTVSA (120)
Mab5              SEQ ID NO:39 (61) PDTVKGRFTISRDNARNTLYLQMSSLKSEDTAIYYC TAHYFGSSGPFAYWGQGTLVTVSA (120)
humanized VH1a    SEQ ID NO:5  (61) PSTVKGRFTVSRDNAKNTLYLQMNSLTSEDTAVYYC AAHYFGSSGPFAYWGQGTLVTVSS (120)
humanized VH1 SEQ ID NO:51     (61) PSTVKGRFTVSRDNAKNTLYLQMNSLTSEDTAIYYC AAHYFGSSGPFAYWGQGTLVTVSA (120)
humanized VHg2    SEQ ID NO:74 (61) ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYC AAHYFGSSGPFAYWGQGTLVTVSS (120)
```

In ▨ : CDR positions allowing any substitution
In ▨ : CDR positions allowing only conservative substitution
In □ : CDR positions not allowing any substitution

FIG.22

Light Chain variable domain alignment

```
Mab2             SEQ ID NO:34  (1)DIQMTQSPASLSASVGETVTITCRAS ENIFSY LAWYQQKQGKSPQLLVY NTK TLAEGVPS (60)
Mab4             SEQ ID NO:38  (1)DIQMTQSPASLSASVGETVTITCRAS ENIYSY FAWYQQKQGKSPQLLVY NAK ILAEGVPS (60)
Mab5             SEQ ID NO:40  (1)DIQMTQSPASLSASVGETVTITCRAS ENIYSY LAWYQQKQGKSPQLLVY NAK TLTEGVPS (60)
humanized VL1    SEQ ID NO:17  (1)DIQMTQSPASLSASVGDTVTITCRAS ENIFSY LAWYQQKPGKSPKLLVY NTK TLAEGVPS (60)
humanized VL1a   SEQ ID NO:23  (1)DIQMTQSPASLSASVGDRVTITCRAS ENIFSY LAWYQQKPGKSPKLLVY NTK TLAEGVPS (60)
humanized VL1c   SEQ ID NO:29  (1)DIQMTQSPASLSASVGDRVTITCRAS ENIFSY LAWYQQKPGKSPKLLVY NTR TLAEGVPS (60)
humanized VL1d   SEQ ID NO:55  (1)DIQMTQSPASLSASVGDTVTITCRAS ENIFSY LAWYQQKPGKSPKLLVY NTR TLAEGVPS (60)
humanized VLg5   SEQ ID NO:75  (1)DIQMTQSPSSLSASVGDRVTITCRAS ENIFSY LAWYQQKPGKAPKLLIY NTK TLQSGVPS (60)

Mab2             SEQ ID NO:34  (61)RFSGSGSGTQFSLKINSLQPEDFGSYYC QHHYGTPFT FGSGTKLEIK (107)
Mab4             SEQ ID NO:38  (61)RFSGSGSGTQFSLKINSLQPEDFGTYYC QHHYGIPFT FGSGTKLELK (107)
Mab5             SEQ ID NO:40  (61)RFSGSGSGTQFSLKINSLQPEDFGSYYC QHHYGTPFT FGSGTKLEIK (107)
humanized VL1    SEQ ID NO:17  (61)RFSGSGSGTQFSLTISSLQPEDFGSYYC QHHYGTPFT FGSGTKLEIK (107)
humanized VL1a   SEQ ID NO:23  (61)RFSGSGSGTDFSLTISSLQPEDFATYYC QHHYGTPFT FGSGTKLEIK (107)
humanized VL1c   SEQ ID NO:29  (61)RFSGSGSGTDFSLTISSLQPEDFATYYC QHHYGTPFT FGSGTKLEIK (107)
humanized VL1d   SEQ ID NO:55  (61)RFSGSGSGTQFSLTISSLQPEDFGSYYC QHHYGTPFT FGSGTKLEIK (107)
humanized VLg5   SEQ ID NO:75  (61)RFSGSGSGTDFTLTISSLQPEDFATYYC QHHYGTPFT FGQGTKLEIK (107)
```

In ▨ : CDR positions allowing any substitution
In ▧ : CDR positions allowing only conservative substitution
In □ : CDR positions not allowing any substitution

FIG.23