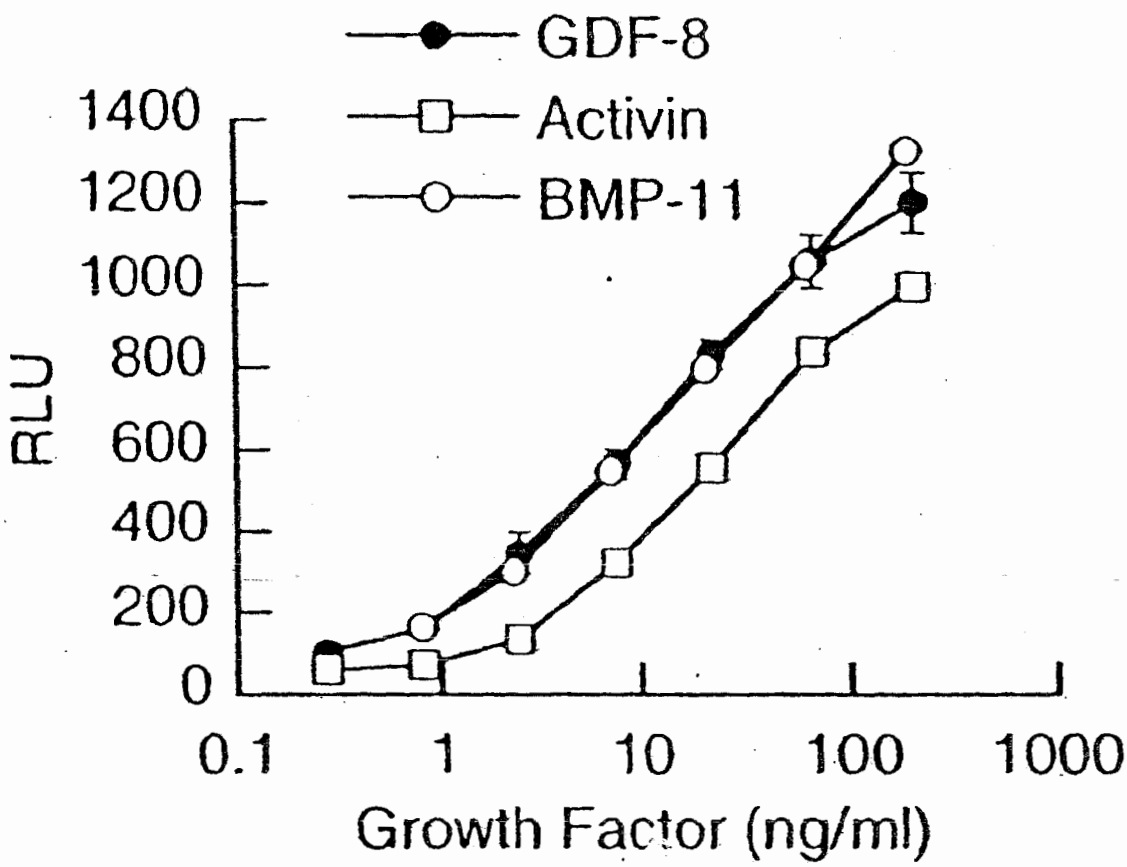

GDF-8
Activin
BMP-11
1400
1200
1000
800
600
400
200
0
RLU
0.1
1
10
100
1000
Growth Factor (ng/ml)

Fig. 1

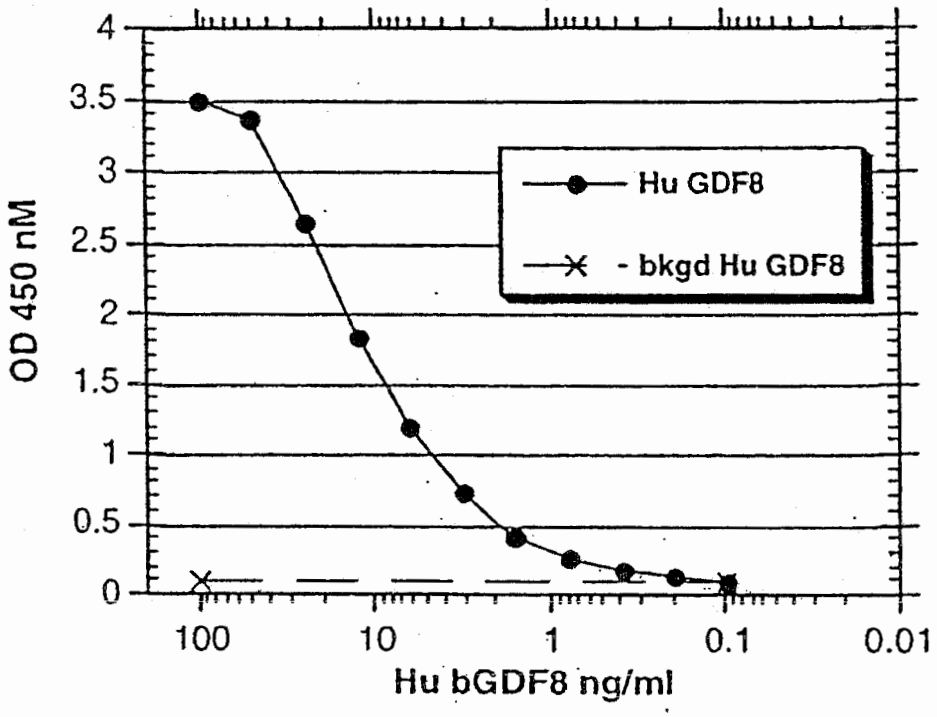

4
3.5
3
2.5
2
1.5
1
0.5
0
OD 450 nM
Hu GDF8
- bkgd Hu GDF8
100
10
1
0.1
0.01
Hu bGDF8 ng/ml

Fig. 2

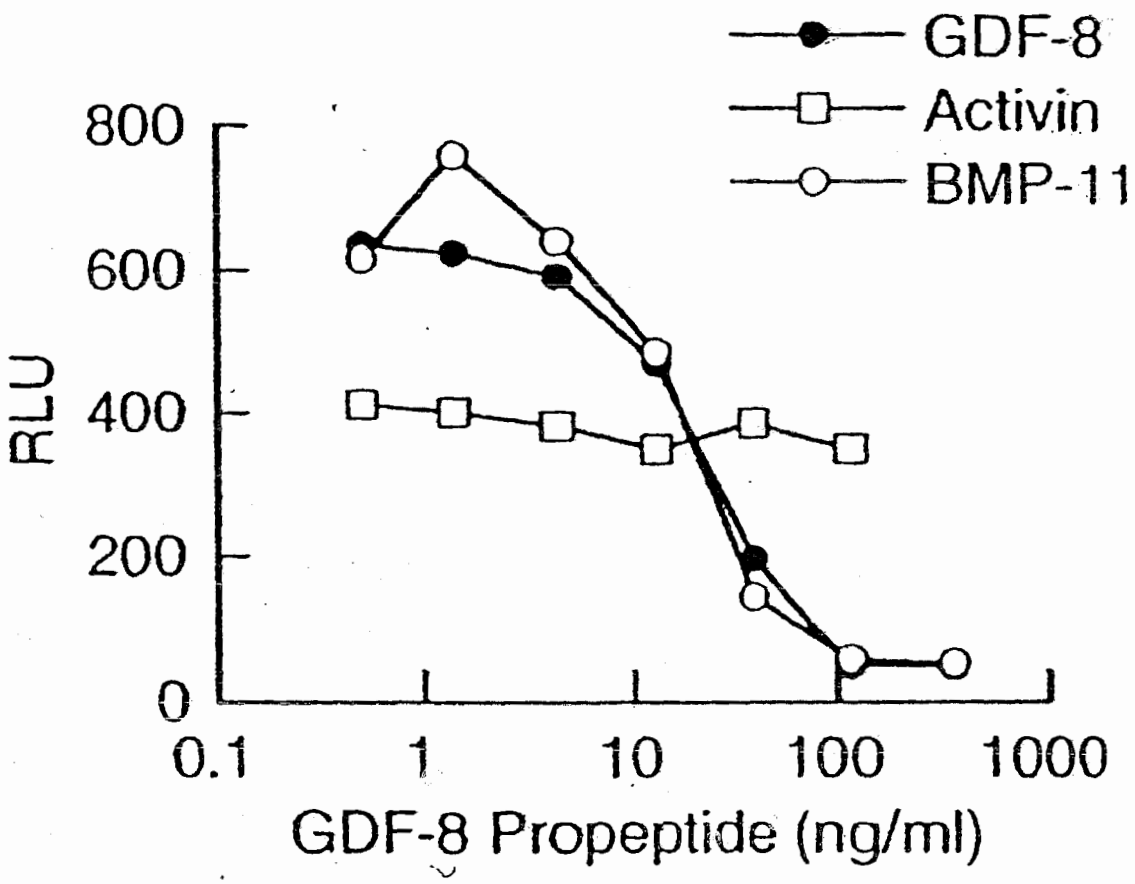

GDF-8
Activin
BMP-11
800
600
400
200
0
RLU
0.1
1
10
100
1000
GDF-8 Propeptide (ng/ml)

Fig. 3

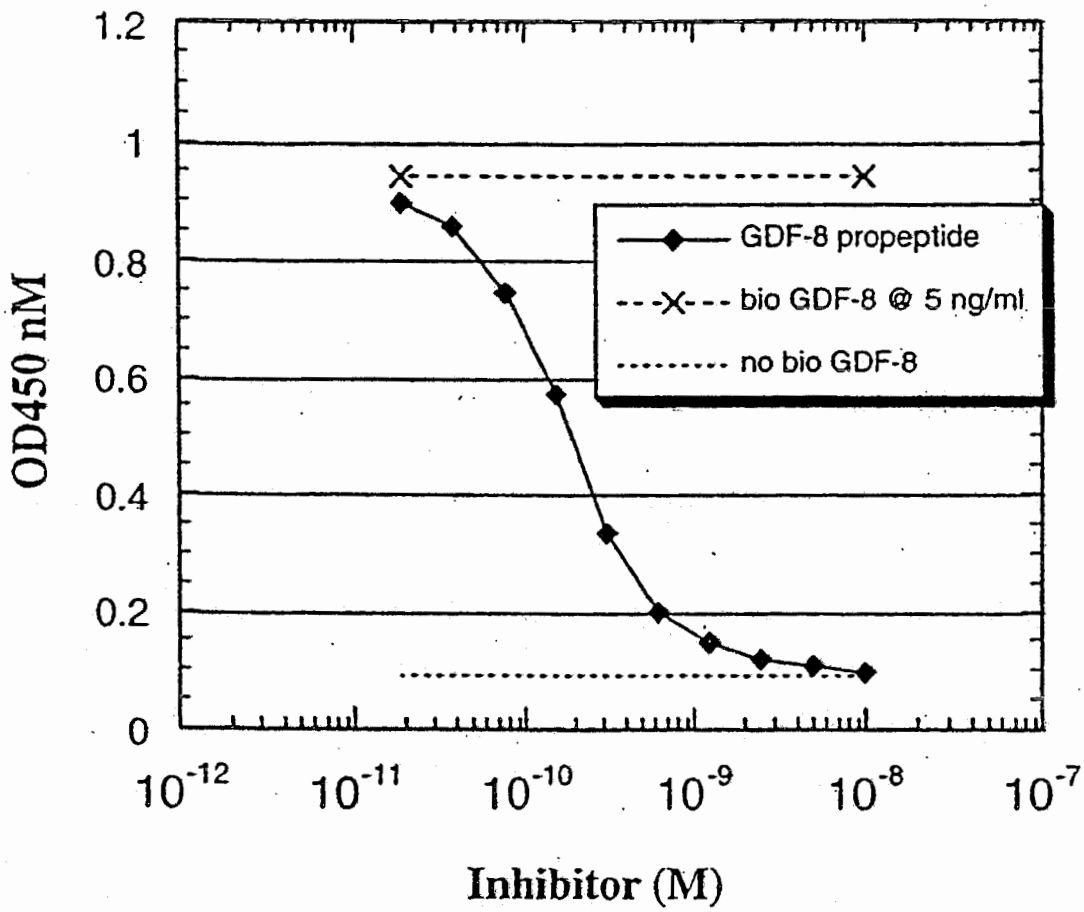

1.2
1
0.8
0.6
0.4
0.2
0
OD450 nM
GDF-8 propeptide
bio GDF-8 @ 5 ng/ml
no bio GDF-8
10-12
10-11
10-10
10-9
10-8
10-7
Inhibitor (M)

Fig. 4

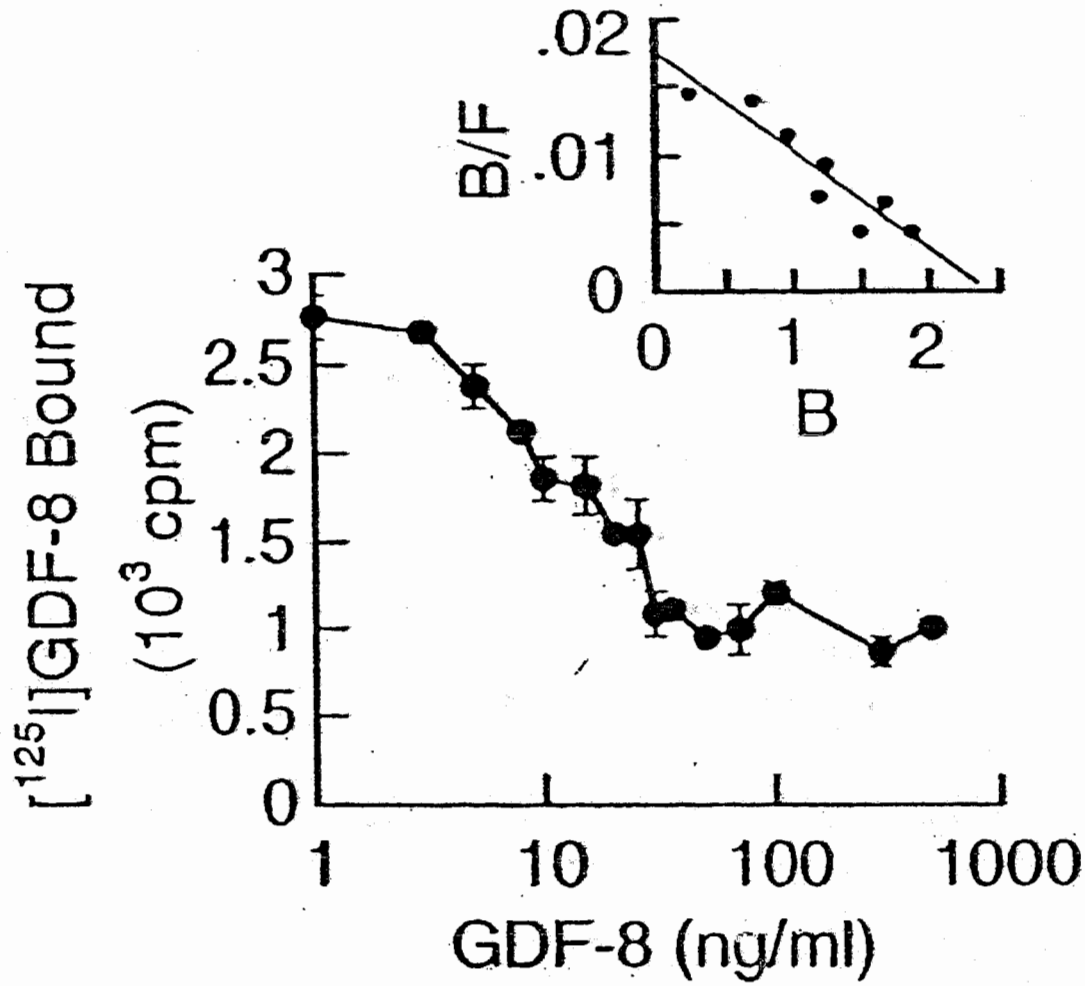

[125I]GDF-8 Bound
(10^3 cpm)
3
2.5
2
1.5
1
0.5
0
1
10
100
1000
GDF-8 (ng/ml)
B/F
.02
.01
0
0
1
2
B

Fig. 5

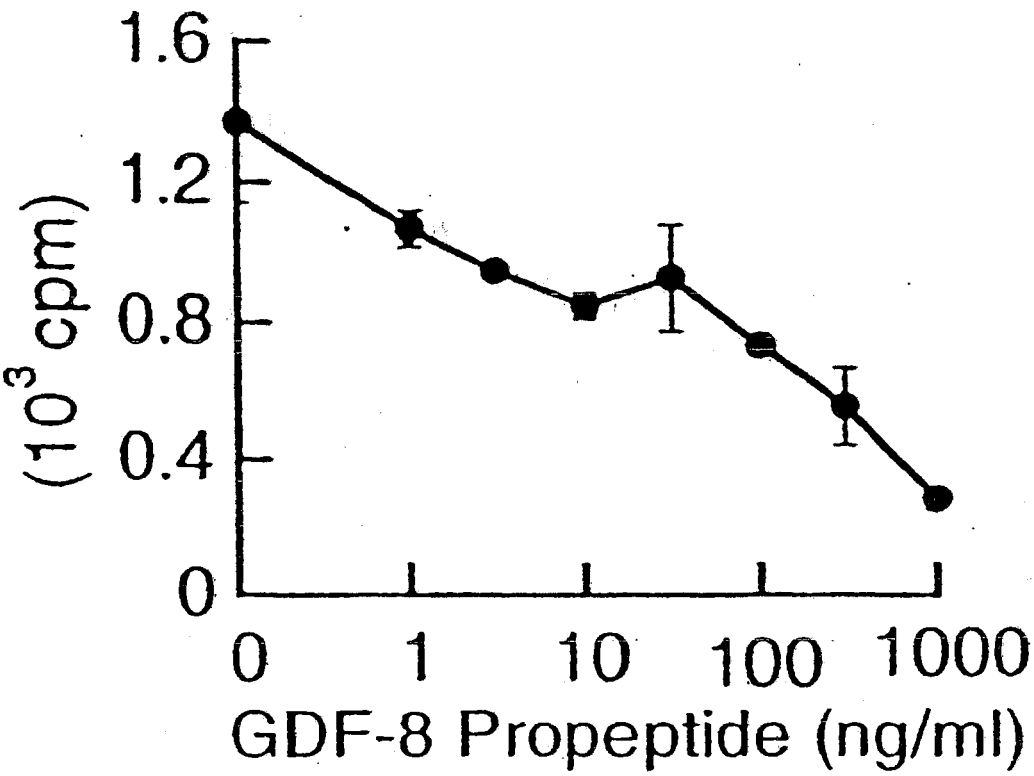
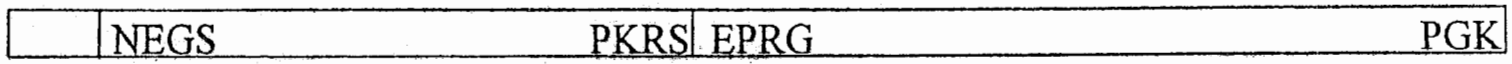


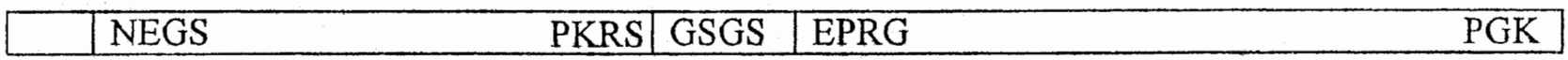
Fig. 6



Secretory leader Mu GDF-8 propeptide Mu IgG2a Fc

MMQKLQMYVYIYLFMLIAAGPVDLNEGSEREENVEKEGLCNACAWRQNTRYSRIEAIKIQILSKLRLET
APNISKDAIRQLLPRAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIITMPTESDFLMQADGKPKC
CFFKFSSKIQYNKVVKAQLWIYLRPVKTPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMSPGTGIWQSI
DVKTVLQNWLKQPESNLGIEIKALDENGHDLAVTFPGPGEDGLNPFLEVKVTDTPKRS**EPRGPTIKPCP**
PCKCPAPNLEGGPSVFIFPPKIKDVLMISLSPIVTCVVVDVSEDDPDVQISWFVNNVEVHTAQTQTHRE
DYNSTLRVVSALPIQHQDWMSGKAFACAVNNKDLPAPIERTISKPKGSVRAPQVYVLPPPEEEMTKKQV
TLTCMVTDFMPEDIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVVHEGL
HNHHTTKSFSRTPGK

Fig. 7A



Secretory leader Mu GDF-8 propeptide Mu IgG2a Fc

MMQKLQMYVYIYLFMLIAAGPVDLNEGSEREENVEKEGLCNACAWRQNTRYSRIEAIKIQILSKLRLET
APNISKDAIRQLLPRAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIITMPTESDFLMQADGKPKC
CFFKFSSKIQYNKVVKAQLWIYLRPVKTPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMSPGTGIWQSI
DVKTVLQNWLKQPESNLGIEIKALDENGHDLAVTFPGPGEDGLNPFLEVKVTDTPKRSGSGS**EPRGPTI**
KPCPPCKCPAPNLEGGPSVFIFPPKIKDVLMISLSPIVTCVVVDVSEDDPDVQISWFVNNVEVHTAQTQ
THREDYNSTLRVVSALPIQHQDWMSGKAFACAVNNKDLPAPIERTISKPKGSVRAPQVYVLPPPEEEMT
KKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVV
HEGLHNHHTTKSFSRTPGK

Fig. 7B

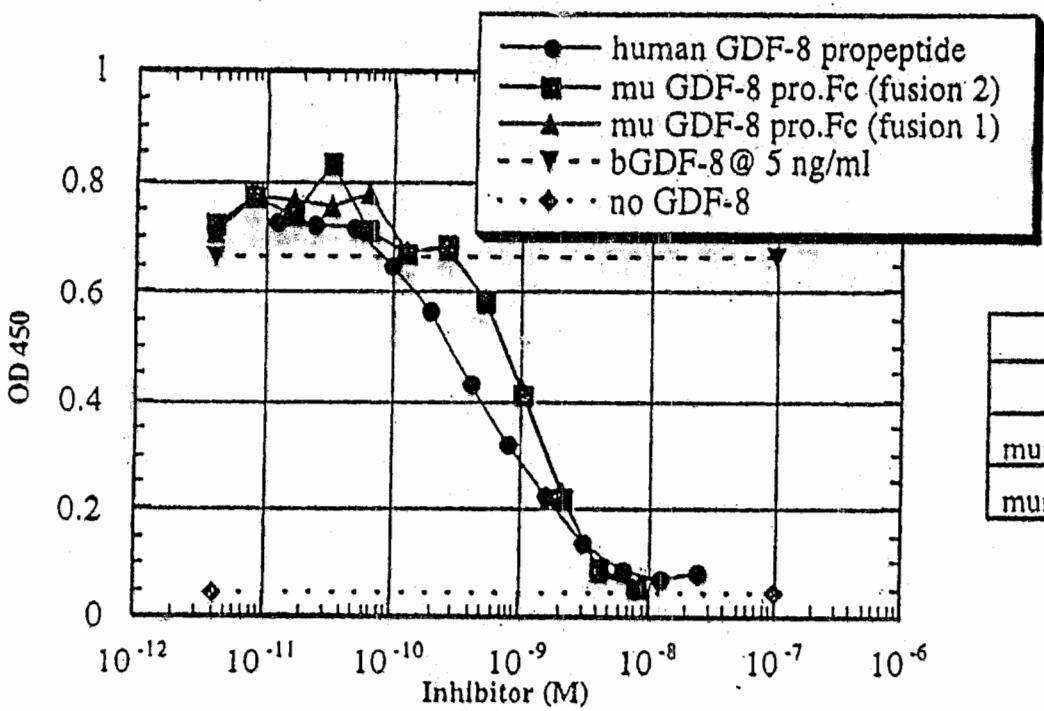


Fig. 8 A

Inhibitor	IC50 (M)
hu GDF-8 propeptide	6 x 10-10
murine GDF-8 pro.Fc (Fusion 1)	1.3 x 10-9
murine GDF-8 pro.Fc (Fusion 2)	1.3 x 10-9

Fig. 8 B

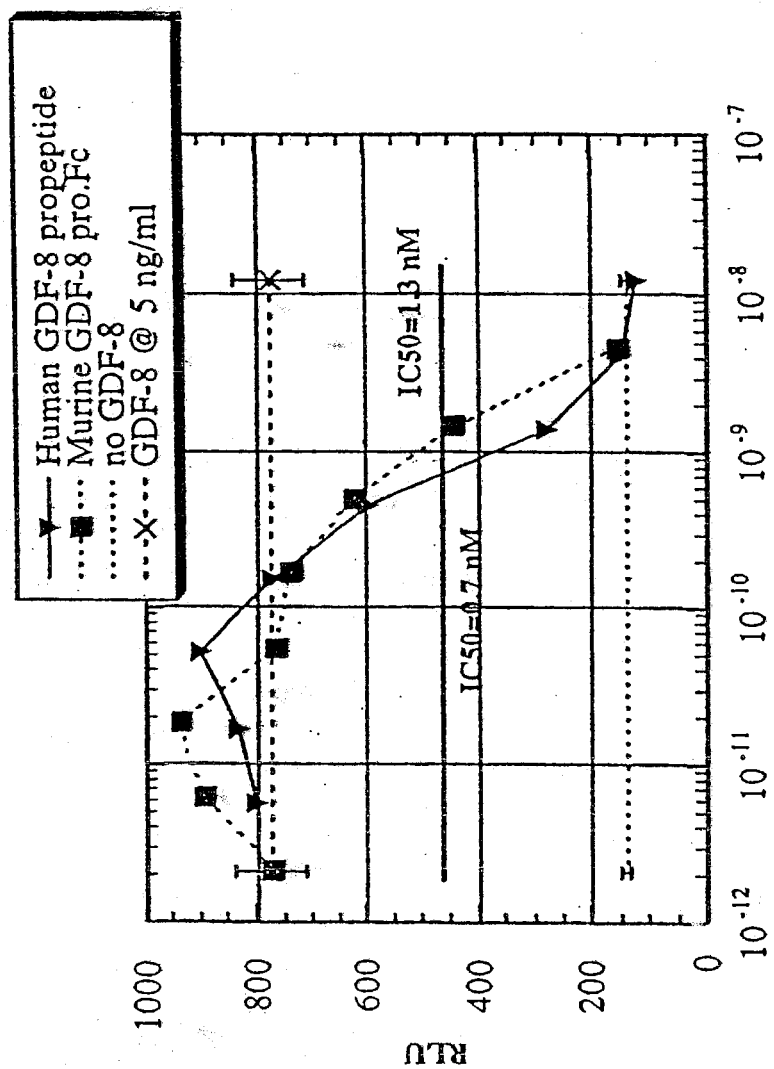

Human GDF-8 propeptide
Murine GDF-8 pro.Fc
no GDF-8
GDF-8 @ 5 ng/ml
IC50=1.3 nM
IC50=0.7 nM
RLU
1000
800
600
400
200
0
10^{-12}
10^{-11}
10^{-10}
10^{-9}
10^{-8}
10^{-7}
Inhibitor (M)

Fig. 9

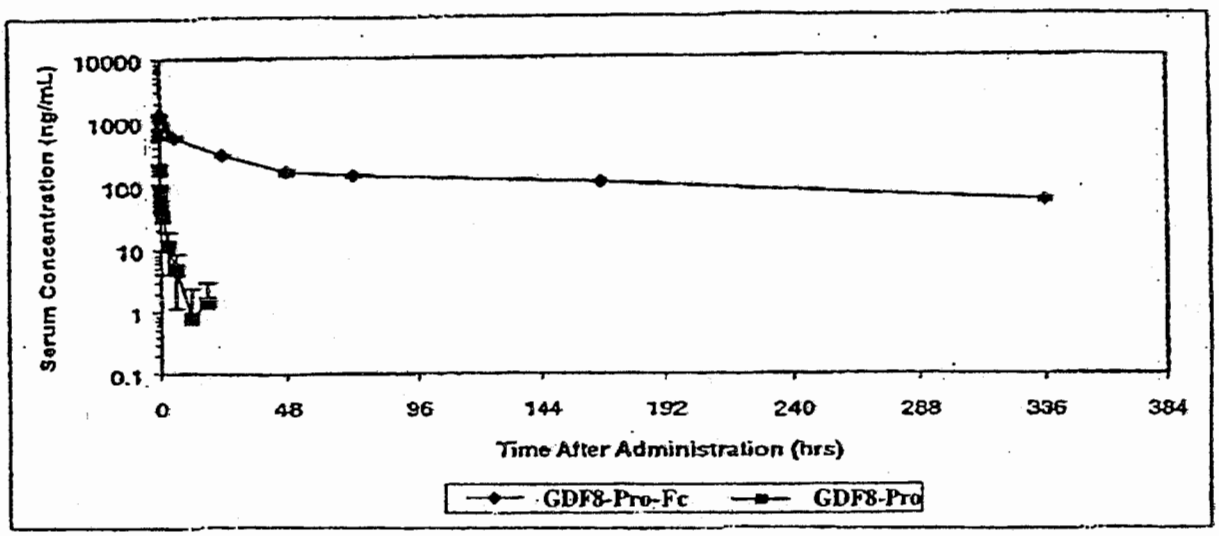
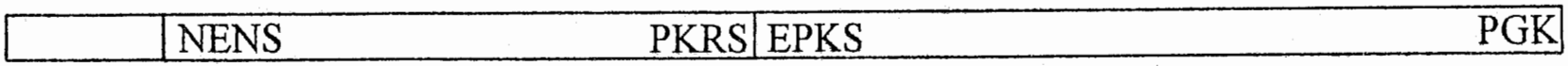

Serum Concentration (ng/mL)
10000
1000
100
10
1
0.1
0
48
96
144
192
240
288
336
384
Time After Administration (hrs)
GDF8-Pro-Fc
GDF8-Pro

Fig. 10



Secretory leader | Hu GDF-8 propeptide | Hu IgG1 Fc

MQKLQLCVYIYLFMLIVAGPVDLNENSEQKENVEKEGLCNACTWRQNTKSSRIEAIKIQILSKLRLETAPN
ISKDVIRQLLPKAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIITMPTESDFLMQVDGKPKCCFFKF
SSKIQYNKVVKAQLWIYLRPVETPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMNPGTGIWQSIDVKTVLQ
NWLKQPESNLGIEIKALDENGHDLAVTFPGPGEDGLNPFLEVKVTDTPKRS**EPKSCDKTHTCPPCPAPELL**
GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI
AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Fig. 11A



Secretory leader

Hu GDF-8 propeptide

Hu IgG1 Fc mutated

MQKLQLCVYIYLFMLIVAGPVDLNENSEQKENVEKEGLCNACTWRQNTKSSRIEAIKIQILSKLRLETAPN
ISKDVIRQLLPKAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIITMPTESDFLMQVDGKPKCCFFKF
SSKIQYNKVVKAQLWIYLRPVETPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMNPGTGIWQSIDVKTVLQ
NWLKQPESNLGIEIKALDENGHDLAVTFPGPGEDGLNPFLEVKVTDTPKRS**DKTHTCPPCPAPEALGAPSV**
FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE
SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Fig. 11B

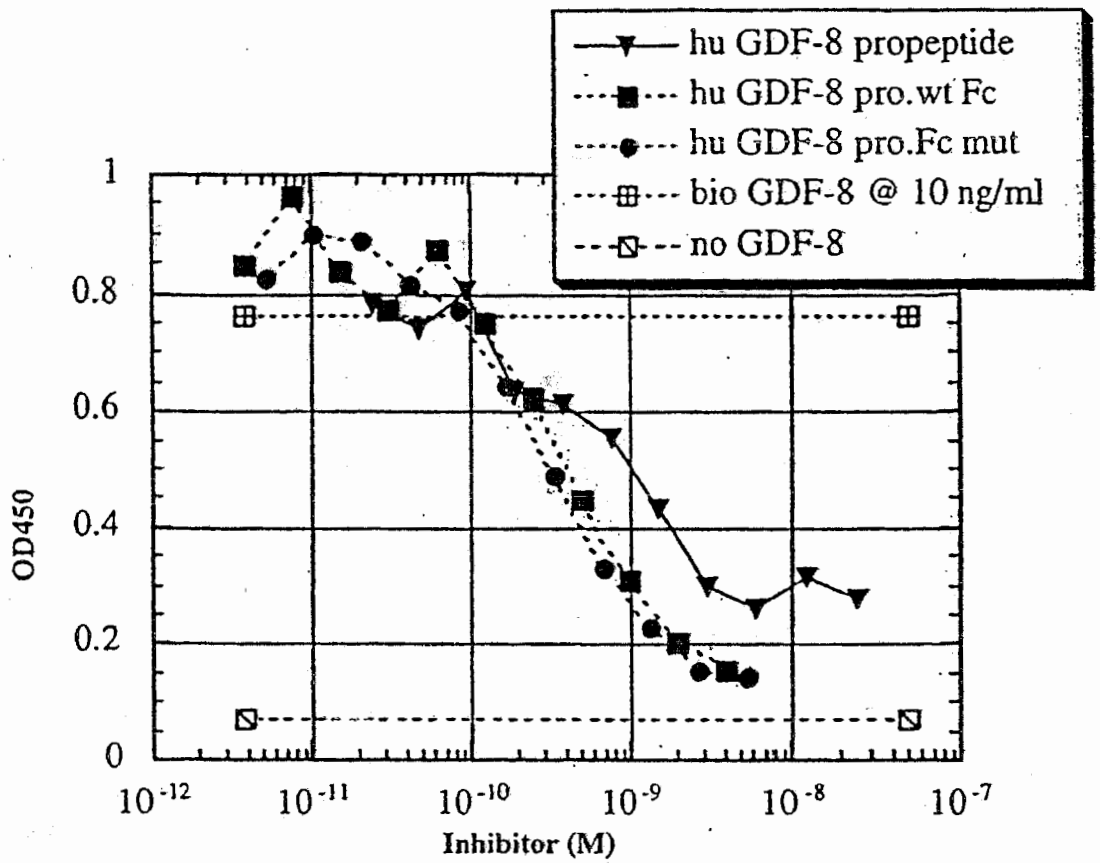

hu GDF-8 propeptide
hu GDF-8 pro.wt Fc
hu GDF-8 pro.Fc mut
bio GDF-8 @ 10 ng/ml
no GDF-8
OD450
1
0.8
0.6
0.4
0.2
0
10-12
10-11
10-10
10-9
10-8
10-7
Inhibitor (M)

Fig. 12

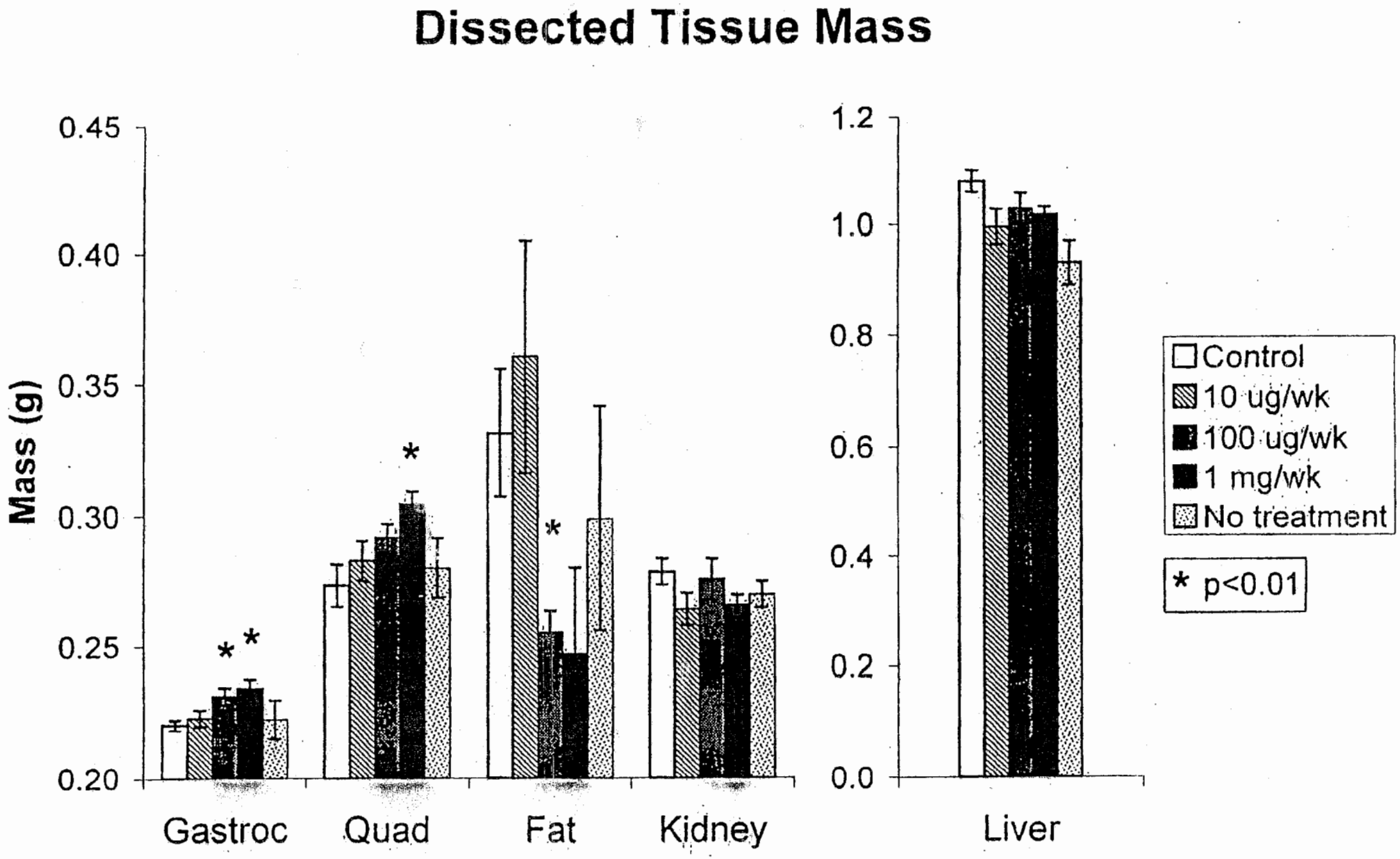

Dissected Tissue Mass
Mass (g)
0.45
0.40
0.35
0.30
0.25
0.20
1.2
1.0
0.8
0.6
0.4
0.2
0.0
Gastroc
Quad
Fat
Kidney
Liver
Control
10 ug/wk
100 ug/wk
1 mg/wk
No treatment
* p<0.01

Figure 13

Fig. 14A

SEQ ID NO:1 Human GDF-8 precursor protein - protein sequence

MQKLQLCVYIYLFMLIVAGPVDLNENSEQKENVEKEGLCNACTWRQNTKSS
RIEAIKIQILSKLRLETAPNISKDVIRQLLPKAPPLRELIDQYDVQRDDSS
DGSLEDDDYHATTETIITMPTESDFLMQVDGKPKCCFFKFSSKIQYNKVVK
AQLWIYLRPVETPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMNPGTGIWQ
SIDVKTVLQNWLKQPESNLGIEIKALDENGHDLAVTFPGPGEDGLNPFLEV
KVTDTPKRSRRDFGLDCDEHSTESRCCRYPLTVDFEAFGWDWIIAPKRYKA
NYCSGECEFVFLQKYPHTHLVHQANPRGSAGPCCTPTKMSPINMLYFNGKE
QIIYGKIPAMVVDRCGCS

Fig. 14B

SEQ ID NO:2 Human GDF-8 precursor protein - DNA sequence

ATGCAAAAACTGCAACTCTGTGTTTATATTTACCTGTTTATGCTGATTGT
TGCTGGTCCAGTGGATCTAAATGAGAACAGTGAGCAAAAAGAAAATGTGG
AAAAAGAGGGGCTGTGTAATGCATGTACTTGGAGACAAAACACTAAATCT
TCAAGAATAGAAGCCATTAAGATACAAATCCTCAGTAAACTTCGTCTGGA
AACAGCTCCTAACATCAGCAAAGATGTTATAAGACAACTTTTACCCAAAG
CTCCTCCACTCCGGGAACTGATTGATCAGTATGATGTCCAGAGGGATGAC
AGCAGCGATGGCTCTTTGGAAGATGACGATTATCACGCTACAACGGAAAC
AATCATTACCATGCCTACAGAGTCTGATTTTCTAATGCAAGTGGATGGAA
AACCCAAATGTTGCTTCTTTAAATTTAGCTCTAAAATACAATACAATAAA
GTAGTAAAGGCCCAACTATGGATATATTTGAGACCCGTCGAGACTCCTAC
AACAGTGTTTGTGCAAATCCTGAGACTCATCAAACCTATGAAAGACGGTA
CAAGGTATACTGGAATCCGATCTCTGAAACTTGACATGAACCCAGGCACT
GGTATTTGGCAGAGCATTGATGTGAAGACAGTGTTGCAAAATTGGCTCAA
ACAACCTGAATCCAACTTAGGCATTGAAATAAAAGCTTTAGATGAGAATG
GTCATGATCTTGCTGTAACCTTCCCAGGACCAGGAGAAGATGGGCTGAAT
CCGTTTTTAGAGGTCAAGGTAACAGACACACCAAAAAGATCCAGAAGGGA
TTTTGGTCTTGACTGTGATGAGCACTCAACAGAATCACGATGCTGTCGTT
ACCCTCTAACTGTGGATTTTGAAGCTTTTGGATGGGATTGGATTATCGCT
CCTAAAAGATATAAGGCCAATTACTGCTCTGGAGAGTGTGAATTTGTATT
TTTACAAAAATATCCTCATACTCATCTGGTACACCAAGCAAACCCCAGAG
GTTCAGCAGGCCCTTGCTGTACTCCCACAAAGATGTCTCCAATTAATATG
CTATATTTTAATGGCAAAGAACAAATAATATATGGGAAAATTCCAGCGAT
GGTAGTAGACCGCTGTGGGTGCTCA

Fig. 14C

SEQ ID NO:3 Human mature GDF-8 - protein sequence

DFGLDCDEHSTESRCCRYPLTVDFEAFGWDWIIAPKRYKANYCSGECEFVF
LQKYPHTHLVHQANPRGSAGPCCTPTKMSPINMLYFNGKEQIIYGKIPAMV
VDRCGCS

Fig. 14D

SEQ ID NO:4 Human mature GDF-8 - DNA sequence

GATTTTGGTCTTGACTGTGATGAGCACTCAACAGAATCACGATGCTGTCG
TTACCCTCTAACTGTGGATTTTGAAGCTTTTGGATGGGATTGGATTATCG
CTCCTAAAAGATATAAGGCCAATTACTGCTCTGGAGAGTGTGAATTTGTA
TTTTTACAAAAATATCCTCATACTCATCTGGTACACCAAGCAAACCCCAG
AGGTTCAGCAGGCCCTTGCTGTACTCCCACAAAGATGTCTCCAATTAATA
TGCTATATTTTAATGGCAAAGAACAAATAATATATGGGAAAATTCCAGCG
ATGGTAGTAGACCGCTGTGGGTGCTCA

Fig.14E

SEQ ID NO:5 Human GDF-8 propeptide - protein sequence

NENSEQKENVEKEGLCNACTWRQNTKSSRIEAIKIQILSKLRLETAPNISK
DVIRQLLPKAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIITMPTES
DFLMQVDGKPKCCFFKFSSKIQYNKVVKAQLWIYLRPVETPTTVFVQILRL
IKPMKDGTRYTGIRSLKLDMNPGTGIWQSIDVKTVLQNWLKQPESNLGIEI
KALDENGHDLAVTFPGPGEDGLNPFLEVKVTDTPKRSRR

Fig. 14F

SEQ ID NO:6 Human GDF-8 propeptide - DNA sequence

AATGAGAACAGTGAGCAAAAAGAAAATGTGGAAAAAGAGGGGCTGTGTAAT
GCATGTACTTGGAGACAAAACACTAAATCTTCAAGAATAGAAGCCATTAAG
ATACAAATCCTCAGTAAACTTCGTCTGGAAACAGCTCCTAACATCAGCAAA
GATGTTATAAGACAACTTTTACCCAAAGCTCCTCCACTCCGGGAACTGATT
GATCAGTATGATGTCCAGAGGGATGACAGCAGCGATGGCTCTTTGGAAGAT
GACGATTATCACGCTACAACGGAAACAATCATTACCATGCCTACAGAGTCT
GATTTTCTAATGCAAGTGGATGGAAAACCCAAATGTTGCTTCTTTAAATTT
AGCTCTAAAATACAATACAATAAAGTAGTAAAGGCCCAACTATGGATATAT
TTGAGACCCGTCGAGACTCCTACAACAGTGTTTGTGCAAATCCTGAGACTC
ATCAAACCTATGAAAGACGGTACAAGGTATACTGGAATCCGATCTCTGAAA
CTTGACATGAACCCAGGCACTGGTATTTGGCAGAGCATTGATGTGAAGACA
GTGTTGCAAAATTGGCTCAAACAACCTGAATCCAACTTAGGCATTGAAATA
AAAGCTTTAGATGAGAATGGTCATGATCTTGCTGTAACCTTCCCAGGACCA
GGAGAAGATGGGCTGAATCCGTTTTTAGAGGTCAAGGTAACAGACACACCA
AAAAGATCCAGAAGG

Fig. 14G

SEQ ID NO:7 Human BMP-11 precursor protein - protein sequence

MVLAAPLLLGFLLLALELRPRGEAAEGPAAAAAAAAAAAAAGVGGERSSRP
APSVAPEPDGCPVCVWRQHSRELRLESIKSQILSKLRLKEAPNISREVVKQ
LLPKAPPLQQILDLHDFQGDALQPEDFLEEDEYHATTETVISMAQETDPAV
QTDGSPLCCHFHFSPKVMFTKVLKAQLWVYLRPVPRPATVYLQILRLKPLT
GEGTAGGGGGRRHIRIRSLKIELHSRSGHWQSIDFKQVLHSWFRQPQSNW
GIEINAFDPSGTDLAVTSLGPGAEGLHPFMELRVLENTKRSRRNLGLDCDE
HSSESRCCRYPLTVDFEAFGWDWIIAPKRYKANYCSGQCEYMFMQKYPHTH
LVQQANPRGSAGPCCTPTKMSPINMLYFNDKQQIIYGKIPGMVVDRCGCS

Fig. 14H

SEQ ID NO:8 Human BMP-11 precursor protein - DNA sequence

ATGGTGCTCGCGGCCCCGCTGCTGCTGGGCTTCCTGCTCCTCGCCCTGGA
GCTGCGGCCCCGGGGGGAGGCGGCCGAGGGCCCCGCGGCGGCGGCGGCGG
CGGCGGCGGCGGCGGCAGCGGCGGGGGTCGGGGGGGAGCGCTCCAGCCGG
CCAGCCCCGTCCGTGGCGCCCGAGCCGGACGGCTGCCCCGTGTGCGTTTG
GCGGCAGCACAGCCGCGAGCTGCGCCTAGAGAGCATCAAGTCGCAGATCT
TGAGCAAACTGCGGCTCAAGGAGGCGCCCAACATCAGCCGCGAGGTGGTG
AAGCAGCTGCTGCCCAAGGCGCCGCCGCTGCAGCAGATCCTGGACCTACA
CGACTTCCAGGGCGACGCGCTGCAGCCCGAGGACTTCCTGGAGGAGGACG
AGTACCACGCCACCACCGAGACCGTCATTAGCATGGCCCAGGAGACGGAC
CCAGCAGTACAGACAGATGGCAGCCCTCTCTGCTGCCATTTTCACTTCAG
CCCCAAGGTGATGTTCACAAAGGTACTGAAGGCCCAGCTGTGGGTGTACC
TACGGCCTGTACCCCGCCCAGCCACAGTCTACCTGCAGATCTTGCGACTA
AAACCCCTAACTGGGGAAGGGACCGCAGGGGGAGGGGGCGGAGGCCGGCG
TCACATCCGTATCCGCTCACTGAAGATTGAGCTGCACTCACGCTCAGGCC
ATTGGCAGAGCATCGACTTCAAGCAAGTGCTACACAGCTGGTTCCGCCAG
CCACAGAGCAACTGGGGCATCGAGATCAACGCCTTTGATCCCAGTGGCAC
AGACCTGGCTGTCACCTCCCTGGGGCCGGGAGCCGAGGGGCTGCATCCAT
TCATGGAGCTTCGAGTCCTAGAGAACACAAAACGTTCCCGGCGGAACCTG
GGTCTGGACTGCGACGAGCACTCAAGCGAGTCCCGCTGCTGCCGATATCC
CCTCACAGTGGACTTTGAGGCTTTCGGCTGGGACTGGATCATCGCACCTA
AGCGCTACAAGGCCAACTACTGCTCCGGCCAGTGCGAGTACATGTTCATG
CAAAAATATCCGCATACCCATTTGGTGCAGCAGGCCAATCCAAGAGGCTC
TGCTGGGCCCTGTTGTACCCCCACCAAGATGTCCCCAATCAACATGCTCT
ACTTCAATGACAAGCAGCAGATTATCTACGGCAAGATCCCTGGCATGGTG
GTGGATCGCTGTGGCTGCTCT

Fig. 14I

SEQ ID NO:9 Human BMP-11 mature - protein sequence

NLGLDCDEHSSESRCCRYPLTVDFEAFGWDWIIAPKRYKANYCSGQCEYMF
MQKYPHTHLVQQANPRGSAGPCCTPTKMSPINMLYFNDKQQIIYGKIPGMV
VDRCGCS

Fig. 14J

SEQ ID NO:10 Human BMP-11 mature - DNA sequence

AACCTGGGTCTGGACTGCGACGAGCACTCAAGCGAGTCCCGCTGCTGCCG
ATATCCCCTCACAGTGGACTTTGAGGCTTTCGGCTGGGACTGGATCATCG
CACCTAAGCGCTACAAGGCCAACTACTGCTCCGGCCAGTGCGAGTACATG
TTCATGCAAAAATATCCGCATACCCATTTGGTGCAGCAGGCCAATCCAAG
AGGCTCTGCTGGGCCCTGTTGTACCCCCACCAAGATGTCCCCAATCAACA
TGCTCTACTTCAATGACAAGCAGCAGATTATCTACGGCAAGATCCCTGGC
ATGGTGGTGGATCGCTGTGGCTGCTCT

Fig. 14K

SEQ ID NO:11 Human BMP-11 propeptide - protein sequence

AEGPAAAAAAAAAAAAAGVGGERSSRPAPSVAPEPDGCPVCVWRQHSRELR
LESIKSQILSKLRLKEAPNISREVVKQLLPKAPPLQQILDLHDFQGDALQP
EDFLEEDEYHATTETVISMAQETDPAVQTDGSPLCCHFHFSPKVMFTKVLK
AQLWVYLRPVPRPATVYLQILRLKPLTGEGTAGGGGGRRHIRIRSLKIEL
HSRSGHWQSIDFKQVLHSWFRQPQSNWGIEINAFDPSGTDLAVTSLGPGAE
GLHPFMELRVLENTKRSRR

Fig. 14L

SEQ ID NO:12 Human BMP-11 propeptide - DNA sequence

GCCGAGGGCCCCGCGGCGGCGGCGGCGGCGGCGGCGGCGGCAGCGGC
GGGGGTCGGGGGGGAGCGCTCCAGCCGGCCAGCCCCGTCCGTGGCGCCCG
AGCCGGACGGCTGCCCCGTGTGCGTTTGGCGGCAGCACAGCCGCGAGCTG
CGCCTAGAGAGCATCAAGTCGCAGATCTTGAGCAAACTGCGGCTCAAGGA
GGCGCCCAACATCAGCCGCGAGGTGGTGAAGCAGCTGCTGCCCAAGGCGC
CGCCGCTGCAGCAGATCCTGGACCTACACGACTTCCAGGGCGACGCGCTG
CAGCCCGAGGACTTCCTGGAGGAGGACGAGTACCACGCCACCACCGAGAC
CGTCATTAGCATGGCCCAGGAGACGGACCCAGCAGTACAGACAGATGGCA
GCCCTCTCTGCTGCCATTTTCACTTCAGCCCCAAGGTGATGTTCACAAAG
GTACTGAAGGCCCAGCTGTGGGTGTACCTACGGCCTGTACCCCGCCCAGC
CACAGTCTACCTGCAGATCTTGCGACTAAAACCCCTAACTGGGGAAGGGA
CCGCAGGGGGAGGGGGCGGAGGCCGGCGTCACATCCGTATCCGCTCACTG
AAGATTGAGCTGCACTCACGCTCAGGCCATTGGCAGAGCATCGACTTCAA
GCAAGTGCTACACAGCTGGTTCCGCCAGCCACAGAGCAACTGGGGCATCG
AGATCAACGCCTTTGATCCCAGTGGCACAGACCTGGCTGTCACCTCCCTG
GGGCCGGGAGCCGAGGGGCTGCATCCATTCATGGAGCTTCGAGTCCTAGA
GAACACAAAACGTTCCCGGCGG

Fig. 14M

SEQ ID NO:13 GDF-8 signal sequence - protein sequence

MQKLQLCVYIYLFMLIVAGPVDL

Fig. 14N

SEQ ID NO:14 BMP-11 signal sequence - protein sequence

MVLAAPLLLGFLLLALELRPRGEA

Fig. 14O

SEQ ID NO:15 Human IgG1-Fc - protein sequence

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV
SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK
EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGK

Fig. 14P

SEQ ID NO:16 Human IgG1-Fc modified - protein sequence

DKTHTCPPCPAPEALGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP
EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY
PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CSVMHEALHNHYTQKSLSLSPGK

SEQUENCE LISTING

<110> American Home Products Corporation

<120> Modified and Stabilized GDF Propeptides and Uses Thereof

<130> 01997.002000

<140> Not-Yet-Assigned
<141> 2001-02-07

<150> US 60/267,509
<151> 2001-02-08

<160> 16

<170> PatentIn version 3.1

<210> 1
<211> 375
<212> PRT
<213> Homo sapiens

<400> 1

```
Met Gln Lys Leu Gln Leu Cys Val Tyr Ile Tyr Leu Phe Met Leu Ile
1               5                  10                  15

Val Ala Gly Pro Val Asp Leu Asn Glu Asn Ser Glu Gln Lys Glu Asn
            20                  25                  30

Val Glu Lys Glu Gly Leu Cys Asn Ala Cys Thr Trp Arg Gln Asn Thr
        35                  40                  45

Lys Ser Ser Arg Ile Glu Ala Ile Lys Ile Gln Ile Leu Ser Lys Leu
    50                  55                  60

Arg Leu Glu Thr Ala Pro Asn Ile Ser Lys Asp Val Ile Arg Gln Leu
65                  70                  75                  80

Leu Pro Lys Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr Asp Val
                85                  90                  95

Gln Arg Asp Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp Tyr His
            100                 105                 110
```

Ala Thr Thr Glu Thr Ile Ile Thr Met Pro Thr Glu Ser Asp Phe Leu
115 120 125

Met Gln Val Asp Gly Lys Pro Lys Cys Cys Phe Phe Lys Phe Ser Ser
130 135 140

Lys Ile Gln Tyr Asn Lys Val Val Lys Ala Gln Leu Trp Ile Tyr Leu
145 150 155 160

Arg Pro Val Glu Thr Pro Thr Thr Val Phe Val Gln Ile Leu Arg Leu
165 170 175

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

Lys Leu Asp Met Asn Pro Gly Thr Gly Ile Trp Gln Ser Ile Asp Val
195 200 205

Lys Thr Val Leu Gln Asn Trp Leu Lys Gln Pro Glu Ser Asn Leu Gly
210 215 220

Ile Glu Ile Lys Ala Leu Asp Glu Asn Gly His Asp Leu Ala Val Thr
225 230 235 240

Phe Pro Gly Pro Gly Glu Asp Gly Leu Asn Pro Phe Leu Glu Val Lys
245 250 255

Val Thr Asp Thr Pro Lys Arg Ser Arg Arg Asp Phe Gly Leu Asp Cys
260 265 270

Asp Glu His Ser Thr Glu Ser Arg Cys Cys Arg Tyr Pro Leu Thr Val
275 280 285

Asp Phe Glu Ala Phe Gly Trp Asp Trp Ile Ile Ala Pro Lys Arg Tyr
290 295 300

Lys Ala Asn Tyr Cys Ser Gly Glu Cys Glu Phe Val Phe Leu Gln Lys

305 310 315 320

Tyr Pro His Thr His Leu Val His Gln Ala Asn Pro Arg Gly Ser Ala
325 330 335

Gly Pro Cys Cys Thr Pro Thr Lys Met Ser Pro Ile Asn Met Leu Tyr
340 345 350

Phe Asn Gly Lys Glu Gln Ile Ile Tyr Gly Lys Ile Pro Ala Met Val
355 360 365

Val Asp Arg Cys Gly Cys Ser
370 375

<210> 2
<211> 1125
<212> DNA
<213> Homo sapiens

<400> 2
atgcaaaaac tgcaactctg tgtttatatt tacctgttta tgctgattgt tgctggtcca
60

gtggatctaa atgagaacag tgagcaaaaa gaaaatgtgg aaaaagaggg gctgtgtaat
120

gcatgtactt ggagacaaaa cactaaatct tcaagaatag aagccattaa gatacaaatc
180

ctcagtaaac ttcgtctgga aacagctcct aacatcagca aagatgttat aagacaactt
240

ttacccaaag ctcctccact ccgggaactg attgatcagt atgatgtcca gagggatgac
300

agcagcgatg gctctttgga agatgacgat tatcacgcta caacggaaac aatcattacc
360

atgcctacag agtctgattt tctaatgcaa gtggatggaa aacccaaatg ttgcttcttt
420

aaatttagct ctaaaataca atacaataaa gtagtaaagg cccaactatg gatatatttg
480

agacccgtcg agactcctac aacagtgttt gtgcaaatcc tgagactcat caaacctatg
540

aaagacggta caaggtatac tggaatccga tctctgaaac ttgacatgaa cccaggcact
600

ggtatttggc agagcattga tgtgaagaca gtgttgcaaa attggctcaa acaacctgaa
660

tccaacttag gcattgaaat aaaagcttta gatgagaatg gtcatgatct tgctgtaacc
720

ttcccaggac caggagaaga tgggctgaat ccgtttttag aggtcaaggt aacagacaca
780

ccaaaaagat ccagaaggga ttttggtctt gactgtgatg agcactcaac agaatcacga
840

tgctgtcgtt accctctaac tgtggatttt gaagcttttg gatgggattg gattatcgct
900

cctaaaagat ataaggccaa ttactgctct ggagagtgtg aatttgtatt tttacaaaaa
960

tatcctcata ctcatctggt acaccaagca aaccccagag gttcagcagg cccttgctgt 1
020

actcccacaa agatgtctcc aattaatatg ctatatttta atggcaaaga acaaataata 1
080

tatgggaaaa ttccagcgat ggtagtagac cgctgtgggt gctca 1
125

<210> 3
<211> 109
<212> PRT
<213> Homo sapiens

<400> 3

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> 4
<211> 327
<212> DNA
<213> Homo sapiens

<400> 4
gattttggtc ttgactgtga tgagcactca acagaatcac gatgctgtcg ttaccctcta
60

actgtggatt ttgaagcttt tggatgggat tggattatcg ctcctaaaag atataaggcc
120

aattactgct ctggagagtg tgaatttgta tttttacaaa aatatcctca tactcatctg
180

gtacaccaag caaaccccag aggttcagca ggcccttgct gtactcccac aaagatgtct
240

ccaattaata tgctatattt taatggcaaa gaacaaataa tatatgggaa aattccagcg
300

atggtagtag accgctgtgg gtgctca
327

<210> 5
<211> 243
<212> PRT
<213> Homo sapiens

<400> 5

Asn Glu Asn Ser Glu Gln Lys Glu Asn Val Glu Lys Glu Gly Leu Cys
1 5 10 15

Asn Ala Cys Thr Trp Arg Gln Asn Thr Lys Ser Ser Arg Ile Glu Ala
20 25 30

Ile Lys Ile Gln Ile Leu Ser Lys Leu Arg Leu Glu Thr Ala Pro Asn
35 40 45

Ile Ser Lys Asp Val Ile Arg Gln Leu Leu Pro Lys Ala Pro Pro Leu
50 55 60

Arg Glu Leu Ile Asp Gln Tyr Asp Val Gln Arg Asp Asp Ser Ser Asp
65 70 75 80

Gly Ser Leu Glu Asp Asp Asp Tyr His Ala Thr Thr Glu Thr Ile Ile
85 90 95

Thr Met Pro Thr Glu Ser Asp Phe Leu Met Gln Val Asp Gly Lys Pro
100 105 110

Lys Cys Cys Phe Phe Lys Phe Ser Ser Lys Ile Gln Tyr Asn Lys Val
115 120 125

Val Lys Ala Gln Leu Trp Ile Tyr Leu Arg Pro Val Glu Thr Pro Thr
130 135 140

Thr Val Phe Val Gln Ile Leu Arg Leu Ile Lys Pro Met Lys Asp Gly
145 150 155 160

Thr Arg Tyr Thr Gly Ile Arg Ser Leu Lys Leu Asp Met Asn Pro Gly
165 170 175

Thr Gly Ile Trp Gln Ser Ile Asp Val Lys Thr Val Leu Gln Asn Trp
180 185 190

Leu Lys Gln Pro Glu Ser Asn Leu Gly Ile Glu Ile Lys Ala Leu Asp
195 200 205

Glu Asn Gly His Asp Leu Ala Val Thr Phe Pro Gly Pro Gly Glu Asp
210 215 220

Gly Leu Asn Pro Phe Leu Glu Val Lys Val Thr Asp Thr Pro Lys Arg
225 230 235 240

Ser Arg Arg

<210> 6
<211> 729
<212> DNA
<213> Homo sapiens

<400> 6
aatgagaaca gtgagcaaaa agaaaatgtg gaaaaagagg ggctgtgtaa tgcatgtact
60

tggagacaaa acactaaatc ttcaagaata gaagccatta agatacaaat cctcagtaaa
120

cttcgtctgg aaacagctcc taacatcagc aaagatgtta taagacaact tttacccaaa
180

gctcctccac tccgggaact gattgatcag tatgatgtcc agagggatga cagcagcgat
240

ggctctttgg aagatgacga ttatcacgct acaacggaaa caatcattac catgcctaca
300

gagtctgatt ttctaatgca agtggatgga aaacccaaat gttgcttctt taaatttagc
360

tctaaaatac aatacaataa agtagtaaag gcccaactat ggatatattt gagacccgtc
420

gagactccta caacagtgtt tgtgcaaatc ctgagactca tcaaacctat gaaagacggt
480

acaaggtata ctggaatccg atctctgaaa cttgacatga acccaggcac tggtatttgg
540

cagagcattg atgtgaagac agtgttgcaa aattggctca aacaacctga atccaactta
600

ggcattgaaa taaaagcttt agatgagaat ggtcatgatc ttgctgtaac cttcccagga
660

ccaggagaag atgggctgaa tccgttttta gaggtcaagg taacagacac accaaaaaga
720

tccagaagg
729

<210> 7
<211> 407
<212> PRT
<213> Homo sapiens

<400> 7

Met Val Leu Ala Ala Pro Leu Leu Leu Gly Phe Leu Leu Leu Ala Leu
1 5 10 15

Glu Leu Arg Pro Arg Gly Glu Ala Ala Glu Gly Pro Ala Ala Ala Ala
20 25 30

Ala Ala Ala Ala Ala Ala Ala Ala Ala Gly Val Gly Gly Glu Arg Ser
35 40 45

Ser Arg Pro Ala Pro Ser Val Ala Pro Glu Pro Asp Gly Cys Pro Val
50 55 60

Cys Val Trp Arg Gln His Ser Arg Glu Leu Arg Leu Glu Ser Ile Lys
65 70 75 80

Ser Gln Ile Leu Ser Lys Leu Arg Leu Lys Glu Ala Pro Asn Ile Ser
85 90 95

Arg Glu Val Val Lys Gln Leu Leu Pro Lys Ala Pro Pro Leu Gln Gln
100 105 110

Ile Leu Asp Leu His Asp Phe Gln Gly Asp Ala Leu Gln Pro Glu Asp
115 120 125

Phe Leu Glu Glu Asp Glu Tyr His Ala Thr Thr Glu Thr Val Ile Ser
130 135 140

Met Ala Gln Glu Thr Asp Pro Ala Val Gln Thr Asp Gly Ser Pro Leu
145 150 155 160

Cys Cys His Phe His Phe Ser Pro Lys Val Met Phe Thr Lys Val Leu
165 170 175

Lys Ala Gln Leu Trp Val Tyr Leu Arg Pro Val Pro Arg Pro Ala Thr
180 185 190

Val Tyr Leu Gln Ile Leu Arg Leu Lys Pro Leu Thr Gly Glu Gly Thr
195 200 205

Ala Gly Gly Gly Gly Gly Gly Arg Arg His Ile Arg Ile Arg Ser Leu
210 215 220

Lys Ile Glu Leu His Ser Arg Ser Gly His Trp Gln Ser Ile Asp Phe
225 230 235 240

Lys Gln Val Leu His Ser Trp Phe Arg Gln Pro Gln Ser Asn Trp Gly
245 250 255

Ile Glu Ile Asn Ala Phe Asp Pro Ser Gly Thr Asp Leu Ala Val Thr
260 265 270

Ser Leu Gly Pro Gly Ala Glu Gly Leu His Pro Phe Met Glu Leu Arg
275 280 285

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

Asp Glu His Ser Ser Glu Ser Arg Cys Cys Arg Tyr Pro Leu Thr Val
305 310 315 320

Asp Phe Glu Ala Phe Gly Trp Asp Trp Ile Ile Ala Pro Lys Arg Tyr
325 330 335

Lys Ala Asn Tyr Cys Ser Gly Gln Cys Glu Tyr Met Phe Met Gln Lys
340 345 350

Tyr Pro His Thr His Leu Val Gln Gln Ala Asn Pro Arg Gly Ser Ala
355 360 365

Gly Pro Cys Cys Thr Pro Thr Lys Met Ser Pro Ile Asn Met Leu Tyr
370 375 380

Phe Asn Asp Lys Gln Gln Ile Ile Tyr Gly Lys Ile Pro Gly Met Val
385 390 395 400

Val Asp Arg Cys Gly Cys Ser
405

<210> 8
<211> 1221
<212> DNA
<213> Homo sapiens

<400> 8
atggtgctcg cggccccgct gctgctgggc ttcctgctcc tcgccctgga gctgcggccc
60

cgggggggagg cggccgaggg ccccgcggcg gcggcggcgg cggcggcggc ggcggcagcg
120

gcgggggtcg gggggggagcg ctccagccgg ccaqccccgt ccgtggcgcc cgagccggac
180

ggctgccccg tgtgcgtttg gcggcagcac agccgcgagc tgcgcctaga gagcatcaag
240

tcgcagatct tgagcaaact gcggctcaag gaggcgccca acatcagccg cgaggtggtg
300

aagcagctgc tgcccaaggc gccgccgctg cagcagatcc tggacctaca cgacttccag
360

ggcgacgcgc tgcagcccga ggacttcctg gaggaggacg agtaccacgc caccaccgag
420

accgtcatta gcatggccca ggagacggac ccagcagtac agacagatgg cagccctctc
480

tgctgccatt ttcacttcag ccccaaggtg atgttcacaa aggtactgaa ggcccagctg
540

tgggtgtacc tacggcctgt accccgccca gccacagtct acctgcagat cttgcgacta
600

aaaccccctaa ctggggaagg gaccgcaggg ggagggggcg gaggccggcg tcacatccgt

660

atccgctcac tgaagattga gctgcactca cgctcaggcc attggcagag catcgacttc
720

aagcaagtgc tacacagctg gttccgccag ccacagagca actggggcat cgagatcaac
780

gcctttgatc ccagtggcac agacctggct gtcacctccc tggggccggg agccgagggg
840

ctgcatccat tcatggagct tcgagtccta gagaacacaa aacgttcccg gcggaacctg
900

ggtctggact gcgacgagca ctcaagcgag tcccgctgct gccgatatcc cctcacagtg
960

gactttgagg ctttcggctg ggactggatc atcgcaccta agcgctacaa ggccaactac 1
020

tgctccggcc agtgcgagta catgttcatg caaaaatatc cgcataccca tttggtgcag 1
080

caggccaatc caagaggctc tgctgggccc tgttgtaccc ccaccaagat gtccccaatc 1
140

aacatgctct acttcaatga caagcagcag attatctacg gcaagatccc tggcatggtg 1
200

gtggatcgct gtggctgctc t 1
221

<210> 9
<211> 109
<212> PRT
<213> Homo sapiens

<400> 9

Asn Leu Gly Leu Asp Cys Asp Glu His Ser Ser 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 Gln Cys Glu
35 40 45

Tyr Met Phe Met Gln Lys Tyr Pro His Thr His Leu Val Gln 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 Asp Lys Gln Gln Ile Ile Tyr Gly
85 90 95

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

<210> 10
<211> 327
<212> DNA
<213> Homo sapiens

<400> 10
aacctgggtc tggactgcga cgagcactca agcgagtccc gctgctgccg atatcccctc
60

acagtggact ttgaggcttt cggctgggac tggatcatcg cacctaagcg ctacaaggcc
120

aactactgct ccggccagtg cgagtacatg ttcatgcaaa aatatccgca tacccatttg
180

gtgcagcagg ccaatccaag aggctctgct gggccctgtt gtacccccac caagatgtcc
240

ccaatcaaca tgctctactt caatgacaag cagcagatta tctacggcaa gatccctggc
300

atggtggtgg atcgctgtgg ctgctct
327

<210> 11
<211> 274
<212> PRT
<213> Homo sapiens

<400> 11

Ala Glu Gly Pro Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala
1 5 10 15

Ala Gly Val Gly Gly Glu Arg Ser Ser Arg Pro Ala Pro Ser Val Ala
20 25 30

Pro Glu Pro Asp Gly Cys Pro Val Cys Val Trp Arg Gln His Ser Arg
35 40 45

Glu Leu Arg Leu Glu Ser Ile Lys Ser Gln Ile Leu Ser Lys Leu Arg
50 55 60

Leu Lys Glu Ala Pro Asn Ile Ser Arg Glu Val Val Lys Gln Leu Leu
65 70 75 80

Pro Lys Ala Pro Pro Leu Gln Gln Ile Leu Asp Leu His Asp Phe Gln
85 90 95

Gly Asp Ala Leu Gln Pro Glu Asp Phe Leu Glu Glu Asp Glu Tyr His
100 105 110

Ala Thr Thr Glu Thr Val Ile Ser Met Ala Gln Glu Thr Asp Pro Ala
115 120 125

Val Gln Thr Asp Gly Ser Pro Leu Cys Cys His Phe His Phe Ser Pro
130 135 140

Lys Val Met Phe Thr Lys Val Leu Lys Ala Gln Leu Trp Val Tyr Leu
145 150 155 160

Arg Pro Val Pro Arg Pro Ala Thr Val Tyr Leu Gln Ile Leu Arg Leu
165 170 175

Lys Pro Leu Thr Gly Glu Gly Thr Ala Gly Gly Gly Gly Gly Gly Arg
180 185 190

Arg His Ile Arg Ile Arg Ser Leu Lys Ile Glu Leu His Ser Arg Ser
195 200 205

Gly His Trp Gln Ser Ile Asp Phe Lys Gln Val Leu His Ser Trp Phe

210 215 220

Arg Gln Pro Gln Ser Asn Trp Gly Ile Glu Ile Asn Ala Phe Asp Pro
225 230 235 240

Ser Gly Thr Asp Leu Ala Val Thr Ser Leu Gly Pro Gly Ala Glu Gly
245 250 255

Leu His Pro Phe Met Glu Leu Arg Val Leu Glu Asn Thr Lys Arg Ser
260 265 270

Arg Arg

<210> 12
<211> 822
<212> DNA
<213> Homo sapiens

<400> 12
gccgagggcc ccgcggcggc ggcggcggcg gcggcggcgg cggcagcggc gggggtcggg
60

ggggagcgct ccagccggcc agccccgtcc gtggcgcccg agccggacgg ctgccccgtg
120

tgcgtttggc ggcagcacag ccgcgagctg cgcctagaga gcatcaagtc gcagatcttg
180

agcaaactgc ggctcaagga ggcgcccaac atcagccgcg aggtggtgaa gcagctgctg
240

cccaaggcgc cgccgctgca gcagatcctg gacctacacg acttccaggg cgacgcgctg
300

cagcccgagg acttcctgga ggaggacgag taccacgcca ccaccgagac cgtcattagc
360

atggcccagg agacggaccc agcagtacag acagatggca gccctctctg ctgccatttt
420

cacttcagcc ccaaggtgat gttcacaaag gtactgaagg cccagctgtg ggtgtaccta
480

cggcctgtac cccgcccagc cacagtctac ctgcagatct tgcgactaaa acccctaact
540

ggggaaggga ccgcaggggg agggggcgga ggccggcgtc acatccgtat ccgctcactg
600

aagattgagc tgcactcacg ctcaggccat tggcagagca tcgacttcaa gcaagtgcta
660

cacagctggt tccgccagcc acagagcaac tggggcatcg agatcaacgc ctttgatccc
720

agtggcacag acctggctgt cacctccctg gggccgggag ccgaggggct gcatccattc
780

atggagcttc gagtcctaga gaacacaaaa cgttcccggc gg
822

<210> 13
<211> 23
<212> PRT
<213> Homo sapiens

<400> 13

Met Gln Lys Leu Gln Leu Cys Val Tyr Ile Tyr Leu Phe Met Leu Ile
1 5 10 15

Val Ala Gly Pro Val Asp Leu
20

<210> 14
<211> 24
<212> PRT
<213> Homo sapiens

<400> 14

Met Val Leu Ala Ala Pro Leu Leu Leu Gly Phe Leu Leu Leu Ala Leu
1 5 10 15

Glu Leu Arg Pro Arg Gly Glu Ala
20

<210> 15
<211> 232
<212> PRT
<213> Homo sapiens

<400> 15

```
Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1               5                  10                  15

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
            20                  25                  30

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
        35                  40                  45

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
    50                  55                  60

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
65                  70                  75                  80

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
                85                  90                  95

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
            100                 105                 110

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
        115                 120                 125

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
    130                 135                 140

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
145                 150                 155                 160

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
                165                 170                 175

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
            180                 185                 190
```

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
195 200 205

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
210 215 220

Ser Leu Ser Leu Ser Pro Gly Lys
225 230

<210> 16
<211> 227
<212> PRT
<213> Homo sapiens

<400> 16

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Leu Gly
1 5 10 15

Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

```
Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
    130                 135                 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145                 150                 155                 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
                165                 170                 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
            180                 185                 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
        195                 200                 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
    210                 215                 220

Pro Gly Lys
225
```