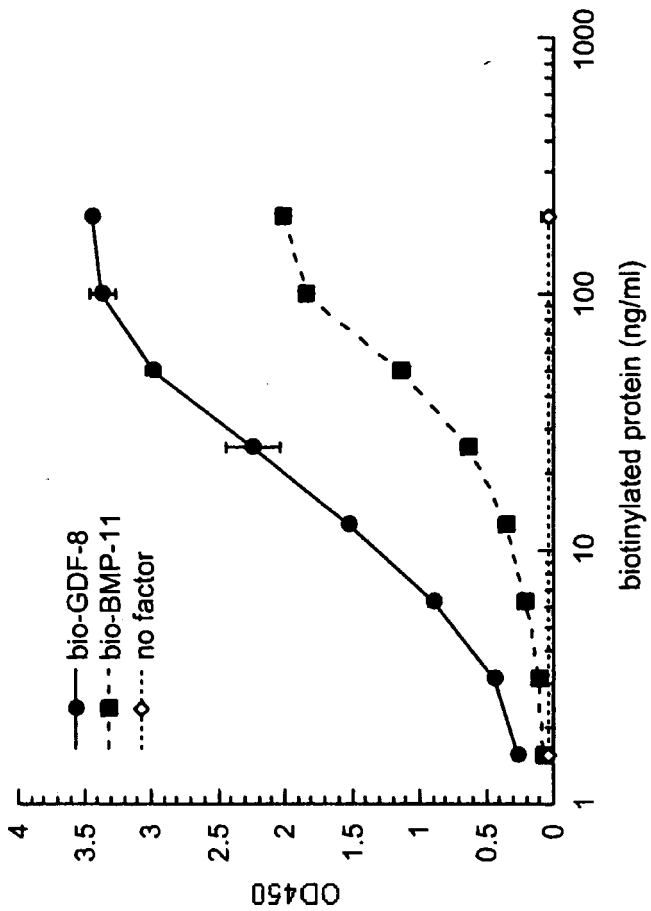

bio-GDF-8
bio-BMP-11
no factor
OD450
4
3.5
3
2.5
2
1.5
1
0.5
0
1
10
100
1000
biotinylated protein (ng/ml)

Fig. 1

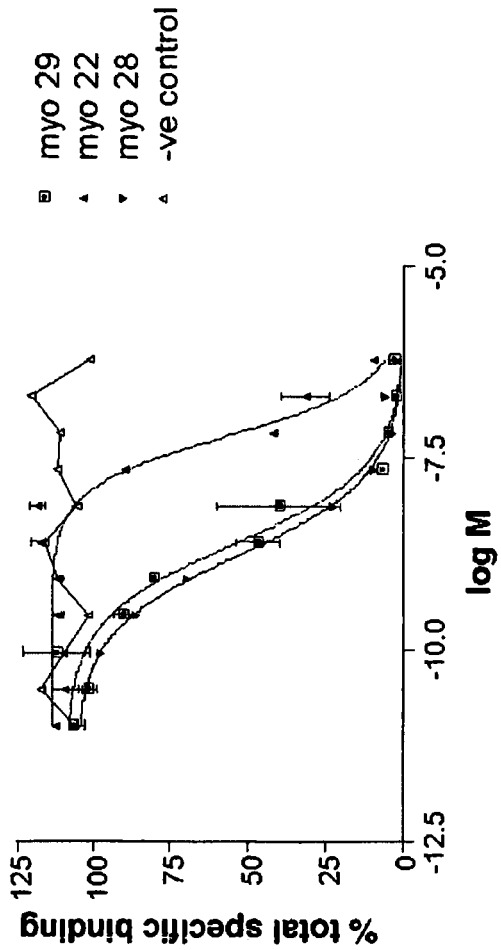

myo 29
myo 22
myo 28
-ve control
% total specific binding
125
100
75
50
25
0
-12.5
-10.0
-7.5
-5.0
log M

Fig. 2

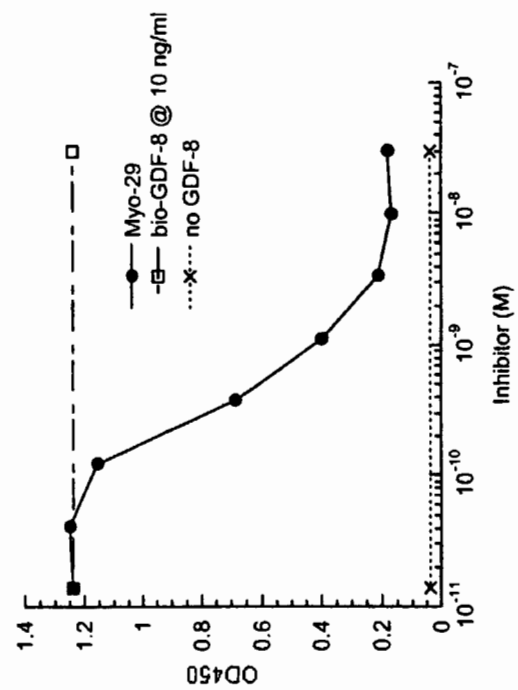

OD450
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Inhibitor (M)
10-11
10-10
10-9
10-8
10-7
Myo-29
bio-GDF-8 @ 10 ng/ml
no GDF-8

FIG. 3A

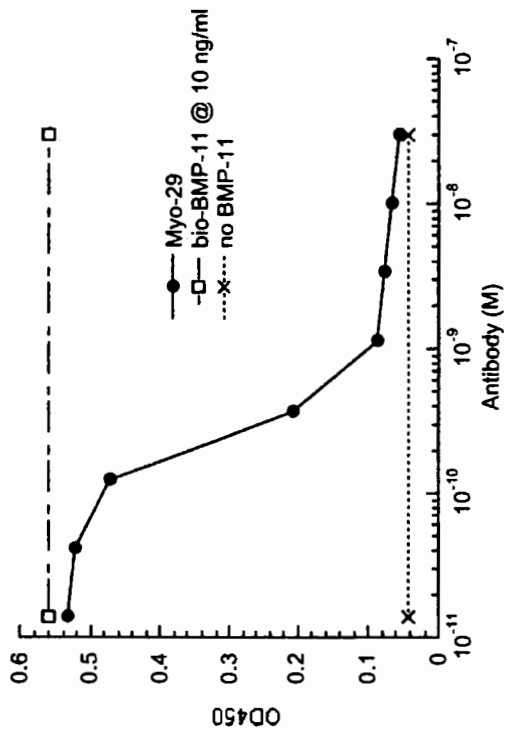

Myo-29
bio-BMP-11 @ 10 ng/ml
no BMP-11
OD450
0.6
0.5
0.4
0.3
0.2
0.1
0
10^{-11}
10^{-10}
10^{-9}
10^{-8}
10^{-7}
Antibody (M)

FIG 3B

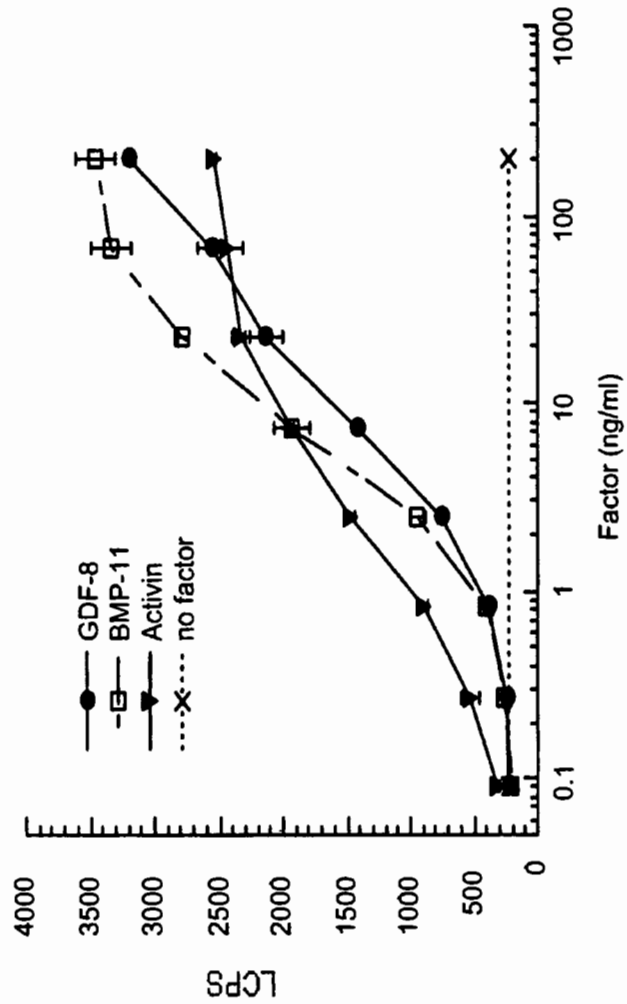

LCPS
4000
3500
3000
2500
2000
1500
1000
500
0
0.1
1
10
100
1000
Factor (ng/ml)
GDF-8
BMP-11
Activin
no factor

Fig. 4A

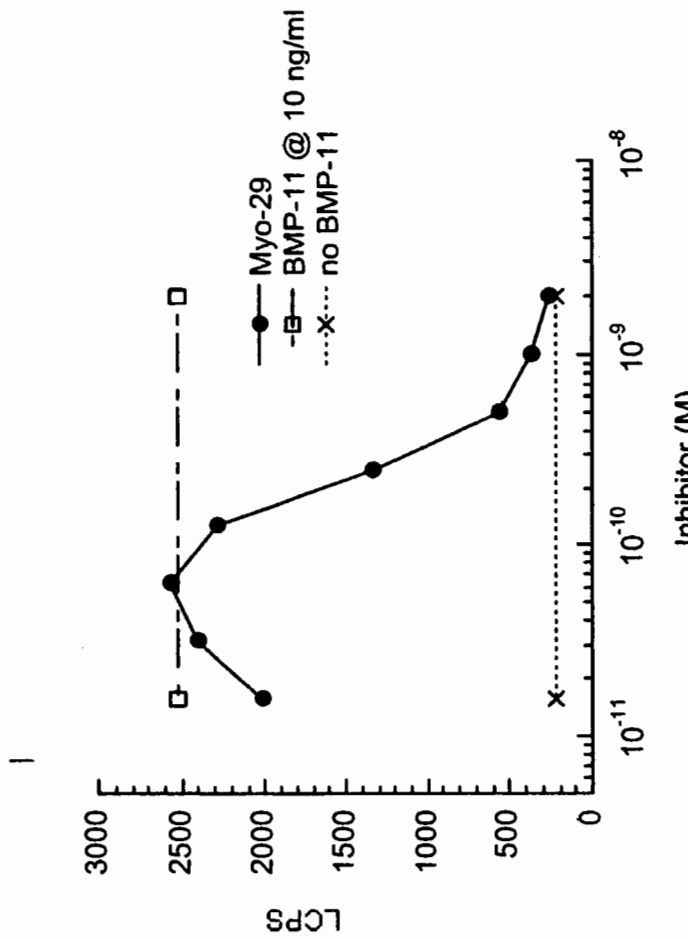

LCPS
3000
2500
2000
1500
1000
500
0
10^{-11}
10^{-10}
10^{-9}
10^{-8}
Inhibitor (M)
Myo-29
BMP-11 @ 10 ng/ml
no BMP-11

Fig. 4B

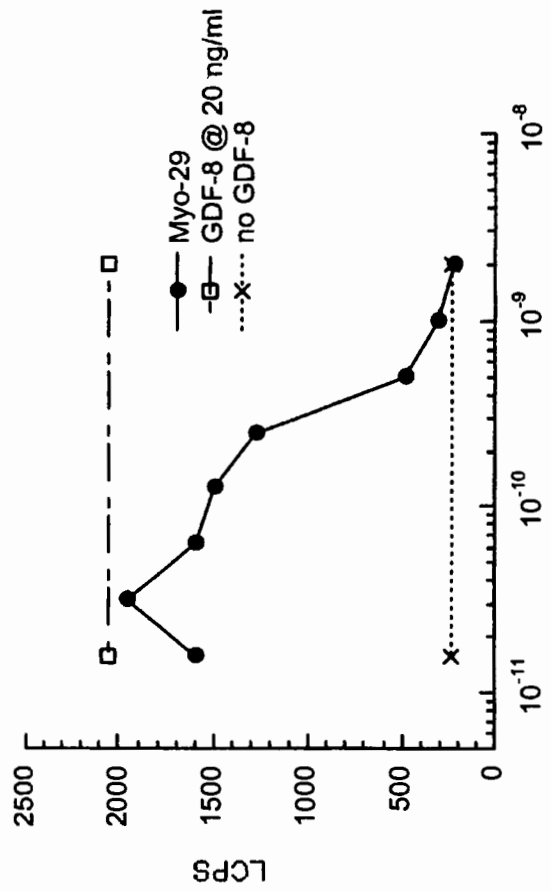

LCPS
2500
2000
1500
1000
500
0
10^{-11}
10^{-10}
10^{-9}
10^{-8}
Inhibitor (M)
Myo-29
GDF-8 @ 20 ng/ml
no GDF-8

Fig. 4C

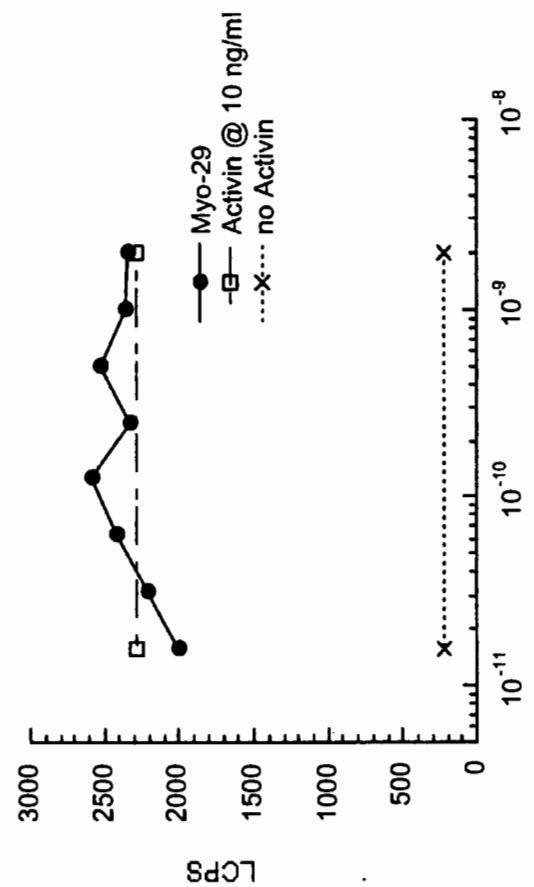

LCPS
3000
2500
2000
1500
1000
500
0
10^{-11}
10^{-10}
10^{-9}
10^{-8}
Inhibitor (M)
Myo-29
Activin @ 10 ng/ml
no Activin

Fig. 4D

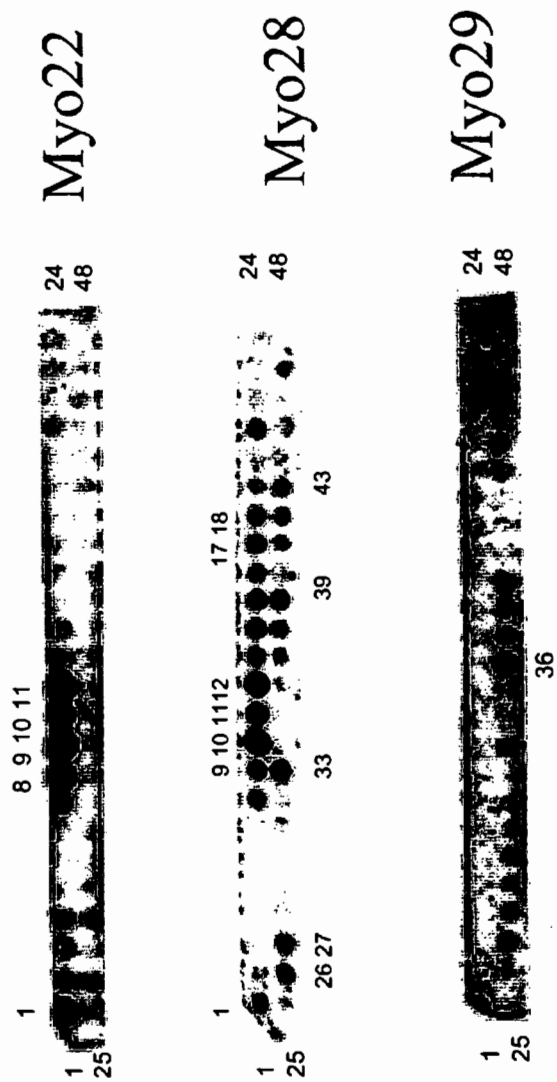

Myo22
Myo28
Myo29
1
8 9 10 11
24
48
1
25
1
9 10 1112
17 18
24
48
43
39
33
26 27
1
25
1
24
48
36
25

Fig. 5

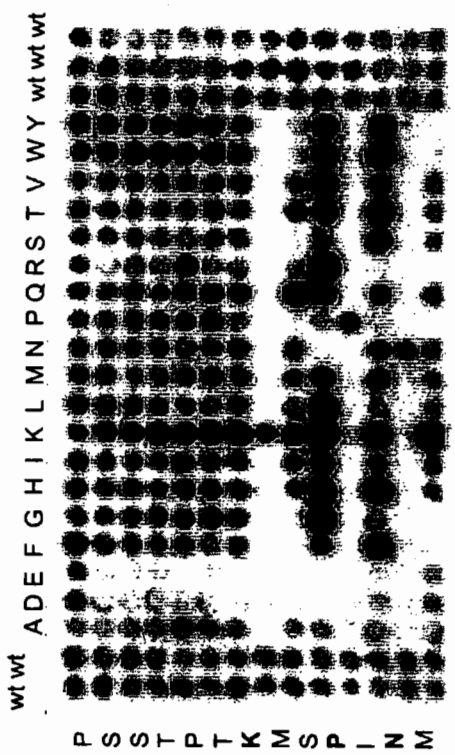


Fig. 6

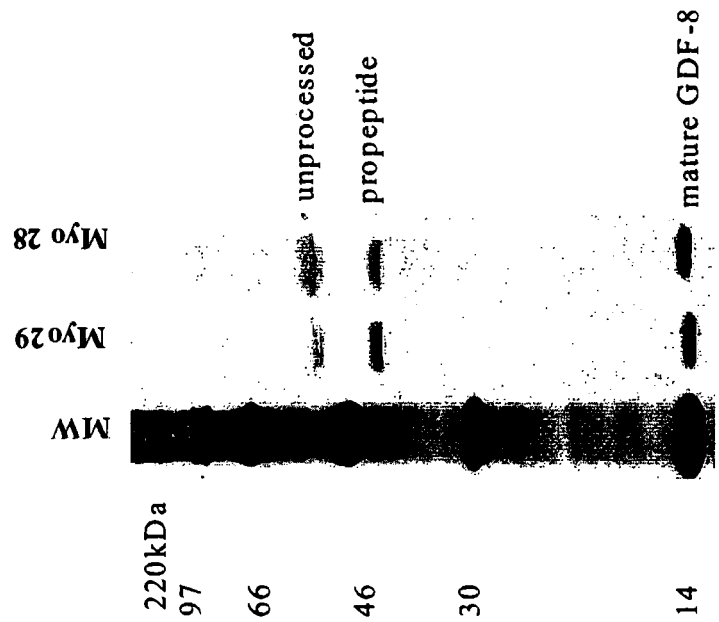

unprocessed
propeptide
mature GDF-8
Myo 28
Myo 29
MW
220kDa
97
66
46
30
14

Fig. 7

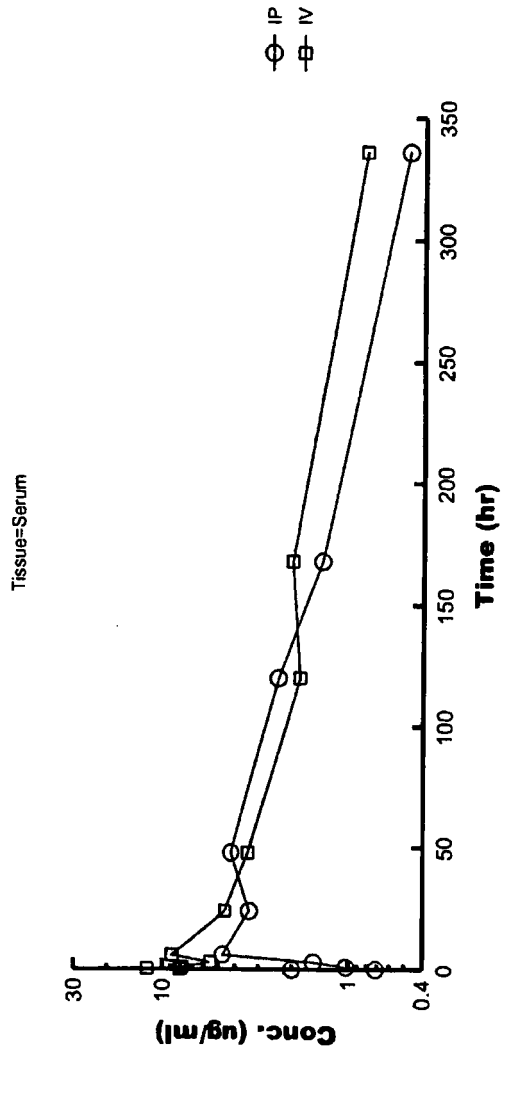

IP
IV
Tissue=Serum
Conc. (ug/ml)
30
10
1
0.4
0
50
100
150
200
250
300
350
Time (hr)

Fig. 8

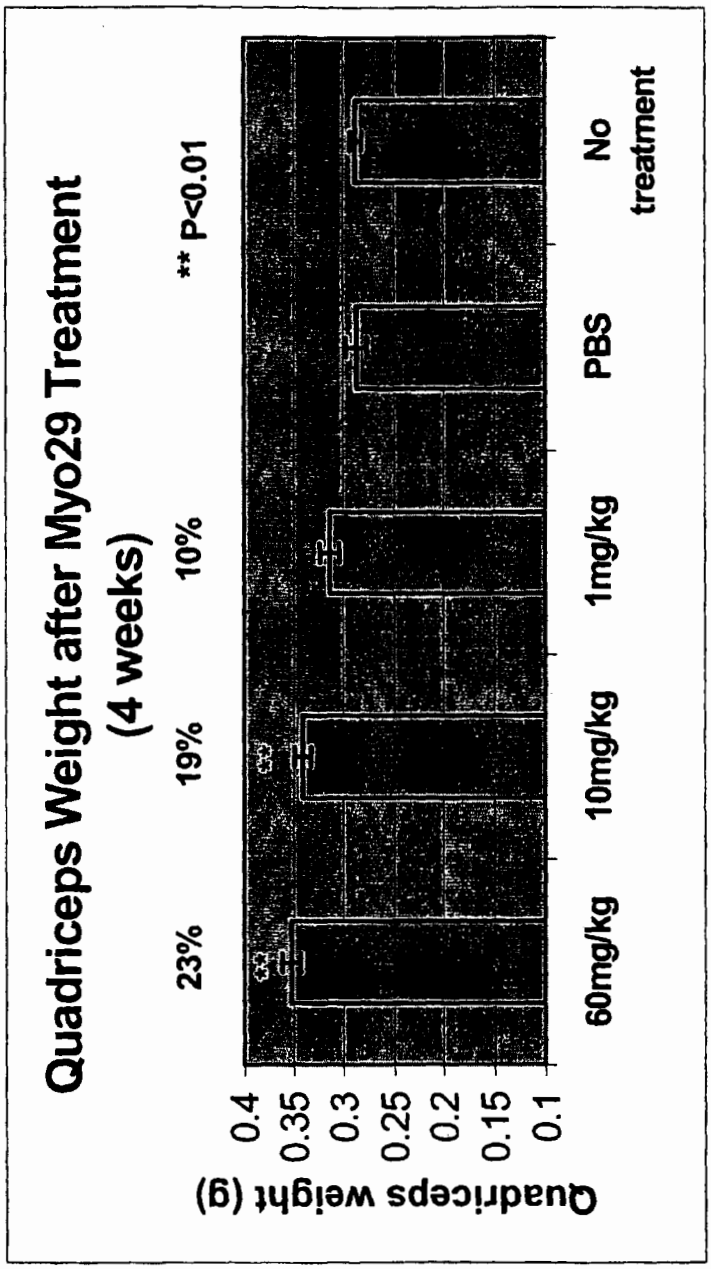

Quadriceps Weight after Myo29 Treatment
(4 weeks)
23%
19%
10%
** P<0.01
Quadriceps weight (g)
0.4
0.35
0.3
0.25
0.2
0.15
0.1
60mg/kg
10mg/kg
1mg/kg
PBS
No treatment

Fig. 9

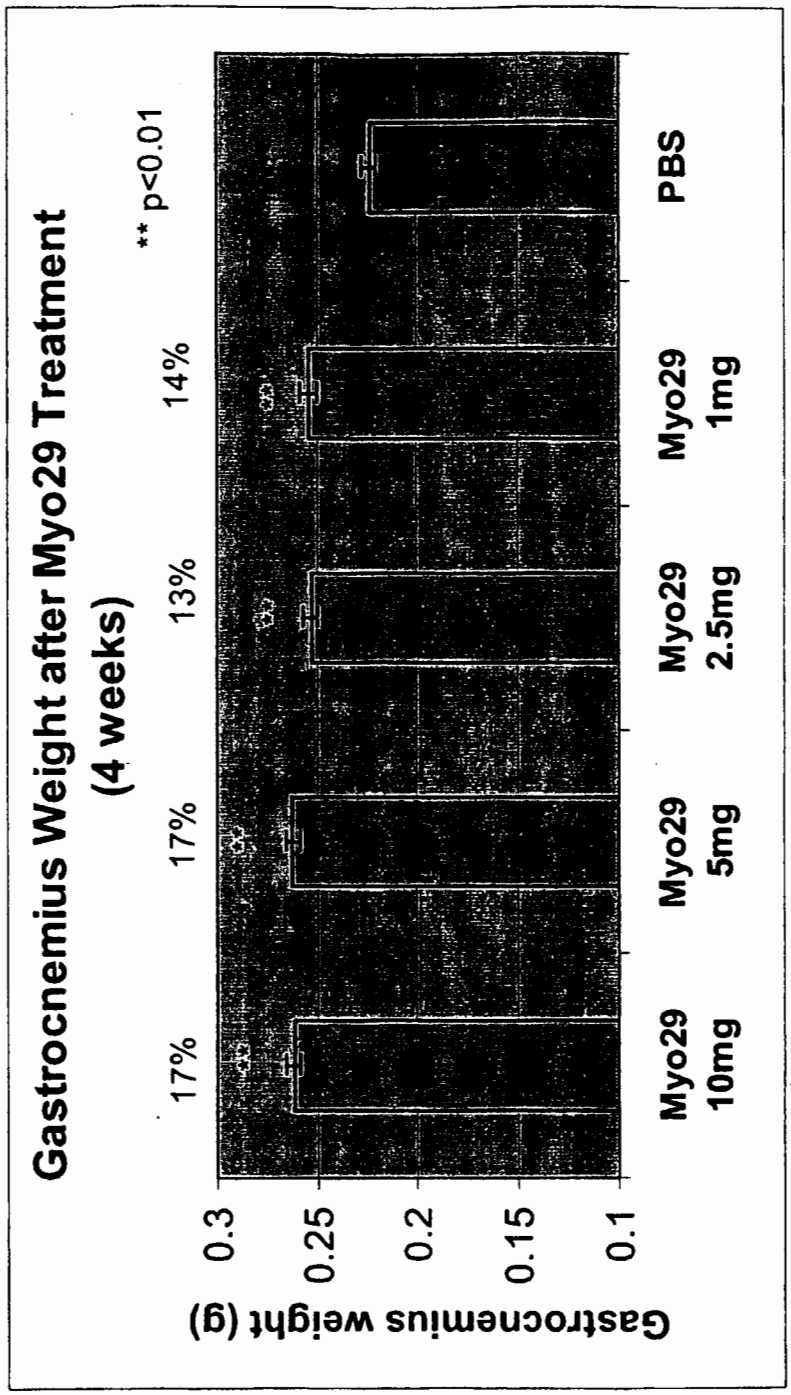

Gastrocnemius Weight after Myo29 Treatment
(4 weeks)
** p<0.01
Gastrocnemius weight (g)
0.3
0.25
0.2
0.15
0.1
17%
17%
13%
14%
Myo29 10mg
Myo29 5mg
Myo29 2.5mg
Myo29 1mg
PBS

FIG. 10A

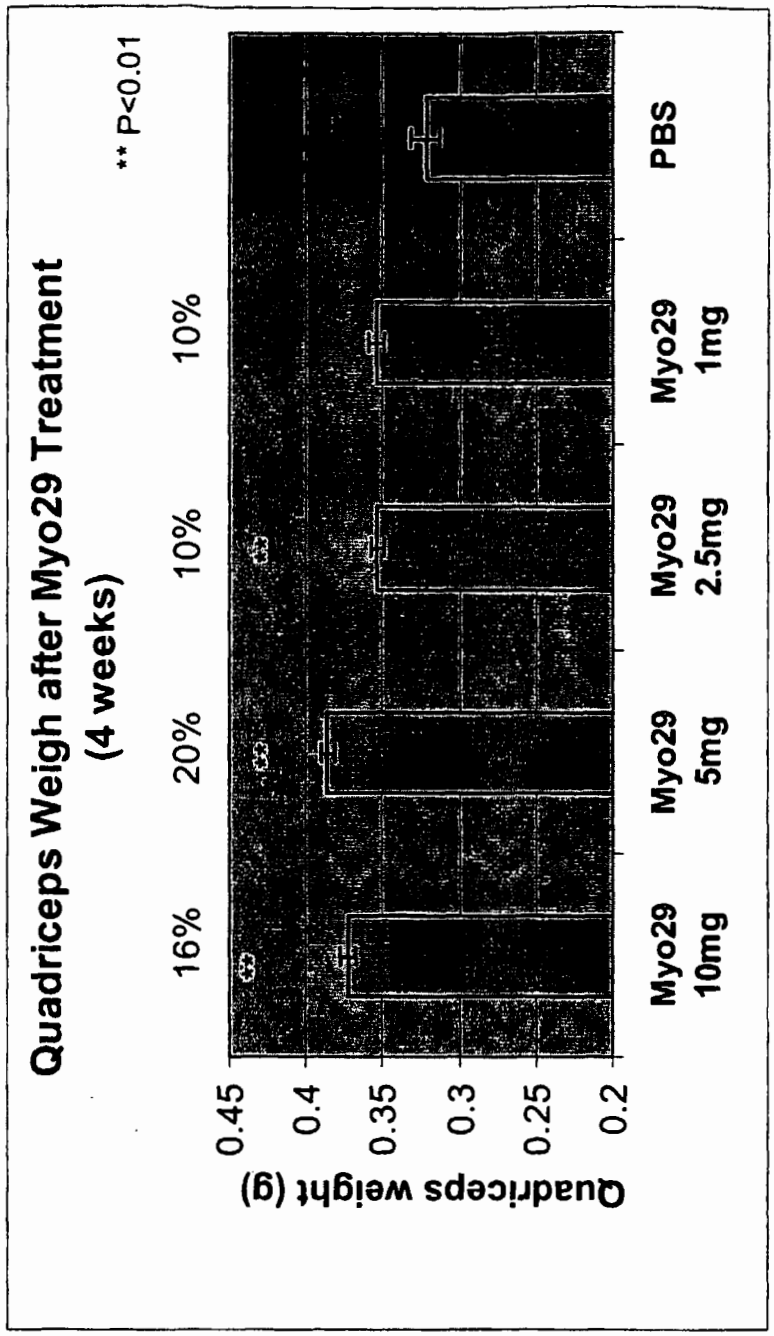

Quadriceps Weigh after Myo29 Treatment
(4 weeks)
** P<0.01
Quadriceps weight (g)
0.45
0.4
0.35
0.3
0.25
0.2
16%
20%
10%
10%
Myo29 10mg
Myo29 5mg
Myo29 2.5mg
Myo29 1mg
PBS

FIG. 10B

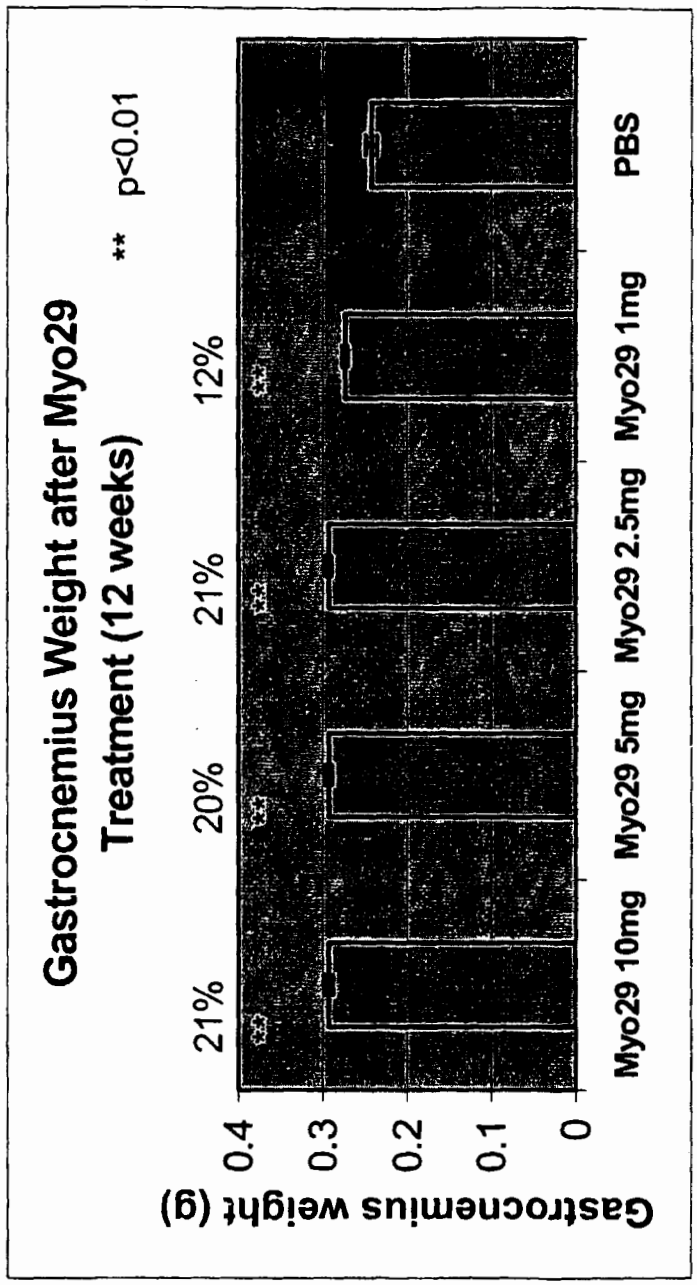

Gastrocnemius Weight after Myo29
Treatment (12 weeks)
** p<0.01
Gastrocnemius weight (g)
0.4
0.3
0.2
0.1
0
21%
20%
21%
12%
Myo29 10mg
Myo29 5mg
Myo29 2.5mg
Myo29 1mg
PBS

FIG. 11A

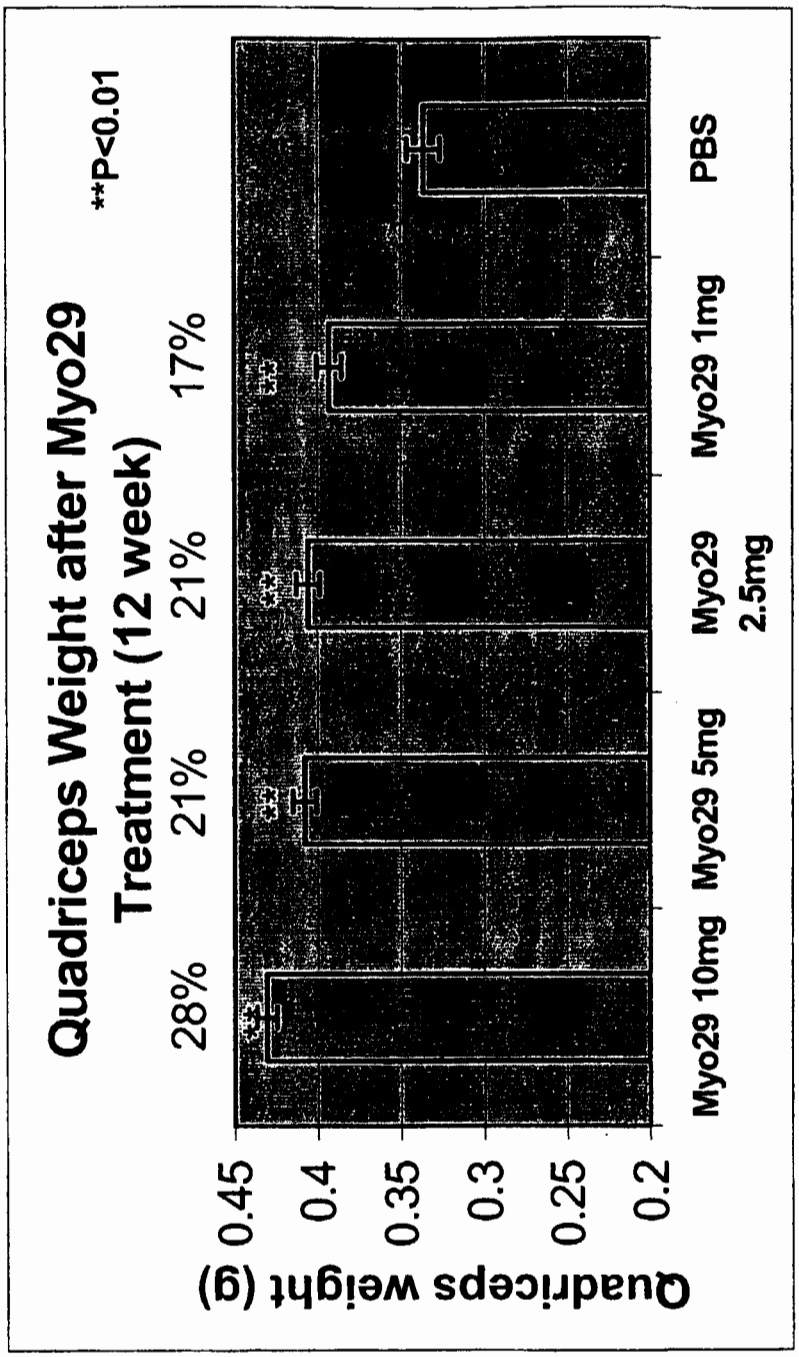

Quadriceps Weight after Myo29 Treatment (12 week)
**P<0.01
28%
21%
21%
17%
Quadriceps weight (g)
0.45
0.4
0.35
0.3
0.25
0.2
Myo29 10mg
Myo29 5mg
Myo29 2.5mg
Myo29 1mg
PBS

FIG. 11B

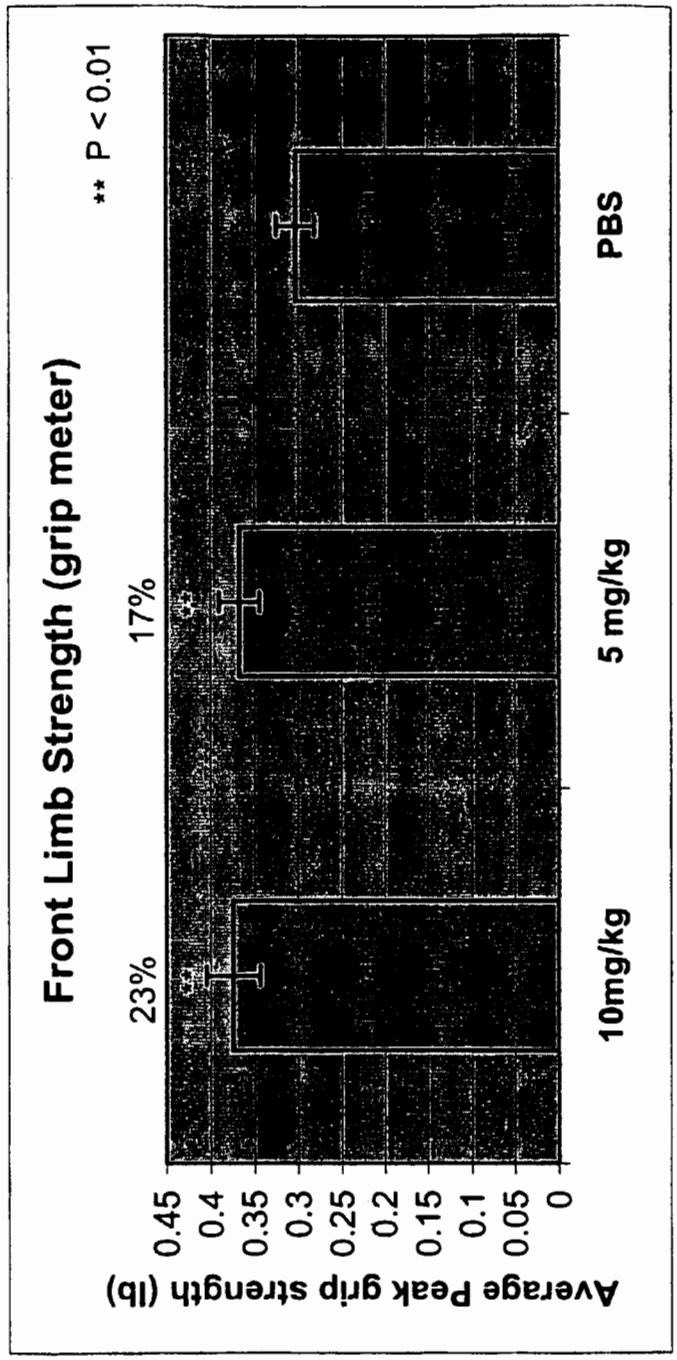

Front Limb Strength (grip meter)
** P < 0.01
23%
17%
Average Peak grip strength (lb)
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
10mg/kg
5 mg/kg
PBS

Fig. 12

SEQUENCE LISTING

<110> Wyeth
Cambridge Antibody Technology

<120> NEUTRALIZING ANTIBODIES AGAINST GDF-8 AND USES THEREFOR

<130> 8702.020-304

<160> 54

<170> PatentIn version 3.1

<210> 1

<211> 786

<212> DNA

<213> Homo sapiens

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ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtga gagaatgggg 300

ccctgtactg gtggaagctg ctacgacacc cttggcaact ggggccgggg caccctggtc 360

accgtctcga gtggaggcgg cggttcaggc ggaggtggct ctggcggtgg cggaagtgca 420

cagtctgtgc tgacgcagcc gccctcagtg tctggggccc cagggcagag ggtcaccatc 480

tcctgcactg ggagcagctc caacatcggg gcaggttatg atgtacactg gtaccagcaa 540

cttccaggcg cggcccccaa actcctcatc aggggtaatg gcaatcggcc ctcaggggtc 600

cctgaccgat tctctgtctc caagtctggc tactcagcct ccctggccat cactgggctg 660

cagcctgccg atgagggtgt ttattactgc cagtcctatg acagcagtct gagtggttcg 720

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catcac 786

<210> 2

<211> 262

<212> PRT

<213> Homo sapiens

<400> 2

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1               5                   10                  15

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

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

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

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr 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

Glu Arg Met Gly Pro Cys Thr Gly Gly Ser Cys Tyr Asp Thr Leu Gly
            100                 105                 110

Asn Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Gln Ser Val Leu
    130                 135                 140

Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln Arg Val Thr Ile
145                 150                 155                 160

Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly Tyr Asp Val His
                165                 170                 175

Trp Tyr Gln Gln Leu Pro Gly Ala Ala Pro Lys Leu Leu Ile Arg Gly
            180                 185                 190

Asn Gly Asn Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Val Ser Lys
        195                 200                 205
```

```
Ser Gly Tyr Ser Ala Ser Leu Ala Ile Thr Gly Leu Gln Pro Ala Asp
    210                 215                 220

Glu Gly Val Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser Leu Ser Gly Ser
225                 230                 235                 240

Lys Val Phe Gly Gln Gly Thr Lys Leu Thr Val Leu Gly Ala Ala Ala
                245                 250                 255

His His His His His His
            260
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<210> 3

<211> 372

<212> DNA

<213> Homo sapiens

<400> 3

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ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac    180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat    240

ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtga gagaatgggg    300

ccctgtactg gtggaagctg ctacgacacc cttggcaact ggggccgggg caccctggtc    360

accgtctcga gt                                                        372
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<210> 4

<211> 124

<212> PRT

<213> Homo sapiens

<400> 4

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Glu Val Gln Leu Leu 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 Thr Phe Ser Ser Tyr
            20                  25                  30

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

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

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr 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

Glu Arg Met Gly Pro Cys Thr Gly Gly Ser Cys Tyr Asp Thr Leu Gly
100 105 110

Asn Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 5

<211> 336

<212> DNA

<213> Homo sapiens

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cttccaggcg cggcccccaa actcctcatc aggggtaatg gcaatcggcc ctcaggggtc 180

cctgaccgat tctctgtctc caagtctggc tactcagcct ccctggccat cactgggctg 240

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aaggtgttcg gccaagggac caagctgacc gtccta 336

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<211> 112

<212> PRT

<213> Homo sapiens

<400> 6

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1 5 10 15

Arg Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly
20 25 30

Tyr Asp Val His Trp Tyr Gln Gln Leu Pro Gly Ala Ala Pro Lys Leu
35 40 45

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

Ser Val Ser Lys Ser Gly Tyr Ser Ala Ser Leu Ala Ile Thr Gly Leu
65 70 75 80

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

Leu Ser Gly Ser Lys Val Phe Gly Gln Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> 7

<211> 774

<212> DNA

<213> Homo sapiens

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ccagggaagg ggctggaatg ggtctcagct attagtgtta ctggtggtag cacggcctac 180

gcagactccg tgaggggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ttgcaaatga atagcctgag agccgaggac acggccgtat attactgtac gaaaggacag 300

tgggaacggg gaagttacta ctttgactac tggggccggg gaaccctggt caccgtctcg 360

agtggaggcg gcggttcagg cggaggtggc tctggcggtg gcggaagtgc acagtctgtg 420

ctgacgcagc cgccctcagt gtctggggcc ccagggcaga gggtcaccat ctcctgcact 480

gggagcagct ccaacatcgg ggacggttat gatgtacact ggtatcagca gcttccagga 540

acagccccca aactcctcat ctatggtaac agtcatcggc cctcaggggt ccctgaccga 600

ttctctggct ccaagtctga cacctctgcc tccctggcca tcactgggct ccaggttgag 660

gatgaggctg attatttctg ccactcctat gacggcagtg tgagtggctg gattttcggc 720

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<210> 8

<211> 258

<212> PRT

<213> Homo sapiens

<400> 8

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Gln Val Thr Leu Lys 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 Thr Phe Ser Arg Tyr
            20                  25                  30

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

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

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr 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

Thr Lys Gly Gln Trp Glu Arg Gly Ser Tyr Tyr Phe Asp Tyr Trp Gly
            100                 105                 110

Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Ala Gln Ser Val Leu Thr Gln Pro
    130                 135                 140

Pro Ser Val Ser Gly Ala Pro Gly Gln Arg Val Thr Ile Ser Cys Thr
145                 150                 155                 160

Gly Ser Ser Ser Asn Ile Gly Asp Gly Tyr Asp Val His Trp Tyr Gln
                165                 170                 175

Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Gly Asn Ser His
            180                 185                 190

Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Asp Thr
        195                 200                 205

Ser Ala Ser Leu Ala Ile Thr Gly Leu Gln Val Glu Asp Glu Ala Asp
    210                 215                 220
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Tyr Phe Cys His Ser Tyr Asp Gly Ser Val Ser Gly Trp Ile Phe Gly
225 230 235 240

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His His

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<211> 363

<212> DNA

<213> Homo sapiens

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ccagggaagg ggctggaatg ggtctcagct attagtgtta ctggtggtag cacggcctac 180

gcagactccg tgaggggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ttgcaaatga atagcctgag agccgaggac acggccgtat attactgtac gaaaggacag 300

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agt 363

<210> 10

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<213> Homo sapiens

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20 25 30

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

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

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr 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

Thr Lys Gly Gln Trp Glu Arg Gly Ser Tyr Tyr Phe Asp Tyr Trp Gly
100 105 110

Arg Gly Thr Leu Val Thr Val Ser Ser
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<210> 11

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<212> DNA

<213> Homo sapiens

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cttccaggaa cagcccccaa actcctcatc tatggtaaca gtcatcggcc ctcaggggtc 180

cctgaccgat tctctggctc caagtctgac acctctgcct ccctggccat cactgggctc 240

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<213> Homo sapiens

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20 25 30

Tyr Asp Val His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu
35 40 45

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

Ser Gly Ser Lys Ser Asp Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu
65 70 75 80

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

Val Ser Gly Trp Ile Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> 13

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<212> DNA

<213> Homo sapiens

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cctggacaag ggcttgagtg gatgggaata atcaacccta gtggtggtag cacaagctac 180

gcacagaagt tccagggcag agtcaccatg accagggaca cgtccacgag cacagtctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagagacgag 300

aactgggggt tcgacccctg gggccaggga accctggtca ccgtctcgag tggaggcggc 360

ggttcaggcg gaggtggctc tggcggtggc ggaagtgcac tttcctatga gctgactcag 420

ccaccctcag tgtccgtgtc tccaggacag acagccacca ttacctgctc tggacatgca 480

ctgggggaca aatttgtttc ctggtatcag cagggatcag gccagtcccc tgtattggtc 540

atctatgacg atacccagcg gccctcaggg atccctgggc gattctctgg ctccaactct 600

gggaacacag ccactctgac catcagcggg acccaggcta tggatgaggc tgactatttt 660

tgtcaggcgt gggacagcag cttcgtattc ggcggaggga ccaaggtcac cgtcctaggt 720

gcggccgcac atcatcatca ccatcac 747

<210> 14

<211> 249

<212> PRT

<213> Homo sapiens

<400> 14

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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 Gly Gly Ser 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

Ala Arg Asp Glu Asn Trp Gly Phe Asp Pro Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Ala Leu Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val
    130                 135                 140

Ser Val Ser Pro Gly Gln Thr Ala Thr Ile Thr Cys Ser Gly His Ala
145                 150                 155                 160

Leu Gly Asp Lys Phe Val Ser Trp Tyr Gln Gln Gly Ser Gly Gln Ser
                165                 170                 175

Pro Val Leu Val Ile Tyr Asp Asp Thr Gln Arg Pro Ser Gly Ile Pro
            180                 185                 190

Gly Arg Phe Ser Gly Ser Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile
        195                 200                 205

Ser Gly Thr Gln Ala Met Asp Glu Ala Asp Tyr Phe Cys Gln Ala Trp
    210                 215                 220

Asp Ser Ser Phe Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu Gly
225                 230                 235                 240
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Ala Ala Ala His His His His His His
245

<210> 15

<211> 351

<212> DNA

<213> Homo sapiens

<400> 15
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tcctgcaagg catctggata caccttcacc agctactata tgcactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaata atcaacccta gtggtggtag cacaagctac 180

gcacagaagt tccagggcag agtcaccatg accagggaca cgtccacgag cacagtctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagagacgag 300

aactgggggt tcgacccctg gggccaggga accctggtca ccgtctcgag t 351

<210> 16

<211> 117

<212> PRT

<213> Homo sapiens

<400> 16

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 Gly Gly Ser 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

Ala Arg Asp Glu Asn Trp Gly Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 17

<211> 315

<212> DNA

<213> Homo sapiens

<400> 17
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acctgctctg gacatgcact gggggacaaa tttgtttcct ggtatcagca gggatcaggc 120

cagtcccctg tattggtcat ctatgacgat acccagcggc cctcagggat ccctgggcga 180

ttctctggct ccaactctgg gaacacagcc actctgacca tcagcgggac ccaggctatg 240

gatgaggctg actatttttg tcaggcgtgg gacagcagct tcgtattcgg cggagggacc 300

aaggtcaccg tccta 315

<210> 18

<211> 105

<212> PRT

<213> Homo sapiens

<400> 18

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

Thr Ala Thr Ile Thr Cys Ser Gly His Ala Leu Gly Asp Lys Phe Val
20 25 30

Ser Trp Tyr Gln Gln Gly Ser Gly Gln Ser Pro Val Leu Val Ile Tyr
35 40 45

Asp Asp Thr Gln Arg Pro Ser Gly Ile Pro Gly Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Met
65 70 75 80

Asp Glu Ala Asp Tyr Phe Cys Gln Ala Trp Asp Ser Ser Phe Val Phe
85 90 95

Gly Gly Gly Thr Lys Val Thr Val Leu
100 105

<210> 19

<211> 774

<212> DNA

<213> Homo sapiens

<400> 19
gaggtccagt tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagt agatatgtca tcaactgggt ccgccaggct 120

ccagggaagg ggctggaatg ggtctcagct attagtgtta ctggtggtag cacggcctac 180

gcagactccg tgaggggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ttgcaaatga atagcctgag agccgaggac acggccgtat attactgtgc gaaaggacag 300

tgggaacggg gaagttacta ctttgactac tggggccggg gaaccctggt caccgtctcg 360

agtggaggcg gcggttcagg cggaggtggc tctggcggtg gcggaagtgc acagtctgtg 420

ctgacgcagc cgccctcagt gtctggggcc ccagggcaga gggtcaccat ctcctgcact 480

gggagcagct ccaacatcgg ggacggttat gatgtacact ggtatcagca gcttccagga 540

acagccccca aactcctcat ctatggtaac agtcatcggc cctcaggggt ccctgaccga 600

ttctctggct ccaagtctgg tacctctgcc tccctggcca tcactgggct ccaggctgag 660

gatgaggctg attattactg ccactcctat gacggcagtg tgagtggctg gattttcggc 720

ggagggacca agctgaccgt cctaggtgcg gccgcacatc atcatcacca tcac 774

<210> 20

<211> 258

<212> PRT

<213> Homo sapiens

<400> 20

Glu Val Gln Leu Leu 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 Thr Phe Ser Arg Tyr
20 25 30

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

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

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr 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 Lys Gly Gln Trp Glu Arg Gly Ser Tyr Tyr Phe Asp Tyr Trp Gly
            100                 105                 110

Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Ala Gln Ser Val Leu Thr Gln Pro
    130                 135                 140

Pro Ser Val Ser Gly Ala Pro Gly Gln Arg Val Thr Ile Ser Cys Thr
145                 150                 155                 160

Gly Ser Ser Ser Asn Ile Gly Asp Gly Tyr Asp Val His Trp Tyr Gln
                165                 170                 175

Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Gly Asn Ser His
            180                 185                 190

Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr
        195                 200                 205

Ser Ala Ser Leu Ala Ile Thr Gly Leu Gln Ala Glu Asp Glu Ala Asp
    210                 215                 220

Tyr Tyr Cys His Ser Tyr Asp Gly Ser Val Ser Gly Trp Ile Phe Gly
225                 230                 235                 240

Gly Gly Thr Lys Leu Thr Val Leu Gly Ala Ala His His His His
                245                 250                 255

His His
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<210> 21

<211> 363

<212> DNA

<213> Homo sapiens

<400> 21
gaggtccagt tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagt agatatgtca tcaactgggt ccgccaggct 120

ccagggaagg ggctggaatg ggtctcagct attagtgtta ctggtggtag cacggcctac 180

gcagactccg tgaggggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ttgcaaatga atagcctgag agccgaggac acggccgtat attactgtgc gaaaggacag 300

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agt 363

<210> 22

<211> 121

<212> PRT

<213> Homo sapiens

<400> 22

Glu Val Gln Leu Leu 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 Thr Phe Ser Arg Tyr
20 25 30

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

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

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr 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 Lys Gly Gln Trp Glu Arg Gly Ser Tyr Tyr Phe Asp Tyr Trp Gly
100 105 110

Arg Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 23

<211> 333

<212> DNA

<213> Homo sapiens

<400> 23
cagtctgtgc tgacgcagcc gccctcagtg tctggggccc cagggcagag ggtcaccatc 60

tcctgcactg ggagcagctc caacatcggg gacggttatg atgtacactg gtatcagcag 120

cttccaggaa cagcccccaa actcctcatc tatggtaaca gtcatcggcc ctcaggggtc 180

cctgaccgat tctctggctc caagtctggt acctctgcct ccctggccat cactgggctc 240

caggctgagg atgaggctga ttattactgc cactcctatg acggcagtgt gagtggctgg 300

attttcggcg gagggaccaa gctgaccgtc cta 333

<210> 24

<211> 111

<212> PRT

<213> Homo sapiens

<400> 24

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

Arg Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Asp Gly
20 25 30

Tyr Asp Val His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu
35 40 45

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

Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys His Ser Tyr Asp Gly Ser
85 90 95

Val Ser Gly Trp Ile Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> 25

<211> 747

<212> DNA

<213> Homo sapiens

<400> 25
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tcctgcaagg catctggata caccttcacc agctactata tgcactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaata atcaacccta gtggtggtag cacaagctac 180

gcacagaagt tccagggcag agtcaccatg accagggaca cgtccacgag cacagtctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagagacgag 300

aactgggggt tcgacccctg gggccaggga accctggtca ccgtctcgag tggaggcggc 360

ggttcaggcg gaggtggctc tggcggtggc ggaagtgcac tttcctatga gctgactcag 420

ccaccctcag tgtccgtgtc tccaggacag acagccagca ttacctgctc tggacatgca 480

ctgggggaca aatttgtttc ctggtatcag cagaagccag gccagtcccc tgtattggtc 540

atctatgacg atacccagcg gccctcaggg atccctgagc gattctctgg ctccaactct 600

gggaacacag ccactctgac catcagcggg acccaggcta tggatgaggc tgactattac 660

tgtcaggcgt gggacagcag cttcgtattc ggcggaggga ccaaggtcac cgtcctaggt 720

gcggccgcac atcaccatca ccatcac 747

<210> 26

<211> 249

<212> PRT

<213> Homo sapiens

<400> 26

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

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Gly Ile Ile Asn Pro Ser Gly Gly Ser 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

Ala Arg Asp Glu Asn Trp Gly Phe Asp Pro Trp Gly Gln Gly Thr Leu
            100                 105                 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Ala Leu Ser Tyr Glu Leu Thr Gln Pro Pro Ser Val
    130                 135                 140

Ser Val Ser Pro Gly Gln Thr Ala Ser Ile Thr Cys Ser Gly His Ala
145                 150                 155                 160

Leu Gly Asp Lys Phe Val Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ser
                165                 170                 175

Pro Val Leu Val Ile Tyr Asp Asp Thr Gln Arg Pro Ser Gly Ile Pro
            180                 185                 190

Glu Arg Phe Ser Gly Ser Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile
        195                 200                 205

Ser Gly Thr Gln Ala Met Asp Glu Ala Asp Tyr Tyr Cys Gln Ala Trp
    210                 215                 220

Asp Ser Ser Phe Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu Gly
225                 230                 235                 240

Ala Ala Ala His His His His His His
                245
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<210> 27

<211> 351

<212> DNA

<213> Homo sapiens

<400> 27
caggtgcagc tggtgcaatc tggggctgag gtgaagaagc ctggggcctc agtgaaggtt 60

tcctgcaagg catctggata caccttcacc agctactata tgcactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggaata atcaacccta gtggtggtag cacaagctac 180

gcacagaagt tccagggcag agtcaccatg accagggaca cgtccacgag cacagtctac 240

atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagagacgag 300

aactgggggt tcgacccctg gggccaggga accctggtca ccgtctcgag t 351

<210> 28

<211> 117

<212> PRT

<213> Homo sapiens

<400> 28

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 Gly Gly Ser 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

Ala Arg Asp Glu Asn Trp Gly Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 29

<211> 315

<212> DNA

<213> Homo sapiens

<400> 29
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acctgctctg gacatgcact gggggacaaa tttgtttcct ggtatcagca gaagccaggc 120

cagtcccctg tattggtcat ctatgacgat acccagcggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacagcc actctgacca tcagcgggac ccaggctatg 240

gatgaggctg actattactg tcaggcgtgg gacagcagct tcgtattcgg cggagggacc 300

aaggtcaccg tccta 315

<210> 30

<211> 105

<212> PRT

<213> Homo sapiens

<400> 30

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

Thr Ala Ser Ile Thr Cys Ser Gly His Ala Leu Gly Asp Lys Phe Val
20 25 30

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

Asp Asp Thr Gln Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Met
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Ala Trp Asp Ser Ser Phe Val Phe
85 90 95

Gly Gly Gly Thr Lys Val Thr Val Leu
100 105

<210> 31

<211> 5

<212> PRT

<213> Homo sapiens

<400> 31

Ser Tyr Tyr Met His
1 5

<210> 32

<211> 17

<212> PRT

<213> Homo sapiens

<400> 32

Ile Ile Asn Pro Ser Gly Gly Ser Thr Ser Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 33

<211> 8

<212> PRT

<213> Homo sapiens

<400> 33

Asp Glu Asn Trp Gly Phe Asp Pro
1 5

<210> 34

<211> 11

<212> PRT

<213> Homo sapiens

<400> 34

Ser Gly His Ala Leu Gly Asp Lys Phe Val Ser
1 5 10

<210> 35

<211> 7

<212> PRT

<213> Homo sapiens

<400> 35

Asp Asp Thr Gln Arg Pro Ser
1 5

<210> 36

<211> 7

<212> PRT

<213> Homo sapiens

<400> 36

Gln Ala Trp Asp Ser Ser Phe
1 5

<210> 37

<211> 5

<212> PRT

<213> Homo sapiens

<400> 37

Arg Tyr Val Ile Asn
1 5

<210> 38

<211> 17

<212> PRT

<213> Homo sapiens

<400> 38

Ala Ile Ser Val Thr Gly Gly Ser Thr Ala Tyr Ala Asp Ser Val Arg
1 5 10 15

Gly

<210> 39

<211> 12

<212> PRT

<213> Homo sapiens

<400> 39

Gly Gln Trp Glu Arg Gly Ser Tyr Tyr Phe Asp Tyr
1 5 10

<210> 40

<211> 14

<212> PRT

<213> Homo sapiens

<400> 40

Thr Gly Ser Ser Ser Asn Ile Gly Asp Gly Tyr Asp Val His
1 5 10

<210> 41

<211> 7

<212> PRT

<213> Homo sapiens

<400> 41

Gly Asn Ser His Arg Pro Ser
1 5

<210> 42

<211> 6

<212> PRT

<213> Homo sapiens

<400> 42

His Ser Tyr Asp Gly Ser
1 5

<210> 43

<211> 5

<212> PRT

<213> Homo sapiens

<400> 43

Ser Tyr Ala Met Ser
1 5

<210> 44

<211> 17

<212> PRT

<213> Homo sapiens

<400> 44

Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 45

<211> 15

<212> PRT

<213> Homo sapiens

<400> 45

Met Gly Pro Cys Thr Gly Gly Ser Cys Tyr Asp Thr Leu Gly Asn
1 5 10 15

<210> 46

<211> 14

<212> PRT

<213> Homo sapiens

<400> 46

Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly Tyr Asp Val His
1 5 10

<210> 47

<211> 7

<212> PRT

<213> Homo sapiens

<400> 47

Gly Asn Gly Asn Arg Pro Ser
1 5

<210> 48

<211> 12

<212> PRT

<213> Homo sapiens

<400> 48

Gln Ser Tyr Asp Ser Ser Leu Ser Gly Ser Lys Val
1 5 10

<210> 49

<211> 109

<212> PRT

<213> Homo sapiens

<400> 49

Asp Phe Gly Leu Asp Cys Asp Glu His Ser Thr Glu Ser Arg Cys Cys
1 5 10 15

Arg Tyr Pro Leu Thr Val Asp Phe Glu Ala Phe Gly Trp Asp Trp Ile
20 25 30

Ile Ala Pro Lys Arg Tyr Lys Ala Asn Tyr Cys Ser Gly Glu Cys Glu
35 40 45

Phe Val Phe Leu Gln Lys Tyr Pro His Thr His Leu Val His Gln Ala
50 55 60

Asn Pro Arg Gly Ser Ala Gly Pro Cys Cys Thr Pro Thr Lys Met Ser
65 70 75 80

Pro Ile Asn Met Leu Tyr Phe Asn Gly Lys Glu Gln Ile Ile Tyr Gly
85 90 95

Lys Ile Pro Ala Met Val Val Asp Arg Cys Gly Cys Ser
100 105

<210> 50

<211> 320

<212> DNA

<213> Homo sapiens

<400> 50
gtcagcccaa ggctgccccc tcggtcactc tgttcccgcc ctcctctgag gagcttcaag 60

ccaacaaggc cacactggtg tgtctcataa gtgacttcta cccgggagcc gtgacagtgg 120

cctggaaggc agatagcagc cccgtcaagg cgggagtgga gaccaccaca ccctccaaac 180

aaagcaacaa caagtacgcg gccagcagct atctgagcct gacgcctgag cagtggaagt 240

cccacagaag ctacagctgc caggtcacgc atgaagggag caccgtggag aagacagtgg 300

cccctacaga atgttcatag 320

<210> 51

<211> 106

<212> PRT

<213> Homo sapiens

<400> 51

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

Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp
20 25 30

Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro
35 40 45

Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn
50 55 60

Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys
65 70 75 80

Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val
85 90 95

Glu Lys Thr Val Ala Pro Thr Glu Cys Ser
100 105

<210> 52

<211> 992

<212> DNA

<213> Homo sapiens

<400> 52
cctccaccaa gggcccatcg gtcttccccc tggcaccctc ctccaagagc acctctgggg 60

gcacagcggc cctgggctgc ctggtcaagg actacttccc cgaaccggtg acggtgtcgt 120

ggaactcagg cgccctgacc agcggcgtgc acaccttccc ggctgtccta cagtcctcag 180

gactctactc cctcagcagc gtggtgaccg tgccctccag cagcttgggc acccagacct 240

acatctgcaa cgtgaatcac aagcccagca acaccaaggt ggacaagaaa gttgagccca 300

aatcttgtga caaaactcac acatgcccac cgtgcccagc acctgaactc ctgggggggac 360

cgtcagtctt cctcttcccc ccaaaaccca aggacaccct catgatctcc cggacccctg 420

aggtcacatg cgtggtggtg gacgtgagcc acgaagaccc tgaggtcaag ttcaactggt 480

acgtggacgg cgtggaggtg cataatgcca agacaaagcc gcgggaggag cagtacaaca 540

gcacgtaccg tgtggtcagc gtcctcaccg tcctgcacca ggactggctg aatggcaagg 600

agtacaagtg caaggtctcc aacaaagccc tcccagcccc catcgagaaa accatctcca 660

aagccaaagg gcagccccga gaaccacagg tgtacaccct gcccccatcc cgggaggaga 720

tgaccaagaa ccaggtcagc ctgacctgcc tggtcaaagg cttctatccc agcgacatcg 780

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agaagagcct ctccctgtcc ccgggtaaat ga 992

<210> 53

<211> 330

<212> PRT

<213> Homo Sapiens

<400> 53

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Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1               5                  10                  15

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220
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Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225                 230                 235                 240

Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
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Lys Xaa Xaa Pro Xaa Asn
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