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

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- (63) Continuation of application No. 10/119,480, filed on Apr. 9, 2002, which is a continuation of application No. PCT/US01/21066, filed on Jun. 29, 2001, and which is a continuation-in-part of application No. PCT/US01/17800, filed on Jun. 1, 2001.
- (60) Provisional application No. 60/220,666, filed on Jul. 25, 2000.

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- (52) **U.S. Cl.** **530/350**; 536/23.2; 435/320.1; 435/183; 435/325; 435/69.1

(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.

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>>/usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA125219
>>subunit 1 of 1, 283 aa, 1 stop
><MW: 31175, pI: 7.51, NX(S/T): 0
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GKELVDKNIDRFIPITKLKYYFAVDTMVYVGRKLGLLFFPYLHQDWEVQYQQDTPVAPRFD
VNAPDLYIPAMAFITYVLVAGLALGTQDRFSPDLLGLQASSALAWLTLEVLAILLSLYLV
TVNTDLTTIDLVAFLGYKYVGMIGGVLMGLLFGKIGYYLVLGWCCVAIFVFMIRTLRLKI
LADAAAEGVPRGARNQLRMYLTMAVAAAQPMLMYWLTFFHLVR
```

Important features of the protein:

Transmembrane domain:

Amino acids 126-142;164-179;215-233

N-myristoylation sites:

Amino acids 54-60;141-147;156-162;201-207;205-211;209-215

Amidation site:

Amino acids 89-93

FIGURE 1A

GCAGCCCTAGCAGGGATGGACATGATGCTGTTGGTGCAGGGTGCCTTGTGCTCGAACCAGTG
GCTGGCGGCGGTGCTCCTCAGCCTGTGCTGCCTGCTACCCTCCTGCCTCCCGGCTGGACAGA
GTGTGGACTTCCCCGGGGCGCCGTGGACAACATGATGGTCAGAAAAGGGGACACGGCGGTG
CTTAGGTGTTATTTGGAAGATGGAGCTTCAAAGGGTGCCTGGCTGAACCGGTCAAGTATTAT
TTTTGCGGGAGGTGATAAGTGGTCAGTGGATCCTCGAGTTTCAATTTCAACATTGAATAAAA
GGGACTACAGCCTCCAGATACAGAATGTAGATGTGACAGATGATGGCCCATACACGTGTTCT
GTTCAGACTCAACATACACCCAGAACAATGCAGGTGCATCTAACTGTGCAAGTTCCCTCTTAA
GATATATGACATCTCAAATGATATGACCGTCAATGAAGGAACCAACGTCACCTTACTTGT
TGGCCACTGGGAAACCAGAGCCTTCCATTTCTTGGCGACACATCTCCCCATCAGCAAAACCA
TTTGAAAATGGACAATATTTGGACATTTATGGAATTACAAGGGACCAGGCTGGGGAATATGA
ATGCAGTGGGAAAATGATGTGTCATTCCCAGATGTGAGGAAAGTAAAAGTTGTTGTCAACT
TTGCTCCTACTATTAGGAAATTAATCTGGCACCGTGACCCCGGACGCAGTGGCCTGATA
AGATGTGAAGGTGCAGGTGTGCCGCTCCAGCCTTTGAATGGTACAAAGGAGAGAAGAAGCT
CTTCAATGGCCAACAAGGAATTATTATTTCAAATTTTAGCACAAAGATCCATTCTCACTGTTA
CCAACGTGACACAGGAGCACTTCGGCAATTATACTTGTGTGGCTGCCAACAAAGCTAGGCACA
ACCAATGCGAGCCTGCCTCTTAACCCTCCAAGTACAGCCCAGTATGGAATTACCGGGAGCGC
TGATGTTCTTTTCTCCTGCTGGTACCTTGTGTTGACACTGTCCTCTTTCACCAGCATATTCT
ACCTGAAGAATGCCATTTCTACAATAAATTTCAAAGACCCATAAAAAGGCTTTTAAAGGATTCTCT
GAAAGTGTGATGGCTGGATCCAATCTGGTACAGTTTGTAAAAGCAGCGTGGGATATAATC
AGCAGTGCCTTACATGGGGATGATCGCCTTCTGTAGAATTGCTCATTATGTAATACTTTAAT
TCTACTCTTTTTGATTAGCTACATTTACCTTGTGAAGCAGTACACATTGTCCTTTTTTTAAG
ACGTGAAAGCTCTGAAATTACTTTTTAGAGGATATTAATTGTGATTTTCATGTTTGAATCTAC
AACTTTTTCAAAGCATTCACTCATGGTCTGCTAGGTTGCAGGCTGTAGTTTACAAAAACGAA
TATTGCAGTGAATATGTGATTCTTTAAGGCTGCAATACAAGCATTGATTTCCCTGTTCAAT
AAGAGTCAATCCACATTTACAAGATGCATTTTTTTCTTTTTTTGATAAAAAAGCAAATAATA
TTGCCTTCAGATTATTTCTTCAAATATAACACATATCTAGATTTTTCTGCTCGCATGATAT
TCAGGTTTCAGGAATGAGCCTTGTAAATATAACTGGCTGTGCAGCTCTGCTTCTCTTTCTGT
AAGTTCAGCATGGGTGTGCCCTTCAACAATAATTTTTCTCTTTGTCTCCAATAATAATA
AATGTTTTGCTAAATCTTACAATTTGAAAGTAAAAATAAACCAGAGTGATCAAGTTAAACCA
TACACTATCTTAAGTAACGAAGGAGCTATGGACTGTAAAAATCTCTTCCCTGCCTGACAA
TGGGGTTTGAGAAATTTGCCCCACACTAACTCAGTTCTTGTGATGAGAGACAATTAATAAC
AGTATAGTAAATATACCATATGATTTCTTTAGTTGTAGCTAAATGTTAGATCCACCGTGGGA
AATCATTTCCCTTTAAATGACAGCACAGTCCACTCAAAGGATTGCCTAGCAATACAGCATCT
TTTCCCTTCACTAGTCCAAGCCAAAAATTTAAGATGATTTGTGAGAAAGGGCACAAAGTCC
TATCACCTAATATTACAAGAGTTGGTAAGCGCTCATTAATTTTATTTTGTGGCAGCTAA
GTTAGTATGACAGAGGCAGTGTCTTGTGGACAGGAGCATTTTGCATATTTCCATCTGAAA
GTATCACTCAGTTGATAGTCTGGAATGCATGTTATATATTTTAAAACCTCCAAAATATATTA
TAACAAACATTTCTATATCGGTATGTAGCAGACCAATCTCTAAAATAGCTAATTCTTCAATAA
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TTCCCTTACATGATATATGTAAGATGCGATCAAATAAAGACAAAACACCAGTGTGAGAATAT
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AACTACATTTTTGAAGGAAAATGCTGTTACTCTAACATTAATTTACAGGAATAGTTTGATGG
TTTCACTCTTTACTAAAGAAAGGCCATCACCTTGAAGCCATTTTACAGGTTTGATGAAGTT
ACCAATTTCACTACACCTAAATTTCTACAATAGTCCCCTTTTACAAGTTGTAACAACAAAG
ACCTATAATAAAATTAGATACAAGAAATTTGAGTGGTTATACATATTTGAGATATCTAG
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CCCAAAGTACATCATAAATCAATTTAATTAGAAAAATGAATCTTAAATGAGGGGACATAAG
TATACTCTTTCCACAAAATGGCAATAATAAGGCATAAAGCTAGTAAATCTACTAACTGTAAT
AAATGTATGACATTATTTGATTGATACATTAAAAAAGAGTTTTTTAGAACAATATGGCATT
TAACTTTATTATTTATTTGCTTTTAAAGAAATATTCTTTGTGGAATTGTTGAATAAACTATAA
AATATTATTTGTATTGCAGCTTTAAAGTGGCACACTCCATAATAATCTACTTACTAGAAAT

FIGURE 1B

AGTGGTGCTACCACAAAAAATGTTAACCATCAGTACCATTGTTTGGGAGAAAGAAACAGATC
AAGAATGCATATTATTTCAGTGACCGCTTTCCTAGAGTTAAAATACCTCCTCTTTGTAAGGTT
TGTAGGTAAATTGAGGTATAAACTATGGATGAACCAAATAATTAGTTCAAAGTGTTGTCATG
ATTCCAAATTTGTGGAGTCTGGTGTTTTTACCATAGAATGTGACAGAAGTACAGTCATAGCT
CAGTAGCTATATGTATTTGCCTTTATGTTAGAAGAGACTTTCCTGAGTGACATTTTTAAATA
GAGGAGGTATTCATATGTTTTCTGTATCACAGCAGCATTCCCTAGTCCTTAGGCCCTCGGA
CAGAGTGAAATCATGAGTATTTATGAGTTC AATATTGTCAAATAAGGCTACAGTATTTGCTT
TTTTGTGTGAATGTATTGCATATAATGTTCAAGTAGATGATTTTACATTTATGGACATATAA
AATGTCTGATTACCCCATTTTATCAGTCCTGACTGTACAAGATTGTTGCAATTCAGAATAG
CAGTTTTATAAATTGATTTATCTTTTAATCTATAACAATTTGTGTTAGCTGTTTCATTTCAGG
ANTATATTTTCTACAAGTTC CACTTGTGGGACTCCTTTTGTGGCCCTATTTTTTTTTAAAG
AAGGAAGAAAGAAAAATAAGTAGCAGTTTAAAAATGAGAATGGAGAGAAAAAGAAAAGAATG
AAAAGGAAAGGCAGTAAAGAGGGGAAAAAAAGGAAGGATGGAAGGAATGAAGGAAGGAAGGG
AGGAAGGGGAGAAGGTAGGAAGAAAGAAAGGATGAGAGGGGAAGGAAGAATCAGAGTATTAGG
GTAGTTAACTTACACATTTGCATTCCTTAGTTTAACTGCAAGTGGTGTAACATGTTTTTCAA
TGATCGCATTTGAAACATAAGTCCTATTATAACCATTAAGTTCCTATTATGCAGCAATTATAT
AATAAAAAGTACTGCCCAAGTTATAGTAATGTGGGTGTTTTTGAGACACTAAAAGATTTGAG
AGGGAGAATTTCAAACCTTAAAGCCACTTTTGGGGGGTTTATAACTTAACTGAAAAATTAATG
CTTCATCATAACATTTAAGCTATATCTAGAAAAGTAGACTGGAGAACTGAGAAAATTACCCAG
GTAATTCAGGGGAAAAAAAAAATATATATATATAAATACCCCTACATTTGAAGTCAGAAA
ACTCTGAAAACTGAATTTATCAAAGTCAATCATCTATAATGATCAAATTTACTGAACAATTG
TTAATTTATCCATTGTGCTTAGCTTTGTGACACAGCCAAAAGTTACCTATTTAATCTTTTCA
ATAAAAAATGTTTTTTGAAATCCAGAAATGATTTAAAAGAGGTCAGGTTTTTAACTATTTA
TTGAAGTATGTGGATGTACAGTATTTCAATAGATATGAATATGAATAAATGGTATGCCTTAA
GATTCCTTTGAATATGTATTTACTTTAAAGACTGGAAAAAGCTCTTCCTGTCTTTTAGTAAAA
CATCCATATTTCATAACCTGATGTAAAATATGTTGTACTGTTTCCAATAGGTGAATATAAAC
TCAGTTTATCAATTAA

FIGURE 2

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></usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA92259
><subunit 1 of 1, 354 aa, 1 stop
><MW: 38719, pI: 6.12, NX(S/T): 6
MDMMLLVQGACCSNQWLA AVL LSLCCLLP SCLPAGQSVDFPWA AVDNMMVRKGD TAVLRCYL
EDGASKGAWLNRSSII FAGGDKWSV DPRVSISTLNKRDYSLQIQNV DVTDDGPYTCSVQTQH
TPRTMQVHLTVQVPPKIYDISNDMTVNEGTVNLTCLATGKPEPSISWRHISPSAKPFENGQ
YLDIYGITRDQAGEYECSAENDVSFPDVRKVKVVVNFAPTIQEIKSGTVTPGRSGLIRCEGA
GVPPPAFEWYKGEKCLFNGQQGIIIQNFSTRSILVTNVTQEHFGNYTCVAANKLGTNASL
PLNPPSTAQYGITGSADVLFSCWYLVLTLSSTSI FYLKNAILQ
```

Important features of the protein:

Signal peptide:

amino acids 1-33

Transmembrane domain:

amino acids 322-343

N-glycosylation sites.

amino acids 73-77, 155-159, 275-279, 286-290, 294-298, 307-311

Tyrosine kinase phosphorylation site.

amino acids 180-188

N-myristoylation sites.

amino acids 9-15, 65-71, 69-75, 153-159, 241-247, 293-299,
304-310, 321-327

Myelin P0 protein.

amino acids 94-123

FIGURE 3

CACTGCCCGTCCGCTCTTCAGCAGCCGGTTCGCGGGCGGTGGAAAAGCGAGTGAAGAGAGCGC
GACGGCGGGCGGGCGGGCGGCAGCTATTGCTGGACGGCCAGTGGGAGAGCGAGGCCCTGAG
CCTCTGCGTCTAGGATCAAAATGCTTTCAATCCCAGAATACTATGAAGGCAAGAACGTCCTC
CTCACAGGAGCTACCGGTTTTCTAGGGAAGGTGCTTCTGGAAAAGTTGCTGAGGTCTTGTC
TAAGGTGAATTCAGTATATGTTTTGGTGAGGCAGAAAGCTGGACAGACACCACAAGAGCGAG
TGGAAGAAGTCCTTAGTGGCAAGCTTTTTGACAGATTGAGAGATGAAAATCCAGATTTTAGA
GAGAAAATTATAGCAATCAACAGCGAACTCACCCAACCTAAACTGGCTCTCAGTGAAGAAGA
TAAAGAGGTGATCATAGATTCTACCAATATTATATCCACTGTGCAGCTACAGTAAGGTTTA
ATGAAAATTTAAGAGATGCTGTTTCAGTTAAATGTGATTGCAACGCGACAGCTTATTCTCCTT
GCACAACAAATGAAGAATCTGGAAGTGTTCATGCATGTATCAACAGCATATGCCTACTGTAA
TCGCAAGCATATTGATGAAGTAGTCTATCCACCACCTGTGGATCCCAAGAAGCTGATTGATTCT
TTAGAGTGGATGGATGATGGCCTAGTAAATGATATCACGCCAAAATTGATAGGAGACAGACC
TAATACATACATATACACAAAAGCATTGGCAGAATATGTTGTACAACAAGAAGGAGCAAAAC
TAAATGTGGCAATTGTAAGGCCATCGATTGTTGGTGCCAGTTGGAAAAGAACCTTTCCAGGA
TGGATTGATAACTTTAATGGACCAAGTGGTCTCTTTATTGCGGCAGGAAAAGGAATTTCTCG
AACAAATACGTGCCTCCAACAATGCCCTGCAGATCTTGTTCCTGTAGATGTAGTTGTCAACA
TGTACTCTGCGGCAGCCTGGTATTCGGGAGTTAATAGACCAAGAAACATCATGGTGTATAAT
TGTACAACAGCAGACTAATCCTTTCCACTGGGGTGAAGTTGAGTACCATGTAATTTCCAC
TTTTCAAGAGGAATCCTCTCGAACAGGCCTTCAGACGGCCCAATGTAATCTAACCTCCAATC
ATCTTTTATATCATTAAGTGGATTGCTGTAAGCCATAAGGCCCCAGCATTCCTGTATGATATC
TACCTCAGGATGACTGGAAGAAGCCCAAGGATGATGAAAACAATAACTCGTCTTCACAAAGC
TATGGTGTCTTGAATATTTACAAGTAATTTCTGGGTTTGGAAATCTGAGAATGTCAATA
TGTTAATGAATCAACTAAACCCTGAAGATAAAAAGACCTTCAATATTGATGTACGGCAGTTA
CATTGGGCAGAATATATAGAGAACTACTGCTTGGGAACTAAGAAGTACGTATTGAATGAAGA
AATGCTGGCCCTCCCTGCAGCCAGAAAACATCTGAACAAGTTGCGGAATATACGTTATGGTT
TTAATACTATCCTTGTGATCCTCATCTGGCGCATTTTTATGCAAGATCACAAATGGCAAGA
AATATCTGGTACTTTGTGGTAGTCTGTGTTACAAGTTTTTGTCAACTCTCCGAGCATCCAG
CACTATGAGATACTGAAGACCAAGGATTGAGCATTGAAACATCTATACATATGGTGTATCAA
ATGTACAAAATGTAAAATGTATAAGTCACTCACTTTTGTCAAGACATTAACCATCTTAG
ATCGGAGTGTGAAGTAAATTTATGGTATATTTTATGTAACATTTTAAATGTTTATGCTCATAAA
ACTTAGTGAACACACTGTGTTATGCCAGCTCAAATCTACAGTAGCCACCAAAACCATGACTT
AATATTTTGGCCCTAGAAGAAAGGGGTGTGCTGAGGACAAGAGTGGGGAAATAGGAACACT
GACCAGTATAACTGTGCAATTCTGGAACATATTAATTAATAATATGCCTTAACATATAGT
GAATTTCTAATTCTAATGTTTCAGTGAATGGAAGACATTTATTTGGACAGTATACTAGCAA
GTTGGTAGATATTTGATCTTTCATTTTTTTGTTTTTTTCATTAGTTGAAGTGGGTTTTAGTTT
TGTTTTAAATTTATAACCAGCGTATTTTACATCATTCTGTAAGTTAAATGATATCAAACATG
AAAGAGATGTTCTCATTTTTCTTTTTCTGATTAAACGTCTGATGCATATCATTTTTCTATAA
GTAATCAGTTGCTTTTAAATCAGAAGGCTATATTAATCTAATGACCCTATTCGATCTAAAT
GGGTTTGAAGTCCATATCAGCAACATACGTGTTTTTTGACAGAAAGTGAACAACAAATCCG
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AATCTTGTGAGATGTTAAAAA

FIGURE 4

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></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA94849
><subunit 1 of 1, 515 aa, 1 stop
><MW: 59357, pI: 9.40, NX(S/T): 3
MVSIP EYYEGKNVLLTGATGFLGKVLLEKLLRSCPKNVSVYVLRQKAGQTPQERVEEVL
SGKLFDRLRDENPDFREKIIAINSELTQPKLALSEEDKEVIIDSTNIIFHCAATVRFNEN
LRDAVQLNVIATRQLILLAQQMKNLEVFMHVSTAYAYCNRKHIDEVVYPPVDPKKLIDS
LEWMDDGLVNDITPKLIGDRPNTYIYTKALAEYVVQQEGAKLNVAIVRPSIVGASWKEPF
PGWIDNFNGPSGLFIAAGKGILRTIRASNNALADLVPVDVVVNMSLAAAWYSGVNRPRNI
MVYNCTTGSTNPFHWGEVEYHVIISTFKRNPLEQAFRRPNVNLTSNHLLYHYWIAVSHKAP
AFLYDIYLRMTGRSPRMMKTITRLHKAMVFLEYFTSNSWVWNTENVNMLMNQLNPEDKKT
FNIDVRQLHWA EYIENYCLGTKKYVLNEEMSGLPAARKHLNKLNRNI RYGFNTILVILIWR
IFIARSQMARNI WYFVVS L CYKFLSYFRASSTMRY
```

Important features of the protein:

Transmembrane domain:

Amino acids 469-488

N-glycosylation sites:

Amino acids 283-287;304-308;341-345

Tyrosine kinase phosphorylation site:

Amino acids 160-169

N-myristoylation sites:

Amino acids 219-225;252-258;260-266;452-458

Leucine zipper pattern:

Amino acids 439-461

FIGURE 6

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA96883
><subunit 1 of 1, 514 aa, 1 stop
><MW: 55687, pI: 8.78, NX(S/T): 2
MPAVSGPGPLFCLLLLLLLDPHSPETGCPPLRRFEYKLSFKGPRRLALPGAGIPFWSHHGDA
ILGLEEVRLTPSMRNRSGAVWSRASVPFSAWEVEVQMRVTGLGRRGAQGMVWYTRGRGH
VGSVLGGLASWDGIGIFFDSPAEDTQDSPAIRVLASDGHIPSEQPGDGASQGLGSCHWDF
RNRPHSFRARITYWQQLRMSLNSGLTPSDPGEFCVDVGPLLLVPGGFFGVSAATGTLAG
EDPTGQVPPQPFLEMQQLRLARQLEGLWARLGLGTREDVTPKSDSEAQGEGERLFDLEET
LGRHRRILQALRGLSKQLAQAERQWKKQLGPPGQARPDGGWALDASCQIPSTPGRGGHLS
MSLNKDSAKVGALLHGQWTLQALQEMRDAAVRMAAEAQVSYLPVGGIEHHFLELDHILGI
LQEELRGPAAKAAKAPRPPGQPPRASSCLQPGIFLFYLLIQTVGFFGYVHFRQELNKS LQ
ECLSTGSLPLGPAPHTPRALGILRRQPLPAMPA
```

Important features of the protein:

Signal peptide:

Amino acids 1-23

Transmembrane domain:

Amino acids 215-232;450-465

N-glycosylation sites:

Amino acids 75-79;476-480

Glycosaminoglycan attachment site:

Amino acids 5-9

N-myristoylation sites:

Amino acids 78-84;122-128;126-132;168-174;172-178;
205-211;226-232;230-236;236-242;356-362

Amidation site:

Amino acids 102-106

FIGURE 8

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></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA96894
><subunit 1 of 1, 361 aa, 1 stop
><MW: 40747, pI: 9.20, NX(S/T): 1
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RTWLGYL FYRQQLRRARNRYPKGHSKTQPRLFNGVKVLP I PVLSDNYSYLI IDTQAQLAV
AVDPSDPRAVQASIEKEGVTLVAILCTHKKHWDHSGGNRDL SRRHRDCRVYGSPQDGI PYL
THPLCHQDVVSVGRLQIRALATPGHTQGHLVYLLDGE PYKGPSCLFSGDLLFLSGCGRTF
EGNAETMLSSLDTVLGLGDDTLLWPGHEYAEENLGFAGVVEPENLARERKMQWVQRQRLE
RKGTCPSTLGEERSYNPFLRTHCLALQEALGPGPGPTGDDDYSRAQLLEELRRLKDMHKS
K
```

Important features of the protein:

Signal peptide:

Amino acids 1-35

N-glycosylation site:

Amino acids 106-110

Glycosaminoglycan attachment site:

Amino acids 234-238

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 301-305

Tyrosine kinase phosphorylation site:

Amino acids 162-171

N-myristoylation sites:

Amino acids 41-47;235-241;242-248;303-309

Prokaryotic membrane lipoprotein lipid attachment site:

Amino acids 6-17

cAMP phosphodiesterases class-II proteins:

Amino acids 144-161

FIGURE 9

GCTGACAATCCCCTTGACGTTCTATCCCAGGAACTCCACCTGGGGCCCAATGTTGGGCGTGA
TGTTCCCTCGCCTGTCTCTGCCTGGAAAAGTGGTCTTCCCAAGCTCCACTGGCAGCCACTTCT
CCATGTTGGGCATCGGAGACATCGTTATGCCTGGTCTCCTACTATGCTTTGTCCTTCGCTAT
GACAACTACAAAAGCAAGCCAGTGGGGACTCCTGTGGGGCCCCTGGACCTGCCAACATCTC
CGGGCGCATGCAGAAGGTCTCCTACTCTCACTGCACCCTCATCGGATACTTTGTAGGCCTGC
TCACTGC'ACT'GTGGCGTCTCGCATTCACCGGGCCGCCAGCCCGCCCTTCTCTATTTGGTG
CCATTTACTTTATTGCCACTCCTCACGATGGCCTATTTAAAGGGCGACCTCCGGCGGATGTG
GTCTGAGCCTTTCCACTCCAAGTCCAGCAGCTCCCGATTCTTGGAAAGTATGATGGATCACGT
GGAAAGTGACCAGATGGCCGTCATAGTCCTTTTCTCTCAACTCATGGTTTGTTCCTCTTAG
AGCTGGCCTGGTACTCAGAAATGTACCTGTGTTTAAGGAACTGCCGTGTGACTGGATTTGGC
ATTGAAAGGGAGCTCGTTTGCAGGAGAGAGGTGCTGGAGCCCTGTTTGGTTCCTTCTCTTCC
TGCGGATGTAGAGGTGGGGCCCCTTCCAAGAGGGACAGGCCTCTCCCAGCGCGCCTTCCCTC
CCACGTTTTTATGGATCTGCACCAGACTGTTACCTTCTGGGGGAGATGGAGATTTGACTGTT
TAAAAACTGAAAACAGCGAGGAGTCTTTCTAGAACTTTTGAACACTAAAAGGATGAAAAAAT
TAGC

FIGURE 10

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA100272
><subunit 1 of 1, 108 aa, 1 stop
><MW: 12055, pI: 4.69, NX(S/T): 0
MMDHVESDQMAVIVLFSQLMVCFLLELAWYSEMYLCLRNCRVTFGFIERELVCRREVLEP
CLVPSLPADVEVGPLPRGTGLSPARLPPTFLWICTRLLPSGGDGLTV
```

Important features of the protein:

Signal peptide:

Amino acids 1-30

N-myristoylation site:

Amino acids 80-86

FIGURE 11

TCGCACACTGGTGGCTTCAGAAGAAATTCTCAACACCTAGCTCGCCAGAGAGTCTATGTATG
GGATTGAACAATCTGTAAACTAAAGGATCCTAATCATGAAAATAAGTATGATAAATTATAAG
TCACTATTGGCACTGTTGTTTATATTAGCCTCCTGGATCATTTTTACAGTTTTCCAGAACTC
CACAAAGGTTTGGTCTGCTCTAAACTTATCCATCTCCCTCCATTACTGGAACAACCTCCACAA
AGTCCTTATTTCCCTAAAACACCACCTGATATCATTAAGCCACTAACAGAGACTGAACTCAGA
ATAAAGGAAATCATAGAGAAACTAGATCAGCAGATCCCACCCAGACCTTTCACCCACGTGAA
CACCACCACCAGCGCCACACATAGCACAGCCACCATCCTCAACCCTCGAGATACGTACTGCA
GGGAGACCAGCTGCACATCCTGCTGGAGGTGAGGGACCCTTGGGACGCAGGAAGCAATAT
GGCGGGGATTTCTGAGGGGCCAGGATGTCTTCCCCAGCGCTGATGGCAGGTGCTTCAGGAAA
GGTGACTIONTCAACAACGGCACCTACCTGGTCAGCTTCACTCTGTTCTGGGAGGGCCAGG
TCTCTCTGTCTCTGCTGCTCATCCACCCAGTGAAGGGGTGTCAGCTCTCTGGAGTGCAAGG
AACCAAGGCTATGACAGGGTGATCTTCACTGGCCAGTTTGTCAATGGCACTTCCCAAGTCCA
CTCTGAATGTGGCCTGATCCTAAACACAAATGCTGAATTGTGCCAGTACCTGGACAACAGAG
ACCAAGAAGGCTTCTACTGTGTGAGGCCTCAACACATGCCCTGTGCTGCACTCACTCACATG
TATTCTAAGAACAAGAAAGTTTCTTATCTTAGCAAACAAGAAAAGAGCCTCTTTGAAAGGTC
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GTCTGGAGAAACACATGGAATCCTGTCTCCTGTAGTTTGGCTACAGTCAAATGAAGGAATGC
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CAAAGCCAGTATCAACACACTGAAGTCAGTGGATCTGCATGAATCTGGAAAATTGCAACACC
AGCTTGCTGTGGATTTGGATAGGAACATCAACATCCAGTGGCAAAAATATTGTTATCCCTTG
ATAGGATCAATGACCTATTCAGTCAAAGAGATGGAGTACCTCACCCGGGCCATTGACAGAAC
TGGAGGAGAAAAAATACTGTCATTGTTATTTCCCTGGGCCAGCATTCAGACCCTTTCCCA
TTGATGTTTTTATCCGAAGGGCCCTCAATGTCCACAAAGCCATTCAGCATCTTCTTCTGAGA
AGCCCAGACACTATGGTTATCATCAAACAGAAAACATCAGGGAGATGTACAATGATGCAGA
AAGATTTAGTGACTTTCATGGTTACATTCATATCTCATATAAAGGACATTTTTCCAGGATC
TCAGTGTGAGTATCATTGATGCCTGGGATATAACAATTGCATATGGCACAAATAATGTACAC
CCACCTCAACATGTAGTCGAAATCAGATTAATATATTATTAACCTATATTTGTTAAATAACAA

FIGURE 12

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></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA108696
><subunit 1 of 1, 544 aa, 1 stop
><MW: 62263, pI: 9.17, NX(S/T): 7
MKISMINYKSLALLFILASWIIFTVFQNSTKVWSALNLSISLHYWNNSTKSLFPKTPLI
SLKPLTETELRIKEIEKLDQQIPPRPFTHVNTTTSATHSTATILNPRDTYCRGDQLHIL
LEVRDHLGRRKQYGGDFLRARMSSPALMAGASGKVTDFNNGTYLVSFTLFWEGQVSLSL
LIHPSEGVSALWSARNQGYDRVIFTGQFVNGTSQVHSECGLILNTNAELCQYLDNRDQEG
FYCVRPQHMPCAALTHMYSKNKKVSYLSKQEKSLFERSNVGVEIMEKFNTISVSKCNKET
VAMKEKCKFGMTSTIPSGHVWRNTWNPVSCSLATVKMKECLRGKLIYLMGDSTIRQWMEY
FKASINTLKSVDLHESGKLOHQLAVDLDRNINIQWQKYCYPLIGSMTYSVKEMEYLTRAI
DRTGGEKNTVIVISLGQHFRPFIDVFIRRALNVHKAIQHLLLRSPDTMVIKKTENIREM
YNDAERFSDFHGYIQYLIKDIKDIKDIKDIKDIKDIKDIKDIKDIKDIKDIKDIKDIKDIK
NYIC
```

Important features of the protein:

Signal peptide:

Amino acids 1-22

N-glycosylation sites:

Amino acids 29-33;38-42;47-51;48-52;92-96;160-164;210-214

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 262-266

Tyrosine kinase phosphorylation site:

Amino acids 236-243;486-494

N-myristoylation sites:

Amino acids 206-212;220-226;310-316;424-430;533-539

Amidation site:

Amino acids 127-131

Cell attachment sequence:

Amino acids 113-116

FIGURE 13

GCAAAGAGAAGACTGAAAGACAAACCTGGGTGCAGCCAGAGAGGTCCAGATAGATGAGCTTG
TGGCATCCATTCCCCAAGTTCAGCCTAGGGACTCCACGTACCCCAGCTGGGTCTCATTGTTC
CAGAACTGCATTAGTTAAGATTACCCAGACTTGGATTTCAAAGGAATACTTTCATTGTTCCG
TCTGTAACACGAAGTAATTGGGGCCAGCTGGATGTCAGGATGCGTGTGGTTACCATTGTAAT
CTTGCTCTGCTTTTGCAAAGCGGCTGAGCTGCGCAAAGCAAGCCCAGGCAGTGTGAGAAGCC
GATGGAATCATGGCCGGGGCGGTGGAGGCCGGAGAGGCTCCAACCCGGTCAAACGCTACGCA
CCAGGCCTCCCGTGTGACGTGTACACATATCTCCATGAGAAAATACTTAGATTGTCAAGAAAG
AAAATTAGTTTATGTGCTGCCTGGTTGGCCTCAGGATTTGCTGCACATGCTGCTAGCAAGAA
ACAAGATCCGCACATTGAAGAACAACATGTTTTCCAAGTTTAAAAAGCTGAAAAGCCTGGAT
CTGCAGCAGAATGAGATCTCTAAAATTGAGAGTGAGGCGTTCTTTGGTTTTAAACAACTCAC
CACCTCTTACTGCAGCACAAACCAGATCAAAGTCTTGACGGAGGAAGTGTTCATTTACACAC
CTCTCTTGAGCTACCTGCGTCTTTATGACAACCCCTGGCACTGTACTTGTGAGATAGAAACG
CTTATTTCAATGTTGCAGATTTCCAGGAACCCGGAATTTGGGGAACACTACGCCAAGTGTGAAAG
TCCACAAGAACAAAAAATAAAAAACTGCGGCAGATAAAATCTGAACAGTTGTGTAATGAAG
AAAAGGAACAATTGGACCCGAAACCCCAAGTGTGAGGGAGACCCCAAGTCAAGCCTGAG
GTGGACTCAACTTTTTGCCACAATTATGTGTTTCCCATACAAACACTGGACTGCAAAAAGGAA
AGAGTTGAAAAAAGTGCCAAACAACATCCCTCCAGATATTGTTAAACTTGACTTGTGCATACA
ATAAAATCAACCAACTTCGACCCAAAGGAATTTGAAGATGTTTCATGAGCTGAAGAAATTAAC
CTCAGCAGCAATGGCATTGAATTCATCGATCCTGCCGCTTTTTTAGGGCTCACACATTTAGA
AGAATTAGATTTATCAAACAACAGTCTGCAAACTTTGACTATGGCGTATTAGAAGACTTGT
ATTTTTTGAAACTCTTGTGGCTCAGAGATAACCCTTGGAGATGTGACTACAACATTCACTAC
CTCTACTACTGGTTAAAGCACCCTACAATGTCCATTTTAATGGCCTGGAATGCAAAACGCT
GAAGAATACAAAGGATGGTCTGTGGGAAAATATATTAGAAGTTACTATGAAGAATGCCCAA
AGACAAGTTACCAGCATATCCTGAGTCATTTGACCAAGACACAGAAGATGATGAATGGGAAA
AAAAACATAGAGATCACACCGCAAAGAAGCAAAGCGTAATAATTACTATAGTAGGATTAAGGT
AGAAATTGTTCTGATTGTAATTAGTTTTGTATTTTCTATACTGGTGTAGAAAACATATGTT
TACATTTGATTAAGTGTGTTGCCTATTTATGCAGGGTAATCCAGCTAAAGGAAGCTTCTTT
AATTATAAGTATTATTGTGACTATTATAGTAATCAAGAGAATGCTATCATCCTGCTTGCCTG
TCCATTTGTGGAACAGCATCTGGTGATATGCAATTCACACTGGTAACCTGCAGCAGTTGGG
TCCTAATGATGGCATTAGACTTTCATAATGTCTGTATAAATGTTTTTACTGCTTTTAGAAA
ATAAAGAAAAAACTTGGTTCATGTTTAAAA

FIGURE 14

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA117935
><subunit 1 of 1, 440 aa, 1 stop
><MW: 51670, pI: 8.70, NX(S/T): 2
MRVVTIVILLCFCKAAELRKASPGSVRSRVNHGRAGGGRRGSGNPVKRYAPGLPCDVYTYL
HEKYLDQCERKLVYVLPGWPDLLHMLLARNKIRTLKNNMFSKFKKLSLDLQQNEISKI
ESEAFFGLNKLTLLLLQHNQIKVLTEEVFIYTPLLSYLRLYDNPWHCTCEIETLISMLQI
PRNRNLGNyakCESPQEQNKKLRQIKSEQLCNEEKEQLDPKPQVSGRPPVIKPEVDSTF
CHNYVFPIQTLDCRKRKELKKVPNNIPDIVKLDLSYNKINQLRPKEFEDVHELKKNLSS
NGIEFIDPAAFLGLTHLEELDLSNNSLQNFYGVLEDLYFLKLLWLRDNPWRCDYNIHYL
YYWLKHHYNVHFNGLECKTPEEYKGWSVGKYIRSYEECPKDKLPAYPESFDQDTEDEW
EKKHRDHTAKKQSVIITIVG
```

Important features of the protein:

Signal peptide:

Amino acids 1-15

N-glycosylation sites:

Amino acids 297-301;324-328

cAMP- and cGMP-dependent protein kinase phosphorylation sites:

Amino acids 19-23;39-43;430-434

N-myristoylation sites:

Amino acids 24-30;37-43

Amidation site:

Amino acids 37-41

FIGURE 15

GCGGCAGCAGCGCGGGCCCCAGCAGCCTCGGCAGCCACAGCCGCTGCAGCCGGGGCAGCCTC
CGCTGCTGTGCGCTCCTCTGATGCGCTTGCCCTCTCCCGCCCCGGGACTCCGGGAGA**ATGT**
GGGTCCTAGGCATCGCGGCAACTTTTTGCGGATTGTTCTTGCTTCCAGGCTTTGCGCTGCAA
ATCCAGTGTACCAGTGTGAAGAATTCAGCTGAACAACGACTGCTCCTCCCCGAGTTCAT
TGTGAATTGCACGGTGAACGTTCAAGACATGTGTGTCAGAAAGAAGTGATGGAGCAAAGTGCCG
GGATCATGTACCGCAAGTCCTGTGCATCATCAGCGGCCGTGTCTCATCGCCTCTGCCGGGTAC
CAGTCCTTCTGCTCCCCAGGGAACTGAACTCAGTTGCATCAGCTGCTGCAACACCCCTCT
TTGTAACGGGCCAAGGCCCAAGAAAAGGGGAAGTTCTGCGCTCGGCCCTCAGGCCAGGGCTCC
GCACCACCATCCTGTTCCCTCAAATTAGCCCTCTTCTCGGCACACTGCT**TGA**AGCTGAAGGAGA
TGCCACCCCTCCTGCATTGTTCTTCCAGCCCTCGCCCCCAACCCCCACCTCCCTGAGTGA
GTTTCTTCTGGGTGTCCTTTTATTCTGGGTAGGGAGCGGGAGTCCGTGTTCTCTTTTGTTC
TGTGCAAATAATGAAAGAGCTCGGTAAAGCATTCTGAATAAATTCAGCCTGACTGAATTTTC
AGTATGTACTTGAAGGAAGGAGGTGGAGTGAAAGTTCACCCCATGTCTGTGTAACCGGAGT
CAAGGCCAGGCTGGCAGAGTCAGTCCTTAGAAGTCACTGAGGTGGGCATCTGCCTTTTGTAA
AGCCTCCAGTGTCCATTCCATCCCTGATGGGGCATAGTTTGGAGCTGCAGAGTGAGAGTGA
CGTTTTCTTAGGGCTGGAGGGCCAGTTCCCCTCAAGGCTCCCTCGCTTGACATTCAAACCT
CATGCTCCTGAAAACCATTCTCTGCAGCAGAATTGGCTGGTTTTCGCGCCTGAGTTGGGCTCT
AGTGAICTCGAGACTCAATGACTGGGACTTAGACTGGGGCTCGGCCCTCGCTTGAAAAGTGCT
TAAGAAAATCTTCTCAGTTCTCCTTGACAGAGGACTGGCGCCGGGACGCGAAGAGCAACGGGC
GCTGCACAAAGCGGGCGCTGTGCGGTGGTGGAGTGCGCATGTACGCGCAGGCGCTTCTCGTGG
TTGGCGTGCTGCAGCGACAGGCGGCAGCACAGCACCTGCACGAACACCCGCCGAAACTGCTG
CGAGGACACCGTGTACAGGAGCGGGTTGATGACCGAGCTGAGGTAGAAAACGTCTCCGAGA
AGGGGAGGAGGATCATGTACGCCGGAAGTAGGACCTCGTCCAGTCGTGCTTGGGTTTGGCC
GCAGCCATGATCCTCCGAATCTGGTTGGGCATCCAGCATAACGGCCAATGTCACAACAATCAG
CCCTGGGCAGACACGAGCAGGAGGGAGAGACAGAGA

FIGURE 16

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA119474
><subunit 1 of 2, 141 aa, 1 stop
><MW: 15240, pI: 8.47, NX(S/T): 1
MWVLGIAATFCGLFLLPGFALQIQCYQCEEFQLNNDCCSSEFIVNCTVNVQDMCQKEVME
QSAGIMYRKSCASSAACLIASAGYQSFCS PGKLNSVCISCCNTPLCNGPRPKKRGSSASA
LRPGLRRTTILFLKLALFSAHC
```

Important features of the protein:

Signal peptide:

Amino acids 1-22

N-glycosylation site:

Amino acids 45-49

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 113-117

N-myristoylation sites:

Amino acids 5-11;115-121;124-130

Ly-6 / u-PAR domain proteins:

Amino acids 94-107

FIGURE 17

CGCAAAGCCGCCCTCGGGGCGCTCATGGCGGGACGCCTCCTGGGAAAGGCTTTAGCCGCGGT
GTCTCTCTCTCTGGCCTTGGCCTCTGTGACTATCAGGTCCTCGCGCTGCCGCGGCATCCAGG
CGTTCAGAACTCGTTTTTCATCTTCTTGGTTTCATCTTAATACCAACGTCATGTCTGGTTCT
AATGGTTCCAAAGAAAATTCTCACATAAGGCTCGGACGTCCTTACCCAGGTTCAAAAAGT
TGAACGAAGCCAGGTTCCATAATGAGAAAGTGGGCTGGCTTGTTGAGTGGCAAGACTATAAGC
CTGTGGAATACACTGCAGTCTCTGTCTTGGCTGGACCCAGGTGGGCAGATCCTCAGATCAGT
GAAAGTAATTTTTCTCCCAAGTTTAACGAAAAGGATGGGCATGTTGAGAGAAAAGAGCAAGAA
TGGCCTGTATGAGATTGAAAATGGAAGACCGAGAAATCCTGCAGGACGGACTGGACTGGTGG
GCCGGGGGCTTTTGGGGCGATGGGGCCCAAATCACGCTGCAGATCCCATTATAACCAGATGG
AAAAGGGATAGCAGTGGAAATAAAATCATGCATCCTGTTTCTGGGAAGCATATCTTACAATT
TGTTGCAATAAAAAGGAAAGACTGTGGAGAATGGGCAATCCAGGGGGGATGGTGGATCCAGGA
GAGAAGATTAGTGCCCACTGAAAAGAGAATTTGGTGAGGAAGCTCTCAACTCCTTACAGAA
AACCAGTGCTGAGAAGAGAGAAATAGAGGAAAAGTTGCACAACTCTTCAGCCAAGACCACC
TAGTGATATATAAGGGATATGTTGATGATCCTCGAAACACTGATAATGCATGGATGGAGACA
GAAGCTGTGAACTACCATGACGAAACAGGTGAGATAATGGATAATCTTATGCTAGAAGCTGG
AGATGATGCTGGAAAAGTAAAATGGGTGGACATCAATGATAAACTGAAGCTTTATGCCAGTC
ACTCTCAATTCATCAAACCTTGTGGCTGAGAAACGAGATGCACACTGGAGCGAGGACTCTGAA
GCTGACTGCCATGCGTTGTAGCTGATGGTCTCCGTGTAAGCCAAAGGCCACAGAGGAGCAT
ATACTGAAAAGAAGGCAGTATCACAGAATTTATACTATAAAAAGGGCAGGGTAGGCCACTTG
GCCTATTTACTTTCAAACAATTTGCATTTAGAGTGTTCGCATCAGAATAACATGAGTAAG
ATGAACTGGAACACAAAATTTTCAGCTCTTTGGTCAAAAAGGAATATAAGTAATCATATTTTG
TATGTATTCGATTTAAGCATGGCTTAAATTAATTTAAACAACATAATGCTCTTTGAAGAATC
ATAATCAGAATAAAGATAAATTCCTTGATCAGCTATA

FIGURE 18

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA119498
><subunit 1 of 1, 350 aa, 1 stop
><MW: 39125, pI: 8.53, NX(S/T): 2
MAGRLLGKALAAVSLALASVTIRSSRCRGIQAFRNSFSSSWFHLNTNVMGSGNSKEN
SHNKARTSPYPGSKVERSQVPNEKVGWLVEWQDYKPVEYTAVSVLAGPRWADPQISESNF
SPKFNEKDGHVVERKSKNGLYEIENGRPRNPAGRTGLVGRGLLGRWGPNAADPIITRWKR
DSSGNKIMHPVSGKHILQFVAIKRKDCGEWAI PGGMVDPEKISATLKREFGEEALNSLQ
K TSAEKREIEEKLHKLFSQDHLVIYKGYVDDPRNTDNAWMETEAVNYHDETGEIMDNLML
EAGDDAGKVKWVDINDKCLKLYASHSQFIKLVAEKRDAAHWESEADCHAL
```

Important features of the protein:

Signal peptide:

Amino acids 1-20

N-glycosylation site:

Amino acids 55-59

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 179-183

N-myristoylation sites:

Amino acids 53-59;56-62

mutT domain signature:

Amino acids 215-235

FIGURE 20

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA119502
><subunit 1 of 1, 667 aa, 1 stop
><MW: 74810, pI: 9.55, NX(S/T): 3
MGSSRLAALLLPLLLIVIDLSDSAGIGFRHLPHWNTRCPLASHTDDSFSGSSAYIPCRTW
WALFSTKPWCVRVWHCSRCLCQHLLSGGSLQRGLFHLLVQKSKKSSTFKFYRRHKMPAP
AQRKLLPRRHLSSEKSHHISIPSPDISHGKLSKRTQPSDPETWESLPRLDSQRHGGPEFS
FDLLPEARAIRVTIISGPEVSVRLCHQWALECEELSSPYDVQKIVSGGHTVELPYEFLLP
CLCIEASYLQEDTVRRKKCPFQSWPEAYGSDFWKSVHFTDYSQHTQVMALTLRCPLKLE
AALCQRHDWHTLCKDLPNATARESDGWYVLEKVDLHPQLCFKFSFGNSSHVECPHQTGSL
TSWNVSMDTQAQQLILHFSSRMHATFSAAWSLPGLGQDTLVPPVYTVSQARGSSPVSLDL
IIPFLRPGCCVLVWRSDVQFAWKHLLCPDVSYRHLGLLILALLALLTLLGVVLALTCRRP
QSGPGPARPVLLLHAADSEAQRRLVGALAELLRAALGGGRDVIVDLWEGRHVARVGPLPW
LWAARTRVAREQGTVLLLWSGADLRPVSGDPRAAPLLALLHAAPRPLLLLAYFSRLCAK
GDIPPLRALPRYRLRLDLPRLLRALDARPF AEATSWGRLGARQRRQRSRLELC SRLERA
ARLADLG
```

Important features of the protein:

Signal peptide:

Amino acids 1-23

Transmembrane domain:

Amino acids 455-472

N-glycosylation sites:

Amino acids 318-322;347-351;364-368

Glycosaminoglycan attachment site:

Amino acids 482-486

cAMP- and cGMP-dependent protein kinase phosphorylation sites:

Amino acids 104-108;645-649

Tyrosine kinase phosphorylation site:

Amino acids 322-329

N-myristoylation sites:

Amino acids 90-96;358-364;470-476

Eukaryotic cobalamin-binding proteins:

Amino acids 453-462

FIGURE 22

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA119516
><subunit 1 of 1, 172 aa, 1 stop
><MW: 18470, pI: 5.45, NX(S/T): 0
MSSSSGGAPGASASSAPPAQEEGMTWWYRWLCRLSGVLGAVSCAISGLFNCITIHPLNIAA
GVWMIMNAFILLLCEAPFCCQFIEFANTVAEKVDRLRSWQKAVFYCGMAVVPIVISLTLT
TL LGNAIAFATGVLYGLSALGKKGDALSYARIQQQRQQADEEKLAETLEGEL
```

Important features of the protein:

Signal peptide:

Amino acids 1-42

Transmembrane domains:

Amino acids 64-77;109-128

Tyrosine kinase phosphorylation site:

Amino acids 142-150

N-myristoylation sites:

Amino acids 5-11;6-12;9-15;35-41;38-44;46-52;124-130;132-138

Amidation site:

Amino acids 140-144

FIGURE 23

GTGAAACACCCATGGTTTTATGCTCTATTTCTCTTTTCCTCATCTTCTTCCACATCCTCTTT
CTGAATGTATCAAACACTTTCCTTGAAGTGGGGCACCAGGAGGGCCACTCCAGTCTCCAATG
CAGGGACTCAGGGGCAGGGATCTCTGAGAAAGTGGCCATCTCGTTATTAAAGCTCTGTCCTC
TGCTTCCCTCTCACCTCAGAAGCAGCCCGTTTATTCAACAGAGCTCCAGGTTGCCAGCTAGG
GGTTTTCGGGACCATAGACCAAGCAACCCCGAGAGACTGAGTACTGACCTGCAGTTGTTCCAG
AAACTCTGCTGGGAATTAGGTTGTGACCTAGAAGTGAACTGACACATAACAGTGAGAAGGCAG
GGTAAGAATGCAGTCTAGAGCGCAACCTTTCTCCACTAGACTTGTAAGTAATTTAAGTGAAT
CCTGTCCCCCTGGGGTTCTATCCTGGCTGGCTCTGCTGGTGAACCTGACTGGCCAGCATAGG
GCACTTGATGAGACCCTGGAATGCTGAGGCCAGTTGGGCAGCAAGCTTTCACCTCATCCTTC
TGCCCATCTATCCAGCCATTCAAACATTCATTCGCCTGAAGACATTTATCAAGCTCCTGCAA
TGGGTCAGGCATCTGCTAGGCACTGGGGACACAGAGCTCACAGTCTCCTGGAGGGGGTGAGA
GATGACTGACAGGTGGTCTGTGGTGCAGTGTGACCTGGGAATGCACACAGTACTGTGGAAAC
ACGGGAGAGGCATCTAGCACAACTGAGAGGGCCAGGGGAGGCTTCCTGGCAGGTTTCCCTT
TAACCATCTTAAGGGAAAGAGGCACTAGGTAGGAAAATAAAGGGACAGTGGTGTCCAGACA
GAGGGCACTCTACATGGAA

FIGURE 24

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA119530
><subunit 1 of 1, 113 aa, 1 stop
><MW: 12799, pI: 7.53, NX(S/T): 1
MVLCSISLFLIFFHILFLNVSNYFLEVGHQEGHSSLQCRDSGAGISEKVAISLLKLCPLL
PSHLRSSPFIQQSSRLPARGFRDHRPSNPERLSTDLQLFQKLCWELGCDLEVN
```

Important features of the protein:

Signal peptide:

Amino acids 1-18

N-glycosylation site:

Amino acids 19-23

Glycosaminoglycan attachment site:

Amino acids 41-45

N-myristoylation site:

Amino acids 42-48

FIGURE 25

CGGGCTCCGCGCGGTCCCACCTCCCGGCTCCCTTCGCCTCCAGGATGCGCTGAGCCCTACAA
CACCCCAGCGGCCCGGGCTCCCCACGAGGTGTGAATGACAGAGGTGGTGCCATCCAGCG
CGCTCAGCGAGGTACGCCTGCGCCTCCTCTGCCACGATGACATAGACACTGTGAAGCACCTG
TGTGGCGACTGGTTCCCATCGAGTACCCAGACTCATGGTATCGTGATATCACATCCAACAA
GAAGTTCTTTCCCTTGCTGCAACCTACAGAGGTGCCATTGTGGGAATGATAGTAGCTGAAA
TTAAGAACAGGACCAAAATACATAAAGAGGATGGAGATATTCTAGCAACCAACTTCTCTGTT
GACACACAAGTTCGCGTACATCCTAAGTCTGGGCGTCGTGAAAGAGTTTCAGGAAGCACGGCAT
AGGTTCCCTCTTACTTGAAAGTTTAAAGGATCACATATCAACCACCGCCAGGACCACTGCA
AAGCCATTTACCTGCATGTCCTCACCACCAACAACACAGCAATAAACTTCTATGAAAACAGA
GACTTCAAGCAGCACCACCTATCTCCCCTATTACTACTCCATTCGAGGGGTCTCAAAGATGG
CTTACCTATGTCTCTACATCAACGGCGGGCACCCTCCCTGGACGATTTTGGACTACATCC
AGCACCTGGGCTCTGCACTAGCCAGCCTGAGCCCCTGCTCCATTCGCGACAGAGTCTACCGC
CAGGCCACAGCCTGCTCTGCAGCTTCTGCCATGGTTCGGGCATCTCTTCCAAGAGTGGCAT
CGAGTACAGCCGGACCATGTGATGTCGGCTGGGCAGCCGCCACCAGGCCCCACCCTTCAGCC
GCCCGCAGAGCCCGCCTTCTGTCCATCTGACCCCTTCTGTTTTCTGCAAGGAGCTGCCAGC
CATCTAACTGGGCTCGTCGGCCTGCCCCAGCTGCAGGCCGGTGCTACACGGGCTCGGGAAC
AGAACATCGTGGGCATGCGCAGAGCATGCCCATCCGTGGCAGGCTCTTCAGCTCCCCCTCCCT
GCTTCTGAAAACCTCTGCCTGCTGCCCTGGCCCTGCCCCCTGCGCATGCACCATCCCCAGG
GCTGACCCAGTGTGGCTGCATTCACTGGGAGGGGCTGCCCTCACTGGGCCTCTCCCACTCCG
CTGCCTGTTCTTGACAGCTCCTTCTGGAAAGCTGGAGGGGACTTTCTCCTGCAAGGGAGGAA
CGCAAGTATTATGGACACACTTGACCGTAAAGGCACAGGAGCCTCGGAACAAGGGGGCGCAA
TAAAGGGAATGGCCCGTCCCCCTCCAGAACCAGCCAAAGAAGCCTGGGGGGTGAGGAGTGG
CCCCACTCCTCCATGAGGGGCTGATGAGGGGTGGGCAGCCTGGGGGAGGCTTTCTCGCAA
GCACAGAGCTCTGAGGCTCAGCCCCCTGGCACAGGCGGTACGCATCAGGACGGTTCCTACT
CCTCAGCACCTTCCGTGCAGTTACCAGTGCCTGGGAGGTCACACTGCCCCGTCCGACCTTGG
CATGCTCCATTCAGCTGACCTGCTGAGGACAGGCATCGCCGAGACTCCTTGGGTCTCCCCG
CCCTCCCTCATGCTGCCACAAGCTGCTGCTCCAAGGCCTGGCCACATGCAGACAGGAGGAAG
CTGAGCTCGACATTAGGCCTCAAGGCTGCCATCTGTCTTGTAGGGCCTGGCCTTGTGGGCAG
GGGCAGTCTGTGCCTTGTGGGCCCTCAGCCTCTGAGGGCAGAGATGCTGTCAGTGCCGCA
GGTGCATCACATACTTCTAGCATCCTCTCCACCCTGCATTCCAAATGCTGCTTGTGCCTGC
CCTGCCCTCCGATGCAGGGGTGGGGTGGGGGGCGGAGTCCCGCCAGCATAGCTGCAGTGTC
ACAAAGCCATGGCAGAGGGTCTAGCGGGGCCACCCTGCCCCAGCCTGAGGAGGAGGGAGAG
GGAGGAACAACCCTGGGCAGACGGGGTCTCAGGGACCTGTGTCCTTCCGCTCCAGAGCTGC
CCAGCCACGGGCTCTCAGGGTGTGGGGCAGCCCCAGGTCCCCTCTTGAACCTCAGCTGGGGC
CAGGGGCCCTCAGAATGAAGGCAGGCACCAGGCAGGAGCAGCATCCCCCTCCTTGACGGTGC
TGGCAGGAGGGCCGCGCCATGCTGACTGCTTGAACCTCTGCTGACCTGACAGTGTGGCGGG
AGGGCCGCACCATGCTGACTGCCTGAATCTCTGCTGAGGCTGCCTGCCTGCCGGGCCAGCT
CAGCGCCCTCTCCACTGCGAATCAGTGGCGATCATGTGATTTCTATTTCTGCCCCACAGGGT
AAGGGACGAGTCTTCTGGAAGGCTCTGCCATGGACATTTGTCCTCGGGCTCAGAGGCCCCAC
CCTGCCCCACACCTGCCCTAATCACTGCAGTGTCCAGCCAGTGTGAAACAGATTGTAGCG
TTCTGTCTCATTACGAGCAAATAAATAGACTTTCATTGGGAAAAAAAAAAAAA

FIGURE 26

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA121772
><subunit 1 of 1, 242 aa, 1 stop
><MW: 27465, pI: 7.72, NX(S/T): 3
MTEVVPSSALSEVSLRLLCHDDIDTVKHLCDWFPPIEYPDSWYRDITSNKKFFSLAATYR
GAIVGMIVAEIKNRTKIHKEDGDILATNFSVDTQVAYILSLGVVKEFRKHGIGSLLLES
KDHISTTAQDHCKAIYLVLTNTNNTAINFYENRDFKQHLYPYYSIRGVLKDGFTYVLY
INGGHPWTILDYIQHLGSALASLSPCSI PHRVYRQAHSLLCSFLPWSGISSKSGIEYSR
TM
```

N-glycosylation sites:

Amino acids 73-77;88-92;143-147

N-myristoylation sites:

Amino acids 61-67;65-71;198-204;235-241

Matrixins cysteine switch motif:

Amino acids 18-31

FIGURE 27

GTTGGGCAGCAGCCACCCGCTCACCTCCATCCCCAGGACTTAGAGGGACGCAGGGCGTTGGG
AACAGAGGACACTCCAGGCGCTGACCCCTGGGAGGCCAGGACCAGGGCCAAAGTCCCGTGGGC
AAGAGGAGTCCTCAGAGGTCCTTCA¹TCAGCGGTCCGGGAGGTCTGGGAAGCCCACGGCCT
GGCTGGGGCAGGGTCAACGCCGCCAGGCCGCC²ATGGCCTGTGCTGGCTGCTGCTTCTGGTG
ATGGCTCTGCCCCCAGGCACGACGGGCGTCAAGGACTGCGTCTTCTGTGAGCTCACCGACTC
CATGCAGTGTCTGGTACCTACATGCACTGTGGCGATGACGAGGACTGCTTACAGGCCACG
GGTTCGCCCCGGGCACTGGTCCGGTCATCAACAAAGGCTGCCTGCGAGCCACCAGCTGCGGC
CTTGAGGAACCCGTCAGCTACAGGGGCGTCACCTACAGCCTCACCACCAACTGCTGCACCGG
CCGCTGTGTAACAGAGCCCCGAGCAGCCAGACAGTGGGGGCCACCACCAGCCTGGCACTGG
GGCTGGGTATGCTGCTT³CCTCCACGTTTGCTG⁴TGACCAACAGGGAGGACAGGGCCTGGGACT
GTTCTCCAGATCCGCCACTCCCCATGTCCCCATGTCTTCCCCACTAAATGGCCAGAGAG
GCCCTGGACAACCTCTTGCGGCCCTGGCTTCATCCCTTCTAAGGCTGTCCACCAGGAGCCCG
GTGCTAGGGGAAGCATCCCCAGGCC⁵TGACTGAGCGGCAGGGGAGCACGGCCCGTGGGTTTGA
TTGTATTACTCTGTTCCACTGGTTCTAAGACGCAGAGCTTCTCACATCTCAATCAGGATGCT
TCTCTCCATTGGTAGCACTTTAGAGTCCATGAAATATGGTAAAAAATATATATATATCATAA
TAAATGACAGCTGATGTT⁶CATGGGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 28

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA125148
><subunit 1 of 1, 124 aa, 1 stop
><MW: 13004, pI: 5.70, NX(S/T): 0
MVLCLLLLLVMALPPGTTGVKDCVFCELTDSMQCPGTYMHCGDDEDCFTGHGVAPGTGPV
INKGCLRATSCGLEEPVSYRGVTYSLTTNCCTGRLCNRAPSSQTVGATTSLALGLGMLLP
PRL
```

Important features of the protein:

Signal peptide:

Amino acids 1-13

N-myristoylation sites:

Amino acids 19-25;52-58;64-70;81-87;106-112

Ly-6 / u-PAR domain proteins:

Amino acids 84-97

FIGURE 29

GGCATT TTTGAAAGCC CAGTGTGCCCAGGGGGCATCTCCTTTGTGTTTATGAGAGACCTGCA
TTCTCCCTGGCTCAGTTCTCTCAGGCTCTCCAGAGCTCAGGACCTCTGAGAAGAATGGAGCC
CTCCTGGCTTCAGGAACATCAGGCTCACCCCTCTTGCTGCTGATCCTCCTCTGCATGTCTC
TGCTGCTGTTTTAGGTAATCAGGTTGTACCAGAGGAGGATGGATGATCAGAGCCCTGCAC
CTGTTTCCTGCACCCCTGCCACTGGTTCTATGGCCACAAGGAGTTTACCCAGTAAAGGA
GTTTGAGGTGTATCATAAGCTGATGGAAAAATACCCATGTGCTGTTCCCTTGTGGGTTGGAC
CCTTTACGATGTTCTTCAGTGTCCATGACCCAGACTATGCCAAGATTCTCCTGAAAAGACAA
GATCCCAAAGTGCTGTTAGCCACAAAATCCTTGAATCCTGGGTTGGTTCGAGGACTTGTGAC
CCTGGATGGTTCTAAATGGAAAAAGCACCGCCAGATTGTGAAACCTGGCTTCAACATCAGCA
TTCTGAAAATATTCATCACCATGATGTCTGAGAGTGTTCGGATGATGCTGAACAAATGGGAG
GAACACATTGCCAAAACACAGTCTGGAGCTCTTCAACATGTCTCCTCCTGATGACCCCTGGA
CAGCATCATGAAGTGTGCCTTCAGCCACCGGAGCATCCAGTTGGACAGTACCCTGGACT
CATACCTGAAAGCAGTGTCAACCTTAGCAAAAATCTCCAACCAGCGCATGAACAATTTTCTA
CATCACAACGACCTGGTTTTCAAATTCAGCTCTCAAGGCCAAAATCTTTTCTAAATTTAACCA
AGAACTTCATCAGTTCACAGAGAAAGTAATCCAGGACCGGAAGGAGTCTCTTAAGGATAAGC
TAAAACAAGATACTACTCAGAAAAGGCGCTGGGATTTTCTGGACATACTTTTGAGTGCCAAA
AGCGAAAACACCAAAGATTTCTCTGAAGCAGATCTCCAGGCTGAAGTGAACCGTTCATGTT
TGCAGGACATGACACCACATCCAGTGCTATCTCCTGGATCCTTTACTGCTTGGCAAAGTACC
CTGAGCATCAGCAGAGATGCCGAGATGAAATCAGGGAACCTTAGGGGATGGGTCTTCTATT
ACCTGGGAACACCTGAGCCAGATGCCTTACACCACGATGTGCATCAAGGAATGCCTCCGCCT
CTACGCACCGGTAGTAAACATATCCCGGTTACTCGACAAAACCCATCACCTTTCCAGATGGAC
GCTCCTTACCTGCAGGAATAACTGTGTTTATCAATATTTGGGCTCTTACCACAACCCCTAT
TTCTGGGAAGACCCCTCAGGTCTTTAACCCCTTGAGATTCTCCAGGGAAAATTTGAAAAAAT
ACATCCCTATGCCCTCATACCATTTCTCAGCTGGATTAAGGAACGCAATGGGCAGCATTTTG
CCATAATTGAGTGTAAGTGGCAGTGGCATTAACTCTGCTCCGCTTCAAGCTGGCTCCAGAC
CACTCAAGGCCTCCCAGCCTGTTTCGTCAGTTGTCTCAAGTCCAAGATGGAATCCATGT
GTTTGCAAAAAAAGTTTGCTAATTTTAAGTCCTTTTCGTATAAGAATTAATGAGACAATTTTCCT
ACCAAAGGAAGAACAAAAGGATAAATAATAACAAAATATATGTATATGGTTGTTTGACAAA
TTATATAACTTAGGATACTTCTGACTGGTTTTGACATCCATTAACAGTAATTTTAATTTCTT
TGCTGTATCTGGTGAAACCCACAAAACACCTGAAAAAACCAAGCTGACTTCCACTGCGAA
GGGAAATTATGGTTTTGTGTAAGTGTGGTAGAGTGGCTTTCAGCATAGTTTGATCAAAAC
TCCACTCAGTATCTGCATTACTTTTATCTCTGCAAATATCTGCATGATAGCTTTATCTCAG
TTATCTTTCCCATATAAAAAATATCTGCCAAA

FIGURE 30

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA125150
><subunit 1 of 1, 505 aa, 1 stop
><MW: 59086, pI: 9.50, NX(S/T): 3
MEPSWLQELMAHPFLLLILLCMSLLLQVIRLYQRRRWMIRALHLFPAPPAHWFYGHKEF
YPVKEFEVYHKLMEKYPYCAVPLWVGPFTMFFSVHDPDYAKILLKRQDPKSAVSHKILES
VGRGLVTLDGSKWKKHRQIVKPGFNISILKIFITMMSESVRMMLNKWEEHIAQNSRLELF
QHVSLMTLDSIMKCAFHQSIQLDSTLDSYLKAVFNLSKISNQRMNFLHHNDLVFKFS
SQGQIFSKFNQELHQFTEKVIQDRKESLKDCLKQDTPQKRRWDFLDILLSAKSENTKDFS
EADLQAEVKTFMFAGHDTTSSAISWILYCLAKYPEHQQRCDREIRELLGDGSSITWEHLS
QMPYTTMCIKECLRLYAPVVNISRLLDKPITFPDGRSLEPAGITVFINIHALHNPYFWED
PQVFNPLRFSRENSSEKIHPYAFIPFSAGLRNCIGQHFAIIECKVAVALTLLRFKLAPDHS
RPPQPVRQVVLKSKNGIHFVFAKKVC
```

Important features of the protein:

Signal peptide:

Amino acids 1-28

Transmembrane domain:

Amino acids 451-470

N-glycosylation sites:

Amino acids 145-149;217-221;381-385

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 264-268

N-myristoylation sites:

Amino acids 243-249;351-357;448-454;454-460

Cytochrome P450 cysteine heme-iron ligand signature:

Amino acids 445-455

Cytochrome P450 cysteine heme-iron ligand proteins:

Amino acids 442-473

FAD-dependent glycerol-3-phosphate dehydrogenase proteins:

Amino acids 124-141

FIGURE 31

TCCGCTGTCGCCCAGTCCCGGCCGC'TGGCGGGA'ACTGACCTGGAGCAAGCAGGACCTTCCCT
CCCACCTCTCCCGCCTGGCCTCCGCGGGAGTCCCCTACGATCCCGCTCAGCAGTGGGGCACT
CGCTGAGGACAGCGAGTCCTGGGAGTGAGCCCAAGGCCACCCCTGGCCAGCCCAGGAGAGAT
AGCCAGGGCAGGCCAGCAGCCGAGGGCCAGGCTCTGGCCACGGCGGTCTCCGACATGGAGA
GACATTGTCTGCTTTTTATCCTGTTAACCTGTCTTCGGTGGTTGTGCCACGACATTCCCCAG
GGTTCAGGTGCCCGGTGGCCGAGGGT'CA'GTCCAGTGGTAGAGCCTTGCTCTCCTAGGCTCAT
CCTGCTGGCGGTCCCTCCTGCTTCTGCTGTGTGGTGT'CA'GACTGGTGTGTCCGGT'TCTGCT
GCCTCCGGAAGCAGGCACAGGCCAGCCACATCTGCCACCAGCACGGCAGCCCTGCGACGTG
GCAGTCATCCCTATGGACAGTGACAGCCCTGTACACAGCACTGT'GAC'CTCCTACAGCTCCGT
GCAGTACCCACTGGGCATGCGGTTGCCCTGCCCT'TTGGGGAGCTGGACCTGGACTCCACGG
CTCCTCCTGCCTACAGCCTGTACACCCCGGAGCCTCCACCCTCCTACGATGAAGCTGTCAAG
ATGGCCAAGCCCAGAGAGGAAGGACCAGCACTCTCCAGAAACCCAGCCCTCTCCTTGGGGC
CTCGGGCC'TAGAG'CACTCCAGTGCCCCAGGAGTCGGGCCCCAATACTCAACTACCACCTT
GTAGCCCTGGT'GCCCCT'TGAAGGAGGTAGGAGAACGGACCAGAGCTTGGAGAACTAATGCTT
GGAGCCAAGGGCCCCAGCCCACCCACCGTCCACACATTGCTGTGGCCCCAACCTCGGTGC
CATGTTACACCGGCCCTGGCGTCACCCACTAGGCAGGCTGCTGC'TTTCAGCCTCAGCCCT
GGCCCAGCCCAGCAGGCCCTCAGCCTGGAAGAGGCCCTTGGGCCTAAGCCTCGGGTGGGA
GCTCAGGGCCACCTGTGACGTCTGCATCTTCTTGGAGAGAGAATAAAGTTTGTATTTAAGTGGT

FIGURE 32

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA125151
><subunit 1 of 1, 194 aa, 1 stop
><MW: 20882, pI: 6.44, NX(S/T): 0
MERHCLLFILLTCLRWLCHDIPQGSGARWPRVSPVVEPCSPRLILLAVLLLLLLCGVTAGC
VRFCCCLRKQAQAQPHLPPARQPCDVAVIPMDSDSPVHSTVTSYSSVQYPLGMRLPLPFGE
LLDLDSTAPPAYSLYTPEPPPSYDEAVKMAKPREEGPALSQKPSPLLGASGLETTVPVQES
GPNTQLPPCSPGAP
```

Important features of the protein:

Signal peptide:

Amino acids 1-20

Transmembrane domain:

Amino acids 39-58

N-myristoylation site:

Amino acids 55-61

Prokaryotic membrane lipoprotein lipid attachment site:

Amino acids 50-61

FIGURE 33

CCTTGCTTGGTGCTTGGCACACACAAATCCAGTGGGCTACACAGGTTTTCCAGAAGCCCCAC
GAGGTGGTAATGGTGCTGCTGATTTCAGACCCTGGGGGCCCTCATGCCCTCGCTGCCCTCCTG
CCTCAGCAACGGCGTGGAGAGGGCAGGGCCCAGCAGGAGCTCACCAGGCTGCTGGAGTTCT
ACGACGCCACCGCCCCTTCGCCAAGGGCTTGGAGATGGCACTGCTCCCCACCTACATGAA
CACAATCTGGTAAAAGTCACGGAGCTGGTGGATGCTGTGTATGATCCATACAAACCCTACCAG
CTGAAGTATGGCGACATGGAAGAGAGCAACCTCCTCATCCAGATGAGTGTGCTGTGCCTCTGGA
GCATGGGGAAGTGATTGACTGTGTGCAGGAGCTGAGCCACTCCGTGAACAAGCTGTTTGGTC
TGGCGTCTGCAGCCGTTGACAGATGCGTCAGATTACCAATGGCCTGGGGACCTGCGGCCCTG
TTGTCAGCCCTGAAATCCCTCTTTGCCAAGTATGTGTCTGATTTACCAGCACTCTCCAGTC
CATAAGAAAGAGTCAAACCTGGACCACATTCCTCCCAACTCCCTCTTCCAGGAAGATTGGA
CGGCTTTTCAGAACTCCATTAGGATAATAGCCACCTGTGGAGAGCTTTTTCGGCATTGTGGG
GACTTCGAGCAGCAGCTAGCCAACAGGATTTTGTCCACAGCTGGGAAGTATCTATCTGATTC
CTGCAGCCCCCGGAGCCTGGCTGGTTTTTCAGGAGAGCATCTTGACAGACAAGAAGAACTCTG
CCAAGAACCCTATGGCAAGAATATAATTACCTCCAGAAAGATAACCCTGCTGAATATGCCAGT
TTAATGGAAATACTTTATAACCCTTAAGGAAAAAGGGTCAAGCAACCACAACCTGCTGGCTGC
ACCTCGAGCAGCGCTGACTCGGCTTAACCAGCAGGCCACCAGCTGGCTTTCGATTCCGTGT
TCCTGCGCATCAAACAACAGCTGTTGCTTATTTTGAAGATGGACAGCTGGAATACGGCTGGC
ATCGGAGAAACCCTCACAGATGAACTGCCCGCCTTTAGTCTACCCCTCTCGAGTACATCAG
CAACATCGGGCAGTACATCATGTCCCTCCCCCTGAATCTTGAGCCATTTGTGACTCAGGAGG
ACTCTGCCTTAGAGTTGGCATTGCACGCTGGAAAGCTGCCATTTCTCCTGAGCAGGGGGAT
GAATTGCCCGAGCTGGACAACATGGCTGACAACCTGGCTGGGCTCGATCGCCAGAGCCACAAT
GCAGACCTACTGTGATGCGATCCTACAGATCCCTGAGCTGAGCCACACTCTGCCAAGCAGC
TGGCCACTGACATCGACTATCTGATCAACGTGATGGATGCCCTGGGCCTGCAGCCGTCCCCG
ACCCTCCAGCACATCGTGACGCTACTGAAGACCAGGCCCTGAGGACTATAGACAGGTCAGCAA
AGGCCTGCCCCGTGCCTGGCCACCACCGTGGCCACCATGCGGAGTGTGAATTACTTGACCCC
ACCACACACCGGACCACCAAGAGAGCCAGGGCTGCTGTTTCGTGACTCACCAGCACAGATTT
GCTCAGAACTCTGCCAAGATTGGGCAGAAGTTACTTTAAAAAGACTTGGTTCAGCTGGTC
ACGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCAAGCCAGATGGATCATGAGGCC
AGGAGTTCGAGACCAGCCTGACCAACATGGTGAACCCCATCTCTACTAAAAATACAAAAAT
TAAACAGCAGAGCGAGACTCTGTCTCAAAAAAAAAAAAAAAAAAAGACTTGGTTCATTTGTATAA
TCAAAAAGAGTTGTAAATTAAGATGTATTATTTATCAGAGAAGACTTTTTAGATAATTTTT
TTAAAGGATCAGATCTTGAAAATGGAATAATAACTACTGTGAAATGCAAAA

FIGURE 34

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA125181
><subunit 1 of 1, 491 aa, 1 stop
><MW: 54759, pI: 5.61, NX(S/T): 0
MVLIIQTLGALMPSLPSCLSNGVERAGPEQELTRLLEFYDATAHFAGKLEMALLPHLHEH
NLVKVTELVDVAVYDPYKPYQLKYGDMEESNLLIQMSAVPLEHGEVIDCVQELSHSVNKL
GLASAAVDRCVRFNGLGTCGLLSALKSLFAKYVSDFTSTLQSIKCKLDHIPPNSLFQ
EDWTAFQNSIRIIATCGELLRHCGDFEQQLANRILSTAGKYLSDSCSPRSLAGFQESILT
DKKNSAKNPWQEYNYLQKDNPAEYASLMEILYTLKEKGSSNHLLAAPRAALTRLNQQAH
QLAFDSVFLRIKQQLLLISKMDSWNTAGIGETLTDELPAFSLTPLYEISNIGQYIMSLPL
NLEPFVTQEDSALELALHAGKLPFPPEQGDELPELDNMADNWLGSIARATMQTYCDAILQ
IPELSPHSKQLATDIDYLINVMDALGLQPSRTLQHIVTLLKTRPEDYRQVSKGLPRRLA
TTVATMRSVNY
```

Important features of the protein:

Signal peptide:

Amino acids 1-20

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 242-246

N-myristoylation sites:

Amino acids 22-28;48-54;121-127;136-142;141-147;328-334;
447-453

Leucine zipper pattern:

Amino acids 295-317

FIGURE 35

GCAAGTGCCACCATGCTAGTGTGATTTGGACTTCAGTAAAAGTTAGTTTGCTTCCTTCCCGT
TGTCCCATCTCACTCCTGGGCCACCC**ATG**GGGCTGCTGGTAGCTGGTGTGTGGCTGCTGCTG
GACTGTGTGGCAGTCCATCCATCTGTGTCAGCAGCCACTGCGGGCCTACTTGCTGGGTGCCAG
CACCGCACTCACCCTGCAGGCGTGGCCAGGAGCGTGAGATCCCCAGAGCCCATGGCCAGTG
AGAGGCGGCCAGGGATAGGTACCCAGGGAATGCCACAGGAGTTTGCTGGGCTCACGGAGCTC
TTTCACTGGTCAGAGAGGAGTGTGTGTAGGAGAGGACTTCTACTTGGTGTGAAGGACAGAT
GGGGTTTGGCTGGGAGAGAGGAGGAATGTGGGCGGGCCTTATAGGCAGGCGAGAAGGTGAGA
GCCAAGGCCCTCTGTGGGCAGGGCGAGGTGGCGTGTGAGGAGACTCGTCCAGCTGGGCAGA
GGCTCATGTT**TGA**GGGATGAGGCAGAGCTGGGGGAGGAGGGAGCCAGAAATGGCAGGTCCCTT
GAATGCAGGTTTGAAGCAGGGACGCCCTGTGAGGGTACAGAGTCTGGGCTGTTACCTTCTG
TGGCTTTGCTAGAAAGGTGAGATGTCAGGGAGGAAGACAGGACTCCAGGATGTCTCCTGTCTCT
CTCTGGAAAAAGGAGGTGGGCCCTTTCTCAGCAGTCAGCTGCTGTTTTTTGAGGTCTTCTCC
ATGGATAATCCACGGTGTGGGAAGTGGTTAAGTAATGGATCCTCATGGGCTTACCATAAAA
ATATCTGGAGGCTGGACCATTTCCCTTAAAACGTTATAAAAAGCTGGAATTGAATGCCATCGG
TGTCACCCCTGGGAAGTGTGCTTTCTCTTGAGCTCTTTTGGCCCCGAGATAGCAGTCACTCC
ATAGTTTCGTGAAGACCAGCCTGGTGTGGCTGGTTTTCTGCCATTAGGGAGCAGCTAGAGG
TCTTCCAGTAGCTCCTGTGTAAAGTGATGAAAGAAAAGGGCTGGGTGCTGACTGCTCCTGGA
GAAAAGCAACACACTCCCAAAGTCTTAATTGCCTGCTTCCAGGGAGCTGTGGTGGTTTTCCCT
TGGGCAGGGCACACGCCCCAGTGGTTGACTTAATAAGGATACATTTTAATCAGAGGACAAAA
ATGTGCCCTGACTTGATTTCCGCATGGGCTTCCAGCATGGTCAAAGG

FIGURE 36

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA125192
><subunit 1 of 1, 139 aa, 1 stop
><MW: 14841, pI: 9.20, NX(S/T): 0
MGLLVAGVWLLLDCAVHPSVSSHCGPTCWVPSTALTTAGVARSVRSPEPMASERRPGIG
TQGMPEFAGLTELFWHSERSVCRRGLLLGVEGQMFGWGERGGMWAGLIGRREGESQGPL
WAGRGGVLRRLVQLGRGSC
```

Important features of the protein:

Signal peptide:

Amino acids 1-22

N-myristoylation sites:

Amino acids 2-8;40-46;86-92;102-108;103-109

Amidation site:

Amino acids 109-113

FIGURE 37

GGCCAGGAATGGGGTCCCCGGGCATGGTGCTGGGCCTCCTGGTGCAGATCTGGGCCCTGCAA
GAAGCCTCAAGCCTGAGCGTGCAGCAGGGGCCAACTTGCTGCAGGTGAGGCAGGGCAGTCA
GGCACCCTGGTCTGCCAGGTGGACCAGGCCACAGCCTGGGAACGGCTCCGTGTTAAGTGGACA
AAGGATGGGGCCATCCTGTGTCAACCGTACATCACCAACGGCAGCCTCAGCCTGGGGGTCTG
CGGGCCCCAGGGACGGCTCTCCTGGCAGGCACCCAGCCATCTCACCTGCAGCTGGACCCTG
TGAGCCTCAACCACAGCGGGGCGTACGTGTGCTGGGCGGCCGTAGAGATTCTTGAGTTGGAG
GAGGCTGAGGGCAACATAACAAGGCTCTTTGTGGACCCAGATGACCCACACAGAACAGAAA
CCGGATCGCAAGCTTCCCAGGATTCCTCTTCGTGCTGCTGGGGGTGGGAAGCATGGGTGTGG
CTGCGATCGTGTGGGGTGCTGGTTCTGGGGCCCGCAGCTGCCAGCAAAGGGACTCAGGA
AATGCATTCTACAGCAACGTCTATAACCGCCCCGGGGGGCCCCAAAGAAGAGTGAGGACTG
CTCTGGAGAGGGGAAGGACCAGAGGGGCCAGAGCATTTATTCAACCTCCTTCCCGCAACCGG
CCCCCGCCAGCCGCACCTGGCGTCAAGACCCTGCCCCAGCCGAGACCCTGCCCCAGCCCC
AGGCCCCGCCACCCCGTCTCTATGGTCAGGGTCTCTCCTAGACCAAGCCCCACCCAGCAGCC
GAGGCCAAAAGGGTTCCCCAAAGTGGGAGAGGAGTGAGAGATCCCAGGAGACCTCAACAGGA
CCCCACCCATAGGTACACACAAAAAAGGGGGGATCGAGGCCAGACACGGTGGCTCACGCCTG
TAATCCCAGCAGTTTGGGAAGCCGAGGCGGGTGAACACTTGAGGTGAGGGGTTGAGACCA
GCCTGGCTTGAACCTGGGAGGCGGAGGTTGCAGTGAGCCGAGATTGCGCCACTGCACTCCAG
CCTGGGCGACAGAGTGAGACTCCGTCTCAAAAAAAAAAACAAAAAGCAGGAGGATTGGGAGCC
TGTCAGCCCCATCTGAGACCCCGTCTCATTCTGTAATGATGGATCTCGCTCCCACCTTC
CCCCAAGAACCTAATAAAGGCTTGTGAAGAAAAAAAAAAAAAAAAAAAA

FIGURE 38

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA125196
><subunit 1 of 1, 278 aa, 1 stop
><MW: 30319, pI: 9.21, NX(S/T): 3
MGSPGMVLGLLVQI WALQEASSLSVQQGPNLLQVRQGSQATLVCQVDQATAWERLRVKWT
KDGAILCQPYITNGSLSLGVCGPQGRLSWQAPSHLTLQLDPVSLNHSGAYVCWAAVEIPE
LEEAEGNITRLFVDPDDPTQNRNRIASFPGFLFVLLGVGSMGVAAIVWGAWFWGRRSCQQ
RDSGNAFYSNVLYRPRGAPKKSEDCSGEGKDQQRGQSIYSTSFQPAPRQPHLASRPCPSP
RPCPSRPGHPVSMVRVSPRPSPTQQPRPKGF PKVGEE
```

Important features of the protein:

Signal peptide:

Amino acids 1-22

Transmembrane domain:

Amino acids 149-166

N-glycosylation sites:

Amino acids 73-77;105-109;127-131

Glycosaminoglycan attachment site:

Amino acids 206-210

N-myristoylation sites:

Amino acids 5-11;37-43;63-69;108-114

Amidation site:

Amino acids 173-179

FIGURE 40

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA125200
><subunit 1 of 1, 290 aa, 1 stop
><MW: 32335, pI: 5.82, NX(S/T): 1
MPLLTLYLLLFWLSGYSIATQITGPTTVNGLERGS�TVQCVRSGWETYLKWWCRGAIWR
DCKILVKTSQSSEQEVKRDVSIKDNQKNRTFTVTMEDLMKTDADTYWCGIEKTGNLDGVT
VQVTIDPAPVTEETSSSPTLTGHHLNDRHKLLKLSVLLPLIFTILLLLLVAASLLAWRM
MKYQQKAAGMSPEQVLQPLEGDLCYADLTLLQLAGTSPRKATTKLSSAQVDQVEVEYVTMA
SLPKEDISYASLTLGAEDQEPTYCNMGHLSHL.PGRGPPEEPTTEYSTISRPF
```

Important features of the protein:

Signal peptide:

Amino acids 1-15

Transmembrane domain:

Amino acids 155-174

N-glycosylation site:

Amino acids 88-92

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 218-222

Tyrosine kinase phosphorylation site:

Amino acids 276-285

N-myristoylation sites:

Amino acids 30-36;109-115;114-120

FIGURE 41

AAGAACACTGTTGCTCTTGGTGGACGGGCCAGAGGAATTCAGAGTTAAACCTTGAGTGCCT
 GCGTCCGTGAGAATTCAGCAATGGAAATGTCTCTACTATTTCTGGGATTTCTGCTCCTGGCTG
 CAAGATTGCCACTTGATGCCGCAAACGATTTTCATGATGTGCTGGGCAATGAAAGACCTTCT
 GCTTACATGAGGGAGCACAATCAATTAATGGCTGGTCTTCTGATGAAAATGACTGGAATGA
 AAAACTCTACCCAGTGTGGAAGCGGGGAGACATGAGGTGGAAAACTCCTGGAAGGGAGGCC
 GTGTGCAGGCGGTCTGACCAGTGACTCACCAGCCCTCGTGGGCTCAAATATAACATTTGCG
 GTGAACCTGATATTTCCCTAGATGCCAAAAGGAAGATGCCAATGGCAACATAGTCTATGAGAA
 GAACTGCAGAAATGAGGCTGGTTTATCTGCTGATCCGTATGTTTACAACCTGGACAGCATGGT
 CAGAGGACAGTGACGGGAAAATGGCACCGGCCAAAAGCCATCATAACGTCTTCCCTGATGGG
 AACCTTTTCCCTCACCACCCCGGATGGAGAAGATGGAATTTTCATCTACGTCTTCCACACACTT
 GGTCAAGTATTTCCAGAAAATGGGACGATGTTCAAGTGAAGTTCCTGTGAACACAGCCAATGT
 GACTTGGGCTCAACTCATGGAAGTGACTGTCTACAGAAGACATGGACGGGCATATGTTT
 CCATCGCACAAGTGAAGATGTGTACGTGGTAACAGATCAGATTCCTGTGTTTGTGACTATG
 TTCCAGAAGAAGATCGAAATTCATCCGACGAAACCTTCCCTCAAAGATCTCCCCATTATGTT
 TGATGCTCTGATTCATGATCCTAGCCACTTCCCTCAATTATTCTACCATTAACATAAAGTGG
 GATTCGGGGATAAATACTGGCCTGTTTGTTCACCAATCATACTGTGAATCACACGTATGTG
 C'CAATGGAACCTTCAGCCTTAACCTCACTGTGAAAGCTGCAGCACCAGGACCTTGTCCGCC
 ACCGCCACCACCACCCAGACCTTCAAAAACCCACCCCTTCTTTAGCAACTACTCTAAAACTT
 ATGATTCAAACACCCACAGGACCTACTGGTGACAACCCCTGGAGCTGAGTAGGATTCCTGAT
 GAAAACCTGCCAGATTAACAGATATGGCCACTTTCAGCCACCATCACAATTGTAGAGGGAAT
 CTTAGAGGTTAACATCATCCAGATGACAGACGTCTGATGCCGGTGCCATGGCCTGAAAGCT
 CCCTAATAGACTTTGTGCTGACCTGCCAAGGGAGCATTCACCGGAGGTCTGTACCATCATT
 TCTGACCCACCTGCGAGATCACCCAGAACACAGTCTGCAGCCCTGTGGATGTGGATGAGAT
 GTGTCTGCTGACTGTGAGACGAACCTTCAATGGGTCTGGGACGTACTGTGTGAACCTCACCC
 TGGGGGATGACACAAGCCTGGCTCTCACGAGCACCCCTGATTTCTGTTTCTGACAGAGACCCA
 GCCTCGCCTTTAAGGATGGCAAACAGTGCCCTGATCTCCGTGGCTGCTTGGCCATATTTGT
 CACTGTGATCTCCCTCTTGGTGTACAAAAACACAAGGAATACAACCCAAATAGAAAATAGTC
 CTGGGAATGTGGTCAGAAGCAAAGGCCCTGAGTGTCTTTCTCAACCGTCAAAAAGCCGTGTT
 TTCCCGGAAACCAGGAAAAGGATCCGCTACTCAAAAACCAAGAATTTAAAGGAGTTTCTTA
AATTTTCGACCTTGTCTTGAAGCTCACTTTTTCAGTGCCATTGATGTGAGATGTGCTGGAGTG
 GCTATTAACCTTTTTTTCCTAAAGATTATTGTTAAATAGATATTGTGGTTTGGGGAAGTTGA
 ATTTTTTATAGGTTAAATGTCATTTTATAGATGGGGAGAGGGATTATACTGCAGGCAGCTTC
 AGCCATGTTGTGAAACTGATAAAAGCAACTTAGCAAGGCTTCTTTTCATTATTTTTTATGTT
 TCACTTATAAAGTCTTAGGTAAC TAGTAGGATAGAAACACTGTGTCCCGAGAGTAAGGAGAG
 AAGCTACTATTGATTAGAGCCTAACCCAGGTTAACTGCAAGAAGAGGCGGATACTTTTCAGC
 TTTCCATGTAACGTATGCATAAAGCCAATGTAGTCCAGTTTCTAAGATCATGTTCCAAGCTA
 ACTGAATCCCACCTTCAATACACACTCATGAACTCCTGATGGAACAATAACAGGCCCAAGCCT
 GTGGTATGATGTGCACACTTGCTAGACTCAGAAAAATACTACTCTCATAAATGGGTGGGAG
 TATTTTGGTGACAACCTACTTTGCTTGGCTGAGTGAAGGAATGATATTCATATATTCATTTA
 TTCCATGGACATTTAGTTAGTGCTTTTTATATAACCAGGCATGATGCTGAGTGACACTCTTGT
 GTATAATTTCAAATTTTTGTACAGTCGCTGCACATATTTGAAATCATATATTAAGACTTTCC
 AAAGATGAGGTCCTGGTTTTTTCATGGCAACTTGATCAGTAAGGATTTACCTCTGTTTGT
 ACTAAAACCATCTACTATATGTTAGACATGACATTCTTTTTCTCTCTTCCCTGAAAAATAAA
 GTGTGGGAAGAGACA

FIGURE 44

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA125219
><subunit 1 of 1, 283 aa, 1 stop
><MW: 31175, pI: 7.51, NX(S/T): 0
MADPHQLFDDTSSAQRSRGYGAQRAPGGLSYPAASPTPHAAFLADPVSNMAMAYGSSSLAAQ
GKELVDKNIDRFIPITKLKYYFAVDVTMYVGRKLGLLFFPYLHQDWEVQYQQDTPVAPRFD
VNAPDLYIPAMAFITYVLVAGLALGTQDRFSPDLLGLQASSALAWLTLEVLAILLSLYLV
TVNTDLTTIDLVAFLGYKYVGMIGGVLMLLFGKIGYYLVLGWCCVAIFVFMIRTLRLKI
LADAAAEGVPVRGARNQLRMYLTMAVAAAQPMLMYWLTFFHLVR
```

Important features of the protein:

Transmembrane domain:

Amino acids 126-142;164-179;215-233

N-myristoylation sites:

Amino acids 54-60;141-147;156-162;201-207;205-211;209-215

Amidation site:

Amino acids 89-93

FIGURE 45

GCTGAGCACCAACAGGAACTATTCCAGTGAAGAGCAAGTGCTGCCCGACCCAGGACCCTGTG
CCAGGCTGGCAGCCCTCCAGCTCCCTCCAGAGAGGAAACCTCTGTCTGGCTGAGGGTGGGAC
TAGCTGGGATGCTCTCACTCCAGTTGCTCAGGTTACCCAGGAAGCTCCTCCGTGGAGTGGCC
AGCCTGATTCTAGCCCTGTCCTCTCTGGCAGCACATGCCACACCTGCCTGGGCCTTCTGCTC
CCTGATGCTTGATGAGCCCCGCTCCTCAATGTTTCTCAAAGACAGACCCCCCTGAGGCCAGC
TTGAATGTGAAGACTGCTGAAGTCAGCTGGCTTCACTTGAGCTGCAGAAAAGGTGGCTGGGA
TGGCCCAGGTGCACCCAGAGGCCCCAGCCCTTTGGCTGCCTTTGGGTTG**TGA**CTTGGGTTGT
CTCTGAGGCCCTGCCAGAGCTGGGCCTGCGGGTGGTGGGCGGTCCGACCTCGGGCAGTCAGT
GCTCCGCAGCCTCAGCACTGCATCCCAGACCCAGTGTCTCAGAGGGAAGAGCCAGCCTCCC
TGCCTCATGGAACCAGGAGTCCCAAAAAGTCAGGAGCCTGGAGGCTCTGAAAGGAGCAGGGA
TTCCATAGTGCCTGAAGCTGAAATAGGGCCCTCCTGGGGAGCCCCAGCAAAACTGTTTTT
CATACCCACTCCAGAACTGCCCGCTCCAGCTCCAGCGCCAGCGCCAGCTGTTGCCAGGC
GTCATTGGAGAGGCCTGGCTGCCCCAGGGGCAGCAGGGAGTGGTGGACCTGTATGGGCTGGC
AGGAGGCCATTGGCCATGCTGACAAGTGTACCTGCCTTCTAGCCTGGAGCCACCCCTCAG
GTGGCCTGCTTGACCTCCTATCCGGAGGTAGCCTGCCCCACCTGTAGGCAGAGGGGGCTCT
TGCTTGAGGCCTGCACAGGAAGCAAGTATAGCCCCGGTGCCCCAGAGTGGGTTCCACTTAGC
CCTGGCGAGATGGCCTGTCTGAGATCTCTGCTCCCAGACCCACCATCTGGGGAGCACAGT
CCTTAGGCTGCCTGGTCCAGGAAGGGGGTGGGCTCTGTGTCAGGAAACCTGGACTCTCAAGGC
CCACCAGCCTCTCCGTGAGTGTAGAAATCACAGATACAGTATATACTTAATTACACTACTC
ACTACTCAAAAAAAAAAAAAAAAAAAAA

FIGURE 46

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA128309
><subunit 1 of 1, 97 aa, 1 stop
><MW: 10112, pI: 8.64, NX(S/T): 0
MSHSSCSGSPRKLLRGVASLILALSSLAHATPAWAFCSLMLDEPLPPQCFSKTDPPPEAS
LNVKTAEVSWLHLSCRKGGWDGPGAPRGPSPIAAFGL
```

Important features of the protein:

Signal peptide:

Amino acids 1-31

FIGURE 47

TTCCGGGCCCTGGCGTCTCGTCTCCTTACCCTGGGGCTACCCTTGCCCCGGTCCTACTGCCCG
CGGTTAACCCGCCGCGAGCCGCCTCTCCCCCCCCGCCCCGACTCAACCCTGCCCTCCCCCGT
GCTTTGCAGACGCCGCCCGGGGGCCCCAGGCGGCTGATGCGTGTGGGCCTCGCGCTGATCTTG
GTGGGCCACGTGAACCTGCTGCTGGGGGCCGTGCTGCATGGCACCGTCCTGCGGCACGTGGC
CAATCCCCGCGGCGCTGTCACGCCGGAGTACACCGTAGCCAATGTCATCTCTGTGCGGCTCGG
GGCTGCTGAGCGTTTCCGTGGGACTTGTGGCCCTCCTGGCGTCCAGGAACCTTCTTCGCCCT
CCACTGCACTGGGTCCCTGCTGGCACTAGCTCTGGTGAACCTGCTCTTGTCCGTTGCCTGCTC
CCTGGGCCTCCTTCTTGTGTGTCACTCACTGTGGCCAACGGTGGCCGCCGCCTTATTGCTG
ACTGCCACCCAGGACTGCTGGATCCTCTGGTACCCTGGATGAGGGGCCGGGACATACTGAC
TGCCCCCTTGACCCCAAGAATCTATGATACAGCCTTGGCTCTCTGGATCCCTTCTTTGCT
CATGTCTGCAGGGGAGGCTGCTCTATCTGGTTACTGCTGTGTGGCTGCACTCACTCTACGTG
GAGTTGGGCCCTGCAGGAAGGACGGACTTCAGGGGCAGCTAGAGGAAATGACAGAGCTTGAA
TCTCCTAAATGTAAGGAGGAGGAAAATGAGCAGCTACTGGATCAAATCAAGAAATCCGGGC
ATCACAGAGAAGTTGGGTTTAGGACAGGTGCTGTTCCGAGACTCAGTCCTAAAGGGTTTTTT
TTCCCACTAAGCAAGGGGCCCTGACCTCGGGATGAGATAACAAATTGTAATAAAGTAACTTC
TCTTTTCTTCTAAA

FIGURE 48

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA129535
><subunit 1 of 1, 222 aa, 1 stop
><MW: 23566, pI: 6.70, NX(S/T): 0
MRVGLALILVGHVNLLLGAVLHGTVLRHVANPRGAVTPEYTVANVISVGSGLLSVSVGLV
ALLASRNLLRPPLHWVLLALALVNLLLSVACSLGLLLAVSILTVANGGRRLIADCHPGLLD
PLVPLDEGPGHTDCPFDPTRIIDTALALWIPSLMSAGEAALSGYCCVAALTLRGVGPCR
KDGLQGQLEEMTELESPKCKRQENEQLLDQDQEIIRASQRSWV
```

Important features of the protein:

Signal peptide:

Amino acids 1-18

Transmembrane domain:

Amino acids 44-60;76-96

N-myristoylation sites:

Amino acids 94-100;175-181

Amidation site:

Amino acids 106-110

Prokaryotic membrane lipoprotein lipid attachment site:

Amino acids 81-92

FIGURE 49

CGTCAGTCTAGAAGGATAAGAGAAAGAAAGTTAAGCAACTACAGGAAATGGCTTTGGGAG
TTCCAATATCAGTCTATCTTTTATTCAACGCAATGACAGCACTGACCGAAGAGGCAGCCG
TGACTGTAACACCTCCAATCACAGCCCAGCAAGCTGACAACATAGAAGGACCCATAGCCT
TGAAGTTCTCACACCTTTGCCTGGAAGATCATAACAGTTACTGCATCAACGGTGCTTGTG
CATTCCACCATGAGCTAGAGAAAGCCATCTGCAGGTGTTTTACTGGTTATACTGGAGAAA
GGTGTGAGCACTTGACTTTAACTTCATATGCTGTGGATTCTTATGAAAAATACATTGCAA
TTGGGATTGGTGTGGATTACTATTAAGTGGTTTTCTTGTTATTTTTTACTGCTATATAA
GAAAGAGGTATGAAAAAGACAAAATATGAAGTCACTTCATATGCAATCGTTTTGACAAATA
GTTATTCAGGCCCTATAATGTGTCAGGCACTGACATGTAAAATTTTTTAAATTA AAAAAG
AGCTGTAATCTGGCAAAAAGTTTCTATGTAATATTTTTTCATGCCTTTTCTCATAAACCCA
GACGAGTGGTAAAAATTTGCCTTCAGTTGTAATAGGAGAGTTCAAACGTACAGTCTCCCT
TCAACCTATCTCTGTCTGCCCATATCAAATTTATAAATGAGGAGGACAGCAGGCCCAAG
AAAGTAGGGACTAAGTATGTCTTGTTCAAATTTGTATATTCAGTGACTTACACTATGCCT
AGCACACAACACACACTGAGTAAATATTTGTTGAGTGAAATAAAATCAAGAAACAAGTAA
AAACTGA

FIGURE 50

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA129549
><subunit 1 of 1, 133 aa, 1 stop
><MW: 14792, pI: 5.97, NX(S/T): 0
MALGVPI SVYLLFNAMTALTEEA AVTVTPPITAQQADNIEGPIALKFSHLCLEDHNSYCI
NGACAFHHELEKAICRCFTGYTGERCEHLTLTSYAVDSYEKYIAIGIGVGLLLSGFLVIF
YCYIRKRYEKDKI
```

Important features of the protein:

Signal peptide:

1-20 (weak)

Transmembrane domain:

103-117

N-myristoylation site.

4-10;106-112;110-116

EGF-like domain cysteine pattern signature.

75-87

Integrins beta chain cysteine-rich domain proteins

66-88

FIGURE 52

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA129580
><subunit 1 of 1, 114 aa, 1 stop
><MW: 12886, pI: 7.04, NX(S/T): 0
MQIQNNLFCCYTVMSAIFKWLLLYSLPALCFLLGTOESESFHSKAEILVTLTSQVIISPA
GPHALTWTHFSPSVIIILVPCWWHAVIVTQHPVANCYVTNHLNIQWLELKAGS
```

Important features of the protein:

Signal peptide:

Amino acids 1-33

Transmembrane domain:

Amino acids 71-86

N-myristoylation site:

Amino acids 35-41

FIGURE 53

TTTTGAAATGGTTTT**ATG**ACCTCTTCCCCACTTCCCCGCTTGCTTTGCTCATTAGTGTTCCTA
GGTGGCTGCTGGGTGACGGGCTTTTCATCATCTCTGATGTGGGCCAGTGCGAAAAGAGCAGCT
GCAACATCTGTTTCTAATTGGGTGCGTGCCTTTATAAACTTCTTGCCTATTTGTCACATTG
CTTCCCTCCCACCCTGTCTTCCCTGGGAGTACTGCAGAACTGTAAGCGTCCCTGGAATGCAC
ACGTGGACCTTGTCAATCCCAAACAGACTTTCTGCTGGTCAGCACTTTGTAATGTTCCGGCTG
TTACAGGCAT**TAG**TCACCTGTGCTCAGAGAGAGACTGTGGTCTTTGGAACTGAAGAAAATGTC
TTTTTTGTTGTTGTTAATTCTTGGCATCCAGTTAGATTTAACTTCTCAAGAGTTTACACAGA
CTTTTAGAAAAACATTCTGTCTCTAAGAAAAAGTGCTCTAGCTTTGTACAGTTTTTGGATT
TTCACACTTGGTGGTTGTTTGTGCTGAAATGCTGTTTTGCTAGTGATTCCCTCCTCCCCCTAT
CTGGGGTTGTAAGCAGCTCTGGGGCTCTGTTCACTTCGGATACCTGTTTCTGGGGACTGCTT
TTCAACAGCGTTTTTCTAAGGGCATATGAGAAAATTTAATTTCTGATGGAATGAAGGTGAAA
CTCTAGTCCCAGGTAAACCTGGGTAGGCTGTAGAGACAGAAAGGGGGCTGCAGGTCTAGGTG
GAAGAACGAGAACGAATGCAGCATGGTATTTCCAGGCCTTTTAGATTCCGGCTTCATCCACAA
CCAATGTGAGTTCTTATCTGCAAAGCGGGCCTAAGTGTAATGGAGGGAAGGTGGGCCAGGCA
CCAGGGTCTGGGTTCTCCCGCGCCTCACTCTGTCTCCACCTGGCCCATGCATAAAGAACAC
TAGTCAAGTAGCCATTGTACCTGTTTCTTATCTGAAAATGAGAAGGTTGGAGAGTATGACT
TCTGTTGAAACAACAAGGCGCTTACAAATTTGGTGAAGTCGAATGAGGGCAGCGTTAAGAG
AAATATCAAAGTTAGTCATTGGATTTCAAGGGCTTAGGGATGGAAACCAGCTGGTAGTAGACT
GGTTGTAGTTATGTCCAAAGGGCAGAGTGGGAAAAATTTGGCCGAAAAGAGTGTGGTGGGGTG
ACCAGCAAATGTTAGAGGTATACATCAGGGCACAGAGGAGAAAAGCTAACATGATACTGATG
ACTTCAAGTCTTCACTGTCCAATTCAGAGGATAGGGGAGGGTTAAGCTGATTAACAGTGG
GCTTTTTTTCTCCTGCAAGAGGGTGGAGGTCTATAACTGTGCAGATTTTATCAGATGCATGC
TAATACATGTTATTCTGGGGGACTCTCTTATACCTTGAAGTAGACATTGCTGCTATTTGCGT
GAAAAAATAGGAGGACTTATTTGAATTGAGAATGGGGATAGGCTGAGTTCCACCGAGATGT
TGGCTTAGAGATGCCTGGGCCATGCTGTACAGTAGGAAGCCCAGCAGAGGAGATTGGGCTGT
GTGGGTGATGACAAAGGGAGTTGTTAGCTTATGGTTGGCTATTAAGTCATGGGCAAGGATG
GGCAAGAAAAGTGTGTAATGAGCTGACAAAAGATAAATATGTTAATTA

FIGURE 54

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA129794
><subunit 1 of 1, 102 aa, 1 stop
><MW: 11382, pI: 8.72, NX(S/T): 0
MTSSPLPRLLCSLVFLGGCWVTGFSSSLMWASAKEQLQHLFLIGSCLYKYFLPICHIASL
PPCLPWSTAESVSVPGMHTWTLSFPNRLSAGQHFVMFGCYRH
```

Important features of the protein:

Signal peptide:

Amino acids 1-21

N-myristoylation site:

Amino acids 18-24

Prokaryotic membrane lipoprotein lipid attachment sites:

Amino acids 9-20;36-47;
89-100

FIGURE 55

ACACTGGCCAAACACTCGCATCCCAGGGCGTCTCCGGCTGCTCCCATTGAGCTGTCTGCTCG
CTGTGCCCCGCTGTGCTGTGCTGTGCCCCGCGCTGTGCGCCGCTGCTACCGCGTCTGCTGGACGCG
GGAGACGCCAGCGAGCTGGTGATTGGAGCCCTGCGGAGAGCTCAAGCGCCCAGCTCTGCCCCG
AGGAGCCCAGGCTGCCCGTGAGTCCCATAGTTTGTCTGCAGGAGTGGAGCCATGAGCTGCGTCT
CTGGGTGGTGTGCATCCCCCTTGGGGCTGCTGTTCCCTGGTCTGCGGATCCCAAGGCTACCTCCT
GCCAACGTCACTCTCTTAGAGGAGCTGCTCAGCAAATACCAGCACAAACGAGTCTCACTCCC
GGGTCCGCAGAGCCATCCCCAGGGAGGACAAGGAGGAGATCCTCATGCTGCACAACAAGCTT
CGGGGCCAGGTGCAGCCTCAGGCC^TCCAACATGGAGTACATGACCTGGGATGACGAACTGGA
GAAGTCTGCTGCAGCGTGGGCCAGTCACTGCATCTGGGAGCACGGGCCACCAGTCTGCTGG
TGTCATCGGGCAGAACC^TGGGCGCTCACTGGGGCAGGTATCGCTCTCCGGGGTTCATGTG
CAGTCTGGTATGACGAGGTGAAGGACTACACCTACCCCTACCCGAGCGAGTGAACCCCTG
GTGTCCAGAGAGGTGCTCGGGCCCTATGTGCACGCAC^TTACACACAGATAGTTTGGGCCACCA
CCAACAAGATCGGTGTGCTGTGAACACCTGCCGGAAGATGACTGTCTGGGGAGAAGTTTGG
GAGAACCGGCTACTTTGTCTGCAATTATTCTCCAAAGGGGAAC^TGGATTGGAGAAGCCCC
CTACAAGAATGGCCGGCCCTGCTCTGAGTGCCCACCCAGCTATGGAGGCAGCTGCAGGAACA
ACTTGTGTTACCGAGAAGAAACCTACACTCCAAAACCTGAAACGGACGAGATGAATGAGGTG
GAAACGGCTCCCATTCTGAAAGAAAACCATGTTTGGCTCCAACCGAGGGT^{GAT}GAGACCCAC
CAAGCCCAAGAAAACCTCTGCGGTCAACTACATGACCCAAGT^{CGT}CAGATGTGACACCAAGA
TGAAGGACAGGTGCAAAGGGTCCACGTGTAACAGGTACCAGT^{GCCC}AGCAGGCTGCCTGAAC
CACAAGGCGAAGATCTTTGGAAGTCTGTTCTATGAAAGCTCGTCTAGCATATGCCGCGCCGC
CATCCACTACGGGATCCTGGATGACAAGGGAGGCCTGGTGGATATCACCAGGAACGGGAAGG
TCCCCCTCTTCGTGAAGTCTGAGAGACACGGCGTGCAGTCCCTCAGCAAATACAAACCTTCC
AGCTCATTCATGGTGTCAAAGTGAAGTGCAGGATTTGGACTGCTACACGACCGTTGCTCA
GCTGTGCCCGTTTGAAGCCAGCAACTCACTGCCCAAGAATCCATTGTCCGGCACACTGCA
AAGACGAACCTTCCTACTGGGCTCCGGTGTGTTGGAACCAACATCTATGCAGATACCTCAAGC
ATCTGCAAGACAGCTGTGCACGCGGGAGTCATCAGCAACGAGAGTGGGGGTGACGTGGACGT
GATGCCCGTGGATAAAAAGAAGACCTACGTGGGCTCGCTCAGGAATGGAGTTCAGTCTGAAA
GCCTGGGGACTCCTCGGGATGGAAAGGCCTTCCGGATCTTTGCTGTCAGGCAGTGAATTCC
AGCACCAGGGGAGAAGGGCGTCTTCAGGAGGGCTTCGGGGTTTGTCTTTATTTTATTTT
GTCATTGCCGGGTATATGGAGAGTCA

FIGURE 56

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA131590
><subunit 1 of 1, 497 aa, 1 stop
><MW: 55906, pI: 8.43, NX(S/T): 4
MSCVLGGVIPLGLLFLVCGSQGYLLPNVTLLEELLSKYQHNESSHRSVRRRAIPREDKEEIL
MLHNKLRGQVQPQASNMEMYMTWDDLEKSAAAWASQCIWEHGPTSLLSVIGQNLGAHWGR
YRSPGFHVQSWYDEVKDYTYYPSECNPWCPERCSGPMCTHYTQIVWATTNKIGCAVNTC
RKMTVWGEVWENAVYFVCNYSKGNWIGEAPYKNGRPCSECPPSYGGSCRNNLCYREETY
TPKPETDEMNEVETAPIPEENHVWLQPRVMRPTKPKKTSAVNYMTQVVRCDTKMKDRCKG
STCNRYQCPAGCLNHHKAKIFGSLFYESSSSICRAAIHYGILDDKGGLVDITRNGKVPFFV
KSERHGVQSLSKYKSSSFMVSKVKVQDLDCYTTVAQLCPFEKPATHCPRIHCPAHCKDE
PSYWAPVFGTNIYADTSSICKTAVHAGVISNESGGDQVMPVDKTKKTYVGSRLRNGVQSES
LGTPRDGKAFRIFAVRQ
```

Important features of the protein:

Signal peptide:

Amino acids 1-22

N-glycosylation sites:

Amino acids 27-31;41-45;451-455

cAMP- and cGMP-dependent protein kinase phosphorylation sites:

Amino acids 181-185;276-280;464-468

Tyrosine kinase phosphorylation site:

Amino acids 385-393

N-myristoylation sites:

Amino acids 111-117;115-121;174-180;204-210;227-233;300-306;
447-453;470-476

Extracellular proteins SCP/Tpx-1/Ag5/PR-1/Sc7 signature 2:

Amino acids 195-207

SCP-like extracellular protein:

Amino acids 56-208

FIGURE 57

GCACGAGGCCAAACACAGCAGCCTCAACATGAAGGTGGTTATGGTCCTCCTGCTTGCTGCCC
TCCCCCTTTACTGCTATGCAGGTTCTGGTTGCGTTCCTTCTGGAGAGCGTCGTGGAAAAGACC
ATCGATCCATCGGTTTCTGTGGAGGAATACAAAGCAGATCTTCAGAGGTTTCATCGACACTGA
GCAAACCGAAGCAGCTGTAGAGGAGTTCAAGGAGTGCTTCCTCAGCCAGAGCAATGAGACTC
TGGCCAACTTCCGAGTCATGGTGCATACGATATATGACAGCCTTTACTGTGCTGCGTATTAA
CTGTCACAAGAACTTTGGCTCAGAGGAATCCAGACGATGCTCACAACCCGACTGTGGACTGG
CAGAAATCTCAACTTTTCCTTTGACTTTCCCCTTTGATCAGTAATATGGAAGACGTTGTTG
AAACCTGAAGTATAGTTAATTTAAATAAACCCACTGCAAGAAAAAAAAAAAAA

FIGURE 58

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA135173
><subunit 1 of 1, 93 aa, 1 stop
><MW: 10456, pI: 4.37, NX(S/T): 1
MKVVMVLLLLAALPLYCYAGSGCVLLESVVEKTIDPSVSVVEEYKADLQRFIDTEQTEAAVE
EFKECFLSQSNETLANFRVMVHTIYDSLYCAAY
```

Important features of the protein:

Signal peptide:

Amino acids 1-18

Prokaryotic membrane lipoprotein lipid attachment site:

Amino acids 12-23

FIGURE 59A

CAAGTCCGTTGAGGCTGCCAGGCGAGTCAGGTCTCTCTGGACCTCGCCTGACTCGGCTGGGC
 TGTGCCTGAAATTGACCCAGCTCCACCATACTCCTTGATTATGAGAAAACAAGGAGTAAGCT
 CAAAGCGGCTGCAATCTTCCGGCCGCAGCCAGTCTAAGGGCGGCGGGGGCTCCCTCGCC
 CGGGAGCCGGAGGTAGAGGAGGAGGTGAAAAAGTCGGTCCTAGGCGGGGGAAACTGCCAAG
 GGGCGCCTGGAGGTCTCCCGGGGAGGATCCAAAGTCTGAAAGAGCGAAAAGGCTTGGAGC
 TAGAGGTGGTGGCCAAGACCTTTCTCTCGGCCCTTCCAGTTCGTCCGTAATTCCTGGCG
 CAGCTCCGGGAAAAGGTGCAGGAAGTGCAGGCGCGGGGTTCTCCAGCAGAACCCTCTCGG
 CATCGCTGTCTTTGTGGCAATTTTACATTTGGTTACATTTAGTAACACTTTTTGAAAATGATC
 GTCATTTCTCTCACCTCTCATCTTTGGAACGGGAGATGACTTTTTCGCACTGAAATGGGACTT
 TATTATTCATACTTCAAGACCATTATTGAAGCACCTTCGTTTTTTGGAAGGACTGTGGATGAT
 TATGAATGACAGGCTTACTGAATATCCTCTTATAATTAATGCAATAAAACGCTTCCATCTTT
 ATCCAGAGGTAATCATAGCCTCCTGGTATTGCACATTCATGGGAATAATGAATTTATTTGGA
 CTAGAAACTAAGACCTGCTGGAATGTCACCAGAATAGAACCTCTTAATGAAGTTCAAAGCTG
 TGAAGGATTGGGAGATCCTGCTTGCTTTTATGTTGGTGTAATCTTTATTTTAAATGGACTAA
 TGATGGGATTGTTCTTCATGTATGGAGCATACCTGAGTGGGACTCAACTGGGAGGTCATTAT
 ACAGTACTGTGCTTCTTTTTCAACCAATGGAGAGGCCACCCGTGTGATGTGGACACCACCTCT
 CCGTGAAAGTTTTTCCCTATCCTTTCCTTGACTTCAGATGTGTATTTAACTTTGATTCTCA
 GGACCTCAAGCAATGATAGAAGGCCCTTCATTTGCACCTGTCTTTCCAATGTGCTTTTATG
 CTTCCCTGGCAATTTGCTCAGTTTATACTTTTTACACAGATAGCATATTATTTCCCATGTA
 TGTGTGGGATACATGAACCAAGCAAATTTCAGAAGATCATTATATGAACATGATTTTCAGTT
 ACCCTTAGTTTTCATTTTTGATGTTTGGAAATTCATGTACTTATCTTCTTATTATTCTTCATC
 TTTGTTAATGACGTGGGCAATAATTCTAAAGAGAAATGAAATTCAAAAACTGGGAGTATCTA
 AACTCAACTTTTGGCTAATTCAGGTAGTGCCTGGTGGTGTGGAACAATCATTTTGAATTT
 CTGACATCTAAAATCTTAGGCGTTTCAGACCACATTCGCCTGAGTGATCTTATAGCAGCCAG
 AATCTTAAGGTATACAGATTTTGATACTTTAATATATACCTGTGCTCCCGAATTTGACTTCA
 TGGAAAAAGCGACTCCGCTGAGATACACAAAGACATTATTGCTTCCAGTTGTTATGGTGATT
 ACATGTTTTATCTTTAAAAGACTGTTTCGTGATATTTTCATATGTTTTAGCTACAAACATTTA
 TCTAAGAAAACAGCTCCTTGAACACAGTGAGCTGGCTTTTTCACACATTCAGTTGTTAGTGT
 TTAGTGCCTTGGCATTTTAATTATGAGGCTAAAGATGTTTTTTGACACCGCACATGTGTGTT
 ATGGCTTCCTTGATATGCTCTCGACAGCTCTTTGGCTGGCTTTTTTCGCAGAGTTCGTTTTGA
 GAAGGTTATCTTTGGCATTTTAACAGTGATGTCAATACAAGGTATGCAAACCTCCGTAATC
 AATGGAGCATAATAGGAGAATTTAATAATTTGCCTCAGGAAGAACTTTTACAGTGGATCAAA
 TACAGTACCACATCAGATGCTGTCTTTGCAGGTGCCATGCCTACAATGGCAAGCATCAAGCT
 GTCTACACTTCATCCCATTTGTGAATCATCCACATTCGAAGATGCAGACTGAGGGCTCGGA
 CAAAAATAGTTTATTCTACATATAGTCGAAAACTGCCAAAGAAGTAAGAGATAAATTGTTG
 GAGTTACATGTGAATTTATGTTTTAGAAAGGCATGGTGTGTTGTGAGAATAAGCCTGG
 TTGCAGTATGCTTGAATCTGGGATGTGGAAGACCCTTCCAATGCAGCTAACCTCCCTTAT
 GTAGCGTCTGCTCGAAGACGCCAGGCCTTACTTCACCACAGTATTTTCCAGATAGTGTGTAC
 AGAGTATTAAGGTTAACTGAGAAGGATCTACCCATTTTACTATGGCACAATGCCGTGTGT
 CAAAAACAATCACCTTTGGCTTATTCACTTAATAAAAAATCACAAAGCTTTAATAACAGACA
 CTAAAAATAAGATAAAAATGGATTGGAAATTTTTCTGATTACTAAAAGGTAATTTACTTTT
 CTGTTCAATTGAATGTCAGCCTTATTAAGCTTGTTCATATAAGTTATTAATCATTTCATGTCAT
 ACTGCATAAACAAATGTTCAATTTTCAAGTTGAAGTGTTTTTAAAACACTTTGTTTTGTAAT
 TTAATAATCAGGGTATGTAAGTCCTTTTTTCATCCAAGTGGTGAATTGCTTCAGATTTTCT
 CTAGTACCAGAGGTTACCTCCTCAAACCTTTTGAACCACTTAAGGCAGAAGAATGCAAGCTC
 TGAAATGACATCCTTAAAATGCTGATACTGGTCCACAGCCTCTTTACCTCTGTGAGGAAATTG
 TAACAGTGTGTCTTTTAAAGGTGTTTTTATTTTACCAGCCCTTAAGAAAGATCTTAATACCT
 TTTAATACTTTTTTTAATAATTTCAAGTTGAAGTGTTTTTAAAACACTTTGTTTTGTAAT
 GTTTTGAATCTCTTGAGATGTGTTTACCCACTAGATACATATTTGCCACTGGTTAGTTCTC
 CATCTAAGCTCAAGAGGTTATTCATCTCTTTTAGATTCCAGTGGCTTTTCTTTAACATCC
 AGGTAAAACAGAACTGCTATGGTATACAACCAAGTTTTGGGGTTAAACATAATCAGAAAAG

FIGURE 59B

AAAATCCAGTTAAATTTATGAAGTGAGATTTTCAGATCCTAGATCTTGAATAAAGGAAAGGT
CTTTTCATCTTGATGGCCCCAAAGCTTGTTGGTCATGGTCTTTATTTCTGGCCACTATCTTC
TTAAATAATATATTTTTAAGCCCTCATTTATTTTTGGTTTTGGGTGAGGAAAGTCATGTTTT
CTAAGTCCTCTCCCCTAATAAAACCTACCCAACAATAGTGCTTTGAAAAGTGGTAGTTATCT
TGAAGATACTCTTGCCAAATGCAAAGATAAACATTCTTTTGTCTGCTTTATAAATATGAAA
TATGCCAGATCTATAGTATTTTAATGTGCATCTACTTTAAATGAGTCATCTTGGGGTTTTTA
TAATTCCTTTATGTTCTTGCCCCTCFACACTTGAAATAACAAAATGCCTTAATTTTTATGGAT
TAGTTCTCTTATAGTAGACAGGCAGCTATATGCAGCAAAAACCAATAAAGTTATTTTTCAACT
TTCATAGTTGTAAAATATCTTATAACCAGAATACAAAACAGCTAAGAAAACATGCCACATTTTAT
TTTAGCATTTTTCAAATAATTTGTTTTTGGTGTAAGCACAGGATAAAAAAGGAGAGCGTCAA
GAAAAGAGACATAACACCTAACATTCATAAAAATTAACAAAGTATATTTTGGATGATGTTTT
TACAGGAAATATTTTAAATAAGTTGGTAGAACTTTTAAATGGTACTGTATTAGCTAATAAA
ATATTCAGTACAAATATATGTTTGGATTTATGCATTAAAAACTAATAAAATTATTTCCAAC
TTTA

FIGURE 60

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA138039
><subunit 1 of 1, 758 aa, 1 stop
><MW: 87354, pI: 9.36, NX(S/T): 1
MRKQGVSSKRLQSSGRSQSKGRRGASLAREPEVEEVEKSVLGGGKLPrgAWRSSPGRIQ
SLKERKGLELEVVAKTFLLGPFQFVRNSLAQLREKVQELQARRFSSRTTLGIAVFVAILH
WLHLVTLFENDRHFSHLSSLEREMTFRTEMGLYYSYFKTIIIEAPSFLEGLWMIMNDRLTE
YPLIINAIAKRFLHYPEVIIASWYCTFMGIMNLFGLTKTCWNVTRIEPLNEVQSCEGLGD
PACFYVGVIFILNGLMMLGFFMYGAYLSGTQLGGLITVLCFFFNHGEATRVMWTPPLRES
FSYPFLVLQMCILTLLIRTSSNDRRPFIALCLSNVAFMLPWQFAQFILFTQIASLFPMYV
VGYIEPSKFQKIIYMNMSVTLSEFILMFGNSMYLSSYSSLLMTWAIILKRNEIQKLGV
SKLNFWLIQGSAAWCGTIIILKFLTSKILGVS DHIRLSDLIAARILRYTDFDTLIYTCAPE
FDFMEKATPLRYTKTLLL PVVMVITCFIFKKTVRDISYVLATNIYLRKQLLEHSELAFT
LQLLVFTALAILIMRLKMFLTPHMCVMASLICSRLFGWLFRRVRFKVIIFGILTVMSIQ
GYANLRNQWSIIIGEFNNLPQEELLQWIKYSTTSDAVFAGAMPTMASIKLSTLHPIVNHPH
YEDADLRARTKIVYSTYSRKSAREVRDKLLELHVNYVLEEAWCVVRTKPGCSMLEIWDV
EDPSNAANPPLCSVLLEDARPYFTTVFQNSVYRVLKVN
```

Important features of the protein:

Transmembrane domain:

Amino acids 109-124;197-213;241-260;266-283;302-315;336-356;
376-391;430-450;495-509;541-560;584-599;634-647

N-glycosylation site:

Amino acids 222-226

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 102-106

Tyrosine kinase phosphorylation site:

Amino acids 511-519

N-myristoylation sites:

Amino acids 24-30;50-56;151-157;254-260;264-270;269-275;
273-279;639-645

Amidation site:

Amino acids 20-24

FIGURE 61

GGCGCGGCCACATCCTTTAAATATGGTCTTTCTTGGGCGCGCGACAATGTGAGGAGTGGG
 GTGGAGCGTGTGTGGTGTGTGGCTGCGGCCTGGGCAAGAGCCGCGCGGACCATGAGCTGAG
 TAAGTTCTGGAGGGATCCTGCCCTTTGGAGCCTTCGCAGCCAGGCAGCTGTGAACTGTGAGC
 TAGAGTGAAGCAGAAATCTAGGAAGATGAGCTCCAAGATGGTCATAAGTGAACCAGGACTGA
 ATTGGGATATTTCCCCCAAAAATGGCCTTAAGACATTTTTCTCTCGAGAAAATTATAAAGAT
 CATTCCATGGCTCCAAGTTTAAAAGAAGTACGTGTTTTATCCAACAGACGTATAGGAGAAAA
 TTTGAATGCCTCAGCAAGTCTGTAGAAAAAGAGCCGGCAGTTAGTTCAGCAACTCAAGCAA
 AGGAAAAAGTTAAAACCACAATGGAATGGTTCTTCTTCCAAAACCAAGAGTTCTTATCCT
 CGTTTCTCTCGTTTCTCACAGAGAGAGCAGAGGAGTTATGTGGACTTGTGGTTAAATACGC
 AAAGATTCCTGCAAATTCCAAAGCTGTTGGAATAAATAAAAATGACTACTTGCAGTACTTGG
 ATATGAAAAAACATGTGAACGAAGAAGTTACTGAGTTCCTAAAGTTTTTGCAGAAATCTGCA
 AAGAAATGTGCGCAGGATTATAATATGCTTTCTGATGATGCCCGTCTCTTACAGAGAAAA'
 TTTAAGAGCTTGCAATTGAACAAGTGAAGAAAGTATTCAGAATCTATACTCTCCACGAGGTCA
 CCAGCTTAATGGGATTCTTCCATTTCAGAGTAGAGATGGGATTAAGTTAGAAAAAACTCTT
 CTCGCATTGGGCAGTGTAAAATATGTGAAAACAGTATTTCCCTCAATGCCTATAAAGTTGCAG
 CTGTCAAAGGACGATATAGCTACCATTGAAACGTCAGAACAAACAGCTGAAGCTATGCATTA
 TGATATTAGTAAAGATCCAAATGCAGAGAAGCTTGT'TTCCAGATATCACCCCTCAGATAGCTC
 TAACTAGTCAGTCATTATTTACCTTATTAATAATCATGGACCAACGTACAAGGAACAGTGG
 GAAATTCAGTGTGTATTCAAGTAATACCTGTTGCAGGTTCAAACCAGTTAAAGTAATATA
 TATTAATTCACCACTTCCCCAAAAGAAAATGACTATGAGAGAGAGAAAATCAAATCTTTCATG
 AAGTTCATTAATAATTTATGATGTCCAAAAACACATCTGTTCCAGTCTCTGCAGTCTTTATG
 GACAAACCTGAAGAGTTTATATCTGAAATGGACATGTCTGTGAAGTCAACGAGTGCCGAAA
 AATTGAGAGTCTTGAAAACCTGTATTTGGATT'T'GATGATGATGTACAGAACTTGAACCTT
 TTGGAGTAACCACCACCACCAAGTATCAAAAATCACCAAGTCCAGCAAGTACTTCCACAGTACCT
 AACATGACAGATGCTCCTACAGCCCCCAAAGCAGGAACTACAACGTGGCCACCAAGTGCACC
 AGACATTTCTGCTAATCTAGAAAGTTTATCTCAGATTCTGATGGAACAATGCAAAAAGGAGA
 AACAGCTGGTCACTGGTATGGATGGTGGCCCTGAGGAATGCAAAAATAAAGATGATCAGGGA
 TTTGAATCATGTGAAAAGGTATCAAATCTGACAAGCCTTTGATACAAGATAGTACTTGA
 AACATCTGATGCCTTACAGTTAGAAAA'TTCTCAGGAAATTGAACTTCTAATAAAAATGATA
 TGACTATAGATATACTACATGCTGATGGTGAAGACCTAATGTTCTAGAAAACCTAGACAAC
 TCAAAGGAAAAGACTGTTGGATCAGAAGCAGCAAAAACCTGAAGATACAGTTCTCTGCAGCAG
 TGATACAGATGAGGAGTGTAAATCATTGATACAGAATGTAAAAAACAGTTATAACAGTG
 TTT**TAA**TTTAGATAAGTTTGAGGGAAAATAATCAGTAGGCAAGAGGAACATTTTTCTGTAGT
 AGCTAGAGTGCCTTGAAAAATGTGTTGGCTATGTGAAGGAATATTTCAACTAAAATGGAAT
 GGTATGCTTTTCACCCTTAAAGTTTGAGGAGGATCTTGATATGTTTTAACATTATCATGGCA
 GGGAAATATATAAGAAGAAAAATATTTTTACATTAAACCTTTTCTAAAAATTGTAATAGA
 AAAATAATTTGGTTTTTTATCAAGAACAACACTTATCGTTATGTATTGTGTTAGTTATATTG
 CCAGTCTGTTGCGACTGACTCAAAAAGTTAAATGTTGCCACTGCTGAAGATGATTATGAGCA
 TCGCAAACTTTGTTTTCTGACCCATTTTGACAGTTTTTATATACTCCTTTAAATGATGAATG
 TTACAGGTTAATAAAGTTAATACCTTTAAA

FIGURE 62

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA139540
><subunit 1 of 1, 592 aa, 1 stop
><MW: 66453, pI: 5.42, NX(S/T): 3
MSSKMVISEPGLNWDISPKNGLKTFFSRENYKDHSMAPSLKELRVLSNRRIGENLNASAS
SVENEPAVSSATQAKEKVKTTIGMVLLPKPRVPYPRFSRFSQREQRSYVDLLVKYAKIPA
NSKAVGINKNDYLQYLDMKKHVNEEVTEFLKFLQNSAKKCAQDYNMLSDDARLFTEKILR
ACIEQVKKYSEFYTLHEVTSLMGFFPFRVEMGLKLEKTLALGKSVKYVKTVPFSPMPIKQ
LSKDDIATIETSEQTAEAMHYDISKDPNAEKLVSRYHPQIALTSQSLEFTLLNNHGPTYKE
QWEIPVCIQVIPVAGSKPVKVIYINSPLPQKKMTMRERNQIFHEVPLKFMMSKNTSVPVS
AVFMDKPEEFIEMDMSCEVNECRKIESLENLYLDFDDDVTELETFGVTTTKVSKSPSPA
STSTVPNMTDAPTAPKAGTTTVAPSAPDISANSRSLSQLMEQLQKEKQLVTGMDGGPEE
CKNKDDQGFESCEKVSNSDKPLIQSDLKTS DALQLENSQEIETS NKNDMTIDILHADGE
RPNVLENLDNSKEKTVGSEAAKTEDTVLCSSDTDEECLIIDTECKKTSYNSV
```

Important features of the protein:

N-glycosylation sites:

Amino acids 56-60;354-358;427-431

cAMP- and cGMP-dependent protein kinase phosphorylation sites:

Amino acids 187-191;331-335;585-589

N-myristoylation sites:

Amino acids 126-132;407-413;557-563

FIGURE 64

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA139602
><subunit 1 of 1, 159 aa, 1 stop
><MW: 15900, pI: 8.07, NX(S/T): 0
MGRPRPFCPRSLVWSAQALLSHITCVVGGPPVPGHRCGRPRPSCPGPPVQVTGVVGGPGP
SVPGHLCGRPRALLYHVTV EGLALEEGRDLALVGAGFQGVACQQEGAGGMGPGGTQGWGA
TAGDCPEAPPGLAIAIVAHGHLVFPQGTTRGGS DAAGHD
```

Important features of the protein:

Signal peptide:

Amino acids 1-25

N-myristoylation sites:

Amino acids 109-115;113-119;119-125;148-154;151-157;152-158

FIGURE 65

GGCGACCACCGCCGCTCCTCACCTGGCCATTGGTGCAGCCCGTTCCCGGCGGGCAGAGAAG
GCAGGCGCGCTCCTTGCGCCACGCCACACCGTCGGGCCCCCGTCGGGTCCCCCTCGGGCCGCA
ATGGTGGGCTCCGCGCGGGCTGGGTCCGGCACTCTTGACCCCTTTGTAACCACCGCGGCGGG
CACCCAGGGAGTTCGAGCAACGAAGTTGGTGACCTGCCCGCTCCCAGGCAGTTTGCTGTTG
GGGCTTTCACGGCTGCTGGAAGGGCATGGCTGTTTGTCCCATCACTGGGCGCCAGCTTCTCA
AAGCTACGTTACAGCAACGCAGTAGGGACTTTCGTGGCAGGCTTTTTTTAAGAGCTGAAAG
AAGGGCGGGAGGGTTTACGTCC**TAG**GGTGATGATTCCTCACCAGACAGCGAAGTATCTATT
GGGAACTCCAGGTGACCGCACCTCCTTCGACAGTTCGCCCCGGGGCAAGTTACCAGCTG
CGTCAGAAAGCAGGTTTGCAAATCCTTGAGAACGGCCTGAGCTAAGGACTGGGGTCAGGA
GGGTTTTAACTCATTCTGATTTTCTTGCAATCATATCTCTTGAAAGTTTTTATATTTTCCC
CAATATTTTTCTGAGTTGCTATATCCAATGAAAACAATGCTGATGTAGAGGTCCACCAGCCA
ATGCTTTATTGGAAGTCAACGAATGAGACCGAGGGTGGCCATAATCAATCTCGGCACGCGG
GAATGTGAACCTCTTCCAAGGTCTGGGCGAGTCCCTAGAGTTACGCAGATGAAGGACATTGG
CCCTCGAGAATCTCACACCAGCAAAGAAGAGCACAACGAAGCGCAAACACTACTTATGATCATT
GTGGCTTTGGGCAAGTTGTTGTAGCTCCCAGCAACAATTTCTCACCTGGAGTGCAGCAATA
AATGATACTGGTGTGCAGGGCAGCTAATAAGCTTCTGAATAATATATGCAAAGTACTTGGC
ACCATGAGCAGAACTCAGTATACCGTCACTGAAGAAATAGCTTATTTAATGATTACACTTTT
CATATGTGCAAGTAAAAGTTTGACTTTTAGGGAGAGCCTCACCTACGGAATGTCTTTTTTAA
ATTTCTTTTTTAATTATACTTTAAGTTCTGGGATACATGTGCAGAACGTGCAGGTTTGTTAC
ACAGGTATACATGTGCCATGGTGGTTTGCAGCACCCATCAACCTTCATCTAGGTTTTAAGC
TCCGCATGCATTAGTTATTTGTCCTAATGCTCTCCCTCCCCTTGTCCCCCACCCCCAACAG
GCCTCAGGGTGTGATGTTCCCCTCCCTGGGTCCATATGTTCTCATTGTTCAACTCCCCTTA
TGATGAGAACATGCAGTGTGGTTTTCTGTTCCCTGTGTTAGTTGCTGAGAATGATGGTTT
CCAGCATCATCCACGTCCCTGCAAAGGACATGAATTCATTCTTTTTTATGGCTGCATGGTAT
TCCATGGTGTATATGTGCCACATTTTCTTCATCCAGTCTATCATTGATGGGCACTTGGGTTG
GTTCCAAGACTTTGTTATTGTGAACAGTGTGCAATAAACATACGTTTGTATGTGTCAAAA
AAAAAAAAAAAAAAAAA

FIGURE 66

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA139632
><subunit 1 of 1, 90 aa, 1 stop
><MW: 9586, pI: 12.18, NX(S/T): 0
MVG SARLGPALLTPFVTTAAGTQGV RATKLVTC PAPRQFAVGAFTAAGRAWLFVPSLGAS
FSKLRSQQRSRDFRGR LFLRAERRAGGFTS
```

Important features of the protein:

Signal peptide:

Amino acids 1-24

N-myristoylation sites:

Amino acids 24-30;42-48;58-64

FIGURE 67

CATGCTAGACTGGGAGCCCTGGGTGGTGCCCGTGCCGGGCTGGGACTGTTGCTGGGTACCG
CCGCCGGCCTTGGATTCTGTGCCCTCCTTTACAGCCAGCGATGGAAACGGACCCAGCGTCAT
GGCCGCAGCCAGAGCCTGCCCACTCCCTGGACTATACGCAGACTTCAGATCCCGGACGCCA
CGTGATGCTCCTGCCGGCTGTCCCAGGTGGGGCTGGAGATGCCTCAGTGCTGCCAGCCTTC
CACGGGAAGGACAGGAGAAGGTGCTGGACCGCCTGGACTTTGTGCTGACCAGCCTTGTGGCG
CTGCCGGCGGGAGGTGGAGGAGCTGAGAAGCAGCCTGCGAGGGCTTGCCGGGGAGATTGTTGG
GGAGGTCCGATGCCACATGGAAGAGAACCAGAGAGTGGCTCGGCCGGCGAAGGTTTCCGTTTG
TCCGGGAGAGGAGTGACTCCACTGGCTCCAGCTCTGTCTACTTCACGGCCTCCTCGGGAGCC
ACGTTACAGATGCTGAGAGTGAAGGGGGTTACACAACAGCCAATGCCGAGTCTGACAATGA
GCGGGACTCTGACAAAGAAAGTGAGGACGGGGAAAGATGAAGTGAGCTGTGAGACTGTGAAGA
TGGGGAGAAAGGATTCTCTTGACTTGGAGGAAGAGGCAGCTTCAGGTGCCTCCAGTGCCCTG
GAGGCTGGAGGTTCTCAGGCTTGGAGGATGTGCTGCCCTCCTGCAGCAGGCCGACGAGCT
GCACAGGGGTGATGAGCAAGGCAAGCGGGAGGGCTTCCAGCTGCTGCTCAACAACAAGCTGG
TGTATGGAAGCCGGCAGGACTTTCTCTGGCGCTGGCCCGAGCCTACAGTGACATGTGTGAG
CTCAC'TGAGGAGGTGAGCGAGAAGAAGTCATATGCCCTAGATGGAAAAGAAGAAGCAGAGG
TGCTCTGGAGAAGGGGGATGAGAGTGCTGACTGTCACCTGTGGTATGCGGTGCTTTGTGGTC
AGCTGGCTGAGCATGAGAGCATCCAGAGGCGCATCCAGAGTGGCTTTAGCTTCAAGGAGCAT
GTGGACAAAGCCATTGCTCTCCAGCCAGAAAACCCCATGGCTCACTTTCTTCTTGGCAGGTG
GTGCTATCAGGTCTCTCACCTGAGCTGGCTAGAAAAAAAAAACTGCTACAGCCTTGCTTGAAA
GCCCTCTCAGTGCCAC'GT'GGAAGATGCCCTCCAGAGCTTCTAAAGGCTGAAGAACTACAG
CCAGGATTTTCCAAAGCAGGAAGGGTATATATTTCCAAGTGCTACAGAGAACTAGGGAAAAA
CTCTGAAGCTAGATGGTGGATGAAGTTGGCCCTGGAGCTGCCAGATGTCACGAAGGAGGATT
TGGCTATCCAGAAGGACCTGGAAGAAGTGAAGTCAATTTTACGAGACT**TAA**CCACGTTTCACT
GGCCTTCATGACTTGATGCCACTATTTAAGGTGGGGGGCGGGGAGGCTTTTTTCTTAGAC
CTTGCTGAGATCAGGAAACCACACAAATCTGTCTCCTGGGTCTGACTGCTACCCACTACCAC
TCCCATTAGTTAATTTATTCTAACCTCTAACCTAATCTAGAATTGGGGCAGTACTCATGGC
TTCCGTTTCTGTTGTTCTCTCCCTTGAGTAATCTCTTAAAAAATCAAGATTCACACCTGCC
CCAGGATTACACATGGGTAGAGCCTGCAAGACCTGAGACCTCCAATTGCTGGTGAGGTGGA
TGAAC'TCAAAGCTATAGGAACAAAGCACATAACTTGTCACTTTAATCTTTTCACTGACTA
ATAGGACTCAGTACATATAGTCTTAAGATCATAACCTTACCTACCAAGGTAAAAAGAGGGATCA
GAGTGGCCACAGACATTGCTTTCTTATCACCTATCATGTGAATTCTACCTGTATTCTGGG
CTGGACCACTTGATAACTTCCAGTGTCTGGCAGCTTTTGGAAATGACAGCAGTGGTATGGGG
TTTATGATGCTATAAAACAATGTCTGAAAAGTTGCCTAGAATATATTTTGTACAAACTTGA
AATAAACCAATTTGATGTT

FIGURE 68

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA139686
><subunit 1 of 1, 470 aa, 1 stop
><MW: 52118, pI: 5.06, NX(S/T): 0
MSRLGALGGARAGLGLLLGTAAGLGFLCLLYSQRWKRTQRHGRSQSLPNSLDYTQTSDPG
RHMVLLRAVPGGAGDASVLPSPREGQEKVLDRLDFVLTSLVALRREVEELRSSLRGLAG
EIVGEVRCHMEENQRVARRRRFPFVRERSDSTGSSSVYFTASSGATFTDAESEGGYTTAN
AESDNERDSKESEDGEDEVSCETVKMGRKDSLDEEEAASGASSALEAGGSSGLEDVLP
LLQQADELHRGDEQKREGFQLLLNNKLVYGSRQDFLWRLARAYSDMCELTEEVSEKSY
ALDGKEEAEEAALEKGDDESADCHLWYAVLCGQLAEHESIQRRIQSGFSFKEHVDKAIALQP
ENPMAHFLLGRWCYQVSHLSWLEKKTATALLESPLSATVEDALQSFLKAEELQPGFSKAG
RVYISKCYRELGKNSEARWWMKLALELPDVTKEDLAIQKDLEEELEVLIRD
```

Important features of the protein:

Signal peptide:

Amino acids 1-32

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 209-213

N-myristoylation sites:

Amino acids 5-11;8-14;9-15;15-21;19-25;72-78;164-170;
174-180;222-228;230-236

Amidation sites:

Amino acids 207-211;254-258

Cell attachment sequence:

Amino acids 250-253

FIGURE 69

CCCACGCGTCCGAAACACTTTAAACCTGACCAGCTAAATGGATAAACCTAGCCTGCATAGCT
TTTAAACTGGGGTCTCATAACAGCACAGGAGGCCACTTGCCTCAAGAAGCTGAAAATCCAGAG
GATGAATTGCTTTATCTGGGAATGGCAAAGCCAGCACAAATAAGGAATGCCAGTTTGTATGG
GGCTACTAGCTCACATGCGGGATCAGAATGGTGTGAATGACAGCCGCACTGTGTATGAAGG
TGGTGGTGGTTTCCGCACAAGAGACCAAATAAGAAGAAAGCTGAGAGAGGGGGGAAACGTTTTT
GGATGACAAAGGATGGGTTTCCATTTAATTACGCAGCTGAAAGGCATGAGTGTGGTGCCTGGT
GCTACTTCTACACTGCTGCTGTGTATGTCTACGGGTGCTCAGAGAGCTTGCCCAAAGAAGCT
GCAGATGTGATGGCAAATTTGTGTACTGTGAGTCTCATGCTTTCGCAGATATCCCTGAGAAC
ATTTCTGGAGGGTCAACAAGCTTATCATTAAGGTTCAACAGCATTTCAGAAGCTCAAATCCAA
TCAGTTTGCCGGCCTTAACCAGCTTATATGGCTTTATCTTGACCATAATTACATTAGCTCAGTG
GATGAAGATGCATTTCAAGGGATCCGTAGACTGAAAGAATTAATTCTAAGCTCCAACAAAAT
TACTTATCTGCACAATAAAACATTTCAACCAGTTCCCAATCTCCGCAATCTGGACCTCTCCT
ACAATAAGCTTCAGACATTGCAATCTGAACAATTTAAAGGCCTTCGGAAACTCATCATTTTG
CACTTGAGATCTAACTCACTAAAGACTGTGCCATAAGAGTTTTTCAAGACTGTCCGAATCT
TGATTTTTTGGATTTGGGTTACAATCGTCTTCAAGCTTGTCCCAGAAATGCATTTGCTGGCC
TCTTGAAGTTAAAGGAGCTCCACCTGGAGCACAAACCAGTTTTCCAAGATCAACTTTGCTCAT
TTTCCACGTCTCTCAACCTCCGCTCAATTTACTTACAATGGAACAGGATTCGCTCCATTAG
CCAAGGTTTGACATGGACTTGGAGTTCCCTTACACAACCTTGGATTTATCAGGGAATGACATCC
AAGGAATTGAGCCGGGCACATTTAAATGCCTCCCAATTTACAAAATTTGAATTTGGATTCC
AACAAGCTCACCAATATCTCACAGGAAACTGTCAATGCGTGGATATCATTAATATCCATCAC
ATTGTCTGGAAATATGTGGGAATGCAGTCGGAGCATTGTCTTTATTTTATTGGCTTAAGA
ATTTCAAAGGAAATAAGGAAAGCACCATGATATGTGCGGGACCTAAGCACATCCAGGGTGAA
AAGGTTAGTGATGCAGTGGAAACATATAATATCTGTTCTGAAGTCCAGGTGGTCAACACAGA
AAGATCACACCTGGTGCSCCAAACCTCCCAAGAAACCTCTGATTATCCCTAGACCTACCATCT
TCAAACCTGACGTCACCAATCCACCTTTGAAACACCAAGCCCTTCCCAAGGGTTTCAGATT
CCTGGCGCAGAGCAAGAGTATGAGCATGTTTCATTTACAAAATTTATTGCCGGGAGTGTGGC
TCTCTTTCTCTCAGTGGCCATGATCCTCTTGGTGATCTATGTGTCTTGGAAACGCTACCCAG
CCAGCATGAAACAACCTCCAGCAACACTCTCTTATGAAGAGGCGGCGGAAAAAGGCCAGAGAG
TCTGAAAGACAAATGAATTTCCCTTTTACAGGAGTATTATGTGGACTACAAGCCTACAAACTC
TGAGACCATGGATATATCGGTTAATGGATCTGGGCCCTGCACATATAACCATCTCTGGCTCCA
GGGAATGTGAGATGCCACACCACATGAAGCCCTTGCCATATTACAGCTATGACCAGCCTGTG
ATCGGGTACTGCCAGGCCACCAGCCACTCCATGTCACCAAGGGCTATGAGACAGTGTCTCC
AGAGCAGGACGAAAGCCCCGGCCTGGAGCTGGGCCGAGACCACAGCTTCAATCGCCACCATCG
CCAGGTCCGGCAGCACCGGCCATCTACCTAGAGAGAATTGCAAACCTAACCGCTGAAGCCAACTC
CTCACTGGGGAGCTCCATGGGGGGGAGGGAGGGCCTTCATCTTAAAGGAGAATGGGTGTCCA
CAATCGCGCAATCGAGCAAGCTCATCGTTTCTGTAAAACATTTATGGCATAGGGAAAAAAA
AAAAAAAAAAAAAAAA

FIGURE 70

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA142392
><subunit 1 of 1, 590 aa, 1 stop
><MW: 67217, pI: 9.26, NX(S/T): 4
MGFHLITQLKGMSVVLVLLPTLLLVMMLTGAQRACPKNCRCDCGKIVYCESHAFADIPENIS
GGSQGLSLRFNSIQKLKSNQFAGLNQLIWLYLDHNYISSVDEDAFQGIIRRLKELILSSNK
ITYLHNKTFHPVFNLRNLDLSYNKLQTLQSEQFKGLRKLIIHLRSNSLKTVPPIRVFQDC
RNLDFLDLGYNRLRSLSRNAFAGLLKLKELHLEHNQFSKINFAHFPRLFNLRSIYLQWNR
IRSISQGLTWTWSSLHNLDSLGNDIQGIIEPGTFKCLPNLQKLNLDLSDSNKLTNISQETVNAW
ISLISITLSGNMWECRSRSCPLFYWLKNEFKGNKESTMICAGPKHIQGEKVS DAVETYNIC
SEVQVVNTERSHLVPQTPQKPLIIPRPTIFKPDVTQSTFETPSPSPGFQIPGAEQEYEHV
SFHKIIAGSVALFLSVAMILLVIYVSWKRY PASMKQLQQHSLMKRRRKKARESERQMNSP
LQEYYVDYKPTNSETMDISVNGSGPCTYTI SSGSRECEMPHMKPLPYYSYDQPVIGYCQA
HQPLHVTKGYETVSPEQDESPGLELGRDHSFIATIARSAAPAIYLERIAN
```

Important features of the protein:

Signal peptide:

Amino acids 1-30

Transmembrane domain:

Amino acids 425-443

N-glycosylation sites:

Amino acids 58-62;126-130;291-295;501-505

Tyrosine kinase phosphorylation site:

Amino acids 136-143

N-myristoylation sites:

Amino acids 29-35;61-67;247-253;267-273;271-277;331-337;
502-508;512-518;562-568

Glycosyl hydrolases family:

Amino acids 310-319

FIGURE 71

TTCCAGTCAGAGTTAAGTTAAAACAGAAAAAAGGAAGATGGCAAGAATATTGTTACTTTTCC
TCCCGGGTCTTGTGGCTGTATGTGCTGTGCATGGAATATTTATGGACCGTCTAGCTTCCAAG
AAGCTCTGTGCAGATGATGAGTGTGTCTATACTATTTCTCTGGCTAGTGCTCAAGAAGATTA
TAATGCCCCGGACTGTAGATTCATTAACGTTAAAAAAGGGCAGCAGATCTATGTGTA~~CT~~CAA
AGCTGGTAAAAGAAAATGGAGCTGGAGAATTTTGGGCTGGCAGTGTTTATGGTGATGGCCAG
GACGAGATGGGAGTCGTGGGTTATTTCCCCAGGAACTTGGTCAAGGAACAGCGTGTGTACCA
GGAAGCTACCAAGGAAGTTCCCACCACGGATATTGACTTCTTCTGCGAGTAAATAATTAGTT
AAAAGTCAAATAGAAAGAAAACACCAAAAATAAAGAAAAGAGCAAAAAGTGCCAAAAAATG
CATGTCTGTAATTTTGGACTGACGT

FIGURE 72

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA143076
><subunit 1 of 1, 128 aa, 1 stop
><MW: 14332, pI: 4.83, NX(S/T): 0
MARILLFLPGLVAVCAVHGIFMDRLASKKLCADDFECVYTI SLASAQEDYNAPDCRFINV
KKGQQIYVYSKLVKENGAGEFWAGSVYGDGQDEMGGVVGYFPRNLVKEQRVYQEATKEVPT
TDIDFFCE
```

Important features of the protein:

Signal peptide:

Amino acids 1-14

N-myristoylation site:

Amino acids 84-90

FIGURE 73

CTCAGATTTGCC**ATG**GAGAAATTTTCAGTCTCGGCAATCCTGCTTCTTGTGGCCATCTCTGG
TACTCTGGCCAAAGACACCACAGTCAAATCTGGATCCAAAAAGGACCCAAAGGACTCTCGAC
CCAAACTACCCCAGACCCTGTCCAGAGGTTGGGGAGATCAGCTCATCTGGACTCAGACTTAC
GAAGAAGCCTTATACAAATCCAAGACAAGCAACAGACCCTTGATGGTCATTCATCACTTGGA
CGAATGCCCCGCACAGTCAAGCTTTAAAGAAAGTGTTGCTGAAAATAAGGAGATCCAGAAATTG
GCAGAGCAGTTTGTTCCTCAACTTGATCTATGAAACAACCTGACAAGCACCTTTCTCCTGA
TGGCCAGTACGTCCCCAGAATTGTGTTTGTGGACCCTTCCCTGACGGTGAGGGCAGACATCA
CCGGAAGATACTCAAACCGTCTCTACGCTTATGAACCTTCTGACACAGCTCTGTTGCACGAC
AACATGAAGAAAGCTCTCAAGTTGCTGAAGACAGAGTTG**TAG**AGTCAACTGTACAGTGCCTC
AGGAGCCGGAAGGCAGAAGCACTGTGGACCTGCCGATGACATTACAGTTTAATGTTACAAC
AAATGTATTTTTTAAACACCCACGTGTGGGGAAACAATATTATTATCTACTACAGACACATG
ATTTTCTAGAAAATAAAGTCTTGTGAGAACTCCAAA

FIGURE 74

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA143294
><subunit 1 of 1, 175 aa, 1 stop, 1 unknown
><MW: 19888.97, pI: 9.08, NX(S/T): 0
MEKFSVSAILLLLVAISGTLAKDTTVKSGSKKDPKDSRPKLPQTLSRGWGDQLIWTQTYEE
ALYKSKTSNRPLMVIHHLDECPHSQALKKVFAENKEIQKLAEQFVLLNLIYETTDKHLSP
DGQYVPRIVFVDPSTLTVRADITGRYSNRLYAYEPSDTALLHDNMKKALKLLKTEL
```

Important features of the protein:

Signal peptide:

Amino acids 1-20

FIGURE 75

GCCGGCGCCAGGGCAGGGCGGGCGGGCTGGCAGCTGTGGCGCCGACATGGCTGCGCTGGTGGAG
CCGCTGGGGCTGGAGCGGGACGTGTCCCGGGCGGTTGAGCTCCTCGAGCGGCTCCAGCGCAG
CGGGGAGCTGCCGCCGAGAAAGCTGCAGGCCCTCCAGCGAGTTCTGCAGAGCCGCTTCTGCT
CCGCTATCCGAGAGGTGTATGAGCAGCTTTATGACACGCTGGACATCACCGGCAGCGCCGAG
ATCCGAGCCCATGCCACAGCCAAGGCCACAGTGGCTGCCTTCACAGCCAGCGAGGGGCCACGC
ACATCCCAGGGTAGTGGAGCTACCCAAGACGGATGAGGGCCTAGGCTTCAACATCATGGGTG
GCAAAGAGCAAAACTCGCCCATCTACATCTCCCGGGTCATCCCAGGGGGTGTGGCTGACCGC
CATGGAGGCTCAAGCGTGGGGATCAACTGTTGTCCGTGAACGGTGTGAGCGTTGAGGGTGA
GCAGCATGAGAAGGCGGTGGAGCTGCTGAAGGCGGCCAGGGCTCGGTGAAGCTGGTTGTCC
GTTACACACCGCGAGTGTGGAGGAGATGGAGGCCCGGTTTCGAGAAGATGCGCTCTGCCCGC
CGGCGCCAACAGCATCAGAGCTACTCGTCCTTGGAGTCTCGAGGTTGAAACCACAGATCTGG
ACGTTACGTGCACTCTCTCCTGTACAGTATTTATTGTTCCCTGGCACTTTATTTAAAGATA
TTTGACCCTCAAAAAAAAAAAAAAAAAAAAAA

FIGURE 76

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA143514
><subunit 1 of 1, 207 aa, 1 stop
><MW: 22896, pI: 8.93, NX(S/T): 0
MAALVEPLGLERDVSRAVELLERLQMSGELPPQKLQALQRVLQSRFCSAIREVYEQLYDT
LDITGSAEIRAHATAKATVAAFTASEGHAPRVVELPKTDEGLGFNIMGGKEQNSPIYIS
RVIPGGVADRHGGLKRGDQLLSVNGVSVEGEQHEKAVELLKAAQGSVKLVRYTPRVLEE
MEARFEKMRSARRRQQHQSYSSLESRC
```

Tyrosine kinase phosphorylation site:

Amino acids 51-59

N-myristoylation sites:

Amino acids 102-108;133-139

Cell attachment sequence:

Amino acids 136-139

PDZ domain (Also known as DHR or GLGF):

Amino acids 93-174

FIGURE 78

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA144841
><subunit 1 of 1, 208 aa, 1 stop
><MW: 22187, pI: 5.08, NX(S/T): 1
MDSDETGFHESGLWVSVLAGLLGACQAHPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHL
EIREDTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGLYGLHFDPEAC
SFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPAPRFLPLPGLPPALPEPPCIL
APQPPDVGSSDPLSMVGPSQGRSPSYAS
```

Important features of the protein:

Signal peptide:

Amino acids 1-27

N-myristoylation sites:

Amino acids 12-18;20-26;23-29;66-72;94-100;107-113;168-174

Prokaryotic membrane lipoprotein lipid attachment site:

Amino acids 15-26

HGF/FGF family proteins:

Amino acids 57-73;80-131

FIGURE 79

AGTCCCAGACGGGCTTTTCCCAGAGAGCTAAAAGAGAAGGGCCAGAGA**ATG**TCGTCCCAG
CCAGCAGGGAACCAGACCTCCCCGGGGCCACAGAGGACTACTCCTATGGCAGCTGGTAC
ATCGATGAGCCCCAGGGGGCGAGGAGCTCCAGCCAGAGGGGGAAGTGCCCTCCTGCCAC
ACCAGCATAACCACCCGGCCTGTACCACGCCTGCCTGGCCTCGCTGTCAATCCTTGTGCTG
CTGCTCCTGGCCATGCTGGTGAGGCGCCGCCAGCTCTGGCCTGACTGTGTGCGTGGCAGG
CCCGGCCTGCCAGCCCTGTGGATTTCTTGGCTGGGGACAGGCCCCGGGCAGTGCCTGCT
GCTGTTTTTCATGGTCCCTCCTGAGCTCCCTGTGTTTGGCTGCTCCCCGACGAGGACGCATTG
CCCTTCTGACTCTCGCCTCAGCACCCAGCCAAGATGGGAAAACCTGAGGCTCCAAGAGGG
GCCTGGAAGATACTGGGACTGTTCTATTATGCTGCCCTTACTACCCTCTGGCTGCCTGT
GCCACGGCTGGCCACACAGCTGCACACCTGCTCGGCAGCACGCTGTCTGGGCCACCTT
GGGTCCAGGTCTGGCAGAGGGCAGAGTGTCCCCAGGTGCCAAGATCTACAAGTACTAC
TCCCTGTGGCCTCCCTGCCTCTCCTGCTGGGCCCTCGGATTCCTGAGCCTTTGGTACCC
GTGCAGCTGGTGAGAAGCTTCAGCCGTAGGACAGGAGCAGGCTCCAAGGGGCTGCAGAGC
AGCTACTCTGAGGAATATCTGAGGAACCTCCTTTGCAGGAAGAAGCTGGGAAGCAGCTAC
CACACCTCCAAGCATGGCTTCCTGTCTGGGCCCGCTCTGCTTGAGACACTGCATCTAC
ACTCCACAGCCAGGATTCATCTCCCCTGAAGCTGGTGTTCAGCTACACTGACAGGG
ACGGCCATTTACCAGGTGGCCCTGCTGCTGCTGGTGGGCGTGGTACCCACTATCCAGAAG
GTGAGGGCAGGGGTACCACGGATGTCTCCTACCTGCTGGCCGGCTTTGGAATCGTGCTC
TCCGAGGACAAGCAGGAGGTGGTGGAGCTGGTGAAGCACCATCTGTGGGCTCTGGAGTG
TGCTACATCTCAGCCTTGGTCTTGTCTGCTTACTCACCTCCTGGTCTGATGCGCTCA
CTGGTGACACACAGGACCAACCTTCGAGCTCTGCACCGAGGAGCTGCCCTGGACTTGAGT
CCCTTGATCGGAGTCCCCATCCCTCCCAGCAAGCCATATTCCTGTTGGATGAGCTTCAGT
GCCTACCAGACGCCCTTATCTGCCTTGGGCTCCTGGTGCAGCAGATCATCTCTTCCTG
GGAACCCAGGCCCTGGCCCTTCTGGTGCCTCATGCCTGTGCTCCATGGCAGGAACCTCCTG
CTCTTCCGTTCCCTGGAGTCTCCTGCGGCCCTTCTGGCTGACTTTGGCCCTGGCTGTGATC
CTGCAGAACATGGCAGCCATTGGGTCTTCTGGAGACTCATGATGGACACCCACAGCTG
ACCAACCGGCGAGTGTCTATGCAGCCACCTTCTTCTCTTCCCCCTCAATGTGCTGGT
GGTGCATGGTGGCCACCTGGCGAGTGTCTCTCTGCCCTCTACAACGCCATCCACCTT
GGCCAGATGGACCTCAGCCTGCTGCCACCGAGAGCCGCCACTCTCGACCCCGGCTACTAC
ACGTACCGAACTTCTTGAAGATTGAAGTCAGCCAGTCGCATCCAGCCATGACAGCCTTC
TGCTCCCTGCTCCTGCAAGCGCAGAGCCTCCTACCCAGGACCATGGCAGCCCCCAGGAC
AGCCTCAGACCAGGGGAGGAAGACGAAGGGATGCAGCTGCTACAGACAAAGGACTCCATG
GCCAAGGGAGCTAGGCCCGGGGCCAGCCGCGGCAGGGCTCGCTGGGGTCTGGCCTACACG
CTGCTGCACAACCCAACCTGCAGGTCTCCGCAAGACGGCCCTGTTGGGTGCCAATGGT
GCCCAGCCC**TGA**GGGCAGGGAAGGTCAACCCACCTGCCATCTGTGCTGAGGCATGTTCC
TGCTACCATCCTCCTCCCTCCCCGGCTCTCCTCCCAGCATCACACCAGCCATGCAGCCA
GCAGGTCTCCGGATCACTGTGGTTGGGTGGAGGTCTGTCTGCACTGGGAGCCTCAGGAG
GGCTCTGCTCCACCCACTTGGCTATGGGAGAGCCAGCAGGGGTTCTGGAGAAAAAACTG
GTGGGTTAGGGCCTTGGTCCAGGAGCCAGTTGAGCCAGGGCAGCCACATCCAGGCGTCTC
CCTACCCCTGGCTCTGCCATCAGCCTTGAAGGGCCTCGATGAAGCCTTCTCTGGAACCACT
CCAGCCCAGCTCCACCTCAGCCTTGGCCTTACGCTGTGGAAGCAGCCAAGGCACTTCTC
CACCCCTCAGCGCCACGGACCTCTCTGGGGAGTGGCCGAAAGCTCCCGTCTCTGGC
CTGCAGGGCAGCCCAAGTCATGACTCAGACCAGGTCCCACACTGAGCTGCCACACTCGA
GAGCCAGATATTTTTGTAGTTTTTATGCC'TTTGGCTATTATGAAAGAGGTTAGTGTGTTT
CCTGCAATAAACTTGTTCCTGAGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 80

Protein File:

MW: 73502.97, pI: 9.26

MSSQPAGNQTSPGATEDYSYGSWYIDEPQGGEELOPEGEVPSCHTSIPPGLYHACLASLS
ILVLLLLAMLVRRRQLWPDVCVRGRPLSPVDFLAGDRPRAVPAAVFMVLLSSLCLLLPD
EDALPFLTLASAPSQDGKTEAPRGAWKILGLFYAALYYPLAACATAGHTAAHLLGSTLS
WAHLGVQVWQRAECPQVPKIYKYSSLASPLLLGLGFLSLWYPVQLVRSFSRRTGAGSK
GLQSSYSEEYLRNLLCRKKLGSSYHTSKHGFLSWARVCLRHCIYTPQPGFHLPLKLVLSA
TLTGTAIYQVALLLVGVVPTIQKVRAGVTTDVSYLLAGFGIVLSEDKQEVVELVKHHLW
ALEVCYISALVLSCLLTFVLVLRSLVTHRTNLRALHRGAALDLSPLHRSPHPSRQAI FCW
MSFSAYQTAFICLGLLVQQIIFFLGTTALAFVLMPVLHGRNLLLFRSLESSWPEWLTTLA
LAVILQNMAAHWVFLETHDGHPQLTNRRLVYAATFLLFPLNVLVGAMVATWRVLLSALYN
AIHLGQMDLSLLPPRAATLDPGYTYRNFLEKIEVSQSHPAMTAFCSLLLOAQSLPRTMA
APQDSL RPGEEDGEMQLLQTKDSMAKGARPGASRGRARWGLAYTLLHNPTLQVFRKTALL
GANGAQP

Important features of the protein:

Transmembrane domains:

Amino acids 54-69;102-119;148-166;207-222;301-320;
364-380;431-451;474-489;512-531

N-glycosylation site:

Amino acids 8-12

N-myristoylation sites:

Amino acids 50-56;176-182;241-247;317-323;341-347;525-531;
627-633;631-637;640-646;661-667

Prokaryotic membrane lipoprotein lipid attachment site:

Amino acids 364-375

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

Amino acids 132-140

FIGURE 81

AAAAAATACAGCAGGTGAAGGAGGTTGGAGAGTAGGGGGTGGAGGGCCCACGCAGCACTTGT
CCTTCACCCTGGAGGGGATCTGTTACATGCCCCAGATTGCTGGTCCCCTAGAAATGTTACTG
AGGCAGCCTCTGCATTTTTCAGGGATTGTTTTCTACTGTTTGACATTCACGTAACCTCCTA
ACGCTGTCTGGGGAAGATGCTACCCCCTGCTCTCCCCGTCTTTCCTGCACTCTCAGCAATGG
GATGGGCTGACTGATGCCCTGTGGGCTGGAAAGCTGACCACAGTTGCTGCAGACCAGACCCC
CTCACATAGTGAGTGCTGGGCTGAGGAATCCAGGAGAGCCCAGGGGGGACACTGAAGGTGT
ATCGTTGGCCCTGCCAGCTGCAAGTGAAGTCTTCTGATGAATTTAATAGGGAGAAAGAAG
TATTTGCTAAGAATGGCAATCCTGACGCTCAGCCTTCAACTCATCTTGTTATTAATACCATC
AATATCCCATGAGGCTCATAAAACGAGTCTTTCTTCTTGAAACATGACCAAGATTGGGCAA
ACGCTCCAACATGACTTTCAGCAACGGAAAACCTAAGAGTCAAAGGCATTTATTACCGGAAT
GCCGACATTTGCTCTCGACATCGCGTAACTCAGCAGGCCTAACTCTGCAGGACCTTCAGCT
ATGGTGTAATTTGAGGTCAGTGGCCAGAGGACAGATCCCGTCTACATTAAGTGAAGCGGAGA
GCTACTGCAGGGTTCTGAGCAGAGTCCTAATTTATATTTTAGAAGAATCATCATGGCTCCTA
GATTAGGAATAAAACGAAGGGGGCCAGGGATGGAAACGATGAGTCCAGTTGGGTTACTGCAA
AGATCCAGGCCAGAAATCCAGGCACAGTGGCACACACCTGAGTCCAGATAATTCCACCTAC
TGGTCCTGCTCTGTGGCCTACTGGTCCGAGTCCAGCCCCGACTGATTTCTGGGCCTGTAATG
TCTAAAAACGCTCCCTGCTGATGTTTTGCAAGTACTGTGTTACTTGAAGGCAGTTCCTAGG
ATAAACTAGTCGCTTTATCATTACAGAAATCATTCACTGAGCATCAACTATGTAACCAGCATT
GGTTGGGTGCCAGAGATCCAAAGCTAAGACACCAAACCTGCTCTCCAGGAAACGAGAGGC
TGAGAA

FIGURE 82

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA149995
><subunit 1 of 1, 95 aa, 1 stop
><MW: 10704, pI: 10.00, NX(S/T): 2
MAILTSLQLILLLLIPSI SHEAHKTSLSWKHDQDWANVSNMTFSNGKLRVKGIIYRNAD
ICSRHRVTSAGLTLQDLQLWCNLRVARGQIPSTL
```

Important features of the protein:

Signal peptide:

Amino acids 1-19

N-glycosylation sites:

Amino acids 38-42;41-45

N-myristoylation site:

Amino acids 89-95

FIGURE 83

AATAGAAGTCCTCAGGACGGAGCAGAGGTGGCCGGCGGGCCCGGCTGACTGCGCCTCTGCTT
TCTTTCCATAACCTTTTCTTTTCGGACTCGAATCACGGCTGCTGCGAAGGGTCTAGTTCCGGA
CACTAGGGTGCCCGAACCGCTGATGCCCCGAGTGCTCGCAGGGCTTCCCCTAACCATGCT
GCCGCCGCCCGGCCCGCAGCTGCCTTGGCGCTGCCTGTGCTCCTGCTACTGCTGGTGGTGC
TGACGCCGCCCGACCGGCGCAAGGCCATCCCCAGGCCAGATTACCTGCGGCGGGCTGG
ATGCGGCTGCTAGCGGAGGGCGAGGGCTGCGCTCCCTGCCGGCCAGAAGAGTGCGCCGCGCC
GCGGGCTGCCTGGCGGGCAGGGTGC CGCAGCGCTGCGGCTGCTGCTGGGAATGCGCCAACC
TCGAGGGCCAGCTCTGCGACCTGGACCCAGTGCTCACTTCTACGGGCACTGCGGCGAGCAG
CTTGAGTGCCGGCTGGACACAGGGCGGCGACTGAGCCGCGGAGAGGTGCCGGAACCTCTGTG
TGCTGTGTTTCGACAGAGTCCGCTCTGCGGGTCCGACGGTACACCTACTCCCAGATCTGCC
GCCTGCAGGAGGCGGCCCGCGCTCGGCCCGATGCCAACCTCACTGTGGCACACCCGGGGGCC
TGCGAATCGGGGCCCGAGATCGTGTACATCCATATGACACTTGGGAATGTGACAGGGCAGGA
TGTGATCTTTGGCTGTGAAGTGTTTGCCTACCCCATGGCCTCCATCGAGTGGAGGAAGGATG
GCTTGGACATCCAGCTGCCAGGGGATGACCCACATCTCTGTGCAGTTTAGGGGTGGACCC
CAGAGGTTTGAGGTGACTGGCTGGCTGCAGATCCAGGCTGTGCGTCCCAGTGATGAGGGCAC
TTACCGCTGCCTTGGCCGCAATGCCCTGGGTCAAGTGGAGGCCCTGCTAGCTTGACAGTGC
TCACACCTGACCAGCTGAACTCTACAGGCATCCCCAGCTGCGATCACTAAACCTGGTTCTCT
GAGGAGGAGGCTGAGAGTGAAGAGAATGACGATTACTACTAGGTCCAGAGCTCTGGCCCATG
GGGTGGGTGAGCGGCTATAGTGTTTCATCCCTGCTCTTGAAAAGACCTGGAAAGGGGAGCAG
GGTCCCTTCATCGACTGCTTTCATGCTGTGCTAGGGATGATCATGGGAGGCCTATTTGACT
CCAAGGTAGCAGTGTGGTAGGATAGAGACAAAAGCTGGAGGAGGGTAGGGAGAGAAGCTGAG
ACCAGGACCGGTGGGGTACAAAGGGGCCCATGCAGGAGATGCCCTGGCCAGTAGGACCTCCA
ACAGGTTGTTTCCCAGGCTGGGGTGGGGCCCTGAGCAGACACAGAGGTGCAGGCACCAGGAT
TCTCCACTTCTTCCAGCCCTGCTGGGCCACAGTTCCTAACTGCCCTTCTCCCAGGCCCTGGT
TCTTGCTATTTCTGCTCCCAACGTTTATCTAGCTTGTGTTGCCCTTCCCCAACTCATCT
TCCAGAACTTTTCCCTCTCTCCTAAGCCCCAGTTGCACCTACTAACTGCAGTCCCTTTTGCT
GTCTGCCGTCTTTTGTACAAGAGAGAGAACAGCGGAGCATGACTTAGTTCAGTGCAGAGAGA
TTT

FIGURE 84

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA167678
><subunit 1 of 1, 304 aa, 1 stop
><MW: 32945, pI: 4.69, NX(S/T): 3
MLPPRPAAALALPVLLLLLVLT PPPTGARPSGPDYLRGWMRLLAEGEGCAPCRPEE
CAAPRGCLAGRVRDACGCCWECANLEGQLCDLDPSAHFYGHCGEQLECRDLDGDLRGE
VPEPLCACRSQSPLCGSDGHTYSQICRLQEAARARPDANLTVAHGPGCESGQIVSHPYD
TWNVTGQDVI FGCEVFAYPMASIEWRKDGLDIQLPGDDPHISVQFRGGPQRFEVTGWI.QI
QAVRPSDEGTYRCLGRNALGQVEAPASLTVLTPDQLNSTGIPQLRSLNLVPEEEAESEEN
DDYY
```

Important features of the protein:

Signal peptide:

Amino acids 1-30

N-glycosylation sites:

Amino acids 159-163;183-187;277-281

Tyrosine kinase phosphorylation site:

Amino acids 244-252

N-myristoylation sites:

Amino acids 52-58;66-72;113-119;249-255

Kazal-type serine protease inhibitor domain:

Amino acids 121-168

Immunoglobulin domain:

Amino acids 186-255

Insulin-like growth factor binding proteins:

Amino acids 53-90

FIGURE 85

CAAAGCGGCGGCTGTCCGCGGTGCCGGCTGGGGGCGGAGAGGCGGCGGTGGGCTCCCTGGGG
TGTGTGAGCCCGGTG**ATG**GAGCCGGGCCCCGACAGCCGCGCAGCGGAGGTGTTGTTGCCGCC
GTGGCTGCCGCTGGGGCTGCTGCTGTGGTCGGGGCTGGCCCTGGGCGCGCTCCCTTCGGCA
GCAGTCCGCACAGGGTCTTCCACGACCTCCTGTGCGAGCAGCAGTTGCTGGAGGTGGAGGAC
TTGTCCCTGTCCCTCCTGCAGGGTGGAGGGCTGGGGCCTCTGTGCTGCCCCGGACCTGCC
GGATCTGGATCCTGAGTGCCGGGAGCTCCTGCTGGACTTCGCCAACAGCAGCGCAGAGCTGA
CAGGGTGTCTGGTGCGCAGCGCCCCGGCCCGTGCGCCCTCTGTCAGACCTGCTACCCCCCTTTC
CAACAGGTCGT**CAG**CAAGATGGACAACATCAGCCGAGCCGCGGGGAATACTTCAGAGAGTCAG
AGTTGTGCCAGAAGTCTCTTAATGGCAGATAGAATGCAAATAGTTGTGATTCTCTCAGAATT
TTTAAATACCACATGGCAGGAGGCAAATTGTGCAAATTGTTTAAACAAACAACAGTGAAGAA
TATCAAACAGCACAGTATATTTCTTAATCTATTTAATCACACCCTGACCTGCTTTGAACAT
AACCTTCAGGGGAATGCACATAGTCTTTTACAGACAAAAAATTATT**CAG**AAGTATGCAAAAA
CTGCCGTGAAGCATACAAACTCTGAGTAGTCTGTACAGTGAAATGCAAAAAATGAATGAAC
TTGAGAATAAGGCTGAACCTGGAACACATTTATGCATTGATGTGGAAGATGCAATGAACATC
ACTCGAAACTATGGAGTCGAACTTTCAACTGTT**CAG**TCCCTTG**CAG**TGACACAGTGCCTGT
AATTGCTGTTTCTGTGTTCA**TTCTCTTTCTACCTGTTGTCTTCTACCTTAGTAGCTTTCTTC**
ACTCAGAGCAAAAGAAACGCAAACTCAT**CTG**CCCAAACGTCTCAAGTCCAGTACCAGTTTT
GCAAATATTCAGGAAAATTCAAACT**TGA**GACCTACAAAATGGAGAATTGACATATCACGTGAA
TGAATGGTGGAAAGACACA**ACTTGGTTTCAGAA**AGAAGATAAACTGTGATTTGACAAGTCAAG
CTCTTAAGAAATACAAGGACTTCAGATCCATTTTTAAATAAGAATTTTCGATTTTTCTTTCC
TTTTCCA**CTTCTTCTAACAGATTTGGATATTTTAAATTTCCAG**

FIGURE 86

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA168028
><subunit 1 of 1, 334 aa, 1 stop
><MW: 37257, pI: 5.95, NX(S/T): 10
MEPGPTAAQRRCSLPPWLPGLLLWSGLALGALPFGSSPHRVFHDLLSEQQLLEVEDLSL
SLLQGGGLGPLSLPPDLPDLDPDPECRELLLDFASSAELTGCLVRSARPVRLCQTCYPLFQ
QVVSMDNISRAAGNTSESQSCARSLLMADRMQIVVILSEFFNTTWQEANCANCLTNNSE
ELSNSTVYFLNLFNHTLTCFEHNLQGNASHLLQTKNYSEVCKNCREAYKTLSSLYSEMOK
MNELENKAEPGTHLCIDVEDAMNITRKLWSRTFNCSVPCSDTVPVIAVSVFILFLPVVY
LSSFLHSEQKRRKLILPKRLKSSTSFANIQENSN
```

Important features of the protein:

Signal peptide:

Amino acids 1-31

Transmembrane domain:

Amino acids 278-300

N-glycosylation sites:

Amino acids 93-97;128-132;135-139;163-167;177-181;
184-188;194-198;216-220;263-267;274-278

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 10-14

N-myristoylation sites:

Amino acids 27-33;206-212;251-257

Leucine zipper pattern:

Amino acids 190-212

FIGURE 87

ATGCTGGTAGCCGGCTTCCTGCTGGCGCTGCCGCCGAGCTGGGCCGCGGGCGCCCCAGGGC
GGGCAGGCGCCCCGCGCGGCCGCGGGGCTGCGCGGACCGGCCGGAGGAGCTACTGGAGCAGC
TGTACGGGCGCCTGGCGGCCGGCGTGCTCAGTGCCCTCCACCACACGCTGCAGCTGGGGCCG
CGTGAGCAGGCGCGCAACGCGAGCTGCCCGGCAGGGGGCAGGCCCCGGCGACCGCCGCTCCG
GCCGCCACCAACCTGCGCAGCGTGTGCCCTGGGCCACAGAATCTCCTACGACCCGGCGA
GGTACCCCAGGTACCTGCCTGAAGCCTACTGCCTGTGCCGGGGCTGCCTGACCGGGCTGTTC
GGCGAGGAGGACGTGCGCTTCCGCAGCGCCCCCTGTCTACATGCCACCGTCGTCCTGCGCCG
CACCCCGCCTGCGCCGGCGGCCGTTCCTGTCTACACCGAGGCCACGTACCATCCCCGTGG
GCTGCACCTGCGTCCCCGAGCCGGAGAAGGACGCAGACAGCATCAACTCCAGCATCGACAAA
CAGGGCGCCAAGCTCCTGCTGGGCCCAACGACGCGCCCGCTGGCCCC**TGA**GGCCGGTCTCTG
CCCCGGGAGGTCTCCCCGGCCCGCATCCCAGGGCGCCCAAGCTGGAGCCGCTGGAGGGGCTC
GGTCGGCGACCTCTGAAGAGAGTGCACCGAGCAAACCAAGTGCCGGAGCACCAGCGCCGCT
TTCCATGGAGACTCGTAAGCAGCTTCATCTGACACGGGCATCCCTGGCTTGCTTTTAGCTAC
AAGCAAGCAGCGTGGCTGGAAGCTGATGGGAAACGACCCGGCACGGGCATCCTGTGTGCGGC
CCGATGGAGGGTTTGAAAAGTTCACGGAGGCTCCCTGAGGAGCCTCTCAGATCGGCTGCT
GCGGGTGCAGGGCGTGACTCACCGCTGGGTGCTTGCCAAAGAGATAGGGACGCATATGCTTT
TTAAAGCAATCTAAAAATAATAAAGTATAGCGACTATATACCTACTTTTAAATCAACTG
TTTTGAATAGAGGCAGAGCTATTTTATATTATCAAATGAGAGCTACTCTGTTACATTTCTTA
ACATATAAACATCGTTTTTTACTTCTTCTGGTAGAATTTTTTAAAGCATAATTGGAATCCTT
GGATAAATTTGTAGCTGGTACACTCTGGCCTGGGTCTCTGAATTCAGCCTGTCACCGATGG
CTGACTGATGAAATGGACACGTCTCATCTGACCCACTCTTCCCTTCCACTGAAGGTCTTCAG
GGCCTCCAGGTGGACCAAGGGATGCACAGGCGGCTCGCATGCCCCAGGGCCAGCTAAGAGT
TCCAAAGATCTCAGATTTGGTTTTAGTCATGAATACATAAACAGTCTCAAACTCGCACAATT
TTTTCCCCCTTTTGAAAGCCACTGGGGCCAATTTGTGGTTAAGAGGTGGTGAGATAAGAAGT
GGAACGTGACATCTTTGCCAGTTGTCAGAAGAATCCAAGCAGGTATGGCTTAGTTGTAAGG
GCTTTAGGATCAGGCTGAATATGAGGACAAAGTGGGCCACGTTAGCATCTGCAGAGATCAAT
CTGGAGGCTTCTGTTTCTGCATTCTGCCACGAGAGCTAGGTCCTTGATCTTTCTTTAGATT
GAAAGTCTGTCTCTGAACACAATTATTTGTAAGTTAGTAGTTCTTTTTTAAATCATTAAA
AGAGGCTTGCTGAAGGAT

FIGURE 88

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA173894
><subunit 1 of 1, 202 aa, 1 stop
><MW: 21879, pI: 9.30, NX(S/T): 2
MLVAGFLLALPPSWAAGAPRAGRPPARPRGCADRPEELLEQLYGRLAAGVLSAFHHTLQL
GPREQARNASC PAGGRPGDRRFRPPTNLRVSPWAYRISYDPARYPRYLPEAYCLCRGCL
TGLFGEEDVRFERSAPVYMPTVVLRRTPACAGGRSVYTEAYVTIPVGCTCVPEPEKDADSI
NSSIDKQGAKLLLGPNDAPAGP
```

Important features of the protein:

Signal peptide:

Amino acids 1-15

N-glycosylation sites:

Amino acids 68-72;181-185

Tyrosine kinase phosphorylation site:

Amino acids 97-106

N-myristoylation sites:

Amino acids 17-23;49-55;74-80;118-124

Amidation site:

Amino acids 21-25

FIGURE 89

CCGGGGCCTCCGGAGAACGCTGTCCCATGAACGTGCGGGGAGCGGCCCGGGCGTCCGCGCG
TCCCCGCGTCCCTGGCAATTCCCGACTTCCCAACGGCTTCCCGCTGGCAGCCCCGAAGCCGC
ACC**ATGT**TCCGCCTCTGGTTGCTGCTGGCCGGGCTCTGCGGCCTCCTGGCGTCAAGACCCGGT
TTTCAAAATTCACCTTCTACAGATCGTAATTCCAGAGAAAATCCAAACAAATACAAATGACAG
TTCAGAAATAGAATATGAACAAATATCCTATATTATTCCAATAGATGAGAAACTGTACTG
TGCACCTTAAACAAAGATATTTTTTAGCAGATAATTTTATGATCTATTTGTACAATCAAGGA
TCTATGAATACTTATTCTTCAGATATTCAGACTCAATGCTACTATCAAGGAAATATTGAAGG
ATATCCAGATTCCATGGTCACACTCAGCACGTGCTCTGGACTAAGAGGAATACTGCAATTTG
AAAATGTTTCTTATGGAATTGAGCCTCTGGAATCTGCAGTTGAATTTAGCATGTTCTTTAC
AAATTAAGAATGAAGACAATGATATTGCAATTTTTATTGACAGAAGCCTGAAAAGAACAACC
AATGGATGACAACATTTTTATAAGTGA AAAATCAGAACCCAGCTGTTCCAGATTTATTTCCCTC
TTTATCTAGAAATGCATATTTGTTGGTGGACAAAACCTTTGTATGATTACTGGGGCTCTGATAGC
ATGATAGTAACAAATAAAGTCATCGAAATTTGTTGGCCTTGCAAATTC AATGTTCCACCAATT
TAAAGTTACTATTTGTGCTGTCATCATTGGAGTTATGGTCAGATGAAAATAAGATTTCTACAG
TTGGTGAGGCAGATGAATTTATGCAAAAATTTTTAGAAATGGAAACAATCTTATCTTAACCTA
AGCCTCATGATATTGCATATCTACTAATTTATATGGATTATCCTCGTTATTGGGAGCAGT
GTTCTCCTGGAAACAATGTGTATTACTCGTTATTCTGCAGGAGTTGCATTGTACCCCAAGGAGA
TAACTCTGGAGGCATTTGCAGTTATTGTACCCAGATGCTGGCACTCAGTCTGGGAATATCA
TATGACGACCCAAAGAAAATGTCAATGTTCCAGAATCCACCTGTATAAATGAATCCAGAAGTTGT
GCAATCCAATGGTGTGAAGACTTTTAGCAGTTGCAGTTTGAGGAGCTTCAAATTTCAATTT
CAAATGTGGGTGTCAAATGTCTTCAGAATAAGCCACAAATGCAAAAAAAATCTCCGAAACCA
GTCTGTGGCAATGGCAGATTGGAGGGAAATGAAATCTGTGATTGTGGTACTGAGGCTCAATG
TGGACCTGCAAGCTGTTGTGATTTTCGAACCTGTGTACTGAAAGACGGAGCAAATGTTATA
AAGGACTGTGCTGCAAAGACTGTCAAATTTTACAATCAGGCGTTGAATGTAGGCCGAAAGCA
CATCCTGAATGTGACATCGCTGAAAATTTGTAATGGAAGCTCACCCAGAATGTGGTCCCTGACAT
AACTTTAATCAATGGACTTTTCATGCAAAAATAATAAGTTTATTTGTTATGACGGAGACTGCC
ATGATCTCGATGCACGTTGTGAGAGTGTATTTGGAAAAGGTTCAAGAAATGCTCCATTTGCC
TGCTATGAAGAAATACAATCTCAATCAGACAGATTTGGGAACCTGTGGTAGGGATAGAAATA
CAAATATGTGTTCTGTGGATGGAGGAATCTTATATGTGGAAGATTAGTTGTACCTACCCTA
CTCGAAAGCCTTTCCATCAAGAAAATGGTGTGATTTATGCTTTCGTACGAGATTCTGTA
TGCATAACTGTAGACTACAAATTGCCTCGAACAGTTCCAGATCCACTGGCTGTCAAAAATGG
CTCTCAGTGTGATATTGGGAGGGTTTGTGTAAATCGTGAATGTGTAGAAATCAAGGATAATTAAG
GCTTCAGCACATGTTTGTTCACAACAGTGTCTGGACATGGAGTGTGTGATTCCAGAAACAA
GTGCCATTGTTTCGCCAGGCTATAAGCCTCCAAACTGCCAAATACGTTCCAAAGGATTTTCCA
TATTTCCCTGAGGAAGATATGGGTTCAATCATGGAAAGAGCATCTGGGAAGACTGAAAACACC
TGGCTTCTAGGTTTCCCTCATTGCTCTTCCTATTCTCATTGTAACAACCGCAATAGTTTGGC
AAGGAAACAGTTGAAAAAGTGGTTTCGCCAAGGAAGAGGAATTCCCAAGTAGCGAATCTAAT
CGGAAGGTAGCACACAGACATATGCCAGCCAATCCAGCTCAGAAGGCAGCACTCAGACATAT
GCCAGCCAAACCAGATCAGAAAGCAGCAGTCAAGCTGATACTAGCAAATCCAAATCAGAAGA
TAGTGCTGAAGCATATACTAGCAGATCCAAATCACAGGACAGTACCCAAACACAAAGCAGTA
GTAAC**TAGT**GATTCCCTTCAGAAGGCAACGGATAACATCGAGAGTCTCGCTAAGAAATGAAAA
TTCTGTCTTTCCCTCCGTGGTCACAGCTGAAAGAAAACAATAAATTGAGTGTGGATC

FIGURE 90

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA176775
><subunit 1 of 1, 787 aa, 1 stop
><MW: 87934, pI: 5.49, NX(S/T): 4
MFRLWLLLAGLCLLASRPGFQNSLLQIIVIPEKIQTNTNDSSEIEYEQISYIIPIDEKLY
TVHLKQRYFLADNFMIYLYNQGSMTYSSDIQTQCYQGNIEGYPDSMVTLSTCSGLRGI
LQFENVSYGIEPLESAVEFQHVLYKLNEDNDIAIFIDRSLKEQPMDDNIFISEKSEPAV
PDLFPLYLEMHIIVDKTLYDYWGSDSMIVTNKVIIEIVGLANSMTQFKVTVLSSLELWS
DENKISTVGEADELLQKFLQKSYLNLRPHDIAYLLIYMDYPRYLGAVFPGTMCITRYS
AGVALYPKEITLEAFVIVTQMLALSGLISYDDPKKCQCSESTCIMNPEVVQSNQVKTFS
SCSLRSFQNFISNVGVKCLQNKPKQKSPKPVCGNGRLEGNEICDCGTEAQCGPASCCD
FRTCVLKDGAKCYKGLCKDCQILQSGVECRPKAHPECEDIAENCNGSSPECGPDITLING
LSCKNNKFICYDGDCHDLARCESVFGKGSRNAPFACYEEIQSQSDRFGNCGRDRNNKYV
FCGWRNLICGRLVCTYPTKPFHQENGDVIYAFVRDVCITVDYKLPRTVPDPLAVKNGS
QCDIGRVCVNRECVESRIKASAHVCSQQCSGHGVCDSRNKCHCSPGYKPPNCQIRSKGF
SIFPEEDMGSIMERASGKTENTWLLGFLIALPILIVTTAIVLARKQLKKWFAKEEEFPSS
ESKSEGSTQTYASQSSSEGSTQTYASQTRSESSSQADTSKSKSEDSAEAYTSRKSQDST
QTQSSSN
```

Important features of the protein:

Signal peptide:

Amino acids 1-16

Transmembrane domain:

Amino acids 309-326;681-705

N-glycosylation sites:

Amino acids 39-43;125-129;465-469;598-602

Glycosaminoglycan attachment site:

Amino acids 631-635

Tyrosine kinase phosphorylation site:

Amino acids 269-276

N-myristoylation sites:

Amino acids 13-19;82-88;99-105;218-224;401-407;634-640;
726-732;739-745

EGF-like domain proteins:

Amino acids 642-654

Disintegrins proteins:

Amino acids 400-407;422-472;403-453;467-517;634-684

Reprolysin (M12B) family zinc metalloprotease:

Amino acids 186-383

Reprolysin family propeptide:

Amino acids 63-176

FIGURE 91

CACCAGACAGCACTCCAGCACTCTGTTTTGGGGGGCATTGAAACAGCAAAATCACTCATAAA
AGGCAAAAATTGCAAAAAAATAGTAATAACCAGCATGGCACTAAATAGACCATGAAAAG
ACATGTGTGTGCAGTATGAAAATTGAGACAGGAAGGCAGAGTGTGAGCTTGTCCACCTCAG
CTGGGAATGTCATCAGGCAACTCAAGTTTTTCACCACGGCATGTGTCTGTGAATGTCCGCA
AAACATTCTCTCTCCCCAGCCTTCATGTGTTAACCTGGGGATGATGTGGACCTGGGCACTGTGG
ATGCTCCCTTCACTCTGCAAATTCAGCCTGGCAGCTCTGCCAGCTAAGCCTGAGAACATTTT
CTGTGTCTACTACTATAGGAAAAATTTAACCTGCACCTGGAGTCCAGGAAAGGAAACCAGTT
ATACCCAGTACACAGTTAAGAGAACTTACGCTTTTGGAGAAAAACATGATAATTGTACAACC
AATAGTTCTACAAGTGAAGTTCGTGCTTCGTGCTCTTTTTTCCCTTCCAAGAATAACGATCCC
AGATAATTATACCATGAGGTGGAAGCTGAAAATGGAGATGGTGTAAATTAATCTCATATGA
CATACTGGAGATTAGAGAACATAGCGAAAACTGAACCACCTAAGATTTCCGTGTGAAACCA
GTTTTGGGCATCAAACGAATGATTCAAATTGAATGGATAAAGCCTGAGTTGGCGCTGTTTC
ATCTGATTTAAAATACACACTTCGATTCAGGACAGTCAACAGTACCAGCTGGATGGAAGTCA
ACTTCGCTAAGAACCCTAAGGATAAAAAACCAAACGTACAACCTCACGGGGCTGCAGCCTTTT
ACAGAATATGTCATAGCTCTGCGATGTGCGGTCAAGGAGTCAAAGTCTGGAGTGAAGTGGAG
CCAAGAAAAATGGGAATGACTGAGGAAGAAGCTCCATGTGGCCTGGAAGTGTGGAGAGTCC
TGAAACCAGCTGAGCGGATGGAAGAAGGCCAGTGCAGTTGTTATGGAAGAAGGCAAGAGGA
GCCCCAGTCTTAGAGAAAACACTTGGCTACAACATATGGTACTATCCAGAAAGCAACACTAA
CCTCACAGAAACAATGAACACTACTAACCAGCAGCTTGAAGTGCATCTGGGAGGCGAGAGCT
TTTGGGTGTCTATGATTTCTTATAATCTCTTGGGAAGTCTCCAGTGGCCACCCTGAGGATT
CCAGCTATTCAGAAAAATCATTTTCAGTGCATTGAGGTCATGCAGGCCTGCGTTGCTGAGGA
CCAGCTAGTGGTGAAGTGGCAAAGCTCTGCTCTAGACGTGAACACTTGGATGATTGAATGGT
TTCCGGATGTGGACTCAGAGCCCACCACCCTTCCCTGGGAATCTGTGTCTCAGGCCACGAAC
TGGACGATCCAGCAAGATAAATAAAACCTTCTGGTGTATAACATCTCTGTGTATCCAAT
GTTGCATGACAAAGTTGGCGAGCCATATCCATCCAGGCTTATGCCAAAGAAGGCGTTCCAT
CAGAAGGTCCTGAGACCAAGGTGGAGAACATTGGCGTGAAGACGGTCACGATCACATGGAAA
GAGATTTCCAAGAGTGAAGAGAAAGGGTATCATCTGCAACTACACCATCTTTTACCAAGCTGA
AGGTGGAAAAGGATTCTGTAAGCACGCCCATAGCGAAGTGGAAAAAACCCCAAGCCCCAGA
TAGATGCTATGGATAGACCTGTTGTAGGCATGGCTCCCCATCTCATTGTGACTTGCAACCT
GGCATGAATCACTTAGCTTCTTTAAATCTCTCTGAAAATGGGGCCAAGAGCACCCACCTTTT
GGGTTTTGGGGTTAAATGAGAGTGAAGTACAGTACCTGAGAGGAGAGTCTGAGGAAAT
GGAAGGAGTTGTTATTAATTTGTCTGGTTAGGCCCTGAATTGACCTCCCGGGAGCTCCCCGA
CCATCATTTCCAGGAATGGCGTGCCTGGCTTAAAGAGTGAAGGAGAACAGACCTTATCTCCTGACATCT
TAAATACTGGGCAAGGCTTGGATTTCTTGTCTTAGGCTAAATAATTTTTTCTTATGGTAAAATA
CACGTAAAATATTTTTCCAGTTTAAACATTTGAAAGTGTACAATTTAGTGGCATTAGAAGCA
TTCACAATATTGTGCAACCATCACCCTATTTCCAGAACTCTTCTATTTCTGCCAAATAGA
AGCCCTATACCCATTATAGTCACTCCCCATTCCTCTCCTCCCACAGCCCTGGCAACTAC
CAAACCTGCTTTGTGTCTCTATGGATTGCCTATTTGGATATTTTCATATACATAGAATCATAA
ANTAAAAA

FIGURE 92

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA177313
><subunit 1 of 1, 582 aa, 1 stop
><MW: 66605, pI: 8.14, NX(S/T): 15
MCIRQLKFFTTACVCECPQNILSPQPSCVNLGMMWTWALWMLPSLCKFSLAALPAKPENI
SCVYYRKNLTCTWSPGKETSQYTVKRTYAFGEKHDNCTTNSSTSENRA SC SF FL PRI
TIPDNYTIEVEAENG DGV I KSHMTYWRLENI AKTEPPKIFRVKPV LGIKRMIQIEWIKPE
LAPVSSDLKYTLRFRTVNSTSWMEVNF AKNRKDKNQTYNLTGLQPFTEYVIALRCAVKES
KFWS DWSQEKMGMT EEEAPCGLELWRV LKPAEADGRRPV RLLWKKARGAPVLEKTLGYN I
WYYPESNTNLTETMNTTNQQLELHLGGESFWVSMISYNSLGKSPVATLRIPAIQEKSFQC
IEVMQACVAEDQLVVKWQSSALDVNTWMI EWFPD VDSEPTT LSWESVSQATNWTIQQDKL
KPFWCYNISVYPMLHDKVGEPYSIQAYAKEGVPSEGPETKVENIGVKT V TITWKEIPKSE
RKGIICNYTIFYQAE GKGFC KHAHSEVEKNPKPQIDAMDRPVVGMAPP SHCDLQPGMNH
LASLN LSENGAKSTHLLGFWGLNESEVTV PERRVLRKWKELL
```

Important features of the protein:

Signal peptide:

Amino acids 1-46

N-glycosylation sites:

Amino acids 59-63;69-73;99-103;103-107;125-129;198-202;
215-219;219-223;309-313;315-319;412-416;
427-431;487-491;545-549;563-567

N-myristoylation sites:

Amino acids 32-38;137-143;483-489;550-556;561-567

Amidation site:

Amino acids 274-278

Growth factor and cytokines receptors family signature 1:

Amino acids 62-75

Fibronectin type III domain:

Amino acids 54-144;154-247

FIGURE 93

ATTCTCCTAGAGCATCTTTGGAAGCATGAGGCCACGATGCTGCATCTTGGCTCTTGTCTGCT
GGATAACAGTCTTCCCTCCTCCAGTGTTCAAAAAGGAACTACAGACGCTCCTGTTGGCTCAGGA
CTGTGGCTGTGCCAGCCGACACCCAGGTGTGGGAACAAGATCTACAACCCTTCAGAGCAGTG
CTGTTATGATGATGCCATCTTATCCTTAAAGGAGACCCGCCGCTGTGGCTCCACCTGCACCT
TCTGGCCCTGCTTTGAGCTCTGCTGTCCCGAGTCTTTTGGCCCCCAGCAGAAGTTTCTTGTG
AAGTTGAGGGTTCTGGGTATGAAGTCTCAGTGTCACTTATCTCCCATCTCCCGGAGCTGTAC
CAGGAACAGGAGGCACGTCTGTACCCATTAAAAACCCCAGGCTCCACTGGCAGACGGCAGAC
AAGGGGAGAAGAGACGAAGCAGCTGGACATCGGAGACTACAGTTGAAC¹TCCGGAGAGAAGCA
ACTTGA²CTTCAGAGGGATGGCTCAATGACATAGCTTTGGAGAGGAGCCCAGCTGGGGATGGC
CAGACTTCAGGGGAAGAATGCCTTCCTGCTTCATCCCCTTCCAGCTCCCCTTCCCGCTGAG
AGCCACTTTCATCGGCAATAAAAATCCCCCACATTTACCATCT

FIGURE 94

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA57700

<subunit 1 of 1, 125 aa, 1 stop

<MW: 14198, pI: 9.01, NX(S/T): 1

MRPRCCILALVCWITVFLQCSKGTTDAPVGSGLWLCQPTPRCGNKIYNPSEQCCYDDAI
LSLKETRRCGSTCTFWPCFELCCPESFGPQQKFLVKLRVLGMKSQCHLSPISRSTRNRR
HVLYP

Important features:

Signal peptide:

Amino acids 1-21

N-myristoylation sites:

Amino acids 33-39;70-76

Anaphylatoxin domain proteins:

Amino acids 50-60

FIGURE 95

GCATTTTGTCTGTGCTCCCTGATCTTCAGGTCACCACCATGAAGTTCTTAGCAGTCCTGGT
ACTCTTGGGAGTTTCCATCTTTCTGGTCTCTGCCCAGAATCCGACAACAGCTGCTCCAGCTG
ACACGTATCCAGCTACTGGTCCTGCTGATGATGAAGCCCCTGATGCTGAAACCACTGCTGCT
GCAACCACTGCGACCACTGCTGCTCCTACCACTGCAACCACCGCTGCTTCTACCACTGCTCG
TAAAGACATTCCAGTTTTACCCAAATGGGTTGGGGATCTCCCGAATGGTAGAGTGTGTCCCT
GAGATGGAATCAGCTTGAGTCTTCTGCAATTGGTCACAACCTATTCATGCTTCCTGTGATTC
ATCCAACCTACTTACCTTGCCTACGATATCCCCTTTATCTCTAATCAGTTATTTTCTTTCAA
ATAAAAAATAACTATGAGCAACATAAAAAAAAAAAAAA

FIGURE 96

```
</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA62872
<subunit 1 of 1, 90 aa, 1 stop
<MW: 9039, pI: 4.37, NX(S/T): 1
MKFLAVLVLLGVSI FLVSAQNPTTAA PADTYPATG PADDEAPDAET TAAATTATTAAPT
ATTAASTTARKDIPVLPKWVGDLPNGRVCP
```

Important features:

Signal peptide:

Amino acids 1-19

FIGURE 97

GGACTCTGAAGGTCCCAAGCAGCTGCTGAGGCCCCCAAGGAAGTGGTTCCAACCTTGGACCC
CTAGGGGTCTGGATTTGCTGGTTAACAAGATAACCTGAGGGCAGGACCCCATAGGGGAATGC
TACCTCCTGCCCTTCCACCTGCCCTGGTGTTCACGGTGGCCTGGTCCCTCCTTGCCGAGAGA
GTGTCCTGGGTACAGGACGCAGAGGACGCTCACAGACTCCAGCCCTTTGTTACCGAGAGGAC
ACTTGGCAAGGTCCAGCGATGGTCCGGAGTCCACACACAGACTGGCGGCAGGGCAGGAGGGG
GACAGTTCTGTTGTGCTTGGTTGGACAGTAAGAGGGTCTTGCCAGTCCAGGGTGGGGGGCG
GCAAACCTCCATAAAGAACCAGAGGGTCTGGGCCCCGCCACAGAGTCATCTGCCCAGCTCCT
CTGCTGCTGGCCAGTGGGAGTGGCACGAGGTGGGGCTTTGTGCCAGTTAAAACCACAGGCTGG
ATTTGCCTGCGGGCCATGGTCCCTGTCTAGGGCAGCAATTCTCAACCTTCTTGCTCTCAGGA
CCCCAAAGAGCTTTCATTGTATCTATTGATTTTTACCACATTAGCAATTA~~AA~~ACTGAGAAAT
GGCCCGGCACGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGTGGAT
CACCTGAGATCAGGAGTTCAAGACCAGCCTGGCCAACATGGTGAAACCTTGTCTACTAAAA
TACAAAAAATTAGCCAGGCACAGTGGTGTGCACTGGTAGTCCCAGTTACTCGGGAGGCTGAG
GCAGGAAAATCGCTTGAACCCAGGAGGCGGACGTTGCGGTGAGCCGAGATCGCGCCGCTGAT
TCCAGCCTGGGCGACAAGAGTGAGACTCCATCTCACACA

FIGURE 98

```
</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA62876  
<subunit 1 of 1, 120 aa, 1 stop  
<MW: 12925, pI: 9.46, NX(S/T): 0  
MLPPALPPALVFTVAWSLLAERVSWVRDAEDAHLQPFVVTERTLGKVQRWSGVHTQTGGR  
AGGGQFCCAWLDSKRVLASPGWGAANSIKNQRVWAPATESSAQLLCCWPFVGVARGGALCQ
```

Important features:

Signal peptide:

Amino acids 1-17

N-myristoylation sites:

Amino acids 58-64;63-69;64-70;83-89;111-117;115-121

FIGURE 100

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA66660
><subunit 1 of 1, 209 aa, 1 stop
><MW: 21588, pI: 5.50, NX(S/T): 0
MRSTILLFCLLGSTRSLPQLKPALGLPPTKLAPDQGTLPNQQSNQVFPSLSLIPLTQML
TLGPDLHLLNPAAGMTPGTQTHPLTLGGLNVQQQLHPHVLPPIFVTQLGAQGTILSSEELP
QIFTSLLIHSLEFPGGILPTSQAGANPDVQDGSLEPAGGAGVNPATQGTTPAGRLPTPSGTD
DFAVTPPAGIQRSTHAIEEATTESANGIQ
```

Important features of the protein:

Signal peptide:

Amino acids 1-16

Leucine zipper patterns:

Amino acids 10-32;17-39

N-myristoylation sites:

Amino acids 12-18;25-31;36-42;74-80;108-114;111-117;
135-141;151-157;159-165;166-172;189-195

FIGURE 101

GGGGTCTCCCTCAGGGCCGGGAGGCACAGCGGTCCCTGCTTGCTGAAGGGCTGGATGTACGC
ATCCGCAGGTTCCCGCGGACTTGGGGGCGCCCGCTGAGCCCCGGCGCCCGCAGAAGACTTGT
GTTTGCCTCCTGCAGCCTCAACCCGGAGGGCAGCGAGGGCCTACCACCATGATCACTGGTGT
GTTCAGCATGCGCTTGTGGACCCAGTGGGCGTCCTGACCTCGCTGGCGTACTGCCTGCACC
AGCGGCGGGTGGCCCTGGCCGAGCTGCAGGAGGCCGATGGCCAGTGTCCGGTCGACCCGCAGC
CTGCTGAAGTTGAAAATGGTGCAGGTCGTGTTTCGACACGGGGCTCGGAGTCCCTCTCAAGCC
GCTCCCCTGGAGGAGCAGGTAGAGTGGAAACCCCCAGCTATTAGAGGTCCCACCCCAAATC
AGTTTGATTACACAGTCACCAATCTAGCTGGTGGTCCGAAACCATATTCTCCTTACGACTCT
CAATACCATGAGACCACCTGAAGGGGGGCATGTTTGCTGGGCAGCTGACCAAGGTGGGCAT
GCAGCAAATGTTTGCCTTGGGAGAGAGACTGAGGAAGAAGTATGTGGAAGACATTCCCTTTC
TTTACCAACCTTCAACCCACAGGAGGTCTTTATTCGTTCCACTAACATTTTTTCGGAATCTG
GAGTCCACCCGTTGTTTGTGCTGGCTGGGCTTTTCCAGTGTGAGAAAGAAGGACCCATCATCAT
CCACACTGATGAAGCAGATTCAGAAGTCTTGTATCCCAACTACCAAAGCTGCTGGAGCCTGA
GGCAGAGAACCAGAGGCCGGAGGCAGACTGCCTCTTTACAGCCAGGAATCTCAGAGGATTTG
AAAAAGGTGAAGGACAGGATGGGCATTGACAGTAGTGATAAAGTGGACTTCTTCATCCTCCT
GGACAACGTGGCTGCCGAGCAGGCACACAACCTCCCAAGCTGCCCATGCTGAAGAGATTTG
CACGGATGATCGAACAGAGAGCTGTGGACACATCCTTGTACATACTGCCCAAGGAAGACAGG
GAAAGTCTTCAGATGGCAGTAGGCCCATTCCTCCACATCCTAGAGAGCAACCTGCTGAAAGC
CATGGACTCTGCCACTGCCCCGACAAGATCAGAAAGCTGTATCTCTATGCGGCTCATGATG
TGACCTTCATACCGCTCTTAATGACCCTGGGGATTTTTGACCACAAATGGCCACCGTTTGCT
GTTGACCTGACCATGGAACTTTACCAGCACCTGGAATCTAAGGAGTGGTTTTGTGCAGCTCTA
TTACCACGGGAAGGAGCAGGTGCCGAGAGGTTGCCCTGATGGGCTCTGCCCGCTGGACATGT
TCTTGAATGCCATGTCAGTTTATACCTTAAGCCCAGAAAAATACCATGCACTCTGCTCTCAA
ACTCAGGTGATGGAAGTTGGAAATGAAGAGTAACTGATTTATAAAAGCAGGATGTGTTGATT
TTAAAAATAAGTGCCTTTATACAATG

FIGURE 102

MITGVFSMRLWTPVGVLTSLAYCLHQRRVALAELQEADGQCPVDRSLKLMVQVVERHGARSPLKPLPLEEQV
EWNPQLLEVPFQTQFDYTVTNLAGGPKPYSYDSQYHETTLKGGMFAGQLTKVGMQMFALGERLRKKNYVEDIP
FLSPTFNPQEVFIRSTNIFRNLESTRCLLAGI.FQCQKEGPIIIHTDEADSEVLYPNYQSCWSLRQRTRGRRQTA
SLQPGISEDLKVKVDRMGIDSSDKVDFIILLDNVAAEQAHNLPSCPMLKRFARMIEQRAVDTSLYILPKEDRES
LQMAVGPFLHILESNTLLKAMDSATAPDKIRKLYLYAAHDVTFIPLLMTLGI FDHKWPPFAVDLTMELYQHLESK
EWFVQLYYHGKEQVPRGCPDGLCPDMFLNAMS VYTLSPKEYHALCSQTQVMEVGNEE

Important features:

Signal sequence:

amino acids 1-23

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 218-222

Casein kinase II phosphorylation site.

amino acids 87-91, 104-108, 320-324

Tyrosine kinase phosphorylation site.

amino acids 280-288

N-myristoylation site.

amino acids 15-21, 117-123, 118-124, 179-185, 240-246, 387-393

Amidation site.

amino acids 216-220

Leucine zipper pattern.

amino acids 10-32

Histidine acid phosphatases phosphohistidine signature.

amino acids 50-65

FIGURE 103

GGGGCGGGTGGACGCGGACTCGAACGCAGTTGCTTCGGGACCCAGGACCCCCCTCGGGCCCCGA
CCCCCAGGAAAGACTGAGGCCGCGGGCTGCCCGCCCGGCTCCCTGCGCCGCGCCGCGCTC
CCGGGACAGAAGATGTCCTCCAGGGTCCCTCTGCTGCTGCCGCTGCTCCTGCTACTGGCCCT
GGGGCCTGGGGTGCAGGGCTGCCCATCCGGCTGCCAGTGCAGCCAGCCACAGACAGTCTTCT
GCACTGCCCGCCAGGGGACCACGGTGCCCCGAGACGTGCCACCCGACACGGTGGGGCTGTAC
GTCTTTGAGAACGGCATCACCATGCTCGACGCAAGCAGCTTTGCCGGCTGCCGGCCCTGCA
GTCCTGGACCTGTCACAGAACCAGATCGCCAGCCTGCGCCTGCCCGCCTGCTGCTGCTGG
ACCTCAGCCACAACAGCCTCCTGGCCCTGGAGCCCGGCATCCTGGACACTGCCAACGTGGAG
GCGCTGCGGCTGGCTGGTCTGGGGCTGCAGCAGCTGGACGAGGGGCTCTTCAGCCGCTTGCG
CAACCTCCACGACCTGGATGTGTCCGACAACCAGCTGGAGCGAGTGCCACCTGTGATCCGAG
GCCTCCGGGGCCTGACGCGCCTGCGGCTGGCCGGCAACACCCGCATTGCCAGCTGCGGCC
GAGGACCTGGCCGGCCTGGCTGCCCTGCAGGAGCTGGATGTGAGCAACCTAAGCCTGCAGGC
CCTGCCTGGCGACCTCTCGGGCCTCTTCCCCCGCCTGCGGCTGCTGGCAGCTGCCCGCAACC
CCTTCAACTGCGTGTGCCCCCTGAGCTGGTTTTGGCCCTGGGTGCGCGAGAGCCACGTACA
CTGGCCAGCCCTGAGGAGACGCGCTGCCACTTCCCGCCAAGAACGCTGGCCGGCTGCTCCT
GGAGCTTGACTACGCCGACTTTGGCTGCCAGCCACCACCACAGCCACAGTGCCACCA
CGAGGCCCGTGGTGCGGGAGCCACAGCCTTGTCTTCTAGCTTGGCTCCTACCTGGCTTAGC
CCCACAGCGCCGGCCACTGAGGCCCCAGCCCGCCCTCCACTGCCACCCGACTGTAGGGCC
TGTCCCCAGCCCCAGGACTGCCACCGTCCACCTGCCTCAATGGGGGCACATGCCACCTGG
GGACACGGCACCACCTGGCGTGCTTGTGCCCCGAAGGCTTACGGGCCTGTACTGTGAGAG
CAGATGGGGCAGGGACAGGCCAGCCCTACACCAGTACGCCGAGGCCACCACGGTCCCT
GACCCCTGGGCATCGAGCCGGTGAACCCACCTCCCTGCGCGTGGGGCTGCAGCGTACCTCC
AGGGGAGCTCCGTGCAGCTCAGGAGCCTCCGTCTCACCTATCGCAACCTATCGGGCCCTGAT
AAGCGCTGGTGACGCTGCGACTGCCTGCCTCGCTCGCTGAGTACACGGTCAACCAGCTGCG
GCCAACGCCACTTACTCCGTCTGTGTCATGCCTTTGGGGCCCGGGCGGGTGCCTGGAGGGCG
AGGAGCCTGCGGGGAGGCCATACACCCAGCCGTCCACTCCAACCACGCCCCAGTCAAC
CAGGCCCGGAGGGCAACCTGCCGCTCCTCATTGCGCCGCCCTGGCCGCGGTGCTCCTGGC
CGCGCTGGCTGCGGTGGGGGACGCTACTGTGTGCGGCGGGGGCGGGCCATGGCAGCAGCGG
CTCAGGACAAAGGGCAGGTGGGGCCAGGGGCTGGGCCCTGGAACCTGGAGGGAGTGAAGGTC
CCCTTGAGCCAGGCCGAAGGCAACAGAGGGCGGTGGAGAGGCCCTGCCAGCGGGTCTGA
GTGTGAGGTGCCACTCATGGGCTTCCAGGGCCTGGCCTCCAGTCAACCCCTCCACGCAAAGC
CCTACATCTAAGCCAGAGAGAGACAGGGCAGCTGGGGCCGGGCTCTCAGCCAGTGAATGGC
CAGCCCCCTCCTGCTGCCACACCACGTAAGTTCTCAGTCCCAACCTCGGGGATGTGTGAG
ATGCTGTGGCCAGCTGACGAGCCCTAACGTCCCCAGAACCAGTGCCTATGAGGACAGTGT
CCGCCCTGCCCTCCGCAACGTGCAGTCCCTGGGCACGCGGGCCCTGCCATGTGCTGGTAAC
GCATGCCTGGGCCCTGCTGGGCTCTCCACTCCAGGCGGACCCTGGGGCCAGTGAAGGAAG
CTCCCGAAAGAGCAGAGGGAGAGCGGGTAGGCGGCTGTGTGACTCTAGTCTTGGCCCCAGG
AAGCGAAGGAACAAAAGAACTGGAAAGGAAGATGCTTTAGGAACATGT'TT'GCTTTTTTAA
AATATATATATATTTATAAGAGATCCTTTCCCATTTATTTCTGGGAAGATGTTTTCAAACCTC
AGAGACAAGGACTTTGGTTTTTGTAAAGACAAACGATGATATGAAGGCCCTTTT'GTAAGAAAAA
ATAAAAAAAAAA

FIGURE 105

CCCACGCGTCCGAAGGCAGACAAAGGTTCAATTTGTAAAGAAGCTCCTTCCAGCACCTCCTCT
CTTCTCCTTTTGCCCAAACCTCACCCAGTGAGTGTGAGCATTTAAGAAGCATCCTCTGCCAAG
ACCAAAAGGAAAGAAGAAAAAGGGCCAAAAGCCAAAATGAAACTGATGGTACTTGTTTTAC
CATTGGGCTAACTTTGCTGCTAGGAGTTCAAGCCATGCCTGCAAATCGCCTCTCTTGCTACA
GAAAGATACTAAAAGATCACAACCTGTCAACCTTCCGGAAGGAGTAGCTGACCTGACACAG
ATTGATGTCAATGTCCAGGATCATTCTGGGATGGGAAGGGATGTGAGATGATCTGTTACTG
CAACTTCAGCGAATTGCTCTGCTGCCAAAAGACGTTTTCTTTGGACCAAAGATCTCTTTTCG
TGATTCCTTGCAACAATCAATTGA GAATCTTCATGTATTCTGGAGAACACCATTCTGATTTTC
CCACAACTGCACTACATCAGTATAACTGCATTTCTAGTTTCTATATAGTGCAATAGAGCAT
AGATTCTATAAATTCTTACTTGTCTAAGACAAGTAAATCTGTGTTAAACAAGTAGTAATAAA
AGTTAATTC AATCTAAAAAAAAAAAAA

FIGURE 106

```
</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA52758  
<subunit 1 of 1, 98 aa, 1 stop  
<MW: 11081, pI: 6.68, NX(S/T): 1  
MKLMVLVFTIGLTLTLLGVQAMPANRLSCYRKILKDHNCHNLPEGVADI.TQIDVNVQDHF  
W  
DGKGCEMICYCNFSELLCCPKDVFFGPKISFVI PCNNQ
```

Important features:

Signal peptide:

Amino acids 1-20

N-glycosylation site:

Amino acids 72-76

Tyrosine kinase phosphorylation site:

Amino acids 63-71

FIGURE 108

```
</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA59849
<subunit 1 of 1, 135 aa, 1 stop
<MW: 14833, pI: 9.78, NX(S/T): 0
MRIMLLFTAILAFSLAQSFQAVCKEPQEEVVPGGGRSKRDPDLYQLLQRLFKSHSSLEGL
LKALSQASTDPKESTSPKRDMDHDFVGLMGKRSVQPEGKTGPFELPSVRVPRPLHPNQLG
STGKSSLGTEEQRPL
```

Important features:

Signal peptide:

Amino acids 1-18

Tyrosine kinase phosphorylation site:

Amino acids 36-45

N-myristoylation sites:

Amino acids 33-39;59-65

Amidation site:

Amino acids 90-94

Leucine zipper pattern:

Amino acids 43-65

Tachykinin family signature:

Amino acids 86-92

FIGURE 109

GCGGCCACACGCAGCTAGCCGGAGCCCGGACCAGGCGCCTGTGCCTCCTCCTCGTCCCTCGC
CGCGTCCGCGAAGCCTGGAGCCGGCGGGAGCCCCGCGCTCGCC**ATGT**CGGGCGAGCTCAGCA
ACAGGTTCCAAGGAGGGAAGGCGTTTCGGCTTGCTCAAAGCCCCGGCAGGAGAGGAGGCTGGCC
GAGATCAACCGGGAGTTTCTGTGTGACCAGAAGTACAGTGATGAAGAGAACCTTCCAGAAAA
GCTCACAGCCTTCAAAGAGAAGTACATGGAGTTTGACCTGAACAATGAAGGCGAGATTGACC
TGATGTCTTTAAAGAGGATGATGGAGAAGCTTGGTGTCCCCAAGACCCACCTGGAGATGAAG
AAGATGATCTCAGAGGTGACAGGAGGGGTGAGTACACTATATCCTACCGAGACTTTGTGAA
CATGATGCTGGGAAACGGTCGGCTGTCTCAAGTTAGTCATGATGTTGAAGGAAAAGCCA
ACGAGAGCAGCCCCAAGCCAGTTGGCCCCCTCCAGAGAGAGACATTGCTAGCCTGCCCT**TGA**
GGACCCCGCCTGGACTCCCCAGCCTTCCCACCCCATACCTCCCTCCCGATCTTGCTGCCCTT
CTTGACACACTGTGATCTCTCTCTCTCATTGTGGTTCATTGAGGGTTTGTGGTGTGTTT
TCATCAATGTCTTTGTAAAGCACAAATTATCTGCCTTAAAGGGGCTCTGGGTGGGGGAATCC
TGAGCCTTGGGTCCCCTCCCTCTCTTCTTCCCTCCTTCCCCGCTCCCTGTGCAGAAGGGCTG
ATATCAAACCAAAAAGTAGAGGGGGCAGGGCCAGGGCAGGGAGGCTTCCAGCCTGTGTTCCC
CTCACTTGGAGGAACCAGCACTCTCCATCCTTTCAGAAAGTCTCCAAGCCAAGTTCAGGCTC
ACTGACCTGGCTCTGACGAGGACCCCAGGCCACTCTGAGAAGACCTTGGAGTAGGGACAAGG
CTGCAGGGCCTCTTTCGGGTTTCCTTGGACAGTGCCATGGTTCAGTGCTCTGGTGTCAACC
AGGACACAGCCACTCGGGGCCCCGCTGCCCCAGCTGATCCCCACTCATTCCACACCTCTTCT
CATCCTCAGTGATGTGAAGGTGGGAAGGAAAGGAGCTTGGCATGGGAGCCCTTCAAGAAGG
TACCAGAAGGAACCCTCCAGTCCTGCTCTTGGCCACACCTGTGCAGGCAGCTGAGAGGCAG
CGTGCAGCCCTACTGTCCCTTACTGGGGCAGCAGAGGGCTTCGGAGGCAGAAGTGAGGCCTG
GGGTTTGGGGGAAAGGTGAGCTCAGTGCTGTTCCACCTTTTACGGAGGATACTGAGGGGAC
CAGGATGGGAGAATGAGGAGTAAAATGCTCACGGCAAAGTCAGCAGCACTGGTAAGCCAAGA
CTGAGAAATACAAGGTTGCTTGTCTGACCCCAATCTGCTTGAAAAAAAAAAAAAAAAAAAAA

FIGURE 110

MSGELSNRFQGGKAFGLLKRQERRLAEINREFLCDQKYSDEENLPEKLTAFKEKYMEFDLN
NEGEIDLMSLKRMMEKLGVPKTHLEMKKMISEVTGGVSDTISYRDFVNMLGKRSAVLKLV
MFEGKANESSPKPVGPPPERDIASLP

FIGURE 111

TAAAACAGCTACAATATTCCAGGGCCAGTCACTTGCCATTTCTCATAACAGCGTCAGAGAGA
AAGAACTGACTGAAACGTTTGAG**ATGA**AAGAAAGTTCTCCTCCTGATCACAGCCATCTTGGCA
GTGGCTGTTGGTTTCCCAGTCTCTCAAGACCAGGAACGAGAAAAAAGAAGTATCAGTGACAG
CGATGAATTAGCTTCAGGGTTTTTTGTGTTCCCTTACCCATATCCATTTGCCCCACTTCCAC
CAATTCCATTTCCAAGATTTCCATGGTTTAGACGTAATTTTCCTATTTCCAATACCTGAATCT
GCCCCTACAACCTCCCCTTCCTAGCGAAAAG**TAA**ACAAGAAGGATAAGTCACGATAAACCTGG
TCACCTGAAATTGAAATTGAGCCACTTCCTTGAAGAATCAAAATTCCTGTTAATAAAAGAAA
AACAAATGTAATTGAAATAGCACACAGCATTCTCTAGTCAATATCTTTAGTGATCTTCTTTA
ATAAACATGAAAGCAAAGATTTTGGTTTCTTAATTTCCACA

FIGURE 112

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA71290
><subunit 1 of 1, 85 aa, 1 stop
><MW: 9700, pI: 9.55, NX(S/T): 0
MKKVLLLITAILAVAVGFPVSQDQEREKRSISDSDELASGFFVFPYPYFRPLPPIPFPR
FPWFRRNFPIPIPIESAPTTPLPSEK
```

Important features of the protein:

Signal peptide:

Amino acids 1-17

Homologous region to B3-hordein:

Amino acids 47-85

FIGURE 113

CTCCTCTTAACATACTTGCAGCTAAAATAAATATTGCTGCTTGGGGACCTCCTTCTAGCCT
TAAATTTTCAGCTCATCACCTTCACCTGCCTTGGTCA**TGG**GCTCTGCTATTCTCCTTGATCCTT
GCCATTTGCACCAGACCTGGATTCCCTAGCGTCTCCATCTGGAGTGGGGCTGGTGGGGGGCCT
CCACCGCTGTGAAGGGCGGGTGGAGGTGGAACAGAAAGGCCAGTGGGGCACCGTGTGTGATG
ACGGCTGGGACATTAAGGACGTGGC'TGTGTTGTGCCGGGAGCTGGGCTGTGGAGCTGCCAGC
GGAACCCCTAGTGGTATTTTGTATGAGCCACCAGCAGAAAAAGAGCAAAAGGTCCATCCA
ATCAGTCAGTTGCACAGGAACAGAAGATACATTTGGCTCAGTGTGAGCAAGAAGAAGTTTATG
ATTGTTACATGATGAAGATGCTGGGGCATCGTGTGAGAACCCAGAGAGCTCTTCTCCCCA
GTCCCAGAGGGTGTGAGGCTGGCTGACGGCCCTGGGCATTGCAAGGGACCGGTGGAAGTGAA
GCACCAGAACCAGTGGTATACCGTGTGCCAGACAGGCTGGAGCCTCCGGGCCGCAAAGGTGG
TGTGCCGGCAGCTGGGATGTGGGAGGGCTGTACTGACTCAAAAACGCTGCAACAAGCATGCC
TATGGCCGAAAACCCATCTGGCTGAGCCAGATGTCATGCTCAGGACGAGAAGCAACCCTTCA
GGATTGCCCTTCTGGGCCCTTGGGGGAAGAACACCTGCAACCATGATGAAGACACGTGGGTGCG
AATGTGAAGATCCCTTTGACTTGAGACTAGTAGGAGGAGACAACCTCTGCTCTGGGGCAGTGTG
GAGGTGCTGCACAAGGGCGTATGGGGCTCTGTCTGTGATGACAACCTGGGGAGAAAAGGAGGA
CCAGGTGGTATGCAAGCAACTGGGCTGTGGGAAGTCCCTCTCTCCCTCCTTCAGAGACCGGA
AATGCTATGGCCCTGGGGTGGCCGCATCTGGCTGGATAATGTTTCGTTGCTCAGGGGAGGAG
CAGTCCCTGGAGCAGTGCCAGCACAGATTTTGGGGGTTTACGACTGCACCCACCAGGAAGA
TGTGGCTGTCATCTGCTCAGTGT**TAG**GTGGGCATCATCTAATCTGTTGAGTGCCTGAATAGAA
GAAAAACACAGAAGAAGGGAGCATTACTGTCTACATGACTGCATGGGATGAACACTGATCT
TCTTCTGCCCTTGGACTGGGACTTATACTTGGTGGCCCTGATTCTCAGGCCTTCAGAGTTGG
ATCAGAACTTACAACATCAGGTCTAGTTCTCAGGCCATCAGACATAGTTTGGAACTACATCA
CCACCTTTCCTATGCTCCACATTGCACACACACACACACACACACACACACACACACACATA
CACTACTTAAATACATTCTCACACACACACACACACACACACACACACACACACACATA
CACCATTTGTCTCTGTTTCTCTGAAGAACTCTGACAAAATACAGATTTTGGTACTGAAAGAGA
TTCTAGAGGAACCGAATTTTAAAGGATAAATTTCTGAATTGGTTATGGGGTTTCTGAAATTG
GCTCTATAATCTAATTAGATATAAAATTTCTGGTAACTTTATTTACAATAATAAGATAGCAC
TATGTGTTCAAA

FIGURE 114

MALLFSLILAICTRPGFLASPSGVRLVGG LHRCEGRVEVEQKGQWGTVCDDGWDIKDVAVLC
RELGCGAASGTPSGILYEPPEAEKEQKVL IQSVSCTGTEDTLAQCEQEVEYDCSHDEDAGASC
ENPESSFSVPPEGVRLADGPGHCKGRVEVKHQNQWYTV CQTGWSLRAAKVVCRQLGCCGRAVL
TQKRCNKHAYGRKPIWLSQMSCSGREATLQDCPSGPGWGN TCNHDEDTWVECEDPFDLRLVG
GDNLCSGRLEVLHKGWVGSVCDDNWGEKEDQVVCKQLGCGKSLSPSFRDRKCYGPGVGRIWL
DNVRCSGEEQSLEQCQHRFWGFHDCTHQEDVAVICSV

Signal sequence:

amino acids 1-15

Casein kinase II phosphorylation site.

amino acids 47-51, 97-101, 115-119, 209-213, 214-218, 234-238,
267-271, 294-298, 316-320, 336-340

N-myristoylation site.

amino acids 29-35, 43-49, 66-72, 68-74, 72-78, 98-104, 137-143,
180-186, 263-269, 286-292

Amidation site.

amino acids 196-200

Speract receptor repeated domain signature.

amino acids 29-67, 249-287

FIGURE 115

CATTTCCAACAAGAGCACTGGCCAAGTCAGCTTCTTCTGAGAGAGTCTCTAGAAGACATGAT
GCTACACTCAGCTTTGGGTCTCTGCCTCTTACTCGTCACAGTTTCTTCCAACCTTGCCATTG
CAATAAAAAAGGAAAAGAGGCCTCCTCAGACACTCTCAAGAGGATGGGGAGATGACATCACT
TGGGTACAACTTATGAAGAAGGTCTCTTTTATGCTCAAAAAAGTAAGAAGCCATTAATGGT
TATTCATCACCTGGAGGATTGTCAATACTCTCAAGCACTAAAGAAAGTATTTGCCCAAAATG
AAGAAATACAAGAAATGGCTCAGAATAAGTTCATCATGCTAAACCTTATGCATGAAACCACT
GATAAGAATTTATCACCTGATGGGCAATATGTGCCTAGAATCATGTTTGTAGACCCTTCTTT
AACAGTTAGAGCTGACATAGCTGGAAGATACTCTAACAGATTGTACACATATGAGCCTCGGG
ATTTACCCCTATTGATAGAAAACATGAAGAAAGCATTAAGACTTATTCAGTCAGAGCTATAA
GAGATGATGGAAAAAGCCTTCACTTCAAAGAAGTCAAATTTTCATGAAGAAAACCTCTGGCA
CATTGACAAATACTAAATGTGCAAGTATATAGATTTTGTAAATATTACTATTTAGTTTTTTTA
ATGTGTTTGCAATAGTCTTATTAATAAATAAATGTTTTTTAAATCTGA

FIGURE 116

```
</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64896
<subunit 1 of 1, 166 aa, 1 stop
<MW: 19171, pI: 8.26, NX(S/T): 1
MMLHSALGLCLLLVTVSSNLAIKKEKRPPQTL SRGWGDDITWVQTYEEGLFYAQKSKK
PLMVIHHLEDCQYSQALKKVFAQNEEIQEMAQNKFIMLNLMHETTDKNLSPDGQYVPRIM
FVDPSLTVRADIAGRYSNRIYTYEPRDLPLLIENMKKALRLIQSEL
```

Important features:

Signal peptide:

Amino acids 1-23

N-myristoylation site:

Amino acids 51-57

FIGURE 117

CCTGGAGCCGGAAGCGGGCTGCAGCAGGGCGAGGCTCCAGGTGGGGTCGGTTCCGCATCCA
GCCTAGCGTGTCCACGATGCGGGCTGGGCTCCGGGACTTTCGCTACCTGTTGCGTAGCGATCG
AGGTGCTAGGGATCGCGGTCTTCCCTTCGGGGATTCTTCCCGGCTCCCGTTCGTTCCCTCTGCC
AGAGCCGGAACACGGAGCGGAGCCCCAGCGCCCGAACCCCTCGGCTGGAGCCAGTTCTAACTG
GACCACGCTGCCACCACCTCTCTTCAGTAAAGTTGTTATTGTTCTGATAGATGCCTTGAGAG
ATGATTTTGTGTTTGGGTCAAAGGGTGTGAAATTTATGCCCTACACAACCTTACCTTGTGGAA
AAAGGAGCATCTCACAGTTTTGTGGCTGAAGCAAAGCCACCTACAGTTACTATGCCTCGAAT
CAAGGCATTGATGACGGGGAGCCTTCCCTGGCTTTGTGACGTCATCAGGAACCTCAATTCTC
CTGCACTGCTGGAAGACAGTGTGATAAGACAAGCAAAGCAGCTGGAAAAAGAATAGTCTTT
TATGGAGATGAAACCTGGGTTAAATTTATCCCAAAGCATTTTGTGGAATATGATGGAACAAC
CTCATTTTTTCGTGTGAGATTACACAGAGGTGGATAATAATGTCACGAGGCATTTGGATAAAG
TATTAAGAGAGGAGATTGGGACATAATTAATCCTCCACTACCTGGGGCTGGACCACATTGGC
CACATTTAGGGCCCAACAGCCCCCTGATTGGGCAGAAGCTGAGCGAGATGGACAGCGTGCT
GATGAAGATCCACACCTCACTGCAGTGAAGGAGAGAGAGACGCCTTACCCAATTTGCTGG
TTCTTTGTGGTGACCATGGCATGTCTGAAACAGGAAGTCACGGGGCCTCCTCCACCGAGGAG
GTGAATACACCTCTGATTTTAATCAGTTCTGCGTTTGAAAGGAAACCCGGTGATATCCGACA
TCCAAAGCACGTCCAATACACGGATGTGGCTGCGACACTGGCGATAGCACTTGGCTTACCGA
TTCCAAAAGACAGTGTAGGGAGCCTCCTATTTCCAGTTGTGGAAGGAAGACCAATGAGAGAG
CAGTTGAGATTTTTACATTTGAATACAGTGCAGCTTAGTAACTGTTGCAAGAGAATGTGCC
GTCATATGAAAAGATCCTGGGTTTGGAGCAGTTTAAATGTGCAAAAGATTGCATGGGAAC
GGATCAGACTGTACTTGGAGGAAAAGCATTGAGAAGTCTATTCAACCTGGGCTCCAAGGTT
CTCAGGCAGTACCTGGATGCTCTGAAGACGCTGAGCTTGTCCCTGAGTGCACAAGTGGCCCA
GTTCTCACCCCTGCTCCTGCTCAGCGTCCCACAGGCACTGCACAGAAAGGCTGAGCTGGAAGTC
CCACTGTATCTCCTGGGTTTTCTCTGCTCTTTTATTTGGTGATCCTGGTCTTTCGGCCGT
TCACGTCAATTGTGTGCACCTCAGCTGAAAGTTCGTGCTACTTCTGTGGCCTCTCGTGGCTGG
CGGCAGGCTGCCTTTCGTTTACCAGACTCTGGTTGAACACCTGGTGTGTGCCAAGTGCTGGC
AGTGCCCTGGACAGGGGGCCTCAGGGAAGGACGTGGAGCAGCCTTATCCCAGGCCTCTGGGT
GTCCCGACACAGGTGTTACCAAGGTGATTGTAAGAGCTGGCGGTACAGAGGAACAAGCCCC
CCAGCTGAGGGGGTGTGTGAATCGGACAGCCTCCCAGCAGAGGTGTGGGAGCTGCAGCTGAG
GGAAGAAGAGACAATCGGCCTGGACACTCAGGAGGGTCAAAGGAGACTTGGTCGCACCACT
CATCCTGCCACCCCCAGAATGCATCCTGCCTCATCAGGTCCAGATTTCTTTCCAAGGCGGAC
GTTTTCTGTTGGAATTTTAGTCCTTGGCCTCGGACACCTTCATTCGTTAGCTGGGGAGTGG
TGGTGAGGCAGTGAAGAAGAGGCGGATGGTCACTCAGATCCACAGAGCCCAGGATCAAGG
GACCCACTGCAGTGGCAGCAGGACTGTTGGGCCCCACCCCAACCCTGCACAGCCCTCATCC
CCTCTTGGCTTGAGCCGTGAGAGGCCCTGTGCTGAGTGTCTGACCGAGACACTCACAGCTTT
GTCATCAGGGCACAGGCTTCTCGGAGCCAGGATGATCTGTGCCACGCTTGCACCTCGGGCC
CATCTGGGCTCATGCTCTCTCTCTGCTATTGAATTAGTACCTAGCTGCACACAGTATGTAG
TTACCAAAGAATAAACGGCAATAATTGAGAAAAAAA

FIGURE 118

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA84920
><subunit 1 of 1, 310 aa, 1 stop
><MW: 33875, pI: 7.08, NX(S/T): 2
MRLGSGTFATCCVAIEVLGIAVFLRGFFPAPVRSSARAEGHGAEPPEPSAGASSNWTTL
PPPLFSKVVIVLIDALRDDFVFCGSKGVKFMPTTYLVEKGASHSFVAEAKPPTVTMPRIK
ALMTGSLPGFVDVIRNLNSPALLEDSVIRQAKAAGKRIVFYGDETWVKLFPKHFEYDGT
TSFFVSDYTEVDNNVTRHLDKVLKRGDWDILILHYLGLDGHIGHISGPN SPLIGQKLSEMD
SVLMKIHTSLQSKERETPLPNLLVLCGDHGMSETGSHGASSTEEVNTPLILISSAFERKP
GDIRHPKHVQ
```

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 119

GCCCACGCGTCCG**ATG**GCGTTACGTTTCGCGGCCCTTCTGCTACATGCTGGCGCTGCTGCTCA
CTGCCGCGCTCATCTTCTTCGCCATTTGGCACATTATAGCATTGATGAGCTGAAGACTGAT
TACAAGAAATCCTATAGACCAGTGTAATACCCTGAATCCCCTTGACTCCCAGAGTACCTCAT
CCACGCTTTCTTCTGTGTCATGTTTCTTTGTGCAGCAGAGTGGCTTACACTGGGTCTCAATA
TGCCCCCTTGGCCATATCATATTTGGAGGTATATGAGTAGACCAGTGATGAGTGGCCCAGGA
CTCTATGACCCTACAAACCATCATGAATGCAGATATTCTAGCATATTGTCAGAAGGAAGGATGG
TGCAAATTAGCTTTTTATCTTCTAGCATTTTTTTTACTACCTATATGGCATGATCTATGTTTT
GGTGAGCTCT**TAGA**AACAACACACAGAAGAATTGGTCCAGTTAAGTGCATGCAAAAAGCCACC
AAATGAAGGGATTCTATCCAGCAAGATCCTGTCCAAGAGTAGCCTGTGGAATCTGATCAGTT
ACTTTAAAAAATGACTCCTTATTTTTTAAATGTTCCACATTTTTTGCTTGTGGAAAGACTGT
TTTCATATGTTATACTCAGATAAAGATTTTTAAATGGTATTACGTATAAATTAATATAAAATG
ATTACCTCTGGTGTGACAGGTTTGAACCTTGCACCTCTTAAGGAACAGCCATAATCCTCTGA
ATGATGCATTAATTACTGACTGTCCTAGTACATTGGAAGCTTTTGTATTATAGGAACCTGTAG
GGCTCATTTTGGTTTTATTGAAACAGTATCTAATTATAAATTAGCTGTAGATATCAGGTGCT
TCTGATGAAGTGAATAATGTATATCTGACTAGTGGGAAACTTCATGGGTTTCCTCATCTGTCA
TGTCGATGATTATATATGGATACATTTACAAAAATAAAAAGCGGGAATTTCCCTTCGCTTG
AATATTATCCCTGTATATTGCATGAATGAGAGATTTCCCATATTTCCATCAGAGTAATAAAT
ATACTTGCTTTAATTCTTAAGCATAAGTAAACATGATATAAAAATATATGCTGAATTAATTG
TGAAGAATGCATTTAAAGCTATTTTAAATGTGTTTTATTTGTAAGACATTACTTATTAAGA
AATTGGTTATTATGCTTACTGTTCTAATCTGGTGGTAAAGGTATTCTTAAGAATTTGCAGGT
ACTACAGATTTTCAAAACTGAATGAGAGAAAATTGTATAACCATCCTGCTGTTTCTTTAGTG
CAATACAATAAAACTCTGAAATTAAGACTC

FIGURE 120

```
</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA23330
<subunit 1 of 1, 144 aa, 1 stop
<MW: 16699, pI: 5.60, NX(S/T): 0
MAFTFAAFCYMLALLLTAALIFFFAIWHIIAFDELKTDYKNPIDQCNTLNPLVLPEYLIHA
FFCVMFLCAAEWLTLGLNMPLLAYHIWRYMSRPVMSGPGLYDPTTIMNADILAYCQKEGW
CKLAFYLLAFFYYLYGMIYVLVSS
```

Important features:

Signal peptide:

Amino acids 1-20

Type II transmembrane domain:

Amino acids 11-31

Other transmembrane domain:

Amino acids 57-77;123-143

Glycosaminoglycan attachment site:

Amino acids 96-100

FIGURE 121

CGGACGCGTGGGCGGACGCGTGGGCGGCCACGGCGCCCGCGGGCTGGGGCGGTTCGCTTCTT
CCTTCTCCGTGGCCTACGAGGGTCCCCAGCCTGGGTAAAGATGGCCCCATGGCCCCCGAAGG
GCCTAGTCCCAGCTGTGCTCTGGGGCCTCAGCCTCTTCTCAACCTCCCAGGACCTATCTGG
CTCCAGCCCTCTCCACCTCCCCAGTCTTCTCCCCGCCTCAGCCCCATCCGTGTCATACCTG
CCGGGACTGGTTGACAGCTTTAACAAGGGCCTGGAGAGAACCATCCGGGACAACCTTGGAG
GTGAAACACTGCCTGGGAGGAAGAGAATTTGTCCAAATACAAAGACAGTGAGACCCGCCTG
GTAGAGGTGCTGGAGGGTGTGTGCAGCAAGTCAGACTTCGAGTGCCACCCGCCTGCTGGAGCT
GAGTGAGGAGCTGGTGGAGAGCTGGTGGTTTACAAAGCAGCAGGAGGCCCGGACCTCTTCC
AGTGGCTGTGCTCAGATTCCTGAAGCTCTGCTGCCCCGAGGCACCTTCGGGGCCCTCCTGC
CTTCCCTGTCTGGGGGAACAGAGAGGCCCTGCGGTGGCTACGGGCAGTGTGAAGGAGAAGG
GACACGAGGGGGCAGCGGGCACTGTGACTGCCAAGCCGGCTACGGGGGTGAGGCCTGTGGCC
AGTGTGGCCTTGGCTACTTTGAGGCAGAACGCAACGCCAGCCATCTGGTATGTTCCGGCTTGT
TTTGGCCCCGTGCCCCGATGCTCAGGACCTGAGGAATCAAACCTGTTTGCAATGCAAGAAGGG
CTGGGCCCTGCATCACCTCAAGTGTGTAGACATTTGATGAGTGTGGCACAGAGGGAGCCAAC
GTGGAGCTGACCAATTCCTGCGTGAACACTGAGGGCTCCTATGAGTGCCGAGACTGTGCCAAG
GCCTGCCTAGGCTGCATGGGGGCAGGGCCAGGTGCGCTGTAAGAAGTGTAGCCCTGGCTATCA
GCAGGTGGGCTCCAAGTGTCTCGATGTGGATGAGTGTGAGACAGAGGTGTGTCCGGGAGAGA
ACAAGCAGTGTGAAAACACCGAGGGCGGTTATCGCTGCATCTGTGCCGAGGGCTACAAGCAG
ATGGAAGGCATCTGTGTGAAGGAGCAGATCCAGAGTCAGCAGGCTTCTTCTCAGAGATGAC
AGAAGACGAGTTGGTGGTGTGTCAGCAGATGTTCTTTGGCATCATCATCTGTGCACTGGCCA
CGCTGGCTGCTAAGGGCGACTTGGTGTTCACCGCCATCTTCATTGGGGCTGTGGCGGCCATG
ACTGGCTACTGGTTGTGAGAGCGCAGTGACCGTGTGCTGGAGGGCTTCATCAAGGGCAGATA
ATCGCGGCCACCACCTGTAGGACCTCCTCCCACCCACGCTGCCCCAGAGCTTGGGCTGCC
TCCTGCTGGACACTCAGGACAGCTTGGTTTTATTTTTGAGAGTGGGGTAAGCACCCCTACCTG
CCTTACAGAGCAGCCCAGGTACCCAGGCCCGGGCAGACAAGGCCCTGGGGTAAAAAGTAGC
CCTGAAGGTGGATAACCATGAGCTCTTACCTGGCGGGACTGGCAGGCTTCACAATGTGTGA
ATTTCAAAGTTTTTCTTAATGGTGGCTGCTAGAGCTTTGGCCCCGTAGGATTAGGTG
GTCCCTCACAGGGGTGGGGCCATCACAGCTCCCTCCTGCCAGCTGCATGCTGCCAGTTCTGT
TCTGTGTTACCACATCCCCACCCCCATTGCCACTTATTTATTCATCTCAGGAAATAAAGA
AAGGTCTTGGAAAGTTAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 122

MAPWPPKGLVPAVLWGLSLFLNLPGPIWLQPSPPPQSSPPPQPHPCHTCRGLVDSFNKGLER
TIRDNFGGGNTAWEEENLSKYKDSETRLVEVLEGVCSKSDFECHRLLLELSEELVESWWFHKQ
QEAPDLFQWLCSDSLKLCCPAGTFGPSCLPCPGGTERPCGGYGQCEGEGTRGGSGHCDCQAG
YGGACGQCGLGYFEAERNASHLVCSACFGPCARCSGPEESNCLQCKKGWAI.HHI.KCVDIDE
CGTEGANCGADQFCVNTEGSYECRDCAKACLGCMGAGPGRCKKCSPGYQQVGSKCLDVDECE
TEVCPGENKQCENTEGGYRCICAEGYKQMEGICVKEQIPESAGFFSEMTEDELVVLQQMFFC
IIICALATLAAKGDVFTAIFIGAVAAMTGYWLSERSDRVLEGFIKGR

Important features:

Signal peptide:

Amino acids 1-29

Transmembrane domain:

Amino acids 342-392

N-glycosylation sites:

Amino acids 79-83;205-209

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 290-294

Aspartic acid and asparagine hydroxylation site:

Amino acids 321-333

EGF-like domain cysteine pattern signature: .

Amino acids 181-193

FIGURE 123

GCAAGCCAAGGCGCTGTTTGAGAAGGTGAAGAAGTCCGGACCCATGTGGAGGAGGGGGACATTGTGTACCGCC
TCTACATGCGGGCAGACCATCATCAAGGTGATCAAGTTCATCCATCATCTGCTACACCGTCTACTACGTGCAC
AACATCAAGTTCGACGTGGACTGCACCGTGGACATTGAGAGCCTGACGGGCTACCGCACCTACCGCTGTGCCA
CCCCCTGGCCACACTCTTCAAGATCCCTGGCGTCTTCTACATCAGCCTAGTCATCTTCTACGGCCTCATCTGCA
TGACACACTGTGGTGGATGCTACGGCGTCCCTCAAGAAGTACTCGTGTGAGTCGATCCGTGAGGAGAGCAGC
TACAGCGACATCCCCGACGTCAAGAACGACTTCGCCTTCATGCTGCACCTCATTGACCAATACGACCCGCTCTA
CTCCAAGCGCTTCGCGTCTTCCCTGTGCGGAGGTGAGTGAGAACAAGCTGCGGCAGCTGAACCTCAACAACGAGT
GGACGCTGGACAAGCTCCGGCAGCGGCTCACCAGAACCGCGCAGGACAAGCTGGAGCTGCACCTGTTTCATGCTC
AGTGGCATCCCTGACACTGTGTTTGCACCTGGTGGAGCTGGAGGTCCTCAAGCTGGAGCTGATCCCCGACGTGAC
CATCCCCGCCAGCATTGCCAGCTCACGGGCTCAAGGAGCTGTGGCTCTACCACACAGCGGCCAAGATFGAAG
CGCTGCGCTGGCCTTCCCTGCGCGAGAACCTGCGGGCGCTGCACATCAAGTTCACCGACATCAAGGAGATCCCG
CTGTGGATCTATAGCCTGAAGACACTGGAGGAGCTGCACCTGACGGGCAACCTGAGCGGGAGAACAACCGCTA
CATCGTCATCGACGGGCTGCGGGAGCTCAAACGCTCAAGGTGCTGCGGCTCAAGAGCAACCTAAGCAAGCTGC
CACAGGTGGTCACAGATGTGGGCGTGCACCTGCAGAAGCTGTCCATCAACAATGAGGGCACCAAGCTCATCGTC
CTCAACAGCCTCAAGAAGATGGCGAACCTGACTGAGCTGGAGCTGATCCGCTGCGACCTGGAGCGCATCCCCA
CTCCATCTTACGCTCCACAACCTGCAGGAGATTGACCTCAAGGACAACAACCTCAAGACCATCGAGGAGATCA
TCAGCTCCAGCACCTGCACCGCTCACCTGCCTTAAGCTGTGGTACAACCACATCGCCTACATCCCCATCCAG
ATCGGCAACCTCACCAACCTGGAGCGCTCTACCTGAACCGCAACAAGATCGAGAAGATCCCCACCCAGCTCTT
CTACTGCCGCAAGCTGCGCTACCTGGACCTCAGCCACAACAACCTGACCTTCTCCCTGCCGACATCGGCCTCC
TGAGAACCTCCAGAACCTAGCCATCAGGGCAACCGGATCGAGACGCTCCCTCCGGAGCTCTTCCAGTGGCCG
AAGCTGCGGGCCCTGCACCTGGGCAACAACGTGCTGCAGTCACTGCCCTCCAGGTGGGCGAGCTGACCAACCT
GACGCAGATCGAGCTGCGGGGCAACCGGCTGGAGTGCCTGCCTGTGGAGCTGGGCGAGTGGCCACTGCTCAAGC
GCAGCGCTTGGTGGTGGAGGAGGACCTGTTCAACACACTGCCACCGAGGTGAAGGAGCGGCTGTGGAGGGCT
GACAAGGAGCAGGCTGAGCGGAGCGGCCCCAGCACAGCAAGCAGCAGGACCGCTGCCAGTCCCTCAGGCCCGG
AGGGCAGGCCTAGCTTCTCCAGAACTCCCGGACAGCCAGGACAGCCTCGCGGCTGGGCGAGGCTGGGGCC
GCTTGTGAGTCAGGCCAGAGCGAGAGGACAGTATCTGTGGGCTGGCCCTTTTCTCCCTTGAGACTCAGCTC
CCCCAGGGCAAGTCTTGTGGAGGAGCAAGTCTCAAGAGCGCAGTATTTGGATAATCAGGGTCTCCTCCCTG
GAGGCCAGCTCTGCCCCAGGGGCTGAGCTGCCACCAGAGTCTGGGACCCTCACTTTAGTCTTGGTATTTAT
TTTTCTCCATCTCCACCTCTTTCATCCAGATAACTATACATTTCCCAAGAAAGTTCAGCCCAGATGGAAGGTG
TTCAGGGAAAGGTGGGCTGCCTTTCCCTTGTCTTATTTAGCGATGCCGCCGGCATTAAACACCCACCTGG
ACTTCAGCAGAGTGGTCCGGGGCGAACCAGCCATGGGACGGTCACCCAGCAGTGGCGGCTGGGCTGTGGGTTG
CGGTCCACGGGAGAGCAGGCCCTCCAGCTGGAAAGGCCAGGCCTGGAGCTTGCCTCTTCAGTTTTTGTGGCAGTT
TTAGTTTTTTGTTTTTTTTTTTTTAAATCAAAAAACAATTTTTTTTAAAAAAAAGCTTTGAAAATGGATGGTTT
GGGTATTTTTTTTTGAAAAAAAACCTTAAAAAAAAGACACTAACGGCCAGTGAAGTGGAGTCTCAGGGCAGG
GTGGCAGTTTCCCTTGAGCAAAGCAGCCAGACGTTGAAGTGTGTTTCCCTTCCCTGGGCGCAGGGTGCAGGGTG
TCTTCCGGATCTGGTGTGACCTTGGTCCAGGAGTCTATTTGTTTCCCTGGGAGGGAGGTTTTTTTTGTTTGT
TTGGTTTTTTTTGGTGTCTTGTTTTCTTCTCCTCCATGTGTCTTGGCAGGCACTATTCTGTGGCTGTCCGC
CAGAGGGAATGTTCTGGAGCTGCCAAGGAGGGAGGAGACTCGGGTTGGCTAATCCCCGGATGAACGGTGTCCA
TTGCACTCCCTCCCTCGTGCCTGCCCTGCCTCTCCACGCACAGTGTAAAGGAGCAAGAGGAGCCACTTCGC
CCAGACTTTGTTTTCCCACTCCTGCGGATGGGTGTGCCAGTGCCACCGCTGGCCTCCGCTGCTTCCATCAG
CCCTGTCGCCACCTGGTCTTATGAAGAGCAGACACTTAGAGGCTGGTCCGGGAATGGGAGGTCGCCCTGGG
AGGGCAGGCGTTGGTCCAAGCCGGTCCCGTCCCTGGCGCTGGAGTGCACACAGCCAGTCCGGCACCTGGTG
GCTGGAAGCCAACCTGCTTTAGATCACTCGGGTCCCACTTAGAAGGGTCCCGCTTAGATCAATCAGGTGG
ACACTAAGGCAGTTTTAGAGTCTCTTGTCTTAATGATATGTCCATCCGTCTGTCCGTCATTTGTGTTTTCT
CGGTCTGTCAATGGATATAATCCTCAGAAATAATGCACACTAGCCTCTGACAACCATGAAGCAAAAATCCGTT
ACATGTGGGTCTGAAGTGTAGACTCGGTACAGTATCAATAAAATCTATAACAGAAAAA

FIGURE 124

MRQTIKVIKFIILICYTVVYVHNIKFDVDCTVDIESLTGYRTRYCAHPLATLFKILASFYI
SLVIFYGLICMYTLWWMRLRRSLKKYSFESIREESSYSDIPDVKNDFAFMLHLIDQYDPLYSK
RFAVFLSEVSENKLRQLNLNNEWTLDKLRQRLTKNAQDKLELHLFMLSIGIPDTVFDLVELEV
LKLELIPDVTIPPSIAQLTGLKELWLYHTAAKIEAPALAFLENLRALHIKFTDIKEIPLWI
YSLKLEELHLTGNLSAENNRIVIDGLRELKRLKVLRLKSNLSKLPQVVTDVGVHLQKISI
NNEGTKLIVLNSLKKMANLTELELIRCDLERIPHSIFSLHNLQEIDLKDNNLKTIEEIIISFQ
HLHRLTCLKLWYNHIAIYIPIQIGNLTNLERLYLNRNKIEKIPTQLFYCRKRLRYLDLSHNNLT
FLPADIGLLQNLQNLAITANRIETLPPELFQCRKLRALHLGNNVLQSLPSRVGELTNLTQIE
LRGNRLECLPVELGECPLLKRSGLVVEEDLFNTLPPEVKERLWRADKEQA

Transmembrane domain:

amino acids 51-75 (type II)

N-glycosylation site.

amino acids 262-266, 290-294, 328-332, 396-400, 432-436, 491-495

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 85-89

Casein kinase II phosphorylation site.

amino acids 91-95, 97-101, 177-181, 253-257, 330-334, 364-368,
398-402, 493-497

N-myristoylation site.

amino acids 173-179, 261-267, 395-401, 441-447

FIGURE 125

GTTGTGTCCTTCAGCAAAACAGTGGATTTAAATCTCCTTGCACAAGCTTGAGAGCAACACAA
TCTATCAGGAAAGAAAGAAAGAAAAAACC GAACCTGACAAAAAGAAGAAAAAGAAGA
AAAAAATCATGAAAACCATCCAGCCAAAAATGCACAATTCTATCTCTTGGGCAATCTTCAC
GGGGCTGGCTGCTCTGTGTCTCTTCCAAGGAGTGCCCGTGCGCAGCGGAGATGCCACCTTCC
CCAAAGCTATGGACAACGTGACGGTCCGGCAGGGGGAGAGCGCCACCCTCAGGTGCACTATT
GACAACCGGGTCACCCGGGTGGCCTGGCTAAACCGCAGCACCATCCTCTATGCTGGGAATGA
CAAGTGGTGCCTGGATCCTCGCGTGGTCTTCTGAGCAACACCCAAACGCAGTACAGCATCG
AGATCCAGAACGTGGATGTGTATGACGAGGGCCCTTACACCTGCTCGGTGCAGACAGACAAC
CACCCAAAGACCTCTAGGGTCCACCTCA'TTGTGCAAGTATCTCCAAAAATTGTAGAGATTC
TTCAGATATCTCCATTAATGAAGGGAACAATATTAGCCTCACCTGCATAGCAACTGGTAGAC
CAGAGCCTACGGTTACTTGGAGACACATCTCTCCCAAAGCGGTTGGCTTTGTGAGTGAAGAC
GAATACTTGGAAATTCAGGGCATCACCCGGGAGCAGTCAGGGGACTACGAGTGCAGTGCCTC
CAATGACGTGGCCGCGCCCGTGGTACGGAGAGTAAAGGTCACCGTGAACCTATCCACCATACA
TTTCAGAAGCCAAGGGTACAGGTGTCCCCGTGGGACAAAAGGGGACACTGCAGTGTGAAGCC
TCAGCAGTCCCCCTCAGCAGAATTCAGTGGTACAAGGATGACAAAAGACTGATTGAAGGAAA
GAAAGGGGTGAAAGTGGAAAACAGACCTTTCCCTCTCAAACCTCATCTTCTTCAATGTCTCTG
AACATGACTATGGGAACTACACTTGCCTGGCCTCCAACAAGCTGGGCCACACCAATGCCAGC
ATCATGCTATTTGGTCCAGGCGCCGTCAGCGAGGTGAGCAACGGCAGCTCGAGGAGGGCAGG
CTGCGTCTGGCTGCTGCCTCTTCTGGTCTTGCACCTGCTTCTCAAATTTTGATGTGAGTGCC
ACTTCCCCACCCGGGAAAGGCTGCCGCCACCACCACCAACACAACAGCAATGGCAACAC
CGACAGCAACCAATCAGATATATACAAATGAAATTAGAAGAAACACAGCCTCATGGGACAGA
AATTTGAGGGAGGGGAACAAAGAATACTTTGGGGGAAAAGAGTTTTAAAAAAGAAATTGAA
AATTGCCTTGAGATATTTAGGTACAATGGAGTTTTCTTTTCCCAAACGGGAAGAACACAGC
ACACCCGGCTTGGACCCACTGCAAGCTGCATCGTGCAACCTCTTTGGTGCCAGTGTGGGCAA
GGGCTCAGCCTCTCTGCCACAGAGTGCCCCACGTGGAACATCTTGGAGCTGGCCATCCCA
AATTCAATCAGTCCATAGAGACGAACAGAATGAGACCTTCCGGCCCAAGCGTGGCGCTGCGG
GCACTTTGGTAGACTGTGCCACCACGGCGTGTGTGTGAAACGTGAAATAAAAAGAGCAAAA
AAAAA

FIGURE 126

MKTIQPKMHNSISWAI FTGLAALCLFQGV PVRSGDATFPKAMDNVTVRQGESATLRCTIDNR
VTRVAWLN RSTILYAGNDKWCLDPRV VLLSNTQTQYSIEIQNV DVYDEGPYTCSVQTDNHPK
TSRVHLIVQVSPKIVEISSDISINEGNNISLTCIATGRPEPTVTWRHISPKAVGFVSEDEYL
EIQGITREQSGDYEC SASNDVAAPV VRRVKVTVNYPPYISEAKGTGVPV GQKGTLQCEASAV
PSAEFQWYKDDKRLIEGKKGVKVENRPF LSKLIFFNVSEHDYGN YTCVASNKLGH TNASIML
FGPGAVSEVSNGTSRRAGCVWLLPLLVLHLLLKF

Important features:

Signal peptide:

amino acids 1-28

FIGURE 127

GGCGCCGGTGCACCGGGCGGGCTGAGCGCCTCCTGCGGGCCCGGCTGCGCGCCCCGGCCCGCCGCGCCGCCAC
GCCCCAACCCCGGCCCGCCCCCTAGCCCCCGCCGGGCCCGCGCCCGCCCGCCAGGTGAGCGCTCCG
CCCGCCGCGAGGCCCGCCCCGGCCCGCCCCCGCCCGCCCGGCCGGGGGAACGGGGCGGATTCCTCGCG
CGTCAAACCACTGATCCATAAAACATTCATCCTCCCGCGGCCCGCGCTGCGAGCGCCCCGCCAGTCCGCGC
CGCCGCCCCCTGCGCCTGTGCGCCTGCGCGCCTGCGCACCCCGCGCCGAGCCAGCCAGAGCCGGGCGGA
GCGGAGCGCGCCGAGCCTCGTCCCGGCGCGGGCCGGGGCCGGCCGTAGCGCGGCCCTGGATGCGGACCCG
GCCGCGGGGAGACGGCGCCCGCCCCGAAACGACTTTCAGTCCCCGACGCGCCCGCCCAACCCCTACGATGAA
GAGGGCGTCCGCTGGAGGGAGCCGGCTGCTGGCATGGGTGCTGTGGCTGCAGGCCTGGCAGGTGGCAGCCCAT
GCCCAGGTGCCTGCGTATGCTACAATGAGCCAAAGTGACGACAGCTGCCCCAGCAGGGCCTGCAGGCTGTG
CCCGTGGGCATCCCTGCTGCCAGCCAGCGCATCTTCCTGCACGGCAACCGCATCTCGCATGTGCCAGTGGCAG
CTTCCGTGCCTGCCGCAACCTCACACACCTCTTCCTGCACGGCAACCGCATCTCCAGCGTGCCCGAGCGCGCTTCCGT
TCACTGGCCTGGCCCTCCTGGAGCAGCTGGACCTCAGCGATAATGCACAGCTCCGGTCTGTGGACCCTGCCACA
TTCACGGCCTGGGCCGCTACACACGCTGCACCTGGACCGCTGCGGCCTGCAGGAGCTGGGCCCGGGCTGTT
CCGCGGCCTGGCTGCCCTGCAGTACCTTACCTGCAGGACAACGCGCTGCAGGCACTGCCATGACACCTTCC
GCGACCTGGGCAACCTCACACACCTCTTCCTGCACGGCAACCGCATCTCCAGCGTGCCCGAGCGCGCTTCCGT
GGGCTGCACAGCCTCGACCGTCTCCTACTGCACCAGAACCAGCGTGGCCCATGTGCACCCGCATGCCTTCCGTGA
CCTTGGCCGCTCATGACACTCTATCTGTTTGCCAACAATCTATCAGCGCTGCCACTGAGGCCCTGGCCCCC
TGGTGCAGAAAGTTCGCGGCTCCTCCTCCGAGGTGCCCTGCAGCCTCCCGCAACGCTGGCTGGCCGTGACCT
CAAACGCCCTAGCTGCCAATGACCTGCAGGGCTGCGCTGTGGCCACCGGCCCTTACCATCCCATCTGGACCGCA
GGGCCACCGATGAGGAGCCGCTGGGGCTTCCCAAGTGTGCCAGCCAGATGCCGCTGACAAGCCCTCAGTACTG
GAGCCTGGAAGACCAGCTTCGGCAGGCAATGCGCTGAAGGGACGCGTGCCGCCCCGCTGACAGCCCGCCGGCAA
CGGCTCTGGCCACGGCACATCAATGACTACCCTTTGGGACTCTGCCTGGCTCTGCTGAGCCCCCGCTCACTG
CAGTGCGGCCCGAGGGCTCCGAGCCACCAGGGTTCCCCACCTCGGGCCCTCGCCGGAGGCCAGGCTGTTACGC
AAGAACCGCACCCGACCCACTGCCGTCTGGGCCAGGACGCGAGCGGGGTGGCCGGACTGTTGACTCAGAAGG
CTCAGGTGCCCTACCCAGCCTCACCTGCAGCCTCACCCCTGGCCCTGGCGCTGGTGTGTTGACAGTGCCTG
GGCCTGCTGACCCCCAGCGGACACAAGAGCGTGTGACAGCCAGGTGTGTGTACATACGGGGTCTCTCTCCA
CGCCGCAAGCCAGCCGGGCGCCGACCCGTGGGGCAGGCCAGGCCAGGTCTCCCTGATGGACGCCTGCCGCC
CGCCACCCCATCTCCACCCCATCATGTTTACAGGGTTCGGCCGAGCGTTTGTTCAGAACGCCGCTCCAC
CCAGATCGCGGTATATAGAGATATGCATTTTATTTTACTTGTGTAAAAATATCGGACGACGTGGAATAAAGAC
CTTTTCTTAAAAAA

FIGURE 128

MKRASAGGSRLLAWVWLQAWQVAAPCPGACVCYNEPKVTTSCFQQGLQAVPVGIPAASQRIFLHG NRISHVPA
ASFRACRNLTILWLHSNVLARIDAAAFTGLALLEQLDLSDNAQLRSVDPATFHGLGRLHTLHLDRCGLQELGPG
LFRGLAALQYLYLQDNALQALPDDTFRDLGNLTHLFLHG NRISVPERAFRGLHSLDRLLLHQNRVAHVHPHAF
RDLGRLMTLYLFANNLSALPTEALAPLRALQYLRLNDNPWVDCRARPLWAWLQKFRGSSSEVPCSLPQRLAGR
DLKRLAANDLQCAVATGPYHP IWTGRATDEEPLGLPKCCQPDAAADKASVLEPGRPASAGNALKGRVPPGDSPP
GNGSGPRHINDSPFGTLPGSAEPPLTAVRPEGSEPPGFPTSGPRRRPGCSRKNRTRSHCRRLGQAGSGGGGTGDS
EGSGALPSLTCSLTPLGLALVLTVLGPC

Important features:

Signal peptide:

amino acids 1-26

Leucine zipper pattern.

amino acids 135-156

Glycosaminoglycan attachment site.

amino acids 436-439

N-glycosylation site.

amino acids 82-85, 179-183, 237-240, 372-375 and 423-426

VWFC domain

amino acids 411-425

FIGURE 129

GCGCCGGGAGCCCATCTGCCCCAGGGGCACGGGGCGGGGGCCGGCTCCCGCCCGGCACATGGCTGCAGCCAC
CTCGCGCGCACCCCGAGGCGCCCGCCAGCTCGCCCGAGGTCCGTCCGAGGCGCCCGCCCGCCCGGAGCCAA
GCAGCAACTGAGCGGGGAAGCGCCCGCTCCGGGGATCGGGATGTCCTCCTCCTCTCTCTCTCTGCTAGTTCC
TACTATGTTGGAACCTTGGGGACTCACACTGAGATCAAGAGAGTGGCAGAGGAAAAGGTCACCTTTGCCCTGCCA
CCATCAACTGGGGCTTCCAGAAAAAGACACTCTGGATATTGAATGGCTGCTCACCGATAATGAAGGGAACCCAAA
AAGTGGTGATCACTTACTCCAGTCGTCATGTCTACAATAACTTGAAGTGGGAAACAGAAAGGGCCGAGTGGCCTTT
GCTTCCAATTTCTGGCAGGAGATGCCTCCTTGCAGATTGAACCTCTGAAGCCAGTGTAGAGGCGCGGTACAC
CTGTAAGGTTAAGAATTCAGGGCGCTACGTGTGGAGCCATGTCTATCTTAAAAGTCTTAGTGAGACCATCCAAGC
CCAAGTGTGAGTTGGAAGGAGAGCTGACAGAAGGAAGTACCTGACTTTGCAAGTGTGAGTCATCCTCTGGCACA
GAGCCATTGTATTACTGGCAGCGAATCCGAGAGAAAGAGGGAGAGGATGAACGTCTGCCTCCCAAATCTAG
GATGACTACAACCACCTGGACGAGTCTGTGCTGAGAATCTTACCATGTCTACTCTGGACTGTACCAGTGCAC
CAGCAGGCAACGAAGCTGGGAAGGAAAGCTGTGTGGTGGCAGTAAGTGTACAGTATGTACAAAGCATCGGCATG
GTTGAGGAGCAGTGAAGGATAGTGGCTGGAGCCCTGCTGATTTTCTCTTGGTGTGGCTGCTAATCCGAAG
GAAAGACAAAGAAATATGAGGAAGAAGAGAGACCTAATGAAATTCGAGAAGATGCTGAAGCTCCAAAAGCCC
GTCTGTGAAACCCAGCTCCTCTTCTCAGGCTCTCGGAGCTCACGCTCTGGTCTTCTCTCCACTCGCTCCACA
GCAATAGTGCTCACGCAGCCAGCGGACACTGTCAACTGACGCAGCACCCAGCCAGGGCTGGCCACCCAGGC
ATACAGCCTAGTGGGGCCAGAGGTGAGAGGTTCTGAACCAAAGAAAGTCCACCATGCTAATCTGACCAAAGCAG
AAACCACACCCAGCATGATCCCCAGCCAGAGCAGAGCCTTCCAAACGGTCTGAATTACAATGGACTTGACTCCC
ACGCTTTCCTAGGAGTCAGGGTCTTTGGACTCTTCTCGTCATTGGAGCTCAAGTCACCAGCCACACACCAGAT
GAGAGGTCATCTAAGTAGCAGTGAAGCATTGCACGGAACAGATTGAGATGAGCATTTCCTTATACAAATACAAA
CAAGCAAAGGATGTAAGCTGATTCATCTGTA AAAAGGCATCTTATTGTGCCTTAGACCAGAGTAAGGGAAAG
CAGGAGTCCAAATCTATTTGTTGACCAGGACCTGTGGTGAGAAGGTTGGGGAAAGGTGAGGTGAATATACCTAA
AACTTTAATGTGGGATATTTGTATCAGTGCTTTGATTACAATTTCAAGAGGAAATGGGATGCTGTTTGT
AATTTCTATGCATTTCTGCAAACCTAATTGGATTATTAGTTATTAGACAGTCAAGCAGAACCCACAGCCTTAT
TACACCTGTCTACACCATGTACTGAGCTAACCCTTCTAAGAAACTCCAAAAAGGAAACATGTGTCTCTATT
CTGACTTAACTTCAATTTGTCATAAGGTTGGATATTAATTTCAAGGGGAGTTGAAATAGTGGGAGATGGAGAAG
AGTGAATGAGTTTCTCCACTCTATACTAATCTCACTATTTGTATTGAGCCCAAATAACTATGAAAGGAGACA
AAAATTTGTGACAAAGGATTGTGAAGAGCTTCCATCTTCATGATGTTATGAGGATTGTTGACAAACATAGAA
ATATATAATGGAGCAATTGTGGATTTCCCTCAAATCAGATGCCTCTAAGGACTTCTCTGCTAGATATTTCTGG
AAGGAGAAAATACAACATGTCAATTTACACGCTCTTAGAAAAGAAATCTTCTAGAGAAAAGGGATCTAGGAAT
GCTGAAAGATTACCCAACATACCATTTATAGTCTCTCTTTCTGAGAAAATGTGAAACCAGAAATGCAAGACTGG
GTGGACTAGAAAGGGAGATTAGATCAGTTTCTCTTAATATGTCAAGGAAGGTAGCCGGGCATGGTGCCAGGCA
CCTGTAGGAAAATCCAGCAGGTGGAGGTTGCAGTGAGCCGAGATTATGCCATTGCACTCCAGCCTGGGTGACAG
AGCGGGACTCCGTCTC

FIGURE 130

MSLLLLLLVSYVGTGLGHTTEIKRVAEEKVTLPCHHQLGLPEKDTLDIEWLLTDNEGNQKVVIYSSRHVYNN
LTEEQKGRVAFASNFLAGDASLQIEPLKPSDEGRYTCVKNSGRYVWSHVILKVLVRPSKPKCELEGELEGS
LTLQCESSSGTEPIVYVWQRIREKEGEDERLPPKSRIDYNIHPGRVLLQNLTMSYSGLYQCTAGNEAGKESC
VVRVTVQYVQSIGMVAGAVTGIVAGALLIFLLVWLLIRRKDKERYEEEEERPNEIREDAEAPKARLVKPS
SSSSSGSRS SRSGSSSTRSTANSASRSQRTLSTDAAPQPGLATQAYSLVGPEVRGSEPKKVHHLTKAET
TPSMIPSQSRAFTV

Important features:

Signal sequence:
amino acids 1-16

Transmembrane domain:
amino acids 232-251

FIGURE 132

```
</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA48314
<subunit 1 of 1, 798 aa, 1 stop
<MW: 87552, pI: 4.84, NX(S/T): 5
MEASGKLICRQRQVLFSFLLGLSLAGAAEPRSYSVVEETEGSSFVTNLAKDLGLEQREFSR
RGVRVVSARGNKLHLQLNQETADLLLNEKLDREDLCGHTEPCVLRFRQVLESPFEFFQAEQV
IDINDHSPVFLDKQMLVKVSESSPPGTTFPLKNAEDLDVGQNNIENYIISPNSYFRVLTRKR
SDGRKYPELVLDKALDREEEAELRLTLTALDGGSPPRSGTAQVYIEVLDVNDNAPEFEQPFY
RVQISEDSPVGFLVVKVSATDVDVTGVNGEISYSLFQASEEIGKTFKINPLTGEIELKKQLDF
EKLQSYEVNIEARDAGTFSGKCTVLIQVIDVNDHAPEVTMSAFTSPIENAPETVVALFSVS
DLDSGENGKISCSIQEDLPFLLKSAENFYTLTTERPLDRESRAEYNITITVTDLGTPLMITQ
LNMTVLIADVNDNAPAFQTQTSYTLFVRENNSPALHIRSVSATDRDSDGTNAQVITYSLLPPQDF
HLPLTSLVSINADNGHLFALRSLDYEALQGFQFRVGASDHGSPALSSEALVRVVVLDANDNS
PFVLYPLQNGSAPCTELVPRAAEPGYLVTKVVAVDGDGSGQNAWLSYQLLKATELGLFGVWAH
NGEVRTARLLSERDAAKHLVVLVKDNGEPPRSATATLHVLLVDGFSQPYLPLPEAAPTQAO
ADLLTVYLVVALASVSSLFLFSVLLFVAVRLCRRSRAASVGRCLVPEGPLPGHLVDMGSTRT
LSQSYQYEVCLAGGSGTNEFKFLKPIIPNFPPQCPGKETQGNSTFPNNFGFNIQ
```

Important features:

Signal peptide:

amino acids 1-26

Transmembrane domain:

amino acids 685-712

Cadherins extracellular repeated domain signature.

amino acids 122-132, 231-241, 336-346, 439-449 and 549-559

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

amino acids 285-292

N-glycosylation site.

amino acids 418-421, 436-439, 567-570 and 786-789

FIGURE 134

MT PQSLLQTTLFLLSLLFLVQGAHGRGHREDFR FCSQRNQTHRSSLHYKPTPDLRISIENSE
EALTVHAPFPAAHPASRSFPDPRGLYHFCLYWNRHAGRLHLLYGKRDFLLSDKASSLLCFQH
QEE SLAQGPPLLATS VTSWWSPQNI SLPSAASF TFSFHSPPH TAAHNASVDMCELKRD LQLL
SQFLKHPQKASRRPSAAPASQQQSLESKLT SVRFMGDMVS FEEDRINATVWKLQPTAGLQD
LHIHSRQEEEQSEIMEYSVLLPRTL FORTKGRSGEAEKRLLLVDFSSQALFQDKNSSQVLGE
KVLGIVVQNTKVANLTPVVLT FQHQLQPKNVT LQCVFWVEDPTLSSPGHWSSAGCETVRRE
TQTSFCFNHLTYFAVLMVSSVEVD AVHKHYLSLLSYVGCVV SALACLVTIAAYLCSRVP LPLC
RRKPRDYTIKVHMNLLLAVFLLDTS FLLSEPVALTGSEAGCRASAI FLHFSLTCLSWMGLE
GYNLYRLVVEVFGTYVPGYLLKLSAMGWGFPI FLVTLVALVDVDNYGPI ILAVHRTPEGVIY
PSMCWIRD SLVSYITNLGLFSLVFLFN MAMLATMVVQILRLRPHTQKWSHVLTLLGLSLVLG
LPWALIFFSFASGTFQLVVLYLFSIITSFQGF LIFIWYWSMRLQARGGPSPLKSNSDSARLP
ISSGSTSSSRI

Important features:

Signal peptide:

amino acids 1-25

Putative transmembrane domains:

amino acids 382-398, 402-420, 445-468, 473-491, 519-537, 568-590
and 634-657

Microbodies C-terminal targeting signal.

amino acids 691-693

cAMP- and cGMP-dependent protein kinase phosphorylation sites.

amino acids 198-201 and 370-373

N-glycosylation sites.

amino acids 39-42, 148-151, 171-174, 234-237, 303-306, 324-327
and 341-344

G-protein coupled receptors family 2 proteins

amino acids 475-504

FIGURE 135

GCCTAGCCAGGCCAAGAATGCAATTGCCCCGGTGGTGGGAGCTGGGAGACCCCTGTGCTTGGACGGGACAGGCTCGG
GGGACACGCAGGATGAGCCCGCGACCCTGGCACATTCTTGCTGACAGTGTACAGTATTTCTCCAAGGTACA
CTCCGATCGGAATGTATACCCATCAGCAGGTGTCTCTTTGTTCATGTTTTGGAAAAGAGAATATTTAAGGGG
AATTTCCACCTTACCCAAAACCTGGCGAGATTAGTAATGATCCCATAACATTTAATACAAATTTAATGGGTTAC
CCAGACCGACCTGGATGGCTTCGATATATCCAAAGGACACCATATAGTGATGGAGTCCATATATGGGTCCCAAC
AGCTGAAAATGTGGGAAGCCAACAATCATTGAGATAACTGCCTACAACAGGCGCACCTTTGAGACTGCAAGGC
ATAATTTGATAATTAATATAATGTCTGCAGAAGACTTCCCGTTGCCATATCAAGCAGAATTCCTTCAITTAAGAAT
ATGAATGTAGAAGAAATGTTGGCCAGTGAGGTTCTTGGAGACTTCTTGGCGCAGTGAAAAATGTGTGGCAGCC
AGAGCGCCTGAACGCCATAAACATCACATCGGCCCTAGACAGGGGTGGCAGGGTGCCACTTCCCATTAATGACC
TGAAGGAGGGCGTTTATGTCATGGTGGTGCAGATGTCCCCTTTCTTCTTGTACGAGAAGTTGAAAATCCA
CAGAATCAATTGAGATGTAGTCAAGAAATGGAGCCTGTAATAACATGTGATAAAAAATTTCTGACTCAATTTA
CATTGACTGGTGCAAAATTTTCAATGGTTGATAAAAACAAAGCAAGTGTCCACCTATCAGGAAGTGATTCTGGAG
AGGGGATTTTACCTGATGGTGGAGAATACAAACCCCTTCTGATTCTTTGAAAAGCAGAGACTATTACACGGAT
TTCTAATTACACTGGCTGTGCCCTCGGCAGTGGCACTGGTCTTTTCTAATACTTGCTTATATCATGTGCTG
CCGACGGGAAGGCGTGGAAAAGAGAAACATGCAAACACCAGACATCCAACCTGGTCCATCACAGTGCTATTCAGA
AATCTACCAAGGAGCTTCGAGACATGTCCAAGAATAGAGAGATAGCATGGCCCCGTCAACGCTTCTCTGTGTTC
CACCTGTGACTGGGAAATCATACCTCTTTACACACAGACAACATGATAGCACAACATGCCATTGATGCA
AACGCAGCAGAACTTGCCACATCAGACTCAGATTTCCCAACAGCAGACTACAGGTAATGGTATCCCTGAGAA
AGAAAACCTGACTGAAGCAATGAATTTATAATCAGACAATATAGCAGTTACATCACATTTCTTTCTCTTCCAAT
AATGCATGAGCTTTTCTGGCATATGTTATGCATGTTGGCAGTATTAAGTGTATACCAAATAATACAACATAACT
TTCATTTACTAATGTATTTTTTGTACTTAAAGCATTTTGACAATTTGTAAAACATTTGATGACTTTATATTT
GTTACAATAAAAGTTGATCTTTAAAATAAATATTATTAATGAAGCCTAAAAA

FIGURE 136

MQLPRWWELGDPCAWTGQGRGTRRMS PattGTfLLTVYSIFSKVHSDRNvYPSAGVLFVHVLEREYFKGEFPPY
PKPGEISNDPITFNTNLMGYPDRPGWLRyIQRTpYSDGVLYGSPTAENVGKPTIEITAYNRRTFETARHNLI
NIMSAEDFPLPYQAEFFIKNMNVEEMLASEVLGDfLGAVKNVWQPERLNAINITSALDRGGRVPLPINDLKEGV
YVMVGADVPFSSCLREVENPQNQLRCSQEMEPVITCDKKFRtQFYIDWCKISLVDKTKQVSTYQEVIRGEGILP
DGGEYKPPSDSLKSRDYTDfLITLAVPSAVALVFLILAYIMCCRREGVEKRNMQTPDIQLVHHSATQKSTKE
LRDMSKNREIAWPLSTLPVFHPVTGEIIPPLHTDNYDSTNMPLMQTQQNLPHQTQIPQQQTGKWYP

signal sequence:
Amino acids 1-46

transmembrane domain:
Amino acids 319-338

N-glycosylation site:
Amino acids 200-204

cAMP- and cGMP-dependent protein kinase phosphorylation site:
Amino acids 23-27

Tyrosine kinase phosphorylation site:
Amino acids 43-52

N-myristoylation sites:
Amino acids 17-23;112-118;116-122;

185-191

FIGURE 137

CAGAAGAGGGGGCTAGCTAGCTGTCTCTGCGGACCAGGGAGACCCCCGCGCCCCCGGTGT
GAGGCGGCCTCACAGGGCCGGGTGGGCTGGCGAGCCGACGCGGCGGCGGAGGAGGCTGTGAG
GAGTGTGTGGAACAGGACCCGGGACAGAGGAACC**ATGG**GCTCCGCAGAACCTGAGCACCTTTT
GCCTGTTGCTGCTATAACCTCATCGGGGCGGTGATTGCCGGACGAGATTTCTATAAGATCTTG
GGGGTGCCTCGAAGTGCCTCTATAAAGGATATTA AAAAGGCCTATAGGAAACTAGCCCTGCA
GCTTCATCCCGACCCGGAACCCCTGATGATCCACAAGCCCAGGAGAAATCCAGGATCTGGGTG
CTGCTTATGAGGTTCTGTGATAGTGAGAAACGGAAACAGTACGATACTTATGGTGAAGAA
GGATTA AAAAGATGGTCATCAGAGCTCCCATGGAGACATTTTTTTCACACTTCTTTGGGGATTT
TGGTTTTCATGTTTTGGAGGAACCCCTCGTCAGCAAGACAGAAATATCCAAGAGGAAGTGATA
TTATTGTAGATCTAGAAGTCAC'TTTGGAAGAAGTATATGCAGGAAATTTTTGTGGAAGTAGTT
AGAAACAAACCTGTGGCAAGGCAGGCTCCTGGCAAACGGAAGTGCAATTGTGCGCAAGAGAT
GCGGACCACCCAGCTGGGCCCTGGGCGCTTCCAAATGACCCAGGAGGTGGTCTGCGACGAAT
GCCCTAATGTCAAACCTAGTGAATGAAGAACGAACGCTGGAAGTAGAAATAGAGCCTGGGGTG
AGAGACGGCATGGAGTACCCCTTTATTGGAGAAGGTGAGCCTCACGTGGATGGGGAGCCTGG
AGATTTACGGTTC CGAATCAAAGTTGTC AAGCACCCCAATATTTGAAAGGAGAGGAGATGATT
TGTACACAAATGTGACAATCTCATTAGTTGAGTCACTGGTTGGCTTTGAGATGGATATTACT
CACTTGGATGGTCACAAGGTACATATTTCCCGGGATAAGATCACCCAGGCCAGGAGCGAAGCT
ATGGAAGAAAGGGGAAGGGCTCCCCAACTTTGACAACAACAATATCAAGGGCTCTTTGATAA
TCACTTTTGATGTGGATTTTCCAAAAGAACAGTTAACAGAGGAAGCGAGAGAAGGTATCAA
CAGCTACTGAAACAAGGGTCAGTGCAGAAGGTATACAATGGACTGCAAGGATAT**TGAG**AGTG
AATAAAATTGGACTTTGTTTAAAATAAGTGAATAAGCGATATTTATTATCTGCAAGGTTTTT
TTGTGTGTGTTTTTTGTTTTTATTTTCAATATGCAAGTTAGGCTTAATTTTTTTTATCTAATGA
TCATCATGAAATGAATAAGAGGGCTTAAAGAATTTGTCCATTTGCATTCGGAAAAGAATGACC
AGCAAAGGTTTACTAATACCTCTCCCTTTGGGGATTTAATGTCTGGTGTGCCGCCTGAGT
TTCAAGAATTAAGCTGCAAGAGGACTCCAGGAGCAAAGAAACACAATATAGAGGGTTGGA
GTTGTTAGCAATTTCAATCAAATGCCAACTGGAGAAGTCTGTTTTTAAATACATTTTGTG
TTATTTTTTA

FIGURE 138

MAPQNLSTFCLLLLYLIGAVIAGRDFYKILGVPRSASIKDIKKAYRKLALQLHPDRNPDDPQAQEKFQDLGAAY
EVLSDSEKRKQYDITYGEEGLKDGHQSSHGDI FSHFFGDFGFMFGGT PRQQDRNI PRGSDI IVDLEVTLEEVYAG
NFVEVVRNKPVARQAPGKRKCNCRQEMRTTQLGPGRFQMTQEVVVCDECPNVKLVNEERTLEVEIEPGVRDGMAY
PFIGEGEPHVDGEPGDLRFRIKVVKHPI FERRGDDLYTNVTISLVESLVGFEMDITHLDGCHKVHISRDKITRPG
AKLWKKGEGLPNFDNNNIKGSLIITFDVDFPKEQLTEEAREFGIKQLLKQGSVQKVYNGLQGY

Important features:

Signal peptide:

amino acids 1-22

Cell attachment sequence.

amino acids 254-257

Nt-dnaJ domain signature.

amino acids 67-87

Homologous region to Nt-dnaJ domain proteins.

amino acids 26-58

N-glycosylation site.

amino acids 5-9, 261-265

Tyrosine kinase phosphorylation site.

amino acids 253-260

N-myristoylation site.

amino acids 18-24, 31-37, 93-99, 215-221

Amidation site.

amino acids 164-168

FIGURE 139

CCAGTCTGTCGCCACCTCACTTGGTGTCTGCTGTCCCCGCCAGGCAAGCCTGGGGTGAGAGC
ACAGAGGAGTGGGCCGGGACC**ATG**CGGGGGACGCGGCTGGCGCTCCTGGCGCTGGTGCTGGC
TGCTGCGGAGAGCTGGCGCCGGCCCTGCGCTGCTACGTCTGTCCGGAGCCCACAGGAGTGT
CGGACTGTGTCACCATCGCCACCTGCACCACCAACGAAACCATGTGCAAGACCACACTCTAC
TCCCGGGAGATAGTGTACCCCTTCCAGGGGGACTCCACGGTGACCAAGTCTGTGCCAGCAA
GTGTAAGCCCTCGGATGTGGATGGCATCGGCCAGACCCTGCCCGTGTCTGTGCAATACTG
AGCTGTGCAATGTAGACGGGGCGCCCGCTCTGAACAGCCTCCACTGCGGGGCCCTCACGCTC
CTCCCACTCTTGAGCCTCCGACT**G****TAG**AGTCCCCGCCACCCCATGGCCCTATGCGGCCCA
GCCCCGAATGCCTTGAAGAAGTGCCCCCTGCACCAGGAAAAAAAAAAAAAAAAAAAA

FIGURE 140

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56405

<subunit 1 of 1, 125 aa, 1 stop

<MW: 13115, pI: 5.90, NX(S/T): 1

MRGTRLALLALVLAACGELAPALRCYVCPEPTGVSDCVTIATCTTNETMCKTTLYSREIVYP
FQGDSTVTKSCASKCKPSDVDGIGQTLPVSCCNTELCNVDGAPALNSLHCGALTLLPLLSLRL

Important features:

Signal peptide:

amino acids 1-17

N-glycosylation site.

amino acids 46-49

FIGURE 141

GGCGCCGCGTAGGCCCGGGAGGCCGGGCCGGCCGGGCTGCGAGCGCCTGCCCCATGCGCCGC
CGCCTCTCCGCACG**ATG**TTCCCTTCGCGGAGGAAAGCGGGCGCAGCTGCCCTGGGAGGACGGC
AGGTCCGGGTGCTCTCCGGCGGCCTCCCTCGGAAGTGTTCCGTCTTCCACCTGTTCGTGGC
CTGCCTCTCGCTGGGCTTCTTCTCCCTACTCTGGCTGCAGCTCAGCTGCTCTGGGGACGTGG
CCCGGGCAGTCAGGGGACNAGGGCAGGAGACCTCGGGCCCTCCCCGTCCCTGCCCCAGAG
CCGCCCTGAGCACTGGGAAGAAGACGCATCCTGGGGCCCCACCCTGGCAGTGTGGT
GCCCTTCCGCGAACGCTTCGAGGAGCTCCTGGTCTTCGTGCCCCACATGCGCCGCTTCCTGA
GCAGGAAGAAGATCCGGCACCATCTACGTGCTCAACCAGGTGGACCACTTCAGGTTCAAC
CGGGCAGCGCTCATCAACGTGGGCTTCTGGAGAGCAGCAACAGCACGGACTACATTGCCAT
GCACGACGTTGACCTGCTCCCTCTCAACGAGGAGCTGGACTATGGCTTTCCTGAGGCTGGGC
CCTTCCACGTGGCCTCCCCGGAGCTCCACCCTCTCTACCCTACAAGACCTATGTCGGCGGC
ATCCTGCTGCTCTCCAAGCAGCACTACCGGCTGTGCAATGGGATGTCCAACCGCTTCTGGGG
CTGGGGCCGCGAGGACGACGAGTTCTACCGGCGCATTAAGGGAGCTGGGCTCCAGCTTTTCC
GCCCCCTCGGGAATCACAACCTGGGTACAAGACATTTGCCACCTGCATGACCCAGCCTGGCGG
AAGAGGGACCAGAAGCGCATCGCAGCTCAAAAACAGGAGCAGTTCAAGGTGGACAGGGAGGG
AGGCCTGAACACTGTGAAGTACCATGTGGCTTCCCGCACTGCCCTGTCTGTGGGGGGGGCCC
CCTGCACTGTCCTCAACATCATGTTGGACTGTGACAAGACCGCCACACCCTGGTGCACATTC
AGCT**CGA**GCTGGATGGACAGTGAGGAAGCCTGTACCTACAGGCCATATTGCTCAGGCTCAGGA
CAAGGCCTCAGGTCGTGGGCCAGCTCTGACAGGATGTGGAGTGGCCAGGACCAAGACAGCA
AGCTACGCAATTGCAGCCACCCGGCCGCAAGGCAGGCTTGGGCTGGGCCAGGACACGTGGG
GTGCCTGGGACGCTGCTTGCCATGCACAGTGATCAGAGAGAGGCTGGGGTGTGTCTGTCCG
GGACCCCCCTGCCTTCCCTGGTCCACCTACTCTGACCTCCTTACAGTGGCCAGGCTGTGGG
TAGTGGGGAGGGCTGAACAGGACAACCTCTCATCACCTACTCTGACCTCCTTACAGTGGCC
AGGCCTGTGGGTAGTGGGGAGGGCTGAACAGGACAACCTCTCATCACCCCCAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 142

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56531
><subunit 1 of 1, 327 aa, 1 stop
><MW: 37406, pI: 9.30, NX(S/T): 1
MFPSRRKAAQLPWEDGRSGLLSGGLPRKCSVFHLFVACL⁷SLGFFSLLWLQLSCSGDVARAVR
GQGQETSGPPRACPEPPPEHWEDASWGP⁷HRLAVLV⁷PF⁷FRERFEELLV⁷FPHMR⁷RFLSRKKI
RHHIYVLN⁷QVDHFRFNRAALIN⁷VGFLESSN⁷STDYIAMHDVDLLPLNEELDYGFPEAGPFHVA
SPELHPLYHYKTYVGGILL⁷LSKQHYRLCNGMSNR⁷FWG⁷WGREDD⁷EYRR⁷IKGAGLQLFRPSGI
TTGYK⁷TFRHLHDP⁷AWRKR⁷DQKRIAAQKQE⁷QFKVDREGGLNTV⁷KYHVASRTALSVGGAPCTVL
NIMLDCDKTATPWCTFS

Signal peptide:
amino acids 1-42

Transmembrane domain:
amino acids 29-49 (type II)

N-glycosylation site.
amino acids 154-158

cAMP- and cGMP-dependent protein kinase phosphorylation site.
amino acids 27-31

Tyrosine kinase phosphorylation site.
amino acids 226-233

N-myristoylation site.
amino acids 19-25, 65-71, 247-253, 285-291, 303-309, 304-310

FIGURE 143

GTGGGATTTATTTGAGTGCAAGATCGTTTTCTCAGTGGTGGTGGAAAGTTGCCTCATCGCAGGCAGATGTTGGGG
CTTTGTCCGAACAGCTCCCCTCTGCCAGCTTCTGTAGATAAGGGTTAAAACTAATATTTATATGACAGAAGAA
AAAGATGTCATCCGTAAGTAAACATCATCATCTTGGTCTGGCTGTTGCTCTCTTCTTACTGGTTTTGCACC
ATAACTTCCCTCAGCTTGAGCAGTTGTAAAGGAATGAGGTTACAGATTCAGGAATTGTAGGGCCTCAACCTATA
GACTTTGTCCCAAATGCTCTCCGACATGCAGTAGATGGGAGACAAGAGGAGATTCTGTGGTCATCGCTGCATC
TGAAGACAGGCTTGGGGGGCCATTGCAGCTATAAACAGCATTCAGCACAACACTCGCTCCAATGTGATTTTCT
ACATTGTTACTCTCAACAATACAGCAGACCATCTCCGGTCTGGCTCAACAGTGATTCCCTGAAAAGCATCAGA
TACAAAATTGTCAATTTTGACCCTAAACTTTTGGAAGGAAAAGTAAAGGAGGATCCTGACCAGGGGAATCCAT
GAAACCTTTAACCTTTGCAAGGTCTACTTGCCAATTCTGGTTCACAGCGCAAAGAAGGCCATATACATGGATG
ATGATGTAATTGTGCAAGGTGATATTCTTGCCCTTTACAATACAGCACTGAAGCCAGGACATGCAGCTGCATTT
TCAGAAGATTGTGATTCAGCCTCTACTAAAGTTGTCATCCGTGGAGCAGGAAACCAGTACAATTACATTGGCTA
TCTTGACTATAAAAAGGAAAGAATTCGTAAGCTTTCCATGAAAGCCAGCACTTGCTCATTTAATCCTGGAGTTT
TTGTTGCAAACCTGACGGAATGGAACGACAGAATATAACTAACCAACTGGAAAAATGGATGAACTCAATGTA
GAAGAGGGACTGTATAGCAGAACCCTGGCTGGTAGCATCACAAACCTCCTCTGCTTATCGTATTTTATCAACA
GCACTCTACCATCGATCCTATGTGGAATGTCCGCCACCTTGGTTCAGTGCTGGAAAACGATATTCACCTCAGT
TTGTAAGGCTGCCAAGTTACTCCATTGGAATGGACATTTGAAGCCATGGGGAAGGACTGCTTCATATACTGAT
GTTTGGGAAAAATGGTATATTCCAGACCCAACAGGCAAATTC AACCTAATCCGAAGATATACCGAGATCTCAA
CATAAAGTGA AACAGAATTTGAACTGTAAGCAAGCATTTCTCAGGAAGTCTGGAAGATAGCATGCATGGGAAG
TAACAGTTGCTAGCTTCAATGCCTATCGGTAGCAAGCCATGGAAAAAGATGTGTCAGCTAGGTAAGATGACA
AACTGCCCTGTCTGGCAGTCAGCTTCCAGACAGACTATAGACTATAAATATGTCTCCATCTGCCTTACCAAGT
GTTTCTTACTACAATGCTGAATGACTGGAAGAAGAAGTACTGATATGGCTAGTTCAGCTAGCTGGTACAGATAAT
TCAAAACTGCTGTGGTTTTAATTTGTAACTGTGCCTGATCTGTAATAAAACTTACATTTTTT

FIGURE 144

MSFRKVNIIILVLAVALFLLVLHFNFLSLSLLRNEVTDSGIVGPQPIDFVFNALRHAVDGR
QEEIPVIAASEDRLGGAIAAINS IQHNTRSNI FYIVTLNNTADHLRSWLNSDSLKSIRYK
IVNFDPKLLEGKVKEDPDQGESMKPLTFARFYLPILVPSAKKAIYMDDDVI VQGDILALYNT
ALKPGHAAAFSEDCDSASTKV VIRGAGNQNYIGYLDYKKERIRKLSMKASTCSFNPGVFVA
NLTEWKRQNI TNQLEKWMKLNVEEGLYSRTL AGSITTPPLLIVFYQQHSTIDPMWNVRHLGS
SAGKRYSPQFVKA AKLLHWNGHLK PWGRTASYTDVWEKWI PDPTGKFNLIRRYTEISNIK

FIGURE 145

AAACTTGACGCCATGAAAGATCCC GGTCCTTCCTGCCGTGGTGCTCCTCTCCCTCCTGGTGCT
CCTCTGCCCAGGGAGCCACCC TGGGTGGTCCTGAGGAAGAAAGCACCATTGAGAATTATG
CGTCACGACCCGAGGCCTTTAACACCCCGTTCTGAAATCGACAAATTGCGATCTGCGTTT
AAGGCTGATGAGTTCCTGAAC TGGCAGCCCTCTTTGAGTCTATCAAAGGAAACTTCCTT
CCTCAACTGGGATGCCTTTCCTAAGCTGAAAGGACTGAGGAGCGCAACTCCTGATGCCCAGT
GACCATGACCTCCACTGGAAGAGGGGGCTAGCGTGAGCGCTGATTCTCAACCTACCATAACT
CTTTCCTGCCTCAGGAACTCCAATAAAACATTTCCATCCAAA

FIGURE 146

MKIPVLPVAVLLSLLVLHSAQGATLGGPEEESTIENYASRPEAFNTPFLNIDKLRSFAKDE
FLNWHALFESIKRKL PFLNWDAFPCLKGLRSATPDAQ

FIGURE 147

CCTCTGTCCACTGCTTTCGTGAAGACAAGATGAAAGTTCACAATTGTCTTTGCTGGACTTCTT
GGAGTCTTTCTAGCTCCTGCCCTAGCTAACTATAATATCAACGTCAATGATGACAACAACAA
TGCTGGAAGTGGGCAGCAGTCAGTGAGTGTCAACAATGAACACAATGTGGCCAATGTTGACA
ATAACAACGGATGGGACTCCTGGAATCCATCTGGGATTATGGAAATGGCTTTGCTGCAACC
AGACTCTTTCAAAGAAGACATGCATTGTGCACAAAATGAACAAGGAAGTCATGCCCTCCAT
TCAATCCCTTGATGCACTGGTCAAGGAAAAGAAGCTTCAGGGTAAGGGACCAGGAGGACCAC
CTCCCAAGGGCCTGATGTACTCAGTCAACCCAAACAAAGTCGATGACCTGAGCAAGTTCGGA
AAAAACATTGCAAACATGTGTGCGTGGGATTCCAACATACATGGCTGAGGAGATGCAAGAGGC
AAGCCTGTTTTTTTACTCAGGAACGTGCTACACGACCAGTGTACTATGGATTGTGGACATTT
CCTTCTGTGGAGACACGGTGGAGAACTAAACAATTTTTTAAAGCCACTATGGATTTAGTCAT
CTGAATATGCTGTGCAGAAAAAATATGGGCTCCAGTGGTTTTTACCATGTCATTCTGAAATT
TTTCTCTACTAGTTATGTTTGATTTCTTTAAGTTTCAATAAAATCATTTAGCATTGAAAAAA

FIGURE 148

MKFTIVFAGLLGVFLAPALANYNINVNDDNNNAGSGQQSVSVNNEHNVANVDNNGWDSWNS
IWDYGNNGFAATRLFQKKTICIVHKMNKEVMPSIQSLDALVKEKKLQKGGPPPKGLMYSVN
PNKVDDLSKFGKNIANMCRGIPTYMAEEMQEASLFFYSGTCYTTSVLWIVDISFCGDTVEN

Signal Peptide:
amino acids 1-20

N-myristoylation Sites:
amino acids 67-72, 118-123, 163-168

Flavodoxin protein homology:
amino acids 156-174

FIGURE 149

GGCACGAGCCAGGAACTAGGAGGTTCTCACTGCCCGAGCAGAGGCCCTACACCCACCGAGGC
ATGGGGCTCCCTGGGCTGTTCTGCTTGGCCGTGCTGGCTGCCAGCAGCTTCTCCAAGGCACG
GGAGGAAGAAATTACCCCTGTGGTCTCCATTGCCTACAAAGTCCTGGAAGTTTTCCCAAAG
GCCGCTGGGTGCTCATAACCTGCTGTGCACCCAGCCACCACCGCCCATCACCTATTCCCTC
TGTGGAACCAAGAACATCAAGGTGGCCAAGAAGGTGGTGAAGACCCACGAGCCGGCCTCCTT
CAACCTCAACGTCACACTCAAGTCCAGTCCAGACCTGCTCACCTACTTCTGCCGGGCGTCTT
CCACCTCAGGTGCCCATGTGGACAGTGCCAGGCTACAGATGCACTGGGAGCTGTGGTCCAAG
CCAGTGTCTGAGCTGCGGGCAACTTCACTCTGCAGGACAGAGGGCAGGCCCCAGGGTGGA
GATGATCTGCCAGGCGTCCTCGGGCAGCCACCTATCACCAACAGCCTGATCGGGAAGGATG
GGCAGGTCCACCTGCAGCAGAGACCATGCCACAGGCAGCCTGCCAACTTCTCCTTCCTGCCG
AGCCAGACATCGGACTGGTTCTGGTGCCAGGCTGCAAACAACGCCAATGTCCAGCACAGCGC
CCTCACAGTGGTGCCCCAGGTGGTGACCAGAAGATGGAGGACTGGCAGGGTCCCCTGGAGA
GCCCCATCCTTGCCTTGCCGCTCTACAGGAGCACCCGCCGTCTGAGTGAAGAGGAGTTGGG
GGGTTCAGGATAGGGAATGGGGAGGTGAGAGGACGCAAAGCAGCAGCCATG**TAG**AATGAACC
GTCCAGAGAGCCAAGCACGGCAGAGGACTGCAGGCCATCAGCGTGCCTGTTTCGATTTTGGG
GTTTCATGCAAAATGAGTGTGTTTTAGCTGCTCTTGCCACAAAAAAAAAAAAAAAAAAAAA

FIGURE 150

MGLPGLFCLAVLAASSFSKAREEEITPVVSIAYKVLEVPKGRWVLITCCAPQPPPPITYSL
CGTKNIKVAKKVVKTHEPASFNLVTLKSSPDLLTYFCRASSTSGAHVDSARLQMHWELWSK
PVSELRANFTLQDRGAGPRVEMICQASSGSPPIITNSLIGKDGQVHLQORPCHRQFANFSFLP
SQTSDWFWCQAANNANVQHSALTVVPPGGDQKMEDWQGPLESPIALPLYRSTRRLSEEEFG
GFRIGNGEVRGRKAAAM

Signal Peptide:

amino acids 1-18

N-glycosylation Sites:

amino acids 86-89, 132-135, 181-184

FIGURE 151

GCGTGGGG**ATG**TCTAGGAGCTCGAAGGTGGTGCTGGGCCTCTCGGTGCTGCTGACGGCGGCC
ACAGTGGCCGGCGTACATGTGAAGCAGCAGTGGGACCAGCAGAGGCTTCGTGACGGAGTTAT
CAGAGACATTGAGAGGCAAATTCGGAAAAAAGAAAACATTCGTCTTTGGGAGAACAGATTA
TTTTGACTGAGCAACTTGAAGCAGAAAGAGAGAAGATGTTATTGGCAAAGGATCTCAAAAA
TC**TGA**CTTGAATGTGAAATATCTGTTGGACAGACAACACGAGTTTGTGTGTGTGTGTGAT
GGAGAGTAGCTTAGTAGTATCTTCATCTTTTTTTTTGGTCACTGTCCTTTTAACTTGATCA
AATAAAGGACAGTGGGTCATATAAGTTACTGCTTTCAGGGTCCCTTATATCTGAATAAAGGA
GTGTGGGCAGACACTTTTTGGAAGAGTCTGTCTGGGTGATCCTGGTAGAAGCCCCATTAGGG
TCACTGTCCAGTGCTTAGGGTTGTTACTGAGAAGCACTGCCGAGCTTGTGAGAAGGAAGGGA
TGGATAGTAGCATCCACCTGAGTAGTCTGATCAGTCGGCATGATGACGAAGCCACGAGAACA
TCGACCTCAGAAGGACTGGAGGAAGGTGAAGTGGAGGGAGAGACGCTCCTGATCGTCGAATCC

FIGURE 152

MSRSSKVVVLGLSVLLTAATVAGVHVKQQWDQQRLRDGVIRDIERQIRKKENIRLLGEQIILT
EQLEAEREKMLLAKGSQKS

FIGURE 153

AATGTGAGAGGGGCTGATGGAAGCTGATAGGCAGGACTGGAGTGTTAGCACCACTACTGGAT
GTGACAGCAGGCAGAGGAGCACTTAGCAGCTTATTCAGTGTCCGATTCTGATTCCGGCAAGG
ATCCAAGCATGGAATGCTGCCGTCGGGCAACTCCTGGCACACTGCTCCTCTTTCTGGCTTTC
CTGCTCCTGAGTTCAGGACCGCACGCTCCGAGGAGGACCGGGACGGCCTATGGGATGCCTG
GGGCCATGGAGTGAATGCTCACGCACCTGCGGGGAGGGGCCTCCTACTCTCTGAGGCGCT
GCCTGAGCAGCAAGAGCTGTGAAGGAAGAAATATCCGATACAGAACATGCAGTAATGTGGAC
TGCCACCAGAAGCAGGTGATTTCCGAGCTCAGCAATGCTCAGCTCATAATGATGTCAAGCA
CCATGGCCAGTTTTTATGAATGGCTTCCTGTGTCTAATGACCCTGACAACCCATGTTCACTCA
AGTGCCAAGCCAAAGGAACAACCCTGGTTGTTGAACTAGCACCTAAGGTCTTAGATGGTACG
CGTTGCTATACAGAATCTTTGGATATGTGCATCAGTGGTTTATGCCAAATTGTTGGCTGCGA
TCACCAGCTGGGAAGCACCGTCAAGGAAGATAACTGTGGGGTCTGCAACGGAGATGGGTCCA
CCTGCCGGCTGGTCCGAGGGCAGTATAAATCCAGCTCTCCGCAACCAAATCGGATGATACT
GTGGTGCACCTCCCTATGGAAGTAGACATATTCGCCTTGTCTTAAAAGGTCTGATCACTT
ATATCTGGAAACAAAACCCTCCAGGGGACTAAAGGTGAAAACAGTCTCAGCTCCACAGGAA
CTTTCCTTGTGGACAATTCTAGTGTGGACTTCCAGAAATTTCCAGACAAAGAGATACTGAGA
ATGGCTGGACCACTCACAGCAGATTTCAATTGTCAAGATTCGTAACCTCGGGCTCCGCTGACAG
TACAGTCCAGTTCATCTTCTATCAACCCATCATCCACCGATGGAGGGAGACGGATTTCTTTC
CTTGCTCAGCAACCTGTGGAGGAGTTATCAGCTGACATCGGCTGAGTGTACGATCTGAGG
AGCAACCGTGTGGTTGCTGACCAATACTGTCACTATTACCCAGAGAACATCAAACCCAAACC
CAAGCTTCAGGAGTGCAACTGGATCCTTGTCCAGCCAGTGACGGATAACAAGCAGATCATGC
CTTATGACCTCTACCATCCCCTTCCTCGGTGGGAGGCCACCCCATGGACCGCGTGTCTCCTCC
TCGTGTGGGGGGGGCATCCAGAGCCGGGCAGTTTCCTGTGTGGAGGAGGACATCCAGGGGCA
TGTCACTTCAGTGGAAGAGTGGAAATGCATGTACACCCCTAAGATGCCATCGCGCAGCCCT
GCAACATTTTTGACTGCCCTAAATGGCTGGCACAGGAGTGGTCTCCGTGCACAGTGACATGT
GGCCAGGGCCTCAGATACCGTGTGGTCTCTGCATCGACCATCGAGGAATGCACACAGGAGG
CTGTAGCCCAAAAACAAAGCCCCACATAAAAGAGGAATGCATCGTACCCACTCCCTGCTATA
AACCCAAAGAGAAACTTCCAGTCGAGGCCAAGTTGCCATGGTTCAAACAAGCTCAAGAGCTA
GAAGAAGGAGCTGCTGTGTGTCAGAGGAGCCCTCGTAAGTTGTAAGCACAGACTGTTCTATA
TTTGAAGTGTGTTTAAAGAAAGCAGTGTCTCACTGGTTGTAGCTTTCATGGGTTCTGA
ACTAAGTGAATCATCTCACCAAAGCTTTTTGGCTCTCAAATTAAGATTGATTAGTTTCAA
AAAAAAAAA

FIGURE 154

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA58847

<subunit 1 of 1, 525 aa, 1 stop

<MW: 58416, pI: 6.62, NX(S/T): 1

MECCRRATPGTLLLFLAFLLLSSRTARSEEDRDGLWDAWGPWSECSRTC GGGASYS LRRLS
SKSCEGRNIRYRTCSNVDCPPEAGDFRAQQCSAHNDVKHHGQFYEWL PVSNDPDPNPSLKCQ
AKGTTLVVELAPKVL DGT RCYTESLDMCISGLCQIVGCDHQLGSTVKEDNCGVCNGDGSTCR
LVRGQYKSQLSATKSDDTVVALPYGSRHIRLV LKGPDLHLYLETKTLQGTKGENSLSSSTGTFL
VDNSSVDFQKFPDKEILRMAGPLTADFIVKIRNSGSADSTVQFIFYQPI IHRWRETDFFP
ATCGGGYQLTSAECYDLRSNRVVADQYCHYYPENIKPKPKLQECNLDPCPASDGYKQIMPYD
LYHPLRWEATPWTACSSSCGGGIQSRVSCVEEDIQGHVTSVEEWKCMYTPKMPIAQPCNI
FDCPKWLAQEWSPCTVTTCGQGLRYRVVLCIDHRGMHTGGCSPKTKPHIKEECIVPTPCYKPK
EKLPVEAKLPWFKQAQAELEEGAAVSEEPS

Important features:

Signal peptide:

amino acids 1-25

N-glycosylation site.

amino acids 251-254

Thrombospondin 1

amino acids 385-399

von Willebrand factor type C domain proteins

amino acids 385-399, 445-459 and 42-56

FIGURE 156

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA59212

><subunit 1 of 1, 440 aa, 1 stop

><MW: 42208, pI: 6.36, NX(S/T): 1

MKFQGPLACLLLALCLGSGEAGPLQSGEESTGTNIGEALGHGLGDALSEGKKAIGKEAGGA
AGSKVSEALGQGTREAVGTGVRQVPGFGAADALGNRVGEAAHALGNTGHEIGRQAEDVIRHG
ADAVRGSWQGVPGHSGAWETSGGHGIFGSQGGGLGGQGNPGCLGTPWVHGYPGNSAGSFGM
NPQGAPWQGGNGGPPNFGTNTQGAVAQPGYGSVRSNQNNEGCTNPPPSGSGGSSNSGGGS
GSQSGSSGSGSNGDNNNGSSSSGSSSSGSSSSGSSSSGSSSSGSSGSSGSSGSSGNSGGSRGDSGSESSW
GSSTGSSSGNHGSGGGNGHKPGCEKPGNEARGSGESGIQGFRRQGVSSNMREISKEGNRLL
GGSGDNYRGQSSWGSGGGDAVGGVNTVNSETSPGMFNFDTFWKNFKSKLGFINWDAINKDQ
RSSRIP

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 157

CCCACGCGTCCGCCACGCGTCCGCCACGCGTCCGCCACGCGTCCGCCACGCGTCCGCC
CACGGTCCGGTGAAGCTCGCGCCGACACTGCCTGGTGGAGGAAGGAGCCGGCGCCTCTCGCGCTCCC
CGCGCCGCGTCCGCACCTCCCACCGCCCGCCGCCGCCGCCGCCGCAAGCATGAGTGAGCCCGCTC
TCTGCAGCTGCCCGGGGCGGAATGGCAGGCTGTTCCGCGGAGTAAAAGGTGGCGCCGTCAGTGGTCTGTTT
CAATGACGGACATTAACCGACTGTCAGATCCTGGGGAGTCCGGAGCCCGAGTTTGGAGTTTTTCCCCCAC
AAGTCACAGTCCGAATGCAGAGGAAAGGAAGGGCGAGGAAGGCGAAGCTCGGGTCCGGCACGTAGTTGG
GAACTTGGCGTCTAGAAGTGCCTCCCGCCTTGGCGGCCGCTTGCAGCCCCGAGCCGAGCAAAAT
GAGCATTGTGCGCTGCCAGATCCGCCCGCCGCGGACCGGGGTGCCTCGGAAACACAGAGGGGTCTTCTC
GCCCTGCATATAATAGCCTGCACACAAAGGGAGCAGCTGAATGGAGGTTGTACTCTCTGGAAAAGGATTTCT
TACCAGGACTGCCGACACCTGTCCGCTCTCTCGTGGAAAGATTCTCGCTAATGGATTCTCTGCTCGGT
CTCTGTCTATACTGGCTGCTGAGGAGGCCCTCGGGGGTGGTCTTGTGTCTGCTGGGGCCCTGCTTTCAGATGCT
GCCCGCCGCCACGCGGTGCCCGAGCTGTGCCGTTGCCGTTGCCAGGGGCGGCTGCTGTACTGCGAGGCGCTCAACC
TCACCAGGCGCCCAACCTGTCCGGCTGCTGGGCTGTCCCTGCGCTACAAACAGCCCTCGGAGCTGCCG
GCCGGCCAGTTACGGGGTTAATGCAGCTCAGTGGCTCTATCTGGATCACAAATCACATCTGCTCCGTGCAGGG
GGACGCTTTCAGAACTGCCCGAGTTAAGGAATCAGCTGAGTTCACACAGATCCCACTCCAGCTTCCGCAAG
CCACCTTCCGGCCATGCCAACCTGCCAGGCTGGACCTCTCGTACAACAAGCTGCAGGCGCTCGCGCCGAC
CTCTTCCACGGGCTGCGGAAGCTCACACGCTGCATATGCGGGCAACGCCATCCAGTTTGTGCCCGTGGCAT
TCCAGGACTGCCGACCTCAAGTTTCTCGACTCGGATACAAATCAGCTCAAGAGTCTGGCGCCCACTCTT
TCGCGGCTTGTTTAAGCTCACCGAGCTGCACCTCGAGCACAACGACTTGGTCAAGGTGAACCTCGCCCACTT
CCGCGCTCATCTGCACTCGCTCTGCTCGGAGGAGCAAGGTGGCCATTGTGGTCAAGTTCGGGACTG
GGTTTGAACCTGGAGAAAATGGACTTGTCCGGCAACGAGATCGAGTACATGGAGCCCATGTGTTCGAGACCG
TGCCGACCTGCAGTCCCTGCAGCTGGACTCAAACCGCTCACCTACATCGAGCCCCGGATCCTCACTCTTGG
AAGTCCAGTGCAGACCTACCTGGCCGGGAACCTGTTGGGATTGCGGGCGCAACGTGTGTGCCGCGCAACTCT
GCTCAGCAACTCCAGGGGGCTACGATGGCAACTGTCAGTGCGCCAGCCCGAGTACGCCAGGGCGAGGACG
TCTGGACCGCTTACGCTTCCACCTGTGCGAGGATGGGGCGAGCCACAGCGCCACCTCTCGGCTCGG
GTCACCAACCGCAGTGATCTGGGCCCCCTGCCAGCTCGGCCACCAGCTCGCGGACGGCGGGGAGGGCGAGCA
CGACGGCACATTCGAGCCTGCCACCTGGCTCTTCCAGGGCGGAGCAGCGCGAGAACGCCGTGCAGATCCACA
AGGTGGTCAAGGACACCTGGCCCTCACT
TGTTTCCAGCCAGCCTCAGGCAAGCTCAGACAGTGTCTTGTACGCAAGCGCAGGAAAGCAAAAGCAGAAACAGAC
CATGATCAGATGGCTGCCATGTCTGCCAGGAATACTACGTTGATTACAACCGCAACTTGGGAGGCC
TGGTGATCATCAACGAGTATGGCTCGTGTACCTGCCACCAGCAGCCCGAGGGAAATGCGAGGTGTGATTTGCC
CAGTGGCTCTCAACCCATGCGCTACCAAAATACGCTGGGCGAGCCGGGACGGGCGGGGACCCAGGCTGGGGT
CTCCTTGTCTGTGCTCTGATATGCTCCTTGAAGTAACTTAAAGGGATCTCTCCAGAGACTTGACATTTTAG
TTTTTGTGTCTTAAAACAAAAGCGAATTAACACAAACAAAACCCACCCACAACCTTCAGGACAGTCT
TATCTTAAATTTCAATATGAGAATCCTTCT
AAAGGTGGCCATAAGACAGAGAGAGAATAATCGTGTCTTTGTTTTATGCTACTCCTCCACCTGCCATGATTA
AACATCATGTATGTAGAAGATCTTAAGTCCATACGCTTTTCAAGAGACCATTGGAAAGAGGAATCTGCAATC
TGGGAGCTTAAGAGCAAATGATGACCATAGAAAGCTATGTTCTTACTTGTGTGTGTGTGTGTGTGTGTGTGT
TTGTGTGTCTTTGTAGGCAAGCAAAGCTTGTCTACACAAACGGGAATTTAGCTCAGATCATTTTCATGCCCTGT
GCCTCTAGCTCTGGAGATTGGTGGGGGGAGGTGGGGGGAAACGGCAGGAATAAGGGAAAGTGGTAGTTTTAACT
AAGTTTTGTAACTTGAATCTTTCTTTCTCAATTAATATCTTTAAGCTCAAGAACTTGTCTGACC
CCTTAAGCAAACCTAAGCATTTAAAAGAGAATCTAATTTTTAAAGGTGTAGCACCTTTTTTTTTATCTTC
CCACAGAGGGTCTAATCTCATTATGCTGTGCTATCTGAAAAGAACTTAAAGCCCAATTCAGCTCTCGTCTG
GGCATTGTGATGGATTGACCCCTCATTGTCAGTACCTTCCAGCTGATTAAGTTTCAAGCAGTGGTATTGAGGTT
TTTCGAAATTTATATAGAAAAGAAAGTCTTTTACATGACAAATGACACTCTCACACAGCTTACCCCTAGTA
GTTTTTGTAGGTTGGACAGAGGAAGCAGGTTAATGAGACCTGTCTCTGCTGCACTCAGAAAAAATAGGCAGT
CCCTGATGCTCAGATCTTAGCCCTGATATTAATAGTTGAGACCCTACCCACAATGCAGCCTATACTCCCAAG
ACTACAAAGTTACCATCGCAAAGGAAAGGTTATTCAGTAAAAGGAAATAGTTTTCTCAACCATTTAAAATAT
TCTTCTGAATCATCAAAGTAGAAGGCCCAACCTTTCTCTCTGCTTCAAGAAAGGCAGACATTTGGTATG
ATTTAGCATCAACAACATTTATGAGTATATGTAAGTAAATCAGAGGGGCAATGCCACTTGTATTCTCCCA
AGTTTTCCAAAGCAAGTACACACAGATCTCTGGTAGGATTAGGGGCCACTTGTGTTTTCCGGCTATTTTAGTCGA
CTTGTACGAAGTTTGTATGCTAGCTCTATCTGACATGGCCAGTAGAACAGGGCATTTGATGGATCACATGAGAT
GGTAGAAGGAACATCATACATACCCCTCTCACAGAGAAAATATCAAAGAACAGAAATTAATCTGTTTTGG
AGCAAGAGTGTCAATGTTTCAGGGTAGTCAAATAAACATAAATTATCTCTCTAGATGAGTGGCGATGTTG
CTGATTTGGGCTGCCATTGACAGAATGTCAAATAAAAGGAATTAGCTAGAATATGACATTAATGTGCTT
CTGAAATATATTTGAGATAGGTTAGAATGTCA

FIGURE 158

MDFLLGLCLYWLLRRPSGVVLCLLGACFQMLPAAPSGCPQLCRCEGRLLYCEALNLTEAPHNLSGLLGLSLRY
NSLSELRAGQFTGLMQLTWLYLDHNNHICSVQGDFAFQKLRVVKELTLSSNQITQLPNTTFRPMPNLRSDLSYNK
LQALAPDLFHGLRKLTLHMRANAIQFVVPVRFQDCRSLKFLDIGYNQLKSLARNSFAGLFKLTLEHLEHNDLV
KVNFAHFPRLLSLHSLCLRRNKVAIVVSSLDWVWNLEKMDLSGNEI EYMEPHVFETVPHIQSLQLDSNRLTYIE
PRILNSWKS LTSITLAGNLWDCGRNVCALASWLSNFQGRYDGNLQCASPEYAQGEDVLDVYAFHLCEDGA EPT
SGHLLSAVTNRSDLGPPASSATTLADGGEGQHDGTFEPATVALPGGEHAENAVQIHKVVTGTMALIFSF LIVVL
VLYVSWKCFPASLRQLRQCFVTQRRKQKQKQTMHQMAAMSAQEY YVDYKPNHIEGALVI INEYGSCTCHQOPAR
ECEV

FIGURE 159

CAGAGAGGAGGCTTTGGGAATTGTCCAGCAGAAACAGAGAAGTCTGAGGTGGTGTCAAGACA
AAAGATGCCTTCAGCTTTGGAAACTTGTTCTCCTGTGCGGCGTGCTCACTGGGACCTCAGAGTCT
CTTCTTGACAATCTTGGCAATGACCTAAGCAATGTCGTGGATAAGCTGGAACCTGTTCTTCA
CGAGGGACTTGAGACAGTTGACAATACTCTTAAAGGCATCCTTGAGAAACTGAAGGTCGACC
TAGGAGTGCTTCAGAAATCCAGTGCTTGGCAACTGGCCAAGCAGAAGGCCAGGAAGCTGAG
AAATTGCTGAACAATGTCATTTCTAAGCTGCTTCCAACAAACACGGACATTTTTGGGTTGAA
AATCAGCAACTCCCTCATCCTGGATGTCAAAGCTGAACCGATCGATGATGGCAAAGGCCTTA
ACCTGAGCTTCCCTGTCACCGCGAATGTCACTGTGGCCGGGCCATCATTGGCCAGATTATC
AACCTGAAAGCCTCCTTGGACCTCCTGACCGCAGTCACAATTGAAACTGATCCCCAGACACA
CCAGCCTGTTGCCGTCCTGGGAGAATGCGCCAGTGACCCAACCAGCATCTCACTTTCCTTGC
TGGACAAACACAGCCAAATCATCAACAAGTTCGTGAATAGCGTGATCAACACGCTGAAAAGC
ACTGTATCCTCCCTGCTGCAGAAGGAGATATGTCCACTGATCCGCATCTTCATCCACTCCCT
GGATGTGAATGTCATTCAGCAGGTCGTCGATAATCCTCAGCACAAAACCCAGCTGCAAACCC
TCATCTGAAGAGAGACGAATGAGGAGGACCACTGTGGTGCATGCTGATTGGTTCCCAGTGGCT
TGCCCCACCCCTTATAGCATCTCCCTCCAGGAAGCTGCTGCCACCACCTAACCAGCGTGAA
AGCCTGAGTCCCACCAGAAGGACCTTCCCAGATACCCCTTCTCCTCACAGTCAGAACAGCAG
CCTCTACACATGTTGTCCTGCCCTGGCAATAAAGGCCCATTTCTGCACCCTTAA

FIGURE 160

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA59622
><subunit 1 of 1, 249 aa, 1 stop
><MW: 27011, pI: 5.48, NX(S/T): 2
MLQLWKLVLCCGVLGTSESLLDNLGNDLSNVVDKLEPVLHEGLETVDNTLKGILEKLV
DLGVLQKSSAWQLAKQKAQEAEKLLNNVISKLLPTNTDIFGLKISNSLIIDVKAEPIDG
KGLNLSFPVTANVTVAGPIIGQIINLKASLDLLTAVTIETDPQTHQPVAVLGECASDPTS
ISLSLLDKHSQIINKFVNSVINTLTKSTVSSLLQKEICPLIRIFIHSLDVNVIQQVVDNPQ
HKTQLQTLI
```

Important features:

Signal peptide:

Amino acids 1-15

N-glycosylation sites:

Amino acids 124-128;132-136

N-myristoylation sites:

Amino acids 12-18;16-22;26-32;101-107;122-128;141-147

Leucine zipper pattern:

Amino acids 44-66

FIGURE 161

CAGCCACAGACGGGTCATGAGCGCGGTATTACTGCTGGCCCTCCTGGGGTTCATCCTCCCAC
TGCCAGGAGTGCAGGCGCTGCTCTGCCAGTTTGGGACAGTTCAGCATGTGTGGAAGGTGTCC
GACCTACCCCGGCAATGGACCCCTAAGAACACCAGCTGCGACAGCGGCTTGGGGTGCCAGGA
CACGTTGATGCTCATTGAGAGCGGACCCCAAGTGAGCCTGGTGTCTCCAAGGGCTGCACGG
AGGCCAAGGACCAGGAGCCCCGCGTCACTGAGCACC GGATGGGCCCCCGGCTCTCCCTGATC
TCTTACACCTTCGTGTGCCGCCAGGAGGACTTCTGCAACAACCTCGTTAACTCCCTCCCGCT
TTGGGCCCCACAGCCCCCAGCAGACCCAGGATCCTTGAGGTGCCAGTCTGCTTGTCTA'TGG
AAGGCTGTCTGGAGGGGACAACAGAGAGATCTGCCCAAGGGGACCACACACTGTTATGAT
GGCTCCTCAGGCTCAGGGGAGGAGGCATCTTCTCCAATCTGAGAGTCCAGGGATGCATGCC
CCAGCCAGGTTGCAACCTGCTCAATGGGACACAGGAAATTGGGCCCGTGGGTATGACTGAGA
ACTGCAATAGGAAAGATTTTCTGACCTGTCAATCGGGGGACCACCATTATGACACACGGAAAC
TTGGCTCAAGAACCCACTGATTGGACCACATCGAATAACCGAGATGTGCGAGGTGGGGCAGGT
GTGTCAGGAGACGCTGCTGCTCATAGATGTAGGACTCACATCAACCCTGGTGGGGACAAAAG
GCTGCAGCACTGTTGGGGCTCAAAATTCCCAGAAGACCACCATCCACTCAGCCCCCTCTGGG
GTGCTTGTGGCCTCCTATACCCACTTCTGCTCCTCGGACCTGTGCAATAGTGCCAGCAGCAG
CAGCGTTCTGCTGAACTCCCTCCCTCCTCAAGCTGCCCCCTGTCCCAGGAGACCGGCAGTGT
CTACCTGTGTGCAGCCCCCTTGGAAACCTGTTCAAGTGGCTCCCCCGAATGACCTGCCCCAGG
GGCGCCACTCATTGTTATGATGGGTACATTCATCTCTCAGGAGGTGGGCTGTCCACCAAAT
GAGCATTACAGGGCTGCGTGGCCCAACCTTCCAGCTTCTTGTGTAACACACCAGACAAATCG
GGATCTTCTCTGCGCGTGAGAAGCGTGATGTGCAGCCTCCTGCCTCTCAGCATGAGGGAGGT
GGGGCTGAGGGCCTGGAGTCTCTCACTTGGGGGGTGGGGCTGGCACTGGCCCCAGCGCTGTG
GTGGGGAGTGGTTTGGCCCTTCTGCTTAACTCTATTACCCCCACGATTCTTACCGCTGCTGA
CCACCCACACTCAACCTCCCTCTGACCTCATAACCTAATGGCCTTGGACACCAGATTCTTTC
CCATTCTGTCCATGAATCATCTTCCCCACACACAATCATTATATCTACTCACCTAACAGCA
ACACTGGGGAGAGCCTGGAGCATCCGGACTTGGCCCTATGGGAGAGGGGACGCTGGAGGAGTG
GCTGCATGTATCTGATAATACAGACCCTGTCCTTTCA

FIGURE 162

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA59847
><subunit 1 of 1, 437 aa, 1 stop
><MW: 46363, pI: 6.22, NX(S/T): 3
MSAVLLLLALLGFILPLPGVQALLCQFGTVQHVKVSDLPQWTPKNTSCDSGLGCQDTLM
LIESGPQVSLVLSKGCTEAKDQEPRVTEHRMGPGLSLISYTFVCRQEDFCNNLVNSLPLW
APQPPADPGSLRCPVCLSMEGCLEGTTEEICPKGTTHCYDGLLRLRGGGIFSNLRVQGCM
PQPGCNLLNGTQEIGPVGMTENCNRKDFLTCHRGTTIMTHGNLAQEPTDWTTSNTEMCEV
GQVCQETLLLIDVGLTSTLVGTKGCSTVGAQNSQKTTIHSAPPGVLVASYTHFCSSDLCN
SASSSVLLNSLPPQAAPVPGDRQCPTCVQPLGTCSSGSPRMTCPRGATHCYDGYIHLG
GGLSTKMSIQGCVAQPSSFLLNHTRQIGIFSAREKRDVQPPASQHEGGGAEGLESLTWGV
GLALAPALWVGVCPCSC
```

Important features of the protein:

Signal peptide:

Amino acids 1-15

Transmembrane domain:

Amino acids 243-260

N-glycosylation sites:

Amino acids 46-50;189-193;382-386

Glycosaminoglycan attachment sites:

Amino acids 51-55;359-363

N-myristoylation sites:

Amino acids 54-60;75-81;141-147;154-160;168-174;169-175;
198-204;254-260;261-267;269-275;284-290;333-339
347-353;360-366;361-367;388-394;408-414;419-425

FIGURE 164

MMVALRGASALLVLFLLAFLPPPQCTQDPAMVHYIYQRFVLEQGLEKCTQATRAYIQEFQEFKSNISVMLGRC
QTYTSEYKSAVGNLALRVERAQREIDYIQYLREADECEIVEDKTLAEMLLQEAEKKIRTLNASCNDMLMGI
KSLKIVKKMMDTHGSWMKDAVYNPKVYLLIGSRNNTVWEFANIRAFMEDNTKPAPRKQILTLSWQGTGQVIYK
GFLFFHNQATSNEIIKYNLQKRTVEDRMLLPGGVGRALVYQHSPTYIDLAVDEHGLWAIHSGPGTHSHLVLT
IEPGTIGVEHSWDTPCRSQDAEASFLLCGVLYVVYSTGGQGPHRITCIYDPIGTISEEDLPNLFPPKRPRSHSM
IHYNPRDKQLYAWNEGNQIIYKLQTKRKLPLK

FIGURE 165

TGGCCTCCCCAGCTTGCCAGGCACAAGGCTGAGCGGGAGGAAGCGAGAGGCATCTAAGCAGGCAGTGTGTTTGCC
TTCACCCCCAAGTGACCATGAGAGGGTGCCACGCGAGTCTCAATCATGCTCCTCCTAGTAACTGTGTCTGACTGTG
CTGTGATCACAGGGGCCTGTGAGCGGGATGTCCAGTGTGGGGCAGGCACCTGCTGTGCCATCAGCCTGTGGCTT
CGAGGGCTGCGGATGTGCACCCCCGCTGGGGCGGGAAGGCGAGGAGTGCCACCCCGGCAGCCACAAGGTCCCCTT
CTTCAGGAAACGCAAGCACCACACCTGTCTTGCTTGCCCAACCTGCTGTGCTCCAGGTCCCAGGCAGGCAGGT
ACCGCTGCTCCATGGACTTGAAGAACATCAATTTTTTAGGGCGCTTGCCTGGTCTCAGGATACCCACCATCCTTTT
CCTGAGCACAGCCTGGATTTTTATTCTGCCATGAAACCCAGCTCCCATGACTCTCCCAGTCCCTACACTGACT
ACCTGATCTCTCTGTCTAGTACGCACATATGCACACAGGCAGACATACCTCCCATCATGACATGGTCCCCAG
GCTGGCCTGAGGATGTACAGCTTGAGGCTGTGGTGTGAAAGGTGGCCAGCCTGGTTCTCTCCCTGCTCAGGC
TGCCAGAGAGGTGGTAAATGGCAGAAAGGACATTCCTCCCTCCCAGGTGACCTGCTCTCTTCCCTGGGC
CCTGCCCCCTCCCCACATGTATCCCTCGGTCTGAATTAGACATTCTGGGCACAGGCTCTGGGTGCATTGCT
CAGAGTCCCAGGTCTGGCCTGACCCTCAGGCCCTTACGTGAGGTCTGTGAGGACCAATTTGTGGGTAGTTCA
TCTTCCCTCGATTGGTTAACTCCTTAGTTTCAGACCACAGACTCAAGATTGGCTCTTCCCAGAGGGCAGCAGAC
AGTCACCCCAAGGCAGGTGTAGGGAGCCCAGGGAGGCCAATCAGCCCCCTGAAGACTCTGGTCCCAGTCAGCCT
GTGGCTTGTGGCCTGTGACCTGTGACCTTCTGCCAGAATTGTATGCCCTCTGAGGCCCTCTTACCACACTTT
ACCAGTTAACCCTGAAGCCCCCAATTCCCACAGCTTTCCATTAAAATGCAAATGGTGGTGGTTCAATCTAAT
CTGATATTGACATATTAGAAGGCAATTAGGGTGTTCCTTAAACAACCTCTTTCCAAGGATCAGCCCTGAGAGC
AGGTTGGTGACTTTGAGGAGGGCAGTCCTCTGTCCAGATTGGGGTGGGAGCAAGGGACAGGGAGCAGGGCAGGG
GCTGAAAGGGGCACTGATTCAGACCAGGGAGGCAACTACACACCAACATGCTGGCTTTAGAATAAAAGCACCAA
CTGAAAAAA

FIGURE 166

MRGATRVSIMLLLVTVSDCAVITGACERDVQCGAGTCCAISLWLRGLRMCTPLGREGECHPGSHKVPFFRKRK
HHTCPCLPNLLCSRFPDGRYRCSMDLKNINF

Important feratures:

Signal peptide:
amino acids 1-19

Tyrosine kinase phosphorylation site:
amino acids 88-95

N-myristoylation sites:
amino acids 33-39, 35-41, 46-52

FIGURE 167

AACTCAAACCTCTCTCTGGGAAAACGCGGTGCTTGCTCCTCCCGGAGTGGCCTTGGCAGGGTGTGGAGCCC
TCGGTCTGCCCCGTCCGGTCTCTGGGGCCAAGGCTGGGTTCCCTCATGTATGGCAAGAGCTCTACTCGTGCGG
TGCTTCTTCTCCTTGGCATAACAGCTCACAGCTCTTTGGCCTATAGCAGCTGTGGAAATTTATACCTCCCGGGT
CTGGAGGCTGTTAATGGGACAGATGCTCGGTTAAAATGCACTTTCTCCAGCTTTGCCCTGTGGGTGATGCTCT
AACAGTGACCTGGAATTTTCGTCTCTAGACGGGGGACCTGAGCAGTTGTATTCTACTACCACATAGATCCCT
TCCAACCCATGAGTGGGCGGTTAAGGACCGGGTGTCTTGGGATGGGAATCCTGAGCGGTACGATGCCTCCATC
CTTCTCTGAAACTGCAGTTCGACGACAATGGGACATACACCTGCCAGGTGAAGAACCCACCTGATGTTGATGG
GGTGATAGGGGAGATCCGGCTCAGCGTCGTGCACACTGTACGCTTCTCTGAGATCCACTTCTGGCTCTGGCCA
TTGGCTCTGCCTGTGCACTGATGATCATAATAGTAATTGTAGTGGTCCCTCTCCAGCATTACCGAAAAAGCGA
TGGGCCGAAAGAGCTCATAAAGTGGTGGAGATAAAATCAAAGAAGAGGAAAGGCTCAACCAAGAGAAAAAGGT
CTCTGTTATTTAGAAGACACAGACTTAACAATTTTAGATGGAAGCTGAGATGATTTCCAAGAACAAAGAACCTA
GTATTTCTGAAGTTAATGGAAACTTTTCTTTGGCTTTTCCAGTTGTGACCCGTTTTCCAACCAGTTCTGCAGC
ATATTAGATTCTAGACAAGCAACACCCCTCTGGAGCCAGCACAGTGTCTCCATATACCAGTCATACACAGC
CTCATTATTAAGGTCTTATTTAATTTTCAGAGTGTAAATTTTTTCAAGTGTCTATTAGTTTTATAAACAAGAAG
CTACATTTTTGCCCTTAAGACACTACTTACAGTGTATGACTTGTATACACATATATTGGTATCAAAGGGGATA
AAAGCCAATTTGTCTGTTACATTCCTTTCACGTATTTCTTTAGCAGCACTTCTGCTACTAAAGTTAATGTGT
TTACTCTCTTCCCTTCCACATTTCTCAATTTAAAGGTGAGCTAAGCCTCCTCGGTGTTTCTGATTAACAGTAAA
TCCTAAATTCAAACTGTTAAATGACATTTTATTTTATGTCTCTCCTTAACTATGAGACACATCTGTTTTAC
TGAATTTCTTTCAATATTCCAGGTGATAGATTTTTGTCTG

FIGURE 168

MYGKSSTRAVLLLLLGIQLTALWPIAAVEIYTSRVLEAVNGTDARLKCTFSSFAPVGDALVTWNFRPLDGGPEQ
FVFYYHIDPFQPMSEGRKDRVSWDGNPERYDASILLWKLQFDDNGTYTCQVKNPPDVDGVIGEIRLSVVHTVRF
SEIHFLALAIQSACALMIIVVVVLFQHYRKKRWAERAHKVVEIKSKEEERLNQEKKVSVYLEDTD

FIGURE 169

GAGCGAACATGGCGAGCGCGTTGGCGGTTTTGGTGTGTCTCTGTGACCATGGTGGTGGCGCTG
CTCATCGTTTTGCGACGTTCCCTCAGCCTCTGCCCAAAGAAAGAAGGAGATGGTGTATCTGA
AAAGGTTAGTCAGCTGATGGAATGGACTAACAAAAGACCTGTAATAAGAATGAATGGAGACA
AGTTCCGTCGCCTTGTGAAAGCCCCACCGAGAAATTACTCCGTTATCGTCATGTTCACTGCT
CTCCAAGTGCATAGACAGTGTGTCGTTTTGCAAGCAAGCTGATGAAGAATCCAGATCCTGGC
AAACTCCTGGCGATACTCCAGTGCATTACCAACAGGATATTTTTTGGCCATGGTGGATTTTG
ATGAAGGCTCTGATGTATTTTCAGATGCTAAACATGAATTCAGCTCCAACCTTTCATCAACTTT
CCTGCAAAAGGGAAACCCAAACGGGGTGATACATATGAGTTACAGGTGCGGGGTTTTTCAGC
TGAGCAGATTGCCCGGTGGATCGCCGACAGAAGCTGATGTCAATATTAGAGTGATTAGACCCC
CAAAATATGCTGGTCCCCTTATGTTGGGATTGCTTTTGGCTGTTATTGGTGGACTTGTGTAT
CTTCGAAGAAGTAATATGGAATTTCTCTTTAATAAACTGGATGGGCTTTTGCAGCTTTGTG
TTTTGTGCTTGCTATGACATCTGGTCAAATGTGGAACCATATAAGAGGACCACCATATGCC
ATAAGAATCCCCACACGGGACATGTGAATTATATCCATGGAAGCAGTCAAGCCCAGTTTGTA
GCTGAAACACACATTTGTTCTTCTGTTAATGGTGGAGTTACCTTAGGAATGGTGTCTTTTATG
TGAAGCTGCTACCTCTGACATGGATATTGGAAAGCGAAAGATAATGTGTGTGGCTGGTATTG
GACTTGTGTATTATTCTTCAGTTGGATGCTCTCTATTTTTTAGATCTAAATATCATGGCTAC
CCATACAGCTTTCTGATGAGTTAAAAAAGGTCAGAGATATATAGACTGGAGTACTGGAA
ATTGAAAACGAAAATCGTGTGTGTTTTGAAAAGAAGAATGCAACTGTATATTTTTGTATTAC
CTTTTTTTTTCAAGTGATTTAAATAGTTAATCATTTAACCAGAAAGATGTGTAGTGCCTTA
ACAAGCAATCCTCTGTCAAAATCTGAGGTATTTGAAAATAATTATCCTCTTAACCTTCTCTT
CCCAGTGAACCTTATGGAACATTTAATTTAGTACAATTAAGTATATTATAAAAATTGTAAAA
CTACTACTTTGTTTTAGTTAGAACAAAGCTCAAACTACTTTAGTTAACTTGGTCATCTGAT
TTTTATATTGCCTTATCCAAAGATGGGGAAAGTAAGTCCTGACCAGGTGTTCCACATATGCC
TGTTACAGATAACTACATTAGGAATTCATTCTTAGCTTCTTCATCTTGTGTGGATGTGTAT
ACTTTACGCATCTTTCCTTTTGGAGTAGAGAAATTATGTGTGTCATGTGGTCTTCTGAAAATG
GAACACCATTCTTCAGAGCACACGTCTAGCCCTCAGCAAGACAGTTGTTTCTCCTCCTCCTT
GCATATTTCTACTGCGCTCCAGCCTGAGTGATAGAGTGAGACTCTGTCTCAAAAAAAGTA
TCTCTAAATACAGGATTATAATTTCTGCTTGAGTATGGTGTAACTACCTTGTATTTAGAAA
GATTTTCAGATTCATTCCATCTCCTTAGTTTTCTTTTAAAGGTGACCCATCTGTGATAAAAATA
TAGCTTAGTGCTAAAATCAGTGTAACTTATACATGGCCTAAAATGTTTCTACAAATTAGAGT
TTGTCACTTATTCCATTTGTACCTAAGAGAAAAATAGGCTCAGTTAGAAAAGGACTCCCTGG
CCAGGCGCAGTGACTTACGCCTGTAATCTCAGCACTTTGGGAGGCCAAGGCAGGCAGATCAC
GAGGTCAGGAGTTCGAGACCATCCTGGCCAACATGGTGAACCCCGTCTCTACTAAAAATAT
AAAAATTAGCTGGGTGTGGTGGCAGGAGCCTGTAATCCCAGCTACACAGGAGGCTGAGGCAC
GAGAATCACTTGAACCTCAGGAGATGGAGGTTTTCAGTGAGCCGAGATCACGCCACTGCACTCC
AGCCTGGCAACAGAGCGGAGACTCCATCTCAAAAAAAAAAAAAA

FIGURE 170

MAARWRFWCVSVTMVVALLIVCDVPSASAQRKKEMVLSEKVSQLMWETNKRVPVIRMNGDKFR
RLVKAPPRNYSVIVMFTALQLHRQCVVCKQADEEFQILANSWRYSSAFTNRIFFAMVDFDEG
SDVFQMLNMNSAPTFINFPKGGKPKRGDTYELQVRGFSAEQIARWIADRTDVNIRVIRPPNY
AGPLMLGLLLAVIGGLVYLRRSNMEFLFNKTGWAFALCFVLAMTSGQMWNHIRGPPYAHKN
PHTGHVNYIHGSSQAQFVAETHIVLLFNNGVTLGMVLLCEAATSMDMIGKRKIMCVAGIGLV
VLFFSWMLSIFRSKYHGYPSFLMS

Signal peptide:

amino acids 1-29

Transmembrane domains:

amino acids 183-205, 217-237, 217-287, 301-321

FIGURE 171

CTCCACTGCAACCACCCAGAGCCATGGCTCCCCGAGGCTGCATCGTAGCTGTCTTTGCCATTTTCTGCATCTCC
AGGCTCCTCTGCTCACACGGAGCCCCAGTGGCCCCCATGACTCCTTACCTGATGCTGTGCCAGCCACACAAGAG
ATGTGGGGACAAGTTCTACGACCCCTGCAGCACTGTTGCTATGATGATGCCGTGCTGCCCTGGCCAGGACCC
AGACGTGTGGAAACTGCACCTTCAGAGTCTGCTTTGAGCAGTGCTGCCCCTGGACCTTCATGGTGAAGCTGATA
AACCAGAAGTGGGACTCAGCCCGGACCTCGGATGACAGGCTTTGTGCGAGTGTGAGCTAATGGAACATCAGGGG
AACGATGACTCCTGGATTCTCCTTCTGGGTGGGCCTGGAGAAAGAGGCTGGTGTACCTGAGATCTGGGATGC
TGAGTGGCTGTTTGGGGCCAGAGAAACACACACTCAACTGCCCACTTCATTCTGTGACCTGTCTGAGGCCAC
CCTGCAGTGCCTGAGGAGGCCACAGGTCCCCTTCTAGAATTCTGGACAGCATGAGATGCCGTGTGCTGATGG
GGCCCAGGGACTCTGAACCTCCTGATGACCCCTATGGCCAACATCAACCCGGCACCACCCCAAGGCTGGCTG
GGGAACCCCTCACCCCTTCTGTGAGATTTTCCATCATCTCAAGTTCTCTTCTATCCAGGAGCAAGCACAGGATC
ATAATAAATTTATGTACTTTATAAATGAAAA

FIGURE 172

MAPRGCIVAVFAIFCISRLLC SHGAPVAPMTPYLMLCQPHKRCGDKFYDPLQHCCYDDAVVPLARTQTCGNCTF
RVCFEQCCPWTFMVKLINQNCDSARTSDDRLCRSVS

Important features:

Signal peptide:

amino acids 1-24

FIGURE 173

GGGGGCGGGTGCCTGGAGCACGGCGCTGGGGCCGCCCGCAGCGCTCACTCGCTCGCACTCAG
TCGCGGGAGGCTTCCCCGCGCCGGCCGCGTCCC GCCCGCTCCCCGGCACCAGAAAGTTCCTCT
GCGCGTCCGACGGCGACATGGGCGTCCCCACGGCCCTGGAGGCCGGCAGCTGGCGCTGGGGA
TCCCTGCTCTTCGCTCTCTTCTGGCTGCGTCCCTAGGTCCGGTGGCAGCCTTCAAGGTGCG
CACGCCGTATTCCCTGTATGTCTGTCCCGAGGGGCAGAACGTCACCCTCACCTGCAGGCTCT
TGGGCCCTGTGGACAAAGGGCACGATGTGACCTTCTACAAGACGTGGTACCGCAGCTCGAGG
GGCGAGGTGCAGACCTGCTCAGAGCGCCGGCCCATCCGCAACCTCACGTTCCAGGACCTTCA
CCTGCACCATGGAGGCCACCAGGCTGCCAACACCAGCCACGACCTGGCTCAGCGCCACGGGC
TGGAGTCGGCCTCCGACCACCATGGCAACTTCTCCATCACCATGCGCAACCTGACCCTGCTG
GATAGCGGCTCTACTGCTGCCTGGTGGTGGAGATCAGGCACCACCCTCGGAGCACAGGGT
CCATGGTGCCATGGAGCTGCAGGTGCAGACAGGCAAAGATGCACCATCCAACCTGTGTGGTGT
ACCCATCCTCCTCCCAGGATAGTGAAAACATCACGGCTGCAGCCCTGGCTACGGGTGCCTGC
ATCGTAGGAATCCTCTGCCTCCCCCTCATCCTGCTCCTGGTCTACAAGCAAAGGCAGGCAGC
CTCCAACCGCCGTGCCAGGAGCTGGTGC GGATGGACAGCAACATTCAAGGGATTGAAAACC
CCGGCTTTGAAGCCTCACCACTGCCAGGGGATACCCGAGGCCAAAGTCAGGCACCCCTG
TCCTATGTGGCCCAGCGGCAGCCTTCTGAGTCTGGGCGGCATCTGCTTTCGGAGCCCAGCAC
CCCCCTGTCTCCTCCAGGCCCGGAGACGCTTCTTCCCATCCCTGGACCCTGTCCCTGACT
CTCCAAACTTTGAGGTCATCTAGCCCAGCTGGGGGACAGTGGGCTGTTGTGGCTGGGTCTGG
GGCAGGTGCATTTGAGCCAGGGCTGGCTCTGTGAGTGGCTCCTTGGCTCGGCCCTGGTTC
CCTCCCTCCTGCTCTGGGCTCAGATACTGTGACATCCCAGAAGCCCAGCCCCTCAACCCCTC
TGGATGCTACATGGGGATGCTGGACGGCTCAGCCCCTGTTCCAAGGATTTTGGGGTGTGAG
ATTCTCCCCTAGAGACCTGAAATTCACCAGCTACAGATGCCAAATGACTTACATCTTAAGAA
GTCTCAGAACGTCCAGCCCTCAGCAGCTCTCGTTCTGAGACATGAGCCTTGGGATGTGGCA
GCATCAGTGGGACAAGATGGACACTGGGCCACCCTCCCAGGCACCAGACACAGGGCACGGTG
GAGAGACTTCTCCCCCGTGGCCGCCTTGGCTCCCCCGTTTTGCCCAGGCTGCTCTTCTGTC
AGACTTCCTCTTTGTACCACAGTGGCTCTGGGGCCAGGCCTGCCTGCCCACTGGCCATCGCC
ACCTTCCCAGCTGCCTCCTACCAGCAGTTTCTCTGAAGATCTGTCAACAGGTTAAGTCAAT
CTGGGGCTTCCACTGCCTGCATTCCAGTCCCAGAGCTTGGTGGTCCCGAAACGGGAAGTAC
ATATTGGGGCATGGTGGCCTCCGTGAGCAAATGGTGTCTTGGGCAATCTGAGGCCAGGACAG
ATGTTGCCCCACCCACTGGAGATGGTGTGAGGGAGGTGGGTGGGGCCTTCTGGGAAGGTGA
GTGGAGAGGGGCACCTGCCCCCGCCCTCCCATCCCCTACTCCCCTGCTCAGCGCGGGCC
ATTGCAAGGGTGCCACACAATGTCTTGTCACCCTGGGACACTTCTGAGTATGAAGCGGGAT
GCTATTA AAAACTACATGGGGAAA

FIGURE 176

MDSLRKMLISVAMLGAGAGVGYALLVIVTPGERRKQEMLKEMPLQDPRSREEAARTQQLLLATLQEATTQENV
AWRKNWMVGGEGGASGRSP

Important features:

Signal peptide:

amino acids 1-18

FIGURE 177

GCCAGGCAGGTGGGCCTCAGGAGGTGCCTCCAGGCGGCCAGTGGGCCTGAGGCCCCAGCAAG
GGCTAGGGTCCATCTCCAGTCCCAGGACACAGCAGCGGCCACCATGGCCACGCCTGGGCTCC
AGCAGCATCAGAGCAGCCCCCTGTGGTTGGCAGCAAAGTTCAGCTTGGCTGGGCCCGCTGTGA
GGGGCTTCGCGCTACGCCCTGCGGTGTCCCGAGGGCTGAGGTCTCCTCATCTTCTCCCTAGC
AGTGGATGAGCAACCCAAACGGGGGCCCCGGGGAGGGGAACCTGGCCCCGAGGGAGAGGAACCCC
AAAGCCACATCTGTAGCCAGGATGAGCAGTGTGAATCCAGGCAGCCCCCAGGACCGGGGAGG
CACAGGTGGCCCCCACCACCCGGAGGAGCAGCTCCTGCCCTGTCCGGGGGATGACTGATTC
TCTCCGCCAGGCCACCCAGAGGAGAAGGCCACCCCGCCTGGAGGCACAGGCCCATGAGGGGC
TCTCAGGAGGTGCTGCTGATGTGGCTTCTGGTGTGGCAGTGGCGGCACAGAGCACGCCTA
CCGGCCCCGGCCGTAGGGTGTGTGCTGTCCGGGCTCACGGGGACCCTGTCTCCGAGTCGTTCCG
TGCAGCGTGTGTACCAGCCCTTCCCTACCACCTGCGACGGGCACCGGGCCTGCAGCACCTAC
CGAACCATCTATAGGACCCTTACCGCCAGCCCTGGGCTGGCCCTGCCAGGCCTCGCTA
CGCGTGCTGCCCGGCTGGAAGAGGACCAGCGGGCTTCCCTGGGGCCTGTGGAGCAGCAATAT
GCCAGCCGCCATGCCGGAACGGAGGGAGCTGTGTCCAGCCTGGCCGCTGCCGCTGCCCTGCA
GGATGGCGGGGTGACACTTGCCAGTCAGATGTGGATGAATGCAGTGCTAGGAGGGGGCGGCTG
TCCCCAGCGCTGCATCAACACCCGCCAGTTACTGGTGCCAGTGTTGGGAGGGGCACAGCC
TGTCTGCAGACGGTACACTCTGTGTGCCCAAGGGAGGGCCCCCAGGGTGGCCCCCAACCCG
ACAGGAGTGGACAGTGCAATGAAGGAAGAAGTGCAGAGGCTGCAGTCCAGGGTGGACCTGCT
GGAGGAGAAGCTGCAGCTGGTGTGGCCCCACTGCACAGCCTGGCCTCGCAGGCACTGGAGC
ATGGGCTCCCGGACCCCGGCAGCCTCCTGGTGCCTCCTTCCAGCAGCTCGGCCGCATCGAC
TCCCTGAGCGAGCAGATTCCTTCCCTGGAGGAGCAGCTGGGGTCCCTGCTCCTGCAAGAAAGA
CTCGTGACTGCCCAGCGCTCCAGGCTGGACTGAGCCCCCTACGCCGCCCTGCAGCCCCCATG
CCCCTGCCCAACATGCTGGGGGTCCAGAAGCCACCTCGGGGTGACTGAGCGGAAGGCCAGGC
AGGGCCTTCCCTCCTTCCCTCCTCCCCTTCCCTCGGGAGGCTCCCCAGACCCTGGCATGGGAT
GGGCTGGGATCTTCTCTGTGAATCCACCCCTGGCTACCCCCACCCTGGCTACCCCAACGGCA
TCCCAAGGCCAGGTGGACCCTCAGCTGAGGGAAGGTACGAGCTCCCTGCTGGAGCCTGGGAC
CCATGGCACAGGCCAGGCAGCCCCGGAGGCTGGGTGGGGCCTCAGTGGGGGCTGCTGCCTGAC
CCCCAGCAATAAAAATGAAACGTG

FIGURE 178

MRGSQEVLLMWLLVLAVGGTEHAYRPGRRVCAVRAHGDPVSESFVQRVYQPFLTTCDGHRAC
STYRTIYRTAYRRSPGLAPARPRYACCPGWKRTSGLPGACGAAICQPPCRNGGSCVQPGRCR
CPAGWRGDTQCSDVDECSARRGGCPQRCINTAGSYWCQCWEGHLSADGTLCVPKGGPPRVA
PNPTGVDSAMKEEVQRLQSRVDLLEEKQLVLAPLHSLASQALEHGLPDPGSLVHSFQQLG
RIDSLSEQISFLEEQLGSCSCKKDS

Signal sequence:

1-19

FIGURE 179

GACAGCTGTGTCTCGATGGAGTAGACTCTCAGAACAGCGCAGTTTGCCCTCCGCTCACGCAG
AGCCTCTCCGTGGCTTCCGCACCTTGAGCATTAGGCCAGTTCTCCTCTTCTCTAATCCAT
CCGTCACCTCTCCTGTCATCCGTTTCCATGCCGTGAGGTCCATTACAGAACACATCC**ATGG**
CTCTCATGCTCAGTTTGGTTCTGAGTCTCCTCAAGCTGGGATCAGGGCAGTGGCAGGTGTTT
GGGCCAGACAAGCCTGTCCAGGCCCTGGTGGGGGAGGACGCAGCATTCTCCTGTTTCTGTC
TCTTAAGACCAATGCAGAGGCCATGGAAGTGCGGTTCTTCAGGGGCCAGTTCTCTAGCGTGG
TCCACCTCTACAGGGACGGGAAGGACCAGCCATTTATGCAGATGCCACAGTATCAAGGCAGG
ACAAAACCTGGTGAAGGATTCTATTGCGGAGGGGCGCATCTCTGAGGCTGGAAAACATTAC
TGTGTTGGATGCTGGCCTCTATGGGTGCAGGATTAAGTCCCAGTCTTACTACCAGAAGGCCA
TCTGGGAGCTACAGTGTGCAGCACTGGGCTCAGTTCTCCTCTCATTTCATCACGGGATATGTT
GATAGAGACATCCAGCTACTCTGTCAGTCCCTCGGGCTGGTTCCCCGGCCACAGCGAAGTG
GAAAGGTCCACAAGGACAGGATTTGTCCACAGACTCCAGGACAAAACAGAGACATGCATGGCC
TGTTTGATGTGGAGATCTCTCTGACCGTCCAAGAGAACGCCGGGAGCATATCCTGTTCCATG
CGGCATGCTCATCTGAGCCGAGAGGTGGAATCCAGGGTACAGATAGGAGATACCTTTTTTCGA
GCCTATATCGTGGCACCTGGCTACCAAAGTACTGGGAATACTCTGCTGTGGCCTATTTTTTTG
GCATTTGTTGGACTGAAGATTTTCTTCTCCAAATTCAGTGGAATAATCCAGGCGGAACTGGAC
TGGAGAAGAAAGCACGGACAGGCAGAATTGAGAGACGCCCGGAAACACGCAGTGGAGGTGAC
TCTGGATCCAGAGACGGCTCACCCGAAGCTCTGCGTTTCTGATCTGAAAACGTAAACCATA
GAAAAGCTCCCCAGGAGGTGCCCTCACTCTGAGAAGAGATTTACAAGGAAGAGTGTGGTGGCT
TCTCAGAGTTTCCAAGCAGGGAAACATTACTGGGAGGTGGACGGAGGACACAATAAAAGGTG
GCGCGTGGGAGTGTGCCGGGATGATGTGGACAGGAGGAAGGAGTACGTGACTTTGTCTCCCG
ATCATGGGTACTGGGTCCTCAGACTGAATGGAGAACATTTGTATTTACATTAATCCCCGT
TTTATCAGCGTCTTCCCCAGGACCCACCTACAAAAATAGGGGTCTTCCCTGGACTATGAGTG
TGGGACCATCTCCTTCTTCAACATAAATGACCAGTCCCTTATTTATACCCTGACATGTCGGT
TTGAAGGCTTATTGAGGCCCTACATTGAGTATCCGTCCTATAATGAGCAAAATGGAACCTCC
ATAGTCATCTGCCAGTCACCCAGGAATCAGAGAAAGAGGCCCTTGGCAAAGGGCCTCTGC
AATCCCAGAGACAAGCAACAGTGAGTCCCTCCTCACAGGCAACCACGCCCTTCTCCCCAGGG
GTGAAATG**TAGG**ATGAATCACATCCCACATTTCTTCTTAGGGATATTAAGGTCTCTCTCCCA
GATCCAAAGTCCCGCAGCAGCCGGCCAAGGTGGCTTCCAGATGAAGGGGGACTGGCCTGTCC
ACATGGGAGTCAGGTGTATGGCTGCCCTGAGCTGGGAGGGGAAGAAGGCTGACATTACATTT
AGTTTGCTCTCACTCCATCTGGCTAAGTGTCTTGAATAACCACCTCTCAGGTGAAGAACC
TCAGGAATTTCCATCTCACAGGCTGTGGTGTAGATTAAGTAGACAAGGAATGTGAATAATGC
TTAGATCTTATTGATGACAGAGTGTATCCTAATGGTTTGTTCATTATATTACACTTCAGTA
AAAAAA

FIGURE 180

MALMLSLVLSLLKLGSGQWQVFGPDKPVQALVGEDAAFSCFLSPKTNAEAMEVRFRRGQFSS
VVHLYRDGKDQPFMQMPQYQGRTKLVKDSIAEGRISLRLENITVLDAGLYGCRISSQSYQK
AIWELQVSALGSVPLISITGYVDRDIQLLCQSSGWFPRTAKWKGPQGDLSTDSRTNRDMH
GLFDVEISLTVQENAGSISCSMRHAHLSREVESRVQIGDTFFEPISWHLATKVLGILCCGLF
FGIVGLKIFFSKFQWKIQAELDWRRKHGQAEIRDARKHAVEVTLDPETAHPKLCVSDLKTVT
HRKAPQEVPHSEKRFRTRKSVVASQS FQAGKHYWEVDGGHNKRWRVGVCRDDVDRRKEYVTLS
PDHGYWVLRNLNGEHL YFTLNPRFISVFPRT PPTKIGVFLDYECGTISFFNINDQSLIYTLTC
RFEGLLRPYIEYPSYNEQNGTPIVICPVTQESEKEASWQRASAI PETSNSSESSQATTPFLP
RGEM

Signal peptide:

amino acids 1-17

Transmembrane domain:

amino acids 239-255

FIGURE 181

GCGATGGTGGCCCCGGTGGCGGTGGCGGGCGGGTTCGGGAGGCTTCCTTGGTGGATTGCAACGAGGAGAAGA
TGACTGACCAACCGACTGGCTGAATGAATGAATGGCGGAGCCGAGCGCGCCATGAGGAGCCTGCCGAGCCTGGG
CGGCCTCGCCCTGTTGTGCTGCGCCGCCGCCCGCCGCCCGCTCGCCTCAGCCGCCCTCGGCGGGGAATGTCACCG
GTGGCGGGGGGCCCGGGGCGAGGTGGACGCGTTCGCCGGGCCCCGGGTTGCGGGGCGAGCCAGCCACCCCTTC
CCTAGGGCGACGGCTCCACAGGCCAGGCCCGAGGACCGGGCCCCCGCGCGCCACCGTCCACCGACCCCTGGC
TGGCACTTCTCCAGCCAGTCCCCGGAGACCACCCTCTTTGGGCGACTGCTGGACCCTCTTCCACCACCTTTC
AGGCGCCGCTCGGCCCTCGCCGACCACCCTCCGGCGCGGGAACGCACTTCGACCACCTCTCAGGCGCCGACC
AGACCCGCGCCGACCACCCTTCGACGACCCTGGCCCCGGCGCCGACCACCCTGTAGCGACCACCGTACCGGC
GCCACGACTCCCCGGACCCCGACCCTCGATCTCCCCAGCAGCAGCAACAGCAGCGTCTCCCCACCCACCTG
CCACCGAGGCCCTCTTCGCCCTCCTCCAGAGTATGTATGTAACCTGCTCTGTGGTGGGAAGCCTGAATGTGAAT
CGCTGCAACCAGACCACAGGGCAGTGTGAGTGTGCGCCAGGTTATCAGGGGCTTACTGTGAAACCTGCAAAGA
GGCCTTTTACCTAAATTACACTTCTGGGCTCTGTGAGCCATGTGACTGTAGTCCACATGGAGCTCTCAGCATA
CGTGCAACAGGTAAGCAACAGAGGGTGGAACTGAAGTTTATTTTATTTTAGCAAGGGAAAAAAAAGGCTGCTA
CTCTCAAGACCATACTGGTTTAAACAAGGAGGATGAGGGTCATAGATTTACAAAATATTTTATATACTTTTA
TTCTCTTACTTTATATGTTATATTTAATGTGAGGATTTAAAAACATCTAATTTACTGATTTAGTTCTTCAAAG
CACTAGAGTCGCCAATTTTCTCTGGGATAATTTCTGTAAATTTTCATGGGAAAAAATTTATGAAGAATAAATCT
GCTTTCTGGAAAGGCTTTTCAGGCATGAAACCTGCTAGGAGGTTTAGAAATGTTCTTATGTTTATTAATATA
TTGGAGTTTGAGGAAATTTGTTGTTTGGTTTATTTTTCTCTAATCAAAATCTACATTTGTTTCTTTGGACA
TCTAAAGCTTAACCTGGGGGTACCCTAATTTATTTAAGTGGTAAGTAGACTGGTTTTACTCTATTTACCAG
TACATTTTGAGACAAAAGTAGATTAAGCAGGAATTATCTTTAACTATTATGTTATTTGGAGGTAATTTAAT
CTAGTGGAATAATGTACTGTTATCTAAGCATTTGCCTTGACTGCACTGAAAGTAATTTCTTTGACCTTATG
TGAGGCACTTGGCTTTTTGTGGACCCCAAGTCAAAAACTGAAGAGACAGTATTAATAATGAAAAAATAATG
ACAGTTTACTCAGTGAACTGGGTATAACCCAAGATCTGCTGCCACTTACGAGCTGTGTTCTTGGGCAAG
TAATTTCTTTCACTGAGCTTGTTCCTCAAGGTTGTTGTGAAGATTAATGAGTTGATATATATAAAATGC
CTAGCACATGTCACTCAATAAATCTGGTTTGTTTTAAATTTCAAAGGAATATTATGGACTGAAATGAGAGAACA
TGTTTTAAGAACCTTTAGCTCCTTGACAAAGAAGTGCTTTATACTTTAGCACTAAATTTTTAAATGCTTTATA
AATGATATTACTGTTATGGAATATTGTATCATATTGTAGTTTATTAATAAATGTAGAAGAGGCTGGGCGGGT
GGCTCACGCCGTGAATCCTAGCACTTTGGGAGGCCAAGGCGGGTGGATCACTTGGAGCCAGGAGTTCTAGATGA
GCCTGGCCAGCACAGTGAACCCCGTCTCTACTAAAAATACAAACAAATTAGCTGGGCGGTGGCAGCACACCT
GTAGTCCCAGTACTCGGGAGGCTGAGGCAGGAGAATCGGTTGAACCCGGGAGGTGGAGGTTGCAGTGAGCTGA
GATCGGCCACTGCACTCCAGCCTGGTGAGAGAGGGAGACTCTGTCTTAAAAAAAATAAAAAAAAAAAAAA

FIGURE 182

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64952
><subunit 1 of 1, 258 aa, 1 stop
><MW: 25716, pI: 8.13, NX(S/T): 5
MRSLSLGGGLALLCCAAAAAASASAASAGNVTGGGGAAGQVDASPGPGLRGEPSHPFPRATA
PTAQAPRTGPPRATVHRPLAATSPAQSPETTPLWATAGPSSTTFQAPLGPSPTTPPAAERTS
TTSQAPTRPAPTTLSTTTGPAPTTVPATTVPAPTTTPRTPTDLPSSSNSSVLPPTPPATEAPS
SPPPEYVCNCSVVGSLNVNRCNQTTGQCECRPGYQGLHCETCKEGFYLNYSGLCQPCDCSP
HGALSIPCNR
```

Important features of the protein:

Signal peptide:

amino acids 1-25

N-glycosylation sites.

amino acids 30-33, 172-175, 195-198, 208-211, 235-238

EGF-like domain cysteine pattern signature.

amino acids 214-226.

FIGURE 183

TGCGGCGCAGTGTAGACCTGGGAGGATGGGCGGCCTGCTGCTGGCTGCTTTTCTGGCTTTGGTCTCGGTGCCCA
GGGCCAGGCCGTGTGGTTGGGAAGACTGGACCCTGAGCAGCTTCTTGGGCCCTGGTACGTGCTTGCCGTGGCC
TCCCGGAAAAGGGCTTTGCCATGGAGAAGGACATGAAGAACGTCGTGGGGTGGTGGTGACCCTCACTCCAGA
AAACAACCTGCGGACGCTGTCTCTCAGCACGGGCTGGGAGGGTGTGACCAGAGTGTGCATGGACCTGATAAAGC
GAAACTCCGATGGGTGTTTGAGAATCCCTCAATAGGCGTGCTGGAGCTCTGGGTGCTGGCCACCAACTTCAGA
GACTATGCCATCATCTTCACTCAGCTGGAGTTCGGGGACGAGCCCTTCAACACCGTGGAGCTGTACAGTCTGAC
GGAGACAGCCAGCCAGGAGGCCATGGGGCTTTCACCAAGTGGAGCAGGAGCCTGGGCTTCTGTACAGTAGC
AGGCCAGCTGCAGAAGGACCTCACCTGTGCTCACAAGATCCTTCTGTGAGTGTGCGTCCCCAGTAGGGATGG
CGCCACAGGGTCTGTGACCTCGGCCAGTGTCACCCACCTCGCTCAGCGGCTCCCGGGGCCAGCACCAGCT
CAGAATAAAGCGATTCCACAGCA

FIGURE 184

MGGLLLAAFLALVSVPRQAQAVWLGRLDPEQLLGPWYVLAVASREKGFAMEKDMKNVVGVVTLTPENNLRTLSS
QHGLGGCDQSVMDLIKRN SGWVFENPSIGVLELWVLATNFRDYAII FTQLEFGDEPFNTVELYSLTETASQEAM
GLFTKWSRSLGFLSQ

Important features:

Signal peptide:
amino acids 1-20

FIGURE 185

GTTCGCAGATGCAGAGGTTGAGGTGGCTGCGGGACTGGAAGTCATCGGGCAGAGGTCTCACAGCAGCCAAGGA
ACCTGGGGCCCGCTCCTCCCCCTCCAGGCCATGAGGATTCTGCAGTTAATCCTGCTTGCTCTGGCAACAGGGC
TTGTAGGGGGAGAGACCAGGATCATCAAGGGGTTTCGAGTGCAAGCCTCACTCCCAGCCCTGGCAGGCAGCCCTG
TTCGAGAAGACGCGGCTACTCTGTGGGGCGACGCTCATCGCCCCAGATGGCTCCTGACAGCAGCCCACTGCCT
CAAGCCCCGCTACATAGTTCACCTGGGGCAGCACAACTCCAGAAGGAGGAGGGCTGTGAGCAGACCCGGACAG
CCACTGAGTCCTTCCCCACCCCGGCTTCAACAACAGCCTCCCAACAAAGACCACCGCAATGACATCATGCTG
GTGAAGATGGCATCGCCAGTCTCCATCACCTGGGCTGTGCGACCCCTCACCTCTCCTCACGCTGTGTCACTGC
TGGCACCAGCTGCCTCATTTCGGCTGGGGCAGCAGTCCAGCCCCAGTTACGCCTGCCTCACACCTTGCGAT
GCGCCAACATCACCATCATTTGAGCACCAGAAGTGTGAGAACGCCCTACCCCGGCAACATCACAGACCCATGGTG
TGTGCCAGCGTGAGGAAGGGGGCAAGGACTCCTGCCAGGGTGACTCCGGGGGCCCTCTGGTCTGTAACCAGTC
TCTTCAAGCATTATCTCCTGGGGCCAGGATCCGTGTGCGATCACCCGAAAGCCTGGTGTCTACACGAAAGTCT
GCAATATGTGGACTGGATCCAGGAGACGATGAAGAACATTAGACTGGACCCACCACAGCCCATCACCC
TCCATTTCCACTTGGTGTGGTTCCTGTTCACTCTGTTAATAAGAAAACCTAAGCCAAGACCCTCTACGAACA
TTCTTTGGGCCTCCTGGACTACAGGAGATGCTGTCACTTAATAATCAACCTGGGGTTCGAAATCAGTGAGACCT
GGATTCAAATTCTGCCTTGAAATATTGTGACTCTGGGAATGACAAACACCTGGTTTGTCTCTGTTGTATCCCCA
GCCCCAAAGACAGCTCCTGGCCATATATCAAGGTTTCAATAAATATTTGCTAAATGAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAA

FIGURE 186

MRILQLILLALATGLVGGETRIIKGFECKPHSQPWQAALFEKTRLLCGATLIAPRWLLTAAHCLKPRYIVHLGQ
HNLQKEEGCEQTRTATESFPHPGFNNSLPNKDHRNDIMLVKMASPVSIWAVRPLTLSSRCVTAGTSCLIISGWG
STSSPQLRLPHTLRCANITIIIEHQKCNAYPGNITDTMVCASVQEGGKDCQGDSCGGPLVCNQSLOGIISWGQD
PCAITRKPGVYTKVCKYVDWIQETMKNN

Important features:

Signal peptide:

amino acids 1-18

Serine proteases, trypsin family, histidine active site.

amino acids 58-63

N-glycosylation sites.

amino acids 99-102, 165-168, 181-184, 210-213

Glycosaminoglycan attachment site.

amino acids 145-148

Kringle domain proteins.

amino acids 197-209, 47-64

Serine proteases, trypsin family, histidine protein

amino acids 199-209, 47-63, 220-243

Apple domain proteins

amino acids 222-249, 189-222

FIGURE 187

GCTCAAGTGCCCTGCCTTGCCCCACCCAGCCAGCCCTGGCCAGAGCCCCCTGGAGAAGGAGC
TCTCTTCTTGCTTGGCAGCTGGACCAAGGGAGCCAGTCTTGGGCGCTGGAGGGCCTGTCTG
ACC**ATGG**TCCCTGCCTGGCTGTGGCTGCTTTGTGTCTCCGTCCCCAGGCTCTCCCCAAGGC
CCAGCCTGCAGAGCTGTCTGTGGAAGTTCCAGAAAATATGGTGGAAATTTCCCTTTATACC
TGACCAAGTTGCCGCTGCCCGTGAGGGGGCTGAAGGCCAGATCGTGTCTGTGAGGGGACTCA
GGCAAGGCAACTGAGGGGCCATTTGCTATGGATCCAGATTCTGGCTTCTGTCTGTGACCAG
GGCCCTGGACCGAGAGGAGCAGGCAGAGTACCAGCTACAGGTCACCCTGGAGATGCAGGATG
GACATGTCTTGTGGGGTCCACAGCCTGTGCTTGTGCACGTGAAGGATGAGAATGACCAGGTG
CCCCATTTCTCTCAAGCCATCTACAGAGCTCGGCTGAGCCGGGGTACCAGGCCTGGCATCCC
CTTCTCTTCCCTGAGGCTTCAGACCGGGATGAGCCAGGCACAGCCAACTCGGATCTTCGAT
TCCACATCCTGAGCCAGGCTCCAGCCCAGCCTTCCCCAGACATGTTCCAGCTGGAGCCTCGG
CTGGGGGCTCTGGCCCTCAGCCCCAAGGGGAGCACCAGCCTTGACCACGCCCTGGAGAGGAC
CTACCAGCTGTTGGTACAGGTCAAGGACATGGGTGACCAGGCCCTCAGGCCACCAGGCCACTG
CCACCGTGGAAGTCTCCATCATAGAGAGCACCTGGGTGTCCCTAGAGCCTATCCACCTGGCA
GAGAATCTCAAAGTCTATACCCGCACCACATGGCCAGGTACACTGGAGTGGGGGTGATGT
GCACTATCACCTGGAGAGCCATCCCCCGGGACCCTTTGAAGTGAATGCAGAGGGAAACCTCT
ACGTGACCAGAGAGCTGGACAGAGAAGCCAGGCCAGTACCTGCTCCAGGTGCGGGCTCAG
AATTCCCATGGCGAGGACTATGCGGGCCCTCTGGAGCTGCACGTGCTGGTGTGATGGATGAGAA
TGACAACGTGCCTATCTGCCCTCCCCGTGACCCACAGTCAGCATCCCTGAGCTCAGTCCAC
CAGGTACTGAAGTGACTAGACTGTGAGCAGAGGATGCAGATGCCCCGGCTCCCCAATTCC
CACGTTGTGTATCAGCTCCTGAGCCCTGAGCCTGAGGATGGGGTAGAGGGGAGAGCCTTCCA
GGTGGACCCCACTTCAGGCAGTGTGACGCTGGGGGTGCTCCCACTCCGAGCAGGCCAGAACA
TCTGCTTCTGGTGTGGCCATGGACCTGGCAGGCGCAGAGGGTGGCTTCAGCAGCACGTGT
GAAGTCGAAGTCGCAGTCACAGATATCAATGATCACGCCCTGAGTTCATCACTTCCCAGAT
TGGGCTATAAGCCTCCCTGAGGATGTGGAGCCCGGGACTCTGGTGGCCATGCTAACAGCCA
TTGATGCTGACCTCGAGCCCGCTTCCGCCTCATGGATTTTGCCATTGAGAGGGGAGACACA
GAAGGGACTTTTGGCCTGGATTGGGAGCCAGACTCTGGGCATGTTAGACTCAGACTCTGCAA
GAACCTCAGTTATGAGGCAGCTCCAAGTCATGAGGTGGTGGTGGTGGTGCAGAGTGTGGCGA
AGCTGGTGGGGCCAGGCCAGGCCCTGGAGCCACCGCCACGGTACTGTGCTAGTGGAGAGA
GTGATGCCACCCCAAGTTGGACCAGGAGAGCTACGAGGCCAGTGTCCCCATCAGTGCCCC
AGCCGGCTCTTTCCTGCTGACCATCCAGCCCTCCGACCCCATCAGCCGAACCTCAGGTTCT
CCCTAGTCAATGACTCAGAGGGCTGGCTCTGCATTGAGAAATCTCCGGGGAGGTGCACACC
GCCAGTCCCTGCAGGGCGCCAGCCTGGGGACACCTACACGGTGTCTGTGGAGGCCAGGA
TACAGCCCTGACTCTTGCCCTGTGCCCTCCCAATACCTCTGCACACCCCGCCAAGACCATG
GCTTGATCGTGAGTGGACCCAGCAAGGACCCCGATCTGGCCAGTGGGACGCTCCCTACAGC
TTCACCCCTGGTCCCAACCCACGGTGAACGGGATTTGGCGCCTCCAGACTCTCAATGGTTC
CCATGCCCTACCTCACCTTGGCCCTGCATTGGGTGGAGCCACGTGAACACATAATCCCCGTGG
TGGTCAGCCACAATGCCAGATGTGGCAGCTCCTGGTTCGAGTGATCGTGTGTGCTGCAAC
GTGGAGGGGACAGTGCATGCGCAAGGTGGGCCGATGAAGGGCATGCCACGAAGCTGTGGC
AGTGGGCATCCTTGTAGGCACCTGGTAGCAATAGGAATCTTCCCTCATCCTCAITTTTACCC
ACTGGACCATGTCAAGGAAGAAGGACCCGGATCAACCAGCAGACAGCGTGGCCCTGAAGGCG
ACTGTCT**TGA**ATGGCCAGGCAGCTCTAGCTGGGAGCTTGGCCTCTGGCTCCATCTGAGTCCC
CTGGGAGAGAGCCAGCACCCCAAGATCCAGCAGGGGACAGGACAGAGTAGAAGCCCCTCCAT
CTGCCCTGGGGTGGAGGCACCATCACCATCACCAGGCATGTCTGCAGAGCCTGGACACCAAC
TTTATGGACTGCCCATGGGAGTGCTCAAATGTCAGGGTGT'TTGCCCAATAATAAAGCCCCA
GAGAACT'GGGCTGGGCCCTATGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAG

FIGURE 188

MVPAWLWLLCVSVPQALPKAQPAELSVVPEVNYGGNFPLYLTKLPLPREGAEGQIVLSGDGSG
KATEGPFAMDPDSGFLLVTRALDREEQAQYQLQVTLEMQDGHVWLGQPVLVHVKDENDQVP
HFSQAIYRARLSRGTRPGIPFLFLEASDRDEPGTANSDLRFHILSQAPAQPSDFMQLPRL
GALALSPKGSTSLDHALERTYQLLVQVKMDGQASGHQATATVEVSIIESTWVSLEPIHLAE
NLKVLYPHHMAQVHWSGGDVHYHLESHPPGPFVNAEGNLYVTRELDREAQAEYLLQVRAQN
SHGEDYAAPLELHVLVMDENDNVPICPPRDPTVSIPELSPPGTEVTRLSAEDADAPGSPNSH
VVYQLLSPEPEDGVEGRAFOVDPTSGSVTLGVLPFRAGQNILLVLLVMDLAGAEGGFSSTCE
VEVAVTDINDHAPEFITSQIGPISLPEDVEPGTLVAMLTAIDADLEPAFRIMDFAIERGDTE
GTFGLDWEPSDGHVRLRLCKNLSYEAPSHEVVVVVQSVAKLVGPGPGGATATVTVLVERV
MPPPKLDQESYEASVPISAPAGSFLLLTIQPSDPISRTLRFSLVNDSEGWLCIEKFSGEVHTA
QSLQGAQPGDYYTVLVEAQDTALTLPVPSQYLCTPRQDHGLIVSGPSKDPDLASGHGPYSF
TLGPNPTVQRDWRLQTLNGSHAYLTLALHWVEPREHIIIPVVVSHNAQMWQLLVRVIVCRCNV
EGQCMRKVGRMKGMPTKLSAVGILVGTLLVAIGIFLILIFTHWTMSRKKDPDQFADSVPLKATV

Signal peptide:

amino acids 1-18

Transmembrane domain:

amino acids 762-784

FIGURE 189

GACTTTGCTTGAATGTTTACATTTTCTGCTCGCTGCTCTACATATCACAATATAGTGTTACGTTTTGTAAAA
CTTTGGGGTGTGAGGAGTTGAGCTTGCTCAGCAAGCCAGCATGGCTAGGATGAGCTTTGTTATAGCAGCTTGCC
AATGGTGCTGGGCCACTAATGACTTCATTAACCGAGTCTCCATACAGAATACTGAGTGCCACAACCTTGC
GTATGTGAAATTCGTCCCTGGTTTACCCACAGTCAACTTACAGAGAAGCCACCCTGTTGATGCAATGACCT
CCGCTTAACAAGGATTCCCAGTAACCTCTCTAGTGACACACAAGTGCTTCTCTTACAGAGCAATAACATCGCGA
AGACTGTGGATGAGCTGCAGCAGCTTTCAACTGACTGAAGTATTTCTCCAAAACACTTTACTAACATT
AAGGAGGTGGGGCTGGCAAACCTAACCAGCTCACACCGCTGCATTTGGAGGAAAATCAGATTACCGAGATGAC
TGATTACTGTCTACAAGACCTCAGCAACCTTCAAGAAGTCTACATCAACCACAACCAATTAGCACTA'TTCTG
CTCATGCTTTTGCAGCTTAAAAATCTATTAAGGCTCCACCTGAACTCCAACAATTTGAAAGTTATTGATAGT
CGCTGGTTTTGATTTACACCCAACTGGAAATTTCTATGATCGGAGAAAACCTGTGATTGGAATTTCTGGATAT
GAACCTCAAACCCCTCGCAAATTTGAGAAGCTTAGTTTTGGCAGGAATGTATCTCACTGATATTCCTGGAAATG
CTTTGGTGGGTCTGGATAGCCTTGAGAGCCTGTCTTTTTATGATAACAACTGGTTAAAGTCCCTCAACTTGCC
CTGCAAAAAGTTCCAAATTTGAAATTTTAGACCTCAACAAAAACCCATTACAAAAATCCAAGAAGGGGACTT
CAAAAATATGCTTCGGTTAAAAGAAGTGGGAATCAACAATATGGGCGAGCTCGTTTTCTGTCGACCGCTATGCCC
TGGATAACTTGCCTGAAGTCAAAAAGCTGGAAGCCACCAATAACCTAAACTCTTTACATCCACCGCTTGCC
TTCCGAAGTGTCCCTGCTCTGGAAAGCTTGATGCTGAACAACAATGCCTTGAATGCCATTTACCAAAAGACAGT
CGAATCCCTCCCAATCTGCGTGAGATCAGTATCCATAGCAATCCCTCAGGTGTGACTGTGTGATCCACTGGA
TTAACTCCAACAAAACCAACATCCGCTTCATGGAGCCCTGTCCATGTTCTGTGCCATGCCGCCGAATATAAA
GGGCACCAGGTGAAGGAAGTTTTAATCCAGGATTCGAGTGAACAGTGCCTCCCAATGATATCTCAGGACAGCTT
CCCAATCGTTTTAAACGTGGATATCGGCACGACGGTTTTCTTAGACTGTGAGCCATGGCTGAGCCAGAACCTG
AAATTTACTGGGTCACTCCCATTTGAAATAAGATAACTGTGGAACCCCTTTAGATAAATAACAAGCTAAGTAGC
GAAGGTACCTTGGAAATACTAACATACAATTTGAAGACTCAGGAAGATACACATGTGTTGCCCAGAATGTCCA
AGGGGCAGACACTCGGGTGGCAACAATTAAGGTTAACGGGACCCTTCTGGATGGTACCAGGTGCTAAAAATAT
ACGTCAAGCAGACAGAATCCCATTCATCTTAGTGTCTGGAAAGTTAATTTCCAATGTCATGACGTCAAACCTA
AAATGGTCTGCTGCCACCATGAAGATTGATAACCCCTCACATAACATATACTGCCAGGGTCCCAGTTCGATGTCCA
TGAATAACAACCTAACGCATCTGCAGCCTTCCACAGATTATGAAGTGTGTCTCACAGTGTCCAATATTCATCAGC
AGACTCAAAGTTCATGCGTAAATGTCAACCAAAAATGCCGCTTCGCGAGTGGACATCTCTGATCAAGAAACC
AGTACAGCCCTTGCTGCAGTAATGGGGTCTATGTTTGGCGTCATTAGCCTTGCCTCCATTGCTGTGACTTTGC
CAAAAGATTTAAGAGAAAAAACTACCACCACTCATTAAAAAGTATATGCAAAAAACCTCTTCAATCCCCTAA
ATGAGCTGTACCCACCACTCATTAACTCTGGGAAGGTGACAGCGAGAAAGACAAAGATGGTTCTGCAGACACC
AAGCCAACCCAGGTGCAGACATCCAGAAGCTATTACATGTTGGTAACTCAGAGGATATTTGCTTCTGGTAGTAA
GGAGCACAAAGACGTTTTTGGCTTATTTCTGCAAAAAGTGAACAAGTTGAAGACTTTTGTATTTTACTTTGCTA
GTTTGTGGCAGAGTGGAGAGGACGGGTGGATATTTCAAATTTTTTAGTATAGCGTATCGCAAGGGTTTGACAC
CGCTGCCAGCGACTCTAGGCTTCCAGTCTGTGTTGGTTTTTATTCTTATCATTATATGATTGTTATATAT
ATTATTTATTTTAGTTGTTGCTGCTAAACTCAATAATGCTGTTCTAACTACAGTGTCAATAAAATGATTAATG
ACAGGAAAAA
AAAA

FIGURE 190

MARMSFVIAACQLVLGLLMTSLTESSIQNSECPQLCVCEIRPWFTPQSTYREATTVDCNDLRLTRIPSNLSSDT
QVLLLSQSNNAIAKTVDLQQLFNLELDFSQNNFTNIKEVGLANLTQLTTLHLEENQITEMTDYCLQDLSNLQEL
YINHNQISTISAHAFAGLKNLLRLHLNSNKLKVIDSRWFDSTPNLEILMIGENPVIIGILDMNFKPLANLRSIVL
AGMYLTDIPGNALVGLDSLESLSFYDNKLVKVPQLALQKVPNLKFLDLNKNPIHKIQEGDFKNMLRLKELGINN
MGELVSVDRYALDNLPELTKLEATNNPKLSYIHLRAFRSVPALLESMLNNNALNAIYOKTVESLPLNREISHS
NPLRCDCVIHWINSNKTNI RFMEPLSMFCAMPPEYKGHQVKEVLIQDSSEQCLPMISHDSFPNRLNVDIGTTVF
LDCRAMAEPEPEIYWVTPIGNKITVETLSDKYKLSSEGTLEISNIQIEDSGRYTCVAQNVOGADTRVATIKVNG
TLLDGTQVLKIYVKQTFESHSLVSWKVNVMVTSNLKWSATMKIDNPHITYTARVPVDVHEYNLTHLQPSTDY
EVCLTVSNIHQQTQKSCVNVTTKNAFAVDISDQETSTALAAVMGSMFAVISLASIAVYFAKRFKRKNYHHSK
KYMQKTSIPLNELYPPLINLWEGDSEKDKDGSADTKPTQVDTSRSYMW

Important features:

Signal peptide:

Amino acids 1-25

Transmembrane domain:

Amino acids 508-530

N-glycosylation sites:

Amino acids 69-73;96-100;106-110;117-121;385-389;517-521;
582-586;611-615

Tyrosine kinase phosphorylation site:

Amino acids 573-582

N-myristoylation sites:

Amino acids 16-22;224-230;464-470;637-643;698-704

FIGURE 191

GGGAGAGAGGATAAAATAGCAGCGTGGCTTCCCTGGCTCCTCTCTGCATCCTTCCCGACCTTC
CCAGCAAT**ATG**CATCTTGCACGTCTGGTCGGCTCCTGCTCCCTCCTTCTGCTACTGGGGGCC
CTGTCTGGATGGGCGGCCAGCGATGACCCCATTTGAGAAGGTCATTGAAGGGATCAACCGAGG
GCTGAGCAATGCAGAGAGAGAGGTGGGCAAGGCCCTGGATGGCATCAACAGTGAATCACGC
ATGCCGGAAGGGAAGTGGAGAAGGTTTTCAACGGACTTAGCAACATGGGGAGCCACACCGGC
AAGGAGTTGGACAAAGCGTCCAGGGGCTCAACCACGGCATGGACAAGGTTGCCCATGAGAT
CAACCATGGTATTGGACAAGCAGGAAAGGAAGCAGAGAAGCTTGGCCATGGGGTCAACAACG
CTGCTGGACAGGCCGGGAAGGAAGCAGACAAAGCGGTCCAAGGGTTCACACTGGGGTCCAC
CAGGCTGGGAAGGAAGCAGAGAAACTTGGCCAAGGGTCAACCATGCTGCTGACCAGGCTGG
AAAGGAAGTGGAGAAGCTTGGCCAAGGTGCCACCATGCTGCTGGCCAGGCCGGGAAGGAGC
TGCAGAATGCTCATAATGGGGTCAACCAAGCCAGCAAGGAGGCCAACCAGCTGCTGAATGGC
AACCATCAAAGCGGATCTTCCAGCCATCAAGGAGGGGCCACAACCACGCCGTTAGCCTCTGG
GGCCTCAGTCAACACGCCTTTCATCAACCTTCCCGCCCTGTGGAGGAGCGTCGCCAACATCA
TGCCCT**TAA**ACTGGCATCCGGCCTTGCTGGGAGAATAATGTCGCCGTTGTCACATCAGCTGAC
ATGACCTGGAGGGGTGGGGGTGGGGGACAGGTTTTCTGAAATCCCTGAAGGGGTTGTACTG
GGATTTGTGAATAAACTTGATACACCA

FIGURE 192

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA66675

><subunit 1 of 1, 247 aa, 1 stop

><MW: 25335, pI: 7.00, NX(S/T): 0

MHLARLVGSCSLLLLLLGALSGWAASDDPIEKVIEGINRGLSNAEREVKGKALDGINSGITHAG
REVEKVFNGLSNMGSHGTGKELDKGVQGLNHGMDKVAHEINHGIGQAGKEAEKLGCHGVNNAAG
QAGKEADKAVQGFHTGVHQAGKEAEKLGQGVNHAADQAGKEVEKLGQGAHHAAGQAGKELQN
AHNGVNQASKEANQLLNNGNHQSGSSSHQGGATTTPLASGASVNTPFINLPALWRSVANIMP

Important features of the protein:

Signal peptide:

amino acids 1-25

Homologous region to circumsporozoite (CS) repeats:

amino acids 35-225

FIGURE 193

GAAGTAGAGGTGTTGTGCTGAGCGGCGCTCGGC~~G~~AACTGTGTGGACCGTCTGCTGGGACTCC
GGCCCTGCGTCCGCTCAGCCCCGTGGCCCCGCGCACCTACTGCC~~ATG~~GAGACGCGGCCTCGT
CTCGGGGCCACCTGTTTGTGGGCTTCAGTTTCCTGCTCCTCGTCATCTCTTCTGATGGACA
TAATGGGCTTGGAAAGGGTTTGGAGATCATATTCATTGGAGGACACTGGAAGATGGGAAGA
AAGAAGCAGCTGCCAGTGGACTGCCCCGTGATGGTGATTATTCATAAAATCCTGGTGTGGAGCT
TGCAAAGCTCTAAAGCCCCAAATTTGCAGAATCTACGGAAATTTCAGAACTCTCCATAATTT
TGTTATGGTAAATCTTGAGGATGAAGAGGAACCCAAAGATGAAGATTTAGCCCTGACGGGG
GTTATATTCACGAATCCTTTTCTGGATCCCAGTGGCAAGGTGCATCCTGAAATCATCAAT
GAGAATGGAACCCAGCTACAAGTATTTTTATGTGTCAGTGCCGAGCAAGTTGTTTCAGGGGAT
GAAGGAAGCTCAGGAAAGGCTGACGGGTGATGCCTTCAGAAAGAAAACATCTTGAAGATGAAT
TG~~TAA~~CATGAATGTGCCCCCTTCTTTCATCAGAGTTAGTGTTCTGGAAGGAAAGCAGCAGGGA
AGGGAATATTGAGGAATCATCTAGAACAATTAAGCCGACCAGGAAACCTCATTCCTACCTAC
ACTGGAAGGAGCGCTCTCACTGTGGAAGAGTTCTGCTAACAGAAGCTGGTCTGCATGTTTGT
GGATCCAGCGGAGAGTGGCAGACTTTCTTCTCCTTTTCCCTCTCACCTAAATGTCAACTTGT
CATTGAATGTAAAGAATGAAACCTTCTGACACAAA

FIGURE 194

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA67300
><subunit 1 of 1, 172 aa, 1 stop
><MW: 19206, pI: 5.36, NX(S/T): 1
METRPRLGATCLLGFSFLLLVISSDGHNGLGKGFGDHIIHWRTLEDGKKEAAASGLPLMVI
IHKSWCGACKALKPKFAESTEISELSHNFVMVNILEDDEEPPKDFDFSPDGGYIPRILFLDP
SGKVHPEIINENGNPSYKYFYVSAEQVVQGMKEAQERLTGDAFRKKHLEDEL
```

Important features of the protein:

Signal peptide:

Amino acids 1-23

Thioredoxin family proteins:

Amino acids 58-75

N-myristoylation sites:

Amino acids 29-35;67-73;150-156

Amidation site:

Amino acid 45-49

FIGURE 195

CGGCTCGAGTGCAGCTGTGGGGAGATTTCAAGTGCATTGCCTCCCCTGGGTGCTCTTCATCTTGGATTTGAAAGT
TGAGAGCAGCATGTTTTGCCCCTGAAACTCATCTGCTGCCAGTGTTACTGGATTATTCCTTGGGCCTGAATG
ACTTGAATGTTTTCCCCGCTGAGCTAACAGTCCATGTGGGTGATTCAGCTCTGATGGGATGTGTTTTCCAGAGC
ACAGAAGACAAATGTATATTCAAGATAGACTGGACTCTGTCACCAGGAGAGACGCCAAGGACGAATATGTGCT
ATACTATTACTCCAATCTCAGTGTGCCTATTGGGCGCTTCCAGAACC GCGTACACTTGATGGGGGACATCTTAT
GCAATGATGGCTCTCTCCTGCTCCAAGATGTGCAAGAGGCTGACCAGGGAACCTATATCTGTGAAATCCGCTC
AAAGGGGAGAGCCAGGTGTTCAAGAAGGCGGTGCTACTGCATGTGCTTCCAGAGGAGCCCAAAGAGCTCATGGT
CCATGTGGGTGGATTGATTCAGATGGGATGTGTTTTCCAGAGCACAGAAGTGAACACGTCACCAAGGTAGAAT
GGATATTTTCAGGACGGCGCGCAAAGGAGGAGATTGTATTCGTTACTACCACAAACTCAGGATGTCTGTGGAG
TACTCCAGAGCTGGGGCCACTTCCAGAATCGTGTGAACCTGGTGGGGGACATTTTCCGCAATGACGGTTCCAT
CATGCTTCAAGGAGTGAGGGAGTCAGATGGAGGAACTACACCTGCAGTATCCACCTAGGGAACCTGGTGTTC
AGAAAACCATTTGCTGCATGTCAGCCCGGAAGAGCCTCGAACACTGGTGACCCCGGCAGCCCTGAGGCCTCTG
GTCTTGGGTGGTAATCAGTTGGTGATCATTGTGGGAATTGTCTGTGCCACAATCCTGCTGCTCCCTGTTCTGAT
ATTGATCGTGAAGAAGACCTGTGGAATAAGAGTTCAAGTGAATTCACAGTCTTGGTGAAGAACACGAAGAAGA
CTAATCCAGAGATAAAAAGAAAAACCTGCCATTTTGAAGATGTGAAGGGGAGAAACACATTTACTCCCCAATA
ATTGTACGGGAGGTGATCGAGGAAGAAGAACCAGTGAATAATCAGAGGCCACCTACATGACCATGCACCCAGT
TTGGCCTTCTCTGAGGTGAGATCGGAACAACCTCACTTGAAAAAAGTCAGGTGGGGGAATGCCAAAAACACAGC
AAGCCTTTTTGAAGAATGGAGAGTCCCTTCATCTCAGCAGCGGTGGAGACTCTCTCCTGTGTGTCTCTGGGC
CACTCTACCAGTGATTTTCAGACTCCCCTCTCCCAGCTGTCTCCTCTGTCATTGTTTGGTCAATACACTGAAG
ATGGAGAATTTGGAGCCTGGCAGAGAGACTGGACAGCTCTGGAGGAACAGGCCTGCTGAGGGGAGGGGAGCATG
GACTTGGCCTCTGGAGTGGGACACTGGCCCTGGGAACCAGGCTGAGCTGAGTGGCCTCAAACCCCCGTTGGAT
CAGACCCTCTGTGGGCAGGTTCTTAGTGATGAGTTACTGGGAAGAATCAGAGATAAAAACCAACCCAAATCAA

FIGURE 196

MFCPLKLILLPVLLDYSLGLNDLNVSPPELTVHVGDSALMGCVFQSTEDKCI FKIDWTLSPGEHAKDEYVLYYY
SNLSVPIGRFQNRVHLMGDI LCNDGSLLLQDVQEADQGTIYICEIRLKGESQVFKKAVLHVLPEEPKELMVHVG
GLIQMGCVFQSTEVKHVTKVEWIFSGRRAKEEIVFRYYHKL RMSVEYSQSWG HFQNRVNLVGDIFRNDGSIMLQ
GVRES DGGNYTCSIHLGNLVFKKTI VLHVSPEEPRTLVT PAALRPLVLGGNQLVIIVGIVCATILLPVLILIV
KKT CGNKSSVNSTVLVKNTKKTNPEI KEKPC HFFRCEGEKHIYSPIIVREVIEEEEEPSEKSEATYMTMHPVWPS
LRSDRNNSLEKKS GGGMPKTOQAF

FIGURE 197

CGCC**ATG**GCCGGGCTATCCCGCGGGTCCGCGCGGCACTGCTCGCCGCCCTGCTGGCGTCGACG
CTGTTGGCGCTGCTCGTGTGCCCCGCGCGGGGTCGCGGCGGCCGGGACCACGGGGACTGGGA
CGAGGCCTCCCGGCTGCCGCCGTACCACCCCGCGAGGACGCGGCGCGCGTGGCCCGCTTCG
TGACGCACGTCTCCGACTGGGGCGCTCTGGCCACCATCTCCACGCTGGAGGCGGTGCGCGGC
CGGCCCTTCGCCGACGTCCCTCTCGCTCAGCGACGGGCCCCCGGGCGCGGCAGCGGCCTGCC
CTATTTCTACCTGAGCCCCTGCAGCTCTCCGTGAGCAACCTGCAGGAGAATCCATATGCTA
CACTGACCATGACTTTGGCACAGACCAACTTCTGCAAGAAACATGGATTTGATCCACAAAGT
CCCCTTTGTGTTACATAAATGCTGTCAGGAAGTGTGACCAAGGTGAATGAAACAGAAATGGA
TATTGCAAAGCATTTCGTTATTCATTCGACACCCTGAGATGAAAACCTGGCCTTCAGCCATA
ATTGGTTCTTTGCTAAGTTGAATATAACCAATATCTGGGTCCTGGACTACTTTGGTGGACCA
AAAATCGTGACACCAGAAGAATATTATAATGTCACAGTTCAG**TGA**ACCAGACTGTGGTGAAT
TTAGCAACACTTATGAAGTTTCTTAAAGTGGCTCATAACACTTAAAAGGCTTAATGTTTCT
CTGGAAAGCGTCCCAGAATATTAGCCAGTTTCTGTG

FIGURE 198

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA71269
><subunit 1 of 1, 220 aa, 1 stop
><MW: 24075, pI: 7.67, NX(S/T): 3
MAGLSRGSARALLAALLASTLLALLVSPARGRGGRDHGDWDEASRLPPLPPREDAARVAR
FVTHVSDWGALATISTLEAVRGRPFADVLSLSDGPPGAGSGVPHYLSPLQLSVSNLQEN
PYATLTMTLAQTNFCKKHGFDPQSPLCVHIMLSGTVTKVNETEMDIAKHSLFIRHPEMKT
WPSSHNWFFAKLNITNIWVLDYFGGPKIVTPEEYYNVTVQ

Important features of the protein:

Transmembrane domain:

Amino acids

11-29

N-glycosylation sites:

Amino acids

160-164;193-197;216-220

N-myristoylation sites:

Amino acids

3-9;7-13;69-75;97-103

FIGURE 199

TCGCCATGGCCTCTGCCGGAATGCAGATCCTGGGAGTCGTCCTGACACTGCTGGGCTGGGTG
AATGGCCTGGTCTCCTGTGCCCTGCCCATGTGGAAGGTGACCGCTTTCATCGGCAACAGCAT
CGTGGTGGCCCAGGTGGTGTGGGAGGGCCTGTGGATGTCCTGCGTGGTGCAGAGCACCGGCC
AGATGCAGTGCAAGGTGTACGACTCACTGCTGGCGCTGCCACAGGACCTGCAGGCTGCACGT
GCCCTCTGTGTCATCGCCCTCCTTGTGGCCCTGTTCGGCTTGCTGGTCTACCTTGCTGGGGC
CAAGTGTACCACCTGTGTGGAGGAGAAGGATTCCAAGGCCCGCCTGGTGTACCTCTGGGA
TTGTCTTTGTCATCTCAGGGGTCCGTACGCTAAATCCCCGTGTGCTGGACGGCGCATGCCATC
ATCCGGGACTTCTATAACCCCTGGTGGCTGAGGCCAAAAGCGGGAGCTGGGGGCCTCCCT
CTACTTGGGCTGGGCGGCCTCAGGCCTTTTGTGCTGGGTGGGGGGTTGCTGTGCTGCACTT
GCCCCFCGGGGGGTCCCAGGGCCCCAGCCATTACATGGCCCGCTACTCAACATCTGCCCT
GCCATCTCTCGGGGGCCCTCTGAGTACCCTACCAAGAATTACGTCTTGACGTGGAGGGGAATG
GGGGCTCCGCTGGCGCTAGAGCCATCCAGAAGTGGCAGTGCCCAACAGCTTGGGATGGGTT
CGTACCTTTTGTCTCTGCCTCCTGCTATTTTTCTTTTACTGAGGATATTTAAAATTCATTT
GAAAACAGGCAAGGTGTTGACTCAGACTCTCACTTAGGCTCTGCTGTTTCTCACCTTGG
ATGATGGAGCCAAAGAGGGGATGCTTTGAGATTCTGGATCTTGACATGCCCATCTTAGAAGC
CAGTCAAGCTATGGAATAATGCGGAGGCTGCTTGCTGTGCTGGCTTTGCAACAAGACAGAC
TGTCCTCCCAAGAGTTCCTGCTGCTGCTGGGGCTGGGCTTCCCTAGATGTCCTGGACAGCTG
CCCCCATCCTACTCAGGTCTCTGGAGCTCCTCTCTTACCCCTGGAAAAACAAATCATCTG
TTAACAAAGGACTGCCACCTCCGGAACCTCTGACCTCTGTTTCCCTCCGTCCTGATAAGACG
TCCACCCCCAGGGCCAGGTCCCAGCTATGTAGACCCCCGCCCCACCTCCAACACTGCACC
CTTCTGCCCTGCCCCCTCGTCTCACCCCTTACACTCACATTTTATCAAATAAAGCATG
TTTTGTTAGTGCA

FIGURE 200

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA73736
><subunit 1 of 1, 220 aa, 1 stop
><MW: 23292, pI: 8.43, NX(S/T): 0
MASAGMQILGVVLTLLGWVNGLVSCALPMWKVTAFIGNSI VVAQVVWEG LWMSCVVQSTGQM
QCKVYD SLLALPQDLQAARALCVIALLV ALFGLLVYLAGAKCTTCVEEKDSKARLVLTSGIV
FVISGVLT LIPVCWTAHAIIRD FYNPLVAEAQKRELGASLYLGWAASGLLLLGGGLLCCTCP
SGGSQGP SHYMARYSTSAP AISRGPSEYPTKNYV
```

Transmembrane domains:

amino acids 8-30 (type II), 82-102, 121-140, 166-186

FIGURE 201

AGTGACAATCTCAGAGCAGCTTCTACACCACAGCCATTTCCAGCATGAAGATCACTGGGGGTCTCCTTCIGCTC
TGTACAGTGGTCTATTTCTGTAGCAGCTCAGAAGCTGCTAGTCTGTCTCCAAAAAAGTGGACTGCAGCATTTA
CAAGAAGTATCCAGTGGTGGCCATCCCCTGCCCATCACATACCTACCAGTTTGTGGTTCTGACTACATCACCT
ATGGGAATGAATGTCACCTGTGTACCGAGAGCTTGAAAAGTAATGGAAGAGTTCAGTTTCTTCACGATGGAAGT
TGCTTAAATTCTCCATGGACATAGAGAGAAAAGGAATGATATTCTCATCATCATCTTCATCATCCCAGGCTCTGAC
TGAGTTTCTTTCAGTTTFACTGATGTCTGGGTGGGGACAGAGCCAGATTCAGAGTAATCTTGACTGAATGGA
GAAAGTTTCTGTGCTACCCCTACAAACCCATGCCTCACTGACAGACCAGCATTTTTTTTTTAAACACGTCAATAA
AAAAATAATCTCCAGA

FIGURE 202

MKITGLLLLLCTVVYFCSSSEAAASLSPKKVDCSIYKYPVVAIPCPITYLPVCGSDYITYGNECHICTESLKSN
GRVQFLHDGSC

Important features:

Signal peptide:

amino acids 1-19

FIGURE 203

CGACGATGCTACGCGCGCCCGGCTGCCTCCTCCGGACCTCCGTAGCGCCTGCCGCGCCCTGGCTGCGGGCGTG
CTCTCGTCGCTTGGCGGCTGCTCTCTTCTAGAGCCGAGGGACCCGGTGGCCTCGTCGCTCAGCCCCATTTCCG
CACCAAGACTCGCTACGAGGATGTC AACCCCGTGCTATTGTGCGGCCCGGAGGCTCCGTGGCGGGACCCCTGAGC
TGCTGGAGGGGACCTGCACCCCGTGCAGCTGGTGCGCCCTATTCCGCCACGGCACCCGCTACCCACGGTCAAA
CAGATCCGCAAGCTGAGGCAGCTGCACGGGTTGCTGCAGGCCCGCGGGTCCAGGGATGGCGGGGCTAGTAGTAC
CGGCAGCCGCGACCTGGGTGCAGCGCTGGCCGACTGGCCTTTGTGGTACGCGGACTGGATGGACGGGCAGCTAG
TAGAGAAGGGACGGCAGGATATGCGACAGCTGGCGCTGCGTCTGGCCTCGCTCTCCCGGCCCTTTTCAGCCGT
GAGAATACGGCCGCTGCGGCTCATCACCAGTCCAAGCACCGCTGCATGGATAGCAGCGCCGCTTCTGCA
GGGGCTGTGGCAGCACTACCACCCCTGGCTTGC CGCCGCGGGACGTCCGAGATATGGAGTTTGGACCTCCAACAG
TTAATGATAAACTAATGAGATTTTTGATCACGTGTGAGAAGTTTTTAACTGAAGTAGAAAAAATGCTACAGCT
CTTTATCACGTGGAAGCCTTCAAACCTGGACCAGAAAATGCAGAACATTTAAAAAAGTTGCAGCTACTTTGCA
AGTGCCAGTAAATGATTTAAATGCAGATTTAATCAAGTAGCCTTTTTCACCTGTTTATTGACCTGGCAATTA
AAGGTGTTAAATCTCCTTGGTGTGATGTTTTTGACATAGATGATGCAAAAGGTATTAGAATATTTAAATGATCTG
AAACAATATTTGAAAAGAGGATATGGGTATACTATTAACAGTCGATCCAGCTGCACCTGTTTCAGGATATCTT
TCAGCACTGGACAAAGCAGTTGAACAGAAACAAAGGCTCAGCCAATTTCTTCTCCAGTCATCCTCCAGTTTG
GTCATGCAGAGACTCTTCTCCACTGCTTCTCTCATGGGCTACTTCAAAGACAAGGAACCCCTAACAGCGTAC
AATTACAAAAACAAATGCATCGGAAGTTCCGAAGTGGTCTCATTGTACCTTATGCCTCGAACCTGATATTTGT
GCTTTACCACTGTGAAAATGCTAAGACTCCTAAAGAACAATTCGAGTGCAGATGTTATTAATGAAAAGGTGT
TACCTTTGGCTTACTCACAAAGAACTGTTTCATTTTATGAAGATCTGAAGAACCCTACAAGGACATCCTTCAG
AGTTGTCAAACCACTGAAGAATGTGAATTAGCAAGGGCTAACAGTACATCTGATGAACTATGAGTAACTGAAGA
ACATTTTTAATCTTTAGGAATCTGCAATGAGTGATTACATGCTTGAATAGGTAGGCAATTCCTTGATTACAG
GAAGCTTTTATTTACTTGAGTATTTCTGTCTTTTACAGAAAAACATTTGGGTTTCTCTGGGTTTGGACATG
AAATGTAAGAAAAGATTTTTCACTGGAGCAGCTCTCTAAGGAGAAAACAAATCTATTTAGAGAAACAGCTGGCC
CTGCAAAATGTTTACAGAAATGAAATTTCTTCTACTTATATAAGAAATCTCACACTGAGATAGAATTTGTGATTT
ATAATAACACTTGAAAAGTGCTGGAGTAACAAAATATCTCAGTTGGACCATCCTTAACTTGATTGAACTGTCTA
GAACTTTTACAGATTGTTCTGCAGTTCTCTCTCTTTTCTCAGGTAGGACAGCTCTAGCATTTCCTTAATCAG
GAAATATTGTGGTAAGCTGGGAGTATCACTCTGGAAGAAAAGTAAACATCTCCAGATGACAATTTGAAACAAGAAAC
AGAGTGGTTGTAAGGACACCTTCACTGAAGCAAGTCGGAAGTACAATGAAAATAAATATTTTTGGTATTTAT
TTATGAAAATATTTGAACATTTTTTCAATAATTCCTTTTACTTCTAGGAAGTCTCAAAGACCATCTAAATTA
TTATATGTTTGGACAATTAGCAACAAGTCAGATAGTTAGAATCGAAGTTTTTCAAATCCATTGCTTAGCTAACT
TTTTTCACTTGTCACTTGGCTTCGATTTTTATATTTTCTTATATATGAAATGTATCTTTTGGTGTGTTGATTT
TTCTTTCTTTTGTAAATAGTTCTGAGTTCTGTCAAATGCCGTGAAAGTATTTGCTATAATAAAGAAAATTC
TTGTGACTTTAAAAAAA

FIGURE 204

MLRAPGCLLRTSVAPAAALAAALLSSLARCSLLEPRDPVASSLSPYFGTKTRYEDVNPVLLSGPEAPWRDPELL
EGTCTPVQLVALIRHGTRYPTVKQIRKLRQLHGLLQARGSRDGGASSTGSRDLGAALADWPLWYADWMDGQOLVE
KGRQDMRQLALRLASLFPALFSRENYGRLRLITSSKHRCMDSSAAFLQGLWQHYHPGLPPPVDADMEFGPPTVN
DKLMRFFDHCEKFLTEVEKNATALYHVEAFKTPGEMQNILKKVAATLQVPVNDLNADLIQVAFFTCSDLAIKG
VKSPWCDVFDIDDAKVLEYLNDLKQYWKRGYGYTINSRSSCTLFQDIFQHLDKAVEQKORSQPISSPVILQFGH
AETLLPLLSLMGYFKDKEPLTAYNYKKQMRKFRSGLIVPYASNLIFVLYHCENAKTPKEQFRVQMLLNEKVL
LAYSQETVSFYEDLKNHYKDILQSCQTSEECELARANSTSDDEL

Important features:

Signal sequence

amino acids 1-30

N-glycosylation sites.

amino acids 242-246, 481-485

N-myristoylation sites.

amino acids 107-113, 113-119, 117-123, 118-124, 128-134

Endoplasmic reticulum targeting sequence.

amino acids 484-489

FIGURE 205

GCGACGCGCGGCGGGGCGGGGAGAGGAAACGCGGGCGCCGGGCCGGGCCCTGGAGATG
GTCCCCGGCGCCGCGGGGCTGGTGTGTCTCGTGCTCTGGCTCCCCGCGTGCGTTCGCGGCCCA
CGGCTTCCGTATCCATGATTATTTGTACTTTCAAGTGCTGAGTCCTGGGGACATTCGATACA
TCTTACAGCCACACCTGCCAAGGACTTTGGTGGTATCTTTACACAAGGTATGAGCAGATT
CACCTTGTCCCGCTGAACCTCCAGAGGCCTGCGGGGAACCTCAGCAACGGTTTCTTCATCCA
GGACCAGATTGCTCTGGTGGAGAGGGGGGCTGCTCCTTCCCTCCAAGACTCGGGTGGTCC
AGGAGCACGGCGGGCGGGCGGTGATCATCTCTGACAACGCAGTTGACAATGACAGCTTCTAC
GTGGAGATGATCCAGGACAGTACCCAGCGCACAGCTGACATCCCCGCCCTCTTCTGCTCGG
CCGAGACGGCTACATGATCCGCCGCTCTCTGGAACAGCATGGGCTGCCATGGGCCATCATT
CCATCCCAGTCAATGTCACCAGCATCCCCACCTTTGAGCTGCTGCAACCGCCCTGGACCTC
TGGTAGAAGAGTTTGTCCACATTCCAGCCATAAGTGACTCTGAGCTGGGAAGGGGAAACCC
AGGAATTTTGCTACTTGAATTTGGAGATAGCATCTGGGGACAAGTGGAGCCAGGTAGAGGA
AAAGGGTTTGGGCGTTGCTAGGCTGAAAGGGAAGCCACCCACTGGCCTTCCCTTCCCCAGG
GCCCCAAGGGTGTCTCATGCTACAAGAAGAGGCAAGAGACAGGCCCCAGGGCTTCTGGCTA
GAACCCGAAACAAAAGGAGCTGAAGGCAGGTGGCCTGAGAGCCATCTGTGACCTGTCACACT
CACCTGGCTCCAGCCTCCCCACCCAGGGTCTCTGCACAGTGACCTTCACAGCAGTTGTTGG
AGTGGTTTAAAGAGCTGGTGTGTTGGGGACTCAATAAACCTCACTGACTTTTGTAGCAATAAA
GCTTCTCATCAGGGTTGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 206

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA76532

><subunit 1 of 1, 188 aa, 1 stop

><MW: 21042, pI: 5.36, NX(S/T): 2

MVPGAAGWCCLVLWLPACVAAHGFRIHDYLYFQVLSPGDIRYIFTATPAKDFGGIFHTRYEQ

IHLVPAEPPEACGELSNGFFIQDQIALVERGGCSFLSKTRVVQEHGGRAVIISDNAVNDNSF

YVEMIQDSTQRTADIPALFLLGRDGYMIRRSLEQHGLPWAIISIPVNVTSIPTFELLOPPWTFW

Signal peptide:

amino acids 1-20

FIGURE 207

CTCGCTTCTTCCTTCTGGATGGGGGCCAGGGGGCCCAGGAGAGTATAAAGCGGATGTGGAG
GGTGCCCGGCACAACCAGACGCCAGTCACAGGCGAGAGCCCTGGG**ATG**CACCGGCCAGAGG
CCATGCTGCTGCTGCTCACGCTTGCCCTCCTGGGGGGCCCCACCTGGGCAGGGAAGATGTAT
GGCCCTGGAGGAGGCAAGTATTTTCAGCACCACTGAAGACTACGACCATGMAATCACAGGGCT
GCGGGTGTCTGTAGGTCTTCTCCTGGTGAAAAGTGTCAGGTGAAACTTGGAGACTCCTGGG
ACGTGAAACTGGGAGCCTTAGGTGGGAATACCCAGGAAGTCACCCTGCAGCCAGGCCAATAC
ATCACAAAAGTCTTTGTCGCCTTCCAAGCTTTCCTCCGGGGTATGGTCATGTACACCAGCAA
GGACCGCTATTTCTATTTTGGGAAGCTTGATGGCCAGATCTCCTCTGCCTACCCAGCCAAG
AGGGGCAGGTGCTGGTGGGCATCTATGGCCAGTATCAACTCCTTGGCATCAAGAGCATTGGC
TTTGAATGGAATTATCCACTAGAGGAGCCGACCACTGAGCCACCAGTTAATCTCACATACTC
AGCAAACCTACCCGTGGGTGCGC**TAG**GGTGGGGTATGGGGCCATCCGAGCTGAGGCCATCTGT
GTGGTGGTGGCTGATGGTACTGGAGTAACTGAGTCGGGACGCTGAATCTGAATCCACCAATA
AATAAAGCTTCTGCAGAAAA

FIGURE 209

GGAGAATGGAGAGAGCAGT GAGAGTGGAGTCCGGGGTCTGGTCCGGGTGGTCTGTCTGCTCCTGGCATGCCCT
GCCACAGCCACTGGGCCGAAGTTGCTCAGCCTGAAGTAGACACCACCCTGGGTGCTGTGCGAGGCCGGCAGGT
GGCGTGAAGGGCACAGACCGCCTTGTGAATGTCTTCTGGGCATTCCATTTGCCAGCCGCCACTGGGCCCTG
ACCGTCTCAGACCCACACCAGCACAGCCCTGGGAGGGTGTGCGGGATGCCAGCACTGGCCCCCAATGTGC
CTACAAGACGTGGAGAGCATGAACAGCAGCAGATTGTCTCAACGGAAAAACAGCAGATCTTCTCCGTTCAGA
GGACTGCCTGGTCTCAACGTCTATAGCCAGCTGAGGTCCCGCAGGGTCCGGTAGGCCGGTCAATGGTATGGC
TCCATGGAGGCCGCTCTGATAACTGGCGCTGCCACTCCTACGATGGATCAGCTCTGGCTGCCATGGGGATGTG
CTCGTGGTACAGTCCAGTACCGCCTTGGGGTCTTGGCTTCTTCCAGCACTGGAGATGACCATGCACCTGGCAA
CCAGGGCTTCCCTAGATGTGGTAGCTGCTTTGCGCTGGGTGCAAGAAAACATCGCCCCCTCGGGGGTGACCTCA
ACTGTGTCACTGTCTTGGTGGATCTGCGGGTGGAGCATCATCTCTGGCCTGGTCTGTCCCAGTGGCTGCA
GGGCTGTTCCACAGAGCCATCACACAGAGTGGGGTCAACACCCAGGGATCATCGACTCTCACCTTGGCC
TTCGGAGTCCCTTCCATGGACGAGAGCTCCCGCTGGCCTTCCAGAGGCCACAGAGGAGGAGAAGCAGCT
AGAAAAGAGGAGAAGAGCTGGTCTTAGCAAGAAGCTGAAAAATACTATCTATCTCTCACCGTGTATGGCAGT
GTCTTCCCAAAGCCCAAGGAACTCCTGAAGGAGAGCCCTTCCACTCTGTGCCCTTCCCTATGGGTGTCAA
CAACCATGAGTTCAGTGGCTCATCCCCAGGGGGTGGGGTCTCCTGGATACAATGGAGCAGATGAGCCGGGAGG
ACATGCTGGCCATCAACACCCGCTTGAACAGCTTGGATGTGCCCTGAGATGATGCCACCCCTCATAGAT
GAATACCTAGGAAGCAACTCGGACGCACAAGCCAAATGCCAGGCGTTCAGGAATTCATGGGTGACGTATTCAI
CAATGTTCCACCGTCACTTTTTCAAGTACCTTCGAGATTCTGGAAGCCCTGTCTTTTTCTATGATTCACGC
ATCGACCCAGTCTTTTGGCAAGATCAAACTGCTGGGTGAAGGCTGATCATGGGGCCAGGGTGTCTTTGTG
TTCGGAGTCCCTTCCATGGACGAGAGCTCCCGCTGGCCTTCCAGAGGCCACAGAGGAGGAGAAGCAGCT
AAGCCTCACCATGATGGCCAGTGGACCCACTTTGCCCGGACAGGGGACCCCAATAGCAAGGCTCTGCCTCCTT
GGCCCCAATCAACACAGCCGGAACAATATCTGGAGATCAACCCAGTGCACCGGCCGGACAGAAGTTCAGGGAG
GCTGGATGACGTCTGGTCAAGACGCTCCCCAGCAAGATAACAACAGTGGCACCAGAAGCAGAAGAACAGGAA
GCCCCAGGAGACCTCTAGAGCCAGCCCTGAACCTTCTTGGCTGGGGCAACCACTCTCAAGTGGTGGCAGAG
TCCCAGCACGGCAGCCCGCTTCCCCCTGCTGAGACTTTAATCTCCACAGCCCTTAAAGTGTGGCCGCTCT
GTGACTGGAGTTATGCTCTTTTGAATGTCAAGGCCGCTCCCACTCTGGGGCATTGTACAAGTCTTCCC
TCTCCCTGAAGTGCCTTCTGCTTCTTCTGTTAGGTTCTAGCACATTCCTCTAGCTTCTGGAGGACTCAC
TCCCCAGGAAGCCTTCCCTGCTTCTGCTGGCTGTGGCCGCGGAGTCTGCGTCCATTAGAGCACAGTCCACCC
GAGGCTAGCACCGTGTCTGTGTCTGTCTCCCTCAGAGGAGCTCTCTCAAATGGGGATTAGCCTAACCCAC
TCTGTACCCACACAGGATCGGGTGGGACCTGGAGCTAGGGGGTGTGCTGAGTGAAGTGAACACAGA
ATATGGGAATGGCAGCTGCTGAACCTGAACCCAGAGCCTTCAAGTGCCAAAGCCATACTCAGGCCCCACCGAC
ATTGTCCACCTGGCCAGAAGGGTGCATGCCAATGGCAGAGACCTGGGATGGGAGAAGTCTGGGGCCAGGG
GATCCAGCCTAGAGCAGACCTTAGCCCTGACTAAGGCCCTCAGACTAGGGCGGGAGGGGTCTCTCCTCTCTGC
TGCCAGTCTGGCCCTGCACAAGACAACAGAAATCCATCAGGGCCATGAGTGTACCCAGACCTGACCCTCAC
CAATTCAGCCCTGACCCCTCAGGACGCTGGATGCCAGCTCCAGCCCAAGTGGCCGGTCCCTCCCTCCCTCCT
GGCTTGGGGAGACCAGTTTCTGGGGAGCTTCCAGAGCACCCACCAAGACACAGCAGGACAGGCCAGGGGAGGG
CATCTGGACCAGGGCATCCGTCCGGCTATTGTACAGAGAAAAGAACAGCCACCCACTCGGGCTGCAAAAGG
TGAAAAGCACAAGAGGTTTTAGATGGAAGTGAAGGTGACAGTGTGCTGGCAGCCCTCACAGCCCTCGCTTGT
CTCTCCCTGCCGCTCTGCTGGGCTCCCACTTTGGCAGCACTTGAAGAGCCCTCAACCCGCGTGCCTGCTGT
AGGAGCCCTTTCTGGGCTGGCCAAGGCCGAGCCAGCTCCCTCAGCTTGGGGGAGGTGGGGAGGAGAGGGG
CGGGCAGGAACCGGGGCTGCGCGCAGCGCTTGGGGCCAGAGTGAAGTCCGGGTGGGCTGGGCTCGCGGGGG
CCCACTCAGAGCAGCTGGCCGGCCCAAGGCACTGAGGGCTTAGCACCTGGGCCAGCAGCTGCTGTGCTCGATT
TCTCGTGGGCTTAGCTGCTCCCGCGGGGCGAGGGCTCGGGACCTGCAGCCCTCCATGCCTGACCCCTCCCC
CACCCCGTGGGCTCTGTGCGGCCGGAGCCTCCCCAAGGAGCGCCGCCCTGCTCCACAGCCCGCAGTCCC
ATCGACCACCAAGGGCTGAGGAGTGGGGTGCACAGCGCGGGACTGGCAGGCAGCTCCACCTGCTGCCCCAGT
GCTGGATCCACTGGGTGAAGCCAGCTGGGCTCTGAGTCTGGTGGGACTTGGAGAACCTTATGTCTAGCTAA
GGGATTGTAATAACCCGATGGGCACTCTGTCTAGCTCAAGGTTTGTAAACACCAATCAGACCCCTGTGT
CTAGCTCAGTGTGTTGTGAATGCACCAATCCACACTCTGTATCTGGCTACTCTGGTGGGACTTGGAGAACCTT
GTGTCCACACTCTGTATCTAGCTAATCTAGTGGGATGTGGAGAACCTTTGTGTCTAGCTCAGGGATCGTAAAC
GCACCAATCAGCACCTGTCAAAACAGACCCTTGACTCTCTGTAAAATGGACCAATCAGCAGGATGTGGGTGG
GGCGAGACAAGACAATAAAGCAGGCTGCCTGAGCCAGCAGTGAACCCCCCTCGGGTCCCTCCACGCCGT
GGAAGCTTTGTCTTTCGCTCTTTGCAATAAACTTGTCTACTGCCAAAA

FIGURE 210

MERAVRVESGVLVGVVCLLLACPATATGPEVAQPEVDTTLGRVVRGRQVGVKGTDRLVNVFLGIPFAQPPLGPDR
FSAPHPAQWEGVRDASTAPPMLQDVESMNSSRFVNLNGKQQIFSVSEDCLVLVNVS PAEVPAGSGRPVMVWVH
GGALITGAATSYDGSALAAAYGDVVVVTVQYRLGVLGFFSTGDEHAPGNQGFLLDVVAALRWVQENIAPFGDLNC
VTVFSGSAGGSIIISGLVLS PVAAGLFHRAITQSGVITTPGIIDSHPWPLAQKIAN TLACSSSSPAEMVQCLQQK
EGEELVLSKKLKNTIYPLTVDGTVPFKSPKELLKEKPFHSVPFLMGVNNHEFSWLI PRGWGLLDTMEQMSREDM
LAISTPVLTSLDVPPEMMPTVIDEYLGNSNDAQAKCAFQEFMGDVFINVPTVSFSRYLRDSGSPVFFYEFQHR
PSSFAKIKPAWVKADHGAEGAFVFGGPFMLDESSRLAFPEATEEEKQLSLTMMAQWTHFARTGDPNSKALPPWP
QFNQAEQYLEINPVPRAGQKFRFAWMQFWSSETLPSKIQQWHQKQKNRKAQEDL

Important features:

Signal peptide:

amino acids 1-27

Transmembrane domain:

amino acids 226-245

N-glycosylation site.

amino acids 105-109

N-myristoylation sites.

amino acids 10-16, 49-55, 62-68, 86-92, 150-156, 155-161, 162-168, 217-223,
227-233, 228-234, 232-238, 262-268, 357-363, 461-467

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 12-23

Carboxylesterases type-B serine active site.

amino acids 216-232

FIGURE 211

AACTTCTACATGGGCCTCCTGCTGCTGGTGCTCTTCCTCAGCCTCCTGCCGGTGGCCTACAC
CATCATGTCCCTCCCACCCTCCTTTGACTGCGGGCCGTTCAAGGTGCAGAGTCTCAGTTGCC
GGGAGCACCTCCCCTCCCGAGGCAGTCTGCTCAGAGGGCCTCGGCCAGAAATCCAGTTCTG
GTTTCATGCCAGCCTGTAAAAGGCCATGGAAC'TTTGGGTGAATCACCGATGCCATTTAAGAG
GGTTTTCTGCCAGGATGGAAATGTTAGGTCGTTCTGTGTCTGCGCTGTTCAATTCAGTAGCC
ACCAGCCACCTGTGGCCGTTGAGTGCTTGAAATGAGGAACTGAGAAAATTAATTTCTCATGT
ATTTTTCTCATTTATTTATTAATTTTAACTGATAGTTGTACATATTTGGGGGTACATGTGA
TATTTGGATACATGTATACAATATATAATGATCAAATCAGGGTAACTGGGATATCCATCACA
TCAAACATTTATTTTTTATTCTTTTTAGACAGAGTCTCACTCTGTCACCCAGGCTGGAGTGC
AGTGGTGCCATCTCAGCTTACTGCAACCTCTGCCTGCCAGGTTCAAGCGATTCTCATGCCTC
CACCTCCAAGTAGCTGGGACTACAGGCATGCACCACAATGCCCAACTAATTTTTGTATTTT
TAGTAGAGACGGGGTTTTGCCATGTTGCCAGGCTGGCCTTGAACCTCTGGCCTCAAACAAT
CCACTTGCCTCGGCCTCCCAAAGTGTTATGATTACAGGCCTGAGCCACCGTGCCTGGCCTAA
ACATTTATCTTTTCTTTGTGTTGGGAAC'TTGAAATTATACAATGAATTATTGTTAACTGTC
ATCTCCCTGCTGTGCTATGGAACACTGGGACTTCTTCCCTCTATCTAACTGTATATTGTAC
CAGTTAACCAACCGTACTTCATCCCCTCCTCTCTATCCTTCCCAACCTCTGATCACCTCA
TTCTACTCTCTACCTCCATGAGATCCACTTTTTTAGCTCCCACATGTGAGTAAGAAAATGCA
ATATTTGTCTTTCTGTGCCTGGCTTATTTCACTTAACATAATGACTTCTGTTCCATCCATG
TTGCTGCAAATGACAGGATTTTCGTTCTTAATTTCAATTAAAATAACCACACATGGCAAAAA

FIGURE 212

MGLLLLVLFLSLLPVAYTIMSLPPSFDCGPFRCRVSVAREHLPSRGSLLRGPRPRIPVLVSC
QPVKGHGTLGESPMPFKRVFCQDGNVRSFCVCAVHFSSHQPPVAVECLK

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 213

AGGGCCCGCGGGTGGAGAGAGCGACGCCCGAGGGG**ATG**GCGGGCAGCGTCCCGGAGCGCCTCT
GGCTGGGCGCTACTGCTGCTGGTGGCACTTTGGCAGCAGCGCGCGGGCCGGCTCCGGCGTCTT
CCAGCTGCAGCTGCAGGAGTTCATCAACGAGCGCGGGCTACTGGCCAGTGGGCGGCCTTGCG
AGCCCGGCTGCCGGACTTTCTTCCGCGTCTGCCTTAAGCACTTCCAGGCGGTCTGTCGCCCC
GGACCCTGCACCTTCGGGACCGTCTCCACGCCGGTATTGGGCACCAACTCCTTCGCTGTCCG
GGACGACAGTAGCGGGGGGGGGCGCAACCCTCTCCAAGTGCCTTCAATTTACCTGGCCGG
GTACCTTCTCGCTCATCATCGAAGCTTGGCACGCGCCAGGAGACGACCTGCGGCCAGAGGCC
TTGCCACCAGATGCACTCATCAGCAAGATCGCCATCCAGGGCTCCCTAGCTGTGGGTGAGAA
CTGGTTATTGGATGAGCAAACCAGCACCTCACAAGGCTGCGCTACTCTTACCGGGTCTATCT
GCAGTGACAACACTATGGAGACAACCTGCTCCCGCCTGTGCAAGAAGCGCAATGACCACTTC
GGCCACTATGTGTGCCAGCCAGATGGCAACTTGTCTTGCCTGCCCGGTGGACTGGGGGAATA
TTGCCAACAGCCTATCTGTCTTTCGGGCTGTCATGAACAGAATGGCTACTGCAGCAAGCCAG
CAGAGTGCCTCTGCCGCCAGGCTGGCAGGGCCGGCTGTGTAACGAATGCATCCCCACAAT
GGCTGTGCCACGGCACCTGCAGCACTCCCTGGCAATGTACTTGTGATGAGGGCTGGGGAGG
CCTGTTTTGTGACCAAGATCTCAACTACTGCACCCACCCTCCCCATGCAAGAATGGGGCAA
CGTGTCCAACAGTGGGCGGGAAGCTACACCTGCACCTGTGCGCCAGGCTACACTGGTGTG
GACTGTGAGCTGGAGCTCAGCGAGTGTGACAGCAACCCTGTGCAATGGAGGCAGCTGTAA
GGACCAGGAGGATGGCTACCACTGCCTGTGTCTCCGGGCTACTATGGCCTGCACTGTGAAC
ACAGCACCTTGAGCTGCGCCGACTCCCCCTGCTTCAATGGGGGCTCCTGCCGGGAGCGCAAC
CAGGGGGCAACTATGCTTGTGAATGTCCCCCAACTTCACCGGCTCCAAGTGCAGAGAAGAA
AGTGGACAGGTGCACCAGCAACCCTGTGCCAACGGGGGACAGTGCCTGAACCGAGGTCCAA
GCCGCATGTGCCGCTGCCGCTCCTGGATTACGGGCACCTACTGTGAACTCCACGTGAGCGAC
TGTGCCCGTAACCCTTGCGCCACGGTGGCACTTGCATGACCTGGAGAATGGGCTCATGTG
CACCTGCCCTGCCGGCTTCTCTGGCCGACGCTGTGAGGTGCGGACATCCATCGATGCCTGTG
CCTCGAGTCCCTGCTTCAACAGGGCCACCTGCTACACCGACCTCTCCACAGACACCTTTGTG
TGCAACTGCCCTTATGGCTTTGTGGGAGCCGCTGCGAGTTCCCCGTGGGGCTTGCCGCCAG
CTTCCCCTGGGTGGCCGCTCTCGCTGGGTGTGGGGCTGGCAGTGTGCTGGTACTGCTGGGCA
TGGTGGCAGTGGCTGTGCGGCAGCTGCGGCTTCGACGGCCGGACGACGGCAGCAGGGAAGCC
ATGAACAACCTGTGCGGACTTCCAGAAGGACAACCTGATTCCTGCCGCCAGCTTAAAAACAC
AAACCAGAAGAAGGAGCTGGAAGTGGACTGTGGCCTGGACAAGTCCAAGTGTGGCAAACAGC
AAAACCACACATTGGACTATAATCTGGCCCCAGGGCCCCCTGGGGCGGGGGACCATGCCAGGA
AAGTTTCCCCACAGTGACAAGAGCTTAGGAGAGAAGGCGCCACTGCGGTTACACAGTGAAAA
GCCAGAGTGTGCGATATCAGCGATATGCTCCCCAGGGACTCCATGTACCAGTCTGTGTGTT
TGATATCAGAGGAGAGGAATGAATGTGTCATTGCCACGGAGGTA**TAA**GGCAGGAGCCTACCT
GGACATCCCTGCTCAGCCCCGCGGCTGGACCTTCCTTCTGCATTGTTTACA

FIGURE 214

MAAASRSASGWALLLLVALWQQRAAGSGVFQLQLQEFINERGVLASGRPCEPGCRTFFRVCL
KHFQAVVSPGPCTFGTVSTPVLGTNSFAVRDDSSGGGRNPLQLPFNFTWPGTFSLIEAWHA
PGDDLRLPEALPPDALISKIAIQGSLAVGQNWLLDEQTSTLTRLRYSYRVICSDNYGDNCSR
LCKKRNDHFGHYVCQPDGNLSCLPGWTGEYCQQPICLSGCHEQNGYCSKPAECLCRPGWQGR
LCNECIPHNGCRHGTCSTPWQCTCDEGWGGLFCDQDLNYCTHHSPCKNGATCSNSGQRSYTC
TCRPGYTGVDCELELSECDNPNCRNGGSKDQEDGYHCLCPPGYGLHCEHSTLSCADSPCF
NGGSCRERNQGANACECPNFTGSNCEKKVDRCTSNPCANGGQCLNRGSPSRMCRCPGFTG
TYCELHVSDCARNPCAAGGTCHELENGLMCTCPAGFSGRRCEVRTSIDACASSPCFNRTC
TDLSTDTFVCNCPYGFVGSRCFPPVGLPPSFPWVAVSLGVGLAVLLVLLGMVAVAVRQLRLR
RPDDGSRREAMNNLSDFQKDNLI PAAQLKNTNQKKELEVDCGLDKSNCGKQQNHTLDYNLAPG
PLGRGTMPEGKFPPIISDKSLGEKAPLRLHSEKPECRISAICSPRDSMYQSVCLISEERNECVIA
TEV

Important features of the protein:

Signal peptide:

amino acids 1-26

Transmembrane domain:

amino acids 530-552

N-glycosylation sites.

amino acids 108-112, 183-187, 205-209, 393-397, 570-574, 610-614

Glycosaminoglycan attachment site.

amino acids 96-100

Tyrosine kinase phosphorylation site.

amino acids 340-347

N-myristoylation sites.

amino acids 42-48, 204-210, 258-264, 277-283, 297-303, 383-389,
415-421, 461-467, 522-528, 535-541, 563-569, 599-605, 625-631

Amidation site.

amino acids 471-475

Aspartic acid and asparagine hydroxylation site.

amino acids 339-351

EGF-like domain cysteine pattern signature.

amino acids 173-185, 206-218, 239-251, 270-282, 310-322,
348-360, 388-400, 426-438, 464-476, 506-518

Calcium-binding EGF-like:

amino acids 224-245, 255-276, 295-316, 333-354, 373-394,
411-432, 449-470

FIGURE 216

```
></usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA82361
><subunit 1 of 1, 352 aa, 1 stop
><MW: 38938, pI: 7.86, NX(S/T): 3
MALLLCFVLLCGVVDFARSLISITTPPEEMIEKAKGETAYLPCKFTLSPEDQGPLDIEWLISPA
DNQKVDQVIILYSGDKIYDDYYPDLKGRVHFTSNDLKSGDASINVTNLQLSDIGTYQCKVKK
APGVANKKIHLVVLVKPSGARCVDGSEEIGSDFKIKCEPKEGSLPLQYEWQKLSDSQKMPT
SWLAEMTSSVISVKNASSEYSGTYSCTVRNRVGSQCLLRLNVVPPSNKAGLIAGAIIGTLL
ALALIGLIIFCCRKKRREEKYEKEVHHDIREDVPPPKSRTSTARSYIGSNHSSLGSMSPSNM
EGYSKTQYNQVPSSEDFERTPQSPTLPPAKFKYPYKTDGITVV
```

Signal sequence.
amino acids 1-19

Transmembrane domain:
amino acids 236-257

N-glycosylation sites.
amino acids 106-110, 201-205, 298-302

Tyrosine kinase phosphorylation sites.
amino acids 31-39, 78-85, 262-270

N-myristoylation sites.
amino acids 116-122, 208-214, 219-225, 237-243, 241-247,
245-251, 296-302

Myelin P0 protein.
amino acids 96-125

FIGURE 217

GATGGCGCAGCCACAGCTTCTGTGAGATTTCGATTTCTCCCCAGTTCCCCTGTGGGTCTGAGG
GGACCAGAAGGGTGAGCTACGTTGGCTTTCTGGAAGGGGAGGCTATATGCGTCAATTCCCCA
AAACAAGTTTTGACATTTCCCCTGAAATGTCATTTCTCTATCTATTCACTGCAAGTGCCTGCT
GTTCCAGGCCCTTACCTGCTGGGCACATAACGGCGGAGCCAGGATGGGGACAGAATAAAGGAGC
CACGACCTGTGCCACCAACTCGCACTCAGACTCTGAACTCAGACCTGAAATCTTCTCTTAC
GGGAGGCTTGGCAGTTTTTCTTACTCCTGTGGTCTCCAGATTTCCAGGCTAAGATGAAAGCC
TCTAGTCTTGCCTTACGCTTCTCTCTGCTGCGTTTTATCTCCTATGGACTCCTTCCACTGG
ACTGAAGACACTCAATTTGGGAAGCTGTGTGATCGCCACAAACCTTCCAGGAAATACGAAATG
GATTTTCTGAGATACGGGGCAGTGTGCAAGCCAAAGATGGAAACATTGACATCAGAATCTTA
AGGAGGACTGAGTCTTTGCAAGACACAAAGCCTGCGAATCGATGCTGCCTCCTGCGCCATTT
GCTAAGACTCTATCTGGACAGGGTATTTAAAAACTACCAGACCCCTGACCAATPATACTCTCC
GGAAGATCAGCAGCCTCGCCAATTCCTTTCTTACCATCAAGAAGGACCTCCGGCTCTCTCAT
GCCCACATGACATGCCATTGTGGGGAGGAAGCAATGAAGAAATACAGCCAGATTCTGAGTCA
CTTTGAAAAGCTGGAACCTCAGGCAGCAGTTGTGAAGGCTTTGGGGGAACTAGACATTCTTC
TGCAATGGATGGAGGAGACAGAAATAGGAGGAAAGTGATGCTGCTGCTAAGAATATTCGAGGT
CAAGAGCTCCAGTCTTCAATACCTGCAGAGGAGGCATGACCCCAAACCACCATCTCTTTACT
GTACTAGTCTTGTGCTGGTCACAGTGTATCTTATTTATGCATTACTTGCTTCCTTGCATGAT
TGTCTTTATGCATCCCCAATCTTAATTGAGACCATACTTGTATAAGATTTTTGTAATATCTT
TCTGCTATTGGATATATTTATTAGTTAATATATTTATTTATTTTTGCTATTTAATGTATTT
ATTTTTTTACTTGGACATGAACTTTAAAAAAATTCACAGATTATATTTATAACCTGACTAG
AGCAGGTGATGTATTTTTATACAGTAAAAAATAAACCTTGTAATTCAGAAAGAGTGGCT
AGGGGGTTATTCATTTGTATTCAACTAAGGACATATTTACTCATGCTGATGCTCTGTGAGA
TATTTGAAATTGAACCAATGACTACTTAGGATGGGTGTGGAATAAGTTTTGATGTGGAATP
GCACATCTACCTTACAATTACTGACCATCCCAGTAGACTCCCAGTCCCATAATTGTGTAT
CTTCCAGCCAGGAATCCTACACGGCCAGCATGTATTTCTACAAATAAAGTTTTCTTTGCATA
CCAAAAAAAAAAAAAAAAAAAAA

FIGURE 218

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA83500

MKASSLAFSLLSAAFYLLWTPSTGLKTLNLGSCVIATNLQEIRNGFSEIRGSVQAKDGN
IDIRILRRTESLQDTKPANRCCLLRHLLRLYLDRVFKNYQTPDHYTI, RKISSLANSTLT
IKKDLRLSHAHMTCHCGEEAMKKYSQILSHFEKLEPQAQAVVKALGELDILLQWMEETE

FIGURE 219

CGCGGAGCCCTGCGCTGGGAGGTGCACGGTGTGCACGCTGGACTGGACCCCCATGCAACCCC
 GCGCCCTGCGCCTTAACCAGGACTGCTCCGCGCGCCCTGAGCCTCGGGCTCCGGCCCGGAC
 CTGCAGCCTCCCAGGTGGCTGGGAAGAAGTCTCCAACAATAAATACATTTGATAAGAAAGAT
GGCTTTAAAAGTGCTACTAGAACAAAGAGAAAACGTTTTTCACTCTTTTAGTATTACTAGGCT
 ATTTGTCATGTAAAGTGACTTGTGAATCAGGAGACTGTAGACAGCAAGAATTCAGGGATCGG
 TCTGGAAACTGTGTTCCCTGCAACCAGTGTGGGCCAGGCATGGAGTTGTCTAAGGAATGTGG
 CTTGCGCTATGGGGAGGATGCACAGTGTGTGACGTGCCGGCTGCACAGGTTCAAGGAGGACT
 GGGGCTTCCAGAAATGCAAGCCCTGTCTGGACTGCGCAGTGGTGAACCGCTTTCAGAAGGCA
 AATTGTTAGCCACCAGTGTATGCCATCTGCGGGGACTGCTTGCCAGGATTTTATAGGAAGAC
 GAAACTTGTGCGGCTTTC AAGACATGGAGTGTGTGCCCTTGTGGAGACCCCTCCTCCTTACG
 AACCGCACTGTGCCAGCAAGGTCAACCTCGTGAAGATCGCGTCCACGGCCTCCAGCCCACGG
 GACACGGCGCTGGCTGCCGTTATCTGCAGCGCTCTGGCCACCGTCTGCTGGCCCTGCTCAT
 CCTCTGTGTCATCTATTGTAAGAGACAGTTTATGGAGAAGAAAACCCAGCTGGTCTCTGCGGT
 CGCAGGACATTCAGTACAACGGCTCTGAGCTGTGCTGTTTTGACAGACCTCAGCTCCACGAA
 TATGCCACAGAGCCTGCTGCCAGTGCCGCGTGACTCAGTGCAGACCTGCCGGGCCGGT'GCG
 CTTGCTCCCATCCATGTGCTGTGAGGAGGCCAGCAGCCCCAACCCGGGACTCTTGGTTGTG
 GGGTGCATTCAGCAGCCAGTCTTCAGGCAAGAAACGCAGGCCAGCCGGGAGATGCTGCCG
 ACTTCTTCGGATCCCTCACGCAGTCCATCTGTGGCGAGTTTTTCAGATGCCTGGCCTCTGAT
 GCAGAATCCCATGGGTGGTGACAACATCTCTTTTTGTGACTCTTATCCTGAACTCACTGGAG
 AAGACATTCATTCTCTCAATCCAGAAGTGAAGCTCAACGTCTTTGGATTCAAATAGCAGT
 CAAGATTTGGTTGGTGGGGCTGTTCCAGTCCAGTCTCAT'CTGAAAACCTTACAGCAGCTAC
 TGATTTATCTAGATATAACAACACACTGGTAGAATCAGCATCAACTCAGGATGCCTAACTA
 TGAGAAGCCAGCTAGATCAGGAGAGTGGCGCTGTATCCACCCAGCCACTCAGACGTCCCTC
 CAGGAAGCTTAAAGAACCTGCTTCTTTCTGCAGTAGAAGCGTGTGCTGGAACCCAAAGAGTA
 CTCCTTTGTTAGGCTTATGGACTGAGCAGTCTGGACCTTGCATGGCTTCTGGGGCAAATA
 AATCTGAACCAAACCTGACGGCATTGTAAGCCTTTCAGCCAGTTGCTTCTGAGCCAGACCAGC
 TGTAAGCTGAAACCTCAATGAATAACAAGAAAAGACTCCAGGCCGACTCATGATACTCTGCA
 TCTTTCCTACATGAGAAGCTTCTCTGCCACAAAAGTGACTTCAAAGACTGATGGGTTGAGCT
 GGCAGCCTATGAGATTTGTGGACATATAACAAGAAAACAGAAATGCCCTCATGCTTATTTTCAI
 GGTGATTGTGGTTTTTACAAGACTGAAGACCCAGAGTATACTTTTTTCTTCCAGAAATAATTT
 CATACCGCCTATGAAATATCAGATAAATTACCTTAGCTTTTATGTAGAATGGGTTCAAAGT
 GAGTGTCTTATTTGAGAAGGACACTTTTTTATCATCTAAACTGATTGCGATAGGTGGTTAG
 AATGGCCCTCATAT'GCCTGCCTAAATCTTGGGTTTATTAGATGAAGTTTACTGAATCAGAG
 GAATCAGACAGAGGAGGATAGCTCTTCCAGAATCCACACTTCTGACCTCAGCCTCGGTCTC
 ATGAACACCCGCTGATCTCAGGAGAACACCTGGGCTAGGGAATGTGCTCGAGAAAGGGCAGC
 CCATTGCCCAGAATTAACACATATTGTAGAGACTTGTATGCAAAGGTTGGCATATTTATATG
 AAAATTAGTTGCTATAGAAAACATTTGTTGCATCTGTCCCTCTGCCTGAGCTTAGAAGGTTAT
 AGAAAAGGGTATTTATAAACATAAATGACTTTTTACTTGCATTGTATCTTATACTAAAGGC
 TTTAGAAATTACAACATATCAGGTTCCCTACT'ACT'GAAGTAGCCTTCCG'GAGAACACACC
 ACATGTTAGGACTAGAAGAAAATGCACAATTTGTAGGGGTTTGGATGAAGCAGCTGTAACCTG
 CCCTAGTGTAGTTTGACCAGGACATTGTCGTGCTCCTCCAATTGTGTAAGATTAGTTAGCA
 CATCATCTCCTACTTTAGCCATCCGGTGTGGATTTAAGAGGACGGTGTCTTCTTCTATTAA
 AGTGTCCATCCCTACCATCTACACATTAGCATTGTCTCTAGAGCTAAGACAGAAATTAAC
 CCCGTTAGTCACAAAGCAGGGAATGGTTTACTCTTAATCTTTATGCCCTGGAGAAGA
 CCTACTTGAACAGGGCATATTTTTTAGACTTCTGAACATCAGTATGTTCCAGGGTACTATGA
 TATTTTGGTTGGAATTGCCCTGCCCAAGTCACTGTCTTTTAACTTTTAACTGAATATTA
 AATGTATCTGTC'TTTCCT

FIGURE 220

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></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA84210
><subunit 1 of 1, 417 aa, 1 stop
><MW: 45305, pI: 5.12, NX(S/T): 6
MALKVLEQEKTFFFTLLVLLGYLSCKVTCESGDCRQQEFRDRSGNCVPCNQCGPGMELSK
ECGFGYGEDAQCVTCLHRFKEDWGFQKCKPCLDCAVVNRFOKANCSATSDAICGDCLPG
FYRKTklVGFQDMECVPCGDPpppyEPHCASKVNLVkiASTASSPRDTALAAVICSALAT
VLLALLILCVIYCKRQFMekkPSWslRSQDIQYNGSELSCFDRPQLHEYAHRACCQCRRD
SVQTCGPVRLLPsmcCEEACSPNPATLGCgVHSAASLQARNAGPAGEMVPTFFGSLTQSI
CGEFSDAWPLMQNPMGGDNISFCDSYPelTGEDIHSLNPELESSTSLDSNSSQDLVGGAV
PVQSHSENFTAATDLsRYNNTLVESASTQDALTMRSQldQESGAVIHpatQTSLQEA
```

Important features of the protein:

Signal peptide:

Amino acids
1-25

Transmembrane domain:

Amino acids
169-192

N-glycosylation sites:

Amino acids
105-109;214-218;319-323;350-354;368-372;379-383

cAMP- and cGMP-dependent protein kinase phosphorylation sites:

Amino acids
200-204;238-242

Tyrosine kinase phosphorylation site:

Amino acids
207-214

N-myristoylation sites:

Amino acids
55-61;215-221;270-276

Prokaryotic membrane lipoprotein lipid attachment site:

Amino acids
259-270

TNFR/NGFR family cysteine-rich region proteins:

Amino acids
89-96

FIGURE 222

MLGLPWKGGLSWALLLLLLLGSQILLIYAWHFHEQRDCDEHNVMARYLPATVEFAVHTFNQQS
KDYYAYRLGHILNSWKEQVESKTVFSMELLGRTRCGKFEDDIDNCHFQESTELNNTFTCFE
TISTRPWMTQFSLLNKTCLEGFH

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 223

AATCGGCTGATTCTGCATCTGGAACTGCCTTCATCTTGAAAGAAAAGCTCCAGGTCCCT
TCTCCAGCCACCCAGCCCCAAGATGGTGATGCTGCTGCTGCTGCTTTCCGCACTGGCTGG
CCTCTTCGGTGCGGCAGAGGGACAAGCATTTCATCTTGGGAAGTGCCCCAATCCTCCGGT
GCAGGAGAATTTTGACGTGAATAAGTATCTCGGAAGATGGTACGAAATGAGAAGATCCC
AACAACTTTGAGAATGGACGCTGCATCCAGGCCAACTACTCACTAATGGAAAACGGAAA
GATCAAAGTGTTAAACCAGGAGTTGAGAGCTGATGGAAGTGAATCAAAATCGAAGGTGA
AGCCACCCAGTTAACCTCACAGAGCCTGCCAAGCTGGAAGTTAAGTTTTCCTGGTTTAT
GCCATCGGCACCGTACTGGATCCTGGCCACCGACTATGAGAAGTATGCCCTCGTGTATTC
CTGTACCTGCATCATCCAACCTTTTTACGTGGATTTTGCTTGGATCTTGGCAAGAAACCC
TAATCTCCCTCCAGAAACAGTGGACTCTCTAAAAAATATCCTGACTTCTAATAACATTGA
TGTCAAGAAAATGACGGTCACAGACCAGGTGAACTGCCCCAAGCTCTCGTAACCAGGTTC
TACAGGGAGGCTGCACCCACTCCATGTTACTTCTGCTTCGCTTTCCCTACCCACCCCC
CCCCATAAAGACAAACCAATCAACCACGACAAAGGAAGTTGACCTGAACATGTAACCAT
GCCCTACCCTGTTACCTTGCTAGCTGCAAATAAACTTGTTGCTGACCTGCTGTGCTCGC
AAAAAA

FIGURE 224

MVMLLLLLSALAGLFGAAEGQAFHLGKCPNPPVQENFDVNKYLGRWYEIEKIPTTFENG
RCIQANYSLMENGKIKVLNQELRADGTVNQIEGEATPVNLTEPAKLEVKFSWFMPSPAY
WILATDYENYALVYSCTCIIQLFHVDFAWILARNPNLPPETVDSLKNILTSNNIDVKKM
TVTQVNCPKLS

Signal sequence

1-16

N-glycosylation site.

65-68

98-101

cAMP- and cGMP-dependent protein kinase phosphorylation site.

175-178

N-myristoylation site.

13-18

16-21

Lipocalin proteins.

36-47

120-130

Lipocalin / cytosolic fatty-acid binding proteins

41-185

FIGURE 225

GGGTGATTGAACTAAACCTTCGCCGCACCGAGTTTGCAGTACGGCCGTCACCCGCACCGCTG
CCTGCTTGCGGTTGGAGAAATCAAGGCCCTACGGGCCCTCCGTAGTCACCTCTCTATAGTGG
GCGTGGCCGAGGCCGGGGTGACCCTGCCGGAGCCTCCGCTGCCAGCGACATGTTC AAGGTAA
TTCAGAGGTCCGTGGGGCCAGCCAGCCTGAGCTTGCTCACCTTCAAAGTCTATGCAGCACCA
AAAAAGGACTCACCTCCCAAAAATTCCGTGAAGGTTGATGAGCTTTCACTCTACTCAGTTCC
TGAGGGTCAATCGAAGTATGTGGAGGAGGCAAGGAGCCAGCTTGAAGAAAGCATCTCACAGC
TCCGACACTATTGCGAGCCATACACAACCTGGTGTGAGGAAACGTACTCCCAAACTAAGCCC
AAGATGCAAAGTTTGGTTCAATGGGGGTTAGACAGCTATGACTATCTCCAAAATGCACCTCC
TGGATTTTTTCCGAGACTTGGTGTATTGGTTTTGCTGGCCTTATTGGACTCCTTTTGGCTA
GAGTTCAAAAATAAAGAAGCTAGTGTATCCGCCTGGTTTCATGGGATTAGCTGCCTCCCTC
TATTATCCACAACAAGCCATCGTGTGTTGCCAGGTCAGTGGGGAGAGATTATATGACTGGGG
TTTACGAGGATATATAGTCATAGAAGATTTGTGGAAGGAGAACTTTCAAAGCCAGGAAATG
TGAAGAATTCACCTGGAACTAAGTAGAAAACCTCCATGCTCTGCCATCTTAATCAGTTATAGG
TAAACATTGGAAACTCCATAGAATAAATCAGTATTTCTACAGAAAAATGGCATAGAAGTCAG
TATTGAATGTATTAAATTGGCTTTCTTCTTCCAGGAAAAACTAGACCAGACCTCTGTTATCTT
CTGTGAAATCATCTACAAGCAAACCTAACCTGGAATCCCTTCACCTAGAGATAATGTACAAG
CCTTAGAACTCCTCATTCTCATGTTGCTATTTATGTACCTAATTTAAACCCAAGTTTAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 226

MFKVIQRSVGPASLSLLTFKVYAAPKKDSPPKNSVKVDELSLYSVPEGQSKYVEEARSQLEE
SISQLRHYCEPYTTWCQETYSQTKPKMQSLVQWGLDSYDYLQNAPPGFFPRLGVIGFAGLIG
LLLARGSKIKKLVYPPGFEMGLAASLYYPQQAIVFAQVSGERLYDWGLRGYIVIEDLWKENFQ
KPGNVKNSPGTK

Important features:

Signal peptide:

Amino acids 1-23

Transmembrane domain:

Amino acids 111-130

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 26-30

Tyrosine kinase phosphorylation site:

Amino acids 36-44

N-myristoylation sites:

Amino acids 124-130;144-150;189-195

FIGURE 227

CACCGGAGGGCACGCAGCTGACGGAGCTGCGCTGCGTTCGCCTCGTTTGCCTCGCGCCCTCC
ACTGGAGCTGTTTCGCGCCTCCCGGCTCCCACCGCAGCCCACCCGGCAGAGGAGTCGCTACCA
GCGCCAGTGCCTCTGTTCAGTCCGCAAACCTCTTTCGCGCCCGCCCCGGGCTGGGCACCAAA
TACCAGGCTACCATGGTCTACAAGACTCTCTTCGCTCTTTGCATCTTAACTGCAGGATGGAG
GGTACAGAGTCTGCCTACATCAGCTCCTTTGTCTGTTTCTCTTCCGACAAACATTTGTACCAC
CGACCACCATCTGGACTAGCTCTCCACAAAACACTGATGCAGACACTGCCTCCCCATCCAAC
GGCACTCACAACAACCTCGGTGCTCCCAGTTACAGCATCAGCCCCAACATCTCTGCTTCCTAA
GAACATTTCCATAGAGTCCAGAGAAGAGGAGATCACCAGCCCAGGTTTGAATTTGGGAAGGCA
CAAACACAGACCCCTCACCTTCTGGGTTCTCGTCAACAAGCGGTGGAGTCCACTTAAACAACC
ACGTTGGAGGAACACAGCTCGGGCACTCCTGAAGCAGGCGTGGCAGCTACACTGTCGCAGTC
CGCTGCTGAGCCTCCCACACTCATCTCCCCTCAAGCTCCAGCCTCATCACCTCATCCCTAT
CAACCTCACCACCTGAGGTCTTTTCTGCCTCCGTTACTACCAACCATAGCTCCACTGTGACC
AGCACCCCAACCCACTGGAGTCCAAGTGCACACAGAGTCCCCGACAGAGGAGTCCAGCTCTGA
CCACACACCCACTTACATGCCACAGCTGAGCCAGTCCCCCAGGAGAAAACACCCCAACAA
CTGTGTCAGGCAAAGTGTGTGTGAGCTCATAGACATGGAGACCACCACCCTTTCCCAGG
GTGATCATGCAGGAAGTAGAACATGCATTAAGTTTCCAGGCAGCATCGCCGCCATTACCGTGAC
AGTCATTGCCGTGGTGTCTGCTGGTGTGTTGGAGTTGCAGCCTACCTAAAAATCAGGCATTCCT
CCTATGGAAGACTTTTGGACGACCATGACTACGGGTCTGGGGAAACTACAACAACCCTCTG
TACGATGACTCCATAAATGGAATATGGCCTGGGATGAGGATTAAGTCTTTATTTATAA
GTGCTTATCCAGTAGAATTAATAAGTACCTGATGCGCATTGAACGACAATCTTAAGCCCTGT
TTTGTGGTATGGTTGTTTTGTTTTTCCCTCCCTCTCCTCTGGCTGCTACAACCTCCCCTTTC
TGGTACAAGAAGAACCATTCTTTAAAGGTGAGTGGAGGCTGATTTGCAGCTGAAGTGGGCCA
GCCTTGCACCAGCCAGGCCAGACCACCATGGTGAAGGCTTCTTTCCCCTGCAGGACCCAC
TTTGAGAAGGATCGAGGAGGAGGATTTGGGTTGTTTTGTTAGGGGTTACTTTCAGGGGAACA
TTTCATTTGTGTTATTTCTTAAACTTCTATTTAGGAAATTACATTAAGTATTAATGAGGGGA
AAGGAAATGAGCTCTACGAGGATTTACCTTGCATGGGAGAGAGCAGGGTTTTCTCAGATTC
CTTTTTAATCTCTATTTATCTGGTTGTTTTCTGACAGGATGCTGCCTGCTTGGCTCTACGAGC
TGGAAGCAGCTTCTTAGCTGCCTAATTAATGAAAGATGAAAATAGGAAGTGCCTGGAGGG
GGCCAGCAGGTCACGGGGCAGAATCTCTCAGGTTGCTGTGGGATCTCAGTGTGCCCCCTACCT
GTTCTCCCCTCCAGGCCACCTGTCTCTGTAAAGGATGTCTGCTCTGTTCAAAGGCAGCTGG
GATCCCAGCCCACAAGTGTATCAGCAGAGTTGCATTTCCAAAGAAAAGGCTATGAGATGAGC
TGAGTATAGAGAGAAAGGGAGAGGCATGTACGGTGTGGGGAAGTGAAGAGAAGCTGGCGG
GGGAGAAGGAGGCTAACCTGCCTGAGTACTTCATTAGGACAAGTGAAGATCAGCTATTGAT
AATGGCCAGAGATATCCACAGCTTGGAGGAGCCCAGAGACTGTTCGCTTTATACCCACACAG
CAACTGGTCCACTGCTTTACTGTCTGTTGGATAATGGCTGTAAAATGTTTAAAAAC

FIGURE 228

MVYKTLFALCILTAGWRVQSLPTSAPLSVSLPTNIVPPTTIWTSSPQNTDADTASPSNGTHN
NSVLPVTASAPTSLLPKNISIESREEEITSPGSNWEGTNTDPSPSGFSSTSGGVHLTTTLEE
HSSGTPEAGVAATLSQSAAPPTLISPQAPASSPSSLSTSPPEVFSASVTTNHSSTVTSTQP
TGAPTAPESPTEESSDHTPTSHATAEPVPEKTPPTTVSGKVMCELIDMETTTTFPRVIMQ
EVEHALSSGSIAAITVTVIAVVLLVFGVAAYLKIRHSSYGRLLDDHDYGSWGNYNPLYDDS

Important features of the protein:

Signal peptide:

amino acids 1-20

Transmembrane domain:

amino acids 258-278

N-glycosylation sites.

amino acids 58-61, 62-65, 80-83, 176-179

Casein kinase II phosphorylation sites.

amino acids 49-52, 85-88, 95-98, 100-103, 120-123, 121-124, 141-144, 164-167, 191-194, 195-198, 200-203

Tyrosine kinase phosphorylation site.

amino acids 289-296

N-myristoylation sites.

amino acids 59-64, 115-120, 128-133, 133-138, 257-262, 297-302

FIGURE 229

CTCCTGCACTAGGCTCTCAGCCAGGGATGATGCGCTGCTGCCGCCGCCGCTGCTGCTGCCGG
CAACCACCCCATGCCCTGAGGCCGTTGCTGTTGCTGCCCCTCGTCCCTTTACCTCCCCTGGC
AGCAGCTGCAGCGGGCCCAAACCGATGTGACACCATATACCAGGGCTTCGCCGAGTGTCTCA
TCCGCTTGGGGGACAGCATGGGCCCGGAGGCGAGCTGGAGACCATCTGCAGGTCTTGGAAT
GACTTCCATGCCTGTGCCTCTCAGGTCCTGTCAGGCTGTCCGGAGGAGGCAGCTGCAGTGTG
GGAATCACTACAGCAAGAAGCTCGCCAGGCCCCCCCGTCCGAATAACTTGCACACTCTGTGCG
GTGCCCCGGTGCATGTTTCGGGAGCGCGGCACAGGC¹CCGAAACCAACCAGGAGACGCTGCCG
GCTACAGCGCCTGCACTCCCCATGGCCCCCTGCGCCCCACTGCTGGCGGCTGCTCTGGCTCTG
GCCTACCTCCTGAGGCCTCTGGCCTAGCCTTGTTGGGTGGGTAGCAGCGCCCGTACCTCCAG
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TTTATATTTGTA

FIGURE 230

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA92265
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GRGGELETICRSWNDFHACASQVLSGCPEEAAAVWESLQQEARQAPRPNNLHTLCGAPVH
VRERGTGSETNQETLRATAPALPMAPAPPLLAALALAYLLRPLA
```

Important features of the protein:

Signal peptide:

Amino acids 1-35

Transmembrane domain:

Amino acids 141-157

N-myristoylation site:

Amino acids 127-133

Prokaryotic membrane lipoprotein lipid attachment site:

Amino acids 77-88

FIGURE 231

AAGTACTTGTGTCCGGGTGGTGGACTGGATTAGCTGCGGAGCCCTGGAAGCTGCCTGTCCTT
CTCCCTGTGCTTAACCAGAGGTGCCCATGGGTTGGACAATGAGGCTGGTCACAGCAGCACTG
TACTGGGTCTCATGATGGTGGTCACTGGAGACGAGGATGAGAACAGCCCGTGTGCCCATGA
GGCCCTCTTGGACGAGGACACCCTCTTTTGGCAGGGCCTTGAAGTTTTCTACCCAGAGTTGG
GGAACATTGGCTGCAAGGTGTTCCTGATTGTAACAACCTACAGACAGAAGATCACCTCCTGG
ATGGAGCCGATAGTCAAGTTCCTGGGGGCCCTGGACGGCGCAACCTATATCCTGGTGATGGT
GGATCCAGATGCCCTAGCAGAGCAGAACCCAGACAGAGATTCTGGAGACATTGGCTGGTAA
CAGATATCAAGGGCGCCGACCTGAAGAAAGGGAAGATTCAGGGCCAGGAGTTATCAGCCTAC
CAGGCTCCCTCCCACCGGCACACAGTGGCTTCCATCGCTACCAGTTCTTTGTCTATCTTCA
GGAAGGAAAAGTCATCTCTCCTTCCCAAGGAAAACAAAACCTCGAGGCTCTTGGAAAATGG
ACAGATTTCTGAACCGCTTCCACCTGGGCGAACCTGAAGCAAGCACCCAGTTCATGACCCAG
AACTACCAGGACTCACCAACCCTCCAGGCTCCAGAGGAAGGGCCAGCGAGCCCAAGCACAA
AACCAGGCAGAGATAGCTGCCTGCTAGATAGCCGGCTTTGCCATCCGGGCATGTGGCCACAC
TGCTCACCACCGACGATGTGGGTATGGAACCCCTCTGGATACAGAACCCCTTCTTTCCAA
ATTAAAAAAAAAATCATCAA

FIGURE 232

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA92274
><subunit 1 of 1, 223 aa, 1 stop
><MW: 25402, pI: 8.14, NX(S/T): 1
MGWTMRLVTAALLLGLMMVVTGDEDENSPCAHEALLDEDTLFCQGLEVFYPELGNIGCKVVP
DCNNYRQKITSWMEPIVKFPGAVDGATYILVMVDPDAPSRAPRQRFWRHWLVTDIKGADLK
KGKIQQQELSAYQAPSPPAHSGFHRYQFFVYLQEGKVISLLPKENKTRGSKMDRFLNRFHL
GEPEASTQFMTQNYQDSPTLQAPRGRASEPKHKTRQR
```

Important features of the protein:

Signal peptide:

amino acids 1-22

N-glycosylation site.

amino acids 169-173

Tyrosine kinase phosphorylation site.

amino acids 59-68

N-myristoylation sites.

amino acids 54-60, 83-89, 130-136

Phosphatidylethanolamine signature.

amino acids 113-157

FIGURE 233

AAGGAGCAGCCC GCAAGCACCAAGTGAGAGGCCATGAAGTTACAGTGTGTTTCCCTTTGGCTC
CTGGGTACAATACTGATATTGTGCTCAGTAGACAACCACGGTCTCAGGAGATGTCTGATTTTC
CACAGACATGCACCATATAGAAGAGAGTTTTCCAAGAAATCAAAAAGAGCCATCCAAGCTAAGG
ACACCTTCCCAAATGTCACTATCCTGTCCACATTTGGAGACTCTGCAGATCATTAAGCCCTTA
GATGTGTGCTGCGTGACCAAGAACCTCCTGGCGTTCTACGTGGACAGGGTGTTC AAGGATCA
TCAGGAGCCAAACCCCAAATCTTGAGAAAAATCAGCAGCATTGCCAACTCTTTCCTCTACA
TGCAGAAAACCTCTGCGGCAATGTCAGGAACAGAGGCAGTGTCACTGCAGGCAGGAAGCCACC
AATGCCACCAGAGTCATCCATGACAACTATGATCAGCTGGAGGTCCACGCTGCTGCCATTAA
ATCCCTGGGAGAGCTCGACGTCTTTCTAGCCTGGATTAATAAGAATCATGAAGTAATGTTCT
CAGCTTGATGACAAGGAACCTGTATAGTGATCCAGGGATGAACACCCCTGTGCGGTTTACT
GTGGGAGACAGCCCACCTTGAAGGGGAAGGAGATGGGGAAGGCCCTTGCAGCTGAAAGTCC
CACTGGCTGGCCTCAGGCTGTCTTATTCCGCTTGAAAATAGGCAAAAAGTCTACTGTGGTAT
TTGTAATAAACTCTATCTGCTGAAAGGGCCTGCAGGCCATCCTGGGAGTAAAGGGCTGCCTT
CCCATCTAATTTATTTGTAAGTCATATAGTCCATGTCTGTGATGTGAGCCAAGTGATATCCT
GTAGTACACATTGTA CTGAGTGGTTTTTCTGAATAAATTCCATATTTTACCTATGA

FIGURE 234

```
></usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA92282
><subunit 1 of 1, 177 aa, 1 stop
><MW: 20452, pI: 8.00, NX(S/T): 2
MKLQCVSLWLLGTILILCSVDNHGLRRCLISTDMHHIEESFQEIKRAIQAKDTFPNVTILST
LETLQI IKPLDVCCVTKNLLAFYVDRVFKDHQEPNPKILRKISSIANSFLYMOKTLRQCQEQ
RQCHCRQEATNATRVIHDNYDQLEVHAAAIKSLGELDVFLAWINKNHEVMFSA
```

Signal sequence:
amino acids 1-18

N-glycosylation sites.
amino acids 56-60, 135-139

cAMP- and cGMP-dependent protein kinase phosphorylation site.
amino acids 102-106

N-myristoylation site.
amino acids 24-30

Actinin-type actin-binding domain signature 1.
amino acids 159-169

FIGURE 235

GCCCCGGGCGGCTGCCCTTGGGTGCTCCCTTCCCTGCCCCGACACCCAGACCCGACCTTGACCGC
CCACCTGGCAGGAGCAGGACAGGACAGGACGGCCGGACGCGGCCATGGCCGAGCTCCCGGGGCCCTT
TCTCTGCGGGGCCCTGCTAGGCTTCCTGTGCCTGAGTGGGCTGGCCGTGGAGGTGAAGGTAC
CCACAGAGCCGCTGAGCACGCCCTGGGGAAGACAGCCGAGCTGACCTGCACCTACAGCACG
TCGGTGGGAGACAGCTTCGCCCTGGAGTGGAGCTTTGTGCAGCCTGGGAAACCCATCTCTGA
GTCCCATCCAATCCTGTACTTCACCAATGGCCATCTGTATCCAACCTGGTTCTAAGTCAAAGC
GGGTGAGCCTGCTTTCAGAACCCCCCACAGTGGGGGTGGCCACACTGAAACTGACTGACGTC
CACCCCTCAGATACTGGAACCTACCTCTGCCAAGTCAACAACCCACCAGATTTCTACACCAA
TGGGTGGGGCTAATCAACCTTACTGTGCTGGTTCCCCCAGTAATCCCTTATGCAGTCAGA
GTGGACAAACCTCTGTGGGAGGCTCTACTGCACTGAGATGCAGCTCTTCCGAGGGGGCTCCT
AAGCCAGTGTACAACCTGGGTGCGTCTTGGAACCTTTTCCCTACACCTTCTCCTGGCAGCATGGT
TCAAGATGAGGTGTCTGGCCAGCTCATTCTCACCAACCTCTCCCTGACCTCCTCGGGCACCT
ACCGCTGTGTGGCCACCAACCAGATGGGCAGTGCATCCTGTGAGCTGACCTCTCTGTGACC
GAACCCTCCCAAGGCCGAGTGGCCGGAGCTCTGATTGGGGTGCTCCTGGGCGTGCTGTTGCT
GTCAGTTGCTGCGTTCTGCCTGGTCAGGTTCCAGAAAGAGAGGGGGGAAGAAGCCCAAGGAGA
CATATGGGGGTAGTGACCTTCGGGAGGATGCCATCGCTCCTGGGATCTCTGAGCACACTTGT
ATGAGGGCTGATTCTAGCAAGGGTTTCCCTGGAAAGACCCTCGTCTGCCAGCACCGTGACGAC
CACCAAGTCCAAGCTCCCTATGGTCGTGTGACTTCTCCCGATCCCTGAGGGCGGTGAGGGGG
AATATCAATAATTAAGTCTGTGGGTACCCTTNAAAAAAAAAA

FIGURE 236

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA108760
><subunit 1 of 1, 327 aa, 1 stop
><MW: 34348, pI: 7.88, NX(S/T): 2
MAELPGPFELCGAII.GFLCLSGLAWEVKVPTEPLSTPLGKTAELTCTYSTSVGDSFALEWS
FVQPGKPISESHPILYFTNGHLYPTGSKSKRVSLLOQPPTVGVATLKLTDVHPSDTGTYL
CQVNNPPDFYTNGLGLINLTVLVPPSNPLCSQSGQTSVGGSTALRCSSSEGAPKPVYNWV
RLGTFPTPSPGSMVQDEVSGQLILTNLSTSSGTYRCVATNQMGASCELTLSVTEPSQG
RVAGALIGVLLGVLLLSVAAFCLVRFQKERGKKPKETYGGSDLREDAIAPGISEHTCMRA
DSSKGFLERPSSASTVTTTTSKLPVV
```

Important features of the protein:

Signal peptide:

Amino acids 1-20

Transmembrane domain:

Amino acids 242-260

N-glycosylation sites:

Amino acids 138-142;206-210

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 90-94

N-myristoylation sites:

Amino acids 11-17;117-123;159-165;213-219;224-230;244-250;
248-254

Amidation site:

Amino acids 270-274

Prokaryotic membrane lipoprotein lipid attachment site:

Amino acids 218-229

FIGURE 237

GGATGCAGCAGAGAGGAGCAGCTGGAAGCCGTGGCTGCGCTCTCTTCCCTCTGCTGGGCG
TCCTGTTCTTCCAGGGTGTTTATATCGTCTTTTCCTTGGAGATTCGTGCAGATGCCCATG
TCCGAGGTTATGTTGGAGAAAAGATCAAGTTGAAATGCACTTCAAGTCAACTTCAGATG
TCACTGACAAGCTTACTATAGACTGGACATATCGCCCTCCCAGCAGCCACACAGTAT
CAATATTTCAATTATCAGTCTTTCCAGTACCCAACCACAGCAGGCACATTTCGGGATCGGA
TTTCCCTGGGTTGGAAATGTATACAAAGGGGATGCATCTATAAGTATAAGCAACCCTACCA
TAAAGGACAATGGGACATTCAGCTGTGCTGTGAAGAATCCCCAGATGTGCACCATAATA
TTCCCATGACAGAGCTAACAGTCACAGAAAGGGGTTTTGGCACCATGCTTTCCTCTGTGG
CCCTTCTTCCATCCTTGTCTTGTGCCCTCAGCCGTGGTGGTTGCTCTGCTGCTGGTGA
GAATGGGGAGGAAGGCTGCTGGGCTGAAGAAGAGGAGCAGGTCTGGCTATAAGAAGTCAT
CTATTGAGGTTTTCCGATGACACTGATCAGGAGGAGGAAGAGGCGTGTATGGCGAGGCTTT
GTGTCCGTTGCGCTGAGTGCTGGATTCACTATGAAGAGACATATGATGAAAGTCTG
TATGACACAAGAAGAGTCACCTAAAGACAGGAAACATCCCATTCCACTGGCAGCTAAAGC
CTGTCAGAGAAAGTGGAGCTGGCCTGGACCATAGCGATGGACAATCCTGGAGATCATCAG
TAAAGACTTTAGGAACCACTTATTTATTGAATAAATGTTCTTGTGTATTATATAAAGTGT
TCAGGAAGTCTCATAAGAGACTCATGACTTCCCCTTCAATGAATTATGCTGTAATTGAA
TGAAGAAATTCTTTTCCCTGAGCA

FIGURE 238

MQQRGAAGSRGCALFPLLGVLFQGVYIVFSLEIRADAHVRGYVGEKIKLKCTFKSTSD
VTDKLTIDWTYRPPSSHTVSI FHYQSFQYPTTAGTFRDRISWVGNVYKGDASISISNP
TIKDNGTFSCAVKNPPDVHHNIPMTELTVTERGFGTMLSSVALLSILVFVPSAVVVALL
LVRMGRKAAGLKKRSRSGYKKSIEVSDDTDQEEEEACMARLCVRCAECLDSYEETY

Transmembrane domain

11-30
157-177

N-glycosylation site

123-127

cAMP- and cGMP-dependent protein kinase phosphorylation site

189-193
197-201

Tyrosine kinase phosphorylation site

63-71

N-myristoylation site

5-11
8-14
124-130
153-159

Amidation site

181-185

FIGURE 239

CAGCGGGCCCCCGCGGGCAGGGCCCTGGACCCGCGGGCTCCCGGGGATGGTGAGCAAGGCGCTGCTGCGCC
TCGTGTCTGCCGTCAACCGCAGGAGGATGAAGCTGCTGCTGGGCATCGCCTTGCTGGCCTACGTCGCCTCTGTT
TGGGGCAACTTCGTTAATATGAGGTCTATCCAGGAAAATGGTGAACAAAAATTGAAAGCAAGATTGAAGAGAT
GGTTGAACCACCTAAGAGAGAAAATCAGAGATTTAGAAAAAGCTTTACCCAGAAAATACCCACCAGTAAAGTTTT
TATCAGAAAAGGATCGGAAAAGAATTTTGATAACAGGAGGCGCAGGGTTCGTGGGCTCCCATCTAACTGACAAA
CTCATGATGGACGGCCACGAGGTGACCGTGGTGGACAATTTCTTACGGGCAGGAAGAGAAAACGTGGAGCACTG
GATCGGACATGAGAACTTCGAGTTGATTAACCACGACGTGGTGGAGCCCCCTACATCGAGGTTGACCAGATAT
ACCATCTGGCATCTCCAGCCTCCCTCCAAACTACATGTATAATCCTATCAAGACATTAAGACCAATACGATT
GGGACATTAACATGTTGGGGCTGGCAAAACGAGTCGGTGCCCGTCTGCTCCTGGCCTCCACATCGGAGGTGTA
TGGAGATCCTGAAGTCCACCCTCAAAGTGAGGATTACTGGGGCCACGTGAATCCAATAGGACCTCGGGCCTGCT
ACGATGAAGGCAAACGTGTTGCAGAGACCATGTGCTATGCCTACATGAAGCAGGAAGGCGTGGAAGTGCAGTG
GCCAGAACTTCAACACCTTTGGGCCACGCATGCACATGAACGATGGGCGAGTAGTCAGCAACTTCATCCTGCA
GGCGCTCCAGGGGGAGCCACTCACGGTATACGGATCCGGGTCTCAGACAAGGGCGTTCAGTACGTGAGCGATC
TAGTGAATGGCCTCGTGGCTCTCATGAACAGCAACGTGAGCAGCCCGGTCAACCTGGGGAACCCAGAAGAACAC
ACAATCCTAGAATTTGCTCAGTTAATTA AAAACCTTGTTGGTAGCGGAAGTGAATTCAGTTTCTCTCCGAAGC
CCAGGATGACCCACAGAAAAGAAAACAGACATCAAAAAGCAAAGCTGATGCTGGGGTGGGAGCCCGTGGTCC
CGCTGGAGGAAGTTTTAAACAAAGCAATTCACTACTTCCGTAAGAAGCTCGAGTACCAGGCAAAATATCAGTAC
ATCCCCAAACCAAGCCTGCCAGAATAAAGAAAGGACGGACTCGCCACAGCTGAACTCCTCACTTTTAGGACAC
AAGACTACCATTGTACACTTGATGGGATGATTTTTGGCTTTTTTTTGGTTGTCGTTTAAAGAAAGACTTTAACA
GGTGTGATGAAGAACAACCTGGAATTTCAATCTGAAGCTTGCTTTAATGAAATGGATGTGCTAAAAGCTCCCC
TCAAAAACCTGCAGATTTTGCCTTGCACTTTTTGAATCTCTCTTTTTATGTAAAATAGCGTAGATGCATCTCTG
CGTATTTCAAGTTTTTTTATCTTGCTGTGAGAGCATATGTTGTGACTGTGCTTGACAGTTTTATTTACTGGTT
TCTTTGTGAAGCTGAAAAGGAACATTAAGCGGGACAAAAAATGCCGATTTTATTTATAAAAAGTGGGTACTTAAT
AAATGATCGTTTATACTATGCATAAAGAAAAATCCTAGCAGTATTGTGAGGTGGTGGTGCGCCGGCATGATTT
TAGGGCAGATAAAAGAATTCTGTGTGAGAGCTTTATGTTTCTTTTTAATTCAGAGTTTTTCCAAGGTCTACTT
TTGAGTTGCAAACCTTGACTTTGAAATATTCCTGTGGTGCATGATCAAGGATATTTGAAATCACTACTGTGTTTT
GCTGCGTATCTGGGGCGGGGGCAGGTTGGGGGGCACAAAGTTAACATATCTTGGTTAACCATGGTTAAATATG
CTATTTTAATAAAAATATTGAAACTCA

FIGURE 240

MVSKALLRLVSAVNRRRMKLLLGIALLAYVASVWGNFVNMRSIQENGELKIESKIEEMVEPL
REKIRDLEKSFTQKYPPVKFLSEKDRKRILITGGAGFVGSHLTDKLMMDGHEVTVVDNFFTG
RKRNVHEHWIGHENFELINHVVVEPLYIEVDQIYHLASPPNYMYPNPIKTLKTNITIGTLNM
LGLAKRVGARLLLASTSEVYGDPEVHPQSEYWGHNPIGPRACYDEGKRVAETMCYAYMKQ
EGVEVRVARI FNTFGPRMIIMNDGRVVS NFILQALQGEPLTVYSGSQTRAFQYVSDLVNGLV
ALMNSNVSSPVNLGNPEEHTILEFAQLIKNLVSGSSEIQFLSEAQDDPQKRKPDIKKAKLML
GWEPVVPLEEGLNKAIHYFRKELEYQANNQYIPKPKPARIKKGRTSHS

Important features:

Signal peptide:

amino acids 1-32

N-glycosylation site:

amino acids 316-320

Tyrosine kinase phosphorylation site:

amino acids 235-244

N-myristoylation sites:

amino acids 35-41,101-107,383-389

Amidation sites:

amino acids 123-127,233-237

FIGURE 241

GCCCAGTGGAGAATTAGGTGCTGCTGGGAGCTCCTGCCTCCCACAGGATTCCAGCTGCAGGG
AGCCTCAGGGACTCTGGGCCGCACGGAGTTGGGGGCATTCCCCAGAGAGCGTCGCC**ATGGTC**
TGCAGGGAGCAGTTATCAAAGAATCAGGTCAAGTGGGTGTTTGGCCGCATTACCTGTGTGTC
TGTGGTGGTCATTGCCGCAATAGTCCTTGCCATCACCCCTGCGGGCCAGGCTGTGAGCTGG
AGGCCTGCAGCCCTGATGCCGACATGCTGGACTACCTGCTGAGCCTGGGCCAGATCAGCCGG
CGAGATGCCTTGGAGGTACCTGGTACCACGCAGCCAACAGCAAGAAAGCCATGACAGCTGC
CCTGAACAGCAACATCACAGTCCTGGAGGCTGACGTCAATGTAGAAGGGCTCGGCACAGCCA
ATGAGACAGGAGTTCCCATCATGGCACACCCCCCCTATCTACAGTGACAACACACTGGAG
CAGTGGCTGGACGCTGTGCTGGGCTCTTCCCAAAGGGCATCAAAGTGGACTTCAAGAACAT
CAAGGCAGTGGGCCCTCCCTGGACCTCCTGCGGCAGCTGACAGAGGAAGGCAAAGTCCGGC
GGCCCATATGGATCAACGCTGACATCTTAAAGGGCCCAACATGCTCATCTCAACTGAGGTC
AATGCCACACAGTTCTTGGCCCTGGTCCAGGAGAAGTATCCCAAGGCTACCCTATCTCCAGG
CTGGACCACCTTCTACATGTCCACGTCCCCAAACAGGACGTACACCCAAGCCATGGTGGAGA
AGATGCACGAGCTGGTGGGAGGAGTGCCCCAGAGGGTACCTTCCCTGTACGGTCTTCCATG
GTGCGGGCTGCCTGGCCCCACTTCAGCTGGCTGCTGAGCCAATCTGAGAGGTACAGCCTGAC
GCTGTGGCAGGCTGCCTCGGACCCCATGTGGTGGAAAGATCTGCTCTACGTCCGGGATAACA
GCCTTGAATGCCACACGGAAACCAATGTACTACACGGGAGGCAGCCTGATCCCTCTTCTCCA
GCTGCCTGGGGATGACGGTCTGAATGTGGAGTGGCTGGTTCCCTGACGTCCAGGGCAGCGGTA
AAACAGCAACAATGACCCCTCCAGACACAGAAGGCATGATCCTGCTGAACACTGGCCTCGAG
GGAAGTGTGGCTGAAAACCCCGTGCCCATTTGTTTACTACTCCAAGTGGCAACATCCTGACGCT
GGAGTCTGCCTGCAGCAGCTGGCCACACATCCCGGACACTGGGGCATCCATTTGCAAATAG
TGGAGCCCGCAGCCCTCCGGCCATCCCTGGCCTTGCTGGCACGCCTCTCCAGCCTTGGCCTC
TTGCATTTGGCCTGTGTGGGTGGGGCCAAAATCTCCCACGGGAGTTTTTCGGTCCCCGGCCA
TGTGGCTGGCAGAGAGCTGCTTACAGCTGTGGCTGAGGTCTTCCCCACGTGACTGTGGCAC
CAGGCTGGCCTGAGGAGGTGCTGGGCAGTGGCTACAGGGAACAGCTGCTCACAGATATGCTA
GAGTTGTGCCAGGGGCTCTGGCAACCTGTGTCTTCCAGATGCAGGCCATGCTGCTGGGCCA
CAGCACAGCTGGAGCCATAGGCAGGCTGCTGGCATCCTCCCCCGGGCCACCGTCACAGTGGAG
CACAACCCAGCTGGGGGGGACTATGCCTCTGTGAGGACAGCATTGCTGGCAGCTAGGGCTGT
GGACAGGACCCGAGTCTACTACAGGCTACCCAGGGCTACCACAAGGACTTGTGGCTCATG
TTGGTAGAAAT**TGA**GCACCCAGGGGTGGTGGGCCAGCGGACCTCAGGGCGGAGGCTTCCCAC
GGGGAGGCAGGAAGAAATAAAGGTCTTTGGCTTTCTCCAGGCAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAG

FIGURE 242

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA119514
><subunit 1 of 1, 585 aa, 1 stop
><MW: 64056, pI: 6.58, NX(S/T): 5
MVCREQLSKNQVKWVFAGITCVSVVVIAAIVLAILRRPGCELEACSPDADMLDYLLSLG
QISRRDALEVTWYHAANSKKAMTAALNSNITVLEADVNVVEGLGTANETGVPIMAHPTIY
SDNTLEQWLDVAVLGSSQKGIKLDKFNKAVGPSLDLLRQLTEEGKVRRIWINADILKGP
NMLISTEVNATQFLALVQEKYPKATLSPGWTFYFYMSTSPNRITYTQAMVEKMHVGGVPG
RVTFFVRRSSMVRAAWPHFSWLLSQSERYSLTLWQAASDPMSVEDLLYVRDNTAVHQVYD
IFEPLLSQFKQLALNATRKPMYYTGGLIPLLQLPGDDGLNVEWLVPDVQSGKTATMTL
PDTEGMILLNTGLEGTVAENPVPIVHTPSGNILTLESCLQQLATHPGHWGIHLQIVEPAA
LRPSLALLARLSSLGLLHWPVWVGAKISHGSFSVPGHVAGRELLTAVAEVFPHTVAPGW
PEEVLGSGYREQLLTDMLELCQGLWQPVSFQMAMLLGHSTAGAIGRLLASSPRATVTVE
HNPAGGDYASVRTALLAARAVDRTRVYYRLPQGYHKDLLAHVGRN
```

Important features of the protein:

Transmembrane domain:

Amino acids 18-37 (Possible type II)

N-glycosylation sites:

Amino acids 89-93;106-110;189-193;220-224;315-319

Tyrosine kinase phosphorylation site:

Amino acids 65-74

N-myristoylation sites:

Amino acids 101-107;351-357;372-378;390-396;444-450;545-551

Aminotransferases class-V pyridoxal-phosphate attachment site:

Amino acids 312-330

FIGURE 243

CTTCAGAACAGGTTCTCCTTCCCCAGTCACCAGTTGCTCGAGTTAGAATTGTCTGCAATGGC
CGCCCTGCAGAAATCTGTGAGCTCTTTCCCTTATGGGGACCCTGGCCACCAGCTGCCTCCTTC
TCTTGGCCCTCTTGGTACAGGGAGGAGCAGCTGCGCCCATCAGCTCCCAC'TGCAGGCTTGAC
AAGTCCAAC'TCCAGCAGCCCTATATCACCAACCGCACCTTCATGCTGGCTAAGGAGGCTAG
CTTGGCTGATAACAACACAGACGTTTCGTCTCATTGGGGAGAACTGTTCCACGGAGTCAGTA
TGAGTGAGCGCTGCTATCTGATGAAGCAGGTGCTGAACTTCACCCTTGAAGAAGTGCTGTTT
CCTCAATCTGATAGGTTCCAGCCTTATATGCAGGAGGTGGTGGCCCTTCCTGGCCAGGCTCAG
CAACAGGCTAAGCACATGTCATATTTGAAGGTGATGACCTGCATATCCAGAGGAATGTGCAAA
AGCTGAAGGACACAGTGAAAAAGCTTGGAGAGAGTGGAGAGATCAAAGCAATTTGGAGAACTG
GATTTGCTGTTTATGTCTCTGAGAAATGCCTGCATTTTGACCCAGAGCAAAGCTGAAAAATGAA
TAACTAACCCCTTTCCCTGCTAGAAATAACAATTAGATGCCCCAAAGCGATTTTTTTTAAAC
CAAAGGAAGATGGGAAGCCAAACTCCATCATGATGGGTGGATTCCAAATGAACCCCTGCGT
TAGTTACAAAGGAAACCAATGCCACTTTTGTATAAGACCAGAAGGTAGACTTTCTAAGCA
TAGATATTTATTGATAACATTTTCATTGTAAC'TGGTGTCTATACACAGAAAACAATTTATTT
TTTAAATAATTGTCTTTTTCCATAAAAAAGATTACTTTCCATTCCCTTTAGGGGAAAAAACCC
CTAAATAGCTTCATGTTTCCATAATCAGTACTTTATATTTATAAATGTATTTATTATTATTA
TAAGACTGCATTTTATTTATATCATTTTATTAATATGGATTTATTTATAGAAACATCATTCCG
ATATTGCTACTTGAGTGTAAGGCTAATATTGATATTTATGACAATAATTATAGAGCTATAAC
ATGTTTATTTGACCTCAATAAACACTTGGATATCCC

FIGURE 244

MAALQKSVSSFLMGTLATSCLLLLLALLVQGGAAAPTSSHCRLDKSNFQQPYITNRTFMLAKE
ASLADNNTDVRLIGEKLFHGVSMSERCYLMKQVLNFTLEEVLPQSDRFQPYMQEVVPFLAR
LSNRLSTCHIEGDDLHIQRNVQKLKDTVKKLGESGEIKAIGELDLLFMSLRNACI

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

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

FIELD OF THE INVENTION

[0001] The present invention relates generally to the identification and isolation of novel DNA and to the recombinant production of novel polypeptides.

BACKGROUND OF THE INVENTION

[0002] 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.

[0003] 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].

[0004] 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.

[0005] Membrane-bound proteins and receptor molecules have various industrial applications, including as pharma-

ceutical 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 for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

[0006] 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 THE INVENTION

[0007] In one embodiment, the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence that encodes a PRO polypeptide.

[0008] 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).

[0009] 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).

[0010] 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).

[0011] 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.

[0012] 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 10 nucleotides in length, alternatively at least about 15 nucleotides in length, alternatively 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 fragments, preferably those PRO polypeptide fragments that comprise a binding site for an anti-PRO antibody.

[0013] In another embodiment, the invention provides isolated PRO polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

[0014] 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 signal peptide, as disclosed herein or any other specifically defined fragment of the full-length amino acid sequence as disclosed herein.

[0015] 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.

[0016] 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.

[0017] 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.

[0018] 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.

[0019] 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.

[0020] 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.

[0021] 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.

[0022] 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.

[0023] 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.

[0024] 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.

[0025] In yet other embodiments, the invention provides oligonucleotide probes which may be useful for isolating genomic and cDNA nucleotide sequences, measuring or detecting expression of an associated gene or as antisense probes, wherein those probes may be derived from any of the above or below described nucleotide sequences. Preferred probe lengths are described above.

[0026] 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 THE DRAWINGS

[0027] FIGS. 1A-1B show a nucleotide sequence (SEQ ID NO:1) of a native sequence PRO6004 cDNA, wherein SEQ ID NO:1 is a clone designated herein as "DNA92259".

[0028] FIG. 2 shows the amino acid sequence (SEQ ID NO:2) derived from the coding sequence of SEQ ID NO:1 shown in FIGS. 1A-1B.

- [0029] FIG. 3 shows a nucleotide sequence (SEQ ID NO:3) of a native sequence PRO4981 cDNA, wherein SEQ ID NO:3 is a clone designated herein as "DNA94849-2960".
- [0030] 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.
- [0031] FIG. 5 shows a nucleotide sequence (SEQ ID NO:5) of a native sequence PRO7174 cDNA, wherein SEQ ID NO:5 is a clone designated herein as "DNA96883-2745".
- [0032] 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.
- [0033] FIG. 7 shows a nucleotide sequence (SEQ ID NO:7) of a native sequence PRO5778 cDNA, wherein SEQ ID NO:7 is a clone designated herein as "DNA96894-2675".
- [0034] 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.
- [0035] FIG. 9 shows a nucleotide sequence (SEQ ID NO:9) of a native sequence PRO4332 cDNA, wherein SEQ ID NO:9 is a clone designated herein as "DNA100272-2969".
- [0036] 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.
- [0037] FIG. 11 shows a nucleotide sequence (SEQ ID NO:11) of a native sequence PRO9799 cDNA, wherein SEQ ID NO:11 is a clone designated herein as "DNA108696-2966".
- [0038] 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.
- [0039] FIG. 13 shows a nucleotide sequence (SEQ ID NO:13) of a native sequence PRO9909 cDNA, wherein SEQ ID NO:13 is a clone designated herein as "DNA117935-2801".
- [0040] 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.
- [0041] FIG. 15 shows a nucleotide sequence (SEQ ID NO:15) of a native sequence PRO9917 cDNA, wherein SEQ ID NO:15 is a clone designated herein as "DNA119474-2803".
- [0042] 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.
- [0043] FIG. 17 shows a nucleotide sequence (SEQ ID NO:17) of a native sequence PRO9771 cDNA, wherein SEQ ID NO:17 is a clone designated herein as "DNA119498-2965".
- [0044] 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.
- [0045] FIG. 19 shows a nucleotide sequence (SEQ ID NO:19) of a native sequence PRO9877 cDNA, wherein SEQ ID NO:19 is a clone designated herein as "DNA119502-2789".
- [0046] 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.
- [0047] FIG. 21 shows a nucleotide sequence (SEQ ID NO:21) of a native sequence PRO9903 cDNA, wherein SEQ ID NO:21 is a clone designated herein as "DNA119516-2797".
- [0048] 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.
- [0049] FIG. 23 shows a nucleotide sequence (SEQ ID NO:23) of a native sequence PRO9830 cDNA, wherein SEQ ID NO:23 is a clone designated herein as "DNA119530-2968".
- [0050] 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.
- [0051] FIG. 25 shows a nucleotide sequence (SEQ ID NO:25) of a native sequence PRO7155 cDNA, wherein SEQ ID NO:25 is a clone designated herein as "DNA121772-2741".
- [0052] 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.
- [0053] FIG. 27 shows a nucleotide sequence (SEQ ID NO:27) of a native sequence PRO9862 cDNA, wherein SEQ ID NO:27 is a clone designated herein as "DNA125148-2782".
- [0054] 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.
- [0055] FIG. 29 shows a nucleotide sequence (SEQ ID NO:29) of a native sequence PRO9882 cDNA, wherein SEQ ID NO:29 is a clone designated herein as "DNA125150-2793".
- [0056] 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.
- [0057] FIG. 31 shows a nucleotide sequence (SEQ ID NO:31) of a native sequence PRO9864 cDNA, wherein SEQ ID NO:31 is a clone designated herein as "DNA125151-2784".
- [0058] 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.
- [0059] FIG. 33 shows a nucleotide sequence (SEQ ID NO:33) of a native sequence PRO10013 cDNA, wherein SEQ ID NO:33 is a clone designated herein as "DNA125181-2804".
- [0060] 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.
- [0061] FIG. 35 shows a nucleotide sequence (SEQ ID NO:35) of a native sequence PRO9885 cDNA, wherein SEQ ID NO:35 is a clone designated herein as "DNA125192-2794".

- [0062] 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.
- [0063] FIG. 37 shows a nucleotide sequence (SEQ ID NO:37) of a native sequence PRO9879 cDNA, wherein SEQ ID NO:37 is a clone designated herein as "DNA125196-2792".
- [0064] 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.
- [0065] FIG. 39 shows a nucleotide sequence (SEQ ID NO:39) of a native sequence PRO10111 cDNA, wherein SEQ ID NO:39 is a clone designated herein as "DNA125200-2810".
- [0066] 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.
- [0067] FIG. 41 shows a nucleotide sequence (SEQ ID NO:41) of a native sequence PRO9925 cDNA, wherein SEQ ID NO:41 is a clone designated herein as "DNA125214-2814".
- [0068] 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.
- [0069] FIG. 43 shows a nucleotide sequence (SEQ ID NO:43) of a native sequence PRO9905 cDNA, wherein SEQ ID NO:43 is a clone designated herein as "DNA125219-2799".
- [0070] 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.
- [0071] FIG. 45 shows a nucleotide sequence (SEQ ID NO:45) of a native sequence PRO10276 cDNA, wherein SEQ ID NO:45 is a clone designated herein as "DNA128309-2825".
- [0072] 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.
- [0073] FIG. 47 shows a nucleotide sequence (SEQ ID NO:47) of a native sequence PRO9898 cDNA, wherein SEQ ID NO:47 is a clone designated herein as "DNA129535-2796".
- [0074] 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.
- [0075] FIG. 49 shows a nucleotide sequence (SEQ ID NO:49) of a native sequence PRO9904 cDNA, wherein SEQ ID NO:49 is a clone designated herein as "DNA129549-2798".
- [0076] 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.
- [0077] FIG. 51 shows a nucleotide sequence (SEQ ID NO:51) of a native sequence PRO19632 cDNA, wherein SEQ ID NO:51 is a clone designated herein as "DNA129580-2863".
- [0078] 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.
- [0079] FIG. 53 shows a nucleotide sequence (SEQ ID NO:53) of a native sequence PRO19672 cDNA, wherein SEQ ID NO:53 is a clone designated herein as "DNA129794-2967".
- [0080] 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.
- [0081] FIG. 55 shows a nucleotide sequence (SEQ ID NO:55) of a native sequence PRO9783 cDNA, wherein SEQ ID NO:55 is a clone designated herein as "DNA131590-2962".
- [0082] 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.
- [0083] FIG. 57 shows a nucleotide sequence (SEQ ID NO:57) of a native sequence PRO10112 cDNA, wherein SEQ ID NO:57 is a clone designated herein as "DNA135173-2811".
- [0084] 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.
- [0085] FIGS. 59A-59B show a nucleotide sequence (SEQ ID NO:59) of a native sequence PRO10284 cDNA, wherein SEQ ID NO:59 is a clone designated herein as "DNA138039-2828".
- [0086] FIG. 60 shows the amino acid sequence (SEQ ID NO:60) derived from the coding sequence of SEQ ID NO:59 shown in FIGS. 59A-59B.
- [0087] FIG. 61 shows a nucleotide sequence (SEQ ID NO:61) of a native sequence PRO10100 cDNA, wherein SEQ ID NO:61 is a clone designated herein as "DNA139540-2807".
- [0088] 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.
- [0089] FIG. 63 shows a nucleotide sequence (SEQ ID NO:63) of a native sequence PRO19628 cDNA, wherein SEQ ID NO:63 is a clone designated herein as "DNA139602-2859".
- [0090] 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.
- [0091] FIG. 65 shows a nucleotide sequence (SEQ ID NO:65) of a native sequence PRO19684 cDNA, wherein SEQ ID NO:65 is a clone designated herein as "DNA139632-2880".
- [0092] 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.
- [0093] FIG. 67 shows a nucleotide sequence (SEQ ID NO:67) of a native sequence PRO10274 cDNA, wherein SEQ ID NO:67 is a clone designated herein as "DNA139686-2823".

- [0094] 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.
- [0095] FIG. 69 shows a nucleotide sequence (SEQ ID NO:69) of a native sequence PRO9907 cDNA, wherein SEQ ID NO:69 is a clone designated herein as "DNA142392-2800".
- [0096] 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.
- [0097] FIG. 71 shows a nucleotide sequence (SEQ ID NO:71) of a native sequence PRO9873 cDNA, wherein SEQ ID NO:71 is a clone designated herein as "DNA143076-2787".
- [0098] 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.
- [0099] FIG. 73 shows a nucleotide sequence (SEQ ID NO:73) of a native sequence PRO10201 cDNA, wherein SEQ ID NO:73 is a clone designated herein as "DNA143294-2818".
- [0100] 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.
- [0101] FIG. 75 shows a nucleotide sequence (SEQ ID NO:75) of a native sequence PRO10200 cDNA, wherein SEQ ID NO:75 is a clone designated herein as "DNA143514-2817".
- [0102] 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.
- [0103] FIG. 77 shows a nucleotide sequence (SEQ ID NO:77) of a native sequence PRO10196 cDNA, wherein SEQ ID NO:77 is a clone designated herein as "DNA144841-2816".
- [0104] 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.
- [0105] FIG. 79 shows a nucleotide sequence (SEQ ID NO:79) of a native sequence PRO10282 cDNA, wherein SEQ ID NO:79 is a clone designated herein as "DNA148380-2827".
- [0106] 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.
- [0107] FIG. 81 shows a nucleotide sequence (SEQ ID NO:81) of a native sequence PRO19650 cDNA, wherein SEQ ID NO:81 is a clone designated herein as "DNA149995-2871".
- [0108] 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.
- [0109] FIG. 83 shows a nucleotide sequence (SEQ ID NO:83) of a native sequence PRO21184 cDNA, wherein SEQ ID NO:83 is a clone designated herein as "DNA167678-2963".
- [0110] 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.
- [0111] FIG. 85 shows a nucleotide sequence (SEQ ID NO:85) of a native sequence PRO21201 cDNA, wherein SEQ ID NO:85 is a clone designated herein as "DNA168028-2956".
- [0112] 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.
- [0113] FIG. 87 shows a nucleotide sequence (SEQ ID NO:87) of a native sequence PRO21175 cDNA, wherein SEQ ID NO:87 is a clone designated herein as "DNA173894-2947".
- [0114] 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.
- [0115] FIG. 89 shows a nucleotide sequence (SEQ ID NO:89) of a native sequence PRO21340 cDNA, wherein SEQ ID NO:89 is a clone designated herein as "DNA176775-2957".
- [0116] 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.
- [0117] FIG. 91 shows a nucleotide sequence (SEQ ID NO:91) of a native sequence PRO21384cDNA, wherein SEQ ID NO:91 is a clone designated herein as "DNA177313-2982".
- [0118] 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.
- [0119] FIG. 93 shows a nucleotide sequence (SEQ ID NO:93) of a native sequence PRO982 cDNA, wherein SEQ ID NO:93 is a clone designated herein as "DNA57700-1408".
- [0120] 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.
- [0121] FIG. 95 shows a nucleotide sequence (SEQ ID NO:95) of a native sequence PRO1160 cDNA, wherein SEQ ID NO:95 is a clone designated herein as "DNA62872-1509".
- [0122] 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.
- [0123] FIG. 97 shows a nucleotide sequence (SEQ ID NO:97) of a native sequence PRO1187 cDNA, wherein SEQ ID NO:97 is a clone designated herein as "DNA62876-1517".
- [0124] 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.
- [0125] FIG. 99 shows a nucleotide sequence (SEQ ID NO:99) of a native sequence PRO1329 cDNA, wherein SEQ ID NO:99 is a clone designated herein as "DNA66660-1585".

- [0126] 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.
- [0127] FIG. 101 shows a nucleotide sequence (SEQ ID NO:101) of a native sequence PRO231 cDNA, wherein SEQ ID NO:101 is a clone designated herein as "DNA34434-1139".
- [0128] 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.
- [0129] FIG. 103 shows a nucleotide sequence (SEQ ID NO:103) of a native sequence PRO357 cDNA, wherein SEQ ID NO:103 is a clone designated herein as "DNA44804-1248".
- [0130] 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.
- [0131] FIG. 105 shows a nucleotide sequence (SEQ ID NO:105) of a native sequence PRO725 cDNA, wherein SEQ ID NO:105 is a clone designated herein as "DNA52758-1399".
- [0132] 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.
- [0133] FIG. 107 shows a nucleotide sequence (SEQ ID NO:107) of a native sequence PRO1155 cDNA, wherein SEQ ID NO:107 is a clone designated herein as "DNA59849-1504".
- [0134] 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.
- [0135] FIG. 109 shows a nucleotide sequence (SEQ ID NO:109) of a native sequence PRO1306 cDNA, wherein SEQ ID NO:109 is a clone designated herein as "DNA65410-1569".
- [0136] 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.
- [0137] FIG. 111 shows a nucleotide sequence (SEQ ID NO:111) of a native sequence PRO1419 cDNA, wherein SEQ ID NO:111 is a clone designated herein as "DNA71290-1630".
- [0138] 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.
- [0139] FIG. 113 shows a nucleotide sequence (SEQ ID NO:113) of a native sequence PRO229 cDNA, wherein SEQ ID NO:113 is a clone designated herein as "DNA33100-1159".
- [0140] 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.
- [0141] FIG. 115 shows a nucleotide sequence (SEQ ID NO:115) of a native sequence PRO1272 cDNA, wherein SEQ ID NO:115 is a clone designated herein as "DNA64896-1539".
- [0142] 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.
- [0143] FIG. 117 shows a nucleotide sequence (SEQ ID NO:117) of a native sequence PRO4405 cDNA, wherein SEQ ID NO:117 is a clone designated herein as "DNA84920-2614".
- [0144] 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.
- [0145] FIG. 119 shows a nucleotide sequence (SEQ ID NO:119) of a native sequence PRO181 cDNA, wherein SEQ ID NO:119 is a clone designated herein as "DNA23330-1390".
- [0146] 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.
- [0147] FIG. 121 shows a nucleotide sequence (SEQ ID NO:121) of a native sequence PRO214 cDNA, wherein SEQ ID NO:121 is a clone designated herein as "DNA32286-1191".
- [0148] 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.
- [0149] FIG. 123 shows a nucleotide sequence (SEQ ID NO:123) of a native sequence PRO247 cDNA, wherein SEQ ID NO:123 is a clone designated herein as "DNA35673-1201".
- [0150] 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.
- [0151] FIG. 125 shows a nucleotide sequence (SEQ ID NO:125) of a native sequence PRO337 cDNA, wherein SEQ ID NO:125 is a clone designated herein as "DNA43316-1237".
- [0152] 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.
- [0153] FIG. 127 shows a nucleotide sequence (SEQ ID NO:127) of a native sequence PRO526 cDNA, wherein SEQ ID NO:127 is a clone designated herein as "DNA44184-1319".
- [0154] 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.
- [0155] FIG. 129 shows a nucleotide sequence (SEQ ID NO:129) of a native sequence PRO363 cDNA, wherein SEQ ID NO:129 is a clone designated herein as "DNA45419-1252".
- [0156] 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.
- [0157] FIG. 131 shows a nucleotide sequence (SEQ ID NO:131) of a native sequence PRO531 cDNA, wherein SEQ ID NO:131 is a clone designated herein as "DNA48314-1320".

- [0158] 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.
- [0159] FIG. 133 shows a nucleotide sequence (SEQ ID NO:133) of a native sequence PRO1083 cDNA, wherein SEQ ID NO:133 is a clone designated herein as "DNA50921-1458".
- [0160] 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.
- [0161] FIG. 135 shows a nucleotide sequence (SEQ ID NO:135) of a native sequence PRO840 cDNA, wherein SEQ ID NO:135 is a clone designated herein as "DNA53987".
- [0162] 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.
- [0163] FIG. 137 shows a nucleotide sequence (SEQ ID NO:137) of a native sequence PRO1080 cDNA, wherein SEQ ID NO:137 is a clone designated herein as "DNA56047-1456".
- [0164] 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.
- [0165] FIG. 139 shows a nucleotide sequence (SEQ ID NO:139) of a native sequence PRO788 cDNA, wherein SEQ ID NO:139 is a clone designated herein as "DNA56405-1357".
- [0166] 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.
- [0167] FIG. 141 shows a nucleotide sequence (SEQ ID NO:141) of a native sequence PRO1478 cDNA, wherein SEQ ID NO:141 is a clone designated herein as "DNA56531-1648".
- [0168] 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.
- [0169] FIG. 143 shows a nucleotide sequence (SEQ ID NO:143) of a native sequence PRO1134 cDNA, wherein SEQ ID NO:143 is a clone designated herein as "DNA56865-1491".
- [0170] 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.
- [0171] FIG. 145 shows a nucleotide sequence (SEQ ID NO:145) of a native sequence PRO826 cDNA, wherein SEQ ID NO:145 is a clone designated herein as "DNA57694-1341".
- [0172] 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.
- [0173] FIG. 147 shows a nucleotide sequence (SEQ ID NO:147) of a native sequence PRO1005 cDNA, wherein SEQ ID NO:147 is a clone designated herein as "DNA57708-1411".
- [0174] 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.
- [0175] FIG. 149 shows a nucleotide sequence (SEQ ID NO:149) of a native sequence PRO809 cDNA, wherein SEQ ID NO:149 is a clone designated herein as "DNA57836-1338".
- [0176] 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.
- [0177] FIG. 151 shows a nucleotide sequence (SEQ ID NO:151) of a native sequence PRO1194 cDNA, wherein SEQ ID NO:151 is a clone designated herein as "DNA57841-1522".
- [0178] 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.
- [0179] FIG. 153 shows a nucleotide sequence (SEQ ID NO:153) of a native sequence PRO1071 cDNA, wherein SEQ ID NO:153 is a clone designated herein as "DNA58847-1383".
- [0180] 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.
- [0181] FIG. 155 shows a nucleotide sequence (SEQ ID NO:155) of a native sequence PRO1411 cDNA, wherein SEQ ID NO:155 is a clone designated herein as "DNA59212-1627".
- [0182] 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.
- [0183] FIG. 157 shows a nucleotide sequence (SEQ ID NO:157) of a native sequence PRO1309 cDNA, wherein SEQ ID NO:157 is a clone designated herein as "DNA59588-1571".
- [0184] 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.
- [0185] FIG. 159 shows a nucleotide sequence (SEQ ID NO:159) of a native sequence PRO1025 cDNA, wherein SEQ ID NO:159 is a clone designated herein as "DNA59622-1334".
- [0186] 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.
- [0187] FIG. 161 shows a nucleotide sequence (SEQ ID NO:161) of a native sequence PRO1181 cDNA, wherein SEQ ID NO:161 is a clone designated herein as "DNA59847-2510".
- [0188] 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.
- [0189] FIG. 163 shows a nucleotide sequence (SEQ ID NO:163) of a native sequence PRO1126 cDNA, wherein SEQ ID NO:163 is a clone designated herein as "DNA60615-1483".

- [0190] 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.
- [0191] FIG. 165 shows a nucleotide sequence (SEQ ID NO:165) of a native sequence PRO1186 cDNA, wherein SEQ ID NO:165 is a clone designated herein as "DNA60621-1516".
- [0192] 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.
- [0193] FIG. 167 shows a nucleotide sequence (SEQ ID NO:167) of a native sequence PRO1192 cDNA, wherein SEQ ID NO:167 is a clone designated herein as "DNA62814-1521".
- [0194] 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.
- [0195] FIG. 169 shows a nucleotide sequence (SEQ ID NO:169) of a native sequence PRO1244 cDNA, wherein SEQ ID NO:169 is a clone designated herein as "DNA64883-1526".
- [0196] FIG. 170 shows the amino acid sequence (SEQ ID NO:170) derived from the coding sequence of SEQ ID NO:169 shown in FIG. 169.
- [0197] FIG. 171 shows a nucleotide sequence (SEQ ID NO:171) of a native sequence PRO1274 cDNA, wherein SEQ ID NO:171 is a clone designated herein as "DNA64889-1541".
- [0198] FIG. 172 shows the amino acid sequence (SEQ ID NO:172) derived from the coding sequence of SEQ ID NO:171 shown in FIG. 171.
- [0199] FIG. 173 shows a nucleotide sequence (SEQ ID NO:173) of a native sequence PRO1412 cDNA, wherein SEQ ID NO:173 is a clone designated herein as "DNA64897-1628".
- [0200] FIG. 174 shows the amino acid sequence (SEQ ID NO:174) derived from the coding sequence of SEQ ID NO:173 shown in FIG. 173.
- [0201] FIG. 175 shows a nucleotide sequence (SEQ ID NO:175) of a native sequence PRO1286 cDNA, wherein SEQ ID NO:175 is a clone designated herein as "DNA64903-1553".
- [0202] FIG. 176 shows the amino acid sequence (SEQ ID NO:176) derived from the coding sequence of SEQ ID NO:175 shown in FIG. 175.
- [0203] FIG. 177 shows a nucleotide sequence (SEQ ID NO:177) of a native sequence PRO1330 cDNA, wherein SEQ ID NO:177 is a clone designated herein as "DNA64907-1163-1".
- [0204] FIG. 178 shows the amino acid sequence (SEQ ID NO:178) derived from the coding sequence of SEQ ID NO:177 shown in FIG. 177.
- [0205] FIG. 179 shows a nucleotide sequence (SEQ ID NO:179) of a native sequence PRO1347 cDNA, wherein SEQ ID NO:179 is a clone designated herein as "DNA64950-1590".
- [0206] FIG. 180 shows the amino acid sequence (SEQ ID NO:180) derived from the coding sequence of SEQ ID NO:179 shown in FIG. 179.
- [0207] FIG. 181 shows a nucleotide sequence (SEQ ID NO:181) of a native sequence PRO1305 cDNA, wherein SEQ ID NO:181 is a clone designated herein as "DNA64952-1568".
- [0208] FIG. 182 shows the amino acid sequence (SEQ ID NO:182) derived from the coding sequence of SEQ ID NO:181 shown in FIG. 181.
- [0209] FIG. 183 shows a nucleotide sequence (SEQ ID NO:183) of a native sequence PRO1273 cDNA, wherein SEQ ID NO:183 is a clone designated herein as "DNA65402-1540".
- [0210] FIG. 184 shows the amino acid sequence (SEQ ID NO:184) derived from the coding sequence of SEQ ID NO:183 shown in FIG. 183.
- [0211] FIG. 185 shows a nucleotide sequence (SEQ ID NO:185) of a native sequence PRO1279 cDNA, wherein SEQ ID NO:185 is a clone designated herein as "DNA65405-1547".
- [0212] FIG. 186 shows the amino acid sequence (SEQ ID NO:186) derived from the coding sequence of SEQ ID NO:185 shown in FIG. 185.
- [0213] FIG. 187 shows a nucleotide sequence (SEQ ID NO:187) of a native sequence PRO1340 cDNA, wherein SEQ ID NO:187 is a clone designated herein as "DNA66663-1598".
- [0214] FIG. 188 shows the amino acid sequence (SEQ ID NO:188) derived from the coding sequence of SEQ ID NO:187 shown in FIG. 187.
- [0215] FIG. 189 shows a nucleotide sequence (SEQ ID NO:189) of a native sequence PRO1338 cDNA, wherein SEQ ID NO:189 is a clone designated herein as "DNA66667".
- [0216] FIG. 190 shows the amino acid sequence (SEQ ID NO:190) derived from the coding sequence of SEQ ID NO:189 shown in FIG. 189.
- [0217] FIG. 191 shows a nucleotide sequence (SEQ ID NO:191) of a native sequence PRO1343 cDNA, wherein SEQ ID NO:191 is a clone designated herein as "DNA66675-1587".
- [0218] FIG. 192 shows the amino acid sequence (SEQ ID NO:192) derived from the coding sequence of SEQ ID NO:191 shown in FIG. 191.
- [0219] FIG. 193 shows a nucleotide sequence (SEQ ID NO:193) of a native sequence PRO1376 cDNA, wherein SEQ ID NO:193 is a clone designated herein as "DNA67300-1605".
- [0220] FIG. 194 shows the amino acid sequence (SEQ ID NO:194) derived from the coding sequence of SEQ ID NO:193 shown in FIG. 193.
- [0221] FIG. 195 shows a nucleotide sequence (SEQ ID NO:195) of a native sequence PRO1387 cDNA, wherein SEQ ID NO:195 is a clone designated herein as "DNA68872-1620".

- [0222] FIG. 196 shows the amino acid sequence (SEQ ID NO:196) derived from the coding sequence of SEQ ID NO:195 shown in FIG. 195.
- [0223] FIG. 197 shows a nucleotide sequence (SEQ ID NO:197) of a native sequence PRO1409 cDNA, wherein SEQ ID NO:197 is a clone designated herein as "DNA71269-1621".
- [0224] FIG. 198 shows the amino acid sequence (SEQ ID NO:198) derived from the coding sequence of SEQ ID NO:197 shown in FIG. 197.
- [0225] FIG. 199 shows a nucleotide sequence (SEQ ID NO:199) of a native sequence PRO1488 cDNA, wherein SEQ ID NO:199 is a clone designated herein as "DNA73736-1657".
- [0226] FIG. 200 shows the amino acid sequence (SEQ ID NO:200) derived from the coding sequence of SEQ ID NO:199 shown in FIG. 199.
- [0227] FIG. 201 shows a nucleotide sequence (SEQ ID NO:201) of a native sequence PRO1474 cDNA, wherein SEQ ID NO:201 is a clone designated herein as "DNA73739-1645".
- [0228] FIG. 202 shows the amino acid sequence (SEQ ID NO:202) derived from the coding sequence of SEQ ID NO:201 shown in FIG. 201.
- [0229] FIG. 203 shows a nucleotide sequence (SEQ ID NO:203) of a native sequence PRO1917 cDNA, wherein SEQ ID NO:203 is a clone designated herein as "DNA76400-2528".
- [0230] FIG. 204 shows the amino acid sequence (SEQ ID NO:204) derived from the coding sequence of SEQ ID NO:203 shown in FIG. 203.
- [0231] FIG. 205 shows a nucleotide sequence (SEQ ID NO:205) of a native sequence PRO1760 cDNA, wherein SEQ ID NO:205 is a clone designated herein as "DNA76532-1702".
- [0232] FIG. 206 shows the amino acid sequence (SEQ ID NO:206) derived from the coding sequence of SEQ ID NO:205 shown in FIG. 205.
- [0233] FIG. 207 shows a nucleotide sequence (SEQ ID NO:207) of a native sequence PRO1567 cDNA, wherein SEQ ID NO:207 is a clone designated herein as "DNA76541-1675".
- [0234] FIG. 208 shows the amino acid sequence (SEQ ID NO:208) derived from the coding sequence of SEQ ID NO:207 shown in FIG. 207.
- [0235] FIG. 209 shows a nucleotide sequence (SEQ ID NO:209) of a native sequence PRO1887 cDNA, wherein SEQ ID NO:209 is a clone designated herein as "DNA79862-2522".
- [0236] FIG. 210 shows the amino acid sequence (SEQ ID NO:210) derived from the coding sequence of SEQ ID NO:209 shown in FIG. 209.
- [0237] FIG. 211 shows a nucleotide sequence (SEQ ID NO:211) of a native sequence PRO1928 cDNA, wherein SEQ ID NO:211 is a clone designated herein as "DNA81754-2532".
- [0238] FIG. 212 shows the amino acid sequence (SEQ ID NO:212) derived from the coding sequence of SEQ ID NO:211 shown in FIG. 211.
- [0239] FIG. 213 shows a nucleotide sequence (SEQ ID NO:213) of a native sequence PRO4341 cDNA, wherein SEQ ID NO:213 is a clone designated herein as "DNA81761-2583".
- [0240] FIG. 214 shows the amino acid sequence (SEQ ID NO:214) derived from the coding sequence of SEQ ID NO:213 shown in FIG. 213.
- [0241] FIG. 215 shows a nucleotide sequence (SEQ ID NO:215) of a native sequence PRO5723 cDNA, wherein SEQ ID NO:215 is a clone designated herein as "DNA82361".
- [0242] FIG. 216 shows the amino acid sequence (SEQ ID NO:216) derived from the coding sequence of SEQ ID NO:215 shown in FIG. 215.
- [0243] FIG. 217 shows a nucleotide sequence (SEQ ID NO:217) of a native sequence PRO1801 cDNA, wherein SEQ ID NO:217 is a clone designated herein as "DNA83500-2506".
- [0244] FIG. 218 shows the amino acid sequence (SEQ ID NO:218) derived from the coding sequence of SEQ ID NO:217 shown in FIG. 217.
- [0245] FIG. 219 shows a nucleotide sequence (SEQ ID NO:219) of a native sequence PRO4333 cDNA, wherein SEQ ID NO:219 is a clone designated herein as "DNA84210-2576".
- [0246] FIG. 220 shows the amino acid sequence (SEQ ID NO:220) derived from the coding sequence of SEQ ID NO:219 shown in FIG. 219.
- [0247] FIG. 221 shows a nucleotide sequence (SEQ ID NO:221) of a native sequence PRO3543 cDNA, wherein SEQ ID NO:221 is a clone designated herein as "DNA86571-2551".
- [0248] FIG. 222 shows the amino acid sequence (SEQ ID NO:222) derived from the coding sequence of SEQ ID NO:221 shown in FIG. 221.
- [0249] FIG. 223 shows a nucleotide sequence (SEQ ID NO:223) of a native sequence PRO3444 cDNA, wherein SEQ ID NO:223 is a clone designated herein as "DNA87997".
- [0250] FIG. 224 shows the amino acid sequence (SEQ ID NO:224) derived from the coding sequence of SEQ ID NO:223 shown in FIG. 223.
- [0251] FIG. 225 shows a nucleotide sequence (SEQ ID NO:225) of a native sequence PRO4302 cDNA, wherein SEQ ID NO:225 is a clone designated herein as "DNA92218-2554".
- [0252] FIG. 226 shows the amino acid sequence (SEQ ID NO:226) derived from the coding sequence of SEQ ID NO:225 shown in FIG. 225.
- [0253] FIG. 227 shows a nucleotide sequence (SEQ ID NO:227) of a native sequence PRO4322 cDNA, wherein SEQ ID NO:227 is a clone designated herein as "DNA92223-2567".

[0254] FIG. 228 shows the amino acid sequence (SEQ ID NO:228) derived from the coding sequence of SEQ ID NO:227 shown in FIG. 227.

[0255] FIG. 229 shows a nucleotide sequence (SEQ ID NO:229) of a native sequence PRO5725 cDNA, wherein SEQ ID NO:229 is a clone designated herein as "DNA92265-2669".

[0256] FIG. 230 shows the amino acid sequence (SEQ ID NO:230) derived from the coding sequence of SEQ ID NO:229 shown in FIG. 229.

[0257] FIG. 231 shows a nucleotide sequence (SEQ ID NO:231) of a native sequence PRO4408 cDNA, wherein SEQ ID NO:231 is a clone designated herein as "DNA92274-2617".

[0258] FIG. 232 shows the amino acid sequence (SEQ ID NO:232) derived from the coding sequence of SEQ ID NO:231 shown in FIG. 231.

[0259] FIG. 233 shows a nucleotide sequence (SEQ ID NO:233) of a native sequence PRO9940 cDNA, wherein SEQ ID NO:233 is a clone designated herein as "DNA92282".

[0260] FIG. 234 shows the amino acid sequence (SEQ ID NO:234) derived from the coding sequence of SEQ ID NO:233 shown in FIG. 233.

[0261] FIG. 235 shows a nucleotide sequence (SEQ ID NO:235) of a native sequence PRO7154 cDNA, wherein SEQ ID NO:235 is a clone designated herein as "DNA108760-2740".

[0262] FIG. 236 shows the amino acid sequence (SEQ ID NO:236) derived from the coding sequence of SEQ ID NO:235 shown in FIG. 235.

[0263] FIG. 237 shows a nucleotide sequence (SEQ ID NO:237) of a native sequence PRO7425 cDNA, wherein SEQ ID NO:237 is a clone designated herein as "DNA108792-2753".

[0264] FIG. 238 shows the amino acid sequence (SEQ ID NO:238) derived from the coding sequence of SEQ ID NO:237 shown in FIG. 237.

[0265] FIG. 239 shows a nucleotide sequence (SEQ ID NO:239) of a native sequence PRO6079 cDNA, wherein SEQ ID NO:239 is a clone designated herein as "DNA111750-2706".

[0266] FIG. 240 shows the amino acid sequence (SEQ ID NO:240) derived from the coding sequence of SEQ ID NO:239 shown in FIG. 239.

[0267] FIG. 241 shows a nucleotide sequence (SEQ ID NO:241) of a native sequence PRO9836 cDNA, wherein SEQ ID NO:241 is a clone designated herein as "DNA119514-2772".

[0268] FIG. 242 shows the amino acid sequence (SEQ ID NO:242) derived from the coding sequence of SEQ ID NO:241 shown in FIG. 241.

[0269] FIG. 243 shows a nucleotide sequence (SEQ ID NO:243) of a native sequence PRO10096 cDNA, wherein SEQ ID NO:243 is a clone designated herein as "DNA125185-2806".

[0270] FIG. 244 shows the amino acid sequence (SEQ ID NO:244) derived from the coding sequence of SEQ ID NO:243 shown in FIG. 243.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0271] 1. Definitions 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 preparation 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.

[0272] 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 acid 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.

[0273] 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.

[0274] 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.

[0275] “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.

[0276] “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.

[0277] 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:

$$100 \text{ times the fraction } \frac{X}{Y}$$

[0278] 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.

[0279] 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.

[0280] 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.

[0281] 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:

$$100 \text{ times the fraction } \frac{X}{Y}$$

[0282] 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.

[0283] "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.

[0284] 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, alter-

natively 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.

[0285] “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.

[0286] 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

[0287] 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.

[0288] 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.

[0289] 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.

[0290] 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

[0291] 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.

[0292] In other embodiments, PRO variant polynucleotides are nucleic acid molecules that encode an active PRO polypeptide and which are capable of hybridizing, prefer-

ably 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.

[0293] “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.

[0294] 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.

[0295] 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.

[0296] 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.

[0297] The term “antibody” is used in the broadest sense and specifically covers, for example, single anti-PRO mono-

clonal 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.

[0298] “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).

[0299] “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.

[0300] “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.

[0301] 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).

[0302] 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.

[0303] “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.

[0304] 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.

[0305] “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.

[0306] “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.

[0307] “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.

[0308] Administration “in combination with” one or more further therapeutic agents includes simultaneous (concurrent) and consecutive administration in any order.

[0309] “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™.

[0310] “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.

[0311] 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.

[0312] “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.

[0313] 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.

[0314] 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.

[0315] 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.

[0316] "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. Preferably, 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).

[0317] 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).

[0318] 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.

[0319] 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.

[0320] 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.

[0321] 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.

[0322] 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.

[0323] A "small molecule" is defined herein to have a molecular weight below about 500 Daltons.

[0324] An "effective amount" of a polypeptide disclosed herein or an agonist or antagonist thereof is an amount sufficient to carry out a specifically stated purpose. An "effective amount" may be determined empirically and in a routine manner, in relation to the stated purpose.

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},

```


TABLE 1-continued

```

* 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, 0xFFFFFFF, 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 */
    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 diags", 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

```

TABLE 1-continued

```

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;
        } 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++;
    }
}

```


TABLE 1-continued

```

        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++;
            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)

```

getmat

TABLE 1-continued

```

    lx = (len0 < len1)? len0 : len1;
else
    lx = (lx < ly)? lx : ly;
pct = 100.*(double)nm/(double)lx;
fprintf(fx, "\n");
fprintf(fx, "< %d match%s in an overlap of %d: %.2f percent similarity\n",
        nm, (nm == 1)? "" : "es", lx, pct);
fprintf(fx, "< gaps in first sequence: %d", gapx);
if (gapx) {
    (void) sprintf(outx, "(%d %s%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%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, DMAT, 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%s, right endgap: %d %s%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;
    register i;
    for (i = 0, lmax = 0; i < 2; i++) {
        nn = stripname(name[i]);
        if (nn > lmax)
            lmax = nn;
        nc[i] = 1;
        ni[i] = 1;
        siz[i] = ij[i] = 0;
        ps[i] = seqx[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 */

```

...getmat

pr_align

...pr_align

TABLE 1-continued

```

        *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) puts("\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])
                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;

```

TABLE 1-continued

```

        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 = name[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++) {
        if (isalpha(*p0) && isalpha(*p1)) {
            if (xbm[*p0-'A']&xbm[*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) */
    {

```

putline

...putline

stars

stripname

TABLE 1-continued

```

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)) {
        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';

    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)))

```

TABLE 1-continued

```

        natgc++;
    }
}
*py++ = '\0';
*py = '\0';
(void) fclose(fp);
dna = natgc > (tlen/3);
return(pseq+4);
}
char *
g__calloc(msg, nx, sz)                                g__calloc
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()                                           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;
        }
        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;
                gapy++;
                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;
            gapx++;
        }
    }
}

```

TABLE 1-continued

```

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);
}

```

[0325]

TABLE 2

PRO	XXXXXXXXXXXXXXXXXX	(Length = 15 amino acids)
Comparison Protein	XXXXXXXXYYYYYYYY	(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%

[0326]

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%

[0327]

TABLE 4

PRO-DNA	NNNNNNNNNNNNNN	(Length = 14 nucleotides)
Comparison DNA	NNNNNNLLLLLLLL	(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%

[0328]

TABLE 5

PRO-DNA	NNNNNNNNNNNN	(Length = 12 nucleotides)
Comparison DNA	NNNNLLLVV	(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%

[0329] II. Compositions and Methods of the Invention**[0330]** A. Full-Length PRO Polypeptides

[0331] 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.

[0332] 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.

[0333] B. PRO Polypeptide Variants

[0334] 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.

[0335] 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 system-

atically 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.

[0336] 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.

[0337] 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 restriction 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.

[0338] 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

[0339] 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:

[0340] (1) hydrophobic: norleucine, met, ala, val, leu, ile;

[0341] (2) neutral hydrophilic: cys, ser, thr;

[0342] (3) acidic: asp, glu;

[0343] (4) basic: asn, gln, his, lys, arg;

[0344] (5) residues that influence chain orientation: gly, pro; and

[0345] (6) aromatic: trp, tyr, phe.

[0346] 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.

[0347] 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.

[0348] 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.); Chothia, *J. Mol. Biol.*, 150:1 (1976)]. If alanine substitution does not yield adequate amounts of variant, an isoteric amino acid can be used.

[0349] C. Modifications of PRO

[0350] 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-(diazocetyl)-2-phenylethane, glutaraldehyde, N-hydroxysuccinimide esters, for example, esters with 4-azidosalicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis(succinimidyl-

propionate), bifunctional maleimides such as bis-N-maleimido-1,8-octane and agents such as methyl-3-[(p-azidophenyl)dithio]propioimidate.

[0351] 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.

[0352] 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.

[0353] 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.

[0354] 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).

[0355] 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. 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).

[0356] 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 U.S. Pat. No. 4,179,337.

[0357] 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.

[0358] 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)].

[0359] 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.

[0360] D. Preparation of PRO

[0361] 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

[0362] 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).

[0363] 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)].

[0364] 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.

[0365] 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.

[0366] 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.

[0367] 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

[0368] 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.

[0369] 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).

[0370] 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 K5772 (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.

[0371] 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. drosophilum* (ATCC 36,906; Van den Berg et al., *Bio/Technology*, 8:135 (1990)), *K. thermotolerans*, and *K. manrius*; *yarrowia* (EP 402,226); *Pichia pastoris* (EP 183,070; Sreekrishna 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]); Schwannomyces such as *Schwannomyces occidentalis* (EP 394,538 published Oct. 31, 1990); and filamentous fungi such as, e.g., Neurospora, Penicillium, Tolypocladium (WO 91/00357 published Jan. 10, 1991), and Aspergillus hosts such as *A. nidulans* (Balance 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).

[0372] 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

[0373] 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.

[0374] 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.

[0375] 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 *2* μ plasmid origin is suitable for yeast, and various viral origins (SV40, polyoma, adenovirus, VSV or BPV) are useful for cloning vectors in mammalian cells.

[0376] 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*.

[0377] 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 *trp1* 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 *trp1* 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)].

[0378] 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.

[0379] 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.

[0380] 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.

[0381] 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.

[0382] 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.

[0383] 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.

[0384] 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

[0385] 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*, 77:5201-5205 (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.

[0386] 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

[0387] 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.

[0388] 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.

[0389] E. Uses for PRO

[0390] 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.

[0391] 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 ³²P or ³⁵S, 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.

[0392] Any EST sequences disclosed in the present application may similarly be employed as probes, using the methods disclosed herein.

[0393] 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).

[0394] 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.

[0395] 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 complexes may be attached to sense or antisense oligonucleotides to modify binding specificities of the antisense or sense oligonucleotide for the target nucleotide sequence.

[0396] Antisense or sense oligonucleotides may be introduced into a cell containing the target nucleic acid sequence by any gene transfer method, including, for example, CaPO₄-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).

[0397] 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.

[0398] Alternatively, a sense or an antisense oligonucleotide may be introduced into a cell 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.

[0399] 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.

[0400] The probes may also be employed in PCR techniques to generate a pool of sequences for identification of closely related PRO coding sequences.

[0401] 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.

[0402] 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.

[0403] 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.

[0404] Alternatively, non-human homologues of PRO can be used to construct a PRO "knockout" 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 estab-

lished 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 (e.g., 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.

[0405] 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.

[0406] 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).

[0407] 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.

[0408] 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.

[0409] 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.

[0410] 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.

[0411] 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.

[0412] 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.

[0413] The route of administration is in accord with known methods, e.g. injection or infusion by intravenous, intraperitoneal, intracerebral, intramuscular, intraocular, intraarterial or intrasplenic routes, topical administration, or by sustained release systems.

[0414] 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.

[0415] 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 U.S. Pat. No. 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.

[0416] 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.

[0417] The sustained-release formulations of these proteins were developed using poly-lactic-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.

[0418] This invention encompasses methods of screening compounds to identify those that mimic the PRO polypep-

ptide (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.

[0419] 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.

[0420] 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.

[0421] 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.

[0422] 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 GALA, 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 GALA-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.

[0423] 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.

[0424] 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.

[0425] 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.

[0426] 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.

[0427] 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.

[0428] 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 control 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.

[0429] 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.

[0430] 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).

[0431] 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.

[0432] 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.

[0433] Diagnostic and therapeutic uses of the herein disclosed molecules may also be based upon the positive functional assay hits disclosed and described below.

[0434] F. Anti-PRO Antibodies

[0435] The present invention further provides anti-PRO antibodies. Exemplary antibodies include polyclonal, monoclonal, humanized, bispecific, and heteroconjugate antibodies.

[0436] 1. Polyclonal Antibodies

[0437] The anti-PRO antibodies may comprise polygonal 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.

[0438] 2. Monoclonal Antibodies

[0439] 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.

[0440] 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.

[0441] 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].

[0442] 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 immunosorbent 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).

[0443] 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.

[0444] 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.

[0445] 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.

[0446] 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 Fe 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.

[0447] 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.

[0448] 3. Human and Humanized Antibodies

[0449] 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)].

[0450] 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.

[0451] 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.* 1365-93 (1995).

[0452] 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.

[0453] 4. Bispecific Antibodies

[0454] 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.

[0455] 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).

[0456] 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 the 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).

[0457] 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.

[0458] 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 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.

[0459] Fab' fragments may be directly recovered from *E. coli* and chemically coupled to form bispecific antibodies. Shalaby et al., *J. Exp. Med.* 175:217-225 (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.

[0460] 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).

[0461] Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt et al., *J. Immunol.* 147:60 (1991).

[0462] 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 (FcγR), such as FcγRI (CD64), FcγRII (CD32) and FcγRIII (CD 16) 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).

[0463] 5. Heteroconjugate Antibodies

[0464] 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.

[0465] 6. Effector Function Engineering

[0466] 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).

[0467] 7. Immunoconjugates

[0468] 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).

[0469] 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, *Phytolaca americana* proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, 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 radionucleotide to the antibody. See WO94/11026.

[0470] 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).

[0471] 8. Immunoliposomes

[0472] 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.

[0473] 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).

[0474] 9. Pharmaceutical Compositions of Antibodies

[0475] 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.

[0476] 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.

[0477] 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 collo-

dal 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.

[0478] The formulations to be used for in vivo administration must be sterile. This is readily accomplished by filtration through sterile filtration membranes.

[0479] 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 γ 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 sulphydryl residues, lyophilizing from acidic solutions, controlling moisture content, using appropriate additives, and developing specific polymer matrix compositions.

[0480] G. Uses for anti-PRO Antibodies

[0481] 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 , ^{14}C , ^{32}P , ^{35}S , or ^{125}I , 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).

[0482] 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 a 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.

[0483] The following examples are offered for illustrative purposes only, and are not intended to limit the scope of the present invention in any way.

[0484] All patent and literature references cited in the present specification are hereby incorporated by reference in their entirety.

EXAMPLES

[0485] 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

[0486] 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* 266:460480 (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.).

[0487] 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.

[0488] 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.

[0489] 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

[0490] 1. Preparation of Oligo dT Primed cDNA Library

[0491] 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.

[0492] 2. Preparation of Random Primed cDNA Library

[0493] 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.

[0494] 3. Transformation and Detection

[0495] 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.

[0496] 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.

[0497] 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 sec71, sec72, sec62, with truncated sec71 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.

[0498] 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 2x10⁶ cells/ml (approx. OD₆₀₀=0.1) into fresh YEPD broth (500 ml) and regrown to 1x10⁷ cells/ml (approx. OD₆₀₀=0.4-0.5).

[0499] 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).

[0500] 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 μ l) were spread onto the selective media previously prepared in 150 mm growth plates (VWR).

[0501] Alternatively, instead of multiple small reactions, the transformation was performed using a single, large scale reaction, wherein reagent amounts were scaled up accordingly.

[0502] 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.

[0503] 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).

[0504] 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.

[0505] 4. Isolation of DNA by PCR Amplification

[0506] When a positive colony was isolated, a portion of it was picked by a toothpick and diluted into sterile water (30 μ l) 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 μ l) was used as a template for the PCR reaction in a 25 μ l volume containing: 0.5 μ l Klentaq (Clontech, Palo Alto, Calif.); 4.0 μ l 10 mM dNTP's (Perkin Elmer-Cetus); 2.5 μ l Kentaq buffer (Clontech); 0.25 μ l forward oligo 1; 0.25 μ l reverse oligo 2; 12.5 μ l distilled water. The sequence of the forward oligonucleotide 1 was:

[0507] 5'-TGTAACACGACGGCCAGTTAAATA-GACCTGCAATTATTAATCT-3' (SEQ ID NO:245)

[0508] The sequence of reverse oligonucleotide 2 was:

[0509] 5'-CAGGAAACAGCTATGACCACCTG-CACACCTGCAAATCCATT-3' (SEQ ID NO:246)

[0510] 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.	

[0511] 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.

[0512] 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

[0513] 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 the 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

[0514] 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 Table 7 below.

TABLE 7

Material	ATCC Dep. No.	Deposit Date
DNA94849-2960	PTA-2306	Jul. 25, 2000
DNA96883-2745	PTA-544	Aug. 17, 1999
DNA96894-2675	PTA-260	Jun. 22, 1999
DNA100272-2969	PTA-2299	Jul. 25, 2000

TABLE 7-continued

Material	ATCC Dep. No.	Deposit Date
DNA108696-2966	PTA-2315	Aug. 1, 2000
DNA117935-2801	PTA-1088	Dec. 22, 1999
DNA119474-2803	PTA-1097	Dec. 22, 1999
DNA119498-2965	PTA-2298	Jul. 25, 2000
DNA119502-2789	PTA-1082	Dec. 22, 1999
DNA119516-2797	PTA-1083	Dec. 22, 1999
DNA119530-2968	PTA-2396	Aug. 8, 2000
DNA121772-2741	PTA-1030	Dec. 7, 1999
DNA125148-2782	PTA-955	Nov. 16, 1999
DNA125150-2793	PTA-1085	Dec. 22, 1999
DNA125151-2784	PTA-1029	Dec. 7, 1999
DNA125181-2804	PTA-1096	Dec. 22, 1999
DNA125192-2794	PTA-1086	Dec. 22, 1999
DNA125196-2792	PTA-1091	Dec. 22, 1999
DNA125200-2810	PTA-1186	Jan. 11, 2000
DNA125214-2814	PTA-1270	Feb. 2, 2000
DNA125219-2799	PTA-1084	Dec. 22, 1999
DNA128309-2825	PTA-1340	Feb. 8, 2000
DNA129535-2796	PTA-1087	Dec. 22, 1999
DNA129549-2798	PTA-1099	Dec. 22, 1999
DNA129580-2863	PTA-1584	Mar. 28, 2000
DNA129794-2967	PTA-2305	Jul. 25, 2000
DNA131590-2962	PTA-2297	Jul. 25, 2000
DNA135173-2811	PTA-1184	Jan. 11, 2000
DNA138039-2828	PTA-1343	Feb. 8, 2000
DNA139540-2807	PTA-1187	Jan. 11, 2000
DNA139602-2859	PTA-1588	Mar. 28, 2000
DNA139632-2880	PTA-1629	Apr. 4, 2000
DNA139686-2823	PTA-1264	Feb. 2, 2000
DNA142392-2800	PTA-1092	Dec. 22, 1999
DNA143076-2787	PTA-1028	Dec. 7, 1999
DNA143294-2818	PTA-1182	Jan. 11, 2000
DNA143514-2817	PTA-1266	Feb. 2, 2000
DNA144841-2816	PTA-1188	Jan. 11, 2000
DNA148380-2827	PTA-1181	Jan. 11, 2000
DNA149995-2871	PTA-1971	May 31, 2000
DNA167678-2963	PTA-2302	Jul. 25, 2000
DNA168028-2956	PTA-2304	Jul. 25, 2000
DNA173894-2947	PTA-2108	Jun. 20, 2000
DNA176775-2957	PTA-2303	Jul. 25, 2000
DNA177313-2982	PTA-2251	Jul. 19, 2000
DNA57700-1408	203583	Jan. 12, 1999
DNA62872-1509	203100	Aug. 4, 1998
DNA62876-1517	203095	Aug. 4, 1998
DNA66660-1585	203279	Sep. 22, 1998
DNA34434-1139	209252	Sep. 16, 1997
DNA44804-1248	209527	Dec. 10, 1997
DNA52758-1399	209773	Apr. 14, 1998
DNA59849-1504	209986	Jun. 16, 1998
DNA65410-1569	203231	Sep. 15, 1998
DNA71290-1630	203275	Sep. 22, 1998
DNA33100-1159	209377	Oct. 16, 1997
DNA64896-1539	203238	Sep. 9, 1998
DNA84920-2614	203966	Apr. 27, 1999
DNA23330-1390	209775	Apr. 14, 1998
DNA32286-1191	209385	Oct. 16, 1997
DNA35673-1201	209418	Oct. 28, 1997
DNA43316-1237	209487	Nov. 21, 1997
DNA44184-1319	209704	Mar. 26, 1998
DNA45419-1252	209616	Feb. 5, 1998
DNA48314-1320	209702	Mar. 26, 1998
DNA50921-1458	209859	May 12, 1998
DNA53987	209858	May 12, 1998
DNA56047-1456	209948	Jun. 9, 1998
DNA56405-1357	209849	May 6, 1998
DNA56531-1648	203286	Sep. 29, 1998
DNA56865-1491	203022	Jun. 23, 1998
DNA57694-1341	203017	Jun. 23, 1998
DNA57708-1411	203021	Jun. 23, 1998
DNA57836-1338	203025	Jun. 23, 1998
DNA57841-1522	203458	Nov. 3, 1998
DNA58847-1383	209879	May 20, 1998
DNA59212-1627	203245	Sep. 9, 1998
DNA59588-1571	203106	Aug. 11, 1998

TABLE 7-continued

Material	ATCC Dep. No.	Deposit Date
DNA59622-1334	209984	Jun. 16, 1998
DNA59847-2510	203576	Jan. 12, 1999
DNA60615-1483	209980	Jun. 16, 1998
DNA60621-1516	203091	Aug. 4, 1998
DNA62814-1521	203093	Aug. 4, 1998
DNA64883-1526	203253	Sep. 9, 1998
DNA64889-1541	203250	Sep. 9, 1998
DNA64897-1628	203216	Sep. 15, 1998
DNA64903-1553	203223	Sep. 15, 1998
DNA64907-1163-1	203242	Sep. 9, 1998
DNA64950-1590	203224	Sep. 15, 1998
DNA64952-1568	203222	Sep. 15, 1998
DNA65402-1540	203252	Sep. 9, 1998
DNA65405-1547	203476	Nov. 17, 1998
DNA66663-1598	203268	Sep. 22, 1998
DNA66667	203267	Sep. 22, 1998
DNA66675-1587	203282	Sep. 22, 1998
DNA67300-1605	203163	Aug. 25, 1998
DNA68872-1620	203160	Aug. 25, 1998
DNA71269-1621	203284	Sep. 22, 1998
DNA73736-1657	203466	Nov. 17, 1998
DNA73739-1645	203270	Sep. 22, 1998
DNA76400-2528	203573	Jan. 12, 1999
DNA76532-1702	203473	Nov. 17, 1998
DNA76541-1675	203409	Oct. 27, 1998
DNA79862-2522	203550	Dec. 22, 1998
DNA81754-2532	203542	Dec. 15, 1998
DNA81761-2583	203862	Mar. 23, 1999
DNA83500-2506	203391	Oct. 29, 1998
DNA84210-2576	203818	Mar. 2, 1999
DNA86571-2551	203660	Feb. 9, 1999
DNA92218-2554	203834	Mar. 9, 1999
DNA92223-2567	203851	Mar. 16, 1999
DNA92265-2669	PTA-256	Jun. 22, 1999
DNA92274-2617	203971	Apr. 27, 1999
DNA108760-2740	PTA-548	Aug. 17, 1999
DNA108792-2753	PTA-617	Aug. 31, 1999
DNA111750-2706	PTA-489	Aug. 3, 1999
DNA119514-2772	PTA-946	Nov. 9, 1999
DNA125185-2806	PTA-1031	Dec. 7, 1999

[0515] 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).

[0516] 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

Isolation of cDNA Clones Encoding Human PRO6004, PRO5723, PRO3444, and PRO9940

[0517] DNA molecules encoding the PRO840, PRO1338, PRO6004, PRO5723, PRO3444, and PRO9940 polypeptides shown in the accompanying figures were obtained through GenBank.

Example 6

Use of PRO as a Hybridization Probe

[0518] The following method describes use of a nucleotide sequence encoding PRO as a hybridization probe.

[0519] 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.

[0520] 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.

[0521] 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 7

Expression of PRO in *E. coli*

[0522] This example illustrates preparation of an unglycosylated form of PRO by recombinant expression in *E. coli*.

[0523] 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.

[0524] 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.

[0525] Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with anti-

biotics. 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.

[0526] 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.

[0527] 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) lon 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.

[0528] *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 sulfate and sodium tetrathionate is added to make final concentrations of 0.1 M 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 Ultra-centrifuge 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.

[0529] 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 proteins from the desired form, the reversed phase step also removes endotoxin from the samples.

[0530] 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.

[0531] Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

Example 8

Expression of PRO in Mammalian Cells

[0532] This example illustrates preparation of a potentially glycosylated form of PRO by recombinant expression in mammalian cells.

[0533] 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.

[0534] 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.

[0535] 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, con-

centrated 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.

[0536] In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran sulfate method described by Sompariyac 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.

[0537] 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.

[0538] 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.

[0539] 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.

[0540] 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.

[0541] 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.

[0542] Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect[®] (Qiagen), Dospert[®] or Fugene[®] (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.

[0543] 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 1.2×10^5 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.

[0544] 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.

[0545] Immuno-adhesin (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.

[0546] Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

Example 9

Expression of PRO in Yeast

[0547] The following method describes recombinant expression of PRO in yeast.

[0548] 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.

[0549] 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.

[0550] Recombinant PRO can subsequently be isolated and purified by removing the yeast 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.

[0551] Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

Example 10

Expression of PRO in Baculovirus-Infected Insect Cells

[0552] The following method describes recombinant expression of PRO in Baculovirus-infected insect cells.

[0553] The sequence coding for PRO is fused upstream of an epitope tag contained within 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.

[0554] 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'Reilly et al., *Baculovirus expression vectors: A Laboratory Manual*, Oxford: Oxford University Press (1994).

[0555] 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.

[0556] 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.

[0557] Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

Example 11

Preparation of Antibodies that Bind PRO

[0558] This example illustrates preparation of monoclonal antibodies which can specifically bind PRO.

[0559] 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.

[0560] 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.

[0561] 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.

[0562] 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.

[0563] 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 12

Purification of PRO Polypeptides Using Specific Antibodies

[0564] 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.

[0565] 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.

[0566] 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.

[0567] 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 13

Drug Screening

[0568] 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.

[0569] 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 an 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.

[0570] 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-forementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the peptide and immobilize it on the solid support.

[0571] 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 14

Rational Drug Design

[0572] 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)).

[0573] In one approach, the three-dimensional structure of the PRO polypeptide, or of an 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).

[0574] 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.

[0575] 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 15

Pericyte c-Fos Induction (Assay 93)

[0576] 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+/-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+1X fungizone. Assay Media=low glucose DMEM+5% FBS.

[0577] The following polypeptides tested positive in this assay: PRO982, PRO1160, PRO1187, and PRO1329.

Example 16

Chondrocyte Re-Differentiation Assay (Assay 110)

[0578] This assay shows that certain polypeptides of the invention act to induce redifferentiation of chondrocytes, therefore, are expected to be useful for the treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis. The assay is performed as follows. Porcine chondrocytes are isolated by overnight collagenase digestion of articular cartilage of metacarpophalangeal joints of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm² in Ham F-12 containing 10% FBS and 4 μ g/ml gentamycin. The culture media is changed every third day and the cells are then seeded in 96 well plates at 5,000 cells/well in 100 μ l of the same media without serum and 100 μ l of the test PRO polypeptide, 5 nM staurosporin (positive control) or medium alone (negative control) is added to give a final volume of 200 μ l/well. After 5 days of incubation at 37° C., a picture of each well is taken and the differentiation state of the chondrocytes is determined. A positive result in the assay occurs when the redifferentiation of the chondrocytes is determined to be more similar to the positive control than the negative control.

[0579] The following polypeptide tested positive in this assay: PRO357.

Example 17

Identification of PRO Polypeptides that Stimulate TNF- α Release in Human Blood (Assay 128)

[0580] 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 aliquoted 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.

[0581] The following PRO polypeptides tested positive in this assay: PRO231; PRO357, PRO725, PRO1155, PRO1306, and PRO1419.

Example 18

Promotion of Chondrocyte Redifferentiation (Assay 129)

[0582] This assay is designed to determine whether PRO polypeptides of the present invention show the ability to induce the proliferation and/or redifferentiation of chondrocytes in culture. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis.

[0583] Porcine chondrocytes are isolated by overnight collagenase digestion of articular cartilage of the metacarpophalangeal joint of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm² in Ham F-12 containing 10% FBS and 4 μ g/ml gentamycin. The culture media is changed every third day. On day 12, the cells are seeded in 96 well plates at 5,000 cells/well in 100 μ l of the same media without serum and 100 μ l of either serum-free medium (negative control), staurosporin (final concentration of 5 nM; positive control) or the test PRO polypeptide are added to give a final volume of 200 μ l/well. After 5 days at 37° C., 22 μ l of media containing 100 μ g/ml Hoechst 33342 and 50 μ g/ml 5-CFDA is added to each well and incubated for an additional 10 minutes at 37° C. A picture of the green fluorescence is taken for each well and the differentiation state of the chondrocytes is calculated by morphometric analysis. A positive result in the assay is obtained when the >50% of the PRO polypeptide treated cells are differentiated (compared to the background obtained by the negative control).

[0584] The following PRO polypeptides tested positive in this assay: PRO229, PRO1272, and PRO4405.

Example 19

Normal Human Dermal Fibroblast Proliferation
(Assay 141)

[0585] This assay is designed to determine whether PRO polypeptides of the present invention show the ability to induce proliferation of human dermal fibroblast cells in culture and, therefore, function as useful growth factors.

[0586] On day 0, human dermal fibroblast cells (from cell lines, maximum of 12-14 passages) were plated in 96-well plates at 1000 cells/well per 100 microliter and incubated overnight in complete media [fibroblast growth media (FGM, Clonetics), plus supplements: insulin, human epithelial growth factor (hEGF), gentamicin (GA-1000), and fetal bovine serum (FBS, Clonetics)]. On day 1, complete media was replaced by basal media [FGM plus 1% FBS] and addition of PRO polypeptides at 1%, 0.1% and 0.01%. On day 7, an assessment of cell proliferation was performed by Alamar Blue assay followed by Crystal Violet. Results are expressed as % of the cell growth observed with control buffer.

[0587] The following PRO polypeptides stimulated normal human dermal fibroblast proliferation in this assay: PRO982, PRO357, PRO725, PRO1306, PRO1419, PRO214, PRO247, PRO337, PRO526, PRO363, PRO531, PRO1083, PRO840, PRO1080, PRO1478, PRO1134, PRO826, PRO1005, PRO809, PRO1071, PRO1411, PRO1309, PRO1025, PRO1181, PRO1126, PRO1186, PRO1192, PRO1244, PRO1274, PRO1412, PRO1286, PRO1330, PRO1347, PRO1305, PRO1273, PRO1279, PRO1340, PRO1338, PRO1343, PRO1376, PRO1387, PRO1409, PRO1474, PRO1917, PRO1760, PRO1567, PRO1887, PRO1928, PRO4341, PRO1801, PRO4333, PRO3543, PRO3444, PRO4322, PRO9940, PRO6079, PRO9836 and PRO10096.

[0588] The following PRO polypeptides inhibited normal human dermal fibroblast proliferation in this assay: PRO181, PRO229, PRO788, PRO1194, PRO1272, PRO1488, PRO4302, PRO4408, PRO5723, PRO5725, PRO7154, and PRO7425.

Example 20

Microarray Analysis to Detect Overexpression of
PRO Polypeptides in Cancerous Tumors

[0589] Nucleic acid microarrays, often containing thousands of gene sequences, are useful for identifying differentially expressed genes in diseased tissues as compared to their normal counterparts. Using nucleic acid microarrays, test and control mRNA samples from test and control tissue samples are reverse transcribed and labeled to generate cDNA probes. The cDNA probes are then hybridized to an array of nucleic acids immobilized on a solid support. The array is configured such that the sequence and position of each member of the array is known. For example, a selection of genes known to be expressed in certain disease states may be arrayed on a solid support. Hybridization of a labeled probe with a particular array member indicates that the sample from which the probe was derived expresses that gene. If the hybridization signal of a probe from a test (disease tissue) sample is greater than hybridization signal of a probe from a control (normal tissue) sample, the gene or

genes overexpressed in the disease tissue are identified. The implication of this result is that an overexpressed protein in a diseased tissue is useful not only as a diagnostic marker for the presence of the disease condition, but also as a therapeutic target for treatment of the disease condition.

[0590] The methodology of hybridization of nucleic acids and microarray technology is well known in the art. In the present example, the specific preparation of nucleic acids for hybridization and probes, slides, and hybridization conditions are all detailed in U.S. Provisional Patent Application Serial No. 60/193,767, filed on Mar. 31, 2000 and which is herein incorporated by reference.

[0591] In the present example, cancerous tumors derived from various human tissues were studied for PRO polypeptide-encoding gene expression relative to non-cancerous human tissue in an attempt to identify those PRO polypeptides which are overexpressed in cancerous tumors. Cancerous human tumor tissue from any of a variety of different human tumors was obtained and compared to a "universal" epithelial control sample which was prepared by pooling non-cancerous human tissues of epithelial origin, including liver, kidney, and lung. mRNA isolated from the pooled tissues represents a mixture of expressed gene products from these different tissues. Microarray hybridization experiments using the pooled control samples generated a linear plot in a 2-color analysis. The slope of the line generated in a 2-color analysis was then used to normalize the ratios of (test:control detection) within each experiment. The normalized ratios from various experiments were then compared and used to identify clustering of gene expression. Thus, the pooled "universal control" sample not only allowed effective relative gene expression determinations in a simple 2-sample comparison, it also allowed multi-sample comparisons across several experiments.

[0592] In the present experiments, nucleic acid probes derived from the herein described PRO polypeptide-encoding nucleic acid sequences were used in the creation of the microarray and RNA from a panel of nine different tumor tissues (listed below) were used for the hybridization thereto. A value based upon the normalized ratio:experimental ratio was designated as a "cutoff ratio". Only values that were above this cutoff ratio were determined to be significant. Table 8 below shows the results of these experiments, demonstrating that various PRO polypeptides of the present invention are significantly overexpressed in various human tumor tissues, as compared to a non-cancerous human tissue control or other human tumor tissues. As described above, these data demonstrate that the PRO polypeptides of the present invention are useful not only as diagnostic markers for the presence of one or more cancerous tumors, but also serve as therapeutic targets for the treatment of those tumors.

TABLE 8

Molecule	is overexpressed in:	as compared to normal control:
PRO6004	colon tumor	universal normal control
PRO4981	colon tumor	universal normal control
PRO4981	lung tumor	universal normal control
PRO7174	colon tumor	universal normal control
PRO5778	lung tumor	universal normal control
PRO5778	breast tumor	universal normal control
PRO5778	liver tumor	universal normal control
PRO4332	colon tumor	universal normal control

TABLE 8-continued

Molecule	is overexpressed in:	as compared to normal control:
PRO9799	colon tumor	universal normal control
PRO9909	colon tumor	universal normal control
PRO9917	colon tumor	universal normal control
PRO9917	lung tumor	universal normal control
PRO9917	breast tumor	universal normal control
PRO9771	colon tumor	universal normal control
PRO9877	colon tumor	universal normal control
PRO9903	colon tumor	universal normal control
PRO9830	colon tumor	universal normal control
PRO7155	colon tumor	universal normal control
PRO7155	lung tumor	universal normal control
PRO7155	prostate tumor	universal normal control
PRO9862	colon tumor	universal normal control
PRO9882	colon tumor	universal normal control
PRO9864	colon tumor	universal normal control
PRO10013	colon tumor	universal normal control
PRO9885	colon tumor	universal normal control
PRO9879	colon tumor	universal normal control
PRO10111	colon tumor	universal normal control
PRO10111	rectal tumor	universal normal control
PRO9925	breast tumor	universal normal control
PRO9925	rectal tumor	universal normal control
PRO9925	colon tumor	universal normal control
PRO9925	lung tumor	universal normal control
PRO9905	colon tumor	universal normal control
PRO10276	colon tumor	universal normal control
PRO9898	colon tumor	universal normal control
PRO9904	colon tumor	universal normal control
PRO19632	colon tumor	universal normal control
PRO19672	colon tumor	universal normal control
PRO9783	colon tumor	universal normal control
PRO9783	lung tumor	universal normal control
PRO9783	breast tumor	universal normal control
PRO9783	prostate tumor	universal normal control
PRO9783	rectal tumor	universal normal control
PRO10112	colon tumor	universal normal control
PRO10284	colon tumor	universal normal control
PRO10100	colon tumor	universal normal control
PRO19628	colon tumor	universal normal control
PRO19684	colon tumor	universal normal control
PRO10274	colon tumor	universal normal control
PRO9907	colon tumor	universal normal control
PRO9873	colon tumor	universal normal control
PRO10201	colon tumor	universal normal control
PRO10200	colon tumor	universal normal control
PRO10196	colon tumor	universal normal control
PRO10282	lung tumor	universal normal control
PRO10282	breast tumor	universal normal control
PRO10282	colon tumor	universal normal control
PRO10282	rectal tumor	universal normal control
PRO19650	colon tumor	universal normal control
PRO21184	lung tumor	universal normal control
PRO21184	breast tumor	universal normal control
PRO21184	colon tumor	universal normal control
PRO21201	breast tumor	universal normal control
PRO21201	colon tumor	universal normal control
PRO21175	breast tumor	universal normal control
PRO21175	colon tumor	universal normal control
PRO21175	lung tumor	universal normal control
PRO21340	colon tumor	universal normal control
PRO21340	prostate tumor	universal normal control
PRO21384	colon tumor	universal normal control
PRO21384	lung tumor	universal normal control
PRO21384	breast tumor	universal normal control

Example 21

Tumor Versus Normal Differential Tissue
Expression Distribution

[0593] 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.

[0594] (1) the DNA94849-2960 molecule is significantly expressed in the following tissues: cartilage, testis, colon tumor, heart, placenta, bone marrow, adrenal gland, prostate, spleen aortic endothelial cells and uterus, and not significantly expressed in the following tissues: HUVEC.

[0595] (2) the DNA100272-2969 molecule is significantly expressed in cartilage, testis, human umbilical vein endothelial cells (HUVEC), colon tumor, heart, placenta, bone marrow, adrenal gland, prostate, spleen and aortic endothelial cells; and not significantly expressed in uterus. Among a panel of normal and tumor cells examined, the DNA100272-2969 was found to be expressed in normal esophagus, esophageal tumor, normal stomach, stomach tumor, normal kidney, kidney tumor, normal lung, lung tumor, normal rectum, rectal tumor, normal liver and liver tumor.

[0596] (3) the DNA108696-2966 molecule is highly expressed in prostate and also expressed in testis, bone marrow and spleen. The DNA108696-2966 molecule is expressed in normal stomach, but not expressed in stomach tumor. The DNA108696-2966 molecule is not expressed in normal kidney, kidney tumor, normal lung, or lung tumor. The DNA108696-2966 molecule is highly expressed in normal rectum, lower expression in rectal tumor. The DNA108696-2966 molecule is not expressed in normal liver or liver tumor. The DNA108696-2966 molecule is not expressed in normal esophagus, esophageal tumor, cartilage, HUVEC, colon tumor, heart, placenta, adrenal gland, aortic endothelial cells and uterus.

[0597] (4) the DNA119498-2965 molecule is significantly expressed in the following tissues: highly expressed in aortic endothelial cells, and also significantly expressed in cartilage, testis, HUVEC, colon tumor, heart, placenta, bone marrow, adrenal gland, prostate and spleen. It is not significantly expressed in uterus.

- [0598] (5) the DNA119530-2968 molecule is expressed in the following tissues: normal esophagus and not expressed in the following tissues: esophageal tumors, stomach tumors, normal stomach, normal kidney, kidney tumor, normal lung, lung tumor, normal rectum, rectal tumors, normal liver or liver tumors.
- [0599] (6) the DNA129794-2967 molecule is significantly expressed in testis and adrenal gland; and not significantly expressed in cartilage, human umbilical vein endothelial cells (HUVEC), colon tumor, heart, placenta, bone marrow, prostate, spleen, aortic endothelial cells and uterus.
- [0600] (7) the DNA131590-2962 molecule is significantly expressed in the following tissues: bone marrow, adrenal gland, prostate, spleen, uterus, cartilage, testis, colon tumor, heart, and placenta, and not significantly expressed in the following tissues: HUVEC, and aortic endothelial cells.
- [0601] (8) the DNA149995-2871 molecule is highly expressed in testis, and adrenal gland; expressed in cartilage, human umbilical vein endothelial cells (HUVEC), colon tumor, heart, prostate and uterus; weakly expressed in bone marrow, spleen and aortic endothelial cells; and not significantly expressed in placenta.
- [0602] (9) the DNA167678-2963 molecule is significantly expressed in the following tissues: normal esophagus, esophageal tumor, highly expressed in normal stomach, stomach tumor, highly expressed in normal kidney, kidney tumor, expressed in lung, lung tumor, normal rectum, rectal tumor, weakly expressed in normal liver, and not significantly expressed in liver tumor.
- [0603] (10) the DNA168028-2956 molecule is highly expressed in bone marrow; expressed in testis, human umbilical vein endothelial cells (HUVEC), colon tumor, heart, placenta, adrenal gland, prostate, spleen, aortic endothelial cells and uterus; and is weakly expressed in cartilage. Among a panel of normal and tumor samples examined, the DNA168028-2956 was found to be expressed in stomach tumor, normal kidney, kidney tumor, lung tumor, normal rectum and rectal tumor; and not expressed in normal esophagus, esophageal tumor, normal stomach, normal lung, normal liver and liver tumor.
- [0604] (11) the DNA176775-2957 molecule is highly expressed in testis; expressed in cartilage and prostate; weakly expressed in adrenal gland, spleen and uterus; and not significantly expressed in human umbilical vein endothelial cells (HUVEC), colon tumor, heart, placenta, bone marrow and aortic endothelial cells.
- [0605] (12) the DNA177313-2982 molecule is significantly expressed in prostate and aortic endothelial cells; and not significantly expressed in cartilage, testis, human umbilical vein endothelial cells (HUVEC), colon tumor, heart, placenta, bone marrow, adrenal gland, spleen and uterus. Among a panel of normal and tumor cells, the DNA177313-2982 molecule was found to be expressed in esophageal tumor but not in normal esophagus, normal stomach, stomach tumor, normal kidney, kidney tumor, normal lung, lung tumor, normal rectum, rectal tumor, normal liver and liver tumor.

SEQUENCE LISTING

The patent application contains a lengthy "Sequence Listing" section. A copy of the "Sequence Listing" is available in electronic form from the USPTO web site (<http://seqdata.uspto.gov/sequence.html?DocID=20030096967>). An electronic copy of the "Sequence Listing" will also be available from the USPTO upon request and payment of the fee set forth in 37 CFR 1.19(b)(3).

What is claimed is:

1. Isolated nucleic acid having at least 80% nucleic acid sequence identity to a nucleotide sequence that encodes an amino acid sequence selected from the group consisting of the amino acid sequence shown in **FIG. 2** (SEQ ID NO:2), **FIG. 4** (SEQ ID NO:4), **FIG. 6** (SEQ ID NO:6), **FIG. 8** (SEQ ID NO:8), **FIG. 10** (SEQ ID NO:10), **FIG. 12** (SEQ ID NO:12), **FIG. 14** (SEQ ID NO:14), **FIG. 16** (SEQ ID NO:16), **FIG. 18** (SEQ ID NO:18), **FIG. 20** (SEQ ID NO:20), **FIG. 22** (SEQ ID NO:22), **FIG. 24** (SEQ ID NO:24), **FIG. 26** (SEQ ID NO:26), **FIG. 28** (SEQ ID NO:28), **FIG. 30** (SEQ ID NO:30), **FIG. 32** (SEQ ID NO:32), **FIG. 34** (SEQ ID NO:34), **FIG. 36** (SEQ ID NO:36), **FIG. 38** (SEQ ID NO:38), **FIG. 40** (SEQ ID NO:40), **FIG. 42** (SEQ ID NO:42), **FIG. 44** (SEQ ID NO:44), **FIG. 46** (SEQ ID NO:46), **FIG. 48** (SEQ ID NO:48), **FIG. 50** (SEQ ID NO:50), **FIG. 52** (SEQ ID NO:52), **FIG. 54** (SEQ ID NO:54), **FIG. 56** (SEQ ID NO:56), **FIG. 58** (SEQ ID NO:58), **FIG. 60** (SEQ ID NO:60), **FIG. 62** (SEQ ID NO:62), **FIG. 64** (SEQ ID NO:64), **FIG. 66** (SEQ ID NO:66), **FIG. 68** (SEQ ID NO:68), **FIG. 70** (SEQ ID NO:70), **FIG. 72** (SEQ ID NO:72), **FIG. 74** (SEQ ID NO:74), **FIG. 76** (SEQ ID NO:76), **FIG. 78** (SEQ ID NO:78), **FIG. 80** (SEQ ID NO:80), **FIG. 82** (SEQ ID NO:82), **FIG. 84** (SEQ ID NO:84), **FIG. 86** (SEQ ID NO:86), **FIG. 88** (SEQ ID NO:88), **FIG. 90** (SEQ ID NO:90), **FIG. 92** (SEQ ID NO:92), **FIG. 94** (SEQ ID NO:94), **FIG. 96** (SEQ ID

NO:96), **FIG. 98** (SEQ ID NO:98), **FIG. 100** (SEQ ID NO:100), **FIG. 102** (SEQ ID NO:102), **FIG. 104** (SEQ ID NO:104), **FIG. 106** (SEQ ID NO:106), **FIG. 108** (SEQ ID NO:108), **FIG. 110** (SEQ ID NO:110), **FIG. 112** (SEQ ID NO:112), **FIG. 114** (SEQ ID NO:114), **FIG. 116** (SEQ ID NO:116), **FIG. 118** (SEQ ID NO:118), **FIG. 120** (SEQ ID NO:120), **FIG. 122** (SEQ ID NO:122), **FIG. 124** (SEQ ID NO:124), **FIG. 126** (SEQ ID NO:126), **FIG. 128** (SEQ ID NO:128), **FIG. 130** (SEQ ID NO:130), **FIG. 132** (SEQ ID NO:132), **FIG. 134** (SEQ ID NO:134), **FIG. 136** (SEQ ID NO:136), **FIG. 138** (SEQ ID NO:138), **FIG. 140** (SEQ ID NO:140), **FIG. 142** (SEQ ID NO:142), **FIG. 144** (SEQ ID NO:144), **FIG. 146** (SEQ ID NO:146), **FIG. 148** (SEQ ID NO:148), **FIG. 150** (SEQ ID NO:150), **FIG. 152** (SEQ ID NO:152), **FIG. 154** (SEQ ID NO:154), **FIG. 156** (SEQ ID NO:156), **FIG. 158** (SEQ ID NO:158), **FIG. 160** (SEQ ID NO:160), **FIG. 162** (SEQ ID NO:162), **FIG. 164** (SEQ ID NO:164), **FIG. 166** (SEQ ID NO:166), **FIG. 168** (SEQ ID NO:168), **FIG. 170** (SEQ ID NO:170), **FIG. 172** (SEQ ID NO:172), **FIG. 174** (SEQ ID NO:174), **FIG. 176** (SEQ ID NO:176), **FIG. 178** (SEQ ID NO:178), **FIG. 180** (SEQ ID NO:180), **FIG. 182** (SEQ ID NO:182), **FIG. 184** (SEQ ID NO:184), **FIG. 186** (SEQ ID NO:186), **FIG. 188** (SEQ ID NO:188), **FIG. 190** (SEQ ID NO:190), **FIG. 192** (SEQ ID NO:192), **FIG. 194** (SEQ ID NO:194), **FIG. 196** (SEQ ID NO:196), **FIG. 198** (SEQ ID NO:198), **FIG. 200** (SEQ ID NO:200), **FIG. 202** (SEQ ID NO:202), **FIG. 204** (SEQ ID NO:204), **FIG. 206** (SEQ ID NO:206), **FIG. 208** (SEQ ID NO:208), **FIG. 210** (SEQ ID NO:210), **FIG. 212** (SEQ ID NO:212), **FIG. 214** (SEQ ID NO:214), **FIG. 216** (SEQ ID NO:216), **FIG. 218** (SEQ ID NO:218), **FIG. 220** (SEQ ID NO:220), **FIG. 222** (SEQ ID NO:222), **FIG. 224** (SEQ ID NO:224), **FIG. 226** (SEQ ID NO:226), **FIG. 228** (SEQ ID NO:228), **FIG. 230** (SEQ ID NO:230), **FIG. 232** (SEQ ID NO:232), **FIG. 234** (SEQ ID NO:234), **FIG. 236** (SEQ ID NO:236), **FIG. 238** (SEQ ID NO:238), **FIG. 240** (SEQ ID NO:240), **FIG. 242** (SEQ ID NO:242), and **FIG. 244** (SEQ ID NO:244).

2. Isolated nucleic acid having at least 80% nucleic acid sequence identity to a nucleotide sequence selected from the group consisting of the nucleotide sequence shown in FIGS. 1A-1B (SEQ ID NO:1), **FIG. 3** (SEQ ID NO:3), **FIG. 5** (SEQ ID NO:5), **FIG. 7** (SEQ ID NO:7), **FIG. 9** (SEQ ID NO:9), **FIG. 11** (SEQ ID NO:11), **FIG. 13** (SEQ ID NO:13), **FIG. 15** (SEQ ID NO:15), **FIG. 17** (SEQ ID NO:17), **FIG. 19** (SEQ ID NO:19), **FIG. 21** (SEQ ID NO:21), **FIG. 23** (SEQ ID NO:23), **FIG. 25** (SEQ ID NO:25), **FIG. 27** (SEQ ID NO:27), **FIG. 29** (SEQ ID NO:29), **FIG. 31** (SEQ ID NO:31), **FIG. 33** (SEQ ID NO:33), **FIG. 35** (SEQ ID NO:35), **FIG. 37** (SEQ ID NO:37), **FIG. 39** (SEQ ID NO:39), **FIG. 41** (SEQ ID NO:41), **FIG. 43** (SEQ ID NO:43), **FIG. 45** (SEQ ID NO:45), **FIG. 47** (SEQ ID NO:47), **FIG. 49** (SEQ ID NO:49), **FIG. 51** (SEQ ID NO:51), **FIG. 53** (SEQ ID NO:53), **FIG. 55** (SEQ ID NO:55), **FIG. 57** (SEQ ID NO:57), FIGS. 59A-59B (SEQ ID NO:59), **FIG. 61** (SEQ ID NO:61), **FIG. 63** (SEQ ID NO:63), **FIG. 65** (SEQ ID NO:65), **FIG. 67** (SEQ ID NO:67), **FIG. 69** (SEQ ID NO:69), **FIG. 71** (SEQ ID NO:71), **FIG. 73** (SEQ ID NO:73), **FIG. 75** (SEQ ID NO:75), **FIG. 77** (SEQ ID NO:77), **FIG. 79** (SEQ ID NO:79), **FIG. 81** (SEQ ID NO:81), **FIG. 83** (SEQ ID NO:83), **FIG. 85** (SEQ ID NO:85), **FIG. 87** (SEQ ID NO:87), **FIG. 89** (SEQ ID NO:89), **FIG. 91** (SEQ ID NO:91), **FIG. 93** (SEQ ID NO:93), **FIG. 95** (SEQ ID

NO:95), **FIG. 97** (SEQ ID NO:97), **FIG. 99** (SEQ ID NO:99), **FIG. 101** (SEQ ID NO:101), **FIG. 103** (SEQ ID NO:103), **FIG. 105** (SEQ ID NO:105), **FIG. 107** (SEQ ID NO:107), **FIG. 109** (SEQ ID NO:109), **FIG. 111** (SEQ ID NO:111), **FIG. 113** (SEQ ID NO:113), **FIG. 115** (SEQ ID NO:115), **FIG. 117** (SEQ ID NO:117), **FIG. 119** (SEQ ID NO:119), **FIG. 121** (SEQ ID NO:121), **FIG. 123** (SEQ ID NO:123), **FIG. 125** (SEQ ID NO:125), **FIG. 127** (SEQ ID NO:127), **FIG. 129** (SEQ ID NO:129), **FIG. 131** (SEQ ID NO:131), **FIG. 133** (SEQ ID NO:133), **FIG. 135** (SEQ ID NO:135), **FIG. 137** (SEQ ID NO:137), **FIG. 139** (SEQ ID NO:139), **FIG. 141** (SEQ ID NO:141), **FIG. 143** (SEQ ID NO:143), **FIG. 145** (SEQ ID NO:145), **FIG. 147** (SEQ ID NO:147), **FIG. 149** (SEQ ID NO:149), **FIG. 151** (SEQ ID NO:151), **FIG. 153** (SEQ ID NO:153), **FIG. 155** (SEQ ID NO:155), **FIG. 157** (SEQ ID NO:157), **FIG. 159** (SEQ ID NO:159), **FIG. 161** (SEQ ID NO:161), **FIG. 163** (SEQ ID NO:163), **FIG. 165** (SEQ ID NO:165), **FIG. 167** (SEQ ID NO:167), **FIG. 169** (SEQ ID NO:169), **FIG. 171** (SEQ ID NO:171), **FIG. 173** (SEQ ID NO:173), **FIG. 175** (SEQ ID NO:175), **FIG. 177** (SEQ ID NO:177), **FIG. 179** (SEQ ID NO:179), **FIG. 181** (SEQ ID NO:181), **FIG. 183** (SEQ ID NO:183), **FIG. 185** (SEQ ID NO:185), **FIG. 187** (SEQ ID NO:187), **FIG. 189** (SEQ ID NO:189), **FIG. 191** (SEQ ID NO:191), **FIG. 193** (SEQ ID NO:193), **FIG. 195** (SEQ ID NO:195), **FIG. 197** (SEQ ID NO:197), **FIG. 199** (SEQ ID NO:199), **FIG. 201** (SEQ ID NO:201), **FIG. 203** (SEQ ID NO:203), **FIG. 205** (SEQ ID NO:205), **FIG. 207** (SEQ ID NO:207), **FIG. 209** (SEQ ID NO:209), **FIG. 211** (SEQ ID NO:211), **FIG. 213** (SEQ ID NO:213), **FIG. 215** (SEQ ID NO:215), **FIG. 217** (SEQ ID NO:217), **FIG. 219** (SEQ ID NO:219), **FIG. 221** (SEQ ID NO:221), **FIG. 223** (SEQ ID NO:223), **FIG. 225** (SEQ ID NO:225), **FIG. 227** (SEQ ID NO:227), **FIG. 229** (SEQ ID NO:229), **FIG. 231** (SEQ ID NO:231), **FIG. 233** (SEQ ID NO:233), **FIG. 235** (SEQ ID NO:235), **FIG. 237** (SEQ ID NO:237), **FIG. 239** (SEQ ID NO:239), **FIG. 241** (SEQ ID NO:241), and **FIG. 243** (SEQ ID NO:243).

3. Isolated nucleic acid having at least 80% nucleic acid sequence identity to a nucleotide sequence selected from the group consisting of the full-length coding sequence of the nucleotide sequence shown in FIGS. 1A-1B (SEQ ID NO:1), **FIG. 3** (SEQ ID NO:3), **FIG. 5** (SEQ ID NO:5), **FIG. 7** (SEQ ID NO:7), **FIG. 9** (SEQ ID NO:9), **FIG. 11** (SEQ ID NO:11), **FIG. 13** (SEQ ID NO:13), **FIG. 15** (SEQ ID NO:15), **FIG. 17** (SEQ ID NO:17), **FIG. 19** (SEQ ID NO:19), **FIG. 21** (SEQ ID NO:21), **FIG. 23** (SEQ ID NO:23), **FIG. 25** (SEQ ID NO:25), **FIG. 27** (SEQ ID NO:27), **FIG. 29** (SEQ ID NO:29), **FIG. 31** (SEQ ID NO:31), **FIG. 33** (SEQ ID NO:33), **FIG. 35** (SEQ ID NO:35), **FIG. 37** (SEQ ID NO:37), **FIG. 39** (SEQ ID NO:39), **FIG. 41** (SEQ ID NO:41), **FIG. 43** (SEQ ID NO:43), **FIG. 45** (SEQ ID NO:45), **FIG. 47** (SEQ ID NO:47), **FIG. 49** (SEQ ID NO:49), **FIG. 51** (SEQ ID NO:51), **FIG. 53** (SEQ ID NO:53), **FIG. 55** (SEQ ID NO:55), **FIG. 57** (SEQ ID NO:57), FIGS. 59A-59B (SEQ ID NO:59), **FIG. 61** (SEQ ID NO:61), **FIG. 63** (SEQ ID NO:63), **FIG. 65** (SEQ ID NO:65), **FIG. 67** (SEQ ID NO:67), **FIG. 69** (SEQ ID NO:69), **FIG. 71** (SEQ ID NO:71), **FIG. 73** (SEQ ID NO:73), **FIG. 75** (SEQ ID NO:75), **FIG. 77** (SEQ ID NO:77), **FIG. 79** (SEQ ID NO:79), **FIG. 81** (SEQ ID NO:81), **FIG. 83** (SEQ ID NO:83), **FIG. 85** (SEQ ID NO:85), **FIG. 87** (SEQ ID NO:87), **FIG. 89** (SEQ ID NO:89), **FIG. 91** (SEQ ID

NO:91), **FIG. 93** (SEQ ID NO:93), **FIG. 95** (SEQ ID NO:95), **FIG. 97** (SEQ ID NO:97), **FIG. 99** (SEQ ID NO:99), **FIG. 101** (SEQ ID NO:101), **FIG. 103** (SEQ ID NO:103), **FIG. 105** (SEQ ID NO:105), **FIG. 107** (SEQ ID NO:107), **FIG. 109** (SEQ ID NO:109), **FIG. 111** (SEQ ID NO:111), **FIG. 113** (SEQ ID NO:113), **FIG. 115** (SEQ ID NO:115), **FIG. 117** (SEQ ID NO:117), **FIG. 119** (SEQ ID NO:119), **FIG. 121** (SEQ ID NO:121), **FIG. 123** (SEQ ID NO:123), **FIG. 125** (SEQ ID NO:125), **FIG. 127** (SEQ ID NO:127), **FIG. 129** (SEQ ID NO:129), **FIG. 131** (SEQ ID NO:131), **FIG. 133** (SEQ ID NO:133), **FIG. 135** (SEQ ID NO:135), **FIG. 137** (SEQ ID NO:137), **FIG. 139** (SEQ ID NO:139), **FIG. 141** (SEQ ID NO:141), **FIG. 143** (SEQ ID NO:143), **FIG. 145** (SEQ ID NO:145), **FIG. 147** (SEQ ID NO:147), **FIG. 149** (SEQ ID NO:149), **FIG. 151** (SEQ ID NO:151), **FIG. 153** (SEQ ID NO:153), **FIG. 155** (SEQ ID NO:155), **FIG. 157** (SEQ ID NO:157), **FIG. 159** (SEQ ID NO:159), **FIG. 161** (SEQ ID NO:161), **FIG. 163** (SEQ ID NO:163), **FIG. 165** (SEQ ID NO:165), **FIG. 167** (SEQ ID NO:167), **FIG. 169** (SEQ ID NO:169), **FIG. 171** (SEQ ID NO:171), **FIG. 173** (SEQ ID NO:173), **FIG. 175** (SEQ ID NO:175), **FIG. 177** (SEQ ID NO:177), **FIG. 179** (SEQ ID NO:179), **FIG. 181** (SEQ ID NO:181), **FIG. 183** (SEQ ID NO:183), **FIG. 185** (SEQ ID NO:185), **FIG. 187** (SEQ ID NO:187), **FIG. 189** (SEQ ID NO:189), **FIG. 191** (SEQ ID NO:191), **FIG. 193** (SEQ ID NO:193), **FIG. 195** (SEQ ID NO:195), **FIG. 197** (SEQ ID NO:197), **FIG. 199** (SEQ ID NO:199), **FIG. 201** (SEQ ID NO:201), **FIG. 203** (SEQ ID NO:203), **FIG. 205** (SEQ ID NO:205), **FIG. 207** (SEQ ID NO:207), **FIG. 209** (SEQ ID NO:209), **FIG. 211** (SEQ ID NO:211), **FIG. 213** (SEQ ID NO:213), **FIG. 215** (SEQ ID NO:215), **FIG. 217** (SEQ ID NO:217), **FIG. 219** (SEQ ID NO:219), **FIG. 221** (SEQ ID NO:221), **FIG. 223** (SEQ ID NO:223), **FIG. 225** (SEQ ID NO:225), **FIG. 227** (SEQ ID NO:227), **FIG. 229** (SEQ ID NO:229), **FIG. 231** (SEQ ID NO:231), **FIG. 233** (SEQ ID NO:233), **FIG. 235** (SEQ ID NO:235), **FIG. 237** (SEQ ID NO:237), **FIG. 239** (SEQ ID NO:239), **FIG. 241** (SEQ ID NO:241), and **FIG. 243** (SEQ ID NO:243).

4. Isolated nucleic acid having at least 80% nucleic acid sequence identity to the full-length coding sequence of the DNA deposited under any ATCC accession number shown in Table 7.

5. A vector comprising the nucleic acid of claim 1.

6. A host cell comprising the vector of claim 5.

7. The host cell of claim 6, wherein said cell is a CHO cell.

8. The host cell of claim 6, wherein said cell is an *E. coli*.

9. The host cell of claim 6, wherein said cell is a yeast cell.

10. A process for producing a PRO polypeptide comprising culturing the host cell of claim 6 under conditions suitable for expression of said PRO polypeptide and recovering said PRO polypeptide from the cell culture.

11. An isolated polypeptide having at least 80% amino acid sequence identity to an amino acid sequence selected from the group consisting of the amino acid sequence shown in **FIG. 2** (SEQ ID NO:2), **FIG. 4** (SEQ ID NO:4), **FIG. 6** (SEQ ID NO:6), **FIG. 8** (SEQ ID NO:8), **FIG. 10** (SEQ ID NO:10), **FIG. 12** (SEQ ID NO:12), **FIG. 14** (SEQ ID NO:14), **FIG. 16** (SEQ ID NO:16), **FIG. 18** (SEQ ID NO:18), **FIG. 20** (SEQ ID NO:20), **FIG. 22** (SEQ ID NO:22), **FIG. 24** (SEQ ID NO:24), **FIG. 26** (SEQ ID NO:26), **FIG. 28** (SEQ ID NO:28), **FIG. 30** (SEQ ID NO:30), **FIG. 32** (SEQ ID NO:32), **FIG. 34** (SEQ ID NO:34), **FIG. 36** (SEQ ID NO:36), **FIG. 38** (SEQ ID

NO:38), **FIG. 40** (SEQ ID NO:40), **FIG. 42** (SEQ ID NO:42), **FIG. 44** (SEQ ID NO:44), **FIG. 46** (SEQ ID NO:46), **FIG. 48** (SEQ ID NO:48), **FIG. 50** (SEQ ID NO:50), **FIG. 52** (SEQ ID NO:52), **FIG. 54** (SEQ ID NO:54), **FIG. 56** (SEQ ID NO:56), **FIG. 58** (SEQ ID NO:58), **FIG. 60** (SEQ ID NO:60), **FIG. 62** (SEQ ID NO:62), **FIG. 64** (SEQ ID NO:64), **FIG. 66** (SEQ ID NO:66), **FIG. 68** (SEQ ID NO:68), **FIG. 70** (SEQ ID NO:70), **FIG. 72** (SEQ ID NO:72), **FIG. 74** (SEQ ID NO:74), **FIG. 76** (SEQ ID NO:76), **FIG. 78** (SEQ ID NO:78), **FIG. 80** (SEQ ID NO:80), **FIG. 82** (SEQ ID NO:82), **FIG. 84** (SEQ ID NO:84), **FIG. 86** (SEQ ID NO:86), **FIG. 88** (SEQ ID NO:88), **FIG. 90** (SEQ ID NO:90), **FIG. 92** (SEQ ID NO:92), **FIG. 94** (SEQ ID NO:94), **FIG. 96** (SEQ ID NO:96), **FIG. 98** (SEQ ID NO:98), **FIG. 100** (SEQ ID NO:100), **FIG. 102** (SEQ ID NO:102), **FIG. 104** (SEQ ID NO:104), **FIG. 106** (SEQ ID NO:106), **FIG. 108** (SEQ ID NO:108), **FIG. 110** (SEQ ID NO:110), **FIG. 112** (SEQ ID NO:112), **FIG. 114** (SEQ ID NO:114), **FIG. 116** (SEQ ID NO:116), **FIG. 118** (SEQ ID NO:118), **FIG. 120** (SEQ ID NO:120), **FIG. 122** (SEQ ID NO:122), **FIG. 124** (SEQ ID NO:124), **FIG. 126** (SEQ ID NO:126), **FIG. 128** (SEQ ID NO:128), **FIG. 130** (SEQ ID NO:130), **FIG. 132** (SEQ ID NO:132), **FIG. 134** (SEQ ID NO:134), **FIG. 136** (SEQ ID NO:136), **FIG. 138** (SEQ ID NO:138), **FIG. 140** (SEQ ID NO:140), **FIG. 142** (SEQ ID NO:142), **FIG. 144** (SEQ ID NO:144), **FIG. 146** (SEQ ID NO:146), **FIG. 148** (SEQ ID NO:148), **FIG. 150** (SEQ ID NO:150), **FIG. 152** (SEQ ID NO:152), **FIG. 154** (SEQ ID NO:154), **FIG. 156** (SEQ ID NO:156), **FIG. 158** (SEQ ID NO:158), **FIG. 160** (SEQ ID NO:160), **FIG. 162** (SEQ ID NO:162), **FIG. 164** (SEQ ID NO:164), **FIG. 166** (SEQ ID NO:166), **FIG. 168** (SEQ ID NO:168), **FIG. 170** (SEQ ID NO:170), **FIG. 172** (SEQ ID NO:172), **FIG. 174** (SEQ ID NO:174), **FIG. 176** (SEQ ID NO:176), **FIG. 178** (SEQ ID NO:178), **FIG. 180** (SEQ ID NO:180), **FIG. 182** (SEQ ID NO:182), **FIG. 184** (SEQ ID NO:184), **FIG. 186** (SEQ ID NO:186), **FIG. 188** (SEQ ID NO:188), **FIG. 190** (SEQ ID NO:190), **FIG. 192** (SEQ ID NO:192), **FIG. 194** (SEQ ID NO:194), **FIG. 196** (SEQ ID NO:196), **FIG. 198** (SEQ ID NO:198), **FIG. 200** (SEQ ID NO:200), **FIG. 202** (SEQ ID NO:202), **FIG. 204** (SEQ ID NO:204), **FIG. 206** (SEQ ID NO:206), **FIG. 208** (SEQ ID NO:208), **FIG. 210** (SEQ ID NO:210), **FIG. 212** (SEQ ID NO:212), **FIG. 214** (SEQ ID NO:214), **FIG. 216** (SEQ ID NO:216), **FIG. 218** (SEQ ID NO:218), **FIG. 220** (SEQ ID NO:220), **FIG. 222** (SEQ ID NO:222), **FIG. 224** (SEQ ID NO:224), **FIG. 226** (SEQ ID NO:226), **FIG. 228** (SEQ ID NO:228), **FIG. 230** (SEQ ID NO:230), **FIG. 232** (SEQ ID NO:232), **FIG. 234** (SEQ ID NO:234), **FIG. 236** (SEQ ID NO:236), **FIG. 238** (SEQ ID NO:238), **FIG. 240** (SEQ ID NO:240), **FIG. 242** (SEQ ID NO:242), and **FIG. 244** (SEQ ID NO:244).

12. An isolated polypeptide having at least 80% amino acid sequence identity to an amino acid sequence encoded by the full-length coding sequence of the DNA deposited under any ATCC accession number shown in Table 7.

13. A chimeric molecule comprising a polypeptide according to claim 11 fused to a heterologous amino acid sequence.

14. The chimeric molecule of claim 13, wherein said heterologous amino acid sequence is an epitope tag sequence.

15. The chimeric molecule of claim 13, wherein said heterologous amino acid sequence is a Fe region of an immunoglobulin.

16. An antibody which specifically binds to a polypeptide according to claim 11.

17. The antibody of claim 16, wherein said antibody is a monoclonal antibody, a humanized antibody or a single-chain antibody.

18. Isolated nucleic acid having at least 80% nucleic acid sequence identity to:

- (a) a nucleotide sequence encoding the polypeptide shown in **FIG. 2** (SEQ ID NO:2), **FIG. 4** (SEQ ID NO:4), **FIG. 6** (SEQ ID NO:6), **FIG. 8** (SEQ ID NO:8), **FIG. 10** (SEQ ID NO:10), **FIG. 12** (SEQ ID NO:12), **FIG. 14** (SEQ ID NO:14), **FIG. 16** (SEQ ID NO:16), **FIG. 18** (SEQ ID NO:18), **FIG. 20** (SEQ ID NO:20), **FIG. 22** (SEQ ID NO:22), **FIG. 24** (SEQ ID NO:24), **FIG. 26** (SEQ ID NO:26), **FIG. 28** (SEQ ID NO:28), **FIG. 30** (SEQ ID NO:30), **FIG. 32** (SEQ ID NO:32), **FIG. 34** (SEQ ID NO:34), **FIG. 36** (SEQ ID NO:36), **FIG. 38** (SEQ ID NO:38), **FIG. 40** (SEQ ID NO:40), **FIG. 42** (SEQ ID NO:42), **FIG. 44** (SEQ ID NO:44), **FIG. 46** (SEQ ID NO:46), **FIG. 48** (SEQ ID NO:48), **FIG. 50** (SEQ ID NO:50), **FIG. 52** (SEQ ID NO:52), **FIG. 54** (SEQ ID NO:54), **FIG. 56** (SEQ ID NO:56), **FIG. 58** (SEQ ID NO:58), **FIG. 60** (SEQ ID NO:60), **FIG. 62** (SEQ ID NO:62), **FIG. 64** (SEQ ID NO:64), **FIG. 66** (SEQ ID NO:66), **FIG. 68** (SEQ ID NO:68), **FIG. 70** (SEQ ID NO:70), **FIG. 72** (SEQ ID NO:72), **FIG. 74** (SEQ ID NO:74), **FIG. 76** (SEQ ID NO:76), **FIG. 78** (SEQ ID NO:78), **FIG. 80** (SEQ ID NO:80), **FIG. 82** (SEQ ID NO:82), **FIG. 84** (SEQ ID NO:84), **FIG. 86** (SEQ ID NO:86), **FIG. 88** (SEQ ID NO:88), **FIG. 90** (SEQ ID NO:90), **FIG. 92** (SEQ ID NO:92), **FIG. 94** (SEQ ID NO:94), **FIG. 96** (SEQ ID NO:96), **FIG. 98** (SEQ ID NO:98), **FIG. 100** (SEQ ID NO:100), **FIG. 102** (SEQ ID NO:102), **FIG. 104** (SEQ ID NO:104), **FIG. 106** (SEQ ID NO:106), **FIG. 108** (SEQ ID NO:108), **FIG. 110** (SEQ ID NO:110), **FIG. 112** (SEQ ID NO:112), **FIG. 114** (SEQ ID NO:114), **FIG. 116** (SEQ ID NO:116), **FIG. 118** (SEQ ID NO:118), **FIG. 120** (SEQ ID NO:120), **FIG. 122** (SEQ ID NO:122), **FIG. 124** (SEQ ID NO:124), **FIG. 126** (SEQ ID NO:126), **FIG. 128** (SEQ ID NO:128), **FIG. 130** (SEQ ID NO:130), **FIG. 132** (SEQ ID NO:132), **FIG. 134** (SEQ ID NO:134), **FIG. 136** (SEQ ID NO:136), **FIG. 138** (SEQ ID NO:138), **FIG. 140** (SEQ ID NO:140), **FIG. 142** (SEQ ID NO:142), **FIG. 144** (SEQ ID NO:144), **FIG. 146** (SEQ ID NO:146), **FIG. 148** (SEQ ID NO:148), **FIG. 150** (SEQ ID NO:150), **FIG. 152** (SEQ ID NO:152), **FIG. 154** (SEQ ID NO:154), **FIG. 156** (SEQ ID NO:156), **FIG. 158** (SEQ ID NO:158), **FIG. 160** (SEQ ID NO:160), **FIG. 162** (SEQ ID NO:162), **FIG. 164** (SEQ ID NO:164), **FIG. 166** (SEQ ID NO:166), **FIG. 168** (SEQ ID NO:168), **FIG. 170** (SEQ ID NO:170), **FIG. 172** (SEQ ID NO:172), **FIG. 174** (SEQ ID NO:174), **FIG. 176** (SEQ ID NO:176), **FIG. 178** (SEQ ID NO:178), **FIG. 180** (SEQ ID NO:180), **FIG. 182** (SEQ ID NO:182), **FIG. 184** (SEQ ID NO:184), **FIG. 186** (SEQ ID NO:186), **FIG. 188** (SEQ ID NO:188), **FIG. 190** (SEQ ID NO:190), **FIG. 192** (SEQ ID NO:192), **FIG. 194** (SEQ ID NO:194), **FIG. 196** (SEQ ID NO:196), **FIG. 198** (SEQ ID NO:198), **FIG. 200** (SEQ ID NO:200), **FIG. 202**

(SEQ ID NO:202), **FIG. 204** (SEQ ID NO:204), **FIG. 206** (SEQ ID NO:206), **FIG. 208** (SEQ ID NO:208), **FIG. 210** (SEQ ID NO:210), **FIG. 212** (SEQ ID NO:212), **FIG. 214** (SEQ ID NO:214), **FIG. 216** (SEQ ID NO:216), **FIG. 218** (SEQ ID NO:218), **FIG. 220** (SEQ ID NO:220), **FIG. 222** (SEQ ID NO:222), **FIG. 224** (SEQ ID NO:224), **FIG. 226** (SEQ ID NO:226), **FIG. 228** (SEQ ID NO:228), **FIG. 230** (SEQ ID NO:230), **FIG. 232** (SEQ ID NO:232), **FIG. 234** (SEQ ID NO:234), **FIG. 236** (SEQ ID NO:236), **FIG. 238** (SEQ ID NO:238), **FIG. 240** (SEQ ID NO:240), **FIG. 242** (SEQ ID NO:242), or **FIG. 244** (SEQ ID NO:244), lacking its associated signal peptide;

- (b) a nucleotide sequence encoding an extracellular domain of the polypeptide shown in **FIG. 2** (SEQ ID NO:2), **FIG. 4** (SEQ ID NO:4), **FIG. 6** (SEQ ID NO:6), **FIG. 8** (SEQ ID NO:8), **FIG. 10** (SEQ ID NO:10), **FIG. 12** (SEQ ID NO:12), **FIG. 14** (SEQ ID NO:14), **FIG. 16** (SEQ ID NO:16), **FIG. 18** (SEQ ID NO:18), **FIG. 20** (SEQ ID NO:20), **FIG. 22** (SEQ ID NO:22), **FIG. 24** (SEQ ID NO:24), **FIG. 26** (SEQ ID NO:26), **FIG. 28** (SEQ ID NO:28), **FIG. 30** (SEQ ID NO:30), **FIG. 32** (SEQ ID NO:32), **FIG. 34** (SEQ ID NO:34), **FIG. 36** (SEQ ID NO:36), **FIG. 38** (SEQ ID NO:38), **FIG. 40** (SEQ ID NO:40), **FIG. 42** (SEQ ID NO:42), **FIG. 44** (SEQ ID NO:44), **FIG. 46** (SEQ ID NO:46), **FIG. 48** (SEQ ID NO:48), **FIG. 50** (SEQ ID NO:50), **FIG. 52** (SEQ ID NO:52), **FIG. 54** (SEQ ID NO:54), **FIG. 56** (SEQ ID NO:56), **FIG. 58** (SEQ ID NO:58), **FIG. 60** (SEQ ID NO:60), **FIG. 62** (SEQ ID NO:62), **FIG. 64** (SEQ ID NO:64), **FIG. 66** (SEQ ID NO:66), **FIG. 68** (SEQ ID NO:68), **FIG. 70** (SEQ ID NO:70), **FIG. 72** (SEQ ID NO:72), **FIG. 74** (SEQ ID NO:74), **FIG. 76** (SEQ ID NO:76), **FIG. 78** (SEQ ID NO:78), **FIG. 80** (SEQ ID NO:80), **FIG. 82** (SEQ ID NO:82), **FIG. 84** (SEQ ID NO:84), **FIG. 86** (SEQ ID NO:86), **FIG. 88** (SEQ ID NO:88), **FIG. 90** (SEQ ID NO:90), **FIG. 92** (SEQ ID NO:92), **FIG. 94** (SEQ ID NO:94), **FIG. 96** (SEQ ID NO:96), **FIG. 98** (SEQ ID NO:98), **FIG. 100** (SEQ ID NO:100), **FIG. 102** (SEQ ID NO:102), **FIG. 104** (SEQ ID NO:104), **FIG. 106** (SEQ ID NO:106), **FIG. 108** (SEQ ID NO:108), **FIG. 110** (SEQ ID NO:110), **FIG. 112** (SEQ ID NO:112), **FIG. 114** (SEQ ID NO:114), **FIG. 116** (SEQ ID NO:116), **FIG. 118** (SEQ ID NO:118), **FIG. 120** (SEQ ID NO:120), **FIG. 122** (SEQ ID NO:122), **FIG. 124** (SEQ ID NO:124), **FIG. 126** (SEQ ID NO:126), **FIG. 128** (SEQ ID NO:128), **FIG. 130** (SEQ ID NO:130), **FIG. 132** (SEQ ID NO:132), **FIG. 134** (SEQ ID NO:134), **FIG. 136** (SEQ ID NO:136), **FIG. 138** (SEQ ID NO:138), **FIG. 140** (SEQ ID NO:140), **FIG. 142** (SEQ ID NO:142), **FIG. 144** (SEQ ID NO:144), **FIG. 146** (SEQ ID NO:146), **FIG. 148** (SEQ ID NO:148), **FIG. 150** (SEQ ID NO:150), **FIG. 152** (SEQ ID NO:152), **FIG. 154** (SEQ ID NO:154), **FIG. 156** (SEQ ID NO:156), **FIG. 158** (SEQ ID NO:158), **FIG. 160** (SEQ ID NO:160), **FIG. 162** (SEQ ID NO:162), **FIG. 164** (SEQ ID NO:164), **FIG. 166** (SEQ ID NO:166), **FIG. 168** (SEQ ID NO:168), **FIG. 170** (SEQ ID NO:170), **FIG. 172** (SEQ ID NO:172), **FIG. 174** (SEQ ID NO:174), **FIG. 176** (SEQ ID NO:176), **FIG. 178** (SEQ ID NO:178), **FIG. 180** (SEQ ID NO:180), **FIG. 182** (SEQ ID NO:182), **FIG. 184** (SEQ ID NO:184), **FIG. 186** (SEQ ID NO:186), **FIG. 188** (SEQ ID

NO:188), **FIG. 190** (SEQ ID NO:190), **FIG. 192** (SEQ ID NO:192), **FIG. 194** (SEQ ID NO:194), **FIG. 196** (SEQ ID NO:196), **FIG. 198** (SEQ ID NO:198), **FIG. 200** (SEQ ID NO:200), **FIG. 202** (SEQ ID NO:202), **FIG. 204** (SEQ ID NO:204), **FIG. 206** (SEQ ID NO:206), **FIG. 208** (SEQ ID NO:208), **FIG. 210** (SEQ ID NO:210), **FIG. 212** (SEQ ID NO:212), **FIG. 214** (SEQ ID NO:214), **FIG. 216** (SEQ ID NO:216), **FIG. 218** (SEQ ID NO:218), **FIG. 220** (SEQ ID NO:220), **FIG. 222** (SEQ ID NO:222), **FIG. 224** (SEQ ID NO:224), **FIG. 226** (SEQ ID NO:226), **FIG. 228** (SEQ ID NO:228), **FIG. 230** (SEQ ID NO:230), **FIG. 232** (SEQ ID NO:232), **FIG. 234** (SEQ ID NO:234), **FIG. 236** (SEQ ID NO:236), **FIG. 238** (SEQ ID NO:238), **FIG. 240** (SEQ ID NO:240), **FIG. 242** (SEQ ID NO:242), or **FIG. 244** (SEQ ID NO:244), with its associated signal peptide; or

- (c) a nucleotide sequence encoding an extracellular domain of the polypeptide shown in **FIG. 2** (SEQ ID NO:2), **FIG. 4** (SEQ ID NO:4), **FIG. 6** (SEQ ID NO:6), **FIG. 8** (SEQ ID NO:8), **FIG. 10** (SEQ ID NO:10), **FIG. 12** (SEQ ID NO:12), **FIG. 14** (SEQ ID NO:14), **FIG. 16** (SEQ ID NO:16), **FIG. 18** (SEQ ID NO:18), **FIG. 20** (SEQ ID NO:20), **FIG. 22** (SEQ ID NO:22), **FIG. 24** (SEQ ID NO:24), **FIG. 26** (SEQ ID NO:26), **FIG. 28** (SEQ ID NO:28), **FIG. 30** (SEQ ID NO:30), **FIG. 32** (SEQ ID NO:32), **FIG. 34** (SEQ ID NO:34), **FIG. 36** (SEQ ID NO:36), **FIG. 38** (SEQ ID NO:38), **FIG. 40** (SEQ ID NO:40), **FIG. 42** (SEQ ID NO:42), **FIG. 44** (SEQ ID NO:44), **FIG. 46** (SEQ ID NO:46), **FIG. 48** (SEQ ID NO:48), **FIG. 50** (SEQ ID NO:50), **FIG. 52** (SEQ ID NO:52), **FIG. 54** (SEQ ID NO:54), **FIG. 56** (SEQ ID NO:56), **FIG. 58** (SEQ ID NO:58), **FIG. 60** (SEQ ID NO:60), **FIG. 62** (SEQ ID NO:62), **FIG. 64** (SEQ ID NO:64), **FIG. 66** (SEQ ID NO:66), **FIG. 68** (SEQ ID NO:68), **FIG. 70** (SEQ ID NO:70), **FIG. 72** (SEQ ID NO:72), **FIG. 74** (SEQ ID NO:74), **FIG. 76** (SEQ ID NO:76), **FIG. 78** (SEQ ID NO:78), **FIG. 80** (SEQ ID NO:80), **FIG. 82** (SEQ ID NO:82), **FIG. 84** (SEQ ID NO:84), **FIG. 86** (SEQ ID NO:86), **FIG. 88** (SEQ ID NO:88), **FIG. 90** (SEQ ID NO:90), **FIG. 92** (SEQ ID NO:92), **FIG. 94** (SEQ ID NO:94), **FIG. 96** (SEQ ID NO:96), **FIG. 98** (SEQ ID NO:98), **FIG. 100** (SEQ ID NO:100), **FIG. 102** (SEQ ID NO:102), **FIG. 104** (SEQ ID NO:104), **FIG. 106** (SEQ ID NO:106), **FIG. 108** (SEQ ID NO:108), **FIG. 110** (SEQ ID NO:110), **FIG. 112** (SEQ ID NO:112), **FIG. 114** (SEQ ID NO:114), **FIG. 116** (SEQ ID NO:116), **FIG. 118** (SEQ ID NO:118), **FIG. 120** (SEQ ID NO:120), **FIG. 122** (SEQ ID NO:122), **FIG. 124** (SEQ ID NO:124), **FIG. 126** (SEQ ID NO:126), **FIG. 128** (SEQ ID NO:128), **FIG. 130** (SEQ ID NO:130), **FIG. 132** (SEQ ID NO:132), **FIG. 134** (SEQ ID NO:134), **FIG. 136** (SEQ ID NO:136), **FIG. 138** (SEQ ID NO:138), **FIG. 140** (SEQ ID NO:140), **FIG. 142** (SEQ ID NO:142), **FIG. 144** (SEQ ID NO:144), **FIG. 146** (SEQ ID NO:146), **FIG. 148** (SEQ ID NO:148), **FIG. 150** (SEQ ID NO:150), **FIG. 152** (SEQ ID NO:152), **FIG. 154** (SEQ ID NO:154), **FIG. 156** (SEQ ID NO:156), **FIG. 158** (SEQ ID NO:158), **FIG. 160** (SEQ ID NO:160), **FIG. 162** (SEQ ID NO:162), **FIG. 164** (SEQ ID NO:164), **FIG. 166** (SEQ ID NO:166), **FIG. 168** (SEQ ID NO:168), **FIG. 170** (SEQ ID NO:170), **FIG. 172** (SEQ ID NO:172), **FIG. 174** (SEQ

ID NO:174), **FIG. 176** (SEQ ID NO:176), **FIG. 178** (SEQ ID NO:178), **FIG. 180** (SEQ ID NO:180), **FIG. 182** (SEQ ID NO:182), **FIG. 184** (SEQ ID NO:184), **FIG. 186** (SEQ ID NO:186), **FIG. 188** (SEQ ID NO:188), **FIG. 190** (SEQ ID NO:190), **FIG. 192** (SEQ ID NO:192), **FIG. 194** (SEQ ID NO:194), **FIG. 196** (SEQ ID NO:196), **FIG. 198** (SEQ ID NO:198), **FIG. 200** (SEQ ID NO:200), **FIG. 202** (SEQ ID NO:202), **FIG. 204** (SEQ ID NO:204), **FIG. 206** (SEQ ID NO:206), **FIG. 208** (SEQ ID NO:208), **FIG. 210** (SEQ ID NO:210), **FIG. 212** (SEQ ID NO:212), **FIG. 214** (SEQ ID NO:214), **FIG. 216** (SEQ ID NO:216), **FIG. 218** (SEQ ID NO:218), **FIG. 220** (SEQ ID NO:220), **FIG. 222** (SEQ ID NO:222), **FIG. 224** (SEQ ID NO:224), **FIG. 226** (SEQ ID NO:226), **FIG. 228** (SEQ ID NO:228), **FIG. 230** (SEQ ID NO:230), **FIG. 232** (SEQ ID NO:232), **FIG. 234** (SEQ ID NO:234), **FIG. 236** (SEQ ID NO:236), **FIG. 238** (SEQ ID NO:238), **FIG. 240** (SEQ ID NO:240), **FIG. 242** (SEQ ID NO:242), or **FIG. 244** (SEQ ID NO:244), lacking its associated signal peptide.

19. An isolated polypeptide having at least 80% amino acid sequence identity to:

- (a) an amino acid sequence of the polypeptide shown in **FIG. 2** (SEQ ID NO:2), **FIG. 4** (SEQ ID NO:4), **FIG. 6** (SEQ ID NO:6), **FIG. 8** (SEQ ID NO:8), **FIG. 10** (SEQ ID NO:10), **FIG. 12** (SEQ ID NO:12), **FIG. 14** (SEQ ID NO:14), **FIG. 16** (SEQ ID NO:16), **FIG. 18** (SEQ ID NO:18), **FIG. 20** (SEQ ID NO:20), **FIG. 22** (SEQ ID NO:22), **FIG. 24** (SEQ ID NO:24), **FIG. 26** (SEQ ID NO:26), **FIG. 28** (SEQ ID NO:28), **FIG. 30** (SEQ ID NO:30), **FIG. 32** (SEQ ID NO:32), **FIG. 34** (SEQ ID NO:34), **FIG. 36** (SEQ ID NO:36), **FIG. 38** (SEQ ID NO:38), **FIG. 40** (SEQ ID NO:40), **FIG. 42** (SEQ ID NO:42), **FIG. 44** (SEQ ID NO:44), **FIG. 46** (SEQ ID NO:46), **FIG. 48** (SEQ ID NO:48), **FIG. 50** (SEQ ID NO:50), **FIG. 52** (SEQ ID NO:52), **FIG. 54** (SEQ ID NO:54), **FIG. 56** (SEQ ID NO:56), **FIG. 58** (SEQ ID NO:58), **FIG. 60** (SEQ ID NO:60), **FIG. 62** (SEQ ID NO:62), **FIG. 64** (SEQ ID NO:64), **FIG. 66** (SEQ ID NO:66), **FIG. 68** (SEQ ID NO:68), **FIG. 70** (SEQ ID NO:70), **FIG. 72** (SEQ ID NO:72), **FIG. 74** (SEQ ID NO:74), **FIG. 76** (SEQ ID NO:76), **FIG. 78** (SEQ ID NO:78), **FIG. 80** (SEQ ID NO:80), **FIG. 82** (SEQ ID NO:82), **FIG. 84** (SEQ ID NO:84), **FIG. 86** (SEQ ID NO:86), **FIG. 88** (SEQ ID NO:88), **FIG. 90** (SEQ ID NO:90), **FIG. 92** (SEQ ID NO:92), **FIG. 94** (SEQ ID NO:94), **FIG. 96** (SEQ ID NO:96), **FIG. 98** (SEQ ID NO:98), **FIG. 100** (SEQ ID NO:100), **FIG. 102** (SEQ ID NO:102), **FIG. 104** (SEQ ID NO:104), **FIG. 106** (SEQ ID NO:106), **FIG. 108** (SEQ ID NO:108), **FIG. 110** (SEQ ID NO:110), **FIG. 112** (SEQ ID NO:112), **FIG. 114** (SEQ ID NO:114), **FIG. 116** (SEQ ID NO:116), **FIG. 118** (SEQ ID NO:118), **FIG. 120** (SEQ ID NO:120), **FIG. 122** (SEQ ID NO:122), **FIG. 124** (SEQ ID NO:124), **FIG. 126** (SEQ ID NO:126), **FIG. 128** (SEQ ID NO:128), **FIG. 130** (SEQ ID NO:130), **FIG. 132** (SEQ ID NO:132), **FIG. 134** (SEQ ID NO:134), **FIG. 136** (SEQ ID NO:136), **FIG. 138** (SEQ ID NO:138), **FIG. 140** (SEQ ID NO:140), **FIG. 142** (SEQ ID NO:142), **FIG. 144** (SEQ ID NO:144), **FIG. 146** (SEQ ID NO:146), **FIG. 148** (SEQ ID NO:148), **FIG. 150** (SEQ ID NO:150), **FIG. 152** (SEQ ID NO:152), **FIG. 154** (SEQ ID NO:154), **FIG.**

ID NO:132), **FIG. 134** (SEQ ID NO:134), **FIG. 136** (SEQ ID NO:136), **FIG. 138** (SEQ ID NO:138), **FIG. 140** (SEQ ID NO:140), **FIG. 142** (SEQ ID NO:142), **FIG. 144** (SEQ ID NO:144), **FIG. 146** (SEQ ID NO:146), **FIG. 148** (SEQ ID NO:148), **FIG. 150** (SEQ ID NO:150), **FIG. 152** (SEQ ID NO:152), **FIG. 154** (SEQ ID NO:154), **FIG. 156** (SEQ ID NO:156), **FIG. 158** (SEQ ID NO:158), **FIG. 160** (SEQ ID NO:160), **FIG. 162** (SEQ ID NO:162), **FIG. 164** (SEQ ID NO:164), **FIG. 166** (SEQ ID NO:166), **FIG. 168** (SEQ ID NO:168), **FIG. 170** (SEQ ID NO:170), **FIG. 172** (SEQ ID NO:172), **FIG. 174** (SEQ ID NO:174), **FIG. 176** (SEQ ID NO:176), **FIG. 178** (SEQ ID NO:178), **FIG. 180** (SEQ ID NO:180), **FIG. 182** (SEQ ID NO:182), **FIG. 184** (SEQ ID NO:184), **FIG. 186** (SEQ ID NO:186), **FIG. 188** (SEQ ID NO:188), **FIG. 190** (SEQ ID NO:190), **FIG. 192** (SEQ ID NO:192), **FIG. 194** (SEQ ID NO:194), **FIG. 196** (SEQ ID NO:196), **FIG. 198** (SEQ ID NO:198), **FIG. 200** (SEQ ID NO:200), **FIG. 202** (SEQ ID NO:202), **FIG. 204** (SEQ ID NO:204), **FIG. 206** (SEQ ID NO:206), **FIG. 208** (SEQ ID NO:208), **FIG. 210** (SEQ ID NO:210), **FIG. 212** (SEQ ID NO:212), **FIG. 214** (SEQ ID NO:214), **FIG. 216** (SEQ ID NO:216), **FIG. 218** (SEQ ID NO:218), **FIG. 220** (SEQ ID NO:220), **FIG. 222** (SEQ ID NO:222), **FIG. 224** (SEQ ID NO:224), **FIG. 226** (SEQ ID NO:226), **FIG. 228** (SEQ ID NO:228), **FIG. 230** (SEQ ID NO:230), **FIG. 232** (SEQ ID NO:232), **FIG. 234** (SEQ ID NO:234), **FIG. 236** (SEQ ID NO:236), **FIG. 238** (SEQ ID NO:238), **FIG. 240** (SEQ ID NO:240), **FIG. 242** (SEQ ID NO:242), or **FIG. 244** (SEQ ID NO:244), lacking its associated signal peptide.

20. A method for stimulating the proliferation of or gene expression in pericyte cells, said method comprising contacting said cells with a PRO982, PRO1160, PRO1187, or PRO1329 polypeptide, wherein the proliferation of or gene expression in said cells is stimulated.

21. A method for stimulating the proliferation or differentiation of chondrocyte cells, said method comprising contacting said cells with a PRO357, PRO229, PRO1272 or PRO4405 polypeptide, wherein the proliferation or differentiation of said cells is stimulated.

22. A method for stimulating the release of TNF- α from human blood, said method comprising contacting said blood with a PRO231, PRO357, PRO725, PRO1155, PRO1306 or PRO1419 polypeptide, wherein the release of TNF- α from said blood is stimulated.

23. A method for stimulating the proliferation of normal human dermal fibroblast cells, said method comprising contacting said cells with a PRO982, PRO357, PRO725, PRO1306, PRO1419, PRO214, PRO247, PRO337, PRO526, PRO363, PRO531, PRO1083, PRO840, PRO1080, PRO1478, PRO1134, PRO826, PRO1005, PRO809, PRO1071, PRO1411, PRO1309, PRO1025, PRO1181, PRO1126, PRO1186, PRO1192, PRO1244, PRO1274, PRO1412, PRO1286, PRO1330, PRO1347, PRO1305, PRO1273, PRO1279, PRO1340, PRO1338, PRO1343, PRO1376, PRO1387, PRO1409, PRO1474, PRO1917, PRO1760, PRO1567, PRO1887, PRO1928, PRO4341, PRO1801, PRO4333, PRO3543, PRO3444, PRO4322, PRO9940, PRO6079, PRO9836 or PRO10096 polypeptide, wherein the proliferation of said cells is stimulated.

24. A method for inhibiting the proliferation of normal human dermal fibroblast cells, said method comprising contacting said cells with a PRO181, PRO229, PRO788, PRO1194, PRO1272, PRO1488, PRO4302, PRO4408, PRO5723, PRO5725, PRO7154, and PRO7425 polypeptide, wherein the proliferation of said cells is inhibited.

25. A method for detecting the presence of tumor in an mammal, said method comprising comparing the level of expression of any PRO polypeptide shown in Table 8 in (a) a test sample of cells taken from said mammal and (b) a control sample of normal cells of the same cell type, wherein a higher level of expression of said PRO polypeptide in the test sample as compared to the control sample is indicative of the presence of tumor in said mammal.

26. The method of claim 25, wherein said tumor is lung tumor, colon tumor, breast tumor, prostate tumor, rectal tumor, or liver tumor.

27. An oligonucleotide probe derived from any of the nucleotide sequences shown in the accompanying figures.

* * * * *