FIG. 1

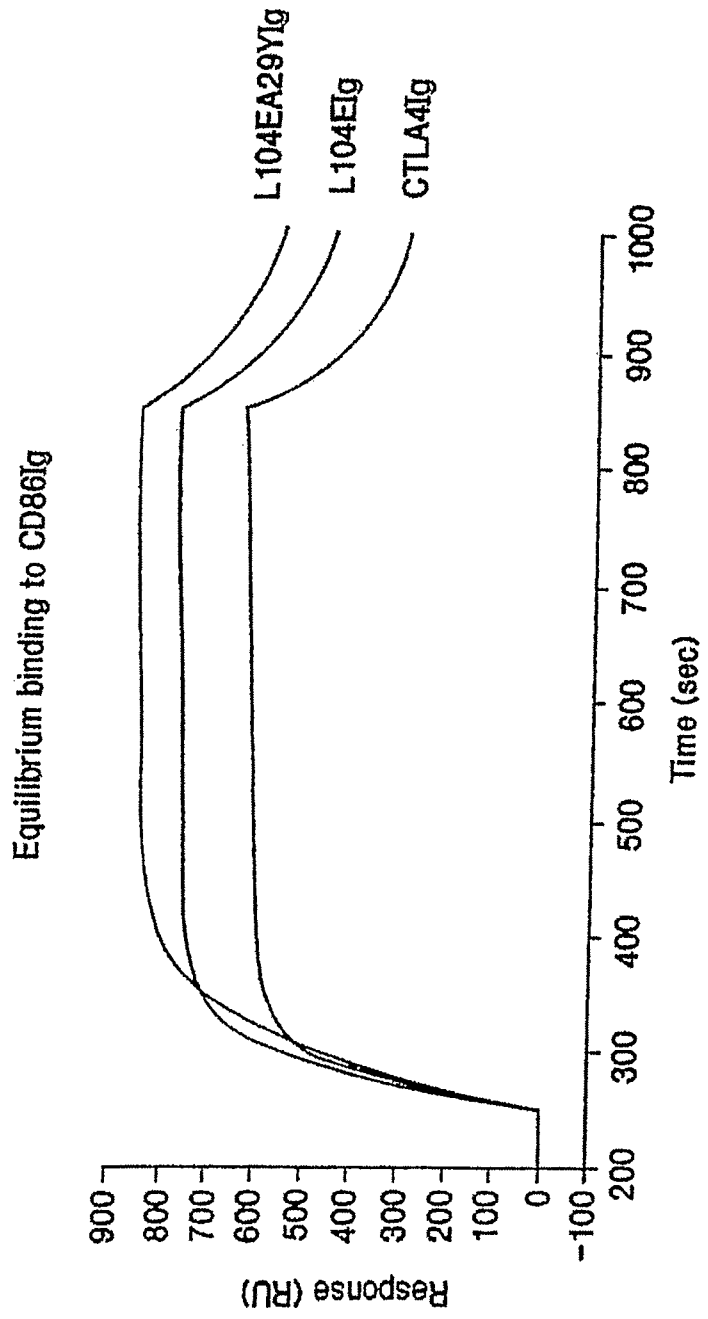

Equilibrium binding to CD86Ig
L104EA29YIg
L104EIg
CTLA4Ig
Response (RU)
900
800
700
600
500
400
300
200
100
0
-100
200
300
400
500
600
700
800
900
1000
Time (sec)

FIG. 2A

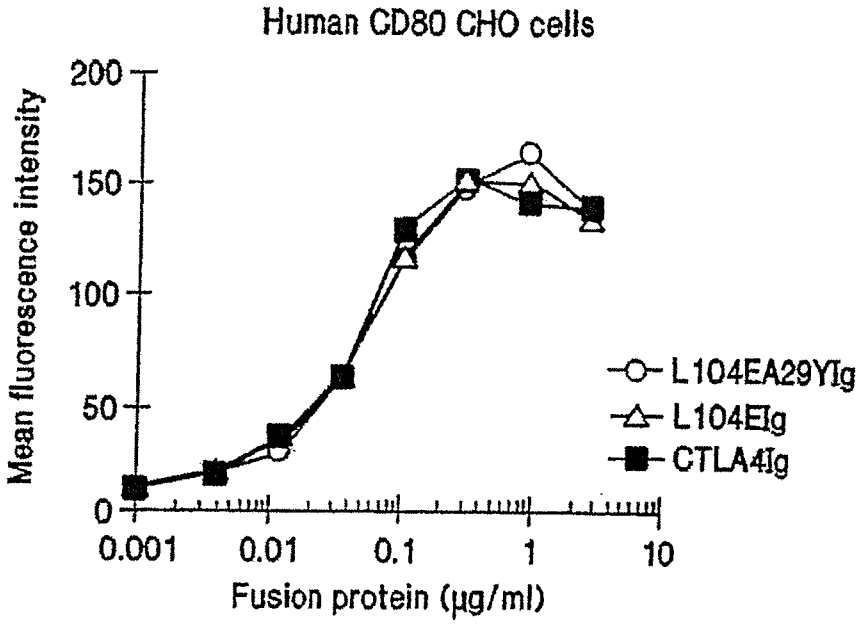

Human CD80 CHO cells
Mean fluorescence intensity
200
150
100
50
0
0.001
0.01
0.1
1
10
Fusion protein (µg/ml)
L104EA29YIg
L104EIg
CTLA4Ig

FIG. 2B

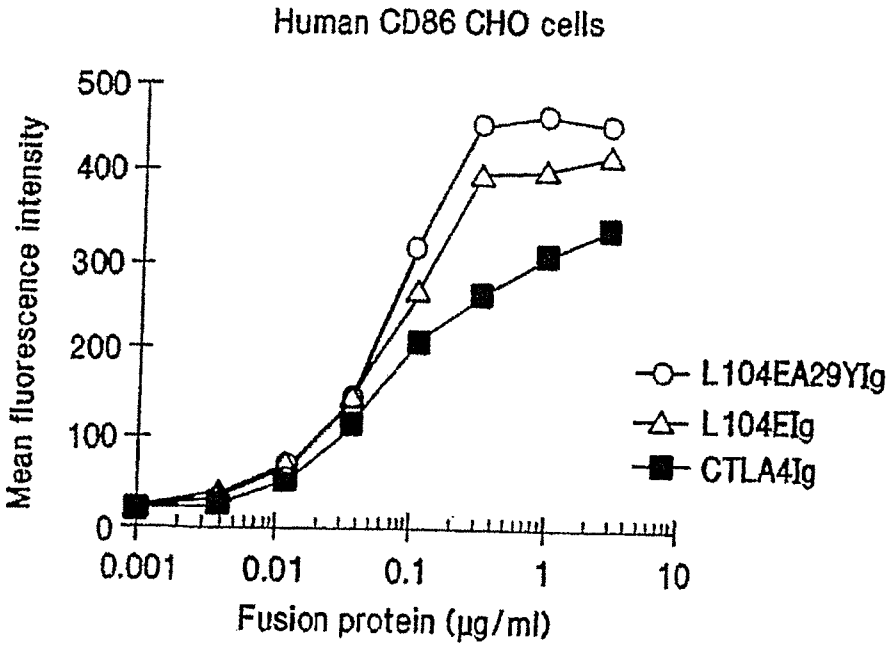

Human CD86 CHO cells
Mean fluorescence intensity
500
400
300
200
100
0
0.001
0.01
0.1
1
10
Fusion protein (µg/ml)
L104EA29YIg
L104EIg
CTLA4Ig

FIG. 3A

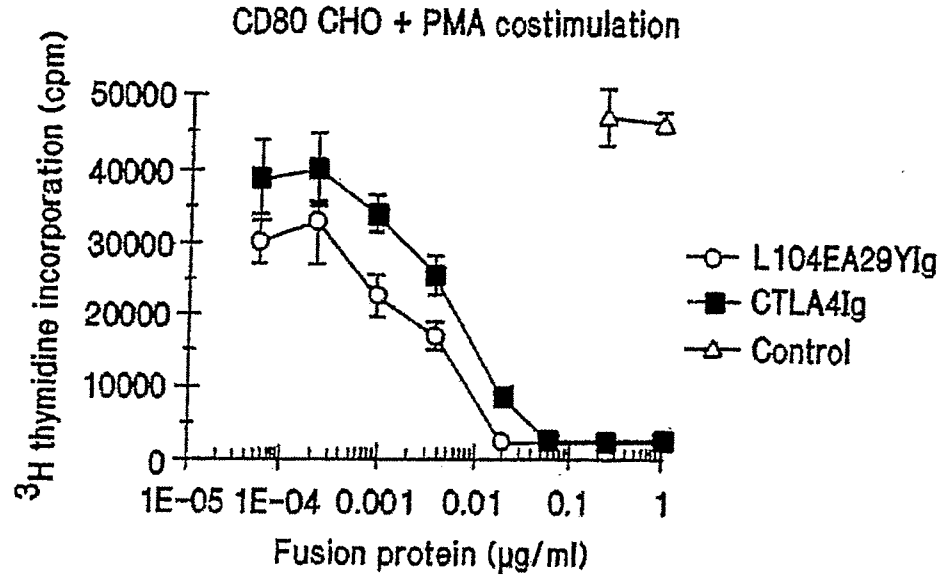

CD80 CHO + PMA costimulation
^{3}H thymidine incorporation (cpm)
50000
40000
30000
20000
10000
0
1E-05 1E-04 0.001 0.01 0.1 1
Fusion protein (μg/ml)
L104EA29YIg
CTLA4Ig
Control

FIG. 3B

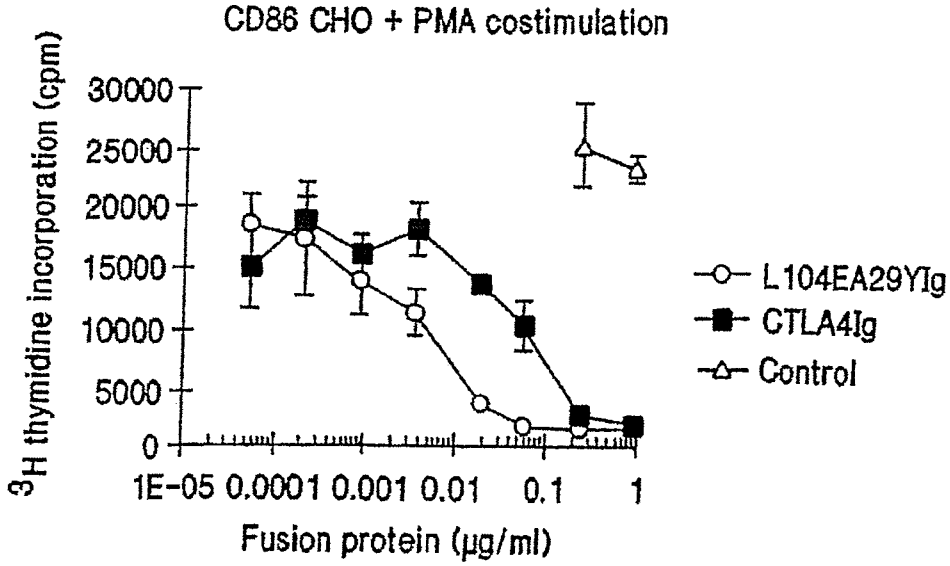

CD86 CHO + PMA costimulation
^{3}H thymidine incorporation (cpm)
30000
25000
20000
15000
10000
5000
0
1E-05 0.0001 0.001 0.01 0.1 1
Fusion protein (μg/ml)
L104EA29YIg
CTLA4Ig
Control

FIG. 4A

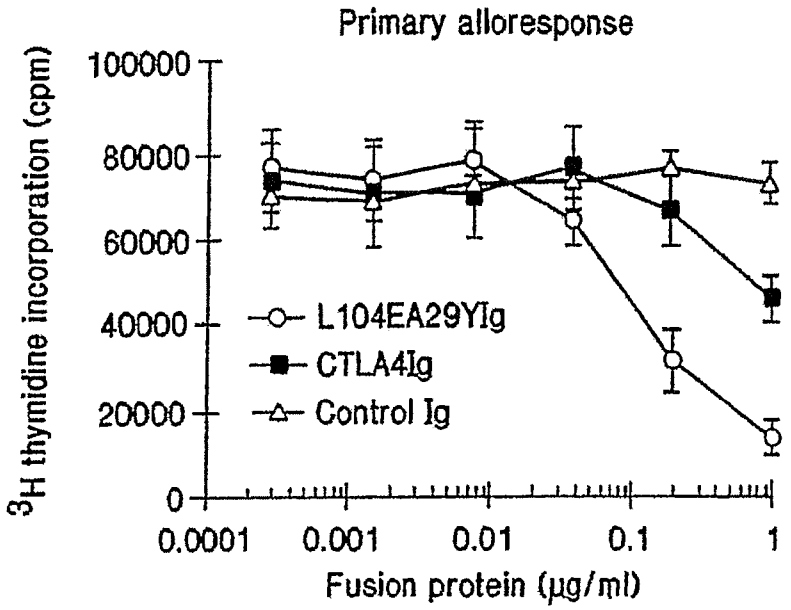

Primary alloresponse
^{3}H thymidine incorporation (cpm)
100000
80000
60000
40000
20000
0
L104EA29YIg
CTLA4Ig
Control Ig
0.0001
0.001
0.01
0.1
1
Fusion protein (μg/ml)

FIG. 4B

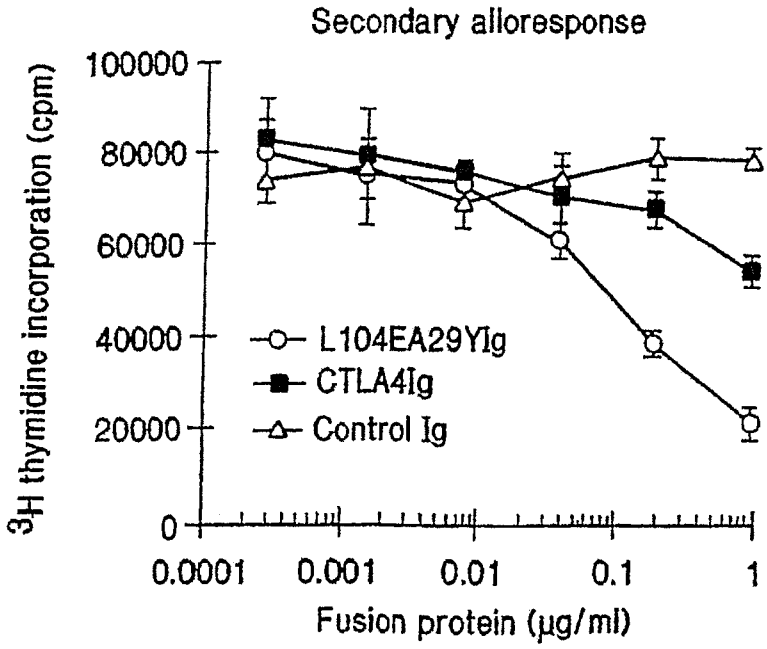

Secondary alloresponse
^{3}H thymidine incorporation (cpm)
100000
80000
60000
40000
20000
0
L104EA29YIg
CTLA4Ig
Control Ig
0.0001
0.001
0.01
0.1
1
Fusion protein (μg/ml)

FIG. 5A

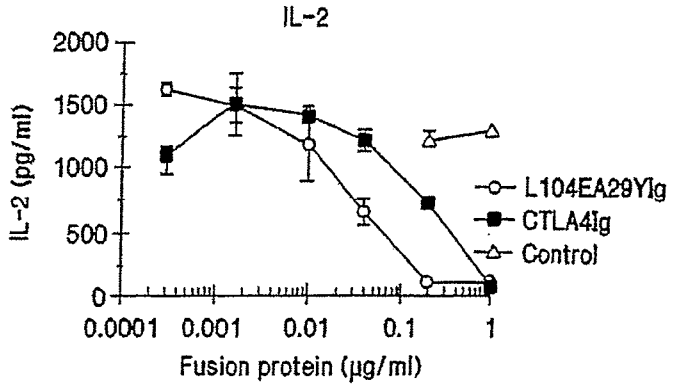


FIG. 5B

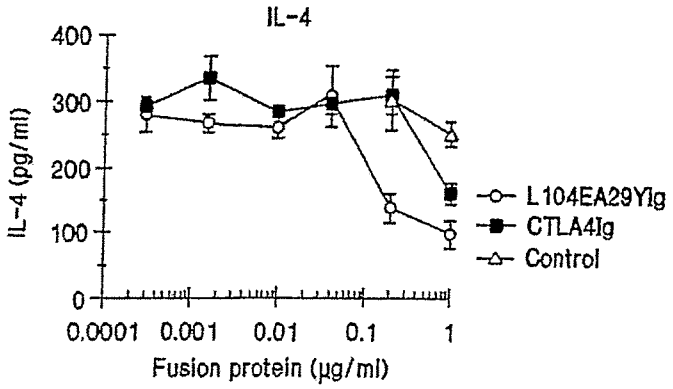


FIG. 5C

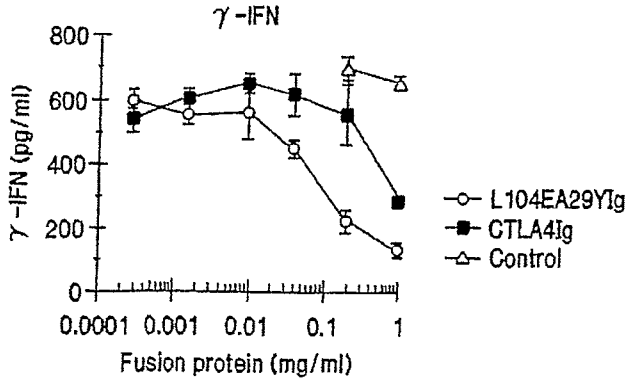


FIG. 6

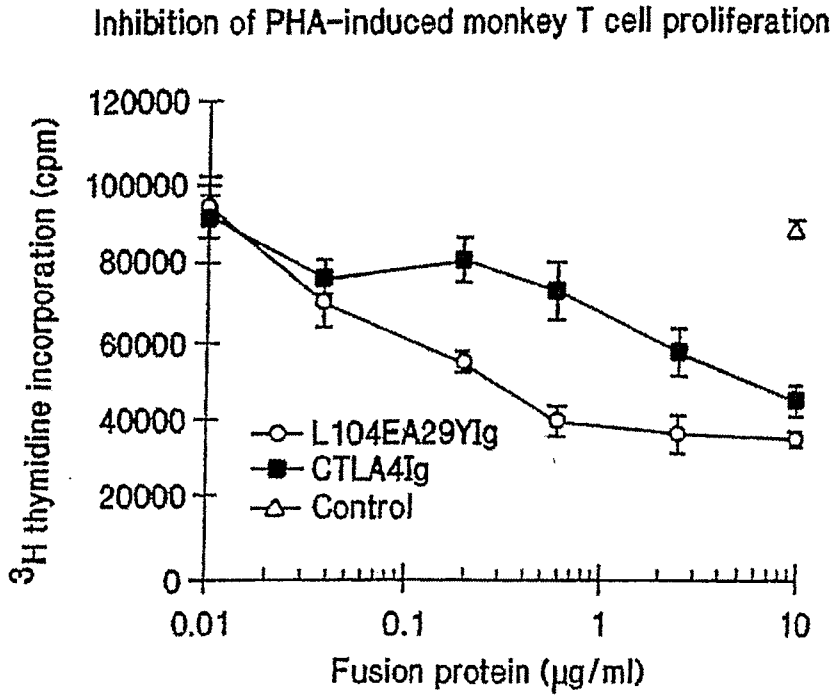

Inhibition of PHA-induced monkey T cell proliferation
^{3}H thymidine incorporation (cpm)
120000
100000
80000
60000
40000
20000
0
0.01
0.1
1
10
Fusion protein (μg/ml)
L104EA29YIg
CTLA4Ig
Control

FIG. 7

```
ATGGGTGTACTGCTCACACAGAGGACGCTGCTCAGTCTGGTCCTTGCACTCCTGTTTCCA      -19
M--G--V--L--L--T--Q--R--T--L--L--S--L--V--L--A--L--L--F--P--      -7

AGCATGGCGAGCATGGCAATGCACGTGGCCCAGCCTGCTGTGGTACTGGCCAGCAGCCGA      +42
S--M--A--S--M--A--M--H--V--A--Q--P--A--V--V--L--A--S--S--R--      +14
                  +1

GGCATCGCTAGCTTTGTGTGTGAGTATGCATCTCCAGGCAAATATACTGAGGTCCGGGTG      +102
G--I--A--S--F--V--C--E--Y--A--S--P--G--K--Y--T--E--V--R--V--      +34

ACAGTGCTTCGGCAGGCTGACAGCCAGGTGACTGAAGTCTGTGCGGCAACCTACATGATG      +162
T--V--L--R--Q--A--D--S--Q--V--T--E--V--C--A--A--T--Y--M--M--      +54

GGGAATGAGTTGACCTTCCTAGATGATTCCATCTGCACGGGCACCTCCAGTGGAAATCAA      +222
G--N--E--L--T--F--L--D--D--S--I--C--T--G--T--S--S--G--N--Q--      +74

GTGAACCTCACTATCCAAGGACTGAGGGCCATGGACACGGGACTCTACATCTGCAAGGTG      +282
V--N--L--T--I--Q--G--L--R--A--M--D--T--G--L--Y--I--C--K--V--      +94

GAGCTCATGTACCCACCGCCATACTACGAGGGCATAGGCAACGGAACCCAGATTTATGTA      +342
E--L--M--Y--P--P--P--Y--Y--E--G--I--G--N--G--T--Q--I--Y--V--      +114

ATTGATCCAGAACCGTGCCCAGATTCTGATCAGGAGCCCAAATCTTCTGACAAAACTCAC      +402
I--D--P--E--P--C--P--D--S--D--Q--E--P--K--S--S--D--K--T--H--      +134

ACATCCCCACCGTCCCCAGCACCTGAACTCCTGGGGGGGATCGTCAGTGTTCCTCTTCCCC      +462
T--S--P--P--S--P--A--P--E--L--L--G--G--S--S--V--F--L--F--P--      +154

CCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTG      +522
P--K--P--K--D--T--L--M--I--S--R--T--P--E--V--T--C--V--V--V--      +174

GACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTG      +582
D--V--S--H--E--D--P--E--V--K--F--N--W--Y--V--D--G--V--E--V--      +194

CATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGC      +642
H--N--A--K--T--K--P--R--E--E--Q--Y--N--S--T--Y--R--V--V--S--      +214

GTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCC      +702
V--L--T--V--L--H--Q--D--W--L--N--G--K--E--Y--K--C--K--V--S--      +234

AACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGA      +762
N--K--A--L--P--A--P--I--E--K--T--I--S--K--A--K--G--Q--P--R--      +254

GAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGC      +822
E--P--Q--V--Y--T--L--P--P--S--R--D--E--L--T--K--N--Q--V--S--      +274

CTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAAT      +882
L--T--C--L--V--K--G--F--Y--P--S--D--I--A--V--E--W--E--S--N--      +294

GGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTC      +942
G--Q--P--E--N--N--Y--K--T--T--P--P--V--L--D--S--D--G--S--F--      +314

TTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCA      +1002
F--L--Y--S--K--L--T--V--D--K--S--R--W--Q--Q--G--N--V--F--S--      +334

TGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCT      +1062
C--S--V--M--H--E--A--L--H--N--H--Y--T--Q--K--S--L--S--L--S--      +354

CCGGGTAAATGA
P--G--K--*
```

FIG. 8

```
ATGGGTGTACTGCTCACACAGAGGACGCTGCTCAGTCTGGTCCTTGCACTCCTGTTTCCA      -19
M--G--V--L--L--T--Q--R--T--L--L--S--L--V--L--A--L--L--F--P--      -7

AGCATGGCGAGCATGGCAATGCACGTGGCCCAGCCTGCTGTGGTACTGGCCAGCAGCCGA      +42
S--M--A--S--M--A--M--H--V--A--Q--P--A--V--V--L--A--S--S--R--      +14
                  +1

GGCATCGCTAGCTTTGTGTGTGAGTATGCATCTCCAGGCAAAGCCACTGAGGTCCGGGTG      +102
G--I--A--S--F--V--C--E--Y--A--S--P--G--K--A--T--E--V--R--V--      +34

ACAGTGCTTCGGCAGGCTGACAGCCAGGTGACTGAAGTCTGTGCGGCAACCTACATGATG      +162
T--V--L--R--Q--A--D--S--Q--V--T--E--V--C--A--A--T--Y--M--M--      +54

GGGAATGAGTTGACCTTCCTAGATGATTCCATCTGCACGGGCACCTCCAGTGGAAATCAA      +222
G--N--E--L--T--F--L--D--D--S--I--C--T--G--T--S--S--G--N--Q--      +74

GTGAACCTCACTATCCAAGGACTGAGGGCCATGGACACGGGACTCTACATCTGCAAGGTG      +282
V--N--L--T--I--Q--G--L--R--A--M--D--T--G--L--Y--I--C--K--V--      +94

GAGCTCATGTACCCACCGCCATACTACCTGGGCATAGGCAACGGAACCCAGATTTATGTA      +342
E--L--M--Y--P--P--P--Y--Y--L--G--I--G--N--G--T--Q--I--Y--V--      +114

ATTGATCCAGAACCGTGCCCAGATTCTGATCAGGAGCCCAAATCTTCTGACAAAACTCAC      +402
I--D--P--E--P--C--P--D--S--D--Q--E--P--K--S--S--D--K--T--H--      +134

ACATCCCCACCGTCCCCAGCACCTGAACTCCTGGGTGGATCGTCAGTCTTCCTCTTCCCC      +462
T--S--P--P--S--P--A--P--E--L--G--G--S--V--F--L--F--P--P--      +154

CCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTG      +522
P--K--P--K--D--T--L--M--I--S--R--T--P--E--V--T--C--V--V--V--      +174

GACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTG      +582
D--V--S--H--E--D--P--E--V--K--F--N--W--Y--V--D--G--V--E--V--      +194

CATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGGGTGGTCAGC      +642
H--N--A--K--T--K--P--R--E--E--Q--Y--N--S--T--Y--R--V--V--S--      +214

GTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCC      +702
V--L--T--V--L--H--Q--D--W--L--N--G--K--E--Y--K--C--K--V--S--      +234

AACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGA      +762
N--K--A--L--P--A--P--I--E--K--T--I--S--K--A--K--G--Q--P--R--      +254

GAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGC      +822
E--P--Q--V--Y--T--L--P--P--S--R--D--E--L--T--K--N--Q--V--S--      +274

CTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAAT      +882
L--T--C--L--V--K--G--F--Y--P--S--D--I--A--V--E--W--E--S--N--      +294

GGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTC      +942
G--Q--P--E--N--N--Y--K--T--T--P--P--V--L--D--S--D--G--S--F--      +314

TTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCA      +1002
F--L--Y--S--K--L--T--V--D--K--S--R--W--Q--Q--G--N--V--F--S--      +334

TGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCT      +1062
C--S--V--M--H--E--A--L--H--N--H--Y--T--Q--K--S--L--S--L--S--      +354

CCGGGTAAATGA
P--G--K--*
```

FIG. 9

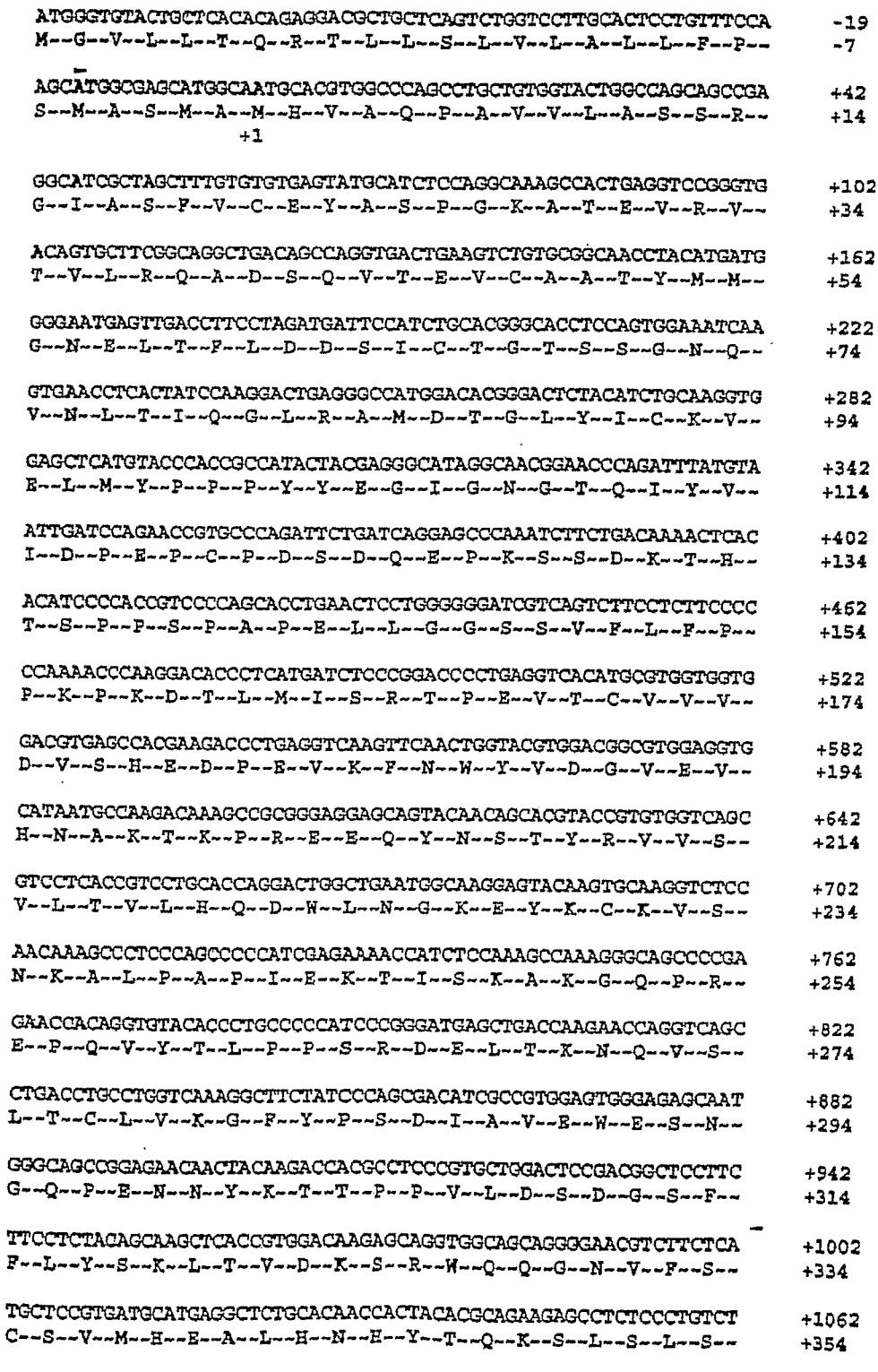

ATGGGTGTACTGCTCACACAGAGGACGCTGCTCAGTCTGGTCCTTGCACTCCTGTTTCCA -19
M--G--V--L--L--T--Q--R--T--L--L--S--L--V--L--A--L--L--F--P-- -7
AGCATGGCGAGCATGGCAATGCACGTGGCCCAGCCTGCTGTGGTACTGGCCAGCAGCCGA +42
S--M--A--S--M--A--M--H--V--A--Q--P--A--V--V--L--A--S--S--R-- +14
+1
GGCATCGCTAGCTTTGTGTGTGAGTATGCATCTCCAGGCAAAGCCACTGAGGTCCGGGTG +102
G--I--A--S--F--V--C--E--Y--A--S--P--G--K--A--T--E--V--R--V-- +34
ACAGTGCTTCGGCAGGCTGACAGCCAGGTGACTGAAGTCTGTGCGGCAACCTACATGATG +162
T--V--L--R--Q--A--D--S--Q--V--T--E--V--C--A--A--T--Y--M--M-- +54
GGGAATGAGTTGACCTTCCTAGATGATTCCATCTGCACGGGCACCTCCAGTGGAAATCAA +222
G--N--E--L--T--F--L--D--D--S--I--C--T--G--T--S--S--G--N--Q-- +74
GTGAACCTCACTATCCAAGGACTGAGGGCCATGGACACGGGACTCTACATCTGCAAGGTG +282
V--N--L--T--I--Q--G--L--R--A--M--D--T--G--L--Y--I--C--K--V-- +94
GAGCTCATGTACCCACCGCCATACTACGAGGGCATAGGCAACGGAACCCAGATTTATGTA +342
E--L--M--Y--P--P--P--Y--Y--E--G--I--G--N--G--T--Q--I--Y--V-- +114
ATTGATCCAGAACCGTGCCCAGATTCTGATCAGGAGCCCAAATCTTCTGACAAAACTCAC +402
I--D--P--E--P--C--P--D--S--D--Q--E--P--K--S--S--D--K--T--H-- +134
ACATCCCCACCGTCCCCAGCACCTGAACTCCTGGGGGGGATCGTCAGTCTTCCTCTTCCCC +462
T--S--P--P--S--P--A--P--E--L--L--G--G--S--S--V--F--L--F--P-- +154
CCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTG +522
P--K--P--K--D--T--L--M--I--S--R--T--P--E--V--T--C--V--V--V-- +174
GACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTG +582
D--V--S--H--E--D--P--E--V--K--F--N--W--Y--V--D--G--V--E--V-- +194
CATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGC +642
H--N--A--K--T--K--P--R--E--E--Q--Y--N--S--T--Y--R--V--V--S-- +214
GTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCC +702
V--L--T--V--L--H--Q--D--W--L--N--G--K--E--Y--K--C--K--V--S-- +234
AACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGA +762
N--K--A--L--P--A--P--I--E--K--T--I--S--K--A--K--G--Q--P--R-- +254
GAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGC +822
E--P--Q--V--Y--T--L--P--P--S--R--D--E--L--T--K--N--Q--V--S-- +274
CTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAAT +882
L--T--C--L--V--K--G--F--Y--P--S--D--I--A--V--E--W--E--S--N-- +294
GGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTC +942
G--Q--P--E--N--N--Y--K--T--T--P--P--V--L--D--S--D--G--S--F-- +314
TTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCA +1002
F--L--Y--S--K--L--T--V--D--K--S--R--W--Q--Q--G--N--V--F--S-- +334
TGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCT +1062
C--S--V--M--H--E--A--L--H--N--H--Y--T--Q--K--S--L--S--L--S-- +354
CCGGGTAAATGA
P--G--K--*

FIG. 10A

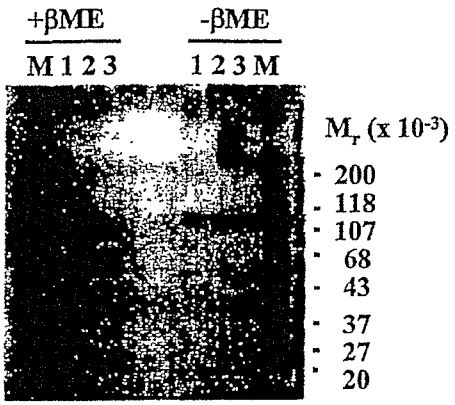


FIG. 10B

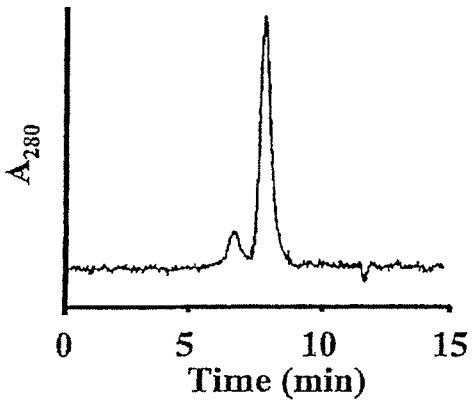
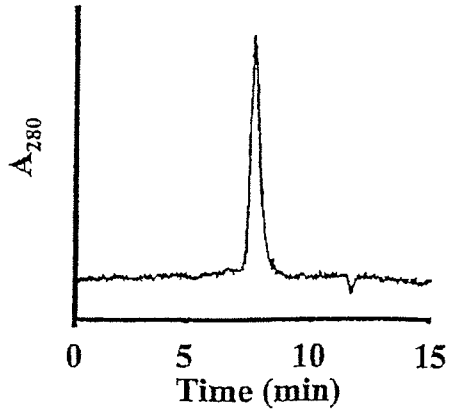


FIG. 10C



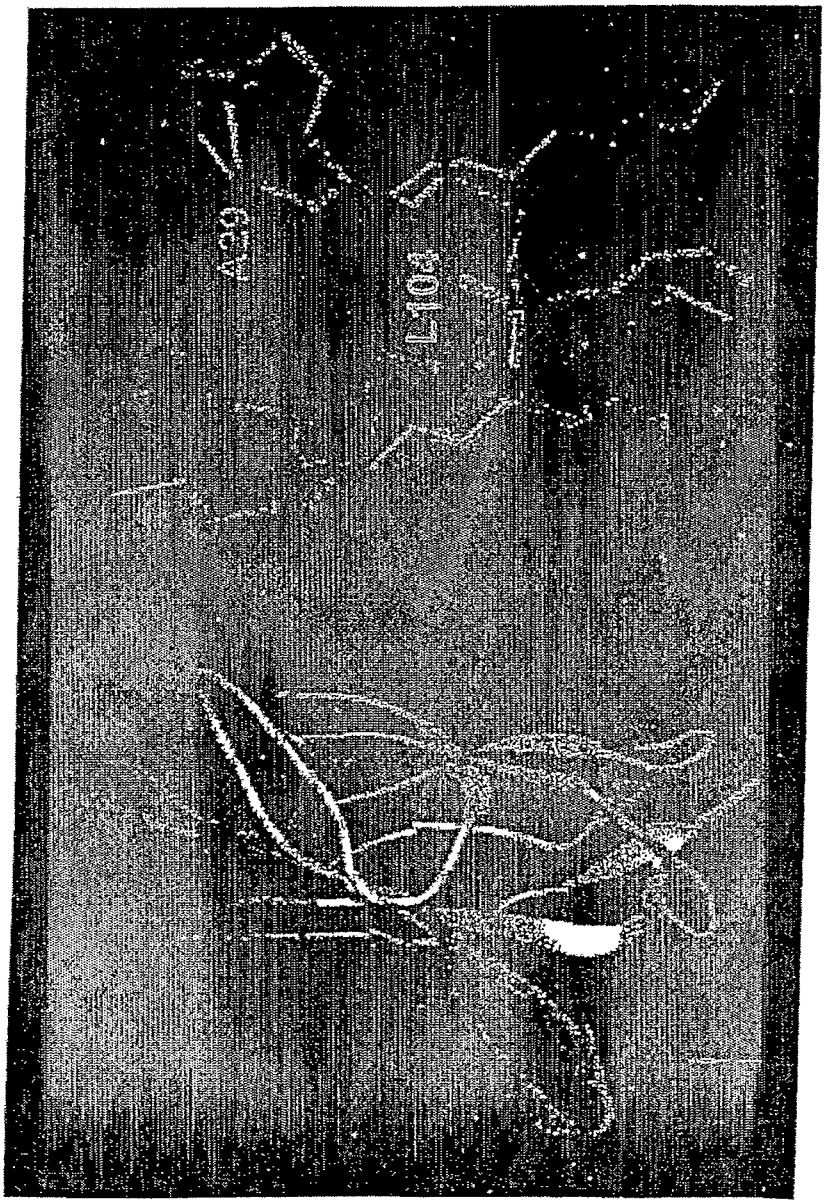


FIG. 11

FIG. 12

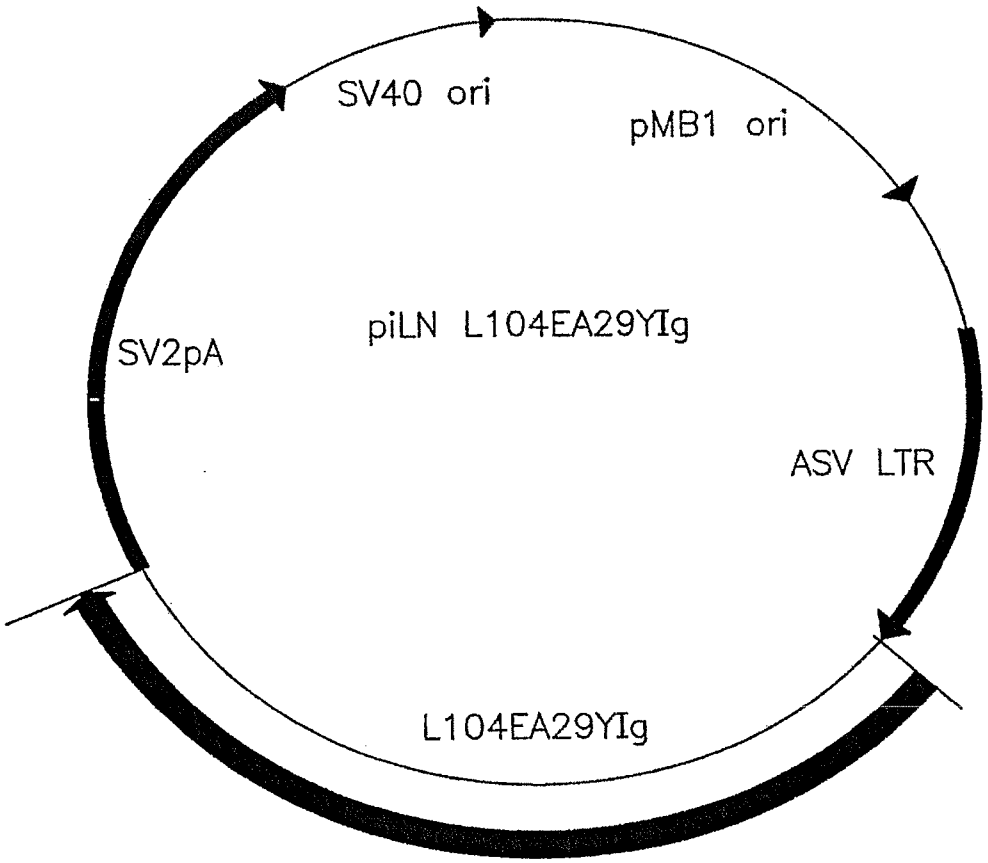
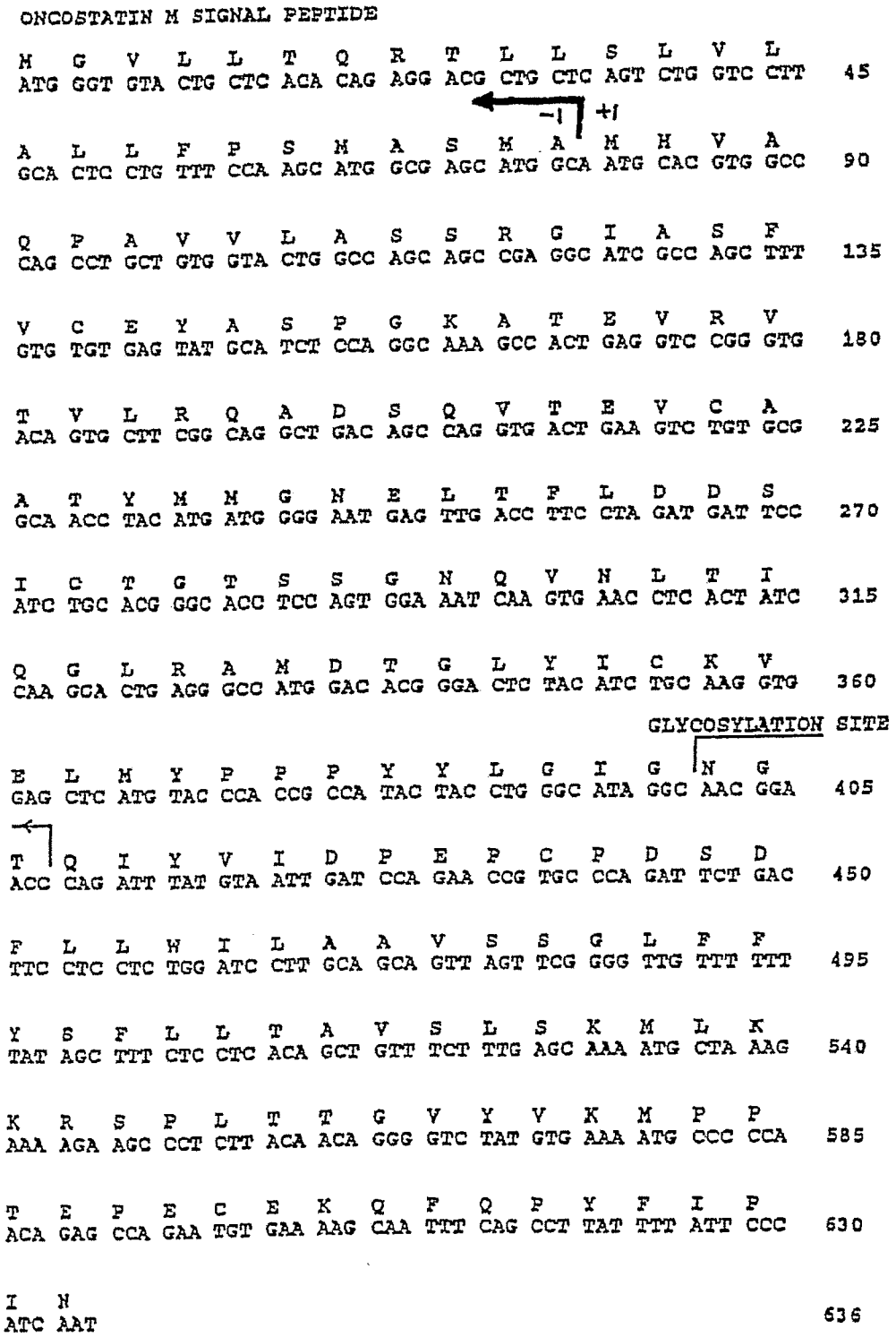

SV40 ori
pMB1 ori
piLN L104EA29YIg
SV2pA
ASV LTR
L104EA29YIg

FIG. 13


ONCOSTATIN M SIGNAL PEPTIDE
M G V L L T Q R T L L S L V L
ATG GGT GTA CTG CTC ACA CAG AGG ACG CTG CTC AGT CTG GTC CTT 45
-1
+1
A L L F P S M A S M A M H V A
GCA CTC CTG TTT CCA AGC ATG GCG AGC ATG GCA ATG CAC GTG GCC 90
Q P A V V L A S S R G I A S F
CAG CCT GCT GTG GTA CTG GCC AGC AGC CGA GGC ATC GCC AGC TTT 135
V C E Y A S P G K A T E V R V
GTG TGT GAG TAT GCA TCT CCA GGC AAA GCC ACT GAG GTC CGG GTG 180
T V L R Q A D S Q V T E V C A
ACA GTG CTT CGG CAG GCT GAC AGC CAG GTG ACT GAA GTC TGT GCG 225
A T Y M M G N E L T F L D D S
GCA ACC TAC ATG ATG GGG AAT GAG TTG ACC TTC CTA GAT GAT TCC 270
I C T G T S S G N Q V N L T I
ATC TGC ACG GGC ACC TCC AGT GGA AAT CAA GTG AAC CTC ACT ATC 315
Q G L R A M D T G L Y I C K V
CAA GGA CTG AGG GCC ATG GAC ACG GGA CTC TAC ATC TGC AAG GTG 360
GLYCOSYLATION SITE
E L M Y P P P Y Y L G I G N G
GAG CTC ATG TAC CCA CCG CCA TAC TAC CTG GGC ATA GGC AAC GGA 405
T Q I Y V I D P E P C P D S D
ACC CAG ATT TAT GTA ATT GAT CCA GAA CCG TGC CCA GAT TCT GAC 450
F L L W I L A A V S S G L F F
TTC CTC CTC TGG ATC CTT GCA GCA GTT AGT TCG GGG TTG TTT TTT 495
Y S F L L T A V S L S K M L K
TAT AGC TTT CTC CTC ACA GCT GTT TCT TTG AGC AAA ATG CTA AAG 540
K R S P L T T G V Y V K M P P
AAA AGA AGC CCT CTT ACA ACA GGG GTC TAT GTG AAA ATG CCC CCA 585
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ATC AAT 636

SEQUENCE LISTING

<110> Bristol-Myers Squibb Company
Hagerty, David
Rusnak, James

<120> METHODS FOR TREATING IMMUNE DISORDERS ASSOCIATED WITH GRAFT TRANSPLANTATION WITH SOLUBLE CTLA4 MUTANT MOLECULES

<130> 10522 PSP

<160> 10

<170> PatentIn version 3.2

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<220>
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<211> 42
<212> DNA
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<223> Oncostatin M CTLA4 (OMCTLA4) Reverse Primer

<400> 2
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<212> DNA
<213> Artificial Sequence

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<223> L104EA29YIg

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ggcatcgcta gctttgtgtg tgagtatgca tctccaggca aatatactga ggtccgggtg 180

acagtgcttc ggcaggctga cagccaggtg actgaagtct gtgcggcaac ctacatgatg 240

gggaatgagt tgaccttcct agatgattcc atctgcacgg gcacctccag tggaaatcaa 300

gtgaacctca ctatccaagg actgagggcc atggacacgg gactctacat ctgcaaggtg 360

gagctcatgt acccaccgcc atactacgag ggcataggca acggaaccca gatttatgta 420

attgatccag aaccgtgccc agattctgat caggagccca aatcttctga caaaactcac 480

acatccccac cgtccccagc acctgaactc ctgggggggat cgtcagtctt cctcttcccc 540

ccaaaaccca aggacaccct catgatctcc cggacccctg aggtcacatg cgtggtggtg 600

gacgtgagcc acgaagaccc tgaggtcaag ttcaactggt acgtggacgg cgtggaggtg 660

cataatgcca agacaaagcc gcgggaggag cagtacaaca gcacgtaccg tgtggtcagc 720

gtcctcaccg tcctgcacca ggactggctg aatggcaagg agtacaagtg caaggtctcc 780

aacaaagccc tcccagcccc catcgagaaa accatctcca aagccaaagg gcagccccga 840

gaaccacagg tgtacaccct gcccccatcc cgggatgagc tgaccaagaa ccaggtcagc 900

ctgacctgcc tggtcaaagg cttctatccc agcgacatcg ccgtggagtg ggagagcaat 960

gggcagccgg agaacaacta caagaccacg cctcccgtgc tggactccga cggctccttc 1020

ttcctctaca gcaagctcac cgtggacaag agcaggtggc agcaggggaa cgtcttctca 1080

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<210> 4
<211> 383
<212> PRT
<213> Artificial Sequence

<220>
<223> L104EA29YIg

<400> 4

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Leu Leu Phe Pro Ser Met Ala Ser Met Ala Met His Val Ala Gln Pro
20 25 30

Ala Val Val Leu Ala Ser Ser Arg Gly Ile Ala Ser Phe Val Cys Glu
35 40 45

Tyr Ala Ser Pro Gly Lys Tyr Thr Glu Val Arg Val Thr Val Leu Arg
50 55 60

Gln Ala Asp Ser Gln Val Thr Glu Val Cys Ala Ala Thr Tyr Met Met
65 70 75 80

Gly Asn Glu Leu Thr Phe Leu Asp Asp Ser Ile Cys Thr Gly Thr Ser
85 90 95

Ser Gly Asn Gln Val Asn Leu Thr Ile Gln Gly Leu Arg Ala Met Asp
100 105 110

Thr Gly Leu Tyr Ile Cys Lys Val Glu Leu Met Tyr Pro Pro Pro Tyr
115 120 125

Tyr Glu Gly Ile Gly Asn Gly Thr Gln Ile Tyr Val Ile Asp Pro Glu
130 135 140

Pro Cys Pro Asp Ser Asp Gln Glu Pro Lys Ser Ser Asp Lys Thr His
145 150 155 160

Thr Ser Pro Pro Ser Pro Ala Pro Glu Leu Leu Gly Gly Ser Ser Val
165 170 175

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
180 185 190

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
195 200 205

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
210 215 220

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
225 230 235 240

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
245 250 255

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
260 265 270

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
275 280 285

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Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
    290                 295                 300

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
305                 310                 315                 320

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
                325                 330                 335

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
            340                 345                 350

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
        355                 360                 365

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
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<212> DNA
<213> Artificial Sequence

<220>
<223> L104EIg

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ggcatcgcta gctttgtgtg tgagtatgca tctccaggca aagccactga ggtccgggtg    180

acagtgcttc ggcaggctga cagccaggtg actgaagtct gtgcggcaac ctacatgatg    240

gggaatgagt tgaccttcct agatgattcc atctgcacgg gcacctccag tggaaatcaa    300

gtgaacctca ctatccaagg actgagggcc atggacacgg gactctacat ctgcaaggtg    360

gagctcatgt acccaccgcc atactacgag ggcataggca acggaaccca gatttatgta    420

attgatccag aaccgtgccc agattctgat caggagccca aatcttctga caaaactcac    480

acatccccac cgtccccagc acctgaactc ctgggggggat cgtcagtctt cctcttcccc    540

ccaaaaccca aggacaccct catgatctcc cggacccctg aggtcacatg cgtggtggtg    600

gacgtgagcc acgaagaccc tgaggtcaag ttcaactggt acgtggacgg cgtggaggtg    660

cataatgcca agacaaagcc gcgggaggag cagtacaaca gcacgtaccg tgtggtcagc    720
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gtcctcaccg tcctgcacca ggactggctg aatggcaagg agtacaagtg caaggtctcc 780

aacaaagccc tcccagcccc catcgagaaa accatctcca aagccaaagg gcagccccga 840

gaaccacagg tgtacaccct gcccccatcc cgggatgagc tgaccaagaa ccaggtcagc 900

ctgacctgcc tggtcaaagg cttctatccc agcgacatcg ccgtggagtg ggagagcaat 960

gggcagccgg agaacaacta caagaccacg cctcccgtgc tggactccga cggctccttc 1020

ttcctctaca gcaagctcac cgtggacaag agcaggtggc agcaggggaa cgtcttctca 1080

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<210> 6
<211> 383
<212> PRT
<213> Artificial Sequence

<220>
<223> L104EIg

<400> 6

Met Gly Val Leu Leu Thr Gln Arg Thr Leu Leu Ser Leu Val Leu Ala
1 5 10 15

Leu Leu Phe Pro Ser Met Ala Ser Met Ala Met His Val Ala Gln Pro
20 25 30

Ala Val Val Leu Ala Ser Ser Arg Gly Ile Ala Ser Phe Val Cys Glu
35 40 45

Tyr Ala Ser Pro Gly Lys Ala Thr Glu Val Arg Val Thr Val Leu Arg
50 55 60

Gln Ala Asp Ser Gln Val Thr Glu Val Cys Ala Ala Thr Tyr Met Met
65 70 75 80

Gly Asn Glu Leu Thr Phe Leu Asp Asp Ser Ile Cys Thr Gly Thr Ser
85 90 95

Ser Gly Asn Gln Val Asn Leu Thr Ile Gln Gly Leu Arg Ala Met Asp
100 105 110

Thr Gly Leu Tyr Ile Cys Lys Val Glu Leu Met Tyr Pro Pro Pro Tyr
115 120 125

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Tyr Glu Gly Ile Gly Asn Gly Thr Gln Ile Tyr Val Ile Asp Pro Glu
    130                 135                 140

Pro Cys Pro Asp Ser Asp Gln Glu Pro Lys Ser Ser Asp Lys Thr His
145                 150                 155                 160

Thr Ser Pro Pro Ser Pro Ala Pro Glu Leu Leu Gly Gly Ser Ser Val
                165                 170                 175

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
            180                 185                 190

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
        195                 200                 205

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
    210                 215                 220

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
225                 230                 235                 240

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
                245                 250                 255

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
            260                 265                 270

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
        275                 280                 285

Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
    290                 295                 300

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
305                 310                 315                 320

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
                325                 330                 335

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
            340                 345                 350
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Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
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His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
370 375 380

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<211> 1152
<212> DNA
<213> Artificial Sequence

<220>
<223> CTLA4Ig

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ggcatcgcta gctttgtgtg tgagtatgca tctccaggca aagccactga ggtccgggtg 180

acagtgcttc ggcaggctga cagccaggtg actgaagtct gtgcggcaac ctacatgatg 240

gggaatgagt tgaccttcct agatgattcc atctgcacgg gcacctccag tggaaatcaa 300

gtgaacctca ctatccaagg actgagggcc atggacacgg gactctacat ctgcaaggtg 360

gagctcatgt acccaccgcc atactacctg ggcataggca acggaaccca gatttatgta 420

attgatccag aaccgtgccc agattctgat caggagccca aatcttctga caaaactcac 480

acatccccac cgtccccagc acctgaactc ctgggtggat cgtcagtctt cctcttcccc 540

ccaaaaccca aggacaccct catgatctcc cggacccctg aggtcacatg cgtggtggtg 600

gacgtgagcc acgaagaccc tgaggtcaag ttcaactggt acgtggacgg cgtggaggtg 660

cataatgcca agacaaagcc gcgggaggag cagtacaaca gcacgtaccg ggtggtcagc 720

gtcctcaccg tcctgcacca ggactggctg aatggcaagg agtacaagtg caaggtctcc 780

aacaaagccc tcccagcccc catcgagaaa accatctcca aagccaaagg gcagccccga 840

gaaccacagg tgtacaccct gcccccatcc cgggatgagc tgaccaagaa ccaggtcagc 900

ctgacctgcc tggtcaaagg cttctatccc agcgacatcg ccgtggagtg ggagagcaat 960

gggcagccgg agaacaacta caagaccacg cctcccgtgc tggactccga cggctccttc 1020

ttcctctaca gcaagctcac cgtggacaag agcaggtggc agcaggggaa cgtcttctca 1080

tgctccgtga tgcatgaggc tctgcacaac cactacacgc agaagagcct ctccctgtct 1140

ccgggtaaat ga 1152

<210> 8
<211> 383
<212> PRT
<213> Artificial Sequence

<220>
<223> CTLA4Ig

<400> 8

Met Gly Val Leu Leu Thr Gln Arg Thr Leu Leu Ser Leu Val Leu Ala
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Leu Leu Phe Pro Ser Met Ala Ser Met Ala Met His Val Ala Gln Pro
20 25 30

Ala Val Val Leu Ala Ser Ser Arg Gly Ile Ala Ser Phe Val Cys Glu
35 40 45

Tyr Ala Ser Pro Gly Lys Ala Thr Glu Val Arg Val Thr Val Leu Arg
50 55 60

Gln Ala Asp Ser Gln Val Thr Glu Val Cys Ala Ala Thr Tyr Met Met
65 70 75 80

Gly Asn Glu Leu Thr Phe Leu Asp Asp Ser Ile Cys Thr Gly Thr Ser
85 90 95

Ser Gly Asn Gln Val Asn Leu Thr Ile Gln Gly Leu Arg Ala Met Asp
100 105 110

Thr Gly Leu Tyr Ile Cys Lys Val Glu Leu Met Tyr Pro Pro Pro Tyr
115 120 125

Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile Tyr Val Ile Asp Pro Glu
130 135 140

Pro Cys Pro Asp Ser Asp Gln Glu Pro Lys Ser Ser Asp Lys Thr His
145 150 155 160

Thr Ser Pro Pro Ser Pro Ala Pro Glu Leu Leu Gly Gly Ser Ser Val
165 170 175

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr

180 185 190

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
195 200 205

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
210 215 220

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
225 230 235 240

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
245 250 255

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
260 265 270

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
275 280 285

Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
290 295 300

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
305 310 315 320

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
325 330 335

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
340 345 350

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
355 360 365

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
370 375 380

<210> 9
<211> 636
<212> DNA
<213> Homo Sapiens

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    -25                 -20                 -15

ctc ctg ttt cca agc atg gcg agc atg gca atg cac gtg gcc cag cct       96
Leu Leu Phe Pro Ser Met Ala Ser Met Ala Met His Val Ala Gln Pro
-10                 -5                  -1  1               5

gct gtg gta ctg gcc agc agc cga ggc atc gcc agc ttt gtg tgt gag      144
Ala Val Val Leu Ala Ser Ser Arg Gly Ile Ala Ser Phe Val Cys Glu
            10                  15                  20

tat gca tct cca ggc aaa gcc act gag gtc cgg gtg aca gtg ctt cgg      192
Tyr Ala Ser Pro Gly Lys Ala Thr Glu Val Arg Val Thr Val Leu Arg
        25                  30                  35

cag gct gac agc cag gtg act gaa gtc tgt gcg gca acc tac atg atg      240
Gln Ala Asp Ser Gln Val Thr Glu Val Cys Ala Ala Thr Tyr Met Met
    40                  45                  50

ggg aat gag ttg acc ttc cta gat gat tcc atc tgc acg ggc acc tcc      288
Gly Asn Glu Leu Thr Phe Leu Asp Asp Ser Ile Cys Thr Gly Thr Ser
55                  60                  65                  70

agt gga aat caa gtg aac ctc act atc caa gga ctg agg gcc atg gac      336
Ser Gly Asn Gln Val Asn Leu Thr Ile Gln Gly Leu Arg Ala Met Asp
                75                  80                  85

acg gga ctc tac atc tgc aag gtg gag ctc atg tac cca ccg cca tac      384
Thr Gly Leu Tyr Ile Cys Lys Val Glu Leu Met Tyr Pro Pro Pro Tyr
            90                  95                  100

tac ctg ggc ata ggc aac gga acc cag att tat gta att gat cca gaa      432
Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile Tyr Val Ile Asp Pro Glu
        105                 110                 115

ccg tgc cca gat tct gac ttc ctc ctc tgg atc ctt gca gca gtt agt      480
Pro Cys Pro Asp Ser Asp Phe Leu Leu Trp Ile Leu Ala Ala Val Ser
    120                 125                 130

tcg ggg ttg ttt ttt tat agc ttt ctc ctc aca gct gtt tct ttg agc      528
Ser Gly Leu Phe Phe Tyr Ser Phe Leu Leu Thr Ala Val Ser Leu Ser
135                 140                 145                 150

aaa atg cta aag aaa aga agc cct ctt aca aca ggg gtc tat gtg aaa      576
Lys Met Leu Lys Lys Arg Ser Pro Leu Thr Thr Gly Val Tyr Val Lys
                155                 160                 165
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atg ccc cca aca gag cca gaa tgt gaa aag caa ttt cag cct tat ttt 624
Met Pro Pro Thr Glu Pro Glu Cys Glu Lys Gln Phe Gln Pro Tyr Phe
170 175 180

att ccc atc aat 636
Ile Pro Ile Asn
185

<210> 10
<211> 212
<212> PRT
<213> Homo Sapiens

<400> 10

Met Gly Val Leu Leu Thr Gln Arg Thr Leu Leu Ser Leu Val Leu Ala
-25 -20 -15

Leu Leu Phe Pro Ser Met Ala Ser Met Ala Met His Val Ala Gln Pro
-10 -5 -1 1 5

Ala Val Val Leu Ala Ser Ser Arg Gly Ile Ala Ser Phe Val Cys Glu
10 15 20

Tyr Ala Ser Pro Gly Lys Ala Thr Glu Val Arg Val Thr Val Leu Arg
25 30 35

Gln Ala Asp Ser Gln Val Thr Glu Val Cys Ala Ala Thr Tyr Met Met
40 45 50

Gly Asn Glu Leu Thr Phe Leu Asp Asp Ser Ile Cys Thr Gly Thr Ser
55 60 65 70

Ser Gly Asn Gln Val Asn Leu Thr Ile Gln Gly Leu Arg Ala Met Asp
75 80 85

Thr Gly Leu Tyr Ile Cys Lys Val Glu Leu Met Tyr Pro Pro Pro Tyr
90 95 100

Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile Tyr Val Ile Asp Pro Glu
105 110 115

Pro Cys Pro Asp Ser Asp Phe Leu Leu Trp Ile Leu Ala Ala Val Ser
120 125 130

Ser Gly Leu Phe Phe Tyr Ser Phe Leu Leu Thr Ala Val Ser Leu Ser

135 140 145 150

Lys Met Leu Lys Lys Arg Ser Pro Leu Thr Thr Gly Val Tyr Val Lys
155 160 165

Met Pro Pro Thr Glu Pro Glu Cys Glu Lys Gln Phe Gln Pro Tyr Phe
170 175 180

Ile Pro Ile Asn
185