FIG. 1

Preprogastrin: M QRLCVYVLIF ALALAAFSEA SWKPRSQQPD APLGTGANRD LELPWLEQQG
-21 -11 -1 +1 11 21

SEQ ID NO:100

PASHHRRQLG PQGPPHLVAD PSKKQGPWLE EEEEAYGWMD FGRRSAEDEN
31 41 51 61 71

Progastrin: SWKPRSQQPD APLGTGANRD LELPWLEQQG
+1 11 21

SEQ ID NO:101

PASHHRRQLG PQGPPHLVAD PSKKQGPWLE EEEEAYGWMD FGRRSAEDEN
31 41 51 61 71

G34: QLG PQGPPHLVAD PSKKQGPWLE EEEEAYGWMD F-NH_2
SEQ ID NO:102 41 51 61 71

G34-Gly: QLG PQGPPHLVAD PSKKQGPWLE EEEEAYGWMD FG
SEQ ID NO:103 41 51 61 71

G17: QGPWLE EEEEAYGWMD F-NH_2
SEQ ID NO:104 61 71

G17-Gly: QGPWLE EEEEAYGWMD FG
SEQ ID NO:105 61 71

CTFP: SAEDEN
SEQ ID NO:106 75

FIG. 2

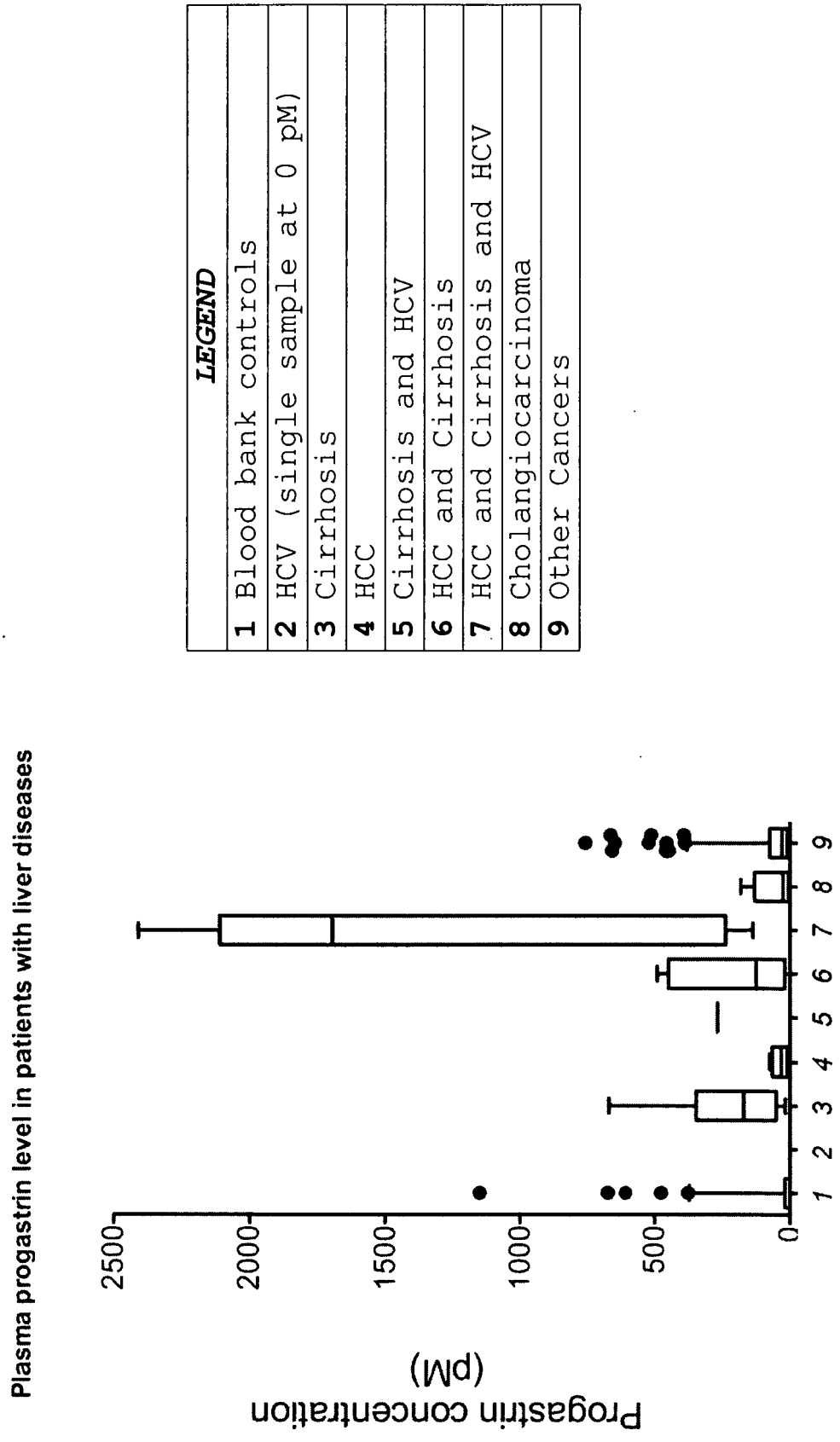

Plasma progastrin level in patients with liver diseases
Progastrin concentration (pM)
2500
2000
1500
1000
500
0
1 2 3 4 5 6 7 8 9
LEGEND
1 Blood bank controls
2 HCV (single sample at 0 pM)
3 Cirrhosis
4 HCC
5 Cirrhosis and HCV
6 HCC and Cirrhosis
7 HCC and Cirrhosis and HCV
8 Cholangiocarcinoma
9 Other Cancers

FIG. 3A

mV_H MAb3

```
gag gtt cag ctc cag cag tct ggg act gtg ctg gca agg cct ggg gct   48
Glu Val Gln Leu Gln Gln Ser Gly Thr Val Leu Ala Arg Pro Gly Ala
1               5                   10                  15

tcc gtg aag atg tcc tgc aag gct tct ggc tac atc ttt acc agc tac   96
Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Ser Tyr
            20                  25                  30

tgg gta cac tgg gtt aaa cag agg cct gga cag ggt cta gaa tgg att  144
Trp Val His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

ggt ggt ttt tat cct gga aat agt gat tct agg tac aac cag aaa ttc  192
Gly Gly Phe Tyr Pro Gly Asn Ser Asp Ser Arg Tyr Asn Gln Lys Phe
    50                  55                  60

aag ggc aag gcc aca ctg act gca gtc aca tcc gcc agt act gcc tac  240
Lys Gly Lys Ala Thr Leu Thr Ala Val Thr Ser Ala Ser Thr Ala Tyr
65                  70                  75                  80

atg gac ctc agc agc ctg aca aat gag gac tct gcg gtc tat ttc tgt  288
Met Asp Leu Ser Ser Leu Thr Asn Glu Asp Ser Ala Val Tyr Phe Cys
                85                  90                  95

aca aga aga gat agt ccc cag tac tgg ggc caa ggc acc act ctc aca  336
Thr Arg Arg Asp Ser Pro Gln Tyr Trp Gly Gln Gly Thr Thr Leu Thr
            100                 105                 110

gtc tcc tca                                                     345
Val Ser Ser
        115
```

FIG. 3B

mV_L MAb3

```
gat gtt ttg atg acc caa act cca ctc tcc ctg cct gtc agt ctt gga   48
Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1               5                  10                  15

gat caa gcc tcc atc tct tgc aga tct agt cag agc att gta cat agt   96
Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Ile Val His Ser
            20                  25                  30

aat gga aac acc tat tta gaa tgg tac ctg cag aaa cca ggc cag tct  144
Asn Gly Asn Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45

cca aag ctc ctg atc tac aaa gtt tcc aac cga ttt tct ggg gtc cca  192
Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60

gac agg ttc agt ggc agt gga tca ggg aca gat ttc aca ctc aag atc  240
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

agc aga ctg gag gct gag gat ctg gga gtt tat tac tgc ttt caa ggt  288
Ser Arg Leu Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Gly
                85                  90                  95

tca cat gtt ccg ttc acg ttc gga ggg ggg acc aag ctg gaa ata aaa  336
Ser His Val Pro Phe Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

FIG. 3C

mV_H MAb4

```
cag gtt cag ttg cag cag tct gga gct gag ctg atg aag cca ggg gcc   48
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Met Lys Pro Gly Ala
1               5                   10                  15

tca gtg aag ata tcc tgc aag gct act ggc tac aca ttc agt agc tcc   96
Ser Val Lys Ile Ser Cys Lys Ala Thr Gly Tyr Thr Phe Ser Ser Ser
            20                  25                  30

tgg ata gag tgg tta aaa cag agg cct gga cat ggc ctt gag tgg att  144
Trp Ile Glu Trp Leu Lys Gln Arg Pro Gly His Gly Leu Glu Trp Ile
        35                  40                  45

gga gag ttt tta cct gga agt ggt agt aca gac tac aat gag aag ttc  192
Gly Glu Phe Leu Pro Gly Ser Gly Ser Thr Asp Tyr Asn Glu Lys Phe
    50                  55                  60

aag ggc aag gcc aca ttc act gca gac aca tcc tcc gac aca gcc tac  240
Lys Gly Lys Ala Thr Phe Thr Ala Asp Thr Ser Ser Asp Thr Ala Tyr
65                  70                  75                  80

atg cta ctc agc agc ctg aca tct gag gac tct gcc gtc tat tac tgt  288
Met Leu Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85                  90                  95

gca act gat ggt aat tat gac tgg ttt gct tac tgg ggc caa ggg act  336
Ala Thr Asp Gly Asn Tyr Asp Trp Phe Ala Tyr Trp Gly Gln Gly Thr
            100                 105                 110

ctg gtc act gtc tct gca                                         354
Leu Val Thr Val Ser Ala
        115
```

FIG. 3D

mV_L MAb4

```
gat ctt gtg atg acc caa act cca ctc tcc ctg cct gtc agt ctt gga   48
Asp Leu Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1               5                  10                  15

gat caa gcc tcc atc tct tgc aga tct agt cag agc ctt gta cac agt   96
Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
            20                  25                  30

agt gga gtc acc tat tta cat tgg tac ctg cag aag cca ggc cag tct  144
Ser Gly Val Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45

cca aag ctc ctg atc tac aaa gtt tcc aac cga ttt tct ggg gtc cca  192
Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
    50                  55                  60

gac agg ttc agt ggc agt gga tca ggg aca gat ttc aca ctc aag atc  240
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

agc aga gtg gag gct gag gat ctg gga gtt tat ttc tgc tct caa agt  288
Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Ser Gln Ser
                85                  90                  95

aca cat gtt cct ccc acg ttc ggc tcg ggg aca aag ttg gaa ata aaa  336
Thr His Val Pro Pro Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

FIG. 3E

mV_H MAb8

```
gaa gtg cag ctg gtg gag tct ggg gga ggc tta gtg aag cct gga ggg   48
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                  10                  15

tcc ctg aaa ctc tcc tgt gca gcc tct gga ttc act ttc act acc tat   96
Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Thr Thr Tyr
            20                  25                  30

gcc atg tct tgg gtt cgc cag act ccg gag aag agg ctg gag tgg gtc  144
Ala Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu Glu Trp Val
        35                  40                  45

gca acc att agt agt ggt ggt act tac acc tac tat cca gac agt gtg  192
Ala Thr Ile Ser Ser Gly Gly Thr Tyr Thr Tyr Tyr Pro Asp Ser Val
    50                  55                  60

aag ggt cga ttc acc atc tcc aga gac aat gcc aag aac gcc cta tac  240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ala Leu Tyr
65                  70                  75                  80

ctg caa atg agc agt ctg agg tct gag gac acg gcc atg tat tac tgt  288
Leu Gln Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95

gca aca cag ggg aat tac tct ttg gac ttc tgg ggc caa ggc acc tct  336
Ala Thr Gln Gly Asn Tyr Ser Leu Asp Phe Trp Gly Gln Gly Thr Ser
            100                 105                 110

ctc aca gtc tcc tca                                             351
Leu Thr Val Ser Ser
        115
```

FIG. 3F

mV_L MAb8

```
gac att gtg atg acg cag gct gca tcc tct aat cca gtc act ctt gga   48
Asp Ile Val Met Thr Gln Ala Ala Ser Ser Asn Pro Val Thr Leu Gly
1               5                  10                  15

aca tcc gct tcc atc tcc tgc agg tct agt aag agt ctc cga cat act   96
Thr Ser Ala Ser Ile Ser Cys Arg Ser Ser Lys Ser Leu Arg His Thr
            20                  25                  30

aaa ggc atc act ttt ttg tat tgg tat ctg cag aag cca ggc cag tct  144
Lys Gly Ile Thr Phe Leu Tyr Trp Tyr Leu Gln Lys Pro Gly Gln Ser
        35                  40                  45

cct cag ctc ctg att tat cag atg tcc aac ctt gcc tca gga gtc cca  192
Pro Gln Leu Leu Ile Tyr Gln Met Ser Asn Leu Ala Ser Gly Val Pro
    50                  55                  60

gac agg ttc agt agc agt ggg tca gga act gat ttc aca ctg aga atc  240
Asp Arg Phe Ser Ser Ser Gly Ser Gly Thr Asp Phe Thr Leu Arg Ile
65                  70                  75                  80

agc aga gtg gag gct gag gat ttg ggt gtt tat tac tgt gct caa aat  288
Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Ala Gln Asn
                85                  90                  95

cta gaa ctt ccg ctc acg ttc ggt gct ggg acc aag ctg gag ctg aaa  336
Leu Glu Leu Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
            100                 105                 110
```

FIG. 3G

mV_H MAb13

```
gag gtg cag ctg gtg gag tct ggg gga ggc ttg gtg cag cct gga ggg   48
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                  10                  15

tcc ctg aaa ctc tcc tgt gca gcc tct gga ttc att ttc agt agc tat   96
Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Ile Phe Ser Ser Tyr
            20                  25                  30

ggc atg tct tgg gtt cgc cag tct cca gac agg agg ctg gag ttg gtc  144
Gly Met Ser Trp Val Arg Gln Ser Pro Asp Arg Arg Leu Glu Leu Val
        35                  40                  45

gca agt att aat act ttt ggt gat aga acc tat tat cca gac agt gtg  192
Ala Ser Ile Asn Thr Phe Gly Asp Arg Thr Tyr Tyr Pro Asp Ser Val
    50                  55                  60

aag ggc cga ttc acc atc tcc aga gac aat gcc aag aac acc ctg tac  240
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65                  70                  75                  80

ctg caa atg acc agt ctg aag tct gag gac aca gcc att tat tac tgt  288
Leu Gln Met Thr Ser Leu Lys Ser Glu Asp Thr Ala Ile Tyr Tyr Cys
                85                  90                  95

gca aga ggg acc gga acc tac tgg ggc caa ggc acc act ctc aca gtc  336
Ala Arg Gly Thr Gly Thr Tyr Trp Gly Gln Gly Thr Thr Leu Thr Val
            100                 105                 110

tcc tca                                                         342
Ser Ser
```

FIG. 3H

mV_L MAb13

```
gat gtt gtg ctg acc cag act cca ctc act ttg tcg gtt acc att gga   48
Asp Val Val Leu Thr Gln Thr Pro Leu Thr Leu Ser Val Thr Ile Gly
1               5                  10                  15

caa cca gcc tcc atc tcc tgc aag tca agt cag agc ctc tta gat agt   96
Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
            20                  25                  30

gat gga aag aca tat ttg aat tgg ttg tta cag agg cca ggc cag tct  144
Asp Gly Lys Thr Tyr Leu Asn Trp Leu Leu Gln Arg Pro Gly Gln Ser
        35                  40                  45

cca aag cgc cta atc tat ctg gtg tct aaa ctg gac tct gga gtc cct  192
Pro Lys Arg Leu Ile Tyr Leu Val Ser Lys Leu Asp Ser Gly Val Pro
    50                  55                  60

gac agg ttc act ggc agt gga tca ggg aca gat ttc aca ctg aaa atc  240
Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

agc aga gtg gag gct gag gat ttg gga gtt tat tat tgc tgg caa ggt  288
Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Trp Gln Gly
                85                  90                  95

aca cat ttt cct cag acg ttc ggt gga ggc acc aag ctg gaa atc aaa  336
Thr His Phe Pro Gln Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

FIG. 3I

mV_H MAb16

```
cag gtc caa ctg cag cag tct ggg gct gaa ctg gtg aag cct ggg gct   48
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala
1               5                   10                  15

tca gtg aag ttg tcc tgc aag gct tct ggc tac acc ttc acc agc tac   96
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

tat atg tac tgg gtg aag cag agg cct gga caa ggc ctt gag tgg att  144
Tyr Met Tyr Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

gga gag att aat cct agc aat ggt ggt act aac ttc aat gag aag ttc  192
Gly Glu Ile Asn Pro Ser Asn Gly Gly Thr Asn Phe Asn Glu Lys Phe
    50                  55                  60

aag agc aag gcc aca ctg act gta gac aaa tcc tcc agc aca gca tac  240
Lys Ser Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80

atg caa ctc agc agc ctg aca tct gag gac tct gcg gtc tat tac tgt  288
Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85                  90                  95

aca aga ggc ggt tac tac ccc ttt gac tac tgg ggc caa ggc acc act  336
Thr Arg Gly Gly Tyr Tyr Pro Phe Asp Tyr Trp Gly Gln Gly Thr Thr
            100                 105                 110

ctc aca gtc tcc tca                                             351
Leu Thr Val Ser Ser
        115
```

FIG. 3J

mV_L MAb16

```
gat gtt gtg atg acc cag act cca ctc act ttg tcg gtt acc att ggg   48
Asp Val Val Met Thr Gln Thr Pro Leu Thr Leu Ser Val Thr Ile Gly
1               5                  10                  15

cgc cca gcc tcc atc tct tgc aag tca agt cag agc ctc tta gac agt   96
Arg Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Leu Asp Ser
            20                  25                  30

gat gga aag aca tat ttg tat tgg ttg tta cag agg cca ggc cag tct  144
Asp Gly Lys Thr Tyr Leu Tyr Trp Leu Leu Gln Arg Pro Gly Gln Ser
        35                  40                  45

cca aag cgc cta atc tat ctg gtg tct gag ctg gac tct gga gtc cct  192
Pro Lys Arg Leu Ile Tyr Leu Val Ser Glu Leu Asp Ser Gly Val Pro
    50                  55                  60

gac agg atc act ggc agt ggg tcg ggg aca gat ttc aca ctg aag atc  240
Asp Arg Ile Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65                  70                  75                  80

agc aga gtg gag gct gag gat ttg gga gtt tat tat tgc tgg caa gga  288
Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Trp Gln Gly
                85                  90                  95

aca cat tct ccg tac acg ttc gga ggg ggg acc aag ctg gaa ata aaa  336
Thr His Ser Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100                 105                 110
```

FIG. 3K

mV_H MAb19

```
gat gtg cag ctt cag gag tcg gga cct ggc ctg gtg aaa cct tct cag   48
Asp Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                  10                  15

tct ctg tcc ctc aca tgc act gtc act ggc tac tca atc acc agt gat   96
Ser Leu Ser Leu Thr Cys Thr Val Thr Gly Tyr Ser Ile Thr Ser Asp
            20                  25                  30

tat gcc tgg aat tgg atc cgg cag ttt cca gga aac aaa ctg gag tgg  144
Tyr Ala Trp Asn Trp Ile Arg Gln Phe Pro Gly Asn Lys Leu Glu Trp
        35                  40                  45

atg ggc tac ata agc ttc agt ggt tac act agt tac aac cca tct ctc  192
Met Gly Tyr Ile Ser Phe Ser Gly Tyr Thr Ser Tyr Asn Pro Ser Leu
    50                  55                  60

aaa agt cga atc tct gtc act cgg gac aca tcc agg aac caa ttc ttc  240
Lys Ser Arg Ile Ser Val Thr Arg Asp Thr Ser Arg Asn Gln Phe Phe
65                  70                  75                  80

ctc cag ttg act tct gtg act act gag gac aca gcc aca tat tac tgt  288
Leu Gln Leu Thr Ser Val Thr Thr Glu Asp Thr Ala Thr Tyr Tyr Cys
                85                  90                  95

gca aga gag gtc aac tat ggg gac tcc tac cac ttt gac tac tgg ggc  336
Ala Arg Glu Val Asn Tyr Gly Asp Ser Tyr His Phe Asp Tyr Trp Gly
            100                 105                 110

caa ggc acc att gtc aca gtc tcc tca                             363
Gln Gly Thr Ile Val Thr Val Ser Ser
        115                 120
```

FIG. 3L

mV_L MAb19

```
caa ctt gcg ctc act cag tca tct tca gcc tct ttc tcc ctg gga gcc   48
Gln Leu Ala Leu Thr Gln Ser Ser Ser Ala Ser Phe Ser Leu Gly Ala
1               5                  10                  15

tca gca aaa cta acg tgc act ttg agt agt caa cac aga acg tac acc   96
Ser Ala Lys Leu Thr Cys Thr Leu Ser Ser Gln His Arg Thr Tyr Thr
            20                  25                  30

att gaa tgg tat cag caa cag tca ctc aag cct cct aag tat gtg atg  144
Ile Glu Trp Tyr Gln Gln Gln Ser Leu Lys Pro Pro Lys Tyr Val Met
        35                  40                  45

gag gtt aag aaa gat gga agc cac agc aca ggt cat ggg att cct gat  192
Glu Val Lys Lys Asp Gly Ser His Ser Thr Gly His Gly Ile Pro Asp
    50                  55                  60

cgc ttc tct gga tcc agt tct ggt gct gat cgc tac ctc agc att tcc  240
Arg Phe Ser Gly Ser Ser Ser Gly Ala Asp Arg Tyr Leu Ser Ile Ser
65                  70                  75                  80

aac atc cag cct gaa gat gaa gca ata tac atc tgt ggt gtg ggt gat  288
Asn Ile Gln Pro Glu Asp Glu Ala Ile Tyr Ile Cys Gly Val Gly Asp
                85                  90                  95

gca att aag gga caa tct gtg ttt gtt ttc ggc ggt ggc acc aag gtc  336
Ala Ile Lys Gly Gln Ser Val Phe Val Phe Gly Gly Gly Thr Lys Val
            100                 105                 110

act gtc cta                                                     345
Thr Val Leu
        115
```

FIG. 4A

hV_H MAb3

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser **Gly Tyr Ile Phe Thr Ser Tyr**
20 25 30

Trp Val His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Gly **Phe Tyr Pro Gly Asn Ser Asp Ser** Arg Tyr Ser Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Arg Asp Ser Pro Gln Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

FIG. 4B

hV_L MAb3

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser **Gln Ser Ile Val His Ser**
20 25 30

Asn Gly Asn Thr Tyr Leu Glu Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr **Lys Val Ser** Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys **Phe Gln Gly**
85 90 95

Ser His Val Pro Phe Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

FIG. 4C

hV_H MAb4

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser **Gly Tyr Thr Phe Ser Ser Ser**
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile **Phe Leu Pro Gly Ser Gly Ser Thr** Asp Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Thr Asp Gly Asn Tyr Asp Trp Phe Ala Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

FIG. 4D

hV_L MAb4

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser **Gln Ser Leu Val His Ser**
20 25 30

Ser Gly Val Thr Tyr Leu Tyr Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr **Lys Val Ser** Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys **Ser Gln Ser**
85 90 95

Thr His Val Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

FIG. 4E

hV_H MAb8(a)

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser **Gly Phe Thr Phe Thr Thr Tyr**
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser **Ile Ser Ser Gly Gly Thr Tyr Thr** Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Thr Gln Gly Asn Tyr Ser Leu Asp Phe Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser
115

FIG. 4F

hV_L MAb8(a)

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser **Lys Ser Leu Arg His Thr**
20 25 30

Lys Gly Ile Thr Phe Leu Tyr Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr **Gln Met Ser** Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys **Ala Gln Asn**
85 90 95

Leu Glu Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

FIG. 4G

hV_H MAb8(b)

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser **Gly Phe Thr Phe Thr Thr Tyr**
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser **Ile Ser Ser Gly Gly Thr Tyr Thr** Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Thr Gln Gly Asn Tyr Ser Leu Asp Phe Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser
115

FIG. 4H

hV_L MAb8(b)

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser **Lys Ser Leu Arg His Thr**
20 25 30

Lys Gly Ile Thr Phe Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr **Gln Met Ser** Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys **Ala Gln Asn**
85 90 95

Leu Glu Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

FIG. 4I

hV_H MAb8(c)

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Thr Thr Tyr
            20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Thr Ile Ser Ser Gly Gly Thr Tyr Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Thr Gln Gly Asn Tyr Ser Leu Asp Phe Trp Gly Gln Gly Thr Thr
            100                 105                 110

Val Thr Val Ser Ser
        115
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FIG. 4J

hV_L MAb8(c)

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser **Lys Ser Leu Arg His Thr**
20 25 30

Lys Gly Ile Thr Phe Leu Tyr Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr **Gln Met Ser** Asn Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys **Ala Gln Asn**
85 90 95

Leu Glu Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

FIG. 4K

hV_H MAb13(a)

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser **Gly Phe Ile Phe Ser Ser Tyr**
20 25 30

Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Asn **Ile Asn Thr Phe Gly Asp Arg Thr** Tyr Tyr Val Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Thr Gly Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
100 105 110

Ser Ser

FIG. 4L

hV_L MAb13(a)

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser **Gln Ser Leu Leu Asp Ser**
20 25 30

Asp Gly Lys Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr **Leu Val Ser** Asn Arg Asp Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys **Trp Gln Gly**
85 90 95

Thr His Phe Pro Gln Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

FIG. 4M

hV_H MAb13(b)

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser **Gly Phe Ile Phe Ser Ser Tyr**
20 25 30

Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Ser **Ile Asn Thr Phe Gly Asp Arg Thr** Tyr Tyr Val Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Thr Gly Thr Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
100 105 110

Ser Ser

FIG. 4N

hV_L MAb13(b)

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser **Gln Ser Leu Leu Asp Ser**
20 25 30

Asp Gly Lys Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr **Leu Val Ser** Lys Arg Asp Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys **Trp Gln Gly**
85 90 95

Thr His Phe Pro Gln Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

FIG. 4O

hV_H MAb16(a)

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser **Gly Tyr Thr Phe Thr Ser Tyr**
20 25 30

Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile **Ile Asn Pro Ser Asn Gly Gly Thr** Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Gly Gly Tyr Tyr Pro Phe Asp Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser
115

FIG. 4P

hV_L MAb16(a)

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser **Gln Ser Leu Leu Asp Ser**
20 25 30

Asp Gly Lys Thr Tyr Leu Tyr Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr **Leu Val Ser** Asn Arg Asp Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys **Trp Gln Gly**
85 90 95

Thr His Ser Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

FIG. 4Q

hV_H MAb16(b)

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser **Gly Tyr Thr Phe Thr Ser Tyr**
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ile **Ile Asn Pro Ser Asn Gly Gly Thr** Ser Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Gly Gly Tyr Tyr Pro Phe Asp Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser
115

FIG. 4R

hV_L MAb16(b)

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser **Gln Ser Leu Leu Asp Ser**
20 25 30

Asp Gly Lys Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr **Leu Val Ser** Asn Arg Asp Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys **Trp Gln Gly**
85 90 95

Thr His Ser Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

FIG. 4S

hV_H MAb16(c)

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser **Gly Tyr Thr Phe Thr Ser Tyr**
20 25 30

Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu **Ile Asn Pro Ser Asn Gly Gly Thr** Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Thr Arg Gly Gly Tyr Tyr Pro Phe Asp Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser
115

FIG. 4T

hV_L MAb16(c)

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser **Gln Ser Leu Leu Asp Ser**
20 25 30

Asp Gly Lys Thr Tyr Leu Tyr Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr **Leu Val Ser** Glu Arg Asp Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys **Trp Gln Gly**
85 90 95

Thr His Ser Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

FIG. 4U

hV_H MAb19(a)

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser **Gly Tyr Ser Ile Thr Ser Asp**
20 25 30

Tyr Ala Trp Asn Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu Trp
35 40 45

Ile Gly Tyr **Ile Ser Phe Ser Gly Tyr Thr** Tyr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Val Asn Tyr Gly Asp Ser Tyr His Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

FIG. 4V

hV_L MAb19(a)

Gln Leu Val Leu Thr Gln Ser Pro Ser Ala Ser Ala Ser Leu Gly Ala
1 5 10 15

Ser Val Lys Leu Thr Cys Thr Leu Ser **Ser Gln His Arg Thr Tyr Thr**
20 25 30

Ile Glu Trp His Gln Gln Gln Pro Glu Lys Gly Pro Arg Tyr Leu Met
35 40 45

Lys **Val Lys Lys Asp Gly Ser His** Ser Lys Gly Asp Gly Ile Pro Asp
50 55 60

Arg Phe Ser Gly Ser Ser Ser Gly Ala Glu Arg Tyr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys **Gly Val Gly Asp**
85 90 95

Ala Ile Lys Gly Gln Ser Val Phe Val Phe Gly Gly Gly Thr Lys Val
100 105 110

Glu Ile Lys
115

FIG. 4W

hV_H MAb19(b)

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser **Gly Tyr Ser Ile Thr Ser Asp**
20 25 30

Tyr Ala Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu Trp
35 40 45

Ile Gly Tyr **Ile Ser Phe Ser Gly Tyr Thr** Tyr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Val Asn Tyr Gly Asp Ser Tyr His Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

FIG. 4X

hV_L MAb19(b)

Gln Leu Val Leu Thr Gln Ser Pro Ser Ala Ser Ala Ser Leu Gly Ala
1 5 10 15

Ser Val Lys Leu Thr Cys Thr Leu Ser **Ser Gln His Arg Thr Tyr Thr**
20 25 30

Ile Ala Trp His Gln Gln Gln Pro Glu Lys Gly Pro Arg Tyr Leu Met
35 40 45

Lys **Val Lys Lys Asp Gly Ser His** Ser Lys Gly Asp Gly Ile Pro Asp
50 55 60

Arg Phe Ser Gly Ser Ser Ser Gly Ala Glu Arg Tyr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys **Gly Val Gly Asp**
85 90 95

Ala Ile Lys Gly Gln Ser Val Phe Val Phe Gly Gly Gly Thr Lys Val
100 105 110

Glu Ile Lys
115

FIG. 4Y

hV_H MAb19(c)

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser **Gly Tyr Ser Ile Thr Ser Asp**
20 25 30

Tyr Ala Trp Asn Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu Trp
35 40 45

Ile Gly Tyr **Ile Ser Phe Ser Gly Tyr Thr** Ser Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Glu Val Asn Tyr Gly Asp Ser Tyr His Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

FIG. 4Z

hV_L MAb19(c)

Gln Leu Val Leu Thr Gln Ser Pro Ser Ala Ser Ala Ser Leu Gly Ala
1 5 10 15

Ser Val Lys Leu Thr Cys Thr Leu Ser **Ser Gln His Arg Thr Tyr Thr**
20 25 30

Ile Glu Trp His Gln Gln Gln Pro Glu Lys Gly Pro Arg Tyr Leu Met
35 40 45

Glu **Val Lys Lys Asp Gly Ser His** Ser Lys Gly Asp Gly Ile Pro Asp
50 55 60

Arg Phe Ser Gly Ser Ser Ser Gly Ala Glu Arg Tyr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys **Gly Val Gly Asp**
85 90 95

Ala Ile Lys Gly Gln Ser Val Phe Val Phe Gly Gly Gly Thr Lys Val
100 105 110

Glu Ile Lys
115