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(54) **SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME**

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(57) **ABSTRACT**

The present invention is directed to novel polypeptides and to nucleic acid molecules encoding those polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.

GGGGCTTCGGCGCCAGCGCCAGCGCTAGTCGGTCTGGTAAGGATTTACAAAAGGTGCAGGTATG
AGCAGGCTCGAAGACTAACATTTTGTGAAGTTGTAAACAGAAAACCTGTTAGAAAATCTGGTGGT
TTCAGCAAGGCCTCAGTTTCCTTCCTTCAGCCCTTGTAAATTTGGACATCTGTGCTTTCATATTT
TCATACATTACTGCAGTAACACTCCACCATATAGACCCGGCTTACCTTATATCAGTGACACTGG
TACAGTAGCTCCAGAAAATGCTTATTTGGGGCAATGCTAAATATTGCGGCAGTTTTATGCATTG
CTACCATTTATGTTTCCTTATAAGCAAGTTCATGCTCTGAGTCCTGAAGAGAACGTTATCATCAA
TTAAACAAGGCTGGCCTTGTACTTGGAACTAGTGTGTTTAGGACTTCTATTGTGGCAAACCTT
CCAGAAAACAACCCCTTTTTGCTGCACATGTAAGTGGAGCTGTGCTTACCTTTGGTATGGGCTCAT
TATATATGTTTGTTCAGACCATCCTTTCCTACCAAATGCAGCCCAAATCCATGGCAAACAAGTC
TTCTGGATCAGACTGTTGTTGGTTATCTGGTGTGGAGTAAGTGCACCTTAGCATGCTGACTTGCTC
ATCAGTTTTGCACAGTGGCAATTTTGGGACTGATTTAGAACAGAAAACCCATTGGAACCCCGAGG
ACAAAGGTTATGTGCTTCACATGATCACTACTGCAGCAGAAATGGTCTATGTCATTTTCCTTCTTT
GGTTTTTTCCTGACTTACATTCGTGATTTTTCAGAAAATTTCTTTACGGGTGGAAGCCAATTTACA
TGGATTAACCCCTCTATGACACTGCACCTTGCCCTATTAACAATGAACGAACACGGCTACTTTCCA
GAGATATTTGATGAAAGGATAAAAATATTTCTGTAATGATTATGATTCTCAGGGATTGGGGAAAGG
TTCACAGAAAGTTGCTTATCTTCTCTGAAATTTTCAACCCTTAATCAAGGCTGACAGTAACACT
GATGAATGCTGATAATCAGGAAACATGAAAGAAGCCATTTGATAGATTATCTAAAGGATATCAT
CAAGAAGACTATTAACACACCTATGCCTATACCTTTTTATCTCAGAAAATAAAGTCAAAAAGACT
ATG

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FIGURE 1

GGGGCTTCGGCGCCAGCGGCCAGCGCTAGTCGGTCTGGTAAGGATTTACAAAAGGTGCAGGTATG
AGCAGGTCTGAAGACTAACATTTTGTGAAGTTGTAAAACAGAAAACCTGTTAGAAATGTGGTGGT
TTCAGCAAGGCCTCAGTTTCCTTCCTTCAGCCCTTGTAATTTGGACATCTGCTGCTTTTCATATTT
TCATACATTACTGCAGTAACACTCCACCATATAGACCCGGCTTTACCTTATATCAGTGACACTGG
TACAGTAGCTCCAGAAAAATGCTTATTTGGGGCAATGCTAAATATTGCGGCAGTTTTATGCATTG
CTACCATTTATGTTTCGTTATAAGCAAGTTCATGCTCTGAGTCCTGAAGAGAACGTTATCATCAA
TTAAACAAGGCTGGCCTTGTACTTGGAATACTGAGTTGTTTAGGACTTTCTATTGTGGCAAACCTT
CCAGAAAACAACCCCTTTTGTCTGCACATGTAAGTGGAGCTGTGCTTACCTTTGGTATGGGCTCAT
TATATATGTTTGTTCAGACCATCCTTTTCCTACCAAATGCAGCCCAAATCCATGGCAAACAAGTC
TTCTGGATCAGACTGTTGTTGGTTATCTGGTGTGGAGTAAGTGCACCTTAGCATGCTGACTTGCTC
ATCAGTTTTGCACAGTGGCAATTTTGGGACTGATTTAGAACAGAACTCCATTGGAACCCCGAGG
ACAAAGGTTATGTGCTTCACATGATCACTACTGCAGCAGAATGGTCTATGTCATTTTCCTTCTTT
GGTTTTTTCCTGACTTACATTCGTGATTTTCAGAAAATTTCTTTACGGGTGGAAGCCAATTTACA
TGGATTAACCCCTCATGACACTGCACCTTGCCCTATTAACAATGAACGAACACGGCTACTTTCCA
GAGATATTTTGATGAAAGGATAAAAATATTTCTGTAATGATTATGATTCTCAGGGATTGGGGAAAGG
TTCACAGAAGTTGCTTATCTTCTCTGAAATTTTCAACCACTTAATCAAGGCTGACAGTAACACT
GATGAATGCTGATAATCAGGAAACATGAAAGAAGCCATTTGATAGATTATCTAAAGGATATCAT
CAAGAAGACTATTAAAAACACCTATGCCTATACTTTTTTATCTCAGAAAATAAAGTCAAAAAGACT
ATG

FIGURE 2

<subunit 1 of 1, 266 aa, 1 stop

<MW: 29766, pI: 8.39, NX(S/T): 0

MWWFQQGLSFLPSALVIWTSAAAFIFSITAVTLHHIDPALPYISDTGTVAPEKCLFGAMLNIAAV
LCIATYVRYKQVHALSPEENVIIKLNKAGLVLGILSCLGLSIVANFQKTTLFAAHVSGAVLTFG
MGSLYMFVQTIILSYQMOPKIHGKQVFWIRLLLVIWCGVSALSMLTCSSVLHSGNFGTDLEQKLHW
NPEDKGYVLHMITTAAEWSMSFSFFGFFLTYIRDFQKISLRVEANLHGLTLYDTAPCPINNERTR
LLSRDI

Important features:

Type II transmembrane domain:

amino acids 13-33

Other Transmembrane domains:

amino acids 54-73, 94-113, 160-180, 122-141

N-myristoylation sites.

amino acids 57-63, 95-101, 99-105, 124-130, 183-189

FIGURE 3

CGGACGCGTGGGCGGACGCGTGGGGGAGAGCCGAGTCCCGGCTGCAGCACCTGGGAGAAGGCAGACC
GTGTGAGGGGGCCTGTGGCCCCAGCGTGTGTGGCCTCGGGGAGTGGGAAGTGGAGGCAGGAGCCTTC
CTTACACTTCGCCATGAGTTTCTCATCGACTCCAGCATCATGATTACCTCCCAGATACTATTTTTTG
GATTTGGGTGGCTTTTCTTCATGCGCCAATTGTTTAAAGACTATGAGATACGT CAGTATGTTGTACAG
GTGATCTTCTCCGTGACGTTTGCATTTTCTTGACCATGTTTGAGCTCATCATCTTTGAAATCTTAGG
AGTATTGAATAGCAGCTCCCGTTATTTTCACTGGAAAATGAACCTGTGTGTAATTCTGCTGATCCTGG
TTTTCATGGTGCCTTTTTTACATTGGCTATTTTATGTGAGCAATATCCGACTACTGCATAAACACGA
CTGCTTTTTTCTGTCTCTTATGGCTGACCTTTATGTATTTCTTCTGGAACTAGGAGATCCCTTTCC
CATTCTCAGCCCAAACATGGGATCTTATCCATAGAACAGCTCATCAGCCGGGTTGGTGTGATTGGAG
TGA CTCTCATGGCTCTTCTTTCTGGATTTGGTGTGTCAACTGCCCATACACTTACATGTCTTACTTC
CTCAGGAATGTGACTGACACGGATATTCTAGCCCTGGAACGGCGACTGCTGCAAACCATGGATATGAT
CATAAGCAAAAAGAAAAGGATGGCAATGGCACGGAGAACAATGTTCCAGAAGGGGGAAGTGCATAACA
AACCATCAGGTTTCTGGGAATGATAAAAAGTGTACCCTTCAGCATCAGGAAGTAAAATCTTACT
CTTATTCAACAGGAAGTGGATGCTTTGGAAGAATTAAGCAGGCAGCTTTTTCTGGAAACAGCTGATCT
ATATGCTACCAAGGAGAGAATAGAATACTCCAAAACCTTCAAGGGGAAATATTTTAATTTTCTGGTT
ACTTTTTCTCTATTTACTGTGTTTGGAAAATTTTCATGGCTACCATCAATATTGTTTTTGATCGAGTT
GGGAAAACGGATCCTGT CACAAGAGGCATTGAGATCACTGTGAATTATCTGGGAATCCAATTTGATGT
GAAGTTTTGGTCCCAACACATTTCTTCATTCTTGTGGAATAATCATCGTCACATCCATCAGAGGAT
TGCTGATCACTCTTACCAAGTTCTTTTATGCCATCTCTAGCAGTAAGTCCCTCCAATGTCATTGTCCTG
CTATTAGCACAGATAATGGGCATGTACTTTGTCTCCTCTGTGCTGCTGATCCGAATGAGTATGCCTTT
AGAATACCGCACCATATAATCACTGAAGTCCTTGGAGAACTGCAGTTCAACTTCTATCACCGTTGGTTG
ATGTGATCTTCTGCTCAGCGCTCTCTCTAGCATACTCTTCTCTATTTGGCTCACAAACAGGCACCA
GAGAAGCAAATGGCACCTTGAACTTAAAGCCTACTACAGACTGTTAGAGGCCAGTGGTTTTCAAATTTA
GATATAAGAGGGGGGAAAATGGAACCAGGGCCTGACATTTTATAAACAAACAAAATGCTATGGTAGC
ATTTTTACCTTCATAGCATACTCTTCCCCGTGAGGTGATACTATGACCATGAGTAGCATCAGCCAG
AACATGAGAGGGGAGAACTAACTCAAGACAATACTCAGCAGAGAGCATCCCGTGTGGATATGAGGCTGG
TG TAGAGGCGGAGAGGAGCCAAGAACTAAAGGTGAAAAATACACTGGAACCTCTGGGGCAAGACATGT
CTATGGTAGCTGAGCCAAACACGTAGGATTTCCGTTTAAAGGTTACATGGAAAAGGTTATAGCTTTG
CCTTGAGATTGACTCATTAAAATCAGAGACTGTAACAAAAAAAAAAAAAAAAAAAAAAAAAGGGCGGCCGCG
ACTCTAGAGTCGACCTGCAGAAGCTTGGCCGCCATGGCCCACTTGTATTATGCAGCTTATAATG

FIGURE 4

MSFLIDSSIMITSQILFFGFGWLFMRQLFKDYEIRQYVVQVIFSVTFAFSCTMFELIIFEILGV
LNSSRYFHWKMNL CVILLILVFMVPFYIGYFIVSNIRLLHKQRLLFSCLLWLTMYFFWKL GDP
FPILSPKHGILSIEQLISRGVIGVTL MALLSGFGAVNCPYTYMSYFLRNVTDDILALERRLLQ
TMDMIISKKRMAMARRTMFQKGEVHNKPSGFWGMIKSVTTSASGSENLT LIQQEVDAL EELSRO
LFLETADLYATKERIEYSKTFKGKYNFLGYFFSIYCVWKIFMATINIVFDRVGGKTD PVTRGIEI
TVNYLGIQFDVKFWSQHISFILVGIIIVTSIRGLLITLTKFFYAISSSKSSNVIVLLLAQIMGY
FVSSVLLIRMSMPLEYRTIITEVLGELQFNFYHRWFDVIFLVSALSSILFLYLAHQAPEKQMAP

Important features:

Signal peptide:

amino acids 1-23

Potential transmembrane domains:

amino acids 37-55, 81-102, 150-168, 288-311, 338-356, 375-398,
425-444

N-glycosylation sites.

amino acids 67-70, 180-183 and 243-246

Eukaryotic cobalamin-binding proteins

amino acids 151-160

FIGURE 5

AGCAGGGAAATCCGGATGTCTCGGTTATGAAGTGGAGCAGTGAGTGTGAGCCTCAACATAGTTCC
AGAACTCTCCATCCGGACTAGTTATTGAGCATCTGCCTCTCATATCACCAGTGGCCATCTGAGGT
GTTTCCCTGGCTCTGAAGGGGTAGGCACGATGGCCAGGTGCTTCAGCCTGGTGTGCTTCTCACT
TCCATCTGGACCACGAGGCTCCTGGTCCAAGGCTCTTTGCGTGCAGAAGAGCTTTCATCCAGGT
GTCATGCAGAATTATGGGGATCACCCCTTGTGAGCAAAAAGGCGAACCAGCAGCTGAATTTACAG
AAGCTAAGGAGGCCTGTAGGCTGCTGGGACTAAGTTTGGCCGGCAAGGACCAAGTTGAAACAGCC
TTGAAAGCTAGCTTTGAAACTTGCAGCTATGGCTGGGTTGGAGATGGATTTCGTGGTCACTCTAG
GATTAGCCCAAACCCCAAGTGTGGGAAAAATGGGGTGGGTGTCTGATTTGGAAGGTTCCAGTGA
GCCGACAGTTTGCAGCCTATTGTTACAACCTCATCTGATACTTGGACTAACTCGTGCATTCAGAA
ATTATCACCACCAAAGATCCCATATTC AACACTCAAACACAAACAACAGAATTTATTGT
CAGTGACAGTACCTACTCGGTGGCATCCCTTACTCTACAATACCTGCCCTACTACTCTCTC
CTGCTCCAGCTTCCACTTCTATTCCACGGAGAAAAAATTGATTTGTGTACAGAAAGTTTTTATG
GAACTAGCACCATGTCTACAGAACTGAACCATTTGTTGAAAATAAAGCAGCATTCAGAATGA
AGCTGCTGGGTTTGGAGGTGTCCCCACGGCTCTGCTAGTGCTTGCTCTCTCTCTTTGGTGCTG
CAGCTGGTCTTGGATTTGCTATGTCAAAGGTATGTGAAGGCCTTCCCTTTTACAAACAAGAAT
CAGCAGAAGGAAATGATCGAAACCAAAGTAGTAAAGGAGGAGAAGGCCAATGATAGCAACCCTAA
TGAGGAATCAAAGAAAACCTGATAAAAACCCAGAAGAGTCCAAGAGTCCAAGCAAAACTACCGTGC
GATGCCTGGAAGCTGAAGTTTAGATGAGACAGAAATGAGGAGACACACCTGAGGCTGGTTTCTTT
CATGCTCCTTACCCTGCCCCAGCTGGGGAAATCAAAGGGCCAAAGAACCAAAGAAGAAAGTCCA
CCCTTGGTTCCCTAACTGGAAATCAGCTCAGGACTGCCATTGGACTATGGAGTGCACCAAAGAGAAT
GCCCTTCTCCTTATTGTAACCCTGTCTGGATCCTATCCTCCTACCTCCAAAGCTTCCCACGGCCT
TTCTAGCCTGGCTATGTCTAATAATATCCCACTGGGAGAAAGGAGTTTGTCAAAGTGCAAGGAC
CTAAAACATCTCATCAGTATCCAGTGGTAAAAGGCCTCCTGGCTGTCTGAGGCTAGGTGGGTTG
AAAGCCAAGGAGTCACTGAGACCAAGGCTTCTCTACTGATTCGCAGCTCAGACCCTTCTTCA
GCTCTGAAAGAGAAACACGTATCCACCTGACATGTCTTCTGAGCCCCGTAAGAGCAAAAGAAT
GGCAGAAAAGTTTAGCCCCTGAAAGCCATGGAGATTCTCATAACTTGAGACCTAATCTCTGTAAA
GCTAAAATAAAGAAATAGAACAAGGCTGAGGATACGACAGTACACTGTCAGCAGGGACTGTAAAC
ACAGACAGGGTCAAAGTGTTTCTCTGAACACATTGAGTTGGAATCACTGTTTAGAACACACACA
CTTACTTTTTCTGGTCTCTACCCTGCTGATATTTTCTCTAGGAAATATACTTTTACAAGTAACA
AAAATAAAAACCTCTATAAAATTTCTATTTTTTATCTGAGTTACAGAAATGATTACTAAGGAAGATT
ACTCAGTAATTTGTTTAAAAGTAATAAAATTC AACAAACATTTGCTGAATAGCTACTATATGTC
AAGTGCTGTGCAAGGTATPACACTCTGTAATTGAATATTATTCTCAAAAAATTGCACATAGTAG
AACGCTATCTGGGAAGCTATTTTTTTCAGTTTTGATATTTCTAGCTTATCTACTTCCAACTAAT
TTTTATTTTTGCTGAGACTAATCTTATTCATTTTTCTCTAATATGGCAACCATTATAACCTTAAT
TATTATTAACATACCTAAGAAGTACATTGTTACCTCTATATACCAAAGCACATTTTAAAAGTGCC
ATTAACAAATGTATCACTAGCCCTCTTTTTTCCAACAAGAAGGGACTGAGAGATGCAGAAATATT
TGTGACAAAAAATTAAGCATTTAGAAACTT

FIGURE 6

MARCFSLVLLLSIWTTTRLLVQGSRLRAEELSIQVSCRIMGITLVSKKANQQLNFTEAKEACRLLG
LSLAGKDQVETALKASFETCSYGWVGDGFVVISRISPKNPKCGKNGVGVLIWKVPVSRQFAAYCYN
SSDTWTNSCIPEIITTKDPIENTQTATQTTEFIVSDSTYSVASPYSTIPAPTTTPPAPASTSIPR
RKKLICVTEVFMETSTMSTETEPFVENKAAFKNEAAGFGGVPTALLVLALLFFGAAAGLGFCYVK
RYVKAFPFTNKNQOKEMIETKVVKEEKANDSNPNEESKKTDKNPEESKSPSKTTVRCLEAEV

Signal sequence:

amino acids 1-16

Transmembrane domain:

amino acids 235-254

N-glycosylation site.

amino acids 53-57, 130-134, 289-293

Casein kinase II phosphorylation site.

amino acids 145-149, 214-218

Tyrosine kinase phosphorylation site.

amino acids 79-88

N-myristoylation site.

amino acids 23-29, 65-71, 234-240, 235-239, 249-255, 253-259

FIGURE 7

CGCCGCGCTCCCGCACCCGCGGCCCGCCACCGCGCCGCTCCCGCATCTGCACCCGCAGCCCGGCG
GGCCTCCCGGCGGGAGCGAGCAGATCCAGTCCGGCCCGCAGCGCAACTCGGTCCAGTCGGGGCGG
CGGCTGCGGGCGCAGAGCGGAGATGCAGCGGCTTGGGGCCACCCTGCTGTGCCTGCTGCTGGCGG
CGGCGGTCCCCACGGCCCCCGCGCCGCTCCGACGGCGACCTCGGCTCCAGTCAAGCCCCGGCCCCG
GCTCTCAGCTACCCGCAGGAGGAGGCCACCCTCAATGAGATGTTCCGCGAGGTTGAGGAAC TGAT
GGAGGACACGCAGCACAAATTCGCGAGCGCGGTGGAAGAGATGGAGGCAGAAGAAGCTGCTGCTA
AAGCATCATCAGAAGTGAACCTGGCAAACCTTACCTCCCAGCTATCACAATGAGACCAACACAGAC
ACGAAGGTTGGAAATAATACCATCCATGTGCACCCGAGAAATTCACAAGATAACCAACAACCAGAC
TGGACAAATGGTCTTTTTAGAGACAGTTATCACATCTGTGGGAGACGAAGAAGGCAGAAGGAGCC
ACGAGTGCATCATCGACGAGGACTGTGGGCCAGCATGTACTGCCAGTTTGCCAGCTTCCAGTAC
ACCTGCCAGCCATGCCGGGGCCAGAGGATGCTCTGCACCCGGGACAGTGAGTGCTGTGGAGACCA
GCTGTGTGTCTGGGGTCACTGCACCAAATGGCCACCAGGGGCAGCAATGGGACCATCTGTGACA
ACCAGAGGGACTGCCAGCCGGGGCTGTGCTGTGCCTTCCAGAGAGGCCTGCTGTCCCTGTGTGC
ACACCCCTGCCCGTGGAGGGCGAGCTTGGCCATGACCCCGCCAGCCGGCTTCTGGACCTCATCAC
CTGGGAGCTAGAGCCTGATGGAGCCTTGGACCGATGCCCTTGTGCCAGTGGCCTCCTCTGCCAGC
CCCACAGCCACAGCCTGGTGTATGTGTGCAAGCCGACCTTCGTGGGGAGCCGTGACCAAGATGGG
GAGATCCTGCTGCCAGAGAGGTCCCCGATGAGTATGAAGTTGGCAGCTTCATGGAGGAGGTGCG
CCAGGAGCTGGAGGACCTGGAGAGGAGCCTGACTGAAGAGATGGCGCTGGGGGAGCCTGCGGCTG
CCGCCGCTGCACTGCTGGGAGGGGAAGAGATTTAGATCTGGACCAGGCTGTGGGTAGATGTGCAA
TAGAAATAGCTAATTTATTTCCCCAGGTGTGTGCTTTAGGCGTGGGCTGACCAGGCTTCTTCCTA
CATCTTCTCCAGTAAGTTTCCCTCTGGCTTGACAGCATGAGGTGTTGTGCATTTGTTGAGCT
CCCCCAGGCTGTTCTCCAGGCTTCACAGTCTGGTGTGGGAGAGTCAGGCAGGGTTAAACTGCA
GGAGCAGTTTGCCACCCCTGTCCAGATTATTGGCTGCTTTGCCTCTACCAGTTGGCAGACAGCCG
TTTGTCTACATGGCTTTGATAAATGTTTGGAGGGGAGGAGATGGAAACAATGTGGAGTCTCCCTC
TGATTGGTTTTGGGAAATGTGGAGAAGAGTGCCCTGCTTTGCAAACATCAACCTGGCAAATG
CAACAAATGAATTTCCACGCAGTTCTTTCCATGGGCATAGGTAAGCTGTGCCTCAGCTGTTGC
AGATGAAATGTTCTGTTACCCTGCATTACATGTGTTTATTCATCCAGCAGTGTGCTCAGCTCC
TACCTCTGTGCCAGGGCAGCATTTTCATATCCAAGATCAATTCCTCTCTCAGCACAGCCTGGGG
AGGGGGTCATTGTTCTCCTCGTCCATCAGGGATCTCAGAGGCTCAGAGACTGCAAGCTGCTTGCC
CAAGTCACACAGCTAGTGAAGACCAGAGCAGTTTCATCTGGTTGTGACTCTAAGCTCAGTGCTCT
CTCCACTACCCACACCAGCCTTGGTGCCACCAAAGTGCTCCCCAAAAGGAAGGAGAATGGGAT
TTTTCTTGAGGCATGCACATCTGGAATTAAGGTCAAAC TAATTCTCACATCCCTCTAAAAGTAAA
CTACTGTTAGGAACAGCAGTGTCTCACAGTGTGGGGCAGCCGTCCTTCTAATGAAGACAATGAT
ATTGACACTGTCCCTCTTGGCAGTTGCATTAGTAACCTTTGAAAGGTATATGACTGAGCGTAGCA
TACAGGTTAACCTGCAGAAACAGTACTTAGGTAATTGTAGGGCGAGGATTATAAATGAAATTTGC
AAAATCACTTAGCAGCAACTGAAGACAATTATCAACCACGTGGAGAAAATCAAACCGAGCAGGGC
TGTGTGAAACATGGTTGTAATATGCGACTGCGAACACTGAACTCTACGCCACTCCACAAATGATG
TTTTCAGGTGTCATGGACTGTTGCCACCATGTATTTCATCCAGAGTCTTAAAGTTTAAAGTTGCA
CATGATTGTATAAGCATGCTTTCTTTGAGTTTTAAATTATGTATAAACATAAGTTGCATTTAGAA
ATCAAGCATAAATCACTTCAACTGCAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 8

MQRLGATLLCLLLAAAVPTAPAPAPTATSAPVKPGPALSYPQEEATLNEMFREVEELMEDTQHKL
RSAVEEMEAEEAAKASSEVNLANLPPSYHNETNTDTKVGNNTIHVHREIHKITNNQTGOMVFSE
TVITSVGDEEGRRSHECIIDEDCGPSMYCQFASFQYTCQPCRGQRMCLTRDSECCGDQLCVWGHC
TKMATRGSNGTICDNQRDCQPLCCAFQRGLLFPVCTPLPVEGELCHDPASRLLDLITWELEPDG
ALDRPCASGLLCQPHSHSLVYVCKPTFVGSRDQDGEILLPREVPDEYEVGSMEEVROLELDLE
RSLTEEMALGEPAAAAAALLGEEI

Signal sequence:

amino acids 1-19

N-glycosylation site.

amino acids 96-100, 106-110, 121-125, 204-208

Casein kinase II phosphorylation site.

amino acids 46-50, 67-71, 98-102, 135-139, 206-210, 312-316,
327-331

N-myristoylation site.

amino acids 202-208, 217-223

Amidation site.

amino acids 140-144

FIGURE 9

CGGACGCGTGGGCGGACGCGTGGGGGCTGTGAGAAAGTGCCAATAAATACATCATGCAACCCAC
GGCCCACCTTGTGAACTCCTCGTGCCCAGGGCTGATGTGCGTCTTCCAGGGCTACTCATCCAAAG
GCCTAATCCAACGTTCTGTCTTCAATCTGCAAATCTATGGGGTCTGGGGCTCTTCTGGACCCTT
AACTGGGTACTGGCCCTGGGCCAATGCGTCTCGCTGGAGCCTTTGCCTCCTTCTACTGGGCCTT
CCACAAGCCCCAGGACATCCCTACCTTCCCCTTAATCTCTGCCTTCATCCGCACACTCCGTTACC
ACACTGGGTCAATTGGCATTGGAGCCCTCATCCTGACCCTTGTGCAGATAGCCCCGGGTCACTTG
GAGTATATTGACCACAAGCTCAGAGGAGTGCAGAACCCTGTAGCCCCTGCATCATGTGCTGTTT
CAAGTGCTGCCTCTGGTGTCTGGAAAAATTTATCAAGTTCCTAAACCGCAATGCATACATCATGA
TCGCCATCTACGGGAAGAATTTCTGTGTCTCAGCCAAAAATGCGTTCATGCTACTCATGCGAAAC
ATTGTCAGGGTGGTTCCTGGACAAAGTCACAGACCTGCTGCTGTTCTTTGGGAAGCTGCTGGT
GGTCCGAGGCGTGGGGTCTGTCTTCTTTTTTCTCCGGTCCGATCCCGGGCTGGGTAAAG
ACTTTAAGAGCCCCACCTCAACTATTACTGGCTGCCCATCATGACCTCCATCCTGGGGGCTAT
GTCATCGCCAGCGGCTTCTTCAGCGTTTTTCGGCATGTGTGTGGACACGCTCTTCTCTGCTTCT
GGAAGACCTGGAGCGGAACAACGGCTCCCTGGACCGGCCCTACTACATGTCCAAGAGCCTTCTAA
AGATTCTGGGCAAGAAGAACGAGGCGCCCCGGACAACAAGAAGAGGAAGAAGTGACAGCTCCGG
CCCTGATCCAGGACTGCACCCACCCACCGTCCAGCCATCCAACCTCACTTCGCCTTACAGGT
CTCCATTTTGTGGTAAAAAAGTTTTAGGCCAGGCGCCGTGGCTCACGCCTGTAATCCAACACT
TTGAGAGGCTGAGGCGGGCGGATCACCTGAGTCAGGAGTTCGAGACCAGCCTGGCCAACATGGTG
AAACCTCCGTCTCTATTAAAAATACAAAAATTAGCCGAGAGTGGTGGCATGCACCTGTGCATCCCA
GCTACTCGGGAGGCTGAGGCAGGAGAATCGCTTGAACCCGGGAGGCAGAGGTTGCAGTGAGCCGA
GATCGCGCCACTGCACTCCAACCTGGGTGACAGACTCTGTCTCCAAAACAAAACAAACAAACAA
AAGATTTTATTAAAGATATTTGTAACTC

FIGURE 10

RTRGRTRGGCEKVPINTSCNPTAHLVNSSCPGLMCFVFGYSSKGLIQRSVFNLQIYGVLGLFWTL
NWLALGQCVLGAFASFYWAFHKPQDIPTFPLISAFIRTLRYHTGSLAFGALILTLVQIARVIL
EYIDHKLRGVQNPVARCIMCCFKCLWCLEKFIKFLNRNAYIMIAIYGKNFCVSAKNAFMLLMRN
IVRVVLDKVTDLLLFFGKLLVVGVGVLSEFFFSGRIPGLGKDFKSPHLNYYWLPIMTSILGAY
VIASGFFSVFGMCDTFLFLCFLEDLERNNGSLDRPYMSKSLKILGKKNEAPPDNKKRKK

Important features:

Transmembrane domains:

amino acids 57-80 (type II), 110-126, 215-231, 254-274

N-glycosylation sites.

amino acids 16-20, 27-31, 289-293

Hypothetical YBR002c family proteins.

amino acids 276-288

Ammonium transporters proteins.

amino acids 204-231

N-myristoylation sites.

amino acids 60-66, 78-84

Amidation site.

amino acids 306-310

FIGURE 11

GCCCCGCGCCCGGGCGCCGGGGCGCCCGAAGCCGGGAGCCACCGCCATGGGGGCCTGCCTGGGAGCCTGC
TCCCTGCTCAGCTGCGCGTCTGCCTCTGCGGCTCTGCCCCCTGCATCCTGTGCAGCTGCTGCCCCGC
CAGCCGCAACTCCACCGTGAGCCGCTCATCTTCACGTTCTTCCTCTTCCTGGGGGTGCTGGTGTCCA
TCATTATGCTGAGCCCGGGCGTGGAGAGTCAGCTCTACAAGCTGCCCTGGGTGTGTGAGGAGGGGGCC
GGGATCCCCACCGTCCCTGCAGGGCCACATCGACTGTGGCTCCCTGCTTGGCTACCGCGCTGTCTACCG
CATGTGCTTCGCCACGGCGGCTTCTTCTTCTTCTTTTTACCCTGCTCATGCTCTGCGTGAGCAGCA
GCCGGGACCCCCGGGTGCCATCCAGAATGGGTTTTGGTTCTTTAAGTTCCTGATCCTGGTGGGCCTC
ACCGTGGGTGCCTTCTACATCCCTGACGGCTCCTTACCAACATCTGGTTCTACTTCGGCGTCGTGGG
CTCCTTCCCTCTCATCCTCATCCAGCTGGTGTGCTCATCGACTTTGCGCACTCCTGGAACCAGCGGT
GGCTGGGCAAGGCCGAGGAGTGCATTCCCCTGCCTGGTACGCAGGCCTCTTCTTCTTCACTCTCCTC
TTCTACTTGCTGTGCATCGCGGCCGTGGCGCTGATGTTTACTACTGAGCCAGCGGGTGC
CGAGGGCAAGGTCTTCATCAGCCTCAACCTCACCTTCTGTGTCTGCGTGTCCATCGCTGCTGTCTGC
CCAAGGTCCAGGACGCCAGCCCAACTCGGGTCTGCTGCAGGCCTCGGTATCACCTCTACACCATG
TTTGTACCTGGTFCAGCCCTATCCAGTATCCCTGAACAGAAATGCAACCCCATTTGCCAACCAGCT
GGGCAACGAGACAGTTGTGGCAGGCCCCGAGGGCTATGAGACCCAGTGGTGGGATGCCCGAGCATTG
TGGGCCTCATCATCTTCCCTCCTGTGCACCCTCTTCATCAGTCTGCGCTCCTCAGACCACGGCAGGT
AACAGCCTGATGCAGACCAGGAGTGCCACCTATGCTAGACGCCACACAGCAGCAGCAGCAGGAT
GGCAGCCTGTGAGGGCCGGGCTTTGACAACGAGCAGGACGGCGTCACCTACAGCTACTCCTTCTTCC
ACTTCTGCCTGGTGTGGCTCACTGCACGTCATGATGACGCTCACCAACTGGTACAAGCCCGGTGAG
ACCCGGAAGATGATCAGCACGTGGACCGCCGTGTGGGTGAAGATCTGTGCCAGCTGGGCAGGGCTGCT
CCTCTACCTGTGGACCCTGGTAGCCCCACTCCTCCTGCGCAACCGCGACTTCAGCTTGAGGCAGCCTCA
CAGCCTGCCATCTGGTGCCTCCTGCCACCTGGTGCCTCTCGGCTCGGTGACAGCCAACCTGCCCCCTC
CCCACACCAATCAGCCAGGCTGAGCCCCACCCCTGCCCCAGCTCCAGGACCTGCCCTGAGCCGGGC
CTTCTAGTTCGTAGTGCCTTCAGGGTCCGAGGAGCATCAGGCTCCTGCAGAGCCCCATCCCCCGCCAC
ACCCACACGGTGGAGCTGCCTCTTCCCTTCCCTCCTCCCTGTTGCCATACTCAGCATCTCGGATGAA
AGGGCTCCCTTGTCTCAGGCTCCACGGGAGCGGGGCTGCTGGAGAGAGCGGGGAACCTCCACCACAG
TGGGGCATCCGGCACTGAAGCCCTGGTGTCTCCTGGTACGTCCTCCAGGGGACCTGCCCCCTCCTG
GACTTCGTGCCTTACTGAGTCTTAAGACTTTTTCTAATAAACAAGCCAGTGCCTGTAAAAAAA

FIGURE 12

MGACLGACSLLSASCCLCGSAPCILSCCPASRNSTVSRLI FTFFLFLGVLVSIIMLSPGVESQL
YKLPWVCEEAGIPIPTVLQGHIDCGSLLGYRAVYRMCFATAAFFFFFFFFFTLLMLCVSSSRDPRAAIQ
NGFWFFKFLILVGLTVGAFYIPDGSFTNIWFYFGVVGSFLFILIQLVLLIDFAHSWNQRWLGKAE
ECDSRAWYAGLFFFTLLFYLLSIAAVALMFMYYTEPSGCHEGKVFISLNLTFVCVVSIAAVLPKV
QDAQPNSGLLQASVITLYTMFVTWSALS SIPEQKCNPHLPTQLGNETVVAGPEGYETQWWDAPSI
VGLIIFLLCTLFISLRSSDHRQVNSLMQTEECPPMLDATQQQQQVAACEGRAFDNEQDGV TYSY
SFFHFCLV LASHVMMTLTNWYKPGETRKMISTWTAVVWKICASWAGLLLLYLWTLVAPLLLRNRD
FS

Signal sequence:

amino acids 1-20

Transmembrane domains:

amino acids 40-58, 101-116, 134-150, 162-178, 206-223, 240-257,
272-283, 324-340, 391-406, 428-444

FIGURE 13

CGGGCCAGCCTGGGGCGGCCGGCCAGGAACCACCCGTTAAGGTGTCTTCTCTTTAGGGATGGTGA
GGTTGGAAAAAGACTCCTGTAACCCTCCTCCAGGATGAACCACCTGCCAGAAGACATGGAGAACG
CTCTCACCGGGAGCCAGAGCTCCCATGCTTCTCTGCGCAATATCCATTCCATCAACCCACACAA
CTCATGGCCAGGATTGAGTCCCTATGAAGGAAGGGAAAAAGGCATATCTGATGTCAGGAGGAC
TTTCTGTTTGTGTTGTCACCTTTGACCTCTTATTGTAACATTACTGTGGATAATAGAGTTAAATG
TGAATGGAGGCATTGAGAACACATTAGAGAAGGAGGTGATGCAGTATGACTACTATTCTTCATAT
TTTGATATATTTCTTCTGGCAGTTTTTTCGATTTAAAGTGTTAATACTTGCATATGCTGTGTGCAG
ACTGCGCCATTGGTGGGCAATAGCGTTGACAACGGCAGTGACCAGTGCCTTTTTACTAGCAAAAG
TGATCCTTTTCGAAGCTTTTCTCTCAAGGGGCTTTTGGCTATGTGCTGCCCATCATTTTCATTCATC
CTTGCCTGGATTGAGACGTGGTTCCTGGATTTCAAAGTGTTACCTCAAGAAGCAGAAGAAGAAAA
CAGACTCCTGATAGTTCAGGATGCTTCAGAGAGGGCAGCACTTATACCTGGTGGTCTTTCTGATG
GTCAGTTTTATTCCCCTCCTGAATCCGAAGCAGGATCTGAAGAAGCTGAAGAAAAACAGGACAGT
GAGAAACCACTTTTAGAACTATGAGTACTACTTTTTGTTAAATGTGAAAAACCCTCACAGAAAGTC
ATCGAGGCAAAAAGAGGCAGGCAGTGGAGTCTCCCTGTGACAGTAAAGTTGAAATGGTGACGTC
CACTGCTGGCTTTATTGAACAGCTAATAAAGATTTATTTATTGTAATACCTCACAAACGTTGTAC
CATATCCATGCACATTTAGTTGCCTGCCTGTGGCTGGTAAGGTAATGTCATGATTCATCCTCTCT
TCAGTGAGACTGAGCCTGATGTGTTAACAAATAGGTGAAGAAAGTCTTGTGCTGTATTCCCTAATC
AAAAGACTTAATATATTGAAGTAACACTTTTTTAGTAAGCAAGATACCTTTTTATTTCAATTCAC
AGAATGGAATTTTTTGTTCATGTCTCAGATTTATTTGTATTTCTTTTTTAACACTCTACAT
TCCCTTGTTTTTTAACTCATGCACATGTGCTCTTTGTACAGTTTTAAAAAGTGAATAAAATCTG
ACATGTCAATGTGGCTAGTTTTATTTTTCTTGTTTTGCATTATGTGTATGGCCTGAAGTGTGGA
CTTGCAAAAGGGGAAGAAAGGAATTGCGAATACATGTAAAATGTCACCAGACATTTGTATTATTT
TTATCATGAAATCATGTTTTCTCTGATTGTTCTGAAATGTTCTAAATACTCTTATTTTGAATGC
ACAAAATGACTTAAACCATTCATATCATGTTTCCTTTGCGTTCAGCCAATTTCAATTAAAAATGAA
CTAAATTAAAA

FIGURE 14

MNHLPEDMENALTGSQSSHASLRNIHSINPTQLMARIESYEGREKKGISDVRRTFCLFVTFDLLF
VTLLWIIELNVNGGIENTLEKEVMQYDYYSSYFDIFLLAVFRFKVLILAYAVCRLRHHWAIALT
AVTSAFLLAKVILSKLFSQGAFGYVLPPIISFILAWIETWFLDFKVLQPQEAEEENRLLIVQDASER
AALIPGGLSDGQFYSPPESEAGSEEAEEKQDSEKPLLEL

Important features of the protein:

Signal peptide:

amino acids 1-20

Transmembrane domains:

amino acids 54-72, 100-118, 130-144, 146-166

N-myristoylation sites.

amino acids 14-20, 78-84, 79-85, 202-208, 217-223

FIGURE 15

ACTCGAACGCAGTTGCTTCGGGACCCAGGACCCCTCGGGCCCGACCCGCCAGGAAAGACTGAGG
CCGCGGCCCTGCCCCGCCCGGCTCCCTGCGCCCGCCGCCCTCCCGGGACAGAAGATGTGCTCCAG
GGTCCCTCTGCTGCTGCCGCTGCTCCTGCTACTGGCCCTGGGGCCTGGGGTGCAGGGCTGCCAT
CCGGCTGCCAGTGCAGCCAGCCACAGACAGTCTTCTGCACTGCCCGCCAGGGGACCACGGTGGCC
CGAGACGTGCCACCCGACACGGTGGGGCTGTACGTCTTTGAGAACGGCATCACCATGCTCGACGC
AGGCAGCTTTGCCGGCTGCCGGGCTGCAGTCTTGGACCTGTACAGAACCAGATCGCCAGCC
TGCCAGCGGGGTCTTCCAGCCACTGCCAACCTCAGCAACCTGGACCTGACGGCCAACAGGCTG
CATGAAATCACCAATGAGACCTTCCGTGGCCGTGGGGCCCTCGAGCGCCTCTACCTGGCAAGAA
CCGATCCGGCCATCCAGCCTGGTGCCCTTCGACACGCTCGACCGCCTCCTGGAGCTCAAGCTGC
AGGACAACGAGCTGCGGGCCTGCCCCGCTGCGCCTGCCCGCCTGCTGCTGCTGGACCTCAGC
CACAAACAGCCTCCTGGCCCTGGAGCCCGGCATCCTGGACACTGCCAACGTGGAGGCGCTGCGGCT
GGCTGGTCTGGGGCTGCAGCAGCTGGACGAGGGGCTCTTACGCCCTTGCACAACCTCCACGACC
TGGATGTGTCCGACAACCAGCTGGAGCGAGTGCCACCTGTGATCCGAGGCCTCCGGGGCTGACG
CGCCTGCGGCTGGCCGGCAACACCCGCATTGCCAGCTGCGGCCCGAGGACCTGGCCGGCCTGGC
TGCCCTGCAGGAGCTGGATGTGAGCAACCTAAGCCTGCAGGCCCTGCCTGGCGACCTCTCGGGCC
TCTTCCCCCGCTGCGGCTGCTGGCAGCTGCCCGCAACCCCTTCAACTGCGTGTGCCCCCTGAGC
TGGTTTGGCCCCCTGGGTGCGCGAGAGCCACGTCAACTGGCCAGCCCTGAGGAGACGCGCTGCCA
CTTCCCGCCCAAGAAGCCTGGCCGGCTGCTCCTGGAGCTTGAATACGCCGACTTTGGCTGCCAG
CCACCACCACACAGCCACAGTGCCACCACGAGGCCCGTGGTGCGGGAGCCACAGCCTTGTCT
TCTAGCTTGGCTCCTACCTGGCTTAGCCCCACAGCGCCGGCCACTGAGGCCCCAGCCCGCCCTC
CACTGCCCCACCGACTGTAGGGCTGTCCCCAGCCCCAGGACTGCCACCCTCCACCTGCCTCA
ATGGGGGCACATGCCACCTGGGGACACGGCACCACCTGGCGTGCTTGTGCCCCGAAGGCTTACG
GGCTGTACTGTGAGAGCCAGATGGGGCAGGGGACACGGCCAGCCCTACACCAGTCACGCCGAG
GCCACCACGGTCCCTGACCCTGGGCATCGAGCCGGTGGAGCCACCTCCCTGCGCGTGGGGCTGC
AGCGCTACCTCCAGGGGAGCTCCGTGCAGCTCAGGAGCCTCCGTCTCACCTATCGCAACCTATCG
GGCCCTGATAAGCGGCTGGTGACGCTGCGACTGCCTGCCTCGCTCGCTGAGTACACGGTCACCCA
GCTGCGGCCCAACGCCACTTACTCCGTCTGTGTATGCCTTTGGGGCCCGGGCGGGTGCCGGAGG
GCGAGGAGGCTGCGGGGAGGCCATACACCCAGCCGTCCACTCCAACCACGCCCCAGTCAAC
CAGGCCCGGAGGGCAACCTGCCGCTCCTCATTGGCCCCGCCCTGGCCCGGGTCTCCTGGCCGC
GCTGGCTGCGGTGGGGCAGCCTACTGTGTGCGGGCGGGGCGGGCCATGGCAGCAGCGGCTCAGG
ACAAAGGGCAGGTGGGGCCAGGGGCTGGGCCCTGGAACCTGGAGGGAGTGAAGGTCCCCTGGAG
CCAGGCCCGAAGGCAACAGAGGGCGGTGGAGAGGCCCTGCCAGCGGGTCTGAGTGTGAGGTGCC
ACTCATGGGCTTCCCAGGGCCTGGCCTCCAGTCAACCCCTCCACGCAAAGCCCTACATCTAAGCCA
GAGAGAGACAGGGCAGCTGGGGCCGGGCTCTCAGCCAGTGAGATGGCCAGCCCCCTCCTGCTGCC
ACACCACGTAAGTCTCAGTCCCAACCTCGGGGATGTGTGCAGACAGGGCTGTGTGACCACAGCT
GGGCCCTGTTCCCTCTGGACCTCGGTCTCCTCATCTGTGAGATGCTGTGGCCAGCTGACGAGCC
CTAACGTCCCCAGAACCGAGTGCCATGAGGACAGTGTCCGCCCTGCCCTCCGCAACGTGCAGTC
CCTGGGCACGGCGGGCCCTGCCATGTGCTGGTAACGCATGCCTGGGTCTGCTGGGCTCTCCAC
TCCAGGCCGACCCGGGGCCAGTGAAGGAAGCTCCCGAAAGAGCAGAGGGAGAGCGGGTAGGC
GGCTGTGTGACTCTAGTCTTGGCCCCAGGAAGCGAAGGAACAAAAGAACTGGAAAGGAAGATGC
TTTAGGAACATGTTTTGCTTTTTTAAAATATATATATTTATAAGAGATCCTTTCCATTTATTCT
GGGAAGATGTTTTCAAACCTCAGAGACAAGGACTTTGGTTTTTTGTAAGACAAACGATGATATGAA
GGCCTTTTTGTAAGAAAAAATAAAGATGAAGTGTGAAA

FIGURE 16

MCSRVPLLLLPLLLLLLALGPGVQGCPSGCQCSQPQTVFCTARQGTTVPRDVPDPTVGLYVFENGI T
MLDAGSFAGLPGLQLLDLSQNQIASLPSGVFQPLANLSNLDLTANRLHEITNETFRGLRRLERLY
LGKNRIRHIQPGAFDTLDRLELKLQDNELRALPPLRRLPRLLLLDLSHNSLLALEPGILD TANVE
ALRLAGLGLQQLDEGLFSRLRNLDLSDNQLERVPPVIRGLRGLTRLRLAGNTRIAQLRPEDL
AGLAALQELDVSNSLSLQALPGDLSGLFPRLRLAAARNPFNCVCPLSWFGPWVRESHVTLASPEE
TRCHFPPKNAGRLLLELDYADFGCPATTTTATVPTTRPVVREPTALSSSLAPTWLSPTAPATEAP
SPPSTAPPTVGPVPQDCPPSTCLNGGTCHLGRHHLACLCEGFTGLYCESOMGQTRPSPTP
VTPRPPRSLTLGIEPVSPSTLRVGLQRYLQSSVQLRSLRLTYRNLSGPDKRLVTLRLPASLAEY
TVTQLRPNATYSVCMPLGPGRVPEGEEACGEAHTPPAVHSNHAPVTQAREGNLPLLIAPALAAV
LLAALAAVGAAYCVRGRAMAAAAQDKGQVGPAGPLELEGVKVPLEPGPKATEGGGEALPSGSE
CEVPLMGFPGLQSPHAKPYI

Important features:

Signal peptide:

amino acids 1-23

Transmembrane domain:

amino acids 579-599

EGF-like domain cysteine pattern signature.

amino acids 430-442

Leucine zipper pattern.

amino acids 197-219, 269-291

N-glycosylation sites.

amino acids 101-105, 117-121, 273-277, 500-504, 528-532

Tyrosine kinase phosphorylation sites.

amino acids 124-131, 337-345

N-myristoylation sites.

amino acids 23-29, 27-33, 70-76, 142-148, 187-193, 348-354,
594-600, 640-646

FIGURE 18

MRVRIGLTLLLCAVLLSLASASSDEEGSQDESILDSKTTLTSDESVDHTTAGRVVAGQIFLDSESEL
ESSIQEEEDSLKSQEGESVTEDISFLESNPENKDYEEPKKVRKPALTAIEGTAHGEPCHFPPFLFDK
EYDECTSDGREDGRLWCATTYDYKADEKWFCEEEEEAAKRRQMQEAEMMYQTGMKILNGSNKKSQKR
EAYRYLQKAASMNHTKALERSYALLFGDYLPQNIQAAREMFEKLTTEEGSPKGTALGFLYASGLGVN
SSQAKALVYYTFGALGGNLI AHMVLVSRL

Important features:

Signal peptide:

amino acids 1-21

N-glycosylation sites.

amino acids 195-199, 217-221, 272-276

Tyrosine kinase phosphorylation site.

amino acids 220-228

N-myristoylation sites.

amino acids 120-126, 253-259, 268-274, 270-274, 285-291, 289-295

Glycosaminoglycan attachment site.

amino acids 267-271

Microbodies C-terminal targeting signal.

amino acids 299-303

Type II fibronectin collagen-binding domain protein.

amino acids 127-169

Fructose-bisphosphate aldolase class-II protein.

amino acids 101-119

FIGURE 20

MLFWVLGLLILCGFLWTRKGLKIEDITDKYIFITGCDSGFGNLAARTFDKKGFEHVIAACLTESG
STALKAETSERLRTVLLDVTDPENVKRTAQWVKNQVGEKGLWGLINNAGVPGVLAPTDWLTLEDY
REPIEVNLFGLISVTLNMLPLVKKAQGRVINVSSVGGRLAIVGGGYTPSKYAVEGFNDSLRRDMK
AFGVHVSCEIEPGLFKTNLADPVKVIKLAWEQLSPDIKQQYGEGYIEKSLDKLKGKNSYVNMD
LSPVVECMDHALTSLFPKTHYAAGKDAKI FWIPLSHMPAALQDFLLLKQKAELANPKAV

Important features of the protein:

Signal peptide:

amino acids 1-17

Transmembrane domain:

amino acids 136-152

N-glycosylation sites.

amino acids 161-163, 187-190 and 253-256

Glycosaminoglycan attachment site.

amino acids 39-42

N-myristoylation sites.

amino acids 36-41, 42-47, 108-113, 166-171, 198-203 and 207-212

FIGURE 21

CTGAGGCGGCGGTAGCATGGAGGGGGAGAGTACGTCGGCGGTGCTCTCGGGCTTTGTGCTCGGCG
CACTCGCTTTCCAGCACCTCAACACGGACTCGGACACGGAAGGTTTTCTTCTTGGGGAAGTAAAA
GGTGAAGCCAAGAACAGCATTACTGATTCCCAAATGGATGATGTTGAAGTTGTTTATACAATTGA
CATTCAGAAATATATTCATGCTATCAGCTTTTTAGCTTTTATAATTCTTCAGGCGAAGTAAATG
AGCAAGCACTGAAGAAAATATTATCAAATGTCAAAAAGAATGTGGTAGGTTGGTACAAATTCCGT
CGTCATTCAGATCAGATCATGACGTTTAGAGAGAGGCTGCTTCACAAAACCTGCAGGAGCATTT
TTCAAACCAAGACCTTGTTTTTCTGCTATTAACACCAAGTATAATAACAGAAAGCTGCTCTACTC
ATCGACTGGAACATTCCTTATATAAACCTCAAAAAGGACTTTTTTCACAGGGTACCTTTAGTGGTT
GCCAATCTGGGCATGCTGAACAACCTGGGTTATAAACTGTATCAGGTTCCCTGTATGTCCACTGG
TTTTAGCCGAGCAGTACAAACACACAGCTCTAAATTTTTTGAAGAAGATGGATCCTTAAAGGAGG
TACATAAGATAAATGAAATGTATGCTTCATTACAAGAGGAATTAAGAGTATATGCAAAAAAGTG
GAAGACAGTGAACAAGCAGTAGATAAACTAGTAAAGGATGTAAACAGATTAAAACGAGAAATTGA
GAAAAGGAGAGGAGCACAGATTCAGGCAGCAAGAGAGAAGAACATCCAAAAGACCCTCAGGAGA
ACATTTTTCTTTGTGTCAGGCATTACGGACCTTTTTTCCAAATCTGAATTTCTTCATTCATGTGTT
ATGTCTTTAAAAAATAGACATGTTTCTAAAAGTAGCTGTAAC TACAACCACCATCTCGATGTAGT
AGACAATCTGACCTTAATGGTAGAACACACTGACATTCCTGAAGCTAGTCCAGCTAGTACACCAC
AAATCATTAAGCATAAAGCCTTAGACTTAGATGACAGATGGCAATTC AAGAGATCTCGGTTGTTA
GATACACAAGACAAACGATCTAAAGCAAATACTGGTAGTAGTAACCAAGATAAAGCATCCAAAAT
GAGCAGCCCAGAAACAGATGAAGAAATTGAAAAGATGAAGGGTTTTGGTGAATATTCACGGTCTC
CTACATTTTGATCTTTTAACCTTACAAGGAGATTTTTTATTTGGCTGATGGGTAAAGCCAAAC
ATTTCTATTGTTTTTACTATGTTGAGCTACTTGCAGTAAGTTCATTTGTTTTTACTATGTTCCACC
TGTTTGCAGTAATACACAGATAACTCTTAGTGCATTTACTTCACAAAGTACTTTTTCAAACATCA
GATGCTTTTATTTCCAAACCTTTTTTTCACCTTTCACTAAGTTGTTGAGGGGAAGGCTTACACAG
ACACATTCCTTTAGAATTGGAAAAGTGAGACCAGGCACAGTGGCTCACACCTGTAATCCCAGCACT
TAGGGAAGACAAGTCAGGAGGATTGATTGAAGCTAGGAGTTAGAGACCAGCCTGGGCAACGTATT
GAGACCATGTCTATTAATAAATAAAATGAAAAGCAAGAATAGCCTTATTTTCAAAAATATGGAAA
GAAATTTATATGAAAATTTATCTGAGTCATTAATAATTCCTTAAGTGATACTTTTTTAGAAGTA
CATTATGGCTAGAGTTGCCAGATAAAATGCTGGATATCATGCAATAAATTTGCAAAACATCATCT
AAAATTTAAAAA AAAAAAAAAAAAAAAAAA

FIGURE 22

MEGESTSAVLSGFVLGALAFQHLNTSDTEGFLLGGEVKGEAKNSITDSQMDDVEVVYTIQKYI
PCYQLFSFYNSSGEVNEQALKKILSNVKNVVGWYKFRRHSDQIMTFRERLLHKNLQEHFSNQLL
VLLLLTPSIIITESCSTHRLEHSLYKPQKGLFHRVPLVVANLGMSEQLGYKTVSGSCMSTGFSSRAV
QTHSSKFFFEEDGSLKEVHKINEMYASLQEELKSICKKVEDSEQAVDKLVKDVNRLKREIEKRRGA
QIQAAREKNIQKDPQENIFLCQALRTFFPNSEFLHSCVMSLKNRHVSKSSCNYNHHLDVVDNLTL
MVEHTDIPEASPASTPQIIKHKALDLDDRWFKRSRLDLDQDKRSKANTGSSNQDKASKMSSPET
DEEIEKMKGFGEYSRSPTF

Important features:

Signal peptide:

amino acids 1-19

N-glycosylation sites.

amino acids 75-79, 322-326

N-myristoylation site.

amino acids 184-154

Growth factor and cytokines receptors family.

amino acids 134-150

FIGURE 23

GGCACAGCCGCGCGGGGAGGGCAGAGTCAGCCGAGCCGAGTCCAGCCGGACGAGCGGACCAGCGCAGGGCAGCCAA
GCAGCGCGCAGCGAACGCCCGCCGCCACACCTCTGCGGTCCCCGCGGGCCTGCCACCTTCCCTCCTTCCCC
GCGTCCCCGCTCGCGGCCAGTCAGCTTGCCGGTTGCGTGCCCCGGAACCCCGAGGTCAACAGCCGCGCTCT
GCTTCCCTGGGCGCGCGCCCTCCACGCCCTCCTTCTCCCTGGCCCGCGCTGGCACCGGGACCGTTGCCTGA
CGCGAGGCCAGCTCTACTTTTGGCCCCGCTCTCTCCGCTGCTCGCTCTTCCACCACTCCAACCTCCTTCTCCC
TCCAGCTCCACTCGCTAGTCCCGACTCCGCCAGCCCTCGGCCCGCTGCCGTAGCGCCGCTTCCCGTCCGGTCCAAA
GGTGGGAACGCGTCCGCCCGGCCCGCACCAATGGCACGGTTGCGCTTGCCCGCGTTCTCTGCACCCCTGGCAGTGCTC
AGCGCCGCGCTGCTGGCTGCCGAGCTCAAGTCGAAAAGTTGCTCGGAAGTGCGACGTCTTTACGTGTCAAAGGCTTC
AACAGAACGATGCCCCCTCCACGAGATCAACGGTGATCATTTGAAGATCTGTCCCCAGGGTTCTACCTGCTGCTCT
CAAGAGATGGAGGAGAAGTACAGCCTGCAAAGTAAAGATGATTTCAAAGTGTGGTCAGCGAACAGTGAATCATTTG
CAAGCTGTCTTTGCTTACGTTACAAGAAGTTTGATGAATTTCTCAAAGAACTACTTGAAAATGCAGAGAAATCCCTG
AATGATATGTTTGTGAAGACATATGGCCATTTATACATGCAAATTTCTGAGCTATTTAAAGATCTCTTGTAGAGTTG
AAACGTTACTACGTGGTGGGAAATGTGAACCTGGAAGAAATGCTAAATGACTTCTGGGCTCGCTCCTGGAGCGGATG
TTCCGCTGGTGAACCTCCAGTACCCTTTACAGATGAGTATCTGGAATGTGTGAGCAAGTATACGGAGCAGCTGAAG
CCCTTCGGAGATGTCCCTCGCAAATGGAAGCTCCAGGTTACTCGTGCTTTTGTAGCAGCCCGTACTTTCGCTCAAGGC
TTAGCGGTTGCGGGAGATGTCGTGAGCAAGGTTCCGTTGTAACCCACAGCCAGTGTACCCATGCCCTGTTGAAG
ATGATCTACTGCTCCACTGCCGGGTTCTCGTACTGTGAAGCCATGTACAACACTGCTCAAACATCATGAGAGGC
TGTGGCCAACCAAGGGGATCTCGATTTGAATGGAACAATTTTCATAGATGCTATGCTGATGGTGGCAGAGAGGCTA
GAGGGTCCTTTCAACATTGAATCGGTCATGGATCCCATCGATGTGAAGATTTCTGATGCTATTATGAACATGCAGGAT
AATAGTGTCAAGTGTCTCAGAAGGTTTTCAGGGATGTGGACCCCCAAGCCCTCCAGCTGGACGAATTTCTCGT
TCCATCTCTGAAAGTGCCTTCAGTGTCTGCTTCAGACCACATCACCCGAGGAACGCCCAACCACAGCAGCTGGCACT
AGTTTGGACCGACTGGTTACTGATGTCAAGGAGAACTGAAACAGGCCAAGAAATTTCTGGTCTCCCTTCGAGCAAC
GTTTGCAACGATGAGAGGATGGCTGCAGGAAACGGCAATGAGGATGACTGTTGGAATGGGAAAGGCAAAGCAGGTAC
CTGTTTGCAGTGACAGGAAATGGATTAGCCAACCAGGGCAACAACCCAGAGGTCCAGGTTGACACCAGCAAACCAGAC
ATACTGATCCTTCGTCAAATCATGGCTCTTCAGTGATGACCAGCAAGATGAAGAATGCATACAATGGGAACGACGTG
GACTTCTTTGATATCAGTGATGAAAGTAGTGGAGAAGGAAGTGAAGTGGCTGTGAGTATCAGCAGTGCCCTTCAGAG
TTTACTACAATGCCACTGACCATGCTGGGAAGAGTGCCAATGAGAAAGCCGACAGTGTGGTGTCCGTCTGGGGCA
CAGGCCTACCTCCTCACTGTCTTCTGCATCTTGTTCCTGGTTATGCAGAGAGAGTGGAGATTAATTCTCAAACCTCTGAG
AAAAAGTGTTCATCAAAAAGTTAAAAGGCACCAGTTATCACTTTCTACCATCCTAGTGACTTTGCTTTTAAATGAA
TGGACAACAATGTACAGTTTTTACTATGTGGCCACTGGTTTAAAGAAGTGTGACTTTGTTTTCTCATTGATTTTGGG
AGGAAAAGGGACTGTGCATTGAGTTGGTTCTGCTCCCCAAACCATGTTAAACGTGGCTAACAGTGTAGGTACAGAA
CTATAGTTAGTTGTGCAATTTGTGATTTTATCACTCTATTATTTGTTTTGATGTTTTTTCTCATTTCGTTTGTGGGTT
TTTTTTCCAACCTGTGATCTCGCTTGTTCCTTACAAGCAAACAGGGTCCCTTCTTGGCACGTACATGTACGTATT
TCTGAAATATTAATAGCTGTACAGAAGCAGGTTTTATTTATCATGTTATCTTATTAAGAAAAAGCCCAAAAAGC

FIGURE 24

MARFGLPALLCTLAVLSAALLAELKSKSCSEVRRLYVSKGFNKNDAPLHEINGDHLKICPQGST
CCSQEMEEKYSLQSKDDFKSVVSEQCNHLQAVFASRYKKFDEFFKELLENAEKSLNDMFVKTYGH
LYMQNSELFKDLFVELKRYVVGNVNLEMLNDFWARLLERMFRVNSQYHFTDEYLECVSKYTE
QLKPFQDVPRKLLQVTRAFVAARTFAQGLAVAGDVVSKVSVVNPTAQCTHALLKMIYCSHCRGL
VTVKPCYNYCSNIMRGCLANQGDLD FEWNNFIDAMLMVAERLEGPFNIESVMDPIDVKISDAIMN
MQDNSVQVSQKVFQCGCPPKPLPAGRISRSISESAFSARFRPHHPEERPTTAAGTSLDRLVTDVK
EKLKQAKKFWSSLPNVCNDERMAAGNGNEDDCWNGKGSRYLFAVTGNGLANQGNPEVQVDT
KPDILILRQIMALRVMTSKMKNAYNNGNDVDFDISDESSGEGSGSGCEYQQCPSEFDYNATDHAG
KSANEKADSAGVRPGAQAYLLTVFCILFLVMQREWR

Important features:

Signal peptide:

amino acids 1-22

ATP/GTP-binding site motif A (P-loop).

amino acids 515-524

N-glycosylation site.

amino acids 514-518

Glycosaminoglycan attachment sites.

amino acids 494-498, 498-502

N-myristoylation sites.

amino acids 63-69, 224-230, 276-282, 438-444, 497-503, 531-537

Glypicans proteins.

amino acids 54-75, 105-157, 238-280, 309-346, 423-460, 468-506

FIGURE 25

CTCGCCCTCAAATGGGAACGCTGGCCTGGGACTAAAGCATAGACCACCAGGCTGAGTATCCTGAC
CTGAGTCATCCCCAGGGATCAGGAGCCTCCAGCAGGGAACCTTCCATTATATTCTTCAAGCAACT
TACAGCTGCACCGACAGTTGCGATGAAAAGTTCTAATCTCTTCCCTCCTCCTGTTGCTGCCACTAA
TGCTGATGTCCATGGTCTCTAGCAGCCTGAATCCAGGGGTCGCCAGAGGCCACAGGGACCGAGGC
CAGGCTTCTAGGAGATGGCTCCAGGAAGGCGGCCAAGAATGTGAGTGCAAAGATTGGTTCCTGAG
AGCCCCGAGAAGAAAATTCATGACAGTGTCTGGGCTGCCAAAGAAGCAGTGCCCCTGTGATCATT
TCAAGGGCAATGTGAAGAAAACAAGACACCAAAGGCACCACAGAAAGCCAAACAAGCATTCCAGA
GCCTGCCAGCAATTTCTCAAACAATGTCAGCTAAGAAGCTTTGCTCTGCCTTTGTAGGAGCTCTG
AGCGCCCACTCTTCCAATTAACATTTCTCAGCCAAGAAGACAGTGAGCACACCTACCAGACACTC
TTCTTCTCCCACCTCACTCTCCCCTGTACCCACCCCTAAATCATTCCAGTGCTCTCAAAAAGCA
TGTTTTTCAAGATCATTTTGTGTTGTTGCTCTCTCTAGTGTCTTCTTCTCTCGTCAGTCTTAGCCT
GTGCCCTCCCCTTACCCAGGCTTAGGCTTAATTACCTGAAAGATTCAGGAAACTGTAGCTTCCT
AGCTAGTGTCAATTAACCTTAAATGCAATCAGGAAAGTAGCAAACAGAAGTCAATAAATATTTTT
AAATGTCAAAAAAAAAAAAAAAAAAAAA

FIGURE 26

MKVLISLLLLLLPLMLMSMVSSSLNPGVARGHRDRGQASRRWLQEGGQECECKDWFLRAPRRKEM
TVSGLPKKQCPCDHFKGNVKKTRHQRRHRKPNKHSRACQQFLKQCQLRSFALPL

Important features:

Signal peptide:

amino acids 1-22

N-myristoylation sites.

amino acids 27-33, 46-52

FIGURE 27

GGACGCCAGCGCCTGCAGAGGCTGAGCAGGGAAAAAGCCAGTGCCCCAGCGGAAGCACAGCTCAG
AGCTGGTCTGCCATGGACATCCTGGTCCCCTCCTGCAGCTGCTGGTGCTGCTTCTTACCCTGCC
CCTGCACCTCATGGCTCTGCTGGGCTGCTGGCAGCCCCGTGTGAAAAGCTACTTCCCCTACCTGA
TGGCCGTGCTGACTCCCAAGAGCAACCGCAAGATGGAGAGCAAGAAACGGGAGCTCTTCAGCCAG
ATAAAGGGGCTTACAGGAGCCTCCGGGAAAGTGGCCCTACTGGAGCTGGGCTGCGGAACCGGAGC
CAACTTTCAGTTCTACCCACCGGGCTGCAGGGTCACCTGCCTAGACCCAAATCCCCACTTTGAGA
AGTTCCTGACAAAGAGCATGGCTGAGAACAGGCACCTCCAATATGAGCGGTTTGTGGTGGCTCCT
GGAGAGGACATGAGACAGCTGGCTGATGGCTCCATGGATGTGGTGGTCTGCACTCTGGTGCTGTG
CTCTGTGCAGAGCCCAAGGAAGGTCTGCAGGAGGTCCGGAGAGTACTGAGACCGGGAGGTGTGC
TCTTTTTCTGGGAGCATGTGGCAGAACCATATGGAAGCTGGGCCTTCATGTGGCAGCAAGTTTTC
GAGCCCACCTGGAAACACATGGGGATGGCTGCTGCCTCACCAGAGAGACCTGGAAGGATCTTGA
GAACGCCCAGTTCTCCGAAATCAAATGGAACGACAGCCCCCTCCCTTGAAGTGGCTACCTGTTG
GGCCCCACATCATGGGAAAGGCTGTCAAACAATCTTTCCCAAGCTCCAAGGCACTCATTGTCTCC
TTCCCCAGCCTCCAATTAGAACAAGCCACCCACCAGCCTATCTATCTTCCACTGAGAGGGACCTA
GCAGAATGAGAGAAGACATTCATGTACCACCTACTAGTCCCTCTCTCCCAACCTCTGCCAGGGC
AATCTCTAACTTCAATCCCGCCTTCGACAGTGAAAAAGCTCTACTTCTACGCTGACCCAGGGAGG
AAACACTAGGACCCTGTTGTATCCTCAACTGCAAGTTTCTGGACTAGTCTCCCAACGTTTGCCTC
CCAATGTTGTCCCTTTCCCTTCGTTCCCATGGTAAAGCTCCTCTCGCTTTCCCTCCTGAGGCTACAC
CCATGCGTCTCTAGGAACTGGTCACAAAAGTCATGGTGCCTGCATCCCTGCCAAGCCCCCTGAC
CCTCTCTCCCCACTACCACCTTCTTCCCTGAGCTGGGGGCACCAGGGAGAATCAGAGATGCTGGGG
ATGCCAGAGCAAGACTCAAAGAGGCAGAGGTTTTGTCTCAAATATTTTTTAATAAATAGACGAA
ACCACG

FIGURE 28

MDILVPLLQLLVLLLTLPPLHLMALLGCWQPLCKSYFPYLMVLTPKSNRKMESKKRELFSSQIKGL
TGASGKVALLELGCGTGANFQFYPPGCRVTCLDPNPHFEKFLTKSMAENRHLQYERFVVAPGEDM
RQLADGSMDVVVCTLVLCVQSPRKVLQEVRRVLRPGGVLFWEHVAEPIYGSWAFMWQQVFEPTW
KHIGDGCCLTRETWKDLENAQFSEIQMERQPPPLKWLPGPHIMGKAVKQSFPSKALICSFPSL
QLEQATHQPIYLPRLGT

Important features:

Signal peptide:

amino acids 1-23

Leucine zipper pattern.

amino acids 10-32

N-myristoylation sites.

amino acids 64-70, 78-84, 80-86, 91-97, 201-207

FIGURE 29

CAATGTTTGCCTATCCACCTCCCCCAAGCCCCTTTACCTATGCTGCTGCTAACGCTGCTGCTGCT
GCTGCTGCTGCTTAAAGGCTCATGCTTGGAGTGGGGACTGGTCGGTGCCCAGAAAGTCTCTTCTG
CCACTGACGCCCCCATCAGGGATTGGGCCTTCTTTCCCCCTTCCTTTCTGTGTCTCCTGCCTCAT
CGGCCTGCCATGACCTGCAGCCAAGCCCAGCCCCGTGGGGAAGGGGAGAAAGTGGGGGATGGCTA
AGAAAGCTGGGAGATAGGGAACAGAAGAGGGTAGTGGGTGGGCTAGGGGGGCTGCCTTATTTAAA
GTGGTTGTTTATGATTCTTATACTAATTTATACAAAGATATTAAGGCCCTGTTTCATTAAGAAATT
GTTCCCTTCCCCTGTGTTCAATGTTTGTAAGATTGTTCTGTGTAAATATGTCTTTATAATAAAC
AGTTAAAAGCTGAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 30

MLLLTLLLLLLLLLKGSCLEWGLVGAQKVSSATDAPIRDWAFFPPSFLCLLPHRPAMTCSQAQPRG
EGEKVGDG

Important features:

Signal peptide:

amino acids 1-15

Growth factor and cytokines receptors family:

amino acids 3-18

FIGURE 31

GTTTGAATTCCTTCAACTATACCCACAGTCCAAAAGCAGACTCACTGTGTCCCAGGCTACCAAGTT
CCTCCAAGCAAGTCATTTCCCTTATTTAACCGATGTGTCCCTCAAACACCTGAGTGCTACTCCCT
ATTTGCATCTGTTTTGATAAATGATGTTGACACCCTCCACCGAATTCTAAGTGGAATCATGTCGG
GAAGAGATAACAATCCTTGGCCTGTGTATCCTCGCATTAGCCTTGCTTTGGCCATGATGTTTACC
TTCAGATTCATCACCACCCTTCTGGTTCACATTTTCATTTCATTGGTTATTTTGGGATTGTTGTT
TGTCTGCGGTGTTTTATGGTGGCTGTATTATGACTATAACCAACGACCTCAGCATAGAATTGGACA
CAGAAAGGGAAAATATGAAGTGCCTGCTGGGGTTTGCTATCGTATCCACAGGCATCAGGGCAGTG
CTGCTCGTCTTGATTTTTGTTCTCAGAAAGAGAATAAAAATTGACAGTTGAGCTTTTCCAAATCAC
AAATAAAGCCATCAGCAGTGCTCCCTTCCCTGCTGTTCCAGCCACTGTGGACATTTGCCATCCTCA
TTTTCTTCTGGGTCTCTGGGTGGCTGTGCTGCTGAGCCTGGGAACTGCAGGAGCTGCCCAGGTT
ATGGAAGGCGGCCAAGTGGAATATAAGCCCCCTTCGGGCATTCGGTACATGTGGTCGTACCATTT
AATTGGCCTCATCTGGACTAGTGAATTCATCCTTGCGTGCCAGCAAATGACTATAGCTGGGGCAG
TGGTTACTTGTATTTCAACAGAAGTAAAAATGATCCTCCTGATCATCCCATCCTTTTCGTCTCTC
TCCATTCTCTTCTTACCATCAAGGAACCGTTGTGAAAGGGTCATTTTAAATCTCTGTGGTGAG
GATTCCGAGAATCATTGTTCATGTACATGCAAACGCACTGAAAGAACAGCAGCATGGTGCATTGT
CCAGGTACCTGTTCCGATGCTGCTACTGCTGTTTTCTGGTGTCTTGACAAAATACCTGCTCCATCTC
AACCAGAATGCATATACTACAACCTGCTATTAATGGGACAGATTTCTGTACATCAGCAAAGATGC
ATTCAAAATCTTGTCCAAGAACTCAAGTCACTTTACATCTATTAAGTCTTTGGAGACTTCATAA
TTTTTCTAGGAAAGGTGTAGTGGTGTGTTTCACTGTTTTTGGAGGACTCATGGCTTTTAACTAC
AATCGGGCATTCCAGGTGTGGGCAGTCCCTCTGTTATTGGTAGCTTTTTTTGCCTACTTAGTAGC
CCATAGTTTTTTATCTGTGTTTGAAACTGTGCTGGATGCACTTTTCCCTGTGTTTTGCTGTTGATC
TGGAAACAAATGATGGATCGTCAGAAAAGCCCTACTTTATGGATCAAGAATTTCTGAGTTTCGTA
AAAAGGAGCAACAAATTAAACAATGCAAGGGCACAGCAGGACAAGCACTCATTAAGGAATGAGGA
GGGAAACAGAACTCCAGGCCATTGTGAGATTAGATACCCATTTAGGTATCTGTACCTGGAAAACATT
TCCTTCTAAGAGCCATTTACAGAATAGAAGATGAGACCACTAGAGAAAAGTTAGTGAATTTTTTT
TTAAAAGACCTAATAAACCCATTCTTCCTCAAAA

FIGURE 32

MSGRDTILGLCILALALSLAMMFTFRFITTLVHIFISLVILGLLFVCGVLWWLYDYTNDLSIE
LDTERENMKCVLGFVAVSTGITAVLLVLI FVLRKRRIKLTVELFQITNKAISSAPFLLFQPLWTF
ILIFFWVLWVAVLLSLGTAGAAQVMEGGQVEYKPLSGIRYMWSYHLIGLIWTSEFILACQOMTIA
GAVVTCYFNRSKNDPPDHPILSSLSILFFYHQGTVVKGSFLISVVRIPRIIVMYMQLKEQQHG
ALSRYLFRCCYCCFWCLDKYLLHLNQNAYTTTAINGTDFCTSADAFKILSKNSSHFTSINCFGD
FIIIFLGKVLVVCFTVFGGLMAFNYNRAFQVWAVPLLLVAFFAYLVAHSFLSVFETVLDALFLCFA
VDLETNDGSSEKPYFMDQEFLSFVKRSNKLNNARAQQDKHS LRNEEGTELQAIVR

Important features:

Signal peptide:

amino acids 1-20

Putative transmembrane domains:

amino acids 35-54, 75-97, 126-146, 185-204, 333-350, 352-371

N-glycosylation sites.

amino acids 204-208, 295-299, 313-317

N-myristoylation sites.

amino acids 147-153, 178-184, 196-202, 296-275, 342-348

FIGURE 34

MRTVVLTMKASVIEMFLVLLVTGVHSNKETAKKIKRPFVTPQINCDVKAGKIIDPEFIVKCPAG
CQDPKYHVYGTDVYASYSSVCGAAVHSGVLDNSGGKILVRKVAGQSGYKGSYSNGVQSLSLPRWR
ESFIVLESKPKKGVTPSALTYSSSKSPAAQAGETTKAYQRPPIPGTTAQFVTLMQLLAVTVAVA
TPTTLPRPSPSAASTTSPRPQSVGHRSEQEMDLWSTATYTSSQNRPRADPGIQRQDPSGAAAFQKP
VGADVSLGLVPKEELSTQSLPEVSLGDPNCKIDLSFLIDGSTSIGKRRFRIQKQLLADVAQALDI
GPAGPLMGVVQYGDNPATHFNLKHTNSRDLKTAIEKITQRGGLSNVGRAISFVTKNFFSKANGN
RSGAPNVVVVMVDGWPTDKVEEASRLARESGINIFFITIEGAAENEKQYVVEPNFANKAVCRTNG
FYSLHVQSWFGLHKTLOPLVKRVCDTDLRACSKTCLNSADIGFVIDGSSSVGTGNFRTVLQFVTN
LTKEFEISDTRIGAVQYTYEQRLFGFDKYSSKPDILNAIKRVGYWSGGTSTGAAINFALEQL
FKKSKPNKRKLMILITDGRSYDDVRIPAMAAHLKGVITYAIGVAWAAQEELEVIATHPARDHSFF
VDEFDNLHQYVPRIIQNICTEFNSQPRN

Important features:

Signal peptide:

amino acids 1-26

Transmembrane domain:

amino acids 181-200

N-glycosylation sites.

amino acids 390-394, 520-524

N-myristoylation sites.

amino acids 23-29, 93-99, 115-121, 262-268, 367-373, 389-395,
431-437, 466-472, 509-515, 570-576, 571-577, 575-581, 627-633

Amidation site.

amino acids 304-308

FIGURE 35

CCGAGCACAGGAGATTGCCTGCCTTAGGAGGTGGCTGCCTTGTGGGAAAAGCTATCAAGGAAGAAATTGC
CAAACCATGTCTTTTTTCTGTTTTTCAGAGTAGTTCACAACAGATCTGAGTGTTTTAATTAAGCATGGAAT
ACAGAAAACAACAAAAAACTTAAGCTTTAATTTTCATCTGGAATTCCACAGTTTTCTTAGCTCCCTGGACCC
GGTTGACCTGTTGGCTCTTCCCCTGGCTGCTCTATCACGTGGTGTCTCCGACTACTCACCCGAGTGTA
AAGAACCTTCGGCTCGCGTGCTTCTGAGCTGCTGTGGATGGCCTCGGCTCTCTGGACTGTCTTCCGAGTA
GGATGTCACCTGAGATCCCTCAAATGGAGCCTCCTGCTGCTGTCACTCCTGAGTTTTCTTTGTGATGTGGTAC
CTCAGCCTTCCCCTACAATGTGATAGAACGCGTGAAGTGGATGTACTTCTATGAGTATGAGCCGATTTA
CAGACAAGACTTTCACCTTCACACTTCGAGAGCATTCAAATGCTCTCATCAAATCCATTTCTGGTCATTCT
TGGTGACCTCCCACCTTCAGATGTGAAAGCCAGGCAGGCCATTAGAGTACTTGGGGTGAAAAAAGTCT
TGGTGGGGATATGAGGTTCTTACATTTTTCTTATTAGGCCAAGAGGCTGAAAAGGAAGACAAAAATGTTGGC
ATTGTCCTTAGAGGATGAACACCTTCTTTATGGTGACATAATCCGACAAGATTTTTTAGACACATATAATA
ACCTGACCTTGAAACCATTATGGCATTACAGGTGGGTAAGTACTGAGTTTTGCCCAATGCCAAGTACGTAATG
AAGACAGACACTGATGTTTTTCATCAATACTGGCAATTTAGTGAAGTATCTTTTAAACCTAAACCACTCAGA
GAAGTTTTTCACAGGTTATCCTCTAATGATAATTATTCCTATAGAGGATTTTACCAAAAACCCATATTT
CTTACCAGGAGTATCCTTTCAGGTGTTCCCTCCATACTGCAGTGGGTTGGGTTATATAATGTCAGAGAT
TTGGTGCCAAGGATCTATGAAATGATGGGTCAGTAAACCCATCAAGTTTGAAGATGTTTATGTCGGGAT
CTGTTTGAATTTATTTAAAGTGAACATTCATATTCAGAAGACACAAATCTTTCTTTCTATATAGAATCC
ATTTGGATGTCTGTCACTGAGACGTGTGATTGCAGCCCATGGCTTTTTCTTCCAAGGAGATCATCACTTTT
TGGCAGGTATGCTAAGGAACACCACATGCCATTATTAACCTTCACATTCTACAAAAGCCTAGAAGGACAG
GATACCTTGTGGAAAGTGTAAATAAAGTAGTACTGTGGAAAATTCATGGGGAGGTCAGTGTGCTGGCTT
ACACTGAACTGAACTCATGAAAACCCAGACTGGAGACTGGAGGGTTACACTTGTGATTTATTAGTCAGG
CCCTTCAAAGATGATATGTGGAGGAATTAATATAAAGGAATTGGAGGTTTTTGCTAAAGAAATTAATAGG
ACCAACAATTTGGACATGTCATTCTGTAGACTAGAATTTCTTAAAAGGGTGTACTGAGTTATAAGCTCA
CTAGGCTGTAAAAACAAAACAATGTAGAGTTTTATTATTGAACAATGTAGTCACTTGAAGGTTTTGTGTA
TATCTTATGTGGATTACCAATTTAAAATATATGTAGTCTGTGTCAAAAACCTTCTTCACTGAAGTTATA
CTGAACAAAATTTTACCTGTTTTTGGTCATTTATAAAGTACTTCAAGATGTTGCAGTATTTACAGTTATT
ATTATTTAAAATTACTTCACTTTGTGTTTTTAAATGTTTGGAGTTTCAATACAAGATAAAAAGGATAG
TGAATCATTTCTTACATGCAACATTTTCCAGTTACTTAACTGATCAGTTTATTATTGATACATCACTCCA
TTAATGTAAAGTCATAGGTCATTATTGCATATCAGTAATCTCTTGGACTTTGTTAAATATTTTACTGTGGT
AATATAGAGAAGAATTAAGCAAGAAAATCTGAAAA

FIGURE 36

MASALWTVLPSRMSLRSLKWSLLLLSLLSFFVMWYLSLPHYNVIERVNWYFYEYEPYRQDFHF
TLREHSNCSHQNPFLVILVTSHPSDVKARQAIRVTWGEKKSWWGYEVLTFLLGQEAEKEDKMLA
LSLEDEHLLYGDIIRQDFLDTYNNLTLKTIMAFRWVTEFCPNAKYVMKTDVDFINTGNLVKYLL
NLNHSEKFFTGYPLIDNYSYRGFYQKTHISYQYEPFKVFPYCSGLGYIMSRDLVPRIYEMMGHV
KPIKFEDVYVGICLNLKVNIIHIPEDTNLFFLYRIHLDVCQLRRVIAAHGFSSKEIITFWQVMLR
NTTCHY

Important features:

Type II transmembrane domain:

amino acids 20-39

N-glycosylation sites.

amino acids 72-76, 154-158, 198-202, 212-216, 326-330

Glycosaminoglycan attachment site.

amino acids 239-243

Ly-6 / u-PAR domain proteins.

amino acids 23-37

N-myristoylation site.

amino acids 271-277

FIGURE 38

MELGCWTQLGLTFLQLLLISSLPREYTVINEACPGAENIMCRECCEYDQIECVCPGKREVVGYT
IPCCRNEENECDSCLIHPGCTIFENCKSCRNGSWGGLDDFYVKGIFYCAECRAGWYGGDCMRCGQ
VLRAPKGQILLESYPLNAHCEWTIHAKPGFVIQLRFVMLSLEFDYMCQYDYVEVRDGDNRDGQII
KRVCGNERPAPIQSIGSSLHVLFHSDGSKNFDGFHAIYEEITACSSSPCFHDGTCVLDKAGSYKC
ACLAGYTGQRCECNLEERNCSDPGGPVNGYQKITGGPGLINGRHAKIGTVVSFFCNNSYVLSGNE
KRTCQQNGEWSGKQPICIKACREPKISDLVRRRVLPMQVQSRETPLHQLYSAAFSKQKLOSAPTK
KPALPFGDLPMGYQHLHTQLQYECISPFYRRLGSSRRTCLRTGKWSGRAPSCIPICGKIENITAP
KTQGLRWPWQAAIYRRTSGVHDGSLHKGAWFLVCSGALVNERTVVVAHCVTDLGKVTMIKTADL
KVVLGKFYRDDDRDEKTIQSLQISAILHPNYDPILLDADIAILKLLDKARISTRVQPICLAASR
DLSTSFQESHITVAGWNVLADVRS PGFKNDTLRSGVVSVVDSLLCEEQHEDHGIPVSVTDNMFCA
SWEPTAPSDICTAETGGIAAVSFPGRASPEPRWHLMLVSWSYDKTCSHRLSTAFTKVLFPFKDWI
ERNMK

Important features of the protein:

Signal peptide:

amino acids 1-23

EGF-like domain cysteine pattern signature.

amino acids 260-272

N-glycosylation sites.

amino acids 96-100, 279-283, 316-320, 451-455, 614-618

N-myristoylation sites.

amino acids 35-41, 97-103, 256-262, 284-290, 298-304, 308-314,
474-480, 491-497, 638-644, 666-672

Amidation site.

amino acids 56-60

Serine proteases, trypsin family.

amino acids 489-506

CUB domain proteins profile.

amino acids 150-167

FIGURE 39

GGTTCCTACATCCTCTCATCTGAGAATCAGAGAGCATAATCTTCTTACGGGCCCGTGATTTATTAACGTGGCTTAATC
 TGAAGGTTCTCAGTCAAATCTTTGTGATCTACTGATTGTGGGGCATGGCAAGGTTTGCTTAAAGGAGCTTGGCTGG
 TTTGGGCCCTTGTAGCTGACAGAAGGTGGCCAGGGAGAATGCAGCACACTGCTCGGAGAATGAAGGCGCTTCTGTTGC
 TGGTCTTGCCTTGGCTCAGTCTGTAACCTACATTGACAATGTGGGCAACCTGCACCTTCCCTGTATTTCAGAACTCTGTA
 AAGGTGCCTCCCACTACGGCCTGACCAAAGATAGGAAGAGGGCGCTCACAAGATGGCTGTCCAGACGGCTGTGCGAGCC
 TCACAGCCACGGCTCCCTCCCCAGAGGTTTCTGCAGCTGCCACCATCTCCTTAATGACAGACGAGCCTGGCCTAGACA
 ACCCTGCCTACGTGTCTCGGCAGAGGACGGGCAGCCAGCAATCAGCCAGTGGACTCTGGCCGGAGCAACCGAACTA
 GGGCACGGCCCTTTGAGAGATCCACTATTAGAAGCAGATCATTTAAAAAATAAATCGAGCTTTGAGTGTCTTCGAA
 GGACAAAGAGCGGGAGTGCAGTTGCCAACCATGCCGACCAGGGCAGGAAAATTCTGAAACACCACTGCCCTGAAG
 TCTTTCCAAGTGTGACCACCTGATTCAGATGGTGAATTAACAGCATCAAGATCAATCGAGTAGATCCAGTGA
 GCCTCTCTATTAGGCTGGTGGGAGTAGCGAAACCCACTGGTCCATATCATTATCCAACACATTTATCGTGATGGGG
 TGATCGCCAGAGACGGCCGGCTACTGCCAGGAGACATCATTTCTAAAGTCAACGGGATGGACATCAGCAATGTCCCTC
 ACAACTACGCTGTGCGTCTCCTGCGGCAGCCCTGCCAGGTGCTGTGGCTGACTGTGATGCGTGAACAGAAGTCCGCA
 GCAGGAACAATGGACAGGCCCGGATGCCTACAGACCCCGAGATGACAGCTTTCATGTGATTCTCAACAAAAGTAGCC
 CCGAGGAGCAGCTTGAATAAACTGGTGGCAAGGTGGATGAGCCTGGGGTTTTTCATCTTCAATGTGCTGGATGGCG
 GTGTGGCATATCGACATGGTGCAGCTTGGGAGAATGACCCTGTGTTAGCCATCAATGGACATGATCTTCGATATGGCA
 GCCAGAAAAGTGGGCTCATCTGATTCAGGCCAGTGAAGACGTGTTACCTCGTGTCCCGCCAGGTTCCGGCAGC
 GGAGCCCTGACATCTTTCAGGAAGCCGGCTGGAACAGCAATGGCAGCTGGTCCCAGGGCCAGGGGAGAGGAGCAACA
 CTCCAAGCCCTCCATCCTACAATTACTTGTGATGAGAAGGTGGTAAATATCCAAAAAGACCCCGGTGAATCTCTCG
 GCATGACCGTGCAGGGGGAGCATCACATAGAGAATGGGATTTGCCTATCTATGTCATCAGTGTGAGCCCGGAGGAG
 TCATAAGCAGAGATGGAAGAATAAAAAAGGTGACATTTTGTGAAATGTGGATGGGGTGAAGTGCAGAGGTGAGCC
 GGAGTGGGAGTGGCATTATTGAAAAGAACATCATCTCGATAGTACTCAAAGCTTTGGAAGTCAAAGAGTATGAGC
 CCCAGGAAGACTGCAGCAGCCCAGCAGCCCTGGACTCCAACCACAACATGGCCCCACCCAGTGAATGGTCCCCATCCT
 GGGTCATGTGGCTGGAATTACCACGGTCTTGTATAACTGTAAAGATATTGTATTACGAAGAAACACAGCTGGAAGTC
 TGGGCTTCTGCATTGTAGGAGGTTATGAAGAATACAATGGAAACAACCTTTTTTTCATCAAAATCCATTGTTGAAGGAA
 CACCAGCATACAATGATGGAAGAATTAGATGTGGTGTATTTCTTCTTGGCTGTCAATGGTAGAAGTACATCAGGAATGA
 TACATGCTTGGCTTGGCAAGACTGCTGAAAGAACTTAAAGGAAGAATTACTCTAACTATTGTTTCTTGGCCTGGCACTT
 TTTTATTAGAATCAATGATGGGTGAGGAAAACAGAAAAATCACAAATAGGCTAAGAAGTTGAAACACTATATTTATC
 TTGTCAGTTTTTATATTTAAAGAAAGAATACATGTAAAAATGTCAGGAAAAGTATGATCATCTAATGAAAGCCAGTT
 ACACCTCAGAAAATATGATTCAAAAAATTAATACTACTAGTTTTTTTTTTCAGTGTGGAGGATTTCTCATTACTCTAC
 AACATTGTTTTATATTTTTCTATTCAATAAAAAGCCCTAAAACAACATAAATGATTGATTTGTATACCCCACTGAATT
 CAAGCTGATTTAAATTTAAATTTGGTATATGCTGAAGTCTGCCAAGGGTACATTATGGCCATTTTTAATTTACAGCT
 AAAATATTTTTTAAATGCATTGCTGAGAAACGTTGCTTTCATCAACAAGAATAAATATTTTTTTCAGAAGTTAAA

FIGURE 40

MKALLLLVLPWLSPANYIDNVGNLHFLYSELCKGASHYGLTKDRKRRSQDGCPCDGCASLTATAPS
PEVSAAATISLMTDEPGLDNPAYVSSAEDGQPAISPVDSGRSNRTRARPFERSTIRSRSEFKKINR
ALSVLRRTKSGSAVANHADQGRENSENTTAPVFPRLYHLIPDGEITSIKINRVDPSESLSIRLV
GGSETPLVHIIIQHIYRDGVIARDGRLLPDGIILKVNMDISNVPHNYAVRLLRQPCQVLWLTVM
REQKFRSRNNGQAPDAYRPRDSSFHVILNKSSPEEQLGIKLVRKVDEPGVFI FNVLDGGVAYRHG
QLEENDRVLAINGHDLRYGSPESAHLIQASERRVHLVVSQRQRSPDIFQEAGWNSNGSWSFG
PGRSNTPKPLHPTITCHEKVVNIQKDPGESLGMTVAGGASHREWDLPYVISVEPPGGVISRDGR
IKTGDILLNVDGVELTEVSRSEAVALLKRTSSSIVLKALEVKEYEPQEDCSSPAALDSNHNMAPP
SDWSPSWMWLELPRCLYNCKDIVLRRNTAGSLGFCIVGGYEEYNGNKPFPIKSIVEGTPAYNDG
RIRCGDILLAVNGRSTSGMIHAACLARLLKELKGRITLTIVSWPGTFL

Important features:

Signal peptide:

amino acids 1-15

N-glycosylation sites.

amino acids 108-112, 157-161, 289-293, 384-388

Tyrosine kinase phosphorylation sites.

amino acids 433-441, 492-500

N-myristoylation sites.

amino acids 51-57, 141-147, 233-239, 344-350, 423-429, 447-453,
467-473, 603-609

FIGURE 41

ACCAGGCATTGTATCTTCAGTTGTCATCAAGTTCGCAATCAGATTGGAAAAGCTCAACTTGAAGCTTT
CTTGCCTGCAGTGAAGCAGAGAGATAGATATTATTACGTAATAAAAAACATGGGCTTCAACCTGACT
TTCCACCTTTCCTACAAATTCGATTACTGTTGCTGTTGACTTTGTGCCTGACAGTGGTGGGTGGGC
CACCAGTAACTACTTCGTGGGTGCCATTCAAGAGATTCCCTAAAGCAAAGGAGTTCATGGCTAATTCC
ATAAGACCCTCATTTTGGGGAAGGGAAAACTCTGACTAATGAAGCATCCACGAAGAAGGTAGAACTT
GACAACTGTCCTTCTGTGTCCTTACCTCAGAGGCCAGAGCAAGCTCATTTTCAAACCAGATCTCAC
TTTGAAGAGGTACAGGCAGAAAATCCCAAAGTGTCCAGAGGCCGGTATCGCCCTCAGGAATGTAAAG
CTTTACAGAGGGTCGCCATCCTCGTTCCCCACCGGAACAGAGAGAAACACCTGATGTACCTGCTGGAA
CATCTGCATCCCTTCTGCAGAGGCAGCAGCTGGATTATGGCATCTACGTATCCACCAGGCTGAAGG
TAAAAAGTTAATCGAGCCAAACTCTTGAATGTGGGCTATCTAGAAGCCCTCAAGGAAGAAAATGGG
ACTGCTTTATATTCCACGATGTGGACCTGGTACCCGAGAATGACTTTAACCTTTACAAGTGTGAGGAG
CATCCAAGCATCTGGTGGTGGCAGGAACAGCACTGGGTACAGGTTACGTTACAGTGGATATTTGG
GGGTGTTACTGCCCTAAGCAGAGAGCAGTTTTTCAAGGTGAATGGATTCTCTAACAACACTACTGGGGAT
GGGGAGGCGAAGACGATGACCTCAGACTCAGGTTGAGCTCCAAAGAATGAAAATTTCCCGGCCCTG
CCTGAAGTGGGTAAATATACAATGGTCTTCCACACTAGAGACAAAGGCAATGAGGTGAACGCAGAACG
GATGAAGCTCTTACACCAAGTGTACGAGTCTGGAGAACAGATGGGTTGAGTAGTTGTTCTTATAAAT
TAGTATCTGTGGAACACAATCCTTTATATATCAACATCACAGTGGATTTCTGGTTTGGTGCATAGACC
TGGATCTTTTGGTGTGTTTGAAGAAGTACTTCTTTGTTGCAATAATTTTGGCTAGAGACTTCAA
ATAGTAGCACACATTAAGAACCTGTTACAGCTCATTGTTGAGCTGAATTTTTCTTTTTGTATTTTCT
TAGCAGAGCTCCTGGTGTAGAGTATAAAACAGTTGTAACAAGACAGCTTTCTTAGTCATTTTGAT
CATGAGGGTTAAATATTGTAATATGGATACTTGAAGGACTTTATATAAAAGGATGACTCAAAGGATAA
AATGAACGCTATTTGAGGACTCTGGTTGAAGGAGATTTATTTAAATTTGAAGTAATATATTATGGGAT
AAAAGGCCACAGGAAATAAGACTGCTGAATGTCTGAGAGAACCAGAGTTGTTCTCGTCCAAGGTAGAA
AGGTACGAAGATAACAATACTGTTATTCAATTTATCCTGTACAATCATCTGTGAAGTGGTGGTGTGAGT
GAGAAGGCGTCCACAAAAGAGGGGAGAAAAGCGACGAATCAGGACACAGTGAACCTGGGAATGAAGA
GGTAGCAGGAGGGTGGAGTGTGCGCTGCAAAGGCAGCAGTAGCTGAGCTGGTTGCAGGTGCTGATAGC
CTTCAGGGGAGGACCTGCCAGGTATGCCTTCCAGTGATGCCACCAGAGAATACATTTCTCTATTAGT
TTTTAAAGAGTTTTTGTAAAATGATTTTGTACAAGTAGGATATGAATTAGCAGTTTACAAGTTTACAT
ATTAACTAATAATAAATATGTCTATCAAATACCTCTGTAGTAAAATGTGAAAAAGCAAAA

FIGURE 42

MGFNLT FHLSYKFRLLLLLTLCLTVVGVWATSNYFVGAIQEIPKAKEFMANFHKTLLILGKGKTLTN
EASTKKVELDNCPSVSPYLRGQSKLIFKPDLTLEEVQAENPKVSRGRYRPQECKALQRVAILVPH
RNREKHLMYLLEHLHPFLQRQQLDYGIYVIHQAEKGFNRKLLNVGYLEALKEENWDCFI FHDV
DLVPENDFNLYKCEEHPKHLVVGRNSTGYRLRYSGYFGGV TALSREQFFKVNGFSNNYWG WGGED
DDLRLRVELQRMKISRPLPEVGKYTMVFHTRDKGNEVNAERMKLLHQVSRVWR TDGLSSCSYKLV
SVEHNPLYINITVDFWFGA

Important features:

Signal peptide:

amino acids 1-27

N-glycosylation sites.

amino acids 4-8, 220-224, 335-339

Xylose isomerase proteins.

amino acids 191-202

FIGURE 44

MALSSQIWAACL LLLLLLLASLTSGSVFPQQTGQLAELQPQDRAGARASWMPMFQRRRRRDTHFPI
CIFCCGCCHRSKCGMCCKT

Important features:

Signal peptide:

amino acids 1-24

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 58-59

N-myristoylation site.

amino acids 44-50

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 1-12

FIGURE 45

GTGGCTTCATTTTCAGTGGCTGACTTCCAGAGAGCAATATGGCTGGTTCCCCAACATGCCTCACCC
TCATCTATATCCTTTGGCAGCTCACAGGGTCAGCAGCCTCTGGACCCGTGAAAGAGCTGGTCGGT
TCCGTTGGTGGGGCCGTGACTTTCCCCCTGAAGTCCAAAGTAAAGCAAGTTGACTCTATTGTCTG
GACCTTCAACACAACCCCTCTTGTACCATAACAGCCAGAAGGGGGCACTATCATAGTGACCCAAA
ATCGTAATAGGGAGAGAGTAGACTTCCCAGATGGAGGCTACTCCCTGAAGCTCAGCAAACCTGAAG
AAGAATGACTCAGGGATCTACTATGTGGGGATATACAGCTCATCACTCCAGCAGCCCTCCACCCA
GGAGTACGTGCTGCATGTCTACGAGCACCTGTCAAAGCCTAAAGTCACCATGGGTCTGCAGAGCA
ATAAGAATGGCACCTGTGTGACCAATCTGACATGCTGCATGGAACATGGGGAAGAGGATGTGATT
TATACCTGGAAGGCCCTGGGGCAAGCAGCCAATGAGTCCCATAATGGGTCCATCCTCCCCATCTC
CTGGAGATGGGGAGAAAGTGATATGACCTTCATCTGCGTTGCCAGGAACCCGTGCAGCAGAACT
TCTCAAGCCCCATCCTTGCCAGGAAGCTCTGTGAAGGTGCTGCTGATGACCCAGATTCTCCATG
GTCCTCCTGTGTCTCCTGTTGGTGCCCCTCCTGCTCAGTCTCTTTGTACTGGGGCTATTTCTTTG
GTTTCTGAAGAGAGAGAGACAAGAAGAGTACATTGAAGAGAAGAAGAGAGTGGACATTTGTCTGGG
AACTCCTAACATATGCCCCATTCTGGAGAGAACACAGAGTACGACACAATCCCTCACACTAAT
AGAACAATCCTAAAGGAAGATCCAGCAAATACGGTTTACTCCACTGTGGAAATACCGAAAAAGAT
GGAAAATCCCCACTCACTGCTCACGATGCCAGACACACCAAGGCTATTTGCCTATGAGAATGTTA
TCTAGACAGCAGTGCCTCCCCCTAAGTCTCTGCTCA

FIGURE 46

MAGSPTCLTLIYILWQLTGSAASGPVKELVGSVGGAVTFPLKSKVKQVDSIVWTFNTTPLVTIQP
EGGTIIIVTQNRNRERVDFFPDGGYSLKLSKLLKKNDSGIYYVGIYSSSLQQPSTQEYVLHVYEHLSK
PKVTMGLQSNKNGTCVTNLTCMEHGEEDVIYTWKALGQAANESHNGSILPISWRWGESDMTFIC
VARNPVSRNFSSPILARKLCEGAADDPDSSMVLLCLLLVPLLLSLFVLGLFLWFLKRERQEEYIE
EKKRVDICRETPNICPHSGENTHEYDTIPHTNRTILKEDPANTVYSTVEIPKCMENPHSLLTMPDT
PRLFAYENVI

Important features:

Signal peptide:

amino acids 1-22

Transmembrane domain:

amino acids 224-250

Leucine zipper pattern.

amino acids 229-251

N-glycosylation sites.

amino acids 98-102, 142-146, 148-152, 172-176, 176-180, 204-208,
291-295

FIGURE 47

GGCTCGAGCGTTTCTGAGCCAGGGGTGACCATGACCTGCTGCGAAGGATGGACATCCTGCAATGG
ATTGAGCCTGCTGGTTCTACTGCTGTTAGGAGTAGTTCTCAATGCGATACCTCTAATTGTCAGCT
TAGTTGAGGAAGACCAATTTTCTCAAAACCCCATCTCTTGCTTTGAGTGGTGGTTCCCAGGAATT
ATAGGAGCAGGTCTGATGGCCATTCCAGCAACAACAATGTCTTGACAGCAAGAAAAAGAGCGTG
CTGCAACAACAGAACTGGAAATGTTTCTTTCATCATTTTTTCAGTGTGATCACAGTCATTGGTGCTC
TGTATTGCATGCTGATATCCATCCAGGCTCTCTTAAAAGGTCTCTCATGTGTAATTCTCCAAGC
AACAGTAATGCCAATTGTGAATTTTCATTGAAAAACATCAGTGACATTCATCCAGAATCCTTCAA
CTTGAGTGGTTTTTCAATGACTCTTGTGCACCTCCTACTGGTTTTCAATAAACCCACCAGTAACG
ACACCATGGCGAGTGGCTGGAGAGCATCTAGTTTCCACTTCGATTCTGAAGAAAACAAACATAGG
CTTATCCACTTCTCAGTATTTTTAGGTCTATTGCTTGTGGAATTCTGGAGGTCTGTTGGGCT
CAGTCAGATAGTCATCGGTTTCCTTGGCTGTCTGTGTTGGAGTCTCTAAGCGAAGAAGTCAAATTG
TGTAGTTTAATGGGAATAAAATGTAAGTATCAGTAGTTTGAAAAAAAAA

FIGURE 48

MTCCEGWTSCTNGFSLLVLLLLLVVLLNVAIPLIVSLVEEDQFSQNPISCFEWWFPGIIGAGLMAIPA
TTMSLTARKRACCNNRTGMFLSSFFSVITVIGALYCLISIQALLKGPLMCNSPNSNANCEFSL
KNISDIHPESFNLQWFFNDSCAPPTGFNKPTSNDTMASGWRASSFHFDSEENKHRLIHFSVFLGL
LLVGILEVLFLGLSQIVIGFLGCLCGVSKRRSQIV

Important features:

Transmembrane domains:

amino acids 10-31 (type II), 50-72, 87-110, 191-213

N-glycosylation sites.

amino acids 80-84, 132-136, 148-152, 163-167

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 223-227

N-myristoylation sites.

amino acids 22-28, 54-60, 83-89, 97-103, 216-222

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 207-218

TNFR/NGFR family cysteine-rich region protein.

amino acids 4-12

FIGURE 49

ATCCGTTCTCTGCGCTGCCAGCTCAGGTGAGCCCTCGCCAAGGTGACCTCGCAGGACACTGGTGA
AGGAGCAGTGAGGAACCTGCAGAGTCACACAGTTGCTGACCAATTGAGCTGTGAGCCTGGAGCAG
ATCCGTGGGCTGCAGACCCCCGCCCCAGTGCCCTCTCCCCCTGCAGCCCTGCCCTCGAACTGTGA
CATGGAGAGAGTGACCCTGGCCCTTCTCCTACTGGCAGGCCTGACTGCCTTGGAAGCCAATGACC
CATTTGCCAATAAAGACGATCCCTTCTACTATGACTGGAAAAACCTGCAGCTGAGCGGACTGATC
TGCGGAGGGCTCCTGGCCATTGCTGGGATCGCGGCAGTTCTGAGTGGCAAATGCAAATACAAGAG
CAGCCAGAAGCAGCACAGTCCGTACCTGAGAAGGCCATCCCACCTCATCACTCCAGGCTCTGCCA
CTACTTGCTTGAGACACAGGACTGGCCCTCAGGGATGGCCTGAAGCCTAACACTGGCCCCCAGCACC
TCCTCCCCTGGGAGGCCTTATCCTCAAGGAAGGACTTCTCTCCAAGGGCAGGCTGTTAGGCCCT
TTCTGATCAGGAGGCTTCTTTATGAATTAAACTCGCCCCACCACCCCTCA

FIGURE 50

MERVTLALLLLAGLTALEANDPFANKDDPFYYDWKNLQLSGLICGLLAIAGIAAVLSGKCKYKS
SQKQHSPVPEKAIPLITPGSATTC

Important features:

Signal peptide:

amino acids 1-16

Transmembrane domain:

amino acids 36-59

N-myristoylation sites.

amino acids 41-47, 45-51, 84-90

Extracellular proteins SCP/Tpx-1/Ag5/PR-1/Sc7.

amino acids 54-67

FIGURE 52

MKFQGPLACLLLLALCLGSGEAGPLQSGEESTGTNIGEALGHGLGDALSEGVGKAIGKEAGGAAGSKVS
EALGQGTREAVGTGVRQVPGFGAADALGNRVGEAAHALGNTGHEIGRQAEDVIRHGADAVRGSWQGVF
GHSGAWETSGGHGI FGSQGGGLGGQGNPGLGTPWVHGYPGNSAGSFGMNPQGAPWGQGGNGGPPNF
GTNTQGAVAQPGYGSVRASNQNEGCTNPPPSGSGGGSSNSGGGSGSQSGSSGSGSNGDNNNGSSSSGGS
SSGSSSGSSSGSSGGSSGGSSGNSGGSRGDSGSESSWGSSTGSSSGNHGGSGGGNGHKPGCEKPGNE
ARGSGESGIQGFRRQGVSSNMREISKEGNRLLGGSGDNYRGQSSWGSGGDAVGGVNTVNSETPGM
FNFDTFWKNFKSKLGFINWDAINKDQRSSRIP

Signal peptide:

amino acids 1-21

N-glycosylation site.

amino acids 265-269

Glycosaminoglycan attachment site.

amino acids 235-239, 237-241, 244-248, 255-259, 324-328, 388-392

Casein kinase II phosphorylation site.

amino acids 26-30, 109-113, 259-263, 300-304, 304-308

N-myristoylation site.

amino acids 17-23, 32-38, 42-48, 50-56, 60-66, 61-67, 64-70, 74-80,
90-96, 96-102, 130-136, 140-146, 149-155, 152-158, 155-161,
159-165, 163-169, 178-184, 190-196, 194-200, 199-205, 218-224,
236-242, 238-244, 239-245, 240-246, 245-251, 246-252, 249-252,
253-259, 256-262, 266-272, 270-276, 271-277, 275-281, 279-285,
283-289, 284-290, 287-293, 288-294, 291-297, 292-298, 295-301,
298-304, 305-311, 311-317, 315-321, 319-325, 322-328, 323-329,
325-331, 343-349, 354-360, 356-362, 374-380, 381-387, 383-389,
387-393, 389-395, 395-401

Cell attachment sequence.

amino acids 301-304

FIGURE 53

GGAGAAGAGGTTGTGTGGGACAAGCTGCTCCCGACAGAAGGATGTCGCTGCTGAGCCTGCCCTGG
CTGGGCCTCAGACCGGTGGCAATGTCCCATGGCTACTCCTGCTGCTGGTTGTGGGCTCCTGGCT
ACTCGCCCGCATCCTGGCTTGGACCTATGCCTTCTATAACAACCTGCCGCCGGCTCCAGTGTTTTCC
CACAGCCCCAAAACGGAACTGGTTTTGGGGTCACTGGGCCTGATCACTCCTACAGAGGAGGGC
TTGAAGGACTCGACCCAGATGTCGGCCACCTATTCAGGGCTTTACGGTATGGCTGGGTCCCAT
CATCCCCTTCATCGTTTTATGCCACCCTGACACCATCCGGTCTATCACCAATGCCTCAGCTGCCA
TTGCACCCAAGGATAATCTCTTCATCAGGTTCTGAAGCCCTGGCTGGGAGAAGGGATACTGCTG
AGTGGCGGTGACAAGTGGAGCCGCCACCCTCGGATGCTGACGCCCCTCCATTTCAACATCCT
GAAGTCTATATAACGATCTTCAACAAGAGTGAAACATCATGCTTGACAAGTGGCAGCACCTGG
CCTCAGAGGGCAGCAGTCGCTCTGGACATGTTTGAGCACATCAGCCTCATGACCTTGGACAGTCTA
CAGAAATGCATCTCAGCTTTGACAGCCATTGTCAGGAGAGGGCCAGTGAATATATTGCCACCAT
CTTGAGCTCAGTGCCCTTGTAGAGAAAAGAAGCCAGCATATCCTCCAGCACATGGACTTTCTGT
ATTACCTCTCCCATGACGGGCGGCGCTTCCACAGGGCCTGCCGCTGGTGCATGACTTCACAGAC
GCTGTGATCCGGGAGCGGCGTGCACCCTCCCCTCAGGGTATTGATGATTTTTTCAAAGACAA
AGCCAAGTCCAAGACTTTGGATTTCAATTGATGTGCTTCTGCTGAGCAAGGATGAAGATGGGAAGG
CATTGTCAGATGAGGATATAAGAGCAGAGGCTGACACCTTCATGTTTGGAGGCCATGACACCACG
GCCAGTGGCCTCTCCTGGGTCTGTACAACCTTGGCAGGCACCCAGAATACCAGGAGCGCTGCCG
ACAGGAGGTGCAAGAGCTTCTGAAGGACCGGATCCTAAAGAGATTGAATGGGACGACCTGGCCC
AGCTGCCCTTCTGACCATGTGCGTGAAGGAGAGCCTGAGGTTACATCCCCCAGCTCCCTTCATC
TCCCGATGCTGCACCCAGGACATTGTTCTCCAGATGGCCGAGTCATCCCCAAAGGCATTACCTG
CCTCATCGATATTATAGGGGTCCATCACAACCCAACTGTGTGGCCGGATCCTGAGGTCTACGACC
CCTTCCGCTTTGACCCAGAGAACAGCAAGGGGAGGTCACTCTGGCTTTTATTCCTTTCTCCGCA
GGGCCAGGAACTGCATCGGGCAGGCGTTCCGCATGGCCGAGATGAAAGTGGTCTGGCGTTGAT
GCTGCTGCACTTCGGTTCCTGCCAGACCACACTGAGCCCCGCAGGAAGCTGGAATTGATCATGC
GCGCCGAGGGCGGGCTTTGGCTGCGGGTGGAGCCCCTGAATGTAGGCTTGCATGACTTTTCTGAC
CCATCCACCTGTTTTTTTTGCAGATTGTCATGAATAAAACGGTGCTGTCAA

FIGURE 54

MSLLSLPWLGLRPVAMSPWLLLLLVVGSWLLARILAWTYAFYNNCRRLQCFPQPCKRNWFWGHLG
LITPTEEGLKDSTQMSATYSQGFTVWLGPIIPFIVLCHPDTIRSITNASAAIAPKDNLFIRFLKP
WLGEGILLSGGDKWSRHRMLTPAFHFNILKSYITIFNKSANIMLDKWQHLASEGSSRLDMFEHI
SLMTLDSLQKCIFSFDSHCQERPSEYIATILELSALVEKRSQHILQHMDFLYYLSHDGRRFHRAC
RLVHDFTDAVIRERRRTLPTQGIDDFKDKAKSKTLDFIDVLLLLSKDEDEGKALSDEDIRAEADTF
MFGGHDTTASGLSWVLYNLARHPEYQERCQEVQELLKDRDPKEIEWDDLAQLPFLTMCVKESLR
LHPPAPFISRCCTQDIVLPDGRVIPKGITCLIDIIGVHHNPTVWPDPEVYDPRFRDPENSKGRSP
LAFIPFSAGPRNCIGQAFAMAEMKVVLALMLLHFRFLPDHTEPRRKLELIMRAEGGLWLRVEPLN
VGLQ

Important features:

Transmembrane domains:

amino acids 13-32 (type II), 77-102

Cytochrome P450 cysteine heme-iron ligand signature.

amino acids 461-471

N-glycosylation sites.

amino acids 112-116, 168-172

FIGURE 56

MGPVKQLKRMFEPTRLIATIMVLLCFALTLCSAFWWHNKGLALIFCILOSLALTWYSLSFIPFAR
DAVKKCFVCLA

Important features:

Signal peptide:

amino acids 1-33

Type II fibronectin collagen-binding domain protein.

amino acids 30-72

FIGURE 58

MLCLCLYVPVIGEAEQTEFQYFESKGLPAELKSIKLSVFIQEFSTYRQWKQKIVQAGDKDLG
QLDFEEFVHYLQDHEKKLRLVFKILDKKNDGRIDAQEIFMQLRDLGVKISEQQAEEKILKSMKNG
TMTIDWNEWRDYHLLHPVENIPEIILYWKHSTIFDVGENLTPDEFTEERQTGMWWRHLVAGGG
AGAVSRTCTAPLDRKVLMOVHASRSNNMGIVGGFTQMIREGGARSLWRGNGINVLKIAPESAIK
FMAYEQIKRLVGSQETLRIHERLVAGSLAGAIQSSIYPMEVLKTRMALRKTGQYSGMLDCARR
ILAREGVAAFYKGYVPNMLGIIPYAGIDLAVYETLKNWLQHYAVNSADPGVFVLLACGTMSSTC
GQLASYPLALVRTRMQAQASIEGAPEVTMSSLEFKHILRTEGAFGLYRGLAPNFMKVIPAVSISYV
VYENLKITLGVQSR

Important features:

Signal peptide:

amino acids 1-16

Putative transmembrane domains:

amino acids 284-304, 339-360, 376-394

Mitochondrial energy transfer proteins signature.

amino acids 206-215, 300-309

N-glycosylation sites.

amino acids 129-133, 169-173

Elongation Factor-hand calcium-binding protein.

amino acids 54-73, 85-104, 121-140

FIGURE 59

GGAAGGCAGCGGCAGCTCCACTCAGCCAGTACCCAGATACGCTGGGAACCTTCCCCAGCCATGGC
TTCCCTGGGGCAGATCCTTCTTCTGGAGCATAATTAGCATCATCATTATTCTGGCTGGAGCAATTG
CACTCATCATTGGCTTTGGTATTTTCAGGGAGACACTCCATCACAGTCACACTGTGCGCCTCAGCT
GGGAACATTGGGGAGGATGGAATCCTGAGCTGCACTTTTGAACCTGACATCAAACCTTCTGATAT
CGTGATACAATGGCTGAAGGAAGGTGTTTTAGGCTTGGTCCATGAGTTCAAAGAAGGCAAAGATG
AGCTGTGCGGAGCAGGATGAAATGTTTCAGAGGCCGGACAGCAGTGTGCTGATCAAGTGATAGTT
GGCAATGCCTCTTTGCGGCTGAAAAACGTGCAACTCACAGATGCTGGCACCTACAAATGTTATAT
CATCACTTCTAAAGGCAAGGGGAATGCTAACCTTGAGTATAAACTGGAGCCTTCAGCATGCCGG
AAGTGAATGTGGACTATAATGCCAGCTCAGAGACCTTGGCGTGTGAGGCTCCCCGATGGTTCCCC
CAGCCCACAGTGGTCTGGGCATCCCAAGTTGACCAGGGAGCCAACCTCTCGGAAGTCTCCAATAC
CAGCTTTGAGCTGAACTCTGAGAATGTGACCATGAAGGTTGTGTCTGTGCTCTACAATGTTACGA
TCAACAACACATACTCCTGTATGATTGAAAATGACATTGCCAAAGCAACAGGGGATATCAAAGTG
ACAGAATCGGAGATCAAAAAGCGGAGTCACTACAGCTGCTAAACTCAAAGGCTTCTCTGTGTGT
CTCTTCTTTCTTTGCCATCAGCTGGGCACCTTCTGCCTCTCAGCCCTTACCTGATGCTAAAATAAT
GTGCCTTGGCCACAAAAAGCATGCAAAGTCATTGTTACAACAGGGATCTACAGAACTATTTAC
CACCAGATATGACCTAGTTTTATATTTCTGGGAGGAAATGAATTCATATCTAGAAGTCTGGAGTG
AGCAAACAAGAGCAAGAAACAAAAAGAAGCCAAAAGCAGAAGGCTCCAATATGAACAAGATAAAT
CTATCTTCAAAGACATATTAGAAGTTGGGAAAATAATTCATGTGAAGTACTAGACAAGTGTGTTAAGA
GTGATAAGTAAATGCACGTGGAGACAAGTGCATCCCAGATCTCAGGGACCTCCCCCTGCCTGT
CACCTGGGGAGTGAGAGGACAGGATAGTGCATGTTCTTTGTCTCTGAATTTTTAGTTATATGTGC
TGTAATGTTGCTCTGAGGAAGCCCCCTGGAAAGTCTATCCCAACATATCCACATCTTATATTCCAC
AAATTAAGCTGTAGTATGTACCCTAAGACGCTGCTAATTGACTGCCACTTCGCAACTCAGGGGCG
GCTGCATTTTAGTAATGGGTCAAATGATCACTTTTTATGATGCTTCCAAAGGTGCCTTGGCTTC
TCTTCCCAACTGACAAATGCCAAAGTTGAGAAAAATGATCATAATTTTAGCATAAACAGAGCAGT
CGGGGACACCGATTTTATAAATAAACTGAGCACCTTCTTTTTAAACAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 60

MASLGQILFWSIISIISIIILAGAIALIIIGFGISGRHSITVTTVASAGNIGEDGILSCTFEPDIKLS
DIVIQWLKEGVLGLVHEFKEGKDELSEQDEMFRGRTAVFADQVIVGNASLRLKNVQLTDAGTYKC
YIITSKGGKGNANLEYKTGAFSMPEVNVVDYNASSETLRCEAPRWFPQPTVVWASQVDQGANFSEVS
NTSFELNSENVTMKVSVLYNVTINNTYSCMIENDIAKATGDIKVTSEIKRRSHLQLLNSKASL
CVSSFFAISWALLPLSPYLMLK

Important features:

Signal peptide:

amino acids 1-28

Transmembrane domain:

amino acids 258-281

N-glycosylation sites.

amino acids 112-116, 160-164, 190-194, 196-200, 205-209, 216-220,
220-224

N-myristoylation sites.

amino acids 52-58, 126-132, 188-194

FIGURE 61

TGACGTCAGAATCACCATGGCCCAGCTATCCTTACCGGCAGGGCTGCCCAGGAGCTGCAGGACAAG
CACCAGGAGCCCCCTCCGGGTAGCTACTACCCTGGACCCCCCAATAGTGGAGGGCAGTATGGTAGT
GGGCTACCCCTGGTGGTGGTTATGGGGGTCTGCCCTGGAGGGCCTTATGGACCACCAGCTGG
TGGAGGGCCCTATGGACACCCCAATCCTGGGATGTTCCCTCTGGAACCCAGGAGGACCATATG
GCGGTGCAGCTCCCGGGGGCCCCATGGTCAGCCACCTCCAAGTTCTACGGTGCCAGCAGCCT
GGGCTTATGGACAGGGTGGCGCCCCCTCCAATGTGGATCCTGAGGCCACTCCTGGTTCAGTC
GGTGGACTCAGATCACAGTGGCTATATCTCCATGAAGGAGCTAAAGCAGGCCCTGGTCAACTGCA
ATTGGTCTTCATTCAATGATGAGACCTGCCTCATGATGATAAACATGTTTGACAAGACCAAGTCA
GGCCGCATCGATGCTACGGCTTCTCAGCCCTGTGGAAATTCATCCAGCAGTGAAGAACCTCTT
CCAGCAGTATGACCGGGACCCTCGGGCTCCATTAGCTACACAGAGCTGCAGCAAGCTCTGTCCC
AAATGGGCTACAACCTGAGCCCCCAGTTCACCCAGCTTCTGGTCTCCCCTACTGCCACGCTCT
GCCAATCCTGCCATGCAGCTTGACCGCTTCATCCAGGTGTGCACCCAGCTGCAGGTGCTGACAGA
GGCTTCCGGGAGAAGGACACAGCTGTACAAGGCAACATCCGGCTCAGCTTCGAGGACTTCGTCA
CCATGACAGCTTCTCGGATGCTATTGACCCCAACCATCTGTGGAGAGTGGAGTGCACCAGGGACCTT
TCCTGGCTTCTTAGAGTGAGAGAAGTATGTGGACATCTCTTCTTTTCTGTCCCTCTAGAAGAAC
ATTCTCCCTTGCTTGATGCAACACTGTTCCAAAAGAGGGTGGAGAGTCTGCATCATAGCCACCA
AATAGTGAGGACCGGGCTGAGGCCACACAGATAGGGGCCTGATGGAGGAGAGGATAGAAGTTGA
ATGTCCTGATGGCCATGAGCAGTTGAGTGGCACAGCCTGGCACCAGGAGCAGGTCCCTTGTAATGG
AGTTAGTGTCCAGTCAGCTGAGCTCCACCCTGATGCCAGTGGTGAGTGTTCATCGGCCTGTTACC
GTTAGTACCTGTGTTCCCTCACCAGGCCATCCTGTCAAACGAGCCCATTTTCTCCAAAGTGAAT
CTGACCAAGCATGAGAGAGATCTGTCTATGGGACCAGTGGCTTGATTCTGCCACACCCATAAAT
CCTTGTGTGTTAACTTCTAGCTGCCTGGGGCTGGCCCTGCTCAGACAAATCTGCTCCCTGGGCAT
CTTTGGCCAGGCTTCTGCCCCCTGCAGCTGGGACCCCTCACTTGCCCTGCCATGCTCTGCTCGGCT
TCAGTCTCCAGGAGACAGTGGTCACCTCTCCCTGCCAATACTTTTTTTAATTTGCATTTTTTTTC
ATTTGGGGCCAAAAGTCCAGTGAATTTGAAGCTTCAATAAAAAGGATGAAACTCTGA

FIGURE 62

MASYPYRQGCPGAAGQAPGAPPGSYYPGPPNSGGQYGSGLPPGGGYGGPAPGGPYGPPAGGGPYG
HPNPGMFPSGTPGGPYGGAAPGGPYGQPPSSYGAQQPGLYGQGGAPPNVDPEAYSWFQSVSDH
SGYISMKELKQALVNCNWSSFNDETCLMMINMFDKTKSGRIDVYGFSALWKFIQQWKNLFQQYDR
DRSGSISYTELQQALSQMGYNLSPQFTQLLVSRYCPRSANPAMQLDRFIQVCTQLQVLTEAFREK
DTAVQGNIRLSFEDFVTMTASRML

Important features of the protein:

Signal peptide:

amino acids 1-19

N-glycosylation site.

amino acids 147-150

Casein kinase II phosphorylation sites.

amino acids 135-138, 150-153, 202-205, 271-274

N-myristoylation sites.

amino acids 9-14, 15-20, 19-24, 33-38, 34-39, 39-44, 43-48, 61-
66, 70-75, 78-83, 83-88, 87-92, 110-115

FIGURE 64

MQGRVAGSCAPLGLLLVCLHLPGLFARSIGVVEEKVSNFGTNLPQLGQPSSTGPSNSEHPQPAL
DPRSNDLARVPLKLSVPPSDGFPPAGGSAVQRWPPSWGLPAMDSWPPEDPWQMMAAAAEDRLGEA
LPEELSYLSSAAALAPGSGPLPGESSPDATGLSPEASLLHQDSESRRLPRSNLSGAGGKILSQRP
PWSLIHRVLPDHPWGTLNPSVSWGGGGPGTGWGTRPMPHPEGIWGINNQPPGTSWGNNINRYPGGS
WGNINRYPGGSWGNINRYPGGSWGNIHLYPGINNFPPGVLRPPGSSWNIPAGFPNPPSPRLQWG

Important features of the protein:

Signal peptide:

amino acids 1-26

Casein kinase II phosphorylation sites.

amino acids 56-59, 155-158

N-myristoylation sites.

amino acids 48-53, 220-225, 221-226, 224-229, 247-252, 258-263,
259-264, 269-274, 270-275, 280-285, 281-286, 305-310

FIGURE 65

AAGGAGAGGCCACCGGGACTTCAGTGTCTCCTCCATCCCAGGAGCGCAGTGGCCACTATGGGGTC
TGGGCTGCCCCTTGTCTCCTCTTGACCCTCCTTGGCAGCTCACATGGAACAGGGCCGGGTATGA
CTTTGCAACTGAAGCTGAAGGAGTCTTTTCTGACAAATTCCTCCTATGAGTCCAGCTTCCTGGAA
TTGCTTGAAAAGCTCTGCCTCCTCCTCCATCTCCCTCAGGGACCAGCGTCACCCCTCCACCATGC
AAGATCTCAACACCATGTTGTCTGCAACACATGACAGCCATTGAAGCCTGTGTCTTCTTGGCCC
GGGCTTTTGGGCCGGGATGCAGGAGGCAGGCCCGACCCTGTCTTTCAGCAGGCCCCCACCCCTC
CTGAGTGGCAATAAATAAAATTCGGTATGCTG

FIGURE 66

MGSGLPLVLLLTLGSSHGTPGPMTLQLKLKESFLTNSSYESSFLELLEKLCLLLHLPSGTSVTL
HHARSQHHVVCNT

Important features:

Signal peptide:

amino acids 1-19

N-glycosylation site.

amino acids 37-41

N-myristoylation sites.

amino acids 15-21, 19-25, 60-66

FIGURE 67

ACGGACCGAGGGTTCGAGGGAGGGACACGGACCAGGAACCTGAGCTAGGTCAAAGACGCCCGGGC
CAGGTGCCCCGTGCGAGGTGCCCTGGCCGGAGATGCGGTAGGAGGGGCGAGCGGAGAAGCCCC
TTCCTCGGGCTGCCAACCCGCCACCCAGCCCATGGCGAACCCCGGGCTGGGGCTGCTTCTGGCG
CTGGGCCTGCCGTTCCCTGCTGGCCCCTGGGGCCGAGCCTGGGGGCAAATACAGACCACTTCTGC
AAATGAGAATAGCACTGTTTTGCCTTCATCCACCAGCTCCAGCTCCGATGGCAACCTGCGTCCGG
AAGCCATCACTGCTATCATCGTGGTCTTCTCCCTCTGGCTGCCTTGCTCCTGGCTGTGGGGCTG
GCACTGTTGGTGCGGAAGCTTCGGGAGAAGCGGCAGACGGAGGGCACCTACCGGCCCAGTAGCGA
GGAGCAGTTCTCCCATGCAGCCGAGGCCCGGGCCCTCAGGACTCCAAGGAGACGGTGCAGGGCT
GCCTGCCCATCTAGGTCCCCTCTCCTGCATCTGTCTCCCTTCATTGCTGTGTGACCTTGGGGAAA
GGCAGTGCCCTCTCTGGGCAGTCAGATCCACCCAGTGCTTAATAGCAGGGAAGAAGGTACTTCAA
AGACTCTGCCCTGAGGTCAAGAGAGGATGGGGCTATTCACCTTTATATATTTATATAAAATTAG
TAGTGAGATGTAAAAAAAAAAAAAAAAAAAA

FIGURE 68

MANPGLGLLLALGLPFLRLRWGRAWGQIQTTSANENSTVLLPSSTSSSSSDGNLRPEAITAIIVVFS
LLAALLLAVGLALLVLRKLREKRQTEGTYRPSSEEQFSHAAEARAPQDSKETVQGCLPI

Important features:

Signal peptide:

amino acids 1-19

Transmembrane domain:

amino acids 56-80

N-glycosylation site.

amino acids 36-40

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 86-90

Tyrosine kinase phosphorylation site.

amino acids 86-94

N-myristoylation sites.

amino acids 7-13, 26-32

FIGURE 70

MGLFRGFVFLLVLCLLHQSNSTSFIKLNNNGFEDIVIVIDPSVPEDEKIIEQIEDMVTTASTYLFE
ATEKRFFFKNVSILIPENWKENPQYKRPKHENHKHADVIVAPP TLPGRDEPYTKQFTECGEKGEY
IHFTPDLLLGGKQNEYGPPGKLFVHEWAHLRWGVFDEYNEDQPFYRAKSKKIEATRC SAGISGRN
RVYKCQGGSCLSRACRIDSTTKLYGKDCQFFPKVQTEKASIMFMQSIDSVVEFCNEKTHNQEAP
SLQNIKCNFRSTWEVISNSEDFKNTIPMVTPPPPPVFESLLKISQRIVCLVLDKSGSMGGKDR LNR
MNQAAKHFLLQTVENG SWVGMVHFDSTATIVNKLIQIKSSDERNTLMAGLPTYPLGGTSICSGIK
YAFQVIGELHSQLDGEVLLLLTDGEDNTASSCIDEVKQSGAIVHFIALGRAADEAVIEMSKITGG
SHFYVSDEAQNNGLIDAFGALTSGNTDLSQKSLQLESKGLTLNSNAWMNDTVIIDSTVGKDTFFL
ITWNSLPPSISLWDPSGTIMENFTVDATSKMAYLSIPGTAKVGTWAYNLQAKANPETLTITVTSR
AANSSVPPI TVNAKMNKDVNSFPSPMIVYAEILQGYVPVLGANVTAFIESQNGHTEVLELLDNCA
GADSFKNDGVYSRYFTAYTENGRYSLKVRAGGANTARLKL RPPLNRAAYIPGWVVNGEIEANPP
RPEIDEDTQTTLED FSRTASGGAFVVSQVPSLPLPDQYPPSQITDL DATVHEDKIILTWTAPGDN
FDVGKVRQRYIIRISASILD LRDSFDDALQVNTDLSPK EANSKESFAFKPENISEENATHIFIAI
KSIDKSNLTSKVS NIAQVTLFIPQANPDDIDPTPTPTPTPTPKSHNSGVNISTLVLSVIGSVVI
VNFILSTTI

Signal peptide:

amino acids 1-21

Putative transmembrane domains:

amino acids 284-300, 617-633

Leucine zipper pattern.

amino acids 469-491, 476-498

N-glycosylation site.

amino acids 20-24, 75-79, 340-344, 504-508, 542-546, 588-592,
628-632, 811-815, 832-836, 837-841, 852-856, 896-900

FIGURE 71

CTCCTTAGGTGAAACCTGGGAGTAGAGTACTGACAGCAAAGACCAGGAAAGACCATACGTCCCCGGGCAGGGTGA
 CAACAGGTGTCATCTTTTGGATCTCGTGTGGCTGCCTTCTATTTCAAGGAAAGACGCCAAGGTAATTTGACCCA
 GAGGAGCAATGATGTAGCCACCTCCTAACCTTCCCTTCTTGAACCCCAAGTTATGCCAGGATTTACTAGAGAGTGCA
 ACTCAACAGCAAGCGGCTCCTTCGGCTTAACTTGTGGTTGGAGGAGAGAACCCTTTGTGGGGCTGCGTTCTCTAGCA
 GTGGCTCAGAAGTGACTTGGCTGAGGGTGGACCAGAAGAAAGGAAAGGTCCTCTTGTCTTGGCTGCACATCAGGAA
 GGCTGTGATGGGAATGAAGGTGAAAACCTGGAGATTTACCTTCAGTCATGTCTTCTGCCTGCAAGATCATCTTTAAA
 AGTAGAGAAGCTGCTCTGTGTGGTGGTTAACTCCAAGAGGCAGAACCTCGTTCTAGAAGGAAATGGATGCAAGCAGCTC
 CGGGGGCCCCAAGCGCATGCTTCTGTGGTCTAGCCAGGGAAGCCCTTCGGTGGGGGGCCCCGGCTTTGAGGGATGCC
 ACCGGTTCGGACGCATGGCTGATTCCTGAAATGATGATGGTTCGCCGGGGGCTGCTTGCCTGGATTTCCCGGGTGGTG
 GTTTTCTGGTCTCCTCTGCTGTGCTATCTGTCTGTACATGTTGGCTGCACCCAAAAGGTGACGAGGAGCAG
 CTGGCACTGCCAGGGCCACAGCCACGGGGAAGGAGGGTACCAGCCCTTCCAGGAGTGGGAGGAGCAGCAC
 CGCAACTACGTGAGCAGCCTGAAGCGGCAGATCGCACAGCTCAAGGAGGAGCTGCAGGAGAGGAGTGCAGCAGCTCAGG
 AATGGGCAGTACCAAGCCAGCGATGCTGCTGGCTGGGTCTGGACAGGAGCCCCAGAGAAAACCAGGCCAGCTC
 CTGGCCTTCTGCACTCGCAGGTGGACAAGGCAGAGGTGAATGCTGGCCTCAAGCTGGCCACAGAGTATGCAGCAGTG
 CCTTTCGATAGCTTACTCTACAGAAGGTGTACCAGCTGGAGACTGGCCTTACCAGCCACCCAGGAGAGAAGCCTGTG
 AGGAAGACAAGCGGGATGAGTTGGTGAAGCCATTGAATCAGCCTTGAGACCCTGAACAATCCTGCAGAGAACAGC
 CCCAATCACCGTCTTACAGGGCTCTGATTTTATAGAAGGGATCTACCGAACAGAAAGGGACAAAGGGACATTGTAT
 GAGCTCACCTTCAAAGGGGACCACAACACGAATTCAAACGGGCTCATCTTATTTCGACCATTCAGCCCCATCATGAAA
 GTGAAAATGAAAAGCTCAACATGGCCAACACGCTTATCAATGTTATCGTCCCTTAGCAAAAAGGGTGGACAAGTTC
 CGGCAGTTCATGCAGAAATTCAGGGAGATGTGCATGAGCAGGATGGGAGAGTCCATCTCACTGTTGTTTACTTTGGG
 AAAGAAGAAATAATGAAGTCAAAGGAATACTTGAACACTTCCAAAGCTGCCAACTTCAGGAACCTTACCTTCATC
 CAGCTGAATGGAGAATTTCTCGGGGAAAGGGACTTGATGTTGGAGCCCGCTTCTGGAAGGGAAGCAACGTCTCTC
 TTTTCTGTGATGTGGACATCTACTTCACATCTGAATTCCTCAATACGTGTAGGCTGAATACACAGCCAGGGGAAGA
 GATTTTATCCAGTCTTTTTCAGTCAGTACAACTCCTGGCATAATATACGGCCACCATGATGCAGTCCCTCCCTTGGAA
 CAGCAGCTGGTCAATAAGAAGGAAACTGGATTTTGGAGAGACTTTGGATTTGGGATGACGTGTCACTATCGGTGAGC
 TTCATCAATATAGTGGGTTTGTATCTGGACATCAAAGGCTGGGGCGGAGAGGATGTGCACCTTTATCGCAAGTATCTC
 CACAGCAACCTCATAGTGGTACGGACGCCTGTGCGAGGACTCTCCACCTCTGGCATGAGAAGCGCTGCATGGCAG
 CTGACCCCGAGCAGTACAAGATGTGCATGCAGTCCAAGGCCATGAACGAGGCATCCACGGCCAGCTGGGCATGCTG
 GTGTTACGGCAGCAGATAGAGGCTCACCTTCGCAACAGAAACAGAAGACAAGTAGCAAAAAACATGAACTCCCGA
 GAAGGATGTGGGAGACACTTTTCTTCTTTGCAATTAAGTGGCTGCAACAGAGAAAAGACTTCCATAAA
 GGACGACAAAAGAAATGGACTGATGGGTGAGAGATGAGAAAGCCTCCGATTTCTCTCTGTTGGGCTTTTACAACAGA
 AATCAAAATCTCCGCTTTCCTGCAAAAAGTAAACCCAGTTGCACCCTGTGAAGTGTCTGACAAGGCAGAAATGCTTGTG
 AGATTATAAGCCTAATGGTGTGGAGGTTTTGATGGTGTTACAATACTGAGACCTGTTGTTTTGTGTGCTCATTGA
 AATATTCATGATTTAAGAGCAGTTTTGTAATAAATTCATTAGCATGAAAGGCAAGCATATTTCTCCTCATATGATGA
 GCCTATCAGCAGGGCTCTAGTTCTAGGAATGCTAAAATATCAGAAGGCAGGAGAGGAGATAGGCTTATATGATACT
 AGTGAGTACATTAAGTAAAATAAATGGACCAGAAAAGAAAAGAAACATAAATATCGTGTCAATTTTTCCCCAAGAT
 TAACCAAAAATAATCTGCTTATCTTTTTGGTGTCTTTTAACTGTCTCCGTTTTTTCTTTTATTTAAAATGCACT
 TTTTTCCCTTGTGAGTTATAGTCTGCTTATTTAATTACCAGTTTGAAGCCTTACAAGAGAGCACAAGTTGGCCTAC
 ATTTTTATATTTTTAAGAAGATACTTTGAGATGCATTATGAGAACTTTCAGTTCAAAGCATCAAATGATGCCATAT
 CCAAGGACATGCCAATGCTGATTCCTGTGAGGCACTGAATGTGAGGATTCAGACATAGGGAAGGAATGGTTGTACT
 AATACAGACGTACAGATACTTCTCTGAAGAGTATTTTCAAGAGGAGCAACTGAACACTGGAGGAAAAGAAAATGAC
 ACTTTCTGCTTACAGAAAAGGAACTCATTGAGACTGGTGATATCGTGTGATGTACCTAAAAGTCAGAAAACCACATTT
 CTCCTCAGAAGTAGGGACCGCTTCTTACCTGTTAAATAAACCAAAGTATACCGTGTGAACCAAACAATCTCTTTT
 AAAACAGGGTGTCTCCTCTGGCTTCTGGCTTCCATAAGAAGAAATGGAGAAAATATATATATATATATATATATGT
 GAAAGATCAATCCATCTGCCAGAATCTAGTGGGATGGAAGTTTTGCTACATGTTATCCACCCAGGCCAGGTGGAAG
 TAACCTGAATATTTTTAAATTAAGCAGTTCTACTCAATCACCAGATGCTTCTGAAAATGCAATTTTATTACCATTT
 CAAACTATTTTTAAAATAAATACAGTTAACATAGAGTGGTTTTCTTCAATCATGTGAAAATTAATTAGCCAGCACCAG
 ATGCATGAGCTAATTATCTCTTTGAGTCTTGGCTTCTGTTTGTCTCACAGTAAACTCATTGTTTAAAGCTCAAGAAC
 ATTCAGCTGTTGGTGTGTTAAAATAATGCATTGTATTGATTGTACTGGTAGTTTATGAAATTAATTAACACAGG
 CCATGAATGGAAGGTGTTATTCACAGCTAATAAATAATGATTTGTGGATATGAA

FIGURE 72

MMVRRGLLAWISRVVLLVLLCCAISVLYMLACTPKGDEEQLALPRANSPTGKEGYQAVLQEW
EQHRNYVSSLKRQIAQLKEELQERSEQLRNGQYQASDAAGLGLDRSPPEKTQADLLAFLHSQVDK
AEVNAGVKLATEYAAVFPDSFTLQKVYQLETGLTRHPEEKPVKDKRDELVEAIESALETLNPA
ENSPNHRPYTASDFIEGIYRTERDKGTLYELTFKGDHKHEFKRLILFRPFSPIMKVKNEKLNMAN
TLINVIVPLAKRVDKFRQFMQNFREMCIEQDGRVHLTVVYFGKEEINEVKGILENTSKAANFRNF
TFIQLNGEFSTRGKGLDVGARFWKGSNVLLFFCDVDIYFTSEFLNLCRLNTQPGKKVFYFVLFESQY
NPGIIYGHHDVAPPLEQQLVIKKETGFWRDFGFGMTCQYRSDFINIGGFDDIKGWGGEDVHLYR
KYLHSNLIIVRTPVRGLFHLWHEKRCMDLTPQYKCMQSKAMNEASHGQLGMLVFRHEIEAHL
RKQKQKTSSKKT

Important features:

Signal peptide:

amino acids 1-27

N-glycosylation sites.

amino acids 315-319, 324-328

N-myristoylation sites.

amino acids 96-102, 136-142, 212-218, 311-317, 339-345, 393-399

Amidation site.

amino acids 377-381

FIGURE 74

MLFSALLLEVIWILAADGGQHWTYEGPHGQDHPASYPECGNNAQSPIDIQTDSVTFDPDLPALQ
PHGYDQPGTEPLDLHNNGHTVQLSLPSTLYLGGLPRKYVAAQLHLHWGQKGSPGGSEHQINSEAT
FAELHIVHYDSYDSLSEAAERPQGLAVLGILIEVGETKNIAYEHILSHLHEVRHKDQKTSVPP
FNLRELLPKQLGQYFRYNGSLTTPCYQSVLWTVFYRRSQISMEQLEKLGTLFSTEEEPSKLLV
QNYRALQPLNQRMVFASFIQAGSSYTTGEMLSLGVGILVGCLCLLLAVYFIARKIRKKRLENRKS
VVFTSAQATTEA

Important features of the protein:

Signal peptide:

amino acids 1-15

Transmembrane domain:

amino acids 291-310

N-glycosylation site.

amino acids 213-216

Eukaryotic-type carbonic anhydrases proteins

amino acids 197-245, 104-140, 22-69

FIGURE 75

TGCCGCTGCCGCCGCTGCTGCTGTTGCTCCTGGCGGCGCCTTGGGGACGGGCAGTTCCTGTGTC
TCTGGTGGTTTGCCTAAACCTGCAAACATCACCTTCTTATCCATCAACATGAAGAATGCCTACA
ATGGACTCCACCAGAGGGTCTTCAAGGAGTTAAAGTTACTTACACTGTGCAGTATTTTCATCACAA
ATTGGCCCACCAGAGGTGGCACTGACTACAGATGAGAAGTCCATTTCTGTTGTCTGACAGCTCC
AGAGAAGTGAAGAGAAATCCAGAAGACCTTCCTGTTTCCATGCAACAAATATACTCCAATCTGA
AGTATAACGTGTCTGTGTTGAATACTAAATCAAACAGAACGTGGTCCCAGTGTGTGACCAACCAC
ACGCTGGTGTCTACCTGGCTGGAGCCGAACACTCTTTACTGCGTACACGTGGAGTCTTTCGTCCC
AGGGCCCCCTCGCCGTGCTCAGCCTTCTGAGAAGCAGTGTGCCAGGACTTTGAAAGATCAATCAT
CAGAGTTCAAGGCTAAAATCATCTTCTGGTATGTTTTGCCATATCTATTACCGTGTTCCTTTTT
TCTGTGATGGGCTATTCCATCTACCGATATATCCACGTTGGCAAAGAGAAACACCCAGCAAATTT
GATTTTGATTTATGGAAATGAATTTGACAAAAGATTCTTTGTGCCTGCTGAAAAAATCGTGATTA
ACTTTATCACCCCTCAATATCTCGGATGATTCTAAAATTTCTCATCAGGATATGAGTTTACTGGGA
AAAAGCAGTGATGTATCCAGCCTTAATGATCCTCAGCCCAGCGGGAACCTGAGGCCCCCTCAGGA
GGAAGAGGAGGTGAAACATTTAGGGTATGCTTCGCATTTGATGGAAATTTTTTGTGACTCTGAAG
AAAACACGGAAGGTACTTCTCTCACCCAGCAAGAGTCCCTCAGCAGAACAATACCCCCGGATAAA
ACAGTCATTGAATATGAATATGATGTGAGAACCCTGACATTTGTGCGGGGCCTGAAGAGCAGGA
GCTCAGTTTGCAGGAGGAGGTGTCCACACAAGGAACATTATTGGAGTCGCAGGCAGCGTTGGCAG
TCTTGGGCCCCGAAACGTTACAGTACTCATAACCCCTCAGCTCCAAGACTTAGACCCCTGGCG
CAGGAGCACACAGACTCGGAGGAGGGGCCGGAGGAAGAGCCATCGACGACCCTGGTCTGACTGGGA
TCCCCAAACTGGCAGGCTGTGTATTCTTTCGCTGTCCAGCTTCGACCAGGATTCAGAGGGCTGCG
AGCCTTCTGAGGGGGATGGGCTCGGAGAGGAGGGTCTTCTATCTAGACTCTATGAGGAGCCGGCT
CCAGACAGGCCACCAGGAGAAAATGAAACCTATCTCATGCAATTCATGGAGGAATGGGGGTTATA
TGTGCAGATGAAAACTGATGCCAACACTTCCTTTTGCCTTTTGTTCCTGTGCAACAAGTGAG
TCACCCCTTTGATCCCAGCCATAAAGTACCTGGGATGAAAGAAGTTTTTCCAGTTTGTGAGTGT
CTGTGAGAATTACTTATTTCTTTTCTATTCTCATAGCACGTGTGTGATTTGGTTCATGCATGTA
GGTCTCTAACAAATGATGGTGGGCTCTGGAGTCCAGGGGCTGGCCGGTTGTTCATGCAGAGAA
AGCAGTCAATAAATGTTTGGCCAGACTGGGTGCAGAATTTATTCAGGTGGGTGT

FIGURE 76

MSYNGLHQRVFKELKLLTLCSISSQIGPPEVALTTDEKSISVVLTAPEKWKRNPEDLPVSMQQIY
SNLKYNVSVLNTKSNRTWSQCVTNHTLVLTWLEPNTLYCVHVESFVPGPPRAQPSEKQCARTLK
DQSSEFKAKIIFWYVLPISITVFLFSVMGYSIYRYIHVGKEKHPANLILIIYGNEFDKRFFVPAEK
IVINFITLNISSDDSKISHQDMSLLGKSSDVSSLNDPQPSGNLRPPQEEEEVKHLGYASHLMEIFC
DSEENTEGTSLTQQEESLRTIPDPKTVIEYEYDVRTTDICAGPEEQELSLQEEVSTQGTLLSQA
ALAVLGPQTLQYSYTPQLQDLPLAQEHTDSEEGPEEPPSTTLVDWDPQTGRLCIPSLSSFDQDS
EGCEPSEGDLGEEGLLSRLYEPPAPDRPPGENETYLMQFMEEWGLYVOMEN

Important features:

Signal peptide:

amino acids 1-28

Transmembrane domain:

amino acids 140-163

N-glycosylation sites.

amino acids 71-74, 80-83, 89-92, 204-207, 423-426

FIGURE 77

GAGGAGCGGGCCGAGGACTCCAGCGTGCCAGGTCTGGCATCCTGCACTTGCTGCCCTCTGACAC
CTGGGAAGATGGCCCGGCCCGTGGACCTTACCCTTCTCTGTGGTTTGCTGGCAGCCACCTTGATC
CAAGCCACCCTCAGTCCCCTGACAGTTCTCATCCTCGGCCAAAAGTCATCAAAGAAAAGCTGAC
ACAGGAGCTGAAGGACCACAACGCCACCAGCATCCTGCAGCAGCTGCCGCTGCTCAGTGCCATGC
GGGAAAAGCCAGCCGGAGGCATCCCTGTGCTGGGCAGCCTGGTGAACACCGTCCCTGAAGCACATC
ATCTGGCTGAAGGTCATCACAGCTAACATCCTCCAGCTGCAGGTGAAGCCCTCGGCCAATGACCA
GGAGCTGCTAGTCAAGATCCCCCTGGACATGGTGGCTGGATTCAACACGCCCTGGTCAAGACCA
TCGTGGAGTTCCACATGACGACTGAGGCCAAGCCACCATCCGCATGGACACCAGTGCAAGTGGC
CCCACCCGCTGGTCCCTCAGTGACTGTGCCACCAGCCATGGGAGCCTGCGCATCCAAGTCTGTA
TAAGCTCTCCTTCCCTGGTGAACGCCTTAGCTAAGCAGGTCATGAACCTCCTAGTGCCATCCCTGC
CCAATCTAGTGAAAACCAGCTGTGTCCCCTGATCGAGGCTTCCCTCAATGGCATGTATGCAGAC
CTCCTGCAGCTGGTGAAGGTGCCCATTTCCCTCAGCATTGACCGTCTGGAGTTTGACCTTCTGTA
TCCTGCCATCAAGGGTGACACCATTGAGCTCTACCTGGGGGCCAAGTTGTTGGACTCACAGGGAA
AGGTGACCAAGTGGTTCAATAACTCTGCAGCTTCCCTGACAATGCCACCCTGGACAACATCCCG
TTCAGCCTCATCGTGAGTCAGGACGTGGTGAAGCTGCAGTGGCTGCTGTGCTCTCTCCAGAAGA
ATTCATGGTCCGTGGACTCTGTGCTTCCCTGAGAGTGCCCATCGGCTGAAGTCAAGCATCGGGC
TGATCAATGAAAAGGCTGCAGATAAGCTGGGATCTACCCAGATCGTGAAGATCCTAACTCAGGAC
ACTCCCAGTTTTTTATAGACCAAGGCCATGCCAAGGTGGCCCAACTGATCGTGCTGGAAGTGT
TCCCTCCAGTGAAGCCCTCCGCCCTTGTTCACCCTGGGCATCGAAGCCAGCTCGGAAGCTCAGT
TTTACACCAAAGGTGACCAACTTATACTCAACTTGAATAACATCAGCTCTGATCGGATCCAGCTG
ATGAACTCTGGGATTGGCTGGTTCCAACCTGATGTTCTGAAAAACATCATCACTGAGATCATCCA
CTCCATCCTGCTGCCGAACCAGAATGGCAAATTAAGATCTGGGGTCCAGTGTGATTGGTGAAGG
CCTTGGGATTCGAGGCAGCTGAGTCCCTCACTGACCAAGGATGCCCTTGTGCTTACTCCAGCCTCC
TTGTGGAAACCCAGCTCTCCTGTCTCCAGTGAAGACTTGGATGGCAGCCATCAGGGAAGGCTGG
GTCCCAGCTGGGAGTATGGGTGTGAGCTCTATAGACCATCCCTCTCTGCAATCAATAAACACTTG
CCTGTGAAAA

FIGURE 78

MAGPWTFTLLCGLLAATLIQATLSPTAVLIILGPKVIKEKLTQELKDHNATSILQQLPLLSAMREK
PAGGIPVLGSLVNTVLKHIIWLKVITANILQLQVKPSANDQELLVKIPLDMVAGENTPLVKTIVE
FHMTTEAQATIRMDTSASGPTRLVLSDCATSHGSLRIQLLYKLSFLVNALAKQVMNLLVPSLPNL
VKNQLCPVIEASFNGMYADLLQLVKVPI SLSIDRLEFDLLYPAIKGDTIQLYLGAKLLDSQGKVT
KWFENSAASLTMP TLDNIPFSLIVSQDVVKA AVAVLSPEEFMVLLDSVLPESAHLKSSIGLIN
EKAADKLGSTQIVKILTQDTPEFFIDQGHAKVAQLIVLEVFPSSSEALRPLFTLGIEASSEAQFYT
KGDQLILNLNINISSDRIQLMNSGIGWFQPDVLKNIITEIIHSILLPNQNGKLRSGVPVSLVKALG
FEAAESSLTKDALVLT PASLWKPSSPVSQ

Important features of the protein:

Signal peptide:

amino acids 1-21

N-glycosylation sites.

amino acids 48-51, 264-267, 401-404

Glycosaminoglycan attachment site.

amino acids 412-415

LBP / BPI / CETP family proteins.

amino acids 407-457

FIGURE 79

GAGAGAAGTCAGCCTGGCAGAGAGACTCTGAAATGAGGGATTAGAGGTGTTCAAGGAGCAAGAGC
TTCAGCCTGAAGACAAGGGAGCAGTCCCTGAAGACGCTTCTACTGAGAGGTCTGCCATGGCCTCT
CTTGGCCTCCAACCTTGTGGGCTACATCCTAGGCCTTCTGGGGCTTTTGGGCACACTGGTTGCCAT
GCTGCTCCCCAGCTGGAAAACAAGTTCTTATGTGGTGCCAGCATTGTGACAGCAGTTGGCTTCT
CCAAGGGCCTCTGGATGGAATGTGCCACACACAGCACAGGCATCACCCAGTGTGACATCTATAGC
ACCCTTCTGGGCCTGCCCCTGACATCCAGGCTGCCAGGCCATGATGGTGACATCCAGTGCAAT
CTCCTCCCTGGCCTGCATTATCTCTGTGGTGGGCATGAGATGCACAGTCTTCTGCCAGGAATCCC
GAGCCAAAGACAGAGTGGCGGTAGCAGGTGGAGTCTTTTTTCATCCTTGGAGGCCCTCTGGGATTC
ATTCCTGTTGCCTGGAATCTTCATGGGATCCTACGGGACTTCTACTCACCCTGGTGCCTGACAG
CATGAAATTTGAGATTGGAGAGGCTCTTTACTTGGGCATTATTTCTTCCCTGTTCTCCCTGATAG
CTGGAATCATCCTCTGCTTTTCTGCTCATCCCAGAGAAATCGCTCCAACCTACTACGATGCCTAC
CAAGCCCAACCTCTTGCCACAAGGAGCTCTCCAAGGCCTGGTCAACCTCCCAAAGTCAAGAGTGA
GTTCAATTCCTACAGCCTGACAGGGTATGTGTGAAGAACCAGGGGCCAGAGCTGGGGGGTGGCTG
GGTCTGTGAAAAACAGTGGACAGCACCCCGAGGGCCACAGGTGAGGGACACTACCACTGGATCGT
GTCAGAAGGTGCTGCTGAGGATAGACTGACTTTGGCCATTGGATTGAGCAAAGGCAGAAATGGGG
GCTAGTGTAACAGCATGCAGGTTGAATGCCAAGGATGCTCGCCATGCCAGCCTTCTGTTTTCC
TCACCTTGCTGCTCCCCTGCCCTAAGTCCCCAACCTCAACTTGAAACCCCATTCCCTTAAGCCA
GGACTCAGAGGATCCCTTTGCCCTCTGGTTTACCTGGGACTCCATCCCCAAACCCTAATCACA
TCCCACTGACTGACCCTCTGTGATCAAAGACCCTCTCTCTGGCTGAGGTTGGCTCTTAGCTCATT
GCTGGGGATGGGAAGGAGAAGCAGTGGCTTTTGTGGGCATTGCTCTAACCTACTTCTCAAGCTTC
CCTCCAAAGAACTGATTGGCCCTGGAACCTCCATCCCACTCTTGTTATGACTCCACAGTGTCCA
GACTAATTTGTGCATGAACTGAAATAAAACCATCTACGGTATCCAGGGAACAGAAAGCAGGATG
CAGGATGGGAGGACAGGAAGGCAGCCTGGGACATTTAAAAAATA

FIGURE 80

MASLGLQLVGYILGLLGLLGTLVAMLLPSWKTSYV GASIVTAVGFSGKGLWMECATHSTGITQCD
IYSTLLGLPADIQAAQAMMVTSSAIISSLACII SVVGMRC TVFCQESRAKDRVAVAGGVFFILGGL
LGFIPVAWNLHGILRDFYSPLVPDSMKFEIGEALYLGII SSLFSLIAGIILCFSCSSQRNRSNYY
DAYQAQPLATRSSPRPGQPPKVKSEFN SYSLTGYV

Important features of the protein:

Signal peptide:

amino acids 1-24

Transmembrane domains:

amino acids 82-102, 117-140, 163-182

N-glycosylation site.

amino acids 190-193

PMP-22 / EMP / MP20 family proteins.

amino acids 46-59

FIGURE 81

CCCACGCGTCCGCGCCTCTCCCTTCTGCTGGACCTTCCTTCGTCTCTCCATCTCTCCCTCCTTTC
CCCGCGTTCTCTTTCCACCTTTCTCTTCTTCCCACCTTAGACCTCCCTTCCTGCCCTCCTTTCCCT
GCCCACCGCTGCTTCCTGGCCCTTCTCCGACCCCGCTCTAGCAGCAGACCTCCTGGGGTCTGTGG
GTTGATCTGTGGCCCTGTGCCTCCGTGTCTTTTCGTCTCCCTTCCTCCCGACTCCGCTCCCGG
ACCAGCGCCTGACCCTGGGAAAGGATGGTTCCCGAGGTGAGGGTCTCTCCTCCTTGCTGGGA
CTCGCGCTGCTCTGGTTCCCCCTGGACTCCCACGCTCGAGCCCGCCAGACATGTTCTGCCTTTT
CCATGGGAAGAGATACTCCCCGGCGAGAGCTGGCACCCTACTTGGAGCCACAAGGCCTGATGT
ACTGCCTGCGCTGTACCTGCTCAGAGGGCGCCCATGTGAGTTGTTACCGCCTCCACTGTCCGCCT
GTCCACTGCCCCAGCCTGTGACGGAGCCACAGCAATGCTGTCCCAAGTGTGTGGAACCTCACAC
TCCCTCTGGACTCCGGGCCCCACCAAAGTCTGCCAGCACAAACGGGACCATGTACCAACACGGAG
AGATCTTCAGTGCCCATGAGCTGTTCCCTCCCGCCTGCCCAACCAGTGTGTCTCTGCAGCTGC
ACAGAGGGCCAGATCTACTGCGGCCTCACAACTGCCCGAACCAGGCTGCCAGCACCCCTCCC
ACTGCCAGACTCCTGCTGCCAAGCCTGCAAAGATGAGGCAAGTGAAGGACAATCGGATGAAGAGGACA
GTGTGCAGTCGCTCCATGGGGTGAGACATCTCAGGATCCATGTTCCAGTGATGCTGGGAGAAAG
AGAGGCCCCGGGCACCCCAAGCCCCACTGGCCTCAGCGCCCCCTGAGCTTCATCCCTCGCCACTT
CAGACCCAAAGGAGCAGGCAGCACAACTGTCAAGATCGTCTGAAGGAGAAACATAAGAAAGCCT
GTGTGCATGGCGGAAGACGTACTCCACGGGGAGGTGTGGCACC CGCCTTCCGTGCCTTCGGC
CCCTTGCCCTGCATCCTATGCACCTGTGAGGATGGCCGCCAGGACTGCCAGCGTGTGACCTGTCC
CACCGAGTACCCCTGCCGTACCCCGAGAAAGTGGCTGGGAAGTGTGCAAGATTTGCCAGAGG
ACAAAGCAGACCCCTGGCCACAGTGAGATCAGTTCTACCAGGTGTCCAAGGCACCGGGCCGGGTC
CTCGTCCACACATCGGTATCCCCAAGCCAGACAACCTGCGTTCGCTTTGCCCTGGAACACGAGGC
CTCGGACTTGGTGGAGATCTACCTCTGGAAGCTGGTAAAAGATGAGGAACTGAGGCTCAGAGAG
GTGAAGTACCTGGCCCAAGGCCACACAGCCAGAATCTTCCACTTGACTCAGATCAAGAAAGTCAG
GAAGCAAGACTTCCAGAAAGAGGCACAGCACTCCGACTGCTCGCTGGCCCCACGAAGGTCCT
GGAACGTCTTCCTAGCCCAGACCCTGGAGCTGAAGGTCACGGCCAGTCCAGACAAAGTGACCAAG
ACATAACAAAGACCTAACAGTTGCAGATATGAGCTGTATAATTGTTGTTATTATATATTAATAAA
TAAGAAGTTGCATTACCCTCAAAAAAAAAAAAAAAAAAAAAA

FIGURE 82

MVPEVRVLSLLGLALLWFPLDSHARARPDMFCLFHGKRYSPGESWHPYLEPQGLMYCLRCTCSE
GAHVSCYRLHCPPVHCPQPVTEPQQCCPKCPEPHTPSGLRAPPKSCQHNGTMYQHGEIFSAHEL
PSRLPNQCVLCSCTEGQIYCGLTTCPEPGCPAPLPLPDSCCQACKDEASEQSDEEDSVQSLHGVR
HPQDPCSSDAGRKRGPPTPAPTGLSAPLSFIPRHFRPKGAGSTTVKIVLKEKHKACVHGGKTYS
HGEVWHPAFRAFGPLPCILCTCEDGRQDCQRVTCPTTEYPCRHPKQVAGKCKICPEDKADPGHSE
ISSTRCPKAPGRVLVHTSVSPSPDNLRRFALEHEASDLVEIYLWKLVKDEETEAQRGEVPGFRPH
SQNLPLDSDQESQEARLPERGTALPTARWPPRRSLERLPSDPGAEGHGQSRQSDQDITKT

Signal peptide:

amino acids 1-25

FIGURE 83

GACAGCTGTGTCTCGATGGAGTAGACTCTCAGAACAGCGCAGTTTGCCCTCCGCTCACGCAGAGCCTCTCC
 GTGGCTTCCGCACCTTGAGCATTAGGCCAGTTCTCCTCTTCTCTCTAATCCATCCGTCACCTCTCCTGTCA
 TCCGTTTCCATGCCGTGAGGTCCATTACAGAACACATCCATGGCTCTCATGCTCAGTTTGGTTCTGAGTC
 TCCTCAAGCTGGGATCAGGGCAGTGGCAGGTGTTTGGGCCAGACAAGCCTGTCCAGGCCTTGGTGGGGGAG
 GACGCAGCATTCTCCTGTTTCTGTCTCCTAAGACCAATGCAGAGGCCATGGAAGTGGGTTCTTCAGGGG
 CCAGTTCTCTAGCGTGGTCCACCTCTACAGGGACGGGAAGGACCAGCCATTTATGCAGATGCCACAGTATC
 AAGGCAGGACAAAACCTGGTGAAGGATTCATTGCGGAGGGGCGCATCTCTCTGAGGCTGGAAAACATTACT
 GTGTTGGATGCTGGCTCTATGGGTGCAGGATTAGTCCCAGTCTTACTACCAGAAGGCCATCTGGGAGCT
 ACAGGTGTCAGCACTGGGCTCAGTTCCCTCTCATTCCATCACGGGATATGTTGATAGAGACATCCAGCTAC
 TCTGTGAGTCTCCTCGGGCTGGTTCCCCCGGCCACAGCGAAGTGGAAAGGTCCACAAGGACAGGATTTGTCC
 ACAGACTCCAGGACAAACAGAGACATGCATGGCCTGTTTGATGTGGAGATCTCTCTGACCCTCCAAGAGAA
 CGCCGGGAGCATATCTGTTCCATGCGGCATGCTCATCTGAGCCGAGAGGTGGAATCCAGGGTACAGATAG
 GAGATACCTTTTTTCGAGCCTATATCGTGGCACCTGGCTACCAAAGTACTGGGAATACTCTGCTGTGGCCTA
 TTTTTTGGCATTGTTGGACTGAAGATTTCTTCTCCAAATTCCAGTGGAAAATCCAGGCGGAACTGGACTG
 GAGAAGAAAGCACGGACAGGCAGAAATGAGAGACGCCCGGAAACACGCAGTGGAGGTGACTCTGGATCCAG
 AGACGGCTCACCCGAAGCTCTGCGTTTCTGATCTGAAAACGTAAACCCATAGAAAAGCTCCCCAGGAGGTG
 CCTCACTCTGAGAAGAGATTTACAAGGAAGAGTGTGGTGGCTTCTCAGAGTTTCCAAGCAGGGAAACATTA
 CTGGGAGGTGGACGGAGGACACAATAAAAGGTGGCGCTGGGAGTGTGCCGGGATGATGTGGACAGGAGGA
 AGGAGTACGTGACTTTGTCTCCCGATCATGGGTACTGGGTCCCTCAGACTGAATGGAGAACATTTGTATTTT
 ACATTAATCCCCGTTTATCAGCGTCTTCCCCAGGACCCACCTACAAAAATAGGGGTCTTCTGGACTA
 TGAGTGTGGGACCATCTCCTTCTTCAACATAAATGACCAGTCCCTTATTTATACCCTGACATGTCGTTTG
 AAGGCTTATTGAGGCCCTACATTGAGTATCCGTCCTATAATGAGCAAAATGGAACCTCCATAGTCATCTGC
 CCAGTCAACCAGGAATCAGAGAAAGAGGCCTCTTGGCAAAGGGCCTCTGCAATCCAGAGACAAGCAACAG
 TGAGTCTCTCACAGGCAACCACGCCCTTCTCCCCAGGGGTGAAATGTAGGATGAATCACATCCCACAT
 TCTTCTTTAGGGATATTAAGGTCTCTCTCCAGATCCAAAGTCCCGCAGCAGCCGGCCAAGGTGGCTTCCA
 GATGAAGGGGGACTGGCCTGTCCACATGGGAGTCAGGTGTCATGGCTGCCCTGAGCTGGGAGGGAAGAAG
 CTGACATTACATTTAGTTTGCTCTCACTCCATCTGGCTAAGTGATCTTGAAATACCACCTCTCAGGTGAAG
 AACCGTCAGGAATCCCATCTCACAGGCTGTGGTGTAGATTAAGTAGACAAGGAATGTGAATAATGCTTAG
 ATCTTATTGATGACAGAGTGATCCTAATGGTTTGTTCATTATATTACACTTTCAGTAAAAAAA

FIGURE 84

MALMLSIVLSLLKLGSGQWQVFGPDKPVQALVGEDAAFSCFLSPKTNAEAMEVRFRRGQFSSVVH
LYRDGKDQPFMQMPQYQGRTKLVKDSIAEGRISLRLENITVLDAGLYGCRISQSYQKAIWELQ
VSALGSVPLISITGYVDRDIQLLCQSSGWFPRTAKWKGPQGDLSTDSRTNRDMHGLFDVEISL
TVQENAGSISCSMRHAHLSREVESRVQIGDTFFEPISWHLATKVLGILCCGLFFGIVGLKIFFSK
FQWKIQAELDWRRKHGQAEIRDARKHAVEVTLDPETAHPKLCVSDLKTVTHRKAPOEVPHSEKRF
TRKSVVASQSFQAGKHYEVDGGHNKRWRVGVCRDDVDRRKEYVTLSPDHGYWVLRNLNGEHLFT
LNPRFISVFPRTPPTKIGVFLDYECGTISFFNINDQSLIYTLTCRFEGLLRPYIEYPSYNEQNGT
PIVICPVTQESEKEASWQRASAI PETSNSESSSQATTPFLPRGEM

Signal peptide:

amino acids 1-17

Transmembrane domain:

amino acids 239-255

FIGURE 85

AACAGACGTTCCCTCGCGGCCCTGGCACCTCTAACCCAGACAATGCTGCTGCTGCTGCTGCCCT
GCTCTGGGGGAGGGAGAGGGCGGAAGGACAGACAAGTAACTGCTGACGATGCAGAGTTCCGTGA
CGGTGCAGGAAGCCTGTGTGTCCATGTGCCCTGCTCCTTCTCCTACCCCTCGCATGGCTGGATT
TACCCTGGCCCAGTAGTTCATGGCTACTGGTTCGGGAAGGGCCAATACAGACCAGGATGCTCC
AGTGGCCACAAACAACCCAGCTCGGGCAGTGTGGGAGGAGACTCGGGACCGATTCCACCTCCTTG
GGGACCCACATAACAGAATTGCACCCCTGAGCATCAGAGATGCCAGAAGAAGTGATCGGGGGAGA
TACTTCTTTCGTATGGAGAAAGGAAGTATAAAATGGAATTATAAACATCACCGGCTCTCTGTGAA
TGTGACAGCCTTGACCCACAGGCCAACATCCTCATCCCAGGCACCCTGGAGTCCGGCTGCCCC
AGAATCTGACCTGCTCTGTGCCCTGGGCCTGTGAGCAGGGGACACCCCTATGATCTCCTGGATA
GGGACCTCCGTGTCCCCCTGGACCCCTCCACCACCCGCTCCTCGGTGCTCACCTCATCCCACA
GCCCCAGGACCATGGCACCAGCCTCACCTGTCAGGTGACCTTCCCTGGGGCCAGCGTGACCACGA
ACAAGACCGTCCATCTCAACGTGTCTACCCGCCTCAGAACTTGACCATGACTGTCTTCCAAGGA
GACGGCACAGTATCCACAGTCTTGGGAAATGGCTCATCTCTGTCACTCCCAGAGGGCCAGTCTCT
GCGCCTGGTCTGTGCAGTTGATGCAGTTGACAGCAATCCCCCTGCCAGGCTGAGCCTGAGCTGGA
GAGGCCTGACCCTGTGCCCTCACAGCCCTCAAACCCGGGGTGCTGGAGCTGCCTTGGGTGCAC
CTGAGGGATGCAGCTGAATTCACCTGCAGAGCTCAGAACCCTCTCGGCTCTCAGCAGGTCTACCT
GAACGTCTCCCTGCAGAGCAAAGCCACATCAGGAGTGACTIONCAGGGGGTGGTCGGGGGAGCTGGAG
CCACAGCCCTGGTCTTCCCTGTCTTCTGCGTCATCTTCGTTGTAGTGAGGTCTGCAGGAAGAAA
TCGGCAAGGCCAGCAGCGGGCGTGGGAGATACGGGCATAGAGGATGCAAACGCTGTGAGGGGTTT
AGCCTCTCAGGGGCCCTGACTGAACCTTGGGCAGAAGACAGTCCCCAGACCAGCCTCCCCAG
CTTCTGCCCCTCCTCAGTGGGGGAAGGAGAGCTCCAGTATGCATCCCTCAGCTTCCAGATGGTG
AAGCCTTGGGACTCGCGGGGACAGGAGGCCACTGACACCGAGTACTCGGAGATCAAGATCCACAG
ATCAGAAACTGCAGAGACTCACCTGATTGAGGGATCACAGCCCTCCAGGCAAGGGAGAAGTCA
GAGGCTGATTCTTGTAGAATTAACAGCCCTCAACGTGATGAGCTATGATAACACTATGAATTATG
TGCAGAGTGAAAAGCACACAGGCTTTAGAGTCAAAGTATCTCAAACCTGAATCCCACTGTGCC
TCCCTTTTATTTTTTAACTAAAAGACAGACAAATTCCTA

FIGURE 86

MLLLLLLPLLLWGRERAEGQTSKLLTMQSSVTVQEGLCVHVPCSFYSPSHGWIYPGPVVHGYWFREG
ANTDQDAPVATNMPARAVWEETRDRFHLLGDPHTKNCTLSIRDARRSDAGRYFFRMEKGSIKWNY
KHHRLSVNVTALTHRPNILIPGTLESGCPQNLTCVWPWACEQGTTPMISWIGTSVSPDPSTTRS
SVLTLIPQPQDHGTSLTCQVTFFGASVTTNKTVHLNVSYPQNLMTVVFQGDGTVSTVLGNGSSL
SLPEGQSLRLVCAVDAVDSNPPARLSLSWRGLTLCPSQPSNPGVLELPWVHLRDAAEFTCRAQNP
LGSQQVYLNVSLSQSKATSGVTQGVVGGAGATALVFLSFCVI FVVVRSCKRKSARPAAGVGDGTGIE
DANAVERGSASQGPLEPWAEDSPPDQPPASARSSVGEELQYASLSFQMVKPWDSRGQEATDTE
YSEIKIHR

Signal peptide:

amino acids 1-15

Transmembrane domain:

amino acids 351-370

FIGURE 87

AGAAAGCTGCACTCTGTTGAGCTCCAGGGCGCAGTGGAGGGAGGGAGTGAAGGAGCTCTCTGTAC
CCAAGGAAAGTGCAGCTGAGACTCAGACAAGATTACAATGAACCAACTCAGCTTCCTGCTGTTTC
TCATAGCGACCACCAGAGGATGGAGTACAGATGAGGCTAATACTTACTTCAAGGAATGGACCTGT
TCTTCGTCTCCATCTCTGCCCAGAAGCTGCAAGGAAATCAAAGACGAATGTCCTAGTGCATTTGA
TGGCCTGTATTTCTCCGCACTGAGAATGGTGTATCTACCAGACCTTCTGTGACATGACCTCTG
GGGGTGGCGGCTGGACCCTGGTGGCCAGCGTGCATGAGAATGACATGCGTGGGAAGTGCACGGTG
GGCGATCGCTGGTCCAGTCAGCAGGGCAGCAAAGCAGACTACCCAGAGGGGGACGGCAACTGGGC
CAACTACAACACCTTTGGATCTGCAGAGGCGGCCACGAGCGATGACTACAAGAACCCTGGCTACT
ACGACATCCAGGCCAAGGACCTGGGCATCTGGCACGTGCCCAATAAGTCCCCCATGCAGCACTGG
AGAAACAGCTCCCTGCTGAGGTACCGCACGGACACTGGCTTCTCCAGACACTGGGACATAATCT
GTTTGGCATCTACCAGAAATATCCAGTGAAATATGGAGAAGGAAAGTGTGGACTGACAACGGCC
CGGTGATCCCTGTGGTCTATGATTTGGCGACGCCAGAAAACAGCATCTTATTACTCACCCCTAT
GGCCAGCGGGAATCACTGCGGGATTTGTTTCAGTTCAGGGTATTTAATAACGAGAGAGCAGCCAA
CGCCTTGTGTGCTGGAAATGAGGGTCACCGGATGTAACACTGAGCATCACTGCATTGGTGGAGGAG
GATACTTCCAGAGGCCAGTCCCAGCAGTGTGGAGATTTTCTGGTTTTGATTGGAGTGGATAT
GGAACTCATGTTGGTTACAGCAGCAGCCGTGAGATAACTGAGGCAGCTGTGCTTCTATTCTATCG
TTGAGAGTTTTGTGGGAGGGAACCCAGACCTCTCCTCCCAACCATGAGATCCCAAGGATGGAGAA
CAACTTACCCAGTAGCTAGAATGTTAATGGCAGAAGAGAAAACAATAAATCATATTGACTCAAGA
AAAAAA

FIGURE 88

MNQLSFLLFLIATTRGWSTDEANTYFKEWTCSSSPSLPRSCKEIKDECPSAFDGLYFLRTENGVI
YQTFCDMTSGGGGWTLVASVHENDMRGKCTVGDRWSSQQGSKADYPEGDGNWANYNTFGSAEAAT
SDDYKNPGYYDIQAKDLGIWHVPNKSPMQHWRNSSLLRYRTDTGFLQTLGHNLFGLIYQKYPVKYG
EGKCWTDNGPVI PVVYDFGDAQKTASYSPYGQREFTAGFVQFRVFNNERAANALCAGMRVTGCN
TEHHCIGGGGYFPEASPOQCDFSGFDWSGYGTHTVGYSSSREITEAAVLLFYR

Important features:

Signal peptide:

amino acids 1-16

N-glycosylation site.

amino acids 163-167

Glycosaminoglycan attachment sites.

amino acids 74-78, 289-293

N-myristoylation sites.

amino acids 76-82, 115-121, 124-130, 253-259, 292-298

FIGURE 89

CTAGATTTGTCGGCTTGCGGGGAGACTTCAGGAGTCGCTGTCTCTGAACTCCAGCCTCAGAGAC
CGCCGCCCTTGTCCCCGAGGGCCATGGGCCGGGTCTCAGGGCTTGTGCCCTCTCGCTTCTGACG
CTCCTGGCGCATCTGGTGGTCGTCATCACCTTATTCTGGTCCCGGGACAGCAACATACAGGCCTG
CCTGCCCTCTCACGTTACCCCCGAGGAGTATGACAAGCAGGACATTCAGCTGGTGGCCGCGCTCT
CTGTCACCCTGGGCCTCTTTGCAGTGGAGCTGGCCGGTTTTCTCTCAGGAGTCTCCATGTTCAAC
AGCACCCAGAGCCTCATCTCCATTGGGGCTCACTGTAGTGCATCCGTGGCCCTGTCCTTCTTCAT
ATTCGAGCGTTGGGAGTGCACTACGTATTGGTACATTTTTGTCTTCTGCAGTGCCCTTCCAGCTG
TCACTGAAATGGCTTTATTCGTCACCGTCTTTGGGCTGAAAAAGAAACCCTTCTTGATTACCTTCA
TGACGGGAACCTAAGGACGAAGCCTACAGGGGCAAGGGCCGCTTCGTATTCCTGGAAGAAGGAAG
GCATAGGCTTCGGTTTTCCCCTCGGAAACTGCTTCTGCTGGAGGATATGTGTTGGAATAATTACG
TCTTGAGTCTGGGATTATCCGCATTGTATTTAGTGCTTTGTAATAAAATATGTTTTGTAGTAACA
TTAAGACTTATATACAGTTTTAGGGGACAATTAATAAAAAAAAAA

FIGURE 90

MGRVSGLVPSRFLTLLAHLVVVITLFWSRDSNIQACLPLTFTPEEYDKQDIQLVAALSVTLGLFA
VELAGFLSGVSMFNSTQSLISIGAHCSASVALSFFIFERWECTTYWYIFVFCALPAVTEMALFV
TVFGLKKKPF

Transmembrane domain:

amino acids 12-28 (type II), 51-66, 107-124

FIGURE 91

CTGGGACCCCGAAAAGAGAAGGGGAGAGCGAGGGGACGAGAGCGGAGGAGGAAGATGCAACTGAC
TCGCTGCTGCTTCGTGTTCTTGGTGCAGGGTAGCCCTATCTGGTCATCTGTGGCCAGGATGATG
GTCCCTCCCGGCTCAGAGGACCCTGAGCGTGATGACCACGAGGGCCAGCCCCGGCCCCGGGTGCC
CGGAAGCGGGGCCACATCTCACCTAAGTCCCGCCCCATGGCCAATTCACCTCTCCTAGGGCTGCT
GGCCCCGCTGGGGAGGCTTGGGGCATCTTGGGCAGCCCCCAACCGCCGAACCACAGCCCC
CACCTCAGCCAAGGTGAAGAAAATCTTTGGCTGGGGCGACTTCTACTCCAACATCAAGACGGTG
GCCCTGAACCTGCTCGTACAGGGAAGATTGTGGACCATGGCAATGGGACCTTCAGCGTCCACTT
CCAACACAATGCCACAGGCCAGGGAACATCTCCATCAGCCTCGTGCCCCCAGTAAAGCTGTAG
AGTTCCACCAGGAACAGCAGATCTTCATCGAAGCCAAGGCTCCAAAATCTTCAACTGCCGGATG
GAGTGGGAGAAGGTAGAACGGGGCCCGGGACCTCGCTTTCACCCACGACCCAGCCAAGATCTG
CTCCCGAGACCACGCTCAGAGCTCAGCCACCTGGAGCTGCTCCAGCCCTTCAAAGTCGTCTGTG
TCTACATCGCTTCTACAGCACGGACTATCGGCTGGTCCAGAAGGTGTGCCAGATTACAACCTAC
CATAGTGATACCCCCTACTACCCATCTGGGTGACCCGGGGCAGGCCACAGAGGCCAGGCCAGGGC
TGGAAGGACAGGCCTGCCATGCAGGAGACCATCTGGACACCGGGCAGGGAAGGGGTTGGGCCTC
AGGCAGGGAGGGGGTGGAGACGAGGAGATGCCAAGTGGGGCCAGGGCCAAGTCTCAAGTGGCAG
AGAAAAGGTCCCAAGTGCTGGTCCCAACCTGAAGCTGTGGAGTGACTAGATCACAGGAGCACTGG
AGGAGGAGTGGGCTCTCTGTGCAGCCTCACAGGGCTTTGCCACGGAGCCACAGAGAGATGCTGGG
TCCCCGAGGCCCTGTGGGCAGGCCGATCAGTGTGGCCCCAGATCAAGTCATGGGAGGAAGCTAAGC
CCTTGGTTCTTGCCATCCTGAGGAAAGATAGCAACAGGGAGGGGGAGATTTTCATCAGTGTGGACA
GCCTGTCAACTTAGGATGGATGGCTGAGAGGGCTTCCTAGGAGCCAGTCAGCAGGGTGGGGTGGG
GCCAGAGGAGCTCTCCAGCCCTGCCTAGTGGGGCCCTGAGCCCCTTGTCTGTGCTGAGCATGG
CATGAGGCTGAAGTGGCAACCCTGGGGTCTTTGATGTCTTGACAGATTGACCATCTGTCTCCAGC
CAGGCCACCCCTTTCCAAAATTCCTCTCTGCCAGTACTCCCCCTGTACCACCCATTGCTGATG
GCACACCCATCCTTAAGCTAAGACAGGACGATTGTGGTCTCCACACTAAGGCCACAGCCCATC
CGCGTGCTGTGTGCCCTCTCCACCCCAACCCCTGCTGGCTCCTCTGGGAGCATCCATGTCCCG
GAGAGGGGTCCCTCAACAGTCAGCCTCACCTGTCAGACCGGGTTCCTCCGGATCTGGATGGCGC
CGCCCTCTCAGCAGCGGGCACGGGTGGGGCGGGGCCGGCCGAGAGCATGTGCTGGATCTGTTC
TGTGTGCTGTCTGTGGGTGGGGGAGGGGAGGGAAGTCTTGTGAAACCGCTGATTGCTGACTTT
TGTGTGAAGAATCGTGTCTTGGAGCAGGAAATAAAGCTTGCCCCGGGGCA

FIGURE 92

MQLTRCCFVFLVQGSLYLVICGQDDGPPGSEDPERDDHEGQPRPRVPRKRGHISPKSRPMANSTL
LGLLAPPGEAWGILGQPPNRPNHSPPPSAKVKKIFGWGDFYSNIKTVALNLLVTGKIVDHGNGTF
SVHFQHNATGQGNISISLVPPSKAVEFHQEQQIFIEAKASKIFNCRMWEKVERGRRTSLCTHDP
AKICSRDHAQSSATWSCSQPFKVVVCVYIAFYSTDYRLVQKVCPCDYNHSDTPYYPSG

Important features of the protein:

Signal peptide:

amino acids 1-14

N-glycosylation sites.

amino acids 62-65, 127-130, 137-140, 143-146

2-oxo acid dehydrogenases acyltransferase

amino acids 61-71

FIGURE 93

CGGTGGCCATGACTGCGGCCGTGTTCTTCGGCTGCGCCTTCATTGCCTTCGGGCCTGCGCTCGCC
CTTTATGTCTTCACCATCGCCATCGAGCCGTTGCGTATCATCTTCCTCATCGCCGGAGCTTTCTT
CTGGTTGGTGTCTCTACTGATTTTCGTCCCTTGTTTGGTTCATGGCAAGAGTCATTATTGACAACA
AAGATGGACCAACACAGAAATATCTGCTGATCTTTGGAGCGTTTGTCTCTGTCTATATCCAAGAA
ATGTTCCGATTTGCATATTATAAACTCTTAAAAAAGCCAGTGAAGGTTTGAAGAGTATAAACCC
AGGTGAGACAGCACCCCTCTATGCGACTGCTGGCCTATGTTTCTGGCTTGGGCTTTGGAATCATGA
GTGGAGTATTTTCCCTTGTGAATACCCTATCTGACTCCTTGGGGCCAGGCACAGTGGGCATTCAT
GGAGATTCTCCTCAATTCTTCCTTTATTTCAGCTTTCATGACGCTGGTCATTATCTTGCTGCATGT
ATTCTGGGGCATTGTATTTTTTGATGGCTGTGAGAAGAAAAAGTGGGGCATCCTCCTTATCGTTC
TCCTGACCCACCTGCTGGTGTGAGCCAGACCTTCATAAGTCTTATTATGGAATAAACCTGGCG
TCAGCATTTATAATCCTGGTGTGCTCATGGGCACCTGGGCATTCTTAGCTGCGGGAGGCAGCTGCCG
AAGCCTGAAACTCTGCCTGCTCTGCCAAGACAAGAACTTTCTTCTTTACAACCAGCGCTCCAGAT
AACCTCAGGGAACCAGCACTTCCCAAACCGCAGACTACATCTTTAGAGGAAGCACAACTGTGCCT
TTTTCTGAAAATCCCTTTTTCTGGTGAATTGAGAAAGAAATAAACTATGCAGATA

FIGURE 94

MTAAVFFGCAFI AFGPALALYVFTIAIEPLRIIFLIAGAFFWLVSLLISSLVWFMARVIIDNKDG
PTQKYLLIFGAFVSVYIQEMFRFAYYKLLKKASEGLKSINPGETAPSMRLLAYVSGLGFGIMSGV
FSFVNTLSDSLPGTGVGIHGDSPOFFLYSAFMTLVIILLHVFWGIVFFDGCERKKWGILLIVLLT
HLLVSAQTFISSYYGINLASAFIILVLMGTWAF LAAGGSCRSLKLCCLLCQDKNFLLYNQSR

Important features of the protein:

Signal peptide:

amino acids 1-19

Transmembrane domains:

amino acids 32-51, 119-138, 152-169, 216-235

Glycosaminoglycan attachment site.

amino acids 120-123

Sodium:neurotransmitter symporter family protein

amino acids 31-65

FIGURE 96

MRSTILLFCLLGSTRSLPQLKPALGLPPTKLAPDQGTLPNQQQSNQVFPSLSLIPLTQM
LTLGPDHLHLLNPAAGMTPGTQTHPLTLGGLNVQQQLHPHVLPIFVTQLGAQGTILSSEE
LPQIFTSLLIHSLEFPGGILPTSQAGANPDVQDGLPAGGAGVNPATQGTPAGRLPTPSG
TDDFAVTTPAGIQRSTHAIEEATTESANGIQ

Signal peptide:

amino acids 1-16

FIGURE 97

GCTCAAGTGCCCTGCCTTGCCCCACCCAGCCAGCCCTGGCCAGAGCCCCCTGGAGAAGGAGCTCT
CTTCTTGCTTGGCAGCTGGACCAAGGGAGCCAGTCTTGGGCGCTGGAGGGCCGTCTCCTGACCATG
GTCCCTGCCTGGCTGTGGCTGCTTTGTGTCTCCGTCCCCCAGGCTCTCCCCAAGGCCAGCCAGCTGC
AGAGCTGTCTGTGGAAGTTCCAGAAAATATGGTGGAAAATTTCCCTTTATACCTGACCAAGTTGC
CGCTGCCCCGTGAGGGGGCTGAAGGCCAGATCGTGTCTGTCAGGGGACTCAGGCAAGGCAACTGAG
GGCCCATTTGCTATGGATCCAGATTCTGGCTTCTGTGCTGGTACCAGGGCCCTGGACCGAGAGGA
GCAGGCAGAGTACCAGCTACAGGTCACCCCTGGAGATGCAGGATGGACATGTCTTGTGGGGTCCAC
AGCCTGTGCTTGTGCACGTGAAGGATGAGAATGACCAGGTGCCCATTTCTCTCAAGCCATCTAC
AGAGCTCGGCTGAGCCGGGGTACCAGGCCCTGGCATCCCCCTCCTCTTCCCTTGAGGCTTCAGACCG
GGATGAGCCAGGCACAGCCAACCTCGGATCTTCGATTCACATCCTGAGCCAGGCTCCAGCCCAGC
CTTCCCCAGACATGTTCCAGCTGGAGCCTCGGCTGGGGGCTCTGGCCCTCAGCCCCAAGGGGAGC
ACCAGCCTTGACCACGCCCTGGAGAGGACCTACCAGCTGTTGGTACAGGTC AAGGACATGGGTGA
CCAGGCCTCAGGCCACCAGGCCACTGCCACCGTGGAAAGTCTCCATCATAGAGAGCACCTGGGTGT
CCCTAGAGCCTATCCACCTGGCAGAGAATCTCAAAGTCCATATACCCGCACCACATGGCCCAGGTA
CACTGGAGTGGGGGTGATGTGCACTATCACCTGGAGAGCCATCCCCCGGGACCCTTTGAAGTGAA
TGCAGAGGGAAACCTCTACGTGACCAGAGAGCTGGACAGAGAAGCCCAGGCTGAGTACCTGCTCC
AGGTGCGGGCTCAGAATTTCCATGGCGAGGACTATGCGGCCCTCTGGAGCTGCACGTGCTGGTG
ATGGATGAGAATGACAACGTGCCATCTGCCCTCCCCGTGACCCACAGTCAGCATCCCTGAGCT
CAGTCCACCAGGTACTGAAGTGACTAGACTGTCAGCAGAGGATGCAGATGCCCCCGGCTCCCCCA
ATTTCCACGTTGTGTATCAGCTCCTGAGCCCTGAGCCTGAGGATGGGGTAGAGGGGAGAGCCATC
CAGGTGGACCCCACTTCAGGCAGTGTGACGCTGGGGGTGCTCCCACTCCGAGCCAGGCCAGAACAT
CCTGCTTCTGGTGCTGGCCATGGACCTGGCAGGCCAGAGGGTGGCTTCAGCAGCACGTGTGAAG
TCGAAGTCGCAGTCACAGATATCAATGATCACGCCCCTGAGTTCATCACCTCCAGATTGGGCCCT
ATAAGCCTCCCTGAGGATGTGGAGCCCCGGGACTCTGGTGGCCATGCTAACAGCCATTGATGCTGA
CCTCGAGCCCGCCTTCCGCCTCATGGATTTTGGCATTGAGAGGGGAGACACAGAAGGGACTTTTG
GCCTGGATTGGGAGCCAGACTCTGGGCATGTTAGACTCAGACTCTGCAAGAACCTCAGTTATGAG
GCAGCTCCAAGTCATGAGGTGGTGGTGGTGGTGCAGAGTGTGGCGAAGCTGGTGGGGCCAGGCC
AGGCCCTGGAGCCACCGCCACGGTGACTGTGCTAGTGGAGAGAGTATGCCACCCCCCAAGTTGG
ACCAGGAGAGCTACGAGGCCAGTGTCCCATCAGTGCCCCAGCCGGCTCTTTCTGCTGACCATC
CAGCCCTCCGACCCCATCAGCCGAACCCTCAGGTTCTCCCTAGTCAATGACTCAGAGGGCTGGCT
CTGCATTGAGAAATTTCTCCGGGGAGGTGCACACCGCCCAGTCCCTGCAGGGCGCCAGCCTGGGG
ACACCTACACGGTGTCTTGTGGAGGCCAGGATACAGCCCTGACTCTTGCCCTGTGCCCTCCCAA
TACCTCTGCACACCCCGCAAGACCATGGCTTGATCGTGAGTGGACCCAGCAAGGACCCCGATCT
GGCCAGTGGGCACGGTCCCTACAGCTTCACCCTTGGTCCCAACCCACGGTGCAACGGGATTGGC
GCCTCCAGACTCTCAATGGTTCCCATGCCTACCTCACCTTGGCCCTGCATTGGGTGGAGCCAGT
GAACACATAATCCCCGTGGTGGT CAGCCACAATGCCCAGATGTGGCAGCTCCTGGTTCGAGTGAT
CGTGTGTGCTGCAACGTGGAGGGGCAGTGCATGCGCAAGGTGGGCCGATGAAGGGCATGCCCA
CGAAGCTGTGCGCAGTGGGCATCCTTGTAGGCACCCCTGGTAGCAATAGGAATCTTCCCTCATCCTC
ATTTTCACCACTGGACCATGTCAAGGAAGAAGGACCCGGATCAACCAGCAGACAGCGTGCCCT
GAAGGCGACTGTCTGAATGGCCCAGGCAGCTCTAGCTGGGAGCTTGGCTCTGGCTCCATCTGAG
TCCCCTGGGAGAGAGCCAGCACCCAAGATCCAGCAGGGGACAGGACAGAGTAGAAGCCCCCTCCA
TCTGCCCTGGGGTGGAGGCACCATCACCATCACCAGGCATGTCTGCAGAGCCTGGACACCAACTT
TATGGACTGCCCATGGGAGTGTCCAAATGTCAGGGTGTFTTGCCCAATAATAAAGCCCCAGAGAA
CTGGGCTGGGCCCTATGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAG

FIGURE 98

MVPAWLWLLCVSVPOALPKAQPAELSVVEVPENYGGNFPLYLTKLPLPREGAEGQIVLSGDSGKAT
EGPFAMDPDSGFLLVTRALDREEQAEYQLQVTLEMQDGHVWGPQVPLVHVKDENDQVPHFSQAI
YRARLSRGTRPGIPFLFLEASDRDEPGTANSDLRFHILSQAPAQSPDMFQLEPRLGALALSPKG
STSLDHALERTYQLLVQVKDMGDQASGHQATATVEVSI IESTWVSLEPIHLAENLKVLYPHHMAQ
VHWSGGDVHYHLESHPPGPFVNAEGNLYVTRELDREAQAEYLLQVRAQNSHGEDYAAPLELHVL
VMDENDNVPICPPRDPTVSIPELSPPGTEVTRLSAEDADAPGSPNSHVYQLLSPEPEDGVEGRA
FQVDPTSGSVTLGVLP L RAGQNILLVLAMDLAGAEGGFSSTCEVEVAVTDINDHAPEFITSQIG
PISLPEDVEPGTLVAMLT AIDADLEPAFRLMDFAI ERGDTEGTFGLDWE PDSGHVRLRLCKNLSY
EAAPSHEVWVWVQSVAKLVGPGPGGATATVTVLVERVMPPPKLDQESYEASVPI SAPAGSFLIT
IQPSDPI SRTLRFSLVNDSEGLWCIEKFSGEVHTAQSLQGAQPGDITYTVLVEAQDTALT LAPVPS
QYLCTPRQDHGLIVSGPSKDPDLASGHGPYSFTLGPNPTVQRDWRLQTLNGSHAYLTLALHWVEP
REHIIPVVVSHNAQMWQLLVRVIVCRCNVEGQCMRKVGRMKGMPTKLSAVGILVGT LVAIGIFLI
LIFTHWTMSRKKDPDQPADSVPLKATV

Signal peptide:

amino acids 1-18

Transmembrane domain:

amino acids 762-784

FIGURE 99

GGCTGACCGTGCTACATTGCCTGGAGGAAGCCTAAGGAACCCAGGCATCCAGCTGCCACGCCTG
AGTCCAAGATTCTTCCCAGGAACACAAACGTAGGAGACCCACGCTCCTGGAAGCACCAGCCTTTA
TCTCTTACCTTCAAGTCCCCTTTCTCAAGAATCCTCTGTTCTTTGCCCTCTAAAGTCTTGGTAC
ATCTAGGACCCAGGCATCTTGCTTTCCAGCCACAAAGAGACAGATGAAGATGCAGAAAGGAAATG
TTCTCCTTATGTTTGGTCTACTATTGCATTTAGAAGCTGCAACAAATTCCAATGAGACTAGCACC
TCTGCCAACACTGGATCCAGTGTGATCTCCAGTGGAGCCAGCACAGCCACCAACTCTGGGTCCAG
TGTGACCTCCAGTGGGGTCAGCACAGCCACCATCTCAGGGTCCAGCGTGACCTCCAATGGGGTCA
GCATAGTCACCAACTCTGAGTTCCATACAACCTCCAGTGGGATCAGCACAGCCACCAACTCTGAG
TTCAGCACAGCGTCCAGTGGGATCAGCATAGCCACCAACTCTGAGTCCAGCACAACTCCAGTGG
GGCCAGCACAGCCACCAACTCTGAGTCCAGCACACCCTCCAGTGGGGCCAGCACAGTCCACCAACT
CTGGGTCCAGTGTGACCTCCAGTGGAGCCAGCACTGCCACCAACTCTGAGTCCAGCACAGTGTCC
AGTAGGGCCAGCACTGCCACCAACTCTGAGTCTAGCACACTCTCCAGTGGGGCCAGCACAGCCAC
CAACTCTGACTCCAGCACAACTCCAGTGGGGCTAGCACAGCCACCAACTCTGAGTCCAGCACAA
CCTCCAGTGGGGCCAGCACAGCCACCAACTCTGAGTCCAGCACAGTGTCCAGTAGGGCCAGCACT
GCCACCAACTCTGAGTCCAGCACAACTCCAGTGGGGCCAGCACAGCCACCAACTCTGAGTCCAG
AACGACCTCCAATGGGGCTGGCACAGCCACCAACTCTGAGTCCAGCACGACCTCCAGTGGGGCCA
GCACAGCCACCAACTCTGACTCCAGCACAGTGTCCAGTGGGGCCAGCACTGCCACCAACTCTGAG
TCCAGCACGACCTCCAGTGGGGCCAGCACAGCCACCAACTCTGAGTCCAGCACGACCTCCAGTGG
GGCTAGCACAGCCACCAACTCTGACTCCAGCACAACTCCAGTGGGGCCGGCACAGCCACCAACT
CTGAGTCCAGCACAGTGTCCAGTGGGATCAGCACAGTCCCAATCTGAGTCCAGCACACCCTCC
AGTGGGGCCAACACAGCCACCAACTCTGAGTCCAGTACGACCTCCAGTGGGGCCAACACAGCCAC
CAACTCTGAGTCCAGCACAGTGTCCAGTGGGGCCAGCACTGCCACCAACTCTGAGTCCAGCACAA
CCTCCAGTGGGGTCAGCACAGCCACCAACTCTGAGTCCAGCACAACTCCAGTGGGGCTAGCACA
GCCACCAACTCTGACTCCAGCACAACTCCAGTGGGGCCAGCACAGCCACCAACTCTGAGTCTAG
CACAGTGTCCAGTGGGATCAGCACAGTCCCAATCTGAGTCCAGCACAACTCCAGTGGGGCCA
ACACAGCCACCAACTCTGGGTCCAGTGTGACCTCTGCAGGCTCTGGAACAGCAGCTCTGACTGGA
ATGCACACAACCTCCCATAGTGCATCTACTGCAGTGTGAGGCAAAGCCTGGTGGGTCCCTGGT
GCCGTGGGAAATCTTCTCATCACCTGGTCTCGGTGTGGCGGCCGTGGGGCTCTTTGCTGGGC
TCTTCTTCTGTGTGAGAAACAGCCTGTCCCTGAGAAACACCTTTAACACAGCTGTCTACCACCT
CATGGCCTCAACCATGGCCTTGGTCCAGGCCCTGGAGGGAATCATGGAGCCCCCACAGGCCAG
GTGGAGTCCTAACCTGGTTCTGGAGGAGACCAGTATCATCGATAGCCATGGAGATGAGCGGGAGGA
ACAGCGGGCCCTGAGCAGCCCCGGAAGCAAGTGCCGCATTCTTCAGGAAGGAAGAGACCTGGGCA
CCCAAGACCTGGTTTCCCTTTCATTCATCCCAGGAGACCCTCCAGCTTTGTTTGGATCCTGAA
AATCTTGAAGAAGGTATTCCCTCACCTTTCTTGCCTTTACCAGACACTGGAAAGAGAATACTATAT
TGCTCATTTAGCTAAGAAATAAATACATCTCATCTAACACACACGACAAAGAGAAGCTGTGCTTG
CCCCGGGGTGGGTATCTAGCTCTGAGATGAACTCAGTTATAGGAGAAAACCTCCATGCTGGACTC
CATCTGGCATTCAAATCTCCACAGTAAAATCCAAAGACCTCAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 100

MKMQKGNVLLMFGLLLHLEAATNSNETSTSAANTGSSVISSGASTATNSGSSVTSSGVSTATISGS
SVTSNGVSIVTNSEFHTTSSGISTATNSEFSTASSGISIATNSESSTTSSGASTATNSESSTPSS
GASTVTNSGSSVTSSGASTATNSESSTVSSRASTATNSESSTLSSGASTATNSDSSTTSSGASTA
TNSESSTTSSGASTATNSESSTVSSRASTATNSESSTTSSGASTATNSESRTTSNGAGTATNSES
STTSSGASTATNSDSSTVSSGASTATNSESSTTSSGASTATNSESSTTSSGASTATNSDSSTTSS
GAGTATNSESSTVSSGISTVTNSESSTPSSGANTATNSESSTTSSGANTATNSESSTVSSGASTA
TNSESSTTSSGVSTATNSESSTTSSGASTATNSDSSTTSSEASTATNSESSTVSSGISTVTNSES
STTSSGANTATNSGSSVTSAGSGTAALTGMHTTSHSASTAVSEAKPGGSLVPWEIFLITLVSVVA
AVGLFAGLFFCVRNSLSLRNTFNTAVYHPHGLNHGLGPGPGGNHGAPHRPRWSPNWFRRPVSSI
AMEMSGRNSGP

Signal peptide:

amino acids 1-20

Transmembrane domain:

amino acids 510-532

FIGURE 101

GGCCGGACGCCTCCGCGTTACGGGATGAATTAACGGCGGGTTCCGCACGGAGGTTGTGACCCCTA
CGGAGCCCCAGCTTGCCACGCACCCCACTCGGCGTCGCGCGGCGTGCCCTGCTTGTCACAGGTG
GGAGGCTGGAACATATCAGGCTGAAAAACAGAGTGGGTACTCTCTTCTGGGAAGCTGGCAACAAAT
GGATGATGTGATATATGCATTCCAGGGGAAGGGAAATTGTGGTGCTTCTGAACCCATGGTCAATT
AACGAGGCAGTTTCTAGCTACTGCACGTACTTCATAAAGCAGGACTCTAAAAGCTTTGGAATCAT
GGTGTTCATGGAAAGGGATTTACTTTATACTGACTCTGTTTTGGGGAAGCTTTTTTTGGAAGCATT
TCATGCTGAGTCCCTTTTTTACCTTTGATGTTTTGTAAACCCATCTTGGTATCGCTGGATCAACAAC
CGCCTTGTGGCAACATGGCTCACCCCTACCTGTGGCATTATTGGAGACCATGTTTGGTGTAAGT
GATTATAACTGGGGATGCATTTGTTCCCTGGAGAAAGAAGTGTCAATTATCATGAACCATCGGACAA
GAATGGACTGGATGTTCCCTGTGGAATTGCCTGATGCGATATAGCTACCTCAGATTGGAGAAAATT
TGCTCAAAGCGAGTCTCAAAGGTGTTCCCTGGATTTGGTTGGGCCATGCAGGCTGCTGCCTATAT
CTTCATTCATAGGAAATGGAAGGATGACAAGAGCCATTTCAAGACATGATTGATTACTTTTTGTG
ATATTCACGAACCACCTCAACTCCTCATATCCCAGAAGGGACTGATCTCACAGAAAACAGCAAG
TCTCGAAGTAATGCATTTGCTGAAAAAATGGACTTCAGAAATATGAATATGTTTTACATCCAAG
AACTACAGGCTTTACTTTTTGTGGTAGACCGTCTAAGAGAAGGTAAGAACCCTTGATGCTGTCCATG
ATATCACTGTGGCGTATCCTCACAACATTCCTCAATCAGAGAAGCACCTCCTCCAAGGAGACTTT
CCCAGGGAAATCCACTTTCACGTCCACCGGTATCCAATAGACACCCTCCCCACATCCAAGGAGGA
CCTTCAACTCTGGTGCCACAAACGGTGGGAAGAGAAAGAAGAGAGGCTGCGTTCCCTTCTATCAAG
GGGAGAAGAATTTTTATTTTACCGGACAGAGTGTCAATCCACCTTGCAAGTCTGAACTCAGGGTC
CTTGTGGTCAAATTGCTCTCTATACTGTATTGGACCCTGTTTCCAGCCCTGCAATGTGCCTACTCAT
ATATTTGTACAGTCTTGTTAAGTGGTATTTTATAATCACCATTGTAATCTTTGTGCTGCAAGAGA
GAATATTTGGTGGACTGGAGATCATAGAACTTGCATGTTACCGACTTTTACACAAACAGCCACAT
TTAAATTCAAAGAAAAATGAGTAAGATTATAAGGTTTGCCATGTGAAAACCTAGAGCATATTTG
GAAATGTTCTAAACCTTCTAAGCTCAGATGCATTTTGCATGACTATGTCGAATATTTCTTACT
GCCATCATTATTTGTTAAAGATATTTTGCACCTTAATTTTGTGGGAAAAATATTGCTACAATTTTT
TTAATCTCTGAATGTAATTTTCGATACTGTGTACATAGCAGGGAGTGATCGGGGTGAAATAACTT
GGCCAGAATATTATTAAACAATCATCAGGCTTTTAAA

FIGURE 102

MHSRGREIVVLLNPWSINEAVSSYCTYFIKQDSKSFIMVSWKGIYFILTLFWGSFFGSI FMLS P
FLPLMFVNPSWYRWINNRLVATWLTLPVALLETMFGVKVIITGDAFVPGERSVIIMNHRTRMDWM
FLWNC LMRYSYLRLEKICLKASLKGVPFGFGWAMQAAAYIFIHRKWKDDKSHFEDMIDYFCDIHEP
LQLLIFPEGTDLTENSRSRNSAFAEKNGLQKYEYVLHPRTTGFTFVVDRLREGKNLDAVHDITVA
YPHNIPQSEKHL LQGDFPREIHFHVHRYPIDTLPTS KEDLQLWCHKRWEEKEERLRSFYQGEKNF
YFTGQSVIPPCKSELRVLVVKLLSILYWTLFSPAMCLLIYLYSLVKWYFIITIVIFVLQERIFGG
LEIIE LACYRLLHKQPHLNSKKNE

Important features of the protein:

Signal peptide:

amino acids 1-22

Transmembrane domains:

amino acids 44-63, 90-108, 354-377

FIGURE 103

CGGCTCGAGCGGCTCGAGTGAAGAGCCCTCCACGGCTCCTGCGCCTGAGACAGCTGGCCTGACC
TCCAAATCATCCATCCACCCCTGCTGTCTGTGTTTTTCATAGTGTGAGATCAACCCACAGGAATA
TCCATGGCTTTTGTGCTCATTGTTGTTCTCAGTTTTCTACGAGCTGGTGTGAGGACAGTGGCAAGT
CACTGGACCGGGCAAGTTTGTCCAGGCCTTGGTGGGGGAGGACGCCGTGTTCTCCTGCTCCCTCT
TTCTTGAGACCAGTGCAGAGGCTATGGAAGTGCGGTTCTTCAGGAATCAGTTCCATGCTGTGGTC
CACCTCTACAGAGATGGGGAAGACTGGGAATCTAAGCAGATGCCACAGTATCGAGGGGAGAACTGA
GTTTGTGAAGGACTCCATTGCAGGGGGGCGTGTCTCTAAGGCTAAAAACATCACTCCCTCGG
ACATCGGCCGTATGGGTGCTGGTTCAGTTCCCAGATTTACGATGAGGAGGCCACCTGGGAGCTG
CGGGTGGCAGCACGGGCTCACTTCCTCTCATTCCATCGTGGGATATGTTGACGGAGGTATCCA
GTTACTCTGCCTGTCTCAGGCTGGTTCCTCCAGCCACAGCCAAGTGGAAAGGTCCACAAGGAC
AGGATTTGCTTCAGACTCCAGAGCAAATGCAGATGGGTACAGCCTGTATGATGTGGAGATCTCC
ATTATAGTCCAGGAAAATGCTGGGAGCATATTGTGTTCCATCCACCTTGCTGAGCAGAGTCATGA
GGTGGAAATCCAAGGTATTGATAGGAGAGACGTTTTCCAGCCCTCACCTTGGCGCCTGGCTTCTA
TTTTACTCGGGTACTCTGTGGTGCCTGTGTGGTGTGTCATGGGGATGATAATTGTTTTCTT
AAATCCAAAGGGAAAATCCAGGCGGAAGTGGAGTGGAGAAGAAAGCACGGACAGGCAGAATTGAG
AGAGCCCCGGAAACAGCAGTGGAGGTACTCTGGATCCAGAGACGGCTCACCCGAAGCTCTGCG
TTTTCTGATCTGAAAACGTAAACCCATAGAAAAGCTCCCCAGGAGGTGCCTCACTCTGAGAAGAGA
TTTACAAGGAAGAGTGTGGTGGCTTCTCAGGGTTTTCCAAGCAGGGAGACATTACTGGGAGGTGGA
CGTGGGACAAAATGTAGGGTGGTATGTGGGAGTGTGTCGGGATGACGTAGACAGGGGGAAGAACA
ATGTGACTTTGTCTCCCAACAATGGGTATTGGGTCTCAGACTGACAACAGAACATTTGTATTT
ACATTCAAATCCCCATTTTATCAGCCTCCCCCCAGCACCCCTCCTACACGAGTAGGGGTCTTCT
GGACTATGAGGGTGGGACCATCTCCTTCTCAATACAAATGACCAGTCCCTTATTTATACCCTGC
TGACATGTCAGTTTGAAGGCTTGTGAGACCCTATATCCAGCATGCGATGTATGACGAGGAAAAG
GGGACTCCCATATTCATATGTCCAGTGTCTGGGGATGAGACAGAGAAGACCCTGCTTAAAGGGC
CCCACACCACAGACCAGACACAGCCAAGGGAGAGTGTCTCCGACAGGTGGCCCCAGCTTCTCT
CCGGAGCCTGCGCACAGAGAGTACAGCCCCCACTCTCCTTTAGGGAGCTGAGGTTCTTCTGCCC
TGAGCCCTGCAGCAGCGGCAGTACAGCTTCCAGATGAGGGGGGATTGGCCTGACCCTGTGGGAG
TCAGAAGCCATGGCTGCCCTGAAGTGGGGACGGAATAGACTCACATTAGGTTTAGTTTTGTGAAA
CTCCATCCAGCTAAGCGATCTTGAACAAGTCACAACCTCCAGGCTCCTCATTTGCTAGTCACGG
ACAGTGATTCTTGCCTCACAGGTGAAGATTAAGAGACAACGAATGTGAATCATGCTTGCAGGTT
TGAGGGCACAGTGTGTTGCTAATGATGTGTTTTTATATTATACATTTTCCCACCATAAACTCTGTT
TGCTTATCCACATTAATTTACTTTTCTCTATACCAAATCACCCATGGAATAGTTATTGAACACC
TGCTTTGTGAGGCTCAAAGAATAAAGAGGAGGTAGGATTTTTCACTGATTTCTATAAGCCCAGCAT
TACCTGATACCAAACAGGCAAAGAAAACAGAAGAAGAGGAAGGAAAACACTACAGGTCCATATCC
CTCATTAACACAGACACAAAATTTCTAAATAAAATTTTAACAAATTAACACTAAACAATATATTTA
AAGATGATATATAACTACTCAGTGTGGTTTTGTCCACAAATGCAGAGTTGGTTTAATATTTAAAT
ATCAACCAGTGTAATTCAGCACATTAATAAAGTAAAAAAGAAAACCATAAAAAAAAAAAAAAAAAA

FIGURE 104

MAFVLILVLSFYELVSGQWQVTGPGKFVQALVGEDAVFSCSLFPETSAAEAMEVRFFRNQFHAVVH
LYRDGEDWESKQMPQYRGRTEFVKDSIAGGRVSLRLKNITPSDIGLYGCWFSSQIYDEEATWELR
VAALGSLPLISIVGYVDGGIQLLCLSSGWFPQPTAKWKGPQGQDLSSDSRANADGYSLYDVEISI
IVQENAGSILCSIHLAEQSHEVESKVLIGETFFQSPWRLASILLGLLCGALCGVVMGMIIVFFK
SKGKIQAELDWRKKGQAELRDARKHAVEVTLDPETAHPKLCVSDLKTVTHRKAQEVPHSEKRF
TRKSVVASQGFQAGRHYWEVDVGVQNVGWYVGVCRDDVDRGKNNVTLSPNNGYWVLRLLTTEHLYFT
FNPHFISLPPSTPPTRVGVFLDYEGGTISFFNTNDQSLIYTLTLCQFEGLLRPYIQHAMYDEEKG
TPIFICPVSWG

Signal peptide:

amino acids 1-17

Transmembrane domains:

amino acids 131-150, 235-259

FIGURE 105

CCTTCACAGGACTCTTCATTGCTGGTTGGCAATGATGTATCGGCCAGATGTGGTGAAGGCTAGGAAAAGAG
TTTGTGGGAACCCTGGGTTATCGGCCTCGTCATCTTCATATCCCTGATTGTCCTGGCAGTGTGCATTGGA
CTCACTGTTTCATTATGTGAGATATAATCAAAAGAAGACCTACAATTACTATAGCACATTGTCATTTACAAC
TGACAAACTATATGCTGAGTTTGGCAGAGAGGCTTCTAACAATTTTACAGAAATGAGCCAGAGACTTGAAT
CAATGGTGAAAAATGCATTTTATAAATCTCCATTAAGGGAAGAATTTGTCAAGTCTCAGGTTATCAAGTTC
AGTCAACAGAAGCATGGAGTGTGGCTCATATGCTGTTGATTTGTAGATTTCACTCTACTGAGGATCCTGA
AACTGTAGATAAAAATGTTCAACTTGTTTTACATGAAAAGCTGCAAGATGCTGTAGGACCCCTAAAGTAG
ATCCTCACTCAGTTAAAATTAATAAATCAACAAGACAGAAACAGACAGCTATCTAAACCATTGCTGCGGA
ACACGAAGAAGTAAAACCTTAGGTCAGAGTCTCAGGATCGTTGGTGGGACAGAAGTAGAAGAGGGTGAATG
GCCCTGGCAGGCTAGCCTGCAGTGGGATGGGAGTCACTCGCTGTGGAGCAACCTTAATTAATGCCACATGGC
TTGTGAGTGTCTCACTGTTTACAACATATAAGAACCCTGCCAGATGGACTGCTTCTCTTTGGAGTAACA
ATAAAACCTTCGAAAATGAAACGGGGTCTCCGGAGAATAATTGTCCATGAAAATACAAACACCCATCACA
TGACTATGATATTTCTCTTGACAGACTTTCTAGCCCTGTTCCCTACACAAATGCAGTACATAGAGTTTGTG
TCCCTGATGCATCCTATGAGTTTCAACCAGGTGATGTGATGTTTGTGACAGGATTTGGAGCACTGAAAAAT
GATGGTTACAGTCAAAATCATCTTCGACAAGCACAGGTGACTCTCATAGACGCTACAACCTTGAATGAACC
TCAAGCTTACAATGACGCCATAACTCCTAGAAATGTTATGTGCTGGCTCCTTAGAAGGAAAAACAGATGCAT
GCCAGGGTACTCTGGAGGACCCTGTTAGTTTCAAGATGCTAGAGATATCTGGTACCTTGCTGGAATAGTG
AGCTGGGGAGATGAATGTGCGAAACCCAAACAGCCTGGTGTTTATACTAGAGTTACGGCCCTGCGGGACTG
GATTACTTCAAAAACGGTATCTAAGAGACAAAAGCCTCATGGAACAGATAACATTTTTTTTTGTTTTTTG
GGTGTGGAGGCCATTTTTAGAGATACAGAATTGGAGAAGACTTGCAAAACAGCTAGATTTGACTGATCTCA
ATAAACTGTTTGCTTGATGCATGTATTTCTTCCCAGCTCTGTTCCGCACGTAAGCATCCTGCTTCTGCCA
GATCAACTCTGTCATCTGTGAGCAATAGTTGAACTTTATGTACATAGAGAAATAGATAATACAATATTAC
ATTACAGCCTGTATTCATTTGTTCTCTAGAAATTTTGTGAGAATTTGACTTGTGACATAAATTTGTAAT
GCATATATACAATTTGAAGCACTCCTTTTCTTCAAGTTCCTCAGCTCCTCTCATTTTCAAGCAAAATATCCATTT
TCAAGGTGCAGAACAAGGAGTGAAGAAAATATAAGAAGAAAAAATCCCTACATTTTATTTGGCACAGAA
AAGTATTAGGTGTTTTTCTTAGTGAATATTAGAAATGATCATATTCATTATGAAAGGTCAAGCAAAGACA
GCAGAATACCAATCACTTCATCATTTAGGAAGTATGGGAAGTAAGTTAAGGAAGTCCAGAAAGAAGCCAAG
ATATATCCTTATTTTCATTTCCAAACAACACTACTATGATAAATGTGAAGAAGATTCTGTTTTTTTTGTGACCT
ATAATAATTATACAACTTCATGCAATGTACTTGTCTAAGCAAATTAAGCAAATATTTATTTAACATTG
TTACTGAGGATGTCAACATATAACAATAAAATATAAATCACCCA

FIGURE 106

MMYRPDVVRARKRVCWEPWVIGLVI F I S L I V L A V C I G L T V H Y V R Y N Q K K T Y N Y Y S T L S F T T D K L Y
A E F G R E A S N N F T E M S Q R L E S M V K N A F Y K S P L R E E F V K S Q V I K F S Q Q K H G V L A H M L L I C R F H S T E D
P E T V D K I V Q L V L H E K L Q D A V G P P K V D P H S V K I K K I N K T E T D S Y L N H C C G T R R S K T L G Q S L R I V G G
T E V E E G E W P W Q A S L Q W D G S H R C G A T L I N A T W L V S A A H C F T T Y K N P A R W T A S F G V T I K P S K M K R G L
R R I I V H E K Y K H P S H D Y D I S L A E L S S P V P Y T N A V H R V C L P D A S Y E F Q P G D V M F V T G F G A L K N D G Y S
Q N H L R Q A Q V T L I D A T T C N E P Q A Y N D A I T P R M L C A G S L E G K T D A C Q G D S G G P L V S S D A R D I W Y L A G
I V S W G D E C A K P N K P G V Y T R V T A L R D W I T S K T G I

Transmembrane domain:

amino acids 21-40 (type II)

FIGURE 107

AGAGAAAGAAGCGTCTCCAGCTGAAGCCAATGCAGCCCTCCGGCTCTCCGCGAAGAAGTTCCCTG
 CCCCAGATGAGCCCCCGCGTGGCTCCCCGACTATCCCCAGGCGGGCGTGGGGCACCGGGCCCAGC
 GCCGACGATCGCTGCCGTTTTGCCCTTGGGAGTAGGATGTGGTGAAAGGATGGGGCTTCTCCCTT
 ACGGGGCTCACAATGGCCAGAGAAGATTCGGTGAAGTGTCTGCGCTGCCTGCTCTACGCCCTCAA
 TCTGCTCTTTTTGGTTAATGTCCATCAGTGTGTTGGCAGTTTTCTGCTTGGATGAGGGACTACCTAA
 ATAATGTTCTCAGTTTTAACTGCAGAAACGAGGGTAGAGGAAGCAGTCATTTTGACTTACTTTCCCT
 GTGGTTCATCCGGTCATGATTGCTGTTGCTGTTTCCCTTATCATTGTGGGGATGTTAGGATATG
 TGAACGGTGAAAAGAAATCTGTTGCTTCTTGCATGGTACTTTGGAAGTTTGTGTGCAATTTTCT
 GTGTAGAACTGGCTTGTGGCGTTTGGACATATGAACAGGAACTTATGGTTCCAGTACAATGGTCA
 GATATGGTCACTTTGAAAGCCAGGATGACAAATTATGGATTACCTAGATATCGGTGGCTTACTCA
 TGCTTGGAAATTTTTTTCAGAGAGAGTTAAGTGTGTGGAGTAGTATATTTCACTGACTGGTTGG
 AAATGACAGAGATGGACTGGCCCCAGATTCCTGCTGTGTTAGAGAATCCCAGGATGTTCCAAA
 CAGGCCCACCAGGAAGATCTCAGTGACCTTTATCAAGAGGGTGTGGGAAGAAAATGATTCCTT
 TTTGAGAGGAACCAACAACCTGCAGGTGCTGAGGTTTTCTGGGAATCTCCATTGGGGTGACACAAA
 TCCTGGCCATGATTCTCACCATTACTCTGCTCTGGGCTCTGTATTATGATAGAAGGGAGCCTGGG
 ACAGACCAATGATGTCCTTGAAGAATGACAACTCTCAGCACCTGTATGTCCCTCAGTAGAACT
 GTTGAACCAAGCCTGTCAAGAATCTTTGAACACACATCCATGGCAAACAGCTTTAATACACACT
 TTGAGATGGAGGATTA~~AAAA~~AGAAATGTCACAGAAGAAAACCACAAACTTGTTTTATTGGACT
 TGTGAATTTTGGAGTACATACTATGTGTTTCAAGAAATATGTAGAAATAAAAATGTTGCCATAAAA
 TAACACCTAAGCATATACTATTCTATGCTTTTAAAAATGAGGATGGAAAAGTTTTCATGTCATAAGTC
 ACCACCTGGACAATAATTGATGCCCTTAAAAATGCTGAAGACAGATGTCATACCCACTGTGTAGCC
 TGTGTATGACTTTTACTGAACACAGTTATGTTTTGAGGCAGCATGGTTTTGATTAGCATTTCGCA
 TCCATGCCAACGAGTCACATATGGTGGGACTGGAGCCATAGTAAAGGTTGATTTACTTCTACCAA
 CTAGTATATAAAGTACTAATTAATGCTAACATAGGAAGTTAGAAAATACTAATAACTTTTTATTA
 CTCAGCGATCTATTCTTCTGATGCTAAATAAATTAATATCAGAAAACCTTCAATATTGGTGACT
 ACCTAAATGTGATTTTTGCTGGTTACTAAAATATTTCTTACCACTTAAAAGAGCAAGCTAACACAT
 TGTCTTAAGCTGATCAGGGATTTTTTGTATATAAGTCTGTGTTAAATCTGTATAATTCAGTCGAT
 TTCAGTTCTGATAATGTTAAGAATAACCATTATGAAAAGGAAAATTTGTCTGTATAGCATCATT
 ATTTTLAGCCTTTCCTGTTAATAAAGCTTTACTATCTGTCTGGGCTTATATTACACATATAAC
 TGTATTTAAATACTTAACCACTAATTTGAAAATTACCAGTGTGATACATAGGAATCATTATTC
 AGAATGTAGTCTGGTCTTTAGGAAGTATTAATAAGAAAATTTGCACATAACTTAGTTGATTGAGA
 AAGGACTGTATGCTGTTTTTCTCCAAATGAAGACTCTTTTGGACACTAAACACTTTTTAAAAA
 GCTTATCTTTGCCTTCTCCAAACAAGAAGCAATAGTCTCCAAGTCAATATAAATTTCTACAGAAA
 TAGTGTCTTTTTTCTCCAGAAAATGCTTGTGAGAATCATTAACATGTGACAATTTAGAGATT
 CTTTGTTTTATTTCACTGATTAATACTGTGGCAAATTACACAGATTATTAATTTTTTTTACAA
 GAGTATAGTATATTTATTTGAAATGGGAAAAGTGCATTTTACTGTATTTTGTGTATTTTGTTTAT
 TTCTCAGAATATGGAAAGAAAATTAATAATGTGTCAATAAATATTTTCTAGAGAGTAA

FIGURE 108

MAREDSVKCLRCLLYALNLLFWLMSISVLAVSAWMRDYLNNVLTTLTAETRVEEAVILTYFPVVHP
VMIAVCCFLIIVGMLGYCGTVKRNLLLLLAWYFGSLLVIFCVELACGVWTYEQELMVPVQWSDMVT
LKARMTNYGLPRYRWLTHAWNFFQREFKCCGVVYFTDWLEMTEMDWPPDSCCVREFPGCSKQAHQ
EDLSDLYQEGCGKMYSLRGTQQLQVLRFLGISIGVTQILAMILTITLLWALYDRREPQTDQM
MSLKNDNSQHLSCPSVELLKPSLSRI FEHTSMANSFNTHFEMEEL

Signal peptide:

amino acids 1-33

Transmembrane domains:

amino acids 12-35, 57-86, 94-114, 226-248

FIGURE 109

CCAAGGCCAGAGCTGTGGACACCTTATCCCACTCATCCTCATCCTTCTCTGATAAAGCCCCCTACCAGTGCT
GATAAAGTCTTTCTCGTGAGAGCCTAGAGGCCCTAAAAAAGTGTGAAAGAGAAGGGGACAAAGGAACA
CCAGTATTAAGAGGATTTTCCAGTGTCTGGCAGTTGGTCCAGAAGGATGCCTCCATTCTGCTTCTCACCTG
CCTCTTCATCACAGGCACCTCCGTGTCACCCGTGGCCCTAGATCCTTGTTCTGCTTACATCAGCCTGAATGAGC
CCTGGAGGAACACTGACCACCAAGTTGGATGAGTCTCAAGGTCTCTCTATGTGACAACCATGTGAATGGGGAG
TGGTACCCTTCACGGGCATGGCGGGAGATGCCATGCCTACCTTCTGCATACCAGAAAACCACTGTGGAACCCA
CGCACCTGTCTGGCTCAATGGCAGCCACCCCTAGAAGGCGACGGCATTGTGCAACGCCAGGCTTGTGCCAGCT
TCAATGGGAACGTGCTGTCTCTGGAACACCACGGTGGAAAGTCAAGGCTTGCCCTGGAGGCTACTATGTGTATCGT
CTGACCAAGCCCAGCGTCTGCTTCCACGTCTACTGTGGTCATTTTTATGACATCTGCCAGCAGGACTGCCATGG
CAGCTGCTCAGATACCAGCGAGTGCACATGCGCTCCAGGAACTGTGCTAGGCCCTGACAGGCAGACATGCTTTG
ATGAAAATGAATGTGAGCAAAACAACGGTGGCTGCAGTGAATCTGTGTGAACCTCAAAAACCTCTACCGCTGT
GAGTGTGGGGTGTGCCGTGTGCTAAGAAGTGTGGAAGACTTGTGAAGACGTTGAAGGATGCCACAATAACAA
TGGTGGCTGCAGCCACTCTTGCCCTGGATCTGAGAAAGGCTACCAGTGTGAATGTCCCCGGGGCTGGTGTCTGT
CTGAGGATAACCACACTTGCCAGTCCCTGTGTTGTGCAAAATCAAATGCCATGGAAGTGAACATCCCCAGGGAG
CTGGTTGGTGGCTGGAGCTCTTCCCTGACCAACACCTCCTGCCGAGGAGTGTCCAACGGCACCCATGTCAACAT
CCTCTTCTCTCAAGACATGTGGTACAGTGGTGCATGTGGTGAATGACAAGATTGTGGCCAGCAACCTCGTGA
CAGGTCTACCCAAGCAGACCCCGGGGAGCAGCGGGGACTTCATCATCCGAACCAGCAAGCTGCTGATCCCCGGT
ACCTGCGAGTTTCCACGCCTGTACACCATTTCTGAAGGATACGTTCCCAACCTTCGAAACTCCCCACTGGAAT
CATGAGCCGAAATCATGGGATCTTCCATTCACTCTGGAGATCTTCAAGGACAATGAGTTTGAAGAGCCTTACC
GGGAAGCTCTGCCACCCTCAAGCTTCTGACTCCCTCTACTTTGGCATTGAGCCCCTGGTGCACGTGAGCGGC
TTGGAAGCTTGGTGGAGAGCTGCTTTGCCACCCACCTCCAAGATCGACGAGGCTCTGAAATACCTACCTCAT
CCGGGATGGCTGTGTTTTCAGATGACTCGGTAAAGCAGTACACATCCCGGGATCACCTAGCAAAGCACTTCCAGG
TCCCTGTCTTCAAGTTTGTGGGCAAAGACCACAAGGAAGTGTCTTCTGCACTGCCGGTCTTGTCTGTGGAGTG
TTGGACGAGCGTTCCTGCTGTGCCAGGGTTCACCCGGCGAATGCGTCTGGGGCAGGAGGAGAGGACTCAGC
CGGTCTACAGGGCCAGACGCTAACAGCGGGCCGATCCGCATCGACTGGGAGGACTAGTTCGTAGCCATACCTC
GAGTCCCTGCATTGGACGGCTCTGCTCTTTGGAGCTTCTCCCCCACCGCCCTCTAAGAACATCTGCCAACAGC
TGGGTTTCAGACTTCACACTGTGAGTTCAGACTCCAGCACCAACTCACTCTGATTCTGGTCCATTGAGTGGGCA
CAGGTCACAGCACTGTGAACAATGTGCCCTGGGTGGGTTTTCATCTTCTAGGGTTGAAAATAAATGTCCA
CCCAGAAAGCACTCACCCATTTCCCTCATTCTTCTTCTACACTTAAATACCTCGTGTATGGTGAATCAGAC
CACAAAATCAGAAGCTGGGTATAATATTTCAAGTTACAAACCTTAGAAAAATAAACAGTTACTGAAATTATGA
CTTAAATACCCAATGACTCCTTAAATATGTAATTATAGTTATACCTTGAATTTCAATTCAAATGCAGACTAA
TTATAGGGAATTTGGAAGTGTATCAATAAACAGTATATAATTTT

FIGURE 110

MPPFLLLTCLFITGTSVSPVALDPCSAYISLNEPWRNTDHQLDESQGPPLCDNHVNGEWYHFTGMAGDAMP
TFCIPENHCGTHAPVWLNGSHPLEGDGIVQRQACASFNGNCCLWNTTVEVKACPGGYVYRLTKPSVCFHV
YCGHFYDICEDEDCHGSCSDTSECTCAPGTVLGPDRQTCFDENECEQNNGGCSEICVNLKNSYRCECGVGRV
LRSDGKTCEDEVEGCHNNNGGCSHSCLGSEKGYQCECPRGLVLSNHTCQVPVLCKSNAIEVNI PRELVGG
LELFLTNTSCRGVSNNGTHVNILESLKTCGTVVVDVNDKIVASNLVTGLPKQTPGSSGDFIIRTSKLLIPVT
CEFPRLYTISEGYVPNLRNSPLEIMSRNHGIFPFTLEIFKDNEFEOPYREALPTLKLRLDSLYFGIEPVVHV
SGLESLVESCFATPTS KIDEVLKYLLIRDGCVSDDSVKQYTSRDHLAKHFQVPVFKFVKGDKHKEVFLHCRV
LVCGVLDERSRCAQGGCHRRMRRGAGGEDSAGLQGGTTLTGGPIRIDWED

Important features of the protein:

Signal peptide:

amino acids 1-16

N-glycosylation sites.

amino acids 89-93, 116-120, 259-263, 291-295, 299-303

Tyrosine kinase phosphorylation sites.

amino acids 411-418, 443-451

N-myristoylation sites.

amino acids 226-232, 233-239, 240-246, 252-258, 296-302, 300-306,
522-528, 531-537

Aspartic acid and asparagine hydroxylation site.

amino acids 197-209

ZP domain proteins.

amino acids 431-457

Calcium-binding EGF-like proteins.

amino acids 191-212, 232-253

FIGURE 111

GAGAGAGGCAGCAGCTTGCTCAGCGGACAAGGATGCTGGGCGTGAGGGACCAAGGCCTGCCCTGCACTCGG
GCCTCCTCCAGCCAGTGCTGACCAGGGACTTCTGACCTGCTGGCCAGCCAGGACCTGTGTGGGGAGGCCCT
CCTGCTGCCCTGGGGTGACAATCTCAGCTCCAGGCTACAGGGAGACCGGGAGGATCACAGAGCCAGCATGT
TACAGGATCCTGACAGTGATCAACCTCTGAACAGCCTCGATGTCAAACCCCTGCGCAAACCCCGTATCCCC
ATGGAGACCTTCAGAAAGGTGGGGATCCCCATCATCATAGCACTACTGAGCCTGGCGAGTATCATCATTGT
GGTTGTCCTCATCAAGGTGATTCTGGATAAAATACTACTTCCCTCTGCGGGCAGCCTCTCCACTTCATCCCGA
GGAAGCAGCTGTGTGACGGAGAGCTGGACTGTCCCTTGGGGGAGGACGAGGAGCACTGTGTCAAGAGCTTC
CCCGAAGGGCCTGCAGTGGCAGTCCGCCCTCTCCAAGGACCGATCCACACTGCAGGTGCTGGACTCGGCCAC
AGGGAAGTGGTTCTCTGCCTGTTTTGACAACCTTCACAGAAGCTCTCGCTGAGACAGCCTGTAGGCAGATGG
GCTACAGCAGAGCTGTGGAGATTGGCCCAGACCAGGATCTGGATGTTGTTGAAATCACAGAAAACAGCCAG
GAGCTTCGCATGCGGAACTCAAGTGGGCCCTGTCTCTCAGGCTCCCTGGTCTCCCTGCCTGTCTTGCCTG
TGGGAAGAGCCTGAAGACCCCGTGTGGTGGGTGGGGAGGAGGCCTCTGTGGATTCTTGGCCTTGGCAGG
TCAGCATCCAGTACGACAAAACAGCACGTCTGTGGAGGGAGCATCCTGGACCCCCACTGGGTCTCACGGCA
GCCCCACTGCTTCAGGAAACATACCGATGTGTTCAACTGGAAGGTGCGGGCAGGCTCAGACAAAAGTGGGCAG
CTTCCCATCCCTGGCTGTGGCCAAGATCATCATCATTTGAATTCAACCCCATGTACCCCAAAGACAATGACA
TCGCCCTCATGAAGCTGCAGTTCCTCACTTTCTCAGGCACAGTCAGGCCCATCTGTCTGCCCTTCTTT
GATGAGGAGCTCACTCCAGCCACCCCACTCTGGATCATTTGGATGGGGCTTTACGAAGCAGAATGGAGGGAA
GATGTCTGACATACTGCTGCAGGCGTCAGTCCAGGTCAATGACAGCACACGGTGAATGCAGACGATGCGT
ACCAGGGGGAAGTCACCGAGAAGATGATGTGTGCAGGCATCCCGAAGGGGGTGTGGACACCTGCCAGGGT
GACAGTGGTGGGCCCTGATGTACCAATCTGACCAGTGGCATGTGGTGGGCATCGTTAGCTGGGGCTATGG
CTGGGGGGCCCGAGCACCCAGGAGTATACACCAAGGTCTCAGCCTATCTCAACTGGATCTACAATGTCT
GGAAGGCTGAGCTGTAATGCTGCTGCCCTTTGCAGTGTGGGAGCCGCTTCCTTCTGCCCTGCCACCT
GGGGATCCCCCAAAGTCAGACACAGAGCAAGAGTCCCTTGGGTACACCCCTCTGCCACAGCCTCAGCAT
TTCTTGGAGCAGCAAAGGGCCTCAATTCCTGTAAGAGACCCTCGCAGCCCAGAGGGCGCCAGAGGAAGTCA
GCAGCCCTAGCTCGGCCACACTTGGTGTCCAGCATCCAGGGAGAGACACAGCCCACTGAACAAGGTCT
CAGGGGTATTGCTAAGCCAAGAAGGAACCTTCCACACTACTGAATGGAAGCAGGCTGTCTTGTAAGGCC
CAGATCACTGTGGCTGGAGAGGAGAAGGAAAGGGTCTGCGCCAGCCCTGTCCGTCTTACCCATCCCCAA
GCCTACTAGAGCAAGAAACCAGTTGTAATATAAAATGCACTGCCCTACTGTTGGTATGACTACCGTTACCT
ACTGTTGTCATTGTTATTACAGCTATGGCCACTATTATTAAGAGCTGTGTAACATCTCTGGCAAAAAAAA
AAAA

FIGURE 112

MLQDPDSQPLNSLDVKPLRKPRIPMETFRKVGIP III IALLSLAS III IVVVLIKVILDKYYFLCG
QPLHFIPRKQLCDGELDCPLGEDEEHCVKSFPEGPAVAVRLSKDRSTLQVLDSATGNWFSACFDN
FTEALAETACRQMGYSRAVEIGPDQDL DVVEITENSQELMRNSSGPCLSGSLVSLHCLACGKSL
KTPRVVGGEEASVDSWPWQVSIQYDKQHVC GGS ILDPHWVLTAAHCFRKHTDVFNWKVRAGSDKL
GSFPSLAVAKI III IEFNPMYPKDNDIALMKLQFPLTFSGTVRPICLPFFDEELTPATPLWIIIGWG
FTKQNGGKMSDILLQASVQVIDSTRCNADDA YQGEVTEKMMCAGIPEGGVDTCQGDSGGPLMYQS
DQWHVVGIVSWGYGCGGPSTPGVYTKVSAYLNWIYNVWKAEL

Transmembrane domain:

amino acids 32-53 (typeII)

FIGURE 113

GGCTGGACTGGAACTCCTGGTCCCAAGTGATCCACCCGCTCAGCCTCCCAAGGTGCTGTGATTA
TAGGTGTAAGCCACCGTGTCTGGCCTCTGAACAACTTTTTCAGCAACTAAAAAGCCACAGGAGT
TGAAGTCTAGGATTCTGACTATGCTGTGGTGGCTAGTGCTCCTACTCCTACCTACATTAAAATC
TGTTTTTTGTTCTCTTGTAACTAGCCTTTACCTTCCTAACACAGAGGATCTGTCACTGTGGCTCT
GGCCCAAACCTGACCTTCACTCTGGAACGAGAACAGAGGTTTCTACCCACACCGTCCCCTCGAAG
CCGGGGACAGCCTCACCTTGCTGGCCTCTCGCTGGAGCAGTGCCCTCACCAACTGTCTCACGTCT
GGAGGCACTGACTCGGGCAGTGCAGGTAGCTGAGCCTCTTGGTAGCTGCGGCTTCAAGGTGGGG
CTTGCCCTGGCCGTAGAAGGGATTGACAAGCCCGAAGATTCATAGGCGATGGCTCCCCTGCCC
AGGCATCAGCCTTGCTGTAGTCAATCACTGCCC TGGGGCCAGGACGGGCCGTGGACACCTGCTCA
GAAGCAGTGGGTGAGACATCACGCTGCCCGCCATCTAACCTTTTCATGTCTGCACATCACCTG
ATCCATGGGCTAATCTGAACCTCTGTCCCAAGGAACCCAGAGCTTGAGTGAGCTGTGGCTCAGACC
CAGAAGGGGTCTGCTTAGACCACCTGGTTTTATGTGACAGGACTTGCAATTCCTGGAACATGAGG
GAACGCCGGAGGAAAAGCAAAGTGGCAGGGAAGGAAC TTGTGCCAAATTATGGGTGAGAAAAGATG
GAGGTGTTGGGTTATCACAAAGGCATCGAGTCTCCTGCATTCAGTGGACATGTGGGGGAAGGGCTG
CCGATGGCGCATGACACACTCGGGACTCACCTCTGGGGCCATCAGACAGCCGTTTCCGCCCCGAT
CCACGTACCAGCTGCTGAAGGGCAACTGCAGGCCGATGCTCTCATCAGCCAGGCAGCAGCCAAAA
TCTGCGATCACCAGCCAGGGGCAGCCGCTCTGGGAAGGAGCAAGCAAAGTGACCATTTCTCCTCCC
CTCCTTCCCTCTGAGAGGCCCTCCTATGTCCC TACTAAAGCCACCAGCAAGACATAGCTGACAGG
GGCTAATGGCTCAGTGTGGCCAGGAGGTGAGCAAGGCCTGAGAGCTGATCAGAAGGGCCTGCT
GTGCCAACACGGAAATGCC TCCAGTAAGCACAGGCTGCAAAATCCCCAGGCAAAGGACTGTGTGG
CTCAATTTAAATCATGTTCTAGTAATTGGAGCTGTCCCCAAGACCAAAGGAGCTAGAGCTTGGTT
CAAATGATCTCCAAGGGCCCTTATACCC CAGGAGACTTTGATTTGAATTTGAAACCCCAAATCCA
AACCTAAGAACCAGGTGCATTAAGAATCAGTTATTGCCGGGTGTGGTGGCCTGTAATGCCAACAT
TTTGGGAGGCCGAGGCGGGTAGATCACCTGAGGTCAGGAGTTCAAGACCAGCCTGGCCAACATGG
TGAAACCCCTGTCTCTACTAAAAATACAAAAAACTAGCCAGGCATGGTGGTGTGTGCCTGTATC
CCAGCTACTCGGGAGGCTGAGACAGGAGAATTACTTGAACCTGGGAGGTGAAGGAGGCTGAGACA
GGAGAATCACTTCAGCCTGAGCAACACAGCGAGACTCTGTCTCAGAAAAATAAAAAAAGAATTA
TGGTTATTTGTAA

FIGURE 114

MLWWLVLLLLPTLKSVFCSLVTSIYLPNTEDLSLWLPKPDHSGTRTEVSTHTVPSKPGTASPC
WPLAGAVPSPTVSRLEALTRAVQVAEPLGSCGFQGGPCPGRRRD

Signal peptide:
amino acids 1-15

FIGURE 115

CAGCAGTGGTCTCTCAGTCCTCTCAAAGCAAGGAAAGAGTACTGTGTGCTGAGAGACCATGGCAA
AGAATCCTCCAGAGAATTGTGAAGACTGTCACATTCTAAATGCAGAAGCTTTTAAATCCAAGAAA
ATATGTAAATCACTTAAGATTTGTGGACTGGTGTGGTATCCTGGCCCTAACTCTAATTGTCTT
GTTTTGGGGGAGCAAGCACTTCTGGCCGGAGGTACCCAAAAAGCCTATGACATGGAGCACACTT
TCTACAGCAATGGAGAGAAGAAGATTTACATGGAATTGATCCTGTGACCAGAAGTAAATA
TTCAGAAGCGGAAATGGCACTGATGAAACATTGGAAGTGCACGACTTTAAAAACGGATACACTGG
CATCTACTTCGTGGTCTTCAAAAATGTTTTATCAAACTCAGATTAAAGTATTCTGAATTTT
CTGAACCAGAAGAGGAAATAGATGAGAATGAAGAAATTACCACAACCTTTCTTTGAACAGTCAGTG
ATTTGGGTCCCAGCAGAAAAGCCTATTGAAAACCGAGATTTTCTTAAAAATTCCAAAATCTGGA
GATTTGTGATAACGTGACCATGTATTGGATCAATCCCACTCTAATATCAGTTTCTGAGTTACAAG
ACTTTGAGGAGGAGGAGAAGATCTTCACTTTCTGCCAACGAAAAAAAAAGGGATTGAACAAAAT
GAACAGTGGGTGGTCCCTCAAGTGAAAGTAGAGAAGACCCGTCACGCCAGACAAGCAAGTGAGGA
AGAACTTCCAATAAATGACTATACTGAAAATGGAATAGAATTTGATCCCATGCTGGATGAGAGAG
GTTATTGTTGTATTTACTGCCGTCGAGGCAACCGCTATTGCCGCCGCTGTGAACTTTACTA
GGCTACTACCCATATCCATACTGCTACCAAGGAGGACGAGTCATCTGTGTCATCATGCCTTG
TAACTGGTGGGTGGCCCGCATGCTGGGGAGGGTTAATAGGAGGTTTGAGCTCAAATGCTTAAAC
TGCTGGCAACATATAATAAATGCATGCTATTCAATGAATTTCTGCCTATGAGGCATCTGGCCCT
GGTAGCCAGCTCTCCAGAATTACTTGTAGGTAATTCCTCTCTTCATGTTCTAATAAACTTCTACA
TTATCACCAAAAAAAAAAAAAAAAAAAAA

FIGURE 116

MAKNPPENCEDCHILNAEAFKSKKICKSLKICGLVFGILALTLIVLFWGSKHFWPEVPKKAYDME
HTFYSNGEKKKIYMEIDPVTRTEIFRSGNGTDETLVHDFKNGYTGIIYFVGLQKCFIKTQIKVIP
EFSEPEEEIDENEEITTTFFEQSVIWWVPAEKPIENRDFLKNKILEICDNVTMYWINPTLISVSE
LQDFEEEGEDLHFPANEKKGIEQNEQWVVPQVKVEKTRHARQASEEELPINDYTENGIEFDPMLD
ERGYCCIIYCRGNRYCRRVCEPLLGYYPYPYCYQGGRVICRVIMPCNWWWVARM LGRV

Important features of the protein:

Signal peptide:

amino acids 1-40

Transmembrane domain:

amino acids 25-47 (type II)

N-glycosylation sites.

amino acids 94-97, 180-183

Glycosaminoglycan attachment sites.

amino acids 92-95, 70-73, 85-88, 133-136, 148-151, 192-195, 239-
242

N-myristoylation sites.

amino acids 33-38, 95-100, 116-121, 215-220, 272-277

Microbodies C-terminal targeting signal.

amino acids 315-317

Cytochrome c family heme-binding site signature.

amino acids 9-14

FIGURE 117

GAGCTCCCCTCAGGAGCGCGTTAGCTTCACACCTTCGGCAGCAGGAGGGCGGCAGCTTCTCGCAGGCGGCA
GGGCGGGCGGCCAGGATCATGTCCACCACCACATGCCAAGTGGTGGCGTTCCTCCTGTCCATCCTGGGGCT
GGCCGGCTGCATCGCGGCCACCGGGATGGACATGTGGAGCACCCAGGACCTGTACGACAACCCCGTCACCT
CCGTGTTCCAGTACGAAGGGCTCTGGAGGAGCTGCGTGAGGCAGAGTTCAGGCTTCACCGAATGCAGGCCC
TATTTACCATCCTGGGACTTCCAGCCATGCTGCAGGCAGTGCAGGCCCTGATGATCGTAGGCATCGTCTCT
GGGTGCCATTGGCTCCTGGTATCCATCTTTGCCCTGAAATGCATCCGCATTGGCAGCATGGAGGACTCTG
CCAAAGCCAACATGACACTGACCTCCGGGATCATGTTTCATGTCTCAGGTCTTTGTGCAATTGCTGGAGTG
TCTGTGTTTGCCAACATGCTGGTGACTAACTTCTGGATGTCCACAGCTAACATGTACACCGGCATGGGTGG
GATGGTGCAGACTGTTCCAGACCAGGTACACATTTGGTGGCGCTCTGTTCTGGGGCTGGGTGCTGGAGGCC
TCACACTAATTGGGGTGTGATGATGTGCATCGCCTGCCGGGCTGGCACCAGAAGAAACCAACTACAAA
GCCGTTTCTTATCATGCCTCAGGCCACAGTGTTCCTACAAGCCTGGAGGCTTCAAGGCCAGCACTGGCTT
TGGGTCCAACACCAAAAAACAAGAAGATATACGATGGAGGTGCCCGCACAGAGGACGAGGTACAATCTTATC
CTTCCAAGCACGACTATGTGTAATGCTCTAAGACCTCTCAGCACGGGCGGAAGAACTCCCGGAGAGCTCA
CCCAAAAAACAAGGAGATCCCATCTAGATTTCTTCTTGCTTTTGACTCACAGCTGGAAGTTAGAAAAGCCT
CGATTTTCATCTTTGGAGAGGCCAAATGGTCTTAGCCTCAGTCTCTGTCTCTAAATATTCCACCATAAAACA
GCTGAGTTATTTATGAATTAGAGGCTATAGCTCACATTTTCAATCCTCTATTTCTTTTTTAAATATAACT
TTCTACTCTGATGAGAGAATGTGGTTTTAATCTCTCTCTCACATTTTGATGATTTAGACAGACTCCCCCTC
TTCCTCCTAGTCAATAAACCCATTGATGATCTATTTCCAGCTTATCCCCAAGAAAACCTTTTGAAGGAAA
GAGTAGACCCAAAGATGTTATTTTTCTGCTGTTTGAATTTTGTCTCCCCACCCCAACTTGGCTAGTAATAA
ACACTTACTGAAGAAGAAGCAATAAGAGAAAGATATTTGTAATCTCTCCAGCCCATGATCTCGGTTTTCTT
ACACTGTGATCTTAAAAGTTACCAACCAAAGTCATTTTCAGTTTGAGGCAACCAACCTTTCTACTGCTG
TTGACATCTTCTTATTACAGCAACACCATTCTAGGAGTTTCTGAGCTCTCCACTGGAGTCTCTTTCTGT
CGCGGGTCAGAAATTGTCCCTAGATGAATGAGAAAATTAATTTTTTAAATTTAAGTCTAAATATAGTTAA
AATAAATAATGTTTTAGTAAAATGATACACTATCTCTGTGAAATAGCCTCACCCCTACATGTGGATAGAAG
GAAATGAAAAATAATTGCTTTGACATTGTCTATATGGTACTTTGTAAAGTCATGCTTAAGTACAAATTC
ATGAAAAGCTCACACCTGTAATCCTAGCACTTTGGGAGGCTGAGGAGGAAGGATCACTTGAGCCCAGAAGT
TCGAGACTAGCCTGGGCAACATGGAGAAGCCCTGTCTCTACAAAATACAGAGAGAAAAATCAGCCAGTCA
TGGTGGCATAACCTGTAGTCCCAGCATTCCGGGAGGCTGAGGTGGGAGGATCACTTGAGCCCAGGGAGGT
TGGGGCTGCAGTGAAGCATGATCACACCACTGCACTCCAGCCAGGTGACATAGCGAGATCCTGTCTAAAAA
AATAAAAAATAAATAATGGAACACAGCAAGTCTTAGGAAGTAGGTTAAAATAATTCTTTAA

FIGURE 118

MSTTTCQVVAFLLSILGLAGCIAATGMDMWSTQDLYDNPVTSVVFQYEGLRSCVVRQSSGFTECRP
YFTILGLPAMLQAVRALMIVGIVLGAIGLLVSIKALKCIKIRIGSMEDSAKANMTLTSGIMFIVSGL
CAIAGVSVFANMLVTNFWMSTANMYTGMGGMVQTVQTRYTFGAALFVGWVAGGLTLIGGVMMCIA
CRGLAPEETNYKAVSYHASGHSVAYKPGGFKASTGFGSNTKNKKIYDGGARTEDEVQSYPSKHDY
V

Signal peptide:

amino acids 1-23

Transmembrane domains:

amino acids 81-100, 121-141, 173-194

FIGURE 119

GGAAAACTGTTCTCTTCTGTGGCACAGAGAACCCTGCTTCAAAGCAGAAGTAGCAGTTCGGAGTCC
AGCTGGCTAAAACTCATCCCAGAGGATAATGGCAACCCATGCCTTAGAAATCGCTGGGCTGTTCTTG
GTGGTGGTGGAAATGGTGGGCACAGTGGCTGTCACTGTCATGCCTCAGTGGAGAGTGTGGCCCTTCATT
GAAAAACAACATCGTGGTTTTTTGAAAACCTCTGGGAAGGACTGTGGATGAATTGCGTGAGGCAGGCTAA
CATCAGGATGCAGTGCAAAATCTATGATTCCTGCTGGCTCTTTCTCCGGACCTACAGGCAGCCAGAG
GACTGATGTGTGCTGCTTCCGTGATGTCCTTCTTGGCTTTCATGATGGCCATCCTTGGCATGAAATGC
ACCAGGTGCACGGGGGACAATGAGAAGGTGAAGGCTCACATTCTGCTGACGGCTGGAATCATCTTCAT
CATCACGGGCATGGTGGTGTCTCATCCCTGTGAGCTGGGTGGCCAATGCCATCATCAGAGATTTCTATA
ACTCAATAGTGAATGTTGCCCAAAAACGTGAGCTTGGAGAAGCTCTCTACTTAGGATGGACCACGGCA
CTGGTGTCTGATTGTTGGAGGAGCTCTGTTCTGCTGCGTTTTTTTGTGCAACGAAAAGAGCAGTAGCTA
CAGATACTCGATACCTTCCCATCGCACAAACCCAAAAAGTTATCACACCGGAAAGAAGTCACCGAGCG
TCTACTCCAGAAGTCAGTATGTGTAGTTGTGTATGTTTTTTAACTTTACTATAAAGCCATGCAAAATG
ACAAAAATCTATATTACTTTCTCAAAATGGACCCCAAAGAACTTTGATTTACTGTTCTTAACTGCCT
AATCTTAATTACAGGAAGTGTGCATCAGCTATTTATGATTTCTATAAGCTATTTTCAGCAGAATGAGATA
TTAAACCCAATGCTTTGATTGTTCTAGAAAGTATAGTAATTTGTTTTCTAAGGTGGTTCAAGCATCTA
CTCTTTTTATCATTTACTTTCAAATGACATTTGCTAAAGACTGCATTATTTTACTACTGTAATTTCTCC
ACGACATAGCATTATGTACATAGATGAGTGTAAACATTTATATCTCACATAGAGACATGCTTATATGGT
TTTATTTAAAATGAAATGCCAGTCCATTACACTGAATAAATAGAAGTCAACTATTGCTTTTCAGGGAA
ATCATGGATAGGGTTGAAGAAGGTTACTATTAATGTTTTAAAAACAGCTTAGGGATTAATGTCTCCCA
TTTATAATGAAGATTAATAATGAAGGCTTTAATCAGCATTGTAAAGGAAATGAATGGCTTTCTGATAT
GCTGTTTTTTAGCCTAGGAGTTAGAAATCCTAACTTCTTTATCCTCTTCTCCAGAGGCTTTTTTTTT
CTTGTTATTAATAAACATTTTTTAAAACGCAGATATTTGTCAAGGGGCTTTGCATTCAAACCTGCTT
TTCCAGGGCTATACTCAGAAGAAAGATAAAAGTGTGATCTAAGAAAAAGTGATGGTTTTAGGAAAGTG
AAAATATTTTTGTTTTTGTATTTGAAGAAGAATGATGCATTTTGACAAGAAATCATATATGTATGGAT
ATATTTTAATAAGTATTTGAGTACAGACTTTGAGGTTTCATCAATATAAATAAAAGAGCAGAAAAATA
TGTCTTGGTTTTCATTTGCTTACCAAAAAACAACAACAAAAAAGTTGTCTTTGAGAACTTCACCT
GCTCCTATGTGGGTACCTGAGTCAAATTTGTCATTTTTGTTCTGTGAAAAATAAATTTCTTCTTGTA
CCATTTCTGTTTAGTTTTACTAAAATCTGTAAATACTGTATTTTTCTGTTTATTCCAAATTTGATGAA
ACTGACAATCCAATTTGAAAGTTTGTGTGACGCTGTCTAGCTTAAATGAATGTGTTCTATTTGCTT
TATACATTTATATTAATAAATTTGTACATTTTTCTAATT

FIGURE 120

MATHALEIAGLEFLGGVGMVGTVAVTVMPOWRVSAFIENNIIVVFENFWEGLWMNCVROANIRMOCK
IYDSSLALSPDLQAARGLMCAASVMSFLAFMMAILGMKCTRCTGDNEKVKAHILLTAGIIFIITG
MVLIPVSWVANAIIRDFYNSIVNVAQKRELGEALYLGWTTALVLIVGGALFCCVFCCNEKSSSY
RYSIPSHRTTQKSYHTGKKSPSVYSRSQYV

Signal peptide:

amino acids 1-17

Transmembrane domains:

amino acids 82-101, 118-145, 164-188

FIGURE 121

GGAGAGAGGCGCGCGGGTGAAGGGCGCATTGATGCAGCCTGCGGGCGGCCTCGGAGCGCGGCGGAG
CCAGACGCTGACCACGTTCCCTCTCCTCGGTCTCCTCCGCCTCCAGCTCCGCGCTGCCCGGCAGCC
GGGAGCCATGCGACCCAGGGCCCCGCCGCCTCCCCGCAGCGGCTCCGCGGCCTCCTGCTGCTCC
TGCTGCTGCAGCTGCCCCGCGCCGTCGAGCGCCTCTGAGATCCCCAAGGGGAAGCAAAGGCGCAG
CTCCGGCAGAGGGAGGTGGTGGACCTGTATAATGGAATGTGCTTACAAGGGCCAGCAGGAGTGCC
TGGTCGAGACGGGAGCCCTGGGGCCAATGTTATTCCGGGTACACCTGGGATCCCAGGTCCGGATG
GATTCAAAGGAGAAAAGGGGGAATGTCTGAGGGAAAGCTTTGAGGAGTCTTGACACCCAACTAC
AAGCAGTGTTCATGGAGTTCATTGAATTATGGCATAGATCTTGGGAAAATTGCGGAGTGTACATT
TACAAAGATGCGTTCAAATAGTGCTCTAAGAGTTTTGTTTCAGTGGCTCACTTCGGCTAAAATGCA
GAAATGCATGCTGTCAGCGTTGGTATTTACATTCAATGGAGCTGAATGTTTCAGGACCTCTTCCC
ATTGAAGCTATAATTTATTTGGACCAAGGAAGCCCTGAAATGAATTCAACAATTAATATTCATCG
CACTTCTTCTGTGGAAGGACTTTGTGAAGGAATTGGTGCTGGATTAGTGGATGTTGCTATCTGGG
TTGGCACTTGTTTCAGATTACCCAAAAGGAGATGCTTCTACTGGATGGAATTCAGTTTCTCGCATC
ATTATTGAAGAACTACCAAATAAATGCTTTAATTTTCATTTGCTACCTCTTTTTTTATTATGCC
TTGGAATGGTTCACTTAAATGACATTTTAAATAAGTTTATGTATACATCTGAATGAAAAGCAAAG
CTAAATATGTTTACAGACCAAAGTGTGATTTCACACTGTTTTTAAATCTAGCATTATTCATTTG
CTTCAATCAAAGTGGTTTCAATATTTTTTTTAGTTGGTTAGAATACTTTCTTCATAGTCACATT
CTCTCAACCTATAATTTGGAATATTGTTGTGGTCTTTTGTTTTTTCTCTTAGTATAGCATTTTTA
AAAAATATAAAAGCTACCAATCTTTGTACAATTTGTAATGTTAAGAATTTTTTTTATATCTGT
TAAATAAAAATTATTTCCAACA

FIGURE 122

MRPQGPAASPQRLRGLLLLLLLLLQLPAPSSASEIPK GKQKAQLRQREVVDLYNGMCLQGPAGVPGR
DGSPGANVIPGTPGIPGRDGFKEKGECLRESFEESWTPNYKQCSWSSLNYGIDLKIAECTFTK
MRSNSALRVLFSGSLRLKCRNACCQRWYFTFNGAECGGLPIEAI IYLDQGSPEMNSTINIHRTS
SVEGLCEGIGAGLVDVAIWVGTCSDYPKGDASTGWNSVSR IIIIEELPK

Signal peptide:

amino acids 1-30

Transmembrane domain:

amino acids 195-217

FIGURE 123

GCTGAGCGTGTGCGCGGTACGGGGCTCTCCTGCCTTCTGGGCTCCAACGCAGCTCTGTGGCTGAA
 CTGGGTGCTCATCACGGAACTGCTGGGCTATGGAATACAGATGTGGCAGCTCAGGTAGCCCCAA
 ATTGCCTGGAAGAATACATCATGTTTTTCGATAAGAAGAAATTGTAGGATCCAGTTTTTTTTTTA
 ACCGCCCCCTCCCCACCCCCCAAAAAAAGCTGTAAAGATGCAAAAACGTAATATCCATGAAGATCC
 TATTACCTAGGAAGATTTTGATGTTTTGCTGCGAATGCGGTGTTGGGATTTATTTGTTCTTGGAG
 TGTTCTGCGTGGCTGGCAAAGAATAATGTTCCAAAATCGGTCCATCTCCCAAGGGGTCCAATTTT
 TCTTCCTGGGTGTGACGCGACCCGACTCACTACAGTGCAGCTGACAGGGGCTGTCATGCAACTG
 GCCCCTAAGCCAAAGCAAAAGACCTAAGGACGACCTTTGAACAATACAAAAGGATGGGTTTCAATG
 TAATTAGGCTACTGAGCGGATCAGCTGTAGCACTGGTTATAGCCCCACTGTCTTACTGACAATG
 CTTTCTTCTGCCGAACGAGGATGCCCTAAGGGCTGTAGGTGTGAAGGCAAAATGGTATATTGTGA
 ATCTCAGAAATTACAGGAGATACCCCTCAAGTATATCTGCTGGTGTCTTAGGTTTGTCCCTTCGCT
 ATAACAGCCTTCAAAAAGCTTAAGTATAATCAATTTAAAGGGCTCAACCAGCTCACCTGGCTATAC
 CTTGACCATAACCATATCAGCAATATTGACGAAAATGCTTTTAAATGGAATACGCAGACTCAAAGA
 GCTGATTCTTAGTTCCAATAGAAATCTCCTATTTTCTTAACAATACCTTCAGACCTGTGACAAAT
 TACGGAACCTGGATCTGTCTATAATCAGCTGCATTCTCTGGGATCTGAACAGTTTCGGGGCTTG
 CGGAAGCTGCTGAGTTTACATTTACGGTCTAACTCCCTGAGAACCATCCCTGTGCGAATATTCCA
 AGACTGCCGCAACCTGGAACCTTTGGACCTGGGATATAACCGGATCCGAAGTTTLAGCCAGGAATG
 TCTTGTCTGGCATGATCAGACTCAAAGAACTTCACCTGGAGCACAATCAATTTTCCAAGCTCAAC
 CTGGCCCTTTTCCAAGGTGGTFCAGCCTTCAGAACCTTTACTTGCAGTGGAAATAAAATCAGTGT
 CATAGGACAGACCATGTCTGGACCTGGAGCTCCTTACAAAAGGCTTGATTTATCAGGCAATGAGA
 TCGAAGCTTTCAGTGGACCCAGTGTTCAGTGTGTCCCGAATCTGCAGCGCCTCAACCTGGAT
 TCCAACAAGCTCACATTTATGGTCAAGAGATTTGGATTCTTGGATATCCCTCAATGACATCAG
 TCTTGTCTGGGAATATATGGGAATGCAGCAGAAATATTTGCTCCCTGTAAACTGGCTGAAAAGTT
 TTAAAGGTCTAAGGGAGAATACAATTTATCTGTGCCAGTCCCAAAGAGCTGCAAGGAGTAAATGTG
 ATCGATGCAGTGAAGAACTACAGCATCTGTGGCAAAGTACTACAGAGAGGTTTGATCTGGCCAG
 GGCTCTCCCAAAGCCGACGTTAAGCCCAAGCTCCCCAGGCCGAAGCATGAGAGCAAACCCCTT
 TGCCCCGACGGTGGGAGCCACAGAGCCCGGCCAGAGACCGATGCTGACGCCGAGCACATCTCT
 TTCCATAAAATCATCGCGGGCAGCGTGGCGCTTTTCTGTCCGTGCTCATCTCTGCTGGTTAT
 CTACGTGTGATGGAAGCGGTACCCCTGCGAGCATGAAGCAGCTGCAGCAGCGCTCCCTCATGCGAA
 GGCACAGGAAAAAGAAAAGACAGTCCCTAAAGCAAATGACTCCAGCACCAGGAATTTTATGTA
 GATTATAAACCACCAACACGGAGACCAGCGAGATGCTGCTGAATGGGACGGGACCCCTGCACCTA
 TAACAAATCGGGCTCCAGGAGTGTGAGGTATGAACCATTGTGATAAAAAGAGCTCTTAAAAGCT
 GGGAAATAAGTGGTGCTTATTGAACTCTGGTGACTATCAAGGGAACGCGATGCCCCCTCCCC
 TTCCCTCTCCCTCTCACTTTGGTGGCAAGATCCTTCCCTGTCCGTTTTAGTGCATTATAATACT
 GGTCATTTTCTCTCATACATAATCAACCCATTGAAATTTAAATACCACAATCAATGTGAAGCTT
 GAACTCCGGTTTAAATATAATACCTATTGTATAAGACCCCTTACTGATTCCATTAATGTGCAATTT
 GTTTAAGATAAAACTTCTTTCATAGGTAAAAA

FIGURE 124

MGFNVIRLLSGSAVALVIAPTVLLTMLSSAERGCPKGCRCCEGKMVYCESQKLQEIPSSISAGCLG
LSLRYNLSLQKLKYNQFKGLNQLTWLYLDHNHISNIDENAFNGIRRLKELILSSNRISYFLNNTFR
PVTNLRNLDLSYNQLHSLGSEQFRGLRKLSSLHLRSNSLRTIPVRI FQDCRNLELLDLGYNRIRS
LARNVFAGMIRLKEHLEHNQFSKLNALFPRLVSLQONLYLQWNKISVIGQTMSTWSSLQRLDL
SGNEIEAFSGPSVFQCVPNLQRLNLDNKLTFIQEILDSWISLNDISLAGNIWECSRNICSLVN
WLKSFKGLRENTIICASPKELQGVNVIDAVKNYSICGKSTTERFDLARALPKPTFKPKLPRPKHE
SKPPLPPTVGATEPGPETDADAHEHISFHKIIAGSVALFLSVLVILLVIYVSWKRYPASKMLQQR
SLMRRHRKRRQSLKQMPSTQEFYVDYKPTNTETSEMLLNGTGPCTYNKSGSRECEV

Important features of the protein:

Signal peptide:

amino acids 1-33

Transmembrane domain:

amino acids 420-442

N-glycosylation sites.

amino acids 126-129, 357-360, 496-499, 504-507

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 465-468

Tyrosine kinase phosphorylation site.

amino acids 136-142

N-myristoylation sites.

amino acids 11-16, 33-38, 245-250, 332-337, 497-502, 507-512

FIGURE 125

CCGTTATCGTCTTGGCGTACTGCTGAATGTCCGTC~~CCCGGAGGAGGAGAGAGGCTTTTGCCGCTG~~
ACCCAGAGATGGCCCCGAGCGAGCAAATTCCTACTGTCCGGCTGCGCGGCTACCGTGGCCGAGCT
AGCAACCTTTCCCCTGGATCTCACAAAACTCGACTCCAAATGCAAGGAGAAGCAGCTCTTGCTC
GGTTGGGAGACGGTGCAAGAGAATCTGCCCCCTATAGGGGAATGGTGCGCACAGCCCTAGGGATC
ATTGAAGAGGAAGGCTTTCTAAAGCTTTGGCAAGGAGTGACACCCGCCATTTACAGACACGTAGT
GTATTCTGGAGGTCGAATGGTCACATATGAACATCTCCGAGAGGTTGTGTTTGGCAAAAGTGAAG
ATGAGCATTATCCCCTTTGGAAATCAGTCATTGGAGGGATGATGGCTGGTGTATTGGCCAGTTT
TTAGCCAATCCAACCTGACCTAGTGAAGGTTTCAGATGCAAATGGAAGGAAAAGGAAACTGGAAGG
AAAACCATTGCGATTTTCGTGGTGACATCATGCATTTGCAAAAATCTTAGCTGAAGGAGGAATAC
GAGGGCTTTGGGCAGGCTGGGTACCCAATATACAAAGAGCAGCACTGGTGAATATGGGAGATTTA
ACCACTTATGATACAGTGAACACTACTTGGTATTGAATACACCACTTGAGGACAATATCATGAC
TCACGGTTTATCAAGTTTATGTTCTGGACTGGTAGCTTCTATTCTGGGAACACCAGCCGATGTCA
TCAAAGCAGAATAATGAATCAACCACGAGATAAACAAGGAAGGGGACTTTTGTATAAATCATCG
ACTGACTGCTTGATTCAGGCTGTTCAAGGTGAAGGATTCATGAGTCTATATAAAGGCTTTTACC
ATCTTGGCTGAGAATGACCCCTTGGTCAATGGTGTCTGGCTTACTTATGAAAAAATCAGAGAGA
TGAGTGGAGTCAGTCCATTTTAA

FIGURE 126

MSVPEEEERLLPLTQRWPRASKFLLSGCAATVAELATFPLDLTKTRLQMQGEAALARLGDGARES
APYRGMVRTALGIIIEEGFLKLWQGVTPAIYRHVVYSGGRMVTYEHLREVVFGKSEDEHYPLWKS
VIGGMMAGVIGQFLANPTDLVKVQMOMEGKRKLEGKPLRFRGVHHAFAKILAEGGIRGLWAGWVP
NIQRAALVNMGDLTTYDVKHYLVLNTPLEDNIMTHGLSSLCSGLVASILGTPADVIKSRIMNQP
RDKQGRGLLYKSSTDCLIQAVQGEFMSLYKGFPSWLRMTPWSMVFWLTYEKIREMSGVSPF

Transmembrane domains:

amino acids 25-38, 130-147, 233-248

FIGURE 127

CGCGGATCGGACCCAAGCAGGT CGGCGGCGGGCGGCAGGAGAGCGGGCCGGGCGTCAGCTCCTCGAC
CCCCGTGTCGGGCTAGTCCAGCGAGGCGGACGGGCGGCGTGGGCCCATGGCCAGGCCCGGCATGG
AGCGGTGGCGCGACCGGCTGGCGCTGGTGACGGGGGCCTCGGGGGGCATCGGCCGCGGCCGTGGCC
CGGGCCCTGGTCCAGCAGGGACTGAAGGTGGTGGGCTGCGCCCCGACTGTGGGCAACATCGAGGA
GCTGGCTGCTGAATGTAAGAGTGCAGGCTACCCCGGGACTTTGATCCCCTACAGATGTGACCTAT
CAAATGAAGAGGACATCCTCTCCATGTTCTCAGCTATCCGTTCTCAGCACAGCGGTGTAGACATC
TGCATCAACAATGCTGGCTTGGCCCGGCCTGACACCCTGCTCTCAGGCAGCACCAGTGGTTGGAA
GGACATGTTCAATGTGAACGTGCTGGCCCTCAGCATCTGCACACGGGAAGCCTACCAGTCCATGA
AGGAGCGGAATGTGGACGATGGGCACATCATTAACATCAATAGCATGTCCTGGCCACCGAGTGTTA
CCCCTGTCTGTGACCCACTTCTATAGTGCCACCAAGTATGCCGTCACTGCGCTGACAGAGGGACT
GAGGCAAGAGCTTCGGGAGGCCAGACCCACATCCGAGCCACGTGCATCTCTCCAGGTGTGGTGG
AGACACAATTCGCCTTCAAACCTCCACGACAAGGACCCTGAGAAGGCAGCTGCCACCTATGAGCAA
ATGAAGTGTCTCAAACCCGAGGATGTGGCCGAGGCTGTTATCTACGTCCCTCAGCACCCCCGCACA
CATCCAGATTGGAGACATCCAGATGAGGCCACGGAGCAGGTGACCTAGTGACTGTGGGAGCTCC
TCCTTCCCTCCCCACCCCTTCATGGCTTGCCCTCCTGCCTCTGGATTTTAGGTGTTGATTTCTGGAT
CACGGGATACCACTTCCCTGTCCACACCCCGACCAGGGGCTAGAAAATTTGTTTGAGATTTTATA
TCATCTTGTCAAATTGCTTCAGTTGTAATGTGAAAAATGGGCTGGGAAAGGAGGTGGTGTCCC
TAATTGTTTTACTTGTTAACTTGTCTTGTGCCCTGGGCACTTGGCCTTTGTCTGCTCTCAGTG
TCTTCCCTTTGACATGGGAAAGGAGTTGTGGCCAAAATCCCCATCTTCTTGACCTCAACGTCTG
TGGCTCAGGGCTGGGGTGGCAGAGGGAGGCCTTACCTTATATCTGTGTTGTTATCCAGGGCTCC
AGACTTCCCTCTGCCTGCCCCACTGCACCCTCTCCCCCTTATCTATCTCCTTCTCGGCTCCCC
AGCCCAGTCTTGCTTCTTGTCCCCCTCTGGGGTCATCCCTCCACTCTGACTCTGACTATGGCAG
CAGAACACCAGGGCCTGGCCAGTGGATTTTCATGGTGATCATTAAAAAAGAAAAATCGCAACCAA
AAAAAAAAA

FIGURE 128

MARPGMERWRDRLALVTGASGGIGAAVARALVQQLKVVGCARTVGNIEELAAECKSAGYPGTLI
PYRCDLSNEEDILSMFSAIRSQHSQVDICINNAGLARPDLLSGSTSGWKDMFNVNVLALSICTR
EAYQSMKERNVDDGHIININSMSGHRVLPPLSVTHFYATKYAVTALTEGLRQELREAQTHIRATC
ISPGVVETQFAFKLHDKDPEKAAATYEQMKCLKPEDVAEAVIYVLSTPAHIQIGDIQMRPTEQVT

Important features of the protein:

Signal peptide:

amino acids 1-17

N-myristoylation sites.

amino acids 18-24, 21-27, 22-28, 24-30, 40-46, 90-96, 109-115,
199-205

Short-chain alcohol dehydrogenase.

amino acids 30-42, 104-114

FIGURE 129

AACTTCTACATGGGCCTCCTGCTGCTGGTGCTCTTCCTCAGCCTCCTGCCGGTGGCTACACCAT
CATGTCCCTCCCACCCTCCTTTGACTGCGGGCCGTTTCAGGTGCAGAGTCTCAGTTGCCCGGGAGC
ACCTCCCCTCCCGAGGCAGTCTGCTCAGAGGGCTCGGCCCAGAATTCAGTTCTGGTTTCATGC
CAGCCTGTAAAAGGCCATGGAAC TTTGGGTGAATCACCGATGCCATTTAAGAGGGTTTTCTGCCA
GGATGGAAATGTTAGGTCGTTCTGTGTCTGCGCTGTTCAATTCAGTAGCCACCAGCCACCTGTGG
CCGTTGAGTGCTTGAAATTGAGGAACTGAGAAAATTAATTTCTCATGTATTTTTCTCATTATTTA
TTAATTTTTAACTGATAGTTGTACATATTTGGGGTACATGTGATATTTGGATACATGTATACAA
TATATAATGATCAAATCAGGGTAACTGGGATATCCATCACATCAAACATTTATTTTTATTCTTT
TTAGACAGAGTCTCACTCTGTACCCAGGCTGGAGTGCAGTGGTGCCATCTCAGCTTACTGCAAC
CTCTGCCTGCCAGGTTCAAGCGATTCTCATGCCTCCACCTCCCAAGTAGCTGGGACTACAGGCAT
GCACCACAATGCCCAACTAATTTTTGTATTTTTAGTAGAGACGGGGTTTTGCCATGTTGCCCAGG
CTGGCCTTGAACCTCTGGCCTCAAACAATCCACTTGCCTCGGCCTCCCAAAGTGTTATGATTACA
GGCGTGAGCCACCGTGCCTGGCCTAAACATTTATCTTTCTTTGTGTTGGGAAC TTTGAAATTAT
ACAATGAATTATTGTTAACTGTCATCTCCCTGCTGTGCTATGGAACACTGGGACTTCTTCCCTCT
ATCTAACTGTATATTTGTACCAGTTAACCAACCGTACTTCATCCCCACTCCTCTCTATCCTTCCC
AACCTCTGATCACCTCATTCTACTCTCTACCTCCATGAGATCCACTTTTTTTAGCTCCACATGTG
AGTAAGAAAATGCAATATTTGTCTTTCTGTGCCTGGCTTATTTCACTTAACATAATGACTTCCTG
TTCCATCCATGTTGCTGCAAATGACAGGATTCGTTCTTAATTTCAATTAATAAATAACCACACATG
GCAAAAA

FIGURE 130

MGLLLLVLFLSLLPVAYTIMSLPPSFDCGPFRCRVSVAREHLPSRGSLLRGPRPRI PVLVSCQPV
KGGHTLGESEMPFKRVFCQDGNVRSFCVCAVHFSSHQPPVAVECLK

Important features of the protein:

Signal peptide:

amino acids 1-18

N-myristoylation site.

amino acids 86-92

Zinc carboxypeptidases, zinc-binding region 2 signature.

amino acids 68-79

FIGURE 131

TTCTGAAGTAACGGAAGCTACCTTGTATAAAGACCTCAACACTGCTGACCATGATCAGCGCAGCCTGGAGC
ATCTTCCTCATCGGGACTAAAATTGGGGCTGTTCCCTCAAGTAGCACCTCTATCAGTTATGGCTAAATCCTG
TCCATCTGTGTGTCGCTGCGATGCGGGTTTCATTTACTGTAATGATCGCTTTCGACATCCATTCCAACAG
GAATACCAGAGGATGCTACAACCTCTCTACCTTCAGAACAACCAAATAAATAATGCTGGGATTCCCTTCAGAT
TTGAAAACTTGCTGAAAGTAGAAAGAATATACCTATACCACAACAGTTTAGATGAATTTCCCTACCAACCT
CCCAAAGTATGTAAAAGAGTTACATTTGCAAGAAAATAACATAAGGACTATCACTTATGATTCACTTTCAA
AAATFCCCTATCTGGAAGAATTACATTTAGATGACAACCTCTGTCTCTGCAGTTAGCATAGAAGAGGGAGCA
TTCCGAGACAGCAACTATCTCCGACTGCTTTTTCTGTCCCGTAATCACCTTAGCACAATTCCCTGGGGTTT
GCCCAGGACTATAGAAGAACTACGCTTGGATGATAATCGCATATCCACTATTTTCATCACCATCTCTTCAAG
GTCTCACTAGTCTAAAACGCCCTGGTTCTAGATGGAAACCTGTTGAACAATCATGGTTTAGGTGACAAAGTT
TTCTTCAACCTAGTTAATTTGACAGAGCTGTCCCTGGTGCGGAATTCCTGACTGCTGCACCAGTAAACCT
TCCAGGCACAAACCTGAGGAAGCTTTATCTTCAAGATAACCACATCAATCGGGTGCCCCAAATGCTTTTT
CTTATCTAAGGCAGCTCTATCGACTGGATATGTCCAATAATAACCTAAGTAATTTACCTCAGGGTATCTTT
GATGATTTGGACAATATAACACAACCTGATTCTTCGCAACAATCCCTGGTATTGCGGGTGCAAGATGAAATG
GGTACGTGACTGGTTACAATCACTACCTGTGAAGGTCAACGTGCGTGGGCTCATGTGCCAAGCCCCAGAAA
AGGTTTCGTGGGATGGCTATTAAGGATCTCAATGCAGAACTGTTTGATTGTAAGGACAGTGGGATTGTAAGC
ACCATTCAGATAACCCTGCAATACCCAACACAGTGTATCCTGCCCAAGGACAGTGGCCAGCTCCAGTGAC
CAAACAGCCAGATATTAAGAACCCCAAGCTCACTAAGGATCAACAAACCACAGGGAGTCCCTCAAGAAAA
CAATFACAATTAAGTGTGAAGTCTGTACCTCTGATACCATTTCATATCTCTTGAAACTTGCTCTACCTATG
ACTGCTTTGAGACTCAGCTGGCTTAAACTGGGCCATAGCCCGGCATTTGGATCTATAACAGAAACAATTTG
AACAGGGGAACGCAGTGAGTACTTGGTCACAGCCCTGGAGCCTGATTCACCCTATAAAGTATGCATGGTTC
CCATGGAAACCAGCAACCTCTACCTATTTGATGAACTCCTGTTTGTATTGAGACTGAAACTGCACCCCTT
CGAATGTACAACCCTACAACCACCTCAATCGAGAGCAAGAGAAAGAACCTTACAAAAACCCCAATTTACC
TTTGGCTGCCATCATTGGTGGGGCTGTGGCCCTGGTTACCATTGCCCTTCTTGCTTTAGTGTGTGGTATG
TTCATAGGAATGGATCGCTCTTCTCAAGGAACCTGTGCATATAGCAAAGGGAGGAGAAAGGATGACTAT
GCAGAACTGGCACTAAGAAGGACAACCTCTATCCTGGAATCAGGGAACTTCTTTTCAGATGTTACCAAT
AAGCAATGAACCCATCTCGAAGGAGGAGTTTGTAAACACACCATATTTCTCCTAATGGAATGAATCTGT
ACAAAAACAATCACAGTGAAGCAGTAGTAACCGAAGCTACAGAGACAGTGGTATTCAGACTCAGATCAC
TCACACTCATGATGCTGAAGGACTCACAGCAGACTTGTGTTTTGGGTTTTTTAAACCTAAGGGAGGTGATG
GT

FIGURE 132

MISAAWSIFLIGTKIGLFLQVAPLSVMAKSCPSVCRCDAGFIYCNDRFLTSIPTGIPEDATTLYL
QNNQINNAGIPSDLKNLLKVERIYLYHNSLDEFPTNLPKYVKELHLQENNIRITITYDSLKIPYL
EELHLDDNSVSAVSIEEGAFRDSNYLRLLFLSRNHLSTIPWGLPRTIEELRLDDNRISTISSPSL
QGLTSLKRLVLDGNLLNNHGLGDKVFFNLVNLTELSLVRNSLTAAPVNLPGTNLRKLYLQDNHIN
RVPPNAFSYLRQLYRLDMSNNNLSNLPQGI FDDL DNITQLILRNNPWYCGCKMKWVRDWLQSLPV
KVNVRGLMCQAPEKVRGMAIKDLNAELFCKD SGIVSTIQITTAIPNTVYPAQGQWPAPVTKQPD
IKNPKLT KDQQTGSPSRKTITITVKS VTS DTHISWKLALPMTALRLSWLKLGHSPA FGSITET
IVTGERSEYLVTALEPDSPYKVCMPMETS NLYLFDETPVC IETETAPLRMYNPTTTLNREQEKE
PYKNPNLPLAAIIGGAVALVTIALLALVCWYVHRNGSLFSRNCAYS KGRRRKDDYAEAGTKKDNS
ILEIRETSFQMLPISNEPISKEEFVIHTIFPPNGMNL YKNNHSESSNRSYRDSGIPDS DSHSHS

Important features of the protein:

Signal peptide:

amino acids 1-28

Transmembrane domain:

amino acids 531-552

N-glycosylation sites.

amino acids 226-229, 282-285, 296-299, 555-558, 626-629, 633-636

Tyrosine kinase phosphorylation site.

amino acids 515-522

N-myristoylation sites.

amino acids 12-17, 172-177, 208-213, 359-364, 534-539, 556-561,
640-645

Amidation site.

amino acids 567-570

Leucine zipper pattern.

amino acids 159-180

Phospholipase A2 aspartic acid active site.

amino acids 34-44

FIGURE 133

CCGTCATCCCCCTGCAGCCACCCTTCCCAGAGTCCTTTGCCAGGCCACCCAGGCTTCTTGCA
GCCCTGCCGGGCCACTTGTCTTCATGTCTGCCAGGGGGAGGTGGGAAGGAGGTGGGAGGAGGGCG
TGCAGAGGCAGTCTGGGCTTGGCCAGAGCTCAGGGTGTGAGCGTGTGACCAGCAGTGTGAGCAGAG
GCCGGCCATGGCCAGCCTGGGGCTGCTGCTCCTGCTCTTACTGACAGCACTGCCACCGCTGTGGT
CCTCCTCACTGCCTGGGCTGGACACTGCTGAAAGTAAAGCCACCATTGCAGACCTGATCCTGTCT
GCGCTGGAGAGAGCCACCGTCTTCTAGAACAGAGGCTGCCTGAAATCAACCTGGATGGCATGGT
GGGGTCCGAGTGTGGAAGAGCAGCTAAAAAGTGTCCGGGAGAAGTGGGCCAGGAGCCCCCTGC
TGCAGCCGCTGAGCCTGCGCGTGGGGATGCTGGGGGAGAAGCTGGAGGCTGCCATCCAGAGATCC
CTCCACTACCTCAAGCTGAGTGATCCCAAGTACCTAAGAGAGTTCCAGCTGACCCCTCCAGCCCCG
GTTTTGGAAGCTCCCACATGCCTGGATCCACACTGATGCCTCCTTGGTGTACCCACGTTCCGGC
CCCAGGACTCATTCTCAGAGGAGAGAAGTGACGTGTGCCTGGTGCAGCTGCTGGGAACCGGGACG
GACAGCAGCGAGCCCTGCGGCCTCTCAGACCTCTGCAGGAGCCTCATGACCAAGCCCCGCTGCTC
AGGCTACTGCCTGTCCCACCAACTGCTCTTCTTCTCTGGGCCAGAATGAGGGGATGCACACAGG
GACCAC'TCCAACAGAGCCAGGACTATATCAACCTCTTCTGCGCCAACATGATGGACTTGAACCGC
AGAGCTGAGGCCATCGGATACGCCTACCCTACCCGGGACATCTTCATGGAAAACATCATGTTCTG
TGAATGGGCGCTTCTCCGACTTCTACAAGCTCCGGTGGCTGGAGGCCATTCTCAGCTGGCAGA
AACAGCAGGAAGGATGCTTCGGGGAGCCTGATGCTGAAGATGAAGAATTATCTAAAGCTATTCAA
TATCAGCAGCATTTTTTCGAGGAGAGTGAAGAGGCGAGAAAAACAATTTCCAGATTCTCGCTCTGT
TGCTCAGGCTGGAGTACAGTGGCGCAATCTCGGCTCACTGCAACCTTTGCCTCCTGGGTCAAGC
AATTCTCTTGCTCATCCTCCCGAGTAGCTGGGACTACAGGAGCGTGCCACCATACTGGCTAAT
TTTTATATTTTTTTAGTAGAGACAGGGTTTCATCATGTTGCTCATGCTGGTCTCGAACTCCTGAT
CTCAAGAGATCCGCCACCTCAGGCTCCCAAAGTGTGGGATTATTAGGTGTGAGCCACCGTGTCTG
GCTGAAAAGCACTTTCAAGAGACTGTGTTGAATAAAGGGCCAAGGTTCTTGCCACCCAGCACTC
ATGGGGGCTCTCTCCCTAGATGGCTGCTCCTCCCACAACACAGCCACAGCAGTGGCAGCCCTGG
GTGGCTTCTATACATCCTGGCAGAATACCCCCAGCAAACAGAGAGCCACACCCATCCACACCG
CCACCACCAAGCAGCCGCTGAGACGGACGGTTCCATGCCAGCTGCCTGGAGGAGGAACAGACCCC
TTTAGTCCTCATCCCTTAGATCCTGGAGGGCACGGATCACATCCTGGGAAGAAGGCATCTGGAGG
ATAAGCAAAGCCACCCCGACACCCAATCTTGAAGCCCTGAGTAGGCAGGGCCAGGGTAGGTGGG
GGCCGGGAGGGACCCAGGTGTGAACGGATGAATAAAGTTCAACTGCAACTGAAAAAAAAAAAA

FIGURE 134

MSARGRWEGGGRRACRGSGLGLARAQGAERVTSSEQRPMASLGLLLLLLLLTALPPLWSSSLPGLD
TAESKATIADLILSALERATVFLEQRLPEINLDGMVGVRVLEEQLKSVREKWAQEPLLQPLSLRV
GMLGEKLEAAIQRSYLHLKLSDPKYLREFQLTLQPGFWKLPHAWIHTDASLVYPTFGPQDSFSEE
RSDVCLVQLLGTGTDSSSEPCGLSDLCRSLMTKPGCSGYCLSHQLLFFLWARMRGCTQGPLQOSQD
YINLFCANMMDLNRRAEAIQYAYPTRDI FMENIMFCGMGGFSDFYKLRWLEAILSQKQEGCFG
EPDAEDEELSKAIQYQOHFSRRVKRREKQFPDSRSVAQAGVQWRNLGSLQPLPPGFKQFSCILIP
SSWDYRSVPPYLANFYIFLVETGFHHVAHAGLELLISRDPTSGSQSVGL

Important features of the protein:

Signal peptide:

amino acids 1-26

Transmembrane domain:

amino acids 39-56

Tyrosine kinase phosphorylation sites.

amino acids 149-156, 274-282

N-myristoylation sites.

amino acids 10-16, 20-26, 63-69, 208-214

Amidation site.

amino acids 10-14

Glycoprotein hormones beta chain signature 1.

amino acids 230-237

FIGURE 135

GGTCTGAGTGCAGAGCTGCTGTCAATGGCGGCCGCTCTGTGGGGCTTCTTTCCCGTCCTGCTGCTG
CTGCTGCTATCGGGGGATGTCCAGAGCTCGGAGGTGCCCGGGGCTGCTGCTGAGGGATCGGGAGG
GAGTGGGGTCGGCATAGGAGATCGCTTCAAGATTGAGGGGCGTGCAGTTGTTCCAGGGGTGAAGC
CTCAGGACTGGATCTCGGCGGCCCGAGTGCTGGTAGACGGAGAAGAGCACGTCGGTTTCCTTAAG
ACAGATGGGAGTTTTGTGGTTCATGATATACCTTCTGGATCTTATGTAGTGGAAAGTTGTATCTCC
AGCTTACAGATTTGATCCCGTTTCGAGTGGATATCACTTCGAAAGGAAAAATGAGAGCAAGATATG
TGAATTACATCAAAACATCAGAGGTTGTCAGACTGCCCTATCCTCTCCAAATGAAATCTTCAGGT
CCACCTTCTTACTTTATTAAAAGGGAATCGTGGGGCTGGACAGACTTTCTAATGAACCCAATGGT
TATGATGATGGTTCTTCCCTTTATTGATATTTGTGCTTCTGCCTAAAGTGGTCAACACAAGTGATC
CTGACATGAGACGGGAAATGGAGCAGTCAATGAATATGCTGAATTCCAACCATGAGTTGCCTGAT
GTTTCTGAGTTCATGACAAGACTCTTCTCTTCAAAATCATCTGGCAAATCTAGCAGCGGCAGCAG
TAAACAGGCAAAAGTGGGGCTGGCAAAGGAGGTAGTCAGGCCGTCCAGAGCTGGCATTTCACAC
AAACACGGCAACACTGGGTGGCATCCAAGTCTTGGAAAACCGTGTGAAGCAACTACTATAAACTT
GAGTCATCCCGACGTTGATCTCTTACAACGTGTGTATGTT
AACTTTTTAGCACATGTTTTGTACTTGGTACACGAGAAAACCCAGCTTTCATCTTTTGTCTGTAT
GAGGTCAATATTGATGTCACCTGAATTAATTACAGTGTCCCTATAGAAAATGCCATTAATAAATTAT
ATGAACTACTATACATTATGTATATTAATTAACATCTTAATCCAGAAATCAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAA

FIGURE 136

MAAALWGFFPVLLLLLLLLSGDVQSSEVPGAAAEGSGGSGVIGDRFKIEGRAVVPGVKPQDWISAA
RVLVDGEEHVGFLKTDGSEFVVHDIPSGSYVVEVVSPAYRFDVPRVDITSKGKMRARYVNYIKTSE
VVRLLPYPLQMKSSGPPSYFIKRESWGWTDFLMNPMVMMVLPPLIFVLLPKVVNTSDPDMRREME
QSMNMLNSNHELDPVSEFMTRLFSSKSSGKSSSGSSKTKGSGAGKRR

Important features of the protein:

Signal sequence:

amino acids 1-23

Transmembrane domain:

amino acids 161-182

N-glycosylation site.

amino acids 184-187

Glycosaminoglycan attachment sites.

amino acids 37-40, 236-239

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 151-154

N-myristoylation sites.

amino acids 33-38, 36-41, 38-44, 229-234

Amidation site.

amino acids 238-241

ATP/GTP-binding site motif A (P-loop).

amino acids 229-236

FIGURE 137

GATGGCGCAGCCACAGCTTCTGTGAGATTTCGATTTCTCCCCAGTTCCCCTGTGGGTCTGAGGGGA
CCAGAAGGGTGAGCTACGTTGGCTTTCTGGAAGGGGAGGCTATATGCGTCAATCCCCAAAACAA
GTTTTGACATTTCCCCTGAAATGTCATTCTCTATCTATTCACTGCAAGTGCCTGCTGTTCCAGGC
CTTACCTGCTGGGCACTAACGGCGGAGCCAGGATGGGGACAGAATAAAGGAGCCACGACCTGTGC
CACCAACTCGCACTCAGACTCTGAACTCAGACCTGAAATCTTCTCTTACGGGAGGCTTGGCAGT
TTTTCTTACTCCTGTGGTCTCCAGATTTTCAGGCCAAGATGAAAGCCTCTAGTCTTGCCTTCAGC
CTTCTCTCTGCTGCGTTTTTATCTCCTATGGACTCCTTCCACTGGACTGAAGACACTCAATTTGGG
AAGCTGTGTGATCGCCACAAACCTTCAGGAAAACGAAATGGATTTTCTGAGATACGGGGCAGTG
TGCAAGCCAAAGATGGAAACATTGACATCAGAATCTTAAGGAGGACTGAGTCTTTGCAAGACACA
AAGCCTGCGAATCGATGCTGCCTCCTGCGCCATTTGCTAAGACTCTATCTGGACAGGGTATTTAA
AAACTACCAGACCCCTGACCATTATACTCTCCGGAAGATCAGCAGCCTCGCCAATTCCTTCTTA
CCATCAAGAAGGACCTCCGGCTCTCTCATGCCCACATGACATGCCATTGTGGGGAGGAAGCAATG
AAGAAATACAGCCAGATTCTGAGTCACTTTGAAAAGCTGGAACCTCAGGCAGCAGTTGTGAAGGC
TTTGGGGGAACTAGACATTCTTCTGCAATGGATGGAGGAGACAGAATAGGAGGAAAGTGATGCTG
CTGCTAAGAATATTCGAGGTCAAGAGCTCCAGTCTTCAATACCTGCAGAGGAGGCATGACCCCAA
ACCACCATCTCTTACTGTACTAGTCTTGTGCTGGTCACAGTGTATCTTATTTATGCATTACTTG
CTTCCTTGCATGATTGTCTTTATGCATCCCCAATCTTAATTGAGACCATACTTGTATAAGATTTT
TGTAATAFCFTTCTGCTATTGGATATATTTATTAGTTAATATATTTATTTATTTTTTGCTATTTA
ATGTATTTATTTTTTACTTGGACATGAACTTTAAAAAAATTCACAGATTATATTTATAACCTG
ACTAGAGCAGGTGATGTATTTTTATACAGTAAAAAAAAAACCTTGTAATTC TAGAAGAGTGG
CTAGGGGGTTATTCATTTGTATTCAACTAAGGACATATTTACTCATGCTGATGCTCTGTGAGAT
ATTTGAAATTGAACCAATGACTACTTAGGATGGGTTGTGGAATAAGTTTTGATGTGGAATTGCAC
ATCTACCTTACAATTACTGACCATCCCCAGTAGACTCCCCAGTCCATAATTGTGTATCTTCCAG
CCAGGAATCCTACACGGCCAGCATGTATTTCTACAAATAAAGTTTTCTTTGCATACCAAAAAAAAA
AAAAAAAAAA

FIGURE 138

MRQFPKTSFDISPEMSFSIYSLQVPAVPGLTWCWALTAEPGWGQNKGATTCATNSHSDSELRPEIF
SSREAWQFFLLLWSPDFRPKMKASSLAFSLLSAAFYLLWTPSTGLKTLNLGSCVIATNLQEIRNG
FSEIRGSVQAKDGNIDIRILRRTESLQDTKPANRCCLLRHLLRLYLDRVFKNYQTPDHYTLRKIS
SLANSFLTIIKKDLRLSHAHMTCHCGEEAMKKYSQILSHFEKLEPQAAVVKALGELDILLOWMEET
E

Important features of the protein:

Signal peptide:

amino acids 1-42

cAMP- and cGMP-dependent protein kinase phosphorylation sites.

amino acids 192-195, 225-228

N-myristoylation sites.

amino acids 42-47, 46-51, 136-141

FIGURE 139

CCTGGAGCCGGAAGCGCGGCTGCAGCAGGGCGAGGCTCCAGGTGGGGTTCGGTTCGGCATCCAGCC
TAGCGTGTCCACGATGCGGCTGGGCTCCGGGACTTTCGCTACCTGTTGCGTAGCGATCGAGGTGC
TAGGGATCGCGGTCTTCCTTCGGGGATTCTTCCCGCTCCCCTTCGTTCCCTCTGCCAGAGCGGAA
CACGGAGCGGAGCCCCAGCGCCCCGAACCTCGGCTGGAGCCAGTTCTAACTGGACCACGCTGCC
ACCACCTCTCTTCAGTAAAGTTGTTATTGTTCTGATAGATGCCCTTGAGAGATGATTTTGTGTTTG
GGTCAAAGGGTGTGAAATTTATGCCCTACACAACTTACCTTGTGGAAAAAGGAGCATCTCACAGT
TTTGTGGCTGAAGCAAAGCCACCTACAGTTACTATGCCCTCGAATCAAGGCATTGATGACGGGGAG
CCTTCTGGCTTTGTGACGTCATCAGGAACCTCAATTCTCCTGCACTGCTGGAAGACAGTGTGA
TAAGACAAGCAAAAGCAGCTGGAAAAAGAATAGTCTTTTATGGAGATGAAACCTGGGTAAATTA
TTCCCAAAGCATTGTGTTGGAATATGATGGAACAACCTCATTTTTCGTGTGAGATTACACAGAGGT
GGATAATAATGTCACGAGGCATTTGGATAAAGTATTAAGAGAGGAGATTGGGACATATTAATCC
TCCACTACCTGGGGCTGGACCACATTTGCCACATTTCAAGGCCAACAGCCCCCTGATTTGGGCAG
AAGCTGAGCGAGATGGACAGCGTGTGATGAAGATCCACACCTCACTGCAGTCAAGGAGAGAGA
GACGCCTTTACCCAATTTGCTGGTTCTTTGTGGTGACCATGGCATGTCTGAAACAGGAAGTCACG
GGCCCTCTCCACGAGGAGGTGAATACACCTCTGATTTTAAATCAGTTCTGCCGTTTGAAGGAAA
CCCGGTGATATCCGACATCCAAAGCACGTCCAATAGACGGATGTGGCTGCGACACTGGCGATAG
ACTTGGCTTACCGATTCCAAAAGACAGTGTAGGGAGCCTCCTATTCAGTTGTGGAAGGAAGAC
CAATGAGAGAGCAGTTGAGATTTTACATTTGAATACAGTGCAGCTTAGTAAACTGTTGCAAGAG
AATGTGCCGTCATATGAAAAAGATCCTGGGTTTGAGCAGTTTAAAATGTCAGAAAGATTGCATGG
GAACTGGATCAGACTGTACTTGGAGGAAAAAGCATTTCAGAAGTCTTATTCAACCTGGGCTCCAAGG
TTCTCAGGCAGTACCTGGATGCTCTGAAGACGCTGAGCTTGTCCCTGAGTGCACAAGTGGCCCAG
TTCTCACCTGCTCCTGCTCAGCGTCCCACAGGCACATGCACAGAAAGGCTGAGCTGGAAGTCCCA
CTGTCATCTCCTGGGTTTTCTCTGCTCTTTTATTTGGTGATCCTGGTTCTTTTCGGCCGTTACAGT
CATTGTGTGCACCTCAGCTGAAAGTTCGTGCTACTTCTGTGGCCTCTCGTGGCTGGCGGCAGGCT
GCCTTTTCGTTTACCAGACTCTGGTTGAACACCTGGTGTGTGCCAAGTGTGTCAGTGCCTGGAC
AGGGGGCTCAGGGAAGGACGTGGAGCAGCCTTATCCCAGGCTCTGGGTGTCCCAGACAGGTG
TTCACATCTGTGCTGTGAGGTCAGATGCCTCAGTTCTTGAAAGCTAGGTTCTGCGACTGTTAC
CAAGGTGATTGTAAAGAGCTGGCGGTACAGAGGAACAAGCCCCCAGCTGAGGGGTGTGTGAA
TCGGACAGCTCCCAGCAGAGGTGTGGGAGCTGCAGCTGAGGGAAGAAGAGACAATCGGCCTGGA
CACTCAGGAGGGTCAAAGGAGACTTGGTTCGCACCACTCATCCTGCCACCCCCAGAATGCATCCT
GCCTCATCAGGTCCAGATTTCTTTCCAAGGCGGACGTTTTCTGTTGGAATTCCTTAGTCCTTGGCC
TCGGACACCTTCATTCGTTAGCTGGGGAGTGGTGGTGAGGCAGTGAAGAAGAGGCGGATGGTCAC
ACTCAGATCCACAGAGCCCAGGATCAAGGGACCCACTGCAGTGGCAGCAGGACTGTTGGGCCCC
ACCCCAACCTGCACAGCCCTCATCCCCTCTTGGCTTGAGCCGTCAGAGGCCCTGTGCTGAGTGT
CTGACCGAGACACTCACAGCTTTGTCATCAGGGCACAGGCTTCCCGGAGCCAGGATGATCTGTG
CCACGCTTGCACCTCGGGCCCATCTGGGCTCATGCTCTCTCTCCTGCTATTGAATTAGTACCTAG
CTGCACACAGTATGTAGTTACCAAAAAGAATAAACGGCAATAATTGAGAAAAAAA

FIGURE 140

MRLGSGTFATCCVAIEVLGIAVFLRGFFPAPVRSSARAEGHGAEPPEPSAGASSNWTTLPPLF
SKVVIVLIDALRDDFVFGSKGVKFMPTTYLVEKGASHSFVAEAKPPTVTMPRIKALMTGSLPGF
VDVIRNLNSPALLEDSVIRQAKAAGKRIVFYGDETWVKLFPKHFVEYDGTTSFFVSDYTEVDNNV
TRHLDKVLKRGDWDILILHYLGLDGHIGHISGPN SPLIGQKLESEMDSVLMKIHTSLQSKERETPLP
NLLVLCGDHGMSETGSHGASSTEEVNTPLILISSAFERKPGDIRHPKHVQ

Important features of the protein:

Signal peptide:

amino acids 1-34

Transmembrane domain:

amino acids 58-76

N-glycosylation sites.

amino acids 56-60, 194-198

N-myristoylation sites.

amino acids 6-12, 52-58, 100-106, 125-131, 233-239, 270-276,
275-281, 278-284

Amidation site.

amino acids 154-158

Cell attachment sequence.

amino acids 205-208

FIGURE 141

GGCACGAGGCAAGCCTTCCAGGTTATCGTGACGCACCTTGAAAGTCTGAGAGCTACTGCCCTACA
GAAAGTTACTAGTGCCCTAAAGCTGGCGCTGGCACTGATGTACTGCTGCTGTTGGAGTACAAC
TCCCTATAGAAAACAACCTGCCAGCACCTTAAGACCACTCACACCTTCAGAGTGAAGAACTTAAAC
CCGAAGAAATTCAGCATTCATGACCAGGATCACAAAGTACTGGTCCTGGACTCTGGGAATCTCAT
AGCAGTTCAGATAAAAACTACATACGCCAGAGATCTTCTTTGCATTAGCCTCATCCTTGAGCT
CAGCCTCTGCGGAGAAAGGAAGTCCGATTCTCCTGGGGTCTCTAAAGGGGAGTTTTGTCTCTAC
TGTGACAAGGATAAAGGACAAAGTCATCCATCCCTTCAGCTGAAGAAGGAGAACTGATGAAGCT
GGCTGCCCAAAGGAATCAGCACGCCGGCCCTTCATCTTTTATAGGGCTCAGGTGGGCTCCTGGA
ACATGCTGGAGTCGGCGGCTCACCCGGATGGTTCATCTGCACCTCCTGCAATTGTAATGAGCCT
GTTGGGTGACAGATAAATTTGAGAACAGGAAACACATTGAATTTTCATTTCAACCAGTTTGCAA
AGCTGAAATGAGCCCCAGTGAGGTCAGCGATTAGGAAACTGCCCCATTGAACGCCTTCCTCGCTA
ATTTGAACTAATTTGTATAAAAACACCAAACCTGCTCACT

FIGURE 142

MLLLLLLEYNFPIENNCQHLKTTHTFRVKNLNPKKFSIHDQDHKVLVLD SGNLI AVDPK NYIRPEI
FFALASSLS S ASAEK GSPILLGVSKGEFCLYCDKDKGQSHPSLQLKKEKLMKLA AQESARRPFI
FYRAQVGSWNMLESA AHPGWFICTSCNCNEPVGVTDKFENRKHIEFSFQPVCKAEMSPSEVSD

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 33-36

N-myristoylation site.

amino acids 50-55, 87-92

Interleukin-1

amino acids 37-182

FIGURE 144

MLGLPWKGGLSWALLLLLLLGSQILLIYAWHFHEQRDCDEHNVMARYLPATVEFAVHTFNQQSKDY
YAYRLGHILNSWKEQVESKTVFSMELLLGRTRCGKFEDDIDNCHFQESTELNNTFTCFFTISTRP
WMTQFSLLNKTCLEGFH

Important features of the protein:

Signal peptide:

amino acids 1-25

N-glycosylation sites.

amino acids 117-121, 139-143

N-myristoylation site.

amino acids 9-15

FIGURE 145

CTGTGCAGCTCGAGGCTCCAGAGGCACACTCCAGAGAGAGCCAAGGTCTGACGCGATGAGGAAG
CACCTGAGCTGGTGGTGGCTGGCCACTGTCTGCATGCTGCTCTTCAGCCACCTCTCTGCGGTCCA
GACGAGGGGCATCAAGCACAGAATCAAGTGGAAACCGGAAGGCCCTGCCAGCACTGCCAGATCA
CTGAGGCCAGGTGGCTGAGAACCGCCCGGGAGCCTTCATCAAGCAAGGCCGCAAGCTCGACATT
GACTTCGGAGCCGAGGGCAACAGGTACTACGAGGCCAACTACTGGCAGTTCCTCGATGGCATCCA
CTACAACGGCTGCTCTGAGGCTAATGTGACCAAGGAGGCATTTGTCACCGGCTGCATCAATGCCA
CCCAGGCGGGCAACCAGGGGGAGTTCCAGAAGCCAGACAACAAGCTCCACCAGCAGGTGCTCTGG
CGGCTGGTCCAGGAGCTCTGCTCCCTCAAGCATTGCGAGTTTTGGTTGGAGAGGGGCGCAGGACT
TCGGGTCACCATGCACCAGCCAGTGCTCCTCTGCCTTCTGGCTTTGATCTGGCTCATGGTGAAT
AAGCTTGCCAGGAGGCTGGCAGTACAGAGCGCAGCAGCGAGCAAATCCTGGCAAGTGACCCAGCT
CTTCTCCCCAAACCCACGCGTGTCTGAAGGTGCCAGGAGCGGGCGATGCACTCGCACTGCAAA
TGCCGCTCCACGTATGCGCCCTGGTATGTGCCTGCGTTCTGATAGATGGGGGACTGTGGCTTCT
CCGTCACTCCATTCTCAGCCCTAGCAGAGCGTCTGGCACACTAGATTAGTAGTAAATGCTTGAT
GAGAAGAACACATCAGGCACTGCGCCACCTGCTTCACAGTACTTCCCAACAACCTCTTAGAGGTAG
GTGTATTCCCGTTTTACAGATAAGGAACTGAGGCCAGAGAGCTGAAGTACTGCACCCAGCATC
ACCAGCTAGAAAGTGGCAGAGCCAGGATTAACCCTGGCTTGCTAACCCAGGTTTTCTGCTCT
GTCCAATCCAGAGCTGTCTGGTGATCACTTTATGTCTCACAGGGACCCACATCCAAACATGTAT
CTCTAATGAAATTGTGAAAGCTCCATGTTTAGAAATAAATGAAAACACCTGA

FIGURE 146

MRKHLSSWWLATVCMLLFSHLSAVQTRGIKHRIKWNRKALPSTAQITEAQVAENRPGAFIKQGRK
LDIDFGAEGNRYYEANYWQFPDGIHYNGCSEANVTKEAFVTGCINATQAANQGEFQKPDNKLHQQ
VLWRLVQELCSLKHCFWLERGAGLRVTMHQPVLLCCLLALIWLMMVK

Important features of the protein:

Signal peptide:

amino acids 1-26

Transmembrane domain:

amino acids 157-171

N-glycosylation sites.

amino acids 98-102, 110-114

Tyrosine kinase phosphorylation site.

amino acids 76-83

N-myristoylation sites.

amino acids 71-77, 88-94, 93-99, 107-113, 154-160

Amidation site.

amino acids 62-66

FIGURE 147

GCCTTGGCCTCCCAAAGGGCTGGGATTATAGGCGTGACCACCATGTCTGGTCCAGAGTCTCATTT
CCTGATGATTTATAGACTCAAAGAAAACTATGTTTCAGAAGCTCTCTTCTTTCTGGCCTCCTCT
CTGTCTTCTTTCCCTCTTTCTTCTTATTTTAATTAGTAGCATCTACTCAGAGTCATGCAAGCTGG
AAATCTTTCATTTTGCTTGTTCAGTGGGGTAGGTCACTGAGTCTTAGTTTTTATTTTTTGAAATTT
CAACTTTCAGATTCAGGGGTACATGTGAAGGTTTGTTTTATGAGTATATTGCATTGATGCTGAGG
TTTGGGGT

FIGURE 148

MFRSLLFWPPLCLLSLFLLLILISSIYSESKLEIFHFACQWGRSLSLSFYFLKFQLSDSGGTCE
GLFYEYIA

Important features of the protein:

Signal peptide:

amino acids 1-25

N-myristoylation site.

amino acids 62-68

FIGURE 149

GTCTCCGCGTCACAGGAACCTCAGCACCCACAGGGCGGACAGCGCTCCCCTCTACCTGGAGACTTGAC
TCCCGCGCGCCCCAACCCCTGCTTATCCCTTGACCGTCGAGTGTGACAGATCCTGCAGCCGCCAGTCC
CGGCCCCCTCTCCCGCCCCACACCCACCCTCCTGGCTCTTCCTGTTTTTACTCCTCCTTTTCATTCATA
ACAAAAGCTACAGCTCCAGGAGCCCAGCGCCGGGCTGTGACCCAAGCCGAGCGTGGAAGAATGGGGTT
CCTCGGGACCGGCACTTGGATTCTGGTGTAGTGCTCCCGATTCAAGCTTTCCCCAACCTGGAGGAA
GCCAAGACAAATCTCTACATAATAGAGAATTAAGTGCAGAAAGACCTTTGAATGAACAGATTGCTGAA
GCAGAAGAAGACAAGATTAATAAACAATATCCTCCAGAAAACAAGCCAGGTGAGAGCAACTATTCTTT
TGTTGATAACTTGAACCTGCTAAAGGCAATAACAGAAAAGGAAAAAATGAGAAAAGAAAGACAATCTA
TAAGAAGCTCCCCACTTGATAATAAGTTGAATGTGGAAGATGTTGATTCAACCAAGAATCGAAAAGT
ATCGATGATTATGACTCTACTAAGAGTGGATTGGATCATAAATTTCAAGATGATCCAGATGGTCTTCA
TCAACTAGACGGGACTCCTTTAACCGCTGAAGACATGTCCATAAAATCGCTGCCAGGATTTATGAAG
AAAATGACAGAGCCGTGTTTGACAAGATTGTTTCTAAACTACTTAATCTCGGCCTTATCACAGAAAGC
CAAGCACATACTGGAAGATGAAGTAGCAGAGGTTTTACAAAAATTAATCTCAAAGGAAGCCAACAA
TTATGAGGAGGATCCCAATAAGCCCACAAGCTGGACTGAGAATCAGGCTGGAAAAATACCAGAGAAAG
TGACTCCAATGGCAGCAATTCAAGATGGTCTTGCTAAGGGAGAAAACGATGAAACAGTATCTAACACA
TTAACCTTGACAAATGGCTTGAAAGGAGAACTAAAACCTACAGTGAAGACAACCTTGAGGAACTCCA
ATATTTCCCAAATTTCTATGCGCTACTGAAAAGTATTGATTGAGAAAAGAAGCAAAAGAGAAAAGAAA
CACTGATTACTATCATGAAAACACTGATTGACTTTGTGAAGATGATGGTGAAATATGGAACAATATCT
CCAGAAGAAGGTGTTTCTACCTTGAAAACCTGGATGAAATGATTGCTCTTCAGACCAAAAAACAAGCT
AGAAAAAATGCTACTGACAATATAAGCAAGCTTTTCCCAGCACCATCAGAGAAGAGTCATGAAGAAA
CAGACAGTACCAAGGAAGAAGCAGCTAAGATGGAAGGAATATGGAAGCTTGAAGGATTCACAAAA
GATGATAACTCCAACCCAGGAGGAAAGACAGATGAACCCAAAGGAAAACAGAAGCCTATTTGGAAGC
CATCAGAAAAAATATTGAATGGTTGAAGAAACATGACAAAAGGGAAATAAAGAAGATTATGACCTTT
CAAAGATGAGAGACTTCATCAATAAACAAGCTGATGCTTATGTGGAGAAAGGCATCCTTGACAAGGAA
GAAGCCGAGGCCATCAAGCGCATTATAGCAGCCTGTAAAAATGGCAAAGATCCAGGAGTCTTCAA
CTGTTTCAGAAAACATAATATAGCTTAAAACACTTCTAATTCTGTGATTAATAATTTTTGACCCCAAGG
GTTATTAGAAAGTGTGAATTTACAGTAGTTAACCTTTTACAAGTGGTTAAACATAGCTTTCTTCCC
GTAAAACTATCTGAAAGTAAAGTTGTATGTAAGCTGAAAAAAAAAAAAAAAAAAAAA

FIGURE 150

MGFLGTGTWILVVLVLP IQAFPKPGGSQDKSLHNRELSAERPLNEQIAEAEEDKIKKTYPPENKPG
QSNYSFVDNLNLLKAITEKEKIEKERQSIRSSPLDNKLNVEDVDSTKNRKLIDDYDSTKSGLDHK
FQDDPDGLHQLDGTPLTAEDIVHKIAARIYEENDRAVFDKIVSKLLNLGLITESQAHTLEDEVAE
VLQKLISKEANNYEEDPNKPTSWTENQAGKIPEKVT PMAAIQDGLAKGENDETVSNTLTLTNGLE
RRTKTYSEDNFEELQYFPNIFYALLKSIDSEKEAKEKETLITIMKTLIDFVKMMVKYGTISPEEGV
SYLENLDEMIALQTKNKLEKNATDNISKLF PAPSEKSHEETDSTKEEAAKMEKEYGSLKDSTKDD
NSNPGGKTDEPKGKTEAYLEAIRKNIEWLKKHKDKGNKEDYDLSKMRDFINKQADAYVEKGILDK
EEAEAIKRIYSSL

N-glycosylation sites:

amino acids 68-71, 346-349, 350-353

Casein kinase II phosphorylation site:

amino acids 70-73, 82-85, 97-100, 125-128, 147-150, 188-191, 217-
220, 265-268, 289-292, 305-308, 320-323, 326-329, 362-365, 368-
341, 369-372, 382-385, 386-389, 387-390

N-myristoylation sites:

amino acids 143-148, 239-244

FIGURE 151

CGGCTCGAGGCTCCCGCCAGGAGAAAGGAACATTTCTGAGGGGAGTCTACACCCTGTGGAGCTCAA
GATGGTCCTGAGTGGGGCGCTGTGCTTCCGAATGAAGGACTCGGCATTGAAGGTGCTTTATCTGC
ATAATAACCAGCTTCTAGCTGGAGGGCTGCATGCAGGGAAGGTCATTAAGGTGAAGAGATCAGC
GTGGTCCCAATCGGTGGCTGGATGCCAGCCTGTCCCCCGTCATCCTGGGTGTCCAGGGTGAAG
CCAGTGCCGTGTCATGTGGGGTGGGGCAGGAGCCGACTCTAACACTAGAGCCAGTGAACATCATGG
AGCTCTATCTTGGTGCCAAGGAATCCAAGAGCTTCACCTTCTACCGGCGGGACATGGGGCTCACC
TCCAGCTTCGAGTCGGCTGCCTACCCGGGTGGTTCCTGTGCACGGTGCCTGAAGCCGATCAGCC
TGTGAGACTCACCCAGCTTCCCGAGAATGGTGGCTGGAATGCCCCCATCACAGACTTCTACTTCC
AGCAGTGTGACTAGGGCAACGTGCCCCCCAGAACTCCCTGGGCAGAGCCAGCTCGGGTGAAGGGT
GAGTGGAGGAGACCCATGGCGGACAATCACTCTCTGCTCTCAGGACCCCCACGTCTGACTTAG
TGGGCACCTGACCACTTTGTCTTCTGGTTCACAGTTTGGATAAATTCTGAGATTTGGAGCTCAGT
CCACGGTCTCCCCCACTGGATGGTGTACTGCTGTGGAACCTTGTA AAAACCATGTGGGGTAAA
CTGGGAATAACATGAAAAGATTTCTGTGGGGTGGGGTGGGGGAGTGGTGGGAATCATTCTGCT
TAATGGTAACTGACAAGTGTACCCTGAGCCCCGAGGCCAACCCATCCCCAGTTGAGCCTTATA
GGGTGAGTACTCTCCACATGAAGTCTGTCACTCACCCTGTGCAGGAGAGGGAGGTGGTCATA
GAGTCAGGGATCTATGGCCCTTGGCCAGCCCCACCCCTTCCCTTTAATCCTGCCACTGTCATA
TGCTACCTTTCCTATCTCTCCCTCATCATCTTGTGTGGGCATGAGGAGGTGGTGTATGTCAGAA
GAAATGGCTCGAGCTCAGAAGATAAAAAGATAAGTAGGGTATGCTGATCCTCTTTTAAAAACCCAA
GATACAATCAAAATCCCAGATGCTGGTCTCTATTTCCCATGAAAAAGTGTCTATGACATATTGAGA
AGACCTACTTACAAAAGTGGCATAATATTGCAATTTATTTAATTAAAAGATACCTATTTATATATT
TCTTTATAGAAAAAGTCTGGAAAGATTTACTTCAATTTAGCAATGTCAGGGTGGTGGCAGTAT
AGGTGATTTTCTTTAATTTCTGTTAATTTATCTGTATTTCTAATTTTCTACAATGAAGATGA
ATTCTTTGTATAAAAAAAGAAAAGAAATTAATCTTGAGGTAAGCAGAGCAGACATCATCTGTA
TTGTCTCAGCCTCCACTTCCCCAGAGTAAATTCAAATGAATCGAGCTCTGCTGCTCTGGTTGG
TTGTAGTAGTGTATCAGGAAACAGATCTCAGCAAAGCCACTGAGGAGGAGGCTGTGCTGAGTTTGT
GTGGCTGGAATCTCTGGGTAAGGAACTTAAAGAACAAAAATCATCTGGTAATTTCTTCTAGAAAG
GATCACAGCCCTGGGATTTCCAAGGCATTGGATCCAGTCTCTAAGAAGGCTGCTGTACTGGTTGA
ATTGTGTCCTCCTCAAATTCACATCTCTTGGAACTCAGTCTGTGAGTTTATTTGGAGATAAG
GTCTCTGCAGATGTAGTTAGTTAAGACAAGGTCATGCTGGATGAAGGTAGACCTAAATTCATAT
GACTGGTTTCTTGTATGAAAAGGAGAGGACACAGAGACAGAGGAGACGCGGGGAAGACTATGTA
AAGATGAAGGCAGAGATCGGAGTTTGCAGCCACAAGCTAAGAAACACCAAGGATTTGGCAACC
ATCAGAAGCTTGAAGAGGCAAAGAAGAAATTTCTCCCTAGAGGCTTTAGAGGGATAACGGCTCTG
CTGAAACCTTAATCTCAGACTTCCAGCCTCCTGAACGAAGAAAGATAAATTTTCGGCTGTTTTAA
GCCACCAAGGATAATTGGTTACAGCAGCTCTAGGAACTAATACAGCTGCTAAAATGATCCCTGT
CTCCTCGTGTTTACATTCTGTGTGTGTCCCCCTCCCAATGTACCAAAGTTGTCTTTGTGACCAA
TAGAATATGGCAGAAGTGTATGGCATGCCACTTCCAAGATTAGGTTATAAAAAGACTGCAGCTTC
TACTTGAGCCCTCTCTCTGCCACCCACCGCCCCCAATCTATCTTGGCTCACTCGCTCTGGGGG
AAGCTAGCTGCCATGCTATGAGCAGGCCTATAAAGAGACTTACGTGGTAAAAAATGAAGTCTCCT
GCCACAGCCACATTAGTGAACCTAGAAGCAGAGACTCTGTGAGATAATCGATGTTGTGTGTTTT
AAGTTGCTCAGTTTTGGTCTAACTTGTATGCAGCAATAGATAAATAATATGCAGAGAAAGAG

FIGURE 152

MVLSGALCFRMKDSALKVLYLHNNQLLAGGLHAGKVIKGEESISVVPNRWLDASLSPVILGVQGG
QCLSCGVGQEP TLTLEPVNIMELYLGAKESKSFTFYRRDMGLTSSFESAAYPGWFLCTVPEADQP
VRLTQLPENGGWNAPITDFYFQQCD

N-myristoylation sites.

amino acids 29-34, 30-35, 60-65, 63-68, 73-78, 91-96, 106-111

Interleukin-1 signature.

amino acids 111-131

Interleukin-1 proteins.

amino acids 8-29, 83-120, 95-134, 64-103

FIGURE 153

CTTCAGAACAGGTTCTCCTTCCCCAGTCACCAGTTGCTCGAGTTAGAATTGTCTGCAATGGCCGC
CCTGCAGAAATCTGTGAGCTCTTTCTTATGGGGACCCTGGCCACCAGCTGCCTCCTTCTCTTGG
CCCTCTTGGTACAGGGAGGAGCAGCTGCGCCCATCAGCTCCCAGTGCAGGCTTGACAAGTCCAAC
TTCCAGCAGCCCTATATCACCAACCGCACCTTCATGCTGGCTAAGGAGGCTAGCTTGGCTGATAA
CAACACAGACGTTCTGTCATTGGGGAGAACTGTTCCACGGAGTCAGTATGAGTGAGCGCTGCT
ATCTGATGAAGCAGGTGCTGAACTTCACCCTTGAAGAAGTGTGTTCCCTCAATCTGATAGGTTT
CAGCCTTATATGCAGGAGGTGGTGCCCTTCTGGCCAGGCTCAGCAACAGGCTAAGCACATGTCA
TATTGAAGGTGATGACCTGCATATCCAGAGGAATGTGCAAAAGCTGAAGGACACAGTGAAAAAGC
TTGGAGAGAGTGGAGAGATCAAAGCAATTGGGAACTGGATTTGCTGTTTATGTCCTGAGAAAT
GCCTGCATTTGACCCAGAGCAAAGCTGAAAAATGAATAACTAACCCCTTTCCCTGCTAGAAATAA
CAATTAGATGCCCCAAAGCGATTTTTTTTAAACCAAAGGAAGATGGGAAGCCAAACTCCATCATG
ATGGGTGGATTCCAAATGAACCCCTGCGTTAGTTACAAAGGAAACCAATGCCACTTTTGTTTATA
AGACCAGAAGGTAGACTTCTAAGCATAGATATTTATTGATAACATTTTATTGTAACGGTGTTC
TATACACAGAAAACAATTTATTTTTTAAATAATTGTCTTTTTCCATAAAAAAGATTACTTTCCAT
TCCTTTAGGGGAAAAAACCCCTAAATAGCTTCATGTTTCCATAATCAGTACTTTATATTTATAAA
TGTATTTATTATTATTATAAGACTGCATTTTATTTATATCATTTTATTAATATGGATTTATTAT
AGAAACATCATTCGATATTGCTACTTGAGTGTAAGGCTAATATTGATATTTATGACAATAATTAT
AGAGCTATAACATGTTTATTGACCTCAATAAACACTTGGATATCCC

FIGURE 154

MAALQKSVSSFLMGTLATSCLLLLALLVQGGAAAPISSHCRLDKSNFQQPYITNRTFMLAKEASL
ADNNTDVRLIGEKLFHGVSMSERCYLMKQVLNFTLEEVLPQSDRFQPYMQEVVPFLARLSNRLS
TCHIEGDDLHIQRNVQKLKDTVKKLGESGEIKAIGELDLLFMSLRNACI

Important features of the protein:

Signal peptide:

amino acids 1-33

N-glycosylation sites.

amino acids 54-58, 68-72, 97-101

N-myristoylation sites.

amino acids 14-20, 82-88

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 10-21

FIGURE 155

GGCTTGCTGAAAATAAAATCAGGACTCCTAACCTGCTCCAGTCAGCCTGCTTCCACGAGGCCTGT
CAGTCAGTGCCCGACTTGTGACTGAGTGTGCAGTGCCCAGCATGTACCAGGTCAGTGCAGAGGGC
TGCTGAGGGCTGTGCTGAGAGGGAGAGGAGCAGAGATGCTGCTGAGGGTGGAGGGAGGCCAAGC
TGCCAGGTTTGGGGCTGGGGGCCAAGTGGAGTGAGAACTGGGATCCCAGGGGGAGGGTGCAGAT
GAGGGAGCGACCCAGATTAGGTGAGGACAGTTCTCTCATTAGCCTTTTCCCTACAGGTGGTTGCAT
TCTTGGCAATGGTCATGGGAACCCACACCTACAGCCACTGGCCCAGCTGCTGCCCCAGCAAAGGG
CAGGACACCTCTGAGGAGCTGCTGAGGTGGAGCACTGTGCCTGTGCCTCCCCTAGAGCCTGCTAG
GCCCAACCGCCACCCAGAGTCCTGTAGGGCCAGTGAAGATGGACCCCTCAACAGCAGGGCCATCT
CCCCCTGGAGATATGAGTTGGACAGAGACTTGAACCGGCTCCCCAGGACCTGTACCACGCCCGT
TGCTGTGCCCCGCACTGCGTCAGCCTACAGACAGGCTCCACATGGACCCCCGGGGCAACTCGGA
GCTGCTCTACCACAACCAGACTGTCTTCTACAGGCGGCCATGCCATGGCGAGAAGGGCACCCACA
AGGGCTACTGCCTGGAGCGCAGGCTGTACCGTGTTCCTTAGCTTGTGTGTGTGTGCGGCCCGT
GTGATGGGCTAGCCGGACCTGCTGGAGGCTGGTCCCTTTTTGGGAAACCTGGAGCCAGGTGTACA
ACCACTTGCCATGAAGGGCCAGGATGCCAGATGCTTGGCCCCTGTGAAGTGTGTCTGGAGCAG
CAGGATCCCGGGACAGGATGGGGGGCTTTGGGGAAAACCTGCACTTCTGCACATTTTGAAAAGAG
CAGCTGCTGCTTAGGGCCGCCGAAGCTGGTGTCTGTCAATTTCTCTCAGGAAAGGTTTTCAA
GTTCTGCCATTTCTGGAGGCCACCACTCCTGTCTCTTCTCTTTTCCCATCCCCTGCTACCCTG
GCCAGCACAGGCACTTTCTAGATATTTCCCCCTTGCTGGAGAAGAAAGAGCCCCTGGTTTTATT
TGTTTGTTTACTCATCACTCAGTGAGCATCTACTTTGGGTGCATTCTAGTGTAGTTACTAGTCTT
TTGACATGGATGATTCTGAGGAGGAAGCTGTTATTGAATGTATAGAGATTTATCCAATAAATAT
CTTTATTTAAAAATGAAAAA

FIGURE 156

MRERPRLGEDSSLISLFLQVVAFLAMVMGTHYSHWPSCCPSKGQDTSEELLRWSTVPVPPLEPA
RPNRHPESCRASEDGPLNSRAISPWRYELDRDLNRLPQDLYHARCLCPHCVSLQTGSHMDPRGNS
ELLYHNQTVFYRRPCHGEKGTGTHKGYCLERRLYRVSLACVCRPRVMG

Important features of the protein:

Signal peptide:

amino acids 1-32

N-glycosylation site.

amino acids 136-140

Tyrosine kinase phosphorylation site.

amino acids 127-135

N-myristoylation sites.

amino acids 44-50, 150-156

FIGURE 157

CCGGCGATGTCGCTCGTGCTGCTAAGCCTGGCCGCGCTGTGCAGGAGCGCCGTACCCCGAGAGCC
GACCGTTC AATGTGGCTCTGAAACTGGGCCATCTCCAGAGTGGATGCTACAACATGATCTAATCC
CCGGAGACTTGAGGGACCTCCGAGTAGAACCTGTTACAACACTAGTGTGCAACAGGGGACTATTCA
ATTTTGATGAATGTAAGCTGGGTACTCCGGGCAGATGCCAGCATCCGCTTGTGTAAGGCCACCAA
GATTTGTGTGACGGGCAAAGCAACTTCCAGTCTTACAGCTGTGTGAGGTGCAATTACACAGAGG
CCTTCCAGACTCAGACCAGACCCTCTGGTGGTAAATGGACATTTTCTTACATCGGCTTCCCTGTA
GAGCTGAACACAGTCTATTTTCATTGGGGCCCATAATATTCCTAATGCAAATATGAATGAAGATGG
CCCTTCCATGTCTGTGAATTTACCTCACCAGGCTGCCTAGACCACATAATGAAATATAAAAAA
AGTGTGTCAAGGCCGGAAGCCTGTGGGATCCGAACATCACTGCTTGTAGAAGAATGAGGAGACA
GTAGAAGTGAACCTCACAACCACTCCCCTGGGAAACAGATACATGGCTCTTATCCAACACAGCAC
TATCATCGGGTTTTCTCAGGTGTTTGAGCCACACCAGAAGAAACAAACGCGAGCTTCAGTGGTGA
TTCCAGTGA CTGGGATAGTGAAGGTGCTACGGTGCAGCTGACTCCATATTTTCTACTTGTGGC
AGCGACTGCATCCGACATAAAGGAACAGTTGTGCTCTGCCACAAACAGGCGTCCCTTTCCCTCT
GGATAACAACAAAAGCAAGCCGGGAGGCTGGCTGCCTCTCCTCCTGCTGTCTCTGCTGGTGGCCA
CATGGGTGCTGGTGGCAGGGATCTATCTAATGTGGAGGCACGAAAGGATCAAGAAGACTTCCTTT
TCTACCACCACACTACTGCCCCCATTAAGGTTCTTGTGGTTTACCCATCTGAAATATGTTTCCA
TCACACAATTTGTTACTTCACTGAATTTCTTCAAACCATTGCAGAAGTGAGGTCATCCTTGAAA
AGTGGCAGAAAAAGAAAATAGCAGAGATGGGTCCAGTGCAGTGGCTTGCCACTCAAAGAAGGCA
GCAGACAAAGTCGTCTTCTTCTTTCCAATGACGTCAACAGTGTGTGCGATGGTACCTGTGGCAA
GAGCGAGGGCAGTCCCAGTGAGAACTCTCAAGACCTCTTCCCCCTTGCCTTTAACCTTTTCTGCA
GTGATCTAAGAAGCCAGATTCATCTGCACAAATACGTGGTGGTCTACTTTAGAGAGATTGATACA
AAAGACGATTACAATGCTCTCAGTGTCTGCCCCAAGTACCACCTCATGAAGGATGCCACTGCTTT
CTGTGCAGAACTTCTCCATGTCAAGCAGCAGGTGTCAGCAGGAAAAAGATCACAAGCCTGCCACG
ATGGCTGCTGCTCCTTGTAG

FIGURE 158

MSLVLLSLAALCRSAVPREPTVQCGSETGPSPEWMLQHDLI PGDLRDLRVEPVTT SVATGDYSILMNVSWV
LRADASIRLLKATKICVTGKSNFQSYSCVRCNYTEAFQTQTRPSGGKWTFSYIGFPVELNTVYFIGAHNIP
NANMNEDGPSMSVNFTSPGCLDHIMKYKKKCVKAGSLWDPNITACKKNEETVEVNFTTTPLGNRYMALIQH
STIIGFSQVFEPHQKKQTRASVVI PVTVGDSEGATVQLTPYFPTCGSDCIRHKGTVVLCPTGVPFPLDNNK
SKPGGWLP LLLLLSLLVATWVVLVAGIYLMWRHERIKKTSFSTTTLLPPIKVLVVYPSEICFHHTICYFTEFL
QNHCRSEVILEKWQKKKIAEMGPVQWLATQKKAADKVV FLLSNDVNSVCDGTCGKSEGSPSENSQDLFPLA
FNLFCSDLRSQIHLHKYVVVYFREIDTKDDYNALSVC PKYHLMKDATAFCAELLHV KQQVSAGKRSQACHD
GCCSL

Important features of the protein:

Signal peptide:

amino acids 1-14

Transmembrane domain:

amino acids 290-309

N-glycosylation sites.

amino acids 67 - 71, 103 - 107, 156 - 160, 183 - 187, 197 - 201 and 283
- 287

cAMP- and cGMP-dependent protein kinase phosphorylation sites.

amino acids 228 - 232 and 319 - 323

Casein kinase II phosphorylation sites.

amino acids 178 - 182, 402 - 406, 414 - 418 and 453 - 457

N-myristoylation site.

amino acids 116-122

Amidation site.

amino acids 488-452

FIGURE 159

AGCCACCAGCGCAACATGACAGTGAAGACCCTGCATGGCCCAGCCATGGTCAAGTACTTGCTGCT
GTCGATATTGGGGCTTGCCTTTCTGAGTGAGGCGGCAGCTCGGAAAATCCCCAAAGTAGGACATA
CTTTTTTCCAAAAGCCTGAGAGTTGCCCGCCTGTGCCAGGAGGTAGTATGAAGCTTGACATTGGC
ATCATCAATGAAAACCAGCGCGTTTCCATGTCACGTAACATCGAGAGCCGCTCCACCTCCCCCTG
GAATTACACTGTCACCTTGGGACCCCAACCGGTACCCCTCGGAAGTTGTACAGGCCCCAGTGTAGGA
ACTTGGGCTGCATCAATGCTCAAGGAAAGGAAGACATCTCCATGAATTCCGTTCCCATCCAGCAA
GAGACCCTGGTCGTCCGGAGGAAGCACCAAGGCTGCTCTGTTTCTTTCCAGTTGGAGAAGGTGCT
GGTGACTGTTGGCTGCACCTGCGTCACCCCTGTCATCCACCATGTGCAGTAAGAGGTGCATATCC
ACTCAGCTGAAGAAG

FIGURE 160

MTVKTLHGPA MVKYL LLSILGLAFLSEAAARKIPKVGHTFFQKPESC PVPVGGSMKLDIGIINEN
QRVSMSRNIESRSTSPWNYT VTWDPNRY PSEVVQAQCRNLGCINAQ GKEDISMNSVPIQQETLVV
RRKHQGC SVSFQLEKVLVTVGCTCVTPVIHHVQ

Signal sequence:

amino acids 1-30

N-glycosylation site.

amino acids 83-87

N-myristoylation sites.

amino acids 106-111, 136-141

FIGURE 161

ACACTGGCCAAACAAAAACGAAAGCACTCCGTGCTGGAAGTAGGAGGAGAGTCAGGACTCCCAGG
ACAGAGAGTGCACAAACTACCCAGCACAGCCCCCTCCGCCCCCTCTGGAGGCTGAAGAGGGATT
CAGCCCCCTGCCACCCACAGACACGGGCTGACTGGGGTGTCTGCCCCCTTGGGGGGGGCAGCAC
AGGGCCTCAGGCCTGGGTGCCACCTGGCACCTAGAAGATGCCTGTGCCCTGGTTCTTGCTGTCT
TGGCACTGGGCCGAAGCCCAGTGGTCTTTCTCTGGAGAGGCTTGTGGGGCTCAGGACGCTACC
CACTGCTCTCCGGGCTCTCCTGCCGCTCTGGGACAGTGACATACTCTGCCTGCCTGGGGACAT
CGTGCCTGCTCCGGGCCCCGTGCTGGCGCTACGCACCTGCAGACAGAGCTGGTGTGAGGTGCC
AGAAGGAGACCGACTGTGACCTCTGTCTGCGTGTGGCTGTCCACTTGGCCGTGCATGGGCACCTGG
GAAGAGCCTGAAGATGAGGAAAAGTTGGAGGAGCAGCTGACTCAGGGGTGGAGGAGCCTAGGAA
TGCCTCTCTCCAGGCCAAGTCTGCTCTCCTTCCAGGCCTACCCTACTGCCCGCTGCGTCTCTGC
TGGAGGTGCAAGTGCCTGCTGCCCTTGTGCAGTTTGGTTCAGTCTGTGGGCTCTGTGGTATATGAC
TGCTTCGAGGCTGCCCTAGGGAGTGGGTACGAATCTGGTCTATACTCAGCCCAGGTACGAGAA
GGAACCTCAACCACACACAGCAGCTGCCTGCCCTGCCCTGGCTCAACGTGTGAGCAGATGGTGACA
ACGTGCATCTGGTTCTGAATGTCTCTGAGGAGCAGCACTTCGGCCTCTCCCTGTACTGGAATCAG
GTCCAGGGCCCCCAAACCCCGGTGGCACAAAACCTGACTGGACCGCAGATCATTACCTTGAA
CCACACAGACCTGGTTCCCTGCCTCTGTATTAGGTGTGGCCTCTGGAACCTGACTCCGTTAGGA
CGAACATCTGCCCTTCAGGGAGGACCCCGCGCACACCAGAACCTCTGGCAAGCCGCCGACTG
CGACTGCTGACCCTGCAGAGCTGGCTGCTGGACGCACCGTGTCTGCTGCCCGCAGAAGCGGCACT
GTGCTGGCGGGCTCCGGGTGGGGACCCCTGCCAGCCACTGGTCCCACCGCTTTCCTGGGAGAAGC
TCACTGTGGACAAGGTTCTCGAGTTCCCATTGCTGAAAGGCCACCCTAACCTCTGTGTTTCAGGTG
AACAGCTCGGAGAAGCTGCAGCTGCAGGAGTGCTTGTGGGCTGACTCCCTGGGGCTCTCAAAGA
CGATGTGCTACTGTTGGAGACACGAGGCCCCAGGACAACAGATCCCTCTGTGCCTTGGAAACCCA
GTGGCTGTACTTCACTACCCAGCAAAGCCTCCACGAGGGCAGCTCGCCTTGGAGAGTACTTACTA
CAAGACCTGCAGTCAGGCCAGTGTCTGCAGCTATGGGACGATGACTTGGGAGCGCTATGGGCCTG
CCCCATGGACAAATACATCCACAAGCGCTGGGCCCTCGTGTGGCTGGCCTGCCTACTCTTTGCCG
CTGCGCTTTCCCTCATCCTCCTTCTCAAAAAGGATCACGCGAAAGGGTGGCTGAGGCTCTTGAAA
CAGGACGTCCGCTCCGGGGCGGGCCGAGGGCCGCGCGGCTCTGCTCCTTACTCAGCCGATGA
CTCGGGTTTCGAGCGCTGGTGGGCGCCCTGGCGTCGGCCCTGTGCCAGCTGCCGCTGCGCGTGG
CCGTAGACCTGTGGAGCCGTGCTGAACTGAGCGCGCAGGGGCCCGTGGCTTGGTTTTCACGCGCAG
CGGCGCCAGACCCTGCAGGAGGGCGGCGTGGTGGTCTTGTCTTTCTCTCCCGGTGCGGTGGCGCT
GTGCAGCGAGTGGCTACAGGATGGGGTGTCCGGGCCCCGGGCGCACGGCCCGCACGACGCTTCC
GCGCCTCGCTCAGCTGCGTGCTGCCGACTTCTTGCAGGGCCGGGCGCCCGGAGCTACGTGGGG
GCCTGCTTCGACAGGCTGCTCCACCCGACGCGTACCGCCCTTTCCGACCGTGCCTGCTT
CACACTGCCCTCCAACTGCCAGACTTCTGGGGCCCTGCAGCAGCCTCGCGCCCCGCGTTCCG
GGCGGCTCCAAGAGAGAGCGGAGCAAGTGTCCCGGGCCCTTCCAGCCAGCCCTGGATAGCTACTTC
CATCCCCGGGACTCCCGCGCCGGGACCGGGGTGGGACCAGGGGCGGGACCTGGGGCGGGGA
CGGGACTTAAATAAAGGCAGACGCTGTTTTTCTAAAAAAA

FIGURE 162

MPVWFLLSLALGRSPVVLSELRVLPQDATHCSPEGLSCRLWSDILCLPGDIVPAPGPVLAPTHLQTELV
LRCQKETDCDLCLRVAVHLAVHGHWEPEDEEKFGGAADSGVEEPRNASLQAQVVLVSFQAYPTARCVLLEV
QVPAALVQFGQSVGSVVYDCFEAALGSEVRIWSYTPRYEKELNHTQQLPALPWLNVSAADGNVHLVNLVS
EEQHFGLSLYWNQVQGPVKPRWHKNTGPPQIITLNTDLVPCLCIQVWPLEPDSVRTNICPFREDPRAHQN
LWQAARLRLLTLQSWLLDAPCSLPAEAALCWRAPGGDPCQPLVPPLSWENVTVDKVFLEFPLLKGHPNLCVQ
VNSSEKLQIQECLWADSLGPKDDVLLLETRGPQDNRSLECALEPSGCTSLPSKASTRAARLGEYLLQDLQS
GQCLQLWDDDLGALWACPMKYIHKRWALVWLACLLFAAALSLILLKDHAKGWLRLKQDVRSGAAARG
RAALLLYSADDSGFERLVGALASALCQLPLRVAVDLWSRRELSAQGPVAVFHAQRRTLQEGGVVLLFSP
GAVALCSEWLQDGVSGPAHGPHDAFRASLSCVLPDFLQGRAPGSYVGACFDRLHPDAVPALFRTVPVET
LPSQLPDFLGALQQPRAPRSGRLQERAEQVSRALQPALDSYFHPPGTPAPGRGVGPGAGPGAGDGT

Signal sequence:

amino acids 1-20

Transmembrane domain.

amino acids 453-475

N-glycosylation sites.

amino acids 118-121, 186-189, 198-201, 211-214, 238-241, 248-251,
334-337, 357-360, 391-394

Glycosaminoglycan attachment site.

amino acids 583-586

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 552-555

N-myristoylation sites.

amino acids 107-112, 152-157, 319-324, 438-443, 516-521, 612-617,
692-697, 696-701, 700-705

FIGURE 163

GGGAGGGCTCTGTGCCAGCCCCGATGAGGACGCTGCTGACCATCTTGACTGTGGGATCCCTGGCT
GCTCAGCCCCCTGAGGACCCCTCGGATCTGCTCCAGCACGTGAAATTCAGTCCAGCAACTTTGA
AAACATCCTGACGTGGGACAGCGGGCCAGAGGGCAGCCACAGACACGGTCTACAGCATCGAGTATA
AGACGTACGGAGAGAGGGACTGGGTGGCAAAGAAGGGCTGTCAGCGGATCACCCGGAAGTCCCTGC
AACCTGACGGTGGAGACGGGCAACCTCACGGAGCTCTACTATGCCAGGGTCAACCGT
GTCAGTGCAGGGAGCCGGTACAGCCACCAAGATGACTGACAGGTTACAGTCTCTGCAGCACACTAC
CCTCAAGCCACCTGATGTGACCTGTATCTCCAAAGTGAGATCGATTAGATGATTGTTTCATCCTA
CCCCACGCCAATCCGTGCAGGCGATGGCCACCGGCTAACCCCTGGAAGACATCTTCCATGACCTG
TTCTACCACTTAGAGCTCCAGGTCAACCGCACCTACCAAATGCACCTTGGAGGGAAGCAGAGAGA
ATATGAGTTCTTCGGCCTGACCCCTGACACAGAGTTCCCTTGGCACCATCATGATTTGCGTTCCTCA
CCTGGGCCAAGGAGAGTGCCTTACATGTGCCGAGTGAAGACACTGCCAGACCCGACATGGACC
TACTCCTTCTCCGGAGCCTTCCCTGTTCTCCATGGGCTTCCCTCGTGCAGTACTCTGCTACCTGAG
CTACAGATATGTCACCAAGCCGCTGCACCTCCCAACTCCCTGAACGTCCAGCGAGTCCCTGACTT
TCCAGCCGTGCGCTTCATCCAGGAGCACGTCTGATCCCTGTCTTTGACCTCAGCGGCCCCAGC
AGTCTGGCCCAGCCTGTCCAGTACTCCCAGATCAGGGTGTCTGGACCCAGGGAGCCCGCAGGAGC
TCCACAGCGGCATAGCCTGTCCGAGATCACCTACTTAGGGCAGCCAGACATCTCCATCCTCCAGC
CCTCCAACGTGCCACCTCCCCAGATCCTCTCCCCACTGTCTATGCCCCAAACGCTGCCCTGAG
GTCGGGCCCCCATCCTATGCACCTCAGGTGACCCCCGAAGCTCAATTCCATTTACGCCCCACA
GGCCATCTCTAAGGTCCAGCCTTCCCTCTATGCCCCCAAGCCACTCCGGACAGCTGGCCTCCCT
CCTATGGGGTATGCATGGAAGGTTCTGGCAAAGACTCCCCACTGGGACACTTCTAGTCCCTAAA
CACCTTAGGCCTAAAGGTGAGCTTCAGAAAGACCACAGTCCGAGTGGAAAGTGCATGTTAGGTGGCCT
TTCTCTGCAGGAGGTGACCTCCTTGGCTATGGAGGAATCCCAAGAAGCAAATCATTGCACCAGC
CCCTGGGGATTTGCACAGAGAACATCTGACCCAAATGTGCTACACAGTGGGGAGGAAGGGACA
CCACGATCTAAAGGGCCAGTCCCCCTCCTCTCCTCAGTCCAGATCGAGGGCCACCCCATGTC
CTCCCTTTGCAACCTCCTTCCGGTCCATGTTCCCCCTCGGACCAAGGTCCAAGTCCCTGGGGCC
TGCTGGAGTCCCTTGTGTGTCCCAAGGATGAAGCCAAAGAGCCAGCCCTGAGACCTCAGACCTG
GAGCAGCCACAGAAGTGGATTCTCTTTTTCAGAGGCTGGCCCTGACTGTGCAGTGGGAGTCCTG
AGGGGAATGGGAAAGGCTTGGTGTCTTCCCTGTCCCTACCCAGTGTACATCCTTGGCTGTCA
ATCCCATGCCTGCCATGCCACACACTCTGCGATCTGGCCTCAGACGGGTGCCCTTGAGAGAAGC
AGAGGGAGTGGCATGCAGGGCCCTGCCATGGGTGCGCTCCTCACCGAACAAGCAGCATGATA
AGGACTGCAGCGGGGAGCTCTGGGGAGCAGCTTGTGTAGACAAGCGCTGCTCGCTGAGCCCTG
CAAGGCAGAAATGACAGTGAAGGAGGAAATGCAGGGAACTCCCGAGGTCCAGAGCCCCACCTC
CTAACACCATGGATTCAAAGTGCTCAGGGAATTTGCCTCTCCTTGCCCCATTCTGGCCAGTTT
ACAATCTAGCTCGACAGAGCATGAGGCCCTGCCTCTCTGTGTCATTGTTCAAAGGTGGGAAGAGA
GCCTGGAAAAGAACCAGGCCCTGGAAAAGAACCAGAAGGAGGCTGGGCAGAACCAGAACAACCTGC
ACTTCTGCCAAGGCCAGGGCCAGCAGGACGGCAGGACTCTAGGGAGGGGTGTGGCCTGCAGCTCA
TTCCAGCCAGGGCAACTGCCTGACGTTGCACGATTTACAGTTTCTTCTGATAGAACAAGC
GAAATGCAGGTCCACCAGGGAGGGAGACACACAAGCTTTTCTGCAGGCAGGAGTTTTCAGACCCT
ATCCTGAGAATGGGGTTTTGAAAGGAAGGTGAGGGCTGTGGCCCTGGACGGGTACAATAACACAC
TGTACTGATGTCACAACCTTTGCAAGCTCTGCCCTGGGTTTCAGCCATCTGGGCTCAAATTCAGC
CTCACCCTCACAAGCTGTGTGACTTCAAACAAATGAAATCAGTCCCCAGAACCTCGGTTTCCCTC
ATCTGTAATGTGGGGATCATAACACCTACCTCATGGAGTTGTGGTGAAGATGAAATGAAGTCATG
TCTTTAAAGTGCTTAATAGTGCTTGGTACATGGGCAGTGCCCAATAAACGGTAGCTATTTAAAAA
AAAAAAA

FIGURE 164

MRTLLTILTVGSLAAHAPEDPSDLLQHVKFQSSNFENILTWDSGPEGTPDTVYSIEYKTYGERDW
VAKKGCQRITRKSCNLTVE TGNLTELYYARVTAVSAGGRSATKMTDRFSSLQHTTLKPPDVTCIS
KVRSIQMIVHPTPTPIRAGDGHRLTLEDIFHDLFYHLELQVNRTYQMHLGGKQREYEFFGLTPDT
EFLGTIMICVPTWAKESAPYMCRVKTLPDRTWTYSFSGAFLFSMGFLVAVLCYLSYRYVTKPPAP
PNSLNVQRVLTTFQPLRFIQEHVLI PVFDLSGPPSSLAQPVQYSQIRVSGPREPAGAPQRHSLSEIT
YLGQPDISILQPSNVPPPQILSPLSYAPNAAPEVGPSPYAPQVTPEAQFPFYAPQAI SKVQPSSY
APQATPDSWPSPSYGVCMEGSGKDSPTGTLSSPKHLRPKGQLQKEPPAGSCMLGGLSLQEVTSLAM
EESQEAKSLHQPLGICTDRSDPNVLHSGEEGTPQYKLGQLPLLSSVQIEGHPMSLPLQPPSGPC
SPSDQGPSPWGLESVCPKDEAKSPAPETSDLEQPTELDSLFRGLALTVQWES

Signal sequence.

amino acids 1-17

Transmembrane domain.

amino acids 233-250

N-glycosylation sites.

amino acids 80-83, 87-90, 172-175

N-myristoylation sites.

amino acids 11-16, 47-52, 102-107, 531-536, 565-570

FIGURE 165

TGGCCTACTGGAAAAAAAAAAAAAAAAAAAAAAAAAAGTCACCCGGGCCCGCGGTGGCCACAACATGG
CTGCGGGCCCGGGGCTGCTCTTCTGGCTGTTCTGTGCTGGGGGCGCTCTGGTGGGTCCCGGGCCAG
TCGGATCTCAGCCACGGACGGCGTTTCTCGGACCTCAAAGTGTGCGGGGACGAAGAGTGCAGCAT
GTTAATGTACCGTGGGAAAGCTCTTGAAGACTTCACGGGCCCTGATTGTCTGTTTTGTGAATTTTA
AAAAAGGTGACGATGTATATGTCTACTACAAACTGGCAGGGGGATCCCTTGAACTTTGGGCTGGA
AGTGTGTAACACAGTTTTGGATATTTCCAAAAGATTTGATCAAGGTACTTCATAAATACACGGA
AGAAGAGCTACATATCCAGCAGATGAGACAGACTTTGTCTGCTTTGAAGGAGGAAGAGATGATT
TTAATAGTTATAATGTAGAAGAGCTTTTAGGATCTTTGGAACTGGAGGACTCTGTACCTGAAGAG
TCGAAGAAAGCTGAAGAAGTTTCTCAGCACAGAGAGAAATCTCCTGAGGAGTCTCGGGGCGTGA
ACTTGACCCTGTGCCTGAGCCCAGGCATTTCAGAGCTGATTCAGAGGATGGAGAAGGTGCTTTCT
CAGAGAGCACCGAGGGGCTGCAGGGACAGCCCTCAGCTCAGGAGAGCCACCCTCACACCAGCGGT
CCTGCGGCTAACGCTCAGGGAGTGCAGTCTTCTGTTGGACACTTTTGAAGAAATTCGCACGATAA
ATTGAAAGTGCCGGGAAGCGAAAGCAGAAGTGGCAATAGTTCTCCTGCCTCGGTGGAGCGGGAGA
AGACAGATGCTTACAAAGTCTGAAAACAGAAATGAGTCAGAGAGGAAGTGGACAGTGCCTTATT
CATTACAGCAAAGATTTCTGTTGGCATCAAATCTAAGTTTGTTTTACAAAGATTGTTTTTTAGTA
CTAAGCTGCCTTGGCAGTTTGCATTTTTGAGCCAAACAAAAATATATTATTTCCCTTCTAAGTA
AAAAAAAAAAAAAAAAAAAAA

FIGURE 166

MAAAPGLLFWLFLVGLALWWVPGQSDLSHGRRFSDLKVCGDDECSMLMYRGKALEDFTGPDCRFVN
FKKGDDVYVYYKLAGGSLELWAGSVEHSFGYFPKDLIKVLHXYTEELHIPAETDFVCFEGGRD
DFNSYNVEELLGSLELEDSVPEESKKAEEVSQHREKSPPEESRGRELDVPEPEAFRAEDGEGA
FSESTEGLOGQPSAQESHPTSGPAANAQGVQSSLDTFEEILHDKLKVPGSESRTGNSSPASVER
EKTDAYKVLKTEMSQRGSGQCVIHYSKGFRRWHQNLSLFYKDCF

Important features of the protein:

Signal peptide:

amino acids 1-22

N-glycosylation site.

amino acids 294-298

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 30-34

Tyrosine kinase phosphorylation site.

amino acids 67-76

N-myristoylation sites.

amino acids 205-211, 225-231, 277-283

Amidation site.

amino acids 28-32

FIGURE 167

CCAGGACCAGGGCGCACCGGCTCAGCCTCTCACTTGTCTAGAGGCCGGGGAAGAGAAGCAAAGCGC
AACGGTGTGGTCCAAGCCGGGGCTTCTGCTTCGCCTCTAGGACATACACGGGACCCCTAAC TTC
AGTCCCCCAAACGCGCACCCCTCGAAGTCTTGAACCTCAGCCCCGCACATCCACGCGCGGCACAGG
CGCGGCAGGCGGCAGGTCCC GGCCGAAGGCGATGCGCGCAGGGGGT CGGGCAGCTGGGCTCGGGC
GGCGGGAGTAGGGCCCGCAGGAGGAGGCTGCATATT CAGAGTCGCGGGCTGCGCCCTG
GGCAGAGGCCGCCCTCGCTCCACGCAACACCTGCTGCTGCCACCGCGCCGCGATGAGCCGCGTGG
TCTCGCTGCTGCTGGGCGCGCTGCTCTGCGGCCACGGAGCCTTCTGCCGCGCGTGGT CAGC
GGCCAAAAGGTGTGTTTTGCTGACTTCAAGCATCCCTGCTACAAAATGGCCTACTTCCATGAACT
GTCCAGCCGAGTGAGCTTTCAGGAGGCACGCCTGGCTTGTGAGAGTGAGGGAGGAGTCCCTCCTCA
GCCTTGAGAATGAAGCAGAACAGAAGTTAATAGAGAGCATGTTGCAAAAACCTGACAAAACCCGGG
ACAGGGATTTCTGATGGTGATTTCTGGATAGGGCTTTGGAGGAATGGAGATGGGCAAACATCTGG
TGCCTGCCCAGATCTCTACCAGTGGTCTGATGGAAGCAATCCCAGTACCGAAACTGGTACACAG
ATGAACCTTCTGCGGAAGTGAAAAGTGTGTTGTGATGTATCACCAACCAACTGCCAATCCTGGC
CTTGGGGGTCCCTACCTTTACCAGTGGAAATGATGACAGGTGTAACATGAAGCACAATTTATATTTG
CAAGTATGAACCAGAGATTAATCCAACAGCCCCTGTAGAAAAGCCTTATCTTACAAATCAACCAG
GAGACACCCATCAGAATGTGGTTGTTACTGAAGCAGGTATAATCCCAATCTAATTTATGTTGTT
ATACCAACAATACCCCTGCTCTTACTGATACTGGTTGCTTTTGGAACTGTTGTTTCCAGATGCT
GCATAAAAGTAAAGGAAGAACA AAAACTAGTCCAAACCAGTCTACACTGTGGATTTCAAAGAGTA
CCAGAAAAGAAAGTGGCATGGAAGTATAATAACTCATTGACTTGGTTCCAGAATTTTGTAAATCT
GGATCTGTATAAGGAATGGCATCAGAACAATAGCTTGGAAATGGCTTGAATCACA AAGGATCTGC
AAGATGAACTGTAAGCTCCCCCTTGAGGCCAAATATTAAGTAATTTTATATGTCTATTATTTCA
TTTAAAGAATATGCTGTGCTAATAATGGAGTGAGACATGCTTATTTTGTAAAGGATGCACCCAA
ACTTCAAACCTCAAGCAAATGAAATGGACAATGCAGATAAAGTTGTTATCAACACGTGCGGGAGTA
TGTGTGTTAGAAGCAATTCCTTTTATTTCTTTCACCTTTCATAAGTTGTTATCTAGTCAATGTAA
TGTATATTGTATTGAAATTTACAGTGTGCAAAAAGTATTTTACCTTTGCATAAGTGTTTGATAAAA
ATGAACTGTTCTAATATTTATTTTTATGGCATCTCATTTTTCAATACATGCTCTTTTGATTAAG
AACTTATTACTGTTGTCAACTGAATTCACACACACACAAATATAGTACCATAGAAAAAGTTTGT
TTTCTCGAAATAATTCATCTTTTCAGCTTCTCTGCTTTTGGTCAATGTCTAGGAAATCTCTTCAGA
AATAAGAAGCTATTTCAATTAAGTGTGATATAAACCTCC TCAAACATTTTACTTAGAGGCAAGGAT
TGTCTAATTTCAATTTGTGCAAGACATGTGCCTTATAAT TATTTTTAGCTTAAAATTAACAGATT
TTGTAATAATGTAACCTTTGTTAATAGGTGCATAAACACTAATGCAGTCAATTTGAACAAAAGAAG
TGACATACACAATATAAATCATATGTCTTCACACGTTGCC TATATAATGAGAAGCAGCTCTCTGA
GGGTTCTGAAATCAATGTGGTCCCTCTCTTGCCCACTAAACAAAGATGGTTGTTCCGGGGTTGGG
ATTGACACTGGAGGCAGATAGTTGCAAAGTTAGTCTAAGGTTTCCCTAGCTGTATTTAGCCTCTG
ACTATATTAGTATACAAAGAGGTCATGTGGTTGAGACCAGGTGAATAGTCACTATCAGTGTGGAG
ACAAGCACAGCACACAGACATTTTAGGAAGGAAAGGAAC TACGAAATCGTGTGAAAATGGGTGG
AACCCATCAGTGATCGCATATTCATTGATGAGGGTTTGC TTGAGATAGAAAATGGTGGCTCCTTT
CTGTCTTATCTCCTAGTTTCTTCAATGCTTACGCC TTTGTTCTTCTCAAGAGAAAGTTGTAACCTCT
CTGGTCTTCATATGTCCCTGTGCTCCTTTTAACCAATAAAGAGTTCTTGTCTTCTGGGGGAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 168

MSRVVSLLLGALLCGHGAFRRVVSQKVCFADEFKHCYKMAVFHELSSRVSFQEARLACESE
GGVLLSLENEAEQKLIESMLQNLTKPGTGISDGDFFWIGLWRNGDGQTSGACPDLYQWSDGSNSQ
YRNWYTDEPSCGSEKCVVMYHQPTANPGLGGPYLYQWNDDRCNMKHNYICKYEPEINPTAPVEK
PYLTNQPGDTHQNVVVTEAGIIPNLIYVVIPTIPLLLLLLILVAFGTCCFQMLHKSkgRTRKTSFNQ
STLWISKSTRKESGMEV

Important features of the protein:

Signal peptide:

amino acids 1-21

Transmembrane domain:

amino acids 214-235

N-glycosylation sites.

amino acids 86-89, 255-258

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 266-269

N-myristoylation sites.

amino acids 27-32, 66-71, 91-96, 93-98, 102-107, 109-114, 140-
145, 212-217

**SECRETED AND TRANSMEMBRANE
POLYPEPTIDES AND NUCLEIC ACIDS
ENCODING THE SAME**

**CROSS REFERENCE TO RELATED
APPLICATIONS**

[0001] This is a continuation application claiming priority under 35 USC § 120 to U.S. Ser. No. 10/006,867 Filed Dec. 6, 2001, and which claims priority under 35 USC § 119 to U.S. provisional serial Nos. 60/063,435 Filed Oct. 29, 1997; 60/064,215 Filed Oct. 29, 1997; 60/082,797 Filed Apr. 22, 1998; 60/083,495 Filed Apr. 29, 1998; 60/085,579 Filed May 15, 1998; 60/087,759 Filed Jun. 2, 1998; 60/088,021 Filed Jun. 4, 1998; 60/088,029 Filed Jun. 4, 1998; 60/088,030 Filed Jun. 4, 1998; 60/088,734 Filed Jun. 10, 1998; 60/088,740 Filed Jun. 10, 1998; 60/088,811 Filed Jun. 10, 1998; 60/088,824 Filed Jun. 10, 1998; 60/088,825 Filed Jun. 10, 1998; 60/088,863 Filed Jun. 11, 1998; 60/089,105 Filed Jun. 12, 1998; 60/089,514 Filed Jun. 16, 1998; 60/089,653 Filed Jun. 17, 1998; 60/089,952 Filed Jun. 19, 1998; 60/090,246 Filed Jun. 22, 1998; 60/090,444 Filed Jun. 24, 1998; 60/090,688 Filed Jun. 25, 1998; 60/090,696 Filed Jun. 25, 1998; 60/090,862 Filed Jun. 26, 1998; 60/091,628 Filed Jul. 2, 1998; 60/096,012 Filed Aug. 10, 1998; 60/096,757 Filed Aug. 17, 1998; 60/096,949 Filed Aug. 18, 1998; 60/096,959 Filed Aug. 18, 1998; 60/097,954 Filed Aug. 26, 1998; 60/097,971 Filed Aug. 26, 1998; 60/097,979 Filed Aug. 26, 1998; 60/098,749 Filed Sep. 1, 1998; 60/099,741 Filed Sep. 10, 1998; 60/099,763 Filed Sep. 10, 1998; 60/099,792 Filed Sep. 10, 1998; 60/099,812 Filed Sep. 10, 1998; 60/099,815 Filed Sep. 10, 1998; 60/100,627 Filed Sep. 16, 1998; 60/100,662 Filed Sep. 16, 1998; 60/100,683 Filed Sep. 17, 1998; 60/100,684 Filed Sep. 17, 1998; 60/100,930 Filed Sep. 17, 1998; 60/101,279 Filed Sep. 22, 1998; 60/101,475 Filed Sep. 23, 1998; 60/101,738 Filed Sep. 24, 1998; 60/101,743 Filed Sep. 24, 1998; 60/101,916 Filed Sep. 24, 1998; 60/102,570 Filed Sep. 30, 1998; 60/103,449 Filed Oct. 6, 1998; 60/103,678 Filed Oct. 8, 1998; 60/103,679 Filed Oct. 8, 1998; 60/103,711 Filed Oct. 8, 1998; 60/105,000 Filed Oct. 20, 1998; 60/105,002 Filed Oct. 20, 1998; 60/105,881 Filed Oct. 27, 1998; 60/106,030 Filed Oct. 28, 1998; 60/106,464 Filed Oct. 30, 1998; 60/106,856 Filed Nov. 3, 1998; 60/108,807 Filed Nov. 17, 1998; 60/112,419 Filed Dec. 15, 1998; 60/112,422 Filed Dec. 15, 1998; 60/112,853 Filed Dec. 16, 1998; 60/113,011 Filed Dec. 16, 1998; 60/112,854 Filed Dec. 16, 1998; 60/113,300 Filed Dec. 22, 1998; 60/113,408 Filed Dec. 22, 1998; 60/113,430 Filed Dec. 23, 1998; 60/113,621 Filed Dec. 23, 1998; 60/114,223 Filed Dec. 30, 1998; 60/115,614 Filed Jan. 12, 1999; 60/116,527 Filed Jan. 20, 1999; 60/116,843 Filed Jan. 22, 1999; 60/119,285 Filed Feb. 9, 1999; 60/119,287 Filed Feb. 9, 1999; 60/119,525 Filed Feb. 10, 1999; 60/119,549 Filed Feb. 10, 1999; 60/120,014 Filed Feb. 11, 1999; 60/129,122 Filed Apr. 13, 1999; 60/129,674 Filed Apr. 16, 1999; 60/131,291 Filed Apr. 27, 1999; 60/138,387 Filed Jun. 9, 1999; 60/144,791 Filed Jul. 20, 1999; 60/169,495 Filed Dec. 7, 1999; 60/175,481 Filed Jan. 11, 2000; 60/191,007 Filed Mar. 21, 2000; 60/199,397 Filed Apr. 25, 2000 and which claims priority under 35 USC § 120 to U.S. patent applications and PCT International Patent Application Ser. Nos. 09/380,139 Filed Aug. 25, 1999; 09/311,832 Filed May 14, 1999; 09/380,137 Filed Aug. 25, 1999, now abandoned; 09/380,138 Filed Aug. 25, 1999, now abandoned; 09/380,142 Filed Aug. 25, 1999, now abandoned; 09/397,342 Filed

Sep. 15, 1999; 09/403,297 Filed Oct. 18, 1999, now abandoned; 09/423,844 Filed Nov. 12, 1999, now abandoned; 09/644,848 Filed Aug. 22, 2000; 09/665,350 Filed Sep. 18, 2000; 09/664,610 Filed Sep. 18, 2000, now abandoned; 09/709,238 Filed Nov. 8, 2000; 09/747,259 Filed Dec. 20, 2000; 09/816,744 Filed Mar. 22, 2001; 09/854,208 Filed May 10, 2001; 09/854,280 Filed May 10, 2001; 09/870,574 Filed May 30, 2001; 09/874,503 Filed Jun. 5, 2001; 09/908,827 Filed Jul. 18, 2001; 09/869,566 Filed Feb. 19, 2002; PCT/US98/19330 Filed Sep. 16, 1998; PCT/US99/05028 Filed Mar. 8, 1999; PCT/US99/10733 Filed May 14, 1999; PCT/US99/12252 Filed Jun. 2, 1999; PCT/US99/20111 Filed Sep. 1, 1999; PCT/US99/21090 Filed Sep. 15, 1999; PCT/US99/21194 Filed Sep. 15, 1999; PCT/US99/30720 Filed Dec. 22, 1999; PCT/US00/04341 Filed Feb. 18, 2000; PCT/US00/04342 Filed Feb. 18, 2000; PCT/US00/04414 Filed Feb. 22, 2000; PCT/US00/05601 Filed Mar. 1, 2000; PCT/US00/08439 Filed Mar. 30, 2000; PCT/US00/14042 Filed May 22, 2000; PCT/US00/15264 Filed Jun. 2, 2000; PCT/US00/23522 Filed Aug. 23, 2000; PCT/US00/23328 Filed Aug. 24, 2000; PCT/US00/30873 Filed Nov. 10, 2000; PCT/US00/32678 Filed Dec. 1, 2000; PCT/US00/34956 Filed Dec. 20, 2000; PCT/US01/06520 Filed Feb. 28, 2001; PCT/US01/06666 Filed Mar. 1, 2001; PCT/US01/17443 Filed May 30, 2001; PCT/US01/17800 Filed Jun. 1, 2001; PCT/US01/19692 Filed Jun. 20, 2001; PCT/US01/21066 Filed Jun. 29, 2001; PCT/US01/21735 Filed Jul. 9, 2001, the entire disclosures of which are hereby incorporated by reference.

BACKGROUND OF THE INVENTION

[0002] The present invention relates generally to the identification and isolation of novel DNA and to the recombinant production of novel polypeptides.

[0003] Extracellular proteins play important roles in, among other things, the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment.

[0004] Secreted proteins have various industrial applications, including as pharmaceuticals, diagnostics, biosensors and bioreactors. Most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane proteins, also have potential as therapeutic or diagnostic agents. Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci. 93:7108-7113 (1996); U.S. Pat. No. 5,536,637].

[0005] Membrane-bound proteins and receptors can play important roles in, among other things, the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesion molecules like selectins and integrins. For instance, transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

[0006] Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interactions. The membrane-bound proteins can also be employed screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

[0007] Efforts are being undertaken by both industry and academia to identify new, native receptor or membrane-bound proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor or membrane-bound proteins.

SUMMARY OF INVENTION

[0008] In one embodiment, the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence that encodes a PRO polypeptide.

[0009] In one aspect, the isolated nucleic acid molecule comprises a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93% nucleic acid sequence identity, alternatively at least about 94% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic

acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity to (a) a DNA molecule encoding a PRO polypeptide having a full-length amino acid sequence as disclosed herein, an amino acid sequence lacking the signal peptide as disclosed herein, an extracellular domain of a transmembrane protein, with or without the signal peptide, as disclosed herein or any other specifically defined fragment of the full-length amino acid sequence as disclosed herein, or (b) the complement of the DNA molecule of (a).

[0010] In other aspects, the isolated nucleic acid molecule comprises a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93% nucleic acid sequence identity, alternatively at least about 94% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity to (a) a DNA molecule comprising the coding sequence of a full-length PRO polypeptide cDNA as disclosed herein, the coding sequence of a PRO polypeptide lacking the signal peptide as disclosed herein, the coding sequence of an extracellular domain of a transmembrane PRO polypeptide, with or without the signal peptide, as disclosed herein or the coding sequence of any other specifically defined fragment of the full-length amino acid sequence as disclosed herein, or (b) the complement of the DNA molecule of (a).

[0011] In a further aspect, the invention concerns an isolated nucleic acid molecule comprising a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93% nucleic acid sequence identity, alternatively at least about 94% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively

at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity to (a) a DNA molecule that encodes the same mature polypeptide encoded by any of the human protein cDNAs deposited with the ATCC as disclosed herein, or (b) the complement of the DNA molecule of (a).

[0012] Another aspect the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence encoding a PRO polypeptide which is either transmembrane domain-deleted or transmembrane domain-inactivated, or is complementary to such encoding nucleotide sequence, wherein the transmembrane domain(s) of such polypeptide are disclosed herein. Therefore, soluble extracellular domains of the herein described PRO polypeptides are contemplated.

[0013] Another embodiment is directed to fragments of a PRO polypeptide coding sequence, or the complement thereof, that may find use as, for example, hybridization probes, for encoding fragments of a PRO polypeptide that may optionally encode a polypeptide comprising a binding site for an anti-PRO antibody or as antisense oligonucleotide probes. Such nucleic acid fragments are usually at least about 20 nucleotides in length, alternatively at least about 30 nucleotides in length, alternatively at least about 40 nucleotides in length, alternatively at least about 50 nucleotides in length, alternatively at least about 60 nucleotides in length, alternatively at least about 70 nucleotides in length, alternatively at least about 80 nucleotides in length, alternatively at least about 90 nucleotides in length, alternatively at least about 100 nucleotides in length, alternatively at least about 110 nucleotides in length, alternatively at least about 120 nucleotides in length, alternatively at least about 130 nucleotides in length, alternatively at least about 140 nucleotides in length, alternatively at least about 150 nucleotides in length, alternatively at least about 160 nucleotides in length, alternatively at least about 170 nucleotides in length, alternatively at least about 180 nucleotides in length, alternatively at least about 190 nucleotides in length, alternatively at least about 200 nucleotides in length, alternatively at least about 250 nucleotides in length, alternatively at least about 300 nucleotides in length, alternatively at least about 350 nucleotides in length, alternatively at least about 400 nucleotides in length, alternatively at least about 450 nucleotides in length, alternatively at least about 500 nucleotides in length, alternatively at least about 600 nucleotides in length, alternatively at least about 700 nucleotides in length, alternatively at least about 800 nucleotides in length, alternatively at least about 900 nucleotides in length and alternatively at least about 1000 nucleotides in length, wherein in this context the term "about" means the referenced nucleotide sequence length plus or minus 10% of that referenced length. It is noted that novel fragments of a PRO polypeptide-encoding nucleotide sequence may be determined in a routine manner by aligning the PRO polypeptide-encoding nucleotide sequence with other known nucleotide sequences using any of a number of well known sequence alignment programs and determining which PRO polypeptide-encoding nucleotide sequence fragment(s) are novel. All of such PRO polypeptide-encoding nucleotide sequences are contemplated herein. Also contemplated are the PRO polypeptide fragments encoded by these nucleotide molecule frag-

ments, preferably those PRO polypeptide fragments that comprise a binding site for an anti-PRO antibody.

[0014] In another embodiment, the invention provides isolated PRO polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

[0015] In a certain aspect, the invention concerns an isolated PRO polypeptide, comprising an amino acid sequence having at least about 80% amino acid sequence identity, alternatively at least about 81% amino acid sequence identity, alternatively at least about 82% amino acid sequence identity, alternatively at least about 83% amino acid sequence identity, alternatively at least about 84% amino acid sequence identity, alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid sequence identity, alternatively at least about 87% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 89% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 96% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity to a PRO polypeptide having a full-length amino acid sequence as disclosed herein, an amino acid sequence lacking the signal peptide as disclosed herein, an extracellular domain of a transmembrane protein, with or without the peptide, as disclosed herein or any other specifically defined fragment of the full-length amino acid sequence as disclosed herein.

[0016] In a further aspect, the invention concerns an isolated PRO polypeptide comprising an amino acid sequence having at least about 80% amino acid sequence identity, alternatively at least about 81% amino acid sequence identity, alternatively at least about 82% amino acid sequence identity, alternatively at least about 83% amino acid sequence identity, alternatively at least about 84% amino acid sequence identity, alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid sequence identity, alternatively at least about 87% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 89% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 96% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity to an amino acid sequence encoded by any of the human protein cDNAs deposited with the ATCC as disclosed herein.

[0017] In a specific aspect, the invention provides an isolated PRO polypeptide without the N-terminal signal sequence and/or the initiating methionine and is encoded by a nucleotide sequence that encodes such an amino acid sequence as hereinbefore described. Processes for producing the same are also herein described, wherein those processes comprise culturing a host cell comprising a vector which comprises the appropriate encoding nucleic acid molecule under conditions suitable for expression of the PRO polypeptide and recovering the PRO polypeptide from the cell culture.

[0018] Another aspect the invention provides an isolated PRO polypeptide which is either transmembrane domain-deleted or transmembrane domain-inactivated. Processes for producing the same are also herein described, wherein those processes comprise culturing a host cell comprising a vector which comprises the appropriate encoding nucleic acid molecule under conditions suitable for expression of the PRO polypeptide and recovering the PRO polypeptide from the cell culture.

[0019] In yet another embodiment, the invention concerns agonists and antagonists of a native PRO polypeptide as defined herein. In a particular embodiment, the agonist or antagonist is an anti-PRO antibody or a small molecule.

[0020] In a further embodiment, the invention concerns a method of identifying agonists or antagonists to a PRO polypeptide which comprise contacting the PRO polypeptide with a candidate molecule and monitoring a biological activity mediated by said PRO polypeptide. Preferably, the PRO polypeptide is a native PRO polypeptide.

[0021] In a still further embodiment, the invention concerns a composition of matter comprising a PRO polypeptide, or an agonist or antagonist of a PRO polypeptide as herein described, or an anti-PRO antibody, in combination with a carrier. Optionally, the carrier is a pharmaceutically acceptable carrier.

[0022] Another embodiment of the present invention is directed to the use of a PRO polypeptide, or an agonist or antagonist thereof as hereinbefore described, or an anti-PRO antibody, for the preparation of a medicament useful in the treatment of a condition which is responsive to the PRO polypeptide, an agonist or antagonist thereof or an anti-PRO antibody.

[0023] In other embodiments of the present invention, the invention provides vectors comprising DNA encoding any of the herein described polypeptides. Host cell comprising any such vector are also provided. By way of example, the host cells may be CHO cells, *E. coli*, or yeast. A process for producing any of the herein described polypeptides is further provided and comprises culturing host cells under conditions suitable for expression of the desired polypeptide and recovering the desired polypeptide from the cell culture.

[0024] In other embodiments, the invention provides chimeric molecules comprising any of the herein described polypeptides fused to a heterologous polypeptide or amino acid sequence. Example of such chimeric molecules comprise any of the herein described polypeptides fused to an epitope tag sequence or a Fc region of an immunoglobulin.

[0025] In another embodiment, the invention provides an antibody which binds, preferably specifically, to any of the

above or below described polypeptides. Optionally, the antibody is a monoclonal antibody, humanized antibody, antibody fragment or single-chain antibody.

[0026] In yet other embodiments, the invention provides oligonucleotide probes useful for isolating genomic and cDNA nucleotide sequences or as antisense probes, wherein those probes may be derived from any of the above or below described nucleotide sequences.

[0027] In yet other embodiments, the present invention is directed to methods of using the PRO polypeptides of the present invention for a variety of uses based upon the functional biological assay data presented in the Examples below.

BRIEF DESCRIPTION OF DRAWINGS

[0028] FIG. 1 shows a nucleotide sequence (SEQ ID NO:1) of a native sequence PRO180 cDNA, wherein SEQ ID NO:1 is a clone designated herein as "DNA26843-1389".

[0029] FIG. 2 shows the amino acid sequence (SEQ ID NO:2) derived from the coding sequence of SEQ ID NO:1 shown in FIG. 1.

[0030] FIG. 3 shows a nucleotide sequence (SEQ ID NO:3) of a native sequence PRO218 cDNA, wherein SEQ ID NO:3 is a clone designated herein as "DNA30867-1335".

[0031] FIG. 4 shows the amino acid sequence (SEQ ID NO:4) derived from the coding sequence of SEQ ID NO:3 shown in FIG. 3.

[0032] FIG. 5 shows a nucleotide sequence (SEQ ID NO:5) of a native sequence PRO263 cDNA, wherein SEQ ID NO:5 is a clone designated herein as "DNA34431-1177".

[0033] FIG. 6 shows the amino acid sequence (SEQ ID NO:6) derived from the coding sequence of SEQ ID NO:5 shown in FIG. 5.

[0034] FIG. 7 shows a nucleotide sequence (SEQ ID NO:7) of a native sequence PRO295 cDNA, wherein SEQ ID NO:7 is a clone designated herein as "DNA38268-1188".

[0035] FIG. 8 shows the amino acid sequence (SEQ ID NO:8) derived from the coding sequence of SEQ ID NO:7 shown in FIG. 7.

[0036] FIG. 9 shows a nucleotide sequence (SEQ ID NO:9) of a native sequence PRO874 cDNA, wherein SEQ ID NO:9 is a clone designated herein as "DNA40621-1440".

[0037] FIG. 10 shows the amino acid sequence (SEQ ID NO:10) derived from the coding sequence of SEQ ID NO:9 shown in FIG. 9.

[0038] FIG. 11 shows a nucleotide sequence (SEQ ID NO:11) of a native sequence PRO300 cDNA, wherein SEQ ID NO:11 is a clone designated herein as "DNA40625-1189".

[0039] FIG. 12 shows the amino acid sequence (SEQ ID NO:12) derived from the coding sequence of SEQ ID NO:11 shown in FIG. 11.

[0040] FIG. 13 shows a nucleotide sequence (SEQ ID NO:13) of a native sequence PRO1864 cDNA, wherein SEQ ID NO:13 is a clone designated herein as "DNA45409-2511".

- [0041] FIG. 14 shows the amino acid sequence (SEQ ID NO:14) derived from the coding sequence of SEQ ID NO:13 shown in FIG. 13.
- [0042] FIG. 15 shows a nucleotide sequence (SEQ ID NO:15) of a native sequence PRO1282 cDNA, wherein SEQ ID NO:15 is a clone designated herein as "DNA45495-1550".
- [0043] FIG. 16 shows the amino acid sequence (SEQ ID NO:16) derived from the coding sequence of SEQ ID NO:15 shown in FIG. 15.
- [0044] FIG. 17 shows a nucleotide sequence (SEQ ID NO:17) of a native sequence PRO1063 cDNA, wherein SEQ ID NO:17 is a clone designated herein as "DNA49820-1427".
- [0045] FIG. 18 shows the amino acid sequence (SEQ ID NO:18) derived from the coding sequence of SEQ ID NO:17 shown in FIG. 17.
- [0046] FIG. 19 shows a nucleotide sequence (SEQ ID NO:19) of a native sequence PRO1773 cDNA, wherein SEQ ID NO:19 is a clone designated herein as "DNA56406-1704".
- [0047] FIG. 20 shows the amino acid sequence (SEQ ID NO:20) derived from the coding sequence of SEQ ID NO:19 shown in FIG. 19.
- [0048] FIG. 21 shows a nucleotide sequence (SEQ ID NO:21) of a native sequence PRO1013 cDNA, wherein SEQ ID NO:21 is a clone designated herein as "DNA56410-1414".
- [0049] FIG. 22 shows the amino acid sequence (SEQ ID NO:22) derived from the coding sequence of SEQ ID NO:21 shown in FIG. 21.
- [0050] FIG. 23 shows a nucleotide sequence (SEQ ID NO:23) of a native sequence PRO937 cDNA, wherein SEQ ID NO:23 is a clone designated herein as "DNA56436-1448".
- [0051] FIG. 24 shows the amino acid sequence (SEQ ID NO:24) derived from the coding sequence of SEQ ID NO:23 shown in FIG. 23.
- [0052] FIG. 25 shows a nucleotide sequence (SEQ ID NO:25) of a native sequence PRO842 cDNA, wherein SEQ ID NO:25 is a clone designated herein as "DNA56855-1447".
- [0053] FIG. 26 shows the amino acid sequence (SEQ ID NO:26) derived from the coding sequence of SEQ ID NO:25 shown in FIG. 25.
- [0054] FIG. 27 shows a nucleotide sequence (SEQ ID NO:27) of a native sequence PRO1180 cDNA, wherein SEQ ID NO:27 is a clone designated herein as "DNA56860-1510".
- [0055] FIG. 28 shows the amino acid sequence (SEQ ID NO:28) derived from the coding sequence of SEQ ID NO:27 shown in FIG. 27.
- [0056] FIG. 29 shows a nucleotide sequence (SEQ ID NO:29) of a native sequence PRO831 cDNA, wherein SEQ ID NO:29 is a clone designated herein as "DNA56862-1343".
- [0057] FIG. 30 shows the amino acid sequence (SEQ ID NO:30) derived from the coding sequence of SEQ ID NO:29 shown in FIG. 29.
- [0058] FIG. 31 shows a nucleotide sequence (SEQ ID NO:31) of a native sequence PRO1115 cDNA, wherein SEQ ID NO:31 is a clone designated herein as "DNA56868-1478".
- [0059] FIG. 32 shows the amino acid sequence (SEQ ID NO:32) derived from the coding sequence of SEQ ID NO:31 shown in FIG. 31.
- [0060] FIG. 33 shows a nucleotide sequence (SEQ ID NO:33) of a native sequence PRO1277 cDNA, wherein SEQ ID NO:33 is a clone designated herein as "DNA56869-1545".
- [0061] FIG. 34 shows the amino acid sequence (SEQ ID NO:34) derived from the coding sequence of SEQ ID NO:33 shown in FIG. 33.
- [0062] FIG. 35 shows a nucleotide sequence (SEQ ID NO:35) of a native sequence PRO1074 cDNA, wherein SEQ ID NO:35 is a clone designated herein as "DNA57704-1452".
- [0063] FIG. 36 shows the amino acid sequence (SEQ ID NO:36) derived from the coding sequence of SEQ ID NO:35 shown in FIG. 35.
- [0064] FIG. 37 shows a nucleotide sequence (SEQ ID NO:37) of a native sequence PRO1344 cDNA, wherein SEQ ID NO:37 is a clone designated herein as "DNA58723-1588".
- [0065] FIG. 38 shows the amino acid sequence (SEQ ID NO:38) derived from the coding sequence of SEQ ID NO:37 shown in FIG. 37.
- [0066] FIG. 39 shows a nucleotide sequence (SEQ ID NO:39) of a native sequence PRO1136 cDNA, wherein SEQ ID NO:39 is a clone designated herein as "DNA57827-1493".
- [0067] FIG. 40 shows the amino acid sequence (SEQ ID NO:40) derived from the coding sequence of SEQ ID NO:39 shown in FIG. 39.
- [0068] FIG. 41 shows a nucleotide sequence (SEQ ID NO:41) of a native sequence PRO1109 cDNA, wherein SEQ ID NO:41 is a clone designated herein as "DNA58737-1473".
- [0069] FIG. 42 shows the amino acid sequence (SEQ ID NO:42) derived from the coding sequence of SEQ ID NO:41 shown in FIG. 41.
- [0070] FIG. 43 shows a nucleotide sequence (SEQ ID NO:43) of a native sequence PRO1003 cDNA, wherein SEQ ID NO:43 is a clone designated herein as "DNA58846-1409".
- [0071] FIG. 44 shows the amino acid sequence (SEQ ID NO:44) derived from the coding sequence of SEQ ID NO:43 shown in FIG. 43.
- [0072] FIG. 45 shows a nucleotide sequence (SEQ ID NO:45) of a native sequence PRO1138 cDNA, wherein SEQ ID NO:45 is a clone designated herein as "DNA58850-1495".

[0073] FIG. 46 shows the amino acid sequence (SEQ ID NO:46) derived from the coding sequence of SEQ ID NO:45 shown in FIG. 45.

[0074] FIG. 47 shows a nucleotide sequence (SEQ ID NO:47) of a native sequence PRO994 cDNA, wherein SEQ ID NO:47 is a clone designated herein as "DNA58855-1422".

[0075] FIG. 48 shows the amino acid sequence (SEQ ID NO:48) derived from the coding sequence of SEQ ID NO:47 shown in FIG. 47.

[0076] FIG. 49 shows a nucleotide sequence (SEQ ID NO:49) of a native sequence PRO1069 cDNA, wherein SEQ ID NO:49 is a clone designated herein as "DNA59211-1450".

[0077] FIG. 50 shows the amino acid sequence (SEQ ID NO:50) derived from the coding sequence of SEQ ID NO:49 shown in FIG. 49.

[0078] FIG. 51 shows a nucleotide sequence (SEQ ID NO:51) of a native sequence PRO1411 cDNA, wherein SEQ ID NO:51 is a clone designated herein as "DNA59212-1627".

[0079] FIG. 52 shows the amino acid sequence (SEQ ID NO:52) derived from the coding sequence of SEQ ID NO:51 shown in FIG. 51.

[0080] FIG. 53 shows a nucleotide sequence (SEQ ID NO:53) of a native sequence PRO1129 cDNA, wherein SEQ ID NO:53 is a clone designated herein as "DNA59213-1487".

[0081] FIG. 54 shows the amino acid sequence (SEQ ID NO:54) derived from the coding sequence of SEQ ID NO:53 shown in FIG. 53.

[0082] FIG. 55 shows a nucleotide sequence (SEQ ID NO:55) of a native sequence PRO1027 cDNA, wherein SEQ ID NO:55 is a clone designated herein as "DNA59605-1418".

[0083] FIG. 56 shows the amino acid sequence (SEQ ID NO:56) derived from the coding sequence of SEQ ID NO:55 shown in FIG. 55.

[0084] FIG. 57 shows a nucleotide sequence (SEQ ID NO:57) of a native sequence PRO1106 cDNA, wherein SEQ ID NO:57 is a clone designated herein as "DNA59609-1470".

[0085] FIG. 58 shows the amino acid sequence (SEQ ID NO:58) derived from the coding sequence of SEQ ID NO:57 shown in FIG. 57.

[0086] FIG. 59 shows a nucleotide sequence (SEQ ID NO:59) of a native sequence PRO1291 cDNA, wherein SEQ ID NO:59 is a clone designated herein as "DNA59610-1556".

[0087] FIG. 60 shows the amino acid sequence (SEQ ID NO:60) derived from the coding sequence of SEQ ID NO:59 shown in FIG. 59.

[0088] FIG. 61 shows a nucleotide sequence (SEQ ID NO:61) of a native sequence PRO3573 cDNA, wherein SEQ ID NO:61 is a clone designated herein as "DNA59837-2545".

[0089] FIG. 62 shows the amino acid sequence (SEQ ID NO:62) derived from the coding sequence of SEQ ID NO:61 shown in FIG. 61.

[0090] FIG. 63 shows a nucleotide sequence (SEQ ID NO:63) of a native sequence PRO3566 cDNA, wherein SEQ ID NO:63 is a clone designated herein as "DNA59844-2542".

[0091] FIG. 64 shows the amino acid sequence (SEQ ID NO:64) derived from the coding sequence of SEQ ID NO:63 shown in FIG. 63.

[0092] FIG. 65 shows a nucleotide sequence (SEQ ID NO:65) of a native sequence PRO1098 cDNA, wherein SEQ ID NO:65 is a clone designated herein as "DNA59854-1459".

[0093] FIG. 66 shows the amino acid sequence (SEQ ID NO:66) derived from the coding sequence of SEQ ID NO:65 shown in FIG. 65.

[0094] FIG. 67 shows a nucleotide sequence (SEQ ID NO:67) of a native sequence PRO1158 cDNA, wherein SEQ ID NO:67 is a clone designated herein as "DNA60625-1507".

[0095] FIG. 68 shows the amino acid sequence (SEQ ID NO:68) derived from the coding sequence of SEQ ID NO:67 shown in FIG. 67.

[0096] FIG. 69 shows a nucleotide sequence (SEQ ID NO:69) of a native sequence PRO1124 cDNA, wherein SEQ ID NO:69 is a clone designated herein as "DNA60629-1481".

[0097] FIG. 70 shows the amino acid sequence (SEQ ID NO:70) derived from the coding sequence of SEQ ID NO:69 shown in FIG. 69.

[0098] FIG. 71 shows a nucleotide sequence (SEQ ID NO:71) of a native sequence PRO1287 cDNA, wherein SEQ ID NO:71 is a clone designated herein as "DNA61755-1554".

[0099] FIG. 72 shows the amino acid sequence (SEQ ID NO:72) derived from the coding sequence of SEQ ID NO:71 shown in FIG. 71.

[0100] FIG. 73 shows a nucleotide sequence (SEQ ID NO:73) of a native sequence PRO1335 cDNA, wherein SEQ ID NO:73 is a clone designated herein as "DNA62812-1594".

[0101] FIG. 74 shows the amino acid sequence (SEQ ID NO:74) derived from the coding sequence of SEQ ID NO:73 shown in FIG. 73.

[0102] FIG. 75 shows a nucleotide sequence (SEQ ID NO:75) of a native sequence PRO1315 cDNA, wherein SEQ ID NO:75 is a clone designated herein as "DNA62815-1576".

[0103] FIG. 76 shows the amino acid sequence (SEQ ID NO:76) derived from the coding sequence of SEQ ID NO:75 shown in FIG. 75.

[0104] FIG. 77 shows a nucleotide sequence (SEQ ID NO:77) of a native sequence PRO1357 cDNA, wherein SEQ ID NO:77 is a clone designated herein as "DNA64881-1602".

[0105] FIG. 78 shows the amino acid sequence (SEQ ID NO:78) derived from the coding sequence of SEQ ID NO:77 shown in FIG. 77.

[0106] FIG. 79 shows a nucleotide sequence (SEQ ID NO:79) of a native sequence PRO1356 cDNA, wherein SEQ ID NO:79 is a clone designated herein as "DNA64886-1601".

[0107] FIG. 80 shows the amino acid sequence (SEQ ID NO:80) derived from the coding sequence of SEQ ID NO:79 shown in FIG. 79.

[0108] FIG. 81 shows a nucleotide sequence (SEQ ID NO:81) of a native sequence PRO1557 cDNA, wherein SEQ ID NO:81 is a clone designated herein as "DNA64902-1667".

[0109] FIG. 82 shows the amino acid sequence (SEQ ID NO:82) derived from the coding sequence of SEQ ID NO:81 shown in FIG. 81.

[0110] FIG. 83 shows a nucleotide sequence (SEQ ID NO:83) of a native sequence PRO1347 cDNA, wherein SEQ ID NO:83 is a clone designated herein as "DNA64950-1590".

[0111] FIG. 84 shows the amino acid sequence (SEQ ID NO:84) derived from the coding sequence of SEQ ID NO:83 shown in FIG. 83.

[0112] FIG. 85 shows a nucleotide sequence (SEQ ID NO:85) of a native sequence PRO1302 cDNA, wherein SEQ ID NO:85 is a clone designated herein as "DNA65403-1565".

[0113] FIG. 86 shows the amino acid sequence (SEQ ID NO:86) derived from the coding sequence of SEQ ID NO:85 shown in FIG. 85.

[0114] FIG. 87 shows a nucleotide sequence (SEQ ID NO:87) of a native sequence PRO1270 cDNA, wherein SEQ ID NO:87 is a clone designated herein as "DNA66308-1537".

[0115] FIG. 88 shows the amino acid sequence (SEQ ID NO:88) derived from the coding sequence of SEQ ID NO:87 shown in FIG. 87.

[0116] FIG. 89 shows a nucleotide sequence (SEQ ID NO:89) of a native sequence PRO1268 cDNA, wherein SEQ ID NO:89 is a clone designated herein as "DNA66519-1535".

[0117] FIG. 90 shows the amino acid sequence (SEQ ID NO:90) derived from the coding sequence of SEQ ID NO:89 shown in FIG. 89.

[0118] FIG. 91 shows a nucleotide sequence (SEQ ID NO:91) of a native sequence PRO1327 cDNA, wherein SEQ ID NO:91 is a clone designated herein as "DNA66521-1583".

[0119] FIG. 92 shows the amino acid sequence (SEQ ID NO:92) derived from the coding sequence of SEQ ID NO:91 shown in FIG. 91.

[0120] FIG. 93 shows a nucleotide sequence (SEQ ID NO:93) of a native sequence PRO1328 cDNA, wherein SEQ ID NO:93 is a clone designated herein as "DNA66658-1584".

[0121] FIG. 94 shows the amino acid sequence (SEQ ID NO:94) derived from the coding sequence of SEQ ID NO:93 shown in FIG. 93.

[0122] FIG. 95 shows a nucleotide sequence (SEQ ID NO:95) of a native sequence PRO1329 cDNA, wherein SEQ ID NO:95 is a clone designated herein as "DNA66660-1585".

[0123] FIG. 96 shows the amino acid sequence (SEQ ID NO:96) derived from the coding sequence of SEQ ID NO:95 shown in FIG. 95.

[0124] FIG. 97 shows a nucleotide sequence (SEQ ID NO:97) of a native sequence PRO1340 cDNA, wherein SEQ ID NO:97 is a clone designated herein as "DNA66663-1598".

[0125] FIG. 98 shows the amino acid sequence (SEQ ID NO:98) derived from the coding sequence of SEQ ID NO:97 shown in FIG. 97.

[0126] FIG. 99 shows a nucleotide sequence (SEQ ID NO:99) of a native sequence PRO1342 cDNA, wherein SEQ ID NO:99 is a clone designated herein as "DNA66674-1599".

[0127] FIG. 100 shows the amino acid sequence (SEQ ID NO:100) derived from the coding sequence of SEQ ID NO:99 shown in FIG. 99.

[0128] FIG. 101 shows a nucleotide sequence (SEQ ID NO:101) of a native sequence PRO3579 cDNA, wherein SEQ ID NO:101 is a clone designated herein as "DNA68862-2546".

[0129] FIG. 102 shows the amino acid sequence (SEQ ID NO:102) derived from the coding sequence of SEQ ID NO:101 shown in FIG. 101.

[0130] FIG. 103 shows a nucleotide sequence (SEQ ID NO:103) of a native sequence PRO1472 cDNA, wherein SEQ ID NO:103 is a clone designated herein as "DNA68866-1644".

[0131] FIG. 104 shows the amino acid sequence (SEQ ID NO:104) derived from the coding sequence of SEQ ID NO:103 shown in FIG. 103.

[0132] FIG. 105 shows a nucleotide sequence (SEQ ID NO:105) of a native sequence PRO1461 cDNA, wherein SEQ ID NO:105 is a clone designated herein as "DNA68871-1638".

[0133] FIG. 106 shows the amino acid sequence (SEQ ID NO:106) derived from the coding sequence of SEQ ID NO:105 shown in FIG. 105.

[0134] FIG. 107 shows a nucleotide sequence (SEQ ID NO:107) of a native sequence PRO1568 cDNA, wherein SEQ ID NO:107 is a clone designated herein as "DNA68880-1676".

[0135] FIG. 108 shows the amino acid sequence (SEQ ID NO:108) derived from the coding sequence of SEQ ID NO:107 shown in FIG. 107.

[0136] FIG. 109 shows a nucleotide sequence (SEQ ID NO:109) of a native sequence PRO1753 cDNA, wherein SEQ ID NO:109 is a clone designated herein as "DNA68883-1691".

[0137] FIG. 110 shows the amino acid sequence (SEQ ID NO:110) derived from the coding sequence of SEQ ID NO:109 shown in FIG. 109.

[0138] FIG. 111 shows a nucleotide sequence (SEQ ID NO:111) of a native sequence PRO1570 cDNA, wherein SEQ ID NO:111 is a clone designated herein as "DNA68885-1678".

[0139] FIG. 112 shows the amino acid sequence (SEQ ID NO:112) derived from the coding sequence of SEQ ID NO:111 shown in FIG. 111.

[0140] FIG. 113 shows a nucleotide sequence (SEQ ID NO:113) of a native sequence PRO1446 cDNA, wherein SEQ ID NO:113 is a clone designated herein as "DNA71277-1636".

[0141] FIG. 114 shows the amino acid sequence (SEQ ID NO:114) derived from the coding sequence of SEQ ID NO:113 shown in FIG. 113.

[0142] FIG. 115 shows a nucleotide sequence (SEQ ID NO:115) of a native sequence PRO1565 cDNA, wherein SEQ ID NO:115 is a clone designated herein as "DNA73727-1673".

[0143] FIG. 116 shows the amino acid sequence (SEQ ID NO:116) derived from the coding sequence of SEQ ID NO:115 shown in FIG. 115.

[0144] FIG. 117 shows a nucleotide sequence (SEQ ID NO:117) of a native sequence PRO1572 cDNA, wherein SEQ ID NO:117 is a clone designated herein as "DNA73734-1680".

[0145] FIG. 118 shows the amino acid sequence (SEQ ID NO:118) derived from the coding sequence of SEQ ID NO:117 shown in FIG. 117.

[0146] FIG. 119 shows a nucleotide sequence (SEQ ID NO:119) of a native sequence PRO1573 cDNA, wherein SEQ ID NO:119 is a clone designated herein as "DNA73735-1681".

[0147] FIG. 120 shows the amino acid sequence (SEQ ID NO:120) derived from the coding sequence of SEQ ID NO:119 shown in FIG. 119.

[0148] FIG. 121 shows a nucleotide sequence (SEQ ID NO:121) of a native sequence PRO1550 cDNA, wherein SEQ ID NO:121 is a clone designated herein as "DNA76393-1664".

[0149] FIG. 122 shows the amino acid sequence (SEQ ID NO:122) derived from the coding sequence of SEQ ID NO:121 shown in FIG. 121.

[0150] FIG. 123 shows a nucleotide sequence (SEQ ID NO:123) of a native sequence PRO1693 cDNA, wherein SEQ ID NO:123 is a clone designated herein as "DNA77301-1708".

[0151] FIG. 124 shows the amino acid sequence (SEQ ID NO:124) derived from the coding sequence of SEQ ID NO:123 shown in FIG. 123.

[0152] FIG. 125 shows a nucleotide sequence (SEQ ID NO:125) of a native sequence PRO1566 cDNA, wherein SEQ ID NO:125 is a clone designated herein as "DNA77568-1626".

[0153] FIG. 126 shows the amino acid sequence (SEQ ID NO:126) derived from the coding sequence of SEQ ID NO:125 shown in FIG. 125.

[0154] FIG. 127 shows a nucleotide sequence (SEQ ID NO:127) of a native sequence PRO1774 cDNA, wherein SEQ ID NO:127 is a clone designated herein as "DNA77626-1705".

[0155] FIG. 128 shows the amino acid sequence (SEQ ID NO:128) derived from the coding sequence of SEQ ID NO:127 shown in FIG. 127.

[0156] FIG. 129 shows a nucleotide sequence (SEQ ID NO:129) of a native sequence PRO1928 cDNA, wherein SEQ ID NO:129 is a clone designated herein as "DNA81754-2532".

[0157] FIG. 130 shows the amino acid sequence (SEQ ID NO:130) derived from the coding sequence of SEQ ID NO:129 shown in FIG. 129.

[0158] FIG. 131 shows a nucleotide sequence (SEQ ID NO:131) of a native sequence PRO1865 cDNA, wherein SEQ ID NO:131 is a clone designated herein as "DNA81757-2512".

[0159] FIG. 132 shows the amino acid sequence (SEQ ID NO:132) derived from the coding sequence of SEQ ID NO:131 shown in FIG. 131.

[0160] FIG. 133 shows a nucleotide sequence (SEQ ID NO:133) of a native sequence PRO1925 cDNA, wherein SEQ ID NO:133 is a clone designated herein as "DNA82302-2529".

[0161] FIG. 134 shows the amino acid sequence (SEQ ID NO:134) derived from the coding sequence of SEQ ID NO:133 shown in FIG. 133.

[0162] FIG. 135 shows a nucleotide sequence (SEQ ID NO:135) of a native sequence PRO1926 cDNA, wherein SEQ ID NO:135 is a clone designated herein as "DNA82340-2530".

[0163] FIG. 136 shows the amino acid sequence (SEQ ID NO:136) derived from the coding sequence of SEQ ID NO:135 shown in FIG. 135.

[0164] FIG. 137 shows a nucleotide sequence (SEQ ID NO:137) of a native sequence PRO1801 cDNA, wherein SEQ ID NO:137 is a clone designated herein as "DNA83500-2506".

[0165] FIG. 138 shows the amino acid sequence (SEQ ID NO:138) derived from the coding sequence of SEQ ID NO:137 shown in FIG. 137.

[0166] FIG. 139 shows a nucleotide sequence (SEQ ID NO:139) of a native sequence PRO4405 cDNA, wherein SEQ ID NO:139 is a clone designated herein as "DNA84920-2614".

[0167] FIG. 140 shows the amino acid sequence (SEQ ID NO:140) derived from the coding sequence of SEQ ID NO:139 shown in FIG. 139.

[0168] FIG. 141 shows a nucleotide sequence (SEQ ID NO:141) of a native sequence PRO3435 cDNA, wherein SEQ ID NO:141 is a clone designated herein as "DNA85066-2534".

[0169] FIG. 142 shows the amino acid sequence (SEQ ID NO:142) derived from the coding sequence of SEQ ID NO:141 shown in FIG. 141.

[0170] FIG. 143 shows a nucleotide sequence (SEQ ID NO:143) of a native sequence PRO3543 cDNA, wherein SEQ ID NO:143 is a clone designated herein as "DNA86571-2551".

[0171] FIG. 144 shows the amino acid sequence (SEQ ID NO:144) derived from the coding sequence of SEQ ID NO:143 shown in FIG. 143.

[0172] FIG. 145 shows a nucleotide sequence (SEQ ID NO:145) of a native sequence PRO3443 cDNA, wherein SEQ ID NO:145 is a clone designated herein as "DNA87991-2540".

[0173] FIG. 146 shows the amino acid sequence (SEQ ID NO:146) derived from the coding sequence of SEQ ID NO:145 shown in FIG. 145.

[0174] FIG. 147 shows a nucleotide sequence (SEQ ID NO:147) of a native sequence PRO3442 cDNA, wherein SEQ ID NO:147 is a clone designated herein as "DNA92238-2539".

[0175] FIG. 148 shows the amino acid sequence (SEQ ID NO:148) derived from the coding sequence of SEQ ID NO:147 shown in FIG. 147.

[0176] FIG. 149 shows a nucleotide sequence (SEQ ID NO:149) of a native sequence PRO5990 cDNA, wherein SEQ ID NO:149 is a clone designated herein as "DNA96042-2682".

[0177] FIG. 150 shows the amino acid sequence (SEQ ID NO:150) derived from the coding sequence of SEQ ID NO:149 shown in FIG. 149.

[0178] FIG. 151 shows a nucleotide sequence (SEQ ID NO:151) of a native sequence PRO4342 cDNA, wherein SEQ ID NO:151 is a clone designated herein as "DNA96787-2534".

[0179] FIG. 152 shows the amino acid sequence (SEQ ID NO:152) derived from the coding sequence of SEQ ID NO:151 shown in FIG. 151.

[0180] FIG. 153 shows a nucleotide sequence (SEQ ID NO:153) of a native sequence PRO10096 cDNA, wherein SEQ ID NO:153 is a clone designated herein as "DNA125185-2806".

[0181] FIG. 154 shows the amino acid sequence (SEQ ID NO:154) derived from the coding sequence of SEQ ID NO:153 shown in FIG. 153.

[0182] FIG. 155 shows a nucleotide sequence (SEQ ID NO:155) of a native sequence PRO10272 cDNA, wherein SEQ ID NO:155 is a clone designated herein as "DNA147531-2821".

[0183] FIG. 156 shows the amino acid sequence (SEQ ID NO:156) derived from the coding sequence of SEQ ID NO:155 shown in FIG. 155.

[0184] FIG. 157 shows a nucleotide sequence (SEQ ID NO:157) of a native sequence PRO5801 cDNA, wherein SEQ ID NO:157 is a clone designated herein as "DNA115291-2681".

[0185] FIG. 158 shows the amino acid sequence (SEQ ID NO:158) derived from the coding sequence of SEQ ID NO:157 shown in FIG. 157.

[0186] FIG. 159 shows a nucleotide sequence (SEQ ID NO:159) of a native sequence PRO20110 cDNA, wherein SEQ ID NO:159 is a clone designated herein as "DNA166819".

[0187] FIG. 160 shows the amino acid sequence (SEQ ID NO:160) derived from the coding sequence of SEQ ID NO:159 shown in FIG. 159.

[0188] FIG. 161 shows a nucleotide sequence (SEQ ID NO:161) of a native sequence PRO20040 cDNA, wherein SEQ ID NO:161 is a clone designated herein as "DNA164625-2890".

[0189] FIG. 162 shows the amino acid sequence (SEQ ID NO:162) derived from the coding sequence of SEQ ID NO:161 shown in FIG. 161.

[0190] FIG. 163 shows a nucleotide sequence (SEQ ID NO:163) of a native sequence PRO20233 cDNA, wherein SEQ ID NO:163 is a clone designated herein as "DNA165608".

[0191] FIG. 164 shows the amino acid sequence (SEQ ID NO:164) derived from the coding sequence of SEQ ID NO:163 shown in FIG. 163.

[0192] FIG. 165 shows a nucleotide sequence (SEQ ID NO:165) of a native sequence PRO19670 cDNA, wherein SEQ ID NO:165 is a clone designated herein as "DNA131639-2874".

[0193] FIG. 166 shows the amino acid sequence (SEQ ID NO:166) derived from the coding sequence of SEQ ID NO:165 shown in FIG. 165.

[0194] FIG. 167 shows a nucleotide sequence (SEQ ID NO:167) of a native sequence PRO1890 cDNA, wherein SEQ ID NO:167 is a clone designated herein as "DNA79230-2525".

[0195] FIG. 168 shows the amino acid sequence (SEQ ID NO:168) derived from the coding sequence of SEQ ID NO:167 shown in FIG. 167.

DETAILED DESCRIPTION

1. Definitions

[0196] The terms "PRO polypeptide" and "PRO" as used herein and when immediately followed by a numerical designation refer to various polypeptides, wherein the complete designation (i.e., PRO/number) refers to specific polypeptide sequences as described herein. The terms "PRO/number polypeptide" and "PRO/number" wherein the term "number" is provided as an actual numerical designation as used herein encompass native sequence polypeptides and polypeptide variants (which are further defined herein). The PRO polypeptides described herein may be isolated from a variety of sources, such as from human tissue types or from another source, or prepared by recombinant or synthetic methods. The term "PRO polypeptide" refers to each individual PRO/number polypeptide disclosed herein. All disclosures in this specification which refer to the "PRO polypeptide" refer to each of the polypeptides individually as well as jointly. For example, descriptions of the prepa-

ration of, purification of, derivation of, formation of antibodies to or against, administration of, compositions containing, treatment of a disease with, etc., pertain to each polypeptide of the invention individually. The term "PRO polypeptide" also includes variants of the PRO/number polypeptides disclosed herein.

[0197] A "native sequence PRO polypeptide" comprises a polypeptide having the same amino acid sequence as the corresponding PRO polypeptide derived from nature. Such native sequence PRO polypeptides can be isolated from nature or can be produced by recombinant or synthetic means. The term "native sequence PRO polypeptide" specifically encompasses naturally-occurring truncated or secreted forms of the specific PRO polypeptide (e.g., an extracellular domain sequence), naturally-occurring variant forms (e.g., alternatively spliced forms) and naturally-occurring allelic variants of the polypeptide. In various embodiments of the invention, the native sequence PRO polypeptides disclosed herein are mature or full-length native sequence polypeptides comprising the full-length amino acids sequences shown in the accompanying figures. Start and stop codons are shown in bold font and underlined in the figures. However, while the PRO polypeptide disclosed in the accompanying figures are shown to begin with methionine residues designated herein as amino acid position 1 in the figures, it is conceivable and possible that other methionine residues located either upstream or downstream from the amino acid position 1 in the figures may be employed as the starting amino acid residue for the PRO polypeptides.

[0198] The PRO polypeptide "extracellular domain" or "ECD" refers to a form of the PRO polypeptide which is essentially free of the transmembrane and cytoplasmic domains. Ordinarily, a PRO polypeptide ECD will have less than 1% of such transmembrane and/or cytoplasmic domains and preferably, will have less than 0.5% of such domains. It will be understood that any transmembrane domains identified for the PRO polypeptides of the present invention are identified pursuant to criteria routinely employed in the art for identifying that type of hydrophobic domain. The exact boundaries of a transmembrane domain may vary but most likely by no more than about 5 amino acids at either end of the domain as initially identified herein. Optionally, therefore, an extracellular domain of a PRO polypeptide may contain from about 5 or fewer amino acids on either side of the transmembrane domain/extracellular domain boundary as identified in the Examples or specification and such polypeptides, with or without the associated signal peptide, and nucleic acid encoding them, are contemplated by the present invention.

[0199] The approximate location of the "signal peptides" of the various PRO polypeptides disclosed herein are shown in the present specification and/or the accompanying figures. It is noted, however, that the C-terminal boundary of a signal peptide may vary, but most likely by no more than about 5 amino acids on either side of the signal peptide C-terminal boundary as initially identified herein, wherein the C-terminal boundary of the signal peptide may be identified pursuant to criteria routinely employed in the art for identifying that type of amino acid sequence element (e.g., Nielsen et al., *Prot. Eng.* 10:1-6 (1997) and von Heinje et al., *Nucl. Acids. Res.* 14:4683-4690 (1986)). Moreover, it is also recognized that, in some cases, cleavage of a signal

sequence from a secreted polypeptide is not entirely uniform, resulting in more than one secreted species. These mature polypeptides, where the signal peptide is cleaved within no more than about 5 amino acids on either side of the C-terminal boundary of the signal peptide as identified herein, and the polynucleotides encoding them, are contemplated by the present invention.

[0200] "PRO polypeptide variant" means an active PRO polypeptide as defined above or below having at least about 80% amino acid sequence identity with a full-length native sequence PRO polypeptide sequence as disclosed herein, a PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Such PRO polypeptide variants include, for instance, PRO polypeptides wherein one or more amino acid residues are added, or deleted, at the N- or C-terminus of the full-length native amino acid sequence. Ordinarily, a PRO polypeptide variant will have at least about 80% amino acid sequence identity, alternatively at least about 81% amino acid sequence identity, alternatively at least about 82% amino acid sequence identity, alternatively at least about 83% amino acid sequence identity, alternatively at least about 84% amino acid sequence identity, alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid sequence identity, alternatively at least about 87% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 89% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 96% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity to a full-length native sequence PRO polypeptide sequence as disclosed herein, a PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other specifically defined fragment of a full-length PRO polypeptide sequence as disclosed herein. Ordinarily, PRO variant polypeptides are at least about 10 amino acids in length, alternatively at least about 20 amino acids in length, alternatively at least about 30 amino acids in length, alternatively at least about 40 amino acids in length, alternatively at least about 50 amino acids in length, alternatively at least about 60 amino acids in length, alternatively at least about 70 amino acids in length, alternatively at least about 80 amino acids in length, alternatively at least about 90 amino acids in length, alternatively at least about 100 amino acids in length, alternatively at least about 150 amino acids in length, alternatively at least about 200 amino acids in length, alternatively at least about 300 amino acids in length, or more.

[0201] "Percent (%) amino acid sequence identity" with respect to the PRO polypeptide sequences identified herein is defined as the percentage of amino acid residues in a

candidate sequence that are identical with the amino acid residues in the specific PRO polypeptide sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared. For purposes herein, however, % amino acid sequence identity values are generated using the sequence comparison computer program ALIGN-2, wherein the complete source code for the ALIGN-2 program is provided in Table 1 below. The ALIGN-2 sequence comparison computer program was authored by Genentech, Inc. and the source code shown in Table 1 below has been filed with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available through Genentech, Inc., South San Francisco, Calif. or may be compiled from the source code provided in Table 1 below. The ALIGN-2 program should be compiled for use on a UNIX operating system, preferably digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary.

[0202] In situations where ALIGN-2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows:

100 times the fraction X/Y

[0203] where X is the number of amino acid residues scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A. As examples of % amino acid sequence identity calculations using this method, Tables 2 and 3 demonstrate how to calculate the % amino acid sequence identity of the amino acid sequence designated "Comparison Protein" to the amino acid sequence designated "PRO", wherein "PRO" represents the amino acid sequence of a hypothetical PRO polypeptide of interest, "Comparison Protein" represents the amino acid sequence of a polypeptide against which the "PRO" polypeptide of interest is being compared, and "X", "Y" and "Z" each represent different hypothetical amino acid residues.

[0204] Unless specifically stated otherwise, all % amino acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the ALIGN-2 computer program. However, % amino acid sequence identity values may also be obtained as described

below by using the WU-BLAST-2 computer program (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Most of the WU-BLAST-2 search parameters are set to the default values. Those not set to default values, i.e., the adjustable parameters, are set with the following values: overlap span=1, overlap fraction=0.125, word threshold (T)=11, and scoring matrix=BLOSUM62. When WU-BLAST-2 is employed, a % amino acid sequence identity value is determined by dividing (a) the number of matching identical amino acid residues between the amino acid sequence of the PRO polypeptide of interest having a sequence derived from the native PRO polypeptide and the comparison amino acid sequence of interest (i.e., the sequence against which the PRO polypeptide of interest is being compared which may be a PRO variant polypeptide) as determined by WU-BLAST-2 by (b) the total number of amino acid residues of the PRO polypeptide of interest. For example, in the statement "a polypeptide comprising an the amino acid sequence A which has or having at least 80% amino acid sequence identity to the amino acid sequence B", the amino acid sequence A is the comparison amino acid sequence of interest and the amino acid sequence B is the amino acid sequence of the PRO polypeptide of interest.

[0205] Percent amino acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., *Nucleic Acids Res.* 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be downloaded from <http://www.ncbi.nlm.nih.gov> or otherwise obtained from the National Institute of Health, Bethesda, Md. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask=yes, strand=all, expected occurrences=10, minimum low complexity length=15/5, multi-pass e-value=0.01, constant for multi-pass=25, dropoff for final gapped alignment=25 and scoring matrix=BLOSUM62.

[0206] In situations where NCBI-BLAST2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows:

100 times the fraction X/Y

[0207] where X is the number of amino acid residues scored as identical matches by the sequence alignment program NCBI-BLAST2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A.

[0208] "PRO variant polynucleotide" or "PRO variant nucleic acid sequence" means a nucleic acid molecule which encodes an active PRO polypeptide as defined below and which has at least about 80% nucleic acid sequence identity with a nucleotide acid sequence encoding a full-length native sequence PRO polypeptide sequence as disclosed herein, a full-length native sequence PRO polypeptide sequence lacking the signal peptide as disclosed herein, an

extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Ordinarily, a PRO variant polynucleotide will have at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93% nucleic acid sequence identity, alternatively at least about 94% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity with a nucleic acid sequence encoding a full-length native sequence PRO polypeptide sequence as disclosed herein, a full-length native sequence PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal sequence, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Variants do not encompass the native nucleotide sequence.

[0209] Ordinarily, PRO variant polynucleotides are at least about 30 nucleotides in length, alternatively at least about 60 nucleotides in length, alternatively at least about 90 nucleotides in length, alternatively at least about 120 nucleotides in length, alternatively at least about 150 nucleotides in length, alternatively at least about 180 nucleotides in length, alternatively at least about 210 nucleotides in length, alternatively at least about 240 nucleotides in length, alternatively at least about 270 nucleotides in length, alternatively at least about 300 nucleotides in length, alternatively at least about 450 nucleotides in length, alternatively at least about 600 nucleotides in length, alternatively at least about 900 nucleotides in length, or more.

[0210] "Percent (%) nucleic acid sequence identity" with respect to PRO-encoding nucleic acid sequences identified herein is defined as the percentage of nucleotides in a candidate sequence that are identical with the nucleotides in the PRO nucleic acid sequence of interest, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity. Alignment for purposes of determining percent nucleic acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. For purposes herein, however, % nucleic acid sequence identity values are generated using the sequence comparison computer program ALIGN-2, wherein the complete source code for the ALIGN-2 program is provided in Table 1 below. The ALIGN-2 sequence comparison computer program was authored by Genentech, Inc.

and the source code shown in Table 1 below has been filed with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available through Genentech, Inc., South San Francisco, Calif. or may be compiled from the source code provided in Table 1 below. The ALIGN-2 program should be compiled for use on a UNIX operating system, preferably digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary.

[0211] In situations where ALIGN-2 is employed for nucleic acid sequence comparisons, the % nucleic acid sequence identity of a given nucleic acid sequence C to, with, or against a given nucleic acid sequence D (which can alternatively be phrased as a given nucleic acid sequence C that has or comprises a certain % nucleic acid sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows:

100 times the fraction W/Z

[0212] where W is the number of nucleotides scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of C and D, and where Z is the total number of nucleotides in D. It will be appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to C. As examples of % nucleic acid sequence identity calculations, Tables 4 and 5, demonstrate how to calculate the % nucleic acid sequence identity of the nucleic acid sequence designated "Comparison DNA" to the nucleic acid sequence designated "PRO-DNA", wherein "PRO-DNA" represents a hypothetical PRO-encoding nucleic acid sequence of interest, "Comparison DNA" represents the nucleotide sequence of a nucleic acid molecule against which the "PRO-DNA" nucleic acid molecule of interest is being compared, and "N", "L" and "V" each represent different hypothetical nucleotides.

[0213] Unless specifically stated otherwise, all % nucleic acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the ALIGN-2 computer program. However, % nucleic acid sequence identity values may also be obtained as described below by using the WU-BLAST-2 computer program (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Most of the WU-BLAST-2 search parameters are set to the default values. Those not set to default values, i.e., the adjustable parameters, are set with the following values: overlap span=1, overlap fraction=0.125, word threshold (T)=11, and scoring matrix=BLOSUM62. When WU-BLAST-2 is employed, a % nucleic acid sequence identity value is determined by dividing (a) the number of matching identical nucleotides between the nucleic acid sequence of the PRO polypeptide-encoding nucleic acid molecule of interest having a sequence derived from the native sequence PRO polypeptide-encoding nucleic acid and the comparison nucleic acid molecule of interest (i.e., the sequence against which the PRO polypeptide-encoding nucleic acid molecule of interest is being compared which may be a variant PRO polynucleotide) as determined by WU-BLAST-2 by (b) the total number of nucleotides of the PRO polypeptide-encoding nucleic acid molecule of interest. For example, in the statement "an isolated nucleic acid

molecule comprising a nucleic acid sequence A which has or having at least 80% nucleic acid sequence identity to the nucleic acid sequence B”, the nucleic acid sequence A is the comparison nucleic acid molecule of interest and the nucleic acid sequence B is the nucleic acid sequence of the PRO polypeptide-encoding nucleic acid molecule of interest.

[0214] Percent nucleic acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., *Nucleic Acids Res.* 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be downloaded from <http://www.ncbi.nlm.nih.gov> or otherwise obtained from the National Institute of Health, Bethesda, Md. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask=yes, strand=all, expected occurrences=10, minimum low complexity length=15/5, multi-pass e-value=0.01, constant for multi-pass=25, dropoff for final gapped alignment=25 and scoring matrix=BLOSUM62.

[0215] In situations where NCBI-BLAST2 is employed for sequence comparisons, the % nucleic acid sequence identity of a given nucleic acid sequence C to, with, or against a given nucleic acid sequence D (which can alternatively be phrased as a given nucleic acid sequence C that has or comprises a certain % nucleic acid sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows:

100 times the fraction W/Z

[0216] where W is the number of nucleotides scored as identical matches by the sequence alignment program NCBI-BLAST2 in that program's alignment of C and D, and where Z is the total number of nucleotides in D. It will be appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to C.

[0217] In other embodiments, PRO variant polynucleotides are nucleic acid molecules that encode an active PRO polypeptide and which are capable of hybridizing, preferably under stringent hybridization and wash conditions, to nucleotide sequences encoding a full-length PRO polypeptide as disclosed herein. PRO variant polypeptides may be those that are encoded by a PRO variant polynucleotide.

[0218] “Isolated,” when used to describe the various polypeptides disclosed herein, means polypeptide that has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials that would typically interfere with diagnostic or therapeutic uses for the polypeptide, and may include enzymes, hormones, and other proteinaceous or non-proteinaceous solutes. In preferred embodiments, the polypeptide will be purified (1) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (2) to homogeneity by SDS-PAGE under non-reducing or reducing conditions using Coomassie blue or, preferably, silver stain. Isolated polypeptide includes polypeptide in situ within recombinant cells, since at least one component of the PRO polypeptide natural environment will not be present. Ordinarily, however, isolated polypeptide will be prepared by at least one purification step.

[0219] An “isolated” PRO polypeptide-encoding nucleic acid or other polypeptide-encoding nucleic acid is a nucleic acid molecule that is identified and separated from at least one contaminant nucleic acid molecule with which it is ordinarily associated in the natural source of the polypeptide-encoding nucleic acid. An isolated polypeptide-encoding nucleic acid molecule is other than in the form or setting in which it is found in nature. Isolated polypeptide-encoding nucleic acid molecules therefore are distinguished from the specific polypeptide-encoding nucleic acid molecule as it exists in natural cells. However, an isolated polypeptide-encoding nucleic acid molecule includes polypeptide-encoding nucleic acid molecules contained in cells that ordinarily express the polypeptide where, for example, the nucleic acid molecule is in a chromosomal location different from that of natural cells.

[0220] The term “control sequences” refers to DNA sequences necessary for the expression of an operably linked coding sequence in a particular host organism. The control sequences that are suitable for prokaryotes, for example, include a promoter, optionally an operator sequence, and a ribosome binding site. Eukaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

[0221] Nucleic acid is “operably linked” when it is placed into a functional relationship with another nucleic acid sequence. For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; or a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation. Generally, “operably linked” means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is accomplished by ligation at convenient restriction sites. If such sites do not exist, the synthetic oligonucleotide adaptors or linkers are used in accordance with conventional practice.

[0222] The term “antibody” is used in the broadest sense and specifically covers, for example, single anti-PRO monoclonal antibodies (including agonist, antagonist, and neutralizing antibodies), anti-PRO antibody compositions with polypeptopic specificity, single chain anti-PRO antibodies, and fragments of anti-PRO antibodies (see below). The term “monoclonal antibody” as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical except for possible naturally-occurring mutations that may be present in minor amounts.

[0223] “Stringency” of hybridization reactions is readily determinable by one of ordinary skill in the art, and generally is an empirical calculation dependent upon probe length, washing temperature, and salt concentration. In general, longer probes require higher temperatures for proper annealing, while shorter probes need lower temperatures. Hybridization generally depends on the ability of denatured DNA to reanneal when complementary strands are present in an environment below their melting temperature. The higher the degree of desired homology between the probe and hybridizable sequence, the higher the relative temperature which can be used. As a result, it follows that

higher relative temperatures would tend to make the reaction conditions more stringent, while lower temperatures less so. For additional details and explanation of stringency of hybridization reactions, see Ausubel et al., *Current Protocols in Molecular Biology*, Wiley Interscience Publishers, (1995).

[0224] “Stringent conditions” or “high stringency conditions”, as defined herein, may be identified by those that: (1) employ low ionic strength and high temperature for washing, for example 0.015 M sodium chloride/0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50° C.; (2) employ during hybridization a denaturing agent, such as formamide, for example, 50% (v/v) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50 mM sodium phosphate buffer at pH 6.5 with 750 mM sodium chloride, 75 mM sodium citrate at 42° C.; or (3) employ 50% formamide, 5×SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5× Denhardt’s solution, sonicated salmon sperm DNA (50 µg/ml), 0.1% SDS, and 10% dextran sulfate at 42° C., with washes at 42° C. in 0.2×SSC (sodium chloride/sodium citrate) and 50% formamide at 55° C., followed by a high-stringency wash consisting of 0.1×SSC containing EDTA at 55° C.

[0225] “Moderately stringent conditions” may be identified as described by Sambrook et al., *Molecular Cloning: A Laboratory Manual*, New York: Cold Spring Harbor Press, 1989, and include the use of washing solution and hybridization conditions (e.g., temperature, ionic strength and % SDS) less stringent than those described above. An example of moderately stringent conditions is overnight incubation at 37° C. in a solution comprising: 20% formamide, 5×SSC (150 mM NaCl, 15 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5× Denhardt’s solution, 10% dextran sulfate, and 20 mg/ml denatured sheared salmon sperm DNA, followed by washing the filters in 1×SSC at about 37-50° C. The skilled artisan will recognize how to adjust the temperature, ionic strength, etc. as necessary to accommodate factors such as probe length and the like.

[0226] The term “epitope tagged” when used herein refers to a chimeric polypeptide comprising a PRO polypeptide fused to a “tag polypeptide”. The tag polypeptide has enough residues to provide an epitope against which an antibody can be made, yet is short enough such that it does not interfere with activity of the polypeptide to which it is fused. The tag polypeptide preferably also is fairly unique so that the antibody does not substantially cross-react with other epitopes. Suitable tag polypeptides generally have at least six amino acid residues and usually between about 8 and 50 amino acid residues (preferably, between about 10 and 20 amino acid residues).

[0227] As used herein, the term “immunoadhesin” designates antibody-like molecules which combine the binding specificity of a heterologous protein (an “adhesin”) with the effector functions of immunoglobulin constant domains. Structurally, the immunoadhesins comprise a fusion of an amino acid sequence with the desired binding specificity which is other than the antigen recognition and binding site of an antibody (i.e., is “heterologous”), and an immunoglobulin constant domain sequence. The adhesin part of an immunoadhesin molecule typically is a contiguous amino acid sequence comprising at least the binding site of a receptor or a ligand. The immunoglobulin constant domain

sequence in the immunoadhesin may be obtained from any immunoglobulin, such as IgG-1, IgG-2, IgG-3, or IgG-4 subtypes, IgA (including IgA-1 and IgA-2), IgE, IgD or IgM.

[0228] “Active” or “activity” for the purposes herein refers to form(s) of a PRO polypeptide which retain a biological and/or an immunological activity of native or naturally-occurring PRO, wherein “biological” activity refers to a biological function (either inhibitory or stimulatory) caused by a native or naturally-occurring PRO other than the ability to induce the production of an antibody against an antigenic epitope possessed by a native or naturally-occurring PRO and an “immunological” activity refers to the ability to induce the production of an antibody against an antigenic epitope possessed by a native or naturally-occurring PRO.

[0229] The term “antagonist” is used in the broadest sense, and includes any molecule that partially or fully blocks, inhibits, or neutralizes a biological activity of a native PRO polypeptide disclosed herein. In a similar manner, the term “agonist” is used in the broadest sense and includes any molecule that mimics a biological activity of a native PRO polypeptide disclosed herein. Suitable agonist or antagonist molecules specifically include agonist or antagonist antibodies or antibody fragments, fragments or amino acid sequence variants of native PRO polypeptides, peptides, antisense oligonucleotides, small organic molecules, etc. Methods for identifying agonists or antagonists of a PRO polypeptide may comprise contacting a PRO polypeptide with a candidate agonist or antagonist molecule and measuring a detectable change in one or more biological activities normally associated with the PRO polypeptide.

[0230] “Treatment” refers to both therapeutic treatment and prophylactic or preventative measures, wherein the object is to prevent or slow down (lessen) the targeted pathologic condition or disorder. Those in need of treatment include those already with the disorder as well as those prone to have the disorder or those in whom the disorder is to be prevented.

[0231] “Chronic” administration refers to administration of the agent(s) in a continuous mode as opposed to an acute mode, so as to maintain the initial therapeutic effect (activity) for an extended period of time. “Intermittent” administration is treatment that is not consecutively done without interruption, but rather is cyclic in nature.

[0232] “Mammal” for purposes of treatment refers to any animal classified as a mammal, including humans, domestic and farm animals, and zoo, sports, or pet animals, such as dogs, cats, cattle, horses, sheep, pigs, goats, rabbits, etc. Preferably, the mammal is human.

[0233] Administration “in combination with” one or more further therapeutic agents includes simultaneous (concurrent) and consecutive administration in any order.

[0234] “Carriers” as used herein include pharmaceutically acceptable carriers, excipients, or stabilizers which are non-toxic to the cell or mammal being exposed thereto at the dosages and concentrations employed. Often the physiologically acceptable carrier is an aqueous pH buffered solution. Examples of physiologically acceptable carriers include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid; low molecular weight

(less than about 10 residues) polypeptide; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as TWEEN™, polyethylene glycol (PEG), and PLURONICS™.

[0235] “Antibody fragments” comprise a portion of an intact antibody, preferably the antigen binding or variable region of the intact antibody. Examples of antibody fragments include Fab, Fab', F(ab)₂, and Fv fragments; diabodies; linear antibodies (Zapata et al., Protein Eng. 8(10): 1057-1062 [1995]); single-chain antibody molecules; and multispecific antibodies formed from antibody fragments.

[0236] Papain digestion of antibodies produces two identical antigen-binding fragments, called “Fab” fragments, each with a single antigen-binding site, and a residual “Fc” fragment, a designation reflecting the ability to crystallize readily. Pepsin treatment yields an F(ab)₂ fragment that has two antigen-combining sites and is still capable of cross-linking antigen.

[0237] “Fv” is the minimum antibody fragment which contains a complete antigen-recognition and -binding site. This region consists of a dimer of one heavy- and one light-chain variable domain in tight, non-covalent association. It is in this configuration that the three CDRs of each variable domain interact to define an antigen-binding site on the surface of the V_H-V_L dimer. Collectively, the six CDRs confer antigen-binding specificity to the antibody. However, even a single variable domain (or half of an Fv comprising only three CDRs specific for an antigen) has the ability to recognize and bind antigen, although at a lower affinity than the entire binding site.

[0238] The Fab fragment also contains the constant domain of the light chain and the first constant domain (CH1) of the heavy chain. Fab fragments differ from Fab' fragments by the addition of a few residues at the carboxy terminus of the heavy chain CH1 domain including one or more cysteines from the antibody hinge region. Fab'-SH is the designation herein for Fab' in which the cysteine residue(s) of the constant domains bear a free thiol group. F(ab)₂ antibody fragments originally were produced as pairs of Fab' fragments which have hinge cysteines between them. Other chemical couplings of antibody fragments are also known.

[0239] The “light chains” of antibodies (immunoglobulins) from any vertebrate species can be assigned to one of two clearly distinct types, called kappa and lambda, based on the amino acid sequences of their constant domains.

[0240] Depending on the amino acid sequence of the constant domain of their heavy chains, immunoglobulins can be assigned to different classes. There are five major classes of immunoglobulins: IgA, IgD, IgE, IgG, and IgM, and several of these may be further divided into subclasses (isotypes), e.g., IgG1, IgG2, IgG3, IgG4, IgA, and IgA2.

[0241] “Single-chain Fv” or “sFv” antibody fragments comprise the V_H and V_L domains of antibody, wherein these domains are present in a single polypeptide chain. Prefer-

ably, the Fv polypeptide further comprises a polypeptide linker between the V_H and V_L domains which enables the sFv to form the desired structure for antigen binding. For a review of sFv, see Pluckthun in *The Pharmacology of Monoclonal Antibodies*, vol.113, Rosenberg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994).

[0242] The term “diabodies” refers to small antibody fragments with two antigen-binding sites, which fragments comprise a heavy-chain variable domain (V_H) connected to a light-chain variable domain (V_L) in the same polypeptide chain (V_H-V_L). By using a linker that is too short to allow pairing between the two domains on the same chain, the domains are forced to pair with the complementary domains of another chain and create two antigen-binding sites. Diabodies are described more fully in, for example, EP 404,097; WO 93/11161; and Hollinger et al., Proc. Natl. Acad. Sci. USA, 90:6444-6448 (1993).

[0243] An “isolated” antibody is one which has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials which would interfere with diagnostic or therapeutic uses for the antibody, and may include enzymes, hormones, and other proteinaceous or nonproteinaceous solutes. In preferred embodiments, the antibody will be purified (1) to greater than 95% by weight of antibody as determined by the Lowry method, and most preferably more than 99% by weight, (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (3) to homogeneity by SDS-PAGE under reducing or nonreducing conditions using Coomassie blue or, preferably, silver stain. Isolated antibody includes the antibody in situ within recombinant cells since at least one component of the antibody's natural environment will not be present. Ordinarily, however, isolated antibody will be prepared by at least one purification step.

[0244] An antibody that “specifically binds to” or is “specific for” a particular polypeptide or an epitope on a particular polypeptide is one that binds to that particular polypeptide or epitope on a particular polypeptide without substantially binding to any other polypeptide or polypeptide epitope.

[0245] The word “label” when used herein refers to a detectable compound or composition which is conjugated directly or indirectly to the antibody so as to generate a “labeled” antibody. The label may be detectable by itself (e.g. radioisotope labels or fluorescent labels) or, in the case of an enzymatic label, may catalyze chemical alteration of a substrate compound or composition which is detectable.

[0246] By “solid phase” is meant a non-aqueous matrix to which the antibody of the present invention can adhere. Examples of solid phases encompassed herein include those formed partially or entirely of glass (e.g., controlled pore glass), polysaccharides (e.g., agarose), polyacrylamides, polystyrene, polyvinyl alcohol and silicones. In certain embodiments, depending on the context, the solid phase can comprise the well of an assay plate; in others it is a purification column (e.g., an affinity chromatography column). This term also includes a discontinuous solid phase of discrete particles, such as those described in U.S. Pat. No. 4,275,149.

[0247] A “liposome” is a small vesicle composed of various types of lipids, phospholipids and/or surfactant which is useful for delivery of a drug (such as a PRO polypeptide or antibody thereto) to a mammal. The components of the liposome are commonly arranged in a bilayer

formation, similar to the lipid arrangement of biological membranes.

[0248] A “small molecule” is defined herein to have a molecular weight below about 500 Daltons

TABLE 1

```

/*
 *
 * C—C increased from 12 to 15
 * Z is average of EQ
 * B is average of ND
 * match with stop is _M; stop—stop = 0; J (joker) match = 0
 */
#define _M -8 /* value of a match with a stop */
int
_day[26][26] = {
/* A B C D E F G H I J K L M N O P Q R S T U V W X Y Z */
/* A */ {2, 0, -2, 0, 0, -4, 1, -1, -1, 0, -1, -2, -1, 0, _M, 1, 0, -2, 1, 1, 0, 0, -6, 0, -3, 0},
/* B */ {0, 3, -4, 3, 2, -5, 0, 1, -2, 0, 0, -3, -2, 2, _M, -1, 1, 0, 0, 0, 0, -2, -5, 0, -3, 1},
/* C */ {-2, -4, 15, -5, -5, -4, -3, -3, -2, 0, -5, -6, -5, -4, _M, -3, -5, -4, 0, -2, 0, -2, -8, 0, 0, -5},
/* D */ {0, 3, -5, 4, 3, -6, 1, 1, -2, 0, 0, -4, -3, 2, _M, -1, 2, -1, 0, 0, 0, -2, -7, 0, -4, 2},
/* E */ {0, 2, -5, 3, 4, -5, 0, 1, -2, 0, 0, -3, -2, 1, _M, -1, 2, -1, 0, 0, 0, -2, -7, 0, -4, 3},
/* F */ {-4, -5, -4, -6, -5, 9, -5, -2, 1, 0, -5, 2, 0, -4, _M, -5, -5, -4, -3, -3, 0, -1, 0, 0, 7, -5},
/* G */ {1, 0, -3, 1, 0, -5, 5, -2, -3, 0, -2, -4, -3, 0, _M, -1, -1, -3, 1, 0, 0, -1, -7, 0, -5, 0},
/* H */ {-1, 1, -3, 1, 1, -2, -2, 6, -2, 0, 0, -2, -2, 2, _M, 0, 3, 2, -1, -1, 0, -2, -3, 0, 0, 2},
/* I */ {-1, -2, -2, -2, -2, 1, -3, -2, 5, 0, -2, 2, 2, -2, _M, -2, -2, -2, -1, 0, 0, 4, -5, 0, -1, -2},
/* J */ {0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, _M, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0},
/* K */ {-1, 0, -5, 0, 0, -5, -2, 0, -2, 0, 5, -3, 0, 1, _M, -1, 1, 3, 0, 0, 0, -2, -3, 0, -4, 0},
/* L */ {-2, -3, -6, -4, -3, 2, -4, -2, 2, 0, -3, 6, 4, -3, _M, -3, -2, -3, -3, -1, 0, 2, -2, 0, -1, -2}
/* M */ {-1, -2, -5, -3, -2, 0, -3, -2, 2, 0, 0, 4, 6, -2, _M, -2, -1, 0, -2, -1, 0, 2, -4, 0, -2, -1},
/* N */ {0, 2, -4, 2, 1, -4, 0, 2, -2, 0, 1, -3, -2, 2, _M, -1, 1, 0, 1, 0, 0, -2, -4, 0, -2, 1},
/* O */ {_M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M, _M},
/* P */ {1, -1, -3, -1, -1, -5, -1, 0, -2, 0, -1, -3, -2, -1, _M, 6, 0, 0, 1, 0, 0, -1, -6, 0, -5, 0},
/* Q */ {0, 1, -5, 2, 2, -5, -1, 3, -2, 0, 1, -2, -1, 1, _M, 0, 4, 1, -1, -1, 0, -2, -5, 0, -4, 3},
/* R */ {-2, 0, -4, -1, -1, -4, -3, 2, -2, 0, 3, -3, 0, 0, _M, 0, 1, 6, 0, -1, 0, -2, 2, 0, -4, 0},
/* S */ {1, 0, 0, 0, 0, -3, 1, -1, -1, 0, 0, -3, -2, 1, _M, 1, -1, 0, 2, 1, 0, -1, -2, 0, -3, 0},
/* T */ {1, 0, -2, 0, 0, -3, 0, -1, 0, 0, 0, -1, -1, 0, _M, 0, -1, -1, 1, 3, 0, 0, -5, 0, -3, 0},
/* U */ {0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, _M, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0},
/* V */ {0, -2, -2, -2, -2, -1, -1, -2, 4, 0, -2, 2, 2, -2, _M, -1, -2, -2, -1, 0, 0, 4, -6, 0, -2, -2},
/* W */ {-6, -5, -8, -7, -7, 0, -7, -3, -5, 0, -3, -2, -4, -4, _M, -6, -5, 2, -2, -5, 0, -6, 17, 0, 0, -6},
/* X */ {0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, _M, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0},
/* Y */ {-3, -3, 0, -4, -4, 7, -5, 0, -1, 0, -4, -1, -2, -2, _M, -5, -4, -4, -3, -3, 0, -2, 0, 0, 10, -4},
/* Z */ {0, 1, -5, 2, 3, -5, 0, 2, -2, 0, 0, -2, -1, 1, _M, 0, 3, 0, 0, 0, 0, -2, -6, 0, -4, 4},
};
/*
 */
#include <stdio.h>
#include <ctype.h>
#define MAXJMP 16 /* max jumps in a diag */
#define MAXGAP 24 /* don't continue to penalize gaps larger than this */
#define JMPS 1024 /* max jmps in an path */
#define MX 4 /* save if there's at least MX-1 bases since last jmp */
#define DMAT 3 /* value of matching bases */
#define DMIS 0 /* penalty for mismatched bases */
#define DINS0 8 /* penalty for a gap */
#define DINS1 1 /* penalty per base */
#define PINS0 8 /* penalty for a gap */
#define PINS1 4 /* penalty per residue */
struct jmp {
    short n[MAXJMP]; /* size of jmp (neg for dely) */
    unsigned short x[MAXJMP]; /* base no. of jmp in seq x */
};
struct diag {
    int score; /* score at last jmp */
    long offset; /* offset of prev block */
    short ijmp; /* current jmp index */
    struct jmp jp; /* list of jmps */
};
struct path {
    int spc; /* number of leading spaces */
    short n[JMPS]; /* size of jmp (gap) */
    int x[JMPS]; /* loc of jmp (last elem before gap) */
};
char *ofile; /* output file name */
char *namex[2]; /* seq names: getseqs() */

```

TABLE 1-continued

```

char      *prog;          /* prog name for err msgs */
char      *seqx[2];      /* seqs: getseqs() */
int       dmax;          /* best diag: nw() */
int       dmax0;        /* final diag */
int       dna;           /* set if dna: main() */
int       endgaps;      /* set if penalizing end gaps */
int       gapx, gapy;    /* total gaps in seqs */
int       len0, len1;    /* seq lens */
int       ngapx, ngapy;  /* total size of gaps */
int       smax;          /* max score: nw() */
int       *xbm;          /* bitmap for matching */
long      offset;        /* current offset in jmp file */
struct    diag *dx;      /* holds diagonals */
struct    path pp[2];    /* holds path for seqs */
char      *calloc(), *malloc(), *index(), *strcpy();
char      *getseq(), *g_calloc();
/* Needleman-Wunsch alignment program
 *
 * usage: prog file1 file2
 * where file1 and file2 are two dna or two protein sequences.
 * The sequences can be in upper- or lower-case and may contain ambiguity
 * Any lines beginning with ';', '>' or '<' are ignored
 * Max file length is 65535 (limited by unsigned short x in the jmp struct)
 * A sequence with 1/3 or more of its elements ACGTU is assumed to be DNA
 * Output is in the file "align.out"
 *
 * The program may create a tmp file in /tmp to hold info about traceback.
 * Original version developed under BSD 4.3 on a vax 8650
 */
#include "nw.h"
#include "day.h"
static  __dbval[26] = {
    1,14,2,13,0,0,4,11,0,0,12,0,3,15,0,0,0,5,6,8,8,7,9,0,10,0
};
static  __pbval[26] = {
    1, 2|(1<<('D'-'A'))|(1<<('N'-'A')), 4, 8, 16, 32, 64,
    128, 256, 0xFFFFFFFF, 1<<10, 1<<11, 1<<12, 1<<13, 1<<14,
    1<<15, 1<<16, 1<<17, 1<<18, 1<<19, 1<<20, 1<<21, 1<<22,
    1<<23, 1<<24, 1<<25|(1<<('E'-'A'))|(1<<('Q'-'A'))
};
main(ac, av)
int      ac;
char     *av[];
{
    prog = av[0];
    if(ac != 3) {
        fprintf(stderr, "usage: %s file1 file2\n", prog);
        fprintf(stderr, "where file1 and file2 are two dna or two protein sequences.\n");
        fprintf(stderr, "The sequences can be in upper- or lower-case\n");
        fprintf(stderr, "Any lines beginning with ';', '>' or '<' are ignored\n");
        fprintf(stderr, "Output is in the file \"align.out\"\n");
        exit(1);
    }
    namex[0] = av[1];
    namex[1] = av[2];
    seqx[0] = getseq(namex[0], &len0);
    seqx[1] = getseq(namex[1], &len1);
    xbm = (dna)? __dbval : __pbval;
    endgaps = 0; /* 1 to penalize endgaps */
    ofile = "align.out"; /* output file */
    nw(); /* fill in the matrix, get the possible jmps */
    readjmps(); /* get the actual jmps */
    print(); /* print stats, alignment */
    cleanup(0); /* unlink any tmp files */
}
/* do the alignment, return best score: main()
 * dna: values in Fitch and Smith, PNAS, 80, 1382-1386, 1983
 * pro: PAM 250 values
 * When scores are equal, we prefer mismatches to any gap, prefer
 * a new gap to extending an ongoing gap, and prefer a gap in seqx
 * to a gap in seq y.
 */
nw()
{
    char     *px, *py; /* seqs and ptrs */
    int      *ndely, *dely; /* keep track of dely */

```

TABLE 1-continued

```

int     ndelx, delx;    /* keep track of delx */
int     *tmp;         /* for swapping row0, row1 */
int     mis;          /* score for each type */
int     ins0, ins1;    /* insertion penalties */
register id;          /* diagonal index */
register ij;          /* jmp index */
register *col0, *col1; /* score for curr, last row */
register xx, yy;      /* index into seqs */
dx = (struct diag *)g_calloc("to get diag", len0+len1+1, sizeof(struct diag));
ndely = (int *)g_calloc("to get ndely", len1+1, sizeof(int));
dely = (int *)g_calloc("to get dely", len1+1, sizeof(int));
col0 = (int *)g_calloc("to get col0", len1+1, sizeof(int));
col1 = (int *)g_calloc("to get col1", len1+1, sizeof(int));
ins0 = (dna)? DINS0 : PINS0;
ins1 = (dna)? DINS1 : PINS1;
smax = -10000;
if (endgaps) {
    for (col0[0] = dely[0] = -ins0, yy = 1; yy <= len1; yy++) {
        col0[yy] = dely[yy] = col0[yy-1] - ins1;
        ndely[yy] = yy;
    }
    col0[0] = 0; /* Waterman Bull Math Biol 84 */
}
else
    for (yy = 1; yy <= len1; yy++)
        dely[yy] = -ins0;
/* fill in match matrix
*/
for (px = seqx[0], xx = 1; xx <= len0; px++, xx++) {
    /* initialize first entry in col
    */
    if (endgaps) {
        if (xx == 1)
            col1[0] = delx = -(ins0+ins1);
        else
            col1[0] = delx = col0[0]-ins1;
        ndelx = xx;
    }
    else {
        col1[0] = 0;
        delx = -ins0;
        ndelx = 0;
    }
}

for (py = seqy[1], yy = 1; yy <= len1; py++, yy++) {
    mis = col0[yy-1];
    if (dna)
        mis += (xbm[*px-'A']&xbm[*py-'A'])? DMAT : DMIS;
    else
        mis += _day[*px-'A'][*py-'A'];
    /* update penalty for del in x seq;
    * favor new del over ongong del
    * ignore MAXGAP if weighting endgaps
    */
    if (endgaps || ndely[yy] < MAXGAP) {
        if (col0[yy] - ins0 >= dely[yy]) {
            dely[yy] = col0[yy] - (ins0+ins1);
            ndely[yy] = 1;
        } else {
            dely[yy] -= ins1;
            ndely[yy]++;
        }
    } else {
        if (col0[yy] - (ins0+ins1) >= dely[yy]) {
            dely[yy] = col0[yy] - (ins0+ins1);
            ndely[yy] = 1;
        } else
            ndely[yy]++;
    }
}
/* update penalty for del in y seq;
* favor new del over ongong del
*/
if (endgaps || ndelx < MAXGAP) {
    if (col1[yy-1] - ins0 >= delx) {
        delx = col1[yy-1] - (ins0+ins1);
        ndelx = 1;
    }
}

```

...nw

TABLE 1-continued

```

    } else {
        delx -= ins1;
        ndelx++;
    }
} else {
    if (col1[yy-1] - (ins0+ins1) >= delx) {
        delx = col1[yy-1] - (ins0+ins1);
        ndelx = 1;
    } else
        ndelx++;
}
/* pick the maximum score; we're favoring
 * mis over any del and delx over dely
 */
id = xx - yy + len1 - 1;
if (mis >= delx && mis >= dely[yy])
    col1[yy] = mis;
else if (delx >= dely[yy]) {
    col1[yy] = delx;
    ij = dx[id].ijmp;
    if (dx[id].jp.n[0] && (!dna || (ndelx >= MAXJMP
    && xx > dx[id].jp.x[ij]+MX) || mis > dx[id].score+DINS0)) {
        dx[id].ijmp++;
        if (++ij >= MAXJMP) {
            writeimps(id);
            ij = dx[id].ijmp = 0;
            dx[id].offset = offset;
            offset += sizeof(struct jmp) + sizeof(offset);
        }
    }
    dx[id].jp.n[ij] = ndelx;
    dx[id].jp.x[ij] = xx;
    dx[id].score = delx;
}
else {
    col1[yy] = dely[yy];
    ij = dx[id].ijmp;
if (dx[id].jp.n[0] && (!dna || (ndely[yy] >= MAXJMP
    && xx > dx[id].jp.x[ij]+MX) || mis > dx[id].score+DINS0)) {
        dx[id].ijmp++;
        if (++ij >= MAXJMP) {
            writeimps(id);
            ij = dx[id].ijmp = 0;
            dx[id].offset = offset;
            offset += sizeof(struct jmp) + sizeof(offset);
        }
    }
    dx[id].jp.n[ij] = ndely[yy];
    dx[id].jp.x[ij] = xx;
    dx[id].score = dely[yy];
}
}
if (xx == len0 && yy < len1) {
    /* last col
    */
    if (endgaps)
        col1[yy] -= ins0+ins1*(len1-yy);
    if (col1[yy] > smax) {
        smax = col1[yy];
        dmax = id;
    }
}
}
if (endgaps && xx < len0)
    col1[yy-1] -= ins0+ins1*(len0-xx);
if (col1[yy-1] > smax) {
    smax = col1[yy-1];
    dmax = id;
}
tmp = col0; col0 = col1; col1 = tmp;
}
(void) free((char *)ndely);
(void) free((char *)dely);
(void) free((char *)col0);
(void) free((char *)col1);
}

```

TABLE 1-continued

```

/*
 *
 * print() -- only routine visible outside this module
 *
 * static:
 * getmat() -- trace back best path, count matches: print()
 * pr_align() -- print alignment of described in array p[]: print()
 * dumpblock() -- dump a block of lines with numbers, stars: pr_align()
 * nums() -- put out a number line: dumpblock()
 * putline() -- put out a line (name, [num], seq, [num]): dumpblock()
 * stars() -- put a line of stars: dumpblock()
 * stripname() -- strip any path and prefix from a seqname
 */
#include "nw.h"
#define SPC 3
#define P_LINE 256 /* maximum output line */
#define P_SPC 3 /* space between name or num and seq */
extern _day[26][26];
int olen; /* set output line length */
FILE *fx; /* output file */
print()
{
    int lx, ly, firstgap, lastgap; /* overlap */
    if ((fx = fopen(ofile, "w")) == 0) {
        fprintf(stderr, "%s: can't write %s\n", prog, ofile);
        cleanup(1);
    }
    fprintf(fx, "<first sequence: %s (length = %d)\n", namex[0], len0);
    fprintf(fx, "<second sequence: %s (length = %d)\n", namex[1], len1);
    olen = 60;
    lx = len0;
    ly = len1;
    firstgap = lastgap = 0;
    if (dmax < len1 - 1) { /* leading gap in x */
        pp[0].spc = firstgap = len1 - dmax - 1;
        ly -= pp[0].spc;
    }
    else if (dmax > len1 - 1) { /* leading gap in y */
        pp[1].spc = firstgap = dmax - (len1 - 1);
        lx -= pp[1].spc;
    }
    if (dmax0 < len0 - 1) { /* trailing gap in x */
        lastgap = len0 - dmax0 - 1;
        lx -= lastgap;
    }
    else if (dmax0 > len0 - 1) { /* trailing gap in y */
        lastgap = dmax0 - (len0 - 1);
        ly -= lastgap;
    }
    getmat(lx, ly, firstgap, lastgap);
    pr_align();
}
/*
 * trace back the best path, count matches
 */
static
getmat(lx, ly, firstgap, lastgap)
    int lx, ly; /* "core" (minus endgaps) */
    int firstgap, lastgap; /* leading trailing overlap */
{
    int nm, i0, i1, siz0, siz1;
    char outx[32];
    double pct;
    register n0, n1;
    register char *p0, *p1;
    /* get total matches, score
    */
    i0 = i1 = siz0 = siz1 = 0;
    p0 = seqx[0] + pp[1].spc;
    p1 = seqx[1] + pp[0].spc;
    n0 = pp[1].spc + 1;
    n1 = pp[0].spc + 1;
    nm = 0;
    while (*p0 && *p1) {
        if (siz0) {
            p1++;

```

TABLE 1-continued

```

        n1++;
        siz0--;
    }
    else if (siz1) {
        p0++;
        n0++;
        siz1--;
    }
    else {
        if (xbm[*p0-'A']&xbm[*p1-'A'])
            nm++;
        if (n0++ == pp[0].x[i0])
            siz0 = pp[0].n[i0++];
        if (n1++ == pp[1].x[i1])
            siz1 = pp[1].n[i1++];
        p0++;
        p1++;
    }
}
/* pct homology:
 * if penalizing endgaps, base is the shorter seq
 * else, knock off overhangs and take shorter core
 */
if (endgaps)
    lx = (len0 < len1)? len0 : len1;
else
    lx = (lx < ly)? lx : ly;
pct = 100.*(double)nm/(double)lx;
fprintf(fx, "\n");
fprintf(fx, "<endgaps in first sequence: %d", gapx);
if (gapx) {
    (void) sprintf(outx, "(%d %s)",
        ngapx, (dna)? "base": "residue", (ngapx == 1)? "" : "s");
    fprintf(fx, "%s", outx);
}
fprintf(fx, ", gaps in second sequence: %d", gapy);
if (gapy) {
    (void) sprintf(outx, "(%d %s)",
        ngapy, (dna)? "base": "residue", (ngapy == 1)? "" : "s");
    fprintf(fx, "%s", outx);
}
if (dna)
    fprintf(fx,
        "\n<score: %d (match = %d, mismatch = %d, gap penalty = %d + %d per base)\n",
        smax, DMAX, DMIS, DINS0, DINS1);
else
    fprintf(fx,
        "\n<score: %d (Dayhoff PAM 250 matrix, gap penalty = %d + %d per residue)\n",
        smax, PINS0, PINS1);
if (endgaps)
    fprintf(fx,
        "<endgaps penalized. left endgap: %d %s, right endgap: %d %s\n",
        firstgap, (dna)? "base": "residue", (firstgap == 1)? "" : "s",
        lastgap, (dna)? "base": "residue", (lastgap == 1)? "" : "s");
else
    fprintf(fx, "<endgaps not penalized\n");
}
static      nm;           /* matches in core -- for checking */
static      lmax;        /* lengths of stripped file names */
static      ij[2];       /* jmp index for a path */
static      nc[2];       /* number at start of current line */
static      ni[2];       /* current elem number -- for gapping */
static      siz[2];
static char *ps[2];      /* ptr to current element */
static char *po[2];      /* ptr to next output char slot */
static char out[2][P_LINE]; /* output line */
static char star[P_LINE]; /* set by stars() */
/*
 * print alignment of described in struct path pp[]
 */
static
pr_align()
{
    int      nn;          /* char count */
    int      more;

```

...getmat

pr_align

TABLE 1-continued

```

register i;
for (i = 0, lmax = 0; i < 2; i++) {
    nn = stripname(name[x[i]);
    if (nn > lmax)
        lmax = nn;
    nc[i] = 1;
    ni[i] = 1;
    siz[i] = ij[i] = 0;
    ps[i] = seq[x[i];
    po[i] = out[i];
}
for (nn = nm = 0, more = 1; more;) {
    for (i = more = 0; i < 2; i++) {
        /*
         * do we have more of this sequence?
         */
        if (!*ps[i])
            continue;
        more++;
        if (pp[i].spc) { /* leading space */
            *po[i]++ = ' ';
            pp[i].spc--;
        }
        else if (siz[i]) { /* in a gap */
            *po[i]++ = '-';
            siz[i]--;
        }
        else { /* we're putting a seq element
            */
            *po[i] = *ps[i];
            if (islower(*ps[i]))
                *ps[i] = toupper(*ps[i]);
            po[i]++;
            ps[i]++;
            /*
             * are we at next gap for this seq?
             */
            if (ni[i] == pp[i].x[ij[i]]) {
                /*
                 * we need to merge all gaps
                 * at this location
                 */
                siz[i] == pp[i].n[ij[i]++];
                while (ni[i] == pp[i].x[ij[i]])
                    siz[i] += pp[i].n[ij[i]++];
            }
            ni[i]++;
        }
    }
    if (++nn == olen || !more && nn) {
        dumpblock();
        for (i = 0; i < 2; i++)
            po[i] = out[i];
        nn = 0;
    }
}
}
/*
 * dump a block of lines, including numbers, stars: pr_align()
 */
static
dumpblock()
{
    register i;
    for (i = 0; i < 2; i++)
        *po[i]-- = '\0';

    (void) putc('\n', fx);
    for (i = 0; i < 2; i++) {
        if (*out[i] && (*out[i] != ' ' || *(po[i]) != ' ')) {
            if (i == 0)
                nums(i);
            if (i == 0 && *out[1])
                stars();
            putline(i);
            if (i == 0 && *out[1])

```

...pr_align

dumpblock

...dumpblock

TABLE 1-continued

```

        fprintf(fx, star);
        if (i == 1)
            nums(i);
    }
}
}
/*
* put out a number line: dumpblock()
*/
static
nums(ix)
int    ix;      /* index in out[] holding seq line */
{
    char    nline[P_LINE];
    register    i, j;
    register char    *pn, *px, *py;
    for(pn = nline, i = 0; i < lmax+P_SPC; i++, pn++)
        *pn = ' ';
    for (i = nc[ix], py = out[ix]; *py; py++, pn++) {
        if (*py == ' ' || *py == '-')
            *pn = ' ';
        else {
            if (i%10 == 0 || (i == 1 && nc[ix] != 1)) {
                j = (i < 0)? -i : i;
                for (px = pn; j; j/= 10, px--)
                    *px = j%10 + '0';
                if (i < 0)
                    *px = '-';
            }
            else
                *pn = ' ';
            i++;
        }
    }
    *pn = '\0';
    nc[ix] = i;
    for (pn = nline; *pn; pn++)
        (void) putc(*pn, fx);
    (void) putc('\n', fx);
}
/*
* put out a line (name, [num], seq. [num]): dumpblock()
*/
static
putline(ix)
int    ix;      {
    int    i;
    register char    *px;
    for (px = namex[ix], i = 0; *px && *px != ':'; px++, i++)
        (void) putc(*px, fx);
    for (i < lmax+P_SPC; i++)
        (void) putc(' ', fx);
    /* these count from 1:
    * ni[] is current element (from 1)
    * nc[] is number at start of current line
    */
    for (px = out[ix]; *px; px++)
        (void) putc(*px&0x7F, fx);
    (void) putc('\n', fx);
}
/*
* put a line of stars (seqs always in out[0], out[1]): dumpblock()
*/
static
stars()
{
    int    i;
    register char    *p0, *p1, cx, *px;
    if (!*out[0] || (*out[0] == ' ' && *(p0[0]) == ' ') ||
        !*out[1] || (*out[1] == ' ' && *(p0[1]) == ' '))
        return;
    px = star;
    for (i = lmax+P_SPC; i; i--)
        *px++ = ' ';
    for (p0 = out[0], p1 = out[1]; *p0 && *p1; p0++, p1++) {

```

nums

putline

...putline

stars

TABLE 1-continued

```

    if (isalpha(*p0) && isalpha(*p1)) {
        if (xbrm[*p0-'A']&xbrm[*p1-'A']) {
            cx = '*';
            nm++;
        }
        else if (!dna && __day[*p0-'A'][*p1-'A'] > 0)
            cx = '.';
        else
            cx = ' ';
    }
    else
        cx = ' ';
    *px++ = cx;
}
*px++ = '\n';
*px = '\0';
}
/*
 * strip path or prefix from pn, return len: pr_align()
 */
static
stripname(pn)
char *pn;          /* file name (may be path) */
{
    register char *px, *py;
    py = 0;
    for (px = pn; *px; px++)
        if (*px == '/')
            py = px + 1;
    if (py)
        (void) strcpy(pn, py);
    return(strlen(pn));
}
/*
 * cleanup() -- cleanup any tmp file
 * getseq() -- read in seq, set dna, len, maxlen
 * g_calloc() -- calloc() with error checkin
 * readjumps() -- get the good jumps, from tmp file if necessary
 * writejumps() -- write a filled array of jumps to a tmp file: nw()
 */
#include "nw.h"
#include <sys/file.h>
char *jname = "/tmp/homgXXXXXX"; /* tmp file for jumps */
FILE *fj;
int cleanup(); /* cleanup tmp file */
long lseek();
/*
 * remove any tmp file if we blow
 */
cleanup(i)
int i;
{
    if (fj)
        (void) unlink(jname);
    exit(i);
}
/*
 * read, return ptr to seq, set dna, len, maxlen
 * skip lines starting with ';', '<', or '>'
 * seq in upper or lower case
 */
char *
getseq(file, len)
char *file; /* file name */
int *len; /* seq len */
{
    char line[1024], *pseq;
    register char *px, *py;
    int natgc, tlen;
    FILE *fp;
    if ((fp = fopen(file, "r")) == 0) {
        fprintf(stderr, "%s: can't read %s\n", prog, file);
        exit(1);
    }
    tlen = natgc = 0;
    while (fgets(line, 1024, fp)) {

```

stripname

cleanup

getseq

TABLE 1-continued

```

    if (*line == ';' || *line == '<' || *line == '>')
        continue;
    for (px = line; *px != '\n'; px++)
        if (isupper(*px) || islower(*px))
            tlen++;
}
if ((pseq = malloc((unsigned)(tlen+6)) == 0) {
    fprintf(stderr, "%s: malloc() failed to get %d bytes for %s\n", prog, tlen+6, file);
    exit(1);
}
pseq[0] = pseq[1] = pseq[2] = pseq[3] = '\0';

```

...getseq

```

py = pseq + 4;
*len = tlen;
rewind(fp);
while (fgets(line, 1024, fp)) {
    if (*line == ';' || *line == '<' || *line == '>')
        continue;
    for (px = line; *px != '\n'; px++) {
        if (isupper(*px))
            *py++ = *px;
        else if (islower(*px))
            *py++ = toupper(*px);
        if (index("ATGCU", *(py-1)))
            natgc++;
    }
}
*py++ = '\0';
*py = '\0';
(void) fclose(fp);
dna = natgc > (tlen/3);
return(pseq+4);
}
char *
g__calloc(msg, nx, sz)
char *msg;          /* program, calling routine */
int nx, sz;         /* number and size of elements */
{
    char *px, *calloc();
    if ((px = calloc((unsigned)nx, (unsigned)sz)) == 0) {
        if (*msg) {
            fprintf(stderr, "%s: g__calloc() failed %s (n= %d, sz= %d)\n", prog, msg, nx, sz);
            exit(1);
        }
    }
    return(px);
}
/*
* get final jmps from dx[] or tmp file, set pp[], reset dmax: main()
*/
readjmps()
{
    int fd = -1;
    int siz, i0, i1;
    register i, j, xx;
    if (fj) {
        (void) fclose(fj);
        if ((fd = open(jname, O_RDONLY, 0)) < 0) {
            fprintf(stderr, "%s: can't open() %s\n", prog, jname);
            cleanup(1);
        }
    }
    for (i = i0 = i1 = 0, dmax0 = dmax, xx = len0; i++) {
        while (1) {
            for (j = dx[dmax].ijmp; j >= 0 && dx[dmax].jp.x[j] >= xx; j--)
                ;
            if (j < 0 && dx[dmax].offset && fj) {
                (void) lseek(fd, dx[dmax].offset, 0);
                (void) read(fd, (char *)&dx[dmax].jp, sizeof(struct jmp));
                (void) read(fd, (char *)&dx[dmax].offset, sizeof(dx[dmax].offset));
                dx[dmax].ijmp = MAXJMP-1;
            }
            else
                break;
        }
    }
}

```

g__calloc

readjmps

...readjmps

TABLE 1-continued

```

    if (i >= JMPS) {
        fprintf(stderr, "%s: too many gaps in alignment\n", prog);
        cleanup(1);
    }
    if (j >= 0) {
        siz = dx[dmax].jp.n[j];
        xx = dx[dmax].jp.x[j];
        dmax += siz;
        if (siz < 0) { /* gap in second seq */
            pp[1].n[i1] = -siz;
            xx += siz;
            /* id = xx - yy + len1 - 1
             */
            pp[1].x[i1] = xx - dmax + len1 - 1;
            gapyy++;
            ngapy -= siz;
/* ignore MAXGAP when doing endgaps */
            siz = (-siz < MAXGAP || endgaps)? -siz : MAXGAP;
            i1++;
        }
        else if (siz > 0) { /* gap in first seq */
            pp[0].n[i0] = siz;
            pp[0].x[i0] = xx;
            gapxx++;
            ngapx += siz;
/* ignore MAXGAP when doing endgaps */
            siz = (siz < MAXGAP || endgaps)? siz : MAXGAP;
            i0++;
        }
    }
    else
        break;
}
/* reverse the order of jmps
*/
for (j = 0, i0--; j < i0; j++, i0--) {
    i = pp[0].n[j]; pp[0].n[j] = pp[0].n[i0]; pp[0].n[i0] = i;
    i = pp[0].x[j]; pp[0].x[j] = pp[0].x[i0]; pp[0].x[i0] = i;
}
for (j = 0, i1--; j < i1; j++, i1--) {
    i = pp[1].n[j]; pp[1].n[j] = pp[1].n[i1]; pp[1].n[i1] = i;
    i = pp[1].x[j]; pp[1].x[j] = pp[1].x[i1]; pp[1].x[i1] = i;
}
if (fd >= 0)
    (void) close(fd);
if (fj) {
    (void) unlink(jname);
    fj = 0;
    offset = 0;
}
}
/*
* write a filled jmp struct offset of the prev one (if any): nw()
*/
writejmps(ix)
int ix;
{
    char *mktemp();
    if (!fj) {
        if (mktemp(jname) < 0) {
            fprintf(stderr, "%s: can't mktemp() %s\n", prog, jname);
            cleanup(1);
        }
        if ((fj = fopen(jname, "w")) == 0) {
            fprintf(stderr, "%s: can't write %s\n", prog, jname);
            exit(1);
        }
    }
    (void) fwrite((char *)&dx[ix].jp, sizeof(struct jmp), 1, fj);
    (void) fwrite((char *)&dx[ix].offset, sizeof(dx[ix].offset), 1, fj);
}

```

writejmps

[0249]

TABLE 2

PRO	XXXXXXXXXXXXXXXXXX	(Length = 15 amino acids)
Comparison Protein	XXXXXXXXYYYYYYY	(Length = 12 amino acids)

% amino acid sequence identity = (the number of identically matching amino acid residues between the two polypeptide sequences as determined by ALIGN-2) divided by (the total number of amino acid residues of the PRO polypeptide) = 5 divided by 15 = 33.3%

[0250]

TABLE 3

PRO	XXXXXXXXXX	(Length = 10 amino acids)
Comparison Protein	XXXXXXXXYYYYZZYZ	(Length = 15 amino acids)

% amino acid sequence identity = (the number of identically matching amino acid residues between the two polypeptide sequences as determined by ALIGN-2) divided by (the total number of amino acid residues of the PRO polypeptide) = 5 divided by 10 = 50%

[0251]

TABLE 4

PRO-DNA	NNNNNNNNNNNNNN	(Length = 14 nucleotides)
Comparison DNA	NNNNNLLLLLLLLLL	(Length = 16 nucleotides)

% nucleic acid sequence identity = (the number of identically matching nucleotides between the two nucleic acid sequences as determined by ALIGN-2) divided by (the total number of nucleotides of the PRO-DNA nucleic acid sequence) = 6 divided by 14 = 42.9%

[0252]

TABLE 5

PRO-DNA	NNNNNNNNNNNN	(Length = 12 nucleotides)
Comparison DNA	NNNLLLLV	(Length = 9 nucleotides)

% nucleic acid sequence identity = (the number of identically matching nucleotides between the two nucleic acid sequences as determined by ALIGN-2) divided by (the total number of nucleotides of the PRO-DNA nucleic acid sequence) = 4 divided by 12 = 33.3%

II. Compositions and Methods of the Invention

A. Full-Length PRO Polypeptides

[0253] The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO polypeptides. In particular, cDNAs encoding various PRO polypeptides have been identified and isolated, as disclosed in further detail in the Examples below. It is noted that proteins produced in separate expression rounds may be given different PRO numbers but the UNQ number is unique for any given DNA and the encoded protein, and will not be changed. However, for sake of simplicity, in the present specification the protein encoded by the full length native nucleic acid molecules disclosed herein as well as all further native homologues and variants included in the foregoing definition of PRO, will be referred to as "PRO/number", regardless of their origin or mode of preparation.

[0254] As disclosed in the Examples below, various cDNA clones have been deposited with the ATCC. The actual nucleotide sequences of those clones can readily be determined by the skilled artisan by sequencing of the deposited clone using routine methods in the art. The predicted amino acid sequence can be determined from the nucleotide sequence using routine skill. For the PRO polypeptides and encoding nucleic acids described herein, Applicants have identified what is believed to be the reading frame best identifiable with the sequence information available at the time.

B. PRO Polypeptide Variants

[0255] In addition to the full-length native sequence PRO polypeptides described herein, it is contemplated that PRO variants can be prepared. PRO variants can be prepared by introducing appropriate nucleotide changes into the PRO DNA, and/or by synthesis of the desired PRO polypeptide. Those skilled in the art will appreciate that amino acid changes may alter post-translational processes of the PRO, such as changing the number or position of glycosylation sites or altering the membrane anchoring characteristics.

[0256] Variations in the native full-length sequence PRO or in various domains of the PRO described herein, can be made, for example, using any of the techniques and guidelines for conservative and non-conservative mutations set forth, for instance, in U.S. Pat. No. 5,364,934. Variations may be a substitution, deletion or insertion of one or more codons encoding the PRO that results in a change in the amino acid sequence of the PRO as compared with the native sequence PRO. Optionally the variation is by substitution of at least one amino acid with any other amino acid in one or more of the domains of the PRO. Guidance in determining which amino acid residue may be inserted, substituted or deleted without adversely affecting the desired activity may be found by comparing the sequence of the PRO with that of homologous known protein molecules and minimizing the number of amino acid sequence changes made in regions of high homology. Amino acid substitutions can be the result of replacing one amino acid with another amino acid having similar structural and/or chemical properties, such as the replacement of a leucine with a serine, i.e., conservative amino acid replacements. Insertions or deletions may optionally be in the range of about 1 to 5 amino acids. The variation allowed may be determined by systematically making insertions, deletions or substitutions of amino acids in the sequence and testing the resulting variants for activity exhibited by the full-length or mature native sequence.

[0257] PRO polypeptide fragments are provided herein. Such fragments may be truncated at the N-terminus or C-terminus, or may lack internal residues, for example, when compared with a full length native protein. Certain fragments lack amino acid residues that are not essential for a desired biological activity of the PRO polypeptide.

[0258] PRO fragments may be prepared by any of a number of conventional techniques. Desired peptide fragments may be chemically synthesized. An alternative approach involves generating PRO fragments by enzymatic digestion, e.g., by treating the protein with an enzyme known to cleave proteins at sites defined by particular amino acid residues, or by digesting the DNA with suitable restric-

tion enzymes and isolating the desired fragment. Yet another suitable technique involves isolating and amplifying a DNA fragment encoding a desired polypeptide fragment, by polymerase chain reaction (PCR). Oligonucleotides that define the desired termini of the DNA fragment are employed at the 5' and 3' primers in the PCR. Preferably, PRO polypeptide fragments share at least one biological and/or immunological activity with the native PRO polypeptide disclosed herein.

[0259] In particular embodiments, conservative substitutions of interest are shown in Table 6 under the heading of preferred substitutions. If such substitutions result in a change in biological activity, then more substantial changes, denominated exemplary substitutions in Table 6, or as further described below in reference to amino acid classes, are introduced and the products screened.

TABLE 6

Original Residue	Exemplary Substitutions	Preferred Substitutions
Ala (A)	val; leu; ile	val
Arg (R)	lys; gln; asn	lys
Asn (N)	gln; his; lys; arg	gln
Asp (D)	glu	glu
Cys (C)	ser	ser
Gln (Q)	asn	asn
Glu (E)	asp	asp
Gly (G)	pro; ala	ala
His (H)	asn; gln; lys; arg	arg
Ile (I)	leu; val; met; ala; phe; norleucine	leu
Leu (L)	norleucine; ile; val; met; ala; phe	ile
Lys (K)	arg; gln; asn	arg
Met (M)	leu; phe; ile	leu
Phe (F)	leu; val; ile; ala; tyr	leu
Pro (P)	ala	ala
Ser (S)	thr	thr
Thr (T)	ser	ser
Trp (W)	tyr; phe	tyr
Tyr (Y)	trp; phe; thr; ser	phe
Val (V)	ile; leu; met; phe; ala; norleucine	leu

[0260] Substantial modifications in function or immunological identity of the PRO polypeptide are accomplished by selecting substitutions that differ significantly in their effect on maintaining (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a sheet or helical conformation, (b) the charge or hydrophobicity of the molecule at the target site, or (c) the bulk of the side chain. Naturally occurring residues are divided into groups based on common side-chain properties:

[0261] (1) hydrophobic: norleucine, met, ala, val, leu, ile;

[0262] (2) neutral hydrophilic: cys, ser, thr;

[0263] (3) acidic: asp, glu;

[0264] (4) basic: asn, gln, his, lys, arg;

[0265] (5) residues that influence chain orientation: gly, pro; and

[0266] (6) aromatic: trp, tyr, phe.

[0267] Non-conservative substitutions will entail exchanging a member of one of these classes for another

class. Such substituted residues also may be introduced into the conservative substitution sites or, more preferably, into the remaining (non-conserved) sites.

[0268] The variations can be made using methods known in the art such as oligonucleotide-mediated (site-directed) mutagenesis, alanine scanning, and PCR mutagenesis. Site-directed mutagenesis [Carter et al., Nucl. Acids Res., 13:4331 (1986); Zoller et al., Nucl. Acids Res., 10:6487 (1987)], cassette mutagenesis [Wells et al., Gene, 34:315 (1985)], restriction selection mutagenesis [Wells et al., Philos. Trans. R. Soc. London SerA, 317:415 (1986)] or other known techniques can be performed on the cloned DNA to produce the PRO variant DNA.

[0269] Scanning amino acid analysis can also be employed to identify one or more amino acids along a contiguous sequence. Among the preferred scanning amino acids are relatively small, neutral amino acids. Such amino acids include alanine, glycine, serine, and cysteine. Alanine is typically a preferred scanning amino acid among this group because it eliminates the side-chain beyond the beta-carbon and is less likely to alter the main-chain conformation of the variant [Cunningham and Wells, Science, 244: 1081-1085 (1989)]. Alanine is also typically preferred because it is the most common amino acid. Further, it is frequently found in both buried and exposed positions [Creighton, The Proteins, (W. H. Freeman & Co., N.Y.); Choithia, J. Mol. Biol., 150:1 (1976)]. If alanine substitution does not yield adequate amounts of variant, an isoteric amino acid can be used.

C. Modifications of PRO

[0270] Covalent modifications of PRO are included within the scope of this invention. One type of covalent modification includes reacting targeted amino acid residues of a PRO polypeptide with an organic derivatizing agent that is capable of reacting with selected side chains or the N- or C-terminal residues of the PRO. Derivatization with bifunctional agents is useful, for instance, for crosslinking PRO to a water-insoluble support matrix or surface for use in the method for purifying anti-PRO antibodies, and vice-versa. Commonly used crosslinking agents include, e.g., 1,1-bis(diazoacetyl)-2-phenylethane, glutaraldehyde, N-hydroxysuccinimide esters, for example, esters with 4-azidosalicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis(succinimidylpropionate), bifunctional maleimides such as bis-N-maleimido-1,8-octane and agents such as methyl-3-[(p-azidophenyl)dithio]propioimide.

[0271] Other modifications include deamidation of glutamyl and asparagyl residues to the corresponding glutamyl and aspartyl residues, respectively, hydroxylation of proline and lysine, phosphorylation of hydroxyl groups of seryl or threonyl residues, methylation of the α -amino groups of lysine, arginine, and histidine side chains [T. E. Creighton, Proteins: Structure and Molecular Properties, W. H. Freeman & Co., San Francisco, pp. 79-86 (1983)], acetylation of the N-terminal amine, and amidation of any C-terminal carboxyl group.

[0272] Another type of covalent modification of the PRO polypeptide included within the scope of this invention comprises altering the native glycosylation pattern of the polypeptide. "Altering the native glycosylation pattern" is

intended for purposes herein to mean deleting one or more carbohydrate moieties found in native sequence PRO (either by removing the underlying glycosylation site or by deleting the glycosylation by chemical and/or enzymatic means), and/or adding one or more glycosylation sites that are not present in the native sequence PRO. In addition, the phrase includes qualitative changes in the glycosylation of the native proteins, involving a change in the nature and proportions of the various carbohydrate moieties present.

[0273] Addition of glycosylation sites to the PRO polypeptide may be accomplished by altering the amino acid sequence. The alteration may be made, for example, by the addition of, or substitution by, one or more serine or threonine residues to the native sequence PRO (for O-linked glycosylation sites). The PRO amino acid sequence may optionally be altered through changes at the DNA level, particularly by mutating the DNA encoding the PRO polypeptide at preselected bases such that codons are generated that will translate into the desired amino acids.

[0274] Another means of increasing the number of carbohydrate moieties on the PRO polypeptide is by chemical or enzymatic coupling of glycosides to the polypeptide. Such methods are described in the art, e.g., in WO 87/05330 published Sep. 11, 1987, and in Aplin and Wriston, *CRC Crit. Rev. Biochem.*, pp. 259-306 (1981).

[0275] Removal of carbohydrate moieties present on the PRO polypeptide may be accomplished chemically or enzymatically or by mutational substitution of codons encoding for amino acid residues that serve as targets for glycosylation. Chemical deglycosylation techniques are known in the art and described, for instance, by Hakimuddin, et al., *Arch. Biochem. Biophys.*, 259:52 (1987) and by Edge et al., *Anal.*

[0276] *Biochem.*, 118:131 (1981). Enzymatic cleavage of carbohydrate moieties on polypeptides can be achieved by the use of a variety of endo- and exo-glycosidases as described by Thotakura et al., *Meth. Enzymol.*, 138:350 (1987).

[0277] Another type of covalent modification of PRO comprises linking the PRO polypeptide to one of a variety of nonproteinaceous polymers, e.g., polyethylene glycol (PEG), polypropylene glycol, or polyoxyalkylenes, in the manner set forth in U.S. Pat. Nos. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192 or 4,179,337.

[0278] The PRO of the present invention may also be modified in a way to form a chimeric molecule comprising PRO fused to another, heterologous polypeptide or amino acid sequence.

[0279] In one embodiment, such a chimeric molecule comprises a fusion of the PRO with a tag polypeptide which provides an epitope to which an anti-tag antibody can selectively bind. The epitope tag is generally placed at the amino- or carboxyl-terminus of the PRO. The presence of such epitope-tagged forms of the PRO can be detected using an antibody against the tag polypeptide. Also, provision of the epitope tag enables the PRO to be readily purified by affinity purification using an anti-tag antibody or another type of affinity matrix that binds to the epitope tag. Various tag polypeptides and their respective antibodies are well known in the art. Examples include poly-histidine (poly-his) or poly-histidine-glycine (poly-his-gly) tags; the flu HA tag polypeptide and its antibody 12CA5 [Field et al., *Mol. Cell.*

Biol., 8:2159-2165 (1988)]; the c-myc tag and the 8F9, 3C7, 6E10, G4, B7 and 9E10 antibodies thereto [Evan et al., *Molecular and Cellular Biology*, 5:3610-3616 (1985)]; and the Herpes Simplex virus glycoprotein D (gD) tag and its antibody [Paborsky et al., *Protein Engineering*, 3(6):547-553 (1990)]. Other tag polypeptides include the Flag-peptide [Hopp et al., *BioTechnology*, 6:1204-1210 (1988)]; the KT3 epitope peptide [Martin et al., *Science*, 255:192-194 (1992)]; an α -tubulin epitope peptide [Skinner et al., *J. Biol. Chem.*, 266:15163-15166 (1991)]; and the T7 gene 10 protein peptide tag [Lutz-Freyermuth et al., *Proc. Natl. Acad. Sci. USA*, 87:6393-6397 (1990)].

[0280] In an alternative embodiment, the chimeric molecule may comprise a fusion of the PRO with an immunoglobulin or a particular region of an immunoglobulin. For a bivalent form of the chimeric molecule (also referred to as an "immunoadhesin"), such a fusion could be to the Fc region of an IgG molecule. The Ig fusions preferably include the substitution of a soluble (transmembrane domain deleted or inactivated) form of a PRO polypeptide in place of at least one variable region within an Ig molecule. In a particularly preferred embodiment, the immunoglobulin fusion includes the hinge, CH2 and CH3, or the hinge, CH1, CH2 and CH3 regions of an IgG1 molecule. For the production of immunoglobulin fusions see also U.S. Pat. No. 5,428,130 issued Jun. 27, 1995.

D. Preparation of PRO

[0281] The description below relates primarily to production of PRO by culturing cells transformed or transfected with a vector containing PRO nucleic acid. It is, of course, contemplated that alternative methods, which are well known in the art, may be employed to prepare PRO. For instance, the PRO sequence, or portions thereof, may be produced by direct peptide synthesis using solid-phase techniques [see, e.g., Stewart et al., *Solid-Phase Peptide Synthesis*, W. H. Freeman Co., San Francisco, Calif. (1969); Merrifield, *J. Am. Chem. Soc.*, 85:2149-2154 (1963)]. In vitro protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be accomplished, for instance, using an Applied Biosystems Peptide Synthesizer (Foster City, Calif.) using manufacturer's instructions. Various portions of the PRO may be chemically synthesized separately and combined using chemical or enzymatic methods to produce the full-length PRO.

1. Isolation of DNA Encoding PRO

[0282] DNA encoding PRO may be obtained from a cDNA library prepared from tissue believed to possess the PRO mRNA and to express it at a detectable level. Accordingly, human PRO DNA can be conveniently obtained from a cDNA library prepared from human tissue, such as described in the Examples. The PRO-encoding gene may also be obtained from a genomic library or by known synthetic procedures (e.g., automated nucleic acid synthesis).

[0283] Libraries can be screened with probes (such as antibodies to the PRO or oligonucleotides of at least about 20-80 bases) designed to identify the gene of interest or the protein encoded by it. Screening the cDNA or genomic library with the selected probe may be conducted using

standard procedures, such as described in Sambrook et al., *Molecular Cloning: A Laboratory Manual* (New York: Cold Spring Harbor Laboratory Press, 1989). An alternative means to isolate the gene encoding PRO is to use PCR methodology [Sambrook et al., supra; Dieffenbach et al., *PCR Primer: A Laboratory Manual* (Cold Spring Harbor Laboratory Press, 1995)].

[0284] The Examples below describe techniques for screening a cDNA library. The oligonucleotide sequences selected as probes should be of sufficient length and sufficiently unambiguous that false positives are minimized. The oligonucleotide is preferably labeled such that it can be detected upon hybridization to DNA in the library being screened. Methods of labeling are well known in the art, and include the use of radiolabels like ^{32}P -labeled ATP, biotinylation or enzyme labeling. Hybridization conditions, including moderate stringency and high stringency, are provided in Sambrook et al., supra.

[0285] Sequences identified in such library screening methods can be compared and aligned to other known sequences deposited and available in public databases such as GenBank or other private sequence databases. Sequence identity (at either the amino acid or nucleotide level) within defined regions of the molecule or across the full-length sequence can be determined using methods known in the art and as described herein.

[0286] Nucleic acid having protein coding sequence may be obtained by screening selected cDNA or genomic libraries using the deduced amino acid sequence disclosed herein for the first time, and, if necessary, using conventional primer extension procedures as described in Sambrook et al., supra, to detect precursors and processing intermediates of mRNA that may not have been reverse-transcribed into cDNA.

2. Selection and Transformation of Host Cells

[0287] Host cells are transfected or transformed with expression or cloning vectors described herein for PRO production and cultured in conventional nutrient media modified as appropriate for inducing promoters, selecting transformants, or amplifying the genes encoding the desired sequences. The culture conditions, such as media, temperature, pH and the like, can be selected by the skilled artisan without undue experimentation. In general, principles, protocols, and practical techniques for maximizing the productivity of cell cultures can be found in *Mammalian Cell Biotechnology: a Practical Approach*, M. Butler, ed. (IRL Press, 1991) and Sambrook et al., supra.

[0288] Methods of eukaryotic cell transfection and prokaryotic cell transformation are known to the ordinarily skilled artisan, for example, CaCl_2 , CaPO_4 , liposome-mediated and electroporation. Depending on the host cell used, transformation is performed using standard techniques appropriate to such cells. The calcium treatment employing calcium chloride, as described in Sambrook et al., supra, or electroporation is generally used for prokaryotes. Infection with *Agrobacterium tumefaciens* is used for transformation of certain plant cells, as described by Shaw et al., *Gene*, 23:315 (1983) and WO 89/05859 published Jun. 29, 1989. For mammalian cells without such cell walls, the calcium phosphate precipitation method of Graham and van der Eb, *Virology*, 52:456-457 (1978) can be employed. General

aspects of mammalian cell host system transfections have been described in U.S. Pat. No. 4,399,216. Transformations into yeast are typically carried out according to the method of Van Solingen et al., *J. Bact.*, 130:946 (1977) and Hsiao et al., *Proc. Natl. Acad. Sci. (USA)*, 76:3829 (1979). However, other methods for introducing DNA into cells, such as by nuclear microinjection, electroporation, bacterial protoplast fusion with intact cells, or polycations, e.g., polybrene, polyornithine, may also be used. For various techniques for transforming mammalian cells, see Keown et al., *Methods in Enzymology*, 185:527-537 (1990) and Mansour et al., *Nature*, 336:348-352 (1988).

[0289] Suitable host cells for cloning or expressing the DNA in the vectors herein include prokaryote, yeast, or higher eukaryote cells. Suitable prokaryotes include but are not limited to eubacteria, such as Gram-negative or Gram-positive organisms, for example, Enterobacteriaceae such as *E. coli*. Various *E. coli* strains are publicly available, such as *E. coli* K12 strain MM294 (ATCC 31,446); *E. coli* X1776 (ATCC 31,537); *E. coli* strain W3110 (ATCC 27,325) and K5 772 (ATCC 53,635). Other suitable prokaryotic host cells include Enterobacteriaceae such as Escherichia, e.g., *E. coli*, Enterobacter, Erwinia, Klebsiella, Proteus, Salmonella, e.g., *Salmonella typhimurium*, Serratia, e.g., *Serratia marcescans*, and Shigella, as well as Bacilli such as *B. subtilis* and *B. licheniformis* (e.g., *B. licheniformis* 41P disclosed in DD 266,710 published Apr. 12, 1989), Pseudomonas such as *P. aeruginosa*, and Streptomyces. These examples are illustrative rather than limiting. Strain W3110 is one particularly preferred host or parent host because it is a common host strain for recombinant DNA product fermentations. Preferably, the host cell secretes minimal amounts of proteolytic enzymes. For example, strain W3110 may be modified to effect a genetic mutation in the genes encoding proteins endogenous to the host, with examples of such hosts including *E. coli* W3110 strain 1A2, which has the complete genotype tonA; *E. coli* W3110 strain 9E4, which has the complete genotype tonA ptr3; *E. coli* W3110 strain 27C7 (ATCC 55,244), which has the complete genotype tonA ptr3 phoA E15 (argF-lac)169 degP ompT kan^r; *E. coli* W3110 strain 37D6, which has the complete genotype tonA ptr3 phoA E15 (argF-lac)169 degP ompT rbs7 ilvG kan^r; *E. coli* W3110 strain 40B4, which is strain 37D6 with a non-kanamycin resistant degP deletion mutation; and an *E. coli* strain having mutant periplasmic protease disclosed in U.S. Pat. No. 4,946,783 issued Aug. 7, 1990. Alternatively, in vitro methods of cloning, e.g., PCR or other nucleic acid polymerase reactions, are suitable.

[0290] In addition to prokaryotes, eukaryotic microbes such as filamentous fungi or yeast are suitable cloning or expression hosts for PRO-encoding vectors. *Saccharomyces cerevisiae* is a commonly used lower eukaryotic host microorganism. Others include *Schizosaccharomyces pombe* (Beach and Nurse, *Nature*, 290: 140 [1981]; EP 139,383 published May 2, 1985); Kluyveromyces hosts (U.S. Pat. No. 4,943,529; Fleer et al., *Bio/Technology*, 9:968-975 (1991)) such as, e.g., *K. lactis* (MW98-8C, CBS683, CBS4574; Louvencourt et al., *J. Bacteriol.*, 154(2):737-742 [1983]), *K. fragilis* (ATCC 12,424), *K. bulgaricus* (ATCC 16,045), *K. wickerhamii* (ATCC 24,178), *K. waltii* (ATCC 56,500), *K. drosophilorum* (ATCC 36,906; Van den Berg et al., *Bio/Technology*, 8:135 (1990)), *K. thermotolerans*, and *K. marxianus*; yarrowia (EP 402,226); *Pichia pastoris* (EP 183,070; Sreerikshna et al., *J. Basic Microbiol.*, 28:265-278

[1988]); *Candida*; *Trichoderma reesia* (EP 244,234); *Neurospora crassa* (Case et al., Proc. Natl. Acad. Sci. USA, 76:5259-5263 [1979]); Schwanniomyces such as *Schwanniomyces occidentalis* (EP 394,538 published Oct. 31, 1990); and filamentous fungi such as, e.g., *Neurospora*, *Penicillium*, *Tolypocladium* (WO 91/000357 published Jan. 10, 1991), and *Aspergillus* hosts such as *A. nidulans* (Ballance et al., Biochem. Biophys. Res. Commun., 112:284-289 [1983]; Tilburn et al., Gene, 26:205-221 [1983]; Yelton et al., Proc. Natl. Acad. Sci. USA, 81: 1470-1474 [1984]) and *A. niger* (Kelly and Hynes, EMBO J., 4:475-479 [1985]). Methylotrophic yeasts are suitable herein and include, but are not limited to, yeast capable of growth on methanol selected from the genera consisting of *Hansenula*, *Candida*, *Kloeckera*, *Pichia*, *Saccharomyces*, *Torulopsis*, and *Rhodotorula*. A list of specific species that are exemplary of this class of yeasts may be found in C. Anthony, The Biochemistry of Methylotrophs, 269 (1982).

[0291] Suitable host cells for the expression of glycosylated PRO are derived from multicellular organisms. Examples of invertebrate cells include insect cells such as *Drosophila* S2 and *Spodoptera* Sf9, as well as plant cells. Examples of useful mammalian host cell lines include Chinese hamster ovary (CHO) and COS cells. More specific examples include monkey kidney CV1 line transformed by SV40 (COS-7, ATCC CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture, Graham et al., J. Gen. Virol., 36:59 (1977)); Chinese hamster ovary cells/-DHFR (CHO, Urlaub and Chasin, Proc. Natl. Acad. Sci. USA, 77:4216 (1980)); mouse sertoli cells (TM4, Mather, Biol. Reprod., 23:243-251 (1980)); human lung cells (W138, ATCC CCL 75); human liver cells (Hep G2, HB 8065); and mouse mammary tumor (MMT 060562, ATCC CCL51). The selection of the appropriate host cell is deemed to be within the skill in the art.

3. Selection and Use of a Replicable Vector

[0292] The nucleic acid (e.g., cDNA or genomic DNA) encoding PRO may be inserted into a replicable vector for cloning (amplification of the DNA) or for expression. Various vectors are publicly available. The vector may, for example, be in the form of a plasmid, cosmid, viral particle, or phage. The appropriate nucleic acid sequence may be inserted into the vector by a variety of procedures. In general, DNA is inserted into an appropriate restriction endonuclease site(s) using techniques known in the art. Vector components generally include, but are not limited to, one or more of a signal sequence, an origin of replication, one or more marker genes, an enhancer element, a promoter, and a transcription termination sequence. Construction of suitable vectors containing one or more of these components employs standard ligation techniques which are known to the skilled artisan.

[0293] The PRO may be produced recombinantly not only directly, but also as a fusion polypeptide with a heterologous polypeptide, which may be a signal sequence or other polypeptide having a specific cleavage site at the N-terminus of the mature protein or polypeptide. In general, the signal sequence may be a component of the vector, or it may be a part of the PRO-encoding DNA that is inserted into the vector. The signal sequence may be a prokaryotic signal sequence selected, for example, from the group of the alkaline phosphatase, penicillinase, lpp, or heat-stable

enterotoxin II leaders. For yeast secretion the signal sequence may be, e.g., the yeast invertase leader, alpha factor leader (including *Saccharomyces* and *Kluyveromyces* α -factor leaders, the latter described in U.S. Pat. No. 5,010, 182), or acid phosphatase leader, the *C. albicans* glucoamylase leader (EP 362,179 published Apr. 4, 1990), or the signal described in WO 90/13646 published Nov. 15, 1990. In mammalian cell expression, mammalian signal sequences may be used to direct secretion of the protein, such as signal sequences from secreted polypeptides of the same or related species, as well as viral secretory leaders.

[0294] Both expression and cloning vectors contain a nucleic acid sequence that enables the vector to replicate in one or more selected host cells. Such sequences are well known for a variety of bacteria, yeast, and viruses. The origin of replication from the plasmid pBR322 is suitable for most Gram-negative bacteria, the 2μ plasmid origin is suitable for yeast, and various viral origins (SV40, polyoma, adenovirus, VSV or BPV) are useful for cloning vectors in mammalian cells.

[0295] Expression and cloning vectors will typically contain a selection gene, also termed a selectable marker. Typical selection genes encode proteins that (a) confer resistance to antibiotics or other toxins, e.g., ampicillin, neomycin, methotrexate, or tetracycline, (b) complement auxotrophic deficiencies, or (c) supply critical nutrients not available from complex media, e.g., the gene encoding D-alanine racemase for *Bacilli*.

[0296] An example of suitable selectable markers for mammalian cells are those that enable the identification of cells competent to take up the PRO-encoding nucleic acid, such as DHFR or thymidine kinase. An appropriate host cell when wild-type DHFR is employed is the CHO cell line deficient in DHFR activity, prepared and propagated as described by Urlaub et al., Proc. Natl. Acad. Sci. USA, 77:4216 (1980). A suitable selection gene for use in yeast is the *trp 1* gene present in the yeast plasmid YRp7 [Stinchcomb et al., Nature, 282:39 (1979); Kingsman et al., Gene, 7:141 (1979); Tschemper et al., Gene, 10:157 (1980)]. The *trp 1* gene provides a selection marker for a mutant strain of yeast lacking the ability to grow in tryptophan, for example, ATCC No. 44076 or PEP4-1 [Jones, Genetics, 85:12 (1977)].

[0297] Expression and cloning vectors usually contain a promoter operably linked to the PRO-encoding nucleic acid sequence to direct mRNA synthesis. Promoters recognized by a variety of potential host cells are well known. Promoters suitable for use with prokaryotic hosts include the β -lactamase and lactose promoter systems [Chang et al., Nature, 275:615 (1978); Goeddel et al., Nature, 281:544 (1979)], alkaline phosphatase, a tryptophan (*trp*) promoter system [Goeddel, Nucleic Acids Res., 8:4057 (1980); EP 36,776], and hybrid promoters such as the *tac* promoter [deBoer et al., Proc. Natl. Acad. Sci. USA, 80:21-25 (1983)]. Promoters for use in bacterial systems also will contain a Shine-Dalgarno (S.D.) sequence operably linked to the DNA encoding PRO.

[0298] Examples of suitable promoting sequences for use with yeast hosts include the promoters for 3-phosphoglycerate kinase [Hitzeman et al., J. Biol. Chem., 255:2073 (1980)] or other glycolytic enzymes [Hess et al., J. Adv. Enzyme Reg., 7:149 (1968); Holland, Biochemistry,

17:4900 (1978)], such as enolase, glyceraldehyde-3-phosphate dehydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase, glucose-6-phosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, phosphoglucose isomerase, and glucokinase.

[0299] Other yeast promoters, which are inducible promoters having the additional advantage of transcription controlled by growth conditions, are the promoter regions for alcohol dehydrogenase 2, isocytochrome C, acid phosphatase, degradative enzymes associated with nitrogen metabolism, metallothionein, glyceraldehyde-3-phosphate dehydrogenase, and enzymes responsible for maltose and galactose utilization. Suitable vectors and promoters for use in yeast expression are further described in EP 73,657.

[0300] PRO transcription from vectors in mammalian host cells is controlled, for example, by promoters obtained from the genomes of viruses such as polyoma virus, fowlpox virus (UK 2,211,504 published Jul. 5, 1989), adenovirus (such as Adenovirus 2), bovine papilloma virus, avian sarcoma virus, cytomegalovirus, a retrovirus, hepatitis-B virus and Simian Virus 40 (SV40), from heterologous mammalian promoters, e.g., the actin promoter or an immunoglobulin promoter, and from heat-shock promoters, provided such promoters are compatible with the host cell systems.

[0301] Transcription of a DNA encoding the PRO by higher eukaryotes may be increased by inserting an enhancer sequence into the vector. Enhancers are cis-acting elements of DNA, usually about from 10 to 300 bp, that act on a promoter to increase its transcription. Many enhancer sequences are now known from mammalian genes (globin, elastase, albumin, α -fetoprotein, and insulin). Typically, however, one will use an enhancer from a eukaryotic cell virus. Examples include the SV40 enhancer on the late side of the replication origin (bp 100-270), the cytomegalovirus early promoter enhancer, the polyoma enhancer on the late side of the replication origin, and adenovirus enhancers. The enhancer may be spliced into the vector at a position 5' or 3' to the PRO coding sequence, but is preferably located at a site 5' from the promoter.

[0302] Expression vectors used in eukaryotic host cells (yeast, fungi, insect, plant, animal, human, or nucleated cells from other multicellular organisms) will also contain sequences necessary for the termination of transcription and for stabilizing the mRNA. Such sequences are commonly available from the 5' and, occasionally 3', untranslated regions of eukaryotic or viral DNAs or cDNAs. These regions contain nucleotide segments transcribed as polyadenylated fragments in the untranslated portion of the mRNA encoding PRO.

[0303] Still other methods, vectors, and host cells suitable for adaptation to the synthesis of PRO in recombinant vertebrate cell culture are described in Gething et al., *Nature*, 293:620-625 (1981); Mantei et al., *Nature*, 281:40-46 (1979); EP 117,060; and EP 117,058.

4. Detecting Gene Amplification/Expression

[0304] Gene amplification and/or expression may be measured in a sample directly, for example, by conventional Southern blotting, Northern blotting to quantitate the transcription of mRNA [Thomas, *Proc. Natl. Acad. Sci. USA*,

77:5201(1980)], dot blotting (DNA analysis), or in situ hybridization, using an appropriately labeled probe, based on the sequences provided herein. Alternatively, antibodies may be employed that can recognize specific duplexes, including DNA duplexes, RNA duplexes, and DNA-RNA hybrid duplexes or DNA-protein duplexes. The antibodies in turn may be labeled and the assay may be carried out where the duplex is bound to a surface, so that upon the formation of duplex on the surface, the presence of antibody bound to the duplex can be detected.

[0305] Gene expression, alternatively, may be measured by immunological methods, such as immunohistochemical staining of cells or tissue sections and assay of cell culture or body fluids, to quantitate directly the expression of gene product. Antibodies useful for immunohistochemical staining and/or assay of sample fluids may be either monoclonal or polyclonal, and may be prepared in any mammal. Conveniently, the antibodies may be prepared against a native sequence PRO polypeptide or against a synthetic peptide based on the DNA sequences provided herein or against exogenous sequence fused to PRO DNA and encoding a specific antibody epitope.

5. Purification of Polypeptide

[0306] Forms of PRO may be recovered from culture medium or from host cell lysates. If membrane-bound, it can be released from the membrane using a suitable detergent solution (e.g. Triton-X 100) or by enzymatic cleavage. Cells employed in expression of PRO can be disrupted by various physical or chemical means, such as freeze-thaw cycling, sonication, mechanical disruption, or cell lysing agents.

[0307] It may be desired to purify PRO from recombinant cell proteins or polypeptides. The following procedures are exemplary of suitable purification procedures: by fractionation on an ion-exchange column; ethanol precipitation; reverse phase HPLC; chromatography on silica or on a cation-exchange resin such as DEAE; chromatofocusing; SDS-PAGE; ammonium sulfate precipitation; gel filtration using, for example, Sephadex G-75; protein A Sepharose columns to remove contaminants such as IgG; and metal chelating columns to bind epitope-tagged forms of the PRO. Various methods of protein purification may be employed and such methods are known in the art and described for example in Deutscher, *Methods in Enzymology*, 182 (1990); Scopes, *Protein Purification: Principles and Practice*, Springer-Verlag, New York (1982). The purification step(s) selected will depend, for example, on the nature of the production process used and the particular PRO produced.

E. Uses for PRO

[0308] Nucleotide sequences (or their complement) encoding PRO have various applications in the art of molecular biology, including uses as hybridization probes, in chromosome and gene mapping and in the generation of anti-sense RNA and DNA. PRO nucleic acid will also be useful for the preparation of PRO polypeptides by the recombinant techniques described herein.

[0309] The full-length native sequence PRO gene, or portions thereof, may be used as hybridization probes for a cDNA library to isolate the full-length PRO cDNA or to isolate still other cDNAs (for instance, those encoding naturally-occurring variants of PRO or PRO from other

species) which have a desired sequence identity to the native PRO sequence disclosed herein. Optionally, the length of the probes will be about 20 to about 50 bases. The hybridization probes may be derived from at least partially novel regions of the full length native nucleotide sequence wherein those regions may be determined without undue experimentation or from genomic sequences including promoters, enhancer elements and introns of native sequence PRO. By way of example, a screening method will comprise isolating the coding region of the PRO gene using the known DNA sequence to synthesize a selected probe of about 40 bases. Hybridization probes may be labeled by a variety of labels, including radionucleotides such as ^{32}P or ^{35}S , or enzymatic labels such as alkaline phosphatase coupled to the probe via avidin/biotin coupling systems. Labeled probes having a sequence complementary to that of the PRO gene of the present invention can be used to screen libraries of human cDNA, genomic DNA or mRNA to determine which members of such libraries the probe hybridizes to. Hybridization techniques are described in further detail in the Examples below.

[0310] Any EST sequences disclosed in the present application may similarly be employed as probes, using the methods disclosed herein.

[0311] Other useful fragments of the PRO nucleic acids include antisense or sense oligonucleotides comprising a single-stranded nucleic acid sequence (either RNA or DNA) capable of binding to target PRO mRNA (sense) or PRO DNA (antisense) sequences. Antisense or sense oligonucleotides, according to the present invention, comprise a fragment of the coding region of PRO DNA. Such a fragment generally comprises at least about 14 nucleotides, preferably from about 14 to 30 nucleotides. The ability to derive an antisense or a sense oligonucleotide, based upon a cDNA sequence encoding a given protein is described in, for example, Stein and Cohen (Cancer Res. 48:2659, 1988) and van der Krol et al. (BioTechniques 6:958, 1988).

[0312] Binding of antisense or sense oligonucleotides to target nucleic acid sequences results in the formation of duplexes that block transcription or translation of the target sequence by one of several means, including enhanced degradation of the duplexes, premature termination of transcription or translation, or by other means. The antisense oligonucleotides thus may be used to block expression of PRO proteins. Antisense or sense oligonucleotides further comprise oligonucleotides having modified sugar-phosphodiester backbones (or other sugar linkages, such as those described in WO 91/06629) and wherein such sugar linkages are resistant to endogenous nucleases. Such oligonucleotides with resistant sugar linkages are stable in vivo (i.e., capable of resisting enzymatic degradation) but retain sequence specificity to be able to bind to target nucleotide sequences.

[0313] Other examples of sense or antisense oligonucleotides include those oligonucleotides which are covalently linked to organic moieties, such as those described in WO 90/10048, and other moieties that increases affinity of the oligonucleotide for a target nucleic acid sequence, such as poly-(L-lysine). Further still, intercalating agents, such as ellipticine, and alkylating agents or metal may be attached to sense or antisense oligonucleotides to modify binding specificities of the antisense or sense oligonucleotide for the target nucleotide sequence.

[0314] Antisense or sense oligonucleotides may be introduced into a cell containing the target nucleic acid sequence by any gene transfer method, including, for example, CaPO_4 -mediated DNA transfection, electroporation, or by using gene transfer vectors such as Epstein-Barr virus. In a preferred procedure, an antisense or sense oligonucleotide is inserted into a suitable retroviral vector. A cell containing the target nucleic acid sequence is contacted with the recombinant retroviral vector, either in vivo or ex vivo. Suitable retroviral vectors include, but are not limited to, those derived from the murine retrovirus M-MuLV, N2 (a retrovirus derived from M-MuLV), or the double copy vectors designated DCT5A, DCT5B and DCT5C (see WO 90/13641).

[0315] Sense or antisense oligonucleotides also may be introduced into a cell containing the target nucleotide sequence by formation of a conjugate with a ligand binding molecule, as described in WO 91/04753. Suitable ligand binding molecules include, but are not limited to, cell surface receptors, growth factors, other cytokines, or other ligands that bind to cell surface receptors. Preferably, conjugation of the ligand binding molecule does not substantially interfere with the ability of the ligand binding molecule to bind to its corresponding molecule or receptor, or block entry of the sense or antisense oligonucleotide or its conjugated version into the cell.

[0316] Alternatively, a sense or an antisense oligonucleotide may be introduced into a containing the target nucleic acid sequence by formation of an oligonucleotide-lipid complex, as described in WO 90/10448. The sense or antisense oligonucleotide-lipid complex is preferably dissociated within the cell by an endogenous lipase.

[0317] Antisense or sense RNA or DNA molecules are generally at least about 5 bases in length, about 10 bases in length, about 15 bases in length, about 20 bases in length, about 25 bases in length, about 30 bases in length, about 35 bases in length, about 40 bases in length, about 45 bases in length, about 50 bases in length, about 55 bases in length, about 60 bases in length, about 65 bases in length, about 70 bases in length, about 75 bases in length, about 80 bases in length, about 85 bases in length, about 90 bases in length, about 95 bases in length, about 100 bases in length, or more.

[0318] The probes may also be employed in PCR techniques to generate a pool of sequences for identification of closely related PRO coding sequences.

[0319] Nucleotide sequences encoding a PRO can also be used to construct hybridization probes for mapping the gene which encodes that PRO and for the genetic analysis of individuals with genetic disorders. The nucleotide sequences provided herein may be mapped to a chromosome and specific regions of a chromosome using known techniques, such as in situ hybridization, linkage analysis against known chromosomal markers, and hybridization screening with libraries.

[0320] When the coding sequences for PRO encode a protein which binds to another protein (example, where the PRO is a receptor), the PRO can be used in assays to identify the other proteins or molecules involved in the binding interaction. By such methods, inhibitors of the receptor/ligand binding interaction can be identified. Proteins involved in such binding interactions can also be used to

screen for peptide or small molecule inhibitors or agonists of the binding interaction. Also, the receptor PRO can be used to isolate correlative ligand(s). Screening assays can be designed to find lead compounds that mimic the biological activity of a native PRO or a receptor for PRO. Such screening assays will include assays amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates. Small molecules contemplated include synthetic organic or inorganic compounds. The assays can be performed in a variety of formats, including protein-protein binding assays, biochemical screening assays, immunoassays and cell based assays, which are well characterized in the art.

[0321] Nucleic acids which encode PRO or its modified forms can also be used to generate either transgenic animals or “knock out” animals which, in turn, are useful in the development and screening of therapeutically useful reagents. A transgenic animal (e.g., a mouse or rat) is an animal having cells that contain a transgene, which transgene was introduced into the animal or an ancestor of the animal at a prenatal, e.g., an embryonic stage. A transgene is a DNA which is integrated into the genome of a cell from which a transgenic animal develops. In one embodiment, cDNA encoding PRO can be used to clone genomic DNA encoding PRO in accordance with established techniques and the genomic sequences used to generate transgenic animals that contain cells which express DNA encoding PRO. Methods for generating transgenic animals, particularly animals such as mice or rats, have become conventional in the art and are described, for example, in U.S. Pat. Nos. 4,736,866 and 4,870,009. Typically, particular cells would be targeted for PRO transgene incorporation with tissue-specific enhancers. Transgenic animals that include a copy of a transgene encoding PRO introduced into the germ line of the animal at an embryonic stage can be used to examine the effect of increased expression of DNA encoding PRO. Such animals can be used as tester animals for reagents thought to confer protection from, for example, pathological conditions associated with its overexpression. In accordance with this facet of the invention, an animal is treated with the reagent and a reduced incidence of the pathological condition, compared to untreated animals bearing the transgene, would indicate a potential therapeutic intervention for the pathological condition.

[0322] Alternatively, non-human homologues of PRO can be used to construct a PRO “knock out” animal which has a defective or altered gene encoding PRO as a result of homologous recombination between the endogenous gene encoding PRO and altered genomic DNA encoding PRO introduced into an embryonic stem cell of the animal. For example, cDNA encoding PRO can be used to clone genomic DNA encoding PRO in accordance with established techniques. A portion of the genomic DNA encoding PRO can be deleted or replaced with another gene, such as a gene encoding a selectable marker which can be used to monitor integration. Typically, several kilobases of unaltered flanking DNA (both at the 5' and 3' ends) are included in the vector [see e.g., Thomas and Capecchi, *Cell*, 51:503 (1987) for a description of homologous recombination vectors]. The vector is introduced into an embryonic stem cell line by electroporation and cells in which the introduced DNA has homologously recombined with the endogenous DNA are selected [see e.g., Li et al., *Cell*, 69:915 (1992)]. The

selected cells are then injected into a blastocyst of an animal (e.g., a mouse or rat) to form aggregation chimeras [see e.g., Bradley, in *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, E. J. Robertson, ed. (IRL, Oxford, 1987), pp. 113-152]. A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and the embryo brought to term to create a “knock out” animal. Progeny harboring the homologously recombined DNA in their germ cells can be identified by standard techniques and used to breed animals in which all cells of the animal contain the homologously recombined DNA. Knock-out animals can be characterized for instance, for their ability to defend against certain pathological conditions and for their development of pathological conditions due to absence of the PRO polypeptide.

[0323] Nucleic acid encoding the PRO polypeptides may also be used in gene therapy. In gene therapy applications, genes are introduced into cells in order to achieve in vivo synthesis of a therapeutically effective genetic product, for example for replacement of a defective gene. “Gene therapy” includes both conventional gene therapy where a lasting effect is achieved by a single treatment, and the administration of gene therapeutic agents, which involves the one time or repeated administration of a therapeutically effective DNA or mRNA. Antisense RNAs and DNAs can be used as therapeutic agents for blocking the expression of certain genes in vivo. It has already been shown that short antisense oligonucleotides can be imported into cells where they act as inhibitors, despite their low intracellular concentrations caused by their restricted uptake by the cell membrane. (Zamecnik et al., *Proc. Natl. Acad. Sci. USA* 83:4143-4146 [1986]). The oligonucleotides can be modified to enhance their uptake, e.g. by substituting their negatively charged phosphodiester groups by uncharged groups.

[0324] There are a variety of techniques available for introducing nucleic acids into viable cells. The techniques vary depending upon whether the nucleic acid is transferred into cultured cells in vitro, or in vivo in the cells of the intended host. Techniques suitable for the transfer of nucleic acid into mammalian cells in vitro include the use of liposomes, electroporation, microinjection, cell fusion, DEAE-dextran, the calcium phosphate precipitation method, etc. The currently preferred in vivo gene transfer techniques include transfection with viral (typically retroviral) vectors and viral coat protein-liposome mediated transfection (Dzau et al., *Trends in Biotechnology* 11, 205-210 [1993]). In some situations it is desirable to provide the nucleic acid source with an agent that targets the target cells, such as an antibody specific for a cell surface membrane protein or the target cell, a ligand for a receptor on the target cell, etc. Where liposomes are employed, proteins which bind to a cell surface membrane protein associated with endocytosis may be used for targeting and/or to facilitate uptake, e.g. capsid proteins or fragments thereof tropic for a particular cell type, antibodies for proteins which undergo internalization in cycling, proteins that target intracellular localization and enhance intracellular half-life. The technique of receptor-mediated endocytosis is described, for example, by Wu et al., *J. Biol. Chem.* 262, 4429-4432 (1987); and Wagner et al., *Proc. Natl. Acad. Sci. USA* 87, 3410-3414 (1990). For review of gene marking and gene therapy protocols see Anderson et al., *Science* 256, 808-813 (1992).

[0325] The PRO polypeptides described herein may also be employed as molecular weight markers for protein electrophoresis purposes and the isolated nucleic acid sequences may be used for recombinantly expressing those markers.

[0326] The nucleic acid molecules encoding the PRO polypeptides or fragments thereof described herein are useful for chromosome identification. In this regard, there exists an ongoing need to identify new chromosome markers, since relatively few chromosome marking reagents, based upon actual sequence data are presently available. Each PRO nucleic acid molecule of the present invention can be used as a chromosome marker.

[0327] The PRO polypeptides and nucleic acid molecules of the present invention may also be used diagnostically for tissue typing, wherein the PRO polypeptides of the present invention may be differentially expressed in one tissue as compared to another, preferably in a diseased tissue as compared to a normal tissue of the same tissue type. PRO nucleic acid molecules will find use for generating probes for PCR, Northern analysis, Southern analysis and Western analysis.

[0328] The PRO polypeptides described herein may also be employed as therapeutic agents. The PRO polypeptides of the present invention can be formulated according to known methods to prepare pharmaceutically useful compositions, whereby the PRO product hereof is combined in admixture with a pharmaceutically acceptable carrier vehicle. Therapeutic formulations are prepared for storage by mixing the active ingredient having the desired degree of purity with optional physiologically acceptable carriers, excipients or stabilizers (Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980)), in the form of lyophilized formulations or aqueous solutions. Acceptable carriers, excipients or stabilizers are nontoxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate and other organic acids; antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone, amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as TWEEN™, PLURONICS™ or PEG.

[0329] The formulations to be used for in vivo administration must be sterile. This is readily accomplished by filtration through sterile filtration membranes, prior to or following lyophilization and reconstitution.

[0330] Therapeutic compositions herein generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

[0331] The route of administration is in accord with known methods, e.g. injection or infusion by intravenous, intraperitoneal, intracerebral, intramuscular, intraocular, intraarterial or intralesional routes, topical administration, or by sustained release systems.

[0332] Dosages and desired drug concentrations of pharmaceutical compositions of the present invention may vary

depending on the particular use envisioned. The determination of the appropriate dosage or route of administration is well within the skill of an ordinary physician. Animal experiments provide reliable guidance for the determination of effective doses for human therapy. Interspecies scaling of effective doses can be performed following the principles laid down by Mordenti, J. and Chappell, W. "The use of interspecies scaling in toxicokinetics" In Toxicokinetics and New Drug Development, Yacobi et al., Eds., Pergamon Press, New York 1989, pp. 42-96.

[0333] When in vivo administration of a PRO polypeptide or agonist or antagonist thereof is employed, normal dosage amounts may vary from about 10 ng/kg to up to 100 mg/kg of mammal body weight or more per day, preferably about 1 μ g/kg/day to 10 mg/kg/day, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature; see, for example, U.S. Pat. Nos. 4,657,760; 5,206,344; or 5,225,212. It is anticipated that different formulations will be effective for different treatment compounds and different disorders, that administration targeting one organ or tissue, for example, may necessitate delivery in a manner different from that to another organ or tissue.

[0334] Where sustained-release administration of a PRO polypeptide is desired in a formulation with release characteristics suitable for the treatment of any disease or disorder requiring administration of the PRO polypeptide, microencapsulation of the PRO polypeptide is contemplated. Microencapsulation of recombinant proteins for sustained release has been successfully performed with human growth hormone (rhGH), interferon- (rhIFN-), interleukin-2, and MN rgp120. Johnson et al., Nat. Med., 2:795-799 (1996); Yasuda, Biomed. Ther., 27:1221-1223 (1993); Hora et al., Bio/Technology, 8:755-758 (1990); Cleland, "Design and Production of Single Immunization Vaccines Using Polylactide Polyglycolide Microsphere Systems," in Vaccine Design: The Subunit and Adjuvant Approach, Powell and Newman, eds, (Plenum Press: New York, 1995), pp. 439-462; WO 97/03692, WO 96/40072, WO 96/07399; and U.S. Pat. No. 5,654,010.

[0335] The sustained-release formulations of these proteins were developed using polylactic-coglycolic acid (PLGA) polymer due to its biocompatibility and wide range of biodegradable properties. The degradation products of PLGA, lactic and glycolic acids, can be cleared quickly within the human body. Moreover, the degradability of this polymer can be adjusted from months to years depending on its molecular weight and composition. Lewis, "Controlled release of bioactive agents from lactide/glycolide polymer," in: M. Chasin and R. Langer (Eds.), Biodegradable Polymers as Drug Delivery Systems (Marcel Dekker: New York, 1990), pp.1-41.

[0336] This invention encompasses methods of screening compounds to identify those that mimic the PRO polypeptide (agonists) or prevent the effect of the PRO polypeptide (antagonists). Screening assays for antagonist drug candidates are designed to identify compounds that bind or complex with the PRO polypeptides encoded by the genes identified herein, or otherwise interfere with the interaction of the encoded polypeptides with other cellular proteins. Such screening assays will include assays amenable to

high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates.

[0337] The assays can be performed in a variety of formats, including protein-protein binding assays, biochemical screening assays, immunoassays, and cell-based assays, which are well characterized in the art.

[0338] All assays for antagonists are common in that they call for contacting the drug candidate with a PRO polypeptide encoded by a nucleic acid identified herein under conditions and for a time sufficient to allow these two components to interact.

[0339] In binding assays, the interaction is binding and the complex formed can be isolated or detected in the reaction mixture. In a particular embodiment, the PRO polypeptide encoded by the gene identified herein or the drug candidate is immobilized on a solid phase, e.g., on a microtiter plate, by covalent or non-covalent attachments. Non-covalent attachment generally is accomplished by coating the solid surface with a solution of the PRO polypeptide and drying. Alternatively, an immobilized antibody, e.g., a monoclonal antibody, specific for the PRO polypeptide to be immobilized can be used to anchor it to a solid surface. The assay is performed by adding the non-immobilized component, which may be labeled by a detectable label, to the immobilized component, e.g., the coated surface containing the anchored component. When the reaction is complete, the non-reacted components are removed, e.g., by washing, and complexes anchored on the solid surface are detected. When the originally non-immobilized component carries a detectable label, the detection of label immobilized on the surface indicates that complexing occurred. Where the originally non-immobilized component does not carry a label, complexing can be detected, for example, by using a labeled antibody specifically binding the immobilized complex.

[0340] If the candidate compound interacts with but does not bind to a particular PRO polypeptide encoded by a gene identified herein, its interaction with that polypeptide can be assayed by methods well known for detecting protein-protein interactions. Such assays include traditional approaches, such as, e.g., cross-linking, co-immunoprecipitation, and co-purification through gradients or chromatographic columns. In addition, protein-protein interactions can be monitored by using a yeast-based genetic system described by Fields and co-workers (Fields and Song, *Nature* (London), 340:245-246 (1989); Chien et al., *Proc. Natl. Acad. Sci. USA*, 88:9578-9582 (1991)) as disclosed by Chevray and Nathans, *Proc. Natl. Acad. Sci. USA*, 89: 5789-5793 (1991). Many transcriptional activators, such as yeast GAL4, consist of two physically discrete modular domains, one acting as the DNA-binding domain, the other one functioning as the transcription-activation domain. The yeast expression system described in the foregoing publications (generally referred to as the "two-hybrid system") takes advantage of this property, and employs two hybrid proteins, one in which the target protein is fused to the DNA-binding domain of GAL4, and another, in which candidate activating proteins are fused to the activation domain. The expression of a GAL1-lacZ reporter gene under control of a GAL4-activated promoter depends on reconstitution of GAL4 activity via protein-protein interaction. Colonies containing interacting polypeptides are detected

with a chromogenic substrate for β -galactosidase. A complete kit (MATCHMAKER™) for identifying protein-protein interactions between two specific proteins using the two-hybrid technique is commercially available from Clontech. This system can also be extended to map protein domains involved in specific protein interactions as well as to pinpoint amino acid residues that are crucial for these interactions.

[0341] Compounds that interfere with the interaction of a gene encoding a PRO polypeptide identified herein and other intra- or extracellular components can be tested as follows: usually a reaction mixture is prepared containing the product of the gene and the intra- or extracellular component under conditions and for a time allowing for the interaction and binding of the two products. To test the ability of a candidate compound to inhibit binding, the reaction is run in the absence and in the presence of the test compound. In addition, a placebo may be added to a third reaction mixture, to serve as positive control. The binding (complex formation) between the test compound and the intra- or extracellular component present in the mixture is monitored as described hereinabove. The formation of a complex in the control reaction(s) but not in the reaction mixture containing the test compound indicates that the test compound interferes with the interaction of the test compound and its reaction partner.

[0342] To assay for antagonists, the PRO polypeptide may be added to a cell along with the compound to be screened for a particular activity and the ability of the compound to inhibit the activity of interest in the presence of the PRO polypeptide indicates that the compound is an antagonist to the PRO polypeptide. Alternatively, antagonists may be detected by combining the PRO polypeptide and a potential antagonist with membrane-bound PRO polypeptide receptors or recombinant receptors under appropriate conditions for a competitive inhibition assay. The PRO polypeptide can be labeled, such as by radioactivity, such that the number of PRO polypeptide molecules bound to the receptor can be used to determine the effectiveness of the potential antagonist. The gene encoding the receptor can be identified by numerous methods known to those of skill in the art, for example, ligand panning and FACS sorting. Coligan et al., *Current Protocols in Immun.*, 1(2): Chapter 5 (1991). Preferably, expression cloning is employed wherein polyadenylated RNA is prepared from a cell responsive to the PRO polypeptide and a cDNA library created from this RNA is divided into pools and used to transfect COS cells or other cells that are not responsive to the PRO polypeptide. Transfected cells that are grown on glass slides are exposed to labeled PRO polypeptide. The PRO polypeptide can be labeled by a variety of means including iodination or inclusion of a recognition site for a site-specific protein kinase. Following fixation and incubation, the slides are subjected to autoradiographic analysis. Positive pools are identified and sub-pools are prepared and re-transfected using an interactive sub-pooling and re-screening process, eventually yielding a single clone that encodes the putative receptor.

[0343] As an alternative approach for receptor identification, labeled PRO polypeptide can be photoaffinity-linked with cell membrane or extract preparations that express the receptor molecule. Cross-linked material is resolved by PAGE and exposed to X-ray film. The labeled complex containing the receptor can be excised, resolved into peptide

fragments, and subjected to protein micro-sequencing. The amino acid sequence obtained from micro-sequencing would be used to design a set of degenerate oligonucleotide probes to screen a cDNA library to identify the gene encoding the putative receptor.

[0344] In another assay for antagonists, mammalian cells or a membrane preparation expressing the receptor would be incubated with labeled PRO polypeptide in the presence of the candidate compound. The ability of the compound to enhance or block this interaction could then be measured.

[0345] More specific examples of potential antagonists include an oligonucleotide that binds to the fusions of immunoglobulin with PRO polypeptide, and, in particular, antibodies including, without limitation, poly- and monoclonal antibodies and antibody fragments, single-chain antibodies, anti-idiotypic antibodies, and chimeric or humanized versions of such antibodies or fragments, as well as human antibodies and antibody fragments. Alternatively, a potential antagonist may be a closely related protein, for example, a mutated form of the PRO polypeptide that recognizes the receptor but imparts no effect, thereby competitively inhibiting the action of the PRO polypeptide.

[0346] Another potential PRO polypeptide antagonist is an antisense RNA or DNA construct prepared using antisense technology, where, e.g., an antisense RNA or DNA molecule acts to block directly the translation of mRNA by hybridizing to targeted mRNA and preventing protein translation. Antisense technology can be used to gene expression through triple-helix formation or antisense DNA or RNA, both of which methods are based on binding of a polynucleotide to DNA or RNA. For example, the 5' coding portion of the polynucleotide sequence, which encodes the mature PRO polypeptides herein, is used to design an antisense RNA oligonucleotide of from about 10 to 40 base pairs in length. A DNA oligonucleotide is designed to be complementary to a region of the gene involved in transcription (triple helix—see Lee et al., *Nucl. Acids Res.*, 6:3073 (1979); Cooney et al., *Science*, 241: 456 (1988); Dervan et al., *Science*, 251:1360 (1991)), thereby preventing transcription and the production of the PRO polypeptide. The antisense RNA oligonucleotide hybridizes to the mRNA *in vivo* and blocks translation of the mRNA molecule into the PRO polypeptide (antisense—Okano, *Neurochem.*, 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression (CRC Press: Boca Raton, Fla., 1988). The oligonucleotides described above can also be delivered to cells such that the antisense RNA or DNA may be expressed *in vivo* to inhibit production of the PRO polypeptide. When antisense DNA is used, oligodeoxyribonucleotides derived from the translation-initiation site, e.g., between about -10 and +10 positions of the target gene nucleotide sequence, are preferred.

[0347] Potential antagonists include small molecules that bind to the active site, the receptor binding site, or growth factor or other relevant binding site of the PRO polypeptide, thereby blocking the normal biological activity of the PRO polypeptide. Examples of small molecules include, but are not limited to, small peptides or peptide-like molecules, preferably soluble peptides, and synthetic non-peptidyl organic or inorganic compounds.

[0348] Ribozymes are enzymatic RNA molecules capable of catalyzing the specific cleavage of RNA. Ribozymes act

by sequence-specific hybridization to the complementary target RNA, followed by endonucleolytic cleavage. Specific ribozyme cleavage sites within a potential RNA target can be identified by known techniques. For further details see, e.g., Rossi, *Current Biology*, 4:469-471 (1994), and PCT publication No. WO 97/33551 (published Sep. 18, 1997).

[0349] Nucleic acid molecules in triple-helix formation used to inhibit transcription should be single-stranded and composed of deoxynucleotides. The base composition of these oligonucleotides is designed such that it promotes triple-helix formation via Hoogsteen base-pairing rules, which generally require sizeable stretches of purines or pyrimidines on one strand of a duplex. For further details see, e.g., PCT publication No. WO 97/33551, *supra*.

[0350] These small molecules can be identified by any one or more of the screening assays discussed hereinabove and/or by any other screening techniques well known for those skilled in the art.

[0351] Diagnostic and therapeutic uses of the herein disclosed molecules may also be based upon the positive functional assay hits disclosed and described below.

F. Anti-PRO Antibodies

[0352] The present invention further provides anti-PRO antibodies. Exemplary antibodies include polyclonal, monoclonal, humanized, bispecific, and heteroconjugate antibodies.

1. Polyclonal Antibodies

[0353] The anti-PRO antibodies may comprise polyclonal antibodies. Methods of preparing polyclonal antibodies are known to the skilled artisan. Polyclonal antibodies can be raised in a mammal, for example, by one or more injections of an immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and/or adjuvant will be injected in the mammal by multiple subcutaneous or intraperitoneal injections. The immunizing agent may include the PRO polypeptide or a fusion protein thereof. It may be useful to conjugate the immunizing agent to a protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. Examples of adjuvants which may be employed include Freund's complete adjuvant and MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate). The immunization protocol may be selected by one skilled in the art without undue experimentation.

2. Monoclonal Antibodies

[0354] The anti-PRO antibodies may, alternatively, be monoclonal antibodies. Monoclonal antibodies may be prepared using hybridoma methods, such as those described by Kohler and Milstein, *Nature*, 256:495 (1975). In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes may be immunized *in vitro*.

[0355] The immunizing agent will typically include the PRO polypeptide or a fusion protein thereof. Generally,

either peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell [Goding, *Monoclonal Antibodies: Principles and Practice*, Academic Press, (1986) pp. 59-103]. Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells may be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

[0356] Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, Calif. and the American Type Culture Collection, Manassas, Va. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies [Kozbor, *J. Immunol.*, 133:3001 (1984); Brodeur et al., *Monoclonal Antibody Production Techniques and Applications*, Marcel Dekker, Inc., New York, (1987) pp. 51-63].

[0357] The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of monoclonal antibodies directed against PRO. Preferably, the binding specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an in vitro binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson and Pollard, *Anal. Biochem.*, 107:220 (1980).

[0358] After the desired hybridoma cells are identified, the clones may be subcloned by limiting dilution procedures and grown by standard methods [Goding, *supra*]. Suitable culture media for this purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells may be grown in vivo as ascites in a mammal.

[0359] The monoclonal antibodies secreted by the subclones may be isolated or purified from the culture medium or ascites fluid by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

[0360] The monoclonal antibodies may also be made by recombinant DNA methods, such as those described in U.S. Pat. No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes

encoding the heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA may be placed into expression vectors, which are then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA also may be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences [U.S. Pat. No. 4,816,567; Morrison et al., *supra*] or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

[0361] The antibodies may be monovalent antibodies. Methods for preparing monovalent antibodies are well known in the art. For example, one method involves recombinant expression of immunoglobulin light chain and modified heavy chain. The heavy chain is truncated generally at any point in the Fc region so as to prevent heavy chain crosslinking. Alternatively, the relevant cysteine residues are substituted with another amino acid residue or are deleted so as to prevent crosslinking.

[0362] In vitro methods are also suitable for preparing monovalent antibodies. Digestion of antibodies to produce fragments thereof, particularly, Fab fragments, can be accomplished using routine techniques known in the art.

3. Human and Humanized Antibodies

[0363] The anti-PRO antibodies of the invention may further comprise humanized antibodies or human antibodies. Humanized forms of non-human (e.g., murine) antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')₂ or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. Humanized antibodies include human immunoglobulins (recipient antibody) in which residues from a complementary determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit having the desired specificity, affinity and capacity. In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies may also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the FR regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin [Jones et al., *Nature*, 321:522-525 (1986); Riechmann et al., *Nature*, 332:323-329 (1988); and Presta, *Curr. Op. Struct. Biol.*, 2:593-596 (1992)].

[0364] Methods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acid residues introduced into it from a source which is non-human. These non-human amino acid residues are often referred to as "import" residues, which are typically taken from an "import" variable domain. Humanization can be essentially performed following the method of Winter and co-workers [Jones et al., *Nature*, 321:522-525 (1986); Riechmann et al., *Nature*, 332:323-327 (1988); Verhoeyen et al., *Science*, 239:1534-1536 (1988)], by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. Accordingly, such "humanized" antibodies are chimeric antibodies (U.S. Pat. No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species. In practice, humanized antibodies are typically human antibodies in which some CDR residues and possibly some FR residues are substituted by residues from analogous sites in rodent antibodies.

[0365] Human antibodies can also be produced using various techniques known in the art, including phage display libraries [Hoogenboom and Winter, *J. Mol. Biol.*, 227:381 (1991); Marks et al., *J. Mol. Biol.*, 222:581 (1991)]. The techniques of Cole et al. and Boerner et al. are also available for the preparation of human monoclonal antibodies (Cole et al., *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, p. 77 (1985) and Boerner et al., *J. Immunol.*, 147(1):86-95 (1991)]. Similarly, human antibodies can be made by introducing of human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, for example, in U.S. Pat. Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in the following scientific publications: Marks et al., *Bio/Technology* 10, 779-783 (1992); Lonberg et al., *Nature* 368 856-859 (1994); Morrison, *Nature* 368, 812-13 (1994); Fishwild et al., *Nature Biotechnology* 14, 845-51 (1996); Neuberger, *Nature Biotechnology* 14, 826 (1996); Lonberg and Huszar, *Intern. Rev. Immunol.* 13 65-93 (1995).

[0366] The antibodies may also be affinity matured using known selection and/or mutagenesis methods as described above. Preferred affinity matured antibodies have an affinity which is five times, more preferably 10 times, even more preferably 20 or 30 times greater than the starting antibody (generally murine, humanized or human) from which the matured antibody is prepared.

4. Bispecific Antibodies

[0367] Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for the PRO, the other one is for any other antigen, and preferably for a cell-surface protein or receptor or receptor subunit.

[0368] Methods for making bispecific antibodies are known in the art. Traditionally, the recombinant production of bispecific antibodies is based on the co-expression of two

immunoglobulin heavy-chain/light-chain pairs, where the two heavy chains have different specificities [Milstein and Cuello, *Nature*, 305:537-539 (1983)]. Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the correct bispecific structure. The purification of the correct molecule is usually accomplished by affinity chromatography steps. Similar procedures are disclosed in WO 93/08829, published May 13, 1993, and in Traunecker et al., *EMBO J.*, 10:3655-3659 (1991).

[0369] Antibody variable domains with the desired binding specificities (antibody-antigen combining sites) can be fused to immunoglobulin constant domain sequences. The fusion preferably is with an immunoglobulin heavy-chain constant domain, comprising at least part of the hinge, CH2, and CH3 regions. It is preferred to have first heavy-chain constant region (CH1) containing the site necessary for light-chain binding present in at least one of the fusions. DNAs encoding the immunoglobulin heavy-chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable host organism. For further details of generating bispecific antibodies see, for example, Suresh et al., *Methods in Enzymology*, 121:210 (1986).

[0370] According to another approach described in WO 96/27011, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers which are recovered from recombinant cell culture. The preferred interface comprises at least a part of the CH3 region of an antibody constant domain. In this method, one or more small amino acid side chains from the interface of the first antibody molecule are replaced with larger side chains (e.g. tyrosine or tryptophan). Compensatory "cavities" of identical or similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (e.g. alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

[0371] Bispecific antibodies can be prepared as full length antibodies or antibody fragments (e.g. F(ab)₂ bispecific antibodies). Techniques for generating bispecific antibodies from antibody fragments have been described in the literature. For example, bispecific antibodies can be prepared using chemical linkage. Brennan et al., *Science* 229:81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate F(ab)₂ fragments. These fragments are reduced in the presence of the dithiol complexing agent sodium arsenite to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

[0372] Fab' fragments may be directly recovered from *E. coli* and chemically coupled to form bispecific antibodies. Shalaby et al., *J. Exp. Med.* 175:217 (1992) describe the production of a fully humanized bispecific antibody F(ab)₂

molecule. Each Fab' fragment was separately secreted from *E. coli* and subjected to directed chemical coupling in vitro to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and normal human T cells, as well as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

[0373] Various technique for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny et al., *J. Immunol.* 148 (5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger et al., *Proc. Natl. Acad. Sci. USA* 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain (V_H) connected to a light-chain variable domain (V_L) by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the V_H and V_L domains of one fragment are forced to pair with the complementary V_L and V_H domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been reported. See, Gruber et al., *J. Immunol.* 152:5368 (1994). Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt et al., *J. Immunol.* 147:60 (1991).

[0374] Exemplary bispecific antibodies may bind to two different epitopes on a given PRO polypeptide herein. Alternatively, an anti-PRO polypeptide arm may be combined with an arm which binds to a triggering molecule on a leukocyte such as a T-cell receptor molecule (e.g. CD2, CD3, CD28, or B7), or Fc receptors for IgG (Fc γ R), such as Fc γ RI (CD64), Fc γ RII (CD32) and Fc γ RIII (CD16) so as to focus cellular defense mechanisms to the cell expressing the particular PRO polypeptide. Bispecific antibodies may also be used to localize cytotoxic agents to cells which express a particular PRO polypeptide. These antibodies possess a PRO-binding arm and an arm which binds a cytotoxic agent or a radionuclide chelator, such as EOTUBE, DPTA, DOTA, or TETA. Another bispecific antibody of interest binds the PRO polypeptide and further binds tissue factor (TF).

5. Heteroconjugate Antibodies

[0375] Heteroconjugate antibodies are also within the scope of the present invention. Heteroconjugate antibodies are composed of two covalently joined antibodies. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells [U.S. Pat. No. 4,676,980], and for treatment of HIV infection [WO 91/00360; WO 92/200373; EP 03089]. It is contemplated that the antibodies may be prepared in vitro using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins may be constructed using a disulfide exchange reaction or by forming a thioether bond. Examples of suitable reagents for

this purpose include iminothiolate and methyl-4-mercaptobutyrimidate and those disclosed, for example, in U.S. Pat. No. 4,676,980.

6. Effector Function Engineering

[0376] It may be desirable to modify the antibody of the invention with respect to effector function, so as to enhance, e.g., the effectiveness of the antibody in treating cancer. For example, cysteine residue(s) may be introduced into the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibody thus generated may have improved internalization capability and/or increased complement-mediated cell killing and antibody-dependent cellular cytotoxicity (ADCC). See Caron et al., *J. Exp. Med.*, 176: 1191-1195 (1992) and Shopes, *J. Immunol.*, 148: 2918-2922 (1992). Homodimeric antibodies with enhanced anti-tumor activity may also be prepared using heterobifunctional cross-linkers as described in Wolff et al. *Cancer Research*, 53: 2560-2565 (1993). Alternatively, an antibody can be engineered that has dual Fc regions and may thereby have enhanced complement lysis and ADCC capabilities. See Stevenson et al., *Anti-Cancer Drug Design*, 3: 219-230 (1989).

7. Immunoconjugates

[0377] The invention also pertains to immunoconjugates comprising an antibody conjugated to a cytotoxic agent such as a chemotherapeutic agent, toxin (e.g., an enzymatically active toxin of bacterial, fungal, plant, or animal origin, or fragments thereof), or a radioactive isotope (i.e., a radioconjugate).

[0378] Chemotherapeutic agents useful in the generation of such immunoconjugates have been described above. Enzymatically active toxins and fragments thereof that can be used include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from *Pseudomonas aeruginosa*), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, *Aleurites fordii* proteins, dianthin proteins, *Phytolacca americana* proteins (PAPI, PAPII, and PAP-S), *momordica charantia* inhibitor, curcumin, croton, *sapaonaria officinalis* inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin, and the tricothecenes. A variety of radionuclides are available for the production of radioconjugated antibodies. Examples include ^{212}Bi , ^{131}I , ^{131}In , ^{90}Y , and ^{186}Re . Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling agents such as N-succinimidyl-3-(2-pyridyldithiol) propionate (SPDP), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimide HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutaraldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in Vitetta et al., *Science*, 238: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyl-diethylene triamine-pentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionuclide to the antibody. See WO 94/11026.

[0379] In another embodiment, the antibody may be conjugated to a "receptor" (such streptavidin) for utilization in

tumor pretargeting wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound conjugate from the circulation using a clearing agent and then administration of a "ligand" (e.g., avidin) that is conjugated to a cytotoxic agent (e.g., a radionucleotide).

8. Immunoliposomes

[0380] The antibodies disclosed herein may also be formulated as immunoliposomes. Liposomes containing the antibody are prepared by methods known in the art, such as described in Epstein et al., Proc. Natl. Acad. Sci. USA, 82: 3688 (1985); Hwang et al., Proc. Natl. Acad. Sci. USA, 77: 4030 (1980); and U.S. Pat. Nos. 4,485,045 and 4,544,545. Liposomes with enhanced circulation time are disclosed in U.S. Pat. No. 5,013,556.

[0381] Particularly useful liposomes can be generated by the reverse-phase evaporation method with a lipid composition comprising phosphatidylcholine, cholesterol, and PEG-derivatized phosphatidylethanolamine (PEG-PE). Liposomes are extruded through filters of defined pore size to yield liposomes with the desired diameter. Fab' fragments of the antibody of the present invention can be conjugated to the liposomes as described in Martin et al., J. Biol. Chem., 257: 286-288 (1982) via a disulfide-interchange reaction. A chemotherapeutic agent (such as Doxorubicin) is optionally contained within the liposome. See Gabizon et al., J. National Cancer Inst., 81(19): 1484 (1989).

9. Pharmaceutical Compositions of Antibodies

[0382] Antibodies specifically binding a PRO polypeptide identified herein, as well as other molecules identified by the screening assays disclosed hereinbefore, can be administered for the treatment of various disorders in the form of pharmaceutical compositions.

[0383] If the PRO polypeptide is intracellular and whole antibodies are used as inhibitors, internalizing antibodies are preferred. However, lipofections or liposomes can also be used to deliver the antibody, or an antibody fragment, into cells. Where antibody fragments are used, the smallest inhibitory fragment that specifically binds to the binding domain of the target protein is preferred. For example, based upon the variable-region sequences of an antibody, peptide molecules can be designed that retain the ability to bind the target protein sequence. Such peptides can be synthesized chemically and/or produced by recombinant DNA technology. See, e.g., Marasco et al., Proc. Natl. Acad. Sci. USA, 90: 7889-7893 (1993). The formulation herein may also contain more than one active compound as necessary for the particular indication being treated, preferably those with complementary activities that do not adversely affect each other. Alternatively, or in addition, the composition may comprise an agent that enhances its function, such as, for example, a cytotoxic agent, cytokine, chemotherapeutic agent, or growth-inhibitory agent. Such molecules are suitably present in combination in amounts that are effective for the purpose intended.

[0384] The active ingredients may also be entrapped in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization, for example, hydroxymethylcellulose or gelatin-microcapsules and poly-(methylmethacrylate) microcapsules, respectively, in colloidal drug delivery systems (for example, liposomes, albumin

microspheres, microemulsions, nano-particles, and nano-capsules) or in macroemulsions. Such techniques are disclosed in Remington's *Pharmaceutical Sciences*, supra.

[0385] The formulations to be used for in vivo administration must be sterile. This is readily accomplished by filtration through sterile filtration membranes.

[0386] Sustained-release preparations may be prepared. Suitable examples of sustained-release preparations include semipermeable matrices of solid hydrophobic polymers containing the antibody, which matrices are in the form of shaped articles, e.g., films, or microcapsules. Examples of sustained-release matrices include polyesters, hydrogels (for example, poly(2-hydroxyethyl-methacrylate), or poly(vinylalcohol)), polylactides (U.S. Pat. No. 3,773,919), copolymers of L-glutamic acid and 65 ethyl-L-glutamate, non-degradable ethylene-vinyl acetate, degradable lactic acid-glycolic acid copolymers such as the LUPRON DEPOT™ (injectable microspheres composed of lactic acid-glycolic acid copolymer and leuprolide acetate), and poly-D-(-)-3-hydroxybutyric acid. While polymers such as ethylene-vinyl acetate and lactic acid-glycolic acid enable release of molecules for over 100 days, certain hydrogels release proteins for shorter time periods. When encapsulated antibodies remain in the body for a long time, they may denature or aggregate as a result of exposure to moisture at 37° C., resulting in a loss of biological activity and possible changes in immunogenicity. Rational strategies can be devised for stabilization depending on the mechanism involved. For example, if the aggregation mechanism is discovered to be intermolecular S—S bond formation through thio-disulfide interchange, stabilization may be achieved by modifying sulfhydryl residues, lyophilizing from acidic solutions, controlling moisture content, using appropriate additives, and developing specific polymer matrix compositions.

C. Uses for Anti-PRO Antibodies

[0387] The anti-PRO antibodies of the invention have various utilities. For example, anti-PRO antibodies may be used in diagnostic assays for PRO, e.g., detecting its expression (and in some cases, differential expression) in specific cells, tissues, or serum. Various diagnostic assay techniques known in the art may be used, such as competitive binding assays, direct or indirect sandwich assays and immunoprecipitation assays conducted in either heterogeneous or homogeneous phases [Zola, *Monoclonal Antibodies: A Manual of Techniques*, CRC Press, Inc. (1987) pp.147-158]. The antibodies used in the diagnostic assays can be labeled with a detectable moiety. The detectable moiety should be capable of producing, either directly or indirectly, a detectable signal. For example, the detectable moiety may be a radioisotope, such as ³H, ¹⁴C, ³²P, ³⁵S, or ¹²⁵I, a fluorescent or chemiluminescent compound, such as fluorescein isothiocyanate, rhodamine, or luciferin, or an enzyme, such as alkaline phosphatase, beta-galactosidase or horseradish peroxidase. Any method known in the art for conjugating the antibody to the detectable moiety may be employed, including those methods described by Hunter et al., *Nature*, 144:945 (1962); David et al., *Biochemistry*, 13:1014 (1974); Pain et al., *J. Immunol. Meth.*, 40:219 (1981); and Nygren, *J. Histochem. and Cytochem.*, 30:407 (1982).

[0388] Anti-PRO antibodies also are useful for the affinity purification of PRO from recombinant cell culture or natural

sources. In this process, the antibodies against PRO are immobilized on a suitable support, such as Sephadex resin or filter paper, using methods well known in the art. The immobilized antibody then is contacted with a sample containing the PRO to be purified, and thereafter the support is washed with a suitable solvent that will remove substantially all the material in the sample except the PRO, which is bound to the immobilized antibody. Finally, the support is washed with another suitable solvent that will release the PRO from the antibody.

[0389] The following examples are offered for illustrative purposes only, and are not intended to limit the scope of the present invention in any way.

[0390] All patent and literature references cited in the present specification are hereby incorporated by reference in their entirety.

EXAMPLES

[0391] Commercially available reagents referred to in the examples were used according to manufacturer's instructions unless otherwise indicated. The source of those cells identified in the following examples, and throughout the specification, by ATCC accession numbers is the American Type Culture Collection, Manassas, Va.

Example 1

Extracellular Domain Homology Screening to Identify Novel Polypeptides and cDNA Encoding Therefor

[0392] The extracellular domain (ECD) sequences (including the secretion signal sequence, if any) from about 950 known secreted proteins from the Swiss-Prot public database were used to search EST databases. The EST databases included public databases (e.g., Dayhoff, GenBank), and proprietary databases (e.g., LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, Calif.). The search was performed using the computer program BLAST or BLAST-2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons with a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Wash.).

[0393] Using this extracellular domain homology screen, consensus DNA sequences were assembled relative to the other identified EST sequences using phrap. In addition, the consensus DNA sequences obtained were often (but not always) extended using repeated cycles of BLAST or BLAST-2 and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above.

[0394] Based upon the consensus sequences obtained as described above, oligonucleotides were then synthesized and used to identify by PCR a cDNA library that contained the sequence of interest and for use as probes to isolate a clone of the full-length coding sequence for a PRO polypeptide. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR

product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5 kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., *Current Protocols in Molecular Biology*, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

[0395] The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, Calif. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to Sall hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

Example 2

Isolation of cDNA Clones by Amylase Screening

[0396] 1. Preparation of oligo dT primed cDNA library

[0397] mRNA was isolated from a human tissue of interest using reagents and protocols from Invitrogen, San Diego, Calif. (Fast Track 2). This RNA was used to generate an oligo dT primed cDNA library in the vector pRK5D using reagents and protocols from Life Technologies, Gaithersburg, Md. (Super Script Plasmid System). In this procedure, the double stranded cDNA was sized to greater than 1000 bp and the Sall/NotI linked cDNA was cloned into XhoI/NotI cleaved vector. pRK5D is a cloning vector that has an sp6 transcription initiation site followed by an SfiI restriction enzyme site preceding the XhoI/NotI cDNA cloning sites.

[0398] 2. Preparation of random primed cDNA library

[0399] A secondary cDNA library was generated in order to preferentially represent the 5' ends of the primary cDNA clones. Sp6 RNA was generated from the primary library (described above), and this RNA was used to generate a random primed cDNA library in the vector pSST-AMY.0 using reagents and protocols from Life Technologies (Super Script Plasmid System, referenced above). In this procedure the double stranded cDNA was sized to 500-1000 bp, linked with blunt to NotI adaptors, cleaved with SfiI, and cloned into SfiI/NotI cleaved vector. pSST-AMY.0 is a cloning vector that has a yeast alcohol dehydrogenase promoter preceding the cDNA cloning sites and the mouse amylase sequence (the mature sequence without the secretion signal) followed by the yeast alcohol dehydrogenase terminator, after the cloning sites. Thus, cDNAs cloned into this vector that are fused in frame with amylase sequence will lead to the secretion of amylase from appropriately transfected yeast colonies.

[0400] 3. Transformation and Detection

[0401] DNA from the library described in paragraph 2 above was chilled on ice to which was added electrocompetent DH10B bacteria (Life Technologies, 20 ml). The bacteria and vector mixture was then electroporated as

recommended by the manufacturer. Subsequently, SOC media (Life Technologies, 1 ml) was added and the mixture was incubated at 37° C. for 30 minutes. The transformants were then plated onto 20 standard 150 mm LB plates containing ampicillin and incubated for 16 hours (37° C.). Positive colonies were scraped off the plates and the DNA was isolated from the bacterial pellet using standard protocols, e.g. CsCl-gradient. The purified DNA was then carried on to the yeast protocols below.

[0402] The yeast methods were divided into three categories: (1) Transformation of yeast with the plasmid/cDNA combined vector; (2) Detection and isolation of yeast clones secreting amylase; and (3) PCR amplification of the insert directly from the yeast colony and purification of the DNA for sequencing and further analysis.

[0403] The yeast strain used was HD56-5A (ATCC-90785). This strain has the following genotype: MAT alpha, ura3-52, leu2-3, leu2-112, his3-11, his3-15, MAL⁺, SUC⁺, GAL⁺. Preferably, yeast mutants can be employed that have deficient post-translational pathways. Such mutants may have translocation deficient alleles in sec 71, sec 72, sec 62, with truncated sec 71 being most preferred. Alternatively, antagonists (including antisense nucleotides and/or ligands) which interfere with the normal operation of these genes, other proteins implicated in this post translation pathway (e.g., SEC61p, SEC72p, SEC62p, SEC63p, TDJ1p or SSA1p-4p) or the complex formation of these proteins may also be preferably employed in combination with the amylase-expressing yeast.

[0404] Transformation was performed based on the protocol outlined by Gietz et al., Nucl. Acid. Res., 20:1425 (1992). Transformed cells were then inoculated from agar into YEPD complex media broth (100 ml) and grown overnight at 30° C. The YEPD broth was prepared as described in Kaiser et al., Methods in Yeast Genetics, Cold Spring Harbor Press, Cold Spring Harbor, N.Y., p. 207 (1994). The overnight culture was then diluted to about 2x10⁷ cells/ml (approx. OD₆₀₀=0.1) into fresh YEPD broth (500 ml) and regrown to 1x10⁷ cells/ml (approx. OD₆₀₀=0.4-0.5).

[0405] The cells were then harvested and prepared for transformation by transfer into GS3 rotor bottles in a Sorval GS3 rotor at 5,000 rpm for 5 minutes, the supernatant discarded, and then resuspended into sterile water, and centrifuged again in 50 ml falcon tubes at 3,500 rpm in a Beckman GS-6KR centrifuge. The supernatant was discarded and the cells were subsequently washed with LiAc/TE (10 ml, 10 mM Tris-HCl, 1 mM EDTA pH 7.5, 100 mM Li₂OOCCH₃), and resuspended into LiAc/TE (2.5 ml).

[0406] Transformation took place by mixing the prepared cells (100 μl) with freshly denatured single stranded salmon testes DNA (Lofstrand Labs, Gaithersburg, Md.) and transforming DNA (1 μg, vol.<10 μl) in microfuge tubes. The mixture was mixed briefly by vortexing, then 40% PEG/TE (600 μl, 40% polyethylene glycol-4000, 10 mM Tris-HCl, 1 mM EDTA, 100 mM Li₂OOCCH₃, pH 7.5) was added. This mixture was gently mixed and incubated at 30° C. while agitating for 30 minutes. The cells were then heat shocked at 42° C. for 15 minutes, and the reaction vessel centrifuged in a microfuge at 12,000 rpm for 5-10 seconds, decanted and resuspended into TE (500 μl, 10 mM Tris-HCl, 1 mM EDTA pH 7.5) followed by recentrifugation. The cells were then

diluted into TE (1 ml) and aliquots (200 μl) were spread onto the selective media previously prepared in 150 mm growth plates (VWR).

[0407] Alternatively, instead of multiple small reactions, the transformation was performed using a single, large scale reaction, wherein reagent amounts were scaled up accordingly.

[0408] The selective media used was a synthetic complete dextrose agar lacking uracil (SCD-Ura) prepared as described in Kaiser et al., Methods in Yeast Genetics, Cold Spring Harbor Press, Cold Spring Harbor, N.Y., p. 208-210 (1994). Transformants were grown at 30° C. for 2-3 days.

[0409] The detection of colonies secreting amylase was performed by including red starch in the selective growth media. Starch was coupled to the red dye (Reactive Red-120, Sigma) as per the procedure described by Biely et al., Anal. Biochem., 172:176-179 (1988). The coupled starch was incorporated into the SCD-Ura agar plates at a final concentration of 0.15% (w/v), and was buffered with potassium phosphate to a pH of 7.0 (50-100 mM final concentration).

[0410] The positive colonies were picked and streaked across fresh selective media (onto 150 mm plates) in order to obtain well isolated and identifiable single colonies. Well isolated single colonies positive for amylase secretion were detected by direct incorporation of red starch into buffered SCD-Ura agar. Positive colonies were determined by their ability to break down starch resulting in a clear halo around the positive colony visualized directly.

[0411] 4. Isolation of DNA by PCR Amplification

[0412] When a positive colony was isolated, a portion of it was picked by a toothpick and diluted into sterile water (30 μl) in a 96 well plate. At this time, the positive colonies were either frozen and stored for subsequent analysis or immediately amplified. An aliquot of cells (5 μl) was used as a template for the PCR reaction in a 25 μl volume containing: 0.5 μl KlenTaq (Clontech, Palo Alto, Calif.); 4.0 μl 10 mM dNTP's (Perkin Elmer-Cetus); 2.5 μl Kentaq buffer (Clontech); 0.25 μl forward oligo 1; 0.25 μl reverse oligo 2; 12.5 μl distilled water. The sequence of the forward oligonucleotide 1 was:

[0413] 5'-TGTA AACGACGGCCAGTTAAATA-GACCTGCAATTATTAATCT-3' (SEQ ID NO:169)

[0414] The sequence of reverse oligonucleotide 2 was:

[0415] 5'-CAGGAAACAGCTATGACCACCTG-CACACCTGCAAATCCATT-3' (SEQ ID NO:170)

[0416] PCR was then performed as follows:

a.	Denature	92° C.,	5 minutes
b.	3 cycles of:	Denature	92° C., 30 seconds
		Anneal	59° C., 30 seconds
		Extend	72° C., 60 seconds
c.	3 cycles of:	Denature	92° C., 30 seconds
		Anneal	57° C., 30 seconds
		Extend	72° C., 60 seconds
d.	25 cycles of:	Denature	92° C., 30 seconds
		Anneal	55° C., 30 seconds
		Extend	72° C., 60 seconds
e.	Hold	4° C.	

[0417] The underlined regions of the oligonucleotides annealed to the ADH promoter region and the amylase region, respectively, and amplified a 307 bp region from vector pSST-AMY.0 when no insert was present. Typically, the first 18 nucleotides of the 5' end of these oligonucleotides contained annealing sites for the sequencing primers. Thus, the total product of the PCR reaction from an empty vector was 343 bp. However, signal sequence-fused cDNA resulted in considerably longer nucleotide sequences.

[0418] Following the PCR, an aliquot of the reaction (5 μ l) was examined by agarose gel electrophoresis in a 1% agarose gel using a Tris-Borate-EDTA (TBE) buffering system as described by Sambrook et al., supra. Clones resulting in a single strong PCR product larger than 400 bp were further analyzed by DNA sequencing after purification with a 96 Qiaquick PCR clean-up column (Qiagen Inc., Chatsworth, Calif.).

Example 3

Isolation of cDNA Clones Using Signal Algorithm Analysis

[0419] Various polypeptide-encoding nucleic acid sequences were identified by applying a proprietary signal sequence finding algorithm developed by Genentech, Inc. (South San Francisco, Calif.) upon ESTs as well as clustered and assembled EST fragments from public (e.g., GenBank) and/or private (LIFESEQ®, Incyte Pharmaceuticals, Inc., Palo Alto, Calif.) databases. The signal sequence algorithm computes a secretion signal score based on the character of the DNA nucleotides surrounding the first and optionally second methionine codon(s) (ATG) at the 5'-end of the sequence or sequence fragment under consideration. The nucleotides following the first ATG must code for at least 35 unambiguous amino acids without any stop codons. If the first ATG has the required amino acids, the second is not examined. If neither meets the requirement, the candidate sequence is not scored. In order to determine whether the EST sequence contains an authentic signal sequence, the DNA and corresponding amino acid sequences surrounding the ATG codon are scored using a set of seven sensors (evaluation parameters) known to be associated with secretion signals. Use of this algorithm resulted in the identification of numerous polypeptide-encoding nucleic acid sequences.

Example 4

Isolation of cDNA Clones Encoding Human PRO Polypeptides

[0420] Using the techniques described in Examples 1 to 3 above, numerous full-length cDNA clones were identified as encoding PRO polypeptides as disclosed herein. These cDNAs were then deposited under the terms of the Budapest Treaty with the American Type Culture Collection, 10801 University Blvd., Manassas, Va. 20110-2209, USA (ATCC) as shown in Tabl 7 below.

TABLE 7

Material	ATCC Dep. No.	Deposit Date
DNA26843-1389	203099	Aug. 4, 1998
DNA30867-1335	209807	Apr. 28, 1998
DNA34431-1177	209399	Oct. 17, 1997
DNA38268-1188	209421	Oct. 28, 1997
DNA40621-1440	209922	Jun. 2, 1998
DNA40625-1189	209788	Apr. 21, 1998
DNA45409-2511	203579	Jan. 12, 1999
DNA45495-1550	203156	Aug. 25, 1998
DNA49820-1427	209932	Jun. 2, 1998
DNA56406-1704	203478	Nov. 17, 1998
DNA56410-1414	209923	Jun. 2, 1998
DNA56436-1448	209902	May 27, 1998
DNA56855-1447	203004	Jun. 23, 1998
DNA56860-1510	209952	Jun. 9, 1998
DNA56862-1343	203174	Sep. 1, 1998
DNA56868-1478	203024	Jun. 23, 1998
DNA56869-1545	203161	Aug. 25, 1998
DNA57704-1452	209953	Jun. 9, 1998
DNA58723-1588	203133	Aug. 18, 1998
DNA57827-1493	203045	Jul. 1, 1998
DNA58737-1473	203136	Aug. 18, 1998
DNA58846-1409	209957	Jun. 9, 1998
DNA58850-1495	209956	Jun. 9, 1998
DNA58855-1422	203018	Jun. 23, 1998
DNA59211-1450	209960	Jun. 9, 1998
DNA59212-1627	203245	Sep. 9, 1998
DNA59213-1487	209959	Jun. 9, 1998
DNA59605-1418	203005	Jun. 23, 1998
DNA59609-1470	209963	Jun. 9, 1998
DNA59610-1556	209990	Jun. 16, 1998
DNA59837-2545	203658	Feb. 9, 1999
DNA59844-2542	203650	Feb. 9, 1999
DNA59854-1459	209974	Jun. 16, 1998
DNA60625-1507	209975	Jun. 16, 1998
DNA60629-1481	209979	Jun. 16, 1998
DNA61755-1554	203112	Aug. 11, 1998
DNA62812-1594	203248	Sep. 9, 1998
DNA62815-1576	203247	Sep. 9, 1998
DNA64881-1602	203240	Sep. 9, 1998
DNA64886-1601	203241	Sep. 9, 1998
DNA64902-1667	203317	Oct. 6, 1998
DNA64950-1590	203224	Sep. 15, 1998
DNA65403-1565	203230	Sep. 15, 1998
DNA66308-1537	203159	Aug. 25, 1998
DNA66519-1535	203236	Sep. 15, 1998
DNA66521-1583	203225	Sep. 15, 1998
DNA66658-1584	203229	Sep. 15, 1998
DNA66660-1585	203279	Sep. 22, 1998
DNA66663-1598	203268	Sep. 22, 1998
DNA66674-1599	203281	Sep. 22, 1998
DNA68862-2546	203652	Feb. 9, 1999
DNA68866-1644	203283	Sep. 22, 1998
DNA68871-1638	203280	Sep. 22, 1998
DNA68880-1676	203319	Oct. 6, 1998
DNA68883-1691	203535	Dec. 15, 1998
DNA68885-1678	203311	Oct. 6, 1998
DNA71277-1636	203285	Sep. 22, 1998
DNA73727-1673	203459	Nov. 3, 1998
DNA73734-1680	203363	Oct. 20, 1998
DNA73735-1681	203356	Oct. 20, 1998
DNA76393-1664	203323	Oct. 6, 1998
DNA77301-1708	203407	Oct. 27, 1998
DNA77568-1626	203134	Aug. 18, 1998
DNA77626-1705	203536	Dec. 15, 1998
DNA81754-2532	203542	Dec. 15, 1998
DNA81757-2512	203543	Dec. 15, 1998
DNA82302-2529	203534	Dec. 15, 1998
DNA82340-2530	203547	Dec. 22, 1998
DNA83500-2506	203391	Oct. 29, 1998
DNA84920-2614	203966	Apr. 27, 1999
DNA85066-2534	203588	Jan. 12, 1999
DNA86571-2551	203660	Feb. 9, 1999
DNA87991-2540	203656	Feb. 9, 1999
DNA92238-2539	203602	Jan. 20, 1999

TABLE 7-continued

Material	ATCC Dep. No.	Deposit Date
DNA96042-2682	PTA-382	Jul. 20, 1999
DNA96787-2534	203589	Jan. 12, 1999
DNA125185-2806	PTA-1031	Dec. 7, 1999
DNA147531-2821	PTA-1185	Jan. 11, 2000
DNA115291-2681	PTA-202	Jun. 8, 1999
DNA164625-28890	PTA-1535	Mar. 21, 2000
DNA131639-2874	PTA-1784	Apr. 25, 2000
DNA79230-2525	203549	Dec. 22, 1998

[0421] These deposits were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement between Genentech, Inc. and ATCC, which assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC § 122 and the Commissioner's rules pursuant thereto (including 37 CFR § 1.14 with particular reference to 886 OG 638).

[0422] The assignee of the present application has agreed that if a culture of the materials on deposit should die or be lost or destroyed when cultivated under suitable conditions, the materials will be promptly replaced on notification with another of the same. Availability of the deposited material is not to be construed as a license to practice the invention in contravention of the rights granted under the authority of any government in accordance with its patent laws.

Example 5

Use of PRO as a Hybridization Probe

[0423] The following method describes use of a nucleotide sequence encoding PRO as a hybridization probe.

[0424] DNA comprising the coding sequence of full-length or mature PRO as disclosed herein is employed as a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of PRO) in human tissue cDNA libraries or human tissue genomic libraries.

[0425] Hybridization and washing of filters containing either library DNAs is performed under the following high stringency conditions. Hybridization of radiolabeled PRO-derived probe to the filters is performed in a solution of 50% formamide, 5×SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2× Denhardt's solution, and 10% dextran sulfate at 42° C. for 20 hours. Washing of the filters is performed in an aqueous solution of 0.1×SSC and 0.1% SDS at 42° C.

[0426] DNAs having a desired sequence identity with the DNA encoding full-length native sequence PRO can then be identified using standard techniques known in the art.

Example 6

Expression of PRO in *E. Coli*

[0427] This example illustrates preparation of an unglycosylated form of PRO by recombinant expression in *E. coli*.

[0428] The DNA sequence encoding PRO is initially amplified using selected PCR primers. The primers should contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector. A variety of expression vectors may be employed. An example of a suitable vector is pBR322 (derived from *E. coli*; see Bolivar et al., Gene, 2:95 (1977)) which contains genes for ampicillin and tetracycline resistance. The vector is digested with restriction enzyme and dephosphorylated. The PCR amplified sequences are then ligated into the vector. The vector will preferably include sequences which encode for an antibiotic resistance gene, a trp promoter, a polyhis leader (including the first six STII codons, polyhis sequence, and enterokinase cleavage site), the PRO coding region, lambda transcriptional terminator, and an argU gene.

[0429] The ligation mixture is then used to transform a selected *E. coli* strain using the methods described in Sambrook et al., supra. Transformants are identified by their ability to grow on LB plates and antibiotic resistant colonies are then selected. Plasmid DNA can be isolated and confirmed by restriction analysis and DNA sequencing.

[0430] Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with antibiotics. The overnight culture may subsequently be used to inoculate a larger scale culture. The cells are then grown to a desired optical density, during which the expression promoter is turned on.

[0431] After culturing the cells for several more hours, the cells can be harvested by centrifugation. The cell pellet obtained by the centrifugation can be solubilized using various agents known in the art, and the solubilized PRO protein can then be purified using a metal chelating column under conditions that allow tight binding of the protein.

[0432] PRO may be expressed in *E. coli* in a poly-His tagged form, using the following procedure. The DNA encoding PRO is initially amplified using selected PCR primers. The primers will contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector, and other useful sequences providing for efficient and reliable translation initiation, rapid purification on a metal chelation column, and proteolytic removal with enterokinase. The PCR-amplified, poly-His tagged sequences are then ligated into an expression vector, which is used to transform an *E. coli* host based on strain 52 (W3110 fuhA(tonA) Ion galE rpoHts (htpRts) clpP(lacIq). Transformants are first grown in LB containing 50 mg/ml carbenicillin at 30° C. with shaking until an O.D.600 of 3-5 is reached. Cultures are then diluted 50-100 fold into CRAP media (prepared by mixing 3.57 g (NH₄)₂SO₄, 0.71 g sodium citrate-2H₂O, 1.07 g KCl, 5.36 g Difco yeast extract, 5.36 g Sheffield hycase SF in 500 mL water, as well as 110 mM MPOS, pH 7.3, 0.55% (w/v) glucose and 7 mM MgSO₄) and grown for approximately 20-30 hours at 30° C. with shaking. Samples are removed to verify expression by SDS-page analysis, and the bulk culture is centrifuged to pellet the cells. Cell pellets are frozen until purification and refolding.

[0433] *E. coli* paste from 0.5 to 1 L fermentations (6-10 g pellets) is resuspended in 10 volumes (w/v) in 7 M guanidine, 20 mM Tris, pH 8 buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1M and 0.02 M, respectively, and the solution is stirred overnight at 4° C. This step results in a denatured protein with all cysteine residues blocked by sulfitolization. The solution is centrifuged at 40,000 rpm in a Beckman Ultracentrifuge for 30 min. The supernatant is diluted with 3-5 volumes of metal chelate column buffer (6 M guanidine, 20 mM Tris, pH 7.4) and filtered through 0.22 micron filters to clarify. The clarified extract is loaded onto a 5 ml Qiagen Ni-NTA metal chelate column equilibrated in the metal chelate column buffer. The column is washed with additional buffer containing 50 mM imidazole (Calbiochem, Utrol grade), pH 7.4. The protein is eluted with buffer containing 250 mM imidazole. Fractions containing the desired protein are pooled and stored at 4° C. Protein concentration is estimated by its absorbance at 280 nm using the calculated extinction coefficient based on its amino acid sequence.

[0434] The proteins are refolded by diluting the sample slowly into freshly prepared refolding buffer consisting of: 20 mM Tris, pH 8.6, 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and 1 mM EDTA. Refolding volumes are chosen so that the final protein concentration is between 50 to 100 micrograms/ml. The refolding solution is stirred gently at 4° C. for 12-36 hours. The refolding reaction is quenched by the addition of TFA to a final concentration of 0.4% (pH of approximately 3). Before further purification of the protein, the solution is filtered through a 0.22 micron filter and acetonitrile is added to 2-10% final concentration. The refolded protein is chromatographed on a Poros R1/H reversed phase column using a mobile buffer of 0.1% TFA with elution with a gradient of acetonitrile from 10 to 80%. Aliquots of fractions with A280 absorbance are analyzed on SDS polyacrylamide gels and fractions containing homogeneous refolded protein are pooled. Generally, the properly refolded species of most proteins are eluted at the lowest concentrations of acetonitrile since those species are the most compact with their hydrophobic interiors shielded from interaction with the reversed phase resin. Aggregated species are usually eluted at higher acetonitrile concentrations. In addition to resolving misfolded forms of from the desired form, the reversed phase step also removes endotoxin from the samples.

[0435] Fractions containing the desired folded PRO polypeptide are pooled and the acetonitrile removed using a gentle stream of nitrogen directed at the solution. Proteins are formulated into 20 mM Hepes, pH 6.8 with 0.14 M sodium chloride and 4% mannitol by dialysis or by gel filtration using G25 Superfine (Pharmacia) resins equilibrated in the formulation buffer and sterile filtered.

[0436] Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

Example 7

Expression of PRO in Mammalian Cells

[0437] This example illustrates preparation of a potentially glycosylated form of PRO by recombinant expression in mammalian cells.

[0438] The vector, pRK5 (see EP 307,247, published Mar. 15, 1989), is employed as the expression vector. Optionally,

the PRO DNA is ligated into pRK5 with selected restriction enzymes to allow insertion of the PRO DNA using ligation methods such as described in Sambrook et al., supra. The resulting vector is called pRK5-PRO.

[0439] In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, nutrient components and/or antibiotics. About 10 μ g pRK5-PRO DNA is mixed with about 1 μ g DNA encoding the VA RNA gene [Thimmappaya et al., Cell, 31:543 (1982)] and dissolved in 500 μ l of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M CaCl₂. To this mixture is added, dropwise, 500 μ l of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM NaPO₄, and a precipitate is allowed to form for 10 minutes at 25° C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37° C. The culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

[0440] Approximately 24 hours after the transfections, the culture medium is removed and replaced with culture medium (alone) or culture medium containing 200 μ Ci/ml ³⁵S-cysteine and 200 μ Ci/ml ³⁵S-methionine. After a 12 hour incubation, the conditioned medium is collected, concentrated on a spin filter, and loaded onto a 15% SDS gel. The processed gel may be dried and exposed to film for a selected period of time to reveal the presence of PRO polypeptide. The cultures containing transfected cells may undergo further incubation (in serum free medium) and the medium is tested in selected bioassays.

[0441] In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran sulfate method described by Somparyrac et al., Proc. Natl. Acad. Sci., 12:7575 (1981). 293 cells are grown to maximal density in a spinner flask and 700 μ g pRK5-PRO DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20% glycerol for 90 seconds, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5 μ g/ml bovine insulin and 0.1 μ g/ml bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed PRO can then be concentrated and purified by any selected method, such as dialysis and/or column chromatography.

[0442] In another embodiment, PRO can be expressed in CHO cells. The pRK5-PRO can be transfected into CHO cells using known reagents such as CaPO₄ or DEAE-dextran. As described above, the cell cultures can be incubated, and the medium replaced with culture medium (alone) or medium containing a radiolabel such as ³⁵S-methionine. After determining the presence of PRO polypeptide, the culture medium may be replaced with serum free medium. Preferably, the cultures are incubated for about 6 days, and then the conditioned medium is harvested. The medium containing the expressed PRO can then be concentrated and purified by any selected method.

[0443] Epitope-tagged PRO may also be expressed in host CHO cells. The PRO may be subcloned out of the pRK5

vector. The subclone insert can undergo PCR to fuse in frame with a selected epitope tag such as a poly-his tag into a Baculovirus expression vector. The poly-his tagged PRO insert can then be subcloned into a SV40 driven vector containing a selection marker such as DHFR for selection of stable clones. Finally, the CHO cells can be transfected (as described above) with the SV40 driven vector. Labeling may be performed, as described above, to verify expression. The culture medium containing the expressed poly-His tagged PRO can then be concentrated and purified by any selected method, such as by Ni²⁺-chelate affinity chromatography.

[0444] PRO may also be expressed in CHO and/or COS cells by a transient expression procedure or in CHO cells by another stable expression procedure.

[0445] Stable expression in CHO cells is performed using the following procedure. The proteins are expressed as an IgG construct (immunoadhesin), in which the coding sequences for the soluble forms (e.g. extracellular domains) of the respective proteins are fused to an IgG1 constant region sequence containing the hinge, CH2 and CH2 domains and/or is a poly-His tagged form.

[0446] Following PCR amplification, the respective DNAs are subcloned in a CHO expression vector using standard techniques as described in Ausubel et al., *Current Protocols of Molecular Biology*, Unit 3.16, John Wiley and Sons (1997). CHO expression vectors are constructed to have compatible restriction sites 5' and 3' of the DNA of interest to allow the convenient shuttling of cDNA's. The vector used expression in CHO cells is as described in Lucas et al., *Nucl. Acids Res.* 24:9 (1774-1779) (1996), and uses the SV40 early promoter/enhancer to drive expression of the cDNA of interest and dihydrofolate reductase (DHFR). DHFR expression permits selection for stable maintenance of the plasmid following transfection.

[0447] Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect® (Quiagen), Dospere® or Eugene® (Boehringer Mannheim). The cells are grown as described in Lucas et al., supra. Approximately 3×10^{-7} cells are frozen in an ampule for further growth and production as described below.

[0448] The ampules containing the plasmid DNA are thawed by placement into water bath and mixed by vortexing. The contents are pipetted into a centrifuge tube containing 10 mLs of media and centrifuged at 1000 rpm for 5 minutes. The supernatant is aspirated and the cells are resuspended in 10 mL of selective media (0.2 μ m filtered PS20 with 5% 0.2 μ m diafiltered fetal bovine serum). The cells are then aliquoted into a 100 mL spinner containing 90 mL of selective media. After 1-2 days, the cells are transferred into a 250 mL spinner filled with 150 mL selective growth medium and incubated at 37° C. After another 2-3 days, 250 mL, 500 mL and 2000 mL spinners are seeded with 3×10^5 cells/mL. The cell media is exchanged with fresh media by centrifugation and resuspension in production medium. Although any suitable CHO media may be employed, a production medium described in U.S. Pat. No. 5,122,469, issued Jun. 16, 1992 may actually be used. A 3L production spinner is seeded at 1.2×10^6 cells/mL. On day 0, the cell number pH is determined. On day 1, the spinner is sampled and sparging with filtered air is commenced. On day 2, the spinner is sampled, the temperature shifted to 33°

C., and 30 mL of 500 g/L glucose and 0.6 mL of 10% antifoam (e.g., 35% polydimethylsiloxane emulsion, Dow Corning 365 Medical Grade Emulsion) taken. Throughout the production, the pH is adjusted as necessary to keep it at around 7.2. After 10 days, or until the viability dropped below 70%, the cell culture is harvested by centrifugation and filtering through a 0.22 μ m filter. The filtrate was either stored at 4° C. or immediately loaded onto columns for purification.

[0449] For the poly-His tagged constructs, the proteins are purified using a Ni-NTA column (Qiagen). Before purification, imidazole is added to the conditioned media to a concentration of 5 mM. The conditioned media is pumped onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4-5 ml/min. at 4° C. After loading, the column is washed with additional equilibration buffer and the protein eluted with equilibration buffer containing 0.25 M imidazole. The highly purified protein is subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 ml G25 Superfine (Pharmacia) column and stored at -80° C.

[0450] Immunoadhesin (Fc-containing) constructs are purified from the conditioned media as follows. The conditioned medium is pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column is washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein is immediately neutralized by collecting 1 ml fractions into tubes containing 275 μ L of 1 M Tris buffer, pH 9. The highly purified protein is subsequently desalted into storage buffer as described above for the poly-His tagged proteins. The homogeneity is assessed by SDS polyacrylamide gels and by N-terminal amino acid sequencing by Edman degradation.

[0451] Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

Example 8

Expression of PRO in Yeast

[0452] The following method describes recombinant expression of PRO in yeast.

[0453] First, yeast expression vectors are constructed for intracellular production or secretion of PRO from the ADH2/GAPDH promoter. DNA encoding PRO and the promoter is inserted into suitable restriction enzyme sites in the selected plasmid to direct intracellular expression of PRO. For secretion, DNA encoding PRO can be cloned into the selected plasmid, together with DNA encoding the ADH2/GAPDH promoter, a native PRO signal peptide or other mammalian signal peptide, or, for example, a yeast alpha-factor or invertase secretory signal/leader sequence, and linker sequences (if needed) for expression of PRO.

[0454] Yeast cells, such as yeast strain AB110, can then be transformed with the expression plasmids described above and cultured in selected fermentation media. The transformed yeast supernatants can be analyzed by precipitation with 10% trichloroacetic acid and separation by SDS-PAGE, followed by staining of the gels with Coomassie Blue stain.

[0455] Recombinant PRO can subsequently be isolated and purified by removing the cells from the fermentation

medium by centrifugation and then concentrating the medium using selected cartridge filters. The concentrate containing PRO may further be purified using selected column chromatography resins.

[0456] Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

Example 9

Expression of PRO in Baculovirus-Infected Insect Cells

[0457] The following method describes recombinant expression of PRO in Baculovirus-infected insect cells.

[0458] The sequence coding for PRO is fused upstream of an epitope tag contained a baculovirus expression vector. Such epitope tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids may be employed, including plasmids derived from commercially available plasmids such as pVL1393 (Novagen). Briefly, the sequence encoding PRO or the desired portion of the coding sequence of PRO such as the sequence encoding the extracellular domain of a transmembrane protein or the sequence encoding the mature protein if the protein is extracellular is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction enzyme sites. The product is then digested with those selected restriction enzymes and subcloned into the expression vector.

[0459] Recombinant baculovirus is generated by co-transfecting the above plasmid and BaculoGold™ virus DNA (PharMingen) into *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4-5 days of incubation at 28° C., the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilley et al., Baculovirus expression vectors: A Laboratory Manual, Oxford: Oxford University Press (1994).

[0460] Expressed poly-his tagged PRO can then be purified, for example, by Ni²⁺-chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by Rupert et al., Nature, 362:175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM MgCl₂; 0.1 mM EDTA; 10% glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% glycerol, pH 7.8) and filtered through a 0.45 μm filter. A Ni²⁺-NTA agarose column (commercially available from Qiagen) is prepared with a bed volume of 5 mL, washed with 25 mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to baseline A₂₈₀ with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 mM phosphate; 300 mM NaCl, 10% glycerol, pH 6.0), which elutes nonspecifically bound protein. After reaching A₂₈₀ baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or Western blot

with Ni²⁺-NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His₁₀-tagged PRO are pooled and dialyzed against loading buffer.

[0461] Alternatively, purification of the IgG tagged (or Fc tagged) PRO can be performed using known chromatography techniques, including for instance, Protein A or protein G column chromatography.

[0462] Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

Example 10

Preparation of Antibodies That Bind PRO

[0463] This example illustrates preparation of monoclonal antibodies which can specifically bind PRO.

[0464] Techniques for producing the monoclonal antibodies are known in the art and are described, for instance, in Goding, supra. Immunogens that may be employed include purified PRO, fusion proteins containing PRO, and cells expressing recombinant PRO on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

[0465] Mice, such as Balb/c, are immunized with the PRO immunogen emulsified in complete Freund's adjuvant and injected subcutaneously or intraperitoneally in an amount from 1-100 micrograms. Alternatively, the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research, Hamilton, Mont.) and injected into the animal's hind foot pads. The immunized mice are then boosted 10 to 12 days later with additional immunogen emulsified in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional immunization injections. Serum samples may be periodically obtained from the mice by retro-orbital bleeding for testing in ELISA assays to detect anti-PRO antibodies.

[0466] After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of PRO. Three to four days later, the mice are sacrificed and the spleen cells are harvested. The spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, available from ATCC, No. CRL 1597. The fusions generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.

[0467] The hybridoma cells will be screened in an ELISA for reactivity against PRO. Determination of "positive" hybridoma cells secreting the desired monoclonal antibodies against PRO is within the skill in the art.

[0468] The positive hybridoma cells can be injected intraperitoneally into syngeneic Balb/c mice to produce ascites containing the anti-PRO monoclonal antibodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks or roller bottles. Purification of the monoclonal antibodies produced in the ascites can be accomplished using ammonium sulfate precipitation, followed by gel exclusion chromatography. Alternatively, affinity chromatography based upon binding of antibody to protein A or protein G can be employed.

Example 11

Purification of PRO Polypeptides Using Specific Antibodies

[0469] Native or recombinant PRO polypeptides may be purified by a variety of standard techniques in the art of protein purification. For example, pro-PRO polypeptide, mature PRO polypeptide, or pre-PRO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the PRO polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the anti-PRO polypeptide antibody to an activated chromatographic resin.

[0470] Polyclonal immunoglobulins are prepared from immune sera either by precipitation with ammonium sulfate or by purification on immobilized Protein A (Pharmacia LKB Biotechnology, Piscataway, N.J.). Likewise, monoclonal antibodies are prepared from mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Partially purified immunoglobulin is covalently attached to a chromatographic resin such as CnBr-activated SEPHAROSE™ (Pharmacia LKB Biotechnology). The antibody is coupled to the resin, the resin is blocked, and the derivative resin is washed according to the manufacturer's instructions.

[0471] Such an immunoaffinity column is utilized in the purification of PRO polypeptide by preparing a fraction from cells containing PRO polypeptide in a soluble form. This preparation is derived by solubilization of the whole cell or of a subcellular fraction obtained via differential centrifugation by the addition of detergent or by other methods well known in the art. Alternatively, soluble PRO polypeptide containing a signal sequence may be secreted in useful quantity into the medium in which the cells are grown.

[0472] A soluble PRO polypeptide-containing preparation is passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of PRO polypeptide (e.g., high ionic strength buffers in the presence of detergent). Then, the column is eluted under conditions that disrupt antibody/PRO polypeptide binding (e.g., a low pH buffer such as approximately pH 2-3, or a high concentration of a chaotrope such as urea or thiocyanate ion), and PRO polypeptide is collected.

Example 12

Drug Screening

[0473] This invention is particularly useful for screening compounds by using PRO polypeptides or binding fragment thereof in any of a variety of drug screening techniques. The PRO polypeptide or fragment employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the PRO polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between PRO polypeptide or a fragment and the agent being tested.

Alternatively, one can examine the diminution in complex formation between the PRO polypeptide and its target cell or target receptors caused by the agent being tested.

[0474] Thus, the present invention provides methods of screening for drugs or any other agents which can affect a PRO polypeptide-associated disease or disorder. These methods comprise contacting such an agent with a PRO polypeptide or fragment thereof and assaying (i) for the presence of a complex between the agent and the PRO polypeptide or fragment, or (ii) for the presence of a complex between the PRO polypeptide or fragment and the cell, by methods well known in the art. In such competitive binding assays, the PRO polypeptide or fragment is typically labeled. After suitable incubation, free PRO polypeptide or fragment is separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of the particular agent to bind to PRO polypeptide or to interfere with the PRO polypeptide/cell complex.

[0475] Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to a polypeptide and is described in detail in WO 84/03564, published on Sep. 13, 1984. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. As applied to a PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. Bound PRO polypeptide is detected by methods well known in the art. Purified PRO polypeptide can also be coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the peptide and immobilize it on the solid support.

[0476] This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding PRO polypeptide specifically compete with a test compound for binding to PRO polypeptide or fragments thereof. In this manner, the antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with PRO polypeptide.

Example 13

Rational Drug Design

[0477] The goal of rational drug design is to produce structural analogs of biologically active polypeptide of interest (i.e., a PRO polypeptide) or of small molecules with which they interact, e.g., agonists, antagonists, or inhibitors. Any of these examples can be used to fashion drugs which are more active or stable forms of the PRO polypeptide or which enhance or interfere with the function of the PRO polypeptide in vivo (c.f., Hodgson, *Bio/Technology*, 9: 19-21(1991)).

[0478] In one approach, the three-dimensional structure of the PRO polypeptide, or of a PRO polypeptide-inhibitor complex, is determined by X-ray crystallography, by computer modeling or, most typically, by a combination of the two approaches. Both the shape and charges of the PRO polypeptide must be ascertained to elucidate the structure and to determine active site(s) of the molecule. Less often, useful information regarding the structure of the PRO polypeptide may be gained by modeling based on the structure of homologous proteins. In both cases, relevant

structural information is used to design analogous PRO polypeptide-like molecules or to identify efficient inhibitors. Useful examples of rational drug design may include molecules which have improved activity or stability as shown by Braxton and Wells, *Biochemistry*, 31:7796-7801 (1992) or which act as inhibitors, agonists, or antagonists of native peptides as shown by Athauda et al., *J. Biochem.*, 113:742-746(1993).

[0479] It is also possible to isolate a target-specific antibody, selected by functional assay, as described above, and then to solve its crystal structure. This approach, in principle, yields a pharmacore upon which subsequent drug design can be based. It is possible to bypass protein crystallography altogether by generating anti-idiotypic antibodies (anti-ids) to a functional, pharmacologically active antibody. As a mirror image of a mirror image, the binding site of the anti-ids would be expected to be an analog of the original receptor. The anti-id could then be used to identify and isolate peptides from banks of chemically or biologically produced peptides. The isolated peptides would then act as the pharmacore.

[0480] By virtue of the present invention, sufficient amounts of the PRO polypeptide may be made available to perform such analytical studies as X-ray crystallography. In addition, knowledge of the PRO polypeptide amino acid sequence provided herein will provide guidance to those employing computer modeling techniques in place of or in addition to X-ray crystallography.

Example 14

Pericyte c-Fos Induction (Assay 93)

[0481] This assay shows that certain polypeptides of the invention act to induce the expression of c-fos in pericyte cells and, therefore, are useful not only as diagnostic markers for particular types of pericyte-associated tumors but also for giving rise to antagonists which would be expected to be useful for the therapeutic treatment of pericyte-associated tumors. Induction of c-fos expression in pericytes is also indicative of the induction of angiogenesis and, as such, PRO polypeptides capable of inducing the expression of c-fos would be expected to be useful for the treatment of conditions where induced angiogenesis would be beneficial including, for example, wound healing, and the like. Specifically, on day 1, pericytes are received from VEC Technologies and all but 5 ml of media is removed from flask. On day 2, the pericytes are trypsinized, washed, spun and then plated onto 96 well plates. On day 7, the media is removed and the pericytes are treated with 100 μ l of PRO polypeptide test samples and controls (positive control=DME+5% serum \pm PDGF at 500 ng/ml; negative control=protein 32). Replicates are averaged and SD/CV are determined. Fold increase over Protein 32 (buffer control) value indicated by chemiluminescence units (RLU) luminometer reading verses frequency is plotted on a histogram. Two-fold above Protein 32 value is considered positive for the assay. ASY Matrix: Growth media=low glucose DMEM=20% FBS+1 \times pen strep+1 \times fungizone. Assay Media=low glucose DMEM+5% FBS.

[0482] The following polypeptides tested positive in this assay: PRO1347 and PRO1340.

Example 15

Ability of PRO Polypeptides to Stimulate the Release of Proteoglycans from Cartilage (Assay 97)

[0483] The ability of various PRO polypeptides to stimulate the release of proteoglycans from cartilage tissue was tested as follows.

[0484] The metacarpophalangeal joint of 4-6 month old pigs was aseptically dissected, and articular cartilage was removed by free hand slicing being careful to avoid the underlying bone. The cartilage was minced and cultured in bulk for 24 hours in a humidified atmosphere of 95% air, 5% CO₂ in serum free (SF) media (DME/F12 1:1) with 0.1% BSA and 100 U/ml penicillin and 100 μ g/ml streptomycin. After washing three times, approximately 100 mg of articular cartilage was aliquoted into microtubes and incubated for an additional 24 hours in the above SF media. PRO polypeptides were then added at 1% either alone or in combination with 18 ng/ml interleukin-1 α , a known stimulator of proteoglycan release from cartilage tissue. The supernatant was then harvested and assayed for the amount of proteoglycans using the 1,9-dimethyl-methylene blue (DMB) colorimetric assay (Farndale and Buttle, *Biochem. Biophys. Acta* 883:173-177 (1985)). A positive result in this assay indicates that the test polypeptide will find use, for example, in the treatment of sports-related joint problems, articular cartilage defects, osteoarthritis or rheumatoid arthritis.

[0485] When various PRO polypeptides were tested in the above assay, the polypeptides demonstrated a marked ability to stimulate release of proteoglycans from cartilage tissue both basally and after stimulation with interleukin-1 α and at 24 and 72 hours after treatment, thereby indicating that these PRO polypeptides are useful for stimulating proteoglycan release from cartilage tissue. As such, these PRO polypeptides are useful for the treatment of sports-related joint problems, articular cartilage defects, osteoarthritis or rheumatoid arthritis. The polypeptides testing positive in this assay are: PRO1565, PRO1693, PRO1801 and PRO10096.

Example 16

Detection of Polypeptides That Affect Glucose or FFA Uptake in Skeletal Muscle (Assay 106)

[0486] This assay is designed to determine whether PRO polypeptides show the ability to affect glucose or FFA uptake by skeletal muscle cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by skeletal muscle would be beneficial including, for example, diabetes or hyper- or hypo-insulinemia.

[0487] In a 96 well format, PRO polypeptides to be assayed are added to primary rat differentiated skeletal muscle, and allowed to incubate overnight. Then fresh media with the PRO polypeptide and \pm insulin are added to the wells. The sample media is then monitored to determine glucose and FFA uptake by the skeletal muscle cells. The insulin will stimulate glucose and FFA uptake by the skeletal muscle, and insulin in media without the PRO polypeptide is used as a positive control, and a limit for scoring. As the PRO polypeptide being tested may either stimulate or inhibit

glucose and FFA uptake, results are scored as positive in the assay if greater than 1.5 times or less than 0.5 times the insulin control.

[0488] The following PRO polypeptides tested positive as either stimulators or inhibitors of glucose and/or FFA uptake in this assay: PRO4405.

Example 17

Identification of PRO Polypeptides That Stimulate TNF- α Release In Human Blood (Assay 128)

[0489] This assay shows that certain PRO polypeptides of the present invention act to stimulate the release of TNF- α in human blood. PRO polypeptides testing positive in this assay are useful for, among other things, research purposes where stimulation of the release of TNF- α would be desired and for the therapeutic treatment of conditions wherein enhanced TNF- α release would be beneficial. Specifically, 200 μ l of human blood supplemented with 50 mM Hepes buffer (pH 7.2) is aliquotted per well in a 96 well test plate. To each well is then added 300 μ l of either the test PRO polypeptide in 50 mM Hepes buffer (at various concentrations) or 50 mM Hepes buffer alone (negative control) and the plates are incubated at 37° C. for 6 hours. The samples are then centrifuged and 50 μ l of plasma is collected from each well and tested for the presence of TNF- α by ELISA assay. A positive in the assay is a higher amount of TNF- α in the PRO polypeptide treated samples as compared to the negative control samples.

[0490] The following PRO polypeptides tested positive in this assay: PRO263, PRO295, PRO1282, PRO1063, PRO1356, PRO3543, and PRO5990.

Example 18

Tumor Versus Normal Differential Tissue Expression Distribution

[0491] Oligonucleotide probes were constructed from some of the PRO polypeptide-encoding nucleotide sequences shown in the accompanying figures for use in quantitative PCR amplification reactions. The oligonucleotide probes were chosen so as to give an approximately 200-600 base pair amplified fragment from the 3' end of its associated template in a standard PCR reaction. The oligonucleotide probes were employed in standard quantitative PCR amplification reactions with cDNA libraries isolated from different human tumor and normal human tissue samples and analyzed by agarose gel electrophoresis so as to obtain a quantitative determination of the level of expression of the PRO polypeptide-encoding nucleic acid in the various tumor and normal tissues tested. β -actin was used as a control to assure that equivalent amounts of nucleic acid was used in each reaction. Identification of the differential expression of the PRO polypeptide-encoding nucleic acid in one or more tumor tissues as compared to one or more normal tissues of the same tissue type renders the molecule useful diagnostically for the determination of the presence or absence of tumor in a subject suspected of possessing a tumor as well as therapeutically as a target for the treatment of a tumor in a subject possessing such a tumor. These assays provided the following results.

Molecule	is more highly expressed in:	as compared to:
DNA26843-1389	normal lung rectum tumor	lung tumor normal rectum
DNA30867-1335	normal kidney	kidney tumor
DNA40621-1440	normal lung	lung tumor
DNA40625-1189	normal lung	lung tumor
DNA45409-2511	melanoma tumor	normal akin
DNA56406-1704	kidney tumor normal skin	normal kidney melanoma tumor
DNA56410-1414	normal stomach	stomach tumor
DNA56436-1448	normal skin	melanoma tumor
DNA56855-1447	normal esophagus rectum tumor	esophageal tumor normal rectum
DNA56860-1510	normal kidney rectum tumor	kidney tumor normal rectum
DNA56862-1343	kidney tumor normal lung	normal kidney lung tumor
DNA56868-1478	normal stomach normal lung	stomach tumor lung tumor
DNA56869-1545	normal esophagus normal skin	esophageal tumor melanoma tumor
DNA57704-1452	normal stomach rectum tumor	stomach tumor normal rectum
DNA58723-1588	normal stomach kidney tumor normal akin	stomach tumor normal kidney melanoma tumor
DNA57827-1493	normal stomach normal skin	stomach tumor melanoma tumor
DNA58737-1473	esophageal tumor normal stomach	normal esophagus stomach tumor
DNA58846-1409	lung tumor	normal lung
DNA58850-1495	esophageal tumor kidney tumor	normal esophagus normal kidney
DNA58855-1422	normal stomach rectum tumor	stomach tumor normal rectum
DNA59211-1450	normal kidney	kidney tumor
DNA59212-1627	normal skin	melanoma tumor
DNA59213-1487	normal stomach normal skin	stomach tumor melanoma tumor
DNA59605-1418	melanoma tumor	normal skin
DNA59609-1470	esophageal tumor	normal esophagus
DNA59610-1556	esophageal tumor lung tumor normal skin	normal esophagus normal lung melanoma tumor
DNA59837-2545	normal skin	melanoma tumor
DNA59844-2542	normal skin esophageal tumor	melanoma tumor normal esophagus
DNA59854-1459	normal esophagus stomach tumor normal lung	esophageal tumor normal stomach lung tumor
DNA60625-1507	normal lung	lung tumor
DNA60629-1481	normal esophagus normal rectum	esophageal tumor rectum tumor
DNA61755-1554	normal stomach kidney tumor	stomach tumor normal kidney
DNA62812-1594	normal stomach normal lung normal rectum normal skin	stomach tumor lung tumor rectum tumor melanoma tumor
DNA62815-1576	esophageal tumor	normal esophagus
DNA64881-1602	normal stomach normal lung	stomach tumor lung tumor
DNA64902-1667	esophageal tumor kidney tumor	normal esophagus normal kidney
DNA65403-1565	normal esophagus	esophageal tumor
DNA66308-1537	normal lung	lung tumor
DNA66519-1535	kidney tumor	normal kidney
DNA66521-1583	normal esophagus normal stomach normal lung normal rectum normal skin	esophageal tumor stomach tumor lung tumor rectum tumor melanoma tumor
DNA66658-1584	normal lung melanoma tumor	lung tumor normal skin
DNA66660-1585	lung tumor	normal lung

-continued

Molecule	is more highly expressed in:	as compared to:
DNA66674-1599	kidney tumor normal lung	normal kidney lung tumor
DNA68862-2546	melanoma tumor	normal skin
DNA68866-1644	normal stomach	stomach tumor
DNA68871-1638	lung tumor normal skin	normal lung melanoma tumor
DNA68880-1676	normal lung normal skin	lung tumor melanoma tumor
DNA68883-1691	esophageal tumor	normal esophagus
DNA68885-1678	lung tumor	normal lung
DNA71277-1636	normal stomach	stomach tumor
DNA73734-1680	normal lung	lung tumor
DNA73735-1681	esophageal tumor normal kidney lung tumor normal skin	normal esophagus kidney tumor normal lung melanoma tumor
DNA76393-1664	esophageal tumor stomach tumor lung tumor rectum tumor	normal esophagus normal stomach normal lung normal rectum
DNA77568-1626	normal stomach lung tumor normal rectum	stomach tumor normal lung rectum tumor
DNA77626-1705	normal skin	melanoma tumor
DNA81754-2532	esophageal tumor	normal esophagus
DNA81757-2512	normal stomach melanoma tumor	stomach tumor normal skin
DNA82302-2529	normal stomach normal lung	stomach tumor lung tumor
DNA82340-2530	normal esophagus	esophageal tumor
DNA85066-2534	lung tumor normal skin	normal lung melanoma tumor
DNA87991-2540	esophageal tumor	normal esophagus
DNA92238-2539	normal skin	melanoma tumor
DNA96787-2534	normal kidney	kidney tumor

Example 19

Identification of Receptor/Ligand Interactions

[0492] In this assay, various PRO polypeptides are tested for ability to bind to a panel of potential receptor or ligand molecules for the purpose of identifying receptor/ligand interactions. The identification of a ligand for a known receptor, a receptor for a known ligand or a novel receptor/ligand pair is useful for a variety of indications including, for example, targeting bioactive molecules (linked to the ligand or receptor) to a cell known to express the receptor or ligand, use of the receptor or ligand as a reagent to detect the presence of the ligand or receptor in a composition suspected of containing the same, wherein the composition may comprise cells suspected of expressing the ligand or receptor, modulating the growth of or another biological or immunological activity of a cell known to express or respond to the receptor or ligand, modulating the immune response of cells or toward cells that express the receptor or ligand, allowing the preparation of agonists, antagonists and/or antibodies directed against the receptor or ligand which will modulate the growth of or a biological or immunological activity of a cell expressing the receptor or ligand, and various other indications which will be readily apparent to the ordinarily skilled artisan.

[0493] The assay is performed as follows. A PRO polypeptide of the present invention suspected of being a ligand for a receptor is expressed as a fusion protein containing the Fc domain of human IgG (an immunoadhesin).

Receptor-ligand binding is detected by allowing interaction of the immunoadhesin polypeptide with cells (e.g. Cos cells) expressing candidate PRO polypeptide receptors and visualization of bound immunoadhesin with fluorescent reagents directed toward the Fc fusion domain and examination by microscope. Cells expressing candidate receptors are produced by transient transfection, in parallel, of defined subsets of a library of cDNA expression vectors encoding PRO polypeptides that may function as receptor molecules. Cells are then incubated for 1 hour in the presence of the PRO polypeptide immunoadhesin being tested for possible receptor binding. The cells are then washed and fixed with paraformaldehyde. The cells are then incubated with fluorescent conjugated antibody directed against the Fc portion of the PRO polypeptide immunoadhesin (e.g. FITC conjugated goat anti-human-Fc antibody). The cells are then washed again and examined by microscope. A positive interaction is judged by the presence of fluorescent labeling of cells transfected with cDNA encoding a particular PRO polypeptide receptor or pool of receptors and an absence of similar fluorescent labeling of similarly prepared cells that have been transfected with other cDNA or pools of cDNA. If a defined pool of cDNA expression vectors is judged to be positive for interaction with a PRO polypeptide immunoadhesin, the individual cDNA species that comprise the pool are tested individually (the pool is "broken down") to determine the specific cDNA that encodes a receptor able to interact with the PRO polypeptide immunoadhesin.

[0494] In another embodiment of this assay, an epitope-tagged potential ligand PRO polypeptide (e.g. 8 histidine "His" tag) is allowed to interact with a panel of potential receptor PRO polypeptide molecules that have been expressed as fusions with the Fc domain of human IgG (immunoadhesins). Following a 1 hour co-incubation with the epitope tagged PRO polypeptide, the candidate receptors are each immunoprecipitated with protein A beads and the beads are washed. Potential ligand interaction is determined by western blot analysis of the immunoprecipitated complexes with antibody directed towards the epitope tag. An interaction is judged to occur if a band of the anticipated molecular weight of the epitope tagged protein is observed in the western blot analysis with a candidate receptor, but is not observed to occur with the other members of the panel of potential receptors.

[0495] Using these assays, the following receptor/ligand interactions have been herein identified:

[0496] (1) PRO10272 binds to PRO5801.

[0497] (2) PRO20110 binds to the human IL-17 receptor (Yao et al., *Cytokine* 9(11):794-800 (1997); also herein designated as PRO1) and to PRO20040.

[0498] (3) PRO10096 binds to PRO20233.

[0499] (4) PRO19670 binds to PRO1890.

[0500] The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the construct deposited, since the deposited embodiment is intended as a single illustration of certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this invention. The deposit of material herein does not constitute an admission that the

written description herein contained is inadequate to enable the practice of any aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims to the specific illustrations that it represents.

Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.

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<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 4

Met Ser Phe Leu Ile Asp Ser Ser Ile Met Ile Thr Ser Gln Ile
 1 5 10 15

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Leu	Phe	Phe	Gly	Phe	Gly	Trp	Leu	Phe	Phe	Met	Arg	Gln	Leu	Phe
				20						25				30
Lys	Asp	Tyr	Glu	Ile	Arg	Gln	Tyr	Val	Val	Gln	Val	Ile	Phe	Ser
				35						40				45
Val	Thr	Phe	Ala	Phe	Ser	Cys	Thr	Met	Phe	Glu	Leu	Ile	Ile	Phe
				50						55				60
Glu	Ile	Leu	Gly	Val	Leu	Asn	Ser	Ser	Ser	Arg	Tyr	Phe	His	Trp
				65						70				75
Lys	Met	Asn	Leu	Cys	Val	Ile	Leu	Leu	Ile	Leu	Val	Phe	Met	Val
				80						85				90
Pro	Phe	Tyr	Ile	Gly	Tyr	Phe	Ile	Val	Ser	Asn	Ile	Arg	Leu	Leu
				95						100				105
His	Lys	Gln	Arg	Leu	Leu	Phe	Ser	Cys	Leu	Leu	Trp	Leu	Thr	Phe
				110						115				120
Met	Tyr	Phe	Phe	Trp	Lys	Leu	Gly	Asp	Pro	Phe	Pro	Ile	Leu	Ser
				125						130				135
Pro	Lys	His	Gly	Ile	Leu	Ser	Ile	Glu	Gln	Leu	Ile	Ser	Arg	Val
				140						145				150
Gly	Val	Ile	Gly	Val	Thr	Leu	Met	Ala	Leu	Leu	Ser	Gly	Phe	Gly
				155						160				165
Ala	Val	Asn	Cys	Pro	Tyr	Thr	Tyr	Met	Ser	Tyr	Phe	Leu	Arg	Asn
				170						175				180
Val	Thr	Asp	Thr	Asp	Ile	Leu	Ala	Leu	Glu	Arg	Arg	Leu	Leu	Gln
				185						190				195
Thr	Met	Asp	Met	Ile	Ile	Ser	Lys	Lys	Lys	Arg	Met	Ala	Met	Ala
				200						205				210
Arg	Arg	Thr	Met	Phe	Gln	Lys	Gly	Glu	Val	His	Asn	Lys	Pro	Ser
				215						220				225
Gly	Phe	Trp	Gly	Met	Ile	Lys	Ser	Val	Thr	Thr	Ser	Ala	Ser	Gly
				230						235				240
Ser	Glu	Asn	Leu	Thr	Leu	Ile	Gln	Gln	Glu	Val	Asp	Ala	Leu	Glu
				245						250				255
Glu	Leu	Ser	Arg	Gln	Leu	Phe	Leu	Glu	Thr	Ala	Asp	Leu	Tyr	Ala
				260						265				270
Thr	Lys	Glu	Arg	Ile	Glu	Tyr	Ser	Lys	Thr	Phe	Lys	Gly	Lys	Tyr
				275						280				285
Phe	Asn	Phe	Leu	Gly	Tyr	Phe	Phe	Ser	Ile	Tyr	Cys	Val	Trp	Lys
				290						295				300
Ile	Phe	Met	Ala	Thr	Ile	Asn	Ile	Val	Phe	Asp	Arg	Val	Gly	Lys
				305						310				315
Thr	Asp	Pro	Val	Thr	Arg	Gly	Ile	Glu	Ile	Thr	Val	Asn	Tyr	Leu
				320						325				330
Gly	Ile	Gln	Phe	Asp	Val	Lys	Phe	Trp	Ser	Gln	His	Ile	Ser	Phe
				335						340				345
Ile	Leu	Val	Gly	Ile	Ile	Ile	Val	Thr	Ser	Ile	Arg	Gly	Leu	Leu
				350						355				360
Ile	Thr	Leu	Thr	Lys	Phe	Phe	Tyr	Ala	Ile	Ser	Ser	Ser	Lys	Ser
				365						370				375
Ser	Asn	Val	Ile	Val	Leu	Leu	Leu	Ala	Gln	Ile	Met	Gly	Met	Tyr
				380						385				390

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Phe Val Ser Ser Val Leu Leu Ile Arg Met Ser Met Pro Leu Glu
 395 400 405

Tyr Arg Thr Ile Ile Thr Glu Val Leu Gly Glu Leu Gln Phe Asn
 410 415 420

Phe Tyr His Arg Trp Phe Asp Val Ile Phe Leu Val Ser Ala Leu
 425 430 435

Ser Ser Ile Leu Phe Leu Tyr Leu Ala His Lys Gln Ala Pro Glu
 440 445 450

Lys Gln Met Ala Pro
 455

<210> SEQ ID NO 5
 <211> LENGTH: 2372
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 5

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agcagggaaa tccggatgtc tcggttatga agtggagcag tgagtgtgag      50
cctcaacata gttccagaac tctccatccg gactagtatt tgagcatctg      100
cctctcatat caccagtggc catctgaggt gtttccttgg ctctgaaggg      150
gtaggcacga tggccaggty cttcagcctg gtgttgcttc tcacttccat      200
ctggaccacg aggctcctgg tccaaggctc tttgctgca gaagagcttt      250
ccatccaggt gtcatgcaga attatgggga tcacccttgt gagcaaaaag      300
gcgaaccagc agctgaatth cacagaagct aaggaggcct gtaggctgct      350
gggactaagt ttggccggca aggaccaagt tgaaacagcc ttgaaagcta      400
gctttgaaac ttgcagctat ggctgggttg gagatggatt cgtggctcgc      450
tctaggatta gcccaaacc caagtgtggg aaaaatgggg tgggtgtcct      500
gatttgggag gttccagtga gccgacagtt tgcagcctat tgttacaact      550
catctgatac ttggactaac tcgtgcattc cagaaattat caccaccaa      600
gatcccatat tcaaacactca aactgcaaca caaacaacag aattttattgt      650
cagtgacagt acctactcgg tggcatcccc ttactctaca atacctgccc      700
ctactactac tcctcctgct ccagcttcca cttctattcc acggagaaaa      750
aaattgattt gtgtcacaga agtttttatg gaaactagca ccatgtctac      800
agaaaactgaa ccatttgttg aaaataaagc agcattcaag aatgaagctg      850
ctgggtttgg aggtgtcccc acggctctgc tagtgcttgc tctcctcttc      900
tttggtgctg cagctggtct tggattttgc tatgtcaaaa ggtatgtgaa      950
ggccttccct tttaaaaca agaatcagca gaaggaaatg atcgaacca      1000
aagtagtaaa ggaggagaag gccaatgata gcaaccctaa tgaggaatca      1050
aagaaaactg ataaaaacc agaagagtcc aagagtcaa gcaaaaactac      1100
cgtgcgatgc ctggaagctg aagtttagat gagacagaaa tgaggagaca      1150
cacctgaggg tggtttcttt catgctcctt accctgcccc agctggggaa      1200
atcaaaaggg ccaaagaacc aaagaagaaa gtccaccctt ggttcctaac      1250
tggaatcagc tcaggactgc cattggacta tggagtgcac caaagagaat      1300
gcccttctoc ttattgtaac cctgtctgga tcctatcctc ctacctcaa      1350
    
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agcttcccac ggcctttcta gcttggtat gtcctaataa tatcccactg      1400
ggagaaagga gttttgcaaa gtgcaaggac ctaaaacatc tcatcagtat      1450
ccagtggtaa aaaggcctcc tggctgtctg aggctagggtg ggttgaaagc      1500
caaggagtca ctgagaccaa ggctttctct actgattccg cagctcagac      1550
cctttcttca gctctgaaag agaaacacgt atcccacctg acatgtcctt      1600
ctgagcccgg taagagcaaa agaatggcag aaaagttag cccctgaaag      1650
ccatggagat tctcataact tgagacctaa tctctgtaaa gctaaaataa      1700
agaaatagaa caaggctgag gatcacgacag tacactgtca gcagggactg      1750
taaacacaga cagggtcaaa gtgttttctc tgaacacatt gagttggaat      1800
cactgttagg aacacacaca cttacttttt ctgggtctcta ccaactgtga      1850
tattttctct aggaaatata cttttacaag taacaaaaat aaaaactctt      1900
ataaatttct atttttatct gagttacaga aatgattact aaggaagatt      1950
actcagtaat ttgtttaaaa agtaataaaa ttcaacaaac atttgctgaa      2000
tagctactat atgtcaagtg ctgtgcaagg tattacactc tgtaattgaa      2050
tattattcct caaaaaattg cacatagtag aacgctatct gggagctat      2100
ttttttcagt tttgatattt ctagcttctc tacttccaaa ctaattttta      2150
tttttgctga gactaatctt attcattttc tctaataatgg caaccattat      2200
aaccttaatt tattattaac atacctaaga agtacattgt tacctctata      2250
taccaaagca ctttttaaaa gtgccattaa caaatgtatc actagccctc      2300
ctttttccaa caagaagggg ctgagagatg cagaaatatt tgtgacaaaa      2350
aattaaagca tttagaaaaa tt                                     2372

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<210> SEQ ID NO 6

<211> LENGTH: 322

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 6

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Met Ala Arg Cys Phe Ser Leu Val Leu Leu Leu Thr Ser Ile Trp
  1           5           10          15
Thr Thr Arg Leu Leu Val Gln Gly Ser Leu Arg Ala Glu Glu Leu
 20          25          30
Ser Ile Gln Val Ser Cys Arg Ile Met Gly Ile Thr Leu Val Ser
 35          40          45
Lys Lys Ala Asn Gln Gln Leu Asn Phe Thr Glu Ala Lys Glu Ala
 50          55          60
Cys Arg Leu Leu Gly Leu Ser Leu Ala Gly Lys Asp Gln Val Glu
 65          70          75
Thr Ala Leu Lys Ala Ser Phe Glu Thr Cys Ser Tyr Gly Trp Val
 80          85          90
Gly Asp Gly Phe Val Val Ile Ser Arg Ile Ser Pro Asn Pro Lys
 95          100         105
Cys Gly Lys Asn Gly Val Gly Val Leu Ile Trp Lys Val Pro Val
110         115         120
Ser Arg Gln Phe Ala Ala Tyr Cys Tyr Asn Ser Ser Asp Thr Trp

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	125		130		135
Thr Asn Ser Cys	Ile Pro Glu Ile Ile	Thr Thr Lys Asp Pro	Ile		
	140		145		150
Phe Asn Thr Gln	Thr Ala Thr Gln Thr	Thr Glu Phe Ile Val	Ser		
	155		160		165
Asp Ser Thr Tyr	Ser Val Ala Ser Pro	Tyr Ser Thr Ile Pro	Ala		
	170		175		180
Pro Thr Thr Thr	Pro Pro Ala Pro Ala	Ser Thr Ser Ile Pro	Arg		
	185		190		195
Arg Lys Lys Leu	Ile Cys Val Thr Glu	Val Phe Met Glu Thr	Ser		
	200		205		210
Thr Met Ser Thr	Glu Thr Glu Pro Phe	Val Glu Asn Lys Ala	Ala		
	215		220		225
Phe Lys Asn Glu	Ala Ala Gly Phe Gly	Gly Val Pro Thr Ala	Leu		
	230		235		240
Leu Val Leu Ala	Leu Leu Phe Phe Gly	Ala Ala Ala Gly Leu	Gly		
	245		250		255
Phe Cys Tyr Val	Lys Arg Tyr Val Lys	Ala Phe Pro Phe Thr	Asn		
	260		265		270
Lys Asn Gln Gln	Lys Glu Met Ile Glu	Thr Lys Val Val Lys	Glu		
	275		280		285
Glu Lys Ala Asn	Asp Ser Asn Pro Asn	Glu Glu Ser Lys Lys	Thr		
	290		295		300
Asp Lys Asn Pro	Glu Glu Ser Lys Ser	Pro Ser Lys Thr Thr	Val		
	305		310		315
Arg Cys Leu Glu	Ala Glu Val				
	320				

<210> SEQ ID NO 7
 <211> LENGTH: 2586
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 7

cgccgcgctc ccgcacccgc ggcccgccca ccgcgcccgt cccgcactctg	50
caccgcgagc ccggcggcct ccggcgggga gcgagcagat ccagtcgggc	100
ccgcagcgca actcgggtcca gtcggggcgg cggtgcggg cgagagcgg	150
agatgcagcg gcttggggcc accctgctgt gctgctgct ggcggcggcg	200
gtccccacgg ccccgcgcc cgcctcgacg gcgacctgg ctccagtcaa	250
gcccggccc gctctcagct acccgcagga ggaggccacc ctcaatgaga	300
tgttccgcga ggttgaggaa ctgatggagg acacgcagca caaattgcgc	350
agcgcggtgg aagagatgga ggcagaagaa gctgctgcta aagcatcatc	400
agaagtgaac ctggcaaaact tacctcccag ctatcacaat gagaccaaca	450
cagacacgaa ggttggaat aataccatcc atgtgcaccg agaaattcac	500
aagataacca acaaccagac tggacaaatg gtcttttcag agacagttat	550
cacatctgtg ggagacgaag aaggcagaag gagccacgag tgcatcatcg	600
acgaggactg tgggccccagc atgtactgcc agtttgccag cttccagtac	650
acctgccagc catgccgggg ccagaggatg ctctgcaccc gggacagtga	700

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gtgctgtgga gaccagctgt gtgtctgggg tcaactgcacc aaaatggcca	750
ccaggggcag caatgggacc atctgtgaca accagaggga ctgccagccg	800
gggctgtgct gtgccttcca gagaggcctg ctgttccctg tgtgcacacc	850
cctgccctg gagggcgagc tttgccatga ccccgccagc cggcttctg	900
acctcatcac ctgggagcta gaggctgatg gagccttga cccgatgccct	950
tgtgccagtg gcctcctctg ccagccccac agccacagcc tgggtgatgt	1000
gtgcaagcgc accttcctgg ggagccgtga ccaagatggg gagatcctgc	1050
tgccacagaga ggtccccgat gagtatgaag ttggcagctt catggaggag	1100
gtgccccag agctggagga cctggagagg agcctgactg aagagatggc	1150
gctggggag cctgcggctg ccgccctgc actgctggga ggggaagaga	1200
tttagatctg gaccagcctg tgggtagatg tgcaatagaa atagctaatt	1250
tatttcccca ggtgtgtgct ttagcgctgg gctgaccagg cttcttctca	1300
catcttcttc ccagtaagtt tccccctctg cttgacagca tgaggtgttg	1350
tgcatattgt cagctcccc aggctgttct ccaggcttca cagtctggtg	1400
cttgggagag tcaggcaggg ttaaactgca ggagcagttt gccaccctg	1450
tccagattat tggctgcttt gcctctacca gttggcagac agccgtttgt	1500
tctacatggc ttgataaatt gtttgagggg aggagatgga aacaatgtgg	1550
agtctccctc tgattggttt tgggaaatg tggagaagag tgccctgctt	1600
tgcaaacatc aacctggcaa aaatgcaaca aatgaatfff ccacgcagtt	1650
ctttccatgg gcataggtaa gctgtgcctt cagctgttgc agatgaaatg	1700
ttctgttacc cctgcattac atgtgtttat tcatccagca gtgttgctca	1750
gctcctacct ctgtgccagg gcagcatttt catatccaag atcaattccc	1800
tctctcagca cagcctgggg agggggtcat tgttctctc gtccatcag	1850
gatctcagag gctcagagac tgcaagctgc ttgcccaagt cacacagcta	1900
gtgaagacca gagcagtttc atctggttgt gactctaagc tcagtgtctt	1950
ctccactacc ccacaccagc ctgtgtgcca ccaaaagtgc tccccaaaag	2000
gaaggagaat gggatttttc ttgagcctg cacatctgga attaagggtca	2050
aactaattct cacatccctc taaaagttaa ctactgttag gaacagcagt	2100
gttctcacag tgtggggcag ccgtccttct aatgaagaca atgatattga	2150
cactgtccct ctttggcagt tgcattagta actttgaaag gtatatgact	2200
gagcgtagca tacaggtaa cctgcagaaa cagtacttag gtaattgtag	2250
ggcgaggatt ataatgaaa ttgcaaaat cacttagcag caactgaaga	2300
caattatcaa ccacgtggag aaaatcaaac cgagcagggc tgtgtgaaac	2350
atggttghaa tatgagactg cgaacactga actctacgcc actccacaaa	2400
tgatgttttc aggtgtcatg gactgttgcc accatgtatt catccagagt	2450
tcttaaagtt taaagttgca catgattgta taagcatgct ttctttgagt	2500
tttaaattat gtataaacat aagttgcatt tagaaatcaa gcataaatca	2550
cttcaactgc aaaaaaaaaa aaaaaaaaaa aaaaaa	2586

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<210> SEQ ID NO 8
<211> LENGTH: 350
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 8

Met  Gln  Arg  Leu  Gly  Ala  Thr  Leu  Leu  Cys  Leu  Leu  Leu  Ala  Ala
  1          5          10          15

Ala  Val  Pro  Thr  Ala  Pro  Ala  Pro  Ala  Pro  Thr  Ala  Thr  Ser  Ala
  20          25          30

Pro  Val  Lys  Pro  Gly  Pro  Ala  Leu  Ser  Tyr  Pro  Gln  Glu  Glu  Ala
  35          40          45

Thr  Leu  Asn  Glu  Met  Phe  Arg  Glu  Val  Glu  Glu  Leu  Met  Glu  Asp
  50          55          60

Thr  Gln  His  Lys  Leu  Arg  Ser  Ala  Val  Glu  Glu  Met  Glu  Ala  Glu
  65          70          75

Glu  Ala  Ala  Ala  Lys  Ala  Ser  Ser  Glu  Val  Asn  Leu  Ala  Asn  Leu
  80          85          90

Pro  Pro  Ser  Tyr  His  Asn  Glu  Thr  Asn  Thr  Asp  Thr  Lys  Val  Gly
  95          100         105

Asn  Asn  Thr  Ile  His  Val  His  Arg  Glu  Ile  His  Lys  Ile  Thr  Asn
  110         115         120

Asn  Gln  Thr  Gly  Gln  Met  Val  Phe  Ser  Glu  Thr  Val  Ile  Thr  Ser
  125         130         135

Val  Gly  Asp  Glu  Glu  Gly  Arg  Arg  Ser  His  Glu  Cys  Ile  Ile  Asp
  140         145         150

Glu  Asp  Cys  Gly  Pro  Ser  Met  Tyr  Cys  Gln  Phe  Ala  Ser  Phe  Gln
  155         160         165

Tyr  Thr  Cys  Gln  Pro  Cys  Arg  Gly  Gln  Arg  Met  Leu  Cys  Thr  Arg
  170         175         180

Asp  Ser  Glu  Cys  Cys  Gly  Asp  Gln  Leu  Cys  Val  Trp  Gly  His  Cys
  185         190         195

Thr  Lys  Met  Ala  Thr  Arg  Gly  Ser  Asn  Gly  Thr  Ile  Cys  Asp  Asn
  200         205         210

Gln  Arg  Asp  Cys  Gln  Pro  Gly  Leu  Cys  Cys  Ala  Phe  Gln  Arg  Gly
  215         220         225

Leu  Leu  Phe  Pro  Val  Cys  Thr  Pro  Leu  Pro  Val  Glu  Gly  Glu  Leu
  230         235         240

Cys  His  Asp  Pro  Ala  Ser  Arg  Leu  Leu  Asp  Leu  Ile  Thr  Trp  Glu
  245         250         255

Leu  Glu  Pro  Asp  Gly  Ala  Leu  Asp  Arg  Cys  Pro  Cys  Ala  Ser  Gly
  260         265         270

Leu  Leu  Cys  Gln  Pro  His  Ser  His  Ser  Leu  Val  Tyr  Val  Cys  Lys
  275         280         285

Pro  Thr  Phe  Val  Gly  Ser  Arg  Asp  Gln  Asp  Gly  Glu  Ile  Leu  Leu
  290         295         300

Pro  Arg  Glu  Val  Pro  Asp  Glu  Tyr  Glu  Val  Gly  Ser  Phe  Met  Glu
  305         310         315

Glu  Val  Arg  Gln  Glu  Leu  Glu  Asp  Leu  Glu  Arg  Ser  Leu  Thr  Glu
  320         325         330

Glu  Met  Ala  Leu  Gly  Glu  Pro  Ala  Ala  Ala  Ala  Ala  Ala  Leu  Leu

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	335	340	345	
Gly Gly Glu Glu Ile				
	350			
<210> SEQ ID NO 9				
<211> LENGTH: 1395				
<212> TYPE: DNA				
<213> ORGANISM: Homo Sapien				
<400> SEQUENCE: 9				
cggacgcgtg ggcggacgcg tggggcgtg gagaaagtgc caataaatac				50
atcatgcaac cccacggccc acctgtgaa ctctcgtgc ccagggctga				100
tgtgcgtctt ccagggctac tcatccaaag gcctaatacca acgttctgtc				150
ttcaatctgc aaatctatgg ggtcctggg ctcttctgga cccttaactg				200
ggtactggcc ctgggccaat gcgtcctcgc tggagccttt gcctccttct				250
actgggcctt ccacaagccc caggacatcc ctacctccc cttaatctct				300
gccttcatcc gcacactccg ttaccacact gggtcattgg catttggagc				350
cctcatcctg acccttgtgc agatagcccg ggtcatcttg gagtatattg				400
accacaagct cagaggagtg cagaaccctg tagcccgtg catcatgtgc				450
tgtttcaagt gctgcctctg gtgtctggaa aaatttatca agttcctaaa				500
ccgcaatgoa tacatcatga tcgccatcta cgggaagaat ttctgtgtct				550
cagccaaaaa tgcgttcatg ctactcatgc gaaacattgt cagggtggtc				600
gtcctggaca aagtacaga cctgctgctg ttctttggga agctgctggt				650
ggtcggaggc gtgggggtcc tgtccttctt tttttctcc ggtgcaccc				700
cgggctggyg taaagacttt aagagcccc acctcaacta ttactggctg				750
cccacatga cctccatcct gggggcctat gtcacgcca gcggcttctt				800
cagcgttttc ggcattgtgt tggacacgct ctctctctgc ttctgggaag				850
acctggagcg gaacaacggc tccctggacc ggccacta catgtccaag				900
agccttctaa agattctggg caagaagaac gaggcgcccc cggacaacaa				950
gaagagggaag aagtacacg tccggcctg atccaggact gcaccccacc				1000
cccaccgtcc agccatccaa cctcacttct ccttacaggt ctccattttg				1050
tggtaaaaaa aggttttagg ccagggcggc tggctcacgc ctgtaatacca				1100
acacttttag aggctgagc gggcgatca cctgagtcag gaggctcgaga				1150
ccagcctggc caacatggtg aaacctcctg ctctattaaa aatacaaaaa				1200
ttagccgaga gtggtggcat gcacctgtca tcccagctac tcgggaggct				1250
gaggcaggag aatcgcttga acccgggagg cagaggttgc agtgagccga				1300
gatcgcgcca ctgcaactca acctgggtga cagactctgt ctccaaaaa				1350
aaacaaacaa acaaaaagat ttattataag atattttggt aactc				1395

<210> SEQ ID NO 10
 <211> LENGTH: 321
 <212> TYPE: PRT
 <213> ORGANISM: Homo Sapien
 <400> SEQUENCE: 10

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Arg Thr Arg Gly Arg Thr Arg Gly Gly Cys Glu Lys Val Pro Ile
 1 5 10 15
 Asn Thr Ser Cys Asn Pro Thr Ala His Leu Val Asn Ser Ser Cys
 20 25 30
 Pro Gly Leu Met Cys Val Phe Gln Gly Tyr Ser Ser Lys Gly Leu
 35 40 45
 Ile Gln Arg Ser Val Phe Asn Leu Gln Ile Tyr Gly Val Leu Gly
 50 55 60
 Leu Phe Trp Thr Leu Asn Trp Val Leu Ala Leu Gly Gln Cys Val
 65 70 75
 Leu Ala Gly Ala Phe Ala Ser Phe Tyr Trp Ala Phe His Lys Pro
 80 85 90
 Gln Asp Ile Pro Thr Phe Pro Leu Ile Ser Ala Phe Ile Arg Thr
 95 100 105
 Leu Arg Tyr His Thr Gly Ser Leu Ala Phe Gly Ala Leu Ile Leu
 110 115 120
 Thr Leu Val Gln Ile Ala Arg Val Ile Leu Glu Tyr Ile Asp His
 125 130 135
 Lys Leu Arg Gly Val Gln Asn Pro Val Ala Arg Cys Ile Met Cys
 140 145 150
 Cys Phe Lys Cys Cys Leu Trp Cys Leu Glu Lys Phe Ile Lys Phe
 155 160 165
 Leu Asn Arg Asn Ala Tyr Ile Met Ile Ala Ile Tyr Gly Lys Asn
 170 175 180
 Phe Cys Val Ser Ala Lys Asn Ala Phe Met Leu Leu Met Arg Asn
 185 190 195
 Ile Val Arg Val Val Val Leu Asp Lys Val Thr Asp Leu Leu Leu
 200 205 210
 Phe Phe Gly Lys Leu Leu Val Val Gly Gly Val Gly Val Leu Ser
 215 220 225
 Phe Phe Phe Phe Ser Gly Arg Ile Pro Gly Leu Gly Lys Asp Phe
 230 235 240
 Lys Ser Pro His Leu Asn Tyr Tyr Trp Leu Pro Ile Met Thr Ser
 245 250 255
 Ile Leu Gly Ala Tyr Val Ile Ala Ser Gly Phe Phe Ser Val Phe
 260 265 270
 Gly Met Cys Val Asp Thr Leu Phe Leu Cys Phe Leu Glu Asp Leu
 275 280 285
 Glu Arg Asn Asn Gly Ser Leu Asp Arg Pro Tyr Tyr Met Ser Lys
 290 295 300
 Ser Leu Leu Lys Ile Leu Gly Lys Lys Asn Glu Ala Pro Pro Asp
 305 310 315
 Asn Lys Lys Arg Lys Lys
 320

<210> SEQ ID NO 11
 <211> LENGTH: 1901
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 11

gccccgcgcc cggcgcggg cgcccgaagc cgggagccac cgccatggg

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gcctgcctgg gagcctgctc cctgctcagc tgcgcgtcct gcctctgctg	100
ctctgcccc tgcacccctgt gcagctgctg ccccgccagc cgcaactcca	150
ccgtgagccg cctcatcttc acgttcttcc tcttctctggg ggtgctggtg	200
tccatcatta tgctgagccc gggcgtggag agtcagctct acaagctgcc	250
ctgggtgtgt gaggaggggg ccgggatccc caccgtcctg cagggccaca	300
tcgactgtgt ctccctgctt ggctaccgcg ctgtctaccg catgtgcttc	350
gccacggcgg ccttcttctt cttctttttc accctgctca tgctctgctg	400
gagcagcagc cgggaccccc gggtgccat ccagaatggg ttttggttct	450
ttaagtctct gatcctgggt ggctcaccg tgggtgcctt ctacatccct	500
gacggctcct tcaccaacat ctggttctac ttccgctcgc tgggctcctt	550
cctctctatc ctcatccagc tgggtgctgt catcgacttt gcgcaactct	600
ggaaccagcg gtggctgggc aaggccgagg agtgcgattc ccgtgcctgg	650
tacgcagcc tcttcttctt cactctcctc ttctacttgc tgtcgatcgc	700
ggccgtggcg ctgatgttca tgtactacac tgagcccagc ggctgccacg	750
agggcaaggt ctcatcagc ctcaacctca cctctgtgt ctgctgttcc	800
atcgctgctg tcctgcccac ggtccaggac gccagccca actcgggtct	850
gctgcagccg tcggctatca ccctctacac catgtttgtc acctggtcag	900
ccctatccag tatccctgaa cagaaatgca acccccattt gccaacccag	950
ctgggcaacg agacagttgt ggcagccccc gagggctatg agaccagtg	1000
gtgggatgoc ccgagcattg tgggcctcat catcttctc ctgtgcaccc	1050
tcttcatcag tctgcgctcc tcagaccacc ggcaggtgaa cagcctgatg	1100
cagaccgagg agtgcccacc tatgctagac gccacacagc agcagcagca	1150
gcaggtgcca gcctgtgagg gccgggcctt tgacaacgag caggacggcg	1200
tcacctacag ctactccttc ttccacttct gcctgggtgct ggctcactg	1250
cacgtcatga tgacgctcac caactggtac aagcccgggtg agaccggaa	1300
gatgatcagc acgtggaccg ccgtgtgggt gaagatctgt gccagctggg	1350
cagggtgctc cctctacctg tggaccctgg tagccccact cctcctgctc	1400
aaccgcgact tcagctgagg cagcctcaca gcctgccatc tggtgctctc	1450
tgccacctgg tgcctctcgg ctcggtgaca gccaacctgc ccctcccca	1500
caccaatcag ccaggctgag cccccacccc tgccccagct ccaggacctg	1550
cccctgagcc gggccttcta gtctagtgc cttcagggtc cgaggagcat	1600
caggctcctg cagagcccca tccccccgc acaccacac ggtggagctg	1650
ccttctcctt ccctcctcc ctggttccca tactcagcat ctcgatgaa	1700
agggctccct tgtcctcagg ctccacggga gggggctgc tggagagagc	1750
ggggaactcc caccacagtg gggcatccgg cactgaagcc ctggtgttcc	1800
tggtcaagtc cccagggga ccctgcccc ttctggact tegtgcctta	1850
ctgagtctct aagacttttt ctaataaaca agccagtgcg tgtaaaaaaa	1900
a	1901

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<210> SEQ ID NO 12
<211> LENGTH: 457
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 12

Met Gly Ala Cys Leu Gly Ala Cys Ser Leu Leu Ser Cys Ala Ser
 1           5           10          15
Cys Leu Cys Gly Ser Ala Pro Cys Ile Leu Cys Ser Cys Cys Pro
 20          25          30
Ala Ser Arg Asn Ser Thr Val Ser Arg Leu Ile Phe Thr Phe Phe
 35          40          45
Leu Phe Leu Gly Val Leu Val Ser Ile Ile Met Leu Ser Pro Gly
 50          55          60
Val Glu Ser Gln Leu Tyr Lys Leu Pro Trp Val Cys Glu Glu Gly
 65          70          75
Ala Gly Ile Pro Thr Val Leu Gln Gly His Ile Asp Cys Gly Ser
 80          85          90
Leu Leu Gly Tyr Arg Ala Val Tyr Arg Met Cys Phe Ala Thr Ala
 95          100         105
Ala Phe Phe Phe Phe Phe Phe Thr Leu Leu Met Leu Cys Val Ser
 110         115         120
Ser Ser Arg Asp Pro Arg Ala Ala Ile Gln Asn Gly Phe Trp Phe
 125         130         135
Phe Lys Phe Leu Ile Leu Val Gly Leu Thr Val Gly Ala Phe Tyr
 140         145         150
Ile Pro Asp Gly Ser Phe Thr Asn Ile Trp Phe Tyr Phe Gly Val
 155         160         165
Val Gly Ser Phe Leu Phe Ile Leu Ile Gln Leu Val Leu Leu Ile
 170         175         180
Asp Phe Ala His Ser Trp Asn Gln Arg Trp Leu Gly Lys Ala Glu
 185         190         195
Glu Cys Asp Ser Arg Ala Trp Tyr Ala Gly Leu Phe Phe Phe Thr
 200         205         210
Leu Leu Phe Tyr Leu Leu Ser Ile Ala Ala Val Ala Leu Met Phe
 215         220         225
Met Tyr Tyr Thr Glu Pro Ser Gly Cys His Glu Gly Lys Val Phe
 230         235         240
Ile Ser Leu Asn Leu Thr Phe Cys Val Cys Val Ser Ile Ala Ala
 245         250         255
Val Leu Pro Lys Val Gln Asp Ala Gln Pro Asn Ser Gly Leu Leu
 260         265         270
Gln Ala Ser Val Ile Thr Leu Tyr Thr Met Phe Val Thr Trp Ser
 275         280         285
Ala Leu Ser Ser Ile Pro Glu Gln Lys Cys Asn Pro His Leu Pro
 290         295         300
Thr Gln Leu Gly Asn Glu Thr Val Val Ala Gly Pro Glu Gly Tyr
 305         310         315
Glu Thr Gln Trp Trp Asp Ala Pro Ser Ile Val Gly Leu Ile Ile
 320         325         330
Phe Leu Leu Cys Thr Leu Phe Ile Ser Leu Arg Ser Ser Asp His

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	335		340		345
Arg Gln Val Asn Ser Leu Met Gln Thr Glu Glu Cys Pro Pro Met	350		355		360
Leu Asp Ala Thr Gln Gln Gln Gln Gln Val Ala Ala Cys Glu	365		370		375
Gly Arg Ala Phe Asp Asn Glu Gln Asp Gly Val Thr Tyr Ser Tyr	380		385		390
Ser Phe Phe His Phe Cys Leu Val Leu Ala Ser Leu His Val Met	395		400		405
Met Thr Leu Thr Asn Trp Tyr Lys Pro Gly Glu Thr Arg Lys Met	410		415		420
Ile Ser Thr Trp Thr Ala Val Trp Val Lys Ile Cys Ala Ser Trp	425		430		435
Ala Gly Leu Leu Leu Tyr Leu Trp Thr Leu Val Ala Pro Leu Leu	440		445		450
Leu Arg Asn Arg Asp Phe Ser	455				

<210> SEQ ID NO 13
 <211> LENGTH: 1572
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 13

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cgggccagcc tggggcggcc ggccaggaac caccogttaa ggtgtcttct      50
ctttagggat ggtgaggttg gaaaaagact cctgtaacct tcctccagga      100
tgaaccacct gccagaagac atggagaacg ctctcaccgg gagccagagc      150
tcccattgctt ctctgcgcaa tatccattcc atcaacccca cacaactcat      200
ggccaggatt gagtccctatg aaggaagggg aaagaaaggc atatctgatg      250
tcaggaggac tttctgtttg tttgtcacct ttgacctctt attcgttaaca      300
ttactgtgga taatagagtt aaatgtgaat ggaggcattg agaacacatt      350
agagaaggag gtgatgcagt atgactacta ttcttcatat tttgatatat      400
ttctctctggc agtttttcga tttaaagtgt taatacttgc atatgctgtg      450
tgacagactgc gccattgggtg ggcaatagcg ttgacaacgg cagtgaccag      500
tgcccttttta ctagcaaaaag tgatcctttc gaagcttttc tctcaagggg      550
cttttggtta tgtgctgccc atcatttcat tcctccttgc ctggattgag      600
acgtggttcc tggatttcaa agtgttacct caagaagcag aagaagaaaa      650
cagactcctg atagttcagg atgcttcaga gagggcagca cttatacctg      700
gtggtctttc tgatggtcag ttttattccc ctctgaatc cgaagcagga      750
tctgaagaag ctgaagaaaa acaggacagt gagaaccac ttttagaact      800
atgagtacta cttttgttaa atgtgaaaaa ccctcacaga aagtcatcga      850
ggcaaaaaga ggcaggcagt ggagtctccc tgtcgacagt aaagttgaaa      900
tggtgacgtc cactgctggc tttattgaac agctaataaa gatttattta      950
ttgtaatacc tcacaaacgt tgtaccatat ccatgcacat ttagttgcct     1000
gcctgtggct ggtaaggtaa tgtcatgatt catcctctct tcagtgagac     1050
    
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tgagcctgat gtgtaacaa ataggatgaag aaagtcttgt gctgtattcc      1100
taatcaaaag acttaataata ttgaagtaac acttttttag taagcaagat      1150
acctttttat ttcaattcac agaatggaat ttttttgttt catgtctcag      1200
atattttttg tatttctttt ttaacactct acatttcctt tgttttttaa      1250
ctcatgcaca tgtgctcttt gtacagtttt aaaaagtgta ataaaatctg      1300
acatgtcaat gtggctagtt ttatttttct tgttttgcac tatgtgtatg      1350
gcttgaagtg ttggacttgc aaaaggggaa gaaaggaatt gcgaatacat      1400
gtaaaatgtc accagacatt tgtattattt ttatcatgaa atcatgtttt      1450
tctctgattg ttctgaaatg ttctaaatc tcttattttg aatgcacaaa      1500
atgacttaaa ccattcatat catgtttcct ttgcgttcag ccaatttcaa      1550
ttaaataatgaa ctaaattaaa aa                                  1572

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<210> SEQ ID NO 14

<211> LENGTH: 234

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 14

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Met Asn His Leu Pro Glu Asp Met Glu Asn Ala Leu Thr Gly Ser
 1          5          10          15
Gln Ser Ser His Ala Ser Leu Arg Asn Ile His Ser Ile Asn Pro
          20          25          30
Thr Gln Leu Met Ala Arg Ile Glu Ser Tyr Glu Gly Arg Glu Lys
          35          40          45
Lys Gly Ile Ser Asp Val Arg Arg Thr Phe Cys Leu Phe Val Thr
          50          55          60
Phe Asp Leu Leu Phe Val Thr Leu Leu Trp Ile Ile Glu Leu Asn
          65          70          75
Val Asn Gly Gly Ile Glu Asn Thr Leu Glu Lys Glu Val Met Gln
          80          85          90
Tyr Asp Tyr Tyr Ser Ser Tyr Phe Asp Ile Phe Leu Leu Ala Val
          95          100          105
Phe Arg Phe Lys Val Leu Ile Leu Ala Tyr Ala Val Cys Arg Leu
          110          115          120
Arg His Trp Trp Ala Ile Ala Leu Thr Thr Ala Val Thr Ser Ala
          125          130          135
Phe Leu Leu Ala Lys Val Ile Leu Ser Lys Leu Phe Ser Gln Gly
          140          145          150
Ala Phe Gly Tyr Val Leu Pro Ile Ile Ser Phe Ile Leu Ala Trp
          155          160          165
Ile Glu Thr Trp Phe Leu Asp Phe Lys Val Leu Pro Gln Glu Ala
          170          175          180
Glu Glu Glu Asn Arg Leu Leu Ile Val Gln Asp Ala Ser Glu Arg
          185          190          195
Ala Ala Leu Ile Pro Gly Gly Leu Ser Asp Gly Gln Phe Tyr Ser
          200          205          210
Pro Pro Glu Ser Glu Ala Gly Ser Glu Glu Ala Glu Glu Lys Gln
          215          220          225
Asp Ser Glu Lys Pro Leu Leu Glu Leu

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230

<210> SEQ ID NO 15

<211> LENGTH: 2768

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 15

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caggaaagac tgagcccgcg gcctgccccg cccggctccc tgcgccgccc	100
ccgcctcccg ggacagaaga tgtgtcccag ggtccctctg ctgctgccgc	150
tgctcctgct actggccctg gggcctgggg tgcagggctg cccatccggc	200
tgccagtgca gccagccaca gacagtcttc tgcactgccc gccaggggac	250
cacggtgccc cgagacgtgc caccgcacac ggtggggctg tacgtctttg	300
agaacggcat caccatgctc gacgcaggca gctttgccgg cctgccggggc	350
ctgcagctcc tggacctgtc acagaaccag atcgcacgcc tgcccagcgg	400
ggtcttccag ccactcgcca acctcagcaa cctggacctg acggccaaca	450
ggctgcatga aatcaccaat gagaccttcc gtggcctgcg gcgcctcgag	500
cgcctctacc tgggcaagaa ccgcctccgc cacatccagc ctggtgcttt	550
cgacacgctc gaccgcctcc tggagctcaa gctgcaggac aacgagctgc	600
gggcactgcc cccgctgccc ctgccccgcc tgcctgctgct ggacctcagc	650
cacaacagcc tcctggccct ggagcccggc atcctggaca ctgccaacgt	700
ggaggcgctg cggctggctg gtctggggct gcagcagctg gacgaggggc	750
tcttcagccg cttgcgcaac ctccacgacc tggatgtgtc cgacaaccag	800
ctggagcgag tgccacctgt gatccgaggc ctccggggcc tgacgcgctt	850
gcggctggcc ggcaaacccc gcattgccc gctgcggccc gaggacctgg	900
ccggcctggc tgccctgcag gagctggatg tgagcaacct aagcctgcag	950
gccctgcctg gcgacctctc gggcctcttc ccccgctgc ggctgctggc	1000
agctgccccg aacccttca actgcgtgtg cccctgagc tggtttgccc	1050
cctgggtgog cgagagccac gtcacactgg ccagccctga ggagacgccc	1100
tgccacttcc cgccaagaa cgctggccgg ctgctcctgg agcttgacta	1150
cgccgacttt ggctgcccag ccaccaccac cacagccaca gtgcccacca	1200
cgaggcccgt ggtgcgggag cccacagcct tgccttctag cttggctcct	1250
acctggctta gcccacagc gccggccact gaggccccca gccgcctctc	1300
cactgcccca ccgactgtag ggctgtccc ccagcccag gactgcccac	1350
cgccacctg cctcaatggg ggcacatgcc acctggggac acggcaccac	1400
ctggcgctgt tgtgccccga aggtctcagc ggcctgtact gtgagagcca	1450
gatggggcag gggacacggc ccagccctac accagtcacg ccgaggccac	1500
cacggtccct gaccctgggc atcgagccgg tgagccccac ctccctgcgc	1550
gtggggctgc agcgtacct ccaggggagc tccgtgcagc tcaggagcct	1600
ccgtctcaac tatcgcaacc tatcggggcc tgataagcgg ctggtgacgc	1650

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tgcgactgcc tgcctcgctc gctgagtaca cggtcaccca gctgcgggccc	1700
aacgccactt actccgtctg tgtcatgcct ttggggcccg ggcgggtgcc	1750
ggagggcgag gaggcctgcg gggaggccca tacaccccca gccgtccact	1800
ccaaccacgc ccagtcacc caggcccgcg agggcaacct gccgtcctc	1850
attgcgcccg ccctggccgc ggtgctcctg gccgcgctgg ctgcggtggg	1900
ggcagcctac tgtgtgcggc gggggcgggc catggcagca gcggtcagg	1950
acaaagggca ggtggggcca ggggctgggc ccctggaact ggagggagtg	2000
aaggtcccct tggagccagg cccgaaggca acagaggcg gtggagaggc	2050
cctgcccagc gggctctgagt gtgaggtgcc actcatgggc ttcccagggc	2100
ctggcctcca gtcacccctc cagcaaaagc cctacatcta agccagagag	2150
agacagggca gctggggccg ggctctcagc cagtgagatg gccagcccc	2200
tctctgtgcc acaccacgta agttctcagt cccaacctcg gggatgtgtg	2250
cagacaggcg tgtgtgacca cagctgggcc ctgttccctc tggacctcgg	2300
tctctctatc tgtgagatgc tgtggcccag ctgacgagcc ctaacgtccc	2350
cagaaccgag tgcctatgag gacagtgtcc gccctgccct ccgcaacctg	2400
cagtcccctg gcacggcggg ccctgccatg tegtggtaac gcatgcctgg	2450
gtcctgtgtg gctctcccac tccaggcggg ccctgggggc cagtgaagga	2500
agctcccgga aagagcagag ggagagcggg taggcccgtg tgtgactcta	2550
gtcttggccc caggaagcga aggaacaaaa gaaactggaa aggaagatgc	2600
tttaggaaca tgttttgctt ttttaaaata tatatattta taagagatcc	2650
tttcccattt attctgggaa gatgttttcc aaactcagag acaaggactt	2700
tggtttttgt aagacaaacg atgatatgaa ggccttttgt aagaaaaaat	2750
aaaagatgaa gtgtgaaa	2768

<210> SEQ ID NO 16

<211> LENGTH: 673

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 16

Met Cys Ser Arg Val Pro Leu Leu Leu Pro Leu Leu Leu Leu Leu	
1 5 10 15	
Ala Leu Gly Pro Gly Val Gln Gly Cys Pro Ser Gly Cys Gln Cys	
20 25 30	
Ser Gln Pro Gln Thr Val Phe Cys Thr Ala Arg Gln Gly Thr Thr	
35 40 45	
Val Pro Arg Asp Val Pro Pro Asp Thr Val Gly Leu Tyr Val Phe	
50 55 60	
Glu Asn Gly Ile Thr Met Leu Asp Ala Gly Ser Phe Ala Gly Leu	
65 70 75	
Pro Gly Leu Gln Leu Leu Asp Leu Ser Gln Asn Gln Ile Ala Ser	
80 85 90	
Leu Pro Ser Gly Val Phe Gln Pro Leu Ala Asn Leu Ser Asn Leu	
95 100 105	
Asp Leu Thr Ala Asn Arg Leu His Glu Ile Thr Asn Glu Thr Phe	

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	110		115		120
Arg Gly Leu Arg Arg Leu Glu Arg Leu Tyr Leu Gly Lys Asn Arg	125		130		135
Ile Arg His Ile Gln Pro Gly Ala Phe Asp Thr Leu Asp Arg Leu	140		145		150
Leu Glu Leu Lys Leu Gln Asp Asn Glu Leu Arg Ala Leu Pro Pro	155		160		165
Leu Arg Leu Pro Arg Leu Leu Leu Leu Asp Leu Ser His Asn Ser	170		175		180
Leu Leu Ala Leu Glu Pro Gly Ile Leu Asp Thr Ala Asn Val Glu	185		190		195
Ala Leu Arg Leu Ala Gly Leu Gly Leu Gln Gln Leu Asp Glu Gly	200		205		210
Leu Phe Ser Arg Leu Arg Asn Leu His Asp Leu Asp Val Ser Asp	215		220		225
Asn Gln Leu Glu Arg Val Pro Pro Val Ile Arg Gly Leu Arg Gly	230		235		240
Leu Thr Arg Leu Arg Leu Ala Gly Asn Thr Arg Ile Ala Gln Leu	245		250		255
Arg Pro Glu Asp Leu Ala Gly Leu Ala Ala Leu Gln Glu Leu Asp	260		265		270
Val Ser Asn Leu Ser Leu Gln Ala Leu Pro Gly Asp Leu Ser Gly	275		280		285
Leu Phe Pro Arg Leu Arg Leu Leu Ala Ala Ala Arg Asn Pro Phe	290		295		300
Asn Cys Val Cys Pro Leu Ser Trp Phe Gly Pro Trp Val Arg Glu	305		310		315
Ser His Val Thr Leu Ala Ser Pro Glu Glu Thr Arg Cys His Phe	320		325		330
Pro Pro Lys Asn Ala Gly Arg Leu Leu Leu Glu Leu Asp Tyr Ala	335		340		345
Asp Phe Gly Cys Pro Ala Thr Thr Thr Thr Ala Thr Val Pro Thr	350		355		360
Thr Arg Pro Val Val Arg Glu Pro Thr Ala Leu Ser Ser Ser Leu	365		370		375
Ala Pro Thr Trp Leu Ser Pro Thr Ala Pro Ala Thr Glu Ala Pro	380		385		390
Ser Pro Pro Ser Thr Ala Pro Pro Thr Val Gly Pro Val Pro Gln	395		400		405
Pro Gln Asp Cys Pro Pro Ser Thr Cys Leu Asn Gly Gly Thr Cys	410		415		420
His Leu Gly Thr Arg His His Leu Ala Cys Leu Cys Pro Glu Gly	425		430		435
Phe Thr Gly Leu Tyr Cys Glu Ser Gln Met Gly Gln Gly Thr Arg	440		445		450
Pro Ser Pro Thr Pro Val Thr Pro Arg Pro Pro Arg Ser Leu Thr	455		460		465
Leu Gly Ile Glu Pro Val Ser Pro Thr Ser Leu Arg Val Gly Leu	470		475		480
Gln Arg Tyr Leu Gln Gly Ser Ser Val Gln Leu Arg Ser Leu Arg	485		490		495

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Leu	Thr	Tyr	Arg	Asn	Leu	Ser	Gly	Pro	Asp	Lys	Arg	Leu	Val	Thr
				500					505					510
Leu	Arg	Leu	Pro	Ala	Ser	Leu	Ala	Glu	Tyr	Thr	Val	Thr	Gln	Leu
				515					520					525
Arg	Pro	Asn	Ala	Thr	Tyr	Ser	Val	Cys	Val	Met	Pro	Leu	Gly	Pro
				530					535					540
Gly	Arg	Val	Pro	Glu	Gly	Glu	Glu	Ala	Cys	Gly	Glu	Ala	His	Thr
				545					550					555
Pro	Pro	Ala	Val	His	Ser	Asn	His	Ala	Pro	Val	Thr	Gln	Ala	Arg
				560					565					570
Glu	Gly	Asn	Leu	Pro	Leu	Leu	Ile	Ala	Pro	Ala	Leu	Ala	Ala	Val
				575					580					585
Leu	Leu	Ala	Ala	Leu	Ala	Ala	Val	Gly	Ala	Ala	Tyr	Cys	Val	Arg
				590					595					600
Arg	Gly	Arg	Ala	Met	Ala	Ala	Ala	Ala	Gln	Asp	Lys	Gly	Gln	Val
				605					610					615
Gly	Pro	Gly	Ala	Gly	Pro	Leu	Glu	Leu	Glu	Gly	Val	Lys	Val	Pro
				620					625					630
Leu	Glu	Pro	Gly	Pro	Lys	Ala	Thr	Glu	Gly	Gly	Gly	Glu	Ala	Leu
				635					640					645
Pro	Ser	Gly	Ser	Glu	Cys	Glu	Val	Pro	Leu	Met	Gly	Phe	Pro	Gly
				650					655					660
Pro	Gly	Leu	Gln	Ser	Pro	Leu	His	Ala	Lys	Pro	Tyr	Ile		
				665					670					

<210> SEQ ID NO 17
 <211> LENGTH: 1672
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 17

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gcgacagctc atgcgggtcc ggatagggct gacgctgctg ctgtgtgcgg	100
tgctgctgag cttggcctcg gcgtcctcgg atgaagaagg cagccaggat	150
gaatccttag attccaagac tactttgaca tcagatgagt cagtaaagga	200
ccatactact gcaggcagag tagttgctgg tcaaatatth cttgattcag	250
aagaatctga attagaatcc tctattcaag aagaggaaga cagcctcaag	300
agccaagagg gggaaagtgt cacagaagat atcagctttc tagagtctcc	350
aaatccagaa aacaaggact atgaagagcc aaagaaagta cggaaaccag	400
ctttgaccgc cattgaaggc acagcacatg gggagccctg ccacttcctt	450
tttcttttcc tagataagga gtatgatgaa tgtacatcag atgggagggg	500
agatggcaga ctgtggtgtg ctacaaccta tgactacaaa gcagatgaaa	550
agtggggctt ttgtgaaact gaagaagagg ctgctaagag acggcagatg	600
caggaagcag aatgatgta tcaaactgga atgaaaatcc ttaatggaag	650
caataagaaa agccaataaa gagaagcata tcggtatctc caaaaggcag	700
caagcatgaa ccataccaaa gccttgagga gagggtcata tgctctttta	750
tttgggtgatt acttgccaca gaatatccag gcagcgagag agatgtttga	800

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gaagctgact gaggaaggct ctccaaggg acagactgct cttggctttc      850
tgtatgcctc tggacttggt gttaattcaa gtcaggcaaa ggctcttgta      900
tattatacat ttggagctct tgggggcaat ctaatagccc acatggtttt      950
ggtaagtaga ctttagtgga aggctaataa tattaacatc agaagaatth      1000
gtggtttata gcggccacaa ctttttcagc tttcatgac cagatttgct      1050
tgtattaaga ccaaatattc agttgaactt ccttcaaatt cttgttaatg      1100
gatataacac atggaatcta catgtaaatg aaagttggtg gagtccacaa      1150
tttttcttta aaatgattag tttggctgat tgcccctaaa aagagagatc      1200
tgataaatgg ctctttttaa attttctctg agttggaatt gtcagaatca      1250
ttttttacat tagattatca taattttaaa aatthttctt tagthtttca      1300
aaatthtgta aatggtggct atagaaaaac aacatgaaat attatacaat      1350
atthtgcaac aatgccctaa gaattgtaa aatcatgga gttatthtg      1400
cagaatgact ccagagagct ctactthctg thttttactt tcatgattg      1450
gctgtcttcc catttattct ggtcatttat tgctagtgac actgtgcttg      1500
cttccagtag tctcattttc cctattttgc taatthgta cttthttctt      1550
gctaattggg aagattaact cattthtaat aaaattatgt ctaagattaa      1600
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa      1650
aaaaaaaaaa aaaaaaaaaa aa                                     1672
    
```

```

<210> SEQ ID NO 18
<211> LENGTH: 301
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien
    
```

<400> SEQUENCE: 18

```

Met Arg Val Arg Ile Gly Leu Thr Leu Leu Leu Cys Ala Val Leu
 1           5           10          15
Leu Ser Leu Ala Ser Ala Ser Ser Asp Glu Glu Gly Ser Gln Asp
 20          25          30
Glu Ser Leu Asp Ser Lys Thr Thr Leu Thr Ser Asp Glu Ser Val
 35          40          45
Lys Asp His Thr Thr Ala Gly Arg Val Val Ala Gly Gln Ile Phe
 50          55          60
Leu Asp Ser Glu Glu Ser Glu Leu Glu Ser Ser Ile Gln Glu Glu
 65          70          75
Glu Asp Ser Leu Lys Ser Gln Glu Gly Glu Ser Val Thr Glu Asp
 80          85          90
Ile Ser Phe Leu Glu Ser Pro Asn Pro Glu Asn Lys Asp Tyr Glu
 95          100         105
Glu Pro Lys Lys Val Arg Lys Pro Ala Leu Thr Ala Ile Glu Gly
110          115         120
Thr Ala His Gly Glu Pro Cys His Phe Pro Phe Leu Phe Leu Asp
125          130         135
Lys Glu Tyr Asp Glu Cys Thr Ser Asp Gly Arg Glu Asp Gly Arg
140          145         150
Leu Trp Cys Ala Thr Thr Tyr Asp Tyr Lys Ala Asp Glu Lys Trp
    
```

-continued

	155		160		165
Gly Phe Cys Glu Thr Glu Glu Glu Ala Ala Lys Arg Arg Gln Met	170		175		180
Gln Glu Ala Glu Met Met Tyr Gln Thr Gly Met Lys Ile Leu Asn	185		190		195
Gly Ser Asn Lys Lys Ser Gln Lys Arg Glu Ala Tyr Arg Tyr Leu	200		205		210
Gln Lys Ala Ala Ser Met Asn His Thr Lys Ala Leu Glu Arg Val	215		220		225
Ser Tyr Ala Leu Leu Phe Gly Asp Tyr Leu Pro Gln Asn Ile Gln	230		235		240
Ala Ala Arg Glu Met Phe Glu Lys Leu Thr Glu Glu Gly Ser Pro	245		250		255
Lys Gly Gln Thr Ala Leu Gly Phe Leu Tyr Ala Ser Gly Leu Gly	260		265		270
Val Asn Ser Ser Gln Ala Lys Ala Leu Val Tyr Tyr Thr Phe Gly	275		280		285
Ala Leu Gly Gly Asn Leu Ile Ala His Met Val Leu Val Ser Arg	290		295		300

Leu

<210> SEQ ID NO 19
 <211> LENGTH: 1508
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 19

```

aattcagatt ttaagcccat tctgcagtgg aatttcatga actagcaaga      50
ggacaccatc ttcttgtatt atacaagaaa ggagtgtacc tatcacacac      100
agggggaaaa atgctctttt ggggtgctagg cctcctaata ctctgtgggt      150
ttctgtggag tcgtaaagga aactaaaga ttgaagacat cactgataag      200
tacattttta tcaactggatg tgactcgggc tttggaaact tggcagccag      250
aacttttgat aaaaagggat ttcattgtaat cgctgcctgt ctgactgaat      300
caggatcaac agctttaaag gcagaaacct cagagagact tcgtactgtg      350
cttctggatg tgaccgaccc agagaatgtc aagaggactg cccagtgggt      400
gaagaaccaa gttggggaga aaggctctctg gggctctgac aataatgctg      450
gtgttcccgg cgtgctggct cccactgact ggctgacact agaggactac      500
agagaaccta ttgaagtga cctgtttgga ctcatcagtg tgacactaaa      550
tatgcttcct ttggtcaaga aagctcaagg gagagttatt aatgtctcca      600
gtgttgagg tcgccttgca atcggtggag ggggctatac tccatccaaa      650
tatgcagtgg aaggtttcaa tgacagctta agacgggaca tgaagcttt      700
tggtgtgcac gtctcatgca ttgaaccagg attgttcaaa acaaacttgg      750
cagatccagt aaaggaatt gaaaaaaac togccatttg ggagcagctg      800
tctccagaca tcaacaaca atatggagaa ggttacattg aaaaaagtct      850
agacaaactg aaaggcaata aatcctatgt gaacatggac ctctctccgg      900
tggtagagtg catggaccac gctctaacaa gtctcttccc taagactcat      950
    
```

-continued

```
tatgccgctg gaaaagatgc caaaattttc tggatacctc tgtctcacat      1000
gccagcagct ttgcaagact ttttattggt gaaacagaaa gcagagctgg      1050
ctaattccaa ggcagtgatga ctacagtaac cacaaatgct tcctccaggc      1100
tatgaaattg gccgatttca agaacacatc tccttttcaa cccattcct      1150
tatctgctcc aacctggact catttagatc gtgcttattt ggattgcaaa      1200
agggagtccc accatcgctg gtggtatccc agggtcctcg ctcaagtttt      1250
ctttgaaaaa gagggctgga atggtacatc acataggcaa gtctgcctcct      1300
gtatttaggc tttgcctgct tgggtgatg taagggaaat tgaagactt      1350
gccattcaa  aatgatcttt accgtggcct gccccatgct tatggtcccc      1400
agcatttaca gtaacttgct aatgtaagt atcatctctt atctaaatat      1450
taaaagataa gtcaacccaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa      1500
aaaaaaaaa      1508
```

```
<210> SEQ ID NO 20
<211> LENGTH: 319
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien
```

```
<400> SEQUENCE: 20
```

```
Met Leu Phe Trp Val Leu Gly Leu Leu Ile Leu Cys Gly Phe Leu
 1           5           10          15
Trp Thr Arg Lys Gly Lys Leu Lys Ile Glu Asp Ile Thr Asp Lys
 20          25          30
Tyr Ile Phe Ile Thr Gly Cys Asp Ser Gly Phe Gly Asn Leu Ala
 35          40          45
Ala Arg Thr Phe Asp Lys Lys Gly Phe His Val Ile Ala Ala Cys
 50          55          60
Leu Thr Glu Ser Gly Ser Thr Ala Leu Lys Ala Glu Thr Ser Glu
 65          70          75
Arg Leu Arg Thr Val Leu Leu Asp Val Thr Asp Pro Glu Asn Val
 80          85          90
Lys Arg Thr Ala Gln Trp Val Lys Asn Gln Val Gly Glu Lys Gly
 95          100         105
Leu Trp Gly Leu Ile Asn Asn Ala Gly Val Pro Gly Val Leu Ala
 110         115         120
Pro Thr Asp Trp Leu Thr Leu Glu Asp Tyr Arg Glu Pro Ile Glu
 125         130         135
Val Asn Leu Phe Gly Leu Ile Ser Val Thr Leu Asn Met Leu Pro
 140         145         150
Leu Val Lys Lys Ala Gln Gly Arg Val Ile Asn Val Ser Ser Val
 155         160         165
Gly Gly Arg Leu Ala Ile Val Gly Gly Gly Tyr Thr Pro Ser Lys
 170         175         180
Tyr Ala Val Glu Gly Phe Asn Asp Ser Leu Arg Arg Asp Met Lys
 185         190         195
Ala Phe Gly Val His Val Ser Cys Ile Glu Pro Gly Leu Phe Lys
 200         205         210
Thr Asn Leu Ala Asp Pro Val Lys Val Ile Glu Lys Lys Leu Ala
```

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	215		220		225
Ile Trp Glu Gln Leu Ser Pro Asp Ile Lys Gln Gln Tyr Gly Glu	230		235		240
Gly Tyr Ile Glu Lys Ser Leu Asp Lys Leu Lys Gly Asn Lys Ser	245		250		255
Tyr Val Asn Met Asp Leu Ser Pro Val Val Glu Cys Met Asp His	260		265		270
Ala Leu Thr Ser Leu Phe Pro Lys Thr His Tyr Ala Ala Gly Lys	275		280		285
Asp Ala Lys Ile Phe Trp Ile Pro Leu Ser His Met Pro Ala Ala	290		295		300
Leu Gln Asp Phe Leu Leu Leu Lys Gln Lys Ala Glu Leu Ala Asn	305		310		315

Pro Lys Ala Val

<210> SEQ ID NO 21
 <211> LENGTH: 1849
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 21

```

ctgaggcggc ggtagcatgg agggggagag tacgtcggcg gtgctctcgg          50
gctttgtgct cggcgcactc gctttccagc acctcaacac ggactcggac          100
acggaaggtt ttcttcttgg ggaagtaaaa ggtgaagcca agaacagcat          150
tactgattcc caaatggatg atgttgaagt tgtttatata attgacattc          200
agaaatatat tccatgctat cagcttttta gcttttataa ttcttcaggc          250
gaagtaaatg agcaagcact gaagaaaata ttatcaaatg tcaaaaagaa          300
tgtggtaggt tgggtacaaat tccgtcgtca ttcagatcag atcatgacgt          350
ttagagagag gctgcttcac aaaaacttgc aggagcattt ttcaaaccaa          400
gacctgtttt ttctgctatt aacaccaagt ataataacag aaagctgctc          450
tactcatcga ctggaacatt cttatataa acctcaaaaa ggactttttc          500
acagggtacc tttagtggtt gccaatctgg gcatgtctga acaactgggt          550
tataaaactg tatcaggttc ctgtatgtcc actggtttta gccgagcagt          600
acaaacacac agctctaaat tttttgaaga agatggatcc ttaaaggagg          650
tacataagat aaatgaaatg tatgcttcat tacaagagga attaaagagt          700
atatgcaaaa aagtgaaga cagtgaacaa gcagtagata aactagtaaa          750
ggatgtaaac agattaaac gagaaattga gaaaaggaga ggagcacaga          800
ttcaggcagc aagagagaag aacatccaaa aagaccctca ggagaacatt          850
tttctttgtc aggcattacg gacctttttt ccaaattctg aatttcttca          900
ttcatgtggt atgtctttaa aaaatagaca tgtttctaaa agtagctgta          950
actacaacca ccatctcgat gtagtagaca atctgacctt aatggtagaa          1000
cactactgaca ttctgaagc tagtccagct agtacaccac aaatcattaa          1050
gcataaagcc ttagacttag atgacagatg gcaattcaag agatctcggg          1100
tgtagtagtac acaagacaaa cgatctaaag caaatactgg tagtagtaac          1150
    
```

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```

caagataaag catccaaaat gagcagccca gaaacagatg aagaaattga      1200
aaagatgaag ggttttggtg aatattcacg gtctoctaca tttgatacct      1250
ttaaactta caaggagatt tttttatttg gctgatgggt aaagccaaac      1300
atctctattg tttttactat gttgagctac ttgcagtaag ttcatttggt      1350
tttactatgt tcacctgttt gcagtaatac acagataact cttagtgcac      1400
ttacttcaca aagtactttt tcaaactca gatgctttta tttccaaacc      1450
tttttttcac ctttcactaa gttgttgagg ggaaggctta cacagacaca      1500
ttctttagaa ttgaaaagt gagaccaggc acagtggctc acacctgtaa      1550
tcccagcact tagggaagac aagtcaggag gattgattga agctaggagt      1600
tagagaccag cctgggcaac gtattgagac catgtctatt aaaaaataaa      1650
atgaaaaagc aagaatagcc ttattttcaa aatatgaaa gaaatttata      1700
tgaaaaatta tctgagtcac taaaattctc ctttaagtat acttttttag      1750
aagtacatta tggctagagt tgccagataa aatgctggat atcatgcaat      1800
aaatttgcaa aacatcatct aaaatttaaa aaaaaaaaaa aaaaaaaaaa      1849

```

<210> SEQ ID NO 22

<211> LENGTH: 409

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 22

```

Met Glu Gly Glu Ser Thr Ser Ala Val Leu Ser Gly Phe Val Leu
  1          5          10          15
Gly Ala Leu Ala Phe Gln His Leu Asn Thr Asp Ser Asp Thr Glu
  20          25          30
Gly Phe Leu Leu Gly Glu Val Lys Gly Glu Ala Lys Asn Ser Ile
  35          40          45
Thr Asp Ser Gln Met Asp Asp Val Glu Val Val Tyr Thr Ile Asp
  50          55          60
Ile Gln Lys Tyr Ile Pro Cys Tyr Gln Leu Phe Ser Phe Tyr Asn
  65          70          75
Ser Ser Gly Glu Val Asn Glu Gln Ala Leu Lys Lys Ile Leu Ser
  80          85          90
Asn Val Lys Lys Asn Val Val Gly Trp Tyr Lys Phe Arg Arg His
  95          100         105
Ser Asp Gln Ile Met Thr Phe Arg Glu Arg Leu Leu His Lys Asn
  110         115         120
Leu Gln Glu His Phe Ser Asn Gln Asp Leu Val Phe Leu Leu Leu
  125         130         135
Thr Pro Ser Ile Ile Thr Glu Ser Cys Ser Thr His Arg Leu Glu
  140         145         150
His Ser Leu Tyr Lys Pro Gln Lys Gly Leu Phe His Arg Val Pro
  155         160         165
Leu Val Val Ala Asn Leu Gly Met Ser Glu Gln Leu Gly Tyr Lys
  170         175         180
Thr Val Ser Gly Ser Cys Met Ser Thr Gly Phe Ser Arg Ala Val
  185         190         195
Gln Thr His Ser Ser Lys Phe Phe Glu Glu Asp Gly Ser Leu Lys

```

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										200						205						210					
Glu	Val	His	Lys	Ile	Asn	Glu	Met	Tyr	Ala	Ser	Leu	Gln	Glu	Glu	215						220						225
Leu	Lys	Ser	Ile	Cys	Lys	Lys	Val	Glu	Asp	Ser	Glu	Gln	Ala	Val	230						235						240
Asp	Lys	Leu	Val	Lys	Asp	Val	Asn	Arg	Leu	Lys	Arg	Glu	Ile	Glu	245						250						255
Lys	Arg	Arg	Gly	Ala	Gln	Ile	Gln	Ala	Ala	Arg	Glu	Lys	Asn	Ile	260						265						270
Gln	Lys	Asp	Pro	Gln	Glu	Asn	Ile	Phe	Leu	Cys	Gln	Ala	Leu	Arg	275						280						285
Thr	Phe	Phe	Pro	Asn	Ser	Glu	Phe	Leu	His	Ser	Cys	Val	Met	Ser	290						295						300
Leu	Lys	Asn	Arg	His	Val	Ser	Lys	Ser	Ser	Cys	Asn	Tyr	Asn	His	305						310						315
His	Leu	Asp	Val	Val	Asp	Asn	Leu	Thr	Leu	Met	Val	Glu	His	Thr	320						325						330
Asp	Ile	Pro	Glu	Ala	Ser	Pro	Ala	Ser	Thr	Pro	Gln	Ile	Ile	Lys	335						340						345
His	Lys	Ala	Leu	Asp	Leu	Asp	Asp	Arg	Trp	Gln	Phe	Lys	Arg	Ser	350						355						360
Arg	Leu	Leu	Asp	Thr	Gln	Asp	Lys	Arg	Ser	Lys	Ala	Asn	Thr	Gly	365						370						375
Ser	Ser	Asn	Gln	Asp	Lys	Ala	Ser	Lys	Met	Ser	Ser	Pro	Glu	Thr	380						385						390
Asp	Glu	Glu	Ile	Glu	Lys	Met	Lys	Gly	Phe	Gly	Glu	Tyr	Ser	Arg	395						400						405

Ser Pro Thr Phe

<210> SEQ ID NO 23

<211> LENGTH: 2651

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 23

```

ggcacagccg cgcgggcgag ggcagagtca gccgagccga gtccagccgg          50
acgagcggac cagcgcaggg cagcccaagc agcgcgcagc gaacgcccgc          100
cgccgcccac accctctgcg gtccccgcgg cgctgcccac ccttccctcc          150
ttccccgcgt ccccgctcgc cgggccagtc agcttgccgg gttcgtgccc          200
ccgcgaaaacc ccgaggtcac cagcccgcgc ctctgcttcc ctgggcccgc          250
cgccgcctcc acgcccctct tctcccctgg cccgggcctt ggcaccgggg          300
accgttgcct gacgcgaggc ccagctctac ttttcgcccc gcgtctctct          350
cgctgctgct cctcttccac caactccaac tccttctccc tccagctcca          400
ctcgtctagtc cccgactccg ccagccctcg gcccgctgcc gtagcgccgc          450
ttcccgctcg gtcccaaagg tgggaacgcg tccgccccgg cccgcacccat          500
ggcacgggtc ggcttgcccg cgcttctctg caccctggca gtgctcagcg          550
ccgcgctgct ggctgcccag ctcaagtoga aaagttgctc ggaagtgcga          600
cgtcttttac tgtccaaagg cttcaacaag aacgatgccc cctccacga          650
    
```

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gatcaacggt gatcatttga agatctgtcc ccagggttct acctgctgct	700
ctcaagagat ggaggagaag tacagcctgc aaagtaaaga tgatttcaaa	750
agtgtggtca gcgaacagtg caatcatttg caagctgtct ttgcttcacg	800
ttacaagaag tttgatgaat tcttcaaaga actacttgaa aatgcagaga	850
aatccctgaa tgatatgttt gtgaagacat atggccatth atacatgcaa	900
aattctgagc tatttaaaga tctctcgtg gagtgaaac gttactacgt	950
ggtgggaaat gtgaacctgg aagaaatgct aaatgacttc tgggctcgcc	1000
tctctggagcg gatgttccgc ctggtgaaact cccagtacca ctttacagat	1050
gagtatctgg aatgtgtgag caagtatacg gagcagctga agcccttcg	1100
agatgtccct cgcaaattga agctccaggt tactcgtgct tttgtagcag	1150
cccgtacttt cgctcaagc ttagcggttg cgggagatgt cgtgagcaag	1200
gtctccgtgg taaacccac agcccagtg acccatgccc tgttgaagat	1250
gatctactgc tcccactgcc ggggtctcgt gactgtgaa ccatgttaca	1300
actactgctc aaacatcatg agaggctgtt tggccaacca aggggatctc	1350
gattttgaat ggaacaattt catagatgct atgctgatgg tggcagagag	1400
gctagagggg cctttcaaca ttgaatcggg catggatccc atcgatgtga	1450
agattttctga tgctattatg aacatgcagg ataatagtgt tcaagtgtct	1500
cagaagggtt tccagggatg tggaccccc aagcccctcc cagctggacg	1550
aatttctcgt tccatctctg aaagtgcctt cagtgtctgc ttcagaccac	1600
atcaccccca ggaacgcca accacagcag ctggcactag tttggaccga	1650
ctggttactg atgtcaagga gaaactgaaa caggccaaga aattctggtc	1700
ctcccttcog agcaacgttt gcaacgatga gaggatggct gcaggaaacg	1750
gcaatgagga tgactgttgg aatgggaaa gcaaaagcag gtacctgttt	1800
gcagtgcagc gaaatggatt agccaaccag ggcaacaacc cagaggcca	1850
ggttgacacc agcaaacag acatactgat ccttcgtcaa atcatggctc	1900
ttcagtgat gaccagcaag atgaagaatg catacaatgg gaacgacgtg	1950
gacttctttg atatcagtga tgaaagtagt ggagaaggaa gtggaagtgg	2000
ctgtgagtat cagcagtgcc cttcagagtt tgactacaat gccactgacc	2050
atgtctggaa gagtgccaat gagaaagccg acagtgtggt tgtccgtcct	2100
ggggcacagg cctacctcct cactgtcttc tgcactctgt tcctggttat	2150
gcagagagag tggagataat tctcaaactc tgagaaaaag tgttcatcaa	2200
aaagttaaaa ggcaccagtt atcacttttc taccatccta tgactttgc	2250
tttttaaatg aatggacaac aatgtacagt ttttactatg tggccactgg	2300
tttaagaagt gctgactttg ttttctcatt cagttttggg aggaaaagg	2350
actgtgcatt gagttggtc ctgctcccc aaaccatggt aaactgtgct	2400
aacagtgtag gtacagaact atagttagtt gtgcatttgt gattttatca	2450
ctctattatt tgtttgtatg ttttttctc atttogtttg tgggttttt	2500
tttccaactg tgatctcgcc ttgtttctta caagcaaac agggctccctt	2550

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cttggcacgt aacatgtacg tatttctgaa atattaaata gctgtacaga      2600
agcagggtttt atttatcatg ttatcttatt aaaagaaaaa gcccaaaaag      2650
c                                                                    2651

```

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<210> SEQ ID NO 24
<211> LENGTH: 556
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien

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<400> SEQUENCE: 24

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```

Met Ala Arg Phe Gly Leu Pro Ala Leu Leu Cys Thr Leu Ala Val
 1          5          10          15
Leu Ser Ala Ala Leu Leu Ala Ala Glu Leu Lys Ser Lys Ser Cys
          20          25          30
Ser Glu Val Arg Arg Leu Tyr Val Ser Lys Gly Phe Asn Lys Asn
          35          40          45
Asp Ala Pro Leu His Glu Ile Asn Gly Asp His Leu Lys Ile Cys
          50          55          60
Pro Gln Gly Ser Thr Cys Cys Ser Gln Glu Met Glu Glu Lys Tyr
          65          70          75
Ser Leu Gln Ser Lys Asp Asp Phe Lys Ser Val Val Ser Glu Gln
          80          85          90
Cys Asn His Leu Gln Ala Val Phe Ala Ser Arg Tyr Lys Lys Phe
          95          100          105
Asp Glu Phe Phe Lys Glu Leu Leu Glu Asn Ala Glu Lys Ser Leu
          110          115          120
Asn Asp Met Phe Val Lys Thr Tyr Gly His Leu Tyr Met Gln Asn
          125          130          135
Ser Glu Leu Phe Lys Asp Leu Phe Val Glu Leu Lys Arg Tyr Tyr
          140          145          150
Val Val Gly Asn Val Asn Leu Glu Glu Met Leu Asn Asp Phe Trp
          155          160          165
Ala Arg Leu Leu Glu Arg Met Phe Arg Leu Val Asn Ser Gln Tyr
          170          175          180
His Phe Thr Asp Glu Tyr Leu Glu Cys Val Ser Lys Tyr Thr Glu
          185          190          195
Gln Leu Lys Pro Phe Gly Asp Val Pro Arg Lys Leu Lys Leu Gln
          200          205          210
Val Thr Arg Ala Phe Val Ala Ala Arg Thr Phe Ala Gln Gly Leu
          215          220          225
Ala Val Ala Gly Asp Val Val Ser Lys Val Ser Val Val Asn Pro
          230          235          240
Thr Ala Gln Cys Thr His Ala Leu Leu Lys Met Ile Tyr Cys Ser
          245          250          255
His Cys Arg Gly Leu Val Thr Val Lys Pro Cys Tyr Asn Tyr Cys
          260          265          270
Ser Asn Ile Met Arg Gly Cys Leu Ala Asn Gln Gly Asp Leu Asp
          275          280          285
Phe Glu Trp Asn Asn Phe Ile Asp Ala Met Leu Met Val Ala Glu
          290          295          300
Arg Leu Glu Gly Pro Phe Asn Ile Glu Ser Val Met Asp Pro Ile

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	305		310		315
Asp Val Lys Ile Ser	Asp Ala Ile Met	Asn Met Gln Asp Asn	Ser		
	320		325		330
Val Gln Val Ser Gln	Lys Val Phe Gln	Gly Cys Gly Pro Pro	Lys		
	335		340		345
Pro Leu Pro Ala Gly	Arg Ile Ser Arg	Ser Ile Ser Glu Ser	Ala		
	350		355		360
Phe Ser Ala Arg Phe	Arg Pro His His	Pro Glu Glu Arg Pro	Thr		
	365		370		375
Thr Ala Ala Gly Thr	Ser Leu Asp Arg	Leu Val Thr Asp Val	Lys		
	380		385		390
Glu Lys Leu Lys Gln	Ala Lys Lys Phe	Trp Ser Ser Leu Pro	Ser		
	395		400		405
Asn Val Cys Asn Asp	Glu Arg Met Ala	Ala Gly Asn Gly Asn	Glu		
	410		415		420
Asp Asp Cys Trp Asn	Gly Lys Gly Lys	Ser Arg Tyr Leu Phe	Ala		
	425		430		435
Val Thr Gly Asn Gly	Leu Ala Asn Gln	Gly Asn Asn Pro Glu	Val		
	440		445		450
Gln Val Asp Thr Ser	Lys Pro Asp Ile	Leu Ile Leu Arg Gln	Ile		
	455		460		465
Met Ala Leu Arg Val	Met Thr Ser Lys	Met Lys Asn Ala Tyr	Asn		
	470		475		480
Gly Asn Asp Val Asp	Phe Phe Asp Ile	Ser Asp Glu Ser Ser	Gly		
	485		490		495
Glu Gly Ser Gly Ser	Gly Cys Glu Tyr	Gln Gln Cys Pro Ser	Glu		
	500		505		510
Phe Asp Tyr Asn Ala	Thr Asp His Ala	Gly Lys Ser Ala Asn	Glu		
	515		520		525
Lys Ala Asp Ser Ala	Gly Val Arg Pro	Gly Ala Gln Ala Tyr	Leu		
	530		535		540
Leu Thr Val Phe Cys	Ile Leu Phe Leu	Val Met Gln Arg Glu	Trp		
	545		550		555

Arg

<210> SEQ ID NO 25

<211> LENGTH: 870

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 25

```

ctcgcctca aatgggaacg ctggcctggg actaaagcat agaccaccag      50
gctgagtatc ctgacctgag tcatccccag ggatcaggag cctccagcag      100
ggaaccttcc attatattct tcaagcaact tacagctgca cgcacagttg      150
cgatgaaagt tctaattctct tcctctctcc tgttgctgcc actaatgctg      200
atgtccatgg tctctagcag cctgaatcca ggggtcgcca gaggccacag      250
ggaccgaggc caggcttcta ggagatggct ccaggaaggc ggccaagaat      300
gtgagtgcaa agattggttc ctgagagccc cgagaagaaa attcatgaca      350
tgtgtctggc tgccaaagaa gcagtgcccc tgtgatcatt tcaagggcaa      400

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tgtgaagaaa acaagacacc aaaggcacca cagaaagcca aacaagcatt	450
ccagagcctg ccagcaattt ctcaacaat gtcagctaag aagctttgct	500
ctgcctttgt aggagctctg agcgccact cttccaatta aacattctca	550
gccaaagaaga cagtgagcac acctaccaga cactcttctt ctcccactc	600
actctcccac tgtaccacc cctaaatcat tccagtgtc tcaaaaagca	650
tgtttttcaa gatcattttg tttgttgctc tctctagtgt cttcttctct	700
cgctcagtctt agcctgtgcc ctccccttac ccaggcttag gcttaattac	750
ctgaaagatt ccaggaaact gtagcttctt agctagtgtc atttaacctt	800
aatgcaatc aggaaagtag caaacagaag tcaataaata tttttaaatg	850
tcaaaaaaaaa aaaaaaaaaa	870

<210> SEQ ID NO 26
 <211> LENGTH: 119
 <212> TYPE: PRT
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 26

Met Lys Val Leu Ile Ser Ser Leu Leu Leu Leu Pro Leu Met	
1 5 10 15	
Leu Met Ser Met Val Ser Ser Ser Leu Asn Pro Gly Val Ala Arg	
20 25 30	
Gly His Arg Asp Arg Gly Gln Ala Ser Arg Arg Trp Leu Gln Glu	
35 40 45	
Gly Gly Gln Glu Cys Glu Cys Lys Asp Trp Phe Leu Arg Ala Pro	
50 55 60	
Arg Arg Lys Phe Met Thr Val Ser Gly Leu Pro Lys Lys Gln Cys	
65 70 75	
Pro Cys Asp His Phe Lys Gly Asn Val Lys Lys Thr Arg His Gln	
80 85 90	
Arg His His Arg Lys Pro Asn Lys His Ser Arg Ala Cys Gln Gln	
95 100 105	
Phe Leu Lys Gln Cys Gln Leu Arg Ser Phe Ala Leu Pro Leu	
110 115	

<210> SEQ ID NO 27
 <211> LENGTH: 1371
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 27

ggacgccagc gcctgcagag gctgagcagg gaaaaagcca gtgcccagc	50
ggaagcacag ctgagagctg gtctgccatg gacatcctgg tcccactcct	100
gcagctgctg gtgctgcttc ttaccctgcc cctgcacctc atggctctgc	150
tgggctgctg gcagcccctg tgcaaaagct acttccccta cctgatggcc	200
gtgctgactc ccaagagcaa ccgcaagatg gagagcaaga aacgggagct	250
cttcagccag ataaagggg ttacaggagc ctccgggaaa gtggccctac	300
tggagctggg ctgcggaacc ggagccaact ttcagttcta cccaccgggc	350
tgcagggtca cctgcctaga cccaaatccc cactttgaga agttcctgac	400

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aaagagcatg gctgagaaca ggcacctcca atatgagcgg tttgtggtgg      450
ctcctggaga ggacatgaga cagctggctg atggctccat ggatgtggtg      500
gtctgcactc tgggtgctgtg ctctgtgcag agcccaagga aggtcctgca      550
ggaggtccgg agagtactga gaccgggagg tgtgctcttt ttctggggagc      600
atgtggcaga accatatgga agctgggcct tcatgtggca gcaagttttc      650
gagcccacct ggaaacacat tggggatggc tegtgcctca ccagagagac      700
ctggaaggat cttgagaacg cccagtcttc cghaatccaa atggaacgac      750
agccccctcc cttgaagtgg ctacctgttg ggccccacat catgggaaaag      800
gctgtcaaac aatctttccc aagctccaag gcaactcatt gctccttccc      850
cagcctccaa ttagaacaag ccaccacca gctatctat ctccactga      900
gagggacctc gcagaatgag agaagacatt catgtaccac ctactagtcc      950
ctctctcccc aacctctgcc agggcaatct ctaactcaa tcccgccttc     1000
gacagtghaa aagctctact tctacgtga cccagggagg aaacctagag     1050
accctgttgt atcctcaact gcaagtttct ggactagtct cccaacgttt     1100
gcctcccaat gttgtccctt tccttcgttc ccatggtaaa gctcctctcg     1150
ctttcctcct gaggctacac ccatgctctc ctaggaactg gtcacaaaag     1200
tcatggtgcc tgcacccctg ccaagcccc ctgaccctct ctccccacta     1250
ccaccttctt cctgagctgg gggcaccagg gagaatcaga gatgctgggg     1300
atgccagagc aagactcaaa gaggcagagg ttttgttctc aaatattttt     1350
taataaatag acgaaaccac g                                     1371

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<210> SEQ ID NO 28

<211> LENGTH: 277

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 28

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Met Asp Ile Leu Val Pro Leu Leu Gln Leu Leu Val Leu Leu Leu
 1           5           10          15
Thr Leu Pro Leu His Leu Met Ala Leu Leu Gly Cys Trp Gln Pro
 20          25          30
Leu Cys Lys Ser Tyr Phe Pro Tyr Leu Met Ala Val Leu Thr Pro
 35          40          45
Lys Ser Asn Arg Lys Met Glu Ser Lys Lys Arg Glu Leu Phe Ser
 50          55          60
Gln Ile Lys Gly Leu Thr Gly Ala Ser Gly Lys Val Ala Leu Leu
 65          70          75
Glu Leu Gly Cys Gly Thr Gly Ala Asn Phe Gln Phe Tyr Pro Pro
 80          85          90
Gly Cys Arg Val Thr Cys Leu Asp Pro Asn Pro His Phe Glu Lys
 95          100         105
Phe Leu Thr Lys Ser Met Ala Glu Asn Arg His Leu Gln Tyr Glu
110          115         120
Arg Phe Val Val Ala Pro Gly Glu Asp Met Arg Gln Leu Ala Asp
125          130         135
Gly Ser Met Asp Val Val Val Cys Thr Leu Val Leu Cys Ser Val

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	140		145		150
Gln Ser Pro Arg Lys Val Leu Gln Glu Val Arg Arg Val Leu Arg	155		160		165
Pro Gly Gly Val Leu Phe Phe Trp Glu His Val Ala Glu Pro Tyr	170		175		180
Gly Ser Trp Ala Phe Met Trp Gln Gln Val Phe Glu Pro Thr Trp	185		190		195
Lys His Ile Gly Asp Gly Cys Cys Leu Thr Arg Glu Thr Trp Lys	200		205		210
Asp Leu Glu Asn Ala Gln Phe Ser Glu Ile Gln Met Glu Arg Gln	215		220		225
Pro Pro Pro Leu Lys Trp Leu Pro Val Gly Pro His Ile Met Gly	230		235		240
Lys Ala Val Lys Gln Ser Phe Pro Ser Ser Lys Ala Leu Ile Cys	245		250		255
Ser Phe Pro Ser Leu Gln Leu Glu Gln Ala Thr His Gln Pro Ile	260		265		270
Tyr Leu Pro Leu Arg Gly Thr	275				

<210> SEQ ID NO 29
 <211> LENGTH: 494
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 29

caatgttgc ctatccacct cccccaagcc cctttaccta tgctgctgct	50
aacgctgctg ctgctgctgc tgctgcttaa aggctcatgc ttggagtggg	100
gactggctgc tgcccagaaa gtctcttctg ccaactgacgc ccccatcagg	150
gattgggoc tctttccccc ttcttttctg tgtctcctgc ctcatcgcc	200
tgccatgacc tgcagccaag cccagccccg tggggaaggg gagaaagtgg	250
gggatggcta agaaagctgg gagatagga acagaagagg gtagtgggtg	300
ggctaggggg gctgccttat ttaaagtgtg tgtttatgat tcttatacta	350
atttatacaa agatattaag gcocctgttca ttaagaaatt gttcccttcc	400
cctgtgttca atgtttgtaa agattgttct gtgtaaatat gtctttataa	450
taaacagtta aaagctgaaa aaaaaaaaaa aaaaaaaaaa aaaa	494

<210> SEQ ID NO 30
 <211> LENGTH: 73
 <212> TYPE: PRT
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 30

Met Leu Leu Leu Thr Leu Leu Leu Leu Leu Leu Leu Lys Gly	1	5	10	15
Ser Cys Leu Glu Trp Gly Leu Val Gly Ala Gln Lys Val Ser Ser	20	25	30	
Ala Thr Asp Ala Pro Ile Arg Asp Trp Ala Phe Phe Pro Pro Ser	35	40	45	
Phe Leu Cys Leu Leu Pro His Arg Pro Ala Met Thr Cys Ser Gln	50	55	60	

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Ala Gln Pro Arg Gly Glu Gly Glu Lys Val Gly Asp Gly
 65 70

<210> SEQ ID NO 31

<211> LENGTH: 1660

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 31

```

gtttgaattc cttcaactat acccacagtc caaaagcaga ctactgtgt      50
cccaggctac cagttcctcc aagcaagtc tttcccttat ttaaccgatg     100
tgtccctcaa acacctgagt gctactccct atttgcattct gttttgataa   150
atgatgttga caccctccac cgaattctaa gtggaatcat gtcgggaaga    200
gatacaatcc ttggcctgtg tatcctcgca ttagccttgt ctttggccat   250
gatgtttacc ttcagattca tcaccaccct tctggttcac attttcattt   300
cattggttat tttgggattg ttgtttgtct goggtgtttt atggtggctg   350
tattatgact ataccaacga cctcagcata gaattggaca cagaaaggga    400
aaatatgaag tgcgtgctgg ggtttgctat cgtatccaca ggcacacagg   450
cagtgtctgt cgtcttgatt tttgttctca gaaagagaat aaaattgaca   500
gttgagcttt tccaaatcac aaataaagcc atcagcagtg ctcccttcct   550
gctgttccag ccaactgtga catttgccat cctcattttc ttctgggtcc   600
tctgggtggc tgtgctgctg agcctgggaa ctgcaggagc tgcccaggtt   650
atggaaggcg gccaaagtga atataagccc ctttcgggca ttcggtacat    700
gtggtcgtac catttaattg gcctcatctg gactagttaa ttcattccttg   750
cgtgccagca aatgactata gctggggcag tggttacttg ttatttcaac    800
agaagtaaaa atgatoctcc tgatcatccc atcctttcgt ctctctccat   850
tctcttcttc taccatcaag gaaccgttgt gaaaggttca tttttaatct   900
ctgtgggtgag gattccgaga atcattgtca tgtacatgca aaacgcactg   950
aaagaacagc agcatggtgc attgtccagg tacctgttcc gatgctgcta  1000
ctgctgtttc tgggtgtctg acaaatacct gctccatctc aaccagaatg  1050
catatactac aactgctatt aatgggacag atttctgtac atcagcaaaa  1100
gatgcattca aaatcttgtc caagaactca agtcacttta catctattaa  1150
ctgctttgga gacttcataa tttttctagg aaagggttga gtgggtgtgt  1200
tcaactgtttt tggaggactc atggcctttta actacaatcg ggcattccag  1250
gtgtgggagc tcctctgttt attggtagct ttttttgctt acttagtagc  1300
ccatagtttt ttatctgtgt ttgaaactgt gctggatgca cttttcctgt  1350
gttttgcgtg tgatctggaa acaaatgatg gatcgtcaga aaagccctac  1400
tttatggatc aagaatttct gagtttcgta aaaaggagca acaaatataa  1450
caatgcaagg gcacagcagg acaagcactc attaaggaat gaggaggaa  1500
cagaactcca ggccattgtg agatagatag ccatttaggt atctgtacct  1550
ggaaaaacatt tccttctaag agccatttac agaatagaag atgagaccac  1600

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tagagaaaag ttagtgaatt tttttttaaa agacctataa aaccctattc 1650

ttcctcaaaa 1660

<210> SEQ ID NO 32

<211> LENGTH: 445

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 32

Met Ser Gly Arg Asp Thr Ile Leu Gly Leu Cys Ile Leu Ala Leu
1 5 10 15Ala Leu Ser Leu Ala Met Met Phe Thr Phe Arg Phe Ile Thr Thr
20 25 30Leu Leu Val His Ile Phe Ile Ser Leu Val Ile Leu Gly Leu Leu
35 40 45Phe Val Cys Gly Val Leu Trp Trp Leu Tyr Tyr Asp Tyr Thr Asn
50 55 60Asp Leu Ser Ile Glu Leu Asp Thr Glu Arg Glu Asn Met Lys Cys
65 70 75Val Leu Gly Phe Ala Ile Val Ser Thr Gly Ile Thr Ala Val Leu
80 85 90Leu Val Leu Ile Phe Val Leu Arg Lys Arg Ile Lys Leu Thr Val
95 100 105Glu Leu Phe Gln Ile Thr Asn Lys Ala Ile Ser Ser Ala Pro Phe
110 115 120Leu Leu Phe Gln Pro Leu Trp Thr Phe Ala Ile Leu Ile Phe Phe
125 130 135Trp Val Leu Trp Val Ala Val Leu Leu Ser Leu Gly Thr Ala Gly
140 145 150Ala Ala Gln Val Met Glu Gly Gly Gln Val Glu Tyr Lys Pro Leu
155 160 165Ser Gly Ile Arg Tyr Met Trp Ser Tyr His Leu Ile Gly Leu Ile
170 175 180Trp Thr Ser Glu Phe Ile Leu Ala Cys Gln Gln Met Thr Ile Ala
185 190 195Gly Ala Val Val Thr Cys Tyr Phe Asn Arg Ser Lys Asn Asp Pro
200 205 210Pro Asp His Pro Ile Leu Ser Ser Leu Ser Ile Leu Phe Phe Tyr
215 220 225His Gln Gly Thr Val Val Lys Gly Ser Phe Leu Ile Ser Val Val
230 235 240Arg Ile Pro Arg Ile Ile Val Met Tyr Met Gln Asn Ala Leu Lys
245 250 255Glu Gln Gln His Gly Ala Leu Ser Arg Tyr Leu Phe Arg Cys Cys
260 265 270Tyr Cys Cys Phe Trp Cys Leu Asp Lys Tyr Leu Leu His Leu Asn
275 280 285Gln Asn Ala Tyr Thr Thr Thr Ala Ile Asn Gly Thr Asp Phe Cys
290 295 300Thr Ser Ala Lys Asp Ala Phe Lys Ile Leu Ser Lys Asn Ser Ser
305 310 315

His Phe Thr Ser Ile Asn Cys Phe Gly Asp Phe Ile Ile Phe Leu

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	320		325		330
Gly Lys Val Leu	Val Val Cys Phe Thr	Val Phe Gly Gly Leu	Met		
	335		340		345
Ala Phe Asn Tyr	Asn Arg Ala Phe Gln	Val Trp Ala Val Pro	Leu		
	350		355		360
Leu Leu Val Ala	Phe Phe Ala Tyr Leu	Val Ala His Ser Phe	Leu		
	365		370		375
Ser Val Phe Glu	Thr Val Leu Asp Ala	Leu Phe Leu Cys Phe	Ala		
	380		385		390
Val Asp Leu Glu	Thr Asn Asp Gly Ser	Ser Glu Lys Pro Tyr	Phe		
	395		400		405
Met Asp Gln Glu	Phe Leu Ser Phe Val	Lys Arg Ser Asn Lys	Leu		
	410		415		420
Asn Asn Ala Arg	Ala Gln Gln Asp Lys	His Ser Leu Arg Asn	Glu		
	425		430		435
Glu Gly Thr Glu	Leu Gln Ala Ile Val	Arg			
	440		445		

<210> SEQ ID NO 33
 <211> LENGTH: 2773
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 33

```

gttcgattag ctctctgag aagaagagaa aaggttcttg gacctctccc      50
tgtttcttcc ttagaataat ttgtatggga tttgtgatgc aggaaagcct      100
aagggaaaaa gaatattcat tctgtgtggt gaaaattttt tgaaaaaaa      150
attgccttct tcaaacaagg gtgtcattct gatatttatg aggactgttg      200
ttctcactat gaaggcatct gttattgaaa tgttccttgt tttgctggtg      250
actggagtac attcaaacaa agaaacggca aagaagatta aaaggcccaa      300
gttcactgtg cctcagatca actgcatgtg caaagccgga aagatcatcg      350
atcctgagtt cattgtgaaa tgtccagcag gatgccaaga ccccaaatac      400
catgtttatg gcactgacgt gtatgcatcc tactccagtg tgtgtggcgc      450
tgccgtacac agtgggtgtg ttgataatc aggagggaaa atacttgttc      500
ggaaggttgc tggacagtct ggttacaag ggagttattc caacggtgtc      550
caatcgttat ccctaccacg atggagagaa tcctttatcg tcttagaaag      600
taaaccctaaa aagggtgtaa cctaccctac agctcttaca tactcatcat      650
cgaaaagtcc agctgcccac gcaggtgaga ccacaaaagc ctatcagagg      700
ccacctattc cagggacaac tgcacagccg gtcactctga tgcagcttct      750
ggctgtcact gtagctgtgg ccacccccac caccttgcca aggccatccc      800
ctttctgtcg ttctaccacc agcatcccca gaccacaatc agtgggcccac      850
aggagccagg agatggatct ctgggtccact gccacctaca caagcagcca      900
aaacaggccc agagctgata caggtatcca aaggcaagat ccttcaggag      950
ctgccttcca gaaacctggt ggagcggatg tcagcctggg acttgttcca      1000
aaagaagaat tgagcacaca gtctttggag ccagtatccc tgggagatcc      1050
    
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aaactgcaaa attgacttgt cgtttttaat tgatgggagc accagcattg	1100
gcaaacggcg attccgaatc cagaagcagc tcctggctga tgttgcccaa	1150
gctcttgaca ttggccctgc cggctcactg atgggtgttg tccagtatgg	1200
agacaacctt gctactcact ttaacctcaa gacacacacg aattctcgag	1250
atctgaagac agccatagag aaaattactc agagaggagg actttctaata	1300
gtaggtcggg ccatctcctt tgtgaccaag aacttctttt ccaaagccaa	1350
tggaaacaga agcggggctc ccaatgtggt ggtgggtgatg gtggatggct	1400
ggccccagga caaagtggag gaggcttcaa gacttgcgag agagtcagga	1450
atcaacattt tcttcatcac cattgaagg tctgctgaaa atgagaagca	1500
gtatgtggtg gagcccaact ttgcaacaa ggccgtgtgc agaacaacg	1550
gcttctactc gctccacgtg cagagctggt ttggcctcca caagacctg	1600
cagcctctgg tgaagcgggt ctgcygacct gaccgcctgg cctgcagcaa	1650
gacctgcttg aactcggtg acattggctt cgtcatcgac ggctccagca	1700
gtgtggggac gggcaacttc cgcacctcc tccagtttgt gaccaacctc	1750
accaaagagt ttgagatttc cgacacggac acgcgcatcg gggccctgca	1800
gtacacctac gaacagcggc tggagtttgg gttcgacaag tacagcagca	1850
agcctgacat cctcaacgcc atcaagaggg tgggctactg gagtgggtggc	1900
accagcacgg gggctgccat caacttcgcc ctggagcagc tcttcaagaa	1950
gtccaagccc aacaagagga agttaatgat cctcatcacc gacgggaggt	2000
cctacgacga cgtccggatc ccagccatgg ctgccatct gaagggagtg	2050
atcaacctat cgataggcgt tgctgggct gcccaagagg agctagaagt	2100
cattgccact caccocgcca gagaccactc cttctttgtg gacgagttt	2150
acaacctcca tcagtatgtc ccaggatca tccagaacat ttgtacagag	2200
ttcaactcac agcctcggaa ctgaattcag agcaggcaga gcaccagcaa	2250
gtgctgcttt actaactgac gtggttgacc accccaccgc ttaatggggc	2300
acgcacggtg catcaagtct tgggcagggc atggagaaac aaatgtctt	2350
ttattattct ttgccatcat gctttttcat attccaaaac ttggagttac	2400
aaagatgatc acaaacgtat agaatgagcc aaaaggctac atcatgttga	2450
gggtgctgga gattttacat tttgacaatt gttttcaaaa taaatgttcg	2500
gaatacagtg cagcccttac gacaggctta cgtagagctt ttgtgagatt	2550
tttaagttgt tatttctgat ttgaactctg taaccctcag caagtttcat	2600
ttttgtcatg acaatgtagg aattgctgaa ttaaatgttt agaaggatga	2650
aaaaataaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa	2700
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa	2750
aaaaaaaaaa aaaaaaaaaa aag	2773

<210> SEQ ID NO 34

<211> LENGTH: 678

<212> TYPE: PR1

<213> ORGANISM: Homo Sapien

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<400> SEQUENCE: 34

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Met Arg Thr Val Val Leu Thr Met Lys Ala Ser Val Ile Glu Met
 1           5           10           15
Phe Leu Val Leu Leu Val Thr Gly Val His Ser Asn Lys Glu Thr
 20           25           30
Ala Lys Lys Ile Lys Arg Pro Lys Phe Thr Val Pro Gln Ile Asn
 35           40           45
Cys Asp Val Lys Ala Gly Lys Ile Ile Asp Pro Glu Phe Ile Val
 50           55           60
Lys Cys Pro Ala Gly Cys Gln Asp Pro Lys Tyr His Val Tyr Gly
 65           70           75
Thr Asp Val Tyr Ala Ser Tyr Ser Ser Val Cys Gly Ala Ala Val
 80           85           90
His Ser Gly Val Leu Asp Asn Ser Gly Gly Lys Ile Leu Val Arg
 95           100          105
Lys Val Ala Gly Gln Ser Gly Tyr Lys Gly Ser Tyr Ser Asn Gly
 110          115          120
Val Gln Ser Leu Ser Leu Pro Arg Trp Arg Glu Ser Phe Ile Val
 125          130          135
Leu Glu Ser Lys Pro Lys Lys Gly Val Thr Tyr Pro Ser Ala Leu
 140          145          150
Thr Tyr Ser Ser Ser Lys Ser Pro Ala Ala Gln Ala Gly Glu Thr
 155          160          165
Thr Lys Ala Tyr Gln Arg Pro Pro Ile Pro Gly Thr Thr Ala Gln
 170          175          180
Pro Val Thr Leu Met Gln Leu Leu Ala Val Thr Val Ala Val Ala
 185          190          195
Thr Pro Thr Thr Leu Pro Arg Pro Ser Pro Ser Ala Ala Ser Thr
 200          205          210
Thr Ser Ile Pro Arg Pro Gln Ser Val Gly His Arg Ser Gln Glu
 215          220          225
Met Asp Leu Trp Ser Thr Ala Thr Tyr Thr Ser Ser Gln Asn Arg
 230          235          240
Pro Arg Ala Asp Pro Gly Ile Gln Arg Gln Asp Pro Ser Gly Ala
 245          250          255
Ala Phe Gln Lys Pro Val Gly Ala Asp Val Ser Leu Gly Leu Val
 260          265          270
Pro Lys Glu Glu Leu Ser Thr Gln Ser Leu Glu Pro Val Ser Leu
 275          280          285
Gly Asp Pro Asn Cys Lys Ile Asp Leu Ser Phe Leu Ile Asp Gly
 290          295          300
Ser Thr Ser Ile Gly Lys Arg Arg Phe Arg Ile Gln Lys Gln Leu
 305          310          315
Leu Ala Asp Val Ala Gln Ala Leu Asp Ile Gly Pro Ala Gly Pro
 320          325          330
Leu Met Gly Val Val Gln Tyr Gly Asp Asn Pro Ala Thr His Phe
 335          340          345
Asn Leu Lys Thr His Thr Asn Ser Arg Asp Leu Lys Thr Ala Ile
 350          355          360
Glu Lys Ile Thr Gln Arg Gly Gly Leu Ser Asn Val Gly Arg Ala
 365          370          375

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Ile Ser Phe Val Thr Lys Asn Phe Phe Ser Lys Ala Asn Gly Asn
 380 385 390

Arg Ser Gly Ala Pro Asn Val Val Val Val Met Val Asp Gly Trp
 395 400 405

Pro Thr Asp Lys Val Glu Glu Ala Ser Arg Leu Ala Arg Glu Ser
 410 415 420

Gly Ile Asn Ile Phe Phe Ile Thr Ile Glu Gly Ala Ala Glu Asn
 425 430 435

Glu Lys Gln Tyr Val Val Glu Pro Asn Phe Ala Asn Lys Ala Val
 440 445 450

Cys Arg Thr Asn Gly Phe Tyr Ser Leu His Val Gln Ser Trp Phe
 455 460 465

Gly Leu His Lys Thr Leu Gln Pro Leu Val Lys Arg Val Cys Asp
 470 475 480

Thr Asp Arg Leu Ala Cys Ser Lys Thr Cys Leu Asn Ser Ala Asp
 485 490 495

Ile Gly Phe Val Ile Asp Gly Ser Ser Ser Val Gly Thr Gly Asn
 500 505 510

Phe Arg Thr Val Leu Gln Phe Val Thr Asn Leu Thr Lys Glu Phe
 515 520 525

Glu Ile Ser Asp Thr Asp Thr Arg Ile Gly Ala Val Gln Tyr Thr
 530 535 540

Tyr Glu Gln Arg Leu Glu Phe Gly Phe Asp Lys Tyr Ser Ser Lys
 545 550 555

Pro Asp Ile Leu Asn Ala Ile Lys Arg Val Gly Tyr Trp Ser Gly
 560 565 570

Gly Thr Ser Thr Gly Ala Ala Ile Asn Phe Ala Leu Glu Gln Leu
 575 580 585

Phe Lys Lys Ser Lys Pro Asn Lys Arg Lys Leu Met Ile Leu Ile
 590 595 600

Thr Asp Gly Arg Ser Tyr Asp Asp Val Arg Ile Pro Ala Met Ala
 605 610 615

Ala His Leu Lys Gly Val Ile Thr Tyr Ala Ile Gly Val Ala Trp
 620 625 630

Ala Ala Gln Glu Glu Leu Glu Val Ile Ala Thr His Pro Ala Arg
 635 640 645

Asp His Ser Phe Phe Val Asp Glu Phe Asp Asn Leu His Gln Tyr
 650 655 660

Val Pro Arg Ile Ile Gln Asn Ile Cys Thr Glu Phe Asn Ser Gln
 665 670 675

Pro Arg Asn

<210> SEQ ID NO 35
 <211> LENGTH: 2095
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 35

c c g a g c a c a g g a g a t t g c c t g c g t t t a g g a g g t g g c t g c g t t g t g g g a a a	50
a g c t a t c a a g g a a g a a t t g c c a a a c c a t g t o t t t t t t t c t g t t t t c a g a	100
g t a g t t c a c a a c a g a t c t g a g t g t t t t a a t t a a g c a t g g a a t a c a g a a a a	150

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caacaaaaa cttaagcttt aatttcac	200
gctccctgga cccggttgac ctggtggctc	250
acgtgggtgct ctccgactac tcaccccgag	300
cgctgcttctg agctgctgtg gatggcctcg	350
gagtaggatg tcaactgagat ccctcaaatg	400
tctctgagttt ctttgtgatg tggtaacctc	450
atagaacgcg tgaactggat gtacttctat	500
acaagacttt cacttcacac ttcgagagca	550
atccatttctt ggtcattctg gtgacctccc	600
aggcaggcca ttagagttac ttggggtgaa	650
tgaggttctt acatttttctt tattaggcca	700
aaatgttggc attgtcctta gaggatgaac	750
atccgacaag atttttttaga cacatataat	800
tatggcattc aggtgggtaa ctgagttttg	850
tgaagacaga cactgatggt ttcacataata	900
cttttaaac taaaccactc agagaagttt	950
tgataattat tcctatagag gattttacca	1000
aggagtatcc tttcaagggt tccctccat	1050
ataatgtcca gagatttggg gccaaagatc	1100
aaaaccatc aagtttgaag atgtttatgt	1150
taaaagtga cattcatatt ccagaagaca	1200
agaatccatt tggatgtctg tcaactgaga	1250
cttttcttcc aaggagatca tcaacttttg	1300
ccacatgcca ttattaactt cacattctac	1350
ataccttggt gaaagtgtta aataaagtag	1400
ggaggtcagt gtgctggctt aactgaact	1450
actggagact ggagggttac acttgtgatt	1500
gatgatatgt ggaggaatta aatataaagg	1550
gaaattaata ggaccaaca atttggacat	1600
ttcttaaaa ggtgttactg agttataagc	1650
aacaatgtag agttttattt attgaacaat	1700
tgtatatctt atgtggatta ccaatttaaa	1750
aaaaaactt ttcactgaag ttatactgaa	1800
gtcatttata aagtacttca agatgttgca	1850
tttaaaatta cttcaacttt gtgtttttaa	1900
caagataaaa aggatagtg atcattcttt	1950
tacttaactg atcagtttat tattgataca	2000
cataggtcat tattgcatat cagtaatctc	2050

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tactgtggta atatagagaa gaattaaagc aagaaaatct gaaaa

2095

<210> SEQ ID NO 36

<211> LENGTH: 331

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 36

```

Met Ala Ser Ala Leu Trp Thr Val Leu Pro Ser Arg Met Ser Leu
 1          5          10          15
Arg Ser Leu Lys Trp Ser Leu Leu Leu Leu Ser Leu Leu Ser Phe
 20          25          30
Phe Val Met Trp Tyr Leu Ser Leu Pro His Tyr Asn Val Ile Glu
 35          40          45
Arg Val Asn Trp Met Tyr Phe Tyr Glu Tyr Glu Pro Ile Tyr Arg
 50          55          60
Gln Asp Phe His Phe Thr Leu Arg Glu His Ser Asn Cys Ser His
 65          70          75
Gln Asn Pro Phe Leu Val Ile Leu Val Thr Ser His Pro Ser Asp
 80          85          90
Val Lys Ala Arg Gln Ala Ile Arg Val Thr Trp Gly Glu Lys Lys
 95          100         105
Ser Trp Trp Gly Tyr Glu Val Leu Thr Phe Phe Leu Leu Gly Gln
 110         115         120
Glu Ala Glu Lys Glu Asp Lys Met Leu Ala Leu Ser Leu Glu Asp
 125         130         135
Glu His Leu Leu Tyr Gly Asp Ile Ile Arg Gln Asp Phe Leu Asp
 140         145         150
Thr Tyr Asn Asn Leu Thr Leu Lys Thr Ile Met Ala Phe Arg Trp
 155         160         165
Val Thr Glu Phe Cys Pro Asn Ala Lys Tyr Val Met Lys Thr Asp
 170         175         180
Thr Asp Val Phe Ile Asn Thr Gly Asn Leu Val Lys Tyr Leu Leu
 185         190         195
Asn Leu Asn His Ser Glu Lys Phe Phe Thr Gly Tyr Pro Leu Ile
 200         205         210
Asp Asn Tyr Ser Tyr Arg Gly Phe Tyr Gln Lys Thr His Ile Ser
 215         220         225
Tyr Gln Glu Tyr Pro Phe Lys Val Phe Pro Pro Tyr Cys Ser Gly
 230         235         240
Leu Gly Tyr Ile Met Ser Arg Asp Leu Val Pro Arg Ile Tyr Glu
 245         250         255
Met Met Gly His Val Lys Pro Ile Lys Phe Glu Asp Val Tyr Val
 260         265         270
Gly Ile Cys Leu Asn Leu Leu Lys Val Asn Ile His Ile Pro Glu
 275         280         285
Asp Thr Asn Leu Phe Phe Leu Tyr Arg Ile His Leu Asp Val Cys
 290         295         300
Gln Leu Arg Arg Val Ile Ala Ala His Gly Phe Ser Ser Lys Glu
 305         310         315
Ile Ile Thr Phe Trp Gln Val Met Leu Arg Asn Thr Thr Cys His
 320         325         330

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Tyr

<210> SEQ ID NO 37

<211> LENGTH: 2846

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 37

cgctcgggca ccagccgcg caaggatgga gctgggttcg tggacgcagt	50
tggggctcac ttttcttcag ctccctctca tctcgtcctt gccaaagagag	100
tacacagctca ttaatgaagc ctgccctgga gcagagtgga atatcatgtg	150
tcgggagtgct tgtgaatatg atcagattga gtgcgtctgc cccggaaaga	200
gggaagtctg gggttatacc atcccttgct gcaggaatga ggagaatgag	250
tgtgactcct gcctgatcca cccaggttgt accatctttg aaaactgcaa	300
gagctgccga aatggctcat ggggggttac cttggatgac ttctatgtga	350
aggggttcta ctgtgcagag tgccgagcag gctggtagcg aggagactgc	400
atgcgatgtg gccaggttct gcgagcccca aagggtcaga tttgtttgga	450
aagctatccc ctaaagtctc actgtgaatg gaccattcat gctaaacctg	500
ggtttgtcat ccaactaaga tttgtcatgt tgagtctgga gtttgactac	550
atgtgccagt atgactatgt tgaggttcgt gatggagaca accgcgatgg	600
ccagatcatc aagcgtgtct gtggcaacga gcggccagct cctatccaga	650
gcataaggatc ctcaactccac gtccctctcc actccgatgg ctccaagaat	700
tttgacggtt tccatgccat ttatgaggag atcacagcat gctcctcatc	750
cccttgtttc catgacggca cgtgcgtcct tgacaaggct ggatcttaca	800
agtggtcctg cttggcaggc tatactgggc agcgtgtga aaatctcctt	850
gaagaaagaa actgctcaga ccctgggggc ccagtcaatg ggtaccagaa	900
aataacaggg ggcctgggc ttatcaacgg acgccatgct aaaattggca	950
ccgtggtgtc tttcttttgt aacaactcct atgttcttag tggcaatgag	1000
aaaagaactt gccagcagaa tggagagtgg tcagggaaac agcccatctg	1050
cataaaagcc tgccgagaac caaagatttc agacctggtg agaaggagag	1100
ttcttccgat gcaggttcag tcaagggaga caccattaca ccagctatac	1150
tcagcggcct tcagcaagca gaaactgcag agtgccccta ccaagaagcc	1200
agcccttccc tttggagatc tgcccatggg ataccaacat ctgcataccc	1250
agctccagta tgagtgcac tcacccttct accgccgcct gggcagcagc	1300
aggaggacat gtctgaggac tgggaagtgg agtgggctgg caccatcctg	1350
catccctatc tgccggaaaa ttgagaacat cactgctcca aagacccaag	1400
ggttgcgctg gccgtggcag gcagccatct acaggaggac cagcgggtg	1450
catgacggca gcctacacaa gggagcgtgg ttcctagtct gcagcgggtc	1500
cctggtgaat gagcgcactg tgggtggtgg tgcccactgt gttactgacc	1550
tggggaaggt caccatgatc aagacagcag acctgaaagt tgttttgggg	1600
aaattctacc gggatgatga ccgggatgag aagaccatcc agagcctaca	1650

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gatttctgct atcattctgc atcccaacta tgaccccatc ctgcttgatg      1700
ctgacatcgc catcctgaag ctctagaca aggcccgat cagcaccgga      1750
gtccagccca tctgcctcgc tgccagtcgg gatctcagca cttccttcca      1800
ggagtcccac atcactgtgg ctggctggaa tgtcctggca gacgtgagga      1850
gccctggctt caagaacgac aactgcgct ctggggtggt cagtgtggtg      1900
gactcgctgc tgtgtgagga gcagcatgag gaccatggca tcccagtgag      1950
tgtcactgat aacatgttct gtgccagctg ggaaccact gcccttctg      2000
atatctgac tgacagaca ggaggcatcg cggtgtgtc cttcccggga      2050
cgagcatctc ctgagccacg ctggcatctg atgggactgg tcagctggag      2100
ctatgataaa acatgcagcc acaggctctc cactgccttc accaaggtgc      2150
tgccctttta agactggatt gaaagaaata tgaatgaac catgctcatg      2200
cactccttga gaagtgtttc tgtatatccg tctgtactgt tgcattgctg      2250
tgaagcagtg tgggcctgaa gtgtgatttg gcctgtgaac ttggctgtgc      2300
cagggcttct gacttcaggg acaaaactca gtgaagggtg agtagactc      2350
cattgctggt aggctgatgc cgcgtccact actaggacag ccaattgga      2400
gatgccaggg cttgcaagaa gtaagtttct tcaagaaga ccatatacaa      2450
aacctctcca ctccactgac ctggtggtct tcccactt tcagttatac      2500
gaatgccatc agcttgacca gggaagatct gggcttcatg aggccccttt      2550
tgaggctctc aagttctaga gagctgcctg tgggacagcc cagggcagca      2600
gagctgggat gtggtgcatg cttttgtgta catggccaca gtacagtctg      2650
gtccttttcc ttcccctct cttgtacaca ttttaataaa ataagggttg      2700
gcttctgaac tacaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa      2750
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa      2800
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaa      2846
    
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<210> SEQ ID NO 38
<211> LENGTH: 720
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien
    
```

<400> SEQUENCE: 38

```

Met Glu Leu Gly Cys Trp Thr Gln Leu Gly Leu Thr Phe Leu Gln
 1             5             10             15
Leu Leu Leu Ile Ser Ser Leu Pro Arg Glu Tyr Thr Val Ile Asn
 20            25            30
Glu Ala Cys Pro Gly Ala Glu Trp Asn Ile Met Cys Arg Glu Cys
 35            40            45
Cys Glu Tyr Asp Gln Ile Glu Cys Val Cys Pro Gly Lys Arg Glu
 50            55            60
Val Val Gly Tyr Thr Ile Pro Cys Cys Arg Asn Glu Glu Asn Glu
 65            70            75
Cys Asp Ser Cys Leu Ile His Pro Gly Cys Thr Ile Phe Glu Asn
 80            85            90
Cys Lys Ser Cys Arg Asn Gly Ser Trp Gly Gly Thr Leu Asp Asp
    
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	95		100		105
Phe Tyr Val Lys Gly Phe Tyr Cys Ala Glu Cys Arg Ala Gly Trp	110		115		120
Tyr Gly Gly Asp Cys Met Arg Cys Gly Gln Val Leu Arg Ala Pro	125		130		135
Lys Gly Gln Ile Leu Leu Glu Ser Tyr Pro Leu Asn Ala His Cys	140		145		150
Glu Trp Thr Ile His Ala Lys Pro Gly Phe Val Ile Gln Leu Arg	155		160		165
Phe Val Met Leu Ser Leu Glu Phe Asp Tyr Met Cys Gln Tyr Asp	170		175		180
Tyr Val Glu Val Arg Asp Gly Asp Asn Arg Asp Gly Gln Ile Ile	185		190		195
Lys Arg Val Cys Gly Asn Glu Arg Pro Ala Pro Ile Gln Ser Ile	200		205		210
Gly Ser Ser Leu His Val Leu Phe His Ser Asp Gly Ser Lys Asn	215		220		225
Phe Asp Gly Phe His Ala Ile Tyr Glu Glu Ile Thr Ala Cys Ser	230		235		240
Ser Ser Pro Cys Phe His Asp Gly Thr Cys Val Leu Asp Lys Ala	245		250		255
Gly Ser Tyr Lys Cys Ala Cys Leu Ala Gly Tyr Thr Gly Gln Arg	260		265		270
Cys Glu Asn Leu Leu Glu Glu Arg Asn Cys Ser Asp Pro Gly Gly	275		280		285
Pro Val Asn Gly Tyr Gln Lys Ile Thr Gly Gly Pro Gly Leu Ile	290		295		300
Asn Gly Arg His Ala Lys Ile Gly Thr Val Val Ser Phe Phe Cys	305		310		315
Asn Asn Ser Tyr Val Leu Ser Gly Asn Glu Lys Arg Thr Cys Gln	320		325		330
Gln Asn Gly Glu Trp Ser Gly Lys Gln Pro Ile Cys Ile Lys Ala	335		340		345
Cys Arg Glu Pro Lys Ile Ser Asp Leu Val Arg Arg Arg Val Leu	350		355		360
Pro Met Gln Val Gln Ser Arg Glu Thr Pro Leu His Gln Leu Tyr	365		370		375
Ser Ala Ala Phe Ser Lys Gln Lys Leu Gln Ser Ala Pro Thr Lys	380		385		390
Lys Pro Ala Leu Pro Phe Gly Asp Leu Pro Met Gly Tyr Gln His	395		400		405
Leu His Thr Gln Leu Gln Tyr Glu Cys Ile Ser Pro Phe Tyr Arg	410		415		420
Arg Leu Gly Ser Ser Arg Arg Thr Cys Leu Arg Thr Gly Lys Trp	425		430		435
Ser Gly Arg Ala Pro Ser Cys Ile Pro Ile Cys Gly Lys Ile Glu	440		445		450
Asn Ile Thr Ala Pro Lys Thr Gln Gly Leu Arg Trp Pro Trp Gln	455		460		465
Ala Ala Ile Tyr Arg Arg Thr Ser Gly Val His Asp Gly Ser Leu	470		475		480

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His Lys Gly Ala Trp Phe Leu Val Cys Ser Gly Ala Leu Val Asn
 485 490 495

Glu Arg Thr Val Val Val Ala Ala His Cys Val Thr Asp Leu Gly
 500 505 510

Lys Val Thr Met Ile Lys Thr Ala Asp Leu Lys Val Val Leu Gly
 515 520 525

Lys Phe Tyr Arg Asp Asp Asp Arg Asp Glu Lys Thr Ile Gln Ser
 530 535 540

Leu Gln Ile Ser Ala Ile Ile Leu His Pro Asn Tyr Asp Pro Ile
 545 550 555

Leu Leu Asp Ala Asp Ile Ala Ile Leu Lys Leu Leu Asp Lys Ala
 560 565 570

Arg Ile Ser Thr Arg Val Gln Pro Ile Cys Leu Ala Ala Ser Arg
 575 580 585

Asp Leu Ser Thr Ser Phe Gln Glu Ser His Ile Thr Val Ala Gly
 590 595 600

Trp Asn Val Leu Ala Asp Val Arg Ser Pro Gly Phe Lys Asn Asp
 605 610 615

Thr Leu Arg Ser Gly Val Val Ser Val Val Asp Ser Leu Leu Cys
 620 625 630

Glu Glu Gln His Glu Asp His Gly Ile Pro Val Ser Val Thr Asp
 635 640 645

Asn Met Phe Cys Ala Ser Trp Glu Pro Thr Ala Pro Ser Asp Ile
 650 655 660

Cys Thr Ala Glu Thr Gly Gly Ile Ala Ala Val Ser Phe Pro Gly
 665 670 675

Arg Ala Ser Pro Glu Pro Arg Trp His Leu Met Gly Leu Val Ser
 680 685 690

Trp Ser Tyr Asp Lys Thr Cys Ser His Arg Leu Ser Thr Ala Phe
 695 700 705

Thr Lys Val Leu Pro Phe Lys Asp Trp Ile Glu Arg Asn Met Lys
 710 715 720

<210> SEQ ID NO 39
 <211> LENGTH: 2571
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 39

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ggttcctaca tcctctcatc tgagaatcag agagcataat cttcttacgg           50
gcccgtgatt tattaacgtg gcttaatctg aaggttctca gtcaaattct           100
ttgtgatcta ctgattgtgg gggcatggca aggtttgctt aaaggagctt           150
ggctggtttg ggcccttgta gctgacagaa ggtggccagg gagaatgcag           200
cacactgctc ggagaatgaa ggcgcttctg ttgctggtct tgccttggtc           250
cagtcctgct aactacattg acaatgtggg caacctgcac ttcctgtatt           300
cagaactctg taaaggtgcc tcccactacg gctgaccaa agataggaag           350
aggcgctcac aagatggctg tccagacggc tgtgagagcc tcacagccac           400
ggctccctcc ccagaggttt ctgcagctgc caccatctcc ttaatgacag           450
acgagcctgg cctagacaac cctgcctacg tgtcctcggc agaggacggg           500
    
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cagccagcaa tcagcccagt ggactctggc cggagcaacc gaactagggc	550
acggcccttt gagagatcca ctattagaag cagatcattt aaaaaataa	600
atcagccttt gagtgttctt cgaaggacaa agagcgggag tgcagttgcc	650
aaccatgcoy accagggcag ggaaaattct gaaaacacca ctgccctga	700
agtctttcca aggtgttacc acctgattcc agatggtgaa attaccagca	750
tcaagatcaa tcgagtagat cccagtgaaa gcctctctat taggctggtg	800
ggaggtagcg aaaccccaact ggtccatcctc attatccaac acatttatcg	850
tgatggggtg atcgccagag acggccggct actgccagga gacatcattc	900
taaaggtcaa cgggatggac atcagcaatg tccctcacia ctacgctgtg	950
cgctctctcg ggcagccctg ccaggtgctg tggctgactg tgatgctgta	1000
acagaagtcc cgcagcagga acaatggaca ggccccgat gcctacagac	1050
cccagatga cagctttcat gtgattctca acaaaagtag ccccgaggag	1100
cagcttgtaa taaaactggt gcgcaaggtg gatgagcctg gggttttcat	1150
cttcaatgtg ctggatggcg gtgtggcata tcgacatggt cagcttgagg	1200
agaatgaccg tgtgttagcc atcaatggac atgatcttcg atatggcagc	1250
ccagaaagtg cggctcatct gattcaggcc agtgaaaagc gtgttcacct	1300
cgctgtgtcc cgccaggttc ggcagcggag ccctgacatc tttcaggaag	1350
ccgcttgtaa cagcaatggc agctggtccc cagggccagg ggagaggagc	1400
aacctctcca agcccccca tcctacaatt acttgatcag agaaggtggt	1450
aaatatccaa aaagaccccc gtgaatctct cggcatgacc gtcgagggg	1500
gagcatcaca tagagaatgg gatttgccta tctatgtcat cagtgttgag	1550
cccggaggag tcataagcag agatggaaaga ataaaaacag gtgacatttt	1600
gttgaatgtg gatggggtcg aactgacaga ggtcagcccg agtgaggcag	1650
tgccattatt gaaaagaaca tcatcctcga tagtactcaa agctttggaa	1700
gtcaaaagat atgagcccca ggaagactgc agcagcccag cagccctgga	1750
ctccaaccac aacatggccc caccagtgca ctggtcccca tcctgggtca	1800
tgtgctgga attaccacgg tgcttgata actgtaaaga tattgtatta	1850
cgaagaaaca cagctggaag tctgggcttc tgcattgtag gaggttatga	1900
agaatacaat ggaacaaac cttttttcat caaatccatt gttgaaggaa	1950
caccagcata caatgatgga agaattagat gtggtgatat tcttcttgct	2000
gtcaatggta gaagtacatc agaatgata catgcttgct tggcaagact	2050
gctgaaagaa cttaaaggaa gaattactct aactattggt tcttgccctg	2100
gcactttttt atagaatcaa tgatgggtca gaggaaaaca gaaaaatcac	2150
aaataggcta agaagttgaa aactatatt tatcttgta gtttttata	2200
ttaaagaaag aatacattgt aaaaatgta ggaagatgat gatcatctaa	2250
tgaaagccag ttacacctca gaaaatgta ttccaaaaaa attaaaacta	2300
ctagtttttt ttcagtgtgg aggatttctc attactctac aacattgttt	2350
atattttttc tattcaataa aaagccctaa aacaactaaa atgattgatt	2400

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tgtatacccc actgaattca agctgattta aatttaaaat ttggtatatg          2450
ctgaagtctg ccaagggtac attatggcca tttttaattt acagctaaaa          2500
tattttttaa aatgcattgc tgagaaacgt tgctttcatc aaacaagaat          2550
aaatattttt cagaagttaa a                                          2571

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<210> SEQ ID NO 40
<211> LENGTH: 632
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 40

```

```

Met Lys Ala Leu Leu Leu Val Leu Pro Trp Leu Ser Pro Ala
 1           5           10          15
Asn Tyr Ile Asp Asn Val Gly Asn Leu His Phe Leu Tyr Ser Glu
 20          25          30
Leu Cys Lys Gly Ala Ser His Tyr Gly Leu Thr Lys Asp Arg Lys
 35          40          45
Arg Arg Ser Gln Asp Gly Cys Pro Asp Gly Cys Ala Ser Leu Thr
 50          55          60
Ala Thr Ala Pro Ser Pro Glu Val Ser Ala Ala Ala Thr Ile Ser
 65          70          75
Leu Met Thr Asp Glu Pro Gly Leu Asp Asn Pro Ala Tyr Val Ser
 80          85          90
Ser Ala Glu Asp Gly Gln Pro Ala Ile Ser Pro Val Asp Ser Gly
 95          100         105
Arg Ser Asn Arg Thr Arg Ala Arg Pro Phe Glu Arg Ser Thr Ile
 110         115         120
Arg Ser Arg Ser Phe Lys Lys Ile Asn Arg Ala Leu Ser Val Leu
 125         130         135
Arg Arg Thr Lys Ser Gly Ser Ala Val Ala Asn His Ala Asp Gln
 140         145         150
Gly Arg Glu Asn Ser Glu Asn Thr Thr Ala Pro Glu Val Phe Pro
 155         160         165
Arg Leu Tyr His Leu Ile Pro Asp Gly Glu Ile Thr Ser Ile Lys
 170         175         180
Ile Asn Arg Val Asp Pro Ser Glu Ser Leu Ser Ile Arg Leu Val
 185         190         195
Gly Gly Ser Glu Thr Pro Leu Val His Ile Ile Ile Gln His Ile
 200         205         210
Tyr Arg Asp Gly Val Ile Ala Arg Asp Gly Arg Leu Leu Pro Gly
 215         220         225
Asp Ile Ile Leu Lys Val Asn Gly Met Asp Ile Ser Asn Val Pro
 230         235         240
His Asn Tyr Ala Val Arg Leu Leu Arg Gln Pro Cys Gln Val Leu
 245         250         255
Trp Leu Thr Val Met Arg Glu Gln Lys Phe Arg Ser Arg Asn Asn
 260         265         270
Gly Gln Ala Pro Asp Ala Tyr Arg Pro Arg Asp Asp Ser Phe His
 275         280         285
Val Ile Leu Asn Lys Ser Ser Pro Glu Glu Gln Leu Gly Ile Lys
 290         295         300

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Leu Val Arg Lys Val Asp Glu Pro Gly Val Phe Ile Phe Asn Val
 305 310 315
 Leu Asp Gly Gly Val Ala Tyr Arg His Gly Gln Leu Glu Glu Asn
 320 325 330
 Asp Arg Val Leu Ala Ile Asn Gly His Asp Leu Arg Tyr Gly Ser
 335 340 345
 Pro Glu Ser Ala Ala His Leu Ile Gln Ala Ser Glu Arg Arg Val
 350 355 360
 His Leu Val Val Ser Arg Gln Val Arg Gln Arg Ser Pro Asp Ile
 365 370 375
 Phe Gln Glu Ala Gly Trp Asn Ser Asn Gly Ser Trp Ser Pro Gly
 380 385 390
 Pro Gly Glu Arg Ser Asn Thr Pro Lys Pro Leu His Pro Thr Ile
 395 400 405
 Thr Cys His Glu Lys Val Val Asn Ile Gln Lys Asp Pro Gly Glu
 410 415 420
 Ser Leu Gly Met Thr Val Ala Gly Gly Ala Ser His Arg Glu Trp
 425 430 435
 Asp Leu Pro Ile Tyr Val Ile Ser Val Glu Pro Gly Gly Val Ile
 440 445 450
 Ser Arg Asp Gly Arg Ile Lys Thr Gly Asp Ile Leu Leu Asn Val
 455 460 465
 Asp Gly Val Glu Leu Thr Glu Val Ser Arg Ser Glu Ala Val Ala
 470 475 480
 Leu Leu Lys Arg Thr Ser Ser Ser Ile Val Leu Lys Ala Leu Glu
 485 490 495
 Val Lys Glu Tyr Glu Pro Gln Glu Asp Cys Ser Ser Pro Ala Ala
 500 505 510
 Leu Asp Ser Asn His Asn Met Ala Pro Pro Ser Asp Trp Ser Pro
 515 520 525
 Ser Trp Val Met Trp Leu Glu Leu Pro Arg Cys Leu Tyr Asn Cys
 530 535 540
 Lys Asp Ile Val Leu Arg Arg Asn Thr Ala Gly Ser Leu Gly Phe
 545 550 555
 Cys Ile Val Gly Gly Tyr Glu Glu Tyr Asn Gly Asn Lys Pro Phe
 560 565 570
 Phe Ile Lys Ser Ile Val Glu Gly Thr Pro Ala Tyr Asn Asp Gly
 575 580 585
 Arg Ile Arg Cys Gly Asp Ile Leu Leu Ala Val Asn Gly Arg Ser
 590 595 600
 Thr Ser Gly Met Ile His Ala Cys Leu Ala Arg Leu Leu Lys Glu
 605 610 615
 Leu Lys Gly Arg Ile Thr Leu Thr Ile Val Ser Trp Pro Gly Thr
 620 625 630
 Phe Leu

<210> SEQ ID NO 41

<211> LENGTH: 1964

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 41

-continued

accaggcatt gtatcttcag ttgtcatcaa gttcgcaatc agattggaaa	50
agctcaactt gaagctttct tgctgcagtg gaagcagaga gatagatatt	100
attcacgtaa taaaaaacat gggcttcaac ctgactttcc acctttccta	150
caaattccga ttactgttgc tgttgacttt gtgcctgaca gtggttgggt	200
gggccaccag taactacttc gtgggtgcca ttcaagagat tcctaaagca	250
aaggagttca tggctaattt ccataagacc ctcatthttg ggaagggaaa	300
aactctgact aatgaagcat ccacgaagaa ggtagaactt gacaactgtc	350
cttctgtgtc tccttacctc agaggccaga gcaagctcat tttcaaacca	400
gatctcactt tggaagaggt acaggcagaa aatcccaaag tgtccagagg	450
ccggtatcgc cctcaggaat gtaaaacttt acagagggtc gccatcctcg	500
ttccccacog gaacagagag aaacacttga tgtactgtct ggaacatctg	550
catcccttcc tgcagaggca gcagctggat tatggcatct acgtcatcca	600
ccaggctgaa ggtaaaaagt ttaatcgagc caaactcttg aatgtgggct	650
atctagaagc cctcaaggaa gaaaattggg actgctttat attccacgat	700
gtggacctgg taccagagaa tgactttaac ctttacaagt gtgaggagca	750
tcccagcat ctggtggttg gcaggaacag cactgggtac aggttacggt	800
acagtggata ttttgggggt gtactgccc taagcagaga gcagtttttc	850
aaggtaatg gattctctaa caactactgg ggatggggag gcgaagacga	900
tgacctcaga ctcagggttg agctccaaag aatgaaaatt tcccggcccc	950
tgctgaaagt gggtaaatat acaatgggtct tccacactag agacaaaggc	1000
aatgagtgta acgcagaacg gatgaagctc ttacaccaag tgtccagagt	1050
ctggagaaca gatgggttga gtagttgttc ttataaatta gtatctgtgg	1100
aacacaatcc tttatatatc aacatcacag tggatttctg gtttggtgca	1150
tgaccttgga tcttttgggt atgtttgtaa gaactgattc tttgtttgca	1200
ataatthttg cctagagact tcaaatagta gcacacatta agaacctggt	1250
acagctcatt gttgagctga atthttcctt tttgtattht cttagcagag	1300
ctcctggtga tgtagagtat aaaacagttg taacaagaca gctthtctag	1350
tcattthtgat catgagggtt aaatattgta atatggatac ttgaaggact	1400
ttatataaaa ggatgactca aaggataaaa tgaacgctat ttgaggactc	1450
tggttgaagg agatthtatt aaatttgaag taatatatta tgggataaaa	1500
ggccacagga aataagactg ctgaatgtct gagagaacca gagttgttct	1550
cgccaaggt agaaaggtac gaagatacaa tactgttatt catttatcct	1600
gtacaatcat ctgtgaagtg gtgggtctag gtgagaaggc gtccacaaaa	1650
gaggggagaa aaggcgacga atcaggacac agtgaacttg ggaatgaaga	1700
ggtagcagga ggggtgagtg tgggtgcaa aggcagcagt agctgagctg	1750
gttgaggtg ctgatagcct tcaggggagg acctgccag gtatgccttc	1800
cagtgatgoc caccagagaa tacattctct attagthttt aaagagthtt	1850
tgtaaaatga tthttgtaca gtaggatag aattagcagt ttacaagtht	1900

-continued

 acatattaac taataataaa tatgtctatc aaatacctct gtagtaaaat 1950

gtgaaaaagc aaaa 1964

<210> SEQ ID NO 42

<211> LENGTH: 344

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 42

Met Gly Phe Asn Leu Thr Phe His Leu Ser Tyr Lys Phe Arg Leu
1 5 10 15Leu Leu Leu Leu Thr Leu Cys Leu Thr Val Val Gly Trp Ala Thr
20 25 30Ser Asn Tyr Phe Val Gly Ala Ile Gln Glu Ile Pro Lys Ala Lys
35 40 45Glu Phe Met Ala Asn Phe His Lys Thr Leu Ile Leu Gly Lys Gly
50 55 60Lys Thr Leu Thr Asn Glu Ala Ser Thr Lys Lys Val Glu Leu Asp
65 70 75Asn Cys Pro Ser Val Ser Pro Tyr Leu Arg Gly Gln Ser Lys Leu
80 85 90Ile Phe Lys Pro Asp Leu Thr Leu Glu Glu Val Gln Ala Glu Asn
95 100 105Pro Lys Val Ser Arg Gly Arg Tyr Arg Pro Gln Glu Cys Lys Ala
110 115 120Leu Gln Arg Val Ala Ile Leu Val Pro His Arg Asn Arg Glu Lys
125 130 135His Leu Met Tyr Leu Leu Glu His Leu His Pro Phe Leu Gln Arg
140 145 150Gln Gln Leu Asp Tyr Gly Ile Tyr Val Ile His Gln Ala Glu Gly
155 160 165Lys Lys Phe Asn Arg Ala Lys Leu Leu Asn Val Gly Tyr Leu Glu
170 175 180Ala Leu Lys Glu Glu Asn Trp Asp Cys Phe Ile Phe His Asp Val
185 190 195Asp Leu Val Pro Glu Asn Asp Phe Asn Leu Tyr Lys Cys Glu Glu
200 205 210His Pro Lys His Leu Val Val Gly Arg Asn Ser Thr Gly Tyr Arg
215 220 225Leu Arg Tyr Ser Gly Tyr Phe Gly Gly Val Thr Ala Leu Ser Arg
230 235 240Glu Gln Phe Phe Lys Val Asn Gly Phe Ser Asn Asn Tyr Trp Gly
245 250 255Trp Gly Gly Glu Asp Asp Asp Leu Arg Leu Arg Val Glu Leu Gln
260 265 270Arg Met Lys Ile Ser Arg Pro Leu Pro Glu Val Gly Lys Tyr Thr
275 280 285Met Val Phe His Thr Arg Asp Lys Gly Asn Glu Val Asn Ala Glu
290 295 300Arg Met Lys Leu Leu His Gln Val Ser Arg Val Trp Arg Thr Asp
305 310 315

-continued

Gly Leu Ser Ser Cys Ser Tyr Lys Leu Val Ser Val Glu His Asn
 320 325 330

Pro Leu Tyr Ile Asn Ile Thr Val Asp Phe Trp Phe Gly Ala
 335 340

<210> SEQ ID NO 43
 <211> LENGTH: 485
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 43

```

gctcaagacc cagcagtggg acagccagac agacggcacg atggcactga      50
gctcccagat ctgggcccgt tgcctcctgc tcctcctcct cctgcgccagc    100
ctgaccagtg gctctgtttt cccacaacag acgggacaac ttgcagagct    150
gcaaccccag gacagagctg gagccagggc cagctggatg cccatgttcc    200
agagggcgaag gaggcgagac acccacttcc ccatotgcat tttctgctgc    250
ggctgctgtc atcgatcaaa gtgtgggatg tgctgcaaga cgtagaacct    300
acctgccctg cccccgtccc ctcccctcct tatttattcc tgctgccccca   350
gaacataggt cttggaataa aatggctggt tcttttgttt tccaaaaaaaa    400
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa    450
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaa                                485
    
```

<210> SEQ ID NO 44
 <211> LENGTH: 84
 <212> TYPE: PRT
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 44

```

Met Ala Leu Ser Ser Gln Ile Trp Ala Ala Cys Leu Leu Leu Leu
  1           5           10           15
Leu Leu Leu Ala Ser Leu Thr Ser Gly Ser Val Phe Pro Gln Gln
  20          25          30
Thr Gly Gln Leu Ala Glu Leu Gln Pro Gln Asp Arg Ala Gly Ala
  35          40          45
Arg Ala Ser Trp Met Pro Met Phe Gln Arg Arg Arg Arg Arg Asp
  50          55          60
Thr His Phe Pro Ile Cys Ile Phe Cys Cys Gly Cys Cys His Arg
  65          70          75
Ser Lys Cys Gly Met Cys Cys Lys Thr
  80
    
```

<210> SEQ ID NO 45
 <211> LENGTH: 1076
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 45

```

gtggcttcat ttcagtggct gacttccaga gagcaatatg gctggttccc      50
caacatgcct caccctcatc tatatccttt ggcagctcac agggtcagca    100
gcctctggac ccgtgaaaga gctggtcggg tccgttggtg gggccgtgac    150
tttcccctg  aagtccaaag taaagcaagt tgactctatt gtctggacct    200
    
```

-continued

```

tcaacacaac ccctcttgtc accatacagc cagaaggggg cactatcata      250
gtgacccaaa atcgtaatag ggagagagta gacttcccag atggaggcta      300
ctccctgaag ctacagaaac tgaagaagaa tgactcaggg atctactatg      350
tggggatata cagctcatca ctccagcagc cctccacca ggagtacgtg      400
ctgcatgtct acgagcacct gtcaaagcct aaagtcacca tgggtctgca      450
gagcaataag aatggcacct gtgtgaccaa tctgacatgc tgcattggaac      500
atggggaaga ggatgtgatt tatacctgga aggcctggg gcaagcagcc      550
aatgagtccc ataatgggct catcctcccc atctcctgga gatggggaga      600
aagtgatatg accttcatct gcgttgccag gaaccctgtc agcagaaact      650
tctcaagccc catccttgcc aggaagctct gtgaaggtgc tgctgatgac      700
ccagattcct ccatggctct cctgtgtctc ctggtgtgtc ccctcctgct      750
cagtctcttt gtactggggc ttttctttg gtttotgaag agagagagac      800
aagaagagta cattgaagag aagaagagag tggacatttg tcgggaaact      850
cctaacatat gcccccattc tgagagaaac acagagtacg acacaatccc      900
tcacactaat agaacaatcc taaaggaaga tccagcaaat acggtttact      950
ccactgtgga aataccgaaa aagatggaaa atccccactc actgctcagc     1000
atgccagaca caccaaggct atttgctat gagaatgta tctagacagc     1050
agtgcactcc cctaagtctc tgctca                                1076
    
```

```

<210> SEQ ID NO 46
<211> LENGTH: 335
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien
    
```

<400> SEQUENCE: 46

```

Met Ala Gly Ser Pro Thr Cys Leu Thr Leu Ile Tyr Ile Leu Trp
 1          5          10          15
Gln Leu Thr Gly Ser Ala Ala Ser Gly Pro Val Lys Glu Leu Val
          20          25          30
Gly Ser Val Gly Gly Ala Val Thr Phe Pro Leu Lys Ser Lys Val
          35          40          45
Lys Gln Val Asp Ser Ile Val Trp Thr Phe Asn Thr Thr Pro Leu
          50          55          60
Val Thr Ile Gln Pro Glu Gly Gly Thr Ile Ile Val Thr Gln Asn
          65          70          75
Arg Asn Arg Glu Arg Val Asp Phe Pro Asp Gly Gly Tyr Ser Leu
          80          85          90
Lys Leu Ser Lys Leu Lys Lys Asn Asp Ser Gly Ile Tyr Tyr Val
          95          100          105
Gly Ile Tyr Ser Ser Ser Leu Gln Gln Pro Ser Thr Gln Glu Tyr
          110          115          120
Val Leu His Val Tyr Glu His Leu Ser Lys Pro Lys Val Thr Met
          125          130          135
Gly Leu Gln Ser Asn Lys Asn Gly Thr Cys Val Thr Asn Leu Thr
          140          145          150
Cys Cys Met Glu His Gly Glu Glu Asp Val Ile Tyr Thr Trp Lys
          155          160          165
    
```


-continued

Ala Leu Gly Gln Ala Ala Asn Glu Ser His Asn Gly Ser Ile Leu
 170 175 180

Pro Ile Ser Trp Arg Trp Gly Glu Ser Asp Met Thr Phe Ile Cys
 185 190 195

Val Ala Arg Asn Pro Val Ser Arg Asn Phe Ser Ser Pro Ile Leu
 200 205 210

Ala Arg Lys Leu Cys Glu Gly Ala Ala Asp Asp Pro Asp Ser Ser
 215 220 225

Met Val Leu Leu Cys Leu Leu Leu Val Pro Leu Leu Leu Ser Leu
 230 235 240

Phe Val Leu Gly Leu Phe Leu Trp Phe Leu Lys Arg Glu Arg Gln
 245 250 255

Glu Glu Tyr Ile Glu Glu Lys Lys Arg Val Asp Ile Cys Arg Glu
 260 265 270

Thr Pro Asn Ile Cys Pro His Ser Gly Glu Asn Thr Glu Tyr Asp
 275 280 285

Thr Ile Pro His Thr Asn Arg Thr Ile Leu Lys Glu Asp Pro Ala
 290 295 300

Asn Thr Val Tyr Ser Thr Val Glu Ile Pro Lys Lys Met Glu Asn
 305 310 315

Pro His Ser Leu Leu Thr Met Pro Asp Thr Pro Arg Leu Phe Ala
 320 325 330

Tyr Glu Asn Val Ile
 335

<210> SEQ ID NO 47
 <211> LENGTH: 766
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 47

```

ggctcgagcg tttctgagcc aggggtgacc atgacctgct gcgaaggatg           50
gacatcctgc aatggattca gcctgctggt tctactgctg ttaggagtag           100
ttctcaatgc gatacctcta attgtcagct tagttgagga agaccaatth           150
tctcaaaacc ccatctcttg ctttgagtgg tggttcccag gaattatagg           200
agcaggctcg atggccattc cagcaacaac aatgtccttg acagcaagaa           250
aaagagcgtg ctgcaacaac agaactggaa tgtttctttc atcatthttc           300
agtgatgatca cagtcattgg tgctctgcat tgcattgctga tatccatcca           350
ggctctctta aaaggtcctc tcatgtgtaa ttctccaagc aacagtaatg           400
ccaattgtga atthtcattg aaaaacatca gtgacattca tccagaatcc           450
ttcaacttgc agtggthttt caatgactct tgtgcacctc ctactggtht           500
caataaacc accagtaacg acaccatggc gagtggctgg agagcatcta           550
gtttccactt cgattctgaa gaaaacaac ataggcttat ccacttctca           600
gtatthttag gtctattgct tgttgaatt ctggaggtcc tgtttgggct           650
cagtcagata gtcacgggtt tccttgctg tctgtgtgga gtctctaagc           700
gaagaagtoa aattgtgtag tttaatggga ataaatgta agtatcagta           750
gtttgaaaaa aaaaaa                                     766
    
```

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<210> SEQ ID NO 48
 <211> LENGTH: 229
 <212> TYPE: PRT
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 48

Met Thr Cys Cys Glu Gly Trp Thr Ser Cys Asn Gly Phe Ser Leu
 1 5 10 15
 Leu Val Leu Leu Leu Leu Gly Val Val Leu Asn Ala Ile Pro Leu
 20 25 30
 Ile Val Ser Leu Val Glu Glu Asp Gln Phe Ser Gln Asn Pro Ile
 35 40 45
 Ser Cys Phe Glu Trp Trp Phe Pro Gly Ile Ile Gly Ala Gly Leu
 50 55 60
 Met Ala Ile Pro Ala Thr Thr Met Ser Leu Thr Ala Arg Lys Arg
 65 70 75
 Ala Cys Cys Asn Asn Arg Thr Gly Met Phe Leu Ser Ser Phe Phe
 80 85 90
 Ser Val Ile Thr Val Ile Gly Ala Leu Tyr Cys Met Leu Ile Ser
 95 100 105
 Ile Gln Ala Leu Leu Lys Gly Pro Leu Met Cys Asn Ser Pro Ser
 110 115 120
 Asn Ser Asn Ala Asn Cys Glu Phe Ser Leu Lys Asn Ile Ser Asp
 125 130 135
 Ile His Pro Glu Ser Phe Asn Leu Gln Trp Phe Phe Asn Asp Ser
 140 145 150
 Cys Ala Pro Pro Thr Gly Phe Asn Lys Pro Thr Ser Asn Asp Thr
 155 160 165
 Met Ala Ser Gly Trp Arg Ala Ser Ser Phe His Phe Asp Ser Glu
 170 175 180
 Glu Asn Lys His Arg Leu Ile His Phe Ser Val Phe Leu Gly Leu
 185 190 195
 Leu Leu Val Gly Ile Leu Glu Val Leu Phe Gly Leu Ser Gln Ile
 200 205 210
 Val Ile Gly Phe Leu Gly Cys Leu Cys Gly Val Ser Lys Arg Arg
 215 220 225
 Ser Gln Ile Val

<210> SEQ ID NO 49
 <211> LENGTH: 636
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 49

atccgttctc tgcgctgcca gctcaggtga gccctcgcca aggtgacctc 50
 gcaggacctt ggtgaaggag cagtgaggaa cctgcagagt cacacagttg 100
 ctgaccaatt gagctgtgag cctggagcag atccgtgggc tgcagacctc 150
 cgccccagtg cctctcccc tgcagccctg ccctcgaac tgtgacatgg 200
 agagagtgac cctggccctt ctctactgg caggcctgac tgccttgtaa 250
 gccaatgacc catttgccaa taaagacgat ccttctact atgactggaa 300

-continued

aaacctgcag ctgagcggac tgatctgcgg agggctcctg gccattgctg	350
ggatcgcggc agttctgagt ggcaaatgca aatacaagag cagccagaag	400
cagcacagtc ctgtacctga gaaggccatc ccaactcatca ctccaggctc	450
tgccactact tgctgagcac aggactggcc tccagggatg gcctgaagcc	500
taaactggc ccccagcacc tcctcccctg ggaggcctta tcctcaagga	550
aggacttctc tccaagggca ggctgttagg cccctttctg atcaggaggc	600
ttctttatga attaaactcg ccccaccacc cctca	636

<210> SEQ ID NO 50
 <211> LENGTH: 89
 <212> TYPE: PRT
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 50

Met Glu Arg Val Thr Leu Ala Leu Leu Leu Leu Ala Gly Leu Thr	
1 5 10 15	
Ala Leu Glu Ala Asn Asp Pro Phe Ala Asn Lys Asp Asp Pro Phe	
20 25 30	
Tyr Tyr Asp Trp Lys Asn Leu Gln Leu Ser Gly Leu Ile Cys Gly	
35 40 45	
Gly Leu Leu Ala Ile Ala Gly Ile Ala Ala Val Leu Ser Gly Lys	
50 55 60	
Cys Lys Tyr Lys Ser Ser Gln Lys Gln His Ser Pro Val Pro Glu	
65 70 75	
Lys Ala Ile Pro Leu Ile Thr Pro Gly Ser Ala Thr Thr Cys	
80 85	

<210> SEQ ID NO 51
 <211> LENGTH: 1734
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 51

gtggactctg agaagcccag gcagttgagg acaggagaga gaaggctgca	50
gaccagagg gagggaggac agggagtctg aaggaggagg acagaggagg	100
gcacagagac gcagagcaag ggcggcaagg aggagaccct ggtgggagga	150
agacactctg gagagagagg gggctgggca gagatgaagt tccaggggcc	200
cctggcctcg ctctgctgg cctctgcct gggcagtggg gaggctggcc	250
ccctgcagag cggagaggaa agcactggga caaatattgg ggaggccctt	300
ggacatggcc tgggagacgc cctgagcgaa ggggtgggaa aggccattgg	350
caaagaggcc ggaggggcag ctggctctaa agtcagttag gcccttggcc	400
aagggaccag agaagcagtt ggcactggag tcaggcaggt tccaggcttt	450
ggcgacagc atgctttggg caacagggtc ggggaagcag cccatgctct	500
gggaaacct gggcacgaga ttggcagaca ggcagaagat gtcattcgac	550
acggagcaga tgctgtccgc ggctcctggc agggggtgcc tggccacagt	600
ggtgcttggg aaacttctgg aggccatggc atctttggct ctcaagtggt	650
ccttggaggc cagggccagg gcaatctgg aggtctgggg actccgtggg	700

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tccacggata ccccggaaac tcagcaggca gctttggaat gaatcctcag      750
ggagctccct ggggtcaagg aggcaatgga gggccaccaa actttgggac      800
caacactcag ggagctgtgg ccagcctgg ctatggttca gtgagagcca      850
gcaaccagaa tgaagggtgc acgaatcccc caccatctgg ctcaggtgga      900
ggctccagca actctggggg aggcagcggc tcacagtcgg gcagcagtg      950
cagtggcagc aatggtgaca acaacaatgg cagcagcagt ggtggcagca     1000
gcagtggcag cagcagtgcc agcagcagtg gcggcagcag tggcggcagc     1050
agtgtgtgca gcagtggcaa cagtgtgtgg agcagaggtg acagcggcag     1100
tgagtcctcc tggggatcca gcaccggctc ctcctccggc aaccacggtg     1150
ggagcggcgg aggaaatgga cataaacccg ggtgtgaaaa gccagggaat     1200
gaagcccgcg ggagcgggga atctgggatt cagggcttca gaggacaggg     1250
agtttccagc aacatgaggg aaataagcaa agagggcaat cgcttcottg     1300
gaggctctg agacaattat cgggggcaag ggtcgagctg gggcagtgga     1350
ggaggtgacg ctgttggtgg agtcaatact gtgaactctg agacgtctcc     1400
tgggatgttt aactttgaca ctttctggaa gaattttaaa tccaagctgg     1450
gtttcatcaa ctgggatgcc ataaacaagg accagagaag ctctcgcac      1500
ccgtgacctc cagacaagga gccaccagat tggatgggag cccccacact     1550
ccctccttaa aacaccacc ctcctcact aatctcagcc cttgcccttg     1600
aaataaacct tagctgcccc aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa     1650
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa     1700
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaa                                     1734

```

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<210> SEQ ID NO 52
<211> LENGTH: 440
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien

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<400> SEQUENCE: 52

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```

Met Lys Phe Gln Gly Pro Leu Ala Cys Leu Leu Leu Ala Leu Cys
 1           5           10
Leu Gly Ser Gly Glu Ala Gly Pro Leu Gln Ser Gly Glu Glu Ser
           20           25           30
Thr Gly Thr Asn Ile Gly Glu Ala Leu Gly His Gly Leu Gly Asp
           35           40           45
Ala Leu Ser Glu Gly Val Gly Lys Ala Ile Gly Lys Glu Ala Gly
           50           55           60
Gly Ala Ala Gly Ser Lys Val Ser Glu Ala Leu Gly Gln Gly Thr
           65           70           75
Arg Glu Ala Val Gly Thr Gly Val Arg Gln Val Pro Gly Phe Gly
           80           85           90
Ala Ala Asp Ala Leu Gly Asn Arg Val Gly Glu Ala Ala His Ala
           95           100          105
Leu Gly Asn Thr Gly His Glu Ile Gly Arg Gln Ala Glu Asp Val
           110          115          120
Ile Arg His Gly Ala Asp Ala Val Arg Gly Ser Trp Gln Gly Val
           125          130          135

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-continued

Pro Gly His Ser Gly Ala Trp Glu Thr Ser Gly Gly His Gly Ile
 140 145 150

Phe Gly Ser Gln Gly Gly Leu Gly Gly Gln Gly Gln Gly Asn Pro
 155 160 165

Gly Gly Leu Gly Thr Pro Trp Val His Gly Tyr Pro Gly Asn Ser
 170 175 180

Ala Gly Ser Phe Gly Met Asn Pro Gln Gly Ala Pro Trp Gly Gln
 185 190 195

Gly Gly Asn Gly Gly Pro Pro Asn Phe Gly Thr Asn Thr Gln Gly
 200 205 210

Ala Val Ala Gln Pro Gly Tyr Gly Ser Val Arg Ala Ser Asn Gln
 215 220 225

Asn Glu Gly Cys Thr Asn Pro Pro Pro Ser Gly Ser Gly Gly Gly
 230 235 240

Ser Ser Asn Ser Gly Gly Gly Ser Gly Ser Gln Ser Gly Ser Ser
 245 250 255

Gly Ser Gly Ser Asn Gly Asp Asn Asn Asn Gly Ser Ser Ser Gly
 260 265 270

Gly Ser Ser Ser Gly Ser Ser Ser Gly Ser Ser Ser Gly Gly Ser
 275 280 285

Ser Gly Gly Ser Ser Gly Gly Ser Ser Gly Asn Ser Gly Gly Ser
 290 295 300

Arg Gly Asp Ser Gly Ser Glu Ser Ser Trp Gly Ser Ser Thr Gly
 305 310 315

Ser Ser Ser Gly Asn His Gly Gly Ser Gly Gly Gly Asn Gly His
 320 325 330

Lys Pro Gly Cys Glu Lys Pro Gly Asn Glu Ala Arg Gly Ser Gly
 335 340 345

Glu Ser Gly Ile Gln Gly Phe Arg Gly Gln Gly Val Ser Ser Asn
 350 355 360

Met Arg Glu Ile Ser Lys Glu Gly Asn Arg Leu Leu Gly Gly Ser
 365 370 375

Gly Asp Asn Tyr Arg Gly Gln Gly Ser Ser Trp Gly Ser Gly Gly
 380 385 390

Gly Asp Ala Val Gly Gly Val Asn Thr Val Asn Ser Glu Thr Ser
 395 400 405

Pro Gly Met Phe Asn Phe Asp Thr Phe Trp Lys Asn Phe Lys Ser
 410 415 420

Lys Leu Gly Phe Ile Asn Trp Asp Ala Ile Asn Lys Asp Gln Arg
 425 430 435

Ser Ser Arg Ile Pro
 440

<210> SEQ ID NO 53
 <211> LENGTH: 1676
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 53

ggagaagagg ttgtgtggga caagctgctc cgcacagaag gatgtcgctg 50
 ctgagcctgc cctggctggg cctcagaccg gtggcaatgt ccccatggct 100

-continued

actcctgctg ctggttggtg gctcctggct actcgcccgc atcctggctt	150
ggacctatgc cttctataac aactgcccgc ggctccagtg tttcccacag	200
ccccaaaaac ggaactgggt ttggggctcac ctgggcctga tcactcctac	250
agaggagggc ttgaaggact cgaccagat gtcggccacc tattcccagg	300
gctttacggt atggctgggt cccatcatcc ccttcactgt tttatgccac	350
cctgacacca tccggtctat caccaatgcc tcagctgcca ttgcacccaa	400
ggataatctc ttcacaggt tcctgaagcc ctggctggga gaagggatac	450
tgctgagtgg cggtgacaag tggagccgcc accgtcggat gctgacgcc	500
gccttcatt tcaacatcct gaagtccat ataacgatct tcaacaagag	550
tgcaaacatc atgcttgaca agtggcagca cctggcctca gagggcagca	600
gtcgtctgga catgtttgag cacatcagcc tcatgacctt ggacagtcta	650
cagaaatgca tcttcagctt tgacagccat tgtcaggaga ggcccagtga	700
atatattgcc accatcttgg agctcagtgc ccttgtagag aaaagaagcc	750
agcatatcct ccagcacatg gactttctgt attacctctc ccatgacggg	800
cggcgcttcc acagggcctg ccgcctggtg catgacttca cagacgctgt	850
catccgggag cggcgtcgca ccctcccac tcagggtatt gatgatttt	900
tcaaagacia agccaagtcc aagacttttg atttcattga tgtgcttctg	950
ctgagcaagg atgaagatgg gaaggcattg tcagatgagg atataagagc	1000
agaggctgac accttcattg ttggaggcca tgacaccacg gccagtggcc	1050
tctcctgggt cctgtacaac cttgcgaggc acccagaata ccaggagcgc	1100
tgccgacagg aggtgcaaga gcttctgaag gaccgcatc ctaaagagat	1150
tgaatgggac gacctggccc agctgccctt cctgaccatg tgcgtgaag	1200
agagcctgag gttacatccc ccagctccct tcactcctcg atgctgcacc	1250
caggacattg ttctcccaga tggccgagtc atccccaaag gcattacctg	1300
cctcatcgat attatagggg tccatcacia cccaactgtg tggccggatc	1350
ctgaggctca cgacccttc cgctttgacc cagagaacag caaggggagg	1400
tcacctctgg cttttattcc tttctccgca gggcccagga actgcatcgg	1450
gcaggcgttc gccatggcgg agatgaaagt ggtcctggcg ttgatgctgc	1500
tgcaacttccg gttcctgcca gaccacactg agccccgag gaagctggaa	1550
ttgatcatgc gcgccgagg cgggcttttg ctgcgggttg agcccctgaa	1600
tgtaggcttg cagtgacttt ctgacccatc cacctgtttt tttgcagatt	1650
gtcatgaata aaacggtgct gtcaaa	1676

<210> SEQ ID NO 54

<211> LENGTH: 524

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 54

Met Ser Leu Leu Ser Leu Pro Trp Leu Gly Leu Arg Pro Val Ala
 1 5 10 15

Met Ser Pro Trp Leu Leu Leu Leu Val Val Gly Ser Trp Leu

-continued

										20						25						30				
Leu	Ala	Arg	Ile	Leu	Ala	Trp	Thr	Tyr	Ala	Phe	Tyr	Asn	Asn	Cys	35					40						45
Arg	Arg	Leu	Gln	Cys	Phe	Pro	Gln	Pro	Pro	Lys	Arg	Asn	Trp	Phe	50					55						60
Trp	Gly	His	Leu	Gly	Leu	Ile	Thr	Pro	Thr	Glu	Glu	Gly	Leu	Lys	65					70						75
Asp	Ser	Thr	Gln	Met	Ser	Ala	Thr	Tyr	Ser	Gln	Gly	Phe	Thr	Val	80					85						90
Trp	Leu	Gly	Pro	Ile	Ile	Pro	Phe	Ile	Val	Leu	Cys	His	Pro	Asp	95					100						105
Thr	Ile	Arg	Ser	Ile	Thr	Asn	Ala	Ser	Ala	Ala	Ile	Ala	Pro	Lys	110					115						120
Asp	Asn	Leu	Phe	Ile	Arg	Phe	Leu	Lys	Pro	Trp	Leu	Gly	Glu	Gly	125					130						135
Ile	Leu	Leu	Ser	Gly	Gly	Asp	Lys	Trp	Ser	Arg	His	Arg	Arg	Met	140					145						150
Leu	Thr	Pro	Ala	Phe	His	Phe	Asn	Ile	Leu	Lys	Ser	Tyr	Ile	Thr	155					160						165
Ile	Phe	Asn	Lys	Ser	Ala	Asn	Ile	Met	Leu	Asp	Lys	Trp	Gln	His	170					175						180
Leu	Ala	Ser	Glu	Gly	Ser	Ser	Arg	Leu	Asp	Met	Phe	Glu	His	Ile	185					190						195
Ser	Leu	Met	Thr	Leu	Asp	Ser	Leu	Gln	Lys	Cys	Ile	Phe	Ser	Phe	200					205						210
Asp	Ser	His	Cys	Gln	Glu	Arg	Pro	Ser	Glu	Tyr	Ile	Ala	Thr	Ile	215					220						225
Leu	Glu	Leu	Ser	Ala	Leu	Val	Glu	Lys	Arg	Ser	Gln	His	Ile	Leu	230					235						240
Gln	His	Met	Asp	Phe	Leu	Tyr	Tyr	Leu	Ser	His	Asp	Gly	Arg	Arg	245					250						255
Phe	His	Arg	Ala	Cys	Arg	Leu	Val	His	Asp	Phe	Thr	Asp	Ala	Val	260					265						270
Ile	Arg	Glu	Arg	Arg	Arg	Thr	Leu	Pro	Thr	Gln	Gly	Ile	Asp	Asp	275					280						285
Phe	Phe	Lys	Asp	Lys	Ala	Lys	Ser	Lys	Thr	Leu	Asp	Phe	Ile	Asp	290					295						300
Val	Leu	Leu	Leu	Ser	Lys	Asp	Glu	Asp	Gly	Lys	Ala	Leu	Ser	Asp	305					310						315
Glu	Asp	Ile	Arg	Ala	Glu	Ala	Asp	Thr	Phe	Met	Phe	Gly	Gly	His	320					325						330
Asp	Thr	Thr	Ala	Ser	Gly	Leu	Ser	Trp	Val	Leu	Tyr	Asn	Leu	Ala	335					340						345
Arg	His	Pro	Glu	Tyr	Gln	Glu	Arg	Cys	Arg	Gln	Glu	Val	Gln	Glu	350					355						360
Leu	Leu	Lys	Asp	Arg	Asp	Pro	Lys	Glu	Ile	Glu	Trp	Asp	Asp	Leu	365					370						375
Ala	Gln	Leu	Pro	Phe	Leu	Thr	Met	Cys	Val	Lys	Glu	Ser	Leu	Arg	380					385						390
Leu	His	Pro	Pro	Ala	Pro	Phe	Ile	Ser	Arg	Cys	Cys	Thr	Gln	Asp	395					400						405

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Ile Val Leu Pro Asp Gly Arg Val Ile Pro Lys Gly Ile Thr Cys
 410 415 420
 Leu Ile Asp Ile Ile Gly Val His His Asn Pro Thr Val Trp Pro
 425 430 435
 Asp Pro Glu Val Tyr Asp Pro Phe Arg Phe Asp Pro Glu Asn Ser
 440 445 450
 Lys Gly Arg Ser Pro Leu Ala Phe Ile Pro Phe Ser Ala Gly Pro
 455 460 465
 Arg Asn Cys Ile Gly Gln Ala Phe Ala Met Ala Glu Met Lys Val
 470 475 480
 Val Leu Ala Leu Met Leu Leu His Phe Arg Phe Leu Pro Asp His
 485 490 495
 Thr Glu Pro Arg Arg Lys Leu Glu Leu Ile Met Arg Ala Glu Gly
 500 505 510
 Gly Leu Trp Leu Arg Val Glu Pro Leu Asn Val Gly Leu Gln
 515 520

<210> SEQ ID NO 55
 <211> LENGTH: 644
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 55

atcgcatcaa ttgggagtag catcttcctc atgggaccag tgaacagct 50
 gaagcgaatg tttgagccta ctggtttgat tgcaactatc atggtgctgt 100
 tgtgttttgc acttaccctg tgtctgcct tttggtggca taacaaggga 150
 cttgcactta tcttctgcat tttgcagtct ttggcattga cgtggtacag 200
 ccttccttc ataccatttg caagggatgc tgtgaagaag tgttttgccg 250
 tgtgtcttgc ataattcatg gccagtttta tgaagctttg gaaggcacta 300
 tggacagaag ctggtggaca gttttgtaac tatcttcgaa acctctgtct 350
 tacagacatg tgccttttat ctgcagcaa tgtgttgctt gtgattcgaa 400
 catttgaggg ttacttttgg aagcaacaat acattctcga acctgaatgt 450
 cagtgcaca ggatgagaag tgggttctgt atcttgtgga gtggaatctt 500
 cctcatgtac ctgtttcctc tctggatggt gtccactga attccatga 550
 atacaaacct attcagcaac agcaaaaaaa aaaaaaaaaa aaaaaaaaaa 600
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaa 644

<210> SEQ ID NO 56
 <211> LENGTH: 77
 <212> TYPE: PRT
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 56

Met Gly Pro Val Lys Gln Leu Lys Arg Met Phe Glu Pro Thr Arg
 1 5 10 15
 Leu Ile Ala Thr Ile Met Val Leu Leu Cys Phe Ala Leu Thr Leu
 20 25 30
 Cys Ser Ala Phe Trp Trp His Asn Lys Gly Leu Ala Leu Ile Phe
 35 40 45

-continued

Cys Ile Leu Gln Ser Leu Ala Leu Thr Trp Tyr Ser Leu Ser Phe
50 55 60

Ile Pro Phe Ala Arg Asp Ala Val Lys Lys Cys Phe Ala Val Cys
65 70 75

Leu Ala

<210> SEQ ID NO 57
<211> LENGTH: 3334
<212> TYPE: DNA
<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 57

```

cggtctgagc tcgagccgaa tcggctcgag gggcagtgga gcaccagca      50
ggccccaac atgctctgtc tgtgctgta cgtgccggtc atcggggaag      100
cccagaccga gttccagtac tttgagtcga aggggctccc tgccgagctg      150
aagtccattt tcaagctcag tgtctctatc ccctcccagg aattctocac      200
ctaccgccag tggaaagcaga aaattgtaca agctggagat aaggaccttg      250
atgggcagct agactttgaa gaatttgtcc attatctcca agatcatgag      300
aagaagctga ggctggtggt taagattttg gacaaaaaga atgatggacg      350
cattgacgog caggagatca tgcagtccct ggggacttg ggagtcaaga      400
tatctgaaca gcaggcagaa aaaattctca agagcatgga taaaaacggc      450
acgatgacca tcgactggaa cgagtggaga gactaccacc tcctccaccc      500
cgtgaaaaac atccccgaga tcatcctcta ctggaagcat tccacgatct      550
ttgatgtggg tgagaatcta acggctcccg atgagttcac agtggaggag      600
aggcagacgg ggatgtggtg gagacacctg gtggcaggag gtggggcagg      650
ggccgtatoc agaacctgca cggccccctt ggacaggctc aagggtctca      700
tgcagggtcca tgcctcccgc agcaacaaca tgggcatcgt tggtggtctc      750
actcagatga ttcgagaagg aggggccagg tcaactctggc ggggcaatgg      800
catcaacgct ctcaaaattg cccccgaatc agccatcaaa ttcatggcct      850
atgagcagat caagcgccct gttgtagtg accaggagac tctgaggatt      900
cacgagaggg ttgtggcagg gtccctggca ggggccatcg cccagagcag      950
catctaccca atggaggtcc tgaagaccgg gatggcgctg cggaagacag     1000
gccagtactc aggaatgctg gactgcgcca ggaggatcct ggccagagag     1050
ggggtggcog ccttctacaa aggctatgtc cccaacatgc tgggcatcat     1100
cccctatgcc ggcacgacc ttgcagtcta cgagacgctc aagaatgcct     1150
ggctgcagca ctatgcagtg aacagcgcgg accccggcgt gtttgtgctc     1200
ctggcctgtg gcaccatgct cagtacctgt ggccagctgg ccagctaccc     1250
cctggcccta gtcaggaccc ggatgcaggc gcaagcctct attgagggcg     1300
ctccggaggt gaccatgagc agcctcttca aacatatact gcggaccgag     1350
ggggccttog ggctgtacag ggggctggcc cccaacttca tgaaggtcat     1400
cccagctgtg agcatcagct acgtgtgcta cgagaacctg aagatcaccc     1450
tgggcgtgca gtcgcggtga cggggggagg gccgccggc agtggactcg     1500

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ctgatcctgg gccgcagcct ggggtgtgca gccatctcat tctgtgaatg	1550
tgccaacact aagctgtctc gagccaagct gtgaaaacc tagacgcacc	1600
cgcaggagg gtggggagag ctggcaggcc cagggcttgt cctgctgacc	1650
ccagcagacc ctctgttgg ttccagcgaa gaccacaggc attccttagg	1700
gtccagggtc agcaggctcc gggctcacat gtgtaaggac aggacathtt	1750
ctgcagtgcc tgccaatagt gagcttggag cctggaggcc ggcttagttc	1800
ttccatttca cccttgcagc cagctgttgg ccacggcccc tgccctctgg	1850
tctgcccgtc atctcccgtt gccctcttgc tgcctgcctg tctgctgagg	1900
taagtgggga ggagggtac agcccacatc ccaccccctc gtccaatccc	1950
ataatccatg atgaaaagtg aggtcacgtg gctcccagg cctgacttcc	2000
caacctacag cattgacgcc aacttggctg tgaaggaaga ggaaggatc	2050
tggccttctg gtcactggca tctgagccct gctgatggct ggggctctcg	2100
ggcatgcttg ggagtgcagg gggctcgggc tgcctggcct ggctgcacag	2150
aaggcaagtg ctggggctca tggctgcttg agctggcctg gaccctgtca	2200
ggatggggcc cacctcagaa ccaaactcac tgtcccact gtggcatgag	2250
ggcagtggag caccatgttt gagggcgaag ggcagagcgt ttgtgtgttc	2300
tggggaggga aggaaaaggt gttggaggcc ttaattatgg actggtggga	2350
aaagggtttt gtccagaagg acaagccgga caaatgagcg acttctgtgc	2400
ttccagagga agacgaggga gcaggagctt ggctgactgc tcagagtctg	2450
ttctgacgcc ctgggggttc ctgtccaacc ccagcagggg cgcagcggga	2500
ccagcccac attccacttg tgtactgct tggaaacctat ttattttgta	2550
tttatttgaa cagagttatg tcctaactat ttttatagat ttgtttaatt	2600
aatagcttgt cattttcaag ttcatTTTTT attcataatt atgttcattg	2650
ttgattgtac cttcccgaag ccgccagtg ggatgggagg aggaggagaa	2700
ggggggcctt gggccgctgc agtcacatct gtccagagaa attccttttg	2750
ggactggagg cagaaaagcg gccagaaggc agcagccctg gctcctttcc	2800
tttgccaggt tggggaaggg cttgcccaca gccttaggat ttcagggttt	2850
gactgggggc gtggagagag agggaggaac ctcaataacc ttgaagggtg	2900
aatccagtta tttcctgcgc tgcgagggtt tctttatttc actcctttct	2950
gaatgtcaag gcagtgaggt gcctctcact gtgaatttgt ggtgggcggg	3000
ggctggagga gagggtggg gctggctcc gtccctccca gccttctgct	3050
gcccttgctt aacaatgccg gccaaactggc gacctcagcg ttgcacttcc	3100
attccaccag aatgacctga tgaggaaatc ttcaatagga tgcaaagatc	3150
aatgcaaaaa ttgttatata tgaacatata actggagtcg tcaaaaagca	3200
aattaagaaa gaattggacg ttagaagttg tcatttaag cagccttcta	3250
ataaagtgtt ttcaagctg aaaaaaaaa aaaaaaaaa aaaaaaaaa	3300
aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaa	3334

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<211> LENGTH: 469

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 58

```

Met Leu Cys Leu Cys Leu Tyr Val Pro Val Ile Gly Glu Ala Gln
 1           5           10          15
Thr Glu Phe Gln Tyr Phe Glu Ser Lys Gly Leu Pro Ala Glu Leu
          20          25          30
Lys Ser Ile Phe Lys Leu Ser Val Phe Ile Pro Ser Gln Glu Phe
          35          40          45
Ser Thr Tyr Arg Gln Trp Lys Gln Lys Ile Val Gln Ala Gly Asp
          50          55          60
Lys Asp Leu Asp Gly Gln Leu Asp Phe Glu Glu Phe Val His Tyr
          65          70          75
Leu Gln Asp His Glu Lys Lys Leu Arg Leu Val Phe Lys Ile Leu
          80          85          90
Asp Lys Lys Asn Asp Gly Arg Ile Asp Ala Gln Glu Ile Met Gln
          95          100         105
Ser Leu Arg Asp Leu Gly Val Lys Ile Ser Glu Gln Gln Ala Glu
          110         115         120
Lys Ile Leu Lys Ser Met Asp Lys Asn Gly Thr Met Thr Ile Asp
          125         130         135
Trp Asn Glu Trp Arg Asp Tyr His Leu Leu His Pro Val Glu Asn
          140         145         150
Ile Pro Glu Ile Ile Leu Tyr Trp Lys His Ser Thr Ile Phe Asp
          155         160         165
Val Gly Glu Asn Leu Thr Val Pro Asp Glu Phe Thr Val Glu Glu
          170         175         180
Arg Gln Thr Gly Met Trp Trp Arg His Leu Val Ala Gly Gly Gly
          185         190         195
Ala Gly Ala Val Ser Arg Thr Cys Thr Ala Pro Leu Asp Arg Leu
          200         205         210
Lys Val Leu Met Gln Val His Ala Ser Arg Ser Asn Asn Met Gly
          215         220         225
Ile Val Gly Gly Phe Thr Gln Met Ile Arg Glu Gly Gly Ala Arg
          230         235         240
Ser Leu Trp Arg Gly Asn Gly Ile Asn Val Leu Lys Ile Ala Pro
          245         250         255
Glu Ser Ala Ile Lys Phe Met Ala Tyr Glu Gln Ile Lys Arg Leu
          260         265         270
Val Gly Ser Asp Gln Glu Thr Leu Arg Ile His Glu Arg Leu Val
          275         280         285
Ala Gly Ser Leu Ala Gly Ala Ile Ala Gln Ser Ser Ile Tyr Pro
          290         295         300
Met Glu Val Leu Lys Thr Arg Met Ala Leu Arg Lys Thr Gly Gln
          305         310         315
Tyr Ser Gly Met Leu Asp Cys Ala Arg Arg Ile Leu Ala Arg Glu
          320         325         330
Gly Val Ala Ala Phe Tyr Lys Gly Tyr Val Pro Asn Met Leu Gly
          335         340         345
Ile Ile Pro Tyr Ala Gly Ile Asp Leu Ala Val Tyr Glu Thr Leu

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	350		355		360
Lys Asn Ala Trp	Leu Gln His Tyr Ala	Val Asn Ser Ala Asp	Pro		
	365		370		375
Gly Val Phe Val	Leu Leu Ala Cys Gly	Thr Met Ser Ser Thr	Cys		
	380		385		390
Gly Gln Leu Ala	Ser Tyr Pro Leu Ala	Leu Val Arg Thr Arg	Met		
	395		400		405
Gln Ala Gln Ala	Ser Ile Glu Gly Ala	Pro Glu Val Thr Met	Ser		
	410		415		420
Ser Leu Phe Lys	His Ile Leu Arg Thr	Glu Gly Ala Phe Gly	Leu		
	425		430		435
Tyr Arg Gly Leu	Ala Pro Asn Phe Met	Lys Val Ile Pro Ala	Val		
	440		445		450
Ser Ile Ser Tyr	Val Val Tyr Glu Asn	Leu Lys Ile Thr Leu	Gly		
	455		460		465
Val Gln Ser Arg					

<210> SEQ ID NO 59

<211> LENGTH: 1658

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 59

```

ggaaggcagc ggcagctcca ctcagccagt acccagatac gctgggaacc          50
tccccagcc atggcttccc tggggcagat cctcttctgg agcataatta          100
gcatcatcat tattctggct ggagcaattg cactcatcat tggctttggt          150
atctcagggg gacactccat cacagtcaact actgtcgctt cagotgggaa          200
cattggggag gatggaatcc tgagctgcac ttttgaacct gacatcaaac          250
tttctgatat cgtgatacaa tggctgaagg aagggtgtttt aggcttggtc          300
catgagtcca aagaaggcaa agatgagctg tcggagcagg atgaaatggt          350
cagaggcccg acagcagtgt ttgctgatca agtgatagtt ggcaatgcct          400
ctttgcccgt gaaaaacgtg caactcacag atgctggcac ctacaaatgt          450
tataatcatc cttctaaagg caagggaat gctaaccttg agtataaac          500
tggagccttc agcatgccg aagtgaatgt ggactataat gccagctcag          550
agaccttgog gtgtgaggct ccccgatggt tccccagcc cacagtggtc          600
tgggcatccc aagttgacca gggagccaac ttctcggaag tctccaatac          650
cagcttttag ctgaactctg agaatgtgac catgaaggtt gtgtctgtgc          700
tctacaatgt tacgatcaac aacacatact cctgtatgat tgaaaatgac          750
attgccaaa gcaacagggg tatcaaatgt acagaatcgg agatcaaaa          800
gcgaggtcac ctacagctgc taaactcaaa ggcttctctg tgtgtctctt          850
ctttctttgc catcagctgg gcaacttctg ctctcagccc ttacctgatg          900
ctaaaaaat gtgccttggc cacaaaaag catgcaaagt cattgttaca          950
acagggatct acagaactat ttcaccacca gatatgacct agttttatat          1000
ttctgggagg aatgaattc atatctagaa gtctggagtg agcaaacaa          1050
agcaagaaac aaaaagaagc caaaagcaga aggctccaat atgaacaaga          1100
    
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taaatctatc ttcaaagaca tattagaagt tgggaaaata attcatgtga      1150
actagacaag tgtgttaaga gtgataagta aaatgcacgt ggagacaagt      1200
gcatccccag atctcagga cctccccctg cctgtcacct ggggagtga      1250
aggacaggat agtgcattgt cttgtctct gaatttttag ttatatgtgc      1300
tgtaatgttg ctctgaggaa gccctggaa agtctatccc aacatatcca      1350
catcttatat tccacaaatt aagctgtagt atgtacccta agacgtgct      1400
aattgactgc cacttcgcaa ctccagggcg gctgcatttt agtaatgggt      1450
caaatgattc actttttatg atgcttccaa aggtgccttg gcttctcttc      1500
ccaactgaca aatgccaaag ttgagaaaaa tgatcataat ttagcataa      1550
acagagcagt cggggacacc gattttataa ataaactgag caccttcttt      1600
ttaaacaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa      1650
aaaaaaaaa      1658

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<210> SEQ ID NO 60

<211> LENGTH: 282

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 60

```

Met Ala Ser Leu Gly Gln Ile Leu Phe Trp Ser Ile Ile Ser Ile
  1           5           10          15
Ile Ile Ile Leu Ala Gly Ala Ile Ala Leu Ile Ile Gly Phe Gly
          20          25          30
Ile Ser Gly Arg His Ser Ile Thr Val Thr Thr Val Ala Ser Ala
          35          40          45
Gly Asn Ile Gly Glu Asp Gly Ile Leu Ser Cys Thr Phe Glu Pro
          50          55          60
Asp Ile Lys Leu Ser Asp Ile Val Ile Gln Trp Leu Lys Glu Gly
          65          70          75
Val Leu Gly Leu Val His Glu Phe Lys Glu Gly Lys Asp Glu Leu
          80          85          90
Ser Glu Gln Asp Glu Met Phe Arg Gly Arg Thr Ala Val Phe Ala
          95          100         105
Asp Gln Val Ile Val Gly Asn Ala Ser Leu Arg Leu Lys Asn Val
          110         115         120
Gln Leu Thr Asp Ala Gly Thr Tyr Lys Cys Tyr Ile Ile Thr Ser
          125         130         135
Lys Gly Lys Gly Asn Ala Asn Leu Glu Tyr Lys Thr Gly Ala Phe
          140         145         150
Ser Met Pro Glu Val Asn Val Asp Tyr Asn Ala Ser Ser Glu Thr
          155         160         165
Leu Arg Cys Glu Ala Pro Arg Trp Phe Pro Gln Pro Thr Val Val
          170         175         180
Trp Ala Ser Gln Val Asp Gln Gly Ala Asn Phe Ser Glu Val Ser
          185         190         195
Asn Thr Ser Phe Glu Leu Asn Ser Glu Asn Val Thr Met Lys Val
          200         205         210
Val Ser Val Leu Tyr Asn Val Thr Ile Asn Asn Thr Tyr Ser Cys

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	215		220		225
Met Ile Glu Asn Asp Ile Ala Lys Ala Thr Gly Asp Ile Lys Val					
	230		235		240
Thr Glu Ser Glu Ile Lys Arg Arg Ser His Leu Gln Leu Leu Asn					
	245		250		255
Ser Lys Ala Ser Leu Cys Val Ser Ser Phe Phe Ala Ile Ser Trp					
	260		265		270
Ala Leu Leu Pro Leu Ser Pro Tyr Leu Met Leu Lys					
	275		280		

<210> SEQ ID NO 61
 <211> LENGTH: 1617
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 61

```

tgacgtcaga atcaccatgg ccagctatcc ttaccggcag ggetgcccag      50
gagctgcagg acaagcacca ggagcccctc cgggtagcta ctaccctgga      100
cccccaata gtggagggca gtatggtagt gggctacccc ctggtggtgg      150
ttatgggggt cctgcccttg gagggcctta tggaccacca gctggtggag      200
ggccctatgg acacccaat cctgggatgt tcccctctgg aactccagga      250
ggaccatatg gcggtgcagc tcccgggggc ccctatggtc agccacctcc      300
aagttcctac ggtgcccagc agcctgggct ttatggacag ggtggcgccc      350
ctcccaatgt ggatcctgag gcctactcct ggttcagtc ggtggactca      400
gatcacagtg gctatatctc catgaaggag ctaaagcagg ccctggtcaa      450
ctgcaattgg tcttcattca atgatgagac ctgcctcatg atgataaaca      500
tgtttgacaa gaccaagtca ggccgcatcg atgtctacgg cttctcagcc      550
ctgtggaaat tcatccagca gtggaagaac ctctccagc agtatgaccg      600
ggaccgctcg ggtccatta gctacacaga gctgcagcaa gctctgtccc      650
aaatgggcta caacctgagc cccagttca cccagcttct ggtctcccgc      700
tactgccac gctctgcca tccctgcatg cagcttgacc gttcatcca      750
ggtgtgcacc cagctgcagg tgctgacaga ggccttccgg gagaaggaca      800
cagctgtaca aggcaacatc cggctcagct tcgaggactt cgtcaccatg      850
acagcttctc ggatgctatg acccaacct ctgtggagag tggagtgcac      900
cagggacctt tcctggcttc ttagagtgag agaagtatgt ggacatctct      950
tcttttctg tccctctaga agaacattct ccctgcttg atgcaaacct      1000
gttcaaaaag aggtggaga gtccctgcatc atagccacca aatagtgagg      1050
accggggctg aggccacaca gataggggccc tgatggagga gaggatagaa      1100
gttgaatgct ctgatggcca tgagcagttg agtggcacag cctggcacca      1150
ggagcaggtc cttgtaatgg agttagtgtc cagtcagctg agctccaccc      1200
tgatgccagt ggtgagtgtt catcggcctg ttaccgttag tacctgtgtt      1250
ccctcaccag gccatcctgt caaacgagcc cattttctcc aaagtggaaat      1300
ctgaccaagc atgagagaga tctgtctatg ggaccagtgg cttggattct      1350
    
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gccacaccca taaatccttg tgtgttaact tctagctgcc tggggctggc      1400
cctgctcaga caaatctgct cctgggcat cttggccag gcttctgccc      1450
cctgcagctg ggacccctca ctgctctgcc atgctctgct cggcttcagt      1500
ctccaggaga cagtgtctac ctctccttgc caatactttt ttttaatttgc      1550
atTTTTTTTtC atttggggcc aaaagtccag tgaaattgta agcttcaata      1600
aaaggatgaa actctga      1617
    
```

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<210> SEQ ID NO 62
<211> LENGTH: 284
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien
    
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<400> SEQUENCE: 62
    
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```

Met Ala Ser Tyr Pro Tyr Arg Gln Gly Cys Pro Gly Ala Ala Gly
 1          5          10          15
Gln Ala Pro Gly Ala Pro Pro Gly Ser Tyr Tyr Pro Gly Pro Pro
 20          25          30
Asn Ser Gly Gly Gln Tyr Gly Ser Gly Leu Pro Pro Gly Gly Gly
 35          40          45
Tyr Gly Gly Pro Ala Pro Gly Gly Pro Tyr Gly Pro Pro Ala Gly
 50          55          60
Gly Gly Pro Tyr Gly His Pro Asn Pro Gly Met Phe Pro Ser Gly
 65          70          75
Thr Pro Gly Gly Pro Tyr Gly Gly Ala Ala Pro Gly Gly Pro Tyr
 80          85          90
Gly Gln Pro Pro Pro Ser Ser Tyr Gly Ala Gln Gln Pro Gly Leu
 95          100         105
Tyr Gly Gln Gly Gly Ala Pro Pro Asn Val Asp Pro Glu Ala Tyr
 110         115         120
Ser Trp Phe Gln Ser Val Asp Ser Asp His Ser Gly Tyr Ile Ser
 125         130         135
Met Lys Glu Leu Lys Gln Ala Leu Val Asn Cys Asn Trp Ser Ser
 140         145         150
Phe Asn Asp Glu Thr Cys Leu Met Met Ile Asn Met Phe Asp Lys
 155         160         165
Thr Lys Ser Gly Arg Ile Asp Val Tyr Gly Phe Ser Ala Leu Trp
 170         175         180
Lys Phe Ile Gln Gln Trp Lys Asn Leu Phe Gln Gln Tyr Asp Arg
 185         190         195
Asp Arg Ser Gly Ser Ile Ser Tyr Thr Glu Leu Gln Gln Ala Leu
 200         205         210
Ser Gln Met Gly Tyr Asn Leu Ser Pro Gln Phe Thr Gln Leu Leu
 215         220         225
Val Ser Arg Tyr Cys Pro Arg Ser Ala Asn Pro Ala Met Gln Leu
 230         235         240
Asp Arg Phe Ile Gln Val Cys Thr Gln Leu Gln Val Leu Thr Glu
 245         250         255
Ala Phe Arg Glu Lys Asp Thr Ala Val Gln Gly Asn Ile Arg Leu
 260         265         270
Ser Phe Glu Asp Phe Val Thr Met Thr Ala Ser Arg Met Leu
 275         280
    
```

-continued

<210> SEQ ID NO 63
 <211> LENGTH: 1234
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien
 <400> SEQUENCE: 63

```

caggatgcag ggcgcgctgg caggagctg cgctcctctg ggctgctcc      50
tggctctgtc tcatctccca ggctctttg cccggagcat cgggtgtgtg      100
gaggagaaa tttcccaaaa ctctgggacc aacttgctc agctcggaca      150
accttctctc actggcccct ctaactctga acatccgcag cccgctctgg      200
accctaggtc taatgacttg gcaagggttc ctctgaagct cagcgtgcct      250
ccatcagatg gcttcccacc tgcaggaggt tctgcagtgc agaggtggcc      300
tccatcgtgg gggctgcctg ccattgattc ctggcccctc gaggatcctt      350
ggcagatgat ggctgctgcg gctgaggacc gcctggggga agcgtgcct      400
gaagaactct cttacctctc cagtgtctcg gccctcgtc cgggcagtgg      450
ccctttgctc ggggagtctt ctcccgatgc cacaggctc tcaactgagg      500
cttactcctc ccaccaggac tcggagtcca gacgactgcc ccgttctaata      550
tcaactgggag ccgggggaaa aatcctttcc caacgccctc cctggtctct      600
catccacagc gttctgcctg atcaccctcg ggtaccctg aatcccagtg      650
tgtcctgggg aggtggaggc cctgggactg gttggggaac gaggcccatg      700
ccacaccctg agggaatctg gggatcaat aatcaacccc caggtaccag      750
ctggggaaaat attaatcggc atccaggagg cagctgggga aatattaatc      800
ggatccacag aggcagctgg gggaatatta atcggtatcc aggaggcagc      850
tgggggaata ttcatctata cccaggtatc aataacccat ttctcctctg      900
agttctccgc cctcctggct ctctctggaa catccagct ggcttcoccta      950
atcctccaag ccctagggtg cagtggggct agagcacgat agagggaaac     1000
ccaacattgg gagttagagt cctgctcccg ccccttgctg tgtgggctca     1050
atccaggccc tgtaacatg tttccagcac tatcccact tttcagtgcc     1100
tcccctgctc atctccaata aaataaaagc acttatgaaa aaaaaaaaaa     1150
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa     1200
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaa                                     1234
    
```

<210> SEQ ID NO 64
 <211> LENGTH: 325
 <212> TYPE: PRT
 <213> ORGANISM: Homo Sapien
 <400> SEQUENCE: 64

```

Met Gln Gly Arg Val Ala Gly Ser Cys Ala Pro Leu Gly Leu Leu
 1           5           10          15
Leu Val Cys Leu His Leu Pro Gly Leu Phe Ala Arg Ser Ile Gly
 20          25          30
Val Val Glu Glu Lys Val Ser Gln Asn Phe Gly Thr Asn Leu Pro
 35          40          45
    
```


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Gln	Leu	Gly	Gln	Pro	Ser	Ser	Thr	Gly	Pro	Ser	Asn	Ser	Glu	His
				50					55					60
Pro	Gln	Pro	Ala	Leu	Asp	Pro	Arg	Ser	Asn	Asp	Leu	Ala	Arg	Val
				65					70					75
Pro	Leu	Lys	Leu	Ser	Val	Pro	Pro	Ser	Asp	Gly	Phe	Pro	Pro	Ala
				80					85					90
Gly	Gly	Ser	Ala	Val	Gln	Arg	Trp	Pro	Pro	Ser	Trp	Gly	Leu	Pro
				95					100					105
Ala	Met	Asp	Ser	Trp	Pro	Pro	Glu	Asp	Pro	Trp	Gln	Met	Met	Ala
				110					115					120
Ala	Ala	Ala	Glu	Asp	Arg	Leu	Gly	Glu	Ala	Leu	Pro	Glu	Glu	Leu
				125					130					135
Ser	Tyr	Leu	Ser	Ser	Ala	Ala	Ala	Leu	Ala	Pro	Gly	Ser	Gly	Pro
				140					145					150
Leu	Pro	Gly	Glu	Ser	Ser	Pro	Asp	Ala	Thr	Gly	Leu	Ser	Pro	Glu
				155					160					165
Ala	Ser	Leu	Leu	His	Gln	Asp	Ser	Glu	Ser	Arg	Arg	Leu	Pro	Arg
				170					175					180
Ser	Asn	Ser	Leu	Gly	Ala	Gly	Gly	Lys	Ile	Leu	Ser	Gln	Arg	Pro
				185					190					195
Pro	Trp	Ser	Leu	Ile	His	Arg	Val	Leu	Pro	Asp	His	Pro	Trp	Gly
				200					205					210
Thr	Leu	Asn	Pro	Ser	Val	Ser	Trp	Gly	Gly	Gly	Gly	Pro	Gly	Thr
				215					220					225
Gly	Trp	Gly	Thr	Arg	Pro	Met	Pro	His	Pro	Glu	Gly	Ile	Trp	Gly
				230					235					240
Ile	Asn	Asn	Gln	Pro	Pro	Gly	Thr	Ser	Trp	Gly	Asn	Ile	Asn	Arg
				245					250					255
Tyr	Pro	Gly	Gly	Ser	Trp	Gly	Asn	Ile	Asn	Arg	Tyr	Pro	Gly	Gly
				260					265					270
Ser	Trp	Gly	Asn	Ile	Asn	Arg	Tyr	Pro	Gly	Gly	Ser	Trp	Gly	Asn
				275					280					285
Ile	His	Leu	Tyr	Pro	Gly	Ile	Asn	Asn	Pro	Phe	Pro	Pro	Gly	Val
				290					295					300
Leu	Arg	Pro	Pro	Gly	Ser	Ser	Trp	Asn	Ile	Pro	Ala	Gly	Phe	Pro
				305					310					315
Asn	Pro	Pro	Ser	Pro	Arg	Leu	Gln	Trp	Gly					
				320					325					

<210> SEQ ID NO 65
 <211> LENGTH: 422
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 65

aaggagagggc caccgggact tcaagtgtctc ctccatocca ggagcgcagt	50
ggccactatg gggctctgggc tgccccttgt cctcctcttg accctccttg	100
gcagctcaca tggaacaggg cggggtatga ctttgcaact gaagctgaag	150
gagtccttttc tgacaaattc ctctctatgag tccagcttcc tggaattgct	200
tgaaaagctc tgcctcctcc tccatctccc ttcagggacc agcgtcacc	250
tccaccatgc aagatctcaa caccatgttg tctgcaacac atgacagcca	300

-continued

```

ttgaagcctg tgtccttctt ggcccgggct tttgggcccgg ggatgcagga      350
ggcaggcccc gacctgtctt ttcagcagcc cccaccctc ctgagtggca      400
ataaataaaa ttcggtatgc tg                                          422

```

```

<210> SEQ ID NO 66
<211> LENGTH: 78
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien

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<400> SEQUENCE: 66

```

```

Met Gly Ser Gly Leu Pro Leu Val Leu Leu Leu Thr Leu Leu Gly
 1           5           10          15
Ser Ser His Gly Thr Gly Pro Gly Met Thr Leu Gln Leu Lys Leu
          20          25          30
Lys Glu Ser Phe Leu Thr Asn Ser Ser Tyr Glu Ser Ser Phe Leu
          35          40          45
Glu Leu Leu Glu Lys Leu Cys Leu Leu Leu His Leu Pro Ser Gly
          50          55          60
Thr Ser Val Thr Leu His His Ala Arg Ser Gln His His Val Val
          65          70          75

```

```

Cys Asn Thr

```

```

<210> SEQ ID NO 67
<211> LENGTH: 744
<212> TYPE: DNA
<213> ORGANISM: Homo Sapien

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<400> SEQUENCE: 67

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```

acggaccgag ggttcgaggg agggacacgg accaggaacc tgagctaggt      50
caaagacgcc cgggccaggt gccccgtcgc aggtgccctt gcccgagat      100
gcggttaggag gggcagagcg gagaagcccc ttcctcggcg ctgccaaacc      150
gccaccagc ccatggcgaa ccccgggctg gggctgcttc tggcgctggg      200
cctgccgttc ctgctggccc gctggggccg agcctggggg caaatacaga      250
ccacttctgc aaatgagaat agcactgttt tgccttcata caccagctcc      300
agctccgatg gcaacctgag tccggaagcc atcactgcta tcatcgtggt      350
cttctccctc ttggtgcctt tgctcctggc tgtggggctg gcaactgttg      400
tgcggaagct tcgggagaag cggcagacgg agggcaccta ccggcccagt      450
agcgaggagc agttctccca tgcagccgag gcccgggccc ctcaggactc      500
caagagagac gtgcagggct gcctgcccac ctaggctccc tctcctgcat      550
ctgtctccct tcattgctgt gtgaccttgg gaaaggcag tgccctctct      600
gggcagtcag atccaccag tgcttaatag caggaagaa ggtacttcaa      650
agactctgcc cctgaggtca agagaggatg gggctattca cttttatata      700
tttatataaa attagtagtg agatgtaaaa aaaaaaaaaa aaaa          744

```

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<210> SEQ ID NO 68
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien

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-continued

<400> SEQUENCE: 68

```

Met Ala Asn Pro Gly Leu Gly Leu Leu Leu Ala Leu Gly Leu Pro
 1           5           10           15
Phe Leu Leu Ala Arg Trp Gly Arg Ala Trp Gly Gln Ile Gln Thr
 20           25           30
Thr Ser Ala Asn Glu Asn Ser Thr Val Leu Pro Ser Ser Thr Ser
 35           40           45
Ser Ser Ser Asp Gly Asn Leu Arg Pro Glu Ala Ile Thr Ala Ile
 50           55           60
Ile Val Val Phe Ser Leu Leu Ala Ala Leu Leu Leu Ala Val Gly
 65           70           75
Leu Ala Leu Leu Val Arg Lys Leu Arg Glu Lys Arg Gln Thr Glu
 80           85           90
Gly Thr Tyr Arg Pro Ser Ser Glu Glu Gln Phe Ser His Ala Ala
 95           100          105
Glu Ala Arg Ala Pro Gln Asp Ser Lys Glu Thr Val Gln Gly Cys
 110          115          120

Leu Pro Ile
    
```

<210> SEQ ID NO 69

<211> LENGTH: 3265

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 69

```

gccaggaata actagagagg aacaatgggg ttattcagag gttttgtttt           50
cctcttagtt ctgtgcctgc tgcaccagtc aaactactcc ttcattaagc           100
tgaataataa tggccttgaa gatattgtca ttggtataga tcctagtgtg           150
ccagaagatg aaaaaataat tgaacaaata gaggatatgg tgactacagc           200
ttctacgtac ctgtttgaag ccacagaaaa aagatTTTTT ttcaaaaatg           250
tatctatatt aattcctgag aattggaagg aaaatcctca gtacaaaagg           300
ccaaaacatg aaaaccataa acatgctgat gttatagttg caccacctac           350
actcccaggt agagatgaac catacaccaa gcagttcaca gaatgtggag           400
agaaaggcga atacattcac ttcaccctcg accttctact tggaaaaaaa           450
caaaatgaat atggaccacc aggcaaaactg tttgtccatg agtgggctca           500
cctccgggtg ggagtgtttg atgagtacaa tgaagatcag cctttctacc           550
gtgctaagtc aaaaaaaatc gaagcaacaa ggtgttccgc aggtatctct           600
ggtagaaata gagtttataa gtgtcaagga ggcagctgtc ttagtagagc           650
atgcagaatt gattctacaa caaaactgta tggaaaagat tgcoaattct           700
ttcctgataa agtacaacaa gaaaaagcat ccataatggt tatgcaaagt           750
attgattctg ttgttgaatt ttgtaacgaa aaaaccata atcaagaagc           800
tccaagccta caaacataa agtgcaatTT tagaagtaca tgggagggtg           850
ttagcaattc tgaggatTTT aaaaacacca taccatggt gacaccacct           900
cctccacctg tcttctcatt gctgaagatc agtcaaagaa ttgtgtgctt           950
agttcttgat aagtctggaa gcatgggggg taaggaccgc ctaaatcgaa           1000
    
```

-continued

tgaatcaagc agcaaaacat ttctgctgc agactgttga aaatggatcc	1050
tgggtgggga tggttcactt tgatagtact gccactattg taataagct	1100
aatccaaata aaaagcagtg atgaaagaaa cacactcatg gcaggattac	1150
ctacatatcc tctgggagga acttccatct gctctggaat taaatatgca	1200
tttcagtgga ttggagagct acattcccaa ctcgatggat ccgaagtact	1250
gctgctgact gatggggagg ataacactgc aagttcttgt attgatgaag	1300
tgaaacaaag tggggccatt gttcatttta ttgctttggg aagagctgct	1350
gatgaagcag taatagagat gagcaagata acaggaggaa gtcattttta	1400
tgtttcagat gaagctcaga acaatggcct cattgatgct tttggggctc	1450
ttacatcagg aaatactgat ctctcccaga agtccctca gctcgaaagt	1500
aagggattaa cactgaatag taatgcctgg atgaacgaca ctgtcataat	1550
tgatagtaca gtgggaaagg acacgttctt tctcatcaca tggaacagtc	1600
tgccctccag tatttctctc tgggatccca gtggaacaat aatggaaaat	1650
ttcacagtgg atgcaacttc caaaatggcc tatctcagta ttccaggaac	1700
tgcaaaaggg ggcacttggg catacaatct tcaagccaaa gcgaaccag	1750
aaacattaac tattacagta acttctcgag cagcaaatc tctgtgcct	1800
ccaatcacag tgaatgctaa aatgaataag gacgtaaaca gtttcccag	1850
cccaatgatt gtttacgcag aaattctaca aggatatgta cctgttcttg	1900
gagccaatgt gactgctttc attgaatcac agaatggaca tacagaagtt	1950
ttggaacttt tggataatgg tgcagcgct gattcttca agaatgatgg	2000
agtctactcc aggtatttta cagcatatac agaaaatggc agatatagct	2050
taaaagttog ggctcatgga ggagcaaa caagcaggct aaaattacgg	2100
cctccactga atagagccgc gtacatacca ggctgggtag tgaacgggga	2150
aattgaagca aaccgcca gacctgaaat tgatgaggat actcagacca	2200
ccttgaggga tttcagcca acagatccg gaggtgcat tgtggtatca	2250
caagtcccaa gccttccctt gcctgaccaa taccaccaa gtcaaatcac	2300
agacctgat gccacagttc atgaggataa gattattctt acatggacag	2350
caccaggaga taattttgat gttgaaaag ttcaacgta tatcataaga	2400
ataagtgcaa gtattcttga tctaagagac agttttgat atgctcttca	2450
agtaaaact actgatctgt caccaaagga ggccaactcc aaggaaagct	2500
ttgcatthaa accagaaaat atctcagaag aaaatgcaac ccacatattt	2550
attgccatta aaagtataga taaaagcaat ttgacatcaa aagtatccaa	2600
cattgcacaa gtaactttgt ttatccctca agcaaatcct gatgacattg	2650
atcctacacc tactcctact cctactccta ctctgataa aagtcataat	2700
tctggagtta atatttctac gctggtattg tctgtgattg ggtctgtgt	2750
aattgttaac tttattttaa gtaccacat ttgaacctta acgaagaaaa	2800
aaatcttcaa gtagacctag aagagagttt taaaaacaa aacaatgtaa	2850
gtaaaggata tttctgaatc ttaaaattca tccatgtgt gatcataaac	2900

-continued

tcataaaaaat aattttaaga tgtcggaaaa ggatactttg attaaataaa	2950
aacactcatg gatagtataa aactgtcaag attaaaattt aatagtttca	3000
tttattttgtt attttatttg taagaaatag tgatgaacaa agatcctttt	3050
tcatactgat acctggttgt atattatttg atgcaacagt tttctgaaat	3100
gatatttcaa attgcatcaa gaaattaaaa tcatctatct gagtagtcaa	3150
aatacaagta aaggagagca aataacaac atttgaaaa aaaaaaaaaa	3200
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa	3250
aaaaaaaaaa aaaaaa	3265

<210> SEQ ID NO 70
 <211> LENGTH: 919
 <212> TYPE: PRT
 <213> ORGANISM: Homo Sapien
 <400> SEQUENCE: 70

Met Gly Leu Phe Arg Gly Phe Val Phe Leu Leu Val Leu Cys Leu	1	5	10	15
Leu His Gln Ser Asn Thr Ser Phe Ile Lys Leu Asn Asn Asn Gly	20	25	30	
Phe Glu Asp Ile Val Ile Val Ile Asp Pro Ser Val Pro Glu Asp	35	40	45	
Glu Lys Ile Ile Glu Gln Ile Glu Asp Met Val Thr Thr Ala Ser	50	55	60	
Thr Tyr Leu Phe Glu Ala Thr Glu Lys Arg Phe Phe Phe Lys Asn	65	70	75	
Val Ser Ile Leu Ile Pro Glu Asn Trp Lys Glu Asn Pro Gln Tyr	80	85	90	
Lys Arg Pro Lys His Glu Asn His Lys His Ala Asp Val Ile Val	95	100	105	
Ala Pro Pro Thr Leu Pro Gly Arg Asp Glu Pro Tyr Thr Lys Gln	110	115	120	
Phe Thr Glu Cys Gly Glu Lys Gly Glu Tyr Ile His Phe Thr Pro	125	130	135	
Asp Leu Leu Leu Gly Lys Lys Gln Asn Glu Tyr Gly Pro Pro Gly	140	145	150	
Lys Leu Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe	155	160	165	
Asp Glu Tyr Asn Glu Asp Gln Pro Phe Tyr Arg Ala Lys Ser Lys	170	175	180	
Lys Ile Glu Ala Thr Arg Cys Ser Ala Gly Ile Ser Gly Arg Asn	185	190	195	
Arg Val Tyr Lys Cys Gln Gly Gly Ser Cys Leu Ser Arg Ala Cys	200	205	210	
Arg Ile Asp Ser Thr Thr Lys Leu Tyr Gly Lys Asp Cys Gln Phe	215	220	225	
Phe Pro Asp Lys Val Gln Thr Glu Lys Ala Ser Ile Met Phe Met	230	235	240	
Gln Ser Ile Asp Ser Val Val Glu Phe Cys Asn Glu Lys Thr His	245	250	255	
Asn Gln Glu Ala Pro Ser Leu Gln Asn Ile Lys Cys Asn Phe Arg				

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	260		265		270
Ser Thr Trp Glu Val	Ile Ser Asn Ser	Glu Asp Phe Lys Asn Thr			
	275		280		285
Ile Pro Met Val Thr	Pro Pro Pro Pro	Pro Val Phe Ser Leu Leu			
	290		295		300
Lys Ile Ser Gln Arg	Ile Val Cys Leu	Val Leu Asp Lys Ser Gly			
	305		310		315
Ser Met Gly Gly Lys	Asp Arg Leu Asn	Arg Met Asn Gln Ala Ala			
	320		325		330
Lys His Phe Leu Leu	Gln Thr Val Glu	Asn Gly Ser Trp Val Gly			
	335		340		345
Met Val His Phe Asp	Ser Thr Ala Thr	Ile Val Asn Lys Leu Ile			
	350		355		360
Gln Ile Lys Ser Ser	Asp Glu Arg Asn	Thr Leu Met Ala Gly Leu			
	365		370		375
Pro Thr Tyr Pro Leu	Gly Gly Thr Ser	Ile Cys Ser Gly Ile Lys			
	380		385		390
Tyr Ala Phe Gln Val	Ile Gly Glu Leu	His Ser Gln Leu Asp Gly			
	395		400		405
Ser Glu Val Leu Leu	Leu Thr Asp Gly	Glu Asp Asn Thr Ala Ser			
	410		415		420
Ser Cys Ile Asp Glu	Val Lys Gln Ser	Gly Ala Ile Val His Phe			
	425		430		435
Ile Ala Leu Gly Arg	Ala Ala Asp Glu	Ala Val Ile Glu Met Ser			
	440		445		450
Lys Ile Thr Gly Gly	Ser His Phe Tyr	Val Ser Asp Glu Ala Gln			
	455		460		465
Asn Asn Gly Leu Ile	Asp Ala Phe Gly	Ala Leu Thr Ser Gly Asn			
	470		475		480
Thr Asp Leu Ser Gln	Lys Ser Leu Gln	Leu Glu Ser Lys Gly Leu			
	485		490		495
Thr Leu Asn Ser Asn	Ala Trp Met Asn	Asp Thr Val Ile Ile Asp			
	500		505		510
Ser Thr Val Gly Lys	Asp Thr Phe Phe	Leu Ile Thr Trp Asn Ser			
	515		520		525
Leu Pro Pro Ser Ile	Ser Leu Trp Asp	Pro Ser Gly Thr Ile Met			
	530		535		540
Glu Asn Phe Thr Val	Asp Ala Thr Ser	Lys Met Ala Tyr Leu Ser			
	545		550		555
Ile Pro Gly Thr Ala	Lys Val Gly Thr	Trp Ala Tyr Asn Leu Gln			
	560		565		570
Ala Lys Ala Asn Pro	Glu Thr Leu Thr	Ile Thr Val Thr Ser Arg			
	575		580		585
Ala Ala Asn Ser Ser	Val Pro Pro Ile	Thr Val Asn Ala Lys Met			
	590		595		600
Asn Lys Asp Val Asn	Ser Phe Pro Ser	Pro Met Ile Val Tyr Ala			
	605		610		615
Glu Ile Leu Gln Gly	Tyr Val Pro Val	Leu Gly Ala Asn Val Thr			
	620		625		630
Ala Phe Ile Glu Ser	Gln Asn Gly His	Thr Glu Val Leu Glu Leu			
	635		640		645

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Leu Asp Asn Gly Ala Gly Ala Asp Ser Phe Lys Asn Asp Gly Val
650 655 660

Tyr Ser Arg Tyr Phe Thr Ala Tyr Thr Glu Asn Gly Arg Tyr Ser
665 670 675

Leu Lys Val Arg Ala His Gly Gly Ala Asn Thr Ala Arg Leu Lys
680 685 690

Leu Arg Pro Pro Leu Asn Arg Ala Ala Tyr Ile Pro Gly Trp Val
695 700 705

Val Asn Gly Glu Ile Glu Ala Asn Pro Pro Arg Pro Glu Ile Asp
710 715 720

Glu Asp Thr Gln Thr Thr Leu Glu Asp Phe Ser Arg Thr Ala Ser
725 730 735

Gly Gly Ala Phe Val Val Ser Gln Val Pro Ser Leu Pro Leu Pro
740 745 750

Asp Gln Tyr Pro Pro Ser Gln Ile Thr Asp Leu Asp Ala Thr Val
755 760 765

His Glu Asp Lys Ile Ile Leu Thr Trp Thr Ala Pro Gly Asp Asn
770 775 780

Phe Asp Val Gly Lys Val Gln Arg Tyr Ile Ile Arg Ile Ser Ala
785 790 795

Ser Ile Leu Asp Leu Arg Asp Ser Phe Asp Asp Ala Leu Gln Val
800 805 810

Asn Thr Thr Asp Leu Ser Pro Lys Glu Ala Asn Ser Lys Glu Ser
815 820 825

Phe Ala Phe Lys Pro Glu Asn Ile Ser Glu Glu Asn Ala Thr His
830 835 840

Ile Phe Ile Ala Ile Lys Ser Ile Asp Lys Ser Asn Leu Thr Ser
845 850 855

Lys Val Ser Asn Ile Ala Gln Val Thr Leu Phe Ile Pro Gln Ala
860 865 870

Asn Pro Asp Asp Ile Asp Pro Thr Pro Thr Pro Thr Pro Thr Pro
875 880 885

Thr Pro Asp Lys Ser His Asn Ser Gly Val Asn Ile Ser Thr Leu
890 895 900

Val Leu Ser Val Ile Gly Ser Val Val Ile Val Asn Phe Ile Leu
905 910 915

Ser Thr Thr Ile

<210> SEQ ID NO 71
 <211> LENGTH: 3877
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 71

ctccttaggt ggaaaccctg ggagtagagt actgacagca aagaccggga	50
aagaccatac gtccccgggc aggggtgaca acaggtgtca tctttttgat	100
ctcgtgtgtg gctgccttcc tatttcaagg aaagacgcca aggtaatttt	150
gaccagagg agcaatgatg tagccacctc ctaaccttcc cttcttgaac	200
ccccagttat gccaggattt actagagagt gtcaactcaa ccagcaagcg	250
gtcctctcgg cttaacttgt ggttgaggga gagaaccttt gtggggctgc	300

-continued

gttctcttag cagtgctcag aagtgacttg cctgagggtg gaccagaaga	350
aaggaaaggt cccctcttgc tgttggtctg acatcaggaa ggctgtgatg	400
ggaatgaagg tgaaaacttg gagatttcac ttcagtcatt gcttctgcct	450
gcaagatcat cctttaaag tagagaagct gctctgtgtg gtggttaact	500
ccaagaggca gaactcgttc tagaaggaaa tggatgcaag cagctccggg	550
ggcccaaac gcatgcttcc tgttggtctag cccagggaag cccttccgtg	600
ggggcccggt ctttgaggga tgccaccggt tctggacgca tggctgattc	650
ctgaatgatg atggttcgcc gggggctgct tgcgtggatt tcccgggtgg	700
tggttttgct ggtgctcctc tgetgtgcta tctctgtcct gtacatgttg	750
gctgcaccc caaaaggtga cgaggagcag ctggcactgc ccagggcaa	800
cagcccaag ggaagagag ggtaccagc cgtccttcag gagtgggagg	850
agcagcaccc caactacgtg agcagcctga agcggcagat cgcacagctc	900
aaggaggagc tgcaggagag gagtgagcag ctcaggaatg ggcagtacca	950
agccagcgat gctgctggcc tgggtctgga caggagcccc ccagagaaaa	1000
cccaggccga cctcctggcc ttcctgcact cgcagggtgga caaggcagag	1050
gtgaatgctg gcgtcaagct ggccacagag tatgcagcag tgcctttcga	1100
tagcttcta ctacagaag tgtaccagct ggagactggc cttaccggcc	1150
accccgagga gaagcctgtg aggaaggaca agcgggatga gttggtgaa	1200
gccattgaat cagccttga gaccctgaac aatcctgcag agaacagccc	1250
caatcacctg ccttacacgg cctctgattt catagaagg atctaccgaa	1300
cagaaaagga caaagggaca ttgtatgagc tcacctcaa aggggaccac	1350
aaacacgaat tcaaacggct catcttattt cgaccattca gcccatcat	1400
gaaagtgaaa aatgaaaagc tcaacatggc caacacgctt atcaatgtta	1450
tcgtgcctct agcaaaaag gtggacaagt tccggcagtt catgcagaat	1500
ttcagggaga tgtgcattga gcaggatggg agagtccatc tcaactgtgt	1550
ttactttggg aaagaagaaa taaatgaagt caaaggaata cttgaaaaca	1600
cttccaaagc tgccaacttc aggaacttta cctcatcca gctgaatgga	1650
gaattttctc ggggaaaggg acttgatgtt ggagcccgtc tctggaaggg	1700
aagcaacgtc cttctctttt tctgtgatgt ggacatctac ttcacatctg	1750
aattcctcaa tacgtgtagg ctgaatacac agccagggaa gaaggtattt	1800
tatccagttc ttttcagtca gtacaatcct ggcataatat acggccacca	1850
tgatgcagtc cctcccttg aacagcagct ggtcataaag aaggaaactg	1900
gattttggag agactttgga tttggatga cgtgtcagta tcggtcagac	1950
ttcatcaata taggtgggtt tgatctggac atcaaaggct ggggaggaga	2000
ggatgtgcac ctttatcgca agtatctcca cagcaacctc atagtggtag	2050
ggacgcctgt gcgaggactc ttcacactct ggcatgagaa gcgctgcagt	2100
gacgagctga cccccagca gtacaagatg tgcatgcagt ccaaggccat	2150
gaacagggca tcccacggcc agctgggcat gctggtgttc aggcacgaga	2200

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tagaggctca ccttcgcaaa cagaaacaga agacaagtag caaaaaaaca 2250
tgaactccca gagaaggatt gtgggagaca ctttttcttt ccttttgcaa 2300
ttactgaaag tggctgcaac agagaaaaga cttccataaa ggacgacaaa 2350
agaattggac tgatgggtca gagatgagaa agcctccgat ttctctctgt 2400
tgggcttttt acaacagaaa tcaaaatctc cgctttgcct gcaaaagtaa 2450
cccagttgca ccctgtgaag tgtctgacaa aggcagaatg cttgtgagat 2500
tataagccta atggtgtgga ggttttgatg gtgtttcaa tacactgaga 2550
cctgtgtgtt tgtgtgctca ttgaaatatt catgatttaa gagcagtttt 2600
gtaaaaaatt cattagcatg aaaggcaagc atatttctcc tcatatgaat 2650
gagcctatca gcagggctct agtttctagg aatgctaaaa taccagaagg 2700
caggagagga gataggctta ttatgatact agtgagtaca ttaagtaaaa 2750
taaaatggac cagaaaagaa aagaaacct aaatatcgtg tcatattttc 2800
cccaagatta accaaaaata atctgcttat ctttttggtt gtccttttaa 2850
ctgtctccgt ttttttcttt ttttaaaaa tgcacttttt ttccctgtgt 2900
agttatagtc tgcttattta attaccactt tgcaagcctt acaagagagc 2950
acaagttggc ctacattttt atatttttta agaagatact ttgagatgca 3000
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gggaaggaat ggtttgact aatacagacg tacagatact ttctctgaag 3150
agtattttog aagaggagca actgaacct ggaggaaaag aaaatgacac 3200
tttctgcttt acagaaaagg aaactcatc agactggtga tctcgtgatg 3250
tacctaaaag tcagaaacca cttttctcc tcagaagtag ggaccgcttt 3300
cttacctgtt taaataaacc aaagtatacc gtgtgaacca aacaatctct 3350
tttcaaaaca ggggtgctct cctggcttct ggcttccata agaagaaatg 3400
gagaaaaata tatatatata tatatatatt gtgaaagatc aatccatctg 3450
ccagaatcta gtgggatgga agtttttgct acatgttatc caccocaggc 3500
caggtggaag taactgaatt attttttaaa ttaagcagtt ctactcaatc 3550
accaagatgc ttctgaaaat tgcattttat taccatttca aactattttt 3600
taaaaaataa tacagttaac atagagtggg ttcttcattc atgtgaaaat 3650
tattagccag caccagatgc atgagctaata tatctctttg agtcoctgct 3700
tctgtttgct cacagtaaac tcattgttta aaagcttcaa gaacattcaa 3750
gctgttggtg tgttaaaaaa tgcattgtat tgatttgtac tggtagttta 3800
tgaaatttaa ttaaaacaca ggccatgaat ggaaggtggt attgcacagc 3850
taataaaaata tgatttggg atatgaa 3877

<210> SEQ ID NO 72

<211> LENGTH: 532

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 72

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Met	Met	Met	Val	Arg	Arg	Gly	Leu	Leu	Ala	Trp	Ile	Ser	Arg	Val
1				5					10					15
Val	Val	Leu	Leu	Val	Leu	Leu	Cys	Cys	Ala	Ile	Ser	Val	Leu	Tyr
				20					25					30
Met	Leu	Ala	Cys	Thr	Pro	Lys	Gly	Asp	Glu	Glu	Gln	Leu	Ala	Leu
				35					40					45
Pro	Arg	Ala	Asn	Ser	Pro	Thr	Gly	Lys	Glu	Gly	Tyr	Gln	Ala	Val
				50					55					60
Leu	Gln	Glu	Trp	Glu	Glu	Gln	His	Arg	Asn	Tyr	Val	Ser	Ser	Leu
				65					70					75
Lys	Arg	Gln	Ile	Ala	Gln	Leu	Lys	Glu	Glu	Leu	Gln	Glu	Arg	Ser
				80					85					90
Glu	Gln	Leu	Arg	Asn	Gly	Gln	Tyr	Gln	Ala	Ser	Asp	Ala	Ala	Gly
				95					100					105
Leu	Gly	Leu	Asp	Arg	Ser	Pro	Pro	Glu	Lys	Thr	Gln	Ala	Asp	Leu
				110					115					120
Leu	Ala	Phe	Leu	His	Ser	Gln	Val	Asp	Lys	Ala	Glu	Val	Asn	Ala
				125					130					135
Gly	Val	Lys	Leu	Ala	Thr	Glu	Tyr	Ala	Ala	Val	Pro	Phe	Asp	Ser
				140					145					150
Phe	Thr	Leu	Gln	Lys	Val	Tyr	Gln	Leu	Glu	Thr	Gly	Leu	Thr	Arg
				155					160					165
His	Pro	Glu	Glu	Lys	Pro	Val	Arg	Lys	Asp	Lys	Arg	Asp	Glu	Leu
				170					175					180
Val	Glu	Ala	Ile	Glu	Ser	Ala	Leu	Glu	Thr	Leu	Asn	Asn	Pro	Ala
				185					190					195
Glu	Asn	Ser	Pro	Asn	His	Arg	Pro	Tyr	Thr	Ala	Ser	Asp	Phe	Ile
				200					205					210
Glu	Gly	Ile	Tyr	Arg	Thr	Glu	Arg	Asp	Lys	Gly	Thr	Leu	Tyr	Glu
				215					220					225
Leu	Thr	Phe	Lys	Gly	Asp	His	Lys	His	Glu	Phe	Lys	Arg	Leu	Ile
				230					235					240
Leu	Phe	Arg	Pro	Phe	Ser	Pro	Ile	Met	Lys	Val	Lys	Asn	Glu	Lys
				245					250					255
Leu	Asn	Met	Ala	Asn	Thr	Leu	Ile	Asn	Val	Ile	Val	Pro	Leu	Ala
				260					265					270
Lys	Arg	Val	Asp	Lys	Phe	Arg	Gln	Phe	Met	Gln	Asn	Phe	Arg	Glu
				275					280					285
Met	Cys	Ile	Glu	Gln	Asp	Gly	Arg	Val	His	Leu	Thr	Val	Val	Tyr
				290					295					300
Phe	Gly	Lys	Glu	Glu	Ile	Asn	Glu	Val	Lys	Gly	Ile	Leu	Glu	Asn
				305					310					315
Thr	Ser	Lys	Ala	Ala	Asn	Phe	Arg	Asn	Phe	Thr	Phe	Ile	Gln	Leu
				320					325					330
Asn	Gly	Glu	Phe	Ser	Arg	Gly	Lys	Gly	Leu	Asp	Val	Gly	Ala	Arg
				335					340					345
Phe	Trp	Lys	Gly	Ser	Asn	Val	Leu	Leu	Phe	Phe	Cys	Asp	Val	Asp
				350					355					360
Ile	Tyr	Phe	Thr	Ser	Glu	Phe	Leu	Asn	Thr	Cys	Arg	Leu	Asn	Thr
				365					370					375

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Gln	Pro	Gly	Lys	Lys	Val	Phe	Tyr	Pro	Val	Leu	Phe	Ser	Gln	Tyr
			380						385					390
Asn	Pro	Gly	Ile	Ile	Tyr	Gly	His	His	Asp	Ala	Val	Pro	Pro	Leu
			395						400					405
Glu	Gln	Gln	Leu	Val	Ile	Lys	Lys	Glu	Thr	Gly	Phe	Trp	Arg	Asp
			410						415					420
Phe	Gly	Phe	Gly	Met	Thr	Cys	Gln	Tyr	Arg	Ser	Asp	Phe	Ile	Asn
				425					430					435
Ile	Gly	Gly	Phe	Asp	Leu	Asp	Ile	Lys	Gly	Trp	Gly	Gly	Glu	Asp
				440					445					450
Val	His	Leu	Tyr	Arg	Lys	Tyr	Leu	His	Ser	Asn	Leu	Ile	Val	Val
				455					460					465
Arg	Thr	Pro	Val	Arg	Gly	Leu	Phe	His	Leu	Trp	His	Glu	Lys	Arg
				470					475					480
Cys	Met	Asp	Glu	Leu	Thr	Pro	Glu	Gln	Tyr	Lys	Met	Cys	Met	Gln
				485					490					495
Ser	Lys	Ala	Met	Asn	Glu	Ala	Ser	His	Gly	Gln	Leu	Gly	Met	Leu
				500					505					510
Val	Phe	Arg	His	Glu	Ile	Glu	Ala	His	Leu	Arg	Lys	Gln	Lys	Gln
				515					520					525
Lys	Thr	Ser	Ser	Lys	Lys	Thr								
				530										

<210> SEQ ID NO 73
 <211> LENGTH: 1701
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien
 <220> FEATURE:
 <221> NAME/KEY: unsure
 <222> LOCATION: 1528
 <223> OTHER INFORMATION: unknown base

<400> SEQUENCE: 73

gagactgcag agggagataa agagagaggg caaagaggca gcaagagatt	50
tgtcctcggg atccagaaac ccatgatacc ctactgaaca ccgaatcccc	100
tggaagccca cagagacaga gacagcaaga gaagcagaga taaatacact	150
cacgccagga gctcgctcgc tctctctctc tctctctcac tcctccctcc	200
ctctctctct gcctgtccta gtcctctagt cctcaaattc ccagtcccct	250
gcaccccttc ctgggacact atgttgttct cgcacctcct gctggagggtg	300
atctggatcc tggctgcaga tgggggtcaa cactggacgt atgaggggcc	350
acatggtcag gaccattggc cagcctctta cctgagtgt ggaacaatg	400
cccagtcgcc catcgatatt cagacagaca gtgtgacatt tgaccctgat	450
ttgcctgctc tgcagcccca cggatatgac cagcctggca ccgagccttt	500
ggacctgcac aacaatggcc acacagtgca actctctctg ccctctaccc	550
tgtatctggg tggacttccc cgaaaatag tagctgcca gctccactg	600
cactggggtc agaaaggatc ccagggggg tcagaacacc agatcaacag	650
tgaagccaca tttgcagagc tccacattgt acattatgac tctgattcct	700
atgacagctt gagtgaggct gctgagagcc ctcagggcct ggctgtctg	750
ggcatcctaa ttgaggtggg tgagactaag aatatagctt atgaacacat	800

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tctgagtcac ttgcatgaag tcaggcataa agatcagaag acctcagtgc      850
ctcccttcaa cctaagagag ctgctcccca aacagctggg gcagtacttc      900
cgctacaatg gctcgctcac aactccccct tgctaccaga gtgtgctctg      950
gacagttttt tatagaaggt cccagatttc aatggaacag ctggaaaagc     1000
ttcaggggac attgttctcc acagaagagg agccctctaa gcttctggta     1050
cagaactacc gagcccttca gcctctcaat cagcgcattg tctttgcttc     1100
tttcatccaa gcaggatcct cgtataccac aggtgaaatg ctgagtctag     1150
gtgtaggaat cttggttggc tgtctctgcc ttctctggc  tgtttatttc     1200
attgctagaa agattcggaa gaagaggctg gaaaaccgaa agagtgtggt     1250
cttcacctca gcacaagcca cgactgaggc ataaattcct tctcagatac     1300
catggatgtg gatgacttcc cttctgcctc atcaggaagc ctctaaaatg     1350
gggtgtagga tctggccaga aacctgttag gagtagtaag cagatgtcct     1400
ccttccccct gacatctctt agagaggaat ggaccocaggc tgtcattcca     1450
ggaagaactg cagagccttc agcctctcca aacatgtagg aggaaatgag     1500
gaaatcgctg tgttgtaaat gcagaganca aactctgttt agttgcaggg     1550
gaagtttggg atatacccca aagtcctcta cccctcact tttatggccc     1600
tttccctaga tatactgagg gatctctcct taggataaag agttgctggt     1650
gaagttgtat atttttgatc aatatatttg gaaattaaag tttctgactt     1700
t                                                                 1701

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<210> SEQ ID NO 74

<211> LENGTH: 337

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 74

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Met Leu Phe Ser Ala Leu Leu Leu Glu Val Ile Trp Ile Leu Ala
 1             5             10            15
Ala Asp Gly Gly Gln His Trp Thr Tyr Glu Gly Pro His Gly Gln
                20            25            30
Asp His Trp Pro Ala Ser Tyr Pro Glu Cys Gly Asn Asn Ala Gln
                35            40            45
Ser Pro Ile Asp Ile Gln Thr Asp Ser Val Thr Phe Asp Pro Asp
                50            55            60
Leu Pro Ala Leu Gln Pro His Gly Tyr Asp Gln Pro Gly Thr Glu
                65            70            75
Pro Leu Asp Leu His Asn Asn Gly His Thr Val Gln Leu Ser Leu
                80            85            90
Pro Ser Thr Leu Tyr Leu Gly Gly Leu Pro Arg Lys Tyr Val Ala
                95            100           105
Ala Gln Leu His Leu His Trp Gly Gln Lys Gly Ser Pro Gly Gly
                110           115           120
Ser Glu His Gln Ile Asn Ser Glu Ala Thr Phe Ala Glu Leu His
                125           130           135
Ile Val His Tyr Asp Ser Asp Ser Tyr Asp Ser Leu Ser Glu Ala
                140           145           150

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Ala Glu Arg Pro Gln Gly Leu Ala Val Leu Gly Ile Leu Ile Glu
 155 160 165

Val Gly Glu Thr Lys Asn Ile Ala Tyr Glu His Ile Leu Ser His
 170 175 180

Leu His Glu Val Arg His Lys Asp Gln Lys Thr Ser Val Pro Pro
 185 190 195

Phe Asn Leu Arg Glu Leu Leu Pro Lys Gln Leu Gly Gln Tyr Phe
 200 205 210

Arg Tyr Asn Gly Ser Leu Thr Thr Pro Pro Cys Tyr Gln Ser Val
 215 220 225

Leu Trp Thr Val Phe Tyr Arg Arg Ser Gln Ile Ser Met Glu Gln
 230 235 240

Leu Glu Lys Leu Gln Gly Thr Leu Phe Ser Thr Glu Glu Glu Pro
 245 250 255

Ser Lys Leu Leu Val Gln Asn Tyr Arg Ala Leu Gln Pro Leu Asn
 260 265 270

Gln Arg Met Val Phe Ala Ser Phe Ile Gln Ala Gly Ser Ser Tyr
 275 280 285

Thr Thr Gly Glu Met Leu Ser Leu Gly Val Gly Ile Leu Val Gly
 290 295 300

Cys Leu Cys Leu Leu Leu Ala Val Tyr Phe Ile Ala Arg Lys Ile
 305 310 315

Arg Lys Lys Arg Leu Glu Asn Arg Lys Ser Val Val Phe Thr Ser
 320 325 330

Ala Gln Ala Thr Thr Glu Ala
 335

<210> SEQ ID NO 75
 <211> LENGTH: 1743
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 75

tgccgctgcc gccgctgctg ctgttctctc tggcggcgcc tggggacgg	50
gcagttccct gtgtctctgg tggtttgcct aaacctgcaa acatcacctt	100
cttatccatc aacatgaaga atgtcctaca atggactcca ccagagggtc	150
ttcaaggagt taaagttact tacactgtgc agtatttcat cacaaattgg	200
cccaccagag gtggcactga ctacagatga gaagtccatt tctgttgctc	250
tgacagctcc agagaagtgg aagagaaatc cagaagacct tcctgtttcc	300
atgcaacaaa tatactcaa tctgaagtat aacgtgtctg tgttgaatac	350
taaatcaaac agaactgggt cccagtgtgt gaccaaccac acgctgggtg	400
tcacctggct ggagccgaac actctttact gogtacacgt ggagtccttc	450
gtcccaggcg cccctcgccg tgctcagcct totgagaagc agtgtgccag	500
gactttgaaa gatcaatcat cagagttcaa ggctaaaaatc atcttctggt	550
atgttttgcc catatctatt accgtgtttc ttttttctgt gatgggctat	600
tccatctacc gatatatcca cgttgcaaaa gagaacacc cagcaaattt	650
gattttgatt tatggaaatg aatttgacaa aagattcttt gtgctgctg	700

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aaaaaatcgt gattaacttt atcaccctca atatctcggg tgattctaaa      750
atttctcatc aggatatgag ttacttgga aaaagcagtg atgtatccag      800
ccttaatgat cctcagccca gcgggaacct gagggcccct caggaggaag      850
aggaggtgaa acatttaggg tatgcttcgc atttgatgga aattttttgt      900
gactctgaag aaaacacgga aggtacttct ctcaccagc aagagtcct      950
cagcagaaca atacccccgg ataaaacagt cattgaatat gaatatgat     1000
tcagaaccac tgacatttgt gcggggcctg aagagcagga gctcagtttg     1050
caggaggagg tgtccacaca aggaacatta ttggagtcgc aggcagcgtt     1100
ggcagtcctg ggcccgcaa cgttacagta ctcatacacc cctcagctcc     1150
aagacttaga cccctggcg caggagcaca cagactcggg ggagggggcg     1200
gaggaagagc catcgacgac cctggtcgc tgggatcccc aaactggcag     1250
gctgtgtatt ccttcgctgt ccagcttcga ccaggattca gagggctgcg     1300
agccttctga ggggatggg ctgggagagg aggtcttct atctagactc     1350
tatgaggagc cggctccaga caggccacca ggagaaaatg aaacctatct     1400
catgcaattc atggaggaat gggggttata tgtgcagatg gaaaactgat     1450
gccaacactt cttttgcct ttgtttcct gtgcaacaa gtgagtcacc     1500
cctttgatcc cagccataaa gtacctggga tgaagaagt tttttccagt     1550
ttgtcagtg ctgtgagaat tacttatttc ttttctctat tctcatagca     1600
cgtgtgtgat tggttcatgc atgtaggctc ctaacaatg atggggggcc     1650
tctggagtc ccgggctggc cggttgttct atgcagagaa agcagtcaat     1700
aaatgtttgc cagactgggt gcagaattta ttcaggtggg tgt          1743
    
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<210> SEQ ID NO 76
<211> LENGTH: 442
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien
    
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<400> SEQUENCE: 76

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Met Ser Tyr Asn Gly Leu His Gln Arg Val Phe Lys Glu Leu Lys
 1             5             10            15
Leu Leu Thr Leu Cys Ser Ile Ser Ser Gln Ile Gly Pro Pro Glu
                20            25            30
Val Ala Leu Thr Thr Asp Glu Lys Ser Ile Ser Val Val Leu Thr
                35            40            45
Ala Pro Glu Lys Trp Lys Arg Asn Pro Glu Asp Leu Pro Val Ser
                50            55            60
Met Gln Gln Ile Tyr Ser Asn Leu Lys Tyr Asn Val Ser Val Leu
                65            70            75
Asn Thr Lys Ser Asn Arg Thr Trp Ser Gln Cys Val Thr Asn His
                80            85            90
Thr Leu Val Leu Thr Trp Leu Glu Pro Asn Thr Leu Tyr Cys Val
                95            100           105
His Val Glu Ser Phe Val Pro Gly Pro Pro Arg Arg Ala Gln Pro
                110           115           120
Ser Glu Lys Gln Cys Ala Arg Thr Leu Lys Asp Gln Ser Ser Glu
                125           130           135
    
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Phe Lys Ala Lys Ile Ile Phe Trp Tyr Val Leu Pro Ile Ser Ile
 140 145 150

Thr Val Phe Leu Phe Ser Val Met Gly Tyr Ser Ile Tyr Arg Tyr
 155 160 165

Ile His Val Gly Lys Glu Lys His Pro Ala Asn Leu Ile Leu Ile
 170 175 180

Tyr Gly Asn Glu Phe Asp Lys Arg Phe Phe Val Pro Ala Glu Lys
 185 190 195

Ile Val Ile Asn Phe Ile Thr Leu Asn Ile Ser Asp Asp Ser Lys
 200 205 210

Ile Ser His Gln Asp Met Ser Leu Leu Gly Lys Ser Ser Asp Val
 215 220 225

Ser Ser Leu Asn Asp Pro Gln Pro Ser Gly Asn Leu Arg Pro Pro
 230 235 240

Gln Glu Glu Glu Glu Val Lys His Leu Gly Tyr Ala Ser His Leu
 245 250 255

Met Glu Ile Phe Cys Asp Ser Glu Glu Asn Thr Glu Gly Thr Ser
 260 265 270

Leu Thr Gln Gln Glu Ser Leu Ser Arg Thr Ile Pro Pro Asp Lys
 275 280 285

Thr Val Ile Glu Tyr Glu Tyr Asp Val Arg Thr Thr Asp Ile Cys
 290 295 300

Ala Gly Pro Glu Glu Gln Glu Leu Ser Leu Gln Glu Glu Val Ser
 305 310 315

Thr Gln Gly Thr Leu Leu Glu Ser Gln Ala Ala Leu Ala Val Leu
 320 325 330

Gly Pro Gln Thr Leu Gln Tyr Ser Tyr Thr Pro Gln Leu Gln Asp
 335 340 345

Leu Asp Pro Leu Ala Gln Glu His Thr Asp Ser Glu Glu Gly Pro
 350 355 360

Glu Glu Glu Pro Ser Thr Thr Leu Val Asp Trp Asp Pro Gln Thr
 365 370 375

Gly Arg Leu Cys Ile Pro Ser Leu Ser Ser Phe Asp Gln Asp Ser
 380 385 390

Glu Gly Cys Glu Pro Ser Glu Gly Asp Gly Leu Gly Glu Glu Gly
 395 400 405

Leu Leu Ser Arg Leu Tyr Glu Glu Pro Ala Pro Asp Arg Pro Pro
 410 415 420

Gly Glu Asn Glu Thr Tyr Leu Met Gln Phe Met Glu Glu Trp Gly
 425 430 435

Leu Tyr Val Gln Met Glu Asn
 440

<210> SEQ ID NO 77
 <211> LENGTH: 1636
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 77

gaggagcggg ccgaggactc cagcgtgccc aggtctggca tcctgcactt 50
 gctgcctct gacacctggg aagatggcgg gccctggac cttcacctt 100

-continued

ctctgtgggtt tgctggcagc caccttgatc caagccaccc tcagtccac	150
tgcaattctc atcctcggcc caaaagtcac caaagaaaag ctgacacagg	200
agctgaagga ccacaacgcc accagcatcc tgcagcagct gccgctgctc	250
agtgccatgc gggaaaagcc agccggaggc atccctgtgc tgggcagcct	300
ggtgaacacc gtcctgaagc acatcatctg gctgaaggtc atcacagcta	350
acatcctcca gctgcagggtg aagccctcgg ccaatgacca ggagctgcta	400
gtcaagatcc ccctggacat ggtggctgga ttcaaacacgc ccctgggtcaa	450
gaccatcgtg gagtccaca tgacgactga ggccaagcc accatccgca	500
tggacaccag tgcaagtggc cccaccggcc tggtoctcag tgactgtgcc	550
accagccatg ggagcctgcg catccaactg ctgtataagc tctccttctc	600
ggtgaacgcc ttagctaagc aggtcatgaa cctcctagtg ccatccctgc	650
ccaatctagt gaaaaaccag ctgtgtcccg tgatcgaggc ttccttcaat	700
ggcatgtatg cagacctcct gcagctgggtg aaggtgccca tttccctcag	750
cattgaccgt ctggagtttg accttctgta tctgcccac aagggtgaca	800
ccattcagct ctacctgggg gccaaattgt tggactcaca gggaaagggtg	850
accaagtgtg tcaataactc tgcagcttcc ctgacaatgc ccaccctgga	900
caacatcccg ttcagcctca tctgtagtcg ggacgtgggtg aaagctgcag	950
tggctgctgt gctctctcca gaagaattca tggtoctggt ggactctgtg	1000
cttctctgaga gtgccatcg gctgaagtca agcatcgggc tgatcaatga	1050
aaaggctgca gataagctgg gatctaccga gatcgtgaag atcctaactc	1100
aggacactcc cgagtttttt atagaccaag gccatgcaa ggtggcccaa	1150
ctgatcgtgc tggaaagtgtt tccctccagt gaagccctcc gccotttgtt	1200
caccctgggc atcgaagcca gctcggaaag tcagttttac accaaagggtg	1250
accaacttat actcaacttg aataacatca gctctgatcg gatccagctg	1300
atgaactctg ggattggctg gttccaacct gatgttctga aaaacatcat	1350
cactgagatc atcactcca tctctgtgcc gaaccagaat ggcaaatata	1400
gatctggggt cccagtgta ttggtgaagg ccttgggatt cgaggcagct	1450
gagtcctcac tgaccaagga tgccttctgt cttactccag cctccttctg	1500
gaaaccagc tctcctgtct cccagtgaa acttggatgg cagccatcag	1550
ggaaggctgg gtcccagctg ggagtatggg tgtgagctct atagaccatc	1600
cctctctgca atcaataaac acttgctctg gaaaaa	1636

<210> SEQ ID NO 78

<211> LENGTH: 484

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 78

Met Ala Gly Pro Trp Thr Phe Thr Leu Leu Cys Gly Leu Leu Ala
 1 5 10 15

Ala Thr Leu Ile Gln Ala Thr Leu Ser Pro Thr Ala Val Leu Ile
 20 25 30

-continued

Leu	Gly	Pro	Lys	Val	Ile	Lys	Glu	Lys	Leu	Thr	Gln	Glu	Leu	Lys	35	40	45
Asp	His	Asn	Ala	Thr	Ser	Ile	Leu	Gln	Gln	Leu	Pro	Leu	Leu	Ser	50	55	60
Ala	Met	Arg	Glu	Lys	Pro	Ala	Gly	Gly	Ile	Pro	Val	Leu	Gly	Ser	65	70	75
Leu	Val	Asn	Thr	Val	Leu	Lys	His	Ile	Ile	Trp	Leu	Lys	Val	Ile	80	85	90
Thr	Ala	Asn	Ile	Leu	Gln	Leu	Gln	Val	Lys	Pro	Ser	Ala	Asn	Asp	95	100	105
Gln	Glu	Leu	Leu	Val	Lys	Ile	Pro	Leu	Asp	Met	Val	Ala	Gly	Phe	110	115	120
Asn	Thr	Pro	Leu	Val	Lys	Thr	Ile	Val	Glu	Phe	His	Met	Thr	Thr	125	130	135
Glu	Ala	Gln	Ala	Thr	Ile	Arg	Met	Asp	Thr	Ser	Ala	Ser	Gly	Pro	140	145	150
Thr	Arg	Leu	Val	Leu	Ser	Asp	Cys	Ala	Thr	Ser	His	Gly	Ser	Leu	155	160	165
Arg	Ile	Gln	Leu	Leu	Tyr	Lys	Leu	Ser	Phe	Leu	Val	Asn	Ala	Leu	170	175	180
Ala	Lys	Gln	Val	Met	Asn	Leu	Leu	Val	Pro	Ser	Leu	Pro	Asn	Leu	185	190	195
Val	Lys	Asn	Gln	Leu	Cys	Pro	Val	Ile	Glu	Ala	Ser	Phe	Asn	Gly	200	205	210
Met	Tyr	Ala	Asp	Leu	Leu	Gln	Leu	Val	Lys	Val	Pro	Ile	Ser	Leu	215	220	225
Ser	Ile	Asp	Arg	Leu	Glu	Phe	Asp	Leu	Leu	Tyr	Pro	Ala	Ile	Lys	230	235	240
Gly	Asp	Thr	Ile	Gln	Leu	Tyr	Leu	Gly	Ala	Lys	Leu	Leu	Asp	Ser	245	250	255
Gln	Gly	Lys	Val	Thr	Lys	Trp	Phe	Asn	Asn	Ser	Ala	Ala	Ser	Leu	260	265	270
Thr	Met	Pro	Thr	Leu	Asp	Asn	Ile	Pro	Phe	Ser	Leu	Ile	Val	Ser	275	280	285
Gln	Asp	Val	Val	Lys	Ala	Ala	Val	Ala	Ala	Val	Leu	Ser	Pro	Glu	290	295	300
Glu	Phe	Met	Val	Leu	Leu	Asp	Ser	Val	Leu	Pro	Glu	Ser	Ala	His	305	310	315
Arg	Leu	Lys	Ser	Ser	Ile	Gly	Leu	Ile	Asn	Glu	Lys	Ala	Ala	Asp	320	325	330
Lys	Leu	Gly	Ser	Thr	Gln	Ile	Val	Lys	Ile	Leu	Thr	Gln	Asp	Thr	335	340	345
Pro	Glu	Phe	Phe	Ile	Asp	Gln	Gly	His	Ala	Lys	Val	Ala	Gln	Leu	350	355	360
Ile	Val	Leu	Glu	Val	Phe	Pro	Ser	Ser	Glu	Ala	Leu	Arg	Pro	Leu	365	370	375
Phe	Thr	Leu	Gly	Ile	Glu	Ala	Ser	Ser	Glu	Ala	Gln	Phe	Tyr	Thr	380	385	390
Lys	Gly	Asp	Gln	Leu	Ile	Leu	Asn	Leu	Asn	Asn	Ile	Ser	Ser	Asp	395	400	405
Arg	Ile	Gln	Leu	Met	Asn	Ser	Gly	Ile	Gly	Trp	Phe	Gln	Pro	Asp			

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	410		415		420
Val Leu Lys Asn	Ile Ile Thr Glu Ile	Ile His Ser Ile Leu	Leu		
	425	430	435		
Pro Asn Gln Asn	Gly Lys Leu Arg Ser	Gly Val Pro Val Ser	Leu		
	440	445	450		
Val Lys Ala Leu	Gly Phe Glu Ala Ala	Glu Ser Ser Leu Thr	Lys		
	455	460	465		
Asp Ala Leu Val	Leu Thr Pro Ala Ser	Leu Trp Lys Pro Ser	Ser		
	470	475	480		
Pro Val Ser Gln					

<210> SEQ ID NO 79
 <211> LENGTH: 1475
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien
 <400> SEQUENCE: 79

```

gagagaagtc agcctggcag agagactctg aatgagggga ttagaggtgt      50
tcaaggagca agagcttcag cctgaagaca agggagcagt ccctgaagac      100
gcttctactg agaggtctgc catggcctct cttggcctcc aacttgtggg      150
ctacatccta ggccttcttg ggcttttggg cacactgggt gccatgctgc      200
tccccagctg gaaaacaagt tcttatgtcg gtgccagcat tgtgacagca      250
gttggtctct ccaagggcct ctggatggaa tgtgccacac acagcacagg      300
catcaccagc tgtgacatct atagaccctt totgggctcg cccgctgaca      350
tccaggctgc ccaggccatg atggtgacat ccagtgcaat ctctccctg      400
gcctgcatta tctctgtggt gggcatgaga tgcacagtct tctgccagga      450
atcccagagc aaagacagag tggcggtagc aggtggagtc tttttcatcc      500
ttggaggcct cctgggattc attcctgttg cctggaatct tcatgggatc      550
ctacgggact tctactcacc actggtgcct gacagcatga aatttgagat      600
tggagaggct ctttacttgg gcattatttc ttccctgttc tccctgatag      650
ctggaatcat cctctgcttt tctgtctcat cccagagaaa tcgctccaac      700
tactacgatg cctaccaagc ccaacctctt gccacaagga gctctccaag      750
gcctgggtcaa cctcccaaag tcaagagtga gttcaattcc tacagcctga      800
cagggtatgt gtgaagaacc aggggccaga gctggggggg ggctgggtct      850
gtgaaaaaca gtggacagca ccccaggggc cacaggtgag ggacactacc      900
actggtactg gtcagaaggt gctgctgagg atagactgac tttggccatt      950
ggattgagca aaggcagaaa tgggggctag tgtaacagca tgcaggttga     1000
attgccaaag atgctcgcca tgccagcctt tctgttttcc tcaccttgct     1050
gtccccctcg cctaagtccc caacctcaa cttgaaacct cattccctta     1100
agccaggact cagaggatcc ctttgccctc tggtttacct gggactocat     1150
ccccaaacct actaatcaca tcccactgac tgaccctctg tgatcaaaga     1200
ccctctctct ggctgagggt ggctcttagc tcattgctgg ggatgggaag     1250
gagaagcagt ggcttttgtg ggcattgctc taacctactt ctcaagcttc     1300
    
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cctccaaaga aactgattgg ccttgaacc tccatcccac tcttgttatg      1350
actccacagt gtccagacta atttgtgcat gaactgaaat aaaaccatcc      1400
tacggtatcc agggaacaga aagcaggatg caggatggga ggacaggaag      1450
gcagcctggg acatttaaaa aaata                                     1475

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<210> SEQ ID NO 80
<211> LENGTH: 230
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien

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<400> SEQUENCE: 80

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```

Met Ala Ser Leu Gly Leu Gln Leu Val Gly Tyr Ile Leu Gly Leu
 1          5          10         15
Leu Gly Leu Leu Gly Thr Leu Val Ala Met Leu Leu Pro Ser Trp
 20         25         30
Lys Thr Ser Ser Tyr Val Gly Ala Ser Ile Val Thr Ala Val Gly
 35         40         45
Phe Ser Lys Gly Leu Trp Met Glu Cys Ala Thr His Ser Thr Gly
 50         55         60
Ile Thr Gln Cys Asp Ile Tyr Ser Thr Leu Leu Gly Leu Pro Ala
 65         70         75
Asp Ile Gln Ala Ala Gln Ala Met Met Val Thr Ser Ser Ala Ile
 80         85         90
Ser Ser Leu Ala Cys Ile Ile Ser Val Val Gly Met Arg Cys Thr
 95        100       105
Val Phe Cys Gln Glu Ser Arg Ala Lys Asp Arg Val Ala Val Ala
110       115       120
Gly Gly Val Phe Phe Ile Leu Gly Gly Leu Leu Gly Phe Ile Pro
125       130       135
Val Ala Trp Asn Leu His Gly Ile Leu Arg Asp Phe Tyr Ser Pro
140       145       150
Leu Val Pro Asp Ser Met Lys Phe Glu Ile Gly Glu Ala Leu Tyr
155       160       165
Leu Gly Ile Ile Ser Ser Leu Phe Ser Leu Ile Ala Gly Ile Ile
170       175       180
Leu Cys Phe Ser Cys Ser Ser Gln Arg Asn Arg Ser Asn Tyr Tyr
185       190       195
Asp Ala Tyr Gln Ala Gln Pro Leu Ala Thr Arg Ser Ser Pro Arg
200       205       210
Pro Gly Gln Pro Pro Lys Val Lys Ser Glu Phe Asn Ser Tyr Ser
215       220       225
Leu Thr Gly Tyr Val
230

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<210> SEQ ID NO 81
<211> LENGTH: 1732
<212> TYPE: DNA
<213> ORGANISM: Homo Sapien

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<400> SEQUENCE: 81

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```

cccacgcgctc cgcgcctctc cttctgtctg gaccttcctt cgtctctcca      50
tctctccctc ctttcccgc gttctctttc cacctttctc ttcttccac      100

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cttagacctc ccttcctgcc ctcccttccct gccaccgct gcttcctggc	150
ccttctccga ccccgctcta gcagcagacc tcctggggtc tgtgggtga	200
tctgtggccc ctgtgctcc gtgtcccttt cgtctccctt cctcccgact	250
ccgctcccgg accagcggcc tgaccctggg gaaaggatgg ttcccgaggt	300
gagggtcctc tcctccttgc tgggactcgc gctgctctgg ttccccctgg	350
actcccacgc tcgagcccgc ccagacatgt tctgcctttt ccatgggaa	400
agatactccc ccggcgagag ctggcaccct tacttgagc cacaaggcct	450
gatgtactgc ctgctctgta cctgctcaga gggcgcccat gtgagtgtt	500
accgctcca ctgtccgctt gtccactgcc cccagcctgt gacggagcca	550
cagcaatgct gtcccaagtg tgtggaacct cacactcctt ctggactccg	600
ggccccacca aagtcctgcc agcacaacgg gaccatgtac caacacggag	650
agatctttag tgcccatgag ctgttcccct cccgctgcc caaccagtgt	700
gtcctctgca gctgcacaga gggccagatc tactgcgccc tcacaactg	750
ccccgaacca ggctgcccag caccctccc actgccagac tcctgctgcc	800
aagcctgcaa agatgaggca agtgagcaat cggatgaaga ggacagtgtg	850
cagtcgctcc atgggggtgag acatcctcag gatccatgtt ccagtgatgc	900
tgggagaaa agaggcccgg gcaccccagc cccactggc ctcagcggcc	950
ctctgagctt catccctcgc cacttcagac ccaagggagc aggcagcaca	1000
actgtcaaga tcgtcctgaa ggagaacat aagaagcct gtgtgcatgg	1050
cgggaagacg tactcccacg gggaggtgtg gcacccggcc ttccgtgcct	1100
tcggcccctt gccctgcac ctatgcacct gtgaggatgg ccgccaggac	1150
tgccagcgtg tgacctgtcc caccgagtac cctgcccgtc accccgagaa	1200
agtgctgctgg aagtgtctga agatttgccc agaggacaaa gcagaccctg	1250
gccacagtga gatcagttct accaggtgtc ccaaggcacc gggccgggtc	1300
ctctccaca catcggatc cccaagccca gacaacctgc gtcgctttgc	1350
cctggaacac gaggcctcgg acttggtgga gatctacctc tggaagctgg	1400
taaaagatga ggaaactgag gctcagagag gtgaagtacc tggccaagg	1450
ccacacagcc agaactctcc acttgactca gatcaagaaa gtcaggaagc	1500
aagacttcca gaaagaggca cagcacttcc gactgctcgc tggccccac	1550
gaaggtcact ggaacgtctt cctagcccag accctggagc tgaaggtcac	1600
ggccagtcca gacaaagtga ccaagacata acaaagacct aacagttgca	1650
gatatgagct gtataattgt tgttattata tattaataaa taagaagttg	1700
cattaccctc aaaaaaaaa aaaaaaaaa aa	1732

<210> SEQ ID NO 82
 <211> LENGTH: 451
 <212> TYPE: PRT
 <213> ORGANISM: Homo Sapien
 <400> SEQUENCE: 82

Met Val Pro Glu Val Arg Val Leu Ser Ser Leu Leu Gly Leu Ala
 1 5 10 15

-continued

Leu Leu Trp Phe Pro Leu Asp Ser His Ala Arg Ala Arg Pro Asp
 20 25 30
 Met Phe Cys Leu Phe His Gly Lys Arg Tyr Ser Pro Gly Glu Ser
 35 40 45
 Trp His Pro Tyr Leu Glu Pro Gln Gly Leu Met Tyr Cys Leu Arg
 50 55 60
 Cys Thr Cys Ser Glu Gly Ala His Val Ser Cys Tyr Arg Leu His
 65 70 75
 Cys Pro Pro Val His Cys Pro Gln Pro Val Thr Glu Pro Gln Gln
 80 85 90
 Cys Cys Pro Lys Cys Val Glu Pro His Thr Pro Ser Gly Leu Arg
 95 100 105
 Ala Pro Pro Lys Ser Cys Gln His Asn Gly Thr Met Tyr Gln His
 110 115 120
 Gly Glu Ile Phe Ser Ala His Glu Leu Phe Pro Ser Arg Leu Pro
 125 130 135
 Asn Gln Cys Val Leu Cys Ser Cys Thr Glu Gly Gln Ile Tyr Cys
 140 145 150
 Gly Leu Thr Thr Cys Pro Glu Pro Gly Cys Pro Ala Pro Leu Pro
 155 160 165
 Leu Pro Asp Ser Cys Cys Gln Ala Cys Lys Asp Glu Ala Ser Glu
 170 175 180
 Gln Ser Asp Glu Glu Asp Ser Val Gln Ser Leu His Gly Val Arg
 185 190 195
 His Pro Gln Asp Pro Cys Ser Ser Asp Ala Gly Arg Lys Arg Gly
 200 205 210
 Pro Gly Thr Pro Ala Pro Thr Gly Leu Ser Ala Pro Leu Ser Phe
 215 220 225
 Ile Pro Arg His Phe Arg Pro Lys Gly Ala Gly Ser Thr Thr Val
 230 235 240
 Lys Ile Val Leu Lys Glu Lys His Lys Lys Ala Cys Val His Gly
 245 250 255
 Gly Lys Thr Tyr Ser His Gly Glu Val Trp His Pro Ala Phe Arg
 260 265 270
 Ala Phe Gly Pro Leu Pro Cys Ile Leu Cys Thr Cys Glu Asp Gly
 275 280 285
 Arg Gln Asp Cys Gln Arg Val Thr Cys Pro Thr Glu Tyr Pro Cys
 290 295 300
 Arg His Pro Glu Lys Val Ala Gly Lys Cys Cys Lys Ile Cys Pro
 305 310 315
 Glu Asp Lys Ala Asp Pro Gly His Ser Glu Ile Ser Ser Thr Arg
 320 325 330
 Cys Pro Lys Ala Pro Gly Arg Val Leu Val His Thr Ser Val Ser
 335 340 345
 Pro Ser Pro Asp Asn Leu Arg Arg Phe Ala Leu Glu His Glu Ala
 350 355 360
 Ser Asp Leu Val Glu Ile Tyr Leu Trp Lys Leu Val Lys Asp Glu
 365 370 375
 Glu Thr Glu Ala Gln Arg Gly Glu Val Pro Gly Pro Arg Pro His
 380 385 390

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Ser	Gln	Asn	Leu	Pro	Leu	Asp	Ser	Asp	Gln	Glu	Ser	Gln	Glu	Ala
				395					400					405
Arg	Leu	Pro	Glu	Arg	Gly	Thr	Ala	Leu	Pro	Thr	Ala	Arg	Trp	Pro
				410					415					420
Pro	Arg	Arg	Ser	Leu	Glu	Arg	Leu	Pro	Ser	Pro	Asp	Pro	Gly	Ala
				425					430					435
Glu	Gly	His	Gly	Gln	Ser	Arg	Gln	Ser	Asp	Gln	Asp	Ile	Thr	Lys
				440					445					450

Thr

<210> SEQ ID NO 83

<211> LENGTH: 2052

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 83

```

gacagctgtg tctcgatgga gtagactctc agaacagcgc agtttgcct      50
ccgctcacgc agagcctctc cgtggcttcc gcaccttgag cattaggcca      100
gttctcctct tctctctaata ccatcctgca cctctcctgt catccgtttc      150
catgccgtga ggtccattca cagaacacat ccatggctct catgctcagt      200
ttggttctga gtctcctcaa gctgggatca gggcagtggc aggtgtttgg      250
gccagacaag cctgtccagg ccttggtggg ggaggacgca gcattctcct      300
gtttcctgtc tcctaagacc aatgcagagg ccatggaagt gcggttcttc      350
aggggccagt tctctagcgt ggtccacctc tacagggacg ggaaggacca      400
gccatttatg cagatgccac agtatcaagg caggacaaaa ctggtgaagg      450
attctattgc ggaggggcgc atctctctga ggctgaaaaa cttactgtg      500
ttggatgctg gcctctatgg gtgcaggatt agttcccagt cttactacca      550
gaagcccatc tgggagctac aggtgtcagc actgggctca gttcctctca      600
tttccatcac gggatatggt gatagagaca tccagctact ctgtcagtcc      650
tcgggctggt tccccggcc cacagcgaag tggaaaggtc cacaaggaca      700
ggatttgtcc acagactcca ggacaacag agacatgcat ggctgtttg      750
atgtggagat ctctctgacc gtccaagaga acgcccggag catatcctgt      800
tccatgcggc atgctcatct gagccgagag gtggaatcca ggttacagat      850
aggagatacc tttttcgagc ctatatcgtg gcacctggct accaaagtac      900
tggaataact ctgctgtggc ctattttttg gcattgttgg actgaagatt      950
ttcttctcca aattccagtg gaaaatccag gcggaactgg actggagaag      1000
aaagcacgga caggcagaat tgagagacgc ccgaaaacac gcagtggagg      1050
tgactctgga tccagagacg gctcaccoga agctctgcgt ttctgatctg      1100
aaaactgtaa cccatagaaa agctccccag gaggtgcctc actctgagaa      1150
gagatttaca aggaagagtg tggtgcttcc tcagagtttc caagcagga      1200
aacattactg ggaggtggac ggaggacaca ataaaagggt gcgogtggga      1250
gtgtgccggg atgatgtgga caggaggaag gactacgtga ctttctctcc      1300
cgatcatggg tactgggtcc tcagactgaa tggagaacat ttgtatttca      1350

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cattaaatcc ccgttttatc agcgtcttcc ccaggacccc acctacaaaa      1400
ataggggtct tcctggacta tgagtgtggg accatctcct tcttcaacat      1450
aatgaccagc tccttatttt ataccctgac atgtcggttt gaaggcttat      1500
tgaggcccta cattgagtat ccgtcctata atgagcaaaa tggaactccc      1550
atagtcatct gcccagtcac ccaggaatca gagaaagagg cctcttggca      1600
aagggcctct gcaatcccag agacaagcaa cagtgagtcc tcctcacag      1650
caaccacgcc cttcctcccc aggggtgaaa tgtaggatga atcacatccc      1700
acattcttct ttagggatat taaggtctct ctcccagatc caaagtcccg      1750
cagcagccgg ccaaggtggc ttccagatga agggggactg gcctgtccac      1800
atgggagtca ggtgtcatgg ctgccctgag ctgggaggga agaaggctga      1850
cattacattt agtttctct cactccatct ggctaagtga tcttgaata      1900
ccacctca ggtgaagaac cgtcaggaat toccatctca caggctgtgg      1950
tgtagattaa gtagacaagg aatgtgaata atgcttagat cttattgatg      2000
acagagtgtg tcctaattgt ttgttcatta tattacactt tcagtaaaaa      2050
aa

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<210> SEQ ID NO 84

<211> LENGTH: 500

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 84

```

Met Ala Leu Met Leu Ser Leu Val Leu Ser Leu Leu Lys Leu Gly
 1             5             10             15
Ser Gly Gln Trp Gln Val Phe Gly Pro Asp Lys Pro Val Gln Ala
                20             25             30
Leu Val Gly Glu Asp Ala Ala Phe Ser Cys Phe Leu Ser Pro Lys
                35             40             45
Thr Asn Ala Glu Ala Met Glu Val Arg Phe Phe Arg Gly Gln Phe
                50             55             60
Ser Ser Val Val His Leu Tyr Arg Asp Gly Lys Asp Gln Pro Phe
                65             70             75
Met Gln Met Pro Gln Tyr Gln Gly Arg Thr Lys Leu Val Lys Asp
                80             85             90
Ser Ile Ala Glu Gly Arg Ile Ser Leu Arg Leu Glu Asn Ile Thr
                95             100            105
Val Leu Asp Ala Gly Leu Tyr Gly Cys Arg Ile Ser Ser Gln Ser
                110            115            120
Tyr Tyr Gln Lys Ala Ile Trp Glu Leu Gln Val Ser Ala Leu Gly
                125            130            135
Ser Val Pro Leu Ile Ser Ile Thr Gly Tyr Val Asp Arg Asp Ile
                140            145            150
Gln Leu Leu Cys Gln Ser Ser Gly Trp Phe Pro Arg Pro Thr Ala
                155            160            165
Lys Trp Lys Gly Pro Gln Gly Gln Asp Leu Ser Thr Asp Ser Arg
                170            175            180
Thr Asn Arg Asp Met His Gly Leu Phe Asp Val Glu Ile Ser Leu
                185            190            195

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Thr Val Gln Glu Asn Ala Gly Ser Ile Ser Cys Ser Met Arg His
 200 205 210

Ala His Leu Ser Arg Glu Val Glu Ser Arg Val Gln Ile Gly Asp
 215 220 225

Thr Phe Phe Glu Pro Ile Ser Trp His Leu Ala Thr Lys Val Leu
 230 235 240

Gly Ile Leu Cys Cys Gly Leu Phe Phe Gly Ile Val Gly Leu Lys
 245 250 255

Ile Phe Phe Ser Lys Phe Gln Trp Lys Ile Gln Ala Glu Leu Asp
 260 265 270

Trp Arg Arg Lys His Gly Gln Ala Glu Leu Arg Asp Ala Arg Lys
 275 280 285

His Ala Val Glu Val Thr Leu Asp Pro Glu Thr Ala His Pro Lys
 290 295 300

Leu Cys Val Ser Asp Leu Lys Thr Val Thr His Arg Lys Ala Pro
 305 310 315

Gln Glu Val Pro His Ser Glu Lys Arg Phe Thr Arg Lys Ser Val
 320 325 330

Val Ala Ser Gln Ser Phe Gln Ala Gly Lys His Tyr Trp Glu Val
 335 340 345

Asp Gly Gly His Asn Lys Arg Trp Arg Val Gly Val Cys Arg Asp
 350 355 360

Asp Val Asp Arg Arg Lys Glu Tyr Val Thr Leu Ser Pro Asp His
 365 370 375

Gly Tyr Trp Val Leu Arg Leu Asn Gly Glu His Leu Tyr Phe Thr
 380 385 390

Leu Asn Pro Arg Phe Ile Ser Val Phe Pro Arg Thr Pro Pro Thr
 395 400 405

Lys Ile Gly Val Phe Leu Asp Tyr Glu Cys Gly Thr Ile Ser Phe
 410 415 420

Phe Asn Ile Asn Asp Gln Ser Leu Ile Tyr Thr Leu Thr Cys Arg
 425 430 435

Phe Glu Gly Leu Leu Arg Pro Tyr Ile Glu Tyr Pro Ser Tyr Asn
 440 445 450

Glu Gln Asn Gly Thr Pro Ile Val Ile Cys Pro Val Thr Gln Glu
 455 460 465

Ser Glu Lys Glu Ala Ser Trp Gln Arg Ala Ser Ala Ile Pro Glu
 470 475 480

Thr Ser Asn Ser Glu Ser Ser Ser Gln Ala Thr Thr Pro Phe Leu
 485 490 495

Pro Arg Gly Glu Met
 500

<210> SEQ ID NO 85
 <211> LENGTH: 1665
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 85

aacagacggtt ccctcgcggc cctggcacct ctaaccccag acatgctgct 50
 gctgctgctg ccctgctct gggggagga gagggcgaa ggacagacaa 100

-continued

gtaaaactgct gacgatgcag agttccgtga cgggtgcagga aggcctgtgt	150
gtccatgtgc cctgctcctt ctectacccc tcgcatggct ggatttacc	200
tggcccaagta gttcatggct actggttccg ggaaggggcc aatacagacc	250
aggatgctcc agtggccaca aacaaccag ctcgggcagt gtgggaggag	300
actcgggacc gattccacct ccttggggac ccacatacca agaattgcac	350
cctgagcatc agagatgcca gaagaagtga tgcggggaga tacttctttc	400
gtatggagaa aggaagtata aaatggaatt ataaacatca cgggtctct	450
gtgaatgtga cagccttgac ccacaggccc aacatcctca tcccaggcac	500
cctggagtcc ggctgcccc agaatctgac ctgctctgtg ccttgggcct	550
gtgagcaggg gacacccct atgatctcct ggataggac ctcogtctcc	600
cccctggacc cctccaccac ccgctcctcg gtgctcacc tcaccccaca	650
gcccaggac catggcacca gcctcacctg tcaggtgacc ttccctggg	700
ccagcgtgac cacgaacaag accgtccatc tcaactgtc ctacccgct	750
cagaacttga ccatgactgt ctccaagga gacggcacag tatccacagt	800
cttgggaaat ggctcatctc tgtactccc agagggccag tctctgccc	850
tggctctgtc agttgatgca gttgacagca atccccctgc caggctgagc	900
ctgagctgga gaggcctgac cctgtgcccc tcacagcct caaacccggg	950
ggctgtggag ctgccttggg tgcacctgag ggatgcagct gaattcacct	1000
gcagagctca gaacctctc ggctctcagc aggtctacct gaactctcc	1050
ctgcagagca aagccacatc aggagtact cagggggtgg tcgggggagc	1100
tggagccaca gccctggtct tcctgtcctt ctgcgtcatc ttogttgtag	1150
tgaggctctg caggaagaaa tcggcaaggc cagcagcggg cgtgggagat	1200
acgggcatag aggatgcaaa cgctgtcagg ggttcagcct ctcaggggcc	1250
cctgactgaa ccttgggcag aagacagtcc cccagaccag cctccccag	1300
cttctgcccc ctctcagtg ggggaaggag agctccagta tgcatcctc	1350
agcttcocaga tggatgaagc ttgggactcg cggggacagg aggccactga	1400
caccgagtac tcggagatca agatccacag atgagaaact gcagagactc	1450
accctgattg agggatcaca gcccctccag gcaagggaga agtcagaggc	1500
tgattcttgt agaattaaca gccctcaacg tgatgagcta tgataacct	1550
atgaattatg tcagagtgga aaagcacaca ggctttagag tcaaagtatc	1600
tcaaactgta atccacactg tgcctccct tttatTTTTT taactaaaag	1650
acagacaaat tccta	1665

<210> SEQ ID NO 86

<211> LENGTH: 463

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 86

Met Leu Leu Leu Leu Leu Pro Leu Leu Trp Gly Arg Glu Arg Ala
 1 5 10 15

Glu Gly Gln Thr Ser Lys Leu Leu Thr Met Gln Ser Ser Val Thr

-continued

															20	25	30
Val	Gln	Glu	Gly	Leu	Cys	Val	His	Val	Pro	Cys	Ser	Phe	Ser	Tyr			
				35					40					45			
Pro	Ser	His	Gly	Trp	Ile	Tyr	Pro	Gly	Pro	Val	Val	His	Gly	Tyr			
				50					55					60			
Trp	Phe	Arg	Glu	Gly	Ala	Asn	Thr	Asp	Gln	Asp	Ala	Pro	Val	Ala			
				65					70					75			
Thr	Asn	Asn	Pro	Ala	Arg	Ala	Val	Trp	Glu	Glu	Thr	Arg	Asp	Arg			
				80					85					90			
Phe	His	Leu	Leu	Gly	Asp	Pro	His	Thr	Lys	Asn	Cys	Thr	Leu	Ser			
				95					100					105			
Ile	Arg	Asp	Ala	Arg	Arg	Ser	Asp	Ala	Gly	Arg	Tyr	Phe	Phe	Arg			
				110					115					120			
Met	Glu	Lys	Gly	Ser	Ile	Lys	Trp	Asn	Tyr	Lys	His	His	Arg	Leu			
				125					130					135			
Ser	Val	Asn	Val	Thr	Ala	Leu	Thr	His	Arg	Pro	Asn	Ile	Leu	Ile			
				140					145					150			
Pro	Gly	Thr	Leu	Glu	Ser	Gly	Cys	Pro	Gln	Asn	Leu	Thr	Cys	Ser			
				155					160					165			
Val	Pro	Trp	Ala	Cys	Glu	Gln	Gly	Thr	Pro	Pro	Met	Ile	Ser	Trp			
				170					175					180			
Ile	Gly	Thr	Ser	Val	Ser	Pro	Leu	Asp	Pro	Ser	Thr	Thr	Arg	Ser			
				185					190					195			
Ser	Val	Leu	Thr	Leu	Ile	Pro	Gln	Pro	Gln	Asp	His	Gly	Thr	Ser			
				200					205					210			
Leu	Thr	Cys	Gln	Val	Thr	Phe	Pro	Gly	Ala	Ser	Val	Thr	Thr	Asn			
				215					220					225			
Lys	Thr	Val	His	Leu	Asn	Val	Ser	Tyr	Pro	Pro	Gln	Asn	Leu	Thr			
				230					235					240			
Met	Thr	Val	Phe	Gln	Gly	Asp	Gly	Thr	Val	Ser	Thr	Val	Leu	Gly			
				245					250					255			
Asn	Gly	Ser	Ser	Leu	Ser	Leu	Pro	Glu	Gly	Gln	Ser	Leu	Arg	Leu			
				260					265					270			
Val	Cys	Ala	Val	Asp	Ala	Val	Asp	Ser	Asn	Pro	Pro	Ala	Arg	Leu			
				275					280					285			
Ser	Leu	Ser	Trp	Arg	Gly	Leu	Thr	Leu	Cys	Pro	Ser	Gln	Pro	Ser			
				290					295					300			
Asn	Pro	Gly	Val	Leu	Glu	Leu	Pro	Trp	Val	His	Leu	Arg	Asp	Ala			
				305					310					315			
Ala	Glu	Phe	Thr	Cys	Arg	Ala	Gln	Asn	Pro	Leu	Gly	Ser	Gln	Gln			
				320					325					330			
Val	Tyr	Leu	Asn	Val	Ser	Leu	Gln	Ser	Lys	Ala	Thr	Ser	Gly	Val			
				335					340					345			
Thr	Gln	Gly	Val	Val	Gly	Gly	Ala	Gly	Ala	Thr	Ala	Leu	Val	Phe			
				350					355					360			
Leu	Ser	Phe	Cys	Val	Ile	Phe	Val	Val	Val	Arg	Ser	Cys	Arg	Lys			
				365					370					375			
Lys	Ser	Ala	Arg	Pro	Ala	Ala	Gly	Val	Gly	Asp	Thr	Gly	Ile	Glu			
				380					385					390			
Asp	Ala	Asn	Ala	Val	Arg	Gly	Ser	Ala	Ser	Gln	Gly	Pro	Leu	Thr			
				395					400					405			

-continued

Glu Pro Trp Ala Glu Asp Ser Pro Pro Asp Gln Pro Pro Pro Ala
 410 415 420

Ser Ala Arg Ser Ser Val Gly Glu Gly Glu Leu Gln Tyr Ala Ser
 425 430 435

Leu Ser Phe Gln Met Val Lys Pro Trp Asp Ser Arg Gly Gln Glu
 440 445 450

Ala Thr Asp Thr Glu Tyr Ser Glu Ile Lys Ile His Arg
 455 460

<210> SEQ ID NO 87

<211> LENGTH: 1176

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 87

```

agaaagctgc actctgttga gctccagggc gcagtgagg gagggagtga      50
aggagctctc tgtaccaag gaaagtgcag ctgagactca gacaagatta      100
caatgaacca actcagcttc ctgctgtttc tcatagcgac caccagagga      150
tggagtacag atgaggctaa tacttacttc aaggaatgga cctgtttctc      200
gtctccatct ctgccagaa gctgcaagga aatcaaagac gaatgtccta      250
gtgcatttga tggcctgtat tttctccgca ctgagaatgg tgttatctac      300
cagaccttot gtgacatgac ctctgggggt ggcggctgga ccctggtggc      350
cagcgtgcat gagaatgaca tgcgtgggaa gtgcacggtg ggcgatcgct      400
ggtccagtca gcagggcagc aaagcagact acccagaggg ggacggcaac      450
tgggccaaat acaacacctt tggatctgca gagggggcca cgagcgatga      500
ctacaagaac cctggctact acgacatcca ggccaaggac ctgggcatct      550
ggcacgtgcc caataagtcc cccatgcagc actggagaaa cagctccctg      600
ctgagggtacc gcacggacac tggcttctc cagacactgg gacataatct      650
gtttggcatc taccagaaat atccagttaa atatggagaa gaaaagtgtt      700
ggactgacaa cggcccgggt atccctgtgg tctatgattt tggcgacgcc      750
cagaaaacag catcttatta ctacacctat ggccagcggg aattcactgc      800
gggatttggt cagttcaggg tatttaataa cgagagagca gccaacgcct      850
tgtgtgctgg aatgagggtc accggatgta aactgagca tcaactgcatt      900
ggtggaggag gatactttcc agaggccagt cccagcagc gtggagattt      950
ttctggtttt gattggagtg gatatggaac tcatgttggg tacagcagca     1000
gccgtgagat aactgaggca gctgtgcttc tattctatcg ttgagagttt     1050
tgtggggagg aaccagacc tctcctccca accatgagat cccaaggatg     1100
gagaacaact taccagtag ctagaatggt aatggcagaa gagaaaacaa     1150
taaatacatat tgactcaaga aaaaaa                                1176

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<210> SEQ ID NO 88

<211> LENGTH: 313

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 88

-continued

Met Asn Gln Leu Ser Phe Leu Leu Phe Leu Ile Ala Thr Thr Arg
 1 5 10 15
 Gly Trp Ser Thr Asp Glu Ala Asn Thr Tyr Phe Lys Glu Trp Thr
 20 25 30
 Cys Ser Ser Ser Pro Ser Leu Pro Arg Ser Cys Lys Glu Ile Lys
 35 40 45
 Asp Glu Cys Pro Ser Ala Phe Asp Gly Leu Tyr Phe Leu Arg Thr
 50 55 60
 Glu Asn Gly Val Ile Tyr Gln Thr Phe Cys Asp Met Thr Ser Gly
 65 70 75
 Gly Gly Gly Trp Thr Leu Val Ala Ser Val His Glu Asn Asp Met
 80 85 90
 Arg Gly Lys Cys Thr Val Gly Asp Arg Trp Ser Ser Gln Gln Gly
 95 100 105
 Ser Lys Ala Asp Tyr Pro Glu Gly Asp Gly Asn Trp Ala Asn Tyr
 110 115 120
 Asn Thr Phe Gly Ser Ala Glu Ala Ala Thr Ser Asp Asp Tyr Lys
 125 130 135
 Asn Pro Gly Tyr Tyr Asp Ile Gln Ala Lys Asp Leu Gly Ile Trp
 140 145 150
 His Val Pro Asn Lys Ser Pro Met Gln His Trp Arg Asn Ser Ser
 155 160 165
 Leu Leu Arg Tyr Arg Thr Asp Thr Gly Phe Leu Gln Thr Leu Gly
 170 175 180
 His Asn Leu Phe Gly Ile Tyr Gln Lys Tyr Pro Val Lys Tyr Gly
 185 190 195
 Glu Gly Lys Cys Trp Thr Asp Asn Gly Pro Val Ile Pro Val Val
 200 205 210
 Tyr Asp Phe Gly Asp Ala Gln Lys Thr Ala Ser Tyr Tyr Ser Pro
 215 220 225
 Tyr Gly Gln Arg Glu Phe Thr Ala Gly Phe Val Gln Phe Arg Val
 230 235 240
 Phe Asn Asn Glu Arg Ala Ala Asn Ala Leu Cys Ala Gly Met Arg
 245 250 255
 Val Thr Gly Cys Asn Thr Glu His His Cys Ile Gly Gly Gly Gly
 260 265 270
 Tyr Phe Pro Glu Ala Ser Pro Gln Gln Cys Gly Asp Phe Ser Gly
 275 280 285
 Phe Asp Trp Ser Gly Tyr Gly Thr His Val Gly Tyr Ser Ser Ser
 290 295 300
 Arg Glu Ile Thr Glu Ala Ala Val Leu Leu Phe Tyr Arg
 305 310

<210> SEQ ID NO 89
 <211> LENGTH: 759
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 89

ctagatttgt cggcttgctg ggagacttca ggagtcgctg tctctgaact 50
 tccagcctca gagaccgccc cccttgctcc cgagggccat gggccgggtc 100

-continued

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tcagggcttg tgccctctcg cttcctgacg ctccctggcgc atctggtggt      150
cgatcatcacc ttattctggt ccggggacag caacatacag gcctgcctgc      200
ctctcacggtt caccoccgag gagtatgaca agcaggacat tcagctgggtg      250
gccgcgctct ctgtcacctt gggcctcttt gcagtggagc tggccggttt      300
cctctcagga gtctccatgt tcaacagcac ccagagcctc atctccattg      350
gggctcactg tagtgcaccc gtggccctgt ccttcttcat attogagcgt      400
tgggagtgca ctacgtattg gtacatcttt gtcttctgca gtgcccttcc      450
agctgtcact gaaatggctt tattcgtcac cgtctttggg ctgaaaaaga      500
aacccttctg attaccttca tgacgggaac ctaaggacga agcctacagg      550
ggcaagggcc gcttcgtatt cctggaagaa ggaaggcata ggcttcggtt      600
ttccocctcg aaactgcttc tgctggagga tatgtgttgg aataattacg      650
tcttgagtct gggattatcc gcattgtatt tagtgctttg taataaaata      700
tgttttgtag taacattaag acttatatac agttttaggg gacaattaa      750
aaaaaaaaa                                                    759
    
```

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<210> SEQ ID NO 90
<211> LENGTH: 140
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien
    
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<400> SEQUENCE: 90

```

Met Gly Arg Val Ser Gly Leu Val Pro Ser Arg Phe Leu Thr Leu
  1           5           10           15
Leu Ala His Leu Val Val Val Ile Thr Leu Phe Trp Ser Arg Asp
          20           25           30
Ser Asn Ile Gln Ala Cys Leu Pro Leu Thr Phe Thr Pro Glu Glu
          35           40           45
Tyr Asp Lys Gln Asp Ile Gln Leu Val Ala Ala Leu Ser Val Thr
          50           55           60
Leu Gly Leu Phe Ala Val Glu Leu Ala Gly Phe Leu Ser Gly Val
          65           70           75
Ser Met Phe Asn Ser Thr Gln Ser Leu Ile Ser Ile Gly Ala His
          80           85           90
Cys Ser Ala Ser Val Ala Leu Ser Phe Phe Ile Phe Glu Arg Trp
          95           100          105
Glu Cys Thr Thr Tyr Trp Tyr Ile Phe Val Phe Cys Ser Ala Leu
          110          115          120
Pro Ala Val Thr Glu Met Ala Leu Phe Val Thr Val Phe Gly Leu
          125          130          135
Lys Lys Lys Pro Phe
          140
    
```

```

<210> SEQ ID NO 91
<211> LENGTH: 1871
<212> TYPE: DNA
<213> ORGANISM: Homo Sapien
    
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<400> SEQUENCE: 91

```

ctgggacccc gaaaagagaa ggggagagcg aggggacgag agcggaggag      50
    
```

-continued

gaagatgcaa ctgactcgct gctgcttcgt gttcctggtg cagggtagcc	100
tctatctggt catctgtggc caggatgatg gtcctcccg ctcagaggac	150
cctgagcgtg atgaccacga gggccagccc cggccccggg tgccctcgaa	200
gcggggccac atctcaccta agtcccggcc catggccaat tccactctcc	250
tagggctgct ggccccgcct ggggaggctt ggggcattct tgggcagccc	300
cccaaccgcc cgaaccacag cccccaccc tcagccaagg tgaagaaaat	350
ctttggctgg ggcgacttct actccaacat caagacggtg gccctgaacc	400
tgctcgtcac agggaagatt gtggaccatg gcaatgggac cttcagcgtc	450
cacttccaac acaatgccac aggccaggga aacatctcca tcagcctcgt	500
gccccccagt aaagctgtag agttccacca ggaacagcag atcttcatcg	550
aagccaaggc ctccaaaatc ttcaactgcc ggatggagtg ggagaaggta	600
gaacggggcc gccggacctc gctttgcacc cacgaccag ccaagatctg	650
ctcccagac cacgctcaga gctcagccac ctggagctgc tcccagccct	700
tcaaagtcgt ctgtgtctac atcgccttct acagcacgga ctatcggctg	750
gtccagaagg tgtgccaga ttacaactac catagtgata ccccctacta	800
cccctctggg tgacccgggg caggccacag aggccaggcc agggctggaa	850
ggacagccct gcccatgcag gagaccatct ggacaccggg cagggaaggg	900
gttgggcctc aggcaggagg ggggggtggag acgaggagat gccaaagtgg	950
gccaggggca agtctcaagt ggcagagaaa gggteccaag tgctggtccc	1000
aacctgaagc tgtggagtga ctagatcaca ggagcactgg aggaggagtg	1050
ggctctctgt gcagcctcac agggctttgc cacggagcca cagagagatg	1100
ctgggtcccc gaggcctgtg ggcaggccga tcagtgtggc cccagatcaa	1150
gtcatgggag gaagctaagc ccttggttct tgccatcctg aggaaagata	1200
gcaacaggga gggggagatt tcatcagtggt ggacagcctg tcaacttagg	1250
atggatggct gagaggcctt cctaggagcc agtcagcagg gtgggggtgg	1300
gccagaggag ctctccagcc ctgacctagt ggcgccctga gcccttgtc	1350
gtgtgctgag catggcatga ggctgaagtg gcaaccctgg ggtctttgat	1400
gtcttgacag attgaccatc tgtctccagc caggccaccc ctttccaaaa	1450
ttccctcttc tgccagtact cccccgtac caccattgc tgatggcaca	1500
cccctcctta agctaagaca ggacgattgt ggtcctcca cactaaggcc	1550
acagcccac cgcgtgctgt gtgtccctct tccaccccaa cccctgctgg	1600
ctcctctggg agcatccatg tcccggagag gggtcctca acagtcagcc	1650
tcacctgtoa gaccgggggt ctcccggatc tggatggcgc cgcctctca	1700
gcagcgggca cgggtggggc gggccgggc cgcagagcat gtgctggatc	1750
tgttctgtgt gtctgtctgt ggggtggggg aggggagggg agtcttgtga	1800
aaccgctgat tgctgacttt tgtgtgaaga atcgtgttct tggagcagga	1850
aataaagctt gccccggggc a	1871

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<211> LENGTH: 252
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 92
Met  Gln  Leu  Thr  Arg  Cys  Cys  Phe  Val  Phe  Leu  Val  Gln  Gly  Ser
  1          5          10          15
Leu  Tyr  Leu  Val  Ile  Cys  Gly  Gln  Asp  Asp  Gly  Pro  Pro  Gly  Ser
          20          25          30
Glu  Asp  Pro  Glu  Arg  Asp  Asp  His  Glu  Gly  Gln  Pro  Arg  Pro  Arg
          35          40          45
Val  Pro  Arg  Lys  Arg  Gly  His  Ile  Ser  Pro  Lys  Ser  Arg  Pro  Met
          50          55          60
Ala  Asn  Ser  Thr  Leu  Leu  Gly  Leu  Leu  Ala  Pro  Pro  Gly  Glu  Ala
          65          70          75
Trp  Gly  Ile  Leu  Gly  Gln  Pro  Pro  Asn  Arg  Pro  Asn  His  Ser  Pro
          80          85          90
Pro  Pro  Ser  Ala  Lys  Val  Lys  Lys  Ile  Phe  Gly  Trp  Gly  Asp  Phe
          95          100          105
Tyr  Ser  Asn  Ile  Lys  Thr  Val  Ala  Leu  Asn  Leu  Leu  Val  Thr  Gly
          110          115          120
Lys  Ile  Val  Asp  His  Gly  Asn  Gly  Thr  Phe  Ser  Val  His  Phe  Gln
          125          130          135
His  Asn  Ala  Thr  Gly  Gln  Gly  Asn  Ile  Ser  Ile  Ser  Leu  Val  Pro
          140          145          150
Pro  Ser  Lys  Ala  Val  Glu  Phe  His  Gln  Glu  Gln  Gln  Ile  Phe  Ile
          155          160          165
Glu  Ala  Lys  Ala  Ser  Lys  Ile  Phe  Asn  Cys  Arg  Met  Glu  Trp  Glu
          170          175          180
Lys  Val  Glu  Arg  Gly  Arg  Arg  Thr  Ser  Leu  Cys  Thr  His  Asp  Pro
          185          190          195
Ala  Lys  Ile  Cys  Ser  Arg  Asp  His  Ala  Gln  Ser  Ser  Ala  Thr  Trp
          200          205          210
Ser  Cys  Ser  Gln  Pro  Phe  Lys  Val  Val  Cys  Val  Tyr  Ile  Ala  Phe
          215          220          225
Tyr  Ser  Thr  Asp  Tyr  Arg  Leu  Val  Gln  Lys  Val  Cys  Pro  Asp  Tyr
          230          235          240
Asn  Tyr  His  Ser  Asp  Thr  Pro  Tyr  Tyr  Pro  Ser  Gly
          245          250

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<210> SEQ ID NO 93
<211> LENGTH: 902
<212> TYPE: DNA
<213> ORGANISM: Homo Sapien

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```

<400> SEQUENCE: 93
cggtggccat gactgcgccc gtgttcttcg gctgcgcctt cattgccttc          50
gggcctgcmc tcgcccttta tgtcttcacc atcgccatcg agcogttgcm          100
tatcatcttc ctcatcgccg gagctttctt ctggttggtg tctctactga          150
tttcgtccct tgtttggttc atggcaagag tcattattga caacaaagat          200
ggaccaacac agaaatatct gctgatcttt ggagcgtttg tctctgtcta          250
tatccaagaa atgttccgat ttgcatatta taaactctta aaaaaagcca          300

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gtgaaggttt gaagagtata aaccaggtg agacagcacc ctctatgca      350
ctgtgctgct atgtttctgg cttgggcttt ggaatcatga gtggagtatt      400
ttcctttgtg aataccctat ctgactcctt ggggccaggc acagtgggca      450
ttcatggaga ttctcctcaa ttcttccttt attcagcttt catgacgctg      500
gtcattatct tgctgcatgt attctggggc attgtatfff ttgatggctg      550
tgagaagaaa aagtggggca tcctccttat cgttctcctg acccacctgc      600
tggtgtcagc ccagacctc ataagttctt attatggaat aaacctggcg      650
tcagcattta taatcctggt gctcatgggc acctgggcat tcttagctgc      700
gggaggcagc tgccgaagcc tgaactctg cctgctctgc caagacaaga      750
actttctctt ttacaaccag cgctccagat aacctcaggg aaccagcact      800
tcccaaacog cagactacat cttagagga agcacaactg tgcotffffc      850
tgaaaatccc tttttctggt ggaattgaga aagaataaa actatgcaga      900
ta                                                                902

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<210> SEQ ID NO 94

<211> LENGTH: 257

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 94

```

Met Thr Ala Ala Val Phe Phe Gly Cys Ala Phe Ile Ala Phe Gly
 1                5                10                15
Pro Ala Leu Ala Leu Tyr Val Phe Thr Ile Ala Ile Glu Pro Leu
                20                25                30
Arg Ile Ile Phe Leu Ile Ala Gly Ala Phe Phe Trp Leu Val Ser
                35                40                45
Leu Leu Ile Ser Ser Leu Val Trp Phe Met Ala Arg Val Ile Ile
                50                55                60
Asp Asn Lys Asp Gly Pro Thr Gln Lys Tyr Leu Leu Ile Phe Gly
                65                70                75
Ala Phe Val Ser Val Tyr Ile Gln Glu Met Phe Arg Phe Ala Tyr
                80                85                90
Tyr Lys Leu Leu Lys Lys Ala Ser Glu Gly Leu Lys Ser Ile Asn
                95                100               105
Pro Gly Glu Thr Ala Pro Ser Met Arg Leu Leu Ala Tyr Val Ser
                110               115               120
Gly Leu Gly Phe Gly Ile Met Ser Gly Val Phe Ser Phe Val Asn
                125               130               135
Thr Leu Ser Asp Ser Leu Gly Pro Gly Thr Val Gly Ile His Gly
                140               145               150
Asp Ser Pro Gln Phe Phe Leu Tyr Ser Ala Phe Met Thr Leu Val
                155               160               165
Ile Ile Leu Leu His Val Phe Trp Gly Ile Val Phe Phe Asp Gly
                170               175               180
Cys Glu Lys Lys Lys Trp Gly Ile Leu Leu Ile Val Leu Leu Thr
                185               190               195
His Leu Leu Val Ser Ala Gln Thr Phe Ile Ser Ser Tyr Tyr Gly
                200               205               210

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-continued

Ile Asn Leu Ala Ser Ala Phe Ile Ile Leu Val Leu Met Gly Thr
 215 220 225
 Trp Ala Phe Leu Ala Ala Gly Gly Ser Cys Arg Ser Leu Lys Leu
 230 235 240
 Cys Leu Leu Cys Gln Asp Lys Asn Phe Leu Leu Tyr Asn Gln Arg
 245 250 255
 Ser Arg

<210> SEQ ID NO 95
 <211> LENGTH: 1073
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 95

aatTTTTcAC cagagtaaAC ttgagaaacc aactggacct tgagtattgt 50
 acatTTTTGCC tcgtggacCC aaaggtagca atctgaaaca tgaggagtac 100
 gattctactg ttttGtcttc taggATCAAC tGGtCatta cCacagctca 150
 AACtGcttt gggactccct cccacaaaac tggctccgga tcagggaaCa 200
 ctacaaaacc AACagcagtc aaatcaggtc tttccttctt taagtctgat 250
 accattaaca cagatgctca cactggggcc agatctgcat ctgttaaAtc 300
 ctgctgcagg aatgacacct ggtaccCaga cccaccCatt gaccctggga 350
 gggttGaatg tacaacagca actgcaccca catgtgttac caatTTTTgt 400
 cacacaactt ggagccCagg gCactatcct aagctcagag gaattgCCac 450
 aaatcttCAC gagcctcatc atccattcct tGttcccgGg aggcacctctg 500
 cccaccagtc aggcaggggc taatccagat gtccaggatg gaagccttcc 550
 agcaggagga gcaggtgtaa atcctgccac cCagggaacc cCagcaggcc 600
 gcctcccaac tcccagtggc acagatgagc actttgcagt gaccaccCct 650
 gcaggcatcc aaaggagcAc acatgccatc gaggaagcca cCacagaatc 700
 agcaaatgga attcagtaag ctgtttcaaa ttttttcaac taagctgcct 750
 cgaatTTggt gatacatgtg aatctttatc attgattata ttatggaata 800
 gattgagaca cattggatag tcttagaaga aattaattct taatttacct 850
 gaaaatattc ttgaaatttc agaaaatag ttctatgtag agaatcccaa 900
 cttttaaaaa caataattca atggataaat ctgtctttga aatataacat 950
 tatgctgcct ggatgatatg catattaaaa catatTTgga aaactggaaa 1000
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1050
 aaaaaaaaaa aaaaaaaaaa aaa 1073

<210> SEQ ID NO 96
 <211> LENGTH: 209
 <212> TYPE: PRT
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 96

Met Arg Ser Thr Ile Leu Leu Phe Cys Leu Leu Gly Ser Thr Arg
 1 5 10 15
 Ser Leu Pro Gln Leu Lys Pro Ala Leu Gly Leu Pro Pro Thr Lys

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														20					25					30
Leu	Ala	Pro	Asp	Gln	Gly	Thr	Leu	Pro	Asn	Gln	Gln	Gln	Ser	Asn	35				40					45
Gln	Val	Phe	Pro	Ser	Leu	Ser	Leu	Ile	Pro	Leu	Thr	Gln	Met	Leu	50				55					60
Thr	Leu	Gly	Pro	Asp	Leu	His	Leu	Leu	Asn	Pro	Ala	Ala	Gly	Met	65				70					75
Thr	Pro	Gly	Thr	Gln	Thr	His	Pro	Leu	Thr	Leu	Gly	Gly	Leu	Asn	80				85					90
Val	Gln	Gln	Gln	Leu	His	Pro	His	Val	Leu	Pro	Ile	Phe	Val	Thr	95				100					105
Gln	Leu	Gly	Ala	Gln	Gly	Thr	Ile	Leu	Ser	Ser	Glu	Glu	Leu	Pro	110				115					120
Gln	Ile	Phe	Thr	Ser	Leu	Ile	Ile	His	Ser	Leu	Phe	Pro	Gly	Gly	125				130					135
Ile	Leu	Pro	Thr	Ser	Gln	Ala	Gly	Ala	Asn	Pro	Asp	Val	Gln	Asp	140				145					150
Gly	Ser	Leu	Pro	Ala	Gly	Gly	Ala	Gly	Val	Asn	Pro	Ala	Thr	Gln	155				160					165
Gly	Thr	Pro	Ala	Gly	Arg	Leu	Pro	Thr	Pro	Ser	Gly	Thr	Asp	Asp	170				175					180
Asp	Phe	Ala	Val	Thr	Thr	Pro	Ala	Gly	Ile	Gln	Arg	Ser	Thr	His	185				190					195
Ala	Ile	Glu	Glu	Ala	Thr	Thr	Glu	Ser	Ala	Asn	Gly	Ile	Gln		200				205					

<210> SEQ ID NO 97
 <211> LENGTH: 2848
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien
 <400> SEQUENCE: 97

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gctcaagtc cctgccttcg cccacccagc ccagcctggc cagagccccc           50
tggagaagga gctctcttct tgcttgccag ctggaccaag ggagccagtc           100
ttgggcgctg gagggcctgt cctgacctg gtcctgcctt ggctgtggct           150
gctttgtgtc tccgtccccc aggtctctcc caaggcccag cctgcagagc           200
tgtctgtgga agttccagaa aactatggtg gaaatttccc tttatactg           250
accaagttgc cgctgccccg tgagggggct gaaggccaga tcgtgctgtc           300
aggggactca ggcaaggcaa ctgagggccc atttgctatg gatccagatt           350
ctggcttctc gctggtgacc agggccctgg accgagagga gcaggcagag           400
taccagctac aggtcaccct ggagatgcag gatggacatg tcttgtgggg           450
tccacagcct gtgcttgtgc acgtgaagga tgagaatgac caggtgcccc           500
atttctctca agccatctac agagctcggc tgagccgggg taccaggcct           550
ggcatccccct tcctcttctc tgaggcttca gaccgggatg agccaggcac           600
agccaactog gatcttcgat tccacatcct gagccaggct ccagcccagc           650
cttccccaga catgttccag ctggagccto ggctgggggc tctggccctc           700
agccccaagg ggagcaccag ccttgaccac gccctggaga ggacctacca           750
    
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gctgttgta caggtcaagg acatgggtga ccaggcctca ggccaccagg	800
ccactgccac cgtggaagtc tccatcatag agagcacctg ggtgtcccta	850
gagcctatcc acctggcaga gaatctcaaa gtcctatacc cgcaccacat	900
ggcccaggtg cactggagtg ggggtgatgt gcactatcac ctggagagcc	950
atccccggg accctttgaa gtgaatgcag agggaaacct ctacgtgacc	1000
agagagctgg acagagaagc ccaggctgag tacctgctcc aggtgcgggc	1050
tcagaattcc catggcgagg actatgcggc ccctctggag ctgcacgtgc	1100
tggtgatgga tgagaatgac aacgtgccta tctgccctcc cctgacccc	1150
acagtacgca tccctgagct cagtccacca ggtactgaag tgactagact	1200
gtcagcagag gatgcagatg cccccggctc cccaattcc cacgttgtgt	1250
atcagctcct gagccctgag cctgaggatg gggtagaggg gagagccttc	1300
caggtggacc ccacttcagg cagtgtgacg ctgggggtgc tcccactccg	1350
agcagggcag aacatcctgc ttctggtgct ggccatggac ctggcagggc	1400
cagaggggtg cttcagcagc acgtgtgaag tcgaagtcgc agtcacagat	1450
atcaatgatc acgcccctga gttcacact tcccagattg ggcctataag	1500
cctccctgag gatgtggagc cgggactct ggtggccatg ctaacagcca	1550
ttgatgctga cctcgagccc gcctccgcc tcatggattt tgccattgag	1600
agggagaca cagaaggagc ttttggcctg gattgggagc cagactctgg	1650
gcatgttaga ctcagactct gcaagaacct cagttatgag gcagctccaa	1700
gtcatgaggt ggtggtggtg gtgcagagtg tggcgaagct ggtggggcca	1750
ggcccaggcc ctggagccac cgccacggtg actgtgctag tggagagagt	1800
gatgccacc cccaagttgg accaggagag ctacaggcc agtgtccca	1850
tcagtcccc agccgctct ttctctgctga ccatccagcc ctccgacccc	1900
atcagccgaa ccctcagggt ctcccctagtc aatgactcag agggctggct	1950
ctgcattgag aaattctccg gggaggtgca caccgcccag tccctcagg	2000
gcgcccagcc tggggacacc tacacggtgc ttgtggaggc ccaggataca	2050
gccctgactc ttgcccctgt gccctcccaa tacctctgca caccccgcca	2100
agaccatggc ttgatcgtga gtggaccag caaggacccc gatctggcca	2150
gtgggcacgg tccctacagc ttcacccctg gtcccaacc cacggtgcaa	2200
cgggattggc gcctccagac tctcaatggt tcccatgcct acctcacctt	2250
ggccctgcat tgggtggagc cacgtgaaca cataatcccc gtggtggtca	2300
gccacaatgc ccagatgtg cagctcctgg ttcgagtgat cgtgtgtcgc	2350
tgcaacgtgg aggggcagtg catgcgcaag gtgggcccga tgaagggcat	2400
gccacgaag ctgtcggcag tgggcatcct tgtaggcacc ctggtagcaa	2450
taggaatctt cctcactctc attttcaacc actggacat gtcaaggaag	2500
aaggaccgg atcaaccagc agacagcgtg cccctgaagg cgaactgtctg	2550
aatggcccag gcagctctag ctgggagctt ggcctctggc tccatctgag	2600
tcccctggga gagagcccag cacccaagat ccagcagggg acaggacaga	2650

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gtagaagccc ctccatctgc cctgggggtgg aggcaccatc accatcacca      2700
ggcatgtctg cagagcctgg acaccaactt tatggactgc ccatggggagt      2750
gtcctcaaatg tcaggggtgt tgcccataa taaagcccca gagaactggg      2800
ctgggcccta tgggaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaag      2848

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<210> SEQ ID NO 98
<211> LENGTH: 807
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien

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<400> SEQUENCE: 98

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Met Val Pro Ala Trp Leu Trp Leu Leu Cys Val Ser Val Pro Gln
 1                    5                    10                   15
Ala Leu Pro Lys Ala Gln Pro Ala Glu Leu Ser Val Glu Val Pro
20                   25                   30
Glu Asn Tyr Gly Gly Asn Phe Pro Leu Tyr Leu Thr Lys Leu Pro
35                   40                   45
Leu Pro Arg Glu Gly Ala Glu Gly Gln Ile Val Leu Ser Gly Asp
50                   55                   60
Ser Gly Lys Ala Thr Glu Gly Pro Phe Ala Met Asp Pro Asp Ser
65                   70                   75
Gly Phe Leu Leu Val Thr Arg Ala Leu Asp Arg Glu Glu Gln Ala
80                   85                   90
Glu Tyr Gln Leu Gln Val Thr Leu Glu Met Gln Asp Gly His Val
95                   100                  105
Leu Trp Gly Pro Gln Pro Val Leu Val His Val Lys Asp Glu Asn
110                  115                  120
Asp Gln Val Pro His Phe Ser Gln Ala Ile Tyr Arg Ala Arg Leu
125                  130                  135
Ser Arg Gly Thr Arg Pro Gly Ile Pro Phe Leu Phe Leu Glu Ala
140                  145                  150
Ser Asp Arg Asp Glu Pro Gly Thr Ala Asn Ser Asp Leu Arg Phe
155                  160                  165
His Ile Leu Ser Gln Ala Pro Ala Gln Pro Ser Pro Asp Met Phe
170                  175                  180
Gln Leu Glu Pro Arg Leu Gly Ala Leu Ala Leu Ser Pro Lys Gly
185                  190                  195
Ser Thr Ser Leu Asp His Ala Leu Glu Arg Thr Tyr Gln Leu Leu
200                  205                  210
Val Gln Val Lys Asp Met Gly Asp Gln Ala Ser Gly His Gln Ala
215                  220                  225
Thr Ala Thr Val Glu Val Ser Ile Ile Glu Ser Thr Trp Val Ser
230                  235                  240
Leu Glu Pro Ile His Leu Ala Glu Asn Leu Lys Val Leu Tyr Pro
245                  250                  255
His His Met Ala Gln Val His Trp Ser Gly Gly Asp Val His Tyr
260                  265                  270
His Leu Glu Ser His Pro Pro Gly Pro Phe Glu Val Asn Ala Glu
275                  280                  285
Gly Asn Leu Tyr Val Thr Arg Glu Leu Asp Arg Glu Ala Gln Ala
290                  295                  300

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Glu Tyr Leu Leu Gln Val Arg Ala Gln Asn Ser His Gly Glu Asp	305	310	315
Tyr Ala Ala Pro Leu Glu Leu His Val Leu Val Met Asp Glu Asn	320	325	330
Asp Asn Val Pro Ile Cys Pro Pro Arg Asp Pro Thr Val Ser Ile	335	340	345
Pro Glu Leu Ser Pro Pro Gly Thr Glu Val Thr Arg Leu Ser Ala	350	355	360
Glu Asp Ala Asp Ala Pro Gly Ser Pro Asn Ser His Val Val Tyr	365	370	375
Gln Leu Leu Ser Pro Glu Pro Glu Asp Gly Val Glu Gly Arg Ala	380	385	390
Phe Gln Val Asp Pro Thr Ser Gly Ser Val Thr Leu Gly Val Leu	395	400	405
Pro Leu Arg Ala Gly Gln Asn Ile Leu Leu Leu Val Leu Ala Met	410	415	420
Asp Leu Ala Gly Ala Glu Gly Gly Phe Ser Ser Thr Cys Glu Val	425	430	435
Glu Val Ala Val Thr Asp Ile Asn Asp His Ala Pro Glu Phe Ile	440	445	450
Thr Ser Gln Ile Gly Pro Ile Ser Leu Pro Glu Asp Val Glu Pro	455	460	465
Gly Thr Leu Val Ala Met Leu Thr Ala Ile Asp Ala Asp Leu Glu	470	475	480
Pro Ala Phe Arg Leu Met Asp Phe Ala Ile Glu Arg Gly Asp Thr	485	490	495
Glu Gly Thr Phe Gly Leu Asp Trp Glu Pro Asp Ser Gly His Val	500	505	510
Arg Leu Arg Leu Cys Lys Asn Leu Ser Tyr Glu Ala Ala Pro Ser	515	520	525
His Glu Val Val Val Val Val Gln Ser Val Ala Lys Leu Val Gly	530	535	540
Pro Gly Pro Gly Pro Gly Ala Thr Ala Thr Val Thr Val Leu Val	545	550	555
Glu Arg Val Met Pro Pro Pro Lys Leu Asp Gln Glu Ser Tyr Glu	560	565	570
Ala Ser Val Pro Ile Ser Ala Pro Ala Gly Ser Phe Leu Leu Thr	575	580	585
Ile Gln Pro Ser Asp Pro Ile Ser Arg Thr Leu Arg Phe Ser Leu	590	595	600
Val Asn Asp Ser Glu Gly Trp Leu Cys Ile Glu Lys Phe Ser Gly	605	610	615
Glu Val His Thr Ala Gln Ser Leu Gln Gly Ala Gln Pro Gly Asp	620	625	630
Thr Tyr Thr Val Leu Val Glu Ala Gln Asp Thr Ala Leu Thr Leu	635	640	645
Ala Pro Val Pro Ser Gln Tyr Leu Cys Thr Pro Arg Gln Asp His	650	655	660
Gly Leu Ile Val Ser Gly Pro Ser Lys Asp Pro Asp Leu Ala Ser	665	670	675
Gly His Gly Pro Tyr Ser Phe Thr Leu Gly Pro Asn Pro Thr Val			

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	680		685		690
Gln Arg Asp Trp Arg Leu Gln Thr Leu Asn Gly Ser His Ala Tyr	695		700		705
Leu Thr Leu Ala Leu His Trp Val Glu Pro Arg Glu His Ile Ile	710		715		720
Pro Val Val Val Ser His Asn Ala Gln Met Trp Gln Leu Leu Val	725		730		735
Arg Val Ile Val Cys Arg Cys Asn Val Glu Gly Gln Cys Met Arg	740		745		750
Lys Val Gly Arg Met Lys Gly Met Pro Thr Lys Leu Ser Ala Val	755		760		765
Gly Ile Leu Val Gly Thr Leu Val Ala Ile Gly Ile Phe Leu Ile	770		775		780
Leu Ile Phe Thr His Trp Thr Met Ser Arg Lys Lys Asp Pro Asp	785		790		795
Gln Pro Ala Asp Ser Val Pro Leu Lys Ala Thr Val	800		805		

<210> SEQ ID NO 99
 <211> LENGTH: 2436
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 99

ggctgaccgt gctacattgc ctggaggaag cctaaggaac ccaggcatcc	50
agctgcccac gcctgagtcc aagattcttc ccaggaacac aaacgttaga	100
gaccacgct cctggaagca ccagccttta tctcttcacc ttcaagtccc	150
ctttctcaag aatcctctgt tctttgccct ctaaagtctt ggtacatcta	200
ggacccaggc atcttgcttt ccagccacaa agagacagat gaagatgcag	250
aaaggaaatg ttctccttat gtttggtcta ctattgcatt tagaagctgc	300
aacaaattcc aatgagacta gcacctctgc caacctgga tccagtgtga	350
tctccagtgg agccagcaca gccaccaact ctgggtccag tgtgacctcc	400
agtggtggca gcacagccac catctcaggg tccagcgtga cctccaatgg	450
ggtcagcata gtcaccaact ctgagttcca tacaacctcc agtgggatca	500
gcacagccac caactctgag ttcagcacag cgtccagtgg gatcagcata	550
gccaccaact ctgagtccag cacaacctcc agtggggcca gcacagccac	600
caactctgag tccagcacac cctccagtgg ggccagcaca gtcaccaact	650
ctgggtccag tgtgacctcc agtggagcca gcaactgccac caactctgag	700
tccagcacag tgtccagttag ggccagcact gccaccaact ctgagtctag	750
cacctctcc agtggggcca gcacagccac caactctgac tccagcacia	800
cctccagtgg ggctagcaca gccaccaact ctgagtccag cacaacctcc	850
agtggtggcca gcacagccac caactctgag tccagcacag tgtccagttag	900
ggccagcaact gccaccaact ctgagtccag cacaacctcc agtggggcca	950
gcacagccac caactctgag tccagaacga cctccaatgg ggtggcaca	1000
gccaccaact ctgagtccag cacgacctcc agtggggcca gcacagccac	1050

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caactctgac tccagcacag tgtccagtgg ggccagcact gccaccaact      1100
ctgagtcag cagcactcc agtggggcca gcacagccac caactctgag      1150
tccagcacga cctccagtgg ggctagcaca gccaccaact ctgactccag      1200
cacaacctcc agtggggccg gcacagccac caactctgag tccagcacag      1250
tgtccagtgg gatcagcaca gtcaccaatt ctgagtcag cacacctcc      1300
agtggggcca acacagccac caactctgag tccagtacga cctccagtgg      1350
ggccaacaca gccaccaact ctgagtcag cacagtgtcc agtggggcca      1400
gcaactgccac caactctgag tccagcaca cctccagtgg ggtcagcaca      1450
gccaccaact ctgagtcag cacaacctcc agtggggcta gcacagccac      1500
caactctgac tccagcaca cctccagtga ggccagcaca gccaccaact      1550
ctgagtcag cacagtgtcc agtgggatca gcacagtcac caattctgag      1600
tccagcaca cctccagtgg ggccaacaca gccaccaact ctgggtocag      1650
tgtgacctct gcaggctctg gaacagcagc tctgactgga atgcacaca      1700
cttcccatag tgcactact gcagtgagt aggcaaagcc tggtggtcc      1750
ctggtgccgt gggaaatctt cctcatcacc ctggtctcgg ttgtggcggc      1800
cgtggggctc tttgctgggc tcttctctg tgtgagaac agcctgtccc      1850
tgagaaacac cttaacaca gctgtctacc accctcatgg cctcaacct      1900
ggccttggtc caggccctgg agggaatcat ggagccccc acaggcccag      1950
gtggagtctt aactggttct ggaggagacc agtatcatcg atagccatgg      2000
agatgagcgg gaggaacagc gggccctgag cagccccgga agcaagtgcc      2050
gcattcttca ggaaggaaga gacctgggca cccaagacct ggtttccttt      2100
cattcatccc aggagacccc tcccagcttt gtttgagatc ctgaaaatct      2150
tgaagaaggt attcctcacc tttctgctt ttaccagaca ctggaaagag      2200
aatactatat tgctcattta gctaagaat aaatacatct catctaacac      2250
acacgacaaa gagaagctgt gcttgccccg gggtggttat ctagctctga      2300
gatgaactca gttataggag aaaacctcca tgctggactc catctggcat      2350
tcaaaatctc cacagtaaaa tccaaagacc tcaaaaaaaaa aaaaaaaaaa      2400
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaa      2436
    
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<210> SEQ ID NO 100
<211> LENGTH: 596
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien
    
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<400> SEQUENCE: 100

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Met Lys Met Gln Lys Gly Asn Val Leu Leu Met Phe Gly Leu Leu
 1           5           10
Leu His Leu Glu Ala Ala Thr Asn Ser Asn Glu Thr Ser Thr Ser
 20          25          30
Ala Asn Thr Gly Ser Ser Val Ile Ser Ser Gly Ala Ser Thr Ala
 35          40          45
Thr Asn Ser Gly Ser Ser Val Thr Ser Ser Gly Val Ser Thr Ala
 50          55          60
    
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Thr	Ile	Ser	Gly	Ser	Ser	Val	Thr	Ser	Asn	Gly	Val	Ser	Ile	Val
			65						70					75
Thr	Asn	Ser	Glu	Phe	His	Thr	Thr	Ser	Ser	Gly	Ile	Ser	Thr	Ala
			80						85					90
Thr	Asn	Ser	Glu	Phe	Ser	Thr	Ala	Ser	Ser	Gly	Ile	Ser	Ile	Ala
			95						100					105
Thr	Asn	Ser	Glu	Ser	Ser	Thr	Thr	Ser	Ser	Gly	Ala	Ser	Thr	Ala
			110						115					120
Thr	Asn	Ser	Glu	Ser	Ser	Thr	Pro	Ser	Ser	Gly	Ala	Ser	Thr	Val
			125						130					135
Thr	Asn	Ser	Gly	Ser	Ser	Val	Thr	Ser	Ser	Gly	Ala	Ser	Thr	Ala
			140						145					150
Thr	Asn	Ser	Glu	Ser	Ser	Thr	Val	Ser	Ser	Arg	Ala	Ser	Thr	Ala
			155						160					165
Thr	Asn	Ser	Glu	Ser	Ser	Thr	Leu	Ser	Ser	Gly	Ala	Ser	Thr	Ala
			170						175					180
Thr	Asn	Ser	Asp	Ser	Ser	Thr	Thr	Ser	Ser	Gly	Ala	Ser	Thr	Ala
			185						190					195
Thr	Asn	Ser	Glu	Ser	Ser	Thr	Thr	Ser	Ser	Gly	Ala	Ser	Thr	Ala
			200						205					210
Thr	Asn	Ser	Glu	Ser	Ser	Thr	Val	Ser	Ser	Arg	Ala	Ser	Thr	Ala
			215						220					225
Thr	Asn	Ser	Glu	Ser	Ser	Thr	Thr	Ser	Ser	Gly	Ala	Ser	Thr	Ala
			230						235					240
Thr	Asn	Ser	Glu	Ser	Arg	Thr	Thr	Ser	Asn	Gly	Ala	Gly	Thr	Ala
			245						250					255
Thr	Asn	Ser	Glu	Ser	Ser	Thr	Thr	Ser	Ser	Gly	Ala	Ser	Thr	Ala
			260						265					270
Thr	Asn	Ser	Asp	Ser	Ser	Thr	Val	Ser	Ser	Gly	Ala	Ser	Thr	Ala
			275						280					285
Thr	Asn	Ser	Glu	Ser	Ser	Thr	Thr	Ser	Ser	Gly	Ala	Ser	Thr	Ala
			290						295					300
Thr	Asn	Ser	Glu	Ser	Ser	Thr	Thr	Ser	Ser	Gly	Ala	Ser	Thr	Ala
			305						310					315
Thr	Asn	Ser	Asp	Ser	Ser	Thr	Thr	Ser	Ser	Gly	Ala	Gly	Thr	Ala
			320						325					330
Thr	Asn	Ser	Glu	Ser	Ser	Thr	Val	Ser	Ser	Gly	Ile	Ser	Thr	Val
			335						340					345
Thr	Asn	Ser	Glu	Ser	Ser	Thr	Pro	Ser	Ser	Gly	Ala	Asn	Thr	Ala
			350						355					360
Thr	Asn	Ser	Glu	Ser	Ser	Thr	Thr	Ser	Ser	Gly	Ala	Asn	Thr	Ala
			365						370					375
Thr	Asn	Ser	Glu	Ser	Ser	Thr	Val	Ser	Ser	Gly	Ala	Ser	Thr	Ala
			380						385					390
Thr	Asn	Ser	Glu	Ser	Ser	Thr	Thr	Ser	Ser	Gly	Val	Ser	Thr	Ala
			395						400					405
Thr	Asn	Ser	Glu	Ser	Ser	Thr	Thr	Ser	Ser	Gly	Ala	Ser	Thr	Ala
			410						415					420
Thr	Asn	Ser	Asp	Ser	Ser	Thr	Thr	Ser	Ser	Glu	Ala	Ser	Thr	Ala
			425						430					435
Thr	Asn	Ser	Glu	Ser	Ser	Thr	Val	Ser	Ser	Gly	Ile	Ser	Thr	Val

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	440		445		450
Thr Asn Ser Glu Ser Ser Thr Thr Ser Ser Gly Ala Asn Thr Ala	455		460		465
Thr Asn Ser Gly Ser Ser Val Thr Ser Ala Gly Ser Gly Thr Ala	470		475		480
Ala Leu Thr Gly Met His Thr Thr Ser His Ser Ala Ser Thr Ala	485		490		495
Val Ser Glu Ala Lys Pro Gly Gly Ser Leu Val Pro Trp Glu Ile	500		505		510
Phe Leu Ile Thr Leu Val Ser Val Val Ala Ala Val Gly Leu Phe	515		520		525
Ala Gly Leu Phe Phe Cys Val Arg Asn Ser Leu Ser Leu Arg Asn	530		535		540
Thr Phe Asn Thr Ala Val Tyr His Pro His Gly Leu Asn His Gly	545		550		555
Leu Gly Pro Gly Pro Gly Gly Asn His Gly Ala Pro His Arg Pro	560		565		570
Arg Trp Ser Pro Asn Trp Phe Trp Arg Arg Pro Val Ser Ser Ile	575		580		585
Ala Met Glu Met Ser Gly Arg Asn Ser Gly Pro	590		595		

<210> SEQ ID NO 101
 <211> LENGTH: 1728
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 101

ggccggagcg ctcgcggtta cgggatgaat taacggcggg ttccgcacgg	50
aggttgtgac ccctacggag ccccagcttg cccacgcacc ccaactggcg	100
tcgcgcggcg tgcctgctt gtcacagtg ggaggctgga actatcaggc	150
tgaaaaacag agtgggtact ctcttctggg aagctggcaa caaatggatg	200
atgtgatata tgcattccag gggaaaggaa attgtggtgc ttctgaacct	250
atgtgcaatt aacgaggcag tttctagcta ctgcacgtac ttcataaagc	300
aggactctaa aagctttgga atcatggtgt catggaaagg gatttacttt	350
atactgactc tgttttgggg aagctttttt ggaagcattt tcatgctgag	400
tcctttttta cctttgatgt ttgtaaaccc atcttggat cgctggatca	450
acaaccgcct tgtggcaaca tggctcacc tacctgtggc attattggag	500
accatgtttg gtgtaaaagt gattataact ggggatgcat ttgttcctgg	550
agaaagaagt gtcattatca tgaaccatcg gacaagaatg gactggatgt	600
tcctgtggaa ttgcctgatg cgatatagct acctcagatt ggagaaaatt	650
tgccctaaa cgagtctcaa aggtgttcct ggatttggtt gggccatgca	700
ggctgctgcc tatatcttca ttcataaggaa atggaaggat gacaagagcc	750
atctcgaaga catgattgat tacttttgtg atattcacga accacttcaa	800
ctcctcatat tcccagaagg gactgatctc acagaaaaca gcaagtctcg	850
aagtaatgca tttgctgaaa aaaatggact tcagaaatat gaatatggtt	900

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tacatccaag aactacaggc ttacttttg tggtagaccg tctaagagaa      950
ggaagaacc ttgatgctgt ccatgatatc actgtggcgt atcctcacia      1000
cattcctcaa tcagagaagc acctcctcca aggagacttt cccagggaaa      1050
tccactttca cgtccaccgg tatccaatag acaccctccc cacatccaag      1100
gaggaccttc aactctggtg ccacaaacgg tgggaagaga aagaagagag      1150
gctgcgttcc ttctatcaag gggagaagaa tttttatfff accggacaga      1200
gtgtcattcc accttgcaag tctgaactca gggccttgt ggtcaaattg      1250
ctctctatac tgtattggac cctgttcagc cctgcaatgt gcctactcat      1300
atatttgtac agtcttgta agtggtatff tataatcacc attgtaatct      1350
ttgtgctgca agagagaata ttgtgtggac tggagatcat agaacttgca      1400
gtttaccgac ttttacacia acagccacat ttaaattcaa agaaaaatga      1450
gtaagattat aaggtttgcc atgtgaaaac ctagagcata ttttgaaat      1500
gttctaaacc tttctaagct cagatgcatt ttgtcatgac tatgtcgaat      1550
atftcttact gccatcatta ttgttaaag atattttgca cttaatfff      1600
tgggaaaaat attgctacia tfttttttaa tctctgaatg taatftcgat      1650
actgtgtaca tagcaggag tagtcgggt gaaataactt gggccagaat      1700
attattaaac aatcatcagc cttttaa      1728

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<210> SEQ ID NO 102

<211> LENGTH: 414

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 102

```

Met His Ser Arg Gly Arg Glu Ile Val Val Leu Leu Asn Pro Trp
 1          5          10          15
Ser Ile Asn Glu Ala Val Ser Ser Tyr Cys Thr Tyr Phe Ile Lys
 20        25        30
Gln Asp Ser Lys Ser Phe Gly Ile Met Val Ser Trp Lys Gly Ile
 35        40        45
Tyr Phe Ile Leu Thr Leu Phe Trp Gly Ser Phe Phe Gly Ser Ile
 50        55        60
Phe Met Leu Ser Pro Phe Leu Pro Leu Met Phe Val Asn Pro Ser
 65        70        75
Trp Tyr Arg Trp Ile Asn Asn Arg Leu Val Ala Thr Trp Leu Thr
 80        85        90
Leu Pro Val Ala Leu Leu Glu Thr Met Phe Gly Val Lys Val Ile
 95       100       105
Ile Thr Gly Asp Ala Phe Val Pro Gly Glu Arg Ser Val Ile Ile
110       115       120
Met Asn His Arg Thr Arg Met Asp Trp Met Phe Leu Trp Asn Cys
125       130       135
Leu Met Arg Tyr Ser Tyr Leu Arg Leu Glu Lys Ile Cys Leu Lys
140       145       150
Ala Ser Leu Lys Gly Val Pro Gly Phe Gly Trp Ala Met Gln Ala
155       160       165
Ala Ala Tyr Ile Phe Ile His Arg Lys Trp Lys Asp Asp Lys Ser

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	170		175		180
His Phe Glu Asp	Met Ile Asp Tyr Phe	Cys Asp Ile His Glu	Pro		
	185		190		195
Leu Gln Leu Leu	Ile Phe Pro Glu Gly	Thr Asp Leu Thr Glu	Asn		
	200		205		210
Ser Lys Ser Arg	Ser Asn Ala Phe Ala	Glu Lys Asn Gly Leu	Gln		
	215		220		225
Lys Tyr Glu Tyr	Val Leu His Pro Arg	Thr Thr Gly Phe Thr	Phe		
	230		235		240
Val Val Asp Arg	Leu Arg Glu Gly Lys	Asn Leu Asp Ala Val	His		
	245		250		255
Asp Ile Thr Val	Ala Tyr Pro His Asn	Ile Pro Gln Ser Glu	Lys		
	260		265		270
His Leu Leu Gln	Gly Asp Phe Pro Arg	Glu Ile His Phe His	Val		
	275		280		285
His Arg Tyr Pro	Ile Asp Thr Leu Pro	Thr Ser Lys Glu Asp	Leu		
	290		295		300
Gln Leu Trp Cys	His Lys Arg Trp Glu	Glu Lys Glu Glu Arg	Leu		
	305		310		315
Arg Ser Phe Tyr	Gln Gly Glu Lys Asn	Phe Tyr Phe Thr Gly	Gln		
	320		325		330
Ser Val Ile Pro	Pro Cys Lys Ser Glu	Leu Arg Val Leu Val	Val		
	335		340		345
Lys Leu Leu Ser	Ile Leu Tyr Trp Thr	Leu Phe Ser Pro Ala	Met		
	350		355		360
Cys Leu Leu Ile	Tyr Leu Tyr Ser Leu	Val Lys Trp Tyr Phe	Ile		
	365		370		375
Ile Thr Ile Val	Ile Phe Val Leu Gln	Glu Arg Ile Phe Gly	Gly		
	380		385		390
Leu Glu Ile Ile	Glu Leu Ala Cys Tyr	Arg Leu Leu His Lys	Gln		
	395		400		405
Pro His Leu Asn	Ser Lys Lys Asn Glu				
	410				

<210> SEQ ID NO 103
 <211> LENGTH: 2403
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien
 <400> SEQUENCE: 103

cggtcgcgagc ggctcgagtg aagagcctct ccacggctcc tgcgcctgag	50
acagctggcc tgacctcaa atcatccatc caccctgct gtcattgtt	100
ttcatagtg gagatcaacc cacaggaata tccatggctt ttgtgctcat	150
tttggttctc agtttctacg agctgggtgc aggacagtgg caagtcactg	200
gaccgggcaa gtttgtccag gccttggtgg gggaggacgc cgtgttctcc	250
tgctccctct ttctgagac cagtgcagag gctatggaag tgcggttctt	300
caggaatcag ttccatgctg tggccacct ctacagagat ggggaagact	350
gggaatctaa gcagatgcca cagtatcgag ggagaactga gtttgtgaag	400
gactccattg caggggggag tgctctctta aggctaaaa acatcactcc	450

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ctcggacatc ggcctgtatg ggtgctggtt cagttcccag atttacgatg	500
aggaggccac ctgggagctg cgggtggcag cactgggctc acttcctctc	550
atttccatcg tgggatatgt tgacggaggt atccagttac tctgcctgtc	600
ctcaggctggt ttccccagc ccacagccaa gtgaaaaggt ccacaaggac	650
aggatttgtc ttcagactcc agagcaaatg cagatgggta cagcctgtat	700
gatgtggaga tctccattat agtccaggaa aatgctggga gcatattgtg	750
ttccatccac cttgctgagc agagtcatga ggtggaatcc aaggatttga	800
taggagagac gtttttccag ccctcacctt ggcgcctggc ttctatttta	850
ctcgggttac tctgtgtgtc cctgtgtggt gttgtcatgg ggatgataat	900
tgttttcttc aaatccaaag ggaaaatcca ggcggaactg gactggagaa	950
gaaagcacgg acaggcagaa ttgagagacg cccggaaca cgcagtggag	1000
gtgactctgg atccagagac ggctcaccgg aagctctgcy tttctgatct	1050
gaaaactgta acccatagaa aagctcccca ggaggtcct cactctgaga	1100
agagatttac aaggaagagt gtggtggctt ctcagggttt ccaagcaggg	1150
agacattact gggaggtgga cgtgggacaa aatgtagggt ggtatgtggg	1200
agtgtgtcgg gatgacgtag acaggggaa gaacaatgtg actttgtctc	1250
ccaacaatgg gtattgggct ctcagactga caacagaaca tttgtatttc	1300
acattcaatc cccattttat cagcctcccc cccagcacc ctcctacacg	1350
agtaggggct ttcttgact atgagggtgg gaccatctcc ttcttcaata	1400
caaatgacca gtcccttatt tatacctcgc tgacatgtca gtttgaaggc	1450
ttgttgagac cctatatcca gcatgcgatg tatgacgagg aaaaggggac	1500
tcccatattc atatgtccag tgtcctgggg atgagacaga gaagaccctg	1550
cttaaaaggc cccacaccac agaccagac acagccaagg gagagtgtc	1600
ccgacaggtg gccccagctt cctctccgga goctgcgcac agagagtcac	1650
gcccccaact ctcttttagg gagctgaggt tctctgccc tgagccctgc	1700
agcagcggca gtcacagctt ccagatgagg ggggattggc ctgaccctgt	1750
gggagtcaga agccatggct gccctgaagt ggggacggaa tagactcaca	1800
ttaggtttag tttgtgaaaa ctccatccag ctaagcgatc ttgaacaagt	1850
cacaacctcc caggctcctc atttgctagt cacggacagt gattcctgcc	1900
tcacagggtg agattaaaga gacaacgaat gtgaatcatg cttgcaggtt	1950
tgagggcaca gtgtttgcta atgatgtgtt tttatattat acattttccc	2000
accataaact ctgtttgctt attccacatt aatttacttt tctctatacc	2050
aaatcaccca tggaatagtt attgaacacc tgctttgtga ggctcaaaga	2100
ataaagagga ggtaggattt ttcactgatt ctataagccc agcattacct	2150
gataccaaaa ccaggcaaaag aaaacagaag aagaggaag aaaactacag	2200
gtccatatcc ctcattaaca cagacacaaa aattcctaat aaaattttaa	2250
caaatataac taaacaatat atttaaagat gatataaac tactcagtgt	2300
ggtttgtccc acaaatgcag agttggttta atattttaat atcaaccagt	2350

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gtaattcagc acattaataa agtaaaaaag aaaaccataa aaaaaaaaaa      2400
aaa                                                                2403
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<210> SEQ ID NO 104

<211> LENGTH: 466

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 104

```
Met Ala Phe Val Leu Ile Leu Val Leu Ser Phe Tyr Glu Leu Val
 1          5          10          15
Ser Gly Gln Trp Gln Val Thr Gly Pro Gly Lys Phe Val Gln Ala
          20          25          30
Leu Val Gly Glu Asp Ala Val Phe Ser Cys Ser Leu Phe Pro Glu
          35          40          45
Thr Ser Ala Glu Ala Met Glu Val Arg Phe Phe Arg Asn Gln Phe
          50          55          60
His Ala Val Val His Leu Tyr Arg Asp Gly Glu Asp Trp Glu Ser
          65          70          75
Lys Gln Met Pro Gln Tyr Arg Gly Arg Thr Glu Phe Val Lys Asp
          80          85          90
Ser Ile Ala Gly Gly Arg Val Ser Leu Arg Leu Lys Asn Ile Thr
          95          100          105
Pro Ser Asp Ile Gly Leu Tyr Gly Cys Trp Phe Ser Ser Gln Ile
          110          115          120
Tyr Asp Glu Glu Ala Thr Trp Glu Leu Arg Val Ala Ala Leu Gly
          125          130          135
Ser Leu Pro Leu Ile Ser Ile Val Gly Tyr Val Asp Gly Gly Ile
          140          145          150
Gln Leu Leu Cys Leu Ser Ser Gly Trp Phe Pro Gln Pro Thr Ala
          155          160          165
Lys Trp Lys Gly Pro Gln Gly Gln Asp Leu Ser Ser Asp Ser Arg
          170          175          180
Ala Asn Ala Asp Gly Tyr Ser Leu Tyr Asp Val Glu Ile Ser Ile
          185          190          195
Ile Val Gln Glu Asn Ala Gly Ser Ile Leu Cys Ser Ile His Leu
          200          205          210
Ala Glu Gln Ser His Glu Val Glu Ser Lys Val Leu Ile Gly Glu
          215          220          225
Thr Phe Phe Gln Pro Ser Pro Trp Arg Leu Ala Ser Ile Leu Leu
          230          235          240
Gly Leu Leu Cys Gly Ala Leu Cys Gly Val Val Met Gly Met Ile
          245          250          255
Ile Val Phe Phe Lys Ser Lys Gly Lys Ile Gln Ala Glu Leu Asp
          260          265          270
Trp Arg Arg Lys His Gly Gln Ala Glu Leu Arg Asp Ala Arg Lys
          275          280          285
His Ala Val Glu Val Thr Leu Asp Pro Glu Thr Ala His Pro Lys
          290          295          300
Leu Cys Val Ser Asp Leu Lys Thr Val Thr His Arg Lys Ala Pro
          305          310          315
Gln Glu Val Pro His Ser Glu Lys Arg Phe Thr Arg Lys Ser Val
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	320		325		330
Val Ala Ser Gln Gly Phe Gln Ala Gly Arg His Tyr Trp Glu Val	335		340		345
Asp Val Gly Gln Asn Val Gly Trp Tyr Val Gly Val Cys Arg Asp	350		355		360
Asp Val Asp Arg Gly Lys Asn Asn Val Thr Leu Ser Pro Asn Asn	365		370		375
Gly Tyr Trp Val Leu Arg Leu Thr Thr Glu His Leu Tyr Phe Thr	380		385		390
Phe Asn Pro His Phe Ile Ser Leu Pro Pro Ser Thr Pro Pro Thr	395		400		405
Arg Val Gly Val Phe Leu Asp Tyr Glu Gly Gly Thr Ile Ser Phe	410		415		420
Phe Asn Thr Asn Asp Gln Ser Leu Ile Tyr Thr Leu Leu Thr Cys	425		430		435
Gln Phe Glu Gly Leu Leu Arg Pro Tyr Ile Gln His Ala Met Tyr	440		445		450
Asp Glu Glu Lys Gly Thr Pro Ile Phe Ile Cys Pro Val Ser Trp	455		460		465

Gly

<210> SEQ ID NO 105
 <211> LENGTH: 2103
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 105

ccttcacagg actcttcatt gctggttggc aatgatgtat cggccagatg	50
tggtgagggc taggaaaaga gtttgttggg aacctgggt tatcgccctc	100
gtcatcttca tatccctgat tgcctggca gtgtgcattg gactcactgt	150
tcattatgtg agatataatc aaaagaagac ctacaattac tatagcacat	200
tgctcattac aactgacaaa ctatatgctg agtttgagcag agaggcttct	250
aacaatttta cagaaatgag ccagagactt gaatcaatgg tgaanaatgc	300
atttataaa tctccattaa gggaagaatt tgtcaagtct caggttatca	350
agttcagtca acagaagcat ggagtgttgg ctcatatgct gttgatttgt	400
agatttcaact ctactgagga tcctgaaact gtagataaaa ttgttcaact	450
tgttttacat gaaaagctgc aagatgctgt aggacccctc aaagtagatc	500
ctcactcagt taaaattaaa aaaatcaaca agacagaaac agacagctat	550
ctaaaccatt gctgcggaac acgaagaagt aaaactctag gtcagagtct	600
caggatcggt ggtgggacag aagtagaaga gggatgaatgg ccctggcagg	650
ctagcctgca gtgggatggg agtcatcgct gtggagcaac cttaattaat	700
gccacatggc ttgtgagtgc tgctcactgt tttacaacat ataagaacc	750
tgccagatgg actgcttctt ttggagtaac aataaaacct tcgaaaatga	800
aacggggtct ccggagaata attgtccatg aaaaatacaa acacccatca	850
catgactatg atatttctct tgccagagctt tctagccctg ttcctacac	900
aaatgcagta catagagttt gtctccctga tgcacccat gagtttcaac	950

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caggatgatgt gatgtttgtg acaggatttg gagcactgaa aaatgatggt      1000
tacagtcaaa atcatcttcg acaagcacag gtgactctca tagacgctac      1050
aacttgcaat gaacctcaag cttaaatga cgccataact cctagaatgt      1100
tatgtgctgg ctcttagaa ggaaaaacag atgcatgccca gggtgactct      1150
ggaggaccac tggtagttc agatgctaga gatatctggt accttgctgg      1200
aatagtgagc tggggagatg aatgtgcaa acccaacaag cctgggtgtt      1250
atactagagt tacggccttg cgggactgga ttacttcaa aactggtatc      1300
taagagaaa aagcctcatg gaacagataa ctttttttt tgttttttg      1350
gtgtggaggc cttttttaga gatacagaat tggagaagac ttgcaaaaca      1400
gctagatttg actgatctca ataaactggt tgcttgatgc atgtattttc      1450
ttcccagctc tgttccgac gtaagcatcc tgcttctgcc agatcaactc      1500
tgtcatctgt gagcaatagt tgaacttta tgtacataga gaaatagata      1550
atacaatatt acattacagc ctgtattcat ttgttctcta gaagttttgt      1600
cagaattttg acttgttgac ataaatttgt aatgcatata tacaatttga      1650
agcactcctt ttcttcagtt cctcagctcc tctcattca gcaaatatcc      1700
atthtcaagg tgcagaacaa ggagtgaaag aaaatataag aagaaaaaaaa      1750
tcccctacat tttattggca cagaaaagta ttagggtgtt ttcttagtgg      1800
aatattagaa atgatcatat tcattatgaa aggtcaagca aagacagcag      1850
aataccaatc acttcatcat ttaggaagta tgggaactaa gtttaaggaag      1900
tccagaaaga agccaagata tacccttatt ttcatttcca acaactact      1950
atgataaatg tgaagaagat tctgtttttt tgtgacctat aataattata      2000
caaacttcat gcaatgtact tgttctaagc aaattaaagc aaatatttat      2050
ttaacattgt tactgaggat gtcaacatat aacaataaaa tataaatcac      2100
cca                                                                2103

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<210> SEQ ID NO 106

<211> LENGTH: 423

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 106

```

Met Met Tyr Arg Pro Asp Val Val Arg Ala Arg Lys Arg Val Cys
 1          5          10          15

Trp Glu Pro Trp Val Ile Gly Leu Val Ile Phe Ile Ser Leu Ile
 20        25        30

Val Leu Ala Val Cys Ile Gly Leu Thr Val His Tyr Val Arg Tyr
 35        40        45

Asn Gln Lys Lys Thr Tyr Asn Tyr Tyr Ser Thr Leu Ser Phe Thr
 50        55        60

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

Phe Thr Glu Met Ser Gln Arg Leu Glu Ser Met Val Lys Asn Ala
 80        85        90

Phe Tyr Lys Ser Pro Leu Arg Glu Glu Phe Val Lys Ser Gln Val

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	95									100										105
Ile	Lys	Phe	Ser	Gln	Gln	Lys	His	Gly	Val	Leu	Ala	His	Met	Leu						
				110					115					120						
Leu	Ile	Cys	Arg	Phe	His	Ser	Thr	Glu	Asp	Pro	Glu	Thr	Val	Asp						
				125					130					135						
Lys	Ile	Val	Gln	Leu	Val	Leu	His	Glu	Lys	Leu	Gln	Asp	Ala	Val						
				140					145					150						
Gly	Pro	Pro	Lys	Val	Asp	Pro	His	Ser	Val	Lys	Ile	Lys	Lys	Ile						
				155					160					165						
Asn	Lys	Thr	Glu	Thr	Asp	Ser	Tyr	Leu	Asn	His	Cys	Cys	Gly	Thr						
				170					175					180						
Arg	Arg	Ser	Lys	Thr	Leu	Gly	Gln	Ser	Leu	Arg	Ile	Val	Gly	Gly						
				185					190					195						
Thr	Glu	Val	Glu	Glu	Gly	Glu	Trp	Pro	Trp	Gln	Ala	Ser	Leu	Gln						
				200					205					210						
Trp	Asp	Gly	Ser	His	Arg	Cys	Gly	Ala	Thr	Leu	Ile	Asn	Ala	Thr						
				215					220					225						
Trp	Leu	Val	Ser	Ala	Ala	His	Cys	Phe	Thr	Thr	Tyr	Lys	Asn	Pro						
				230					235					240						
Ala	Arg	Trp	Thr	Ala	Ser	Phe	Gly	Val	Thr	Ile	Lys	Pro	Ser	Lys						
				245					250					255						
Met	Lys	Arg	Gly	Leu	Arg	Arg	Ile	Ile	Val	His	Glu	Lys	Tyr	Lys						
				260					265					270						
His	Pro	Ser	His	Asp	Tyr	Asp	Ile	Ser	Leu	Ala	Glu	Leu	Ser	Ser						
				275					280					285						
Pro	Val	Pro	Tyr	Thr	Asn	Ala	Val	His	Arg	Val	Cys	Leu	Pro	Asp						
				290					295					300						
Ala	Ser	Tyr	Glu	Phe	Gln	Pro	Gly	Asp	Val	Met	Phe	Val	Thr	Gly						
				305					310					315						
Phe	Gly	Ala	Leu	Lys	Asn	Asp	Gly	Tyr	Ser	Gln	Asn	His	Leu	Arg						
				320					325					330						
Gln	Ala	Gln	Val	Thr	Leu	Ile	Asp	Ala	Thr	Thr	Cys	Asn	Glu	Pro						
				335					340					345						
Gln	Ala	Tyr	Asn	Asp	Ala	Ile	Thr	Pro	Arg	Met	Leu	Cys	Ala	Gly						
				350					355					360						
Ser	Leu	Glu	Gly	Lys	Thr	Asp	Ala	Cys	Gln	Gly	Asp	Ser	Gly	Gly						
				365					370					375						
Pro	Leu	Val	Ser	Ser	Asp	Ala	Arg	Asp	Ile	Trp	Tyr	Leu	Ala	Gly						
				380					385					390						
Ile	Val	Ser	Trp	Gly	Asp	Glu	Cys	Ala	Lys	Pro	Asn	Lys	Pro	Gly						
				395					400					405						
Val	Tyr	Thr	Arg	Val	Thr	Ala	Leu	Arg	Asp	Trp	Ile	Thr	Ser	Lys						
				410					415					420						

Thr Gly Ile

<210> SEQ ID NO 107
 <211> LENGTH: 2397
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 107

agagaaagaa gcgtctccag ctgaagccaa tgcagccctc cggctctccg

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cgaagaagtt ccctgccccg atgagcccc gccgtgcgtc cccgactatc	100
cccaggcggg cgtggggcac cgggccagc gccgacgac gctgccgttt	150
tgcccttggg agtaggatgt ggtgaaagga tggggcttct cccttacggg	200
gctcacaatg gccagagaag attccgtgaa gtgtctgcgc tgctgctct	250
acgcccctca tctgctcttt tggttaatgt ccatcagtggt gttggcagtt	300
tctgcttgga tgagggacta cctaaataat gttctcactt taactgcaga	350
aacgagggta gaggaagcag tcattttgac ttactttcct gtggttcacc	400
cggtcatgat tgctgtttgc tgtttcctta tcattgtggg gatgtagga	450
tattgtgga cggtgaaaag aaatctgttg cttcttgcac ggtactttgg	500
aagtttgctt gtcattttct gtgtagaact ggcttgggc gtttgacat	550
atgaacagga acttatgggt ccagtacaat ggtcagatat ggtcactttg	600
aaagccagga tgacaaatta tggattacct agatatacggg ggttactca	650
tgcttggaat ttttttcaga gagagtttaa gtgctgtgga gtagtatatt	700
tcactgactg gttgaaatg acagagatgg actggcccc agattcctgc	750
tgtgttagag aattcccagg atgttccaaa caggcccacc aggaagatct	800
cagtgcactt tatcaagagg gttgtgggaa gaaaatgtat tccttttga	850
gaggaaccaa acaactgcag gtgctgaggt ttctgggaat ctccattggg	900
gtgacacaaa tcctggccat gattctcacc attactctgc tctgggctct	950
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atgacaactc tcagcacctg tcatgtccct cagtagaact gttgaaacca	1050
agcctgtcaa gaatccttga acacacatcc atggcaaaca gctttaatac	1100
acactttgag atggaggagt tataaaaaga aatgtcacag aagaaaacca	1150
caaacttggt ttattggact tgtgaatfff tgagtacata ctatgtggtt	1200
cagaaatatg tagaaataaa aatgttgcca taaaataaca cctaagcata	1250
tactattcta tgcttataaa tgaggatgga aaagtttcat gtcataagtc	1300
accactgga caataattga tgcccttaa atgctgaaga cagatgtcat	1350
accactgtg tagcctgtgt atgactttta ctgaacacag ttatgttttg	1400
aggcagcatg gtttgattag catttccgca tccatgcaa cgagtcacat	1450
atggtgggac tggagccata gtaaagggtg atttacttct accaactagt	1500
atataaagta ctaattaaat gctaacatag gaagttagaa aataactaata	1550
acttttatta ctcagcgatc tattcttctg atgctaaata aattatata	1600
cagaaaactt tcaatattgg tgactaccta aatgtgattt ttgctgggta	1650
ctaaaaatatt cttaccactt aaaagagcaa gctaacacat tgtcttaagc	1700
tgatcagga ttttttgat ataagtctgt gttaaactctg tataattcag	1750
tcgatttcag ttctgataat gtaagaata accattatga aaaggaaaat	1800
ttgtcctgta tagcatcatt attttagacc tttcctgtta ataaagcttt	1850
actattctgt cctgggctta tattacacat ataactgtta tttaaatact	1900
taaccactaa ttttgaanaat taccagtggt atacatagga atcattattc	1950

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agaatgtagt ctggtcttta ggaagtatta ataagaaaat ttgcacataa      2000
cttagttgat tcagaaagga cttgtatgct gtttttctcc caaatgaaga      2050
ctctttttga cactaaacac tttttaaaaa gcttatcttt gcctttctcca      2100
aacaagaagc aatagtctcc aagtcaatat aaattctaca gaaaatagtg      2150
ttctttttct ccagaaaaat gcttgtgaga atcattaataa catgtgacaa      2200
tttagagatt cttgttttta ttctactgat taatatactg tggcaaatta      2250
cacagattat taaatTTTTT tacaagagta tagtatattt atttgaatg      2300
ggaaaagtgc attttactgt attttgtgta ttttgtttat ttctcagaat      2350
atggaagaa aattaaaatg tgcaataaa tattttctag agagtaa          2397

```

<210> SEQ ID NO 108

<211> LENGTH: 305

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 108

```

Met Ala Arg Glu Asp Ser Val Lys Cys Leu Arg Cys Leu Leu Tyr
 1          5          10          15
Ala Leu Asn Leu Leu Phe Trp Leu Met Ser Ile Ser Val Leu Ala
 20          25          30
Val Ser Ala Trp Met Arg Asp Tyr Leu Asn Asn Val Leu Thr Leu
 35          40          45
Thr Ala Glu Thr Arg Val Glu Glu Ala Val Ile Leu Thr Tyr Phe
 50          55          60
Pro Val Val His Pro Val Met Ile Ala Val Cys Cys Phe Leu Ile
 65          70          75
Ile Val Gly Met Leu Gly Tyr Cys Gly Thr Val Lys Arg Asn Leu
 80          85          90
Leu Leu Leu Ala Trp Tyr Phe Gly Ser Leu Leu Val Ile Phe Cys
 95          100         105
Val Glu Leu Ala Cys Gly Val Trp Thr Tyr Glu Gln Glu Leu Met
 110         115         120
Val Pro Val Gln Trp Ser Asp Met Val Thr Leu Lys Ala Arg Met
 125         130         135
Thr Asn Tyr Gly Leu Pro Arg Tyr Arg Trp Leu Thr His Ala Trp
 140         145         150
Asn Phe Phe Gln Arg Glu Phe Lys Cys Cys Gly Val Val Tyr Phe
 155         160         165
Thr Asp Trp Leu Glu Met Thr Glu Met Asp Trp Pro Pro Asp Ser
 170         175         180
Cys Cys Val Arg Glu Phe Pro Gly Cys Ser Lys Gln Ala His Gln
 185         190         195
Glu Asp Leu Ser Asp Leu Tyr Gln Glu Gly Cys Gly Lys Lys Met
 200         205         210
Tyr Ser Phe Leu Arg Gly Thr Lys Gln Leu Gln Val Leu Arg Phe
 215         220         225
Leu Gly Ile Ser Ile Gly Val Thr Gln Ile Leu Ala Met Ile Leu
 230         235         240
Thr Ile Thr Leu Leu Trp Ala Leu Tyr Tyr Asp Arg Arg Glu Pro

```

-continued

	245		250		255
Gly Thr Asp Gln Met Met Ser Leu Lys Asn Asp Asn Ser Gln His					
	260		265		270
Leu Ser Cys Pro Ser Val Glu Leu Leu Lys Pro Ser Leu Ser Arg					
	275		280		285
Ile Phe Glu His Thr Ser Met Ala Asn Ser Phe Asn Thr His Phe					
	290		295		300
Glu Met Glu Glu Leu					
	305				

<210> SEQ ID NO 109
 <211> LENGTH: 2339
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 109

```

ccaaggccag agctgtggac accttatccc actcatcctc atcctcttcc      50
tctgataaag cccctaccag tgctgataaa gtctttctcg tgagagccta      100
gaggccttaa aaaaaaaaaagt gcttgaaga gaaggggaca aaggaacacc      150
agtattaaga ggattttcca gtgtttctgg cagttgggcc agaaggatgc      200
ctccattcct gcttctcacc tgctcttcca tcacaggcac ctccgtgtca      250
cccgtggccc tagatccttg ttctgcttac atcagcctga atgagccctg      300
gaggaacct gaccaccagt tggatgagtc tcaaggtcct cctctatgtg      350
acaacctatg gaatggggag tggatccact tcacgggcat ggcgggagat      400
gccatgccta ccttctgcat accagaaaac cactgtggaa cccacgcacc      450
tgtctggctc aatggcagcc accccctaga aggcgacggc attgtgcaac      500
gccaggcttg tgccagcttc aatgggaact gotgtctctg gaacaccacg      550
gtggaagtca aggcttgccc tggaggctac tatgtgtatc gtctgaccaa      600
gcccagcgtc tgcttccacg tctactgtgg tcatttttat gacatctgcg      650
acgaggactg ccatggcagc tgctcagata ccagcgagtg cacatgcgct      700
ccaggaactg tgctaggccc tgacaggcag acatgctttg atgaaaatga      750
atgtgagcaa aacaacggtg gctgcagtga gatctgtgtg aacctcaaaa      800
actcctaccg ctgtgagtgt ggggttggcc gtgtgctaag aagtgatggc      850
aagacttgtg aagacgttga aggatgccac aataacaatg gtggctgcag      900
ccactcttgc cttggatctg agaaaggcta ccagtgtgaa tgtccccggg      950
gcttggtgct gtctgaggat aaccacactt gccaaagccc tgtgttgtgc     1000
aaatcaaatg ccattgaagt gaacatcccc agggagctgg ttggtggcct     1050
ggagctcttc ctgaccaaca cctcctgccg aggagtgtcc aacggcacc     1100
atgtcaacat cctcttctct ctcaagacat gtggtacagt ggtogatgtg     1150
gtgaatgaca agatttgtgc cagcaacctc gtgacaggtc taccoaagca     1200
gaccccgggg agcagcgggg acttcatcat ccgaaccagc aagctgctga     1250
tcccggtgac ctgcgagttt ccacgcctgt acaccatttc tgaagatac     1300
gttccaaccc ttcgaaactc cccactggaa atcatgagcc gaaatcatgg     1350
    
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gatcttccca ttcactctgg agatcttcaa ggacaatgag ttggaagagc      1400
cttaccggga agctctgccc accctcaagc ttcgtgactc cctctacttt      1450
ggcattgagc ccgtggtgca cgtgagcggc ttgaaaagct tggtgagag      1500
ctgtctttgcc acccccacct ccaagatcga cgaggctctg aaatactacc      1550
tcatccggga tggctgtggt tcagatgact cggtaaagca gtacacatcc      1600
cgggatcacc tagcaaagca cttccaggtc cctgtcttca agtttgtggg      1650
caaagaccac aaggaagtgt ttctgcactg cggggttctt gtctgtggag      1700
tgttggacga gcgttccgc tgtgccagg gttgccaccg gcgaatgcgt      1750
cgtggggcag gaggagagga ctacagcggc ctacagggcc agacgctaac      1800
aggcggcccg atccgcatcg actgggagga ctagtctgta gccatactc      1850
gagtcctcgc attggacggc tctgtctctt ggagcttctc cccccaccgc      1900
cctctaagaa catctgcaa cagctggggt cagacttcac actgtgagtt      1950
cagactccca gcaccaactc actctgattc tggtcattc agtgggcaca      2000
ggtcacagca ctgctgaaca atgtgcctg ggtggggttt catctttcta      2050
ggggtgaaaa ctaaactgtc caccagaaa gacactcacc ccatttcct      2100
catttctttc ctacacttaa atacctcgtg tatggtgcaa tcagaccaca      2150
aaatcagaag ctgggtataa tatttcaagt tacaaccct agaaaaatta      2200
aacagttact gaaattatga cttaaatacc caatgactcc ttaaataatgt      2250
aaattatagt tataccttga aatttcaatt caaatgcaga ctaattatag      2300
ggaatttga agtgtatcaa taaaacagta tataatttt      2339

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<210> SEQ ID NO 110

<211> LENGTH: 545

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 110

```

Met Pro Pro Phe Leu Leu Leu Thr Cys Leu Phe Ile Thr Gly Thr
  1           5           10           15
Ser Val Ser Pro Val Ala Leu Asp Pro Cys Ser Ala Tyr Ile Ser
  20          25          30
Leu Asn Glu Pro Trp Arg Asn Thr Asp His Gln Leu Asp Glu Ser
  35          40          45
Gln Gly Pro Pro Leu Cys Asp Asn His Val Asn Gly Glu Trp Tyr
  50          55          60
His Phe Thr Gly Met Ala Gly Asp Ala Met Pro Thr Phe Cys Ile
  65          70          75
Pro Glu Asn His Cys Gly Thr His Ala Pro Val Trp Leu Asn Gly
  80          85          90
Ser His Pro Leu Glu Gly Asp Gly Ile Val Gln Arg Gln Ala Cys
  95          100         105
Ala Ser Phe Asn Gly Asn Cys Cys Leu Trp Asn Thr Thr Val Glu
  110         115         120
Val Lys Ala Cys Pro Gly Gly Tyr Tyr Val Tyr Arg Leu Thr Lys
  125         130         135
Pro Ser Val Cys Phe His Val Tyr Cys Gly His Phe Tyr Asp Ile

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	140			145					150
Cys Asp Glu Asp Cys His Gly Ser Cys Ser Asp Thr Ser Glu Cys	155			160					165
Thr Cys Ala Pro Gly Thr Val Leu Gly Pro Asp Arg Gln Thr Cys	170			175					180
Phe Asp Glu Asn Glu Cys Glu Gln Asn Asn Gly Gly Cys Ser Glu	185			190					195
Ile Cys Val Asn Leu Lys Asn Ser Tyr Arg Cys Glu Cys Gly Val	200			205					210
Gly Arg Val Leu Arg Ser Asp Gly Lys Thr Cys Glu Asp Val Glu	215			220					225
Gly Cys His Asn Asn Asn Gly Gly Cys Ser His Ser Cys Leu Gly	230			235					240
Ser Glu Lys Gly Tyr Gln Cys Glu Cys Pro Arg Gly Leu Val Leu	245			250					255
Ser Glu Asp Asn His Thr Cys Gln Val Pro Val Leu Cys Lys Ser	260			265					270
Asn Ala Ile Glu Val Asn Ile Pro Arg Glu Leu Val Gly Gly Leu	275			280					285
Glu Leu Phe Leu Thr Asn Thr Ser Cys Arg Gly Val Ser Asn Gly	290			295					300
Thr His Val Asn Ile Leu Phe Ser Leu Lys Thr Cys Gly Thr Val	305			310					315
Val Asp Val Val Asn Asp Lys Ile Val Ala Ser Asn Leu Val Thr	320			325					330
Gly Leu Pro Lys Gln Thr Pro Gly Ser Ser Gly Asp Phe Ile Ile	335			340					345
Arg Thr Ser Lys Leu Leu Ile Pro Val Thr Cys Glu Phe Pro Arg	350			355					360
Leu Tyr Thr Ile Ser Glu Gly Tyr Val Pro Asn Leu Arg Asn Ser	365			370					375
Pro Leu Glu Ile Met Ser Arg Asn His Gly Ile Phe Pro Phe Thr	380			385					390
Leu Glu Ile Phe Lys Asp Asn Glu Phe Glu Glu Pro Tyr Arg Glu	395			400					405
Ala Leu Pro Thr Leu Lys Leu Arg Asp Ser Leu Tyr Phe Gly Ile	410			415					420
Glu Pro Val Val His Val Ser Gly Leu Glu Ser Leu Val Glu Ser	425			430					435
Cys Phe Ala Thr Pro Thr Ser Lys Ile Asp Glu Val Leu Lys Tyr	440			445					450
Tyr Leu Ile Arg Asp Gly Cys Val Ser Asp Asp Ser Val Lys Gln	455			460					465
Tyr Thr Ser Arg Asp His Leu Ala Lys His Phe Gln Val Pro Val	470			475					480
Phe Lys Phe Val Gly Lys Asp His Lys Glu Val Phe Leu His Cys	485			490					495
Arg Val Leu Val Cys Gly Val Leu Asp Glu Arg Ser Arg Cys Ala	500			505					510
Gln Gly Cys His Arg Arg Met Arg Arg Gly Ala Gly Gly Glu Asp	515			520					525

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Ser Ala Gly Leu Gln Gly Gln Thr Leu Thr Gly Gly Pro Ile Arg
530 535 540

Ile Asp Trp Glu Asp
545

<210> SEQ ID NO 111

<211> LENGTH: 2063

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 111

gagagagggca	gcagcttgct	cagcggacaa	ggatgctggg	cgtgagggac	50
caaggcctgc	cctgcactcg	ggcctcctcc	agccagtgct	gaccagggac	100
ttctgacctg	ctggccagcc	aggacctgtg	tggggagggc	ctcctgctgc	150
cttgggggtg	caatctcagc	tccaggctac	agggagaccg	ggaggatcac	200
agagccagca	tgttacagga	tcctgacagt	gatcaacctc	tgaacagcct	250
cgatgtcaaa	cccctgcgca	aaccctgat	cccctgagag	acctcagaa	300
aggtggggat	cccctcctc	atagcactac	tgagcctggc	gagtatcctc	350
attgtggttg	tcctcatcaa	ggtgattctg	gataaatact	acttcctctg	400
cgggcagcct	ctccacttca	tcccaggagaa	gcagctgtgt	gacggagagc	450
tggactgtcc	cttgggggag	gacgaggagc	actgtgtcaa	gagcttcccc	500
gaagggcctg	cagtggcagt	ccgcctctcc	aaggaccgat	ccacactgca	550
ggtgctggac	tcggccacag	ggaactgggt	ctctgcctgt	ttcgacaact	600
tcacagaagc	tctcgctgag	acagcctgta	ggcagatggg	ctacagcaga	650
gctgtggaga	ttggcccaga	ccaggatctg	gatgtgtttg	aaatcacaga	700
aaacagccag	gagcttcgca	tgcggaactc	aagtggggccc	tgtctctcag	750
gctccctggg	ctcctctcac	tgtcttgcc	gtgggaagag	cctgaagacc	800
ccccgtgtgg	tgggtgggga	ggaggcctct	gtggattctt	ggccttggca	850
ggtcagcctc	cagtacgaca	aacagcacgt	ctgtggaggg	agcatcctgg	900
acccccactg	ggtcctcacg	gcagcccact	gcttcaggaa	acataccgat	950
gtgttcaact	ggaaggtgcg	ggcaggtc	gacaaaactgg	gcagcttccc	1000
atccctggct	gtggccaaga	tcctcatcat	tgaattcaac	cccatgtacc	1050
ccaaagacaa	tgacatcgcc	ctcatgaagc	tgcagttccc	actcactttc	1100
tcaggccacg	tcaggcccat	ctgtctgccc	ttctttgatg	aggagctcac	1150
tccagccaac	ccactctgga	tcattggatg	gggctttacg	aagcagaatg	1200
gagggaaagt	gtctgacata	ctgctgcagg	cgctcagcca	ggtcattgac	1250
agcacacggg	gcaatgcaga	cgatgcgtac	caggggggag	tcaccgagaa	1300
gatgatgtgt	gcaggcatcc	cggaaggggg	tgtggacacc	tgccaggggtg	1350
acagtgggtg	gcccctgatg	taccaatctg	accagtggca	tgtggtgggc	1400
atcgttagct	ggggctatgg	ctgcgggggc	ccgagcacc	caggagtata	1450
caccaaggtc	tcagcctatc	tcaactggat	ctacaatgtc	tggaaaggctg	1500
agctgtaagt	ctgctgcccc	tttgacgtgc	tgggagccgc	ttccttctctg	1550

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cctgcccac ctgggatcc cccaaagtca gacacagagc aagagtcccc      1600
ttgggtacac ccctctgccc acagcctcag catttcttgg agcagcaaag      1650
ggcctcaatt cctgtaagag accctcgag cccagaggcg cccagaggaa      1700
gtcagcagcc ctagctcggc cacacttggg gctcccagca tcccaggagg      1750
agacacagcc cactgaacaa ggtctcaggg gtattgctaa gccagaaggg      1800
aactttccca cactactgaa tggaagcagg ctgtcttgta aaagcccaga      1850
tcactgtggg ctggagagga gaaggaaagg gtctgcgcca gccctgtccg      1900
tcttcaccca tcccgaagcc tactagagca agaaaccagt tgtaataataa      1950
aatgcactgc cctactgttg gtatgactac cgttacctac tgttgcatt      2000
gttattacag ctatggccac tattattaaa gagctgtgta acatctctgg      2050
caaaaaaaaa aaa                                             2063
    
```

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<210> SEQ ID NO 112
<211> LENGTH: 432
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien
    
```

<400> SEQUENCE: 112

```

Met Leu Gln Asp Pro Asp Ser Asp Gln Pro Leu Asn Ser Leu Asp
 1          5          10          15
Val Lys Pro Leu Arg Lys Pro Arg Ile Pro Met Glu Thr Phe Arg
 20          25          30
Lys Val Gly Ile Pro Ile Ile Ile Ala Leu Leu Ser Leu Ala Ser
 35          40          45
Ile Ile Ile Val Val Val Leu Ile Lys Val Ile Leu Asp Lys Tyr
 50          55          60
Tyr Phe Leu Cys Gly Gln Pro Leu His Phe Ile Pro Arg Lys Gln
 65          70          75
Leu Cys Asp Gly Glu Leu Asp Cys Pro Leu Gly Glu Asp Glu Glu
 80          85          90
His Cys Val Lys Ser Phe Pro Glu Gly Pro Ala Val Ala Val Arg
 95          100         105
Leu Ser Lys Asp Arg Ser Thr Leu Gln Val Leu Asp Ser Ala Thr
 110         115         120
Gly Asn Trp Phe Ser Ala Cys Phe Asp Asn Phe Thr Glu Ala Leu
 125         130         135
Ala Glu Thr Ala Cys Arg Gln Met Gly Tyr Ser Arg Ala Val Glu
 140         145         150
Ile Gly Pro Asp Gln Asp Leu Asp Val Val Glu Ile Thr Glu Asn
 155         160         165
Ser Gln Glu Leu Arg Met Arg Asn Ser Ser Gly Pro Cys Leu Ser
 170         175         180
Gly Ser Leu Val Ser Leu His Cys Leu Ala Cys Gly Lys Ser Leu
 185         190         195
Lys Thr Pro Arg Val Val Gly Gly Glu Glu Ala Ser Val Asp Ser
 200         205         210
Trp Pro Trp Gln Val Ser Ile Gln Tyr Asp Lys Gln His Val Cys
 215         220         225
    
```

-continued

Gly Gly Ser Ile Leu Asp Pro His Trp Val Leu Thr Ala Ala His
 230 235 240

Cys Phe Arg Lys His Thr Asp Val Phe Asn Trp Lys Val Arg Ala
 245 250 255

Gly Ser Asp Lys Leu Gly Ser Phe Pro Ser Leu Ala Val Ala Lys
 260 265 270

Ile Ile Ile Ile Glu Phe Asn Pro Met Tyr Pro Lys Asp Asn Asp
 275 280 285

Ile Ala Leu Met Lys Leu Gln Phe Pro Leu Thr Phe Ser Gly Thr
 290 295 300

Val Arg Pro Ile Cys Leu Pro Phe Phe Asp Glu Glu Leu Thr Pro
 305 310 315

Ala Thr Pro Leu Trp Ile Ile Gly Trp Gly Phe Thr Lys Gln Asn
 320 325 330

Gly Gly Lys Met Ser Asp Ile Leu Leu Gln Ala Ser Val Gln Val
 335 340 345

Ile Asp Ser Thr Arg Cys Asn Ala Asp Asp Ala Tyr Gln Gly Glu
 350 355 360

Val Thr Glu Lys Met Met Cys Ala Gly Ile Pro Glu Gly Gly Val
 365 370 375

Asp Thr Cys Gln Gly Asp Ser Gly Gly Pro Leu Met Tyr Gln Ser
 380 385 390

Asp Gln Trp His Val Val Gly Ile Val Ser Trp Gly Tyr Gly Cys
 395 400 405

Gly Gly Pro Ser Thr Pro Gly Val Tyr Thr Lys Val Ser Ala Tyr
 410 415 420

Leu Asn Trp Ile Tyr Asn Val Trp Lys Ala Glu Leu
 425 430

<210> SEQ ID NO 113
 <211> LENGTH: 1768
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 113

```

ggctggactg gaactcctgg tcccaagtga tccaccgcc tcagcctccc           50
aaggtgctgt gattataggt gtaagccacc gtgtctggcc tctgaacaac           100
ttttcagca actaaaaaag ccacaggagt tgaactgcta ggattctgac           150
tatgctgtgg tggctagtgc tcctactcct acctacatta aaatctgttt           200
ttgttctct tgtaactagc ctttaccttc ctaacacaga ggatctgtca           250
ctgtggctct ggcccaaacc tgaccttcac tctggaacga gaacagaggt           300
ttctaccac accgtcccct cgaagccggg gacagcctca ccttgctggc           350
ctctcgctgg agcagtgcc tcaccaactg tctcacgtct ggaggcactg           400
actcgggcag tgcaggtagc tgagcctctt ggtagctgcg gctttcaagg           450
tgggccttgc cctggccgta gaagggattg acaagccoga agatttcata           500
ggcgatggct cccactgccc aggcacagc cttgctgtag tcaatcactg           550
ccctggggcc aggacgggcc gtggacacct gctcagaagc agtgggtgag           600
acatcacgct gcccgccat ctaacctttt catgtcctgc acatcacctg           650
    
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atccatgggc taatctgaac tctgtcccaa ggaaccaga gcttgagtga      700
gctgtggctc agaccagaa ggggtctgct tagaccacct ggtttatgtg      750
acaggacttg cattctcctg gaacatgagg gaacgccgga gaaagcaaaa      800
gtggcagggg aggaacttgt gccaaattat gggtcagaaa agatggaggt      850
gttgggttat cacaaggcat cgagtctcct gcattcagtg gacatgtggg      900
ggaagggctg ccgatggcgc atgacacact cgggactcac ctctggggcc      950
atcacagacg cgtttccgcc ccgatccacg taccagctgc tgaagggcaa     1000
ctgcaggccg atgctctcat cagccaggca gcagcaaaa tctgcgatca     1050
ccagccaggg gcagccgtct gggaaaggag aagcaaatg accatttctc     1100
ctccccctct tccctctgag aggcctcct atgtccctac taaagccacc     1150
agcaagacat agctgacagg ggctaattgg tcagtgttgg cccaggaggt     1200
cagcaaggcc tgagagctga tcagaagggc ctgctgtgcy aacacggaaa     1250
tgccctcagt aagcacaggc tgcaaatcc ccaggcaaag gactgtgtgg     1300
ctcaatttaa atcatgttct agtaattgga gctgtcccca agaccaaggg     1350
agctagagct tggttcaaat gatctccaag ggccttata ccccaggaga     1400
ctttgatttg aatttgaac cccaaatcca aacctaagaa ccaggtgcat     1450
taagaatcag ttattgccgg gtgtggtggc ctgtaatgcc aacattttgg     1500
gaggccgagg cgggtagatc acctgaggtc aggagttaa gaccagcctg     1550
gccaacatg  tgaaacccct gtcttacta aaaatacaaa aaaactagcc     1600
aggcatggtg gtgtgtgcct gtatcccagc tactcgggag gctgagacag     1650
gagaattact tgaacctggg aggtgaagga ggctgagaca ggagaatcac     1700
ttcagcctga gcaacacagc gagactctgt ctcaaaaaa ataaaaaaag     1750
aattatggtt atttghaa     1768

```

<210> SEQ ID NO 114

<211> LENGTH: 109

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 114

```

Met Leu Trp Trp Leu Val Leu Leu Leu Pro Thr Leu Lys Ser
 1           5           10           15
Val Phe Cys Ser Leu Val Thr Ser Leu Tyr Leu Pro Asn Thr Glu
 20          25          30
Asp Leu Ser Leu Trp Leu Trp Pro Lys Pro Asp Leu His Ser Gly
 35          40          45
Thr Arg Thr Glu Val Ser Thr His Thr Val Pro Ser Lys Pro Gly
 50          55          60
Thr Ala Ser Pro Cys Trp Pro Leu Ala Gly Ala Val Pro Ser Pro
 65          70          75
Thr Val Ser Arg Leu Glu Ala Leu Thr Arg Ala Val Gln Val Ala
 80          85          90
Glu Pro Leu Gly Ser Cys Gly Phe Gln Gly Gly Pro Cys Pro Gly
 95          100         105
Arg Arg Arg Asp

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<210> SEQ ID NO 115
 <211> LENGTH: 1197
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 115

```

cagcagtggt ctctcagtcc tctcaaagca aggaaagagt actgtgtgct      50
gagagaccat ggcaaagaat cctccagaga attgtgaaga ctgtcacatt      100
ctaaatgcag aagcttttaa atccaagaaa atatgtaaat cacttaagat      150
ttgtggactg gtgtttgta tcctggccct aactctaatt gtcctgtttt      200
gggggagcaa gcacttctgg cgggaggtac ccaaaaaagc ctatgacatg      250
gagcacactt tctacagcaa tggagagaag aagaagattht acatggaaat      300
tgatcctgtg accagaactg aaatattcag aagcggaaat ggcactgatg      350
aaacattgga agtgcacgac tttaaaaacg gatacactgg catctacttc      400
gtgggtcttc aaaaatgttt tatcaaaact cagattaaag tgattcctga      450
atthttctgaa ccagaagagg aaatagatga gaatgaagaa attaccacaa      500
ctthtttga acagtcatg atttgggtcc cagcagaaaa gcctattgaa      550
aaccgagatt ttcttaaaaa ttccaaaatt ctggagattht gtgataacgt      600
gaccatgtat tggatcaatc cactctaat atcagthttct gagttacaag      650
actthtgagga ggaggagaa gatcttcaat ttctgcca cgaaaaaaaaa      700
gggattgaac aaaaatgaaca gtgggtggtc cctcaagtga aagtagagaa      750
gaccctgac gccagacaag caagtgagga agaacttcca ataatgact      800
atactgaaaa tggaatagaa thtgatccca tgctggatga gagaggtht      850
tgthtgattht actgccgtcg aggcaaccgc thttgccgc gcgtctgtga      900
acctthtacta ggctactacc catatccata ctgctaccaa ggaggacgag      950
tcatctgtcg tgtcatcatg ccttgtaact ggtgggtggc ccgcatgctg     1000
gggagggtct aataggaggt thgagctcaa atgcttaaac tgctggcaac     1050
atataataaa tgcattctat tcaatgaatt tctgcctatg aggcattctg     1100
cccctgtgag ccagctctcc agaattactt gtaggtaatt cctctcttca     1150
tgthtctaata aacttctaca ttatcaccaa aaaaaaaaaa aaaaaaa      1197
    
```

<210> SEQ ID NO 116
 <211> LENGTH: 317
 <212> TYPE: PRT
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 116

```

Met Ala Lys Asn Pro Pro Glu Asn Cys Glu Asp Cys His Ile Leu
 1          5          10         15
Asn Ala Glu Ala Phe Lys Ser Lys Lys Ile Cys Lys Ser Leu Lys
          20          25          30
Ile Cys Gly Leu Val Phe Gly Ile Leu Ala Leu Thr Leu Ile Val
          35          40          45
Leu Phe Trp Gly Ser Lys His Phe Trp Pro Glu Val Pro Lys Lys
          50          55          60
    
```

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Ala Tyr Asp Met Glu His Thr Phe Tyr Ser Asn Gly Glu Lys Lys
 65 70 75

Lys Ile Tyr Met Glu Ile Asp Pro Val Thr Arg Thr Glu Ile Phe
 80 85 90

Arg Ser Gly Asn Gly Thr Asp Glu Thr Leu Glu Val His Asp Phe
 95 100 105

Lys Asn Gly Tyr Thr Gly Ile Tyr Phe Val Gly Leu Gln Lys Cys
 110 115 120

Phe Ile Lys Thr Gln Ile Lys Val Ile Pro Glu Phe Ser Glu Pro
 125 130 135

Glu Glu Glu Ile Asp Glu Asn Glu Glu Ile Thr Thr Thr Phe Phe
 140 145 150

Glu Gln Ser Val Ile Trp Val Pro Ala Glu Lys Pro Ile Glu Asn
 155 160 165

Arg Asp Phe Leu Lys Asn Ser Lys Ile Leu Glu Ile Cys Asp Asn
 170 175 180

Val Thr Met Tyr Trp Ile Asn Pro Thr Leu Ile Ser Val Ser Glu
 185 190 195

Leu Gln Asp Phe Glu Glu Glu Gly Glu Asp Leu His Phe Pro Ala
 200 205 210

Asn Glu Lys Lys Gly Ile Glu Gln Asn Glu Gln Trp Val Val Pro
 215 220 225

Gln Val Lys Val Glu Lys Thr Arg His Ala Arg Gln Ala Ser Glu
 230 235 240

Glu Glu Leu Pro Ile Asn Asp Tyr Thr Glu Asn Gly Ile Glu Phe
 245 250 255

Asp Pro Met Leu Asp Glu Arg Gly Tyr Cys Cys Ile Tyr Cys Arg
 260 265 270

Arg Gly Asn Arg Tyr Cys Arg Arg Val Cys Glu Pro Leu Leu Gly
 275 280 285

Tyr Tyr Pro Tyr Pro Tyr Cys Tyr Gln Gly Gly Arg Val Ile Cys
 290 295 300

Arg Val Ile Met Pro Cys Asn Trp Trp Val Ala Arg Met Leu Gly
 305 310 315

Arg Val

<210> SEQ ID NO 117
 <211> LENGTH: 2121
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 117

```

gagctcccct caggagcgcg ttagcttcac accttcggca gcaggagggc      50
ggcagcttct cgcaggcggc agggcgggcg gccaggatca tgtccaccac      100
cacatgccaa gtggtggcgt tcctcctgtc catcctgggg ctggccggct      150
gcacgcgggc caccgggatg gacatgtgga gcaccagga cctgtacgac      200
aaccccgtca cctccgtggt ccagtacgaa gggctctgga ggagctgcgt      250
gaggcagagt tcaggcttca ccgaatgcag gccctatttc accatcctgg      300
gacttcagc  catgctgcag gcagtgcgag ccctgatgat cgtaggcatc      350
    
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gtcctgggtg ccattggcct cctggtatcc atctttgccc tgaatgcat	400
ccgcattggc agcatggagg actctgcaa agccaacatg aactgacct	450
ccggatcat gttcattgtc tcaggctttt gtgcaattgc tggagtgtct	500
gtgtttgcca acatgctggt gactaacttc tggatgtcca cagctaacat	550
gtacaccggc atgggtggga tgggtcagac tgttcagacc aggtacacat	600
ttggtggcgc tctgttcgtg ggctgggtcg ctggaggcct cacactaatt	650
gggggtgtga tgatgtgcat cgctgcccgg ggctggcac cagaagaaac	700
caactacaaa gccgtttcct atcatgcctc aggccacagt gttgcctaca	750
agcctggagg cttcaaggcc agcactggct ttgggtcaa caccaaaaac	800
aagaagatat acgatggagg tgcgccaca gaggacgagg tacaatctta	850
tccttccaag cactgactatg tgtaatgctc taagacctct cagcacgggc	900
ggaagaaact cccggagagc tcacccaaaa aacaaggaga tcccatctag	950
atctctctct gcttttgact cacagctgga agttagaaaa gcctcgattt	1000
catctttgga gaggccaaat ggtcttagcc tcagtctctg tctctaaata	1050
ttccaccata aaacagctga gttatattat aattagaggc tatagctcac	1100
attttcaact ctctatttct ttttttaaat ataactttct actctgatga	1150
gagaatgtgg ttttaatctc tctctcacat tttgatgatt tagacagact	1200
ccccctcttc ctctagtca ataaacccat tgatgatcta tttcccagct	1250
tatccccaa aaaacttttg aaaggaaaga gtagaccaa agatgttatt	1300
ttctgctggt tgaattttgt ctccccacc ccaacttggc tagtaataaa	1350
cacttactga agaagaagca ataagagaaa gatatttga atctctccag	1400
cccctgatct cggttttcct aactgtgat cttaaaagt accaaaacaa	1450
agtcattttc agtttgaggc aaccaaactc ttctactgct gttgacatct	1500
tcttattaca gcaacacatc tctaggagtt tctgagctc tccactggag	1550
tctctttctc gtcgcggtc agaaattgtc cctagatgaa tgagaaaatt	1600
atttttttta atttaagtcc taaatatagt taaaataaat aatgttttag	1650
taaaatgata cactatctct gtgaaatagc ctcccccta catgtggata	1700
gaagaaaatg aaaaaataat tgctttgaca ttgtctatat ggtactttgt	1750
aaagtcatgc ttaagtacaa attccatgaa aagctcacac ctgtaatcct	1800
agcactttgg gaggctgagg aggaaggatc acttgagccc agaagttcga	1850
gactagcctg ggcaacatgg agaagccctg tctctacaaa atacagagag	1900
aaaaaatcag ccagtcatgg tggcatacac ctgtagtccc agcattccgg	1950
gaggctgagg tgggagatc acttgagccc agggaggttg gggctgcagt	2000
gagccatgat cacaccactg cactccagcc aggtgacata gcgagatcct	2050
gtctaaaaaa ataaaaaata aataatggaa cacagcaagt cctaggaagt	2100
aggttaaac taattcttta a	2121

<210> SEQ ID NO 118

<211> LENGTH: 261

<212> TYPE: PRT

-continued

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 118

Met Ser Thr Thr Thr Cys Gln Val Val Ala Phe Leu Leu Ser Ile
 1 5 10 15
 Leu Gly Leu Ala Gly Cys Ile Ala Ala Thr Gly Met Asp Met Trp
 20 25 30
 Ser Thr Gln Asp Leu Tyr Asp Asn Pro Val Thr Ser Val Phe Gln
 35 40 45
 Tyr Glu Gly Leu Trp Arg Ser Cys Val Arg Gln Ser Ser Gly Phe
 50 55 60
 Thr Glu Cys Arg Pro Tyr Phe Thr Ile Leu Gly Leu Pro Ala Met
 65 70 75
 Leu Gln Ala Val Arg Ala Leu Met Ile Val Gly Ile Val Leu Gly
 80 85 90
 Ala Ile Gly Leu Leu Val Ser Ile Phe Ala Leu Lys Cys Ile Arg
 95 100 105
 Ile Gly Ser Met Glu Asp Ser Ala Lys Ala Asn Met Thr Leu Thr
 110 115 120
 Ser Gly Ile Met Phe Ile Val Ser Gly Leu Cys Ala Ile Ala Gly
 125 130 135
 Val Ser Val Phe Ala Asn Met Leu Val Thr Asn Phe Trp Met Ser
 140 145 150
 Thr Ala Asn Met Tyr Thr Gly Met Gly Gly Met Val Gln Thr Val
 155 160 165
 Gln Thr Arg Tyr Thr Phe Gly Ala Ala Leu Phe Val Gly Trp Val
 170 175 180
 Ala Gly Gly Leu Thr Leu Ile Gly Gly Val Met Met Cys Ile Ala
 185 190 195
 Cys Arg Gly Leu Ala Pro Glu Glu Thr Asn Tyr Lys Ala Val Ser
 200 205 210
 Tyr His Ala Ser Gly His Ser Val Ala Tyr Lys Pro Gly Gly Phe
 215 220 225
 Lys Ala Ser Thr Gly Phe Gly Ser Asn Thr Lys Asn Lys Lys Ile
 230 235 240
 Tyr Asp Gly Gly Ala Arg Thr Glu Asp Glu Val Gln Ser Tyr Pro
 245 250 255
 Ser Lys His Asp Tyr Val
 260

<210> SEQ ID NO 119

<211> LENGTH: 2010

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 119

ggaaaaactg ttctctctcg tggcacagag aacctgctt caaagcagaa 50
 gtagcagttc cggagtccag ctggctaaaa ctcatcccag aggataatg 100
 caacccatgc cttagaaatc gctgggctgt ttcttggtgg tgttggatg 150
 gtgggcacag tggctgtcac tgtcatgcct cagtggagag tgtcggcctt 200
 cattgaaaac aacatcgtgg tttttgaaaa cttctgggaa ggactgtgga 250

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tgaattgctg	gaggcaggct	aacatcagga	tgcaagtcaa	aatctatgat	300
tccctgctgg	ctctttctcc	ggacctacag	gcagccagag	gactgatgtg	350
tgctgcttcc	gtgatgtcct	tcttgctttt	catgatggcc	atccttggca	400
tgaaatgcac	caggtgcacg	ggggacaatg	agaaggtgaa	ggctcacatt	450
ctgctgacgg	ctggaatcat	cttcatcatc	acgggcatgg	tggtgctcat	500
ccctgtgagc	tggtttgcca	atgccatcat	cagagatttc	tataactcaa	550
tagtgaatgt	tgcccaaaaa	cgtgagcttg	gagaagctct	ctacttagga	600
tggaccacgg	cactggtgct	gattgttggg	ggagctctgt	tctgctgcgt	650
ttttgttggc	aacgaaaaga	gcagtagcta	cagatactcg	ataccttccc	700
atcgacaac	caaaaaaagt	tatcacaccg	gaaagaagtc	accgagcgtc	750
tactccagaa	gtcagtatgt	gtagttgtgt	atgttttttt	aactttacta	800
taaagccatg	caaatgacaa	aaatctatat	tactttctca	aaatggacc	850
caaaagaaat	ttgatttact	gttcttaact	gctaatctt	aattacagga	900
actgtgcac	agctatttat	gattctataa	gctatttcag	cagaatgaga	950
tattaaacc	aatgctttga	ttgttctaga	aagtatagta	atttgttttc	1000
taaggtgggt	caagcatcta	ctotttttat	catttacttc	aaaatgacat	1050
tgctaaagac	tgcaattatt	tactactgta	atttctccac	gacatagcat	1100
tatgtacata	gatgagtgtg	acatttatat	ctcacataga	gacatgctta	1150
tatgtgttta	tttaaaatga	aatgccagtc	cattacactg	aataaataga	1200
actcaactat	tgcttttcag	ggaaatcatg	gatagggttg	aagaaggtta	1250
ctattaattg	tttaaaaaa	gcttagggat	taatgtcctc	cattttataat	1300
gaagattaaa	atgaaggctt	taatcagcat	tgtaaaggaa	attgaatggc	1350
tttctgatat	gctgtttttt	agcctaggag	ttagaaatcc	taacttcttt	1400
atcctcttct	cccagaggct	ttttttttct	tgtgtattaa	attaacattt	1450
ttaaaacgca	gatattttgt	caaggggctt	tgcaattcaa	ctgcttttcc	1500
agggtatata	tcagaagaaa	gataaaagtg	tgatctaaga	aaaagtgatg	1550
gttttaggaa	agtgaaaata	tttttgtttt	tgtatttgaa	gaagaatgat	1600
gcattttgac	aagaaatcat	atatgtatgg	atatatttta	ataagtattt	1650
gagtacagac	tttgaggttt	catcaatata	aataaaagag	cagaaaaata	1700
tgtcttggtt	ttcatttgct	taccaaaaa	acaacaaca	aaaaagtgtg	1750
cotttgagaa	cttcacctgc	tcctatgtgg	gtacctgagt	caaaattgct	1800
atttttgttc	tgtgaaaaat	aaatttcctt	ctgtaccat	ttctgtttag	1850
ttttactaaa	atctgtaaat	actgtatttt	tctgtttatt	ccaaatttga	1900
tgaaactgac	aatccaattt	gaaagtgttg	gtcgacgtct	gtctagctta	1950
aatgaatgtg	ttctatttgc	tttatacatt	tatattaata	aattgtacat	2000
ttttctaatt					2010

<210> SEQ ID NO 120

<211> LENGTH: 225

<212> TYPE: PRT

-continued

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 120

Met Ala Thr His Ala Leu Glu Ile Ala Gly Leu Phe Leu Gly Gly
 1 5 10 15
 Val Gly Met Val Gly Thr Val Ala Val Thr Val Met Pro Gln Trp
 20 25 30
 Arg Val Ser Ala Phe Ile Glu Asn Asn Ile Val Val Phe Glu Asn
 35 40 45
 Phe Trp Glu Gly Leu Trp Met Asn Cys Val Arg Gln Ala Asn Ile
 50 55 60
 Arg Met Gln Cys Lys Ile Tyr Asp Ser Leu Leu Ala Leu Ser Pro
 65 70 75
 Asp Leu Gln Ala Ala Arg Gly Leu Met Cys Ala Ala Ser Val Met
 80 85 90
 Ser Phe Leu Ala Phe Met Met Ala Ile Leu Gly Met Lys Cys Thr
 95 100 105
 Arg Cys Thr Gly Asp Asn Glu Lys Val Lys Ala His Ile Leu Leu
 110 115 120
 Thr Ala Gly Ile Ile Phe Ile Ile Thr Gly Met Val Val Leu Ile
 125 130 135
 Pro Val Ser Trp Val Ala Asn Ala Ile Ile Arg Asp Phe Tyr Asn
 140 145 150
 Ser Ile Val Asn Val Ala Gln Lys Arg Glu Leu Gly Glu Ala Leu
 155 160 165
 Tyr Leu Gly Trp Thr Thr Ala Leu Val Leu Ile Val Gly Gly Ala
 170 175 180
 Leu Phe Cys Cys Val Phe Cys Cys Asn Glu Lys Ser Ser Ser Tyr
 185 190 195
 Arg Tyr Ser Ile Pro Ser His Arg Thr Thr Gln Lys Ser Tyr His
 200 205 210
 Thr Gly Lys Lys Ser Pro Ser Val Tyr Ser Arg Ser Gln Tyr Val
 215 220 225

<210> SEQ ID NO 121

<211> LENGTH: 1257

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 121

ggagagaggg gcgcggtga aaggcgatt gatgcagcct gcggcggcct 50
 cggagcgcgg cggagccaga cgctgaccac gttcctctcc tcggctcct 100
 ccgcctccag ctccgcgctg cccggcagcc gggagccatg cgaccccagg 150
 gcccgcgcc ctccccgag cggtccgcg gcctcctgct gctcctgctg 200
 ctgcagctgc ccgcgcgctc gagcgcctct gagatcocca aggggaagca 250
 aaaggcgag ctccggcaga gggaggtggt ggacctgtat aatggaatgt 300
 gttacaagg gccagcagga gtgcctggtc gagacgggag ccctggggcc 350
 aatgttattc cgggtacacc tgggatccca ggtcgggatg gattcaaagg 400
 agaaaagggg gaatgtctga gggaaagctt tgaggagtcc tggacacca 450
 actacaagca gtgttcattg agttcattga attatggcat agatcttggg 500

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aaaattgctg agtgtacatt tacaaagatg cgttcaaata gtgctctaag      550
agttttgttc agtggctcac ttgggctaaa atgcagaaat gcatgctgtc      600
agcgttggtta tttcacattc aatggagctg aatgttcagg acctcttccc      650
attgaagcta taattttatt ggaccaagga agccctgaaa tgaattcaac      700
aattaatatt catcgcaactt cttctgtgga aggactttgt gaaggaattg      750
gtgctgggatt agtggatggt gctatctggg ttggcacttg ttcagattac      800
ccaaaaggag atgcttctac tggatggaat tcagtttctc gcatcattat      850
tgaagaacta ccaaaataaa tgctttaatt ttcatttctc acctcttttt      900
ttattatgoc ttggaatggt tcacttaaat gacattttaa ataagtttat      950
gtatacatct gaatgaaaag caaagctaaa tatgtttaca gaccaaagtg     1000
tgatttcaca ctgtttttaa atctagcatt attcattttg cttcaatcaa     1050
aagtggtttc aatatttttt ttagttggtt agaatacttt cttcatagtc     1100
acattctctc aacctataat ttggaatatt gttgtgtctt tttgtttttt     1150
ctcttagtat agcattttta aaaaaatata aaagctacca atctttgtac     1200
aatttgtaaa tgtaagaat tttttttata tctgttaaat aaaaattatt     1250
tccaaca                                             1257
    
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<210> SEQ ID NO 122
<211> LENGTH: 243
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien
    
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<400> SEQUENCE: 122

```

Met Arg Pro Gln Gly Pro Ala Ala Ser Pro Gln Arg Leu Arg Gly
 1          5          10
Leu Leu Leu Leu Leu Leu Leu Gln Leu Pro Ala Pro Ser Ser Ala
          20          25          30
Ser Glu Ile Pro Lys Gly Lys Gln Lys Ala Gln Leu Arg Gln Arg
          35          40          45
Glu Val Val Asp Leu Tyr Asn Gly Met Cys Leu Gln Gly Pro Ala
          50          55          60
Gly Val Pro Gly Arg Asp Gly Ser Pro Gly Ala Asn Val Ile Pro
          65          70          75
Gly Thr Pro Gly Ile Pro Gly Arg Asp Gly Phe Lys Gly Glu Lys
          80          85          90
Gly Glu Cys Leu Arg Glu Ser Phe Glu Glu Ser Trp Thr Pro Asn
          95          100          105
Tyr Lys Gln Cys Ser Trp Ser Ser Leu Asn Tyr Gly Ile Asp Leu
          110          115          120
Gly Lys Ile Ala Glu Cys Thr Phe Thr Lys Met Arg Ser Asn Ser
          125          130          135
Ala Leu Arg Val Leu Phe Ser Gly Ser Leu Arg Leu Lys Cys Arg
          140          145          150
Asn Ala Cys Cys Gln Arg Trp Tyr Phe Thr Phe Asn Gly Ala Glu
          155          160          165
Cys Ser Gly Pro Leu Pro Ile Glu Ala Ile Ile Tyr Leu Asp Gln
          170          175          180
    
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Gly Ser Pro Glu Met Asn Ser Thr Ile Asn Ile His Arg Thr Ser
 185 190 195
 Ser Val Glu Gly Leu Cys Glu Gly Ile Gly Ala Gly Leu Val Asp
 200 205 210
 Val Ala Ile Trp Val Gly Thr Cys Ser Asp Tyr Pro Lys Gly Asp
 215 220 225
 Ala Ser Thr Gly Trp Asn Ser Val Ser Arg Ile Ile Ile Glu Glu
 230 235 240
 Leu Pro Lys

<210> SEQ ID NO 123
 <211> LENGTH: 2379
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 123

gctgagcgtg tgcgcggtac ggggctctcc tgccttctgg gctccaacgc 50
 agctctgtgg ctgaactggg tgctcatcac gggaaactgct gggctatgga 100
 atacagatgt ggcagctcag gtagcccaaa attgcttggga agaatacatc 150
 atgtttttgg ataagaagaa attgtaggat ccagtttttt ttttaaccgc 200
 cccctcccca cccccaaaa aaactgtaaa gatgcaaaaa cgtaatatcc 250
 atgaagatcc tattacctag gaagattttg atgttttggc gcgaatgcgg 300
 tgttgggatt tatttgttct tggagtgttc tgcgtggctg gcaaagaata 350
 atgttccaaa atcgggtccat ctccaaggg gtccaatttt tcttctggg 400
 tgtcagcggc ccctgactca ctacagtgca gctgacaggg gctgtcatgc 450
 aactggcccc taagccaaag caaaagacct aaggacgacc tttgaacaat 500
 acaaaggatg ggtttcaatg taattaggct actgagcggg tcagctgtag 550
 cactgggtat agccccact gtcttactga caatgctttc tctgcccga 600
 cgaggatgcc ctaagggctg taggtgtgaa ggcaaatgg tatattgtga 650
 atctcagaaa ttacaggaga taccctcaag tataatctgct gtttgcttag 700
 gtttgcctc tcgctataac agcctcaaaa aacttaagta taatcaattt 750
 aaagggtcca accagctcac ctggctatac cttgaccata accatatcag 800
 caatattgac gaaaatgctt ttaatggaat acgcagactc aaagagctga 850
 ttcttagttc caatagaatc tcctattttc ttaacaatac ctccagacct 900
 gtgacaaaatt tacggaactt ggatctgtcc tataatcagc tgcattctct 950
 gggatctgaa cagtttcggg gcttgccgaa gctgctgagt ttacatttac 1000
 ggtctaactc cctgagaacc atccctgtgc gaatattcca agactgccgc 1050
 aacctggaac ttttggacct gggatataac cggatccgaa gtttagccag 1100
 gaatgtcttt gctggcatga tcagactcaa agaacttcac ctggagcaca 1150
 atcaattttc caagctcaac ctggcccttt ttccaagggt ggtoagcctt 1200
 cagaaccttt acttgacgtg gaataaaatc agtgtcatag gacagacct 1250
 gtccctggacc tggagctcct taaaaaggct tgatttatca ggcaatgaga 1300
 tcgaagcttt cagtggacct agtgttttcc agtgtgtccc gaatctgcag 1350

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cgctcaacc tggattccaa caagctcaca tttattggtc aagagatddd      1400
ggattccttg atatccctca atgacatcag tcttgctggg aatatatggg      1450
aatgcagcag aaatatttgc tcccttgtaa actggctgaa aagttttaa      1500
ggtctaaggg agaatacaat tatctgtgcc agtcccaaag agctgcaagg      1550
agtaaatgtg atcgatgcag tgaagaacta cagcatctgt ggcaaaagta      1600
ctacagagag gttgatctg gccagggctc tcccaaagcc gacgtttaag      1650
cccaagctcc ccaggccgaa gcatgagagc aaacccctt tgccccgac      1700
ggtgaggacc acagagcccg gccagagagc cgatgctgac gccgagcaca      1750
tctctttcca taaatcatc gcgggacgcg tggcgctttt cctgtccgtg      1800
ctcgtcatcc tgctggttat ctacgtgtca tggaagcggg accctgcgag      1850
catgaagcag ctgcagcagc gctccctcat gogaaggcac aggaaaaaga      1900
aaagacagtc cctaaagcaa atgactccca gcaccagga attttatgta      1950
gattataaac ccaccaacac ggagaccagc gagatgctgc tgaatgggac      2000
gggaccctgc acctataaca aatcgggctc cagggagtgt gaggtatgaa      2050
ccattgtgat aaaaagagct cttaaaagct gggaaataag tggtgcttta      2100
ttgaactctg gtgactatca agggaacgcg atgccccccc tccccttccc      2150
tctccctctc actttggtgg caagatcctt cctgtccgtt ttagtgcat      2200
tcataatact ggtcattttc ctctcataca taatcaacc attgaaattt      2250
aaataccaca atcaatgtga agcttgaact ccggtttaat ataataccta      2300
ttgtataaga ccctttactg attccattaa tgctgcattt gttttaagat      2350
aaaacttctt tcataggtaa aaaaaaaaa      2379

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<210> SEQ ID NO 124

<211> LENGTH: 513

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 124

```

Met Gly Phe Asn Val Ile Arg Leu Leu Ser Gly Ser Ala Val Ala
  1             5             10             15
Leu Val Ile Ala Pro Thr Val Leu Leu Thr Met Leu Ser Ser Ala
  20            25            30
Glu Arg Gly Cys Pro Lys Gly Cys Arg Cys Glu Gly Lys Met Val
  35            40
Tyr Cys Glu Ser Gln Lys Leu Gln Glu Ile Pro Ser Ser Ile Ser
  50            55            60
Ala Gly Cys Leu Gly Leu Ser Leu Arg Tyr Asn Ser Leu Gln Lys
  65            70            75
Leu Lys Tyr Asn Gln Phe Lys Gly Leu Asn Gln Leu Thr Trp Leu
  80            85            90
Tyr Leu Asp His Asn His Ile Ser Asn Ile Asp Glu Asn Ala Phe
  95           100           105
Asn Gly Ile Arg Arg Leu Lys Glu Leu Ile Leu Ser Ser Asn Arg
 110           115           120
Ile Ser Tyr Phe Leu Asn Asn Thr Phe Arg Pro Val Thr Asn Leu

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										125						130						135	
Arg	Asn	Leu	Asp	Leu	Ser	Tyr	Asn	Gln	Leu	His	Ser	Leu	Gly	Ser	140	Leu	His	Ser	Leu	Gly	Ser	145	150
Glu	Gln	Phe	Arg	Gly	Leu	Arg	Lys	Leu	Leu	Ser	Leu	His	Leu	Arg	155	Leu	Ser	Leu	His	Leu	Arg	160	165
Ser	Asn	Ser	Leu	Arg	Thr	Ile	Pro	Val	Arg	Ile	Phe	Gln	Asp	Cys	170	Arg	Ile	Phe	Gln	Asp	Cys	175	180
Arg	Asn	Leu	Glu	Leu	Leu	Asp	Leu	Gly	Tyr	Asn	Arg	Ile	Arg	Ser	185	Leu	Asn	Arg	Ile	Arg	Ser	190	195
Leu	Ala	Arg	Asn	Val	Phe	Ala	Gly	Met	Ile	Arg	Leu	Lys	Glu	Leu	200	Ile	Arg	Leu	Lys	Glu	Leu	205	210
His	Leu	Glu	His	Asn	Gln	Phe	Ser	Lys	Leu	Asn	Leu	Ala	Leu	Phe	215	Leu	Asn	Leu	Ala	Leu	Phe	220	225
Pro	Arg	Leu	Val	Ser	Leu	Gln	Asn	Leu	Tyr	Leu	Gln	Trp	Asn	Lys	230	Leu	Gln	Trp	Asn	Lys	235	240	
Ile	Ser	Val	Ile	Gly	Gln	Thr	Met	Ser	Trp	Thr	Trp	Ser	Ser	Leu	245	Trp	Thr	Trp	Ser	Ser	Leu	250	255
Gln	Arg	Leu	Asp	Leu	Ser	Gly	Asn	Glu	Ile	Glu	Ala	Phe	Ser	Gly	260	Ile	Glu	Ala	Phe	Ser	Gly	265	270
Pro	Ser	Val	Phe	Gln	Cys	Val	Pro	Asn	Leu	Gln	Arg	Leu	Asn	Leu	275	Leu	Gln	Arg	Leu	Asn	Leu	280	285
Asp	Ser	Asn	Lys	Leu	Thr	Phe	Ile	Gly	Gln	Glu	Ile	Leu	Asp	Ser	290	Gln	Glu	Ile	Leu	Asp	Ser	295	300
Trp	Ile	Ser	Leu	Asn	Asp	Ile	Ser	Leu	Ala	Gly	Asn	Ile	Trp	Glu	305	Ala	Gly	Asn	Ile	Trp	Glu	310	315
Cys	Ser	Arg	Asn	Ile	Cys	Ser	Leu	Val	Asn	Trp	Leu	Lys	Ser	Phe	320	Asn	Trp	Leu	Lys	Ser	Phe	325	330
Lys	Gly	Leu	Arg	Glu	Asn	Thr	Ile	Ile	Cys	Ala	Ser	Pro	Lys	Glu	335	Cys	Ala	Ser	Pro	Lys	Glu	340	345
Leu	Gln	Gly	Val	Asn	Val	Ile	Asp	Ala	Val	Lys	Asn	Tyr	Ser	Ile	350	Val	Lys	Asn	Tyr	Ser	Ile	355	360
Cys	Gly	Lys	Ser	Thr	Thr	Glu	Arg	Phe	Asp	Leu	Ala	Arg	Ala	Leu	365	Leu	Ala	Arg	Ala	Leu	370	375	
Pro	Lys	Pro	Thr	Phe	Lys	Pro	Lys	Leu	Pro	Arg	Pro	Lys	His	Glu	380	Pro	Arg	Pro	Lys	His	Glu	385	390
Ser	Lys	Pro	Pro	Leu	Pro	Pro	Thr	Val	Gly	Ala	Thr	Glu	Pro	Gly	395	Gly	Ala	Thr	Glu	Pro	Gly	400	405
Pro	Glu	Thr	Asp	Ala	Asp	Ala	Glu	His	Ile	Ser	Phe	His	Lys	Ile	410	Ile	Ser	Phe	His	Lys	Ile	415	420
Ile	Ala	Gly	Ser	Val	Ala	Leu	Phe	Leu	Ser	Val	Leu	Val	Ile	Leu	425	Ser	Val	Leu	Val	Ile	Leu	430	435
Leu	Val	Ile	Tyr	Val	Ser	Trp	Lys	Arg	Tyr	Pro	Ala	Ser	Met	Lys	440	Tyr	Pro	Ala	Ser	Met	Lys	445	450
Gln	Leu	Gln	Gln	Arg	Ser	Leu	Met	Arg	Arg	His	Arg	Lys	Lys	Lys	455	Arg	His	Arg	Lys	Lys	Lys	460	465
Arg	Gln	Ser	Leu	Lys	Gln	Met	Thr	Pro	Ser	Thr	Gln	Glu	Phe	Tyr	470	Ser	Thr	Gln	Glu	Phe	Tyr	475	480
Val	Asp	Tyr	Lys	Pro	Thr	Asn	Thr	Glu	Thr	Ser	Glu	Met	Leu	Leu	485	Thr	Ser	Glu	Met	Leu	Leu	490	495
Asn	Gly	Thr	Gly	Pro	Cys	Thr	Tyr	Asn	Lys	Ser	Gly	Ser	Arg	Glu	500	Lys	Ser	Gly	Ser	Arg	Glu	505	510

-continued

Cys Glu Val

<210> SEQ ID NO 125

<211> LENGTH: 998

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 125

```

ccgttatcgt cttgcgctac tgctgaatgt ccgtcccgga ggaggaggag      50
aggcttttgc cgctgacctca gagatggccc cgagcgagca aattcctact      100
gtccggctgc gcggtaccg tggccgagct agcaaccttt cccctggatc      150
tcacaaaaac tcgactccaa atgcaaggag aagcagctct tgctcggttg      200
ggagacggtg caagagaatc tgcccctat aggggaatgg tgcgcacagc      250
cctagggatc attgaagagg aaggctttct aaagctttgg caaggagtga      300
caccgcocat ttacagacac gtagtgatt ctggaggtcg aatggtcaca      350
tatgaacatc tccgagaggt tgtgtttggc aaaagtgaag atgagcatta      400
tcccctttgg aatcagtc tggagggat gatggctggt gttattggcc      450
agtttttagc caatccaact gacctagtga aggttcagat gcaaatggaa      500
ggaaaaagga aactggaagg aaaaccattg cgatttcgtg gtgtacatca      550
tgcatattgca aaaatcttag ctgaaggagg aatacagagg ctttgggcag      600
gctgggtacc caatatacaa agagcagcac tgggtaatat gggagattta      650
accacttatg atacagtgaa aactactctg gtattgaata caccacttga      700
ggacaatatc atgactcacg gtttatcaag tttatgttct ggaactggtag      750
cttctattct gggaacacca gccgatgtca tcaaaagcag aataatgaat      800
caaccacgag ataacaagg aaggggactt ttgtataaat catcgactga      850
ctgcttgatt caggctgttc aaggtgaagg attcatgagt ctatataaag      900
gctttttacc atcttgctg agaatgacct cttggtaaat ggtgttctgg      950
cttacttatg aaaaaatcag agagatgagt ggagtcagtc cattttaa      998

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<210> SEQ ID NO 126

<211> LENGTH: 323

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 126

```

Met Ser Val Pro Glu Glu Glu Arg Leu Leu Pro Leu Thr Gln      15
 1          5          10
Arg Trp Pro Arg Ala Ser Lys Phe Leu Leu Ser Gly Cys Ala Ala      30
 20          25          30
Thr Val Ala Glu Leu Ala Thr Phe Pro Leu Asp Leu Thr Lys Thr      45
 35          40          45
Arg Leu Gln Met Gln Gly Glu Ala Ala Leu Ala Arg Leu Gly Asp      60
 50          55          60
Gly Ala Arg Glu Ser Ala Pro Tyr Arg Gly Met Val Arg Thr Ala      75
 65          70          75
Leu Gly Ile Ile Glu Glu Glu Gly Phe Leu Lys Leu Trp Gln Gly      90
 80          85          90

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Val Thr Pro Ala Ile Tyr Arg His Val Val Tyr Ser Gly Gly Arg
 95 100 105

Met Val Thr Tyr Glu His Leu Arg Glu Val Val Phe Gly Lys Ser
 110 115 120

Glu Asp Glu His Tyr Pro Leu Trp Lys Ser Val Ile Gly Gly Met
 125 130 135

Met Ala Gly Val Ile Gly Gln Phe Leu Ala Asn Pro Thr Asp Leu
 140 145 150

Val Lys Val Gln Met Gln Met Glu Gly Lys Arg Lys Leu Glu Gly
 155 160 165

Lys Pro Leu Arg Phe Arg Gly Val His His Ala Phe Ala Lys Ile
 170 175 180

Leu Ala Glu Gly Gly Ile Arg Gly Leu Trp Ala Gly Trp Val Pro
 185 190 195

Asn Ile Gln Arg Ala Ala Leu Val Asn Met Gly Asp Leu Thr Thr
 200 205 210

Tyr Asp Thr Val Lys His Tyr Leu Val Leu Asn Thr Pro Leu Glu
 215 220 225

Asp Asn Ile Met Thr His Gly Leu Ser Ser Leu Cys Ser Gly Leu
 230 235 240

Val Ala Ser Ile Leu Gly Thr Pro Ala Asp Val Ile Lys Ser Arg
 245 250 255

Ile Met Asn Gln Pro Arg Asp Lys Gln Gly Arg Gly Leu Leu Tyr
 260 265 270

Lys Ser Ser Thr Asp Cys Leu Ile Gln Ala Val Gln Gly Glu Gly
 275 280 285

Phe Met Ser Leu Tyr Lys Gly Phe Leu Pro Ser Trp Leu Arg Met
 290 295 300

Thr Pro Trp Ser Met Val Phe Trp Leu Thr Tyr Glu Lys Ile Arg
 305 310 315

Glu Met Ser Gly Val Ser Pro Phe
 320

<210> SEQ ID NO 127
 <211> LENGTH: 1505
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 127

```

cgcggatcgg acccaagcag gtcggcggcg gcggcaggag agcggccggg          50
cgtcagctcc tcgacccccg tgtcgggcta gtccagcgag gcggaacggg          100
ggcgtgggccc catggccagg cccggcatgg agcggtgggc cgaccggctg          150
gcgctgtgta cgggggcctc ggggggcatc ggcgcggccg tggcccgggc          200
cctggtccag cagggactga aggtggtggg ctgcccgcgc actgtgggca          250
acatcgagga gctggctgct gaatgtaaga gtgcaggcta ccccgggact          300
ttgatccccc acagatgtga cctatcaaat gaagaggaca tcctctccat          350
gttctcagct atccgttctc agcacagcgg tgtagacatc tgcatcaaca          400
atgctggctt ggcccggcct gacacctgc tctcaggcag caccagtgg          450
tggaaggaca tgttcaatgt gaacgtgctg gccctcagca tctgcacacg          500
    
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ggaagcctac cagtccatga aggagcggaa tgtggacgat gggcacatca      550
ttaacatcaa tagcatgtct gccaccgag tgttaccctt gtctgtgacc      600
cactttcata gtgccaccaa gtatgccctc actgcgctga cagagggact      650
gaggcaagag cttcgggagg cccagacca catccgagcc acgtgcatct      700
ctccaggtgt ggtggagaca caattgcctt tcaaactcca cgacaaggac      750
cctgagaagg cagctgccac ctatgagcaa atgaagtgtc tcaaaccgca      800
ggatgtggcc gaggtgtta tctacgtcct cagcaccctc gcacacatcc      850
agattggaga catccagatg aggcccacgg agcaggtgac ctagtgactg      900
tgggagctcc tccttcctc cccacccttc atggcttgcc tcctgcctct      950
ggattttagg tgttgatttc tggatcacgg gataaccactt cctgtccaca     1000
ccccgaccag gggctagaaa atttgtttga gatttttata tcatctgttc     1050
aaattgcttc agttgtaaat gtgaaaaatg ggctggggaa aggaggtggt     1100
gtccctaatt gttttacttg ttaacttgtt cttgtgcccc tgggcacttg     1150
gcctttgtct gctctcagtg tcttcctttt gacatgggaa aggagtgtg     1200
gccaaaaatc ccatcttctt gcacctcaac gtctgtggct cagggctggg     1250
gtggcagagg gaggccttca ccttatatct gtgttggtat ccagggctcc     1300
agacttcctc ctctgcctgc cccactgcac cctctcccc ttatctatct     1350
ccttctcggc tcccagccc agtcttggtt tcttgtcccc tcctggggtc     1400
atccctccac tctgactctg actatggcag cagaacacca gggcctggcc     1450
cagtggtatt catggtgatc attaaaaaag aaaaatcgca accaaaaaaa     1500
aaaaa                                                    1505

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<210> SEQ ID NO 128

<211> LENGTH: 260

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 128

```

Met Ala Arg Pro Gly Met Glu Arg Trp Arg Asp Arg Leu Ala Leu
 1          5          10          15
Val Thr Gly Ala Ser Gly Gly Ile Gly Ala Ala Val Ala Arg Ala
          20          25          30
Leu Val Gln Gln Gly Leu Lys Val Val Gly Cys Ala Arg Thr Val
          35          40          45
Gly Asn Ile Glu Glu Leu Ala Ala Glu Cys Lys Ser Ala Gly Tyr
          50          55          60
Pro Gly Thr Leu Ile Pro Tyr Arg Cys Asp Leu Ser Asn Glu Glu
          65          70          75
Asp Ile Leu Ser Met Phe Ser Ala Ile Arg Ser Gln His Ser Gly
          80          85          90
Val Asp Ile Cys Ile Asn Asn Ala Gly Leu Ala Arg Pro Asp Thr
          95          100          105
Leu Leu Ser Gly Ser Thr Ser Gly Trp Lys Asp Met Phe Asn Val
          110          115          120

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Asn	Val	Leu	Ala	Leu	Ser	Ile	Cys	Thr	Arg	Glu	Ala	Tyr	Gln	Ser
		125							130					135
Met	Lys	Glu	Arg	Asn	Val	Asp	Asp	Gly	His	Ile	Ile	Asn	Ile	Asn
				140					145					150
Ser	Met	Ser	Gly	His	Arg	Val	Leu	Pro	Leu	Ser	Val	Thr	His	Phe
				155					160					165
Tyr	Ser	Ala	Thr	Lys	Tyr	Ala	Val	Thr	Ala	Leu	Thr	Glu	Gly	Leu
				170					175					180
Arg	Gln	Glu	Leu	Arg	Glu	Ala	Gln	Thr	His	Ile	Arg	Ala	Thr	Cys
				185					190					195
Ile	Ser	Pro	Gly	Val	Val	Glu	Thr	Gln	Phe	Ala	Phe	Lys	Leu	His
				200					205					210
Asp	Lys	Asp	Pro	Glu	Lys	Ala	Ala	Ala	Thr	Tyr	Glu	Gln	Met	Lys
				215					220					225
Cys	Leu	Lys	Pro	Glu	Asp	Val	Ala	Glu	Ala	Val	Ile	Tyr	Val	Leu
				230					235					240
Ser	Thr	Pro	Ala	His	Ile	Gln	Ile	Gly	Asp	Ile	Gln	Met	Arg	Pro
				245					250					255
Thr	Glu	Gln	Val	Thr										
				260										

<210> SEQ ID NO 129
 <211> LENGTH: 1177
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 129

aactctaca tgggcctcct gctgctggtg ctcttcctca gcctcctgcc	50
ggtgacctac accatcatgt cctccccacc ctcctttgac tgcggggcgt	100
tcagggtgac agtctcagtt gcccgggagc acctcccctc ccgaggcagt	150
ctgctcagag ggctcgggcc cagaattcca gttctggttt catgccagcc	200
tgtaaaaggc catggaactt tgggtgaatc accgatgcca tttaaagagg	250
ttttctgcca ggatggaaat gttaggtcgt tctgtgtctg cgctgttcat	300
ttcagtagcc accagccacc tgtggccgtt gagtgctga aatgaggaac	350
tgagaaaatt aatttctcat gtatttttct cattatttta ttaattttta	400
actgatagtt gtacatatat gggggtacat gtgatatttg gatacatgta	450
tacaatatat aatgatcaaa tcagggtaac tgggatatcc atcacatcaa	500
acatttattt tttattcttt ttagacagag tctcactctg tcaccaggc	550
tggagtgcag tggtgccatc tcagcttact gcaacctctg cctgccaggt	600
tcaagcgatt ctcatgcctc cacctcccaa gtactggtga ctacaggcat	650
gcaccacaat gcccaactaa tttttgtatt tttagtagag acgggggttt	700
gccatgttgc ccaggctggc cttgaactcc tggcctcaaa caatccactt	750
gcctcggcct cccaaagtgt tatgattaca ggcgtgagcc accgtgctg	800
gcctaaacat ttatcttttc tttgtgttgg gaactttgaa attatacaat	850
gaattattgt taactgtcat ctccctgctg tgctatggaa cactgggact	900
tcttcctct atctaactgt atattgtac cagttaacca accgtacttc	950

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atccccactc ctctctatcc ttccaacct ctgatcacct cattctactc      1000
tctacctcca tgagatccac ttttttagct cccacatgtg agtaagaaaa      1050
tgcaaatattt gtctttctgt gcctggctta tttcacttaa cataatgact      1100
tctctgttcca tccatgttgc tgcaaatgac aggatttcgt tcttaatttc      1150
aattaaataa accacacatg gcaaaaaa                                1177

```

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<210> SEQ ID NO 130
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien

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<400> SEQUENCE: 130

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```

Met Gly Leu Leu Leu Leu Val Leu Phe Leu Ser Leu Leu Pro Val
 1           5           10          15
Ala Tyr Thr Ile Met Ser Leu Pro Pro Ser Phe Asp Cys Gly Pro
          20          25          30
Phe Arg Cys Arg Val Ser Val Ala Arg Glu His Leu Pro Ser Arg
          35          40          45
Gly Ser Leu Leu Arg Gly Pro Arg Pro Arg Ile Pro Val Leu Val
          50          55          60
Ser Cys Gln Pro Val Lys Gly His Gly Thr Leu Gly Glu Ser Pro
          65          70          75
Met Pro Phe Lys Arg Val Phe Cys Gln Asp Gly Asn Val Arg Ser
          80          85          90
Phe Cys Val Cys Ala Val His Phe Ser Ser His Gln Pro Pro Val
          95          100         105
Ala Val Glu Cys Leu Lys
          110

```

```

<210> SEQ ID NO 131
<211> LENGTH: 2061
<212> TYPE: DNA
<213> ORGANISM: Homo Sapien

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<400> SEQUENCE: 131

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```

ttctgaagta acggaagcta ccttgtataa agacctcaac actgctgacc      50
atgatcagcg cagcctggag catcttcctc atcgggacta aaattgggct      100
gttccttcaa gtagcacctc tatcagttat ggctaaatcc tgtccatctg      150
tgtgtcgctg cgatgcgggt ttcatttact gtaatgatcg ctttctgaca      200
tccattccaa caggaatacc agaggatgct acaactctct accttcagaa      250
caaccaaata aataatgctg ggattccttc agatttgaaa aacttgctga      300
aagtagaaaag aatataccta taccacaaca gtttagatga atttcctacc      350
aacctcccaa agtatgtaaa agagttacat ttgcaagaaa ataacataag      400
gactatcact tatgattcac tttcaaaaat tocctatctg gaagaattac      450
atntagatga caactctgtc tctgcagtta gcatagaaga gggagcattc      500
cgagacagca actatctccg actgcttttc ctgtcccgta atcaccttag      550
cacaattccc tggggtttgc ccaggactat agaagaacta cgcttggatg      600
ataatgcgat atccactatt tcatcaccat ctcttcaagg tctcactagt      650

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ctaaaaacgcc tggttctaga tggaaacctg ttgaacaatc atggtttagg	700
tgacaaagtt ttcttcaacc tagttaattt gacagagctg tccctgggtc	750
ggaattccct gactgctgca ccagtaaacc ttccaggcac aaacctgagg	800
aagctttatc ttcaagataa ccacatcaat cgggtgcccc caaatgcttt	850
ttcttatcta aggcagctct atcgactgga tatgtccaat aataacctaa	900
gtaatttacc tcaggtatc tttgatgatt tggacaatat aacacaactg	950
attcttcgca acaatccctg gtattgctgg tgcaagatga aatgggtacg	1000
tgactgggta caatcactac ctgtgaaggc caactgctg gggctcatgt	1050
gccaaagccc agaaaagggt cgtgggatgg ctattaagga tctcaatgca	1100
gaactgtttg attgtaagga cagtgggatt gtaagcacca ttcagataac	1150
cactgcaata cccaacacag tgatcctgct ccaaggacag tggccagctc	1200
cagtgaccaa acagccagat attaagaacc ccaagctcac taaggatcaa	1250
caaaccacag ggagtccctc aagaaaaaca attacaatta ctgtgaagtc	1300
tgtcacctct gataccattc atatctcttg gaaacttgct ctacctatga	1350
ctgcttttag actcagctgg cttaaactgg gccatagccc ggcatttggg	1400
tctataacag aaacaattgt aacaggggaa cgcagtgagt acttggtcac	1450
agccctggag cctgattcac cctataaagt atgcatggtt cccatggaaa	1500
ccagcaacct ctacctattt gatgaaactc ctgtttgat tgagactgaa	1550
actgcacccc ttcgaatgta caaccctaca accaccctca atcgagagca	1600
agagaaagaa ccttacaaaa accccaattt accttggtc gccatcattg	1650
gtggggctgt ggcctgggtt accattgccc ttcttgcttt agtggtgttg	1700
tatgttcata ggaatggatc gctcttctca aggaactgtg catatagcaa	1750
agggaggaga agaaaggatg actatgcaga agctggcact aagaaggaca	1800
actctatcct ggaaatcagg gaaacttctt ttcagatggt accaataagc	1850
aatgaaccca tctcgaagga ggagtttgta atacacacca tatttctctc	1900
taatggaatg aatctgtaca aaaacaatca cagtgaaagc agtagtaacc	1950
gaagctacag agacagtgtt attccagact cagatcactc aactcatga	2000
tgctgaagga ctcacagcag acttggtgtt tgggtttttt aaacctaaag	2050
gaggtgatgg t	2061

<210> SEQ ID NO 132

<211> LENGTH: 649

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 132

Met	Ile	Ser	Ala	Ala	Trp	Ser	Ile	Phe	Leu	Ile	Gly	Thr	Lys	Ile
1				5					10					15
Gly	Leu	Phe	Leu	Gln	Val	Ala	Pro	Leu	Ser	Val	Met	Ala	Lys	Ser
			20						25					30
Cys	Pro	Ser	Val	Cys	Arg	Cys	Asp	Ala	Gly	Phe	Ile	Tyr	Cys	Asn
				35					40					45
Asp	Arg	Phe	Leu	Thr	Ser	Ile	Pro	Thr	Gly	Ile	Pro	Glu	Asp	Ala

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															50	55	60
Thr	Thr	Leu	Tyr	Leu	Gln	Asn	Asn	Gln	Ile	Asn	Asn	Ala	Gly	Ile	65	70	75
Pro	Ser	Asp	Leu	Lys	Asn	Leu	Leu	Lys	Val	Glu	Arg	Ile	Tyr	Leu	80	85	90
Tyr	His	Asn	Ser	Leu	Asp	Glu	Phe	Pro	Thr	Asn	Leu	Pro	Lys	Tyr	95	100	105
Val	Lys	Glu	Leu	His	Leu	Gln	Glu	Asn	Asn	Ile	Arg	Thr	Ile	Thr	110	115	120
Tyr	Asp	Ser	Leu	Ser	Lys	Ile	Pro	Tyr	Leu	Glu	Glu	Leu	His	Leu	125	130	135
Asp	Asp	Asn	Ser	Val	Ser	Ala	Val	Ser	Ile	Glu	Glu	Gly	Ala	Phe	140	145	150
Arg	Asp	Ser	Asn	Tyr	Leu	Arg	Leu	Leu	Phe	Leu	Ser	Arg	Asn	His	155	160	165
Leu	Ser	Thr	Ile	Pro	Trp	Gly	Leu	Pro	Arg	Thr	Ile	Glu	Glu	Leu	170	175	180
Arg	Leu	Asp	Asp	Asn	Arg	Ile	Ser	Thr	Ile	Ser	Ser	Pro	Ser	Leu	185	190	195
Gln	Gly	Leu	Thr	Ser	Leu	Lys	Arg	Leu	Val	Leu	Asp	Gly	Asn	Leu	200	205	210
Leu	Asn	Asn	His	Gly	Leu	Gly	Asp	Lys	Val	Phe	Phe	Asn	Leu	Val	215	220	225
Asn	Leu	Thr	Glu	Leu	Ser	Leu	Val	Arg	Asn	Ser	Leu	Thr	Ala	Ala	230	235	240
Pro	Val	Asn	Leu	Pro	Gly	Thr	Asn	Leu	Arg	Lys	Leu	Tyr	Leu	Gln	245	250	255
Asp	Asn	His	Ile	Asn	Arg	Val	Pro	Pro	Asn	Ala	Phe	Ser	Tyr	Leu	260	265	270
Arg	Gln	Leu	Tyr	Arg	Leu	Asp	Met	Ser	Asn	Asn	Asn	Leu	Ser	Asn	275	280	285
Leu	Pro	Gln	Gly	Ile	Phe	Asp	Asp	Leu	Asp	Asn	Ile	Thr	Gln	Leu	290	295	300
Ile	Leu	Arg	Asn	Asn	Pro	Trp	Tyr	Cys	Gly	Cys	Lys	Met	Lys	Trp	305	310	315
Val	Arg	Asp	Trp	Leu	Gln	Ser	Leu	Pro	Val	Lys	Val	Asn	Val	Arg	320	325	330
Gly	Leu	Met	Cys	Gln	Ala	Pro	Glu	Lys	Val	Arg	Gly	Met	Ala	Ile	335	340	345
Lys	Asp	Leu	Asn	Ala	Glu	Leu	Phe	Asp	Cys	Lys	Asp	Ser	Gly	Ile	350	355	360
Val	Ser	Thr	Ile	Gln	Ile	Thr	Thr	Ala	Ile	Pro	Asn	Thr	Val	Tyr	365	370	375
Pro	Ala	Gln	Gly	Gln	Trp	Pro	Ala	Pro	Val	Thr	Lys	Gln	Pro	Asp	380	385	390
Ile	Lys	Asn	Pro	Lys	Leu	Thr	Lys	Asp	Gln	Gln	Thr	Thr	Gly	Ser	395	400	405
Pro	Ser	Arg	Lys	Thr	Ile	Thr	Ile	Thr	Val	Lys	Ser	Val	Thr	Ser	410	415	420
Asp	Thr	Ile	His	Ile	Ser	Trp	Lys	Leu	Ala	Leu	Pro	Met	Thr	Ala	425	430	435

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Leu Arg Leu Ser Trp Leu Lys Leu Gly His Ser Pro Ala Phe Gly
 440 445 450
 Ser Ile Thr Glu Thr Ile Val Thr Gly Glu Arg Ser Glu Tyr Leu
 455 460 465
 Val Thr Ala Leu Glu Pro Asp Ser Pro Tyr Lys Val Cys Met Val
 470 475 480
 Pro Met Glu Thr Ser Asn Leu Tyr Leu Phe Asp Glu Thr Pro Val
 485 490 495
 Cys Ile Glu Thr Glu Thr Ala Pro Leu Arg Met Tyr Asn Pro Thr
 500 505 510
 Thr Thr Leu Asn Arg Glu Gln Glu Lys Glu Pro Tyr Lys Asn Pro
 515 520 525
 Asn Leu Pro Leu Ala Ala Ile Ile Gly Gly Ala Val Ala Leu Val
 530 535 540
 Thr Ile Ala Leu Leu Ala Leu Val Cys Trp Tyr Val His Arg Asn
 545 550 555
 Gly Ser Leu Phe Ser Arg Asn Cys Ala Tyr Ser Lys Gly Arg Arg
 560 565 570
 Arg Lys Asp Asp Tyr Ala Glu Ala Gly Thr Lys Lys Asp Asn Ser
 575 580 585
 Ile Leu Glu Ile Arg Glu Thr Ser Phe Gln Met Leu Pro Ile Ser
 590 595 600
 Asn Glu Pro Ile Ser Lys Glu Glu Phe Val Ile His Thr Ile Phe
 605 610 615
 Pro Pro Asn Gly Met Asn Leu Tyr Lys Asn Asn His Ser Glu Ser
 620 625 630
 Ser Ser Asn Arg Ser Tyr Arg Asp Ser Gly Ile Pro Asp Ser Asp
 635 640 645
 His Ser His Ser

<210> SEQ ID NO 133
 <211> LENGTH: 1882
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 133

ccgctcatccc cctgcagcca cccttcccag agtcctttgc ccaggccacc 50
 ccaggcttct tggcagccct gccgggccac ttgttctcat gtctgccagg 100
 gggagggtgg aaggaggtgg gaggaggcgc tgcagaggca gtctgggctt 150
 ggccagagct cagggtgctg agcgtgtgac cagcagtgag cagaggccgg 200
 ccatggccag cctggggctg ctgctcctgc tcttactgac agcactgcca 250
 ccgctgtggt cctcctcact gcctgggctg gacactgctg aaagtaaagc 300
 caccattgca gacctgatcc tgtctgcgct ggagagagcc accgtcttcc 350
 tagaacagag gctgcctgaa atcaacctgg atggcatggt gggggctccga 400
 gtgctggaag agcagctaaa aagtgtccgg gagaagtggg cccaggagcc 450
 cctgctgacg ccgctgagcc tgcgcgtggg gatgctgggg gagaagctgg 500
 aggctgccat ccagagatcc ctccactacc tcaagctgag tgatcccaag 550
 tacctaagag agttccagct gaccctccag cccgggtttt ggaagctccc 600

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acatgcctgg atccacactg atgcctcctt ggtgtacccc acgttcgggc      650
cccaggactc attctcagag gagagaagtg acgtgtgcct ggtgcagctg      700
ctgggaaccg ggacggacag cagcagagccc tgcggcctct cagacctctg      750
caggagcctc atgaccaagc ccggctgctc aggctactgc ctgtcccacc      800
aactgctctt cttcctctgg gccagaatga ggggatgcac acagggacca      850
ctccaacaga gccaggacta tatcaacctc ttctgcgcca acatgatgga      900
cttgaaccgc agagctgagg ccatcgagata cgcctaccct acccgggaca      950
tcttcatgga aaacatcatg ttctgtggaa tgggaggctt ctccgacttc     1000
tacaagctcc ggtggctgga ggccattctc agctggcaga aacagcagga     1050
aggatgcttc ggggagcctg atgctgaaga tgaagaatta tctaaagcta     1100
ttcaatatca gcagcattht tcgaggagag tgaagaggcg aaaaaaaca     1150
tttccagatt ctcgctctgt tgctcaggct ggagtacagt ggcgcaatct     1200
cggctcactg caacctttgc ctctcgggtt caagcaattc tcttgctca     1250
tctcccagag tagctgggac tacaggagcg tgccaccata cctggctaatt     1300
ttttatattt ttttagtaga gacagggttt catcatgttg ctcatgctgg     1350
tctcgaactc ctgatctcaa gagatccgcc cacctcaggc tcccaaagtg     1400
tggtattata ggtgtgagcc accgtgtctg gotgaaaagc actttcaaag     1450
agactgtgtt gaataaaggg ccaaggttct tgccaccag cactcatggg     1500
ggctctctcc cctagatggc tgctcctccc acaacacagc cacagcagtg     1550
gcagccctgg gtggcttctc atacatcctg gcagaatacc cccagcaaa     1600
cagagagcca cacccatcca caccgccacc accaagcagc cgctgagacg     1650
gacggttcca tgccagctgc ctggaggagg aacagacccc tttagtctc     1700
atcccttaga tcctggaggg caccgatcac atcctgggaa gaaggcatct     1750
ggagataaag caaagccacc ccgacacca atcttgaag ccctgagtag     1800
gcagggccag ggtaggtggg ggccgggagg gaccaggtg tgaacggatg     1850
aataaagttc aactgcaact gaaaaaaaa aa                          1882

```

<210> SEQ ID NO 134

<211> LENGTH: 440

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 134

```

Met Ser Ala Arg Gly Arg Trp Glu Gly Gly Gly Arg Arg Ala Cys
 1           5           10           15
Arg Gly Ser Leu Gly Leu Ala Arg Ala Gln Gly Ala Glu Arg Val
 20           25           30
Thr Ser Ser Glu Gln Arg Pro Ala Met Ala Ser Leu Gly Leu Leu
 35           40           45
Leu Leu Leu Leu Leu Thr Ala Leu Pro Pro Leu Trp Ser Ser Ser
 50           55           60
Leu Pro Gly Leu Asp Thr Ala Glu Ser Lys Ala Thr Ile Ala Asp
 65           70           75

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Leu	Ile	Leu	Ser	Ala	Leu	Glu	Arg	Ala	Thr	Val	Phe	Leu	Glu	Gln	80	85	90
Arg	Leu	Pro	Glu	Ile	Asn	Leu	Asp	Gly	Met	Val	Gly	Val	Arg	Val	95	100	105
Leu	Glu	Glu	Gln	Leu	Lys	Ser	Val	Arg	Glu	Lys	Trp	Ala	Gln	Glu	110	115	120
Pro	Leu	Leu	Gln	Pro	Leu	Ser	Leu	Arg	Val	Gly	Met	Leu	Gly	Glu	125	130	135
Lys	Leu	Glu	Ala	Ala	Ile	Gln	Arg	Ser	Leu	His	Tyr	Leu	Lys	Leu	140	145	150
Ser	Asp	Pro	Lys	Tyr	Leu	Arg	Glu	Phe	Gln	Leu	Thr	Leu	Gln	Pro	155	160	165
Gly	Phe	Trp	Lys	Leu	Pro	His	Ala	Trp	Ile	His	Thr	Asp	Ala	Ser	170	175	180
Leu	Val	Tyr	Pro	Thr	Phe	Gly	Pro	Gln	Asp	Ser	Phe	Ser	Glu	Glu	185	190	195
Arg	Ser	Asp	Val	Cys	Leu	Val	Gln	Leu	Leu	Gly	Thr	Gly	Thr	Asp	200	205	210
Ser	Ser	Glu	Pro	Cys	Gly	Leu	Ser	Asp	Leu	Cys	Arg	Ser	Leu	Met	215	220	225
Thr	Lys	Pro	Gly	Cys	Ser	Gly	Tyr	Cys	Leu	Ser	His	Gln	Leu	Leu	230	235	240
Phe	Phe	Leu	Trp	Ala	Arg	Met	Arg	Gly	Cys	Thr	Gln	Gly	Pro	Leu	245	250	255
Gln	Gln	Ser	Gln	Asp	Tyr	Ile	Asn	Leu	Phe	Cys	Ala	Asn	Met	Met	260	265	270
Asp	Leu	Asn	Arg	Arg	Ala	Glu	Ala	Ile	Gly	Tyr	Ala	Tyr	Pro	Thr	275	280	285
Arg	Asp	Ile	Phe	Met	Glu	Asn	Ile	Met	Phe	Cys	Gly	Met	Gly	Gly	290	295	300
Phe	Ser	Asp	Phe	Tyr	Lys	Leu	Arg	Trp	Leu	Glu	Ala	Ile	Leu	Ser	305	310	315
Trp	Gln	Lys	Gln	Gln	Glu	Gly	Cys	Phe	Gly	Glu	Pro	Asp	Ala	Glu	320	325	330
Asp	Glu	Glu	Leu	Ser	Lys	Ala	Ile	Gln	Tyr	Gln	Gln	His	Phe	Ser	335	340	345
Arg	Arg	Val	Lys	Arg	Arg	Glu	Lys	Gln	Phe	Pro	Asp	Ser	Arg	Ser	350	355	360
Val	Ala	Gln	Ala	Gly	Val	Gln	Trp	Arg	Asn	Leu	Gly	Ser	Leu	Gln	365	370	375
Pro	Leu	Pro	Pro	Gly	Phe	Lys	Gln	Phe	Ser	Cys	Leu	Ile	Leu	Pro	380	385	390
Ser	Ser	Trp	Asp	Tyr	Arg	Ser	Val	Pro	Pro	Tyr	Leu	Ala	Asn	Phe	395	400	405
Tyr	Ile	Phe	Leu	Val	Glu	Thr	Gly	Phe	His	His	Val	Ala	His	Ala	410	415	420
Gly	Leu	Glu	Leu	Leu	Ile	Ser	Arg	Asp	Pro	Pro	Thr	Ser	Gly	Ser	425	430	435
Gln	Ser	Val	Gly	Leu	440												

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<210> SEQ ID NO 135

<211> LENGTH: 884

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 135

```

ggctctgagtg cagagctgct gtcattggcg ccgctctgtg gggcttcttt      50
cccgtcctgc tgctgctgct gctatcgggg gatgtccaga gctcggaggt      100
gcccggggct gctgctgagg gatcgggagg gagtggggtc ggcataggag      150
atcgcttcaa gattgagggg cgtgcagttg ttccaggggt gaagcctcag      200
gactggatct cggcggcccc agtgctggtg gacggagaag agcacgtcgg      250
tttccttaag acagatggga gttttgtggt tcatgatata ccttctggat      300
cttatgtagt ggaagttgta tctccagctt acagatttga tcccgttcga      350
gtggatatca cttcgaagg aaaaatgaga gcaagatatg tgaattacat      400
caaaacatca gaggttgta gactgcctca tcctctcaa atgaaatctt      450
caggtccacc ttcttacttt attaaaagg aatcgtgggg ctggacagac      500
tttctaatga acccaatggt tatgatgatg gttcttctt tattgatatt      550
tgtgcttctg cctaaagtgg tcaacacaag tgatcctgac atgagacggg      600
aaatggagca gtcaatgaat atgctgaatt ccaacatga gttgcctgat      650
gtttctgagt tcatgacaag actcttctct tcaaaatcat ctggcaaatc      700
tagcagcggc agcagtaaaa caggcaaaa tggggctggc aaaaggaggt      750
agtcaggccg tccagagctg gcatttcac aaacacggca acaactgggtg      800
gcatccaagt cttgaaaaac cgtgtgaagc aactactata aacttgagtc      850
atcccagact tgatctctta caactgtgta tggt      884

```

<210> SEQ ID NO 136

<211> LENGTH: 242

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 136

```

Met Ala Ala Ala Leu Trp Gly Phe Phe Pro Val Leu Leu Leu Leu
  1           5           10          15
Leu Leu Ser Gly Asp Val Gln Ser Ser Glu Val Pro Gly Ala Ala
  20          25          30
Ala Glu Gly Ser Gly Gly Ser Gly Val Gly Ile Gly Asp Arg Phe
  35          40          45
Lys Ile Glu Gly Arg Ala Val Val Pro Gly Val Lys Pro Gln Asp
  50          55          60
Trp Ile Ser Ala Ala Arg Val Leu Val Asp Gly Glu Glu His Val
  65          70          75
Gly Phe Leu Lys Thr Asp Gly Ser Phe Val Val His Asp Ile Pro
  80          85          90
Ser Gly Ser Tyr Val Val Glu Val Val Ser Pro Ala Tyr Arg Phe
  95          100         105
Asp Pro Val Arg Val Asp Ile Thr Ser Lys Gly Lys Met Arg Ala
  110         115         120
Arg Tyr Val Asn Tyr Ile Lys Thr Ser Glu Val Val Arg Leu Pro

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	125		130		135
Tyr Pro Leu Gln Met Lys Ser Ser Gly Pro Pro Ser Tyr Phe Ile	140		145		150
Lys Arg Glu Ser Trp Gly Trp Thr Asp Phe Leu Met Asn Pro Met	155		160		165
Val Met Met Met Val Leu Pro Leu Leu Ile Phe Val Leu Leu Pro	170		175		180
Lys Val Val Asn Thr Ser Asp Pro Asp Met Arg Arg Glu Met Glu	185		190		195
Gln Ser Met Asn Met Leu Asn Ser Asn His Glu Leu Pro Asp Val	200		205		210
Ser Glu Phe Met Thr Arg Leu Phe Ser Ser Lys Ser Ser Gly Lys	215		220		225
Ser Ser Ser Gly Ser Ser Lys Thr Gly Lys Ser Gly Ala Gly Lys	230		235		240

Arg Arg

<210> SEQ ID NO 137

<211> LENGTH: 1571

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 137

```

gatggcgcag ccacagcttc tgtgagattc gatttctccc cagttcccct      50
gtgggtctga ggggaccaga aggggtgagct acgttggtt tctggaagg      100
gaggctatat gcgtcaattc cccaaaacaa gttttgacat ttcccctgaa      150
atgtcattot ctatctattc actgcaagtg cctgctgttc caggccttac      200
ctgctgggca ctaacggcgg agccaggatg gggacagaat aaaggagcca      250
cgacctgtgc caccaactcg cactcagact ctgaactcag acctgaaatc      300
ttctcttcac gggaggcttg gcagtttttc ttactcctgt ggtctccaga      350
tttcaggcct aagatgaaag cctctagtct tgccttcagc cttctctctg      400
ctgcgtttta tctcctatgg actccttcca ctggactgaa gacactcaat      450
ttgggaagct gtgtgatcgc cacaaacctt caggaaatac gaaatggatt      500
ttctgagata cggggcagtg tgcaagccaa agatggaaac attgacatca      550
gaatcttaag gaggactgag tctttgcaag acacaaagcc tgcgaatcga      600
tgctgcctcc tgcgccatth gctaagactc tatctggaca gggtatthaa      650
aaactaccag acccctgacc attatactct cgggaagatc agcagcctcg      700
ccaattcctt tcttaccatc aagaaggacc tccggctctc tcatgcccac      750
atgacatgcc attgtgggga ggaagcaatg aagaaatata gccagattct      800
gagtcacttt gaaaagctgg aacctcaggc agcagttgtg aaggctttgg      850
gggaactaga cattcttctg caatggatgg aggagacaga ataggaggaa      900
agtgatgctg ctgctaagaa tattcgaggt caagagctcc agtcttcaat      950
acctgcagag gaggcatgac cccaaaccac catctcttta ctgtactagt     1000
cttgtgctgg tcacagtgta tcttatttat goattacttg ctctctgca     1050
tgattgtctt tatgcatccc caatcttaat tgagaccata cttgtataag     1100

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-continued

```

atTTTTgtaa tatctttctg ctattggata tatttattag ttaatatatt      1150
tattttatTTT ttgctattta atgtatttat ttttttactt ggacatgaaa      1200
cttttaaaaa attcacagat tatatttata acctgactag agcaggtgat      1250
gtatttttat acagtaaaaa aaaaaaacct tgtaaattct agaagagtgg      1300
ctaggggggt tattcatttg tattcaacta aggacatatt tactcatgct      1350
gatgctctgt gagatatttg aaattgaacc aatgactact taggatgggt      1400
tgtggaataa gttttgatgt ggaattgcac atctacctta caattactga      1450
ccatccccag tagactcccc agtcccataa ttgtgtatct tccagccagg      1500
aatcctacac gccagcatg tatttctaca aataaagttt tctttgcata      1550
ccaaaaaaaa aaaaaaaaaa a      1571
    
```

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<210> SEQ ID NO 138
<211> LENGTH: 261
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien
    
```

<400> SEQUENCE: 138

```

Met Arg Gln Phe Pro Lys Thr Ser Phe Asp Ile Ser Pro Glu Met
 1           5           10           15
Ser Phe Ser Ile Tyr Ser Leu Gln Val Pro Ala Val Pro Gly Leu
          20           25           30
Thr Cys Trp Ala Leu Thr Ala Glu Pro Gly Trp Gly Gln Asn Lys
          35           40           45
Gly Ala Thr Thr Cys Ala Thr Asn Ser His Ser Asp Ser Glu Leu
          50           55           60
Arg Pro Glu Ile Phe Ser Ser Arg Glu Ala Trp Gln Phe Phe Leu
          65           70           75
Leu Leu Trp Ser Pro Asp Phe Arg Pro Lys Met Lys Ala Ser Ser
          80           85           90
Leu Ala Phe Ser Leu Leu Ser Ala Ala Phe Tyr Leu Leu Trp Thr
          95           100          105
Pro Ser Thr Gly Leu Lys Thr Leu Asn Leu Gly Ser Cys Val Ile
          110          115          120
Ala Thr Asn Leu Gln Glu Ile Arg Asn Gly Phe Ser Glu Ile Arg
          125          130          135
Gly Ser Val Gln Ala Lys Asp Gly Asn Ile Asp Ile Arg Ile Leu
          140          145          150
Arg Arg Thr Glu Ser Leu Gln Asp Thr Lys Pro Ala Asn Arg Cys
          155          160          165
Cys Leu Leu Arg His Leu Leu Arg Leu Tyr Leu Asp Arg Val Phe
          170          175          180
Lys Asn Tyr Gln Thr Pro Asp His Tyr Thr Leu Arg Lys Ile Ser
          185          190          195
Ser Leu Ala Asn Ser Phe Leu Thr Ile Lys Lys Asp Leu Arg Leu
          200          205          210
Ser His Ala His Met Thr Cys His Cys Gly Glu Glu Ala Met Lys
          215          220          225
Lys Tyr Ser Gln Ile Leu Ser His Phe Glu Lys Leu Glu Pro Gln
          230          235          240
    
```


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Ala Ala Val Val Lys Ala Leu Gly Glu Leu Asp Ile Leu Leu Gln
 245 250 255
 Trp Met Glu Glu Thr Glu
 260

<210> SEQ ID NO 139

<211> LENGTH: 2395

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 139

```

cctggagcgc gaagcgcggc tgcagcaggg cgaggctcca ggtggggctg      50
gttccgcata cagcctagcg tgtccacgat gcggtggggc tccgggactt      100
tcgtacacct ttgcgtagcg atcgaggtgc tagggatcgc ggtcttctt      150
cggggattct tcccggctcc cgttcgttcc tctgccagag cggaacacgg      200
agcggagccc ccagcgcggc aaccctcggc tggagccagt tctaactgga      250
ccacgctgcc accacctctc ttcagtaaag ttgttattgt tctgatagat      300
gccttgagag atgattttgt gtttggttca aaggggtgta aatttatgcc      350
ctacacaact taccttgtag aaaaaggagc atctcacagt tttgtggctg      400
aagcaaagcc acctacagtt actatgcctc gaatcaaggc attgatgacg      450
gggagccttc ctggctttgt cgacgtcatc aggaacctca attctcctgc      500
actgctggaa gacagtgtga taagacaagc aaaagcagct ggaaaaagaa      550
tagtctttta tggagatgaa acctgggtta aattattccc aaagcatttt      600
gtggaatatg atggaacaac ctcaattttc gtgtcagatt acacagaggt      650
ggataataat gtcacgaggc atttgataa agtattaaaa agaggagatt      700
gggacataat aatcctccac tacctggggc tggaccacat tggccacatt      750
tcagggccca acagcccctc gattggggcag aagctgagcg agatggacag      800
cgtgctgatg aagatccaca cctcactgca gtcgaaggag agagagacgc      850
ctttacccaa tttgctggtt ctttgtggtg accatggcat gctgaaaca      900
ggaagtcaag gggcctcctc caccgaggag gtgaatacac ctctgatatt      950
aatcagttct gcgtttgaaa ggaaacccgg tgatatccga catccaaagc     1000
acgtccaata gacggatgtg gctgcgacac tggcgatagc acttggctta     1050
cogattccaa aagacagtgt agggagcctc ctattcccag ttgtggaagg     1100
aagaccaatg agagagcagt tgagattttt acatttgaat acagtgcagc     1150
ttagtaaaact gttgcaagag aatgtgccgt catatgaaaa agatcctggg     1200
tttgagcagt ttaaaatgtc agaaagattg catgggaact ggatcagact     1250
gtacttgagg gaaaagcatt cagaagtctc attcaacctg ggctccaagg     1300
ttctcaggca gtacctggat gctctgaaga cgctgagctt gtcctgaggt     1350
gcacaagtgg ccagttctc accctgctcc tgctcagcgt cccacaggca     1400
ctgcacagaa aggctgagct ggaagtccca ctgtcatctc ctgggttttc     1450
tctgctcttt tatttggtga tcctggttct ttcggccggt cacgtcattg     1500
tgtgcacctc agctgaaagt tcgtgtactt tctgtggcct ctctggctg     1550

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gcggcaggct gcctttcggt taccagactc tggttgaaca cctgggtgtg      1600
gccaaagtgt ggcagtgcc  tggacagggg gcctcagga  aggacgtgga      1650
gcagccttat cccaggcctc tgggtgtccc gacacaggtg ttcacatctg      1700
tgctgtcagg tcagatgcct cagttcttgg aaagctaggt tcctgcgact      1750
gttaccaagg tgattgtaaa gagctggcgg tcacagagga acaagcccc      1800
cagctgaggg ggtgtgtgaa tcggacagcc tcccagcaga ggtgtgggag      1850
ctgcagctga gggaagaaga gacaatcggc ctggacactc aggagggtca      1900
aaaggagact tggctgcacc actcatcctg ccacccccag aatgcaccc      1950
gcctcatcag gtccagattt cttccaagg  cggacgtttt ctggtggaat      2000
tcttagtctt tggcctcgga cacctcatt  cgtagctgg  ggagtgggtg      2050
tgaggcagtg aagaagaggc gtaggtcac  actcagatcc acagagcca      2100
ggatcaaggg acccaactgca gtggcagcag gactggtggg cccccacccc      2150
aacctgcac  agcctcacc  ccctcttggc ttgagccgtc agaggccctg      2200
tgctgagtg  ctgaccgaga cactcacagc tttgtcatca gggcacaggc      2250
ttcctcggag ccaggatgat ctgtgccagc cttgcacctc gggcccatct      2300
gggctcatgc tctctctcct gctattgaat tagtacctag ctgcacacag      2350
tatgtagtta caaaagaat  aaacggcaat aattgagaaa aaaaa      2395

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<210> SEQ ID NO 140

<211> LENGTH: 310

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 140

```

Met Arg Leu Gly Ser Gly Thr Phe Ala Thr Cys Cys Val Ala Ile
 1          5          10          15
Glu Val Leu Gly Ile Ala Val Phe Leu Arg Gly Phe Phe Pro Ala
 20          25          30
Pro Val Arg Ser Ser Ala Arg Ala Glu His Gly Ala Glu Pro Pro
 35          40          45
Ala Pro Glu Pro Ser Ala Gly Ala Ser Ser Asn Trp Thr Thr Leu
 50          55          60
Pro Pro Pro Leu Phe Ser Lys Val Val Ile Val Leu Ile Asp Ala
 65          70          75
Leu Arg Asp Asp Phe Val Phe Gly Ser Lys Gly Val Lys Phe Met
 80          85          90
Pro Tyr Thr Thr Tyr Leu Val Glu Lys Gly Ala Ser His Ser Phe
 95          100         105
Val Ala Glu Ala Lys Pro Pro Thr Val Thr Met Pro Arg Ile Lys
 110         115         120
Ala Leu Met Thr Gly Ser Leu Pro Gly Phe Val Asp Val Ile Arg
 125         130         135
Asn Leu Asn Ser Pro Ala Leu Leu Glu Asp Ser Val Ile Arg Gln
 140         145         150
Ala Lys Ala Ala Gly Lys Arg Ile Val Phe Tyr Gly Asp Glu Thr
 155         160         165

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Trp	Val	Lys	Leu	Phe	Pro	Lys	His	Phe	Val	Glu	Tyr	Asp	Gly	Thr
			170						175					180
Thr	Ser	Phe	Phe	Val	Ser	Asp	Tyr	Thr	Glu	Val	Asp	Asn	Asn	Val
			185						190					195
Thr	Arg	His	Leu	Asp	Lys	Val	Leu	Lys	Arg	Gly	Asp	Trp	Asp	Ile
			200						205					210
Leu	Ile	Leu	His	Tyr	Leu	Gly	Leu	Asp	His	Ile	Gly	His	Ile	Ser
			215						220					225
Gly	Pro	Asn	Ser	Pro	Leu	Ile	Gly	Gln	Lys	Leu	Ser	Glu	Met	Asp
			230						235					240
Ser	Val	Leu	Met	Lys	Ile	His	Thr	Ser	Leu	Gln	Ser	Lys	Glu	Arg
			245						250					255
Glu	Thr	Pro	Leu	Pro	Asn	Leu	Leu	Val	Leu	Cys	Gly	Asp	His	Gly
			260						265					270
Met	Ser	Glu	Thr	Gly	Ser	His	Gly	Ala	Ser	Ser	Thr	Glu	Glu	Val
			275						280					285
Asn	Thr	Pro	Leu	Ile	Leu	Ile	Ser	Ser	Ala	Phe	Glu	Arg	Lys	Pro
			290						295					300
Gly	Asp	Ile	Arg	His	Pro	Lys	His	Val	Gln					
			305						310					

<210> SEQ ID NO 141
 <211> LENGTH: 754
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 141

ggcacgagggc aagccttcca ggttatcgtg acgcaccttg aaagtctgag	50
agctactgcc ctacagaaag ttactagtgc cctaaagctg gcgctggcac	100
tgatgttaact gctgctggtg gagtacaact tccctataga aaacaactgc	150
cagcacctta agaccactca caccttcaga gtgaagaact taaaccggaa	200
gaaattcagc attcatgacc aggatcacia agtactggtc ctggactctg	250
ggaatctcat agcagttcca gataaaaact acatacgccc agagatcttc	300
tttgcattag cctcatcctt gagctcagcc tctgcggaga aaggaagtcc	350
gattctcctg ggggtctcta aaggggagtt ttgtctctac tgtgacaagg	400
ataaaggaca aagtcattcca tccttcagc tgaagaagga gaaactgatg	450
aagctggctg cccaaaagga atcagcacgc cggcccttca tcttttatag	500
ggctcaggtg ggctcctgga acatgctgga gtcggcggct caccocggat	550
ggttcactcg cacctcctgc aattgtaatg agcctgttgg ggtgacagat	600
aaatttgaga acaggaaaca cattgaattt tcatttcaac cagtttgcaa	650
agctgaaatg agccccagtg aggtcagcga ttaggaaact gccccattga	700
acgccttctc cgctaatttg aactaattgt ataaaaacac caaacctgct	750
caact	754

<210> SEQ ID NO 142
 <211> LENGTH: 193
 <212> TYPE: PRT
 <213> ORGANISM: Homo Sapien

-continued

<400> SEQUENCE: 142

Met Leu Leu Leu Leu Leu Glu Tyr Asn Phe Pro Ile Glu Asn Asn
 1 5 10 15
 Cys Gln His Leu Lys Thr Thr His Thr Phe Arg Val Lys Asn Leu
 20 25 30
 Asn Pro Lys Lys Phe Ser Ile His Asp Gln Asp His Lys Val Leu
 35 40 45
 Val Leu Asp Ser Gly Asn Leu Ile Ala Val Pro Asp Lys Asn Tyr
 50 55 60
 Ile Arg Pro Glu Ile Phe Phe Ala Leu Ala Ser Ser Leu Ser Ser
 65 70 75
 Ala Ser Ala Glu Lys Gly Ser Pro Ile Leu Leu Gly Val Ser Lys
 80 85 90
 Gly Glu Phe Cys Leu Tyr Cys Asp Lys Asp Lys Gly Gln Ser His
 95 100 105
 Pro Ser Leu Gln Leu Lys Lys Glu Lys Leu Met Lys Leu Ala Ala
 110 115 120
 Gln Lys Glu Ser Ala Arg Arg Pro Phe Ile Phe Tyr Arg Ala Gln
 125 130 135
 Val Gly Ser Trp Asn Met Leu Glu Ser Ala Ala His Pro Gly Trp
 140 145 150
 Phe Ile Cys Thr Ser Cys Asn Cys Asn Glu Pro Val Gly Val Thr
 155 160 165
 Asp Lys Phe Glu Asn Arg Lys His Ile Glu Phe Ser Phe Gln Pro
 170 175 180
 Val Cys Lys Ala Glu Met Ser Pro Ser Glu Val Ser Asp
 185 190

<210> SEQ ID NO 143

<211> LENGTH: 961

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 143

ctagagagta tagggcagaa ggatggcaga tgagtgactc cacatccaga 50
 gctgcctccc ttaaatccag gatcctgtcc ttcctgtcct gtaggagtgc 100
 ctgttgccag tgtgggggtga gacaagtttg tcccacaggg ctgtctgagc 150
 agataagatt aagggtctggg tctgtgctca attaactcct gtgggcacgg 200
 gggctgggaa gagcaaagtc agcgggtcct acagtcagca ccatgctggg 250
 cctgccgtgg aaggagggtc tgtcctgggc gctgctgctg cttctcttag 300
 gctcccagat cctgctgata tatgcctggc atttccacga gcaaaggac 350
 tgtgatgaac acaatgtcat ggctcgttac ctccctgccca cagtggagtt 400
 tgctgtccac acattcaacc aacagagcaa ggactactat gcctacagac 450
 tggggcacat cttgaattcc tggaaggagc aggtggagtc caagactgta 500
 ttctcaatgg agctactgct ggggagaact aggtgtggga aatttgaaga 550
 cgacattgac aactgccatt tccaagaaag cacagagctg aacaatactt 600
 tcacctgctt cttcaccatc agcaccaggc cctggatgac tcagttcagc 650
 ctctgaaca agacctgctt ggagggatc cactgagtga aaccactca 700

-continued

```

caggcttgtc catgtgctgc tcccacattc cgtggacatc agcactactc          750
tcttgaggac tcttcagtgg ctgagcagct ttggacttgt ttgttatcct          800
atcttgcatg tgtttgagat ctgagatcag tgttttagaa aatccacaca          850
tcttgagcct aatcatgtag tgtagatcat taaacatcag cattttaaga          900
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa          950
aaaaaaaaaa a          961

```

<210> SEQ ID NO 144

<211> LENGTH: 147

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 144

```

Met Leu Gly Leu Pro Trp Lys Gly Gly Leu Ser Trp Ala Leu Leu
  1             5             10             15
Leu Leu Leu Leu Gly Ser Gln Ile Leu Leu Ile Tyr Ala Trp His
             20             25             30
Phe His Glu Gln Arg Asp Cys Asp Glu His Asn Val Met Ala Arg
             35             40             45
Tyr Leu Pro Ala Thr Val Glu Phe Ala Val His Thr Phe Asn Gln
             50             55             60
Gln Ser Lys Asp Tyr Tyr Ala Tyr Arg Leu Gly His Ile Leu Asn
             65             70             75
Ser Trp Lys Glu Gln Val Glu Ser Lys Thr Val Phe Ser Met Glu
             80             85             90
Leu Leu Leu Gly Arg Thr Arg Cys Gly Lys Phe Glu Asp Asp Ile
             95             100            105
Asp Asn Cys His Phe Gln Glu Ser Thr Glu Leu Asn Asn Thr Phe
            110             115            120
Thr Cys Phe Phe Thr Ile Ser Thr Arg Pro Trp Met Thr Gln Phe
            125             130            135
Ser Leu Leu Asn Lys Thr Cys Leu Glu Gly Phe His
            140             145

```

<210> SEQ ID NO 145

<211> LENGTH: 1157

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 145

```

ctgtgcagct cgaggctcca gaggcacact ccagagagag ccaaggttct          50
gacgcgatga ggaagcacct gagctggtgg tggctggcca ctgtctgcat          100
gtgctctctt agccacctct ctgcggtcca gacgaggggc atcaagcaca          150
gaatcaagtg gaaccggaag gccctgcca gactgcca gatcaactgag          200
gcccaggtgg ctgagaaccg cccgggagcc ttcatacagc aaggccgcaa          250
gtcgcacatt gacttcggag ccgagggcaa caggtactac gaggccaact          300
actggcagtt cccgatggc atocactaca acggctgctc tgaggctaatt          350
gtgaccaagg aggcatttgt caccggtgct atcaatgcca cccaggcggc          400
gaaccagggg gaggctccaga agccagacaa caagctccac cagcaggtgc          450

```

-continued

```

tctggcggct ggtccaggag ctctgctccc tcaagcattg cgagttttgg          500
ttggagaggg gcgcaggact tcgggtcacc atgcaccagc cagtgtctct          550
ctgccttctg gctttgatct ggctcatggt gaaataagct tgccaggagg          600
ctggcagtac agagcgcagc agcgagcaaa tcctggcaag tgaccagct          650
cttctcccc aaaccacgc gtgttctgaa ggtgcccagg agcggcgatg          700
cactcgcact gcaaatgccg ctcccacgta tgcgccctgg tatgtgctg          750
cgttctgata gatgggggac tgtggcttct cgtcactcc attctcagcc          800
cctagcagag cgtctggcac actagattag tagtaaatgc ttgatgagaa          850
gaacacatca ggcactgcgc cacctgcttc acagtacttc ccaacaactc          900
ttagaggtag gtgtattccc gttttacaga taaggaaact gaggcccaga          950
gagctgaagt actgcacca gcatcaccag ctagaaagtg gcagagccag          1000
gattcaacc tggttctgct aaccccaggt tttctgctct gtccaattcc          1050
agagctgtct ggtgatcact ttatgtctca cagggacca catocaaaca          1100
tgtatctcta atgaaattgt gaaagctcca tgtttagaaa taaatgaaa          1150
cacctga                                                              1157

```

<210> SEQ ID NO 146

<211> LENGTH: 176

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 146

```

Met Arg Lys His Leu Ser Trp Trp Trp Leu Ala Thr Val Cys Met
 1           5           10           15
Leu Leu Phe Ser His Leu Ser Ala Val Gln Thr Arg Gly Ile Lys
 20          25          30
His Arg Ile Lys Trp Asn Arg Lys Ala Leu Pro Ser Thr Ala Gln
 35          40          45
Ile Thr Glu Ala Gln Val Ala Glu Asn Arg Pro Gly Ala Phe Ile
 50          55          60
Lys Gln Gly Arg Lys Leu Asp Ile Asp Phe Gly Ala Glu Gly Asn
 65          70          75
Arg Tyr Tyr Glu Ala Asn Tyr Trp Gln Phe Pro Asp Gly Ile His
 80          85          90
Tyr Asn Gly Cys Ser Glu Ala Asn Val Thr Lys Glu Ala Phe Val
 95          100         105
Thr Gly Cys Ile Asn Ala Thr Gln Ala Ala Asn Gln Gly Glu Phe
 110         115         120
Gln Lys Pro Asp Asn Lys Leu His Gln Gln Val Leu Trp Arg Leu
 125         130         135
Val Gln Glu Leu Cys Ser Leu Lys His Cys Glu Phe Trp Leu Glu
 140         145         150
Arg Gly Ala Gly Leu Arg Val Thr Met His Gln Pro Val Leu Leu
 155         160         165
Cys Leu Leu Ala Leu Ile Trp Leu Met Val Lys
 170         175

```

-continued

<210> SEQ ID NO 147

<211> LENGTH: 333

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 147

```

gccttggcct cccaaagggc tgggattata ggcgtgacca ccatgtctgg          50
tccagagtct catttcctga tgatttatag actcaaagaa aactcatggt          100
cagaagctct cttctcttct ggctctctct ctgtcttctt tcctctttc          150
ttcttatttt aattagtagc atctactcag agtcatgcaa gctggaaatc          200
tttcattttg cttgtcagtg gggtaggtca ctgagcttta gtttttattt          250
tttgaatttt caactttcag attcaggggg tacatgtgaa ggtttgtttt          300
atgagtatat tgcatgatgc tgaggtttgg ggt                                333

```

<210> SEQ ID NO 148

<211> LENGTH: 73

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 148

```

Met Phe Arg Ser Ser Leu Leu Phe Trp Pro Pro Leu Cys Leu Leu
 1             5             10             15
Ser Leu Phe Leu Leu Ile Leu Ile Ser Ser Ile Tyr Ser Glu Ser
                20             25             30
Cys Lys Leu Glu Ile Phe His Phe Ala Cys Gln Trp Gly Arg Ser
                35             40             45
Leu Ser Leu Ser Phe Tyr Phe Leu Lys Phe Gln Leu Ser Asp Ser
                50             55             60
Gly Gly Thr Cys Glu Gly Leu Phe Tyr Glu Tyr Ile Ala
                65             70

```

<210> SEQ ID NO 149

<211> LENGTH: 1893

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 149

```

gtctccgctg cacaggaact tcagcaccca cagggcggac agcgtcccc          50
tctacctgga gacttgactc cgcgcgccc caaccctgct tatcccttga          100
ccgtcgagtg tcagagatcc tgcagccgcc cagtccggc ccctctcccg          150
ccccacaccc accctcctgg ctcttctctgt ttttactcct ccttttcatt          200
cataacaaaa gctacagctc caggagccca ggcggggct gtgacccaag          250
ccgagcgtgg aagaatgggg ttcctcggga cggcacttg gattctggtg          300
ttagtgtcc  cgattcaagc tttcccaaa cctggaggaa gccaagacaa          350
atctctacat aatagagaat taagtgcaga aagaccttg aatgaacaga          400
ttgtgtaagc agaagaagac aagattaaaa aaacatatcc tccagaaaac          450
aagccaggtc agagcaacta ttcttttgtt gataacttga acctgctaaa          500
ggcaataaca gaaaaggaaa aaattgagaa agaaagacaa tctataagaa          550
gtccccact  tgataataag ttgaatgtgg aagatgttga ttcaaccaag          600

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aatcgaaaac tgatcgatga ttatgactct actaagagtg gattggatca      650
taaatttcaa gatgatccag atggcttca tcaactagac gggactcctt      700
taaccgctga agacattgtc cataaaatcg ctgccaggat ttatgaagaa      750
aatgacagag ccgtgtttga caagattgtt tctaaactac ttaatctcgg      800
ccttatcaca gaaagccaag cacatacact ggaagatgaa gtagcagagg      850
ttttacaaaa attaatctca aaggaagcca acaattatga ggaggatccc      900
aataagccca caagctggac tgagaatcag gctggaaaaa taccagagaa      950
agtgactcca atggcagcaa ttcaagatgg tcttgctaag ggagaaaacg     1000
atgaaacagt atctaacaca ttaaccttga caaatggctt ggaaggaga     1050
actaaaacct acagtgaaga caactttgag gaactccaat atttccaaa     1100
tttctatgcg ctactgaaa gtattgatcc agaaaaagaa gcaaaagaga     1150
aagaaacact gattactatc atgaaaacac tgattgactt tgtgaagatg     1200
atggtgaaat atggaacaat atctccagaa gaaggtgttt cctaccttga     1250
aaacttgatg gaaatgattg ctcttcagac caaaaacaag ctagaaaaaa     1300
atgctactga caatataagc aagcttttcc cagcaccatc agagaagagt     1350
catgaagaaa cagacagtac caaggaagaa gcagctaaga tggaaaagga     1400
atatggaagc ttgaaggatt ccacaaaaga tgataactcc aaccaggag     1450
gaaagacaga tgaaccctaa ggaaaaacag aagcctatct ggaagccatc     1500
agaaaaaata ttgaatgggt gaagaacatc gacaaaaagg gaaataaaga     1550
agattatgac ctttcaaaga tgagagactt catcaataaa caagctgatg     1600
cttatgtgga gaaaggcatc ctgacaagg aagaagccga ggccatcaag     1650
cgcatttata gcagcctgta aaaatggcaa aagatccagg agtotttcaa     1700
ctgtttcaga aaacataata tagcttaaaa cacttctaata tctgtgatta     1750
aaatTTTTTg acccaagggt tattgaaag tgctgaattt acagtagtta     1800
accttttaca agtgggttaa acatagcttt cttcccgtaa aaactatctg     1850
aaagtaaagt tgtatgtaag ctgaaaaaaa aaaaaaaaaa aaa           1893

```

<210> SEQ ID NO 150

<211> LENGTH: 468

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 150

```

Met Gly Phe Leu Gly Thr Gly Thr Trp Ile Leu Val Leu Val Leu
 1             5             10            15
Pro Ile Gln Ala Phe Pro Lys Pro Gly Gly Ser Gln Asp Lys Ser
 20            25            30
Leu His Asn Arg Glu Leu Ser Ala Glu Arg Pro Leu Asn Glu Gln
 35            40            45
Ile Ala Glu Ala Glu Glu Asp Lys Ile Lys Lys Thr Tyr Pro Pro
 50            55            60
Glu Asn Lys Pro Gly Gln Ser Asn Tyr Ser Phe Val Asp Asn Leu
 65            70            75
Asn Leu Leu Lys Ala Ile Thr Glu Lys Glu Lys Ile Glu Lys Glu

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										80											85											90
Arg	Gln	Ser	Ile	Arg	Ser	Ser	Pro	Leu	Asp	Asn	Lys	Leu	Asn	Val	95	100	105															
Glu	Asp	Val	Asp	Ser	Thr	Lys	Asn	Arg	Lys	Leu	Ile	Asp	Asp	Tyr	110	115	120															
Asp	Ser	Thr	Lys	Ser	Gly	Leu	Asp	His	Lys	Phe	Gln	Asp	Asp	Pro	125	130	135															
Asp	Gly	Leu	His	Gln	Leu	Asp	Gly	Thr	Pro	Leu	Thr	Ala	Glu	Asp	140	145	150															
Ile	Val	His	Lys	Ile	Ala	Ala	Arg	Ile	Tyr	Glu	Glu	Asn	Asp	Arg	155	160	165															
Ala	Val	Phe	Asp	Lys	Ile	Val	Ser	Lys	Leu	Leu	Asn	Leu	Gly	Leu	170	175	180															
Ile	Thr	Glu	Ser	Gln	Ala	His	Thr	Leu	Glu	Asp	Glu	Val	Ala	Glu	185	190	195															
Val	Leu	Gln	Lys	Leu	Ile	Ser	Lys	Glu	Ala	Asn	Asn	Tyr	Glu	Glu	200	205	210															
Asp	Pro	Asn	Lys	Pro	Thr	Ser	Trp	Thr	Glu	Asn	Gln	Ala	Gly	Lys	215	220	225															
Ile	Pro	Glu	Lys	Val	Thr	Pro	Met	Ala	Ala	Ile	Gln	Asp	Gly	Leu	230	235	240															
Ala	Lys	Gly	Glu	Asn	Asp	Glu	Thr	Val	Ser	Asn	Thr	Leu	Thr	Leu	245	250	255															
Thr	Asn	Gly	Leu	Glu	Arg	Arg	Thr	Lys	Thr	Tyr	Ser	Glu	Asp	Asn	260	265	270															
Phe	Glu	Glu	Leu	Gln	Tyr	Phe	Pro	Asn	Phe	Tyr	Ala	Leu	Leu	Lys	275	280	285															
Ser	Ile	Asp	Ser	Glu	Lys	Glu	Ala	Lys	Glu	Lys	Glu	Thr	Leu	Ile	290	295	300															
Thr	Ile	Met	Lys	Thr	Leu	Ile	Asp	Phe	Val	Lys	Met	Met	Val	Lys	305	310	315															
Tyr	Gly	Thr	Ile	Ser	Pro	Glu	Glu	Gly	Val	Ser	Tyr	Leu	Glu	Asn	320	325	330															
Leu	Asp	Glu	Met	Ile	Ala	Leu	Gln	Thr	Lys	Asn	Lys	Leu	Glu	Lys	335	340	345															
Asn	Ala	Thr	Asp	Asn	Ile	Ser	Lys	Leu	Phe	Pro	Ala	Pro	Ser	Glu	350	355	360															
Lys	Ser	His	Glu	Glu	Thr	Asp	Ser	Thr	Lys	Glu	Glu	Ala	Ala	Lys	365	370	375															
Met	Glu	Lys	Glu	Tyr	Gly	Ser	Leu	Lys	Asp	Ser	Thr	Lys	Asp	Asp	380	385	390															
Asn	Ser	Asn	Pro	Gly	Gly	Lys	Thr	Asp	Glu	Pro	Lys	Gly	Lys	Thr	395	400	405															
Glu	Ala	Tyr	Leu	Glu	Ala	Ile	Arg	Lys	Asn	Ile	Glu	Trp	Leu	Lys	410	415	420															
Lys	His	Asp	Lys	Lys	Gly	Asn	Lys	Glu	Asp	Tyr	Asp	Leu	Ser	Lys	425	430	435															
Met	Arg	Asp	Phe	Ile	Asn	Lys	Gln	Ala	Asp	Ala	Tyr	Val	Glu	Lys	440	445	450															
Gly	Ile	Leu	Asp	Lys	Glu	Glu	Ala	Glu	Ala	Ile	Lys	Arg	Ile	Tyr	455	460	465															

-continued

Ser Ser Leu

<210> SEQ ID NO 151

<211> LENGTH: 2598

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 151

cggctcgagg ctcccgccag gagaaaggaa cattctgagg ggagtctaca 50
ccctgtggag ctcaagatgg tcctgagtg ggcgctgtgc ttccgaatga 100
aggactcggc attgaaggtg ctttatctgc ataataacca gcttctagct 150
ggagggtctgc atgcagggaa ggtcattaaa ggtgaagaga tcagcgtggt 200
ccccaatcgg tggctggatg ccagcctgtc ccccgtcac ctaggtgtcc 250
agggtggaag ccagtgcctg tcatgtgggg tggggcagga gccgactcta 300
acactagagc cagtgaacat catggagctc tatcttggtg ccaaggaatc 350
caagagcttc accttctacc ggcgggacat ggggtcacc tccagcttcg 400
agtcggctgc ctacccgggc tggttctctg gcacggtgcc tgaagccgat 450
cagcctgtca gactcaccca gtttcccag aatggtggct ggaatgcccc 500
catcacagac ttctacttcc agcagtgtga ctagggcaac gtgccccca 550
gaactccctg ggcagagcca gctcgggtga ggggtgagtg gaggagacct 600
atggcggaca atcactctct ctgctctcag gacccccacg tctgacttag 650
tgggcacctg accactttgt cttctggttc ccagtttga taaattctga 700
gatttgagc tcagtccacg gtctccccc actggatggt gctactgctg 750
tggaaccttg taaaaacctg tggggtaaa ctgggaataa catgaaaaga 800
tttctgtggg ggtgggggtg gggagtggtg ggaatcattc ctgcttaatg 850
gtaactgaca agtgttacc tgagccccg aggccaaacc atccccagtt 900
gagccttata ggtcagtag ctctccacat gaagtcctgt cactcaccac 950
tgtgcaggag agggagtggt tcatagatc agggatctat ggcccttggc 1000
ccagccccac ccccttccct ttaatcctgc cactgtcata tgctaccttt 1050
cctatctctt ccctcatcat cttgtgtggt gcatgaggag gtggtgatgt 1100
cagaagaaat ggctcgagct cagaagataa aagataagta gggtatgctg 1150
atcctctttt aaaaacccaa gatacaatca aaatcccaga tgctgtctc 1200
tattcccatg aaaaagtgtc catgacatat tgagaagacc tacttacaaa 1250
gtggcatata ttgcaattta ttttaattaa aagataccta tttatatatt 1300
tctttataga aaaaagtctg gaagagtta cttcaattgt agcaatgtca 1350
gggtgggtgc agtatagggt atttttcttt taattctggt aatttatctg 1400
tatttcctaa tttttctaca atgaagatga attccttgta taaaaataag 1450
aaaagaaatt aatcttgagg taagcagagc agacatcatc tctgattgtc 1500
ctcagcctcc acttcccag agtaaatca aattgaatcg agctctgctg 1550
ctctggttgg ttgtagtagt gatcaggaag cagatctcag caaagccact 1600
gaggaggagg ctgtgctgag tttgtgtggc tggaatctct gggtaaggaa 1650

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cttaaagaac aaaatcatc tggttaattct ttcctagaag gatcacagcc      1700
cctgggattc caaggcattg gatccagtct ctaagaaggc tgctgtactg      1750
gttgaattgt gtccccctca aattcacatc cttcttgaa tctcagtctg      1800
tgagtttatt tggagataag gtctctgcag atgtagttag ttaagacaag      1850
gtcatgctgg atgaagtag acctaattc aatagactg gtttccttgt      1900
atgaaaagga gaggacacag agacagagga gacgcgggga agactatgta      1950
aagatgaagg cagagatcgg agttttgcag ccacaagcta agaaacacca      2000
aggattgtgg caaccatcag aagcttgaa gaggcaaaga agaattcttc      2050
cctagaggct ttagagggat aacggctctg ctgaaacctt aatctcagac      2100
ttccagcctc ctgaacgaag aaagaataaa tttcggctgt ttttaagccac      2150
caaggataat tggttacagc agctctagga aactaataca gctgctaaaa      2200
tgatccctgt ctctcctgtt ttacattctg tgtgtgtccc ctcccacaat      2250
gtaccaaaag tgtctttgtg accaatagaa tatggcagaa gtgatggcat      2300
gccacttcca agattaggtt ataaaagaca ctgcagcttc tacttgagcc      2350
ctctctctct gccaccacc gcccacaatc tatcttgct cactcgtctc      2400
gggggaagct agctgccatg ctatgagcag gcctataaag agacttacgt      2450
ggtaaaaaat gaagtctcct gccacagcc acattagtga acctagaagc      2500
agagactctg tgagataatc gatgtttgtt gttttaagtt gctcagtttt      2550
ggcttaactt gttatgcagc aatagataaa taatatgcag agaagag      2598

```

<210> SEQ ID NO 152

<211> LENGTH: 155

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 152

```

Met Val Leu Ser Gly Ala Leu Cys Phe Arg Met Lys Asp Ser Ala
 1             5             10            15
Leu Lys Val Leu Tyr Leu His Asn Asn Gln Leu Leu Ala Gly Gly
                20             25            30
Leu His Ala Gly Lys Val Ile Lys Gly Glu Glu Ile Ser Val Val
                35             40            45
Pro Asn Arg Trp Leu Asp Ala Ser Leu Ser Pro Val Ile Leu Gly
                50             55            60
Val Gln Gly Gly Ser Gln Cys Leu Ser Cys Gly Val Gly Gln Glu
                65             70            75
Pro Thr Leu Thr Leu Glu Pro Val Asn Ile Met Glu Leu Tyr Leu
                80             85            90
Gly Ala Lys Glu Ser Lys Ser Phe Thr Phe Tyr Arg Arg Asp Met
                95             100           105
Gly Leu Thr Ser Ser Phe Glu Ser Ala Ala Tyr Pro Gly Trp Phe
                110            115           120
Leu Cys Thr Val Pro Glu Ala Asp Gln Pro Val Arg Leu Thr Gln
                125            130           135
Leu Pro Glu Asn Gly Gly Trp Asn Ala Pro Ile Thr Asp Phe Tyr
                140            145           150

```

-continued

Phe Gln Gln Cys Asp
155

<210> SEQ ID NO 153

<211> LENGTH: 1152

<212> TYPE: DNA

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 153

```

cttcagaaca ggttctcctt ccccgctcac cagttgctcg agttagaatt      50
gtctgcaatg gccgccctgc agaaatctgt gagctctttc cttatgggga      100
ccctggccac cagctgcctc cttctcttgg ccctcttggg acagggagga      150
gcagctgccc ccatcagctc ccaactgcagg cttgacaagt ccaacttcca      200
gcagccctat atcaccaacc gcaccttcat gctggctaag gaggctagct      250
tggctgataa caacacagac gttcgtctca ttggggagaa actggttocac      300
ggagtcagta tgagtgagcg ctgctatctg atgaagcagg tgctgaactt      350
cacccttgaa gaagtgtctg tccctcaatc tgataggttc cagccttata      400
tgaggagggt ggtgcccttc ctggccaggc tcagcaacag gctaagcaca      450
tgtcatattg aaggatgatg cctgcatatc cagaggaatg tgcaaaagct      500
gaaggacaca gtgaaaaagc ttggagagag tggagagatc aaagcaattg      550
gagaactgga tttgctgttt atgtctctga gaaatgcctg catttgacca      600
gagcaaaagt gaaaaatgaa taactaaccc ctttccctg ctagaaataa      650
caattgatag ccccaaagcg atttttttta accaaaagga agatggggaag      700
ccaaactcca tcatgatggg tggattccaa atgaaccctt gcgttagtta      750
caaaggaaac caatgccact ttgttttata agaccagaag gtagactttc      800
taagcataga tatttattga taacatttca ttgtaactgg tgttctatac      850
acagaaaaca atttattttt taaataattg tctttttcca taaaaaagat      900
tactttccat tccttttagg gaaaaaaccc ctaaatagct tcatgtttcc      950
ataatcagta ctttatattt ataaatgtat ttattattat tataagactg     1000
cattttattt atatcatttt attaatatgg atttatttat agaaacatca     1050
ttcgatattg ctacttgagt gtaaggctaa tattgatatt tatgacaata     1100
attatagagc tataacatgt ttatttgacc tcaataaaca cttggatata     1150
cc                                                                1152

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<210> SEQ ID NO 154

<211> LENGTH: 179

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 154

```

Met Ala Ala Leu Gln Lys Ser Val Ser Ser Phe Leu Met Gly Thr
 1           5           10          15
Leu Ala Thr Ser Cys Leu Leu Leu Leu Ala Leu Leu Val Gln Gly
          20          25          30
Gly Ala Ala Ala Pro Ile Ser Ser His Cys Arg Leu Asp Lys Ser
          35          40          45

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Asn	Phe	Gln	Gln	Pro	Tyr	Ile	Thr	Asn	Arg	Thr	Phe	Met	Leu	Ala
				50					55					60
Lys	Glu	Ala	Ser	Leu	Ala	Asp	Asn	Asn	Thr	Asp	Val	Arg	Leu	Ile
				65					70					75
Gly	Glu	Lys	Leu	Phe	His	Gly	Val	Ser	Met	Ser	Glu	Arg	Cys	Tyr
				80					85					90
Leu	Met	Lys	Gln	Val	Leu	Asn	Phe	Thr	Leu	Glu	Glu	Val	Leu	Phe
				95					100					105
Pro	Gln	Ser	Asp	Arg	Phe	Gln	Pro	Tyr	Met	Gln	Glu	Val	Val	Pro
				110					115					120
Phe	Leu	Ala	Arg	Leu	Ser	Asn	Arg	Leu	Ser	Thr	Cys	His	Ile	Glu
				125					130					135
Gly	Asp	Asp	Leu	His	Ile	Gln	Arg	Asn	Val	Gln	Lys	Leu	Lys	Asp
				140					145					150
Thr	Val	Lys	Lys	Leu	Gly	Glu	Ser	Gly	Glu	Ile	Lys	Ala	Ile	Gly
				155					160					165
Glu	Leu	Asp	Leu	Leu	Phe	Met	Ser	Leu	Arg	Asn	Ala	Cys	Ile	
				170					175					

<210> SEQ ID NO 155
 <211> LENGTH: 1320
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 155

ggcttgctga aaataaaatc aggactccta acctgctcca gtcagcctgc	50
ttccacgagg cctgtcagtc agtgcccagc ttgtgactga gtgtgcagtg	100
cccagcatgt accaggctcag tgcagagggc tgcctgaggg ctgtgctgag	150
agggagagga gcagagatgc tgctgagggt ggaggaggc caagctgccca	200
ggtttggggc tgggggcca gtaggtgag aaactgggat cccaggggga	250
gggtgcagat gaggagcga cccagattag gtgaggacag ttctctcatt	300
agccttttcc tacagtggtg tgcatctctg gcaatggtca tgggaacca	350
cacctacagc cactggccca gctgctgccc cagcaaaggc caggcacct	400
ctgaggagct gctgaggtgg agcactgtgc ctgtgcctcc cctagagcct	450
gctaggccca accgccacc agagtctgt agggccagt aagatggacc	500
cctcaacagc agggccatct ccccctggag atatgagttg gacagagact	550
tgaaccggct ccccaggac ctgtaccag cccgttgctt gtgccgcac	600
tgctgcagcc tacagacag cteccacatg gacccccggg gcaactcgga	650
gctgctctac cacaaccaga ctgtcttcta caggcggcca tgccatggcg	700
agaagggcac ccacaaggc tactgccttg agcgcaggct gtaccgtgtt	750
tccttagctt gtgtgtgtgt ggggccccgt gtgatgggct agccggacct	800
gctgaggctt ggtccctttt tgggaaacct ggagccaggt gtacaaccac	850
ttgccatgaa gggccaggat gccagatgc ttggcccctg tgaagtgtctg	900
tctggagcag caggatcccg ggacaggatg gggggctttg gggaaaacct	950
gcacttctgc acatthttaa aagagcagct gctgcttagg gccgccgaa	1000

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gctggtgtcc tgtcattttc tctcaggaag ggttttcaaa gttctgcccc      1050
tttctggagg ccaccactcc tgtctcttcc tcttttccca tcccctgcta      1100
ccctggcccc gcacaggcac tttctagata tttccccctt gctggagaag      1150
aaagagcccc tggttttatt tgtttgttta ctcatcactc agtgagcadc      1200
tactttgggt gcattctagt gtagttacta gtcttttgac atggatgatt      1250
ctgaggagga agctgttatt gaatgtatag agatttatcc aaataaatat      1300
ctttatttaa aaatgaaaaa      1320

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<210> SEQ ID NO 156
<211> LENGTH: 177
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien

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<400> SEQUENCE: 156

```

```

Met Arg Glu Arg Pro Arg Leu Gly Glu Asp Ser Ser Leu Ile Ser
 1           5           10          15
Leu Phe Leu Gln Val Val Ala Phe Leu Ala Met Val Met Gly Thr
          20          25          30
His Thr Tyr Ser His Trp Pro Ser Cys Cys Pro Ser Lys Gly Gln
          35          40          45
Asp Thr Ser Glu Glu Leu Leu Arg Trp Ser Thr Val Pro Val Pro
          50          55          60
Pro Leu Glu Pro Ala Arg Pro Asn Arg His Pro Glu Ser Cys Arg
          65          70          75
Ala Ser Glu Asp Gly Pro Leu Asn Ser Arg Ala Ile Ser Pro Trp
          80          85          90
Arg Tyr Glu Leu Asp Arg Asp Leu Asn Arg Leu Pro Gln Asp Leu
          95          100         105
Tyr His Ala Arg Cys Leu Cys Pro His Cys Val Ser Leu Gln Thr
          110         115         120
Gly Ser His Met Asp Pro Arg Gly Asn Ser Glu Leu Leu Tyr His
          125         130         135
Asn Gln Thr Val Phe Tyr Arg Arg Pro Cys His Gly Glu Lys Gly
          140         145         150
Thr His Lys Gly Tyr Cys Leu Glu Arg Arg Leu Tyr Arg Val Ser
          155         160         165
Leu Ala Cys Val Cys Val Arg Pro Arg Val Met Gly
          170         175

```

```

<210> SEQ ID NO 157
<211> LENGTH: 1515
<212> TYPE: DNA
<213> ORGANISM: Homo Sapien

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<400> SEQUENCE: 157

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```

ccggcgatgt cgctcgtgct gctaagcctg gccgcgctgt gcaggagcgc      50
cgtaccocga gagccgaccg ttcaatgtgg ctctgaaact gggccatctc      100
cagagtggat gctacaacat gatctaatacc cgggagactt gagggacctc      150
cgagtagaac ctgttacaac tagtgttgca acaggggact attcaatddd      200
gatgaatgta agctgggtac tccgggcaga tgccagcadc cgcttgttga      250

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agggcaccaa gatttgtgtg acgggcaaaa gcaacttcca gtcctacagc      300
tgtgtgaggt gcaattacac agaggccttc cagactcaga ccagaccctc      350
tgggtggtaaa tggacatttt cctacatcgg cttccctgta gagctgaaca      400
cagtctattt cattggggcc cataatatcc ctaatgcaaa tatgaatgaa      450
gatggccctt ccatgtctgt gaatttcacc tcaccaggct gcctagacca      500
cataatgaaa tataaaaaaa agtgtgtcaa ggccggaagc ctgtgggatc      550
cgaacatcac tgcttgaag aagaatgagg agacagtaga agtgaacttc      600
acaaccactc ccctgggaaa cagatacatg gctcttatcc aacacagcac      650
tatcatcggg ttttctcagg tgtttgagcc acaccagaag aaacaaacgc      700
gagcttcagt ggtgattcca gtgactgggg atagtgaagg tgctacggtg      750
cagctgactc catattttcc tacttgtggc agcgactgca tccgacataa      800
aggaacagtt gtgctctgcc cacaaacagg cgtcccttcc cctctggata      850
acaacaaaag caagccggga ggctggctgc ctctctcctc gctgtctctg      900
ctggtggcca catgggtgct ggtggcaggg atctatctaa tgtggaggca      950
cgaaaggatc aagaagactt ccttttctac caccacacta ctgcccccca     1000
ttaaggttct tgtggtttac ccatctgaaa tatgtttcca tcacacaatt     1050
tgttacttca ctgaatttct tcaaaaccat tgcagaagtg aggtcatcct     1100
tgaaaagtgg cagaaaaaga aatagcaga gatgggtcca gtgcagtggc     1150
ttgccactca aaagaaggca gcagacaaag togtcttctc tctttccaat     1200
gacgtcaaca gtgtgtgcca tggtaacctg ggcaagagcg agggcagtc     1250
cagtgagaac tctcaagacc tcttccccct tgcctttaac cttttctgca     1300
gtgatctaag aagccagatt catctgcaca aatacgtggt ggtotacttt     1350
agagagattg atacaaaaga cgattacaat gctctcagtg tctgccccaa     1400
gtaccacctc atgaaggatg ccaactgcttt ctgtgcagaa cttctccatg     1450
tcaagcagca ggtgtcagca ggaaaaagat cacaagcctg ccacgatggc     1500
tgctgctcct tgtag                                           1515

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<210> SEQ ID NO 158

<211> LENGTH: 502

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 158

```

Met Ser Leu Val Leu Leu Ser Leu Ala Ala Leu Cys Arg Ser Ala
 1           5           10          15
Val Pro Arg Glu Pro Thr Val Gln Cys Gly Ser Glu Thr Gly Pro
 20          25          30
Ser Pro Glu Trp Met Leu Gln His Asp Leu Ile Pro Gly Asp Leu
 35          40          45
Arg Asp Leu Arg Val Glu Pro Val Thr Thr Ser Val Ala Thr Gly
 50          55          60
Asp Tyr Ser Ile Leu Met Asn Val Ser Trp Val Leu Arg Ala Asp
 65          70          75
Ala Ser Ile Arg Leu Leu Lys Ala Thr Lys Ile Cys Val Thr Gly

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Tyr His Leu Met Lys Asp Ala Thr Ala Phe Cys Ala Glu Leu Leu
 470 475 480
 His Val Lys Gln Gln Val Ser Ala Gly Lys Arg Ser Gln Ala Cys
 485 490 495
 His Asp Gly Cys Cys Ser Leu
 500

<210> SEQ ID NO 159
 <211> LENGTH: 535
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 159
 agccaccagc gcaacatgac agtgaagacc ctgcatggcc cagccatggt 50
 caagtacttg ctgctgtcga tattggggct tgcctttctg agtgaggcgg 100
 cagctcggaa aatccccaaa gtaggacata cttttttcca aaagcctgag 150
 agttgcccgc ctgtgccagg aggtagtatg aagcttgaca ttggcatcat 200
 caatgaaaac cagcgcgttt ccatgtcacg taacatcgag agccgctcca 250
 cctccccctg gaattacact gtcacttggg accccaaccg gtaccctctg 300
 gaagttgtac aggcccagtg taggaacttg ggctgcatca atgotcaagg 350
 aaaggaagc atctccatga attccgttcc catccagcaa gagaccctgg 400
 tcgtccggag gaagcaccaa ggctgctctg tttctttcca gttggagaag 450
 gtgctggtga ctgttggtg cactgctgc acccctgtca tccaccatgt 500
 gcagtaagag gtgcatatcc actcagctga agaag 535

<210> SEQ ID NO 160
 <211> LENGTH: 163
 <212> TYPE: PRT
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 160
 Met Thr Val Lys Thr Leu His Gly Pro Ala Met Val Lys Tyr Leu
 1 5 10 15
 Leu Leu Ser Ile Leu Gly Leu Ala Phe Leu Ser Glu Ala Ala Ala
 20 25 30
 Arg Lys Ile Pro Lys Val Gly His Thr Phe Phe Gln Lys Pro Glu
 35 40 45
 Ser Cys Pro Pro Val Pro Gly Gly Ser Met Lys Leu Asp Ile Gly
 50 55 60
 Ile Ile Asn Glu Asn Gln Arg Val Ser Met Ser Arg Asn Ile Glu
 65 70 75
 Ser Arg Ser Thr Ser Pro Trp Asn Tyr Thr Val Thr Trp Asp Pro
 80 85 90
 Asn Arg Tyr Pro Ser Glu Val Val Gln Ala Gln Cys Arg Asn Leu
 95 100 105
 Gly Cys Ile Asn Ala Gln Gly Lys Glu Asp Ile Ser Met Asn Ser
 110 115 120
 Val Pro Ile Gln Gln Glu Thr Leu Val Val Arg Arg Lys His Gln
 125 130 135
 Gly Cys Ser Val Ser Phe Gln Leu Glu Lys Val Leu Val Thr Val

-continued

	140	145	150	
Gly Cys Thr Cys Val Thr Pro Val Ile His His Val Gln				
	155	160		
 <210> SEQ ID NO 161				
<211> LENGTH: 2380				
<212> TYPE: DNA				
<213> ORGANISM: Homo Sapien				
 <400> SEQUENCE: 161				
acactggcca acaaaaaacg aaagcactcc gtgctggaag taggaggaga				50
gtcaggactc ccaggacaga gagtgacaaa actaccacgc acagccccct				100
ccgccccctc tggaggctga agagggatcc cagcccctgc caccacaga				150
cacgggtgta ctggggtgtc tgccccctt gggggggggc agcacagggc				200
ctcaggcctg ggtgccacct ggcacctaga agatgcctgt gccctggttc				250
ttgctgtcct tggcactggg ccgaagccca gtggtccttt ctctggagag				300
gcttggtggg cctcaggacg ctaccactg ctctccgggc ctctcctgcc				350
gcctctggga cagtgcata ctctgcctgc ctggggacat cgtgcctgct				400
ccgggccccg tgctggcgcg tacgcacctg cagacagagc tgggtctgag				450
gtgccagaag gagaccgact gtgacctctg tctgcgtgtg gctgtccact				500
tggccgtgca tgggacttgg gaagagcctg aagatgagga aaagtttgga				550
ggagcagctg actcaggggg ggaggagcct agaatgcct ctctccaggc				600
ccaagtctg ctctccttcc aggcctaccc tactgcccgc tgcgtcctgc				650
tggagggtgca agtgccctgct gcctctgtgc agtttgggtca gctgtggggc				700
tctgtgtgat atgactgctt cgaggctgcc ctagggagtg aggtacgaat				750
ctggtcctat actcagccca ggtacgagaa ggaactcaac cacacacagc				800
agctgcctgc cctgccctgg ctcaactgtg cagcagatgg tgacaactgt				850
catctgtgtc tgaatgtctc tgaggagcag cacttcggcc tctccctgta				900
ctggaatcag gtccagggcc ccccaaaacc ccggtggcac aaaaacctga				950
ctggaccgca gatcattacc ttgaaccaca cagacctggt tccctgcctc				1000
tgtattcagg tgtggcctct ggaacctgac tccgttagga cgaacatctg				1050
ccccttcagg gaggaccccc gcgcacacca gaacctctgg caagccgccc				1100
gactgcgact gctgacctg cagagctggc tgctggacgc accgtgctcg				1150
ctgcccgcag aagcggcact gtgctggcgg gctccgggtg gggaccctg				1200
ccagccactg gtcccaccgc tttcctggga gaacgtcact gtggacaagg				1250
ttctcgagtt cccattgctg aaaggccacc ctaacctctg tgttcagggt				1300
aacagctcgg agaagctgca gctgcaggag tgcttgtggg ctgactccct				1350
ggggcctctc aaagacgatg tgctactgtt ggagacacga ggcccccagg				1400
acaacagatc cctctgtgcc ttggaaccga gtggtgttac ttcactacco				1450
agcaaaagct ccacgagggc agctcgcctt ggagagtact tactacaaga				1500
cctgcagtoa ggcagtgctc tgacgctatg ggacgatgac ttgggagcgc				1550
tatgggcctg ccccatggac aaatacatcc acaagcgtg ggcctcgtg				1600

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tggtggcct gcctactcct tgccgctgcg ctttccctca tcctccttct      1650
caaaaaggat cacgcgaaa ggtggctgag gctcttgaag caggacgtcc      1700
gctcgggggc ggccgccagg ggccgcgcgg ctctgctcct ctactcagcc      1750
gatgactcgg gtttcgagcg cctggtgggc gccctggcgt cggccctgtg      1800
ccagctgccg ctgcccgtgg ccgtagacct gtggagccgt cgtgaactga      1850
gcgcgcaggg gcccggtggct tggtttcacg cgcagcggcg ccagaccctg      1900
caggaggggc gcgtggtggt ctgtctcttc tctcccgtg cggtggcgct      1950
gtgcagcgag tggctacagg atgggggtgc cgggcccggg gcgcacggcc      2000
cgcacgacgc cttccgcgcc tcgctcagct gcgtgctgcc cgacttcttg      2050
cagggccggg cgcccggcag ctacgtgggg gcctgcttcg acaggctgct      2100
ccaccggagc gccgtaccgg cccttttccg caccgtgccc gtcttcacac      2150
tgccctccca actgccagac ttctggggg cctgcagca gcctcgcgcc      2200
ccgcgttccg ggcggtcca agagagagcg gagcaagtgt cccggggcct      2250
tcagccagcc ctggatagct acttccatcc cccggggact cccgcgccgg      2300
gacgcggggt gggaccaggg gcgggacctg gggcggggga cgggacttaa      2350
ataaaggcag acgctgtttt tctaaaaaaa      2380

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<210> SEQ ID NO 162

<211> LENGTH: 705

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 162

```

Met Pro Val Pro Trp Phe Leu Leu Ser Leu Ala Leu Gly Arg Ser
  1             5             10            15
Pro Val Val Leu Ser Leu Glu Arg Leu Val Gly Pro Gln Asp Ala
          20             25            30
Thr His Cys Ser Pro Gly Leu Ser Cys Arg Leu Trp Asp Ser Asp
          35             40            45
Ile Leu Cys Leu Pro Gly Asp Ile Val Pro Ala Pro Gly Pro Val
          50             55            60
Leu Ala Pro Thr His Leu Gln Thr Glu Leu Val Leu Arg Cys Gln
          65             70            75
Lys Glu Thr Asp Cys Asp Leu Cys Leu Arg Val Ala Val His Leu
          80             85            90
Ala Val His Gly His Trp Glu Glu Pro Glu Asp Glu Glu Lys Phe
          95            100           105
Gly Gly Ala Ala Asp Ser Gly Val Glu Glu Pro Arg Asn Ala Ser
          110           115           120
Leu Gln Ala Gln Val Val Leu Ser Phe Gln Ala Tyr Pro Thr Ala
          125           130           135
Arg Cys Val Leu Leu Glu Val Gln Val Pro Ala Ala Leu Val Gln
          140           145           150
Phe Gly Gln Ser Val Gly Ser Val Val Tyr Asp Cys Phe Glu Ala
          155           160           165
Ala Leu Gly Ser Glu Val Arg Ile Trp Ser Tyr Thr Gln Pro Arg
          170           175           180

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Tyr	Glu	Lys	Glu	Leu	Asn	His	Thr	Gln	Gln	Leu	Pro	Ala	Leu	Pro	
				185					190					195	
Trp	Leu	Asn	Val	Ser	Ala	Asp	Gly	Asp	Asn	Val	His	Leu	Val	Leu	
				200					205					210	
Asn	Val	Ser	Glu	Glu	Gln	His	Phe	Gly	Leu	Ser	Leu	Tyr	Trp	Asn	
				215					220					225	
Gln	Val	Gln	Gly	Pro	Pro	Lys	Pro	Arg	Trp	His	Lys	Asn	Leu	Thr	
				230					235					240	
Gly	Pro	Gln	Ile	Ile	Thr	Leu	Asn	His	Thr	Asp	Leu	Val	Pro	Cys	
				245					250					255	
Leu	Cys	Ile	Gln	Val	Trp	Pro	Leu	Glu	Pro	Asp	Ser	Val	Arg	Thr	
				260					265					270	
Asn	Ile	Cys	Pro	Phe	Arg	Glu	Asp	Pro	Arg	Ala	His	Gln	Asn	Leu	
				275					280					285	
Trp	Gln	Ala	Ala	Arg	Leu	Arg	Leu	Leu	Thr	Leu	Gln	Ser	Trp	Leu	
				290					295					300	
Leu	Asp	Ala	Pro	Cys	Ser	Leu	Pro	Ala	Glu	Ala	Ala	Leu	Cys	Trp	
				305					310					315	
Arg	Ala	Pro	Gly	Gly	Asp	Pro	Cys	Gln	Pro	Leu	Val	Pro	Pro	Leu	
				320					325					330	
Ser	Trp	Glu	Asn	Val	Thr	Val	Asp	Lys	Val	Leu	Glu	Phe	Pro	Leu	
				335					340					345	
Leu	Lys	Gly	His	Pro	Asn	Leu	Cys	Val	Gln	Val	Asn	Ser	Ser	Glu	
				350					355					360	
Lys	Leu	Gln	Leu	Gln	Glu	Cys	Leu	Trp	Ala	Asp	Ser	Leu	Gly	Pro	
				365					370					375	
Leu	Lys	Asp	Asp	Val	Leu	Leu	Leu	Glu	Thr	Arg	Gly	Pro	Gln	Asp	
				380					385					390	
Asn	Arg	Ser	Leu	Cys	Ala	Leu	Glu	Pro	Ser	Gly	Cys	Thr	Ser	Leu	
				395					400					405	
Pro	Ser	Lys	Ala	Ser	Thr	Arg	Ala	Ala	Arg	Leu	Gly	Glu	Tyr	Leu	
				410					415					420	
Leu	Gln	Asp	Leu	Gln	Ser	Gly	Gln	Cys	Leu	Gln	Leu	Trp	Asp	Asp	
				425					430					435	
Asp	Leu	Gly	Ala	Leu	Trp	Ala	Cys	Pro	Met	Asp	Lys	Tyr	Ile	His	
				440					445					450	
Lys	Arg	Trp	Ala	Leu	Val	Trp	Leu	Ala	Cys	Leu	Leu	Phe	Ala	Ala	
				455					460					465	
Ala	Leu	Ser	Leu	Ile	Leu	Leu	Leu	Lys	Lys	Asp	His	Ala	Lys	Gly	
				470					475					480	
Trp	Leu	Arg	Leu	Leu	Lys	Gln	Asp	Val	Arg	Ser	Gly	Ala	Ala	Ala	
				485					490					495	
Arg	Gly	Arg	Ala	Ala	Leu	Leu	Leu	Tyr	Ser	Ala	Asp	Asp	Ser	Gly	
				500					505					510	
Phe	Glu	Arg	Leu	Val	Gly	Ala	Leu	Ala	Ser	Ala	Leu	Cys	Gln	Leu	
				515					520					525	
Pro	Leu	Arg	Val	Ala	Val	Asp	Leu	Trp	Ser	Arg	Arg	Glu	Leu	Ser	
				530					535					540	
Ala	Gln	Gly	Pro	Val	Ala	Trp	Phe	His	Ala	Gln	Arg	Arg	Gln	Thr	
				545					550					555	

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Leu Gln Glu Gly Gly Val Val Val Leu Leu Phe Ser Pro Gly Ala
 560 565 570

Val Ala Leu Cys Ser Glu Trp Leu Gln Asp Gly Val Ser Gly Pro
 575 580 585

Gly Ala His Gly Pro His Asp Ala Phe Arg Ala Ser Leu Ser Cys
 590 595 600

Val Leu Pro Asp Phe Leu Gln Gly Arg Ala Pro Gly Ser Tyr Val
 605 610 615

Gly Ala Cys Phe Asp Arg Leu Leu His Pro Asp Ala Val Pro Ala
 620 625 630

Leu Phe Arg Thr Val Pro Val Phe Thr Leu Pro Ser Gln Leu Pro
 635 640 645

Asp Phe Leu Gly Ala Leu Gln Gln Pro Arg Ala Pro Arg Ser Gly
 650 655 660

Arg Leu Gln Glu Arg Ala Glu Gln Val Ser Arg Ala Leu Gln Pro
 665 670 675

Ala Leu Asp Ser Tyr Phe His Pro Pro Gly Thr Pro Ala Pro Gly
 680 685 690

Arg Gly Val Gly Pro Gly Ala Gly Pro Gly Ala Gly Asp Gly Thr
 695 700 705

<210> SEQ ID NO 163
 <211> LENGTH: 2478
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 163

gtcagtgcgg gaggccggtc agccaccaag atgactgaca ggttcagctc 50

tctgcagcac actaccctca agccacctga tgtgacctgt atctccaaag 100

tgagatcgat tcagatgatt gttcatccta cccccacgcc aatccgtgca 150

ggcgatggcc accggctaac cctggaagac atcttccatg acctgttcta 200

ccacttagag ctccaggtca accgcaccta ccaaatgcac cttggaggga 250

agcagagaga atatgagttc ttcggcctga cccctgacac agagttcctt 300

ggcaccatca tgatttgctg tcccacctgg gccaaggaga gtgccccta 350

catgtgccga gtgaagacac tgccagaccg gacatggacc tactccttct 400

ccggagcctt cctgtttctc atgggcttcc tcgtcgcagt actctgctac 450

ctgagctaca gatatgtcac caagcgcct gcacctocca actccctgaa 500

cgctccagca gtcctgactt tccagccgct gcgcttcac caggagcacg 550

tctgatccc tgtctttgac ctccagggcc ccagcagtct ggcccagcct 600

gtccagtact cccagatcag ggtgtctgga cccagggagc ccgcaggagc 650

tccacagcgg catagcctgt ccgagatcac ctacttaggg cagccagaca 700

tctccatcct ccagccctcc aacgtgccac ctccccagat cctctcccca 750

ctgtctatg ccccaaagc tgcccctgag gtcgggcccc catcctatgc 800

acctcagtg acccccgaag ctcaattccc attctacgcc ccacaggcca 850

tctctaaggt ccagccttcc tcctatgccc ctcaagccac tccggacagc 900

tggcctccct cctatggggt atgcatggaa ggttctggca aagactcccc 950

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cactgggaca ctttctagtc ctaaacacct taggcctaaa ggtcagcttc      1000
agaaagagcc accagctgga agctgcatgt taggtggcct ttctctgcag      1050
gaggtgacct ccttgctat ggaggaatcc caagaagcaa aatcattgca      1100
ccagcccctg gggatttga cagacagAAC atctgaccca aatgtgctac      1150
acagtgggga ggaagggaca ccacagtacc taaagggccA gctcccctc      1200
ctctcctcag tccagatcga gggccacccc atgtccctcc ctttgcaacc      1250
tccttcctgg ccatgttccc cctcggacca aggtccaagt ccctggggcc      1300
tgctggagtc ccttgtgtgt cccaaggatg aagccaagag cccagcccct      1350
gagacctcag acctggagca gccacagaaA ctggattctc ttttcagagg      1400
cctggccctg actgtgcagt gggagtccctg aggggaatgg gaaaggcttg      1450
gtgcttcctc cctgtcccta cccagtgtca catccttggc tgtcaatccc      1500
atgcctgccc atgccacaca ctctgcgata tggcctcaga cgggtgccct      1550
tgagagaagc agagggagtg gcatgcaggg cccctgccat ggggtgcctc      1600
ctcaccggaa caaagcagca tgataaggac tgcagcgggg gagctctggg      1650
gagcagcttg tgtagacaag cgcgtgctcg ctgagccctg caaggcagaa      1700
atgacagtgc aaggaggaaa tgcagggaaa ctcccgaggt ccagagcccc      1750
acctcctaac acctggatt caaagtgtct agggaatttg cctctccttg      1800
ccccattcct ggccagtttc acaatctagc tcgacagagc atgaggcccc      1850
tgctctctot gtcattgttc aaagtgggga agagagcctg gaaaagaacc      1900
aggcctggaa aagaaccaga aggaggcttg gcagaaccag aacaacctgc      1950
acttctgcca aggccaagggc cagcaggagc gcaggactct agggaggggt      2000
gtggcctgca gctcattccc agccagggca actgctgac gttgcaagat      2050
ttcagcttca ttctctgat agaacaaagc gaaatgcagg tccaccaggg      2100
agggagacac acaagccttt tctgcaggca ggagtctcag acctatcct      2150
gagaatgggg tttgaaagga aggtgagggc tgtggcccct ggacgggtac      2200
aataacacac tgtactgatg tcacaacttt gcaagctctg ccttgggttc      2250
agcccatctg ggctcaaat ccagcctcac cactcacaag ctgtgtgact      2300
tcaaacaatA gaaatcagtg cccagaacct cggtttcctc atctgtaatg      2350
tggggatcat aacacctacc tcatggagtt gtggtgaaga tgaatgaag      2400
tcatgtcttt aaagtctta atagtcctg gtacatgggc agtgcccaat      2450
aaacggtagc tatttaaaaa aaaaaaaaa      2478

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<210> SEQ ID NO 164

<211> LENGTH: 574

<212> TYPE: PRT

<213> ORGANISM: Homo Sapien

<400> SEQUENCE: 164

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

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His Ala Pro Glu Asp Pro Ser Asp Leu Leu Gln His Val Lys Phe
 20             25             30

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Gln	Ser	Ser	Asn	Phe	Glu	Asn	Ile	Leu	Thr	Trp	Asp	Ser	Gly	Pro
			35						40					45
Glu	Gly	Thr	Pro	Asp	Thr	Val	Tyr	Ser	Ile	Glu	Tyr	Lys	Thr	Tyr
			50						55					60
Gly	Glu	Arg	Asp	Trp	Val	Ala	Lys	Lys	Gly	Cys	Gln	Arg	Ile	Thr
			65						70					75
Arg	Lys	Ser	Cys	Asn	Leu	Thr	Val	Glu	Thr	Gly	Asn	Leu	Thr	Glu
			80						85					90
Leu	Tyr	Tyr	Ala	Arg	Val	Thr	Ala	Val	Ser	Ala	Gly	Gly	Arg	Ser
			95						100					105
Ala	Thr	Lys	Met	Thr	Asp	Arg	Phe	Ser	Ser	Leu	Gln	His	Thr	Thr
			110						115					120
Leu	Lys	Pro	Pro	Asp	Val	Thr	Cys	Ile	Ser	Lys	Val	Arg	Ser	Ile
			125						130					135
Gln	Met	Ile	Val	His	Pro	Thr	Pro	Thr	Pro	Ile	Arg	Ala	Gly	Asp
			140						145					150
Gly	His	Arg	Leu	Thr	Leu	Glu	Asp	Ile	Phe	His	Asp	Leu	Phe	Tyr
			155						160					165
His	Leu	Glu	Leu	Gln	Val	Asn	Arg	Thr	Tyr	Gln	Met	His	Leu	Gly
			170						175					180
Gly	Lys	Gln	Arg	Glu	Tyr	Glu	Phe	Phe	Gly	Leu	Thr	Pro	Asp	Thr
			185						190					195
Glu	Phe	Leu	Gly	Thr	Ile	Met	Ile	Cys	Val	Pro	Thr	Trp	Ala	Lys
			200						205					210
Glu	Ser	Ala	Pro	Tyr	Met	Cys	Arg	Val	Lys	Thr	Leu	Pro	Asp	Arg
			215						220					225
Thr	Trp	Thr	Tyr	Ser	Phe	Ser	Gly	Ala	Phe	Leu	Phe	Ser	Met	Gly
			230						235					240
Phe	Leu	Val	Ala	Val	Leu	Cys	Tyr	Leu	Ser	Tyr	Arg	Tyr	Val	Thr
			245						250					255
Lys	Pro	Pro	Ala	Pro	Pro	Asn	Ser	Leu	Asn	Val	Gln	Arg	Val	Leu
			260						265					270
Thr	Phe	Gln	Pro	Leu	Arg	Phe	Ile	Gln	Glu	His	Val	Leu	Ile	Pro
			275						280					285
Val	Phe	Asp	Leu	Ser	Gly	Pro	Ser	Ser	Leu	Ala	Gln	Pro	Val	Gln
			290						295					300
Tyr	Ser	Gln	Ile	Arg	Val	Ser	Gly	Pro	Arg	Glu	Pro	Ala	Gly	Ala
			305						310					315
Pro	Gln	Arg	His	Ser	Leu	Ser	Glu	Ile	Thr	Tyr	Leu	Gly	Gln	Pro
			320						325					330
Asp	Ile	Ser	Ile	Leu	Gln	Pro	Ser	Asn	Val	Pro	Pro	Pro	Gln	Ile
			335						340					345
Leu	Ser	Pro	Leu	Ser	Tyr	Ala	Pro	Asn	Ala	Ala	Pro	Glu	Val	Gly
			350						355					360
Pro	Pro	Ser	Tyr	Ala	Pro	Gln	Val	Thr	Pro	Glu	Ala	Gln	Phe	Pro
			365						370					375
Phe	Tyr	Ala	Pro	Gln	Ala	Ile	Ser	Lys	Val	Gln	Pro	Ser	Ser	Tyr
			380						385					390
Ala	Pro	Gln	Ala	Thr	Pro	Asp	Ser	Trp	Pro	Pro	Ser	Tyr	Gly	Val
			395						400					405
Cys	Met	Glu	Gly	Ser	Gly	Lys	Asp	Ser	Pro	Thr	Gly	Thr	Leu	Ser

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	410		415		420
Ser Pro Lys His	Leu Arg Pro Lys Gly	Gln Leu Gln Lys Glu	Pro		
	425		430		435
Pro Ala Gly Ser	Cys Met Leu Gly Gly	Leu Ser Leu Gln Glu	Val		
	440		445		450
Thr Ser Leu Ala	Met Glu Glu Ser Gln	Glu Ala Lys Ser Leu	His		
	455		460		465
Gln Pro Leu Gly	Ile Cys Thr Asp Arg	Thr Ser Asp Pro Asn	Val		
	470		475		480
Leu His Ser Gly	Glu Glu Gly Thr Pro	Gln Tyr Leu Lys Gly	Gln		
	485		490		495
Leu Pro Leu Leu	Ser Ser Val Gln Ile	Glu Gly His Pro Met	Ser		
	500		505		510
Leu Pro Leu Gln	Pro Pro Ser Gly Pro	Cys Ser Pro Ser Asp	Gln		
	515		520		525
Gly Pro Ser Pro	Trp Gly Leu Leu Glu	Ser Leu Val Cys Pro	Lys		
	530		535		540
Asp Glu Ala Lys	Ser Pro Ala Pro Glu	Thr Ser Asp Leu Glu	Gln		
	545		550		555
Pro Thr Glu Leu	Asp Ser Leu Phe Arg	Gly Leu Ala Leu Thr	Val		
	560		565		570
Gln Trp Glu Ser					

<210> SEQ ID NO 165
 <211> LENGTH: 1060
 <212> TYPE: DNA
 <213> ORGANISM: Homo Sapien

<400> SEQUENCE: 165

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    ctggggggcgc tctgggtgggt cccggggccag tcggatctca gccacggacg          150
    gcgtttctcg gacctcaaag tgtgcgggga cgaagagtgc agcatgttaa          200
    tgtaccgtgg gaaagctcct gaagacttca cgggccctga ttgtcgtttt          250
    gtgaatttta aaaaagtgta cgatgtatat gtctactaca aactggcagg          300
    gggatccctt gaactttggg ctggaagtgt tgaacacagt tttggatatt          350
    ttccaaaaga tttgatcaag gtacttcata aatacacgga agaagagcta          400
    catattccag cagatgagac agactttgtc tgctttgaag gaggaagaga          450
    tgattttaat agttataatg tagaagagct tttaggatct ttggaactgg          500
    aggactctgt acctgaagag tcgaagaaag ctgaagaagt ttctcagcac          550
    agagagaaat ctctgagga gtctcggggg cgtgaacttg accctgtgcc          600
    tgagcccagc gcattcagag ctgattcaga ggatggagaa ggtgctttct          650
    cagagagcac cgaggggctg cagggacagc cctcagctca ggagagccac          700
    cctcacacca gcggtcctgc ggctaacgct cagggagtgc agtctctggt          750
    ggacactttt gaagaaattc tgacacataa attgaaagtg ccggaagcgc          800
    aaagcagaac tggcaatagt tctcctgcct cgggtggagcg ggagaagaca          850
    
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<210> SEQ ID NO 167				
<211> LENGTH: 2570				
<212> TYPE: DNA				
<213> ORGANISM: Homo Sapien				
<400> SEQUENCE: 167				
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tctaggacat acacgggacc ccctaacttc agtcccccaa acgcgcaccc				150
tcgaagtctt gaactccagc cccgcacatc cacgcgcggc acagggcggg				200
cagggcggag gtcccggccg aaggcgatgc gcgcaggggg tcgggcagct				250
gggctcgggc ggcgggagta gggcccggca gggaggcagc gaggtgcat				300
attcagagtc gcgggctgcg ccctggggcag aggcgcacct cgctccacgc				350
aacacctgct gctgccaccg cgcgcgatg agccgcgtgg tctogctgct				400
gctggggccc gcgctgctct gcggccaccg agccttctgc cgcgcgtgg				450
tcagcggcca aaaggtgtgt ttgtctgact tcaagcatcc ctgotacaaa				500
atggcctact tccatgaact gtccagccga gtgagctttc aggaggcacg				550
cctgcttgtt gagagtgagg gaggagtcct cctcagcctt gagaatgaag				600
cagaacagaa gttaatagag agcatgttgc aaaacctgac aaaaccgggg				650
acagggattt ctgatgtga ttcttgata gggctttgga ggaatggaga				700
tgggcaaaaca tctggtgcct gccagatct ctaccagtgg tctgatggaa				750
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aagccttacc ttacaaatca accagagac acccatcaga atgtggttgt				1000
tactgaagca ggtataattc ccaatctaatt ttatgttgtt ataccaacaa				1050
taccctgct cttactgata ctgggtgctt ttggaacctg ttgtttccag				1100
atgctgcata aaagtaaagg aagaacaaaa actagtccaa accagtctac				1150
actgtggatt tcaaagagta ccagaaaaga aagtggcatg gaagtataat				1200
aactcattga cttgggtcca gaattttgta attctggatc tgtataagga				1250
atggcatcag aacaatagct tggaatggct tgaatcaca aaggatctgc				1300
aagatgaact gtaagctccc ccttgaggca aatattaaag taatttttat				1350
atgtctatta ttccatttaa agaataatgct gtgctaataa tggagtgaga				1400
catgcttatt ttgctaaagg atgcacccaa acttcaaact tcaagcaaat				1450
gaaatggaca atgcagataa agttgttatc aacacgtcgg gagtatgtgt				1500
gttagaagca attcctttta ttctttcac ctttcataag ttgttatcta				1550
gtcaatgtaa tgtatattgt attgaaatth acagtgctga aaagtatth				1600

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acctttgcat aagtgttga taaaaatgaa ctgttctaatt atttattttt      1650
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ctgtttgtcaa ctgaattcac acacacacaa atatagtacc atagaaaaag      1750
tttgttttct cgaataaatt catctttcag cttctctgct ttgtgtcaat      1800
gtctaggaaa tctcttcaga aataagaagc tatttcatta agtgtgatat      1850
aaacctcctc aaacatttta cttagaggca aggattgtct aatttcaatt      1900
gtgcaagaca tgtgccttat aattattttt agcttaaaat taaacagatt      1950
ttgtaataat gtaactttgt taataggtgc ataaacacta atgcagtcaa      2000
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ttgcctatat aatgagaagc agctctctga gggttctgaa atcaatgtgg      2100
tccctctctt gcccaactaaa caaagatggt tgttcggggg ttgggattga      2150
cactggaggc agatagttgc aaagttagtc taaggtttcc cttagctgtat      2200
ttagcctctg actatattag tatacaaaaga ggtcatgtgg ttgagaccag      2250
gtgaatagtc actatcagtg tggagacaag cacagcacac agacatttta      2300
ggaaggaaa gaaactacgaa atcgtgtgaa aatgggttgg aacctatcag      2350
tgatcgcata ttcattgatg agggtttgct tgagatagaa aatggtggct      2400
cctttctgtc ttatctccta gtttcttcaa tgcttacgcc ttgttcttct      2450
caagagaaa ttgtaactct ctggtcttca tatgtccctg tgctcctttt      2500
aaccaataaa agagtctctg tttctggggg aaaaaaaaaa aaaaaaaaaa      2550
aaaaaaaaaa aaaaaaaaaa      2570
    
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<210> SEQ ID NO 168
<211> LENGTH: 273
<212> TYPE: PRT
<213> ORGANISM: Homo Sapien
    
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<400> SEQUENCE: 168

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Met Ser Arg Val Val Ser Leu Leu Leu Gly Ala Ala Leu Leu Cys
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Gly His Gly Ala Phe Cys Arg Arg Val Val Ser Gly Gln Lys Val
  20          25          30

Cys Phe Ala Asp Phe Lys His Pro Cys Tyr Lys Met Ala Tyr Phe
  35          40          45

His Glu Leu Ser Ser Arg Val Ser Phe Gln Glu Ala Arg Leu Ala
  50          55          60

Cys Glu Ser Glu Gly Gly Val Leu Leu Ser Leu Glu Asn Glu Ala
  65          70          75

Glu Gln Lys Leu Ile Glu Ser Met Leu Gln Asn Leu Thr Lys Pro
  80          85          90

Gly Thr Gly Ile Ser Asp Gly Asp Phe Trp Ile Gly Leu Trp Arg
  95          100         105

Asn Gly Asp Gly Gln Thr Ser Gly Ala Cys Pro Asp Leu Tyr Gln
  110         115         120

Trp Ser Asp Gly Ser Asn Ser Gln Tyr Arg Asn Trp Tyr Thr Asp
  125         130         135

Glu Pro Ser Cys Gly Ser Glu Lys Cys Val Val Met Tyr His Gln
    
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140	145	150
Pro Thr Ala Asn	Pro Gly Leu Gly Gly	Pro Tyr Leu Tyr Gln Trp
155	160	165
Asn Asp Asp Arg	Cys Asn Met Lys His	Asn Tyr Ile Cys Lys Tyr
170	175	180
Glu Pro Glu Ile	Asn Pro Thr Ala Pro	Val Glu Lys Pro Tyr Leu
185	190	195
Thr Asn Gln Pro	Gly Asp Thr His Gln	Asn Val Val Val Thr Glu
200	205	210
Ala Gly Ile Ile	Pro Asn Leu Ile Tyr	Val Val Ile Pro Thr Ile
215	220	225
Pro Leu Leu Leu	Leu Ile Leu Val Ala	Phe Gly Thr Cys Cys Phe
230	235	240
Gln Met Leu His	Lys Ser Lys Gly Arg	Thr Lys Thr Ser Pro Asn
245	250	255
Gln Ser Thr Leu	Trp Ile Ser Lys Ser	Thr Arg Lys Glu Ser Gly
260	265	270
Met Glu Val		

<210> SEQ ID NO 169
 <211> LENGTH: 43
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic oligonucleotide probe

<400> SEQUENCE: 169

tgtaaaacga cggccagtta aatagacctg caattattaa tct 43

<210> SEQ ID NO 170
 <211> LENGTH: 41
 <212> TYPE: DNA
 <213> ORGANISM: Artificial Sequence
 <220> FEATURE:
 <223> OTHER INFORMATION: Synthetic oligonucleotide probe

<400> SEQUENCE: 170

caggaaacag ctatgaccac ctgcacacct gcaaatccat t 41

1. An isolated nucleic acid having at least 80% nucleic acid sequence identity to:

- a nucleic acid sequence encoding the polypeptide shown in FIG. 14 (SEQ ID NO:14);
- a nucleic acid sequence encoding the polypeptide shown in FIG. 14 (SEQ ID NO:14), lacking its associated signal peptide;
- a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in FIG. 14 (SEQ ID NO:14);
- a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in FIG. 14 (SEQ ID NO:14), lacking its associated signal peptide;
- the nucleic acid sequence shown in FIG. 13 (SEQ ID NO:13);
- the full-length coding sequence of the nucleic acid sequence shown in FIG. 13 (SEQ ID NO:13); or

(g) the full-length coding sequence of the cDNA deposited under ATCC accession number 209788.

2. The isolated nucleic acid of claim 1 having at least 85% nucleic acid sequence identity to:

- a nucleic acid sequence encoding the polypeptide shown in FIG. 14 (SEQ ID NO:14);
- a nucleic acid sequence encoding the polypeptide shown in FIG. 14 (SEQ ID NO:14), lacking its associated signal peptide;
- a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in FIG. 14 (SEQ ID NO:14);
- a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in FIG. 14 (SEQ ID NO:14), lacking its associated signal peptide;
- the nucleic acid sequence shown in FIG. 13 (SEQ ID NO:13);

- (f) the full-length coding sequence of the nucleic acid sequence shown in **FIG. 13** (SEQ ID NO:13); or
- (g) the full-length coding sequence of the cDNA deposited under ATCC accession number 209788.
3. The isolated nucleic acid of claim 1 having at least 90% nucleic acid sequence identity to:
- (a) a nucleic acid sequence encoding the polypeptide shown in **FIG. 14** (SEQ ID NO:14);
- (b) a nucleic acid sequence encoding the polypeptide shown in **FIG. 14** (SEQ ID NO:14), lacking its associated signal peptide;
- (c) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in **FIG. 14** (SEQ ID NO:14);
- (d) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in **FIG. 14** (SEQ ID NO:14), lacking its associated signal peptide;
- (e) the nucleic acid sequence shown in **FIG. 13** (SEQ ID NO:13);
- (f) the full-length coding sequence of the nucleic acid sequence shown in **FIG. 13** (SEQ ID NO:13); or
- (g) the full-length coding sequence of the cDNA deposited under ATCC accession number 209788.
4. The isolated nucleic acid of claim 1 having at least 95% nucleic acid sequence identity to:
- (a) a nucleic acid sequence encoding the polypeptide shown in **FIG. 14** (SEQ ID NO:14);
- (b) a nucleic acid sequence encoding the polypeptide shown in **FIG. 14** (SEQ ID NO:14), lacking its associated signal peptide;
- (c) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in **FIG. 14** (SEQ ID NO:14);
- (d) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in **FIG. 14** (SEQ ID NO:14), lacking its associated signal peptide;
- (e) the nucleic acid sequence shown in **FIG. 13** (SEQ ID NO:13);
- (f) the full-length coding sequence of the nucleic acid sequence shown in **FIG. 13** (SEQ ID NO:13); or
- (g) the full-length coding sequence of the cDNA deposited under ATCC accession number 209788.
5. The isolated nucleic acid of claim 1 having at least 99% nucleic acid sequence identity to:
- (a) a nucleic acid sequence encoding the polypeptide shown in **FIG. 14** (SEQ ID NO:14);
- (b) a nucleic acid sequence encoding the polypeptide shown in **FIG. 14** (SEQ ID NO:14), lacking its associated signal peptide;
- (c) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in **FIG. 14** (SEQ ID NO:14);
- (d) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in **FIG. 14** (SEQ ID NO:14), lacking its associated signal peptide;
- (e) the nucleic acid sequence shown in **FIG. 13** (SEQ ID NO:13);
- (f) the full-length coding sequence of the nucleic acid sequence shown in **FIG. 13** (SEQ ID NO:13); or
- (g) the full-length coding sequence of the cDNA deposited under ATCC accession number 209788.
6. An isolated nucleic acid comprising:
- (a) a nucleic acid sequence encoding the polypeptide shown in **FIG. 14** (SEQ ID NO:14);
- (b) a nucleic acid sequence encoding the polypeptide shown in **FIG. 14** (SEQ ID NO:14), lacking its associated signal peptide;
- (c) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in **FIG. 14** (SEQ ID NO:14);
- (d) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in **FIG. 14** (SEQ ID NO:14), lacking its associated signal peptide;
- (e) the nucleic acid sequence shown in **FIG. 13** (SEQ ID NO:13);
- (f) the full-length coding sequence of the nucleic acid sequence shown in **FIG. 13** (SEQ ID NO:13); or
- (g) the full-length coding sequence of the cDNA deposited under ATCC accession number 209788.
7. The isolated nucleic acid of claim 6 comprising a nucleic acid sequence encoding the polypeptide shown in **FIG. 14** (SEQ ID NO:14).
8. The isolated nucleic acid of claim 6 comprising a nucleic acid sequence encoding the polypeptide shown in **FIG. 14** (SEQ ID NO:14), lacking its associated signal peptide.
9. The isolated nucleic acid of claim 6 comprising a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in **FIG. 14** (SEQ ID NO:14).
10. The isolated nucleic acid of claim 6 comprising a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in **FIG. 14** (SEQ ID NO:14), lacking its associated signal peptide.
11. The isolated nucleic acid of claim 6 comprising the nucleic acid sequence shown in **FIG. 13** (SEQ ID NO:13).
12. The isolated nucleic acid of claim 6 comprising the full-length coding sequence of the nucleic acid sequence shown in **FIG. 13** (SEQ ID NO:13).
13. The isolated nucleic acid of claim 6 comprising the full-length coding sequence of the cDNA deposited under ATCC accession number 209788.
14. An isolated nucleic acid that hybridizes to:
- (a) a nucleic acid sequence encoding the polypeptide shown in **FIG. 14** (SEQ ID NO:14);
- (b) a nucleic acid sequence encoding the polypeptide shown in **FIG. 14** (SEQ ID NO:14), lacking its associated signal peptide;
- (c) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in **FIG. 14** (SEQ ID NO:14);

- (d) a nucleic acid sequence encoding the extracellular domain of the polypeptide shown in **FIG. 14** (SEQ ID NO:14), lacking its associated signal peptide;
- (e) the nucleic acid sequence shown in **FIG. 13** (SEQ ID NO:13);
- (f) the full-length coding sequence of the nucleic acid sequence shown in **FIG. 13** (SEQ ID NO:13); or
- (g) the full-length coding sequence of the cDNA deposited under ATCC accession number 209788.
- 15.** The isolated nucleic acid of claim 14, wherein said hybridization occurs under stringent conditions.
- 16.** The isolated nucleic acid of claim 14 which is at least 10 nucleotides in length.
- 17.** A vector comprising the nucleic acid of claim 1.
- 18.** The vector of claim 17, wherein said nucleic acid is operably linked to control sequences recognized by a host cell transformed with the vector.
- 19.** A host cell comprising the vector of claim 17.
- 20.** The host cell of claim 19, wherein said cell is a CHO cell, an *E. coli* or a yeast cell.
- * * * * *