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(54) Titre : POLYPEPTIDES SECRETES ET TRANSMEMBRANAIRES ET ACIDES NUCLEIQUES CODANT CES POLYPEPTIDES

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

MSTMFADTLLIVFISVCTALLAEGITWVLVYRTDKYKRLKAEVEKQSKKLEKKKETITESAGR

QQKKKIERQEEKLKNNNRDLSMVRMKSMFAIGFCFTALMGMFNSIFDGRVVAKLPFTPLSYIQ

GLSHRNLLGDDTTDCSFIFLYILCTMSIRQNIQKILGLAPSRAATKQAGGFLGPPPPSGKFS

Important features:

Signal peptide:

amino acids 1-22

N-myristoylation sites.

amino acids 103-109, 163-169

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 53-57

(57) Abrégé/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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(54) Title: SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME

MSTMFADTLLIVFISVCTALLAEGITWVLVYRTDKYKRLKAEVEKQSKKLEKKKETITESAGR
QQKKKIERQEEKLKNNNRDLSMVRMKSMFAIGFCFTALMGMFNSIFDGRVVAKLPFTPLSYIQ
GLSHRNLLGDDTTDCSFIFLYILCTMSIRQNIQKILGLAPSRAATKQAGGFLGPPPPSGKFS

Important features:

Signal peptide:

amino acids 1-22

N-myristoylation sites.

amino acids 103-109, 163-169

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 53-57

(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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SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME

FIELD OF THE INVENTION

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

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.

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. Patent No. 5,536,637)].

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 adhesin 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.

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

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

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

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).

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).

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).

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.

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.

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

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.

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.

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.

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.

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.

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.

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.

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.

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.

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.

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.

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.

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

Figure 1 shows a nucleotide sequence (SEQ ID NO:1) of a native sequence PRO177 cDNA, wherein SEQ ID NO:1 is a clone designated herein as "DNA16438-1387".

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

Figure 3 shows a nucleotide sequence (SEQ ID NO:3) of a native sequence PRO3574 cDNA, wherein SEQ ID NO:3 is a clone designated herein as "DNA19360-2552".

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

Figure 5 shows a nucleotide sequence (SEQ ID NO:5) of a native sequence PRO1280 cDNA, wherein SEQ ID NO:5 is a clone designated herein as "DNA33455-1548".

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

Figure 7 shows a nucleotide sequence (SEQ ID NO:7) of a native sequence PRO4984 cDNA, wherein SEQ ID NO:7 is a clone designated herein as "DNA37155-2651".

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

Figure 9 shows a nucleotide sequence (SEQ ID NO:9) of a native sequence PRO4988 cDNA, wherein SEQ ID NO:9 is a clone designated herein as "DNA38269-2654".

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

Figure 11 shows a nucleotide sequence (SEQ ID NO:11) of a native sequence PRO305 cDNA, wherein SEQ ID NO:11 is a clone designated herein as "DNA40619-1220".

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

Figure 13 shows a nucleotide sequence (SEQ ID NO:13) of a native sequence PRO1866 cDNA, wherein SEQ ID NO:13 is a clone designated herein as "DNA44174-2513".

Figure 14 shows the amino acid sequence (SEQ ID NO:14) derived from the coding sequence of SEQ ID NO:13 shown in Figure 13.

Figure 15 shows a nucleotide sequence (SEQ ID NO:15) of a native sequence PRO4996 cDNA, wherein SEQ ID NO:15 is a clone designated herein as "DNA44675-2662".

Figure 16 shows the amino acid sequence (SEQ ID NO:16) derived from the coding sequence of SEQ ID NO:15 shown in Figure 15.

Figure 17 shows a nucleotide sequence (SEQ ID NO:17) of a native sequence PRO4406 cDNA, wherein SEQ ID NO:17 is a clone designated herein as "DNA45408-2615".

Figure 18 shows the amino acid sequence (SEQ ID NO:18) derived from the coding sequence of SEQ ID NO:17 shown in Figure 17.

Figure 19 shows a nucleotide sequence (SEQ ID NO:19) of a native sequence PRO1120 cDNA, wherein SEQ ID NO:19 is a clone designated herein as "DNA48606-1479".

Figure 20 shows the amino acid sequence (SEQ ID NO:20) derived from the coding sequence of SEQ ID NO:19 shown in Figure 19.

Figure 21 shows a nucleotide sequence (SEQ ID NO:21) of a native sequence PRO4990 cDNA, wherein SEQ ID NO:21 is a clone designated herein as "DNA52753-2656".

Figure 22 shows the amino acid sequence (SEQ ID NO:22) derived from the coding sequence of SEQ ID NO:21 shown in Figure 21.

Figure 23 shows a nucleotide sequence (SEQ ID NO:23) of a native sequence PRO738 cDNA, wherein SEQ ID NO:23 is a clone designated herein as "DNA53915-1258".

Figure 24 shows the amino acid sequence (SEQ ID NO:24) derived from the coding sequence of SEQ ID NO:23 shown in Figure 23.

Figure 25 shows a nucleotide sequence (SEQ ID NO:25) of a native sequence PRO3577 cDNA, wherein SEQ ID NO:25 is a clone designated herein as "DNA53991-2553".

Figure 26 shows the amino acid sequence (SEQ ID NO:26) derived from the coding sequence of SEQ ID NO:25 shown in Figure 25.

Figure 27 shows a nucleotide sequence (SEQ ID NO:27) of a native sequence PRO1879 cDNA, wherein SEQ ID NO:27 is a clone designated herein as "DNA54009-2517".

Figure 28 shows the amino acid sequence (SEQ ID NO:28) derived from the coding sequence of SEQ ID NO:27 shown in Figure 27.

Figure 29 shows a nucleotide sequence (SEQ ID NO:29) of a native sequence PRO1471 cDNA, wherein SEQ ID NO:29 is a clone designated herein as "DNA56055-1643".

Figure 30 shows the amino acid sequence (SEQ ID NO:30) derived from the coding sequence of SEQ ID NO:29 shown in Figure 29.

Figure 31 shows a nucleotide sequence (SEQ ID NO:31) of a native sequence PRO1114 cDNA, wherein SEQ ID NO:31 is a clone designated herein as "DNA57033-1403".

Figure 32 shows the amino acid sequence (SEQ ID NO:32) derived from the coding sequence of SEQ ID NO:31 shown in Figure 31.

Figure 33 shows a nucleotide sequence (SEQ ID NO:33) of a native sequence PRO1076 cDNA, wherein SEQ ID NO:33 is a clone designated herein as "DNA57252-1453".

Figure 34 shows the amino acid sequence (SEQ ID NO:34) derived from the coding sequence of SEQ ID NO:33 shown in Figure 33.

Figure 35 shows a nucleotide sequence (SEQ ID NO:35) of a native sequence PRO1483 cDNA, wherein SEQ ID NO:35 is a clone designated herein as "DNA58799-1652".

Figure 36 shows the amino acid sequence (SEQ ID NO:36) derived from the coding sequence of SEQ ID NO:35 shown in Figure 35.

Figure 37 shows a nucleotide sequence (SEQ ID NO:37) of a native sequence PRO4985 cDNA, wherein SEQ ID NO:37 is a clone designated herein as "DNA59770-2652".

Figure 38 shows the amino acid sequence (SEQ ID NO:38) derived from the coding sequence of SEQ ID NO:37 shown in Figure 37.

Figure 39 shows a nucleotide sequence (SEQ ID NO:39) of a native sequence PRO5000 cDNA, wherein SEQ ID NO:39 is a clone designated herein as "DNA59774-2665".

Figure 40 shows the amino acid sequence (SEQ ID NO:40) derived from the coding sequence of SEQ ID NO:39 shown in Figure 39.

Figure 41 shows a nucleotide sequence (SEQ ID NO:41) of a native sequence PRO1881 cDNA, wherein SEQ ID NO:41 is a clone designated herein as "DNA60281-2518".

Figure 42 shows the amino acid sequence (SEQ ID NO:42) derived from the coding sequence of SEQ ID NO:41 shown in Figure 41.

Figure 43 shows a nucleotide sequence (SEQ ID NO:43) of a native sequence PRO4314 cDNA, wherein SEQ ID NO:43 is a clone designated herein as "DNA60736-2559".

Figure 44 shows the amino acid sequence (SEQ ID NO:44) derived from the coding sequence of SEQ ID NO:43 shown in Figure 43.

Figure 45 shows a nucleotide sequence (SEQ ID NO:45) of a native sequence PRO4987 cDNA, wherein SEQ ID NO:45 is a clone designated herein as "DNA61875-2653".

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

Figure 47 shows a nucleotide sequence (SEQ ID NO:47) of a native sequence PRO4313 cDNA, wherein SEQ ID NO:47 is a clone designated herein as "DNA62312-2558".

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

Figure 49 shows a nucleotide sequence (SEQ ID NO:49) of a native sequence PRO4799 cDNA, wherein SEQ ID NO:49 is a clone designated herein as "DNA62849-1604".

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

Figure 51 shows a nucleotide sequence (SEQ ID NO:51) of a native sequence PRO4995 cDNA, wherein SEQ ID NO:51 is a clone designated herein as "DNA66307-2661".

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

Figure 53 shows a nucleotide sequence (SEQ ID NO:53) of a native sequence PRO1341 cDNA, wherein SEQ ID NO:53 is a clone designated herein as "DNA66677-2535".

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

Figure 55 shows a nucleotide sequence (SEQ ID NO:55) of a native sequence PRO1777 cDNA, wherein SEQ ID NO:55 is a clone designated herein as "DNA71235-1706".

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

Figure 57 shows a nucleotide sequence (SEQ ID NO:57) of a native sequence PRO3580 cDNA, wherein SEQ ID NO:57 is a clone designated herein as "DNA71289-2547".

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

Figure 59 shows a nucleotide sequence (SEQ ID NO:59) of a native sequence PRO1779 cDNA, wherein SEQ ID NO:59 is a clone designated herein as "DNA73775-1707".

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

Figure 61 shows a nucleotide sequence (SEQ ID NO:61) of a native sequence PRO1754 cDNA, wherein SEQ ID NO:61 is a clone designated herein as "DNA76385-1692".

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

Figure 63 shows a nucleotide sequence (SEQ ID NO:63) of a native sequence PRO1906 cDNA, wherein SEQ ID NO:63 is a clone designated herein as "DNA76395-2527".

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

Figure 65 shows a nucleotide sequence (SEQ ID NO:65) of a native sequence PRO1870 cDNA, wherein SEQ ID NO:65 is a clone designated herein as "DNA77622-2516".

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

Figure 67 shows a nucleotide sequence (SEQ ID NO:67) of a native sequence PRO4329 cDNA, wherein SEQ ID NO:67 is a clone designated herein as "DNA77629-2573".

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

Figure 69 shows a nucleotide sequence (SEQ ID NO:69) of a native sequence PRO4979 cDNA, wherein SEQ ID NO:69 is a clone designated herein as "DNA77645-2648".

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

Figure 71 shows a nucleotide sequence (SEQ ID NO:71) of a native sequence PRO1885 cDNA, wherein SEQ ID NO:71 is a clone designated herein as "DNA79302-2521".

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

Figure 73 shows a nucleotide sequence (SEQ ID NO:73) of a native sequence PRO1882 cDNA, wherein SEQ ID NO:73 is a clone designated herein as "DNA79865-2519".

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

Figure 75 shows a nucleotide sequence (SEQ ID NO:75) of a native sequence PRO4989 cDNA, wherein SEQ ID NO:75 is a clone designated herein as "DNA80135-2655".

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

Figure 77 shows a nucleotide sequence (SEQ ID NO:77) of a native sequence PRO4323 cDNA, wherein SEQ ID NO:77 is a clone designated herein as "DNA80794-2568".

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

Figure 79 shows a nucleotide sequence (SEQ ID NO:79) of a native sequence PRO1886 cDNA, wherein SEQ ID NO:79 is a clone designated herein as "DNA80796-2523".

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

Figure 81 shows a nucleotide sequence (SEQ ID NO:81) of a native sequence PRO4395 cDNA, wherein SEQ ID NO:81 is a clone designated herein as "DNA80840-2605".

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

Figure 83 shows a nucleotide sequence (SEQ ID NO:83) of a native sequence PRO1782 cDNA, wherein SEQ ID NO:83 is a clone designated herein as "DNA80899-2501".

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

Figure 85 shows a nucleotide sequence (SEQ ID NO:85) of a native sequence PRO4338 cDNA, wherein SEQ ID NO:85 is a clone designated herein as "DNA81228-2580".

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

Figure 87 shows a nucleotide sequence (SEQ ID NO:87) of a native sequence PRO4341 cDNA, wherein SEQ ID NO:87 is a clone designated herein as "DNA81761-2583".

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

Figure 89 shows a nucleotide sequence (SEQ ID NO:89) of a native sequence PRO5990 cDNA, wherein SEQ ID NO:89 is a clone designated herein as "DNA96042-2682".

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

Figure 91 shows a nucleotide sequence (SEQ ID NO:91) of a native sequence PRO3438 cDNA, wherein SEQ ID NO:91 is a clone designated herein as "DNA82364-2538".

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

Figure 93 shows a nucleotide sequence (SEQ ID NO:93) of a native sequence PRO4321 cDNA, wherein SEQ ID NO:93 is a clone designated herein as "DNA82424-2566".

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

Figure 95 shows a nucleotide sequence (SEQ ID NO:95) of a native sequence PRO4304 cDNA, wherein SEQ ID NO:95 is a clone designated herein as "DNA82430-2557".

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

Figure 97 shows a nucleotide sequence (SEQ ID NO:97) of a native sequence PRO1801 cDNA, wherein SEQ ID NO:97 is a clone designated herein as "DNA83500-2506".

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

Figure 99 shows a nucleotide sequence (SEQ ID NO:99) of a native sequence PRO4403 cDNA, wherein SEQ ID NO:99 is a clone designated herein as "DNA83509-2612".

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

Figure 101 shows a nucleotide sequence (SEQ ID NO:101) of a native sequence PRO4324 cDNA, wherein SEQ ID NO:101 is a clone designated herein as "DNA83560-2569".

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

Figure 103 shows a nucleotide sequence (SEQ ID NO:103) of a native sequence PRO4303 cDNA, wherein SEQ ID NO:103 is a clone designated herein as "DNA84139-2555".

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

Figure 105 shows a nucleotide sequence (SEQ ID NO:105) of a native sequence PRO4305 cDNA, wherein SEQ ID NO:105 is a clone designated herein as "DNA84141-2556".

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

Figure 107 shows a nucleotide sequence (SEQ ID NO:107) of a native sequence PRO4404 cDNA, wherein SEQ ID NO:107 is a clone designated herein as "DNA84142-2613".

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

Figure 109 shows a nucleotide sequence (SEQ ID NO:109) of a native sequence PRO1884 cDNA, wherein SEQ ID NO:109 is a clone designated herein as "DNA84318-2520".

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

Figure 111 shows a nucleotide sequence (SEQ ID NO:111) of a native sequence PRO4349 cDNA, wherein SEQ ID NO:111 is a clone designated herein as "DNA84909-2590".

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

Figure 113 shows a nucleotide sequence (SEQ ID NO:113) of a native sequence PRO4401 cDNA, wherein SEQ ID NO:113 is a clone designated herein as "DNA84912-2610".

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

Figure 115 shows a nucleotide sequence (SEQ ID NO:115) of a native sequence PRO1867 cDNA, wherein SEQ ID NO:115 is a clone designated herein as "DNA84925-2514".

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

Figure 117 shows a nucleotide sequence (SEQ ID NO:117) of a native sequence PRO4319 cDNA, wherein SEQ ID NO:117 is a clone designated herein as "DNA84928-2564".

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

Figure 119 shows a nucleotide sequence (SEQ ID NO:119) of a native sequence PRO4991 cDNA, wherein SEQ ID NO:119 is a clone designated herein as "DNA84932-2657".

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

Figure 121 shows a nucleotide sequence (SEQ ID NO:121) of a native sequence PRO4398 cDNA, wherein SEQ ID NO:121 is a clone designated herein as "DNA86592-2607".

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

Figure 123 shows a nucleotide sequence (SEQ ID NO:123) of a native sequence PRO4346 cDNA, wherein SEQ ID NO:123 is a clone designated herein as "DNA86594-2587".

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

Figure 125 shows a nucleotide sequence (SEQ ID NO:125) of a native sequence PRO4350 cDNA, wherein SEQ ID NO:125 is a clone designated herein as "DNA86647-2591".

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

Figure 127 shows a nucleotide sequence (SEQ ID NO:127) of a native sequence PRO4318 cDNA, wherein SEQ ID NO:127 is a clone designated herein as "DNA87185-2563".

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

Figure 129 shows a nucleotide sequence (SEQ ID NO:129) of a native sequence PRO4340 cDNA, wherein SEQ ID NO:129 is a clone designated herein as "DNA87656-2582".

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

Figure 131 shows a nucleotide sequence (SEQ ID NO:131) of a native sequence PRO4400 cDNA, wherein SEQ ID NO:131 is a clone designated herein as "DNA87974-2609".

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

Figure 133 shows a nucleotide sequence (SEQ ID NO:133) of a native sequence PRO4320 cDNA, wherein SEQ ID NO:133 is a clone designated herein as "DNA88001-2565".

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

Figure 135 shows a nucleotide sequence (SEQ ID NO:135) of a native sequence PRO4409 cDNA, wherein SEQ ID NO:135 is a clone designated herein as "DNA88004-2575".

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

Figure 137 shows a nucleotide sequence (SEQ ID NO:137) of a native sequence PRO4399 cDNA, wherein SEQ ID NO:137 is a clone designated herein as "DNA89220-2608".

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

Figure 139 shows a nucleotide sequence (SEQ ID NO:139) of a native sequence PRO4418 cDNA, wherein SEQ ID NO:139 is a clone designated herein as "DNA89947-2618".

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

Figure 141 shows a nucleotide sequence (SEQ ID NO:141) of a native sequence PRO4330 cDNA, wherein SEQ ID NO:141 is a clone designated herein as "DNA90842-2574".

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

Figure 143 shows a nucleotide sequence (SEQ ID NO:143) of a native sequence PRO4339 cDNA, wherein SEQ ID NO:143 is a clone designated herein as "DNA91775-2581".

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

Figure 145 shows a nucleotide sequence (SEQ ID NO:145) of a native sequence PRO4326 cDNA, wherein SEQ ID NO:145 is a clone designated herein as "DNA91779-2571".

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

Figure 147 shows a nucleotide sequence (SEQ ID NO:147) of a native sequence PRO6014 cDNA, wherein SEQ ID NO:147 is a clone designated herein as "DNA92217-2697".

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

Figure 149 shows a nucleotide sequence (SEQ ID NO:149) of a native sequence PRO3446 cDNA, wherein SEQ ID NO:149 is a clone designated herein as "DNA92219-2541".

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

Figure 151 shows a nucleotide sequence (SEQ ID NO:151) of a native sequence PRO4322 cDNA, wherein SEQ ID NO:151 is a clone designated herein as "DNA92223-2567".

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

Figure 153 shows a nucleotide sequence (SEQ ID NO:153) of a native sequence PRO4381 cDNA, wherein SEQ ID NO:153 is a clone designated herein as "DNA92225-2603".

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

Figure 155 shows a nucleotide sequence (SEQ ID NO:155) of a native sequence PRO4348 cDNA, wherein SEQ ID NO:155 is a clone designated herein as "DNA92232-2589".

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

Figure 157 shows a nucleotide sequence (SEQ ID NO:157) of a native sequence PRO4371 cDNA, wherein SEQ ID NO:157 is a clone designated herein as "DNA92233-2599".

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

Figure 159 shows a nucleotide sequence (SEQ ID NO:159) of a native sequence PRO3742 cDNA, wherein SEQ ID NO:159 is a clone designated herein as "DNA92243-2549".

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

Figure 161 shows a nucleotide sequence (SEQ ID NO:161) of a native sequence PRO5773 cDNA, wherein SEQ ID NO:161 is a clone designated herein as "DNA92253-2671".

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

Figure 163 shows a nucleotide sequence (SEQ ID NO:163) of a native sequence PRO5774 cDNA, wherein SEQ ID NO:163 is a clone designated herein as "DNA92254-2672".

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

Figure 165 shows a nucleotide sequence (SEQ ID NO:165) of a native sequence PRO4343 cDNA, wherein SEQ ID NO:165 is a clone designated herein as "DNA92255-2584".

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

Figure 167 shows a nucleotide sequence (SEQ ID NO:167) of a native sequence PRO4325 cDNA, wherein SEQ ID NO:167 is a clone designated herein as "DNA92269-2570".

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

Figure 169 shows a nucleotide sequence (SEQ ID NO:169) of a native sequence PRO4347 cDNA, wherein SEQ ID NO:169 is a clone designated herein as "DNA92288-2588".

Figure 170 shows the amino acid sequence (SEQ ID NO:170) derived from the coding sequence of SEQ ID NO:169 shown in Figure 169.

Figure 171 shows a nucleotide sequence (SEQ ID NO:171) of a native sequence PRO3743 cDNA, wherein SEQ ID NO:171 is a clone designated herein as "DNA92290-2550".

Figure 172 shows the amino acid sequence (SEQ ID NO:172) derived from the coding sequence of SEQ ID NO:171 shown in Figure 171.

Figure 173 shows a nucleotide sequence (SEQ ID NO:173) of a native sequence PRO4426 cDNA, wherein SEQ ID NO:173 is a clone designated herein as "DNA93012-2622".

Figure 174 shows the amino acid sequence (SEQ ID NO:174) derived from the coding sequence of SEQ ID NO:173 shown in Figure 173.

Figure 175 shows a nucleotide sequence (SEQ ID NO:175) of a native sequence PRO4500 cDNA, wherein SEQ ID NO:175 is a clone designated herein as "DNA93020-2642".

Figure 176 shows the amino acid sequence (SEQ ID NO:176) derived from the coding sequence of SEQ ID NO:175 shown in Figure 175.

Figure 177 shows a nucleotide sequence (SEQ ID NO:177) of a native sequence PRO4389 cDNA, wherein SEQ ID NO:177 is a clone designated herein as "DNA94830-2604".

Figure 178 shows the amino acid sequence (SEQ ID NO:178) derived from the coding sequence of SEQ ID NO:177 shown in Figure 177.

Figure 179 shows a nucleotide sequence (SEQ ID NO:179) of a native sequence PRO4337 cDNA, wherein SEQ ID NO:179 is a clone designated herein as "DNA94833-2579".

Figure 180 shows the amino acid sequence (SEQ ID NO:180) derived from the coding sequence of SEQ ID NO:179 shown in Figure 179.

Figure 181 shows a nucleotide sequence (SEQ ID NO:181) of a native sequence PRO4992 cDNA, wherein SEQ ID NO:181 is a clone designated herein as "DNA94838-2658".

Figure 182 shows the amino acid sequence (SEQ ID NO:182) derived from the coding sequence of SEQ ID NO:181 shown in Figure 181.

Figure 183 shows a nucleotide sequence (SEQ ID NO:183) of a native sequence PRO5996 cDNA, wherein SEQ ID NO:183 is a clone designated herein as "DNA94844-2686".

Figure 184 shows the amino acid sequence (SEQ ID NO:184) derived from the coding sequence of SEQ ID NO:183 shown in Figure 183.

Figure 185 shows a nucleotide sequence (SEQ ID NO:185) of a native sequence PRO4345 cDNA, wherein SEQ ID NO:185 is a clone designated herein as "DNA94854-2586".

Figure 186 shows the amino acid sequence (SEQ ID NO:186) derived from the coding sequence of SEQ ID NO:185 shown in Figure 185.

Figure 187 shows a nucleotide sequence (SEQ ID NO:187) of a native sequence PRO4978 cDNA, wherein SEQ ID NO:187 is a clone designated herein as "DNA95930".

Figure 188 shows the amino acid sequence (SEQ ID NO:188) derived from the coding sequence of SEQ ID NO:187 shown in Figure 187.

Figure 189 shows a nucleotide sequence (SEQ ID NO:189) of a native sequence PRO5780 cDNA, wherein SEQ ID NO:189 is a clone designated herein as "DNA96868-2677".

Figure 190 shows the amino acid sequence (SEQ ID NO:190) derived from the coding sequence of SEQ ID NO:189 shown in Figure 189.

Figure 191 shows a nucleotide sequence (SEQ ID NO:191) of a native sequence PRO5992 cDNA, wherein SEQ ID NO:191 is a clone designated herein as "DNA96871-2683".

Figure 192 shows the amino acid sequence (SEQ ID NO:192) derived from the coding sequence of SEQ ID NO:191 shown in Figure 191.

Figure 193 shows a nucleotide sequence (SEQ ID NO:193) of a native sequence PRO4428 cDNA, wherein SEQ ID NO:193 is a clone designated herein as "DNA96880-2624".

Figure 194 shows the amino acid sequence (SEQ ID NO:194) derived from the coding sequence of SEQ ID NO:193 shown in Figure 193.

Figure 195 shows a nucleotide sequence (SEQ ID NO:195) of a native sequence PRO4994 cDNA, wherein SEQ ID NO:195 is a clone designated herein as "DNA96986-2660".

Figure 196 shows the amino acid sequence (SEQ ID NO:196) derived from the coding sequence of SEQ ID NO:195 shown in Figure 195.

Figure 197 shows a nucleotide sequence (SEQ ID NO:197) of a native sequence PRO5995 cDNA, wherein SEQ ID NO:197 is a clone designated herein as "DNA96988-2685".

Figure 198 shows the amino acid sequence (SEQ ID NO:198) derived from the coding sequence of SEQ ID NO:197 shown in Figure 197.

Figure 199 shows a nucleotide sequence (SEQ ID NO:199) of a native sequence PRO6094 cDNA, wherein SEQ ID NO:199 is a clone designated herein as "DNA96995-2709".

Figure 200 shows the amino acid sequence (SEQ ID NO:200) derived from the coding sequence of SEQ ID NO:199 shown in Figure 199.

Figure 201 shows a nucleotide sequence (SEQ ID NO:201) of a native sequence PRO4317 cDNA, wherein SEQ ID NO:201 is a clone designated herein as "DNA97004-2562".

Figure 202 shows the amino acid sequence (SEQ ID NO:202) derived from the coding sequence of SEQ ID NO:201 shown in Figure 201.

Figure 203 shows a nucleotide sequence (SEQ ID NO:203) of a native sequence PRO5997 cDNA, wherein SEQ ID NO:203 is a clone designated herein as "DNA97005-2687".

Figure 204 shows the amino acid sequence (SEQ ID NO:204) derived from the coding sequence of SEQ ID NO:203 shown in Figure 203.

Figure 205 shows a nucleotide sequence (SEQ ID NO:205) of a native sequence PRO5005 cDNA, wherein SEQ ID NO:205 is a clone designated herein as "DNA97009-2668".

Figure 206 shows the amino acid sequence (SEQ ID NO:206) derived from the coding sequence of SEQ ID NO:205 shown in Figure 205.

Figure 207 shows a nucleotide sequence (SEQ ID NO:207) of a native sequence PRO5004 cDNA, wherein SEQ ID NO:207 is a clone designated herein as "DNA97013-2667".

Figure 208 shows the amino acid sequence (SEQ ID NO:208) derived from the coding sequence of SEQ ID NO:207 shown in Figure 207.

Figure 209 shows a nucleotide sequence (SEQ ID NO:209) of a native sequence PRO6001 cDNA, wherein SEQ ID NO:209 is a clone designated herein as "DNA98380-2690".

Figure 210 shows the amino acid sequence (SEQ ID NO:210) derived from the coding sequence of SEQ ID NO:209 shown in Figure 209.

Figure 211 shows a nucleotide sequence (SEQ ID NO:211) of a native sequence PRO6013 cDNA, wherein SEQ ID NO:211 is a clone designated herein as "DNA98561-2696".

Figure 212 shows the amino acid sequence (SEQ ID NO:212) derived from the coding sequence of SEQ ID NO:211 shown in Figure 211.

Figure 213 shows a nucleotide sequence (SEQ ID NO:213) of a native sequence PRO4502 cDNA, wherein SEQ ID NO:213 is a clone designated herein as "DNA98575-2644".

Figure 214 shows the amino acid sequence (SEQ ID NO:214) derived from the coding sequence of SEQ ID NO:213 shown in Figure 213.

Figure 215 shows a nucleotide sequence (SEQ ID NO:215) of a native sequence PRO6007 cDNA, wherein SEQ ID NO:215 is a clone designated herein as "DNA98593-2694".

Figure 216 shows the amino acid sequence (SEQ ID NO:216) derived from the coding sequence of SEQ ID NO:215 shown in Figure 215.

Figure 217 shows a nucleotide sequence (SEQ ID NO:217) of a native sequence PRO6028 cDNA, wherein SEQ ID NO:217 is a clone designated herein as "DNA98600-2703".

Figure 218 shows the amino acid sequence (SEQ ID NO:218) derived from the coding sequence of SEQ ID NO:217 shown in Figure 217.

Figure 219 shows a nucleotide sequence (SEQ ID NO:219) of a native sequence PRO100 cDNA, wherein SEQ ID NO:219 is a clone designated herein as "DNA99333".

Figure 220 shows the amino acid sequence (SEQ ID NO:220) derived from the coding sequence of SEQ ID NO:219 shown in Figure 219.

Figure 221 shows a nucleotide sequence (SEQ ID NO:221) of a native sequence PRO4327 cDNA, wherein SEQ ID NO:221 is a clone designated herein as "DNA99391-2572".

Figure 222 shows the amino acid sequence (SEQ ID NO:222) derived from the coding sequence of SEQ ID NO:221 shown in Figure 221.

Figure 223 shows a nucleotide sequence (SEQ ID NO:223) of a native sequence PRO4315 cDNA, wherein SEQ ID NO:223 is a clone designated herein as "DNA99393-2560".

Figure 224 shows the amino acid sequence (SEQ ID NO:224) derived from the coding sequence of SEQ ID NO:223 shown in Figure 223.

Figure 225 shows a nucleotide sequence (SEQ ID NO:225) of a native sequence PRO5993 cDNA, wherein SEQ ID NO:225 is a clone designated herein as "DNA100276-2684".

Figure 226 shows the amino acid sequence (SEQ ID NO:226) derived from the coding sequence of SEQ ID NO:225 shown in Figure 225.

Figure 227 shows a nucleotide sequence (SEQ ID NO:227) of a native sequence PRO4503 cDNA, wherein SEQ ID NO:227 is a clone designated herein as "DNA100312-2645".

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

Figure 229 shows a nucleotide sequence (SEQ ID NO:229) of a native sequence PRO4976 cDNA, wherein SEQ ID NO:229 is a clone designated herein as "DNA100902-2646".

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

Figure 231 shows a nucleotide sequence (SEQ ID NO:231) of a native sequence PRO5798 cDNA, wherein SEQ ID NO:231 is a clone designated herein as "DNA102899-2679".

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

Figure 233 shows a nucleotide sequence (SEQ ID NO:233) of a native sequence PRO6242 cDNA, wherein SEQ ID NO:233 is a clone designated herein as "DNA104875-2720".

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

Figure 235 shows a nucleotide sequence (SEQ ID NO:235) of a native sequence PRO6095 cDNA, wherein SEQ ID NO:235 is a clone designated herein as "DNA105680-2710".

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

Figure 237 shows a nucleotide sequence (SEQ ID NO:237) of a native sequence PRO6093 cDNA, wherein SEQ ID NO:237 is a clone designated herein as "DNA105779-2708".

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

Figure 239 shows a nucleotide sequence (SEQ ID NO:239) of a native sequence PRO6012 cDNA, wherein SEQ ID NO:239 is a clone designated herein as "DNA105794-2695".

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

Figure 241 shows a nucleotide sequence (SEQ ID NO:241) of a native sequence PRO6027 cDNA, wherein SEQ ID NO:241 is a clone designated herein as "DNA105838-2702".

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

Figure 243 shows a nucleotide sequence (SEQ ID NO:243) of a native sequence PRO6181 cDNA, wherein SEQ ID NO:243 is a clone designated herein as "DNA107698-2715".

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

Figure 245 shows a nucleotide sequence (SEQ ID NO:245) of a native sequence PRO6097 cDNA, wherein SEQ ID NO:245 is a clone designated herein as "DNA107701-2711".

Figure 246 shows the amino acid sequence (SEQ ID NO:246) derived from the coding sequence of SEQ ID NO:245 shown in Figure 245.

Figure 247 shows a nucleotide sequence (SEQ ID NO:247) of a native sequence PRO6090 cDNA, wherein SEQ ID NO:247 is a clone designated herein as "DNA107781-2707".

Figure 248 shows the amino acid sequence (SEQ ID NO:248) derived from the coding sequence of SEQ ID NO:247 shown in Figure 247.

Figure 249 shows a nucleotide sequence (SEQ ID NO:249) of a native sequence PRO7171 cDNA, wherein SEQ ID NO:249 is a clone designated herein as "DNA108670-2744".

Figure 250 shows the amino acid sequence (SEQ ID NO:250) derived from the coding sequence of SEQ ID NO:249 shown in Figure 249.

Figure 251 shows a nucleotide sequence (SEQ ID NO:251) of a native sequence PRO6258 cDNA, wherein SEQ ID NO:251 is a clone designated herein as "DNA108688-2725".

Figure 252 shows the amino acid sequence (SEQ ID NO:252) derived from the coding sequence of SEQ ID NO:251 shown in Figure 251.

Figure 253 shows a nucleotide sequence (SEQ ID NO:253) of a native sequence PRO9820 cDNA, wherein SEQ ID NO:253 is a clone designated herein as "DNA108769-2765".

Figure 254 shows the amino acid sequence (SEQ ID NO:254) derived from the coding sequence of SEQ ID NO:253 shown in Figure 253.

Figure 255 shows a nucleotide sequence (SEQ ID NO:255) of a native sequence PRO6243 cDNA, wherein SEQ ID NO:255 is a clone designated herein as "DNA108935-2721".

Figure 256 shows the amino acid sequence (SEQ ID NO:256) derived from the coding sequence of SEQ ID NO:255 shown in Figure 255.

Figure 257 shows a nucleotide sequence (SEQ ID NO:257) of a native sequence PRO6182 cDNA, wherein SEQ ID NO:257 is a clone designated herein as "DNA110700-2716".

Figure 258 shows the amino acid sequence (SEQ ID NO:258) derived from the coding sequence of SEQ ID NO:257 shown in Figure 257.

Figure 259 shows a nucleotide sequence (SEQ ID NO:259) of a native sequence PRO6079 cDNA, wherein SEQ ID NO:259 is a clone designated herein as "DNA111750-2706".

Figure 260 shows the amino acid sequence (SEQ ID NO:260) derived from the coding sequence of SEQ ID NO:259 shown in Figure 259.

Figure 261 shows a nucleotide sequence (SEQ ID NO:261) of a native sequence PRO7434 cDNA, wherein SEQ ID NO:261 is a clone designated herein as "DNA123430-2755".

Figure 262 shows the amino acid sequence (SEQ ID NO:262) derived from the coding sequence of SEQ ID NO:261 shown in Figure 261.

Figure 263 shows a nucleotide sequence (SEQ ID NO:263) of a native sequence PRO9865 cDNA, wherein SEQ ID NO:263 is a clone designated herein as "DNA125154-2785".

Figure 264 shows the amino acid sequence (SEQ ID NO:264) derived from the coding sequence of SEQ ID NO:263 shown in Figure 263.

Figure 265 shows a nucleotide sequence (SEQ ID NO:265) of a native sequence PRO9828 cDNA, wherein SEQ ID NO:265 is a clone designated herein as "DNA142238-2768".

Figure 266 shows the amino acid sequence (SEQ ID NO:266) derived from the coding sequence of SEQ ID NO:265 shown in Figure 265.

Figure 267 shows a nucleotide sequence (SEQ ID NO:267) of a native sequence PRO196 cDNA, wherein SEQ ID NO:267 is a clone designated herein as "DNA22779-1130".

Figure 268 shows the amino acid sequence (SEQ ID NO:268) derived from the coding sequence of SEQ ID NO:267 shown in Figure 267.

Figure 269 shows a nucleotide sequence (SEQ ID NO:269) of a native sequence PRO197 cDNA, wherein SEQ ID NO:269 is a clone designated herein as "DNA22780-1078".

Figure 270 shows the amino acid sequence (SEQ ID NO:270) derived from the coding sequence of SEQ ID NO:269 shown in Figure 269.

Figure 271 shows a nucleotide sequence (SEQ ID NO:271) of a native sequence PRO195 cDNA, wherein SEQ ID NO:271 is a clone designated herein as "DNA26847-1395".

Figure 272 shows the amino acid sequence (SEQ ID NO:272) derived from the coding sequence of SEQ ID NO:271 shown in Figure 271.

Figure 273 shows a nucleotide sequence (SEQ ID NO:273) of a native sequence PRO187 cDNA, wherein SEQ ID NO:273 is a clone designated herein as "DNA27864-1155".

Figure 274 shows the amino acid sequence (SEQ ID NO:274) derived from the coding sequence of SEQ ID NO:273 shown in Figure 273.

Figure 275 shows a nucleotide sequence (SEQ ID NO:275) of a native sequence PRO182 cDNA, wherein SEQ ID NO:275 is a clone designated herein as "DNA27865-1091".

Figure 276 shows the amino acid sequence (SEQ ID NO:276) derived from the coding sequence of SEQ ID NO:275 shown in Figure 275.

Figure 277 shows a nucleotide sequence (SEQ ID NO:277) of a native sequence PRO188 cDNA, wherein SEQ ID NO:277 is a clone designated herein as "DNA28497-1130".

Figure 278 shows the amino acid sequence (SEQ ID NO:278) derived from the coding sequence of SEQ ID NO:277 shown in Figure 277.

Figure 279 shows a nucleotide sequence (SEQ ID NO:279) of a native sequence PRO183 cDNA, wherein SEQ ID NO:279 is a clone designated herein as "DNA28498".

Figure 280 shows the amino acid sequence (SEQ ID NO:280) derived from the coding sequence of SEQ ID NO:279 shown in Figure 279.

Figure 281 shows a nucleotide sequence (SEQ ID NO:281) of a native sequence PRO184 cDNA, wherein SEQ ID NO:281 is a clone designated herein as "DNA28500".

Figure 282 shows the amino acid sequence (SEQ ID NO:282) derived from the coding sequence of SEQ ID NO:281 shown in Figure 281.

Figure 283 shows a nucleotide sequence (SEQ ID NO:283) of a native sequence PRO185 cDNA, wherein SEQ ID NO:283 is a clone designated herein as "DNA28503".

Figure 284 shows the amino acid sequence (SEQ ID NO:284) derived from the coding sequence of SEQ ID NO:283 shown in Figure 283.

Figure 285 shows a nucleotide sequence (SEQ ID NO:285) of a native sequence PRO200 cDNA, wherein SEQ ID NO:285 is a clone designated herein as "DNA29101-1122".

Figure 286 shows the amino acid sequence (SEQ ID NO:286) derived from the coding sequence of SEQ ID NO:285 shown in Figure 285.

Figure 287 shows a nucleotide sequence (SEQ ID NO:287) of a native sequence PRO202 cDNA, wherein SEQ ID NO:287 is a clone designated herein as "DNA30869".

Figure 288 shows the amino acid sequence (SEQ ID NO:288) derived from the coding sequence of SEQ ID NO:287 shown in Figure 287.

Figure 289 shows a nucleotide sequence (SEQ ID NO:289) of a native sequence PRO214 cDNA, wherein SEQ ID NO:289 is a clone designated herein as "DNA32286-1191".

Figure 290 shows the amino acid sequence (SEQ ID NO:290) derived from the coding sequence of SEQ ID NO:289 shown in Figure 289.

Figure 291 shows a nucleotide sequence (SEQ ID NO:291) of a native sequence PRO215 cDNA, wherein SEQ ID NO:291 is a clone designated herein as "DNA32288-1132".

Figure 292 shows the amino acid sequence (SEQ ID NO:292) derived from the coding sequence of SEQ ID NO:291 shown in Figure 291.

Figure 293 shows a nucleotide sequence (SEQ ID NO:293) of a native sequence PRO219 cDNA, wherein SEQ ID NO:293 is a clone designated herein as "DNA32290-1164".

Figure 294 shows the amino acid sequence (SEQ ID NO:294) derived from the coding sequence of SEQ ID NO:293 shown in Figure 293.

Figure 295 shows a nucleotide sequence (SEQ ID NO:295) of a native sequence PRO211 cDNA, wherein SEQ ID NO:295 is a clone designated herein as "DNA32292-1131".

Figure 296 shows the amino acid sequence (SEQ ID NO:296) derived from the coding sequence of SEQ ID NO:295 shown in Figure 295.

Figure 297 shows a nucleotide sequence (SEQ ID NO:297) of a native sequence PRO220 cDNA, wherein SEQ ID NO:297 is a clone designated herein as "DNA32298-1132".

Figure 298 shows the amino acid sequence (SEQ ID NO:298) derived from the coding sequence of SEQ ID NO:297 shown in Figure 297.

Figure 299 shows a nucleotide sequence (SEQ ID NO:299) of a native sequence PRO366 cDNA, wherein SEQ ID NO:299 is a clone designated herein as "DNA33085-1110".

Figure 300 shows the amino acid sequence (SEQ ID NO:300) derived from the coding sequence of SEQ ID NO:299 shown in Figure 299.

Figure 301 shows a nucleotide sequence (SEQ ID NO:301) of a native sequence PRO216 cDNA, wherein SEQ ID NO:301 is a clone designated herein as "DNA33087-1158".

Figure 302 shows the amino acid sequence (SEQ ID NO:302) derived from the coding sequence of SEQ ID NO:301 shown in Figure 301.

Figure 303 shows a nucleotide sequence (SEQ ID NO:303) of a native sequence PRO221 cDNA, wherein SEQ ID NO:303 is a clone designated herein as "DNA33089-1132".

Figure 304 shows the amino acid sequence (SEQ ID NO:304) derived from the coding sequence of SEQ ID NO:303 shown in Figure 303.

Figure 305 shows a nucleotide sequence (SEQ ID NO:305) of a native sequence PRO228 cDNA, wherein SEQ ID NO:305 is a clone designated herein as "DNA33092-1202".

Figure 306 shows the amino acid sequence (SEQ ID NO:306) derived from the coding sequence of SEQ ID NO:305 shown in Figure 305.

Figure 307 shows a nucleotide sequence (SEQ ID NO:307) of a native sequence PRO217 cDNA, wherein SEQ ID NO:307 is a clone designated herein as "DNA33094-1131".

Figure 308 shows the amino acid sequence (SEQ ID NO:308) derived from the coding sequence of SEQ ID NO:307 shown in Figure 307.

Figure 309 shows a nucleotide sequence (SEQ ID NO:309) of a native sequence PRO222 cDNA, wherein SEQ ID NO:309 is a clone designated herein as "DNA33107-1135".

Figure 310 shows the amino acid sequence (SEQ ID NO:310) derived from the coding sequence of SEQ ID NO:309 shown in Figure 309.

Figure 311 shows a nucleotide sequence (SEQ ID NO:311) of a native sequence PRO224 cDNA, wherein SEQ ID NO:311 is a clone designated herein as "DNA33221-1133".

Figure 312 shows the amino acid sequence (SEQ ID NO:312) derived from the coding sequence of SEQ ID NO:311 shown in Figure 311.

Figure 313 shows a nucleotide sequence (SEQ ID NO:313) of a native sequence PRO230 cDNA, wherein SEQ ID NO:313 is a clone designated herein as "DNA33223-1136".

Figure 314 shows the amino acid sequence (SEQ ID NO:314) derived from the coding sequence of SEQ ID NO:313 shown in Figure 313.

Figure 315 shows a nucleotide sequence (SEQ ID NO:315) of a native sequence PRO198 cDNA, wherein SEQ ID NO:315 is a clone designated herein as "DNA33457-1078".

Figure 316 shows the amino acid sequence (SEQ ID NO:316) derived from the coding sequence of SEQ ID NO:315 shown in Figure 315.

Figure 317 shows a nucleotide sequence (SEQ ID NO:317) of a native sequence PRO226 cDNA, wherein SEQ ID NO:317 is a clone designated herein as "DNA33460-1166".

Figure 318 shows the amino acid sequence (SEQ ID NO:318) derived from the coding sequence of SEQ ID NO:317 shown in Figure 317.

Figure 319 shows a nucleotide sequence (SEQ ID NO:319) of a native sequence PRO261 cDNA, wherein SEQ ID NO:319 is a clone designated herein as "DNA33473-1176".

Figure 320 shows the amino acid sequence (SEQ ID NO:320) derived from the coding sequence of SEQ ID NO:319 shown in Figure 319.

Figure 321 shows a nucleotide sequence (SEQ ID NO:321) of a native sequence PRO242 cDNA, wherein SEQ ID NO:321 is a clone designated herein as "DNA33785-1143".

Figure 322 shows the amino acid sequence (SEQ ID NO:322) derived from the coding sequence of SEQ ID NO:321 shown in Figure 321.

Figure 323 shows a nucleotide sequence (SEQ ID NO:323) of a native sequence PRO227 cDNA, wherein SEQ ID NO:323 is a clone designated herein as "DNA33786-1132".

Figure 324 shows the amino acid sequence (SEQ ID NO:324) derived from the coding sequence of SEQ ID NO:323 shown in Figure 323.

Figure 325 shows a nucleotide sequence (SEQ ID NO:325) of a native sequence PRO237 cDNA, wherein SEQ ID NO:325 is a clone designated herein as "DNA34353-1428".

Figure 326 shows the amino acid sequence (SEQ ID NO:326) derived from the coding sequence of SEQ ID NO:325 shown in Figure 325.

Figure 327 shows a nucleotide sequence (SEQ ID NO:327) of a native sequence PRO241 cDNA, wherein SEQ ID NO:327 is a clone designated herein as "DNA34392-1170".

Figure 328 shows the amino acid sequence (SEQ ID NO:328) derived from the coding sequence of SEQ ID NO:327 shown in Figure 327.

Figure 329 shows a nucleotide sequence (SEQ ID NO:329) of a native sequence PRO231 cDNA, wherein SEQ ID NO:329 is a clone designated herein as "DNA34434-1139".

Figure 330 shows the amino acid sequence (SEQ ID NO:330) derived from the coding sequence of SEQ ID NO:329 shown in Figure 329.

Figure 331 shows a nucleotide sequence (SEQ ID NO:331) of a native sequence PRO235 cDNA, wherein SEQ ID NO:331 is a clone designated herein as "DNA35558-1167".

Figure 332 shows the amino acid sequence (SEQ ID NO:332) derived from the coding sequence of SEQ ID NO:331 shown in Figure 331.

Figure 333 shows a nucleotide sequence (SEQ ID NO:333) of a native sequence PRO323 cDNA, wherein SEQ ID NO:333 is a clone designated herein as "DNA35595-1228".

Figure 334 shows the amino acid sequence (SEQ ID NO:334) derived from the coding sequence of SEQ ID NO:333 shown in Figure 333.

Figure 335 shows a nucleotide sequence (SEQ ID NO:335) of a native sequence PRO245 cDNA, wherein SEQ ID NO:335 is a clone designated herein as "DNA35638-1216".

Figure 336 shows the amino acid sequence (SEQ ID NO:336) derived from the coding sequence of SEQ ID NO:335 shown in Figure 335.

Figure 337 shows a nucleotide sequence (SEQ ID NO:337) of a native sequence PRO246 cDNA, wherein SEQ ID NO:337 is a clone designated herein as "DNA35639-1172".

Figure 338 shows the amino acid sequence (SEQ ID NO:338) derived from the coding sequence of SEQ ID NO:337 shown in Figure 337.

Figure 339 shows a nucleotide sequence (SEQ ID NO:339) of a native sequence PRO288 cDNA, wherein SEQ ID NO:339 is a clone designated herein as "DNA35663-1129".

Figure 340 shows the amino acid sequence (SEQ ID NO:340) derived from the coding sequence of SEQ ID NO:339 shown in Figure 339.

Figure 341 shows a nucleotide sequence (SEQ ID NO:341) of a native sequence PRO248 cDNA, wherein SEQ ID NO:341 is a clone designated herein as "DNA35674-1142".

Figure 342 shows the amino acid sequence (SEQ ID NO:342) derived from the coding sequence of SEQ ID NO:341 shown in Figure 341.

Figure 343 shows a nucleotide sequence (SEQ ID NO:343) of a native sequence PRO257 cDNA, wherein SEQ ID NO:343 is a clone designated herein as "DNA35841-1173".

Figure 344 shows the amino acid sequence (SEQ ID NO:344) derived from the coding sequence of SEQ ID NO:343 shown in Figure 343.

Figure 345 shows a nucleotide sequence (SEQ ID NO:345) of a native sequence PRO172 cDNA, wherein SEQ ID NO:345 is a clone designated herein as "DNA35916-1161".

Figure 346 shows the amino acid sequence (SEQ ID NO:346) derived from the coding sequence of SEQ ID NO:345 shown in Figure 345.

Figure 347 shows a nucleotide sequence (SEQ ID NO:347) of a native sequence PRO258 cDNA, wherein SEQ ID NO:347 is a clone designated herein as "DNA35918-1174".

Figure 348 shows the amino acid sequence (SEQ ID NO:348) derived from the coding sequence of SEQ ID NO:347 shown in Figure 347.

Figure 349 shows a nucleotide sequence (SEQ ID NO:349) of a native sequence PRO265 cDNA, wherein SEQ ID NO:349 is a clone designated herein as "DNA36350-1158".

Figure 350 shows the amino acid sequence (SEQ ID NO:350) derived from the coding sequence of SEQ ID NO:349 shown in Figure 349.

Figure 351 shows a nucleotide sequence (SEQ ID NO:351) of a native sequence PRO326 cDNA, wherein SEQ ID NO:351 is a clone designated herein as "DNA37140-1234".

Figure 352 shows the amino acid sequence (SEQ ID NO:352) derived from the coding sequence of SEQ ID NO:351 shown in Figure 351.

Figure 353 shows a nucleotide sequence (SEQ ID NO:353) of a native sequence PRO266 cDNA, wherein SEQ ID NO:353 is a clone designated herein as "DNA37150-1178".

Figure 354 shows the amino acid sequence (SEQ ID NO:354) derived from the coding sequence of SEQ ID NO:353 shown in Figure 353.

Figure 355 shows a nucleotide sequence (SEQ ID NO:355) of a native sequence PRO269 cDNA, wherein SEQ ID NO:355 is a clone designated herein as "DNA38260-1180".

Figure 356 shows the amino acid sequence (SEQ ID NO:356) derived from the coding sequence of SEQ ID NO:355 shown in Figure 355.

Figure 357 shows a nucleotide sequence (SEQ ID NO:357) of a native sequence PRO285 cDNA, wherein SEQ ID NO:357 is a clone designated herein as "DNA40021-1154".

Figure 358 shows the amino acid sequence (SEQ ID NO:358) derived from the coding sequence of SEQ ID NO:357 shown in Figure 357.

Figure 359 shows a nucleotide sequence (SEQ ID NO:359) of a native sequence PRO328 cDNA, wherein SEQ ID NO:359 is a clone designated herein as "DNA40587-1231".

Figure 360 shows the amino acid sequence (SEQ ID NO:360) derived from the coding sequence of SEQ ID NO:359 shown in Figure 359.

Figure 361 shows a nucleotide sequence (SEQ ID NO:361) of a native sequence PRO344 cDNA, wherein SEQ ID NO:361 is a clone designated herein as "DNA40592-1242".

Figure 362 shows the amino acid sequence (SEQ ID NO:362) derived from the coding sequence of SEQ ID NO:361 shown in Figure 361.

Figure 363 shows a nucleotide sequence (SEQ ID NO:363) of a native sequence PRO272 cDNA, wherein SEQ ID NO:363 is a clone designated herein as "DNA40620-1183".

Figure 364 shows the amino acid sequence (SEQ ID NO:364) derived from the coding sequence of SEQ ID NO:363 shown in Figure 363.

Figure 365 shows a nucleotide sequence (SEQ ID NO:365) of a native sequence PRO301 cDNA, wherein SEQ ID NO:365 is a clone designated herein as "DNA40628-1216".

Figure 366 shows the amino acid sequence (SEQ ID NO:366) derived from the coding sequence of SEQ ID NO:365 shown in Figure 365.

Figure 367 shows a nucleotide sequence (SEQ ID NO:367) of a native sequence PRO331 cDNA, wherein SEQ ID NO:367 is a clone designated herein as "DNA40981-1234".

Figure 368 shows the amino acid sequence (SEQ ID NO:368) derived from the coding sequence of SEQ ID NO:367 shown in Figure 367.

Figure 369 shows a nucleotide sequence (SEQ ID NO:369) of a native sequence PRO332 cDNA, wherein SEQ ID NO:369 is a clone designated herein as "DNA40982-1235".

Figure 370 shows the amino acid sequence (SEQ ID NO:370) derived from the coding sequence of SEQ ID NO:369 shown in Figure 369.

Figure 371 shows a nucleotide sequence (SEQ ID NO:371) of a native sequence PRO353 cDNA, wherein SEQ ID NO:371 is a clone designated herein as "DNA41234-1242".

Figure 372 shows the amino acid sequence (SEQ ID NO:372) derived from the coding sequence of SEQ ID NO:371 shown in Figure 371.

Figure 373 shows a nucleotide sequence (SEQ ID NO:373) of a native sequence PRO310 cDNA, wherein SEQ ID NO:373 is a clone designated herein as "DNA43046-1225".

Figure 374 shows the amino acid sequence (SEQ ID NO:374) derived from the coding sequence of SEQ ID NO:373 shown in Figure 373.

Figure 375 shows a nucleotide sequence (SEQ ID NO:375) of a native sequence PRO337 cDNA, wherein SEQ ID NO:375 is a clone designated herein as "DNA43316-1237".

Figure 376 shows the amino acid sequence (SEQ ID NO:376) derived from the coding sequence of SEQ ID NO:375 shown in Figure 375.

Figure 377 shows a nucleotide sequence (SEQ ID NO:377) of a native sequence PRO346 cDNA, wherein SEQ ID NO:377 is a clone designated herein as "DNA44167-1243".

Figure 378 shows the amino acid sequence (SEQ ID NO:378) derived from the coding sequence of SEQ ID NO:377 shown in Figure 377.

Figure 379 shows a nucleotide sequence (SEQ ID NO:379) of a native sequence PRO350 cDNA, wherein SEQ ID NO:379 is a clone designated herein as "DNA44175-1314".

Figure 380 shows the amino acid sequence (SEQ ID NO:380) derived from the coding sequence of SEQ ID NO:379 shown in Figure 379.

Figure 381 shows a nucleotide sequence (SEQ ID NO:381) of a native sequence PRO526 cDNA, wherein SEQ ID NO:381 is a clone designated herein as "DNA44184-1319".

Figure 382 shows the amino acid sequence (SEQ ID NO:382) derived from the coding sequence of SEQ ID NO:381 shown in Figure 381.

Figure 383 shows a nucleotide sequence (SEQ ID NO:383) of a native sequence PRO381 cDNA, wherein SEQ ID NO:383 is a clone designated herein as "DNA44194-1317".

Figure 384 shows the amino acid sequence (SEQ ID NO:384) derived from the coding sequence of SEQ ID NO:383 shown in Figure 383.

Figure 385 shows a nucleotide sequence (SEQ ID NO:385) of a native sequence PRO846 cDNA, wherein SEQ ID NO:385 is a clone designated herein as "DNA44196-1353".

Figure 386 shows the amino acid sequence (SEQ ID NO:386) derived from the coding sequence of SEQ ID NO:385 shown in Figure 385.

Figure 387 shows a nucleotide sequence (SEQ ID NO:387) of a native sequence PRO363 cDNA, wherein SEQ ID NO:387 is a clone designated herein as "DNA45419-1252".

Figure 388 shows the amino acid sequence (SEQ ID NO:388) derived from the coding sequence of SEQ ID NO:387 shown in Figure 387.

Figure 389 shows a nucleotide sequence (SEQ ID NO:389) of a native sequence PRO365 cDNA, wherein SEQ ID NO:389 is a clone designated herein as "DNA46777-1253".

Figure 390 shows the amino acid sequence (SEQ ID NO:390) derived from the coding sequence of SEQ ID NO:389 shown in Figure 389.

Figure 391 shows a nucleotide sequence (SEQ ID NO:391) of a native sequence PRO1310 cDNA, wherein SEQ ID NO:391 is a clone designated herein as "DNA47394-1572".

Figure 392 shows the amino acid sequence (SEQ ID NO:392) derived from the coding sequence of SEQ ID NO:391 shown in Figure 391.

Figure 393 shows a nucleotide sequence (SEQ ID NO:393) of a native sequence PRO731 cDNA, wherein SEQ ID NO:393 is a clone designated herein as "DNA48331-1329".

Figure 394 shows the amino acid sequence (SEQ ID NO:394) derived from the coding sequence of SEQ ID NO:393 shown in Figure 393.

Figure 395 shows a nucleotide sequence (SEQ ID NO:395) of a native sequence PRO322 cDNA, wherein SEQ ID NO:395 is a clone designated herein as "DNA48336-1309".

Figure 396 shows the amino acid sequence (SEQ ID NO:396) derived from the coding sequence of SEQ ID NO:395 shown in Figure 395.

Figure 397 shows a nucleotide sequence (SEQ ID NO:397) of a native sequence PRO536 cDNA, wherein SEQ ID NO:397 is a clone designated herein as "DNA49142-1430".

Figure 398 shows the amino acid sequence (SEQ ID NO:398) derived from the coding sequence of SEQ ID NO:397 shown in Figure 397.

Figure 399 shows a nucleotide sequence (SEQ ID NO:399) of a native sequence PRO719 cDNA, wherein SEQ ID NO:399 is a clone designated herein as "DNA49646-1327".

Figure 400 shows the amino acid sequence (SEQ ID NO:400) derived from the coding sequence of SEQ ID NO:399 shown in Figure 399.

Figure 401 shows a nucleotide sequence (SEQ ID NO:401) of a native sequence PRO619 cDNA, wherein SEQ ID NO:401 is a clone designated herein as "DNA49821-1562".

Figure 402 shows the amino acid sequence (SEQ ID NO:402) derived from the coding sequence of SEQ ID NO:401 shown in Figure 401.

Figure 403 shows a nucleotide sequence (SEQ ID NO:403) of a native sequence PRO771 cDNA, wherein SEQ ID NO:403 is a clone designated herein as "DNA49829-1346".

Figure 404 shows the amino acid sequence (SEQ ID NO:404) derived from the coding sequence of SEQ ID NO:403 shown in Figure 403.

Figure 405 shows a nucleotide sequence (SEQ ID NO:405) of a native sequence PRO1083 cDNA, wherein SEQ ID NO:405 is a clone designated herein as "DNA50921-1458".

Figure 406 shows the amino acid sequence (SEQ ID NO:406) derived from the coding sequence of SEQ ID NO:405 shown in Figure 405.

Figure 407 shows a nucleotide sequence (SEQ ID NO:407) of a native sequence PRO862 cDNA, wherein SEQ ID NO:407 is a clone designated herein as "DNA52187-1354".

Figure 408 shows the amino acid sequence (SEQ ID NO:408) derived from the coding sequence of SEQ ID NO:407 shown in Figure 407.

Figure 409 shows a nucleotide sequence (SEQ ID NO:409) of a native sequence PRO733 cDNA, wherein SEQ ID NO:409 is a clone designated herein as "DNA52196-1348".

Figure 410 shows the amino acid sequence (SEQ ID NO:410) derived from the coding sequence of SEQ ID NO:409 shown in Figure 409.

Figure 411 shows a nucleotide sequence (SEQ ID NO:411) of a native sequence PRO1188 cDNA, wherein SEQ ID NO:411 is a clone designated herein as "DNA52598-1518".

Figure 412 shows the amino acid sequence (SEQ ID NO:412) derived from the coding sequence of SEQ ID NO:411 shown in Figure 411.

Figure 413 shows a nucleotide sequence (SEQ ID NO:413) of a native sequence PRO770 cDNA, wherein SEQ ID NO:413 is a clone designated herein as "DNA54228-1366".

Figure 414 shows the amino acid sequence (SEQ ID NO:414) derived from the coding sequence of SEQ ID NO:413 shown in Figure 413.

Figure 415 shows a nucleotide sequence (SEQ ID NO:415) of a native sequence PRO1080 cDNA, wherein SEQ ID NO:415 is a clone designated herein as "DNA56047-1456".

Figure 416 shows the amino acid sequence (SEQ ID NO:416) derived from the coding sequence of SEQ ID NO:415 shown in Figure 415.

Figure 417 shows a nucleotide sequence (SEQ ID NO:417) of a native sequence PRO1017 cDNA, wherein SEQ ID NO:417 is a clone designated herein as "DNA56112-1379".

Figure 418 shows the amino acid sequence (SEQ ID NO:418) derived from the coding sequence of SEQ ID NO:417 shown in Figure 417.

Figure 419 shows a nucleotide sequence (SEQ ID NO:419) of a native sequence PRO1016 cDNA, wherein SEQ ID NO:419 is a clone designated herein as "DNA56113-1378".

Figure 420 shows the amino acid sequence (SEQ ID NO:420) derived from the coding sequence of SEQ ID NO:419 shown in Figure 419.

Figure 421 shows a nucleotide sequence (SEQ ID NO:421) of a native sequence PRO792 cDNA, wherein SEQ ID NO:421 is a clone designated herein as "DNA56352-1358".

Figure 422 shows the amino acid sequence (SEQ ID NO:422) derived from the coding sequence of SEQ ID NO:421 shown in Figure 421.

Figure 423 shows a nucleotide sequence (SEQ ID NO:423) of a native sequence PRO938 cDNA, wherein SEQ ID NO:423 is a clone designated herein as "DNA56433-1406".

Figure 424 shows the amino acid sequence (SEQ ID NO:424) derived from the coding sequence of SEQ ID NO:423 shown in Figure 423.

Figure 425 shows a nucleotide sequence (SEQ ID NO:425) of a native sequence PRO1012 cDNA, wherein SEQ ID NO:425 is a clone designated herein as "DNA56439-1376".

Figure 426 shows the amino acid sequence (SEQ ID NO:426) derived from the coding sequence of SEQ ID NO:425 shown in Figure 425.

Figure 427 shows a nucleotide sequence (SEQ ID NO:427) of a native sequence PRO1008 cDNA, wherein SEQ ID NO:427 is a clone designated herein as "DNA57530-1375".

Figure 428 shows the amino acid sequence (SEQ ID NO:428) derived from the coding sequence of SEQ ID NO:427 shown in Figure 427.

Figure 429 shows a nucleotide sequence (SEQ ID NO:429) of a native sequence PRO1075 cDNA, wherein SEQ ID NO:429 is a clone designated herein as "DNA57689-1385".

Figure 430 shows the amino acid sequence (SEQ ID NO:430) derived from the coding sequence of SEQ ID NO:429 shown in Figure 429.

Figure 431 shows a nucleotide sequence (SEQ ID NO:431) of a native sequence PRO1007 cDNA, wherein SEQ ID NO:431 is a clone designated herein as "DNA57690-1374".

Figure 432 shows the amino acid sequence (SEQ ID NO:432) derived from the coding sequence of SEQ ID NO:431 shown in Figure 431.

Figure 433 shows a nucleotide sequence (SEQ ID NO:433) of a native sequence PRO1056 cDNA, wherein SEQ ID NO:433 is a clone designated herein as "DNA57693-1424".

Figure 434 shows the amino acid sequence (SEQ ID NO:434) derived from the coding sequence of SEQ ID NO:433 shown in Figure 433.

Figure 435 shows a nucleotide sequence (SEQ ID NO:435) of a native sequence PRO791 cDNA, wherein SEQ ID NO:435 is a clone designated herein as "DNA57838-1337".

Figure 436 shows the amino acid sequence (SEQ ID NO:436) derived from the coding sequence of SEQ ID NO:435 shown in Figure 435.

Figure 437 shows a nucleotide sequence (SEQ ID NO:437) of a native sequence PRO1111 cDNA, wherein SEQ ID NO:437 is a clone designated herein as "DNA58721-1475".

Figure 438 shows the amino acid sequence (SEQ ID NO:438) derived from the coding sequence of SEQ ID NO:437 shown in Figure 437.

Figure 439 shows a nucleotide sequence (SEQ ID NO:439) of a native sequence PRO812 cDNA, wherein SEQ ID NO:439 is a clone designated herein as "DNA59205-1421".

Figure 440 shows the amino acid sequence (SEQ ID NO:440) derived from the coding sequence of SEQ ID NO:439 shown in Figure 439.

Figure 441 shows a nucleotide sequence (SEQ ID NO:441) of a native sequence PRO1066 cDNA, wherein SEQ ID NO:441 is a clone designated herein as "DNA59215-1425".

Figure 442 shows the amino acid sequence (SEQ ID NO:442) derived from the coding sequence of SEQ ID NO:441 shown in Figure 441.

Figure 443 shows a nucleotide sequence (SEQ ID NO:443) of a native sequence PRO1185 cDNA, wherein SEQ ID NO:443 is a clone designated herein as "DNA59220-1514".

Figure 444 shows the amino acid sequence (SEQ ID NO:444) derived from the coding sequence of SEQ ID NO:443 shown in Figure 443.

Figure 445 shows a nucleotide sequence (SEQ ID NO:445) of a native sequence PRO1031 cDNA, wherein SEQ ID NO:445 is a clone designated herein as "DNA59294-1381".

Figure 446 shows the amino acid sequence (SEQ ID NO:446) derived from the coding sequence of SEQ ID NO:445 shown in Figure 445.

Figure 447 shows a nucleotide sequence (SEQ ID NO:447) of a native sequence PRO1360 cDNA, wherein SEQ ID NO:447 is a clone designated herein as "DNA59488-1603".

Figure 448 shows the amino acid sequence (SEQ ID NO:448) derived from the coding sequence of SEQ ID NO:447 shown in Figure 447.

Figure 449 shows a nucleotide sequence (SEQ ID NO:449) of a native sequence PRO1309 cDNA, wherein SEQ ID NO:449 is a clone designated herein as "DNA59588-1571".

Figure 450 shows the amino acid sequence (SEQ ID NO:450) derived from the coding sequence of SEQ ID NO:449 shown in Figure 449.

Figure 451 shows a nucleotide sequence (SEQ ID NO:451) of a native sequence PRO1107 cDNA, wherein SEQ ID NO:451 is a clone designated herein as "DNA59606-1471".

Figure 452 shows the amino acid sequence (SEQ ID NO:452) derived from the coding sequence of SEQ ID NO:451 shown in Figure 451.

Figure 453 shows a nucleotide sequence (SEQ ID NO:453) of a native sequence PRO836 cDNA, wherein SEQ ID NO:453 is a clone designated herein as "DNA59620-1463".

Figure 454 shows the amino acid sequence (SEQ ID NO:454) derived from the coding sequence of SEQ ID NO:453 shown in Figure 453.

Figure 455 shows a nucleotide sequence (SEQ ID NO:455) of a native sequence PRO1132 cDNA, wherein SEQ ID NO:455 is a clone designated herein as "DNA59767-1489".

Figure 456 shows the amino acid sequence (SEQ ID NO:456) derived from the coding sequence of SEQ ID NO:455 shown in Figure 455.

Figure 457 shows a nucleotide sequence (SEQ ID NO:457) of a native sequence PRO1131 cDNA, wherein SEQ ID NO:457 is a clone designated herein as "DNA59777-1480".

Figure 458 shows the amino acid sequence (SEQ ID NO:458) derived from the coding sequence of SEQ ID NO:457 shown in Figure 457.

Figure 459 shows a nucleotide sequence (SEQ ID NO:459) of a native sequence PRO1130 cDNA, wherein SEQ ID NO:459 is a clone designated herein as "DNA59814-1486".

Figure 460 shows the amino acid sequence (SEQ ID NO:460) derived from the coding sequence of SEQ ID NO:459 shown in Figure 459.

Figure 461 shows a nucleotide sequence (SEQ ID NO:461) of a native sequence PRO844 cDNA, wherein SEQ ID NO:461 is a clone designated herein as "DNA59839-1461".

Figure 462 shows the amino acid sequence (SEQ ID NO:462) derived from the coding sequence of SEQ ID NO:461 shown in Figure 461.

Figure 463 shows a nucleotide sequence (SEQ ID NO:463) of a native sequence PRO1154 cDNA, wherein SEQ ID NO:463 is a clone designated herein as "DNA59846-1503".

Figure 464 shows the amino acid sequence (SEQ ID NO:464) derived from the coding sequence of SEQ ID NO:463 shown in Figure 463.

Figure 465 shows a nucleotide sequence (SEQ ID NO:465) of a native sequence PRO1181 cDNA, wherein SEQ ID NO:465 is a clone designated herein as "DNA59847-1511".

Figure 466 shows the amino acid sequence (SEQ ID NO:466) derived from the coding sequence of SEQ ID NO:465 shown in Figure 465.

Figure 467 shows a nucleotide sequence (SEQ ID NO:467) of a native sequence PRO1126 cDNA, wherein SEQ ID NO:467 is a clone designated herein as "DNA60615-1483".

Figure 468 shows the amino acid sequence (SEQ ID NO:468) derived from the coding sequence of SEQ ID NO:467 shown in Figure 467.

Figure 469 shows a nucleotide sequence (SEQ ID NO:469) of a native sequence PRO1186 cDNA, wherein SEQ ID NO:469 is a clone designated herein as "DNA60621-1516".

Figure 470 shows the amino acid sequence (SEQ ID NO:470) derived from the coding sequence of SEQ ID NO:469 shown in Figure 469.

Figure 471 shows a nucleotide sequence (SEQ ID NO:471) of a native sequence PRO1198 cDNA, wherein SEQ ID NO:471 is a clone designated herein as "DNA60622-1525".

Figure 472 shows the amino acid sequence (SEQ ID NO:472) derived from the coding sequence of SEQ ID NO:471 shown in Figure 471.

Figure 473 shows a nucleotide sequence (SEQ ID NO:473) of a native sequence PRO1159 cDNA, wherein SEQ ID NO:473 is a clone designated herein as "DNA60627-1508".

Figure 474 shows the amino acid sequence (SEQ ID NO:474) derived from the coding sequence of SEQ ID NO:473 shown in Figure 473.

Figure 475 shows a nucleotide sequence (SEQ ID NO:475) of a native sequence PRO1265 cDNA, wherein SEQ ID NO:475 is a clone designated herein as "DNA60764-1533".

Figure 476 shows the amino acid sequence (SEQ ID NO:476) derived from the coding sequence of SEQ ID NO:475 shown in Figure 475.

Figure 477 shows a nucleotide sequence (SEQ ID NO:477) of a native sequence PRO1250 cDNA, wherein SEQ ID NO:477 is a clone designated herein as "DNA60775-1532".

Figure 478 shows the amino acid sequence (SEQ ID NO:478) derived from the coding sequence of SEQ ID NO:477 shown in Figure 477.

Figure 479 shows a nucleotide sequence (SEQ ID NO:479) of a native sequence PRO1475 cDNA, wherein SEQ ID NO:479 is a clone designated herein as "DNA61185-1646".

Figure 480 shows the amino acid sequence (SEQ ID NO:480) derived from the coding sequence of SEQ ID NO:479 shown in Figure 479.

Figure 481 shows a nucleotide sequence (SEQ ID NO:481) of a native sequence PRO1312 cDNA, wherein SEQ ID NO:481 is a clone designated herein as "DNA61873-1574".

Figure 482 shows the amino acid sequence (SEQ ID NO:482) derived from the coding sequence of SEQ ID NO:481 shown in Figure 481.

Figure 483 shows a nucleotide sequence (SEQ ID NO:483) of a native sequence PRO1308 cDNA, wherein SEQ ID NO:483 is a clone designated herein as "DNA62306-1570".

Figure 484 shows the amino acid sequence (SEQ ID NO:484) derived from the coding sequence of SEQ ID NO:483 shown in Figure 483.

Figure 485 shows a nucleotide sequence (SEQ ID NO:485) of a native sequence PRO1326 cDNA, wherein SEQ ID NO:485 is a clone designated herein as "DNA62808-1582".

Figure 486 shows the amino acid sequence (SEQ ID NO:486) derived from the coding sequence of SEQ ID NO:485 shown in Figure 485.

Figure 487 shows a nucleotide sequence (SEQ ID NO:487) of a native sequence PRO1192 cDNA, wherein SEQ ID NO:487 is a clone designated herein as "DNA62814-1521".

Figure 488 shows the amino acid sequence (SEQ ID NO:488) derived from the coding sequence of SEQ ID NO:487 shown in Figure 487.

Figure 489 shows a nucleotide sequence (SEQ ID NO:489) of a native sequence PRO1246 cDNA, wherein SEQ ID NO:489 is a clone designated herein as "DNA64885-1529".

Figure 490 shows the amino acid sequence (SEQ ID NO:490) derived from the coding sequence of SEQ ID NO:489 shown in Figure 489.

Figure 491 shows a nucleotide sequence (SEQ ID NO:491) of a native sequence PRO1356 cDNA, wherein SEQ ID NO:491 is a clone designated herein as "DNA64886-1601".

Figure 492 shows the amino acid sequence (SEQ ID NO:492) derived from the coding sequence of SEQ ID NO:491 shown in Figure 491.

Figure 493 shows a nucleotide sequence (SEQ ID NO:493) of a native sequence PRO1275 cDNA, wherein SEQ ID NO:493 is a clone designated herein as "DNA64888-1542".

Figure 494 shows the amino acid sequence (SEQ ID NO:494) derived from the coding sequence of SEQ ID NO:493 shown in Figure 493.

Figure 495 shows a nucleotide sequence (SEQ ID NO:495) of a native sequence PRO1274 cDNA, wherein SEQ ID NO:495 is a clone designated herein as "DNA64889-1541".

Figure 496 shows the amino acid sequence (SEQ ID NO:496) derived from the coding sequence of SEQ ID NO:495 shown in Figure 495.

Figure 497 shows a nucleotide sequence (SEQ ID NO:497) of a native sequence PRO1358 cDNA, wherein SEQ ID NO:497 is a clone designated herein as "DNA64890-1612".

Figure 498 shows the amino acid sequence (SEQ ID NO:498) derived from the coding sequence of SEQ ID NO:497 shown in Figure 497.

Figure 499 shows a nucleotide sequence (SEQ ID NO:499) of a native sequence PRO1286 cDNA, wherein SEQ ID NO:499 is a clone designated herein as "DNA64903-1553".

Figure 500 shows the amino acid sequence (SEQ ID NO:500) derived from the coding sequence of SEQ ID NO:499 shown in Figure 499.

Figure 501 shows a nucleotide sequence (SEQ ID NO:501) of a native sequence PRO1294 cDNA, wherein SEQ ID NO:501 is a clone designated herein as "DNA64905-1558".

Figure 502 shows the amino acid sequence (SEQ ID NO:502) derived from the coding sequence of SEQ ID NO:501 shown in Figure 501.

Figure 503 shows a nucleotide sequence (SEQ ID NO:503) of a native sequence PRO1273 cDNA, wherein SEQ ID NO:503 is a clone designated herein as "DNA65402-1540".

Figure 504 shows the amino acid sequence (SEQ ID NO:504) derived from the coding sequence of SEQ ID NO:503 shown in Figure 503.

Figure 505 shows a nucleotide sequence (SEQ ID NO:505) of a native sequence PRO1279 cDNA, wherein SEQ ID NO:505 is a clone designated herein as "DNA65405-1547".

Figure 506 shows the amino acid sequence (SEQ ID NO:506) derived from the coding sequence of SEQ ID NO:505 shown in Figure 505.

Figure 507 shows a nucleotide sequence (SEQ ID NO:507) of a native sequence PRO1195 cDNA, wherein SEQ ID NO:507 is a clone designated herein as "DNA65412-1523".

Figure 508 shows the amino acid sequence (SEQ ID NO:508) derived from the coding sequence of SEQ ID NO:507 shown in Figure 507.

Figure 509 shows a nucleotide sequence (SEQ ID NO:509) of a native sequence PRO1271 cDNA, wherein SEQ ID NO:509 is a clone designated herein as "DNA66309-1538".

Figure 510 shows the amino acid sequence (SEQ ID NO:510) derived from the coding sequence of SEQ ID NO:509 shown in Figure 509.

Figure 511 shows a nucleotide sequence (SEQ ID NO:511) of a native sequence PRO1338 cDNA, wherein SEQ ID NO:511 is a clone designated herein as "DNA66667-1596".

Figure 512 shows the amino acid sequence (SEQ ID NO:512) derived from the coding sequence of SEQ ID NO:511 shown in Figure 511.

Figure 513 shows a nucleotide sequence (SEQ ID NO:513) of a native sequence PRO1343 cDNA, wherein SEQ ID NO:513 is a clone designated herein as "DNA66675-1587".

Figure 514 shows the amino acid sequence (SEQ ID NO:514) derived from the coding sequence of SEQ ID NO:513 shown in Figure 513.

Figure 515 shows a nucleotide sequence (SEQ ID NO:515) of a native sequence PRO1434 cDNA, wherein SEQ ID NO:515 is a clone designated herein as "DNA68818-2536".

Figure 516 shows the amino acid sequence (SEQ ID NO:516) derived from the coding sequence of SEQ ID NO:515 shown in Figure 515.

Figure 517 shows a nucleotide sequence (SEQ ID NO:517) of a native sequence PRO1418 cDNA, wherein SEQ ID NO:517 is a clone designated herein as "DNA68864-1629".

Figure 518 shows the amino acid sequence (SEQ ID NO:518) derived from the coding sequence of SEQ ID NO:517 shown in Figure 517.

Figure 519 shows a nucleotide sequence (SEQ ID NO:519) of a native sequence PRO1387 cDNA, wherein SEQ ID NO:519 is a clone designated herein as "DNA68872-1620".

Figure 520 shows the amino acid sequence (SEQ ID NO:520) derived from the coding sequence of SEQ ID NO:519 shown in Figure 519.

Figure 521 shows a nucleotide sequence (SEQ ID NO:521) of a native sequence PRO1384 cDNA, wherein SEQ ID NO:521 is a clone designated herein as "DNA71159-1617".

Figure 522 shows the amino acid sequence (SEQ ID NO:522) derived from the coding sequence of SEQ ID NO:521 shown in Figure 521.

Figure 523 shows a nucleotide sequence (SEQ ID NO:523) of a native sequence PRO1565 cDNA, wherein SEQ ID NO:523 is a clone designated herein as "DNA73727-1673".

Figure 524 shows the amino acid sequence (SEQ ID NO:524) derived from the coding sequence of SEQ ID NO:523 shown in Figure 523.

Figure 525 shows a nucleotide sequence (SEQ ID NO:525) of a native sequence PRO1474 cDNA, wherein SEQ ID NO:525 is a clone designated herein as "DNA73739-1645".

Figure 526 shows the amino acid sequence (SEQ ID NO:526) derived from the coding sequence of SEQ ID NO:525 shown in Figure 525.

Figure 527 shows a nucleotide sequence (SEQ ID NO:527) of a native sequence PRO1917 cDNA, wherein SEQ ID NO:527 is a clone designated herein as "DNA76400-2528".

Figure 528 shows the amino acid sequence (SEQ ID NO:528) derived from the coding sequence of SEQ ID NO:527 shown in Figure 527.

Figure 529 shows a nucleotide sequence (SEQ ID NO:529) of a native sequence PRO1787 cDNA, wherein SEQ ID NO:529 is a clone designated herein as "DNA76510-2504".

Figure 530 shows the amino acid sequence (SEQ ID NO:530) derived from the coding sequence of SEQ ID NO:529 shown in Figure 529.

Figure 531 shows a nucleotide sequence (SEQ ID NO:531) of a native sequence PRO1556 cDNA, wherein SEQ ID NO:531 is a clone designated herein as "DNA76529-1666".

Figure 532 shows the amino acid sequence (SEQ ID NO:532) derived from the coding sequence of SEQ ID NO:531 shown in Figure 531.

Figure 533 shows a nucleotide sequence (SEQ ID NO:533) of a native sequence PRO1561 cDNA, wherein SEQ ID NO:533 is a clone designated herein as "DNA76538-1670".

Figure 534 shows the amino acid sequence (SEQ ID NO:534) derived from the coding sequence of SEQ ID NO:533 shown in Figure 533.

Figure 535 shows a nucleotide sequence (SEQ ID NO:535) of a native sequence PRO1693 cDNA, wherein SEQ ID NO:535 is a clone designated herein as "DNA77301-1708".

Figure 536 shows the amino acid sequence (SEQ ID NO:536) derived from the coding sequence of SEQ ID NO:535 shown in Figure 535.

Figure 537 shows a nucleotide sequence (SEQ ID NO:537) of a native sequence PRO1868 cDNA, wherein SEQ ID NO:537 is a clone designated herein as "DNA77624-2515".

Figure 538 shows the amino acid sequence (SEQ ID NO:538) derived from the coding sequence of SEQ ID NO:537 shown in Figure 537.

Figure 539 shows a nucleotide sequence (SEQ ID NO:539) of a native sequence PRO1890 cDNA, wherein SEQ ID NO:539 is a clone designated herein as "DNA79230-2525".

Figure 540 shows the amino acid sequence (SEQ ID NO:540) derived from the coding sequence of SEQ ID NO:539 shown in Figure 539.

Figure 541 shows a nucleotide sequence (SEQ ID NO:541) of a native sequence PRO1887 cDNA, wherein SEQ ID NO:541 is a clone designated herein as "DNA79862-2522".

Figure 542 shows the amino acid sequence (SEQ ID NO:542) derived from the coding sequence of SEQ ID NO:541 shown in Figure 541.

Figure 543 shows a nucleotide sequence (SEQ ID NO:543) of a native sequence PRO4353 cDNA, wherein SEQ ID NO:543 is a clone designated herein as "DNA80145-2594".

Figure 544 shows the amino acid sequence (SEQ ID NO:544) derived from the coding sequence of SEQ ID NO:543 shown in Figure 543.

Figure 545 shows a nucleotide sequence (SEQ ID NO:545) of a native sequence PRO1801 cDNA, wherein SEQ ID NO:545 is a clone designated herein as "DNA83500-2506".

Figure 546 shows the amino acid sequence (SEQ ID NO:546) derived from the coding sequence of SEQ ID NO:545 shown in Figure 545.

Figure 547 shows a nucleotide sequence (SEQ ID NO:547) of a native sequence PRO4357 cDNA, wherein SEQ ID NO:547 is a clone designated herein as "DNA84917-2597".

Figure 548 shows the amino acid sequence (SEQ ID NO:548) derived from the coding sequence of SEQ ID NO:547 shown in Figure 547.

Figure 549 shows a nucleotide sequence (SEQ ID NO:549) of a native sequence PRO4302 cDNA, wherein SEQ ID NO:549 is a clone designated herein as "DNA92218-2554".

Figure 550 shows the amino acid sequence (SEQ ID NO:550) derived from the coding sequence of SEQ ID NO:549 shown in Figure 549.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

I. 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.

A "native sequence PRO polypeptide" comprises a polypeptide having the same amino acid sequence as the corresponding PRO polypeptide derived from nature. Such native sequence PRO polypeptides can be

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

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 comtemplated by the present invention.

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.

"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.

"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, California 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.

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

100 times the fraction X/Y

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.

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.

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.

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

100 times the fraction X/Y

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.

"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.

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

"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, California 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.

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

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.

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.

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.

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

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.

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

"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.

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.

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.

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.

The term "antibody" is used in the broadest sense and specifically covers, for example, single anti-PRO monoclonal antibodies (including agonist, antagonist, and neutralizing antibodies), anti-PRO antibody compositions with polyepitopic 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.

"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).

"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/50mM 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 x SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x 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 x SSC (sodium chloride/sodium citrate) and 50% formamide at 55°C, followed by a high-stringency wash consisting of 0.1 x SSC containing EDTA at 55°C.

"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 that those described above. An example of moderately stringent conditions is overnight incubation at 37°C in a solution comprising: 20% formamide, 5 x SSC (150 mM NaCl, 15 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5 x Denhardt's solution, 10% dextran sulfate, and 20 mg/ml denatured sheared salmon sperm DNA, followed by washing the filters in 1 x 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.

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).

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.

"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.

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.

"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.

"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.

"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.

Administration "in combination with" one or more further therapeutic agents includes simultaneous (concurrent) and consecutive administration in any order.

"Carriers" as used herein include pharmaceutically acceptable carriers, excipients, or stabilizers which are nontoxic 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 dextrins; 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™.

"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.

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.

"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.

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.

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.

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.

"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, Rosenburg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994).

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).

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.

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.

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.

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. Patent No. 4,275,149.

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.

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

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},
/* H */  {-1, 1,-3, 1, 1,-2,-2, 6,-2, 0, 0,-2,-2, 2,_M, 0, 3, 2,-1,-1, 0,-2,-3, 0, 0, 2},
/* I */  {-1,-2,-2,-2,-2, 1,-3,-2, 5, 0,-2, 2, 2,-2,_M,-2,-2,-2,-1, 0, 0, 4,-5, 0,-1,-2},
/* J */  { 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,_M, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0},
/* K */  {-1, 0,-5, 0, 0,-5,-2, 0,-2, 0, 5,-3, 0, 1,_M,-1, 1, 3, 0, 0, 0,-2,-3, 0,-4, 0},
/* L */  {-2,-3,-6,-4,-3, 2,-4,-2, 2, 0,-3, 6, 4,-3,_M,-3,-2,-3,-3,-1, 0, 2,-2, 0,-1,-2},
/* M */  {-1,-2,-5,-3,-2, 0,-3,-2, 2, 0, 0, 4, 6,-2,_M,-2,-1, 0,-2,-1, 0, 2,-4, 0,-2,-1},
/* N */  { 0, 2,-4, 2, 1,-4, 0, 2,-2, 0, 1,-3,-2, 2,_M,-1, 1, 0, 1, 0, 0,-2,-4, 0,-2, 1},
/* O */  {_M,_M,_M,_M,_M,_M,_M,_M,_M,_M,_M,_M,_M,_M, 0,_M,_M,_M,_M,_M,_M,_M,_M,_M,_M,_M},
/* P */  { 1,-1,-3,-1,-1,-5,-1, 0,-2, 0,-1,-3,-2,-1,_M, 6, 0, 0, 1, 0, 0,-1,-6, 0,-5, 0},
/* Q */  { 0, 1,-5, 2, 2,-5,-1, 3,-2, 0, 1,-2,-1, 1,_M, 0, 4, 1,-1,-1, 0,-2,-5, 0,-4, 3},
/* R */  {-2, 0,-4,-1,-1,-4,-3, 2,-2, 0, 3,-3, 0, 0,_M, 0, 1, 6, 0,-1, 0,-2, 2, 0,-4, 0},
/* S */  { 1, 0, 0, 0, 0,-3, 1,-1,-1, 0, 0,-3,-2, 1,_M, 1,-1, 0, 2, 1, 0,-1,-2, 0,-3, 0},
/* T */  { 1, 0,-2, 0, 0,-3, 0,-1, 0, 0, 0,-1,-1, 0,_M, 0,-1,-1, 1, 3, 0, 0,-5, 0,-3, 0},
/* U */  { 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,_M, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0},
/* V */  { 0,-2,-2,-2,-2,-1,-1,-2, 4, 0,-2, 2, 2,-2,_M,-1,-2,-2,-1, 0, 0, 4,-6, 0,-2,-2},
/* W */  {-6,-5,-8,-7,-7, 0,-7,-3,-5, 0,-3,-2,-4,-4,_M,-6,-5, 2,-2,-5, 0,-6,17, 0, 0,-6},
/* X */  { 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0,_M, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0},
/* Y */  {-3,-3, 0,-4,-4, 7,-5, 0,-1, 0,-4,-1,-2,-2,_M,-5,-4,-4,-3,-3, 0,-2, 0, 0,10,-4},
/* Z */  { 0, 1,-5, 2, 3,-5, 0, 2,-2, 0, 0,-2,-1, 1,_M, 0, 3, 0, 0, 0, 0,-2,-6, 0,-4, 4}
};
```

Table 1 (cont')

```
/*
 */
#include <stdio.h>
#include <ctype.h>

#define  MAXJMP      16      /* max jumps in a diag */
#define  MAXGAP      24      /* don't continue to penalize gaps larger than this */
#define  JMPS        1024    /* max jmps in an path */
#define  MX          4       /* save if there's at least MX-1 bases since last jmp */

#define  DMAT        3       /* value of matching bases */
#define  DMIS        0       /* penalty for mismatched bases */
#define  DINS0       8       /* penalty for a gap */
#define  DINS1       1       /* penalty per base */
#define  PINS0       8       /* penalty for a gap */
#define  PINS1       4       /* penalty per residue */

struct jmp {
        short           n[MAXJMP];      /* size of jmp (neg for dely) */
        unsigned short  x[MAXJMP];      /* base no. of jmp in seq x */
};                                      /* limits seq to 2^16 -1 */

struct diag {
        int             score;          /* score at last jmp */
        long            offset;         /* offset of prev block */
        short           ijmp;           /* current jmp index */
        struct jmp      jp;             /* list of jmps */
};

struct path {
        int     spc;            /* number of leading spaces */
        short   n[JMPS];/* size of jmp (gap) */
        int     x[JMPS];/* loc of jmp (last elem before gap) */
};

char            *ofile;         /* output file name */
char            *namex[2];      /* seq names: getseqs() */
char            *prog;          /* prog name for err msgs */
char            *seqx[2];       /* seqs: getseqs() */
int             dmax;           /* best diag: nw() */
int             dmax0;          /* final diag */
int             dna;            /* set if dna: main() */
int             endgaps;        /* set if penalizing end gaps */
int             gapx, gapy;     /* total gaps in seqs */
int             len0, len1;     /* seq lens */
int             ngapx, ngapy;   /* total size of gaps */
int             smax;           /* max score: nw() */
int             *xbm;           /* bitmap for matching */
long            offset;         /* current offset in jmp file */
struct  diag    *dx;            /* holds diagonals */
struct  path    pp[2];          /* holds path for seqs */

char            *calloc(), *malloc(), *index(), *strcpy();
char            *getseq(), *g_calloc();
```

Table 1 (cont')

```
/* Needleman-Wunsch alignment program
 *
 * usage: progs file1 file2
 *   where file1 and file2 are two dna or two protein sequences.
 *   The sequences can be in upper- or lower-case an may contain ambiguity
 *   Any lines beginning with ';', '>' or '<' are ignored
 *   Max file length is 65535 (limited by unsigned short x in the jmp struct)
 *   A sequence with 1/3 or more of its elements ACGTU is assumed to be DNA
 *   Output is in the file "align.out"
 *
 * The program may create a tmp file in /tmp to hold info about traceback.
 * Original version developed under BSD 4.3 on a vax 8650
 */
#include "nw.h"
#include "day.h"

static  _dbval[26] = {
        1,14,2,13,0,0,4,11,0,0,12,0,3,15,0,0,0,5,6,8,8,7,9,0,10,0
};

static  _pbval[26] = {
        1, 2|(1<<('D'-'A'))|(1<<('N'-'A')), 4, 8, 16, 32, 64,
        128, 256, 0xFFFFFFFF, 1<<10, 1<<11, 1<<12, 1<<13, 1<<14,
        1<<15, 1<<16, 1<<17, 1<<18, 1<<19, 1<<20, 1<<21, 1<<22,
        1<<23, 1<<24, 1<<25|(1<<('E'-'A'))|(1<<('Q'-'A'))
};

main(ac, av)                                                    main
        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 */
}
```

Table 1 (cont')

```
/* 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()                                                                    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
                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;
                }
```

Table 1 (cont')

...nw

```
for (py = seqx[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
         */
```

Table 1 (cont')

...nw

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

Table 1 (cont')

```
/*
 *
 * print() -- only routine visible outside this module
 *
 * static:
 * getmat() -- trace back best path, count matches: print()
 * pr_align() -- print alignment of described in array p[]: print()
 * dumpblock() -- dump a block of lines with numbers, stars: pr_align()
 * nums() -- put out a number line: dumpblock()
 * putline() -- put out a line (name, [num], seq, [num]): dumpblock()
 * stars() - -put a line of stars: dumpblock()
 * stripname() -- strip any path and prefix from a seqname
 */

#include "nw.h"

#define SPC     3
#define P_LINE  256     /* maximum output line */
#define P_SPC   3       /* space between name or num and seq */

extern  _day[26][26];
int     olen;           /* set output line length */
FILE    *fx;            /* output file */

print()                                                          print
{
        int     lx, ly, firstgap, lastgap;      /* overlap */

        if ((fx = fopen(ofile, "w")) == 0) {
                fprintf(stderr,"%s: can't write %s\n", prog, ofile);
                cleanup(1);
        }
        fprintf(fx, "< first sequence: %s (length = %d)\n", namex[0], len0);
        fprintf(fx, "< second sequence: %s (length = %d)\n", namex[1], len1);
        olen = 60;
        lx = len0;
        ly = len1;
        firstgap = lastgap = 0;
        if (dmax < len1 - 1) {          /* leading gap in x */
                pp[0].spc = firstgap = len1 - dmax - 1;
                ly -= pp[0].spc;
        }
        else if (dmax > len1 - 1) {  /* leading gap in y */
                pp[1].spc = firstgap = dmax - (len1 - 1);
                lx -= pp[1].spc;
        }
        if (dmax0 < len0 - 1) {         /* trailing gap in x */
                lastgap = len0 - dmax0 -1;
                lx -= lastgap;
        }
        else if (dmax0 > len0 - 1) { /* trailing gap in y */
                lastgap = dmax0 - (len0 - 1);
                ly -= lastgap;
        }
        getmat(lx, ly, firstgap, lastgap);
        pr_align();
}
```

Table 1 (cont')

```
/*
 * trace back the best path, count matches
 */
static
getmat(lx, ly, firstgap, lastgap)                                    getmat
        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)
                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);
```

Table 1 (cont')

```
        fprintf(fx, "<gaps in first sequence: %d", gapx);                    ...getmat
        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()                                                           pr_align
        {
                int             nn;     /* char count */
                int             more;
                register        i;

                for (i =  0, lmax = 0; i < 2; i++) {
                        nn = stripname(namex[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];                 }
```

Table 1 (cont')

...pr_align

```
for (nn = nm = 0, more = 1; more; ) {
        for (i = more = 0; i < 2; i++) {
                /*
                 * do we have more of this sequence?
                 */
                if (!*ps[i])
                        continue;

                more++;

                if (pp[i].spc) {        /* leading space */
                        *po[i]++ = ' ';
                        pp[i].spc--;
                }
                else if (siz[i]) {      /* in a gap */
                        *po[i]++ = '-';
                        siz[i]--;
                }
                else {                  /* we're putting a seq element
                                         */
                        *po[i] = *ps[i];
                        if (islower(*ps[i]))
                                *ps[i] = toupper(*ps[i]);
                        po[i]++;
                        ps[i]++;

                        /*
                         * are we at next gap for this seq?
                         */
                        if (ni[i] == pp[i].x[ij[i]]) {
                                /*
                                 * we need to merge all gaps
                                 * at this location
                                 */
                                siz[i] = pp[i].n[ij[i]++];
                                while (ni[i] == pp[i].x[ij[i]])
                                        siz[i] += pp[i].n[ij[i]++];
                        }
                        ni[i]++;
                }
        }
        if (++nn == olen || !more && nn) {
                dumpblock();
                for (i = 0; i < 2; i++)
                        po[i] = out[i];
                nn = 0;
        }
}
}
```

dumpblock

```
/*
 * dump a block of lines, including numbers, stars: pr_align()
 */
static
dumpblock()
{
        register  i;

        for (i = 0; i < 2; i++)
                *po[i]-- = '\0';
```

Table 1 (cont')

...dumpblock

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

/*
 * put out a number line: dumpblock()
 */
static
nums(ix)
```

nums

```
        int     ix;     /* index in out[] holding seq line */
{
        char            nline[P_LINE];
        register        i, j;
        register char   *pn, *px, *py;

        for (pn = nline, i = 0; i < lmax+P_SPC; i++, pn++)
                *pn = ' ';
        for (i = nc[ix], py = out[ix]; *py; py++, pn++) {
                if (*py == ' ' || *py == '-')
                        *pn = ' ';
                else {
                        if (i%10 == 0 || (i == 1 && nc[ix] != 1)) {
                                j = (i < 0)? -i : i;
                                for (px = pn; j; j /= 10, px--)
                                        *px = j%10 + '0';
                                if (i < 0)
                                        *px = '-';
                        }
                        else
                                *pn = ' ';
                        i++;
                }
        }
        *pn = '\0';
        nc[ix] = i;
        for (pn = nline; *pn; pn++)
                (void) putc(*pn, fx);
        (void) putc('\n', fx);
}

/*
 * put out a line (name, [num], seq, [num]): dumpblock()
 */
static
putline(ix)
```

putline

```
        int     ix;                     {
```

Table 1 (cont')

...putline

```
        int             i;
        register char   *px;

        for (px = namex[ix], i = 0; *px && *px != ':'; px++, i++)
                (void) putc(*px, fx);
        for (; i < lmax+P_SPC; i++)
                (void) putc(' ', fx);

        /* these count from 1:
         * ni[] is current element (from 1)
         * nc[] is number at start of current line
         */
        for (px = out[ix]; *px; px++)
                (void) putc(*px&0x7F, fx);
        (void) putc('\n', fx);
}

/*
 * put a line of stars (seqs always in out[0], out[1]): dumpblock()
 */
static
stars()
{
        int             i;
        register char   *p0, *p1, cx, *px;

        if (!*out[0] || (*out[0] == ' ' && *(po[0]) == ' ') ||
            !*out[1] || (*out[1] == ' ' && *(po[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';
}
```

...stars

Table 1 (cont')

```
/*
 * strip path or prefix from pn, return len: pr_align()
 */
static
stripname(pn)                                                    stripname
        char    *pn;    /* file name (may be path) */
{
        register char   *px, *py;

        py = 0;
        for (px = pn; *px; px++)
                if (*px == '/')
                        py = px + 1;
        if (py)
                (void) strcpy(pn, py);
        return(strlen(pn));

}
```

Table 1 (cont')

```
/*
 * cleanup() -- cleanup any tmp file
 * getseq() -- read in seq, set dna, len, maxlen
 * g_calloc() -- calloc() with error checkin
 * readjmps() -- get the good jmps, from tmp file if necessary
 * writejmps() -- write a filled array of jmps to a tmp file: nw()
 */
#include "nw.h"
#include <sys/file.h>

char    *jname = "/tmp/homgXXXXXX";             /* tmp file for jmps */
FILE    *fj;

int     cleanup();                              /* cleanup tmp file */
long    lseek();

/*
 * remove any tmp file if we blow
 */
cleanup(i)                                                          cleanup
        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)                                                   getseq
        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';
```

Table 1 (cont')

...getseq

```
        py = pseq + 4;
        *len = tlen;
        rewind(fp);

        while (fgets(line, 1024, fp)) {
                if (*line == ';' || *line == '<' || *line == '>')
                        continue;
                for (px = line; *px != '\n'; px++) {
                        if (isupper(*px))
                                *py++ = *px;
                        else if (islower(*px))
                                *py++ = toupper(*px);
                        if (index("ATGCU",*(py-1)))
                                natgc++;
                        }
                }
                *py++ = '\0';
                *py = '\0';
                (void) fclose(fp);
                dna = natgc > (tlen/3);
                return(pseq+4);
        }

        char    *
        g_calloc(msg, nx, sz)                                                    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--)
                                        ;
```

Table 1 (cont')

...readjmps

```
                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++;
                        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;
}                                       }
```

Table 1 (cont')

writejmps

```
/*
 * 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);
}
```

Table 2

PRO	XXXXXXXXXXXXXXX	(Length = 15 amino acids)
Comparison Protein	XXXXXYYYYYYY	(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%

Table 3

PRO	XXXXXXXXXX	(Length = 10 amino acids)
Comparison Protein	XXXXXYYYYYYZZZYZ	(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%

Table 4

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

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%

II. Compositions and Methods of the Invention

A. Full-Length PRO Polypeptides

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.

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

B. PRO Polypeptide Variants

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.

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

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.

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.

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

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:

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

(2) neutral hydrophilic: cys, ser, thr;

(3) acidic: asp, glu;

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

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

(6) aromatic: trp, tyr, phe.

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.

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.

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.

C. Modifications of PRO

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

octane and agents such as methyl-3-[(p-azidophenyl)dithio]propioimidate.

Other modifications include deamidation of glutaminyl and asparaginyl 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.

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.

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.

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 11 September 1987, and in Aplin and Wriston, CRC Crit. Rev. Biochem., pp. 259-306 (1981).

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).

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. Patent Nos. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192 or 4,179,337.

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.

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)].

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 US Patent No. 5,428,130 issued June 27, 1995.

D. Preparation of PRO

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, CA (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, CA) 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

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).

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)].

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.

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

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

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.

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 29 June 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. Patent 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).

Suitable host cells for cloning or expressing the DNA in the vectors herein include prokaryote, yeast, or higher eukaryote cells. Suitable prokaryotes include but are not limited to eubacteria, such as Gram-negative or Gram-positive organisms, for example, Enterobacteriaceae such as *E. coli*. Various *E. coli* strains are publicly available, such as *E. coli* K12 strain MM294 (ATCC 31,446); *E. coli* X1776 (ATCC 31,537); *E. coli* strain W3110 (ATCC 27,325) and K5 772 (ATCC 53,635). Other suitable prokaryotic host cells include Enterobacteriaceae such as *Escherichia*, e.g., *E. coli*, *Enterobacter*, *Erwinia*, *Klebsiella*, *Proteus*, *Salmonella*, e.g., *Salmonella typhimurium*, *Serratia*, e.g., *Serratia marcescans*, and *Shigella*, as well as *Bacilli* such as *B. subtilis* and *B. licheniformis* (e.g., *B. licheniformis* 41P disclosed in DD 266,710 published 12 April 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. Patent No. 4,946,783 issued 7 August 1990. Alternatively, *in vitro* methods of cloning, e.g., PCR or other nucleic acid polymerase reactions, are suitable.

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 2 May 1985); *Kluyveromyces* hosts (U.S. Patent 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. wickeramii* (ATCC 24,178), *K. waltii* (ATCC 56,500), *K. drosophilarum* (ATCC 36,906; Van den Berg et al., Bio/Technology, 8:135 (1990)), *K. thermotolerans*, and *K. marxianus; yarrowia* (EP 402,226); *Pichia pastoris* (EP 183,070; 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]); *Schwanniomyces* such as *Schwanniomyces occidentalis* (EP 394,538 published 31 October 1990); and filamentous fungi such as, e.g., *Neurospora, Penicillium, Tolypocladium* (WO 91/00357 published 10 January 1991), and *Aspergillus* hosts such as *A. nidulans* (Ballance et al., Biochem. Biophys. Res. Commun., 112:284-289 [1983]; Tilburn et al.,

Gene, 26:205-221 [1983]; Yelton et al., Proc. Natl. Acad. Sci. USA, 81: 1470-1474 [1984]) and *A. niger* (Kelly and Hynes, EMBO J., 4:475-479 [1985]). Methylotropic 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).

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

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.

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. Patent No. 5,010,182), or acid phosphatase leader, the *C. albicans* glucoamylase leader (EP 362,179 published 4 April 1990), or the signal described in WO 90/13646 published 15 November 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.

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

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*.

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

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.

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.

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.

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 5 July

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.

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.

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.

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

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.

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

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.

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

E. Uses for PRO

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.

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

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

Other useful fragments of the PRO nucleic acids include antisense or sense oligonucleotides comprising a singe-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).

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.

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.

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

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.

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.

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.

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

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.

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.

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. Patent 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.

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

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.

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).

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.

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.

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.

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 dextrins; 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.

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.

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.

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

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.

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 μg/kg/day to 10 mg/kg/day, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature; see, for example, U.S. Pat. Nos. 4,657,760; 5,206,344; or 5,225,212. It is anticipated that different formulations will be effective for different treatment compounds and different disorders, that administration targeting one organ or tissue, for example, may necessitate delivery in a manner different from that to another organ or tissue.

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.

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.

This invention encompasses methods of screening compounds to identify those that mimic the PRO polypeptide (agonists) or prevent the effect of the PRO polypeptide (antagonists). Screening assays for antagonist drug candidates are designed to identify compounds that bind or complex with the PRO polypeptides

encoded by the genes identified herein, or otherwise interfere with the interaction of the encoded polypeptides with other cellular proteins. Such screening assays will include assays amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates.

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.

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.

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.

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

domains involved in specific protein interactions as well as to pinpoint amino acid residues that are crucial for these interactions.

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.

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.

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.

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.

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.

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, FL, 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.

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.

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 September 18, 1997).

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*.

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.

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

F. Anti-PRO Antibodies

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

1. Polyclonal Antibodies

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

2. Monoclonal Antibodies

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*.

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.

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, California and the American Type Culture Collection, Manassas, Virginia. 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].

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

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.

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.

The monoclonal antibodies may also be made by recombinant DNA methods, such as those described in U.S. Patent 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. Patent 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.

The antibodies may be monovalent antibodies. Methods for preparing monovalent antibodies are well known in the art. For example, one method involves recombinant expression of immunoglobulin light chain and modified heavy chain. The heavy chain is truncated generally at any point in the Fc region so as to prevent

heavy chain crosslinking. Alternatively, the relevant cysteine residues are substituted with another amino acid residue or are deleted so as to prevent crosslinking.

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

3. Human and Humanized Antibodies

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)].

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. Patent 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.

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. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in the following scientific publications: Marks *et al.*, Bio/Technology 10, 779-783 (1992); Lonberg *et al.*, Nature 368 856-859 (1994); Morrison, Nature 368, 812-13 (1994); Fishwild *et al.*, Nature Biotechnology 14, 845-51 (1996); Neuberger, Nature Biotechnology 14, 826 (1996); Lonberg and Huszar, Intern. Rev. Immunol. 13 65-93 (1995).

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

4. Bispecific Antibodies

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.

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 13 May 1993, and in Traunecker et al., EMBO J., 10:3655-3659 (1991).

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).

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.

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.

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.

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

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

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 (CD16) so as to focus cellular defense mechanisms to the cell expressing the particular PRO polypeptide. Bispecific antibodies may also be used to localize cytotoxic agents to cells which express a particular PRO polypeptide. These antibodies possess a PRO-binding arm and an arm which binds a cytotoxic agent or a radionuclide chelator, such as EOTUBE, DPTA, DOTA, or TETA. Another bispecific antibody of interest binds the PRO polypeptide and further binds tissue factor (TF).

5. Heteroconjugate Antibodies

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. Patent 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. Patent No. 4,676,980.

6. Effector Function Engineering

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

7. Immunoconjugates

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).

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 adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutareldehyde), 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-methyldiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the antibody. See WO94/11026.

In another embodiment, the antibody may be conjugated to a "receptor" (such streptavidin) for utilization in tumor pretargeting wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound conjugate from the circulation using a clearing agent and then administration of a "ligand" (*e.g.*, avidin) that is conjugated to a cytotoxic agent (*e.g.*, a radionucleotide).

8. Immunoliposomes

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. Patent No. 5,013,556.

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

9. Pharmaceutical Compositions of Antibodies

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.

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.

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-(methylmethacylate) microcapsules, respectively, in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nano-particles, and nanocapsules) or in macroemulsions. Such techniques are disclosed in Remington's Pharmaceutical Sciences, *supra*.

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

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 sulfhydryl residues, lyophilizing from acidic solutions, controlling moisture content, using appropriate additives, and developing specific polymer matrix compositions.

G. Uses for anti-PRO Antibodies

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 ^{3}H, ^{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).

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 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.

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

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

EXAMPLES

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

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, CA). The search was performed using the computer program BLAST or BLAST-2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons with a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, WA).

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.

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 1-1.5kbp. 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.

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, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI 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

1. Preparation of oligo dT primed cDNA library

mRNA was isolated from a human tissue of interest using reagents and protocols from Invitrogen, San Diego, CA (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 SalI/NotI linkered 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.

2. Preparation of random primed cDNA library

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, linkered 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.

3. Transformation and Detection

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.

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.

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

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, NY, p. 207 (1994). The overnight culture was then diluted to about 2 x 10^6 cells/ml (approx. OD_{600}=0.1) into fresh YEPD broth (500 ml) and regrown to 1 x 10^7 cells/ml (approx. OD_{600}=0.4-0.5).

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 Li_2OOCCH_3), and resuspended into LiAc/TE (2.5 ml).

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 Li_2OOCCH_3, pH 7.5) was added. This mixture was gently mixed and incubated at 30°C while agitating for 30 minutes. The cells were then heat shocked at 42°C for 15 minutes, and the reaction vessel centrifuged in a microfuge at 12,000 rpm for 5-10 seconds, decanted and resuspended into TE (500 μl, 10 mM Tris-HCl, 1 mM EDTA pH 7.5) followed by recentrifugation. The cells

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

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

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, NY, p. 208-210 (1994). Transformants were grown at 30°C for 2-3 days.

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).

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.

4. Isolation of DNA by PCR Amplification

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

5'-TGTAAAACGACGGCCAGTTAAATAGACCTGCAATTATTAATCT-3' (SEQ ID NO:553)

The sequence of reverse oligonucleotide 2 was:

5'-CAGGAAACAGCTATGACCACCTGCACACCTGCAAATCCATT-3' (SEQ ID NO:554)

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

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.

Following the PCR, an aliquot of the reaction (5 μl) 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, CA).

EXAMPLE 3: Isolation of cDNA Clones Using Signal Algorithm Analysis

Various polypeptide-encoding nucleic acid sequences were identified by applying a proprietary signal sequence finding algorithm developed by Genentech, Inc. (South San Francisco, CA) upon ESTs as well as clustered and assembled EST fragments from public (e.g., GenBank) and/or private (LIFESEQ®, Incyte Pharmaceuticals, Inc., Palo Alto, CA) 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

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
DNA16438-1387	209771	April 14, 1998
DNA19360-2552	203654	February 9, 1999
DNA33455-1548	PTA-127	May 25, 1999
DNA37155-2651	PTA-429	July 27, 1999
DNA38269-2654	PTA-432	July 27, 1999
DNA40619-1220	209525	December 10, 1997

Table 7 (cont')

Material	ATCC Dep. No.	Deposit Date
DNA44174-2513	203577	January 12, 1999
DNA44675-2662	PTA-430	July 27, 1999
DNA45408-2615	PTA-203	June 8, 1999
DNA48606-1479	203040	July 1, 1998
DNA52753-2656	PTA-611	August 31, 1999
DNA53915-1258	209593	January 21, 1998
DNA53991-2553	203649	February 9, 1999
DNA54009-2517	203574	January 12, 1999
DNA56055-1643	PTA-129	May 25, 1999
DNA57033-1403	209905	May 27, 1998
DNA57252-1453	203585	January 12, 1999
DNA58799-1652	203665	February 9, 1999
DNA59770-2652	PTA-427	July 27, 1999
DNA59774-2665	PTA-615	August 31, 1999
DNA60281-2518	203582	January 12, 1999
DNA60736-2559	203838	March 9, 1999
DNA61875-2653	PTA-428	July 27, 1999
DNA62312-2558	203836	March 9, 1999
DNA62849-1604	PTA-205	June 8, 1999
DNA66307-2661	PTA-431	July 27, 1999
DNA66677-2535	203659	February 9, 1999
DNA71235-1706	203584	January 12, 1999
DNA71289-2547	PTA-126	May 25, 1999
DNA73775-1707	PTA-128	May 25, 1999
DNA76385-1692	203664	February 9, 1999
DNA76395-2527	203578	January 12, 1999
DNA77622-2516	203554	December 22, 1998
DNA77629-2573	203850	March 16, 1999
DNA77645-2648	PTA-45	May 11, 1999
DNA79302-2521	203545	December 22, 1998
DNA79865-2519	203544	December 22, 1998
DNA80135-2655	PTA-234	June 15, 1999
DNA80794-2568	203848	March 16, 1999
DNA80796-2523	203555	December 22, 1998
DNA80840-2605	203949	April 20, 1999
DNA80899-2501	203539	December 15, 1998
DNA81228-2580	203871	March 23, 1999
DNA81761-2583	203862	March 23, 1999
DNA82358-2738	PTA-510	August 10, 1999
DNA82364-2538	203603	January 20, 1999
DNA82424-2566	203813	March 2, 1999
DNA82430-2557	203812	March 2, 1999
DNA83500-2506	203391	October 29, 1998
DNA83509-2612	203965	April 27, 1999
DNA83560-2569	203816	March 2, 1999
DNA84139-2555	203814	March 2, 1999
DNA84141-2556	203810	March 2, 1999
DNA84142-2613	PTA-22	May 4, 1999
DNA84318-2520	203580	January 12, 1999
DNA84909-2590	203889	March 30, 1999
DNA84912-2610	203964	April 27, 1999
DNA84925-2514	203548	December 22, 1998
DNA84928-2564	203817	March 2, 1999
DNA84932-2657	PTA-235	June 15, 1999

Table 7 (cont')

Material	ATCC Dep. No.	Deposit Date
DNA86592-2607	203968	April 27, 1999
DNA86594-2587	203894	March 30, 1999
DNA86647-2591	203893	March 30, 1999
DNA87185-2563	203811	March 2, 1999
DNA87656-2582	203867	March 23, 1999
DNA87974-2609	203963	April 27, 1999
DNA88001-2565	203815	March 2, 1999
DNA88004-2575	203890	March 30, 1999
DNA89220-2608	PTA-130	May 25, 1999
DNA89947-2618	203970	April 27, 1999
DNA90842-2574	203845	March 16, 1999
DNA91775-2581	203861	March 23, 1999
DNA91779-2571	203844	March 16, 1999
DNA92217-2697	PTA-513	August 10, 1999
DNA92219-2541	203663	February 9, 1999
DNA92223-2567	203851	March 16, 1999
DNA92225-2603	203950	April 20, 1999
DNA92232-2589	203895	March 30, 1999
DNA92233-2599	PTA-134	May 25, 1999
DNA92243-2549	203852	March 16, 1999
DNA92253-2671	PTA-258	June 22, 1999
DNA92254-2672	PTA-259	June 22, 1999
DNA92255-2584	203866	March 23, 1999
DNA92269-2570	203853	March 16, 1999
DNA92288-2588	203892	March 30, 1999
DNA92290-2550	203847	March 16, 1999
DNA93012-2622	PTA-21	May 4, 1999
DNA93020-2642	PTA-121	May 25, 1999
DNA94830-2604	203951	April 20, 1999
DNA94833-2579	203869	March 23, 1999
DNA94838-2658	PTA-232	June 15, 1999
DNA94844-2686	PTA-385	July 20, 1999
DNA94854-2586	203864	March 23, 1999
DNA96868-2677	PTA-262	June 22, 1999
DNA96871-2683	PTA-381	July 20, 1999
DNA96880-2624	PTA-15	May 4, 1999
DNA96986-2660	PTA-239	June 15, 1999
DNA96988-2685	PTA-384	July 20, 1999
DNA96995-2709	PTA-475	August 3, 1999
DNA97004-2562	203854	March 16, 1999
DNA97005-2687	PTA-378	July 20, 1999
DNA97009-2668	PTA-257	June 22, 1999
DNA97013-2667	PTA-231	June 15, 1999
DNA98380-2690	PTA-388	July 20, 1999
DNA98561-2696	PTA-620	August 31, 1999
DNA98575-2644	PTA-118	May 25, 1999
DNA98593-2694	PTA-477	August 3, 1999
DNA98600-2703	PTA-488	August 3, 1999
DNA99391-2572	203849	March 16, 1999
DNA99393-2560	203837	March 9, 1999
DNA100276-2684	PTA-380	July 20, 1999
DNA100312-2645	PTA-44	May 11, 1999
DNA100902-2646	PTA-42	May 11, 1999
DNA102899-2679	PTA-123	May 25, 1999

Table 7 (cont')

Material	ATCC Dep. No.	Deposit Date
DNA104875-2720	PTA-482	August 3, 1999
DNA105680-2710	PTA-483	August 3, 1999
DNA105779-2708	PTA-485	August 3, 1999
DNA105794-2695	PTA-480	August 3, 1999
DNA105838-2702	PTA-476	August 3, 1999
DNA107698-2715	PTA-472	August 3, 1999
DNA107701-2711	PTA-487	August 3, 1999
DNA107781-2707	PTA-484	August 3, 1999
DNA108670-2744	PTA-546	August 17, 1999
DNA108688-2725	PTA-515	August 10, 1999
DNA108769-2765	PTA-861	October 19, 1999
DNA108935-2721	PTA-518	August 10, 1999
DNA110700-2716	PTA-512	August 10, 1999
DNA111750-2706	PTA-489	August 3, 1999
DNA123430-2755	PTA-614	August 31, 1999
DNA125154-2785	PTA-957	November 16,1999
DNA142238-2768	PTA-819	October 5, 1999
DNA22779-1130	209280	September 18, 1997
DNA26847-1395	209772	April 14, 1998
DNA27864-1155	209375	October 16, 1997
DNA27865-1091	209296	September 23, 1997
DNA28497-1130	209279	September 18, 1997
DNA29101-1122	209653	March 5, 1998
DNA32286-1191	209385	October 16, 1997
DNA32288-1132	209261	September 16, 1997
DNA32290-1164	209384	October 16, 1997
DNA32292-1131	209258	September 16, 1997
DNA32298-1132	209257	September 16, 1997
DNA33085-1110	209087	May 30, 1997
DNA33087-1158	209381	October 16, 1997
DNA33089-1132	209262	September 16, 1997
DNA33092-1202	209420	October 28, 1997
DNA33094-1131	209256	September 16, 1997
DNA33107-1135	209251	September 16, 1997
DNA33221-1133	209263	September 16, 1997
DNA33223-1136	209264	September 16, 1997
DNA33460-1166	209376	October 16, 1997
DNA33473-1176	209391	October 17, 1997
DNA33785-1143	209417	October 28, 1997
DNA33786-1132	209253	September 16, 1997
DNA34353-1428	209855	May 12, 1998
DNA34392-1170	209526	December 10, 1997
DNA34434-1139	209252	September 16, 1997
DNA35558-1167	209374	October 16, 1997
DNA35595-1228	209528	December 10, 1997
DNA35638-1216	209265	September 16, 1997
DNA35639-1172	209396	October 17, 1997
DNA35663-1129	209201	August 18, 1997
DNA35674-1142	209416	October 28, 1997
DNA35841-1173	209403	October 17, 1997
DNA35916-1161	209419	October 28, 1997
DNA35918-1174	209402	October 17, 1997
DNA36350-1158	209378	October 16, 1997
DNA37140-1234	209489	November 21, 1997

Table 7 (cont')

Material	ATCC Dep. No.	Deposit Date
DNA37150-1178	209401	October 17, 1997
DNA38260-1180	209397	October 17, 1997
DNA40021-1154	209389	October 17, 1997
DNA40587-1231	209438	November 7, 1997
DNA40592-1242	209492	November 21, 1997
DNA40620-1183	209388	October 17, 1997
DNA40628-1216	209432	November 7, 1997
DNA40981-1234	209439	November 7, 1997
DNA40982-1235	209433	November 7, 1997
DNA41234-1242	209618	February 5, 1998
DNA43046-1225	209484	November 21, 1997
DNA43316-1237	209487	November 21, 1997
DNA44167-1243	209434	November 7, 1997
DNA44184-1319	209704	March 26, 1998
DNA44194-1317	209808	April 28, 1998
DNA44196-1353	209847	May 6, 1998
DNA45419-1252	209616	February 5, 1998
DNA46777-1253	209619	February 5, 1998
DNA47394-1572	203109	August 11, 1998
DNA48331-1329	209715	March 31, 1998
DNA48336-1309	209669	March 11, 1998
DNA49142-1430	203002	June 23, 1998
DNA49646-1327	209705	March 26, 1998
DNA49821-1562	209981	June 16, 1998
DNA49829-1346	209749	April 7, 1998
DNA50921-1458	209859	May 12, 1998
DNA52187-1354	209845	May 6, 1998
DNA52196-1348	209748	April 7, 1998
DNA52598-1518	203107	August 11, 1998
DNA54228-1366	209801	April 23, 1998
DNA56047-1456	209948	June 9, 1998
DNA56112-1379	209883	May 20, 1998
DNA56113-1378	203049	July 1, 1998
DNA56352-1358	209846	May 6, 1998
DNA56433-1406	209857	May 12, 1998
DNA56439-1376	209864	May 14, 1998
DNA57530-1375	209880	May 20, 1998
DNA57689-1385	209869	May 14, 1998
DNA57690-1374	209950	June 9, 1998
DNA57693-1424	203008	June 23, 1998
DNA57838-1337	203014	June 23, 1998
DNA58721-1475	203110	August 11, 1998
DNA59205-1421	203009	June 23, 1998
DNA59215-1425	209961	June 9, 1998
DNA59220-1514	209962	June 9, 1998
DNA59294-1381	209866	May 14, 1998
DNA59488-1603	203157	August 25, 1998
DNA59588-1571	203106	August 11, 1998
DNA59606-1471	209945	June 9, 1998
DNA59620-1463	209989	June 16, 1998
DNA59767-1489	203108	August 11, 1998
DNA59777-1480	203111	August 11, 1998
DNA59814-1486	203359	October 20, 1998
DNA59839-1461	209988	June 16, 1998

Table 7 (cont')

Material	ATCC Dep. No.	Deposit Date
DNA59846-1503	209978	June 16, 1998
DNA59847-1511	203098	August 4, 1998
DNA60615-1483	209980	June 16, 1998
DNA60621-1516	203091	August 4, 1998
DNA60622-1525	203090	August 4, 1998
DNA60627-1508	203092	August 4, 1998
DNA60764-1533	203452	November 10, 1998
DNA60775-1532	203173	September 1, 1998
DNA61185-1646	203464	November 17, 1998
DNA61873-1574	203132	August 18, 1998
DNA62306-1570	203254	September 9, 1998
DNA62808-1582	203358	October 20, 1998
DNA62814-1521	203093	August 4, 1998
DNA64885-1529	203457	November 3, 1998
DNA64886-1601	203241	September 9, 1998
DNA64888-1542	203249	September 9, 1998
DNA64889-1541	203250	September 9, 1998
DNA64890-1612	203131	August 18, 1998
DNA64903-1553	203223	September 15, 1998
DNA64905-1558	203233	September 15, 1998
DNA65402-1540	203252	September 9, 1998
DNA65405-1547	203476	November 17, 1998
DNA65412-1523	203094	August 4, 1998
DNA66309-1538	203235	September 15, 1998
DNA66667-1596	203267	September 22, 1998
DNA66675-1587	203282	September 22, 1998
DNA68818-2536	203657	February 9, 1999
DNA68864-1629	203276	September 22, 1998
DNA68872-1620	203160	August 25, 1998
DNA71159-1617	203135	August 18, 1998
DNA73727-1673	203459	November 3, 1998
DNA73739-1645	203270	September 22, 1998
DNA76400-2528	203573	January 12, 1999
DNA76510-2504	203477	November 17, 1998
DNA76529-1666	203315	October 6, 1998
DNA76538-1670	203313	October 6, 1998
DNA77301-1708	203407	October 27, 1998
DNA77624-2515	203553	December 22, 1998
DNA79230-2525	203549	December 22, 1998
DNA79862-2522	203550	December 22, 1998
DNA80145-2594	PTA-204	June 8, 1999
DNA83500-2506	203391	October 29, 1998
DNA84917-2597	203863	March 23, 1999
DNA92218-2554	203834	March 9, 1999
DNA96042-2682	PTA-382	July 20, 1999

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).

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

EXAMPLE 5: Use of PRO as a hybridization probe

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

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.

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, 5x SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2x Denhardt's solution, and 10% dextran sulfate at 42°C for 20 hours. Washing of the filters is performed in an aqueous solution of 0.1x SSC and 0.1% SDS at 42°C.

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

EXAMPLE 6: Expression of PRO in *E. coli*

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

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.

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.

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

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.

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 $(NH_4)_2SO_4$, 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 $MgSO_4$) 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.

E. coli paste from 0.5 to 1 L fermentations (6-10 g pellets) is resuspended in 10 volumes (w/v) in 7 M guanidine, 20 mM Tris, pH 8 buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1M and 0.02 M, respectively, and the solution is stirred overnight at 4°C. This step results in a denatured protein with all cysteine residues blocked by sulfitolization. The solution is centrifuged at 40,000 rpm in a Beckman Ultracentifuge 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.

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.

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.

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

EXAMPLE 7: Expression of PRO in mammalian cells

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

The vector, pRK5 (see EP 307,247, published March 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.

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 μg pRK5-PRO DNA is mixed with about 1 μg DNA encoding the VA RNA gene [Thimmappaya et al., Cell, 31:543 (1982)] and dissolved in 500 μl of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M $CaCl_2$. To this mixture is added, dropwise, 500 μl of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM $NaPO_4$, 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.

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

In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran sulfate method described by Somparyrac et al., Proc. Natl. Acad. Sci., 12:7575 (1981). 293 cells are grown to maximal density in a spinner flask and 700 μg 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 μg/ml bovine insulin and 0.1 μg/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.

In another embodiment, PRO can be expressed in CHO cells. The pRK5-PRO can be transfected into CHO cells using known reagents such as $CaPO_4$ 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 ^{35}S-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.

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 Ni^{2+}-chelate affinity chromatography.

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.

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.

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.

Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect® (Quiagen), Dosper® or Fugene® (Boehringer

Mannheim). The cells are grown as described in Lucas et al., supra. Approximately 3 x 10^{-7} cells are frozen in an ampule for further growth and production as described below.

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 μm filtered PS20 with 5% 0.2 μm 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 x 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. Patent No. 5,122,469, issued June 16, 1992 may actually be used. A 3L production spinner is seeded at 1.2 x 10^6 cells/mL. On day 0, the cell number pH ie 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 μm filter. The filtrate was either stored at 4°C or immediately loaded onto columns for purification.

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.

Immunoadhesin (Fc-containing) constructs are purified from the conditioned media as follows. The conditioned medium is pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column is washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein is immediately neutralized by collecting 1 ml fractions into tubes containing 275 μL 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.

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

EXAMPLE 8: Expression of PRO in Yeast

The following method describes recombinant expression of PRO in yeast.

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.

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.

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.

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

EXAMPLE 9: Expression of PRO in Baculovirus-Infected Insect Cells

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

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.

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

Expressed poly-his tagged PRO can then be purified, for example, by Ni^{2+}-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 $MgCl_2$; 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 Ni^{2+}-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 A_{280} 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 A_{280} 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 Ni^{2+}-NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His_{10}-tagged PRO are pooled and dialyzed against loading buffer.

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.

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

EXAMPLE 10: Preparation of Antibodies that Bind PRO

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

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.

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, MT) 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.

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.

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.

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

EXAMPLE 11: Purification of PRO Polypeptides Using Specific Antibodies

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.

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.

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.

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

EXAMPLE 12: Drug Screening

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.

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.

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 September 13, 1984. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. As applied to a PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. Bound PRO polypeptide is detected by methods well known in the art. Purified PRO polypeptide can also be coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the peptide and immobilize it on the solid support.

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

EXAMPLE 13: Rational Drug Design

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)).

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).

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.

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

EXAMPLE 14: Identification of PRO Polypeptides That Stimulate TNF-α Release In Human Blood (Assay 128)

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 μl of human blood supplemented with 50mM Hepes buffer (pH 7.2) is aliquoted per well in a 96 well test plate. To each well is then added 300μl 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 50μl 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.

The following PRO polypeptides tested positive in this assay: PRO195, PRO202, PRO215, PRO221, PRO217, PRO222, PRO198, PRO245, PRO172, PRO265, PRO266, PRO344, PRO337, PRO322, PRO1286, PRO1279, PRO1338 and PRO1343.

EXAMPLE 15: Detection of Polypeptides That Affect Glucose or FFA Uptake in Skeletal Muscle (Assay 106)

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

In a 96 well format, PRO polypeptides to be assayed are added to primary rat differentiated skeletal muscle, and allowed to incubate overnight. Then fresh media with the PRO polypeptide and +/- insulin are added to the wells. The sample media is then monitored to determine glucose and FFA uptake by the skeletal muscle cells. The insulin will stimulate glucose and FFA uptake by the skeletal muscle, and insulin in media without the PRO polypeptide is used as a positive control, and a limit for scoring. As the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay if greater than 1.5 times or less than 0.5 times the insulin control.

The following PRO polypeptides tested positive as being capable of affecting glucose and/or FFA uptake by skeletal muscle in this assay: PRO182, PRO366, PRO198, PRO172 and PRO719.

EXAMPLE 16: Chondrocyte Re-differentiation Assay (Assay 110)

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 articulary cartilage of metacarpophalangeal joints of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm^2 in Ham F-12 containing 10% FBS and 4 μg/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 100μl of the same media without serum and 100 μl of the test PRO polypeptide, 5 nM staurosporin (positive control) or medium alone (negative control) is added to give a final volume of 200 μl/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.

The following polypeptide tested positive in this assay: PRO182, PRO366, PRO198 and PRO1868.

EXAMPLE 17: Chondrocyte Proliferation Assay (Assay 111)

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.

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/cm^2 in Ham F-12 containing 10% FBS and 4 μg/ml gentamycin. The culture media is changed every third day and the cells are reseeded to 25,000 cells/cm^2 every five days. On day 12, the cells are seeded in 96 well plates at 5,000 cells/well in 100μl of the same media without serum and 100 μl 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 μl/well. After 5 days at 37°C, 20 μl of Alamar blue is added to each well and the plates are incubated for an additional 3 hours at 37°C. The fluorescence is then measured in each well (Ex:530 nm; Em: 590 nm). The fluorescence of a plate containing 200 μl of the serum-free medium is measured to obtain the background. A positive result in the assay is obtained when the fluorescence of the PRO polypeptide treated sample is more like that of the positive control than the negative control.

The following PRO polypeptides tested positive in this assay: PRO202, PRO224, PRO172 and PRO1312.

EXAMPLE 18: Detection of PRO Polypeptides That Affect Glucose or FFA Uptake by Primary Rat Adipocytes (Assay 94)

This assay is designed to determine whether PRO polypeptides show the ability to affect glucose or FFA uptake by adipocyte cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by adipocytes

would be beneficial including, for example, obesity, diabetes or hyper- or hypo-insulinemia.

In a 96 well format, PRO polypeptides to be assayed are added to primary rat adipocytes, and allowed to incubate overnight. Samples are taken at 4 and 16 hours and assayed for glycerol, glucose and FFA uptake. After the 16 hour incubation, insulin is added to the media and allowed to incubate for 4 hours. At this time, a sample is taken and glycerol, glucose and FFA uptake is measured. Media containing insulin without the PRO polypeptide is used as a positive reference control. As the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay if greater than 1.5 times or less than 0.5 times the insulin control.

The following PRO polypeptides tested positive as being capable of affecting glucose and/or FFA uptake in this assay: PRO202, PRO211, PRO344 and PRO1338.

EXAMPLE 19: Gene Expression in Bovine Pericytes (Assay 105)

This assay is designed to identify PRO polypeptides which activate gene expression in pericytes. Such polypeptides would be expected to be useful as growth factors and/or for situations where the activation of gene expression is desired or beneficial. Bovine pericytes are plated on 60mm culture dishes in growth media for1 week. On day 1, various PRO polypeptides are diluted (1%) and incubated with the pericytes for 1, 4 and 24 hr. timepoints. The cells are harvested and the RNA isolated using TRI-Reagent following the included instructions. The RNA is then quantified by reading the 260/280 OD using a spectrophotometer. The gene expression analysis is done by TaqMan reactions using Perkin Elmer reagents and specially designed bovine probes and primers. Expression of the following genes is analyzed: GAPDH, beta-integrin, connective tissue growth factor (CTGF), ICAM-1, monocyte chemoattractant protein-1 (MCP-1), osteopontin, transforming growth factor-beta (TGF-beta), TGF-beta receptor, tissue inhibitor of metalloproteinase (TIMP), tissue factor (TF), VEGF-α, thrombospondin, VEGF-β, angiopoeitin-2, and collagenase. Replicates are then averaged and the SD determined. The gene expression levels are then normalized to GAPDH. These are then normalized to the expression levels obtained with a protein (PIN32) which does not significantly induce gene expression in bovine pericytes when compared to untreated controls. Any PRO polypeptide that gives a gene expression level 2-fold or higher over the PIN32 control is considered a positive hit.

The following PRO polypeptides tested positive in this assay: PRO366.

EXAMPLE 20: Identification of PRO Polypeptides That Activate Pericytes (Assay 125)

This assay shows that certain polypeptides of the invention act to activate proliferation of 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. Such PRO polypeptides also would be expected to be useful as growth factors and/or for situations where the induction of cell proliferation is desired or beneficial. Activation of pericyte proliferation also correlates with the induction of angiogenesis and, as such, PRO polypeptides capable of inducing pericyte proliferation 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 media is removed from the flask. On day 2, the pericytes are trypsinized, washed, spun and plated on 96 well plates. On day 7, the media is removed and the pericytes are treated with 100 μl of either the specific PRO polypeptide or control treatments (positive control = DME+5%+/- PDGF @ 500ng/μl; negative control=PIN32, a polypeptide determined to have no significant effect on pericyte proliferation). C-fos and GAPDH gene expression levels are then determined and the replicates are averaged and the SD is determined. The c-fos values are normalized to GAPDH and the results are expressed as fold increase over PIN32. Anything providing at least a 2-fold or higher response as compared to the negative control is considered positive for the assay.

The following polypeptides tested positive in this assay: PRO366.

EXAMPLE 21: Ability of PRO Polypeptides to Stimulate the Release of Proteoglycans from Cartilage (Assay 97)

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

The metacarphophalangeal joint of 4-6 month old pigs was aseptically dissected, and articular cartilage was removed by free hand slicing being careful to avoid the underlying bone. The cartilage was minced and cultured in bulk for 24 hours in a humidified atmosphere of 95% air, 5% CO_2 in serum free (SF) media (DME/F12 1:1) with 0.1% BSA and 100U/ml penicillin and 100μg/ml streptomycin. After washing three times, approximately 100 mg of articular cartilage was aliquoted into micronics tubes and incubated for an additional 24 hours in the above SF media. PRO polypeptides were then added at 1% either alone or in combination with 18 ng/ml interleukin-1α, a known stimulator of proteoglycan release from cartilage tissue. The supernatant was then harvested and assayed for the amount of proteoglycans using the 1,9-dimethyl-methylene blue (DMB) colorimetric assay (Farndale and Buttle, Biochem. Biophys. Acta 883:173-177 (1985)). A positive result in this assay indicates that the test polypeptide will find use, for example, in the treatment of sports-related joint problems, articular cartilage defects, osteoarthritis or rheumatoid arthritis.

When various PRO polypeptides were tested in the above assay, the polypeptides demonstrated a marked ability to stimulate release of proteoglycans from cartilage tissue both basally and after stimulation with interleukin-1α and at 24 and 72 hours after treatment, thereby indicating that these PRO polypeptides are useful for stimulating proteoglycan release from cartilage tissue. As such, these PRO polypeptides are useful for the treatment of sports-related joint problems, articular cartilage defects, osteoarthritis or rheumatoid arthritis. The polypeptides testing positive in this assay are : PRO216.

EXAMPLE 22: Proliferation of Rat Utricular Supporting Cells (Assay 54)

This assay shows that certain polypeptides of the invention act as potent mitogens for inner ear supporting cells which are auditory hair cell progenitors and, therefore, are useful for inducing the regeneration of auditory hair cells and treating hearing loss in mammals. The assay is performed as follows. Rat UEC-4 utricular epithelial cells are aliquoted into 96 well plates with a density of 3000 cells/well in 200 μl of serum-containing medium at 33°C. The cells are cultured overnight and are then switched to serum-free medium at

37°C. Various dilutions of PRO polypeptides (or nothing for a control) are then added to the cultures and the cells are incubated for 24 hours. After the 24 hour incubation, ^{3}H-thymidine (1 μCi/well) is added and the cells are then cultured for an additional 24 hours. The cultures are then washed to remove unincorporated radiolabel, the cells harvested and Cpm per well determined. Cpm of at least 30% or greater in the PRO polypeptide treated cultures as compared to the control cultures is considered a positive in the assay.

The following polypeptides tested positive in this assay: PRO172.

EXAMPLE 23: Stimulatory Activity in Mixed Lymphocyte Reaction (MLR) Assay (Assay 24)

This example shows that certain polypeptides of the invention are active as a stimulator of the proliferation of stimulated T-lymphocytes. Compounds which stimulate proliferation of lymphocytes are useful therapeutically where enhancement of an immune response is beneficial. A therapeutic agent may take the form of antagonists of the polypeptide of the invention, for example, murine-human chimeric, humanized or human antibodies against the polypeptide.

The basic protocol for this assay is described in Current Protocols in Immunology, unit 3.12; edited by J E Coligan, A M Kruisbeek, D H Marglies, E M Shevach, W Strober, National Institutes of Health, Published by John Wiley & Sons, Inc.

More specifically, in one assay variant, peripheral blood mononuclear cells (PBMC) are isolated from mammalian individuals, for example a human volunteer, by leukopheresis (one donor will supply stimulator PBMCs, the other donor will supply responder PBMCs). If desired, the cells are frozen in fetal bovine serum and DMSO after isolation. Frozen cells may be thawed overnight in assay media (37°C, 5% CO_2) and then washed and resuspended to $3x10^6$ cells/ml of assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate). The stimulator PBMCs are prepared by irradiating the cells (about 3000 Rads).

The assay is prepared by plating in triplicate wells a mixture of:

100:l of test sample diluted to 1% or to 0.1%,

50 :l of irradiated stimulator cells, and

50 :l of responder PBMC cells.

100 microliters of cell culture media or 100 microliter of CD4-IgG is used as the control. The wells are then incubated at 37°C, 5% CO_2 for 4 days. On day 5, each well is pulsed with tritiated thymidine (1.0 mC/well; Amersham). After 6 hours the cells are washed 3 times and then the uptake of the label is evaluated.

In another variant of this assay, PBMCs are isolated from the spleens of Balb/c mice and C57B6 mice. The cells are teased from freshly harvested spleens in assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate) and the PBMCs are isolated by overlaying these cells over Lympholyte M (Organon Teknika), centrifuging at 2000 rpm for 20 minutes, collecting and washing the mononuclear cell layer in assay media and resuspending the cells to $1x10^7$ cells/ml of assay media. The assay is then conducted as described above.

Positive increases over control are considered positive with increases of greater than or equal to 180% being preferred. However, any value greater than control indicates a stimulatory effect for the test protein.

The following PRO polypeptides tested positive in this assay: PRO344.

EXAMPLE 24: Pericyte c-Fos Induction (Assay 93)

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 μl 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 + 1X pen strep + 1X fungizone. Assay Media = low glucose DMEM +5% FBS.

The following polypeptides tested positive in this assay: PRO301, PRO619, PRO1066 and PRO1265.

EXAMPLE 25: Cytokine Release Assay (Assay 120)

This assay is designed to determine whether PRO polypeptides of the present invention are capable of inducing the release of cytokines from peripheral blood mononuclear cells (PBMCs). PRO polypeptides capable of inducing the release of cytokines from PBMCs are useful from the treatment of conditions which would benefit from enhanced cytokine release and will be readily evident to those of ordinary skill in the art. Specifically, $1x10^6$ cells/ml of peripheral blood mononuclear cells (PBMC) are cultured with 1% of a PRO polypeptide for 3 days in complete RPMI media. The supernatant is then harvested and tested for increased concentrations of various cytokines by ELISA as compared to a human IgG treated control. A positive in the assay is a 10-fold or greater increase in cytokine concentration in the PRO polypeptide treated sample as compared to the human IgG treated control.

The following polypeptides tested positive in this assay: PRO526 and PRO1343.

EXAMPLE 26: Inhibition of A-Peptide Binding to Factor VIIA (Assay 118)

This assay is designed to identify PRO polypeptides which are capable of inhibiting the binding of A-peptide to factor VIIA, thereby affecting the blood coagulation cascade. PRO polypeptides testing positive in this assay are expected to be useful for the treatment of conditions where alteration of the blood coagulation cascade would be beneficial including, for example, stroke, heart attack and various coagulation disorders. These PRO polypeptides are also useful for the identification of agonist and antagonist molecules which would

also be useful for treatment of those conditions.

Specifically, 384 well plates are coated with soluble factor VIIA and are incubated overnight at 4°C. The wells are then decanted and are blocked by the addition of 0.5% BSA for 1 hour. The wells are then washed and 20μl of biotinylated A-peptide and either various concentration of the PRO polypeptide (test) or nothing (negative control) are added to each well. The plates are then incubated for 1 hour at room temperature. The wells are again washed and then 40μl of streptavidin-europium is added to each well. The plates are then incubated for 30 minutes at room temperature and then washed. 40μl of a fluorescence enhancement solution is then added to each well, the plates incubated for 5 minutes at room temperature and each well is then read on Wallac Victor reader under europium delayed fluorescence settings. Percent inhibition of binding of the A-peptide to the factor VIIA is then determined (as compared to the negative control), wherein a positive in the assay is a percent inhibition of 30% or greater.

The following PRO polypeptides tested positive in this assay: PRO182.

EXAMPLE 27: Inhibition of Adipocyte Differentiation Assay (Assay 66)

This assay is designed to identify PRO polypeptides which are capable of inhibiting insulin-induced differentiation of adipocytes. PRO polypeptides testing positive in this assay would be expected to be useful for the treatment of conditions associated with obesity, diabetes, etc.

Specifically, 3T3-L1 cells are seeded into the wells of 96 well plates at $6x10^4$ cells/well and allowed to grow to confluency for 7 days. At day 7, the cells are treated with various concentrations of the PRO polypeptide (or nothing for the negative control) in the presence of 1μg/ml insulin, $0.25x10^{-6}$ M dexamethasone and 0.5mM IBMX. The samples are then incubated at 37°C in 7% CO_2 for 2 days. After the incubation, the media is removed by aspiration and the cells are washed with PBS and re-exposed to the PRO polypeptide (or nothing for the negative control) and 1μg/ml insulin. After 5 days, the media is removed and replaced with fresh PRO polypeptide (or nothing for the negative control) and insulin. After 5 days, the cells are lysed and the cell lysate is assayed using Sigma's Triglyceride [INT] kit (Sigma procedure #336). A positive in the assay is 20% greater inhibition of adipocyte differentiation in the PRO polypeptide treated samples as compared to the negative control.

The following PRO polypeptides tested positive in this assay: PRO185 and PRO198.

EXAMPLE 28: HUVEC Stimulation by PRO Polypeptides (Assay 131)

This assay is designed to identify PRO polypeptides which are capable of stimulating the proliferation of HUVEC cells. PRO polypeptides testing positive in this assay would be expected to be useful for inducing angiogenesis for the treatmnent of conditions where angiogenesis would be beneficial including, for example, wound healing, and the like. Antagonists of these PRO polypeptides would be expected to be useful for inhibiting angiogenesis for the treatment of, for example, tumors, and the like.

Specifically, COSTAR® flat bottom black plates are treated with fibronectin for 20 minutes and then washed twice with PBS. HUVEC cells are then plated at 2000 cells/well in an appropriate growth medium. The plates are then incubated overnight and then the PRO polypeptide (1% final concentration), nothing (negative

control) or IL1β (3.3 ng/ml final concentration; positive control) is added. The plates are again incubated overnight, stained with ICAM1-Cy5 and read on FMAT. A positive in the assay is a 2-fold or greater increase in fluorescence as compared to the positive control.

The following PRO polypeptides tested positive in this assay: PRO222.

EXAMPLE 29: Promotion of Chondrocyte Redifferentiation (Assay 129)

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.

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/cm^2 in Ham F-12 containing 10% FBS and 4 μg/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 100μl of the same media without serum and 100 μl 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 μl/well. After 5 days at 37°C, 22 μl of media comtaining 100μg/ml Hoechst 33342 and 50 μg/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).

The following PRO polypeptides tested positive in this assay: PRO301.

EXAMPLE 30: Microarray Analysis to Detect Overexpression of PRO Polypeptides in Cancerous Tumors

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.

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 March 31, 2000 and which is herein incorporated by reference.

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. Two sets of experimental data were generated. In one set, cancerous human colon tumor tissue and matched non-cancerous human colon tumor tissue from the same patient ("matched colon control") were obtained and analyzed for PRO polypeptide expression using the above described microarray technology. In the second set of data, 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.

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 the tumor tissues listed above 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 preent invention are significantly overexpressed in various human tumor tissues as compared to a non-cancerous human tissue control. 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:
PRO177	breast tumor	universal normal control
PRO177	liver tumor	universal normal control
PRO177	lung tumor	universal normal control
PRO3574	breast tumor	universal normal control
PRO3574	colon tumor	matched normal colon control
PRO1280	breast tumor	universal normal control
PRO1280	lung tumor	universal normal control
PRO4984	lung tumor	universal normal control
PRO4988	colon tumor	universal normal control
PRO4988	lung tumor	universal normal control
PRO305	lung tumor	universal normal control
PRO305	colon tumor	universal normal control
PRO1866	prostate tumor	universal normal control

Table 8 (cont')

Molecule	is overexpressed in:	as compared to:
PRO1866	lung tumor	universal normal control
PRO1866	colon tumor	universal normal control
PRO4996	breast tumor	universal normal control
PRO4996	lung tumor	universal normal control
PRO4406	lung tumor	universal normal control
PRO4406	colon tumor	universal normal control
PRO1120	colon tumor	universal normal control
PRO1120	breast tumor	universal normal control
PRO1120	rectal tumor	universal normal control
PRO4990	lung tumor	universal normal control
PRO738	cervical tumor	universal normal control
PRO738	lung tumor	universal normal control
PRO738	breast tumor	universal normal control
PRO3577	lung tumor	universal normal control
PRO1879	breast tumor	universal normal control
PRO1879	lung tumor	universal normal control
PRO1879	colon tumor	universal normal control
PRO1471	lung tumor	universal normal control
PRO1076	prostate tumor	universal normal control
PRO1483	lung tumor	universal normal control
PRO4985	rectal tumor	universal normal control
PRO4985	colon tumor	universal normal control
PRO4985	breast tumor	universal normal control
PRO4985	lung tumor	universal normal control
PRO5000	lung tumor	universal normal control
PRO1881	liver tumor	universal normal control
PRO1881	lung tumor	universal normal control
PRO1881	breast tumor	universal normal control
PRO4314	lung tumor	universal normal control
PRO4314	breast tumor	universal normal control
PRO4987	lung tumor	universal normal control
PRO4313	lung tumor	universal normal control
PRO4313	breast tumor	universal normal control
PRO4799	colon tumor	universal normal control
PRO4995	liver tumor	universal normal control
PRO4995	colon tumor	universal normal control
PRO4995	colon tumor	matched normal colon control
PRO1341	prostate tumor	universal normal control
PRO1341	lung tumor	universal normal control
PRO1341	colon tumor	universal normal control
PRO1341	colon tumor	matched normal colon control
PRO1777	lung tumor	universal normal control
PRO1777	colon tumor	matched normal colon control
PRO3580	lung tumor	universal normal control
PRO3580	prostate tumor	universal normal control
PRO1779	lung tumor	universal normal control
PRO1779	colon tumor	universal normal control
PRO1779	cervical tumor	universal normal control
PRO1754	breast tumor	universal normal control
PRO1754	lung tumor	universal normal control
PRO1906	breast tumor	universal normal control
PRO1906	colon tumor	universal normal control
PRO1906	prostate tumor	universal normal control
PRO1870	breast tumor	universal normal control

Table 8 (cont')

Molecule	is overexpressed in:	as compared to:
PRO4329	lung tumor	universal normal control
PRO4979	colon tumor	universal normal control
PRO1885	rectal tumor	universal normal control
PRO1885	colon tumor	universal normal control
PRO1885	colon tumor	matched normal colon control
PRO1882	prostate tumor	universal normal control
PRO1882	lung tumor	universal normal control
PRO1882	colon tumor	universal normal control
PRO1882	breast tumor	universal normal control
PRO1882	cervical tumor	universal normal control
PRO4989	rectal tumor	universal normal control
PRO4989	breast tumor	universal normal control
PRO4989	colon tumor	matched normal colon control
PRO4989	colon tumor	universal normal control
PRO4323	lung tumor	universal normal control
PRO4323	liver tumor	universal normal control
PRO1886	breast tumor	universal normal control
PRO1886	lung tumor	universal normal control
PRO1886	rectal tumor	universal normal control
PRO4395	colon tumor	universal normal control
PRO4395	prostate tumor	universal normal control
PRO4395	lung tumor	universal normal control
PRO4395	cervical tumor	universal normal control
PRO1782	colon tumor	universal normal control
PRO1782	lung tumor	universal normal control
PRO4388	lung tumor	universal normal control
PRO4341	breast tumor	universal normal control
PRO4341	lung tumor	universal normal control
PRO3438	lung tumor	universal normal control
PRO4321	breast tumor	universal normal control
PRO4321	lung tumor	universal normal control
PRO4321	colon tumor	universal normal control
PRO4304	breast tumor	universal normal control
PRO4304	lung tumor	universal normal control
PRO4403	colon tumor	universal normal control
PRO4403	breast tumor	universal normal control
PRO4403	lung tumor	universal normal control
PRO4324	lung tumor	universal normal control
PRO4324	breast tumor	universal normal control
PRO4303	cervical tumor	universal normal control
PRO4303	lung tumor	universal normal control
PRO4303	breast tumor	universal normal control
PRO4303	colon tumor	universal normal control
PRO4303	prostate tumor	universal normal control
PRO4305	breast tumor	universal normal control
PRO4305	lung tumor	universal normal control
PRO4305	colon tumor	universal normal control
PRO4305	liver tumor	universal normal control
PRO4404	lung tumor	universal normal control
PRO4404	breast tumor	universal normal control
PRO4404	rectal tumor	universal normal control
PRO1884	lung tumor	universal normal control
PRO4349	colon tumor	universal normal control
PRO4349	lung tumor	universal normal control

Table 8 (cont')

Molecule	is overexpressed in:	as compared to:
PRO4401	colon tumor	universal normal control
PRO4401	lung tumor	universal normal control
PRO1867	lung tumor	universal normal control
PRO1867	liver tumor	universal normal control
PRO4319	breast tumor	universal normal control
PRO4319	lung tumor	universal normal control
PRO4991	lung tumor	universal normal control
PRO4991	colon tumor	universal normal control
PRO4398	lung tumor	universal normal control
PRO4346	lung tumor	universal normal control
PRO4350	colon tumor	universal normal control
PRO4350	prostate tumor	universal normal control
PRO4350	lung tumor	universal normal control
PRO4318	prostate tumor	universal normal control
PRO4318	lung tumor	universal normal control
PRO4340	breast tumor	universal normal control
PRO4340	lung tumor	universal normal control
PRO4400	breast tumor	universal normal control
PRO4400	lung tumor	universal normal control
PRO4320	lung tumor	universal normal control
PRO4409	lung tumor	universal normal control
PRO4409	cervical tumor	universal normal control
PRO4409	colon tumor	universal normal control
PRO4399	lung tumor	universal normal control
PRO4399	breast tumor	universal normal control
PRO4418	lung tumor	universal normal control
PRO4418	breast tumor	universal normal control
PRO4330	cervical tumor	universal normal control
PRO4330	colon tumor	matched normal colon control
PRO4339	breast tumor	universal normal control
PRO4339	colon tumor	universal normal control
PRO4326	lung tumor	universal normal control
PRO4326	colon tumor	universal normal control
PRO6014	breast tumor	universal normal control
PRO3446	colon tumor	universal normal control
PRO3446	lung tumor	universal normal control
PRO4322	lung tumor	universal normal control
PRO4322	rectal tumor	universal normal control
PRO4322	colon tumor	matched normal colon control
PRO4381	breast tumor	universal normal control
PRO4381	lung tumor	universal normal control
PRO4381	colon tumor	universal normal control
PRO4348	lung tumor	universal normal control
PRO4348	prostate tumor	universal normal control
PRO4371	breast tumor	universal normal control
PRO3742	colon tumor	universal normal control
PRO3742	lung tumor	universal normal control
PRO5773	lung tumor	universal normal control
PRO5773	colon tumor	universal normal control
PRO5773	prostate tumor	universal normal control
PRO5774	colon tumor	universal normal control
PRO4343	colon tumor	universal normal control
PRO4325	lung tumor	universal normal control
PRO4347	lung tumor	universal normal control

Table 8 (cont')

Molecule	is overexpressed in:	as compared to:
PRO4347	colon tumor	universal normal control
PRO4347	rectal tumor	universal normal control
PRO3743	colon tumor	universal normal control
PRO3743	lung tumor	universal normal control
PRO3743	prostate tumor	universal normal control
PRO4426	colon tumor	universal normal control
PRO4500	colon tumor	universal normal control
PRO4389	breast tumor	universal normal control
PRO4389	lung tumor	universal normal control
PRO4337	colon tumor	universal normal control
PRO4337	breast tumor	universal normal control
PRO4337	lung tumor	universal normal control
PRO4992	lung tumor	universal normal control
PRO5996	lung tumor	universal normal control
PRO4345	lung tumor	universal normal control
PRO4345	colon tumor	universal normal control
PRO5780	lung tumor	universal normal control
PRO5780	breast tumor	universal normal control
PRO5992	lung tumor	universal normal control
PRO5992	colon tumor	universal normal control
PRO5992	breast tumor	universal normal control
PRO4428	prostate tumor	universal normal control
PRO4994	lung tumor	universal normal control
PRO5995	lung tumor	universal normal control
PRO5995	colon tumor	universal normal control
PRO6094	lung tumor	universal normal control
PRO6094	colon tumor	universal normal control
PRO4317	lung tumor	universal normal control
PRO4317	colon tumor	universal normal control
PRO4317	liver tumor	universal normal control
PRO4317	colon tumor	matched normal colon control
PRO5997	colon tumor	universal normal control
PRO5997	lung tumor	universal normal control
PRO5005	lung tumor	universal normal control
PRO5005	colon tumor	universal normal control
PRO5004	colon tumor	universal normal control
PRO6001	breast tumor	universal normal control
PRO6013	colon tumor	universal normal control
PRO4502	lung tumor	universal normal control
PRO4502	colon tumor	universal normal control
PRO6007	breast tumor	universal normal control
PRO6028	breast tumor	universal normal control
PRO6028	colon tumor	universal normal control
PRO4327	prostate tumor	universal normal control
PRO4315	colon tumor	universal normal control
PRO5993	lung tumor	universal normal control
PRO5993	colon tumor	universal normal control
PRO4503	colon tumor	universal normal control
PRO4976	lung tumor	universal normal control
PRO5798	lung tumor	universal normal control
PRO5798	colon tumor	universal normal control
PRO6242	colon tumor	universal normal control
PRO6242	colon tumor	matched normal colon control
PRO6242	breast tumor	universal normal control

Table 8 (cont')

Molecule	is overexpressed in:	as compared to:
PRO6242	liver tumor	universal normal control
PRO6242	rectal tumor	universal normal control
PRO6095	breast tumor	universal normal control
PRO6095	lung tumor	universal normal control
PRO6093	colon tumor	universal normal control
PRO6093	breast tumor	universal normal control
PRO6093	lung tumor	universal normal control
PRO6093	colon tumor	matched normal colon control
PRO6012	colon tumor	universal normal control
PRO6027	lung tumor	universal normal control
PRO6027	colon tumor	universal normal control
PRO6027	rectal tumor	universal normal control
PRO6181	prostate tumor	universal normal control
PRO6181	lung tumor	universal normal control
PRO6181	colon tumor	universal normal control
PRO6097	colon tumor	universal normal control
PRO6097	lung tumor	universal normal control
PRO6090	lung tumor	universal normal control
PRO7171	lung tumor	universal normal control
PRO7171	colon tumor	universal normal control
PRO7171	breast tumor	universal normal control
PRO6258	prostate tumor	universal normal control
PRO6258	breast tumor	universal normal control
PRO6258	cervical tumor	universal normal control
PRO6258	liver tumor	universal normal control
PRO6258	colon tumor	universal normal control
PRO9820	prostate tumor	universal normal control
PRO6243	lung tumor	universal normal control
PRO6182	lung tumor	universal normal control
PRO6079	lung tumor	universal normal control
PRO6079	colon tumor	universal normal control
PRO6079	breast tumor	universal normal control
PRO6079	prostate tumor	universal normal control
PRO7434	lung tumor	universal normal control
PRO9865	colon tumor	universal normal control
PRO9828	colon tumor	universal normal control
PRO196	colon tumor	universal normal control
PRO196	lung tumor	universal normal control
PRO196	breast tumor	universal normal control
PRO197	colon tumor	universal normal control
PRO197	lung tumor	universal normal control
PRO197	breast tumor	universal normal control
PRO195	colon tumor	universal normal control
PRO195	lung tumor	universal normal control
PRO195	breast tumor	universal normal control
PRO187	lung tumor	universal normal control
PRO187	liver tumor	universal normal control
PRO182	colon tumor	universal normal control
PRO182	lung tumor	universal normal control
PRO182	breast tumor	universal normal control
PRO188	rectal tumor	universal normal control
PRO183	colon tumor	universal normal control
PRO183	lung tumor	universal normal control
PRO183	breast tumor	universal normal control

Table 8 (cont')

Molecule	is overexpressed in:	as compared to:
PRO183	rectal tumor	universal normal control
PRO184	lung tumor	universal normal control
PRO184	breast tumor	universal normal control
PRO185	lung tumor	universal normal control
PRO200	colon tumor	universal normal control
PRO200	lung tumor	universal normal control
PRO200	breast tumor	universal normal control
PRO200	rectal tumor	universal normal control
PRO202	colon tumor	universal normal control
PRO202	lung tumor	universal normal control
PRO202	breast tumor	universal normal control
PRO202	rectal tumor	universal normal control
PRO202	liver tumor	universal normal control
PRO214	colon tumor	universal normal control
PRO214	lung tumor	universal normal control
PRO215	colon tumor	universal normal control
PRO215	lung tumor	universal normal control
PRO215	breast tumor	universal normal control
PRO219	colon tumor	universal normal control
PRO219	lung tumor	universal normal control
PRO219	breast tumor	universal normal control
PRO219	liver tumor	universal normal control
PRO211	lung tumor	universal normal control
PRO211	breast tumor	universal normal control
PRO220	colon tumor	universal normal control
PRO220	lung tumor	universal normal control
PRO220	breast tumor	universal normal control
PRO366	colon tumor	universal normal control
PRO366	lung tumor	universal normal control
PRO366	breast tumor	universal normal control
PRO216	lung tumor	universal normal control
PRO221	colon tumor	universal normal control
PRO221	lung tumor	universal normal control
PRO221	breast tumor	universal normal control
PRO228	lung tumor	universal normal control
PRO228	breast tumor	universal normal control
PRO217	lung tumor	universal normal control
PRO217	breast tumor	universal normal control
PRO222	colon tumor	universal normal control
PRO222	lung tumor	universal normal control
PRO222	breast tumor	universal normal control
PRO224	colon tumor	universal normal control
PRO224	lung tumor	universal normal control
PRO224	breast tumor	universal normal control
PRO224	prostate tumor	universal normal control
PRO224	rectal tumor	universal normal control
PRO230	colon tumor	universal normal control
PRO230	lung tumor	universal normal control
PRO230	breast tumor	universal normal control
PRO230	prostate tumor	universal normal control
PRO198	colon tumor	universal normal control
PRO198	lung tumor	universal normal control
PRO198	breast tumor	universal normal control
PRO198	liver tumor	universal normal control

Table 8 (cont')

Molecule	is overexpressed in:	as compared to:
PRO226	lung tumor	universal normal control
PRO226	breast tumor	universal normal control
PRO261	lung tumor	universal normal control
PRO242	colon tumor	universal normal control
PRO242	lung tumor	universal normal control
PRO242	breast tumor	universal normal control
PRO227	colon tumor	universal normal control
PRO227	lung tumor	universal normal control
PRO237	colon tumor	universal normal control
PRO237	lung tumor	universal normal control
PRO237	breast tumor	universal normal control
PRO237	prostate tumor	universal normal control
PRO241	colon tumor	universal normal control
PRO241	lung tumor	universal normal control
PRO241	breast tumor	universal normal control
PRO231	colon tumor	universal normal control
PRO231	lung tumor	universal normal control
PRO231	breast tumor	universal normal control
PRO231	rectal tumor	universal normal control
PRO235	colon tumor	universal normal control
PRO235	lung tumor	universal normal control
PRO235	breast tumor	universal normal control
PRO235	liver tumor	universal normal control
PRO323	lung tumor	universal normal control
PRO323	breast tumor	universal normal control
PRO323	rectal tumor	universal normal control
PRO245	colon tumor	universal normal control
PRO245	lung tumor	universal normal control
PRO245	breast tumor	universal normal control
PRO245	cervical tumor	universal normal control
PRO245	liver tumor	universal normal control
PRO246	colon tumor	universal normal control
PRO246	lung tumor	universal normal control
PRO246	breast tumor	universal normal control
PRO288	lung tumor	universal normal control
PRO288	breast tumor	universal normal control
PRO248	lung tumor	universal normal control
PRO248	rectal tumor	universal normal control
PRO257	colon tumor	universal normal control
PRO257	lung tumor	universal normal control
PRO257	prostate tumor	universal normal control
PRO172	colon tumor	universal normal control
PRO172	lung tumor	universal normal control
PRO172	breast tumor	universal normal control
PRO258	colon tumor	universal normal control
PRO258	lung tumor	universal normal control
PRO258	breast tumor	universal normal control
PRO265	lung tumor	universal normal control
PRO265	breast tumor	universal normal control
PRO265	rectal tumor	universal normal control
PRO326	colon tumor	universal normal control
PRO326	lung tumor	universal normal control
PRO326	breast tumor	universal normal control
PRO326	liver tumor	universal normal control

Table 8 (cont')

Molecule	is overexpressed in:	as compared to:
PRO266	colon tumor	universal normal control
PRO266	lung tumor	universal normal control
PRO266	breast tumor	universal normal control
PRO269	lung tumor	universal normal control
PRO269	rectal tumor	universal normal control
PRO285	colon tumor	universal normal control
PRO285	lung tumor	universal normal control
PRO285	breast tumor	universal normal control
PRO328	colon tumor	universal normal control
PRO328	lung tumor	universal normal control
PRO328	breast tumor	universal normal control
PRO344	breast tumor	universal normal control
PRO272	lung tumor	universal normal control
PRO301	colon tumor	universal normal control
PRO301	lung tumor	universal normal control
PRO301	breast tumor	universal normal control
PRO331	colon tumor	universal normal control
PRO331	lung tumor	universal normal control
PRO331	breast tumor	universal normal control
PRO332	colon tumor	universal normal control
PRO332	lung tumor	universal normal control
PRO332	breast tumor	universal normal control
PRO353	colon tumor	universal normal control
PRO353	lung tumor	universal normal control
PRO353	breast tumor	universal normal control
PRO310	colon tumor	universal normal control
PRO310	lung tumor	universal normal control
PRO310	breast tumor	universal normal control
PRO310	rectal tumor	universal normal control
PRO337	colon tumor	universal normal control
PRO337	lung tumor	universal normal control
PRO337	breast tumor	universal normal control
PRO346	lung tumor	universal normal control
PRO350	lung tumor	universal normal control
PRO350	breast tumor	universal normal control
PRO526	colon tumor	universal normal control
PRO526	lung tumor	universal normal control
PRO526	breast tumor	universal normal control
PRO381	colon tumor	universal normal control
PRO381	lung tumor	universal normal control
PRO381	breast tumor	universal normal control
PRO381	prostate tumor	universal normal control
PRO846	colon tumor	universal normal control
PRO846	lung tumor	universal normal control
PRO363	colon tumor	universal normal control
PRO363	lung tumor	universal normal control
PRO365	lung tumor	universal normal control
PRO365	breast tumor	universal normal control
PRO1310	breast tumor	universal normal control
PRO731	colon tumor	universal normal control
PRO731	lung tumor	universal normal control
PRO731	breast tumor	universal normal control
PRO322	colon tumor	universal normal control
PRO322	lung tumor	universal normal control

Table 8 (cont')

Molecule	is overexpressed in:	as compared to:
PRO322	breast tumor	universal normal control
PRO322	rectal tumor	universal normal control
PRO322	liver tumor	universal normal control
PRO536	lung tumor	universal normal control
PRO536	breast tumor	universal normal control
PRO536	liver tumor	universal normal control
PRO719	colon tumor	universal normal control
PRO719	lung tumor	universal normal control
PRO719	breast tumor	universal normal control
PRO619	colon tumor	universal normal control
PRO619	lung tumor	universal normal control
PRO619	breast tumor	universal normal control
PRO771	colon tumor	universal normal control
PRO771	lung tumor	universal normal control
PRO771	breast tumor	universal normal control
PRO1083	colon tumor	universal normal control
PRO1083	lung tumor	universal normal control
PRO1083	breast tumor	universal normal control
PRO1083	prostate tumor	universal normal control
PRO862	colon tumor	universal normal control
PRO862	lung tumor	universal normal control
PRO862	breast tumor	universal normal control
PRO733	colon tumor	universal normal control
PRO733	lung tumor	universal normal control
PRO733	breast tumor	universal normal control
PRO733	liver tumor	universal normal control
PRO1188	lung tumor	universal normal control
PRO1188	breast tumor	universal normal control
PRO1188	rectal tumor	universal normal control
PRO770	lung tumor	universal normal control
PRO770	breast tumor	universal normal control
PRO1080	colon tumor	universal normal control
PRO1080	lung tumor	universal normal control
PRO1080	breast tumor	universal normal control
PRO1017	colon tumor	universal normal control
PRO1017	lung tumor	universal normal control
PRO1017	breast tumor	universal normal control
PRO1016	colon tumor	universal normal control
PRO1016	lung tumor	universal normal control
PRO1016	breast tumor	universal normal control
PRO1016	rectal tumor	universal normal control
PRO792	lung tumor	universal normal control
PRO938	colon tumor	universal normal control
PRO938	lung tumor	universal normal control
PRO938	breast tumor	universal normal control
PRO1012	colon tumor	universal normal control
PRO1012	lung tumor	universal normal control
PRO1012	rectal tumor	universal normal control
PRO1012	liver tumor	universal normal control
PRO1008	lung tumor	universal normal control
PRO1075	colon tumor	universal normal control
PRO1075	lung tumor	universal normal control
PRO1007	colon tumor	universal normal control
PRO1007	lung tumor	universal normal control

Table 8 (cont')

Molecule	is overexpressed in:	as compared to:
PRO1007	breast tumor	universal normal control
PRO1007	rectal tumor	universal normal control
PRO1056	colon tumor	universal normal control
PRO1056	lung tumor	universal normal control
PRO1056	breast tumor	universal normal control
PRO791	colon tumor	universal normal control
PRO791	lung tumor	universal normal control
PRO791	breast tumor	universal normal control
PRO791	rectal tumor	universal normal control
PRO1111	colon tumor	universal normal control
PRO1111	lung tumor	universal normal control
PRO1111	breast tumor	universal normal control
PRO812	lung tumor	universal normal control
PRO812	breast tumor	universal normal control
PRO812	rectal tumor	universal normal control
PRO1066	lung tumor	universal normal control
PRO1185	colon tumor	universal normal control
PRO1185	lung tumor	universal normal control
PRO1185	breast tumor	universal normal control
PRO1031	lung tumor	universal normal control
PRO1360	lung tumor	universal normal control
PRO1360	breast tumor	universal normal control
PRO1309	lung tumor	universal normal control
PRO1309	breast tumor	universal normal control
PRO1107	lung tumor	universal normal control
PRO1107	breast tumor	universal normal control
PRO836	colon tumor	universal normal control
PRO836	lung tumor	universal normal control
PRO1132	lung tumor	universal normal control
PRO1132	breast tumor	universal normal control
PRO1131	colon tumor	universal normal control
PRO1131	lung tumor	universal normal control
PRO1131	breast tumor	universal normal control
PRO1131	liver tumor	universal normal control
PRO1130	colon tumor	universal normal control
PRO1130	lung tumor	universal normal control
PRO1130	breast tumor	universal normal control
PRO844	colon tumor	universal normal control
PRO844	lung tumor	universal normal control
PRO844	breast tumor	universal normal control
PRO844	rectal tumor	universal normal control
PRO1154	colon tumor	universal normal control
PRO1154	lung tumor	universal normal control
PRO1154	rectal tumor	universal normal control
PRO1154	liver tumor	universal normal control
PRO1181	lung tumor	universal normal control
PRO1181	breast tumor	universal normal control
PRO1126	colon tumor	universal normal control
PRO1126	lung tumor	universal normal control
PRO1126	breast tumor	universal normal control
PRO1126	adrenal tumor	universal normal control
PRO1186	colon tumor	universal normal control
PRO1186	lung tumor	universal normal control
PRO1186	breast tumor	universal normal control

Table 8 (cont')

Molecule	is overexpressed in:	as compared to:
PRO1186	liver tumor	universal normal control
PRO1198	colon tumor	universal normal control
PRO1198	lung tumor	universal normal control
PRO1159	lung tumor	universal normal control
PRO1159	breast tumor	universal normal control
PRO1159	liver tumor	universal normal control
PRO1265	colon tumor	universal normal control
PRO1265	breast tumor	universal normal control
PRO1250	colon tumor	universal normal control
PRO1250	lung tumor	universal normal control
PRO1250	breast tumor	universal normal control
PRO1475	colon tumor	universal normal control
PRO1475	breast tumor	universal normal control
PRO1312	colon tumor	universal normal control
PRO1312	lung tumor	universal normal control
PRO1312	breast tumor	universal normal control
PRO1308	colon tumor	universal normal control
PRO1308	lung tumor	universal normal control
PRO1308	liver tumor	universal normal control
PRO1326	colon tumor	universal normal control
PRO1325	lung tumor	universal normal control
PRO1326	breast tumor	universal normal control
PRO1192	colon tumor	universal normal control
PRO1192	lung tumor	universal normal control
PRO1192	breast tumor	universal normal control
PRO1246	colon tumor	universal normal control
PRO1246	lung tumor	universal normal control
PRO1246	breast tumor	universal normal control
PRO1246	prostate tumor	universal normal control
PRO1356	colon tumor	universal normal control
PRO1356	lung tumor	universal normal control
PRO1356	breast tumor.	universal normal control
PRO1275	lung tumor	universal normal control
PRO1275	breast tumor	universal normal control
PRO1274	lung tumor	universal normal control
PRO1358	colon tumor	universal normal control
PRO1358	lung tumor	universal normal control
PRO1358	prostate tumor	universal normal control
PRO1286	colon tumor	universal normal control
PRO1286	lung tumor	universal normal control
PRO1286	prostate tumor	universal normal control
PRO1286	rectal tumor	universal normal control
PRO1294	colon tumor	universal normal control
PRO1294	lung tumor	universal normal control
PRO1294	breast tumor	universal normal control
PRO1294	rectal tumor	universal normal control
PRO1273	lung tumor	universal normal control
PRO1273	rectal tumor	universal normal control
PRO1279	colon tumor	universal normal control
PRO1279	lung tumor	universal normal control
PRO1195	lung tumor	universal normal control
PRO1195	breast tumor	universal normal control
PRO1271	lung tumor	universal normal control
PRO1271	breast tumor	universal normal control

Table 8 (cont')

Molecule	is overexpressed in:	as compared to:
PRO1271	liver tumor	universal normal control
PRO1338	colon tumor	universal normal control
PRO1338	lung tumor	universal normal control
PRO1338	breast tumor	universal normal control
PRO1343	colon tumor	universal normal control
PRO1343	lung tumor	universal normal control
PRO1343	breast tumor	universal normal control
PRO1343	rectal tumor	universal normal control
PRO1434	lung tumor	universal normal control
PRO1418	lung tumor	universal normal control
PRO1418	liver tumor	universal normal control
PRO1387	colon tumor	universal normal control
PRO1387	lung tumor	universal normal control
PRO1387	prostate tumor	universal normal control
PRO1387	rectal tumor	universal normal control
PRO1384	colon tumor	universal normal control
PRO1384	lung tumor	universal normal control
PRO1565	colon tumor	universal normal control
PRO1565	lung tumor	universal normal control
PRO1565	prostate tumor	universal normal control
PRO1474	colon tumor	universal normal control
PRO1474	lung tumor	universal normal control
PRO1474	breast tumor	universal normal control
PRO1474	rectal tumor	universal normal control
PRO1917	colon tumor	universal normal control
PRO1917	lung tumor	universal normal control
PRO1917	breast tumor	universal normal control
PRO1787	colon tumor	universal normal control
PRO1787	lung tumor	universal normal control
PRO1787	breast tumor	universal normal control
PRO1556	lung tumor	universal normal control
PRO1556	breast tumor	universal normal control
PRO1561	colon tumor	universal normal control
PRO1561	lung tumor	universal normal control
PRO1561	rectal tumor	universal normal control
PRO1693	colon tumor	universal normal control
PRO1693	lung tumor	universal normal control
PRO1693	breast tumor	universal normal control
PRO1868	lung tumor	universal normal control
PRO1868	breast tumor	universal normal control
PRO1890	colon tumor	universal normal control
PRO1890	lung tumor	universal normal control
PRO1890	breast tumor	universal normal control
PRO1890	prostate tumor	universal normal control
PRO1887	colon tumor	universal normal control
PRO1887	breast tumor	universal normal control
PRO4353	lung tumor	universal normal control
PRO4353	breast tumor	universal normal control
PRO1801	colon tumor	universal normal control
PRO1801	lung tumor	universal normal control
PRO4357	lung tumor	universal normal control
PRO4357	breast tumor	universal normal control
PRO4302	colon tumor	universal normal control
PRO4302	lung tumor	universal normal control

Table 8 (cont')

Molecule	is overexpressed in:	as compared to:
PRO4302	breast tumor	universal normal control
PRO4302	prostate tumor	universal normal control
PRO5990	colon tumor	universal normal control
PRO5990	lung tumor	universal normal control
PRO5990	breast tumor	universal normal control

EXAMPLE 31: Identification of Receptor/Ligand Interactions

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

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

In another embodiment of this assay, an epitope-tagged potential ligand PRO polypeptide (e.g. 8 histidine "His" tag) is allowed to interact with a panel of potential receptor PRO polypeptide molecules that have

been expressed as fusions with the Fc domain of human IgG (immunoadhesins). Following a 1 hour co-incubation with the epitope tagged PRO polypeptide, the candidate receptors are each immunoprecipitated with protein A beads and the beads are washed. Potential ligand interaction is determined by western blot analysis of the immunoprecipitated complexes with antibody directed towards the epitope tag. An interaction is judged to occur if a band of the anticipated molecular weight of the epitope tagged protein is observed in the western blot analysis with a candidate receptor, but is not observed to occur with the other members of the panel of potential receptors.

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

(1) PRO1801 binds to PRO1114 and PRO4978.

(2) PRO100 binds to PRO1114.

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the construct deposited, since the deposited embodiment is intended as a single illustration of certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this invention. The deposit of material herein does not constitute an admission that the written description herein contained is inadequate to enable the practice of any aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims to the specific illustrations that it represents. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.

PCT P3330R1

Original (for **SUBMISSION**) - printed on 01.12.2000 02:57:35 PM

0-1	**Form - PCT/RO/134 (EASY) Indications Relating to Deposited Microorganism(s) or Other Biological Material (PCT Rule 13bis)**	
0-1-1	Prepared using	PCT-EASY Version 2.91 (updated 10.10.2000)
0-2	**International Application No.**	
0-3	**Applicant's or agent's file reference**	P3330R1
1	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
1-1	page	98
1-2	line	34
1-3	**Identification of Deposit**	
1-3-1	Name of depositary institution	American Type Culture Collection
1-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
1-3-3	Date of deposit	14 April 1998 (14.04.1998)
1-3-4	Accession Number	ATCC 209771
1-4	**Additional Indications**	NONE
1-5	**Designated States for Which Indications are Made**	all designated States
1-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
2	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
2-1	page	98
2-2	line	35
2-3	**Identification of Deposit**	
2-3-1	Name of depositary institution	American Type Culture Collection
2-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
2-3-3	Date of deposit	09 February 1999 (09.02.1999)
2-3-4	Accession Number	ATCC 203654
2-4	**Additional Indications**	NONE
2-5	**Designated States for Which Indications are Made**	all designated States
2-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
3	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
3-1	page	98
3-2	line	36

PCT P3330R1

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3-3	**Identification of Deposit**	
3-3-1	Name of depositary institution	**American Type Culture Collection**
3-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
3-3-3	Date of deposit	**25 May 1999 (25.05.1999)**
3-3-4	Accession Number	**ATCC PTA-127**
3-4	**Additional Indications**	**NONE**
3-5	**Designated States for Which Indications are Made**	**all designated States**
3-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
4	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
4-1	page	**98**
4-2	line	**37**
4-3	**Identification of Deposit**	
4-3-1	Name of depositary institution	**American Type Culture Collection**
4-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
4-3-3	Date of deposit	**27 July 1999 (27.07.1999)**
4-3-4	Accession Number	**ATCC PTA-429**
4-4	**Additional Indications**	**NONE**
4-5	**Designated States for Which Indications are Made**	**all designated States**
4-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
5	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
5-1	page	**98**
5-2	line	**38**
5-3	**Identification of Deposit**	
5-3-1	Name of depositary institution	**American Type Culture Collection**
5-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
5-3-3	Date of deposit	**27 July 1999 (27.07.1999)**
5-3-4	Accession Number	**ATCC PTA-432**
5-4	**Additional Indications**	**NONE**
5-5	**Designated States for Which Indications are Made**	**all designated States**
5-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	

PCT P3330R1

Original (for **SUBMISSION**) - printed on 01.12.2000 02:57:35 PM

6	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
6-1	page	98
6-2	line	39
6-3	**Identification of Deposit**	
6-3-1	Name of depositary institution	American Type Culture Collection
6-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
6-3-3	Date of deposit	10 December 1997 (10.12.1997)
6-3-4	Accession Number	ATCC 209525
6-4	**Additional Indications**	NONE
6-5	**Designated States for Which Indications are Made**	all designated States
6-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
7	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
7-1	page	99
7-2	line	2
7-3	**Identification of Deposit**	
7-3-1	Name of depositary institution	American Type Culture Collection
7-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
7-3-3	Date of deposit	12 January 1999 (12.01.1999)
7-3-4	Accession Number	ATCC 203577
7-4	**Additional Indications**	NONE
7-5	**Designated States for Which Indications are Made**	all designated States
7-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
8	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
8-1	page	99
8-2	line	3
8-3	**Identification of Deposit**	
8-3-1	Name of depositary institution	American Type Culture Collection
8-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
8-3-3	Date of deposit	27 July 1999 (27.07.1999)
8-3-4	Accession Number	ATCC PTA-430
8-4	**Additional Indications**	NONE
8-5	**Designated States for Which Indications are Made**	all designated States

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8-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
9	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
9-1	page	**99**
9-2	line	**4**
9-3	**Identification of Deposit**	
9-3-1	Name of depositary institution	**American Type Culture Collection**
9-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
9-3-3	Date of deposit	**08 June 1999 (08.06.1999)**
9-3-4	Accession Number	**ATCC PTA-203**
9-4	**Additional Indications**	**NONE**
9-5	**Designated States for Which Indications are Made**	**all designated States**
9-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
10	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
10-1	page	**99**
10-2	line	**5**
10-3	**Identification of Deposit**	
10-3-1	Name of depositary institution	**American Type Culture Collection**
10-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
10-3-3	Date of deposit	**01 July 1998 (01.07.1998)**
10-3-4	Accession Number	**ATCC 203040**
10-4	**Additional Indications**	**NONE**
10-5	**Designated States for Which Indications are Made**	**all designated States**
10-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
11	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
11-1	page	**99**
11-2	line	**6**
11-3	**Identification of Deposit**	
11-3-1	Name of depositary institution	**American Type Culture Collection**
11-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
11-3-3	Date of deposit	**31 August 1999 (31.08.1999)**
11-3-4	Accession Number	**ATCC PTA-611**

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11-4	**Additional Indications**	**NONE**
11-5	**Designated States for Which Indications are Made**	all designated States
11-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
12	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
12-1	page	99
12-2	line	7
12-3	**Identification of Deposit**	
12-3-1	Name of depositary institution	American Type Culture Collection
12-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
12-3-3	Date of deposit	21 January 1998 (21.01.1998)
12-3-4	Accession Number	ATCC 209593
12-4	**Additional Indications**	**NONE**
12-5	**Designated States for Which Indications are Made**	all designated States
12-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
13	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
13-1	page	99
13-2	line	8
13-3	**Identification of Deposit**	
13-3-1	Name of depositary institution	American Type Culture Collection
13-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
13-3-3	Date of deposit	09 February 1999 (09.02.1999)
13-3-4	Accession Number	ATCC 203649
13-4	**Additional Indications**	**NONE**
13-5	**Designated States for Which Indications are Made**	all designated States
13-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
14	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
14-1	page	99
14-2	line	9

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14-3	**Identification of Deposit**	
14-3-1	Name of depositary institution	**American Type Culture Collection**
14-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
14-3-3	Date of deposit	**12 January 1999 (12.01.1999)**
14-3-4	Accession Number	**ATCC 203574**
14-4	**Additional Indications**	**NONE**
14-5	**Designated States for Which Indications are Made**	**all designated States**
14-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
15	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
15-1	page	**99**
15-2	line	**10**
15-3	**Identification of Deposit**	
15-3-1	Name of depositary institution	**American Type Culture Collection**
15-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
15-3-3	Date of deposit	**25 May 1999 (25.05.1999)**
15-3-4	Accession Number	**ATCC PTA-129**
15-4	**Additional Indications**	**NONE**
15-5	**Designated States for Which Indications are Made**	**all designated States**
15-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
16	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
16-1	page	**99**
16-2	line	**11**
16-3	**Identification of Deposit**	
16-3-1	Name of depositary institution	**American Type Culture Collection**
16-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
16-3-3	Date of deposit	**27 May 1998 (27.05.1998)**
16-3-4	Accession Number	**ATCC 209905**
16-4	**Additional Indications**	**NONE**
16-5	**Designated States for Which Indications are Made**	**all designated States**
16-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	

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17	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
17-1	page	99
17-2	line	12
17-3	**Identification of Deposit**	
17-3-1	Name of depositary institution	American Type Culture Collection
17-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
17-3-3	Date of deposit	12 January 1999 (12.01.1999)
17-3-4	Accession Number	ATCC 203585
17-4	**Additional Indications**	NONE
17-5	**Designated States for Which Indications are Made**	all designated States
17-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
18	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
18-1	page	99
18-2	line	13
18-3	**Identification of Deposit**	
18-3-1	Name of depositary institution	American Type Culture Collection
18-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
18-3-3	Date of deposit	09 February 1999 (09.02.1999)
18-3-4	Accession Number	ATCC 203665
18-4	**Additional Indications**	NONE
18-5	**Designated States for Which Indications are Made**	all designated States
18-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
19	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
19-1	page	99
19-2	line	14
19-3	**Identification of Deposit**	
19-3-1	Name of depositary institution	American Type Culture Collection
19-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
19-3-3	Date of deposit	27 July 1999 (27.07.1999)
19-3-4	Accession Number	ATCC PTA-427
19-4	**Additional Indications**	NONE
19-5	**Designated States for Which Indications are Made**	all designated States

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19-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
20	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
20-1	page	**99**
20-2	line	**15**
20-3	**Identification of Deposit**	
20-3-1	Name of depositary institution	**American Type Culture Collection**
20-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
20-3-3	Date of deposit	**31 August 1999 (31.08.1999)**
20-3-4	Accession Number	**ATCC PTA-615**
20-4	**Additional Indications**	**NONE**
20-5	**Designated States for Which Indications are Made**	**all designated States**
20-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
21	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
21-1	page	**99**
21-2	line	**16**
21-3	**Identification of Deposit**	
21-3-1	Name of depositary institution	**American Type Culture Collection**
21-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
21-3-3	Date of deposit	**12 January 1999 (12.01.1999)**
21-3-4	Accession Number	**ATCC 203582**
21-4	**Additional Indications**	**NONE**
21-5	**Designated States for Which Indications are Made**	**all designated States**
21-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
22	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
22-1	page	**99**
22-2	line	**17**
22-3	**Identification of Deposit**	
22-3-1	Name of depositary institution	**American Type Culture Collection**
22-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
22-3-3	Date of deposit	**09 March 1999 (09.03.1999)**
22-3-4	Accession Number	**ATCC 203838**

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22-4	**Additional Indications**	**NONE**
22-5	**Designated States for Which Indications are Made**	**all designated States**
22-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
23	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
23-1	page	**99**
23-2	line	**18**
23-3	**Identification of Deposit**	
23-3-1	Name of depositary institution	**American Type Culture Collection**
23-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
23-3-3	Date of deposit	**27 July 1999 (27.07.1999)**
23-3-4	Accession Number	**ATCC PTA-428**
23-4	**Additional Indications**	**NONE**
23-5	**Designated States for Which Indications are Made**	**all designated States**
23-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
24	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
24-1	page	**99**
24-2	line	**19**
24-3	**Identification of Deposit**	
24-3-1	Name of depositary institution	**American Type Culture Collection**
24-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
24-3-3	Date of deposit	**09 March 1999 (09.03.1999)**
24-3-4	Accession Number	**ATCC 203836**
24-4	**Additional Indications**	**NONE**
24-5	**Designated States for Which Indications are Made**	**all designated States**
24-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
25	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
25-1	page	**99**
25-2	line	**20**

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25-3	**Identification of Deposit**	
25-3-1	Name of depositary institution	**American Type Culture Collection**
25-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
25-3-3	Date of deposit	**08 June 1999 (08.06.1999)**
25-3-4	Accession Number	**ATCC PTA-205**
25-4	**Additional Indications**	**NONE**
25-5	**Designated States for Which Indications are Made**	**all designated States**
25-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
26	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
26-1	page	**99**
26-2	line	**21**
26-3	**Identification of Deposit**	
26-3-1	Name of depositary institution	**American Type Culture Collection**
26-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
26-3-3	Date of deposit	**27 July 1999 (27.07.1999)**
26-3-4	Accession Number	**ATCC PTA-431**
26-4	**Additional Indications**	**NONE**
26-5	**Designated States for Which Indications are Made**	**all designated States**
26-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
27	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
27-1	page	**99**
27-2	line	**22**
27-3	**Identification of Deposit**	
27-3-1	Name of depositary institution	**American Type Culture Collection**
27-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
27-3-3	Date of deposit	**09 February 1999 (09.02.1999)**
27-3-4	Accession Number	**ATCC 203659**
27-4	**Additional Indications**	**NONE**
27-5	**Designated States for Which Indications are Made**	**all designated States**
27-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	

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28	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
28-1	page	99
28-2	line	23
28-3	**Identification of Deposit**	
28-3-1	Name of depositary institution	American Type Culture Collection
28-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
28-3-3	Date of deposit	12 January 1999 (12.01.1999)
28-3-4	Accession Number	ATCC 203584
28-4	**Additional Indications**	NONE
28-5	**Designated States for Which Indications are Made**	all designated States
28-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
29	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
29-1	page	99
29-2	line	24
29-3	**Identification of Deposit**	
29-3-1	Name of depositary institution	American Type Culture Collection
29-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
29-3-3	Date of deposit	25 May 1999 (25.05.1999)
29-3-4	Accession Number	ATCC PTA-126
29-4	**Additional Indications**	NONE
29-5	**Designated States for Which Indications are Made**	all designated States
29-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
30	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
30-1	page	99
30-2	line	25
30-3	**Identification of Deposit**	
30-3-1	Name of depositary institution	American Type Culture Collection
30-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
30-3-3	Date of deposit	25 May 1999 (25.05.1999)
30-3-4	Accession Number	ATCC PTA-128
30-4	**Additional Indications**	NONE
30-5	**Designated States for Which Indications are Made**	all designated States

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30-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
31	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
31-1	page	99
31-2	line	26
31-3	**Identification of Deposit**	
31-3-1	Name of depositary institution	American Type Culture Collection
31-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
31-3-3	Date of deposit	09 February 1999 (09.02.1999)
31-3-4	Accession Number	ATCC 203664
31-4	**Additional Indications**	NONE
31-5	**Designated States for Which Indications are Made**	all designated States
31-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
32	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
32-1	page	99
32-2	line	27
32-3	**Identification of Deposit**	
32-3-1	Name of depositary institution	American Type Culture Collection
32-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
32-3-3	Date of deposit	12 January 1999 (12.01.1999)
32-3-4	Accession Number	ATCC 203578
32-4	**Additional Indications**	NONE
32-5	**Designated States for Which Indications are Made**	all designated States
32-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
33	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
33-1	page	99
33-2	line	28
33-3	**Identification of Deposit**	
33-3-1	Name of depositary institution	American Type Culture Collection
33-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
33-3-3	Date of deposit	22 December 1998 (22.12.1998)
33-3-4	Accession Number	ATCC 203554

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33-4	**Additional Indications**	**NONE**
33-5	**Designated States for Which Indications are Made**	all designated States
33-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
34	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
34-1	page	99
34-2	line	29
34-3	**Identification of Deposit**	
34-3-1	Name of depositary institution	American Type Culture Collection
34-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
34-3-3	Date of deposit	16 March 1999 (16.03.1999)
34-3-4	Accession Number	ATCC 203850
34-4	**Additional Indications**	**NONE**
34-5	**Designated States for Which Indications are Made**	all designated States
34-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
35	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
35-1	page	99
35-2	line	30
35-3	**Identification of Deposit**	
35-3-1	Name of depositary institution	American Type Culture Collection
35-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
35-3-3	Date of deposit	11 May 1999 (11.05.1999)
35-3-4	Accession Number	ATCC PTA-45
35-4	**Additional Indications**	**NONE**
35-5	**Designated States for Which Indications are Made**	all designated States
35-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
36	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
36-1	page	99
36-2	line	31

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36-3	**Identification of Deposit**	
36-3-1	Name of depositary institution	**American Type Culture Collection**
36-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
36-3-3	Date of deposit	**22 December 1998 (22.12.1998)**
36-3-4	Accession Number	**ATCC 203545**
36-4	**Additional Indications**	**NONE**
36-5	**Designated States for Which Indications are Made**	**all designated States**
36-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
37	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
37-1	page	**99**
37-2	line	**32**
37-3	**Identification of Deposit**	
37-3-1	Name of depositary institution	**American Type Culture Collection**
37-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
37-3-3	Date of deposit	**22 December 1998 (22.12.1998)**
37-3-4	Accession Number	**ATCC 203544**
37-4	**Additional Indications**	**NONE**
37-5	**Designated States for Which Indications are Made**	**all designated States**
37-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
38	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
38-1	page	**99**
38-2	line	**33**
38-3	**Identification of Deposit**	
38-3-1	Name of depositary institution	**American Type Culture Collection**
38-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
38-3-3	Date of deposit	**15 June 1999 (15.06.1999)**
38-3-4	Accession Number	**ATCC PTA-234**
38-4	**Additional Indications**	**NONE**
38-5	**Designated States for Which Indications are Made**	**all designated States**
38-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**

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39	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
39-1	page	99
39-2	line	34
39-3	**Identification of Deposit**	
39-3-1	Name of depositary institution	American Type Culture Collection
39-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
39-3-3	Date of deposit	16 March 1999 (16.03.1999)
39-3-4	Accession Number	ATCC 203848
39-4	**Additional Indications**	NONE
39-5	**Designated States for Which Indications are Made**	all designated States
39-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
40	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
40-1	page	99
40-2	line	35
40-3	**Identification of Deposit**	
40-3-1	Name of depositary institution	American Type Culture Collection
40-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
40-3-3	Date of deposit	22 December 1998 (22.12.1998)
40-3-4	Accession Number	ATCC 203555
40-4	**Additional Indications**	NONE
40-5	**Designated States for Which Indications are Made**	all designated States
40-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
41	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
41-1	page	99
41-2	line	36
41-3	**Identification of Deposit**	
41-3-1	Name of depositary institution	American Type Culture Collection
41-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
41-3-3	Date of deposit	20 April 1999 (20.04.1999)
41-3-4	Accession Number	ATCC 203949
41-4	**Additional Indications**	NONE
41-5	**Designated States for Which Indications are Made**	all designated States

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41-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
42	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
42-1	page	99
42-2	line	37
42-3	**Identification of Deposit**	
42-3-1	Name of depositary institution	American Type Culture Collection
42-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
42-3-3	Date of deposit	15 December 1998 (15.12.1998)
42-3-4	Accession Number	ATCC 203539
42-4	**Additional Indications**	NONE
42-5	**Designated States for Which Indications are Made**	all designated States
42-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
43	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
43-1	page	99
43-2	line	38
43-3	**Identification of Deposit**	
43-3-1	Name of depositary institution	American Type Culture Collection
43-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
43-3-3	Date of deposit	23 March 1999 (23.03.1999)
43-3-4	Accession Number	ATCC 203871
43-4	**Additional Indications**	NONE
43-5	**Designated States for Which Indications are Made**	all designated States
43-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
44	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
44-1	page	99
44-2	line	39
44-3	**Identification of Deposit**	
44-3-1	Name of depositary institution	American Type Culture Collection
44-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
44-3-3	Date of deposit	23 March 1999 (23.03.1999)
44-3-4	Accession Number	ATCC 203862

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44-4	**Additional Indications**	**NONE**
44-5	**Designated States for Which Indications are Made**	all designated States
44-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
45	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
45-1	page	99
45-2	line	40
45-3	**Identification of Deposit**	
45-3-1	Name of depositary institution	American Type Culture Collection
45-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
45-3-3	Date of deposit	10 August 1999 (10.08.1999)
45-3-4	Accession Number	ATCC PTA-510
45-4	**Additional Indications**	**NONE**
45-5	**Designated States for Which Indications are Made**	all designated States
45-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
46	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
46-1	page	99
46-2	line	41
46-3	**Identification of Deposit**	
46-3-1	Name of depositary institution	American Type Culture Collection
46-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
46-3-3	Date of deposit	20 January 1999 (20.01.1999)
46-3-4	Accession Number	ATCC 203603
46-4	**Additional Indications**	**NONE**
46-5	**Designated States for Which Indications are Made**	all designated States
46-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
47	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
47-1	page	99
47-2	line	42

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47-3	**Identification of Deposit**	
47-3-1	Name of depositary institution	**American Type Culture Collection**
47-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
47-3-3	Date of deposit	**02 March 1999 (02.03.1999)**
47-3-4	Accession Number	**ATCC 203813**
47-4	**Additional Indications**	**NONE**
47-5	**Designated States for Which Indications are Made**	**all designated States**
47-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
48	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
48-1	page	**99**
48-2	line	**43**
48-3	**Identification of Deposit**	
48-3-1	Name of depositary institution	**American Type Culture Collection**
48-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
48-3-3	Date of deposit	**02 March 1999 (02.03.1999)**
48-3-4	Accession Number	**ATCC 203812**
48-4	**Additional Indications**	**NONE**
48-5	**Designated States for Which Indications are Made**	**all designated States**
48-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
49	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
49-1	page	**99**
49-2	line	**44**
49-3	**Identification of Deposit**	
49-3-1	Name of depositary institution	**American Type Culture Collection**
49-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
49-3-3	Date of deposit	**29 October 1998 (29.10.1998)**
49-3-4	Accession Number	**ATCC 203391**
49-4	**Additional Indications**	**NONE**
49-5	**Designated States for Which Indications are Made**	**all designated States**
49-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	

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50	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
50-1	page	99
50-2	line	45
50-3	**Identification of Deposit**	
50-3-1	Name of depositary institution	American Type Culture Collection
50-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
50-3-3	Date of deposit	27 April 1999 (27.04.1999)
50-3-4	Accession Number	ATCC 203965
50-4	**Additional Indications**	NONE
50-5	**Designated States for Which Indications are Made**	all designated States
50-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
51	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
51-1	page	99
51-2	line	46
51-3	**Identification of Deposit**	
51-3-1	Name of depositary institution	American Type Culture Collection
51-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
51-3-3	Date of deposit	02 March 1999 (02.03.1999)
51-3-4	Accession Number	ATCC 203816
51-4	**Additional Indications**	NONE
51-5	**Designated States for Which Indications are Made**	all designated States
51-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
52	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
52-1	page	99
52-2	line	47
52-3	**Identification of Deposit**	
52-3-1	Name of depositary institution	American Type Culture Collection
52-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
52-3-3	Date of deposit	02 March 1999 (02.03.1999)
52-3-4	Accession Number	ATCC 203814
52-4	**Additional Indications**	NONE
52-5	**Designated States for Which Indications are Made**	all designated States

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52-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
53	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
53-1	page	99
53-2	line	48
53-3	**Identification of Deposit**	
53-3-1	Name of depositary institution	American Type Culture Collection
53-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
53-3-3	Date of deposit	02 March 1999 (02.03.1999)
53-3-4	Accession Number	ATCC 203810
53-4	**Additional Indications**	NONE
53-5	**Designated States for Which Indications are Made**	all designated States
53-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
54	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
54-1	page	99
54-2	line	49
54-3	**Identification of Deposit**	
54-3-1	Name of depositary institution	American Type Culture Collection
54-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
54-3-3	Date of deposit	04 May 1999 (04.05.1999)
54-3-4	Accession Number	ATCC PTA-22
54-4	**Additional Indications**	NONE
54-5	**Designated States for Which Indications are Made**	all designated States
54-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
55	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
55-1	page	99
55-2	line	50
55-3	**Identification of Deposit**	
55-3-1	Name of depositary institution	American Type Culture Collection
55-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
55-3-3	Date of deposit	12 January 1999 (12.01.1999)
55-3-4	Accession Number	ATCC 203580

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55-4	**Additional Indications**	**NONE**
55-5	**Designated States for Which Indications are Made**	all designated States
55-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
56	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
56-1	page	99
56-2	line	51
56-3	**Identification of Deposit**	
56-3-1	Name of depositary institution	American Type Culture Collection
56-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
56-3-3	Date of deposit	30 March 1999 (30.03.1999)
56-3-4	Accession Number	ATCC 203889
56-4	**Additional Indications**	**NONE**
56-5	**Designated States for Which Indications are Made**	all designated States
56-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
57	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
57-1	page	99
57-2	line	52
57-3	**Identification of Deposit**	
57-3-1	Name of depositary institution	American Type Culture Collection
57-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
57-3-3	Date of deposit	27 April 1999 (27.04.1999)
57-3-4	Accession Number	ATCC 203964
57-4	**Additional Indications**	**NONE**
57-5	**Designated States for Which Indications are Made**	all designated States
57-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
58	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
58-1	page	99
58-2	line	53

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58-3	**Identification of Deposit**	
58-3-1	Name of depositary institution	American Type Culture Collection
58-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
58-3-3	Date of deposit	22 December 1998 (22.12.1998)
58-3-4	Accession Number	ATCC 203548
58-4	**Additional Indications**	NONE
58-5	**Designated States for Which Indications are Made**	all designated States
58-6	**Separate Furnishing of Indications**	NONE
	These indications will be submitted to the International Bureau later	
59	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
59-1	page	99
59-2	line	54
59-3	**Identification of Deposit**	
59-3-1	Name of depositary institution	American Type Culture Collection
59-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
59-3-3	Date of deposit	02 March 1999 (02.03.1999)
59-3-4	Accession Number	ATCC 203817
59-4	**Additional Indications**	NONE
59-5	**Designated States for Which Indications are Made**	all designated States
59-6	**Separate Furnishing of Indications**	NONE
	These indications will be submitted to the International Bureau later	
60	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
60-1	page	99
60-2	line	55
60-3	**Identification of Deposit**	
60-3-1	Name of depositary institution	American Type Culture Collection
60-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
60-3-3	Date of deposit	15 June 1999 (15.06.1999)
60-3-4	Accession Number	ATCC PTA-235
60-4	**Additional Indications**	NONE
60-5	**Designated States for Which Indications are Made**	all designated States
60-6	**Separate Furnishing of Indications**	NONE
	These indications will be submitted to the International Bureau later	

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61	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
61-1	page	100
61-2	line	2
61-3	**Identification of Deposit**	
61-3-1	Name of depositary institution	American Type Culture Collection
61-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
61-3-3	Date of deposit	27 April 1999 (27.04.1999)
61-3-4	Accession Number	ATCC 203968
61-4	**Additional Indications**	NONE
61-5	**Designated States for Which Indications are Made**	all designated States
61-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
62	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
62-1	page	100
62-2	line	3
62-3	**Identification of Deposit**	
62-3-1	Name of depositary institution	American Type Culture Collection
62-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
62-3-3	Date of deposit	30 March 1999 (30.03.1999)
62-3-4	Accession Number	ATCC 203894
62-4	**Additional Indications**	NONE
62-5	**Designated States for Which Indications are Made**	all designated States
62-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
63	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
63-1	page	100
63-2	line	4
63-3	**Identification of Deposit**	
63-3-1	Name of depositary institution	American Type Culture Collection
63-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
63-3-3	Date of deposit	30 March 1999 (30.03.1999)
63-3-4	Accession Number	ATCC 203893
63-4	**Additional Indications**	NONE
63-5	**Designated States for Which Indications are Made**	all designated States

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63-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
64	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
64-1	page	100
64-2	line	5
64-3	**Identification of Deposit**	
64-3-1	Name of depositary institution	American Type Culture Collection
64-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
64-3-3	Date of deposit	02 March 1999 (02.03.1999)
64-3-4	Accession Number	ATCC 203811
64-4	**Additional Indications**	**NONE**
64-5	**Designated States for Which Indications are Made**	all designated States
64-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
65	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
65-1	page	100
65-2	line	6
65-3	**Identification of Deposit**	
65-3-1	Name of depositary institution	American Type Culture Collection
65-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
65-3-3	Date of deposit	23 March 1999 (23.03.1999)
65-3-4	Accession Number	ATCC 203867
65-4	**Additional Indications**	**NONE**
65-5	**Designated States for Which Indications are Made**	all designated States
65-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
66	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
66-1	page	100
66-2	line	7
66-3	**Identification of Deposit**	
66-3-1	Name of depositary institution	American Type Culture Collection
66-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
66-3-3	Date of deposit	27 April 1999 (27.04.1999)
66-3-4	Accession Number	ATCC 203963

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66-4	**Additional Indications**	**NONE**
66-5	**Designated States for Which Indications are Made**	all designated States
66-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
67	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
67-1	page	100
67-2	line	8
67-3	**Identification of Deposit**	
67-3-1	Name of depositary institution	American Type Culture Collection
67-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
67-3-3	Date of deposit	02 March 1999 (02.03.1999)
67-3-4	Accession Number	ATCC 203815
67-4	**Additional Indications**	**NONE**
67-5	**Designated States for Which Indications are Made**	all designated States
67-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
68	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
68-1	page	100
68-2	line	9
68-3	**Identification of Deposit**	
68-3-1	Name of depositary institution	American Type Culture Collection
68-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
68-3-3	Date of deposit	30 March 1999 (30.03.1999)
68-3-4	Accession Number	ATCC 203890
68-4	**Additional Indications**	**NONE**
68-5	**Designated States for Which Indications are Made**	all designated States
68-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
69	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
69-1	page	100
69-2	line	10

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69-3	**Identification of Deposit**	
69-3-1	Name of depositary institution	**American Type Culture Collection**
69-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
69-3-3	Date of deposit	**25 May 1999 (25.05.1999)**
69-3-4	Accession Number	**ATCC PTA-130**
69-4	**Additional Indications**	**NONE**
69-5	**Designated States for Which Indications are Made**	**all designated States**
69-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
70	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
70-1	page	**100**
70-2	line	**11**
70-3	**Identification of Deposit**	
70-3-1	Name of depositary institution	**American Type Culture Collection**
70-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
70-3-3	Date of deposit	**27 April 1999 (27.04.1999)**
70-3-4	Accession Number	**ATCC 203970**
70-4	**Additional Indications**	**NONE**
70-5	**Designated States for Which Indications are Made**	**all designated States**
70-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
71	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
71-1	page	**100**
71-2	line	**12**
71-3	**Identification of Deposit**	
71-3-1	Name of depositary institution	**American Type Culture Collection**
71-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
71-3-3	Date of deposit	**16 March 1999 (16.03.1999)**
71-3-4	Accession Number	**ATCC 203845**
71-4	**Additional Indications**	**NONE**
71-5	**Designated States for Which Indications are Made**	**all designated States**
71-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	

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72	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
72-1	page	100
72-2	line	13
72-3	**Identification of Deposit**	
72-3-1	Name of depositary institution	American Type Culture Collection
72-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
72-3-3	Date of deposit	23 March 1999 (23.03.1999)
72-3-4	Accession Number	ATCC 203861
72-4	**Additional Indications**	NONE
72-5	**Designated States for Which Indications are Made**	all designated States
72-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
73	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
73-1	page	100
73-2	line	14
73-3	**Identification of Deposit**	
73-3-1	Name of depositary institution	American Type Culture Collection
73-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
73-3-3	Date of deposit	16 March 1999 (16.03.1999)
73-3-4	Accession Number	ATCC 203844
73-4	**Additional Indications**	NONE
73-5	**Designated States for Which Indications are Made**	all designated States
73-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
74	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
74-1	page	100
74-2	line	15
74-3	**Identification of Deposit**	
74-3-1	Name of depositary institution	American Type Culture Collection
74-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
74-3-3	Date of deposit	10 August 1999 (10.08.1999)
74-3-4	Accession Number	ATCC PTA-513
74-4	**Additional Indications**	NONE
74-5	**Designated States for Which Indications are Made**	all designated States

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74-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
75	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
75-1	page	100
75-2	line	16
75-3	**Identification of Deposit**	
75-3-1	Name of depositary institution	American Type Culture Collection
75-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
75-3-3	Date of deposit	09 February 1999 (09.02.1999)
75-3-4	Accession Number	ATCC 203663
75-4	**Additional Indications**	**NONE**
75-5	**Designated States for Which Indications are Made**	all designated States
75-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
76	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
76-1	page	100
76-2	line	17
76-3	**Identification of Deposit**	
76-3-1	Name of depositary institution	American Type Culture Collection
76-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
76-3-3	Date of deposit	16 March 1999 (16.03.1999)
76-3-4	Accession Number	ATCC 203851
76-4	**Additional Indications**	**NONE**
76-5	**Designated States for Which Indications are Made**	all designated States
76-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
77	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
77-1	page	100
77-2	line	18
77-3	**Identification of Deposit**	
77-3-1	Name of depositary institution	American Type Culture Collection
77-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
77-3-3	Date of deposit	20 April 1999 (20.04.1999)
77-3-4	Accession Number	ATCC 203950

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77-4	**Additional Indications**	**NONE**
77-5	**Designated States for Which Indications are Made**	all designated States
77-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
78	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
78-1	page	100
78-2	line	19
78-3	**Identification of Deposit**	
78-3-1	Name of depositary institution	American Type Culture Collection
78-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
78-3-3	Date of deposit	30 March 1999 (30.03.1999)
78-3-4	Accession Number	ATCC 203895
78-4	**Additional Indications**	**NONE**
78-5	**Designated States for Which Indications are Made**	all designated States
78-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
79	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
79-1	page	100
79-2	line	20
79-3	**Identification of Deposit**	
79-3-1	Name of depositary institution	American Type Culture Collection
79-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
79-3-3	Date of deposit	25 May 1999 (25.05.1999)
79-3-4	Accession Number	ATCC PTA-134
79-4	**Additional Indications**	**NONE**
79-5	**Designated States for Which Indications are Made**	all designated States
79-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
80	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
80-1	page	100
80-2	line	21

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80-3	**Identification of Deposit**	
80-3-1	Name of depositary institution	**American Type Culture Collection**
80-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
80-3-3	Date of deposit	**16 March 1999 (16.03.1999)**
80-3-4	Accession Number	**ATCC 203852**
80-4	**Additional Indications**	**NONE**
80-5	**Designated States for Which Indications are Made**	**all designated States**
80-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
81	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
81-1	page	**100**
81-2	line	**22**
81-3	**Identification of Deposit**	
81-3-1	Name of depositary institution	**American Type Culture Collection**
81-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
81-3-3	Date of deposit	**22 June 1999 (22.06.1999)**
81-3-4	Accession Number	**ATCC PTA-258**
81-4	**Additional Indications**	**NONE**
81-5	**Designated States for Which Indications are Made**	**all designated States**
81-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
82	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
82-1	page	**100**
82-2	line	**23**
82-3	**Identification of Deposit**	
82-3-1	Name of depositary institution	**American Type Culture Collection**
82-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
82-3-3	Date of deposit	**22 June 1999 (22.06.1999)**
82-3-4	Accession Number	**ATCC PTA-259**
82-4	**Additional Indications**	**NONE**
82-5	**Designated States for Which Indications are Made**	**all designated States**
82-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**

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83	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
83-1	page	100
83-2	line	24
83-3	**Identification of Deposit**	
83-3-1	Name of depositary institution	American Type Culture Collection
83-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
83-3-3	Date of deposit	23 March 1999 (23.03.1999)
83-3-4	Accession Number	ATCC 203866
83-4	**Additional Indications**	NONE
83-5	**Designated States for Which Indications are Made**	all designated States
83-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
84	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
84-1	page	100
84-2	line	25
84-3	**Identification of Deposit**	
84-3-1	Name of depositary institution	American Type Culture Collection
84-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
84-3-3	Date of deposit	16 March 1999 (16.03.1999)
84-3-4	Accession Number	ATCC 203853
84-4	**Additional Indications**	NONE
84-5	**Designated States for Which Indications are Made**	all designated States
84-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
85	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
85-1	page	100
85-2	line	26
85-3	**Identification of Deposit**	
85-3-1	Name of depositary institution	American Type Culture Collection
85-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
85-3-3	Date of deposit	30 March 1999 (30.03.1999)
85-3-4	Accession Number	ATCC 203892
85-4	**Additional Indications**	NONE
85-5	**Designated States for Which Indications are Made**	all designated States

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85-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
86	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
86-1	page	100
86-2	line	27
86-3	**Identification of Deposit**	
86-3-1	Name of depositary institution	American Type Culture Collection
86-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
86-3-3	Date of deposit	16 March 1999 (16.03.1999)
86-3-4	Accession Number	ATCC 203847
86-4	**Additional Indications**	NONE
86-5	**Designated States for Which Indications are Made**	all designated States
86-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
87	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
87-1	page	100
87-2	line	28
87-3	**Identification of Deposit**	
87-3-1	Name of depositary institution	American Type Culture Collection
87-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
87-3-3	Date of deposit	04 May 1999 (04.05.1999)
87-3-4	Accession Number	ATCC PTA-21
87-4	**Additional Indications**	NONE
87-5	**Designated States for Which Indications are Made**	all designated States
87-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
88	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
88-1	page	100
88-2	line	29
88-3	**Identification of Deposit**	
88-3-1	Name of depositary institution	American Type Culture Collection
88-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
88-3-3	Date of deposit	25 May 1999 (25.05.1999)
88-3-4	Accession Number	ATCC PTA-121

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88-4	**Additional Indications**	**NONE**
88-5	**Designated States for Which Indications are Made**	all designated States
88-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
89	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
89-1	page	100
89-2	line	30
89-3	**Identification of Deposit**	
89-3-1	Name of depositary institution	American Type Culture Collection
89-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
89-3-3	Date of deposit	20 April 1999 (20.04.1999)
89-3-4	Accession Number	ATCC 203951
89-4	**Additional Indications**	**NONE**
89-5	**Designated States for Which Indications are Made**	all designated States
89-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
90	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
90-1	page	100
90-2	line	31
90-3	**Identification of Deposit**	
90-3-1	Name of depositary institution	American Type Culture Collection
90-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
90-3-3	Date of deposit	23 March 1999 (23.03.1999)
90-3-4	Accession Number	ATCC 203869
90-4	**Additional Indications**	**NONE**
90-5	**Designated States for Which Indications are Made**	all designated States
90-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
91	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
91-1	page	100
91-2	line	32

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91-3	**Identification of Deposit**	
91-3-1	Name of depositary institution	**American Type Culture Collection**
91-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
91-3-3	Date of deposit	**15 June 1999 (15.06.1999)**
91-3-4	Accession Number	**ATCC PTA-232**
91-4	**Additional Indications**	**NONE**
91-5	**Designated States for Which Indications are Made**	**all designated States**
91-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
92	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
92-1	page	**100**
92-2	line	**33**
92-3	**Identification of Deposit**	
92-3-1	Name of depositary institution	**American Type Culture Collection**
92-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
92-3-3	Date of deposit	**20 July 1999 (20.07.1999)**
92-3-4	Accession Number	**ATCC PTA-385**
92-4	**Additional Indications**	**NONE**
92-5	**Designated States for Which Indications are Made**	**all designated States**
92-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
93	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
93-1	page	**100**
93-2	line	**34**
93-3	**Identification of Deposit**	
93-3-1	Name of depositary institution	**American Type Culture Collection**
93-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
93-3-3	Date of deposit	**23 March 1999 (23.03.1999)**
93-3-4	Accession Number	**ATCC 203864**
93-4	**Additional Indications**	**NONE**
93-5	**Designated States for Which Indications are Made**	**all designated States**
93-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	

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94	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
94-1	page	100
94-2	line	35
94-3	**Identification of Deposit**	
94-3-1	Name of depositary institution	American Type Culture Collection
94-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
94-3-3	Date of deposit	22 June 1999 (22.06.1999)
94-3-4	Accession Number	ATCC PTA-262
94-4	**Additional Indications**	NONE
94-5	**Designated States for Which Indications are Made**	all designated States
94-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
95	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
95-1	page	100
95-2	line	36
95-3	**Identification of Deposit**	
95-3-1	Name of depositary institution	American Type Culture Collection
95-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
95-3-3	Date of deposit	20 July 1999 (20.07.1999)
95-3-4	Accession Number	ATCC PTA-381
95-4	**Additional Indications**	NONE
95-5	**Designated States for Which Indications are Made**	all designated States
95-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
96	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
96-1	page	100
96-2	line	37
96-3	**Identification of Deposit**	
96-3-1	Name of depositary institution	American Type Culture Collection
96-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
96-3-3	Date of deposit	04 May 1999 (04.05.1999)
96-3-4	Accession Number	ATCC PTA-15
96-4	**Additional Indications**	NONE
96-5	**Designated States for Which Indications are Made**	all designated States

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96-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
97	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
97-1	page	100
97-2	line	38
97-3	**Identification of Deposit**	
97-3-1	Name of depositary institution	American Type Culture Collection
97-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
97-3-3	Date of deposit	15 June 1999 (15.06.1999)
97-3-4	Accession Number	ATCC PTA-239
97-4	**Additional Indications**	NONE
97-5	**Designated States for Which Indications are Made**	all designated States
97-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
98	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
98-1	page	100
98-2	line	39
98-3	**Identification of Deposit**	
98-3-1	Name of depositary institution	American Type Culture Collection
98-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
98-3-3	Date of deposit	20 July 1999 (20.07.1999)
98-3-4	Accession Number	ATCC PTA-384
98-4	**Additional Indications**	NONE
98-5	**Designated States for Which Indications are Made**	all designated States
98-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
99	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
99-1	page	100
99-2	line	40
99-3	**Identification of Deposit**	
99-3-1	Name of depositary institution	American Type Culture Collection
99-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
99-3-3	Date of deposit	03 August 1999 (03.08.1999)
99-3-4	Accession Number	ATCC PTA-475

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99-4	**Additional Indications**	**NONE**
99-5	**Designated States for Which Indications are Made**	all designated States
99-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
100	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
100-1	page	100
100-2	line	41
100-3	**Identification of Deposit**	
100-3-1	Name of depositary institution	American Type Culture Collection
100-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
100-3-3	Date of deposit	16 March 1999 (16.03.1999)
100-3-4	Accession Number	ATCC 203854
100-4	**Additional Indications**	**NONE**
100-5	**Designated States for Which Indications are Made**	all designated States
100-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
101	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
101-1	page	100
101-2	line	42
101-3	**Identification of Deposit**	
101-3-1	Name of depositary institution	American Type Culture Collection
101-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
101-3-3	Date of deposit	20 July 1999 (20.07.1999)
101-3-4	Accession Number	ATCC PTA-378
101-4	**Additional Indications**	**NONE**
101-5	**Designated States for Which Indications are Made**	all designated States
101-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
102	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
102-1	page	100
102-2	line	43

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102-3	**Identification of Deposit**	
102-3-1	Name of depositary institution	**American Type Culture Collection**
102-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
102-3-3	Date of deposit	**22 June 1999 (22.06.1999)**
102-3-4	Accession Number	**ATCC PTA-257**
102-4	**Additional Indications**	**NONE**
102-5	**Designated States for Which Indications are Made**	**all designated States**
102-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
103	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
103-1	page	**100**
103-2	line	**44**
103-3	**Identification of Deposit**	
103-3-1	Name of depositary institution	**American Type Culture Collection**
103-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
103-3-3	Date of deposit	**15 June 1999 (15.06.1999)**
103-3-4	Accession Number	**ATCC PTA-231**
103-4	**Additional Indications**	**NONE**
103-5	**Designated States for Which Indications are Made**	**all designated States**
103-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
104	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
104-1	page	**100**
104-2	line	**45**
104-3	**Identification of Deposit**	
104-3-1	Name of depositary institution	**American Type Culture Collection**
104-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
104-3-3	Date of deposit	**20 July 1999 (20.07.1999)**
104-3-4	Accession Number	**ATCC PTA-388**
104-4	**Additional Indications**	**NONE**
104-5	**Designated States for Which Indications are Made**	**all designated States**
104-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**

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105	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
105-1	page	100
105-2	line	46
105-3	**Identification of Deposit**	
105-3-1	Name of depositary institution	American Type Culture Collection
105-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
105-3-3	Date of deposit	31 August 1999 (31.08.1999)
105-3-4	Accession Number	ATCC PTA-620
105-4	**Additional Indications**	NONE
105-5	**Designated States for Which Indications are Made**	all designated States
105-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
106	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
106-1	page	100
106-2	line	47
106-3	**Identification of Deposit**	
106-3-1	Name of depositary institution	American Type Culture Collection
106-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
106-3-3	Date of deposit	25 May 1999 (25.05.1999)
106-3-4	Accession Number	ATCC PTA-118
106-4	**Additional Indications**	NONE
106-5	**Designated States for Which Indications are Made**	all designated States
106-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
107	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
107-1	page	100
107-2	line	48
107-3	**Identification of Deposit**	
107-3-1	Name of depositary institution	American Type Culture Collection
107-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
107-3-3	Date of deposit	03 August 1999 (03.08.1999)
107-3-4	Accession Number	ATCC PTA-477
107-4	**Additional Indications**	NONE
107-5	**Designated States for Which Indications are Made**	all designated States

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107-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
108	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
108-1	page	100
108-2	line	49
108-3	**Identification of Deposit**	
108-3-1	Name of depositary institution	American Type Culture Collection
108-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
108-3-3	Date of deposit	03 August 1999 (03.08.1999)
108-3-4	Accession Number	ATCC PTA-488
108-4	**Additional Indications**	NONE
108-5	**Designated States for Which Indications are Made**	all designated States
108-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
109	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
109-1	page	100
109-2	line	50
109-3	**Identification of Deposit**	
109-3-1	Name of depositary institution	American Type Culture Collection
109-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
109-3-3	Date of deposit	16 March 1999 (16.03.1999)
109-3-4	Accession Number	ATCC 203849
109-4	**Additional Indications**	NONE
109-5	**Designated States for Which Indications are Made**	all designated States
109-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
110	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
110-1	page	100
110-2	line	51
110-3	**Identification of Deposit**	
110-3-1	Name of depositary institution	American Type Culture Collection
110-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
110-3-3	Date of deposit	09 March 1999 (09.03.1999)
110-3-4	Accession Number	ATCC 203837

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110-4	**Additional Indications**	**NONE**
110-5	**Designated States for Which Indications are Made**	all designated States
110-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
111	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
111-1	page	100
111-2	line	52
111-3	**Identification of Deposit**	
111-3-1	Name of depositary institution	American Type Culture Collection
111-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
111-3-3	Date of deposit	20 July 1999 (20.07.1999)
111-3-4	Accession Number	ATCC PTA-380
111-4	**Additional Indications**	**NONE**
111-5	**Designated States for Which Indications are Made**	all designated States
111-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
112	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
112-1	page	100
112-2	line	53
112-3	**Identification of Deposit**	
112-3-1	Name of depositary institution	American Type Culture Collection
112-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
112-3-3	Date of deposit	11 May 1999 (11.05.1999)
112-3-4	Accession Number	ATCC PTA-44
112-4	**Additional Indications**	**NONE**
112-5	**Designated States for Which Indications are Made**	all designated States
112-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
113	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
113-1	page	100
113-2	line	54

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113-3	**Identification of Deposit**	
113-3-1	Name of depositary institution	**American Type Culture Collection**
113-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
113-3-3	Date of deposit	**11 May 1999 (11.05.1999)**
113-3-4	Accession Number	**ATCC PTA-42**
113-4	**Additional Indications**	**NONE**
113-5	**Designated States for Which Indications are Made**	**all designated States**
113-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
114	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
114-1	page	**100**
114-2	line	**55**
114-3	**Identification of Deposit**	
114-3-1	Name of depositary institution	**American Type Culture Collection**
114-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
114-3-3	Date of deposit	**25 May 1999 (25.05.1999)**
114-3-4	Accession Number	**ATCC PTA-123**
114-4	**Additional Indications**	**NONE**
114-5	**Designated States for Which Indications are Made**	**all designated States**
114-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
115	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
115-1	page	**101**
115-2	line	**2**
115-3	**Identification of Deposit**	
115-3-1	Name of depositary institution	**American Type Culture Collection**
115-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
115-3-3	Date of deposit	**03 August 1999 (03.08.1999)**
115-3-4	Accession Number	**ATCC PTA-482**
115-4	**Additional Indications**	**NONE**
115-5	**Designated States for Which Indications are Made**	**all designated States**
115-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	

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116	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
116-1	page	101
116-2	line	3
116-3	**Identification of Deposit**	
116-3-1	Name of depositary institution	American Type Culture Collection
116-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
116-3-3	Date of deposit	03 August 1999 (03.08.1999)
116-3-4	Accession Number	ATCC PTA-483
116-4	**Additional Indications**	NONE
116-5	**Designated States for Which Indications are Made**	all designated States
116-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
117	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
117-1	page	101
117-2	line	4
117-3	**Identification of Deposit**	
117-3-1	Name of depositary institution	American Type Culture Collection
117-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
117-3-3	Date of deposit	03 August 1999 (03.08.1999)
117-3-4	Accession Number	ATCC PTA-485
117-4	**Additional Indications**	NONE
117-5	**Designated States for Which Indications are Made**	all designated States
117-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
118	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
118-1	page	101
118-2	line	5
118-3	**Identification of Deposit**	
118-3-1	Name of depositary institution	American Type Culture Collection
118-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
118-3-3	Date of deposit	03 August 1999 (03.08.1999)
118-3-4	Accession Number	ATCC PTA-480
118-4	**Additional Indications**	NONE
118-5	**Designated States for Which Indications are Made**	all designated States

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118-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
119	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
119-1	page	101
119-2	line	6
119-3	**Identification of Deposit**	
119-3-1	Name of depositary institution	American Type Culture Collection
119-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
119-3-3	Date of deposit	03 August 1999 (03.08.1999)
119-3-4	Accession Number	ATCC PTA-476
119-4	**Additional Indications**	**NONE**
119-5	**Designated States for Which Indications are Made**	all designated States
119-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
120	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
120-1	page	101
120-2	line	7
120-3	**Identification of Deposit**	
120-3-1	Name of depositary institution	American Type Culture Collection
120-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
120-3-3	Date of deposit	03 August 1999 (03.08.1999)
120-3-4	Accession Number	ATCC PTA-472
120-4	**Additional Indications**	**NONE**
120-5	**Designated States for Which Indications are Made**	all designated States
120-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
121	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
121-1	page	101
121-2	line	8
121-3	**Identification of Deposit**	
121-3-1	Name of depositary institution	American Type Culture Collection
121-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
121-3-3	Date of deposit	03 August 1999 (03.08.1999)
121-3-4	Accession Number	ATCC PTA-487

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121-4	**Additional Indications**	NONE
121-5	**Designated States for Which Indications are Made**	all designated States
121-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
122	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
122-1	page	101
122-2	line	9
122-3	**Identification of Deposit**	
122-3-1	Name of depositary institution	American Type Culture Collection
122-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
122-3-3	Date of deposit	03 August 1999 (03.08.1999)
122-3-4	Accession Number	ATCC PTA-484
122-4	**Additional Indications**	NONE
122-5	**Designated States for Which Indications are Made**	all designated States
122-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
123	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
123-1	page	101
123-2	line	10
123-3	**Identification of Deposit**	
123-3-1	Name of depositary institution	American Type Culture Collection
123-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
123-3-3	Date of deposit	17 August 1999 (17.08.1999)
123-3-4	Accession Number	ATCC PTA-546
123-4	**Additional Indications**	NONE
123-5	**Designated States for Which Indications are Made**	all designated States
123-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
124	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
124-1	page	101
124-2	line	11

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124-3	**Identification of Deposit**	
124-3-1	Name of depositary institution	**American Type Culture Collection**
124-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
124-3-3	Date of deposit	**10 August 1999 (10.08.1999)**
124-3-4	Accession Number	**ATCC PTA-515**
124-4	**Additional Indications**	**NONE**
124-5	**Designated States for Which Indications are Made**	**all designated States**
124-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
125	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
125-1	page	**101**
125-2	line	**12**
125-3	**Identification of Deposit**	
125-3-1	Name of depositary institution	**American Type Culture Collection**
125-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
125-3-3	Date of deposit	**19 October 1999 (19.10.1999)**
125-3-4	Accession Number	**ATCC PTA-861**
125-4	**Additional Indications**	**NONE**
125-5	**Designated States for Which Indications are Made**	**all designated States**
125-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
126	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
126-1	page	**101**
126-2	line	**13**
126-3	**Identification of Deposit**	
126-3-1	Name of depositary institution	**American Type Culture Collection**
126-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
126-3-3	Date of deposit	**10 August 1999 (10.08.1999)**
126-3-4	Accession Number	**ATCC PTA-518**
126-4	**Additional Indications**	**NONE**
126-5	**Designated States for Which Indications are Made**	**all designated States**
126-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	

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127	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
127-1	page	101
127-2	line	14
127-3	**Identification of Deposit**	
127-3-1	Name of depositary institution	American Type Culture Collection
127-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
127-3-3	Date of deposit	10 August 1999 (10.08.1999)
127-3-4	Accession Number	ATCC PTA-512
127-4	**Additional Indications**	NONE
127-5	**Designated States for Which Indications are Made**	all designated States
127-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
128	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
128-1	page	101
128-2	line	15
128-3	**Identification of Deposit**	
128-3-1	Name of depositary institution	American Type Culture Collection
128-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
128-3-3	Date of deposit	03 August 1999 (03.08.1999)
128-3-4	Accession Number	ATCC PTA-489
128-4	**Additional Indications**	NONE
128-5	**Designated States for Which Indications are Made**	all designated States
128-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
129	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
129-1	page	101
129-2	line	16
129-3	**Identification of Deposit**	
129-3-1	Name of depositary institution	American Type Culture Collection
129-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
129-3-3	Date of deposit	31 August 1999 (31.08.1999)
129-3-4	Accession Number	ATCC PTA-614
129-4	**Additional Indications**	NONE
129-5	**Designated States for Which Indications are Made**	all designated States

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129-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
130	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
130-1	page	101
130-2	line	17
130-3	**Identification of Deposit**	
130-3-1	Name of depositary institution	American Type Culture Collection
130-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
130-3-3	Date of deposit	16 November 1999 (16.11.1999)
130-3-4	Accession Number	ATCC PTA-957
130-4	**Additional Indications**	**NONE**
130-5	**Designated States for Which Indications are Made**	all designated States
130-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
131	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
131-1	page	101
131-2	line	18
131-3	**Identification of Deposit**	
131-3-1	Name of depositary institution	American Type Culture Collection
131-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
131-3-3	Date of deposit	05 October 1999 (05.10.1999)
131-3-4	Accession Number	ATCC PTA-819
131-4	**Additional Indications**	**NONE**
131-5	**Designated States for Which Indications are Made**	all designated States
131-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
132	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
132-1	page	101
132-2	line	19
132-3	**Identification of Deposit**	
132-3-1	Name of depositary institution	American Type Culture Collection
132-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
132-3-3	Date of deposit	18 September 1997 (18.09.1997)
132-3-4	Accession Number	ATCC 209280

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132-4	**Additional Indications**	**NONE**
132-5	**Designated States for Which Indications are Made**	all designated States
132-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
133	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
133-1	page	101
133-2	line	20
133-3	**Identification of Deposit**	
133-3-1	Name of depositary institution	American Type Culture Collection
133-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
133-3-3	Date of deposit	14 April 1998 (14.04.1998)
133-3-4	Accession Number	ATCC 209772
133-4	**Additional Indications**	**NONE**
133-5	**Designated States for Which Indications are Made**	all designated States
133-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
134	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
134-1	page	101
134-2	line	21
134-3	**Identification of Deposit**	
134-3-1	Name of depositary institution	American Type Culture Collection
134-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
134-3-3	Date of deposit	16 October 1997 (16.10.1997)
134-3-4	Accession Number	ATCC 209375
134-4	**Additional Indications**	**NONE**
134-5	**Designated States for Which Indications are Made**	all designated States
134-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
135	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
135-1	page	101
135-2	line	22

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135-3	**Identification of Deposit**	
135-3-1	Name of depositary institution	**American Type Culture Collection**
135-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
135-3-3	Date of deposit	**23 September 1997 (23.09.1997)**
135-3-4	Accession Number	**ATCC 209296**
135-4	**Additional Indications**	**NONE**
135-5	**Designated States for Which Indications are Made**	**all designated States**
135-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
136	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
136-1	page	**101**
136-2	line	**23**
136-3	**Identification of Deposit**	
136-3-1	Name of depositary institution	**American Type Culture Collection**
136-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
136-3-3	Date of deposit	**18 September 1997 (18.09.1997)**
136-3-4	Accession Number	**ATCC 209279**
136-4	**Additional Indications**	**NONE**
136-5	**Designated States for Which Indications are Made**	**all designated States**
136-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
137	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
137-1	page	**101**
137-2	line	**24**
137-3	**Identification of Deposit**	
137-3-1	Name of depositary institution	**American Type Culture Collection**
137-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
137-3-3	Date of deposit	**05 March 1998 (05.03.1998)**
137-3-4	Accession Number	**ATCC 209653**
137-4	**Additional Indications**	**NONE**
137-5	**Designated States for Which Indications are Made**	**all designated States**
137-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	

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138	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
138-1	page	101
138-2	line	25
138-3	**Identification of Deposit**	
138-3-1	Name of depositary institution	American Type Culture Collection
138-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
138-3-3	Date of deposit	16 October 1997 (16.10.1997)
138-3-4	Accession Number	ATCC 209385
138-4	**Additional Indications**	NONE
138-5	**Designated States for Which Indications are Made**	all designated States
138-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
139	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
139-1	page	101
139-2	line	26
139-3	**Identification of Deposit**	
139-3-1	Name of depositary institution	American Type Culture Collection
139-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
139-3-3	Date of deposit	16 September 1997 (16.09.1997)
139-3-4	Accession Number	ATCC 209261
139-4	**Additional Indications**	NONE
139-5	**Designated States for Which Indications are Made**	all designated States
139-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
140	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
140-1	page	101
140-2	line	27
140-3	**Identification of Deposit**	
140-3-1	Name of depositary institution	American Type Culture Collection
140-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
140-3-3	Date of deposit	16 October 1997 (16.10.1997)
140-3-4	Accession Number	ATCC 209384
140-4	**Additional Indications**	NONE
140-5	**Designated States for Which Indications are Made**	all designated States

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140-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
141	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
141-1	page	101
141-2	line	28
141-3	**Identification of Deposit**	
141-3-1	Name of depositary institution	American Type Culture Collection
141-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
141-3-3	Date of deposit	16 September 1997 (16.09.1997)
141-3-4	Accession Number	ATCC 209258
141-4	**Additional Indications**	**NONE**
141-5	**Designated States for Which Indications are Made**	all designated States
141-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
142	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
142-1	page	101
142-2	line	29
142-3	**Identification of Deposit**	
142-3-1	Name of depositary institution	American Type Culture Collection
142-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
142-3-3	Date of deposit	16 September 1997 (16.09.1997)
142-3-4	Accession Number	ATCC 209257
142-4	**Additional Indications**	**NONE**
142-5	**Designated States for Which Indications are Made**	all designated States
142-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
143	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
143-1	page	101
143-2	line	30
143-3	**Identification of Deposit**	
143-3-1	Name of depositary institution	American Type Culture Collection
143-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
143-3-3	Date of deposit	30 May 1997 (30.05.1997)
143-3-4	Accession Number	ATCC 209087

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143-4	**Additional Indications**	**NONE**
143-5	**Designated States for Which Indications are Made**	all designated States
143-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
144	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
144-1	page	101
144-2	line	31
144-3	**Identification of Deposit**	
144-3-1	Name of depositary institution	American Type Culture Collection
144-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
144-3-3	Date of deposit	16 October 1997 (16.10.1997)
144-3-4	Accession Number	ATCC 209381
144-4	**Additional Indications**	**NONE**
144-5	**Designated States for Which Indications are Made**	all designated States
144-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
145	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
145-1	page	101
145-2	line	32
145-3	**Identification of Deposit**	
145-3-1	Name of depositary institution	American Type Culture Collection
145-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
145-3-3	Date of deposit	16 September 1997 (16.09.1997)
145-3-4	Accession Number	ATCC 209262
145-4	**Additional Indications**	**NONE**
145-5	**Designated States for Which Indications are Made**	all designated States
145-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
146	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
146-1	page	101
146-2	line	33

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146-3	**Identification of Deposit**	
146-3-1	Name of depositary institution	**American Type Culture Collection**
146-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
146-3-3	Date of deposit	**28 October 1997 (28.10.1997)**
146-3-4	Accession Number	**ATCC 209420**
146-4	**Additional Indications**	**NONE**
146-5	**Designated States for Which Indications are Made**	**all designated States**
146-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
147	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
147-1	page	**101**
147-2	line	**34**
147-3	**Identification of Deposit**	
147-3-1	Name of depositary institution	**American Type Culture Collection**
147-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
147-3-3	Date of deposit	**16 September 1997 (16.09.1997)**
147-3-4	Accession Number	**ATCC 209256**
147-4	**Additional Indications**	**NONE**
147-5	**Designated States for Which Indications are Made**	**all designated States**
147-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
148	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
148-1	page	**101**
148-2	line	**35**
148-3	**Identification of Deposit**	
148-3-1	Name of depositary institution	**American Type Culture Collection**
148-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
148-3-3	Date of deposit	**16 September 1997 (16.09.1997)**
148-3-4	Accession Number	**ATCC 209251**
148-4	**Additional Indications**	**NONE**
148-5	**Designated States for Which Indications are Made**	**all designated States**
148-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	

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149	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
149-1	page	101
149-2	line	36
149-3	**Identification of Deposit**	
149-3-1	Name of depositary institution	American Type Culture Collection
149-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
149-3-3	Date of deposit	16 September 1997 (16.09.1997)
149-3-4	Accession Number	ATCC 209263
149-4	**Additional Indications**	NONE
149-5	**Designated States for Which Indications are Made**	all designated States
149-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
150	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
150-1	page	101
150-2	line	37
150-3	**Identification of Deposit**	
150-3-1	Name of depositary institution	American Type Culture Collection
150-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
150-3-3	Date of deposit	16 September 1997 (16.09.1997)
150-3-4	Accession Number	ATCC 209264
150-4	**Additional Indications**	NONE
150-5	**Designated States for Which Indications are Made**	all designated States
150-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
151	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
151-1	page	101
151-2	line	38
151-3	**Identification of Deposit**	
151-3-1	Name of depositary institution	American Type Culture Collection
151-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
151-3-3	Date of deposit	16 October 1997 (16.10.1997)
151-3-4	Accession Number	ATCC 209376
151-4	**Additional Indications**	NONE
151-5	**Designated States for Which Indications are Made**	all designated States

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151-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
152	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
152-1	page	101
152-2	line	39
152-3	**Identification of Deposit**	
152-3-1	Name of depositary institution	American Type Culture Collection
152-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
152-3-3	Date of deposit	17 October 1997 (17.10.1997)
152-3-4	Accession Number	ATCC 209391
152-4	**Additional Indications**	NONE
152-5	**Designated States for Which Indications are Made**	all designated States
152-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
153	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
153-1	page	101
153-2	line	40
153-3	**Identification of Deposit**	
153-3-1	Name of depositary institution	American Type Culture Collection
153-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
153-3-3	Date of deposit	28 October 1997 (28.10.1997)
153-3-4	Accession Number	ATCC 209417
153-4	**Additional Indications**	NONE
153-5	**Designated States for Which Indications are Made**	all designated States
153-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
154	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
154-1	page	101
154-2	line	41
154-3	**Identification of Deposit**	
154-3-1	Name of depositary institution	American Type Culture Collection
154-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
154-3-3	Date of deposit	16 September 1997 (16.09.1997)
154-3-4	Accession Number	ATCC 209253

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154-4	**Additional Indications**	**NONE**
154-5	**Designated States for Which Indications are Made**	**all designated States**
154-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
155	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
155-1	page	**101**
155-2	line	**42**
155-3	**Identification of Deposit**	
155-3-1	Name of depositary institution	**American Type Culture Collection**
155-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
155-3-3	Date of deposit	**12 May 1998 (12.05.1998)**
155-3-4	Accession Number	**ATCC 209855**
155-4	**Additional Indications**	**NONE**
155-5	**Designated States for Which Indications are Made**	**all designated States**
155-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
156	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
156-1	page	**101**
156-2	line	**43**
156-3	**Identification of Deposit**	
156-3-1	Name of depositary institution	**American Type Culture Collection**
156-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
156-3-3	Date of deposit	**10 December 1997 (10.12.1997)**
156-3-4	Accession Number	**ATCC 209526**
156-4	**Additional Indications**	**NONE**
156-5	**Designated States for Which Indications are Made**	**all designated States**
156-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
157	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
157-1	page	**101**
157-2	line	**44**

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157-3	**Identification of Deposit**	
157-3-1	Name of depositary institution	American Type Culture Collection
157-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
157-3-3	Date of deposit	16 September 1997 (16.09.1997)
157-3-4	Accession Number	ATCC 209252
157-4	**Additional Indications**	NONE
157-5	**Designated States for Which Indications are Made**	all designated States
157-6	**Separate Furnishing of Indications**	NONE
	These indications will be submitted to the International Bureau later	
158	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
158-1	page	101
158-2	line	45
158-3	**Identification of Deposit**	
158-3-1	Name of depositary institution	American Type Culture Collection
158-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
158-3-3	Date of deposit	16 October 1997 (16.10.1997)
158-3-4	Accession Number	ATCC 20937/4
158-4	**Additional Indications**	NONE
158-5	**Designated States for Which Indications are Made**	all designated States
158-6	**Separate Furnishing of Indications**	NONE
	These indications will be submitted to the International Bureau later	
159	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
159-1	page	101
159-2	line	46
159-3	**Identification of Deposit**	
159-3-1	Name of depositary institution	American Type Culture Collection
159-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
159-3-3	Date of deposit	10 December 1997 (10.12.1997)
159-3-4	Accession Number	ATCC 209528
159-4	**Additional Indications**	NONE
159-5	**Designated States for Which Indications are Made**	all designated States
159-6	**Separate Furnishing of Indications**	NONE
	These indications will be submitted to the International Bureau later	

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160	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
160-1	page	101
160-2	line	47
160-3	**Identification of Deposit**	
160-3-1	Name of depositary institution	American Type Culture Collection
160-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
160-3-3	Date of deposit	16 September 1997 (16.09.1997)
160-3-4	Accession Number	ATCC 209265
160-4	**Additional Indications**	NONE
160-5	**Designated States for Which Indications are Made**	all designated States
160-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
161	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
161-1	page	101
161-2	line	48
161-3	**Identification of Deposit**	
161-3-1	Name of depositary institution	American Type Culture Collection
161-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
161-3-3	Date of deposit	17 October 1997 (17.10.1997)
161-3-4	Accession Number	ATCC 209396 .
161-4	**Additional Indications**	NONE
161-5	**Designated States for Which Indications are Made**	all designated States
161-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
162	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
162-1	page	101
162-2	line	49
162-3	**Identification of Deposit**	
162-3-1	Name of depositary institution	American Type Culture Collection
162-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
162-3-3	Date of deposit	18 August 1997 (18.08.1997)
162-3-4	Accession Number	ATCC 209201
162-4	**Additional Indications**	NONE
162-5	**Designated States for Which Indications are Made**	all designated States

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162-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
163	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
163-1	page	101
163-2	line	50
163-3	**Identification of Deposit**	
163-3-1	Name of depositary institution	American Type Culture Collection
163-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
163-3-3	Date of deposit	28 October 1997 (28.10.1997)
163-3-4	Accession Number	ATCC 209416
163-4	**Additional Indications**	**NONE**
163-5	**Designated States for Which Indications are Made**	all designated States
163-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
164	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
164-1	page	101
164-2	line	51
164-3	**Identification of Deposit**	
164-3-1	Name of depositary institution	American Type Culture Collection
164-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
164-3-3	Date of deposit	17 October 1997 (17.10.1997)
164-3-4	Accession Number	ATCC 209403
164-4	**Additional Indications**	**NONE**
164-5	**Designated States for Which Indications are Made**	all designated States
164-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
165	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
165-1	page	101
165-2	line	52
165-3	**Identification of Deposit**	
165-3-1	Name of depositary institution	American Type Culture Collection
165-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
165-3-3	Date of deposit	28 October 1997 (28.10.1997)
165-3-4	Accession Number	ATCC 209419

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165-4	**Additional Indications**	**NONE**
165-5	**Designated States for Which Indications are Made**	**all designated States**
165-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
166	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
166-1	page	**101**
166-2	line	**53**
166-3	**Identification of Deposit**	
166-3-1	Name of depositary institution	**American Type Culture Collection**
166-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
166-3-3	Date of deposit	**17 October 1997 (17.10.1997)**
166-3-4	Accession Number	**ATCC 209402**
166-4	**Additional Indications**	**NONE**
166-5	**Designated States for Which Indications are Made**	**all designated States**
166-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
167	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
167-1	page	**101**
167-2	line	**54**
167-3	**Identification of Deposit**	
167-3-1	Name of depositary institution	**American Type Culture Collection**
167-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
167-3-3	Date of deposit	**16 October 1997 (16.10.1997)**
167-3-4	Accession Number	**ATCC 209378**
167-4	**Additional Indications**	**NONE**
167-5	**Designated States for Which Indications are Made**	**all designated States**
167-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
168	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
168-1	page	**101**
168-2	line	**55**

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168-3	**Identification of Deposit**	
168-3-1	Name of depositary institution	**American Type Culture Collection**
168-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
168-3-3	Date of deposit	**21 November 1997 (21.11.1997)**
168-3-4	Accession Number	**ATCC 209489**
168-4	**Additional Indications**	**NONE**
168-5	**Designated States for Which Indications are Made**	**all designated States**
168-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
169	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
169-1	page	**102**
169-2	line	**2**
169-3	**Identification of Deposit**	
169-3-1	Name of depositary institution	**American Type Culture Collection**
169-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
169-3-3	Date of deposit	**17 October 1997 (17.10.1997)**
169-3-4	Accession Number	**ATCC 209401**
169-4	**Additional Indications**	**NONE**
169-5	**Designated States for Which Indications are Made**	**all designated States**
169-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
170	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
170-1	page	**102**
170-2	line	**3**
170-3	**Identification of Deposit**	
170-3-1	Name of depositary institution	**American Type Culture Collection**
170-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
170-3-3	Date of deposit	**17 October 1997 (17.10.1997)**
170-3-4	Accession Number	**ATCC 209397**
170-4	**Additional Indications**	**NONE**
170-5	**Designated States for Which Indications are Made**	**all designated States**
170-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	

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171	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
171-1	page	102
171-2	line	4
171-3	**Identification of Deposit**	
171-3-1	Name of depositary institution	American Type Culture Collection
171-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
171-3-3	Date of deposit	17 October 1997 (17.10.1997)
171-3-4	Accession Number	ATCC 209389
171-4	**Additional Indications**	NONE
171-5	**Designated States for Which Indications are Made**	all designated States
171-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
172	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
172-1	page	102
172-2	line	5
172-3	**Identification of Deposit**	
172-3-1	Name of depositary institution	American Type Culture Collection
172-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
172-3-3	Date of deposit	07 November 1997 (07.11.1997)
172-3-4	Accession Number	ATCC 209438
172-4	**Additional Indications**	NONE
172-5	**Designated States for Which Indications are Made**	all designated States
172-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
173	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
173-1	page	102
173-2	line	6
173-3	**Identification of Deposit**	
173-3-1	Name of depositary institution	American Type Culture Collection
173-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
173-3-3	Date of deposit	21 November 1997 (21.11.1997)
173-3-4	Accession Number	ATCC 209492
173-4	**Additional Indications**	NONE
173-5	**Designated States for Which Indications are Made**	all designated States

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173-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
174	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
174-1	page	102
174-2	line	7
174-3	**Identification of Deposit**	
174-3-1	Name of depositary institution	American Type Culture Collection
174-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
174-3-3	Date of deposit	17 October 1997 (17.10.1997)
174-3-4	Accession Number	ATCC 209388
174-4	**Additional Indications**	**NONE**
174-5	**Designated States for Which Indications are Made**	all designated States
174-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
175	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
175-1	page	102
175-2	line	8
175-3	**Identification of Deposit**	
175-3-1	Name of depositary institution	American Type Culture Collection
175-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
175-3-3	Date of deposit	07 November 1997 (07.11.1997)
175-3-4	Accession Number	ATCC 209432
175-4	**Additional Indications**	**NONE**
175-5	**Designated States for Which Indications are Made**	all designated States
175-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
176	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
176-1	page	102
176-2	line	9
176-3	**Identification of Deposit**	
176-3-1	Name of depositary institution	American Type Culture Collection
176-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
176-3-3	Date of deposit	07 November 1997 (07.11.1997)
176-3-4	Accession Number	ATCC 209439

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176-4	**Additional Indications**	**NONE**
176-5	**Designated States for Which Indications are Made**	all designated States
176-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
177	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
177-1	page	102
177-2	line	10
177-3	**Identification of Deposit**	
177-3-1	Name of depositary institution	**American Type Culture Collection**
177-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
177-3-3	Date of deposit	**07 November 1997 (07.11.1997)**
177-3-4	Accession Number	**ATCC 209433**
177-4	**Additional Indications**	**NONE**
177-5	**Designated States for Which Indications are Made**	all designated States
177-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
178	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
178-1	page	102
178-2	line	11
178-3	**Identification of Deposit**	
178-3-1	Name of depositary institution	**American Type Culture Collection**
178-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
178-3-3	Date of deposit	**05 February 1998 (05.02.1998)**
178-3-4	Accession Number	**ATCC 209618**
178-4	**Additional Indications**	**NONE**
178-5	**Designated States for Which Indications are Made**	all designated States
178-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
179	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
179-1	page	102
179-2	line	12

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179-3	**Identification of Deposit**	
179-3-1	Name of depositary institution	**American Type Culture Collection**
179-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
179-3-3	Date of deposit	**21 November 1997 (21.11.1997)**
179-3-4	Accession Number	**ATCC 209484**
179-4	**Additional Indications**	**NONE**
179-5	**Designated States for Which Indications are Made**	**all designated States**
179-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
180	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
180-1	page	**102**
180-2	line	**13**
180-3	**Identification of Deposit**	
180-3-1	Name of depositary institution	**American Type Culture Collection**
180-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
180-3-3	Date of deposit	**21 November 1997 (21.11.1997)**
180-3-4	Accession Number	**ATCC 209487**
180-4	**Additional Indications**	**NONE**
180-5	**Designated States for Which Indications are Made**	**all designated States**
180-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
181	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
181-1	page	**102**
181-2	line	**14**
181-3	**Identification of Deposit**	
181-3-1	Name of depositary institution	**American Type Culture Collection**
181-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
181-3-3	Date of deposit	**07 November 1997 (07.11.1997)**
181-3-4	Accession Number	**ATCC 209434**
181-4	**Additional Indications**	**NONE**
181-5	**Designated States for Which Indications are Made**	**all designated States**
181-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	

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182	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
182-1	page	102
182-2	line	15
182-3	**Identification of Deposit**	
182-3-1	Name of depositary institution	American Type Culture Collection
182-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
182-3-3	Date of deposit	26 March 1998 (26.03.1998)
182-3-4	Accession Number	ATCC 209704
182-4	**Additional Indications**	NONE
182-5	**Designated States for Which Indications are Made**	all designated States
182-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
183	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
183-1	page	102
183-2	line	16
183-3	**Identification of Deposit**	
183-3-1	Name of depositary institution	American Type Culture Collection
183-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
183-3-3	Date of deposit	28 April 1998 (28.04.1998)
183-3-4	Accession Number	ATCC 209808
183-4	**Additional Indications**	NONE
183-5	**Designated States for Which Indications are Made**	all designated States
183-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
184	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
184-1	page	102
184-2	line	17
184-3	**Identification of Deposit**	
184-3-1	Name of depositary institution	American Type Culture Collection
184-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
184-3-3	Date of deposit	06 May 1998 (06.05.1998)
184-3-4	Accession Number	ATCC 209847
184-4	**Additional Indications**	NONE
184-5	**Designated States for Which Indications are Made**	all designated States

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184-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
185	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
185-1	page	102
185-2	line	18
185-3	**Identification of Deposit**	
185-3-1	Name of depositary institution	American Type Culture Collection
185-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
185-3-3	Date of deposit	05 February 1998 (05.02.1998)
185-3-4	Accession Number	ATCC 209616
185-4	**Additional Indications**	NONE
185-5	**Designated States for Which Indications are Made**	all designated States
185-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
186	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
186-1	page	102
186-2	line	19
186-3	**Identification of Deposit**	
186-3-1	Name of depositary institution	American Type Culture Collection
186-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
186-3-3	Date of deposit	05 February 1998 (05.02.1998)
186-3-4	Accession Number	ATCC 209619
186-4	**Additional Indications**	NONE
186-5	**Designated States for Which Indications are Made**	all designated States
186-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
187	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
187-1	page	102
187-2	line	20
187-3	**Identification of Deposit**	
187-3-1	Name of depositary institution	American Type Culture Collection
187-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
187-3-3	Date of deposit	11 August 1998 (11.08.1998)
187-3-4	Accession Number	ATCC 203109

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187-4	**Additional Indications**	**NONE**
187-5	**Designated States for Which Indications are Made**	**all designated States**
187-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
188	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
188-1	page	**102**
188-2	line	**21**
188-3	**Identification of Deposit**	
188-3-1	Name of depositary institution	**American Type Culture Collection**
188-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
188-3-3	Date of deposit	**31 March 1998 (31.03.1998)**
188-3-4	Accession Number	**ATCC 209715**
188-4	**Additional Indications**	**NONE**
188-5	**Designated States for Which Indications are Made**	**all designated States**
188-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
189	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
189-1	page	**102**
189-2	line	**22**
189-3	**Identification of Deposit**	
189-3-1	Name of depositary institution	**American Type Culture Collection**
189-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
189-3-3	Date of deposit	**11 March 1998 (11.03.1998)**
189-3-4	Accession Number	**ATCC 209669**
189-4	**Additional Indications**	**NONE**
189-5	**Designated States for Which Indications are Made**	**all designated States**
189-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
190	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
190-1	page	**102**
190-2	line	**23**

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190-3	**Identification of Deposit**	
190-3-1	Name of depositary institution	**American Type Culture Collection**
190-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
190-3-3	Date of deposit	**23 June 1998 (23.06.1998)**
190-3-4	Accession Number	**ATCC 203002**
190-4	**Additional Indications**	**NONE**
190-5	**Designated States for Which Indications are Made**	**all designated States**
190-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
191	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
191-1	page	**102**
191-2	line	**24**
191-3	**Identification of Deposit**	
191-3-1	Name of depositary institution	**American Type Culture Collection**
191-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
191-3-3	Date of deposit	**26 March 1998 (26.03.1998)**
191-3-4	Accession Number	**ATCC 209705**
191-4	**Additional Indications**	**NONE**
191-5	**Designated States for Which Indications are Made**	**all designated States**
191-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
192	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
192-1	page	**102**
192-2	line	**25**
192-3	**Identification of Deposit**	
192-3-1	Name of depositary institution	**American Type Culture Collection**
192-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
192-3-3	Date of deposit	**16 June 1998 (16.06.1998)**
192-3-4	Accession Number	**ATCC 209981**
192-4	**Additional Indications**	**NONE**
192-5	**Designated States for Which Indications are Made**	**all designated States**
192-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**

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193	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
193-1	page	102
193-2	line	26
193-3	**Identification of Deposit**	
193-3-1	Name of depositary institution	American Type Culture Collection
193-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
193-3-3	Date of deposit	07 April 1998 (07.04.1998)
193-3-4	Accession Number	ATCC 209749
193-4	**Additional Indications**	NONE
193-5	**Designated States for Which Indications are Made**	all designated States
193-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
194	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
194-1	page	102
194-2	line	27
194-3	**Identification of Deposit**	
194-3-1	Name of depositary institution	American Type Culture Collection
194-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
194-3-3	Date of deposit	12 May 1998 (12.05.1998)
194-3-4	Accession Number	ATCC 209859
194-4	**Additional Indications**	NONE
194-5	**Designated States for Which Indications are Made**	all designated States
194-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
195	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
195-1	page	102
195-2	line	28
195-3	**Identification of Deposit**	
195-3-1	Name of depositary institution	American Type Culture Collection
195-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
195-3-3	Date of deposit	06 May 1998 (06.05.1998)
195-3-4	Accession Number	ATCC 209845
195-4	**Additional Indications**	NONE
195-5	**Designated States for Which Indications are Made**	all designated States

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195-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
196	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
196-1	page	102
196-2	line	29
196-3	**Identification of Deposit**	
196-3-1	Name of depositary institution	American Type Culture Collection
196-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
196-3-3	Date of deposit	07 April 1998 (07.04.1998)
196-3-4	Accession Number	ATCC 209748
196-4	**Additional Indications**	NONE
196-5	**Designated States for Which Indications are Made**	all designated States
196-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
197	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
197-1	page	102
197-2	line	30
197-3	**Identification of Deposit**	
197-3-1	Name of depositary institution	American Type Culture Collection
197-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
197-3-3	Date of deposit	11 August 1998 (11.08.1998)
197-3-4	Accession Number	ATCC 203107
197-4	**Additional Indications**	NONE
197-5	**Designated States for Which Indications are Made**	all designated States
197-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
198	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
198-1	page	102
198-2	line	31
198-3	**Identification of Deposit**	
198-3-1	Name of depositary institution	American Type Culture Collection
198-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
198-3-3	Date of deposit	23 April 1998 (23.04.1998)
198-3-4	Accession Number	ATCC 209801

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198-4	**Additional Indications**	**NONE**
198-5	**Designated States for Which Indications are Made**	**all designated States**
198-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
199	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
199-1	page	**102**
199-2	line	**32**
199-3	**Identification of Deposit**	
199-3-1	Name of depositary institution	**American Type Culture Collection**
199-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
199-3-3	Date of deposit	**09 June 1998 (09.06.1998)**
199-3-4	Accession Number	**ATCC 209948**
199-4	**Additional Indications**	**NONE**
199-5	**Designated States for Which Indications are Made**	**all designated States**
199-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
200	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
200-1	page	**102**
200-2	line	**33**
200-3	**Identification of Deposit**	
200-3-1	Name of depositary institution	**American Type Culture Collection**
200-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
200-3-3	Date of deposit	**20 May 1998 (20.05.1998)**
200-3-4	Accession Number	**ATCC 209883**
200-4	**Additional Indications**	**NONE**
200-5	**Designated States for Which Indications are Made**	**all designated States**
200-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
201	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
201-1	page	**102**
201-2	line	**34**

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201-3	**Identification of Deposit**	
201-3-1	Name of depositary institution	**American Type Culture Collection**
201-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
201-3-3	Date of deposit	**01 July 1998 (01.07.1998)**
201-3-4	Accession Number	**ATCC 203049**
201-4	**Additional Indications**	**NONE**
201-5	**Designated States for Which Indications are Made**	**all designated States**
201-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
202	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
202-1	page	**102**
202-2	line	**35**
202-3	**Identification of Deposit**	
202-3-1	Name of depositary institution	**American Type Culture Collection**
202-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
202-3-3	Date of deposit	**06 May 1998 (06.05.1998)**
202-3-4	Accession Number	**ATCC 209846**
202-4	**Additional Indications**	**NONE**
202-5	**Designated States for Which Indications are Made**	**all designated States**
202-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
203	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
203-1	page	**102**
203-2	line	**36**
203-3	**Identification of Deposit**	
203-3-1	Name of depositary institution	**American Type Culture Collection**
203-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
203-3-3	Date of deposit	**12 May 1998 (12.05.1998)**
203-3-4	Accession Number	**ATCC 209857**
203-4	**Additional Indications**	**NONE**
203-5	**Designated States for Which Indications are Made**	**all designated States**
203-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	

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204	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
204-1	page	102
204-2	line	37
204-3	**Identification of Deposit**	
204-3-1	Name of depositary institution	American Type Culture Collection
204-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
204-3-3	Date of deposit	14 May 1998 (14.05.1998)
204-3-4	Accession Number	ATCC 209864
204-4	**Additional Indications**	NONE
204-5	**Designated States for Which Indications are Made**	all designated States
204-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
205	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
205-1	page	102
205-2	line	38
205-3	**Identification of Deposit**	
205-3-1	Name of depositary institution	American Type Culture Collection
205-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
205-3-3	Date of deposit	20 May 1998 (20.05.1998)
205-3-4	Accession Number	ATCC 209880
205-4	**Additional Indications**	NONE
205-5	**Designated States for Which Indications are Made**	all designated States
205-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
206	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
206-1	page	102
206-2	line	39
206-3	**Identification of Deposit**	
206-3-1	Name of depositary institution	American Type Culture Collection
206-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
206-3-3	Date of deposit	14 May 1998 (14.05.1998)
206-3-4	Accession Number	ATCC 209869
206-4	**Additional Indications**	NONE
206-5	**Designated States for Which Indications are Made**	all designated States

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206-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
207	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
207-1	page	102
207-2	line	40
207-3	**Identification of Deposit**	
207-3-1	Name of depositary institution	American Type Culture Collection
207-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
207-3-3	Date of deposit	09 June 1998 (09.06.1998)
207-3-4	Accession Number	ATCC 209950
207-4	**Additional Indications**	NONE
207-5	**Designated States for Which Indications are Made**	all designated States
207-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
208	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
208-1	page	102
208-2	line	41
208-3	**Identification of Deposit**	
208-3-1	Name of depositary institution	American Type Culture Collection
208-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
208-3-3	Date of deposit	23 June 1998 (23.06.1998)
208-3-4	Accession Number	ATCC 203008
208-4	**Additional Indications**	NONE
208-5	**Designated States for Which Indications are Made**	all designated States
208-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
209	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
209-1	page	102
209-2	line	42
209-3	**Identification of Deposit**	
209-3-1	Name of depositary institution	American Type Culture Collection
209-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
209-3-3	Date of deposit	23 June 1998 (23.06.1998)
209-3-4	Accession Number	ATCC 203014

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209-4	**Additional Indications**	**NONE**
209-5	**Designated States for Which Indications are Made**	all designated States
209-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
210	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
210-1	page	102
210-2	line	43
210-3	**Identification of Deposit**	
210-3-1	Name of depositary institution	American Type Culture Collection
210-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
210-3-3	Date of deposit	11 August 1998 (11.08.1998)
210-3-4	Accession Number	ATCC 203110
210-4	**Additional Indications**	**NONE**
210-5	**Designated States for Which Indications are Made**	all designated States
210-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
211	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
211-1	page	102
211-2	line	44
211-3	**Identification of Deposit**	
211-3-1	Name of depositary institution	American Type Culture Collection
211-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
211-3-3	Date of deposit	23 June 1998 (23.06.1998)
211-3-4	Accession Number	ATCC 203009
211-4	**Additional Indications**	**NONE**
211-5	**Designated States for Which Indications are Made**	all designated States
211-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
212	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
212-1	page	102
212-2	line	45

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212-3	**Identification of Deposit**	
212-3-1	Name of depositary institution	**American Type Culture Collection**
212-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
212-3-3	Date of deposit	**09 June 1998 (09.06.1998)**
212-3-4	Accession Number	**ATCC 209961**
212-4	**Additional Indications**	**NONE**
212-5	**Designated States for Which Indications are Made**	**all designated States**
212-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
213	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
213-1	page	**102**
213-2	line	**46**
213-3	**Identification of Deposit**	
213-3-1	Name of depositary institution	**American Type Culture Collection**
213-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
213-3-3	Date of deposit	**09 June 1998 (09.06.1998)**
213-3-4	Accession Number	**ATCC 209962**
213-4	**Additional Indications**	**NONE**
213-5	**Designated States for Which Indications are Made**	**all designated States**
213-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
214	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
214-1	page	**102**
214-2	line	**47**
214-3	**Identification of Deposit**	
214-3-1	Name of depositary institution	**American Type Culture Collection**
214-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
214-3-3	Date of deposit	**14 May 1998 (14.05.1998)**
214-3-4	Accession Number	**ATCC 209866**
214-4	**Additional Indications**	**NONE**
214-5	**Designated States for Which Indications are Made**	**all designated States**
214-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**

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215	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
215-1	page	102
215-2	line	48
215-3	**Identification of Deposit**	
215-3-1	Name of depositary institution	American Type Culture Collection
215-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
215-3-3	Date of deposit	25 August 1998 (25.08.1998)
215-3-4	Accession Number	ATCC 203157
215-4	**Additional Indications**	NONE
215-5	**Designated States for Which Indications are Made**	all designated States
215-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
216	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
216-1	page	102
216-2	line	49
216-3	**Identification of Deposit**	
216-3-1	Name of depositary institution	American Type Culture Collection
216-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
216-3-3	Date of deposit	11 August 1998 (11.08.1998)
216-3-4	Accession Number	ATCC 203106
216-4	**Additional Indications**	NONE
216-5	**Designated States for Which Indications are Made**	all designated States
216-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
217	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
217-1	page	102
217-2	line	50
217-3	**Identification of Deposit**	
217-3-1	Name of depositary institution	American Type Culture Collection
217-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
217-3-3	Date of deposit	09 June 1998 (09.06.1998)
217-3-4	Accession Number	ATCC 209945
217-4	**Additional Indications**	NONE
217-5	**Designated States for Which Indications are Made**	all designated States

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217-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
218	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
218-1	page	102
218-2	line	51
218-3	**Identification of Deposit**	
218-3-1	Name of depositary institution	American Type Culture Collection
218-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
218-3-3	Date of deposit	16 June 1998 (16.06.1998)
218-3-4	Accession Number	ATCC 209989
218-4	**Additional Indications**	NONE
218-5	**Designated States for Which Indications are Made**	all designated States
218-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
219	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
219-1	page	102
219-2	line	52
219-3	**Identification of Deposit**	
219-3-1	Name of depositary institution	American Type Culture Collection
219-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
219-3-3	Date of deposit	11 August 1998 (11.08.1998)
219-3-4	Accession Number	ATCC 203108
219-4	**Additional Indications**	NONE
219-5	**Designated States for Which Indications are Made**	all designated States
219-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
220	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
220-1	page	102
220-2	line	53
220-3	**Identification of Deposit**	
220-3-1	Name of depositary institution	American Type Culture Collection
220-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
220-3-3	Date of deposit	11 August 1998 (11.08.1998)
220-3-4	Accession Number	ATCC 203111

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220-4	**Additional Indications**	**NONE**
220-5	**Designated States for Which Indications are Made**	**all designated States**
220-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
221	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
221-1	page	**102**
221-2	line	**54**
221-3	**Identification of Deposit**	
221-3-1	Name of depositary institution	**American Type Culture Collection**
221-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
221-3-3	Date of deposit	**20 October 1998 (20.10.1998)**
221-3-4	Accession Number	**ATCC 203359**
221-4	**Additional Indications**	**NONE**
221-5	**Designated States for Which Indications are Made**	**all designated States**
221-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
222	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
222-1	page	**102**
222-2	line	**55**
222-3	**Identification of Deposit**	
222-3-1	Name of depositary institution	**American Type Culture Collection**
222-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
222-3-3	Date of deposit	**16 June 1998 (16.06.1998)**
222-3-4	Accession Number	**ATCC 209988**
222-4	**Additional Indications**	**NONE**
222-5	**Designated States for Which Indications are Made**	**all designated States**
222-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
223	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
223-1	page	**103**
223-2	line	**2**

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223-3	**Identification of Deposit**	
223-3-1	Name of depositary institution	**American Type Culture Collection**
223-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
223-3-3	Date of deposit	**16 June 1998 (16.06.1998)**
223-3-4	Accession Number	**ATCC 209978**
223-4	**Additional Indications**	**NONE**
223-5	**Designated States for Which Indications are Made**	**all designated States**
223-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
224	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
224-1	page	**103**
224-2	line	**3**
224-3	**Identification of Deposit**	
224-3-1	Name of depositary institution	**American Type Culture Collection**
224-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
224-3-3	Date of deposit	**04 August 1998 (04.08.1998)**
224-3-4	Accession Number	**ATCC 203098**
224-4	**Additional Indications**	**NONE**
224-5	**Designated States for Which Indications are Made**	**all designated States**
224-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
225	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
225-1	page	**103**
225-2	line	**4**
225-3	**Identification of Deposit**	
225-3-1	Name of depositary institution	**American Type Culture Collection**
225-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
225-3-3	Date of deposit	**16 June 1998 (16.06.1998)**
225-3-4	Accession Number	**ATCC 209980**
225-4	**Additional Indications**	**NONE**
225-5	**Designated States for Which Indications are Made**	**all designated States**
225-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**

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226	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
226-1	page	103
226-2	line	5
226-3	**Identification of Deposit**	
226-3-1	Name of depositary institution	American Type Culture Collection
226-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
226-3-3	Date of deposit	04 August 1998 (04.08.1998)
226-3-4	Accession Number	ATCC 203091
226-4	**Additional Indications**	NONE
226-5	**Designated States for Which Indications are Made**	all designated States
226-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
227	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
227-1	page	103
227-2	line	6
227-3	**Identification of Deposit**	
227-3-1	Name of depositary institution	American Type Culture Collection
227-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
227-3-3	Date of deposit	04 August 1998 (04.08.1998)
227-3-4	Accession Number	ATCC 203090
227-4	**Additional Indications**	NONE
227-5	**Designated States for Which Indications are Made**	all designated States
227-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
228	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
228-1	page	103
228-2	line	7
228-3	**Identification of Deposit**	
228-3-1	Name of depositary institution	American Type Culture Collection
228-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
228-3-3	Date of deposit	04 August 1998 (04.08.1998)
228-3-4	Accession Number	ATCC 203092
228-4	**Additional Indications**	NONE
228-5	**Designated States for Which Indications are Made**	all designated States

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228-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
229	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
229-1	page	103
229-2	line	8
229-3	**Identification of Deposit**	
229-3-1	Name of depositary institution	American Type Culture Collection
229-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
229-3-3	Date of deposit	10 November 1998 (10.11.1998)
229-3-4	Accession Number	ATCC 203452
229-4	**Additional Indications**	NONE
229-5	**Designated States for Which Indications are Made**	all designated States
229-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
230	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
230-1	page	103
230-2	line	9
230-3	**Identification of Deposit**	
230-3-1	Name of depositary institution	American Type Culture Collection
230-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
230-3-3	Date of deposit	01 September 1998 (01.09.1998)
230-3-4	Accession Number	ATCC 203173
230-4	**Additional Indications**	NONE
230-5	**Designated States for Which Indications are Made**	all designated States
230-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
231	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
231-1	page	103
231-2	line	10
231-3	**Identification of Deposit**	
231-3-1	Name of depositary institution	American Type Culture Collection
231-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
231-3-3	Date of deposit	17 November 1998 (17.11.1998)
231-3-4	Accession Number	ATCC 203464

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231-4	**Additional Indications**	**NONE**
231-5	**Designated States for Which Indications are Made**	**all designated States**
231-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
232	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
232-1	page	**103**
232-2	line	**11**
232-3	**Identification of Deposit**	
232-3-1	Name of depositary institution	**American Type Culture Collection**
232-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
232-3-3	Date of deposit	**18 August 1998 (18.08.1998)**
232-3-4	Accession Number	**ATCC 203132**
232-4	**Additional Indications**	**NONE**
232-5	**Designated States for Which Indications are Made**	**all designated States**
232-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
233	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
233-1	page	**103**
233-2	line	**12**
233-3	**Identification of Deposit**	
233-3-1	Name of depositary institution	**American Type Culture Collection**
233-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
233-3-3	Date of deposit	**09 September 1998 (09.09.1998)**
233-3-4	Accession Number	**ATCC 203254**
233-4	**Additional Indications**	**NONE**
233-5	**Designated States for Which Indications are Made**	**all designated States**
233-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
234	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
234-1	page	**103**
234-2	line	**13**

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234-3	**Identification of Deposit**	
234-3-1	Name of depositary institution	**American Type Culture Collection**
234-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
234-3-3	Date of deposit	**20 October 1998 (20.10.1998)**
234-3-4	Accession Number	**ATCC 203358**
234-4	**Additional Indications**	**NONE**
234-5	**Designated States for Which Indications are Made**	**all designated States**
234-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
235	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
235-1	page	**103**
235-2	line	**14**
235-3	**Identification of Deposit**	
235-3-1	Name of depositary institution	**American Type Culture Collection**
235-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
235-3-3	Date of deposit	**04 August 1998 (04.08.1998)**
235-3-4	Accession Number	**ATCC 203093**
235-4	**Additional Indications**	**NONE**
235-5	**Designated States for Which Indications are Made**	**all designated States**
235-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
236	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
236-1	page	**103**
236-2	line	**15**
236-3	**Identification of Deposit**	
236-3-1	Name of depositary institution	**American Type Culture Collection**
236-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
236-3-3	Date of deposit	**03 November 1998 (03.11.1998)**
236-3-4	Accession Number	**ATCC 203457**
236-4	**Additional Indications**	**NONE**
236-5	**Designated States for Which Indications are Made**	**all designated States**
236-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	

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237	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
237-1	page	103
237-2	line	16
237-3	**Identification of Deposit**	
237-3-1	Name of depositary institution	American Type Culture Collection
237-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
237-3-3	Date of deposit	09 September 1998 (09.09.1998)
237-3-4	Accession Number	ATCC 203241
237-4	**Additional Indications**	NONE
237-5	**Designated States for Which Indications are Made**	all designated States
237-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
238	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
238-1	page	103
238-2	line	17
238-3	**Identification of Deposit**	
238-3-1	Name of depositary institution	American Type Culture Collection
238-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
238-3-3	Date of deposit	09 September 1998 (09.09.1998)
238-3-4	Accession Number	ATCC 203249
238-4	**Additional Indications**	NONE
238-5	**Designated States for Which Indications are Made**	all designated States
238-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
239	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
239-1	page	103
239-2	line	18
239-3	**Identification of Deposit**	
239-3-1	Name of depositary institution	American Type Culture Collection
239-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
239-3-3	Date of deposit	09 September 1998 (09.09.1998)
239-3-4	Accession Number	ATCC 203250
239-4	**Additional Indications**	NONE
239-5	**Designated States for Which Indications are Made**	all designated States

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239-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
240	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
240-1	page	103
240-2	line	19
240-3	**Identification of Deposit**	
240-3-1	Name of depositary institution	American Type Culture Collection
240-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
240-3-3	Date of deposit	18 August 1998 (18.08.1998)
240-3-4	Accession Number	ATCC 203131
240-4	**Additional Indications**	**NONE**
240-5	**Designated States for Which Indications are Made**	all designated States
240-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
241	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
241-1	page	103
241-2	line	20
241-3	**Identification of Deposit**	
241-3-1	Name of depositary institution	American Type Culture Collection
241-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
241-3-3	Date of deposit	15 September 1998 (15.09.1998)
241-3-4	Accession Number	ATCC 203223
241-4	**Additional Indications**	**NONE**
241-5	**Designated States for Which Indications are Made**	all designated States
241-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
242	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
242-1	page	103
242-2	line	21
242-3	**Identification of Deposit**	
242-3-1	Name of depositary institution	American Type Culture Collection
242-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
242-3-3	Date of deposit	15 September 1998 (15.09.1998)
242-3-4	Accession Number	ATCC 203233

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242-4	**Additional Indications**	**NONE**
242-5	**Designated States for Which Indications are Made**	all designated States
242-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
243	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
243-1	page	103
243-2	line	22
243-3	**Identification of Deposit**	
243-3-1	Name of depositary institution	**American Type Culture Collection**
243-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
243-3-3	Date of deposit	09 September 1998 (09.09.1998)
243-3-4	Accession Number	**ATCC 203252**
243-4	**Additional Indications**	**NONE**
243-5	**Designated States for Which Indications are Made**	all designated States
243-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
244	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
244-1	page	103
244-2	line	23
244-3	**Identification of Deposit**	
244-3-1	Name of depositary institution	**American Type Culture Collection**
244-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
244-3-3	Date of deposit	17 November 1998 (17.11.1998)
244-3-4	Accession Number	**ATCC 203476**
244-4	**Additional Indications**	**NONE**
244-5	**Designated States for Which Indications are Made**	all designated States
244-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
245	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
245-1	page	103
245-2	line	24

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245-3	**Identification of Deposit**	
245-3-1	Name of depositary institution	**American Type Culture Collection**
245-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
245-3-3	Date of deposit	**04 August 1998 (04.08.1998)**
245-3-4	Accession Number	**ATCC 203094**
245-4	**Additional Indications**	**NONE**
245-5	**Designated States for Which Indications are Made**	**all designated States**
245-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
246	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
246-1	page	**103**
246-2	line	**25**
246-3	**Identification of Deposit**	
246-3-1	Name of depositary institution	**American Type Culture Collection**
246-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
246-3-3	Date of deposit	**15 September 1998 (15.09.1998)**
246-3-4	Accession Number	**ATCC 203235**
246-4	**Additional Indications**	**NONE**
246-5	**Designated States for Which Indications are Made**	**all designated States**
246-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
247	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
247-1	page	**103**
247-2	line	**26**
247-3	**Identification of Deposit**	
247-3-1	Name of depositary institution	**American Type Culture Collection**
247-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
247-3-3	Date of deposit	**22 September 1998 (22.09.1998)**
247-3-4	Accession Number	**ATCC 203267**
247-4	**Additional Indications**	**NONE**
247-5	**Designated States for Which Indications are Made**	**all designated States**
247-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**

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248	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
248-1	page	103
248-2	line	27
248-3	**Identification of Deposit**	
248-3-1	Name of depositary institution	American Type Culture Collection
248-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
248-3-3	Date of deposit	22 September 1998 (22.09.1998)
248-3-4	Accession Number	ATCC 203282
248-4	**Additional Indications**	NONE
248-5	**Designated States for Which Indications are Made**	all designated States
248-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
249	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
249-1	page	103
249-2	line	28
249-3	**Identification of Deposit**	
249-3-1	Name of depositary institution	American Type Culture Collection
249-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
249-3-3	Date of deposit	09 February 1999 (09.02.1999)
249-3-4	Accession Number	ATCC 203657
249-4	**Additional Indications**	NONE
249-5	**Designated States for Which Indications are Made**	all designated States
249-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
250	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
250-1	page	103
250-2	line	29
250-3	**Identification of Deposit**	
250-3-1	Name of depositary institution	American Type Culture Collection
250-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
250-3-3	Date of deposit	22 September 1998 (22.09.1998)
250-3-4	Accession Number	ATCC 203276
250-4	**Additional Indications**	NONE
250-5	**Designated States for Which Indications are Made**	all designated States

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250-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
251	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
251-1	page	103
251-2	line	30
251-3	**Identification of Deposit**	
251-3-1	Name of depositary institution	American Type Culture Collection
251-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
251-3-3	Date of deposit	25 August 1998 (25.08.1998)
251-3-4	Accession Number	ATCC 203160
251-4	**Additional Indications**	**NONE**
251-5	**Designated States for Which Indications are Made**	all designated States
251-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
252	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
252-1	page	103
252-2	line	31
252-3	**Identification of Deposit**	
252-3-1	Name of depositary institution	American Type Culture Collection
252-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
252-3-3	Date of deposit	18 August 1998 (18.08.1998)
252-3-4	Accession Number	ATCC 203135
252-4	**Additional Indications**	**NONE**
252-5	**Designated States for Which Indications are Made**	all designated States
252-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
253	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
253-1	page	103
253-2	line	32
253-3	**Identification of Deposit**	
253-3-1	Name of depositary institution	American Type Culture Collection
253-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
253-3-3	Date of deposit	03 November 1998 (03.11.1998)
253-3-4	Accession Number	ATCC 203459

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253-4	**Additional Indications**	**NONE**
253-5	**Designated States for Which Indications are Made**	**all designated States**
253-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
254	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
254-1	page	**103**
254-2	line	**33**
254-3	**Identification of Deposit**	
254-3-1	Name of depositary institution	**American Type Culture Collection**
254-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
254-3-3	Date of deposit	**22 September 1998 (22.09.1998)**
254-3-4	Accession Number	**ATCC 203270**
254-4	**Additional Indications**	**NONE**
254-5	**Designated States for Which Indications are Made**	**all designated States**
254-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
255	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
255-1	page	**103**
255-2	line	**34**
255-3	**Identification of Deposit**	
255-3-1	Name of depositary institution	**American Type Culture Collection**
255-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
255-3-3	Date of deposit	**12 January 1999 (12.01.1999)**
255-3-4	Accession Number	**ATCC 203573**
255-4	**Additional Indications**	**NONE**
255-5	**Designated States for Which Indications are Made**	**all designated States**
255-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
256	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
256-1	page	**103**
256-2	line	**35**

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256-3	**Identification of Deposit**	
256-3-1	Name of depositary institution	**American Type Culture Collection**
256-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
256-3-3	Date of deposit	**17 November 1998 (17.11.1998)**
256-3-4	Accession Number	**ATCC 203477**
256-4	**Additional Indications**	**NONE**
256-5	**Designated States for Which Indications are Made**	**all designated States**
256-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
257	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
257-1	page	**103**
257-2	line	**36**
257-3	**Identification of Deposit**	
257-3-1	Name of depositary institution	**American Type Culture Collection**
257-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
257-3-3	Date of deposit	**06 October 1998 (06.10.1998)**
257-3-4	Accession Number	**ATCC 203315**
257-4	**Additional Indications**	**NONE**
257-5	**Designated States for Which Indications are Made**	**all designated States**
257-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	
258	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
258-1	page	**103**
258-2	line	**37**
258-3	**Identification of Deposit**	
258-3-1	Name of depositary institution	**American Type Culture Collection**
258-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
258-3-3	Date of deposit	**06 October 1998 (06.10.1998)**
258-3-4	Accession Number	**ATCC 203313**
258-4	**Additional Indications**	**NONE**
258-5	**Designated States for Which Indications are Made**	**all designated States**
258-6	**Separate Furnishing of Indications**	**NONE**
	These indications will be submitted to the International Bureau later	

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259	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
259-1	page	103
259-2	line	38
259-3	**Identification of Deposit**	
259-3-1	Name of depositary institution	American Type Culture Collection
259-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
259-3-3	Date of deposit	27 October 1998 (27.10.1998)
259-3-4	Accession Number	ATCC 203407
259-4	**Additional Indications**	NONE
259-5	**Designated States for Which Indications are Made**	all designated States
259-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
260	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
260-1	page	103
260-2	line	39
260-3	**Identification of Deposit**	
260-3-1	Name of depositary institution	American Type Culture Collection
260-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
260-3-3	Date of deposit	22 December 1998 (22.12.1998)
260-3-4	Accession Number	ATCC 203553
260-4	**Additional Indications**	NONE
260-5	**Designated States for Which Indications are Made**	all designated States
260-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	NONE
261	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
261-1	page	103
261-2	line	40
261-3	**Identification of Deposit**	
261-3-1	Name of depositary institution	American Type Culture Collection
261-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
261-3-3	Date of deposit	22 December 1998 (22.12.1998)
261-3-4	Accession Number	ATCC 203549
261-4	**Additional Indications**	NONE
261-5	**Designated States for Which Indications are Made**	all designated States

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261-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
262	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
262-1	page	103
262-2	line	41
262-3	**Identification of Deposit**	
262-3-1	Name of depositary institution	American Type Culture Collection
262-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
262-3-3	Date of deposit	22 December 1998 (22.12.1998)
262-3-4	Accession Number	ATCC 203550
262-4	**Additional Indications**	**NONE**
262-5	**Designated States for Which Indications are Made**	all designated States
262-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
263	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
263-1	page	103
263-2	line	42
263-3	**Identification of Deposit**	
263-3-1	Name of depositary institution	American Type Culture Collection
263-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
263-3-3	Date of deposit	08 June 1999 (08.06.1999)
263-3-4	Accession Number	ATCC PTA-204
263-4	**Additional Indications**	**NONE**
263-5	**Designated States for Which Indications are Made**	all designated States
263-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
264	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
264-1	page	103
264-2	line	43
264-3	**Identification of Deposit**	
264-3-1	Name of depositary institution	American Type Culture Collection
264-3-2	Address of depositary institution	10801 University Blvd., Manassas, Virginia 20110-2209United States of America
264-3-3	Date of deposit	29 October 1998 (29.10.1998)
264-3-4	Accession Number	ATCC 203391

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264-4	**Additional Indications**	**NONE**
264-5	**Designated States for Which Indications are Made**	**all designated States**
264-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
265	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
265-1	page	**103**
265-2	line	**44**
265-3	**Identification of Deposit**	
265-3-1	Name of depositary institution	**American Type Culture Collection**
265-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
265-3-3	Date of deposit	**23 March 1999 (23.03.1999)**
265-3-4	Accession Number	**ATCC 203863**
265-4	**Additional Indications**	**NONE**
265-5	**Designated States for Which Indications are Made**	**all designated States**
265-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
266	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
266-1	page	**103**
266-2	line	**45**
266-3	**Identification of Deposit**	
266-3-1	Name of depositary institution	**American Type Culture Collection**
266-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
266-3-3	Date of deposit	**09 March 1999 (09.03.1999)**
266-3-4	Accession Number	**ATCC 203834**
266-4	**Additional Indications**	**NONE**
266-5	**Designated States for Which Indications are Made**	**all designated States**
266-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**
267	**The indications made below relate to the deposited microorganism(s) or other biological material referred to in the description on:**	
267-1	page	**103**
267-2	line	**46**

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267-3	**Identification of Deposit**	
267-3-1	Name of depositary institution	**American Type Culture Collection**
267-3-2	Address of depositary institution	**10801 University Blvd., Manassas, Virginia 20110-2209United States of America**
267-3-3	Date of deposit	**20 July 1999 (20.07.1999)**
267-3-4	Accession Number	**ATCC PTA-382**
267-4	**Additional Indications**	**NONE**
267-5	**Designated States for Which Indications are Made**	**all designated States**
267-6	**Separate Furnishing of Indications** These indications will be submitted to the International Bureau later	**NONE**

FOR RECEIVING OFFICE USE ONLY

0-4	**This form was received with the international application:** (yes or no)	
0-4-1	Authorized officer	

FOR INTERNATIONAL BUREAU USE ONLY

0-5	**This form was received by the international Bureau on:**	
0-5-1	Authorized officer	

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 Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), Figure 6 (SEQ ID NO:6), Figure 8 (SEQ ID NO:8), Figure 10 (SEQ ID NO:10), Figure 12 (SEQ ID NO:12), Figure 14 (SEQ ID NO:14), Figure 16 (SEQ ID NO:16), Figure 18 (SEQ ID NO:18), Figure 20 (SEQ ID NO:20), Figure 22 (SEQ ID NO:22), Figure 24 (SEQ ID NO:24), Figure 26 (SEQ ID NO:26), Figure 28 (SEQ ID NO:28), Figure 30 (SEQ ID NO:30), Figure 32 (SEQ ID NO:32), Figure 34 (SEQ ID NO:34), Figure 36 (SEQ ID NO:36), Figure 38 (SEQ ID NO:38), Figure 40 (SEQ ID NO:40), Figure 42 (SEQ ID NO:42), Figure 44 (SEQ ID NO:44), Figure 46 (SEQ ID NO:46), Figure 48 (SEQ ID NO:48), Figure 50 (SEQ ID NO:50), Figure 52 (SEQ ID NO:52), Figure 54 (SEQ ID NO:54), Figure 56 (SEQ ID NO:56), Figure 58 (SEQ ID NO:58), Figure 60 (SEQ ID NO:60), Figure 62 (SEQ ID NO:62), Figure 64 (SEQ ID NO:64), Figure 66 (SEQ ID NO:66), Figure 68 (SEQ ID NO:68), Figure 70 (SEQ ID NO:70), Figure 72 (SEQ ID NO:72), Figure 74 (SEQ ID NO:74), Figure 76 (SEQ ID NO:76), Figure 78 (SEQ ID NO:78), Figure 80 (SEQ ID NO:80), Figure 82 (SEQ ID NO:82), Figure 84 (SEQ ID NO:84), Figure 86 (SEQ ID NO:86), Figure 88 (SEQ ID NO:88), Figure 90 (SEQ ID NO:90), Figure 92 (SEQ ID NO:92), Figure 94 (SEQ ID NO:94), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:98), Figure 100 (SEQ ID NO:100), Figure 102 (SEQ ID NO:102), Figure 104 (SEQ ID NO:104), Figure 106 (SEQ ID NO:106), Figure 108 (SEQ ID NO:108), Figure 110 (SEQ ID NO:110), Figure 112 (SEQ ID NO:112), Figure 114 (SEQ ID NO:114), Figure 116 (SEQ ID NO:116), Figure 118 (SEQ ID NO:118), Figure 120 (SEQ ID NO:120), Figure 122 (SEQ ID NO:122), Figure 124 (SEQ ID NO:124), Figure 126 (SEQ ID NO:126), Figure 128 (SEQ ID NO:128), Figure 130 (SEQ ID NO:130), Figure 132 (SEQ ID NO:132), Figure 134 (SEQ ID NO:134), Figure 136 (SEQ ID NO:136), Figure 138 (SEQ ID NO:138), Figure 140 (SEQ ID NO:140), Figure 142 (SEQ ID NO:142), Figure 144 (SEQ ID NO:144), Figure 146 (SEQ ID NO:146), Figure 148 (SEQ ID NO:148), Figure 150 (SEQ ID NO:150), Figure 152 (SEQ ID NO:152), Figure 154 (SEQ ID NO:154), Figure 156 (SEQ ID NO:156), Figure 158 (SEQ ID NO:158), Figure 160 (SEQ ID NO:160), Figure 162 (SEQ ID NO:162), Figure 164 (SEQ ID NO:164), Figure 166 (SEQ ID NO:166), Figure 168 (SEQ ID NO:168), Figure 170 (SEQ ID NO:170), Figure 172 (SEQ ID NO:172), Figure 174 (SEQ ID NO:174), Figure 176 (SEQ ID NO:176), Figure 178 (SEQ ID NO:178), Figure 180 (SEQ ID NO:180), Figure 182 (SEQ ID NO:182), Figure 184 (SEQ ID NO:184), Figure 186 (SEQ ID NO:186), Figure 188 (SEQ ID NO:188), Figure 190 (SEQ ID NO:190), Figure 192 (SEQ ID NO:192), Figure 194 (SEQ ID NO:194), Figure 196 (SEQ ID NO:196), Figure 198 (SEQ ID NO:198), Figure 200 (SEQ ID NO:200), Figure 202 (SEQ ID NO:202), Figure 204 (SEQ ID NO:204), Figure 206 (SEQ ID NO:206), Figure 208 (SEQ ID NO:208), Figure 210 (SEQ ID NO:210), Figure 212 (SEQ ID NO:212), Figure 214 (SEQ ID NO:214), Figure 216 (SEQ ID NO:216), Figure 218 (SEQ ID NO:218), Figure 220 (SEQ ID NO:220), Figure 222 (SEQ ID NO:222), Figure 224 (SEQ ID NO:224), Figure 226 (SEQ ID NO:226), Figure 228 (SEQ ID NO:228), Figure 230 (SEQ ID NO:230), Figure 232 (SEQ ID NO:232), Figure 234 (SEQ ID NO:234), Figure 236 (SEQ ID NO:236), Figure 238 (SEQ ID NO:238), Figure 240 (SEQ ID NO:240), Figure 242 (SEQ ID NO:242), Figure 244 (SEQ ID NO:244), Figure 246 (SEQ ID NO:246), Figure 248 (SEQ ID NO:248), Figure 250 (SEQ ID NO:250), Figure 252 (SEQ ID NO:252), Figure 254 (SEQ ID

NO:254), Figure 256 (SEQ ID NO:256), Figure 258 (SEQ ID NO:258), Figure 260 (SEQ ID NO:260), Figure 262 (SEQ ID NO:262), Figure 264 (SEQ ID NO:264), Figure 266 (SEQ ID NO:266), Figure 268 (SEQ ID NO:268), Figure 270 (SEQ ID NO:270), Figure 272 (SEQ ID NO:272), Figure 274 (SEQ ID NO:274), Figure 276 (SEQ ID NO:276), Figure 278 (SEQ ID NO:278), Figure 280 (SEQ ID NO:280), Figure 282 (SEQ ID NO:282), Figure 284 (SEQ ID NO:284), Figure 286 (SEQ ID NO:286), Figure 288 (SEQ ID NO:288), Figure 290 (SEQ ID NO:290), Figure 292 (SEQ ID NO:292), Figure 294 (SEQ ID NO:294), Figure 296 (SEQ ID NO:296), Figure 298 (SEQ ID NO:298), Figure 300 (SEQ ID NO:300), Figure 302 (SEQ ID NO:302), Figure 304 (SEQ ID NO:304), Figure 306 (SEQ ID NO:306), Figure 308 (SEQ ID NO:308), Figure 310 (SEQ ID NO:310), Figure 312 (SEQ ID NO:312), Figure 314 (SEQ ID NO:314), Figure 316 (SEQ ID NO:316), Figure 318 (SEQ ID NO:318), Figure 320 (SEQ ID NO:320), Figure 322 (SEQ ID NO:322), Figure 324 (SEQ ID NO:324), Figure 326 (SEQ ID NO:326), Figure 328 (SEQ ID NO:328), Figure 330 (SEQ ID NO:330), Figure 332 (SEQ ID NO:332), Figure 334 (SEQ ID NO:334), Figure 336 (SEQ ID NO:336), Figure 338 (SEQ ID NO:338), Figure 340 (SEQ ID NO:340), Figure 342 (SEQ ID NO:342), Figure 344 (SEQ ID NO:344), Figure 346 (SEQ ID NO:346), Figure 348 (SEQ ID NO:348), Figure 350 (SEQ ID NO:350), Figure 352 (SEQ ID NO:352), Figure 354 (SEQ ID NO:354), Figure 356 (SEQ ID NO:356), Figure 358 (SEQ ID NO:358), Figure 360 (SEQ ID NO:360), Figure 362 (SEQ ID NO:362), Figure 364 (SEQ ID NO:364), Figure 366 (SEQ ID NO:366), Figure 368 (SEQ ID NO:368), Figure 370 (SEQ ID NO:370), Figure 372 (SEQ ID NO:372), Figure 374 (SEQ ID NO:374), Figure 376 (SEQ ID NO:376), Figure 378 (SEQ ID NO:378), Figure 380 (SEQ ID NO:380), Figure 382 (SEQ ID NO:382), Figure 384 (SEQ ID NO:384), Figure 386 (SEQ ID NO:386), Figure 388 (SEQ ID NO:388), Figure 390 (SEQ ID NO:390), Figure 392 (SEQ ID NO:392), Figure 394 (SEQ ID NO:394), Figure 396 (SEQ ID NO:396), Figure 398 (SEQ ID NO:398), Figure 400 (SEQ ID NO:400), Figure 402 (SEQ ID NO:402), Figure 404 (SEQ ID NO:404), Figure 406 (SEQ ID NO:406), Figure 408 (SEQ ID NO:408), Figure 410 (SEQ ID NO:410), Figure 412 (SEQ ID NO:412), Figure 414 (SEQ ID NO:414), Figure 416 (SEQ ID NO:416), Figure 418 (SEQ ID NO:418), Figure 420 (SEQ ID NO:420), Figure 422 (SEQ ID NO:422), Figure 424 (SEQ ID NO:424), Figure 426 (SEQ ID NO:426), Figure 428 (SEQ ID NO:428), Figure 430 (SEQ ID NO:430), Figure 432 (SEQ ID NO:432), Figure 434 (SEQ ID NO:434), Figure 436 (SEQ ID NO:436), Figure 438 (SEQ ID NO:438), Figure 440 (SEQ ID NO:440), Figure 442 (SEQ ID NO:442), Figure 444 (SEQ ID NO:444), Figure 446 (SEQ ID NO:446), Figure 448 (SEQ ID NO:448), Figure 450 (SEQ ID NO:450), Figure 452 (SEQ ID NO:452), Figure 454 (SEQ ID NO:454), Figure 456 (SEQ ID NO:456), Figure 458 (SEQ ID NO:458), Figure 460 (SEQ ID NO:460), Figure 462 (SEQ ID NO:462), Figure 464 (SEQ ID NO:464), Figure 466 (SEQ ID NO:466), Figure 468 (SEQ ID NO:468), Figure 470 (SEQ ID NO:470), Figure 472 (SEQ ID NO:472), Figure 474 (SEQ ID NO:474), Figure 476 (SEQ ID NO:476), Figure 478 (SEQ ID NO:478), Figure 480 (SEQ ID NO:480), Figure 482 (SEQ ID NO:482), Figure 484 (SEQ ID NO:484), Figure 486 (SEQ ID NO:486), Figure 488 (SEQ ID NO:488), Figure 490 (SEQ ID NO:490), Figure 492 (SEQ ID NO:492), Figure 494 (SEQ ID NO:494), Figure 496 (SEQ ID NO:496), Figure 498 (SEQ ID NO:498), Figure 500 (SEQ ID NO:500), Figure 502 (SEQ ID NO:502), Figure 504 (SEQ ID NO:504), Figure 506 (SEQ ID NO:506), Figure 508 (SEQ ID NO:508), Figure 510 (SEQ ID NO:510), Figure 512 (SEQ ID NO:512), Figure 514 (SEQ ID NO:514), Figure 516 (SEQ ID NO:516), Figure 518 (SEQ ID NO:518), Figure 520 (SEQ ID

NO:520), Figure 522 (SEQ ID NO:522), Figure 524 (SEQ ID NO:524), Figure 526 (SEQ ID NO:526), Figure 528 (SEQ ID NO:528), Figure 530 (SEQ ID NO:530), Figure 532 (SEQ ID NO:532), Figure 534 (SEQ ID NO:534), Figure 536 (SEQ ID NO:536), Figure 538 (SEQ ID NO:538), Figure 540 (SEQ ID NO:540), Figure 542 (SEQ ID NO:542), Figure 544 (SEQ ID NO:544), Figure 546 (SEQ ID NO:546), Figure 548 (SEQ ID NO:548) and Figure 550 (SEQ ID NO:550).

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 Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:3), Figure 5 (SEQ ID NO:5), Figure 7 (SEQ ID NO:7), Figure 9 (SEQ ID NO:9), Figure 11 (SEQ ID NO:11), Figure 13 (SEQ ID NO:13), Figure 15 (SEQ ID NO:15), Figure 17 (SEQ ID NO:17), Figure 19 (SEQ ID NO:19), Figure 21 (SEQ ID NO:21), Figure 23 (SEQ ID NO:23), Figure 25 (SEQ ID NO:25), Figure 27 (SEQ ID NO:27), Figure 29 (SEQ ID NO:29), Figure 31 (SEQ ID NO:31), Figure 33 (SEQ ID NO:33), Figure 35 (SEQ ID NO:35), Figure 37 (SEQ ID NO:37), Figure 39 (SEQ ID NO:39), Figure 41 (SEQ ID NO:41), Figure 43 (SEQ ID NO:43), Figure 45 (SEQ ID NO:45), Figure 47 (SEQ ID NO:47), Figure 49 (SEQ ID NO:49), Figure 51 (SEQ ID NO:51), Figure 53 (SEQ ID NO:53), Figure 55 (SEQ ID NO:55), Figure 57 (SEQ ID NO:57), Figure 59 (SEQ ID NO:59), Figure 61 (SEQ ID NO:61), Figure 63 (SEQ ID NO:63), Figure 65 (SEQ ID NO:65), Figure 67 (SEQ ID NO:67), Figure 69 (SEQ ID NO:69), Figure 71 (SEQ ID NO:71), Figure 73 (SEQ ID NO:73), Figure 75 (SEQ ID NO:75), Figure 77 (SEQ ID NO:77), Figure 79 (SEQ ID NO:79), Figure 81 (SEQ ID NO:81), Figure 83 (SEQ ID NO:83), Figure 85 (SEQ ID NO:85), Figure 87 (SEQ ID NO:87), Figure 89 (SEQ ID NO:89), Figure 91 (SEQ ID NO:91), Figure 93 (SEQ ID NO:93), Figure 95 (SEQ ID NO:95), Figure 97 (SEQ ID NO:97), Figure 99 (SEQ ID NO:99), Figure 101 (SEQ ID NO:101), Figure 103 (SEQ ID NO:103), Figure 105 (SEQ ID NO:105), Figure 107 (SEQ ID NO:107), Figure 109 (SEQ ID NO:109), Figure 111 (SEQ ID NO:111), Figure 113 (SEQ ID NO:113), Figure 115 (SEQ ID NO:115), Figure 117 (SEQ ID NO:117), Figure 119 (SEQ ID NO:119), Figure 121 (SEQ ID NO:121), Figure 123 (SEQ ID NO:123), Figure 125 (SEQ ID NO:125), Figure 127 (SEQ ID NO:127), Figure 129 (SEQ ID NO:129), Figure 131 (SEQ ID NO:131), Figure 133 (SEQ ID NO:133), Figure 135 (SEQ ID NO:135), Figure 137 (SEQ ID NO:137), Figure 139 (SEQ ID NO:1390), Figure 141 (SEQ ID NO:141), Figure 143 (SEQ ID NO:143), Figure 145 (SEQ ID NO:145), Figure 147 (SEQ ID NO:147), Figure 149 (SEQ ID NO:149), Figure 151 (SEQ ID NO:151), Figure 153 (SEQ ID NO:153), Figure 155 (SEQ ID NO:155), Figure 157 (SEQ ID NO:157), Figure 159 (SEQ ID NO:159), Figure 161 (SEQ ID NO:161), Figure 163 (SEQ ID NO:163), Figure 165 (SEQ ID NO:165), Figure 167 (SEQ ID NO:167), Figure 169 (SEQ ID NO:169), Figure 171 (SEQ ID NO:171), Figure 173 (SEQ ID NO:173), Figure 175 (SEQ ID NO:175), Figure 177 (SEQ ID NO:177), Figure 179 (SEQ ID NO:179), Figure 181 (SEQ ID NO:181), Figure 183 (SEQ ID NO:183), Figure 185 (SEQ ID NO:185), Figure 187 (SEQ ID NO:187), Figure 189 (SEQ ID NO:189), Figure 191 (SEQ ID NO:191), Figure 193 (SEQ ID NO:193), Figure 195 (SEQ ID NO:195), Figure 197 (SEQ ID NO:197), Figure 199 (SEQ ID NO:199), Figure 201 (SEQ ID NO:201), Figure 203 (SEQ ID NO:203), Figure 205 (SEQ ID NO:205), Figure 207 (SEQ ID NO:207), Figure 209 (SEQ ID NO:209), Figure 211 (SEQ ID NO:211), Figure 213 (SEQ ID NO:213), Figure 215 (SEQ ID NO:215), Figure 217 (SEQ ID NO:217), Figure 219 (SEQ ID NO:219), Figure 221 (SEQ ID

NO:221), Figure 223 (SEQ ID NO:223), Figure 225 (SEQ ID NO:225), Figure 227 (SEQ ID NO:227), Figure 229 (SEQ ID NO:229), Figure 231 (SEQ ID NO:231), Figure 233 (SEQ ID NO:233), Figure 235 (SEQ ID NO:235), Figure 237 (SEQ ID NO:237), Figure 239 (SEQ ID NO:239), Figure 241 (SEQ ID NO:241), Figure 243 (SEQ ID NO:243), Figure 245 (SEQ ID NO:245), Figure 247 (SEQ ID NO:247), Figure 249 (SEQ ID NO:249), Figure 251 (SEQ ID NO:251), Figure 253 (SEQ ID NO:253), Figure 255 (SEQ ID NO:255), Figure 257 (SEQ ID NO:257), Figure 259 (SEQ ID NO:259), Figure 261 (SEQ ID NO:261), Figure 263 (SEQ ID NO:263), Figure 265 (SEQ ID NO:265), Figure 267 (SEQ ID NO:267), Figure 269 (SEQ ID NO:269), Figure 271 (SEQ ID NO:271), Figure 273 (SEQ ID NO:273), Figure 275 (SEQ ID NO:275), Figure 277 (SEQ ID NO:277), Figure 279 (SEQ ID NO:279), Figure 281 (SEQ ID NO:281), Figure 283 (SEQ ID NO:283), Figure 285 (SEQ ID NO:285), Figure 287 (SEQ ID NO:287), Figure 289 (SEQ ID NO:289), Figure 291 (SEQ ID NO:291), Figure 293 (SEQ ID NO:293), Figure 295 (SEQ ID NO:295), Figure 297 (SEQ ID NO:297), Figure 299 (SEQ ID NO:299), Figure 301 (SEQ ID NO:301), Figure 303 (SEQ ID NO:303), Figure 305 (SEQ ID NO:305), Figure 307 (SEQ ID NO:307), Figure 309 (SEQ ID NO:309), Figure 311 (SEQ ID NO:311), Figure 313 (SEQ ID NO:313), Figure 315 (SEQ ID NO:315), Figure 317 (SEQ ID NO:317), Figure 319 (SEQ ID NO:319), Figure 321 (SEQ ID NO:321), Figure 323 (SEQ ID NO:323), Figure 325 (SEQ ID NO:325), Figure 327 (SEQ ID NO:327), Figure 329 (SEQ ID NO:329), Figure 331 (SEQ ID NO:331), Figure 333 (SEQ ID NO:333), Figure 335 (SEQ ID NO:335), Figure 337 (SEQ ID NO:337), Figure 339 (SEQ ID NO:339), Figure 341 (SEQ ID NO:341), Figure 343 (SEQ ID NO:343), Figure 345 (SEQ ID NO:345), Figure 347 (SEQ ID NO:347), Figure 349 (SEQ ID NO:349), Figure 351 (SEQ ID NO:351), Figure 353 (SEQ ID NO:353), Figure 355 (SEQ ID NO:355), Figure 357 (SEQ ID NO:357), Figure 359 (SEQ ID NO:359), Figure 361 (SEQ ID NO:361), Figure 363 (SEQ ID NO:363), Figure 365 (SEQ ID NO:365), Figure 367 (SEQ ID NO:367), Figure 369 (SEQ ID NO:369), Figure 371 (SEQ ID NO:371), Figure 373 (SEQ ID NO:373), Figure 375 (SEQ ID NO:375), Figure 377 (SEQ ID NO:377), Figure 379 (SEQ ID NO:379), Figure 381 (SEQ ID NO:381), Figure 383 (SEQ ID NO:383), Figure 385 (SEQ ID NO:385), Figure 387 (SEQ ID NO:387), Figure 389 (SEQ ID NO:389), Figure 391 (SEQ ID NO:391), Figure 393 (SEQ ID NO:393), Figure 395 (SEQ ID NO:395), Figure 397 (SEQ ID NO:397), Figure 399 (SEQ ID NO:399), Figure 401 (SEQ ID NO:401), Figure 403 (SEQ ID NO:403), Figure 405 (SEQ ID NO:405), Figure 407 (SEQ ID NO:407), Figure 409 (SEQ ID NO:409), Figure 411 (SEQ ID NO:411), Figure 413 (SEQ ID NO:413), Figure 415 (SEQ ID NO:415), Figure 417 (SEQ ID NO:417), Figure 419 (SEQ ID NO:419), Figure 421 (SEQ ID NO:421), Figure 423 (SEQ ID NO:423), Figure 425 (SEQ ID NO:425), Figure 427 (SEQ ID NO:427), Figure 429 (SEQ ID NO:429), Figure 431 (SEQ ID NO:431), Figure 433 (SEQ ID NO:433), Figure 435 (SEQ ID NO:435), Figure 437 (SEQ ID NO:437), Figure 439 (SEQ ID NO:439), Figure 441 (SEQ ID NO:441), Figure 443 (SEQ ID NO:443), Figure 445 (SEQ ID NO:445), Figure 447 (SEQ ID NO:447), Figure 449 (SEQ ID NO:449), Figure 451 (SEQ ID NO:451), Figure 453 (SEQ ID NO:453), Figure 455 (SEQ ID NO:455), Figure 457 (SEQ ID NO:457), Figure 459 (SEQ ID NO:459), Figure 461 (SEQ ID NO:461), Figure 463 (SEQ ID NO:463), Figure 465 (SEQ ID NO:465), Figure 467 (SEQ ID NO:467), Figure 469 (SEQ ID NO:469), Figure 471 (SEQ ID NO:471), Figure 473 (SEQ ID NO:473), Figure 475 (SEQ ID NO:475), Figure 477 (SEQ ID NO:477), Figure 479 (SEQ ID NO:479), Figure 481 (SEQ ID NO:481), Figure 483 (SEQ ID NO:483), Figure 485 (SEQ ID NO:485), Figure 487 (SEQ ID

NO:487), Figure 489 (SEQ ID NO:489), Figure 491 (SEQ ID NO:491), Figure 493 (SEQ ID NO:493), Figure 495 (SEQ ID NO:495), Figure 497 (SEQ ID NO:497), Figure 499 (SEQ ID NO:499), Figure 501 (SEQ ID NO:501), Figure 503 (SEQ ID NO:503), Figure 505 (SEQ ID NO:505), Figure 507 (SEQ ID NO:507), Figure 509 (SEQ ID NO:509), Figure 511 (SEQ ID NO:511), Figure 513 (SEQ ID NO:513), Figure 515 (SEQ ID NO:515), Figure 517 (SEQ ID NO:517), Figure 519 (SEQ ID NO:519), Figure 521 (SEQ ID NO:521), Figure 523 (SEQ ID NO:523), Figure 525 (SEQ ID NO:525), Figure 527 (SEQ ID NO:527), Figure 529 (SEQ ID NO:529), Figure 531 (SEQ ID NO:531), Figure 533 (SEQ ID NO:533), Figure 535 (SEQ ID NO:535), Figure 537 (SEQ ID NO:537), Figure 539 (SEQ ID NO:539), Figure 541 (SEQ ID NO:541), Figure 543 (SEQ ID NO:543), Figure 545 (SEQ ID NO:545), Figure 547 (SEQ ID NO:547) and Figure 549 (SEQ ID NO:549).

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 Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:3), Figure 5 (SEQ ID NO:5), Figure 7 (SEQ ID NO:7), Figure 9 (SEQ ID NO:9), Figure 11 (SEQ ID NO:11), Figure 13 (SEQ ID NO:13), Figure 15 (SEQ ID NO:15), Figure 17 (SEQ ID NO:17), Figure 19 (SEQ ID NO:19), Figure 21 (SEQ ID NO:21), Figure 23 (SEQ ID NO:23), Figure 25 (SEQ ID NO:25), Figure 27 (SEQ ID NO:27), Figure 29 (SEQ ID NO:29), Figure 31 (SEQ ID NO:31), Figure 33 (SEQ ID NO:33), Figure 35 (SEQ ID NO:35), Figure 37 (SEQ ID NO:37), Figure 39 (SEQ ID NO:39), Figure 41 (SEQ ID NO:41), Figure 43 (SEQ ID NO:43), Figure 45 (SEQ ID NO:45), Figure 47 (SEQ ID NO:47), Figure 49 (SEQ ID NO:49), Figure 51 (SEQ ID NO:51), Figure 53 (SEQ ID NO:53), Figure 55 (SEQ ID NO:55), Figure 57 (SEQ ID NO:57), Figure 59 (SEQ ID NO:59), Figure 61 (SEQ ID NO:61), Figure 63 (SEQ ID NO:63), Figure 65 (SEQ ID NO:65), Figure 67 (SEQ ID NO:67), Figure 69 (SEQ ID NO:69), Figure 71 (SEQ ID NO:71), Figure 73 (SEQ ID NO:73), Figure 75 (SEQ ID NO:75), Figure 77 (SEQ ID NO:77), Figure 79 (SEQ ID NO:79), Figure 81 (SEQ ID NO:81), Figure 83 (SEQ ID NO:83), Figure 85 (SEQ ID NO:85), Figure 87 (SEQ ID NO:87), Figure 89 (SEQ ID NO:89), Figure 91 (SEQ ID NO:91), Figure 93 (SEQ ID NO:93), Figure 95 (SEQ ID NO:95), Figure 97 (SEQ ID NO:97), Figure 99 (SEQ ID NO:99), Figure 101 (SEQ ID NO:101), Figure 103 (SEQ ID NO:103), Figure 105 (SEQ ID NO:105), Figure 107 (SEQ ID NO:107), Figure 109 (SEQ ID NO:109), Figure 111 (SEQ ID NO:111), Figure 113 (SEQ ID NO:113), Figure 115 (SEQ ID NO:115), Figure 117 (SEQ ID NO:117), Figure 119 (SEQ ID NO:119), Figure 121 (SEQ ID NO:121), Figure 123 (SEQ ID NO:123), Figure 125 (SEQ ID NO:125), Figure 127 (SEQ ID NO:127), Figure 129 (SEQ ID NO:129), Figure 131 (SEQ ID NO:131), Figure 133 (SEQ ID NO:133), Figure 135 (SEQ ID NO:135), Figure 137 (SEQ ID NO:137), Figure 139 (SEQ ID NO:1390), Figure 141 (SEQ ID NO:141), Figure 143 (SEQ ID NO:143), Figure 145 (SEQ ID NO:145), Figure 147 (SEQ ID NO:147), Figure 149 (SEQ ID NO:149), Figure 151 (SEQ ID NO:151), Figure 153 (SEQ ID NO:153), Figure 155 (SEQ ID NO:155), Figure 157 (SEQ ID NO:157), Figure 159 (SEQ ID NO:159), Figure 161 (SEQ ID NO:161), Figure 163 (SEQ ID NO:163), Figure 165 (SEQ ID NO:165), Figure 167 (SEQ ID NO:167), Figure 169 (SEQ ID NO:169), Figure 171 (SEQ ID NO:171), Figure 173 (SEQ ID NO:173), Figure 175 (SEQ ID NO:175), Figure 177 (SEQ ID NO:177), Figure 179 (SEQ ID NO:179), Figure 181 (SEQ ID NO:181), Figure 183 (SEQ ID NO:183), Figure 185 (SEQ ID NO:185), Figure 187 (SEQ ID NO:187), Figure 189 (SEQ ID NO:189), Figure 191 (SEQ

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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. The vector of Claim 5 operably linked to control sequences recognized by a host cell transformed with the vector.

7. A host cell comprising the vector of Claim 5.

8. The host cell of Claim 7, wherein said cell is a CHO cell.

9. The host cell of Claim 7, wherein said cell is an *E. coli*.

10. The host cell of Claim 7, wherein said cell is a yeast cell.

11. A process for producing a PRO polypeptides comprising culturing the host cell of Claim 7 under conditions suitable for expression of said PRO polypeptide and recovering said PRO polypeptide from the cell culture.

12. 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 Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), Figure 6 (SEQ ID NO:6), Figure 8 (SEQ ID NO:8), Figure 10 (SEQ ID NO:10),

Figure 12 (SEQ ID NO:12), Figure 14 (SEQ ID NO:14), Figure 16 (SEQ ID NO:16), Figure 18 (SEQ ID NO:18), Figure 20 (SEQ ID NO:20), Figure 22 (SEQ ID NO:22), Figure 24 (SEQ ID NO:24), Figure 26 (SEQ ID NO:26), Figure 28 (SEQ ID NO:28), Figure 30 (SEQ ID NO:30), Figure 32 (SEQ ID NO:32), Figure 34 (SEQ ID NO:34), Figure 36 (SEQ ID NO:36), Figure 38 (SEQ ID NO:38), Figure 40 (SEQ ID NO:40), Figure 42 (SEQ ID NO:42), Figure 44 (SEQ ID NO:44), Figure 46 (SEQ ID NO:46), Figure 48 (SEQ ID NO:48), Figure 50 (SEQ ID NO:50), Figure 52 (SEQ ID NO:52), Figure 54 (SEQ ID NO:54), Figure 56 (SEQ ID NO:56), Figure 58 (SEQ ID NO:58), Figure 60 (SEQ ID NO:60), Figure 62 (SEQ ID NO:62), Figure 64 (SEQ ID NO:64), Figure 66 (SEQ ID NO:66), Figure 68 (SEQ ID NO:68), Figure 70 (SEQ ID NO:70), Figure 72 (SEQ ID NO:72), Figure 74 (SEQ ID NO:74), Figure 76 (SEQ ID NO:76), Figure 78 (SEQ ID NO:78), Figure 80 (SEQ ID NO:80), Figure 82 (SEQ ID NO:82), Figure 84 (SEQ ID NO:84), Figure 86 (SEQ ID NO:86), Figure 88 (SEQ ID NO:88), Figure 90 (SEQ ID NO:90), Figure 92 (SEQ ID NO:92), Figure 94 (SEQ ID NO:94), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:98), Figure 100 (SEQ ID NO:100), Figure 102 (SEQ ID NO:102), Figure 104 (SEQ ID NO:104), Figure 106 (SEQ ID NO:106), Figure 108 (SEQ ID NO:108), Figure 110 (SEQ ID NO:110), Figure 112 (SEQ ID NO:112), Figure 114 (SEQ ID NO:114), Figure 116 (SEQ ID NO:116), Figure 118 (SEQ ID NO:118), Figure 120 (SEQ ID NO:120), Figure 122 (SEQ ID NO:122), Figure 124 (SEQ ID NO:124), Figure 126 (SEQ ID NO:126), Figure 128 (SEQ ID NO:128), Figure 130 (SEQ ID NO:130), Figure 132 (SEQ ID NO:132), Figure 134 (SEQ ID NO:134), Figure 136 (SEQ ID NO:136), Figure 138 (SEQ ID NO:138), Figure 140 (SEQ ID NO:140), Figure 142 (SEQ ID NO:142), Figure 144 (SEQ ID NO:144), Figure 146 (SEQ ID NO:146), Figure 148 (SEQ ID NO:148), Figure 150 (SEQ ID NO:150), Figure 152 (SEQ ID NO:152), Figure 154 (SEQ ID NO:154), Figure 156 (SEQ ID NO:156), Figure 158 (SEQ ID NO:158), Figure 160 (SEQ ID NO:160), Figure 162 (SEQ ID NO:162), Figure 164 (SEQ ID NO:164), Figure 166 (SEQ ID NO:166), Figure 168 (SEQ ID NO:168), Figure 170 (SEQ ID NO:170), Figure 172 (SEQ ID NO:172), Figure 174 (SEQ ID NO:174), Figure 176 (SEQ ID NO:176), Figure 178 (SEQ ID NO:178), Figure 180 (SEQ ID NO:180), Figure 182 (SEQ ID NO:182), Figure 184 (SEQ ID NO:184), Figure 186 (SEQ ID NO:186), Figure 188 (SEQ ID NO:188), Figure 190 (SEQ ID NO:190), Figure 192 (SEQ ID NO:192), Figure 194 (SEQ ID NO:194), Figure 196 (SEQ ID NO:196), Figure 198 (SEQ ID NO:198), Figure 200 (SEQ ID NO:200), Figure 202 (SEQ ID NO:202), Figure 204 (SEQ ID NO:204), Figure 206 (SEQ ID NO:206), Figure 208 (SEQ ID NO:208), Figure 210 (SEQ ID NO:210), Figure 212 (SEQ ID NO:212), Figure 214 (SEQ ID NO:214), Figure 216 (SEQ ID NO:216), Figure 218 (SEQ ID NO:218), Figure 220 (SEQ ID NO:220), Figure 222 (SEQ ID NO:222), Figure 224 (SEQ ID NO:224), Figure 226 (SEQ ID NO:226), Figure 228 (SEQ ID NO:228), Figure 230 (SEQ ID NO:230), Figure 232 (SEQ ID NO:232), Figure 234 (SEQ ID NO:234), Figure 236 (SEQ ID NO:236), Figure 238 (SEQ ID NO:238), Figure 240 (SEQ ID NO:240), Figure 242 (SEQ ID NO:242), Figure 244 (SEQ ID NO:244), Figure 246 (SEQ ID NO:246), Figure 248 (SEQ ID NO:248), Figure 250 (SEQ ID NO:250), Figure 252 (SEQ ID NO:252), Figure 254 (SEQ ID NO:254), Figure 256 (SEQ ID NO:256), Figure 258 (SEQ ID NO:258), Figure 260 (SEQ ID NO:260), Figure 262 (SEQ ID NO:262), Figure 264 (SEQ ID NO:264), Figure 266 (SEQ ID NO:266), Figure 268 (SEQ ID NO:268), Figure 270 (SEQ ID NO:270), Figure 272 (SEQ ID NO:272), Figure 274 (SEQ ID NO:274), Figure 276 (SEQ ID NO:276), Figure 278 (SEQ ID NO:278), Figure 280 (SEQ ID NO:280), Figure 282 (SEQ ID NO:282), Figure

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Figure 550 (SEQ ID NO:550).

13. 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.

14. A chimeric molecule comprising a polypeptide according to Claim 12 fused to a heterologous amino acid sequence.

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

16. The chimeric molecule of Claim 14, wherein said heterologous amino acid sequence is a Fc region of an immunoglobulin.

17. An antibody which specifically binds to a polypeptide according to Claim 12.

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

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

(a) a nucleotide sequence encoding the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), Figure 6 (SEQ ID NO:6), Figure 8 (SEQ ID NO:8), Figure 10 (SEQ ID NO:10), Figure 12 (SEQ ID NO:12), Figure 14 (SEQ ID NO:14), Figure 16 (SEQ ID NO:16), Figure 18 (SEQ ID NO:18), Figure 20 (SEQ ID NO:20), Figure 22 (SEQ ID NO:22), Figure 24 (SEQ ID NO:24), Figure 26 (SEQ ID NO:26), Figure 28 (SEQ ID NO:28), Figure 30 (SEQ ID NO:30), Figure 32 (SEQ ID NO:32), Figure 34 (SEQ ID NO:34), Figure 36 (SEQ ID NO:36), Figure 38 (SEQ ID NO:38), Figure 40 (SEQ ID NO:40), Figure 42 (SEQ ID NO:42), Figure 44 (SEQ ID NO:44), Figure 46 (SEQ ID NO:46), Figure 48 (SEQ ID NO:48), Figure 50 (SEQ ID NO:50), Figure 52 (SEQ ID NO:52), Figure 54 (SEQ ID NO:54), Figure 56 (SEQ ID NO:56), Figure 58 (SEQ ID NO:58), Figure 60 (SEQ ID NO:60), Figure 62 (SEQ ID NO:62), Figure 64 (SEQ ID NO:64), Figure 66 (SEQ ID NO:66), Figure 68 (SEQ ID NO:68), Figure 70 (SEQ ID NO:70), Figure 72 (SEQ ID NO:72), Figure 74 (SEQ ID NO:74), Figure 76 (SEQ ID NO:76), Figure 78 (SEQ ID NO:78), Figure 80 (SEQ ID NO:80), Figure 82 (SEQ ID NO:82), Figure 84 (SEQ ID NO:84), Figure 86 (SEQ ID NO:86), Figure 88 (SEQ ID NO:88), Figure 90 (SEQ ID NO:90), Figure 92 (SEQ ID NO:92), Figure 94 (SEQ ID NO:94), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:98), Figure 100 (SEQ ID NO:100), Figure 102 (SEQ ID NO:102), Figure 104 (SEQ ID NO:104), Figure 106 (SEQ ID NO:106), Figure 108 (SEQ ID NO:108), Figure 110 (SEQ ID NO:110), Figure 112 (SEQ ID NO:112), Figure 114 (SEQ ID NO:114), Figure 116 (SEQ ID NO:116), Figure 118 (SEQ ID NO:118), Figure 120 (SEQ ID NO:120), Figure 122 (SEQ ID NO:122), Figure 124 (SEQ

ID NO:124), Figure 126 (SEQ ID NO:126), Figure 128 (SEQ ID NO:128), Figure 130 (SEQ ID NO:130), Figure 132 (SEQ ID NO:132), Figure 134 (SEQ ID NO:134), Figure 136 (SEQ ID NO:136), Figure 138 (SEQ ID NO:138), Figure 140 (SEQ ID NO:140), Figure 142 (SEQ ID NO:142), Figure 144 (SEQ ID NO:144), Figure 146 (SEQ ID NO:146), Figure 148 (SEQ ID NO:148), Figure 150 (SEQ ID NO:150), Figure 152 (SEQ ID NO:152), Figure 154 (SEQ ID NO:154), Figure 156 (SEQ ID NO:156), Figure 158 (SEQ ID NO:158), Figure 160 (SEQ ID NO:160), Figure 162 (SEQ ID NO:162), Figure 164 (SEQ ID NO:164), Figure 166 (SEQ ID NO:166), Figure 168 (SEQ ID NO:168), Figure 170 (SEQ ID NO:170), Figure 172 (SEQ ID NO:172), Figure 174 (SEQ ID NO:174), Figure 176 (SEQ ID NO:176), Figure 178 (SEQ ID NO:178), Figure 180 (SEQ ID NO:180), Figure 182 (SEQ ID NO:182), Figure 184 (SEQ ID NO:184), Figure 186 (SEQ ID NO:186), Figure 188 (SEQ ID NO:188), Figure 190 (SEQ ID NO:190), Figure 192 (SEQ ID NO:192), Figure 194 (SEQ ID NO:194), Figure 196 (SEQ ID NO:196), Figure 198 (SEQ ID NO:198), Figure 200 (SEQ ID NO:200), Figure 202 (SEQ ID NO:202), Figure 204 (SEQ ID NO:204), Figure 206 (SEQ ID NO:206), Figure 208 (SEQ ID NO:208), Figure 210 (SEQ ID NO:210), Figure 212 (SEQ ID NO:212), Figure 214 (SEQ ID NO:214), Figure 216 (SEQ ID NO:216), Figure 218 (SEQ ID NO:218), Figure 220 (SEQ ID NO:220), Figure 222 (SEQ ID NO:222), Figure 224 (SEQ ID NO:224), Figure 226 (SEQ ID NO:226), Figure 228 (SEQ ID NO:228), Figure 230 (SEQ ID NO:230), Figure 232 (SEQ ID NO:232), Figure 234 (SEQ ID NO:234), Figure 236 (SEQ ID NO:236), Figure 238 (SEQ ID NO:238), Figure 240 (SEQ ID NO:240), Figure 242 (SEQ ID NO:242), Figure 244 (SEQ ID NO:244), Figure 246 (SEQ ID NO:246), Figure 248 (SEQ ID NO:248), Figure 250 (SEQ ID NO:250), Figure 252 (SEQ ID NO:252), Figure 254 (SEQ ID NO:254), Figure 256 (SEQ ID NO:256), Figure 258 (SEQ ID NO:258), Figure 260 (SEQ ID NO:260), Figure 262 (SEQ ID NO:262), Figure 264 (SEQ ID NO:264), Figure 266 (SEQ ID NO:266), Figure 268 (SEQ ID NO:268), Figure 270 (SEQ ID NO:270), Figure 272 (SEQ ID NO:272), Figure 274 (SEQ ID NO:274), Figure 276 (SEQ ID NO:276), Figure 278 (SEQ ID NO:278), Figure 280 (SEQ ID NO:280), Figure 282 (SEQ ID NO:282), Figure 284 (SEQ ID NO:284), Figure 286 (SEQ ID NO:286), Figure 288 (SEQ ID NO:288), Figure 290 (SEQ ID NO:290), Figure 292 (SEQ ID NO:292), Figure 294 (SEQ ID NO:294), Figure 296 (SEQ ID NO:296), Figure 298 (SEQ ID NO:298), Figure 300 (SEQ ID NO:300), Figure 302 (SEQ ID NO:302), Figure 304 (SEQ ID NO:304), Figure 306 (SEQ ID NO:306), Figure 308 (SEQ ID NO:308), Figure 310 (SEQ ID NO:310), Figure 312 (SEQ ID NO:312), Figure 314 (SEQ ID NO:314), Figure 316 (SEQ ID NO:316), Figure 318 (SEQ ID NO:318), Figure 320 (SEQ ID NO:320), Figure 322 (SEQ ID NO:322), Figure 324 (SEQ ID NO:324), Figure 326 (SEQ ID NO:326), Figure 328 (SEQ ID NO:328), Figure 330 (SEQ ID NO:330), Figure 332 (SEQ ID NO:332), Figure 334 (SEQ ID NO:334), Figure 336 (SEQ ID NO:336), Figure 338 (SEQ ID NO:338), Figure 340 (SEQ ID NO:340), Figure 342 (SEQ ID NO:342), Figure 344 (SEQ ID NO:344), Figure 346 (SEQ ID NO:346), Figure 348 (SEQ ID NO:348), Figure 350 (SEQ ID NO:350), Figure 352 (SEQ ID NO:352), Figure 354 (SEQ ID NO:354), Figure 356 (SEQ ID NO:356), Figure 358 (SEQ ID NO:358), Figure 360 (SEQ ID NO:360), Figure 362 (SEQ ID NO:362), Figure 364 (SEQ ID NO:364), Figure 366 (SEQ ID NO:366), Figure 368 (SEQ ID NO:368), Figure 370 (SEQ ID NO:370), Figure 372 (SEQ ID NO:372), Figure 374 (SEQ ID NO:374), Figure 376 (SEQ ID NO:376), Figure 378 (SEQ ID NO:378), Figure 380 (SEQ ID NO:380), Figure 382 (SEQ ID NO:382), Figure 384 (SEQ ID NO:384), Figure 386 (SEQ ID NO:386), Figure 388 (SEQ ID NO:388), Figure 390 (SEQ

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(b) a nucleotide sequence encoding an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), Figure 6 (SEQ ID NO:6), Figure 8 (SEQ ID NO:8), Figure 10 (SEQ ID NO:10), Figure 12 (SEQ ID NO:12), Figure 14 (SEQ ID NO:14), Figure 16 (SEQ ID NO:16), Figure 18 (SEQ ID NO:18), Figure 20 (SEQ ID NO:20), Figure 22 (SEQ ID NO:22), Figure 24 (SEQ ID NO:24), Figure 26 (SEQ ID NO:26), Figure 28 (SEQ ID NO:28), Figure 30 (SEQ ID NO:30), Figure 32 (SEQ ID NO:32), Figure 34 (SEQ ID NO:34), Figure 36 (SEQ ID NO:36), Figure 38 (SEQ ID NO:38), Figure 40 (SEQ ID NO:40), Figure 42 (SEQ ID NO:42), Figure 44 (SEQ ID NO:44), Figure 46 (SEQ ID NO:46), Figure 48 (SEQ ID NO:48), Figure 50 (SEQ ID NO:50), Figure 52 (SEQ ID NO:52), Figure 54 (SEQ ID NO:54), Figure 56 (SEQ ID NO:56), Figure 58 (SEQ ID NO:58), Figure 60 (SEQ ID NO:60), Figure 62 (SEQ ID NO:62), Figure 64 (SEQ ID NO:64), Figure 66 (SEQ ID NO:66), Figure 68 (SEQ ID NO:68), Figure 70 (SEQ ID NO:70), Figure 72 (SEQ ID NO:72), Figure 74 (SEQ ID NO:74), Figure 76 (SEQ ID NO:76), Figure 78 (SEQ ID NO:78), Figure 80 (SEQ ID NO:80), Figure 82 (SEQ ID NO:82), Figure 84 (SEQ ID NO:84), Figure 86 (SEQ ID NO:86), Figure 88 (SEQ ID NO:88), Figure 90 (SEQ ID NO:90), Figure 92 (SEQ ID NO:92), Figure 94 (SEQ ID NO:94), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:98), Figure 100 (SEQ ID NO:100),

Figure 102 (SEQ ID NO:102), Figure 104 (SEQ ID NO:104), Figure 106 (SEQ ID NO:106), Figure 108 (SEQ ID NO:108), Figure 110 (SEQ ID NO:110), Figure 112 (SEQ ID NO:112), Figure 114 (SEQ ID NO:114), Figure 116 (SEQ ID NO:116), Figure 118 (SEQ ID NO:118), Figure 120 (SEQ ID NO:120), Figure 122 (SEQ ID NO:122), Figure 124 (SEQ ID NO:124), Figure 126 (SEQ ID NO:126), Figure 128 (SEQ ID NO:128), Figure 130 (SEQ ID NO:130), Figure 132 (SEQ ID NO:132), Figure 134 (SEQ ID NO:134), Figure 136 (SEQ ID NO:136), Figure 138 (SEQ ID NO:138), Figure 140 (SEQ ID NO:140), Figure 142 (SEQ ID NO:142), Figure 144 (SEQ ID NO:144), Figure 146 (SEQ ID NO:146), Figure 148 (SEQ ID NO:148), Figure 150 (SEQ ID NO:150), Figure 152 (SEQ ID NO:152), Figure 154 (SEQ ID NO:154), Figure 156 (SEQ ID NO:156), Figure 158 (SEQ ID NO:158), Figure 160 (SEQ ID NO:160), Figure 162 (SEQ ID NO:162), Figure 164 (SEQ ID NO:164), Figure 166 (SEQ ID NO:166), Figure 168 (SEQ ID NO:168), Figure 170 (SEQ ID NO:170), Figure 172 (SEQ ID NO:172), Figure 174 (SEQ ID NO:174), Figure 176 (SEQ ID NO:176), Figure 178 (SEQ ID NO:178), Figure 180 (SEQ ID NO:180), Figure 182 (SEQ ID NO:182), Figure 184 (SEQ ID NO:184), Figure 186 (SEQ ID NO:186), Figure 188 (SEQ ID NO:188), Figure 190 (SEQ ID NO:190), Figure 192 (SEQ ID NO:192), Figure 194 (SEQ ID NO:194), Figure 196 (SEQ ID NO:196), Figure 198 (SEQ ID NO:198), Figure 200 (SEQ ID NO:200), Figure 202 (SEQ ID NO:202), Figure 204 (SEQ ID NO:204), Figure 206 (SEQ ID NO:206), Figure 208 (SEQ ID NO:208), Figure 210 (SEQ ID NO:210), Figure 212 (SEQ ID NO:212), Figure 214 (SEQ ID NO:214), Figure 216 (SEQ ID NO:216), Figure 218 (SEQ ID NO:218), Figure 220 (SEQ ID NO:220), Figure 222 (SEQ ID NO:222), Figure 224 (SEQ ID NO:224), Figure 226 (SEQ ID NO:226), Figure 228 (SEQ ID NO:228), Figure 230 (SEQ ID NO:230), Figure 232 (SEQ ID NO:232), Figure 234 (SEQ ID NO:234), Figure 236 (SEQ ID NO:236), Figure 238 (SEQ ID NO:238), Figure 240 (SEQ ID NO:240), Figure 242 (SEQ ID NO:242), Figure 244 (SEQ ID NO:244), Figure 246 (SEQ ID NO:246), Figure 248 (SEQ ID NO:248), Figure 250 (SEQ ID NO:250), Figure 252 (SEQ ID NO:252), Figure 254 (SEQ ID NO:254), Figure 256 (SEQ ID NO:256), Figure 258 (SEQ ID NO:258), Figure 260 (SEQ ID NO:260), Figure 262 (SEQ ID NO:262), Figure 264 (SEQ ID NO:264), Figure 266 (SEQ ID NO:266), Figure 268 (SEQ ID NO:268), Figure 270 (SEQ ID NO:270), Figure 272 (SEQ ID NO:272), Figure 274 (SEQ ID NO:274), Figure 276 (SEQ ID NO:276), Figure 278 (SEQ ID NO:278), Figure 280 (SEQ ID NO:280), Figure 282 (SEQ ID NO:282), Figure 284 (SEQ ID NO:284), Figure 286 (SEQ ID NO:286), Figure 288 (SEQ ID NO:288), Figure 290 (SEQ ID NO:290), Figure 292 (SEQ ID NO:292), Figure 294 (SEQ ID NO:294), Figure 296 (SEQ ID NO:296), Figure 298 (SEQ ID NO:298), Figure 300 (SEQ ID NO:300), Figure 302 (SEQ ID NO:302), Figure 304 (SEQ ID NO:304), Figure 306 (SEQ ID NO:306), Figure 308 (SEQ ID NO:308), Figure 310 (SEQ ID NO:310), Figure 312 (SEQ ID NO:312), Figure 314 (SEQ ID NO:314), Figure 316 (SEQ ID NO:316), Figure 318 (SEQ ID NO:318), Figure 320 (SEQ ID NO:320), Figure 322 (SEQ ID NO:322), Figure 324 (SEQ ID NO:324), Figure 326 (SEQ ID NO:326), Figure 328 (SEQ ID NO:328), Figure 330 (SEQ ID NO:330), Figure 332 (SEQ ID NO:332), Figure 334 (SEQ ID NO:334), Figure 336 (SEQ ID NO:336), Figure 338 (SEQ ID NO:338), Figure 340 (SEQ ID NO:340), Figure 342 (SEQ ID NO:342), Figure 344 (SEQ ID NO:344), Figure 346 (SEQ ID NO:346), Figure 348 (SEQ ID NO:348), Figure 350 (SEQ ID NO:350), Figure 352 (SEQ ID NO:352), Figure 354 (SEQ ID NO:354), Figure 356 (SEQ ID NO:356), Figure 358 (SEQ ID NO:358), Figure 360 (SEQ ID NO:360), Figure 362 (SEQ ID NO:362), Figure 364 (SEQ ID NO:364), Figure 366 (SEQ ID NO:366),

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(c) a nucleotide sequence encoding an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), Figure 6 (SEQ ID NO:6), Figure 8 (SEQ ID NO:8), Figure 10 (SEQ ID NO:10), Figure 12 (SEQ ID NO:12), Figure 14 (SEQ ID NO:14), Figure 16 (SEQ ID NO:16), Figure 18 (SEQ ID NO:18), Figure 20 (SEQ ID NO:20), Figure 22 (SEQ ID NO:22), Figure 24 (SEQ ID NO:24), Figure 26 (SEQ ID NO:26), Figure 28 (SEQ ID NO:28), Figure 30 (SEQ ID NO:30), Figure 32 (SEQ ID NO:32), Figure 34 (SEQ ID NO:34), Figure 36 (SEQ ID NO:36), Figure 38 (SEQ ID NO:38), Figure 40 (SEQ ID NO:40), Figure 42 (SEQ ID NO:42), Figure 44 (SEQ ID NO:44), Figure 46 (SEQ ID NO:46), Figure 48 (SEQ ID NO:48), Figure 50 (SEQ ID NO:50), Figure 52 (SEQ ID NO:52), Figure 54 (SEQ ID NO:54), Figure 56 (SEQ ID NO:56), Figure 58 (SEQ ID NO:58), Figure 60 (SEQ ID NO:60), Figure 62 (SEQ ID NO:62), Figure 64 (SEQ ID NO:64), Figure 66 (SEQ ID NO:66), Figure 68 (SEQ ID NO:68), Figure 70 (SEQ ID NO:70), Figure 72 (SEQ ID NO:72), Figure 74 (SEQ ID NO:74), Figure 76 (SEQ ID NO:76), Figure 78 (SEQ ID

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

(a) an amino acid sequence of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), Figure 6 (SEQ ID NO:6), Figure 8 (SEQ ID NO:8), Figure 10 (SEQ ID NO:10), Figure 12 (SEQ ID NO:12), Figure 14 (SEQ ID NO:14), Figure 16 (SEQ ID NO:16), Figure 18 (SEQ ID NO:18), Figure 20 (SEQ ID NO:20), Figure 22 (SEQ ID NO:22), Figure 24 (SEQ ID NO:24), Figure 26 (SEQ ID NO:26), Figure 28 (SEQ ID NO:28), Figure 30 (SEQ ID NO:30), Figure 32 (SEQ ID NO:32), Figure 34 (SEQ ID NO:34), Figure 36 (SEQ ID NO:36), Figure 38 (SEQ ID NO:38), Figure 40 (SEQ ID NO:40), Figure 42 (SEQ ID

NO:42), Figure 44 (SEQ ID NO:44), Figure 46 (SEQ ID NO:46), Figure 48 (SEQ ID NO:48), Figure 50 (SEQ ID NO:50), Figure 52 (SEQ ID NO:52), Figure 54 (SEQ ID NO:54), Figure 56 (SEQ ID NO:56), Figure 58 (SEQ ID NO:58), Figure 60 (SEQ ID NO:60), Figure 62 (SEQ ID NO:62), Figure 64 (SEQ ID NO:64), Figure 66 (SEQ ID NO:66), Figure 68 (SEQ ID NO:68), Figure 70 (SEQ ID NO:70), Figure 72 (SEQ ID NO:72), Figure 74 (SEQ ID NO:74), Figure 76 (SEQ ID NO:76), Figure 78 (SEQ ID NO:78), Figure 80 (SEQ ID NO:80), Figure 82 (SEQ ID NO:82), Figure 84 (SEQ ID NO:84), Figure 86 (SEQ ID NO:86), Figure 88 (SEQ ID NO:88), Figure 90 (SEQ ID NO:90), Figure 92 (SEQ ID NO:92), Figure 94 (SEQ ID NO:94), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:98), Figure 100 (SEQ ID NO:100), Figure 102 (SEQ ID NO:102), Figure 104 (SEQ ID NO:104), Figure 106 (SEQ ID NO:106), Figure 108 (SEQ ID NO:108), Figure 110 (SEQ ID NO:110), Figure 112 (SEQ ID NO:112), Figure 114 (SEQ ID NO:114), Figure 116 (SEQ ID NO:116), Figure 118 (SEQ ID NO:118), Figure 120 (SEQ ID NO:120), Figure 122 (SEQ ID NO:122), Figure 124 (SEQ ID NO:124), Figure 126 (SEQ ID NO:126), Figure 128 (SEQ ID NO:128), Figure 130 (SEQ ID NO:130), Figure 132 (SEQ ID NO:132), Figure 134 (SEQ ID NO:134), Figure 136 (SEQ ID NO:136), Figure 138 (SEQ ID NO:138), Figure 140 (SEQ ID NO:140), Figure 142 (SEQ ID NO:142), Figure 144 (SEQ ID NO:144), Figure 146 (SEQ ID NO:146), Figure 148 (SEQ ID NO:148), Figure 150 (SEQ ID NO:150), Figure 152 (SEQ ID NO:152), Figure 154 (SEQ ID NO:154), Figure 156 (SEQ ID NO:156), Figure 158 (SEQ ID NO:158), Figure 160 (SEQ ID NO:160), Figure 162 (SEQ ID NO:162), Figure 164 (SEQ ID NO:164), Figure 166 (SEQ ID NO:166), Figure 168 (SEQ ID NO:168), Figure 170 (SEQ ID NO:170), Figure 172 (SEQ ID NO:172), Figure 174 (SEQ ID NO:174), Figure 176 (SEQ ID NO:176), Figure 178 (SEQ ID NO:178), Figure 180 (SEQ ID NO:180), Figure 182 (SEQ ID NO:182), Figure 184 (SEQ ID NO:184), Figure 186 (SEQ ID NO:186), Figure 188 (SEQ ID NO:188), Figure 190 (SEQ ID NO:190), Figure 192 (SEQ ID NO:192), Figure 194 (SEQ ID NO:194), Figure 196 (SEQ ID NO:196), Figure 198 (SEQ ID NO:198), Figure 200 (SEQ ID NO:200), Figure 202 (SEQ ID NO:202), Figure 204 (SEQ ID NO:204), Figure 206 (SEQ ID NO:206), Figure 208 (SEQ ID NO:208), Figure 210 (SEQ ID NO:210), Figure 212 (SEQ ID NO:212), Figure 214 (SEQ ID NO:214), Figure 216 (SEQ ID NO:216), Figure 218 (SEQ ID NO:218), Figure 220 (SEQ ID NO:220), Figure 222 (SEQ ID NO:222), Figure 224 (SEQ ID NO:224), Figure 226 (SEQ ID NO:226), Figure 228 (SEQ ID NO:228), Figure 230 (SEQ ID NO:230), Figure 232 (SEQ ID NO:232), Figure 234 (SEQ ID NO:234), Figure 236 (SEQ ID NO:236), Figure 238 (SEQ ID NO:238), Figure 240 (SEQ ID NO:240), Figure 242 (SEQ ID NO:242), Figure 244 (SEQ ID NO:244), Figure 246 (SEQ ID NO:246), Figure 248 (SEQ ID NO:248), Figure 250 (SEQ ID NO:250), Figure 252 (SEQ ID NO:252), Figure 254 (SEQ ID NO:254), Figure 256 (SEQ ID NO:256), Figure 258 (SEQ ID NO:258), Figure 260 (SEQ ID NO:260), Figure 262 (SEQ ID NO:262), Figure 264 (SEQ ID NO:264), Figure 266 (SEQ ID NO:266), Figure 268 (SEQ ID NO:268), Figure 270 (SEQ ID NO:270), Figure 272 (SEQ ID NO:272), Figure 274 (SEQ ID NO:274), Figure 276 (SEQ ID NO:276), Figure 278 (SEQ ID NO:278), Figure 280 (SEQ ID NO:280), Figure 282 (SEQ ID NO:282), Figure 284 (SEQ ID NO:284), Figure 286 (SEQ ID NO:286), Figure 288 (SEQ ID NO:288), Figure 290 (SEQ ID NO:290), Figure 292 (SEQ ID NO:292), Figure 294 (SEQ ID NO:294), Figure 296 (SEQ ID NO:296), Figure 298 (SEQ ID NO:298), Figure 300 (SEQ ID NO:300), Figure 302 (SEQ ID NO:302), Figure 304 (SEQ ID NO:304), Figure 306 (SEQ ID NO:306), Figure 308 (SEQ ID NO:308), Figure 310 (SEQ ID NO:310), Figure 312 (SEQ ID NO:312),

Figure 314 (SEQ ID NO:314), Figure 316 (SEQ ID NO:316), Figure 318 (SEQ ID NO:318), Figure 320 (SEQ ID NO:320), Figure 322 (SEQ ID NO:322), Figure 324 (SEQ ID NO:324), Figure 326 (SEQ ID NO:326), Figure 328 (SEQ ID NO:328), Figure 330 (SEQ ID NO:330), Figure 332 (SEQ ID NO:332), Figure 334 (SEQ ID NO:334), Figure 336 (SEQ ID NO:336), Figure 338 (SEQ ID NO:338), Figure 340 (SEQ ID NO:340), Figure 342 (SEQ ID NO:342), Figure 344 (SEQ ID NO:344), Figure 346 (SEQ ID NO:346), Figure 348 (SEQ ID NO:348), Figure 350 (SEQ ID NO:350), Figure 352 (SEQ ID NO:352), Figure 354 (SEQ ID NO:354), Figure 356 (SEQ ID NO:356), Figure 358 (SEQ ID NO:358), Figure 360 (SEQ ID NO:360), Figure 362 (SEQ ID NO:362), Figure 364 (SEQ ID NO:364), Figure 366 (SEQ ID NO:366), Figure 368 (SEQ ID NO:368), Figure 370 (SEQ ID NO:370), Figure 372 (SEQ ID NO:372), Figure 374 (SEQ ID NO:374), Figure 376 (SEQ ID NO:376), Figure 378 (SEQ ID NO:378), Figure 380 (SEQ ID NO:380), Figure 382 (SEQ ID NO:382), Figure 384 (SEQ ID NO:384), Figure 386 (SEQ ID NO:386), Figure 388 (SEQ ID NO:388), Figure 390 (SEQ ID NO:390), Figure 392 (SEQ ID NO:392), Figure 394 (SEQ ID NO:394), Figure 396 (SEQ ID NO:396), Figure 398 (SEQ ID NO:398), Figure 400 (SEQ ID NO:400), Figure 402 (SEQ ID NO:402), Figure 404 (SEQ ID NO:404), Figure 406 (SEQ ID NO:406), Figure 408 (SEQ ID NO:408), Figure 410 (SEQ ID NO:410), Figure 412 (SEQ ID NO:412), Figure 414 (SEQ ID NO:414), Figure 416 (SEQ ID NO:416), Figure 418 (SEQ ID NO:418), Figure 420 (SEQ ID NO:420), Figure 422 (SEQ ID NO:422), Figure 424 (SEQ ID NO:424), Figure 426 (SEQ ID NO:426), Figure 428 (SEQ ID NO:428), Figure 430 (SEQ ID NO:430), Figure 432 (SEQ ID NO:432), Figure 434 (SEQ ID NO:434), Figure 436 (SEQ ID NO:436), Figure 438 (SEQ ID NO:438), Figure 440 (SEQ ID NO:440), Figure 442 (SEQ ID NO:442), Figure 444 (SEQ ID NO:444), Figure 446 (SEQ ID NO:446), Figure 448 (SEQ ID NO:448), Figure 450 (SEQ ID NO:450), Figure 452 (SEQ ID NO:452), Figure 454 (SEQ ID NO:454), Figure 456 (SEQ ID NO:456), Figure 458 (SEQ ID NO:458), Figure 460 (SEQ ID NO:460), Figure 462 (SEQ ID NO:462), Figure 464 (SEQ ID NO:464), Figure 466 (SEQ ID NO:466), Figure 468 (SEQ ID NO:468), Figure 470 (SEQ ID NO:470), Figure 472 (SEQ ID NO:472), Figure 474 (SEQ ID NO:474), Figure 476 (SEQ ID NO:476), Figure 478 (SEQ ID NO:478), Figure 480 (SEQ ID NO:480), Figure 482 (SEQ ID NO:482), Figure 484 (SEQ ID NO:484), Figure 486 (SEQ ID NO:486), Figure 488 (SEQ ID NO:488), Figure 490 (SEQ ID NO:490), Figure 492 (SEQ ID NO:492), Figure 494 (SEQ ID NO:494), Figure 496 (SEQ ID NO:496), Figure 498 (SEQ ID NO:498), Figure 500 (SEQ ID NO:500), Figure 502 (SEQ ID NO:502), Figure 504 (SEQ ID NO:504), Figure 506 (SEQ ID NO:506), Figure 508 (SEQ ID NO:508), Figure 510 (SEQ ID NO:510), Figure 512 (SEQ ID NO:512), Figure 514 (SEQ ID NO:514), Figure 516 (SEQ ID NO:516), Figure 518 (SEQ ID NO:518), Figure 520 (SEQ ID NO:520), Figure 522 (SEQ ID NO:522), Figure 524 (SEQ ID NO:524), Figure 526 (SEQ ID NO:526), Figure 528 (SEQ ID NO:528), Figure 530 (SEQ ID NO:530), Figure 532 (SEQ ID NO:532), Figure 534 (SEQ ID NO:534), Figure 536 (SEQ ID NO:536), Figure 538 (SEQ ID NO:538), Figure 540 (SEQ ID NO:540), Figure 542 (SEQ ID NO:542), Figure 544 (SEQ ID NO:544), Figure 546 (SEQ ID NO:546), Figure 548 (SEQ ID NO:548) or Figure 550 (SEQ ID NO:550), lacking its associated signal peptide;

(b) an amino acid sequence of an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), Figure 6 (SEQ ID NO:6), Figure 8 (SEQ ID NO:8), Figure 10 (SEQ ID NO:10), Figure 12 (SEQ ID NO:12), Figure 14 (SEQ ID NO:14), Figure 16 (SEQ ID NO:16), Figure 18 (SEQ

ID NO:18), Figure 20 (SEQ ID NO:20), Figure 22 (SEQ ID NO:22), Figure 24 (SEQ ID NO:24), Figure 26 (SEQ ID NO:26), Figure 28 (SEQ ID NO:28), Figure 30 (SEQ ID NO:30), Figure 32 (SEQ ID NO:32), Figure 34 (SEQ ID NO:34), Figure 36 (SEQ ID NO:36), Figure 38 (SEQ ID NO:38), Figure 40 (SEQ ID NO:40), Figure 42 (SEQ ID NO:42), Figure 44 (SEQ ID NO:44), Figure 46 (SEQ ID NO:46), Figure 48 (SEQ ID NO:48), Figure 50 (SEQ ID NO:50), Figure 52 (SEQ ID NO:52), Figure 54 (SEQ ID NO:54), Figure 56 (SEQ ID NO:56), Figure 58 (SEQ ID NO:58), Figure 60 (SEQ ID NO:60), Figure 62 (SEQ ID NO:62), Figure 64 (SEQ ID NO:64), Figure 66 (SEQ ID NO:66), Figure 68 (SEQ ID NO:68), Figure 70 (SEQ ID NO:70), Figure 72 (SEQ ID NO:72), Figure 74 (SEQ ID NO:74), Figure 76 (SEQ ID NO:76), Figure 78 (SEQ ID NO:78), Figure 80 (SEQ ID NO:80), Figure 82 (SEQ ID NO:82), Figure 84 (SEQ ID NO:84), Figure 86 (SEQ ID NO:86), Figure 88 (SEQ ID NO:88), Figure 90 (SEQ ID NO:90), Figure 92 (SEQ ID NO:92), Figure 94 (SEQ ID NO:94), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:98), Figure 100 (SEQ ID NO:100), Figure 102 (SEQ ID NO:102), Figure 104 (SEQ ID NO:104), Figure 106 (SEQ ID NO:106), Figure 108 (SEQ ID NO:108), Figure 110 (SEQ ID NO:110), Figure 112 (SEQ ID NO:112), Figure 114 (SEQ ID NO:114), Figure 116 (SEQ ID NO:116), Figure 118 (SEQ ID NO:118), Figure 120 (SEQ ID NO:120), Figure 122 (SEQ ID NO:122), Figure 124 (SEQ ID NO:124), Figure 126 (SEQ ID NO:126), Figure 128 (SEQ ID NO:128), Figure 130 (SEQ ID NO:130), Figure 132 (SEQ ID NO:132), Figure 134 (SEQ ID NO:134), Figure 136 (SEQ ID NO:136), Figure 138 (SEQ ID NO:138), Figure 140 (SEQ ID NO:140), Figure 142 (SEQ ID NO:142), Figure 144 (SEQ ID NO:144), Figure 146 (SEQ ID NO:146), Figure 148 (SEQ ID NO:148), Figure 150 (SEQ ID NO:150), Figure 152 (SEQ ID NO:152), Figure 154 (SEQ ID NO:154), Figure 156 (SEQ ID NO:156), Figure 158 (SEQ ID NO:158), Figure 160 (SEQ ID NO:160), Figure 162 (SEQ ID NO:162), Figure 164 (SEQ ID NO:164), Figure 166 (SEQ ID NO:166), Figure 168 (SEQ ID NO:168), Figure 170 (SEQ ID NO:170), Figure 172 (SEQ ID NO:172), Figure 174 (SEQ ID NO:174), Figure 176 (SEQ ID NO:176), Figure 178 (SEQ ID NO:178), Figure 180 (SEQ ID NO:180), Figure 182 (SEQ ID NO:182), Figure 184 (SEQ ID NO:184), Figure 186 (SEQ ID NO:186), Figure 188 (SEQ ID NO:188), Figure 190 (SEQ ID NO:190), Figure 192 (SEQ ID NO:192), Figure 194 (SEQ ID NO:194), Figure 196 (SEQ ID NO:196), Figure 198 (SEQ ID NO:198), Figure 200 (SEQ ID NO:200), Figure 202 (SEQ ID NO:202), Figure 204 (SEQ ID NO:204), Figure 206 (SEQ ID NO:206), Figure 208 (SEQ ID NO:208), Figure 210 (SEQ ID NO:210), Figure 212 (SEQ ID NO:212), Figure 214 (SEQ ID NO:214), Figure 216 (SEQ ID NO:216), Figure 218 (SEQ ID NO:218), Figure 220 (SEQ ID NO:220), Figure 222 (SEQ ID NO:222), Figure 224 (SEQ ID NO:224), Figure 226 (SEQ ID NO:226), Figure 228 (SEQ ID NO:228), Figure 230 (SEQ ID NO:230), Figure 232 (SEQ ID NO:232), Figure 234 (SEQ ID NO:234), Figure 236 (SEQ ID NO:236), Figure 238 (SEQ ID NO:238), Figure 240 (SEQ ID NO:240), Figure 242 (SEQ ID NO:242), Figure 244 (SEQ ID NO:244), Figure 246 (SEQ ID NO:246), Figure 248 (SEQ ID NO:248), Figure 250 (SEQ ID NO:250), Figure 252 (SEQ ID NO:252), Figure 254 (SEQ ID NO:254), Figure 256 (SEQ ID NO:256), Figure 258 (SEQ ID NO:258), Figure 260 (SEQ ID NO:260), Figure 262 (SEQ ID NO:262), Figure 264 (SEQ ID NO:264), Figure 266 (SEQ ID NO:266), Figure 268 (SEQ ID NO:268), Figure 270 (SEQ ID NO:270), Figure 272 (SEQ ID NO:272), Figure 274 (SEQ ID NO:274), Figure 276 (SEQ ID NO:276), Figure 278 (SEQ ID NO:278), Figure 280 (SEQ ID NO:280), Figure 282 (SEQ ID NO:282), Figure 284 (SEQ ID NO:284), Figure 286 (SEQ ID NO:286), Figure 288 (SEQ ID NO:288), Figure 290 (SEQ ID

NO:290), Figure 292 (SEQ ID NO:292), Figure 294 (SEQ ID NO:294), Figure 296 (SEQ ID NO:296), Figure 298 (SEQ ID NO:298), Figure 300 (SEQ ID NO:300), Figure 302 (SEQ ID NO:302), Figure 304 (SEQ ID NO:304), Figure 306 (SEQ ID NO:306), Figure 308 (SEQ ID NO:308), Figure 310 (SEQ ID NO:310), Figure 312 (SEQ ID NO:312), Figure 314 (SEQ ID NO:314), Figure 316 (SEQ ID NO:316), Figure 318 (SEQ ID NO:318), Figure 320 (SEQ ID NO:320), Figure 322 (SEQ ID NO:322), Figure 324 (SEQ ID NO:324), Figure 326 (SEQ ID NO:326), Figure 328 (SEQ ID NO:328), Figure 330 (SEQ ID NO:330), Figure 332 (SEQ ID NO:332), Figure 334 (SEQ ID NO:334), Figure 336 (SEQ ID NO:336), Figure 338 (SEQ ID NO:338), Figure 340 (SEQ ID NO:340), Figure 342 (SEQ ID NO:342), Figure 344 (SEQ ID NO:344), Figure 346 (SEQ ID NO:346), Figure 348 (SEQ ID NO:348), Figure 350 (SEQ ID NO:350), Figure 352 (SEQ ID NO:352), Figure 354 (SEQ ID NO:354), Figure 356 (SEQ ID NO:356), Figure 358 (SEQ ID NO:358), Figure 360 (SEQ ID NO:360), Figure 362 (SEQ ID NO:362), Figure 364 (SEQ ID NO:364), Figure 366 (SEQ ID NO:366), Figure 368 (SEQ ID NO:368), Figure 370 (SEQ ID NO:370), Figure 372 (SEQ ID NO:372), Figure 374 (SEQ ID NO:374), Figure 376 (SEQ ID NO:376), Figure 378 (SEQ ID NO:378), Figure 380 (SEQ ID NO:380), Figure 382 (SEQ ID NO:382), Figure 384 (SEQ ID NO:384), Figure 386 (SEQ ID NO:386), Figure 388 (SEQ ID NO:388), Figure 390 (SEQ ID NO:390), Figure 392 (SEQ ID NO:392), Figure 394 (SEQ ID NO:394), Figure 396 (SEQ ID NO:396), Figure 398 (SEQ ID NO:398), Figure 400 (SEQ ID NO:400), Figure 402 (SEQ ID NO:402), Figure 404 (SEQ ID NO:404), Figure 406 (SEQ ID NO:406), Figure 408 (SEQ ID NO:408), Figure 410 (SEQ ID NO:410), Figure 412 (SEQ ID NO:412), Figure 414 (SEQ ID NO:414), Figure 416 (SEQ ID NO:416), Figure 418 (SEQ ID NO:418), Figure 420 (SEQ ID NO:420), Figure 422 (SEQ ID NO:422), Figure 424 (SEQ ID NO:424), Figure 426 (SEQ ID NO:426), Figure 428 (SEQ ID NO:428), Figure 430 (SEQ ID NO:430), Figure 432 (SEQ ID NO:432), Figure 434 (SEQ ID NO:434), Figure 436 (SEQ ID NO:436), Figure 438 (SEQ ID NO:438), Figure 440 (SEQ ID NO:440), Figure 442 (SEQ ID NO:442), Figure 444 (SEQ ID NO:444), Figure 446 (SEQ ID NO:446), Figure 448 (SEQ ID NO:448), Figure 450 (SEQ ID NO:450), Figure 452 (SEQ ID NO:452), Figure 454 (SEQ ID NO:454), Figure 456 (SEQ ID NO:456), Figure 458 (SEQ ID NO:458), Figure 460 (SEQ ID NO:460), Figure 462 (SEQ ID NO:462), Figure 464 (SEQ ID NO:464), Figure 466 (SEQ ID NO:466), Figure 468 (SEQ ID NO:468), Figure 470 (SEQ ID NO:470), Figure 472 (SEQ ID NO:472), Figure 474 (SEQ ID NO:474), Figure 476 (SEQ ID NO:476), Figure 478 (SEQ ID NO:478), Figure 480 (SEQ ID NO:480), Figure 482 (SEQ ID NO:482), Figure 484 (SEQ ID NO:484), Figure 486 (SEQ ID NO:486), Figure 488 (SEQ ID NO:488), Figure 490 (SEQ ID NO:490), Figure 492 (SEQ ID NO:492), Figure 494 (SEQ ID NO:494), Figure 496 (SEQ ID NO:496), Figure 498 (SEQ ID NO:498), Figure 500 (SEQ ID NO:500), Figure 502 (SEQ ID NO:502), Figure 504 (SEQ ID NO:504), Figure 506 (SEQ ID NO:506), Figure 508 (SEQ ID NO:508), Figure 510 (SEQ ID NO:510), Figure 512 (SEQ ID NO:512), Figure 514 (SEQ ID NO:514), Figure 516 (SEQ ID NO:516), Figure 518 (SEQ ID NO:518), Figure 520 (SEQ ID NO:520), Figure 522 (SEQ ID NO:522), Figure 524 (SEQ ID NO:524), Figure 526 (SEQ ID NO:526), Figure 528 (SEQ ID NO:528), Figure 530 (SEQ ID NO:530), Figure 532 (SEQ ID NO:532), Figure 534 (SEQ ID NO:534), Figure 536 (SEQ ID NO:536), Figure 538 (SEQ ID NO:538), Figure 540 (SEQ ID NO:540), Figure 542 (SEQ ID NO:542), Figure 544 (SEQ ID NO:544), Figure 546 (SEQ ID NO:546), Figure 548 (SEQ ID NO:548) or Figure 550 (SEQ ID NO:550), with its associated signal peptide; or

(c) an amino acid sequence of an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), Figure 6 (SEQ ID NO:6), Figure 8 (SEQ ID NO:8), Figure 10 (SEQ ID NO:10), Figure 12 (SEQ ID NO:12), Figure 14 (SEQ ID NO:14), Figure 16 (SEQ ID NO:16), Figure 18 (SEQ ID NO:18), Figure 20 (SEQ ID NO:20), Figure 22 (SEQ ID NO:22), Figure 24 (SEQ ID NO:24), Figure 26 (SEQ ID NO:26), Figure 28 (SEQ ID NO:28), Figure 30 (SEQ ID NO:30), Figure 32 (SEQ ID NO:32), Figure 34 (SEQ ID NO:34), Figure 36 (SEQ ID NO:36), Figure 38 (SEQ ID NO:38), Figure 40 (SEQ ID NO:40), Figure 42 (SEQ ID NO:42), Figure 44 (SEQ ID NO:44), Figure 46 (SEQ ID NO:46), Figure 48 (SEQ ID NO:48), Figure 50 (SEQ ID NO:50), Figure 52 (SEQ ID NO:52), Figure 54 (SEQ ID NO:54), Figure 56 (SEQ ID NO:56), Figure 58 (SEQ ID NO:58), Figure 60 (SEQ ID NO:60), Figure 62 (SEQ ID NO:62), Figure 64 (SEQ ID NO:64), Figure 66 (SEQ ID NO:66), Figure 68 (SEQ ID NO:68), Figure 70 (SEQ ID NO:70), Figure 72 (SEQ ID NO:72), Figure 74 (SEQ ID NO:74), Figure 76 (SEQ ID NO:76), Figure 78 (SEQ ID NO:78), Figure 80 (SEQ ID NO:80), Figure 82 (SEQ ID NO:82), Figure 84 (SEQ ID NO:84), Figure 86 (SEQ ID NO:86), Figure 88 (SEQ ID NO:88), Figure 90 (SEQ ID NO:90), Figure 92 (SEQ ID NO:92), Figure 94 (SEQ ID NO:94), Figure 96 (SEQ ID NO:96), Figure 98 (SEQ ID NO:98), Figure 100 (SEQ ID NO:100), Figure 102 (SEQ ID NO:102), Figure 104 (SEQ ID NO:104), Figure 106 (SEQ ID NO:106), Figure 108 (SEQ ID NO:108), Figure 110 (SEQ ID NO:110), Figure 112 (SEQ ID NO:112), Figure 114 (SEQ ID NO:114), Figure 116 (SEQ ID NO:116), Figure 118 (SEQ ID NO:118), Figure 120 (SEQ ID NO:120), Figure 122 (SEQ ID NO:122), Figure 124 (SEQ ID NO:124), Figure 126 (SEQ ID NO:126), Figure 128 (SEQ ID NO:128), Figure 130 (SEQ ID NO:130), Figure 132 (SEQ ID NO:132), Figure 134 (SEQ ID NO:134), Figure 136 (SEQ ID NO:136), Figure 138 (SEQ ID NO:138), Figure 140 (SEQ ID NO:140), Figure 142 (SEQ ID NO:142), Figure 144 (SEQ ID NO:144), Figure 146 (SEQ ID NO:146), Figure 148 (SEQ ID NO:148), Figure 150 (SEQ ID NO:150), Figure 152 (SEQ ID NO:152), Figure 154 (SEQ ID NO:154), Figure 156 (SEQ ID NO:156), Figure 158 (SEQ ID NO:158), Figure 160 (SEQ ID NO:160), Figure 162 (SEQ ID NO:162), Figure 164 (SEQ ID NO:164), Figure 166 (SEQ ID NO:166), Figure 168 (SEQ ID NO:168), Figure 170 (SEQ ID NO:170), Figure 172 (SEQ ID NO:172), Figure 174 (SEQ ID NO:174), Figure 176 (SEQ ID NO:176), Figure 178 (SEQ ID NO:178), Figure 180 (SEQ ID NO:180), Figure 182 (SEQ ID NO:182), Figure 184 (SEQ ID NO:184), Figure 186 (SEQ ID NO:186), Figure 188 (SEQ ID NO:188), Figure 190 (SEQ ID NO:190), Figure 192 (SEQ ID NO:192), Figure 194 (SEQ ID NO:194), Figure 196 (SEQ ID NO:196), Figure 198 (SEQ ID NO:198), Figure 200 (SEQ ID NO:200), Figure 202 (SEQ ID NO:202), Figure 204 (SEQ ID NO:204), Figure 206 (SEQ ID NO:206), Figure 208 (SEQ ID NO:208), Figure 210 (SEQ ID NO:210), Figure 212 (SEQ ID NO:212), Figure 214 (SEQ ID NO:214), Figure 216 (SEQ ID NO:216), Figure 218 (SEQ ID NO:218), Figure 220 (SEQ ID NO:220), Figure 222 (SEQ ID NO:222), Figure 224 (SEQ ID NO:224), Figure 226 (SEQ ID NO:226), Figure 228 (SEQ ID NO:228), Figure 230 (SEQ ID NO:230), Figure 232 (SEQ ID NO:232), Figure 234 (SEQ ID NO:234), Figure 236 (SEQ ID NO:236), Figure 238 (SEQ ID NO:238), Figure 240 (SEQ ID NO:240), Figure 242 (SEQ ID NO:242), Figure 244 (SEQ ID NO:244), Figure 246 (SEQ ID NO:246), Figure 248 (SEQ ID NO:248), Figure 250 (SEQ ID NO:250), Figure 252 (SEQ ID NO:252), Figure 254 (SEQ ID NO:254), Figure 256 (SEQ ID NO:256), Figure 258 (SEQ ID NO:258), Figure 260 (SEQ ID NO:260), Figure 262 (SEQ ID NO:262), Figure 264 (SEQ ID NO:264), Figure 266 (SEQ ID NO:266), Figure 268 (SEQ ID NO:268), Figure

270 (SEQ ID NO:270), Figure 272 (SEQ ID NO:272), Figure 274 (SEQ ID NO:274), Figure 276 (SEQ ID NO:276), Figure 278 (SEQ ID NO:278), Figure 280 (SEQ ID NO:280), Figure 282 (SEQ ID NO:282), Figure 284 (SEQ ID NO:284), Figure 286 (SEQ ID NO:286), Figure 288 (SEQ ID NO:288), Figure 290 (SEQ ID NO:290), Figure 292 (SEQ ID NO:292), Figure 294 (SEQ ID NO:294), Figure 296 (SEQ ID NO:296), Figure 298 (SEQ ID NO:298), Figure 300 (SEQ ID NO:300), Figure 302 (SEQ ID NO:302), Figure 304 (SEQ ID NO:304), Figure 306 (SEQ ID NO:306), Figure 308 (SEQ ID NO:308), Figure 310 (SEQ ID NO:310), Figure 312 (SEQ ID NO:312), Figure 314 (SEQ ID NO:314), Figure 316 (SEQ ID NO:316), Figure 318 (SEQ ID NO:318), Figure 320 (SEQ ID NO:320), Figure 322 (SEQ ID NO:322), Figure 324 (SEQ ID NO:324), Figure 326 (SEQ ID NO:326), Figure 328 (SEQ ID NO:328), Figure 330 (SEQ ID NO:330), Figure 332 (SEQ ID NO:332), Figure 334 (SEQ ID NO:334), Figure 336 (SEQ ID NO:336), Figure 338 (SEQ ID NO:338), Figure 340 (SEQ ID NO:340), Figure 342 (SEQ ID NO:342), Figure 344 (SEQ ID NO:344), Figure 346 (SEQ ID NO:346), Figure 348 (SEQ ID NO:348), Figure 350 (SEQ ID NO:350), Figure 352 (SEQ ID NO:352), Figure 354 (SEQ ID NO:354), Figure 356 (SEQ ID NO:356), Figure 358 (SEQ ID NO:358), Figure 360 (SEQ ID NO:360), Figure 362 (SEQ ID NO:362), Figure 364 (SEQ ID NO:364), Figure 366 (SEQ ID NO:366), Figure 368 (SEQ ID NO:368), Figure 370 (SEQ ID NO:370), Figure 372 (SEQ ID NO:372), Figure 374 (SEQ ID NO:374), Figure 376 (SEQ ID NO:376), Figure 378 (SEQ ID NO:378), Figure 380 (SEQ ID NO:380), Figure 382 (SEQ ID NO:382), Figure 384 (SEQ ID NO:384), Figure 386 (SEQ ID NO:386), Figure 388 (SEQ ID NO:388), Figure 390 (SEQ ID NO:390), Figure 392 (SEQ ID NO:392), Figure 394 (SEQ ID NO:394), Figure 396 (SEQ ID NO:396), Figure 398 (SEQ ID NO:398), Figure 400 (SEQ ID NO:400), Figure 402 (SEQ ID NO:402), Figure 404 (SEQ ID NO:404), Figure 406 (SEQ ID NO:406), Figure 408 (SEQ ID NO:408), Figure 410 (SEQ ID NO:410), Figure 412 (SEQ ID NO:412), Figure 414 (SEQ ID NO:414), Figure 416 (SEQ ID NO:416), Figure 418 (SEQ ID NO:418), Figure 420 (SEQ ID NO:420), Figure 422 (SEQ ID NO:422), Figure 424 (SEQ ID NO:424), Figure 426 (SEQ ID NO:426), Figure 428 (SEQ ID NO:428), Figure 430 (SEQ ID NO:430), Figure 432 (SEQ ID NO:432), Figure 434 (SEQ ID NO:434), Figure 436 (SEQ ID NO:436), Figure 438 (SEQ ID NO:438), Figure 440 (SEQ ID NO:440), Figure 442 (SEQ ID NO:442), Figure 444 (SEQ ID NO:444), Figure 446 (SEQ ID NO:446), Figure 448 (SEQ ID NO:448), Figure 450 (SEQ ID NO:450), Figure 452 (SEQ ID NO:452), Figure 454 (SEQ ID NO:454), Figure 456 (SEQ ID NO:456), Figure 458 (SEQ ID NO:458), Figure 460 (SEQ ID NO:460), Figure 462 (SEQ ID NO:462), Figure 464 (SEQ ID NO:464), Figure 466 (SEQ ID NO:466), Figure 468 (SEQ ID NO:468), Figure 470 (SEQ ID NO:470), Figure 472 (SEQ ID NO:472), Figure 474 (SEQ ID NO:474), Figure 476 (SEQ ID NO:476), Figure 478 (SEQ ID NO:478), Figure 480 (SEQ ID NO:480), Figure 482 (SEQ ID NO:482), Figure 484 (SEQ ID NO:484), Figure 486 (SEQ ID NO:486), Figure 488 (SEQ ID NO:488), Figure 490 (SEQ ID NO:490), Figure 492 (SEQ ID NO:492), Figure 494 (SEQ ID NO:494), Figure 496 (SEQ ID NO:496), Figure 498 (SEQ ID NO:498), Figure 500 (SEQ ID NO:500), Figure 502 (SEQ ID NO:502), Figure 504 (SEQ ID NO:504), Figure 506 (SEQ ID NO:506), Figure 508 (SEQ ID NO:508), Figure 510 (SEQ ID NO:510), Figure 512 (SEQ ID NO:512), Figure 514 (SEQ ID NO:514), Figure 516 (SEQ ID NO:516), Figure 518 (SEQ ID NO:518), Figure 520 (SEQ ID NO:520), Figure 522 (SEQ ID NO:522), Figure 524 (SEQ ID NO:524), Figure 526 (SEQ ID NO:526), Figure 528 (SEQ ID NO:528), Figure 530 (SEQ ID NO:530), Figure 532 (SEQ ID NO:532), Figure 534 (SEQ ID NO:534), Figure

536 (SEQ ID NO:536), Figure 538 (SEQ ID NO:538), Figure 540 (SEQ ID NO:540), Figure 542 (SEQ ID NO:542), Figure 544 (SEQ ID NO:544), Figure 546 (SEQ ID NO:546), Figure 548 (SEQ ID NO:548) or Figure 550 (SEQ ID NO:550), lacking its associated signal peptide.

21. A method of detecting a PRO1801 polypeptide in a sample suspected of containing a PRO1801 polypeptide, said method comprising contacting said sample with a PRO1114 or PRO4978 polypeptide and determining the formation of a PRO1801/PRO1114 or PRO1801/PRO4978 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1801 polypeptide in said sample.

22. The method according to Claim 21, wherein said sample comprises cells suspected of expressing said PRO1801 polypeptide.

23. The method according to Claim 21, wherein said PRO1114 or PRO4978 polypeptide is labeled with a detectable label.

24. The method according to Claim 21, wherein said PRO1114 or PRO4978 polypeptide is attached to a solid support.

25. A method of detecting a PRO1114 or PRO4978 polypeptide in a sample suspected of containing a PRO1114 or PRO4978 polypeptide, said method comprising contacting said sample with a PRO1801 polypeptide and determining the formation of a PRO1801/PRO1114 or PRO1801/PRO4978 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1114 or PRO4978 polypeptide in said sample.

26. The method according to Claim 25, wherein said sample comprises cells suspected of expressing said PRO1114 or PRO4978 polypeptide.

27. The method according to Claim 25, wherein said PRO1801 polypeptide is labeled with a detectable label.

28. The method according to Claim 25, wherein said PRO1801 polypeptide is attached to a solid support.

29. A method of linking a bioactive molecule to a cell expressing a PRO1801 polypeptide, said method comprising contacting said cell with a PRO1114 or PRO4978 polypeptide that is bound to said bioactive molecule and allowing said PRO1801 and said PRO1114 or PRO4978 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

30. The method according to Claim 29, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

31. The method according to Claim 29, wherein said bioactive molecule causes the death of said cell.

32. A method of linking a bioactive molecule to a cell expressing a PRO1114 or PRO4978 polypeptide, said method comprising contacting said cell with a PRO1801 polypeptide that is bound to said bioactive molecule and allowing said PRO1801 and said PRO1114 or PRO4978 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

33. The method according to Claim 32, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

34. The method according to Claim 32, wherein said bioactive molecule causes the death of said cell.

35. A method of modulating at least one biological activity of a cell expressing a PRO1801 polypeptide, said method comprising contacting said cell with a PRO1114 or PRO4978 polypeptide or an anti-PRO1801 polypeptide antibody, whereby said PRO1114 or PRO4978 polypeptide or anti-PRO1801 polypeptide antibody binds to said PRO1801 polypeptide, thereby modulating at least one biological activity of said cell.

36. The method according to Claim 35, wherein said cell is killed.

37. A method of modulating at least one biological activity of a cell expressing a PRO1114 or PRO4978 polypeptide, said method comprising contacting said cell with a PRO1801 polypeptide or an anti-PRO1114 or anti-PRO4978 polypeptide antibody, whereby said PRO1801 polypeptide or anti-PRO1114 or anti-PRO4978 polypeptide antibody binds to said PRO1114 or PRO4978 polypeptide, thereby modulating at least one biological activity of said cell.

38. The method according to Claim 37, wherein said cell is killed.

39. A method of detecting a PRO1114 polypeptide in a sample suspected of containing a PRO1114 polypeptide, said method comprising contacting said sample with a PRO100 polypeptide and determining the formation of a PRO100/PRO1114 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1114 polypeptide in said sample.

40. The method according to Claim 39, wherein said sample comprises cells suspected of expressing said PRO1114 polypeptide.

41. The method according to Claim 39, wherein said PRO100 polypeptide is labeled with a detectable label.

42. The method according to Claim 39, wherein said PRO100 polypeptide is attached to a solid support.

43. A method of detecting a PRO100 polypeptide in a sample suspected of containing a PRO100 polypeptide, said method comprising contacting said sample with a PRO1114 polypeptide and determining the formation of a PRO100/PRO1114 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO100 polypeptide in said sample.

44. The method according to Claim 43, wherein said sample comprises cells suspected of expressing said PRO100 polypeptide.

45. The method according to Claim 43, wherein said PRO1114 polypeptide is labeled with a detectable label.

46. The method according to Claim 43, wherein said PRO1114 polypeptide is attached to a solid support.

47. A method of linking a bioactive molecule to a cell expressing a PRO100 polypeptide, said method comprising contacting said cell with a PRO1114 polypeptide that is bound to said bioactive molecule and allowing said PRO100 and said PRO1114 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

48. The method according to Claim 47, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

49. The method according to Claim 47, wherein said bioactive molecule causes the death of said cell.

50. A method of linking a bioactive molecule to a cell expressing a PRO1114 polypeptide, said method comprising contacting said cell with a PRO100 polypeptide that is bound to said bioactive molecule and allowing said PRO100 and said PRO1114 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

51. The method according to Claim 50, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

52. The method according to Claim 50, wherein said bioactive molecule causes the death of said cell.

53. A method of modulating at least one biological activity of a cell expressing a PRO100 polypeptide, said method comprising contacting said cell with a PRO1114 polypeptide or an anti-PRO100 polypeptide antibody, whereby said PRO1114 polypeptide or anti-PRO100 polypeptide antibody binds to said PRO100 polypeptide, thereby modulating at least one biological activity of said cell.

54. The method according to Claim 53, wherein said cell is killed.

55. A method of modulating at least one biological activity of a cell expressing a PRO1114 polypeptide, said method comprising contacting said cell with a PRO100 polypeptide or an anti-PRO1114 polypeptide antibody, whereby said PRO100 polypeptide or anti-PRO1114 polypeptide antibody binds to said PRO1114 polypeptide, thereby modulating at least one biological activity of said cell.

56. The method according to Claim 55, wherein said cell is killed.

57. A method for stimulating the release of TNF-α from human blood, said method comprising contacting said blood with a PRO195, PRO202, PRO215, PRO221, PRO217, PRO222, PRO198, PRO245, PRO172, PRO265, PRO266, PRO344, PRO337, PRO322, PRO1286, PRO1279, PRO1338 or PRO1343 polypeptide, wherein the release of TNF-α from said blood is stimulated.

58. A method for modulating the uptake of glucose or FFA by skeletal muscle cells, said method comprising contacting said cells with a PRO182, PRO366, PRO198, PRO172 or PRO719 polypeptide, wherein the uptake of glucose or FFA by said cells is modulated.

59. A method for stimulating the proliferation or differentiation of chondrocyte cells, said method comprising contacting said cells with a PRO182, PRO366, PRO198, PRO1868, PRO202, PRO224, PRO172, PRO301 or PRO1312 polypeptide, wherein the proliferation or differentiation of said cells is stimulated.

60. A method for modulating the uptake of glucose or FFA by adipocyte cells, said method comprising contacting said cells with a PRO202, PRO211, PRO344 or PRO1338 polypeptide, wherein the uptake of glucose or FFA by said cells is modulated.

61. A method for stimulating the proliferation of or gene expression in pericyte cells, said method comprising contacting said cells with a PRO366 polypeptide, wherein the proliferation of or gene expression in said cells is stimulated.

62. A method for stimulating the release of proteoglycans from cartilage, said method comprising contacting said cartilage with a PRO216 polypeptide, wherein the release of proteoglycans from said cartilage is stimulated.

63. A method for stimulating the proliferation of inner ear utricular supporting cells, said method comprising contacting said cells with a PRO172 polypeptide, wherein the proliferation of said cells is stimulated.

64. A method for stimulating the proliferation of T-lymphocyte cells, said method comprising contacting said cells with a PRO344 polypeptide, wherein the proliferation of said cells is stimulated.

65. A method for stimulating the release of a cytokine from PBMC cells, said method comprising contacting said cells with a PRO526 or PRO1343 polypeptide, wherein the release of a cytokine from said cells is stimulated.

66. A method for inhibiting the binding of A-peptide to factor VIIA, said method comprising contacting a composition comprising said A-peptide and said factor VIIA with a PRO182 polypeptide, wherein the binding of said A-peptide to said factor VIIA is inhibited.

67. A method for inhibiting the differentiation of adipocyte cells, said method comprising contacting said cells with a PRO185 or PRO198 polypeptide, wherein the differentiation of said cells is inhibited.

68. A method for stimulating the proliferation of endothelial cells, said method comprising contacting said cells with a PRO222 polypeptide, wherein the proliferation of said cells is inhibited.

69. 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.

70. The method of Claim 69, wherein said tumor is lung tumor, colon tumor, breast tumor, prostate tumor, rectal tumor, cervical tumor or liver tumor.

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

DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 2
CONTENANT LES PAGES 1 À 343

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JUMBO APPLICATIONS/PATENTS

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FIGURE 1

GTTACTCGGTGGTGGCGGAGTCTACGGAAGCCGTTTTCGCTTCACTTTTCCTGGCTGTAGAGC

GCTTTCCCCCTGGCGGGTGAGAGTGCAGAGACGAAGGTGCGAG**ATG**AGCACTATGTTCGCGGA

CACTCTCCTCATCGTTTTTATCTCTGTGTGCACGGCTCTGCTCGCAGAGGGCATAACCTGGGT

CCTGGTTTACAGGACAGACAAGTACAAGAGACTGAAGGCAGAAGTGGAAAAACAGAGTAAAAA

ATTGGAAAAGAAGAAGGAAACAATAACAGAGTCAGCTGGTCGACAACAGAAAAAGAAAATAGA

GAGACAAGAAGAGAAACTGAAGAATAACAACAGAGATCTATCAATGGTTCGAATGAAATCCAT

GTTTGCTATTGGCTTTTGTTTTACTGCCCTAATGGGAATGTTCAATTCCATATTTGATGGTAG

AGTGGTGGCAAAGCTTCCTTTTACCCCTCTTTCTTACATCCAAGGACTGTCTCATCGAAATCT

GCTGGGAGATGACACCACAGACTGTTCCTTCATTTTCCTGTATATTCTCTGTACTATGTCGAT

TCGACAGAACATTCAGAAGATTCTCGGCCTTGCCCCTTCACGAGCCGCCACCAAGCAGGCAGG

TGGATTTCTTGGCCCACCACCTCCTTCTGGGAAGTTCTCT**TGA**ACTCAAGAACTCTTTATTTT

CTATCATTCTTTCTAGACACACACACATCAGACTGGCAACTGTTTTGTAGCAAGAGCCATAGG

TAGCCTTACTACTTGGGCCTCTTTCTAGTTTTGAATTATTTCTAAGCCTTTTGGGTATGATTA

GAGTGAAAATGGCAGCCAGCAAACTTGATAGTGCTTTTGGTCCTAGATGATTTTTATCAAATA

AGTGGATTGATTAGTTAAGTTCAGGTAATGTTTATGTAATGAAAAACAAATAGCATCCTTCTT

GTTTCATTTACATAAGTATTTTCTGTGGGACCGACTCTCAAGGCACTGTGTATGCCCTGCAAG

TTGGCTGTCTATGAGCATTTAGAGATTTAGAAGAAAAATTTAGTTTGTTTAACCCTTGTAACT

GTTTGTTTTGTTGTTGTTTTTTTTTCAAGCCAAATACATGACATAAGATCAATAAAGAGGCCA

AATTTTTAGCTGTTTTATGTACAAGGAGAGATCTGTTTCATTTTGTTTTGCCGTATTTCTAGA

TATAAGTTTTAGCATGGGCCAGGAAGGACTAAAATAAAAGTTTTTAAGGTACAAAAAAAAAAA

AAAA

FIGURE 2

MSTMFADTLLIVFISVCTALLAEGITWVLVYRTDKYKRLKAEVEKQSKKLEKKKETITESAGR
QQKKKIERQEEKLKNNNRDLSMVRMKSMFAIGFCFTALMGMFNSIFDGRVVAKLPFTPLSYIQ
GLSHRNLLGDDTTDCSFIFLYILCTMSIRQNIQKILGLAPSRAATKQAGGFLGPPPPSGKFS

Important features:

Signal peptide:

amino acids 1-22

N-myristoylation sites.

amino acids 103-109, 163-169

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 53-57

FIGURE 3

AGCCGGGGGCGGGTTTGAAGACGCGTCGTTGGGTTTTGGAGGCCGTGAAACAGCCGTTTGAGT

TTGGCTGCGGGTGGAGAACGTTTGTCAGGGGCCCGGCCAAGAAGGAGGCCCGCCTGTTACG**AT**

GGTGTCCATGAGTTTCAAGCGGAACCGCAGTGACCGGTTCTACAGCACCCGGTGCTGCGGCTG

TTGCCATGTCCGCACCGGGACGATCATCCTGGGGACCTGGTACATGGTAGTAAACCTATTGAT

GGCAATTTTGCTGACTGTGGAAGTGACTCATCCAAACTCCATGCCAGCTGTCAACATTCAGTA

TGAAGTCATCGGTAATTACTATTCGTCTGAGAGAATGGCTGATAATGCCTGTGTTCTTTTTGC

CGTCTCTGTTCTTATGTTTATAATCAGTTCAATGCTGGTTTATGGAGCAATTTCTTATCAAGT

GGGTTGGCTGATTCCATTCTTCTGTTACCGACTTTTTGACTTCGTCCTCAGTTGCCTGGTTGC

TATTAGTTCTCTCACCTATTTGCCAAGAATCAAAGAATATCTGGATCAACTACCTGATTTTCC

CTACAAAGATGACCTCCTGGCCTTGGACTCCAGCTGCCTCCTGTTCATTGTTCTTGTGTTCTT

TGCCTTATTCATCATTTTTAAGGCTTATCTAATTAACTGTGTTTGGAACTGCTATAAATACAT

CAACAACCGAAACGTGCCGGAGATTGCTGTGTACCCTGCCTTTGAAAGCACCTCCTCAGTACG

TTTTGCCAACCTATGAAATGGCCGTGAAAATGCCTGAAAAAGAACCACCACCTCCTTACTTAC

CTGCCTGAAGAAATTCTGCCTTTGACAATAAATCCTATACCAGCTTTTTGTTTGTTTATGTTA

CAGAATGCTGCAATTCAGGGCTCTTCAAACTTGTTTGATATAAAATATGTTGTCTTTTGTTTA

AGCATTTATTTTCAAACACTAAGGAGCTTTTTGACATCTGTTAAACGTCTTTTTGTTTTTTTG

TTAAGTCTTTTACATTTTAATAGTTTTTGAAGACAATCTAGGTTAAGCAAGAGCAAAGTGCCA

TTGTTTGCCTTTAATTGGGGGGTGGGAAGGGAAAGAGGGTACTTGCCACATAGTTTCCTTTTT

AACTGCACTTTCTTTATATAATCGTTTGCATTTTGTTACTTGCTACCCTGAGTACTTTCAGGA

AGACTGACTTAAATATTCGGGGTGAGTAAGTAGTTGGGTATAAGATCTGAACTTTTCATCTGC

AGAGGCAAGAAAAATATTTGACATTGTGACTTGACTGTGGAAGATGATGGTTGCATGTTTCTA

GTTTGTATATGTTTCCATCTTTGTGATAAGATGATTTAATAAATCTCTTTAAATACTAAAAAA

AAAAAAAAA

FIGURE 4

MVSMSFKRNRSDRFYSTRCCGCCHVRTGTIILGTWYMVVNLLMAILLTVEVTHPNSMPAVNIQ
YEVIGNYYSSERMADNACVLFAVSVLMFIISSMLVYGAISYQVGWLIPFFCYRLFDFVLSCLV
AISSLTYLPRIKEYLDQLPDFPYKDDLLALDSSCLLFIVLVFFALFIIFKAYLINCVWNCYKY
INNRNVPEIAVYPAFESTSSVRFANL

Important features of the protein:

Transmembrane domain (Possible type II transmembrane protein):

amino acids 30-49, 81-100, 111-131, 158-175

N-glycosylation site.

amino acids 9-13

Tyrosine kinase phosphorylation sites.

amino acids 8-16, 193-202

N-myristoylation site.

amino acids 68-74

FIGURE 5

CCCGCTGGCCCGTCAGTGCTCTCCCCGTCGTTTGCCCTCTCCAGTTCCCCCAGTGCCTGCCCT

ACGCACCCCG**ATG**GCGGAGCTGCGGCCTAGCGGCGCCCCCGGCCCCACCGCGCCCCCGGCCCC

TGGCCCGACTGCCCCCCCCGGCCTTCGCTTCGCTCTTTCCCCCGGGACTGCACGCCATCTACGG

AGAGTGCCGCCGCCTTTACCCTGACCAGCCGAACCCGCTCCAGGTTACCGCTATCGTCAAGTA

CTGGTTGGGTGGCCCAGACCCCTTGGACTATGTTAGCATGTACAGGAATGTGGGGAGCCCTTC

TGCTAACATCCCCGAGCACTGGCACTACATCAGCTTCGGCCTGAGTGATCTCTATGGTGACAA

CAGAGTCCATGAGTTTACAGGAACAGATGGACCTAGTGGTTTTGGCTTTGAGTTGACCTTTCG

TCTGAAGAGAGAAACTGGGGAGTCTGCCCCACCAACATGGCCCGCAGAGTTAATGCAGGGCTT

GGCACGATACGTGTTCCAGTCAGAGAACACCTTCTGCAGTGGGGACCATGTGTCCTGGCACAG

CCCTTTGGATAACAGTGAGTCAAGAATTCAGCACATGCTGCTGACAGAGGACCCACAGATGCA

GCCCGTGCAGACACCCTTTGGGGTAGTTACCTTCCTCCAGATCGTTGGTGTCTGCACTGAAGA

GCTACACTCAGCCCAGCAGTGGAACGGGCAGGGCATCCTGGAGCTGCTGCGGACAGTGCCTAT

TGCTGGCGGCCCCTGGCTGATAACTGACATGCGGAGGGGAGAGACCATATTTGAGATCGATCC

ACACCTGCAAGAGAGAGTTGACAAAGGCATCGAGACAGATGGCTCCAACCTGAGTGGTGTCAG

TGCCAAGTGTGCCTGGGATGACCTGAGCCGGCCCCCCGAGGATGACGAGGACAGCCGGAGCAT

CTGCATCGGCACACAGCCCCGGCGACTCTCTGGCAAAGACACAGAGCAGATCCGGGAGACCCT

GAGGAGAGGACTCGAGATCAACAGCAAACCTGTCCTTCCACCAATCAACCCTCAGCGGCAGAA

TGGCCTCGCCCACGACCGGGCCCCGAGCCGCAAAGACAGCCTGGAAAGTGACAGCTCCACGGC

CATCATTCCCCATGAGCTGATTCGCACGCGGCAGCTTGAGAGCGTACATCTGAAATTCAACCA

GGAGTCCGGAGCCCTCATTCCTCTCTGCCTAAGGGGCAGGCTCCTGCATGGACGGCACTTTAC

ATATAAAAGTATCACAGGTGACATGGCCATCACGTTTGTCTCCACGGGAGTGGAAGGCGCCTT

TGCCACTGAGGAGCATCCTTACGCGGCTCATGGACCCTGGTTACAACTC**TGA**ACCTATCCTCG

GAGCTCTGCCCTCCCGTCCTGGAACGTCTTTCTGCCCTGAGGAGAGGGTAGTCAGCATCTCCA

ATTTTCAGCAGCTCAAGAACCTTGGCCCCCACAGGACTTCGCAGATGTCACATTGCCCCTCAG

TCCCCTGAATGCCCTTCGGACCCAACCCCAATTCCCCAAGCCCCTGACCCCCTAGCTGCCGGG

GTTCCCACTCCCAGTGCCACAACCCCCTCACCTCCCCTGGCAGCCCCTCAGCGAGCCTGAGGC

CCAGCACCCGCTGGCTCCCCAGCACATGGTCCCCTCCCATGGGCTGTTGCCCAGGGAACCGGG

GCGCGGTGGGAACGAGCTGCTGGCCTCGGCATGTTTCAATAAAGTTGCTGTGCTGGGAG

FIGURE 6

MAELRPSGAPGPTAPPAPGPTAPPAFASLFPPGLHAIYGECRRLYPDQPNPLQVTAIVKYWLG
GPDPLDYVSMYRNVGSPSANIPEHWHYISFGLSDLYGDNRVHEFTGTDGPSGFGFELTFRLKR
ETGESAPPTWPAELMQGLARYVFQSENTFCSGDHVSWHSPLDNSESRIQHMLLTEDPQMQPVQ
TPFGVVTFLQIVGVCTEELHSAQQWNGQGILELLRTVPIAGGPWLITDMRRGETIFEIDPHLQ
ERVDKGIETDGSNLSGVSAKCAWDDLSRPPEDDEDSRSICIGTQPRRLSGKDTEQIRETLRRG
LEINSKPVLPPINPQRQNGLAHDRAPSRKDSLESDSSTAIIPHELIRTRQLESVHLKFNQESG
ALIPLCLRGRLLHGRHFTYKSITGDMAITFVSTGVEGAFATEEHPYAAHGPWLQL

Important features:

N-glycosylation site.

amino acids 265-268

FIGURE 7

CGCGAATGAAGTTTGCATTTTCCTCTGTTCTTGAGCCCAGCTTCTTCTCGTCTCCCACCCCAG
CTTCCCGGCATTGGAAGAAGGGACCGTCCTCTTCCTTGTCTTGGCCACCCAAATCCTGGTATC
GAAAGGGTTGAACGGACCGGAAGTGTGCAGCAGCGACGGGTCCCCAGCTAATCGACGCCGGAA
GTAGCAATTACTAGACAAGCATTCCGCCGCCGGCTTCGCT**ATG**GCGGCAATTCCCCCAGATTC
CTGGCAGCCACCCAACGTTTACTTGGAGACCAGCATGGGAATCATTGTGCTGGAGCTGTACTG
GAAGCATGCTCCAAAGACCTGTAAGAACTTTGCTGAGTTGGCTCGTCGAGGTTACTACAATGG
CACAAAATTCCACAGAATTATCAAAGACTTCATGATCCAAGGAGGTGACCCAACAGGGACAGG
TCGAGGTGGTGCATCTATCTATGGCAAACAATTTGAAGATGAACTTCATCCAGACTTGAAATT
CACGGGGGCTGGAATTCTCGCAATGGCCAATGCGGGGCCAGATACCAATGGCAGCCAGTTCTT
TGTGACCCTCGCCCCCACCCAGTGGCTTGACGGCAAACACACCATTTTTGGCCGAGTGTGTCA
GGGCATAGGAATGGTGAATCGCGTGGGAATGGTAGAAACAAACTCCCAGGACCGCCCTGTGGA
CGACGTGAAGATCATTAAGGCATACCCTTCTGGG**TAG**ACTTGCTACCCTCTTGAGCAGCTCTT
CTGAGATGGCCCCAGTGAACCAGCTTCTAGATGACATAGAATGACATGTAATGCTAAATTTCA
TTTTGGCTTTGCAAGTCATGAAGCTTAGGAGGCCTGGCATCTTGGGTGAGTTAGAGATGGAAG
TACATTTTAATAGGATGCTTCTTTTCTCTTCCCCCAGTGCCTAGGTTGCCAGAGCATTTGCAC
AAATGCCCCTGTTTATCAATAGGTGACTACTTACTACACATGAACCATAATGCTGCTTCTTGT
GCATGTCTGCTCTGATATACGTCGAACAATGTAGCAGCCACTGTCATTTCTCAGTGGTTTTGC
CTAACCAAACTTCTTCCTAAGGAGATTTATATTCTGGCCTACACAGCAGTCCTTGATGGCTGA
CAGCCACAGAATTCCAAACCAAGTAGTGTCTGTCAGCCCTCTTAACTCTGTGCACGCCCTATT
TCAGTCTTTTACATTTGTTCTTCTAGGGAATGTATGCATCTCTATATATATTTTCCCTCTCAA
AACCAGAACATCAACAGTGCTGTTTCTGACACTTCAGACATCCCACGCAAAGCCACATTGAAT
TTTTGCCAAATGAAAAACACATCCAACAATCAAGTTTCTAAGAAGGTGTCAAGTGGGGAATAA
TAATAATGTATAATAATCAAGAAATTAGTTTATTAAAAGGAAGCAGAAGCATTGACCATTTTT
TCCCAGAGAAGAGGAGAAATCTGTAGTGAGCAAAGGACAGACCATGAATCCTCCTTGAGAAGT
AGTACTCTCAGAAAGGAGAAGCGCCACTCAAGTTCTTTTAACCCAAGACTTTAGAGAAATTAG
GTCCAAGATTTTTATATGTTCAGTTGTTTATGTATAAAAATAACTTTCTGGATTTTGTGGGGA
GGAGCAGGAGAGGAAGGAAGTTAATACCTATGTAATACATAGAAACTTCCACAATAAAATGCC
ATTGATGGTTAAAAAAAAAAAAAAAAAA

FIGURE 8

MAAIPPDSWQPPNVYLETSMGIIVLELYWKHAPKTCKNFAELARRGYYNGTKFHRIIKDFMIQ

GGDPTGTGRGGASIYGKQFEDELHPDLKFTGAGILAMANAGPDTNGSQFFVTLAPTQWLDGKH

TIFGRVCQGIGMVNRVGMVETNSQDRPVDDVKIIKAYPSG

Important features:

N-glycosylation sites:

amino acids 49-52, 108-111

N-myristoylation sites:

amino acids 64-69, 69-74, 143-148

Cyclophilin-type peptidyl-prolyl cis-trans isomerase signature:

amino acids 48-65

FIGURE 9

CGGACGCGTGGGCGCGCGCGAGCGCAGCGGTGGGAGGCGGCGACCAGCCGGTTGAGGCCCCAG
GCTTGGCCTCACCACA**ATG**TGGCACGAGGCTCGGAAGCATGAGCGGAAGCTTCGAGGCATGAT
GGTCGACTACAAGAAGAGGGCGGAGCGGAGACGGGAGTATTATGAAAAGATCAAGAAGGACCC
AGCCCAGTTCCTGCAGGTACATGGCCGAGCTTGCAAGGTGCACCTGGATTCTGCAGTCGCCCT
GGCCGCTGAGAGCCCTGTTAATATGATGCCCTGGCAGGGGGACACCAACAACATGATTGACCG
ATTCGATGTCCGTGCCCACCTGGACCACATCCCCGACTACACCCCCCCTCTGCTCACCACCAT
CTCCCCAGAACAGGAGTCGGACGAACGGAAGTGTAACTACGAGCGCTACAGAGGCCTGGTGCA
GAACGACTTTGCCGGCATCTCAGAGGAGCAGTGCCTGTACCAGATCTACATTGATGAGTTGTA
CGGAGGCCTCCAGAGACCCAGCGAAGATGAGAAGAAGAAGCTGGCAGAGAAGAAGGCTTCCAT
CGGTTATACCTACGAGGACAGCACGGTGGCCGAGGTAGAGAAGGCGGCAGAAAAGCCAGAGGA
GGAGGAGTCAGCGGCCGAGGAGGAGAGCAACTCGGACGAAGATGAGGTCATCCCCGACATCGA
CGTGGAGGTGGACGTGGATGAATTGAACCAGGAGCAGGTGGCAGATCTCAACAAACAGGCCAC
GACTTATGGCATGGCCGACGGTGACTTCGTCAGGATGCTCCGGAAAGACAAGGAGGAGGCAGA
GGCCATCAAGCATGCCAAGGCTCTTGAGGAGGAGAAGGCCATGTACTCGGGACGCCGCTCTCG
ACGCCAGCGGAGAGAGTTTCGGGAGAAGCGGCTGAGGGGTCGCAAGATCAGCCCACCCAGCTA
TGCCCGCCGAGACAGCCCCACCTATGACCCCTATAAGCGGTCACCCTCGGAGTCCAGCTCAGA
GTCCCGCTCCCGCTCCCGCTCCCCGACCCCGGGCCGCGAGGAGAAGATCACGTTCATCACCAG
TTTTGGGGGCAGCGATGAGGAGGCAGCCGCAGCCGCTGCTGCCGCAGCAGCATCAGGAGTCAC
CACAGGGAAGCCCCCCGCACCTCCCCAGCCTGGCGGCCCCGCCCCGGGACGTAATGCCAGCGC
CCGCCGCCGCTCCTCCTCCTCCTCCTCCTCCTCTTCTGCCTCGAGGACCTCCAGCTCCCGCTC
CAGCTCTCGCTCCAGCTCCCGCTCTCGCCGTGGTGGGGGCTACTACCGTTCCGGCCGCCACGC
CCGCTCCCGGTCCCGCTCCTGGTCCCGCTCCCGCTCCCGCTCCCGGCGCTATTCCCGGTCCCG
TAGCCGTGGCCGGCGGCACTCAGGTGGGGGCTCCCGAGACGGACACCGGTACTCCCGCTCGCC
CGCCCGGCGTGGTGGTTACGGGCCCCGGCGCAGAAGCAGGAGCCGCTCCCACTCAGGGGACCG
CTACAGGCGGGGCGGCCGGGGCCTCAGGCACCACAGCAGTAGCCGCAGCCGCAGCAGCTGGTC
CCTCAGCCCGTCCCGCAGTCGCAGCCTGACTCGCAGCCGCAGCCATAGCCCCAGCCCCAGCCA
GAGCCGCAGCCGCAGCCGCAGCCGCAGCCAGAGCCCCTCGCCATCACCCGCAAGAGAGAAGCT
GACCAGGCCGGCCGCGTCCCCTGCTGTGGGCGAGAAGCTGAAAAAGACCGAACCTGCCGCTGG
TAAAGAGACAGGAGCTGCCAAAGTCACCCAAGCTGACGCCTCAGGAGAAGCTGAAACTGAGGA
TGCAGAAGGCGCTGAACAGGCAGTTCAAGGCGGA**TAA**GAAGGCGGCACAAGAAAAGATGATCC
AGCAGGAGCATGAGCGGCAGGAGCGGGAAGACGAGCTTCGAGCCATGGCCCGCAAGATCCGCA
TGAAGGAGCGGGAACGCCGAGAGAAGGAGAGAGAAGAGTGGGAACGCCAGTACAGCCGGCAGA
GCCGCTCACCCTCCCCCCGATACAGTCGAGAATACAGCTCTTCTCGAAGGCGCTCAAGGTCCC
GATCCCGAAGCCCCCATTACCGACATTAGGCAGAAGAGTGGGGGGTGGGGAGGACAAGGGGGT
GGGTAAGGGGCTCAAGCTGTGATGCTGCTGGTTTTATCTCTAGTGAAATAAAGTCAAAAGTTA
TTTAATTCCCGTCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAA

FIGURE 10

MWHEARKHERKLRGMMVDYKKRAERRREYYEKIKKDPAQFLQVHGRACKVHLDSAVALAAESP
VNMMPWQGDTNNMIDRFDVRAHLDHIPDYTPPLLTTISPEQESDERKCNYERYRGLVQNDFAG
ISEEQCLYQIYIDELYGGLQRPSEDEKKKLAEKKASIGYTYEDSTVAEVEKAAEKPEEEESAA
EEESNSDEDEVIPDIDVEVDVDELNQEQVADLNKQATTYGMADGDFVRMLRKDKEEAEAIKHA
KALEEEKAMYSGRRSRRQRREFREKRLRGRKISPPSYARRDSPTYDPYKRSPSESSSESRSRS
RSPTPGREEKITFITSFGGSDEEAAAAAAAAAASGVTTGKPPAPPQPGGPAPGRNASARRRSS
SSSSSSSASRTSSSRSSSRSSSRSRRGGGYYRSGRHARSRSRSWSRSRSRSRRYSRSRSRGRR
HSGGGSRDGHRYSRSPARRGGYGPRRRSRSRSHSGDRYRRGGRGLRHHSSSRSRSSWSLSPSR
SRSLTRSRSHSPSPSQSRSRSRSRSQSPSPSPAREKLTRPAASPAVGEKLKKTEPAAGKETGA
AKVTQADASGEAETEDAEGAEQAVQGG

Important features:

N-glycosylation site:

amino acids 370-373

Glycosaminoglycan attachment site:

amino acids 443-446

cAMP- and cGMP-dependent protein kinase phosphorylation site:

amino acids 159-162, 282-285, 291-294, 374-377, 375-378, 430-433, 440-443, 466-469

Casein kinase II phosphorylation site:

amino acids 149-152, 166-169, 171-174, 187-190, 193-196, 195-198, 303-306, 307-310, 335-338, 571-574

N-myristoylation sites:

amino acids 118-123, 229-234, 350-355, 446-451, 586-591

Amidation sites:

amino acids 263-266, 280-283, 438-441

FIGURE 11

GGTAGGCGCGCCCAGACCTGAGACGGGTTGGGACTGGGCTGCGTCACGCGCGGGCTCTAAGCG
CCCGGGGCCCCGCCCAGTGGCCGGCACAGCCAATCGCAGCGCGGGAAGGCGGTGGGGGCGGGG
AAGGCCGCCTGGAAACTTAAATCCCGAGGCGGGCGAACCTGCACCAGACCGCGGACGTCTGTA
ATCTCAGAGGCTTGTTTGCTGAGGGTGCCTGCGCAGCTGCGACGGCTGCTGGTTTTGAAAC**AT**
GAATCTTTCGCTCGTCCTGGCTGCCTTTTGCTTGGGAATAGCCTCCGCTGTTCCAAAATTTGA
CCAAAATTTGGATACAAAGTGGTACCAGTGGAAGGCAACACACAGAAGATTATATGGCGCGAA
TGAAGAAGGATGGAGGAGAGCAGTGTGGGAAAAGAATATGAAAATGATTGAACTGCACAATGG
GGAATACAGCCAAGGGAAACATGGCTTCACAATGGCCATGAATGCTTTTGGTGACATGACCAA
TGAAGAATTCAGGCAGATGATGGGTTGCTTTCGAAACCAGAAATTCAGGAAGGGGAAAGTGTT
CCGTGAGCCTCTGTTTCTTGATCTTCCCAAATCTGTGGATTGGAGAAAGAAAGGCTACGTGAC
GCCAGTGAAGAATCAGAAACAGTGTGGTTCTTGTTGGGCTTTTAGTGCGACTGGTGCTCTTGA
AGGACAGATGTTCCGGAAAACTGGGAAACTTGTCTCACTGAGCGAGCAGAATCTGGTGGACTG
TTCGCGTCCTCAAGGCAATCAGGGCTGCAATGGTGGCTTCATGGCTAGGGCCTTCCAGTATGT
CAAGGAGAACGGAGGCCTGGACTCTGAGGAATCCTATCCATATGTAGCAGTGGATGAAATCTG
TAAGTACAGACCTGAGAATTCTGTTGCTAATGACACTGGCTTCACAGTGGTCGCACCTGGAAA
GGAGAAGGCCCTGATGAAAGCAGTCGCAACTGTGGGGCCCATCTCCGTTGCTATGGATGCAGG
CCATTCGTCCTTCCAGTTCTACAAATCAGGCATTTATTTTGAACCAGACTGCAGCAGCAAAAA
CCTGGATCATGGTGTTCTGGTGGTTGGCTACGGCTTTGAAGGAGCAAATTCGAATAACAGCAA
GTATTGGCTCGTCAAAAACAGCTGGGGTCCAGAATGGGGCTCGAATGGCTATGTAAAAATAGC
CAAAGACAAGAACAACCACTGTGGAATCGCCACAGCAGCCAGCTACCCCAATGTG**TGA**GCTGA
TGGATGGTGAGGAGGAAGGACTTAAGGACAGCATGTCTGGGGAAATTTTATCTTGAAACTGAC
CAAACGCTTATTGTGTAAGATAAACCAGTTGAATCATGGAGGATCCAAGTTGAGATTTTAATT
CTGTGACATTTTTACAAGGGTAAAATGTTACCACTACTTTAATTATTGTTATACACAGCTTTA
TGATATCAAAGACTCATTGCTTAATTCTAAGACTTTTGAATTTTCATTTTTTAAAAAGATGTA
CAAAACAGTTTGAAATAAATTTTAATTCGTATATA

FIGURE 12

MNLSLVLAAFCLGIASAVPKFDQNLDTKWYQWKATHRRLYGANEEGWRRAVWEKNMKMIELHN
GEYSQGKHGFTMAMNAFGDMTNEEFRQMMGCFRNQKFRKGKVFREPLFLDLPKSVDWRKKGYV
TPVKNQKQCGSCWAFSATGALEGQMFRKTGKLVSLSEQNLVDCSRPQGNQGCNGGFMARAFQY
VKENGGLDSEESYPYVAVDEICKYRPENSVANDTGFTVVAPGKEKALMKAVATVGPISVAMDA
GHSSFQFYKSGIYFEPDCSSKNLDHGVLVVGYGFEGANSNNSKYWLVKNSWGPEWGSNGYVKI
AKDKNNHCGIATAASYPNV

Important features:

Signal sequence

amino acids 1-17

N-glycosylation sites.

amino acids 2-6, 221-225, 292-296

N-myristoylation sites.

amino acids 13-19, 93-99, 136-142, 145-151, 174-180, 177-183, 180-186, 194-200, 288-294, 324-330

Eukaryotic thiol (cysteine) proteases cysteine active site.

amino acids 132-144

Eukaryotic thiol (cysteine) proteases histidine active site.

amino acids 275-286

FIGURE 13

GGCGGCGTCATGTGATCCGCTTCCCTGCTCCTTTAAGCGTCCACAGGCGGCGGAGCGGCCACA
ATCACAGCTCCGGGCATTGGGGGAACCCGAGCCGGCTGCGCCGGGGGAATCCGTGCGGGCGCC
TTCCGTCCCGGTCCCATCCTCGCCGCGCTCCAGCACCTCTGAAGTTTTGCAGCGCCCAGAAAG
GAGGCGAGGAAGGAGGGAGTGTGTGAGAGGAGGGAGCAAAAAGCTCACCCTAAAACATTTATT
TCAAGGAGAAAAGAAAAAGGGGGGGCGCAAAA**ATG**GCTGGGGCAATTATAGAAAACATGAGCA
CCAAGAAGCTGTGCATTGTTGGTGGGATTCTGCTCGTGTTCCAAATCATCGCCTTTCTGGTGG
GAGGCTTGATTGCTCCAGGGCCCACAACGGCAGTGTCCTACATGTCGGTGAAATGTGTGGATG
CCCGTAAGAACCATCACAAGACAAAATGGTTCGTGCCTTGGGGACCCAATCATTGTGACAAGA
TCCGAGACATTGAAGAGGCAATTCCAAGGGAAATTGAAGCCAATGACATCGTGTTTTCTGTTC
ACATTCCCCTCCCCCACATGGAGATGAGTCCTTGGTTCCAATTCATGCTGTTTATCCTGCAGC
TGGACATTGCCTTCAAGCTAAACAACCAAATCAGAGAAAATGCAGAAGTCTCCATGGACGTTT
CCCTGGCTTACCGTGATGACGCATTTGCTGAGTGGACTGAAATGGCCCATGAAAGAGTACCAC
GGAAACTCAAATGCACCTTCACATCTCCCAAGACTCCAGAGCATGAGGGCCGTTACTATGAAT
GTGATGTCCTTCCTTTCATGGAAATTGGGTCTGTGGCCCATAAGTTTTACCTTTTAAACATCC
GGCTGCCTGTGAATGAGAAGAAGAAAATCAATGTGGGAATTGGGGAGATAAAGGATATCCGGT
TGGTGGGGATCCACCAAAATGGAGGCTTCACCAAGGTGTGGTTTGCCATGAAGACCTTCCTTA
CGCCCAGCATCTTCATCATTATGGTGTGGTATTGGAGGAGGATCACCATGATGTCCCGACCCC
CAGTGCTTCTGGAAAAAGTCATCTTTGCCCTTGGGATTTCCATGACCTTTATCAATATCCCAG
TGGAATGGTTTTCCATCGGGTTTGACTGGACCTGGATGCTGCTGTTTGGTGACATCCGACAGG
GCATCTTCTATGCGATGCTTCTGTCCTTCTGGATCATCTTCTGTGGCGAGCACATGATGGATC
AGCACGAGCGGAACCACATCGCAGGGTATTGGAAGCAAGTCGGACCCATTGCCGTTGGCTCCT
TCTGCCTCTTCATATTTGACATGTGTGAGAGAGGGGTACAACTCACGAATCCCTTCTACAGTA
TCTGGACTACAGACATTGGAACAGAGCTGGCCATGGCCTTCATCATCGTGGCTGGAATCTGCC
TCTGCCTCTACTTCCTGTTTCTATGCTTCATGGTATTTCAGGTGTTTCGGAACATCAGTGGGA
AGCAGTCCAGCCTGCCAGCTATGAGCAAAGTCCGGCGGCTACACTATGAGGGGCTAATTTTTA
GGTTCAAGTTCCTCATGCTTATCACCTTGGCCTGCGCTGCCATGACTGTCATCTTCTTCATCG
TTAGTCAGGTAACGGAAGGCCATTGGAAATGGGGCGGCGTCACAGTCCAAGTGAACAGTGCCT
TTTTCACAGGCATCTATGGGATGTGGAATCTGTATGTCTTTGCTCTGATGTTCTTGTATGCAC
CATCCCATAAAAACTATGGAGAAGACCAGTCCAATGGCGATCTGGGTGTCCATAGTGGGGAAG
AACTCCAGCTCACCACCACTATCACCCATGTGGACGGACCCACTGAGATCTACAAGTTGACCC
GCAAGGAGGCCCAGGAG**TAG**GAGGCTGCAGCGCCCGGCTGGGACGGTCTCTCCATACCCCAGC
CCCTCTAACTAGAGTGGGGAGCATGCCAGAGAGAGCTCAATGTACAAATGAATGCCTCATGGC
TCTTAGCTGTGGTTTCTTGGACCAGCGGCATGGACATTTGTCAGTTTGCCTTCTGACGGTAGC
TTTTGGAGGAAGATTCCTGCAGCCACTAATGCATTGTGTATGATAACAAAAACTCTGGTATGA
CACATTTTCTGTGATCATTGTTAATTAGTGACATAGTAACATCTGTAGCAGCTGGTTAGTAAA
CCTCATGTGGGGGTGGGGTGGGGGTGTATTCCTTGGGGGATGGTTTGGGCCGAATGGGGAGTG
GAATATTTGACATTTTTCCTGTTTTAAATTCTAGGATAGATTTTAACATCCTTTGCGGTCCCA
GTCCAAGGTAGGCTGGTGTCATAGTCTTCTCACTCCTAATCCATGACCACTGTTTTTTTCCTA
TTTATATCACCAGGTAGCCTACTGAGTTAATATTTAAGTTGTCAATAGATAAGTGTCCCTGTT
TTGTGGCATAATATAACTGAATTTCATGAGAAGATTTATTCCACCAGGGGTATTTCAGCTTTG
AAACCAAATCTGTGTATCTAATACTAACCAATCTGTTGGATGTGGATTTTAAAAAATGTTTGC
TAAACTACCCAAGTAAGATTTACTGTATTAAATGGCCTTCGGGTCTGAAAAGCTTTTTTAACC
TCTTGCTTAAAATGCGTTTTATTTTGATAAGATACTTCAAATAGCCTCCAAAAGTGTAGATCC
AATCACTTAAATAAACCTGTATGTATATGCAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 14

MAGAIIENMSTKKLCIVGGILLVFQIIAFLVGGLIAPGPTTAVSYMSVKCVDARKNHHKTKWF
VPWGPNHCDKIRDIEEAIPREIEANDIVFSVHIPLPHMEMSPWFQFMLFILQLDIAFKLNNQI
RENAEVSMDVSLAYRDDAFAEWTEMAHERVPRKLKCTFTSPKTPEHEGRYYECDVLPFMEIGS
VAHKFYLLNIRLPVNEKKKINVGIGEIKDIRLVGIHQNGGFTKVWFAMKTFLTPSIFIIMVWY
WRRITMMSRPPVLLEKVIFALGISMTFINIPVEWFSIGFDWTWMLLFGDIRQGIFYAMLLSFW
IIFCGEHMMDQHERNHIAGYWKQVGPIAVGSFCLFIFDMCERGVQLTNPFYSIWTTDIGTELA
MAFIIVAGICLCLYFLFLCFMVFQVFRNISGKQSSLPAMSKVRRLHYEGLIFRFKFLMLITLA
CAAMTVIFFIVSQVTEGHWKWGGVTVQVNSAFFTGIYGMWNLYVFALMFLYAPSHKNYGEDQS
NGDLGVHSGEELQLTTTITHVDGPTEIYKLTRKEAQE

Important features of the protein:

Signal peptide:

amino acids 1-42

Transmembrane domains:

amino acids 239-253, 269-284, 302-318, 338-352, 377-399, 434-452, 471-488

N-glycosylation sites.

amino acids 8-12, 406-410

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 254-258

N-myristoylation sites.

amino acids 223-229, 274-280, 305-311, 358-364, 374-380, 386-392, 509-515

FIGURE 15

GTGAGGGGAACAGCTGATCCGTCTGTTGGGAGGACAGATATCTCAAGGCCAGG**ATG**GAAGAAT
CACCACTAAGCCGGGCACCATCCCGTGGTGGAGTCAACTTTCTCAATGTAGCCCGGACCTACA
TCCCCAACACCAAGGTGGAATGTCACTACACCCTTCCCCCAGGCACCATGCCCAGTGCCAGTG
ACTGGATTGGCATCTTCAAGGTGGAGGCTGCCTGTGTTCGGGATTACCACACATTTGTGTGGT
CTTCCGTGCCTGAAAGTACAACTGATGGTTCCCCCATTCACACCAGTGTCCAGTTCCAAGCCA
GCTACCTGCCCAAACCAGGAGCTCAGCTCTACCAGTTCCGATATGTGAACCGCCAGGGCCAGG
TGTGTGGGCAGAGCCCCCCTTTCCAGTTCCGAGAGCCAAGGCCCATGGATGAACTGGTGACCC
TGGAGGAGGCTGATGGGGGCTCTGACATCCTGCTGGTTGTCCCCAAGGCAACTGTGTTACAGA
ACCAGCTCGATGAGAGCCAGCAAGAACGGAATGACCTGATGCAGCTGAAGCTACAGCTGGAGG
GACAGGTGACAGAGCTGAGGAGCCGAGTGCAGGAGCTCGAGAGGGCTCTGGCAACTGCCAGGC
AGGAGCACACGGAGCTGATGGAACAGTACAAGGGGATTTCCCGGTCCCATGGGGAGATCACAG
AAGAGAGGGACATCCTGAGCCGGCAACAGGGAGACCATGTGGCACGCATCCTGGAGCTAGAGG
ATGACATCCAGACCATCAGTGAGAAAGTGCTGACGAAGGAAGTGGAGCTGGACAGGCTTAGAG
ACACAGTGAAGGCCCTGACTCGGGAACAAGAGAAGCTCCTTGGGCAACTGAAAGAAGTACAAG
CAGACAAGGAGCAAAGTGAGGCTGAGCTCCAAGTGGCACAACAGGAGAACCATCACTTAAATT
TGGACCTGAAGGAGGCGAAGAGCTGGCAAGAGGAGCAGAGTGCTCAGGCTCAGCGACTGAAAG
ACAAGGTGGCCCAGATGAAGGACACCCTAGGCCAGGCCCAGCAGCGGGTGGCCGAGCTGGAGC
CCTTGAAGGAGCAGCTTCGAGGGGCCCAGGAGCTTGCAGCCTCAAGCCAGCAGAAAGCCACCC
TTCTTGGGGAGGAGTTGGCCAGTGCAGCAGCAGCCAGGGACCGCACCATAGCCGAACTACACC
GCAGCCGCCTGGAAGTGGCTGAAGTTAACGGCAGGCTGGCTGAGCTCGGTTTGCACTTGAAGG
AAGAAAAATGCCAATGGAGCAAGGAGCGGGCAGGGCTGCTGCAGAGTGTGGAGGCAGAGAAGG
ACAAGATCCTGAAGCTGAGTGCAGAGATACTTCGATTGGAGAAGGCAGTTCAGGAGGAGAGGA
CCCAAAACCAAGTGTTCAAGACTGAGCTGGCCCGGGAGAAGGATTCTAGCCTGGTACAGTTGT
CAGAAAGTAAGCGGGAGCTGACAGAGCTGCGGTCAGCCCTGCGTGTGCTCCAGAAGGAAAAGG
AGCAGTTACAGGAGGAGAAACAGGAATTGCTAGAGTACATGAGAAAGCTAGAGGCCCGCCTGG
AGAAGGTGGCAGATGAGAAGTGGAATGAGGATGCCACCACAGAGGATGAGGAGGCCGCTGTGG
GGCTGAGCTGCCCGGCAGCTCTGACAGACTCAGAGGACGAGTCCCCAGAAGACATGAGGCTCC
CACCCTATGGCCTTTGTGAGCGTGGAGACCCAGGCTCCTCTCCTGCTGGGCCTCGAGAGGCTT
CTCCCCTTGTTGTCATCAGCCAGCCGGCTCCCATTTCTCCTCACCTCTCTGGGCCAGCTGAGG
ACAGTAGCTCTGACTCGGAGGCTGAAGATGAGAAGTCAGTCCTGATGGCAGCTGTGCAGAGTG
GGGGTGAGGAGGCCAACTTACTGCTTCCTGAACTGGGCAGTGCCTTCTATGACATGGCCAGTG
GCTTTACAGTGGGTACCCTGTCAGAAACCAGCACTGGGGGCCCTGCCACCCCCACATGGAAGG
AGTGTCCTATCTGTAAGGAGCGCTTTCCTGCTGAGAGTGACAAGGATGCCCTGGAGGACCACA
TGGATGGACACTTCTTTTTCAGCACCCAGGACCCCTTCACCTTTGAG**TGA**TCTTACTCCCTCG
TACATGCACAAATACACACTCATGCACACACACACTCACACACATGCATACACTTAGGTTTCA
TGCCCATTTTCTATCACACTGGGCTCCATGATATTCTGTTCCCTAAGAACTGCTTCTGTGTGC
CCTGTTTTCATCCCAAGATTTCTCACTTCATCCTCTCCTACCTGGCTCTTTTGTCCCAGGGAG
GGGTCCTGTTCGGAAGCAGTGGCTGAATTTATCCCCTGAAAGTGGTTTTGGAGGAACCGGGAT
GGAGGAGGCCTTCCCCCTGTGGGAATAGAATCGTCCACTCCTAGCCCTGGTTGCTTCTGATACA
CAGCCACTGCACACACACACTCACACTCACACTCCCTTGTCTGATGCCCCAAAGCCAATTCCT
GGGGCACCCTACCCTCTCTTATTTGGAGTTTCCGTTGGTTTACCTGAGTTTTCTCTGGGGTCT
GCACAGAGGCAGCAGCATGGACATCATGGCCTCTCAGGTCCCTTTTGGTTCTCAGTTTCATTG
GTTCCTCTTTCTGTTCCCCCATTGACTTCTGTGCCCCACCCTAGCCTTTTCCATAACCTTAGG
TATTCAGTTTGGAGGGGTTTTTTGTATTTTTGAGGATTCCTGTATTCTGTATCCTCTCCTCGC
ATCTCCTCACATGGAAAGAAATAATGTATTTGTGCCTTCTGTGAGGAATGGGGGGAACAAGTG
GTCCCAGGTATCCCCATTTCCAAGGCCCCCCTCCCTCTCCAGGTCCCCCCACAGCAATAAAAG
CTTCCCCCTGATATCCATCCCTTTGTAGTTTGAACAAATATATTTATATGATATGTAA

FIGURE 16

MEESPLSRAPSRGGVNFLNVARTYIPNTKVECHYTLPPGTMPSASDWIGIFKVEAACVRDYHT
FVWSSVPESTTDGSPIHTSVQFQASYLPKPGAQLYQFRYVNRQGQVCGQSPPFQFREPRPMDE
LVTLEEADGGSDILLVVPKATVLQNQLDESQQERNDLMQLKLQLEGQVTELRSRVQELERALA
TARQEHTELMEQYKGISRSHGEITEERDILSRQQGDHVARILELEDDIQTISEKVLTKEVELD
RLRDTVKALTREQEKLLGQLKEVQADKEQSEAELQVAQQENHHLNLDLKEAKSWQEEQSAQAQ
RLKDKVAQMKDTLGQAQQRVAELEPLKEQLRGAQELAASSQQKATLLGEELASAAAARDRTIA
ELHRSRLEVAEVNGRLAELGLHLKEEKCQWSKERAGLLQSVEAEKDKILKLSAEILRLEKAVQ
EERTQNQVFKTELAREKDSSLVQLSESKRELTELRSALRVLQKEKEQLQEEKQELLEYMRKLE
ARLEKVADEKWNEDATTEDEEAAVGLSCPAALTDSEDESPEDMRLPPYGLCERGDPGSSPAGP
REASPLVVISQPAPISPHLSGPAEDSSSDSEAEDEKSVLMAAVQSGGEEANLLLPELGSAFYD
MASGFTVGTLSETSTGGPATPTWKECPICKERFPAESDKDALEDHMDGHFFFSTQDPFTFE

Important features:

Casein kinase II phosphorylation sites:

amino acids 28-31, 43-46, 68-71, 72-75, 129-132, 156-159, 208-211, 239-242, 282-285, 305-308, 376-379, 383-383, 468-471, 520-523, 521-524, 537-540, 539-542, 543-546, 593-596, 595-598, 597-600, 612-615, 639-642, 652-655, 667-670, 683-686

N-myristoylation sites:

amino acids 39-44, 107-112, 204-209, 414-419, 561-566, 613-618

Cell attachment sequence:

amino acids 557-559

Leucine zipper pattern sequence:

amino acids 163-184, 475-496, 482-503

FIGURE 17

GCAAGTTGGGAATTTTAGACTGTCACTGCACATGGACCTCTGGGAAGACGTCTGGCGAGAGCT
AGGCCCACTGGCCCTACAGACGGATCTTGCTGGCTCACCTGTCCCTGTGGAGGTTCCCCTGGG
AAGGCAAG**ATG**CCCAACAACAGCACTGCTCTGTCATTGGCCAATGTTACCTACATCACCATGG
AAATTTTCATTGGACTCTGCGCCATAGTGGGCAACGTGCTGGTCATCTGCGTGGTCAAGCTGA
ACCCCAGCCTGCAGACCACCACCTTCTATTTCATTGTCTCTCTAGCCCTGGCTGACATTGCTG
TTGGGGTGCTGGTCATGCCTTTGGCCATTGTTGTCAGCCTGGGCATCACAATCCACTTCTACA
GCTGCCTTTTTTATGACTTGCCTACTGCTTATCTTTACCCACGCCTCCATCATGTCCTTGCTGG
CCATCGCTGTGGACCGATACTTGCGGGTCAAGCTTACCGTCAGATTCAGAATTCCTGGGCTCC
CTGGGTGCATTCTATCATTCCAGTTGAAAGTTTGCTTCCTTCCAGTCATGTGGCTCTTCATTC
TACTCTCCTTGGCTCTCATTTCAGATGCCATGGTCATGGATGAAAAGGTCAAGAGAAGCTTTG
TGCTGGACACGGCTTCTGCCATCTGCAACTACAATGCCCACTACAAGAATCACCCCAAATACT
GGTGCCGAGGCTATTTCCGTGACTACTGCAACATCATCGCCTTCTCCCCTAACAGCACCAATC
ATGTGGCCCTGAGGGACACAGGGAACCAGCTCATTGTCACTATGTCCTGCCTGACCAAAGAGG
ACACGGGCTGGTACTGGTGTGGCATCCAGCGGGACTTTGCCAGGGATGACATGGATTTTACAG
AGCTGATTGTAACTGACGACAAAGGAACCCTGGCCAATGACTTTTGGTCTGGGAAAGACCTAT
CAGGCAACAAAACCAGAAGCTGCAAGGCTCCCAAAGTTGTCCGCAAGGCTGACCGCTCCAGGA
CGTCCATTCTCATCATTTGCATACTGATCACGGGTTTGGGAATCATCTCTGTAATCAGTCATT
TGACCAAAAGGAGGAGAAGTCAAAGGAATAGAAGGGTAGGCAACACTTTGAAGCCCTTCTCGC
GTGTCCTGACTCCAAAGGAAATGGCTCCTACTGAACAGATG**TGA**CTGAAGATTTTTTTTAATTT
AGTTCATAAAGTGATGCTACAACAGAATAATCACCATGACAACTGGCCCACACCTCAGAGACT
GATTCTGATCTCCCAGGAATTCTGAAGGACCCTCTATCCTTGACAACAATCATTTGCAGCCAG
GTAGCAACGGCGGTAGTCAGAGGAGCTATGATAGACCACACCCAAGCAAGGCTGCCCTCAAAT
AACATCTCAAGATCTTAGTTCTTATGCATTCCATCAGTCAGAAGTGAAGAAGAGGTGGAGAAT
CTGGATTGGGGACCAGGAAATCACTTGTATTTTGTTAGCCAATAAATTCCTAGCCAGTGTTGA
ATGAAAAAAAAAAAAA

FIGURE 18

MPNNSTALSLANVTYITMEIFIGLCAIVGNVLVICVVKLNPSLQTTTFYFIVSLALADIAVGV
LVMPLAIVVSLGITIHFYSCLFMTCLLLIFTHASIMSLLAIAVDRYLRVKLTVRFRIPGLPGC
ILSFQLKVCFLPVMWLFILLSLALISDAMVMDEKVKRSFVLDTASAICNYNAHYKNHPKYWCR
GYFRDYCNIIAFSPNSTNHVALRDTGNQLIVTMSCLTKEDTGWYWCGIQRDFARDDMDFTELI
VTDDKGTLANDFWSGKDLSGNKTRSCKAPKVVRKADRSRTSILIICILITGLGIISVISHLTK
RRRSQRNRRVGNTLKPFSRVLTPKEMAPTEQM

Important features of the protein:

Transmembrane domains:

amino acids 16-35, 62-80, 89-101, 134-152, 292-311

N-glycosylation sites.

amino acids 3-7, 4-8, 12-16, 204-208, 273-277

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 316-320

N-myristoylation sites.

amino acids 122-128, 125-131, 258-264

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 214-225

G-protein coupled receptors proteins.

amino acids 29-59, 76-116

FIGURE 19

CTCGGGCGCGCACAGGCAGCTCGGTTTGCCCTGCGATTGAGCTGCGGGTCGCGGCCGGCGCCGGCCTCTCCAATG
GCAAATGTGTGTGGCTGGAGGCGAGCGCGAGGCTTTCGGCAAAGGCAGTCGAGTGTTTGCAGACCGGGGCGAGTC
CTGTGAAAGCAGATAAAAGAAAACATTTATTAACGTGTCATTACGAGGGGAGCGCCCGGCCGGGGCTGTCGCACT
CCCCGCGGAACATTTGGCTCCCTCCAGCTCCGAGAGAGGAGAAGAAGAAAGCGGAAAAGAGGCAGATTCACGTCG
TTTCCAGCCAAGTGGACCTGATCGATGGCCCTCCTGAATTTATCACGATATTTGATTTATTAGCGATGCCCCCTG
GTTTGTGTGTTACGCACACACACGTGCACACAAGGCTCTGGCTCGCTTCCCTCCCTCGTTTCCAGCTCCTGGGCG
AATCCCACATCTGTTTCAACTCTCCGCCGAGGGCGAGCAGGAGCGAGAGTGTGTCGAATCTGCGAGTGAAGAGGG
ACGAGGGAAAAGAAACAAAGCCACAGACGCAACTTGAGACTCCCGCATCCCAAAAGAAGCACCAGATCAGCAAAA
AAAGAAG**ATG**GGCCCCCCGAGCCTCGTGCTGTGCTTGCTGTCCGCAACTGTGTTCTCCCTGCTGGGTGGAAGCTC
GGCCTTCCTGTCGCACCACCGCCTGAAAGGCAGGTTTCAGAGGGACCGCAGGAACATCCGCCCCAACATCATCCT
GGTGCTGACGGACGACCAGGATGTGGAGCTGGGTTCCATGCAGGTGATGAACAAGACCCGGCGCATCATGGAGCA
GGGCGGGGCGCACTTCATCAACGCCTTCGTGACCACACCCATGTGCTGCCCCTCACGCTCCTCCATCCTCACTGG
CAAGTACGTCCACAACCACAACACCTACACCAACAATGAGAACTGCTCCTCGCCCTCCTGGCAGGCACAGCACGA
GAGCCGCACCTTTGCCGTGTACCTCAATAGCACTGGCTACCGGACAGCTTTCTTCGGGAAGTATCTTAATGAATA
CAACGGCTCCTACGTGCCACCCGGCTGGAAGGAGTGGGTCGGACTCCTTAAAAACTCCCGCTTTTATAACTACAC
GCTGTGTCGGAACGGGGTGAAAGAGAAGCACGGCTCCGACTACTCCAAGGATTACCTCACAGACCTCATCACCAA
TGACAGCGTGAGCTTCTTCCGCACGTCCAAGAAGATGTACCCGCACAGGCCAGTCCTCATGGTCATCAGCCATGC
AGCCCCCCACGGCCCTGAGGATTCAGCCCCACAATATTCACGCCTCTTCCCAAACGCATCTCAGCACATCACGCC
GAGCTACAACTACGCGCCCAACCCGGACAAACACTGGATCATGCGCTACACGGGGCCCATGAAGCCCATCCACAT
GGAATTCACCAACATGCTCCAGCGGAAGCGCTTGCAGACCCTCATGTCGGTGGACGACTCCATGGAGACGATTTA
CAACATGCTGGTTGAGACGGGCGAGCTGGACAACACGTACATCGTATACACCGCCGACCACGGTTACCACATCGG
CCAGTTTGGCCTGGTGAAAGGGAAATCCATGCCATATGAGTTTGACATCAGGGTCCCGTTCTACGTGAGGGGCCC
CAACGTGGAAGCCGGCTGTCTGAATCCCCACATCGTCCTCAACATTGACCTGGCCCCCACCATCCTGGACATTGC
AGGCCTGGACATACCTGCGGATATGGACGGGAAATCCATCCTCAAGCTGCTGGACACGGAGCGGCCGGTGAATCG
GTTTCACTTGAAAAAGAAGATGAGGGTCTGGCGGGACTCCTTCTTGGTGGAGAGAGGCAAGCTGCTACACAAGAG
AGACAATGACAAGGTGGACGCCCAGGAGGAGAACTTTCTGCCCAAGTACCAGCGTGTGAAGGACCTGTGTCAGCG
TGCTGAGTACCAGACGGCGTGTGAGCAGCTGGGACAGAAGTGGCAGTGTGTGGAGGACGCCACGGGGAAGCTGAA
GCTGCATAAGTGCAAGGGCCCCATGCGGCTGGGCGGCAGCAGAGCCCTCTCCAACCTCGTGCCCAAGTACTACGG
GCAGGGCAGCGAGGCCTGCACCTGTGACAGCGGGGACTACAAGCTCAGCCTGGCCGGACGCCGGAAAAAACTCTT
CAAGAAGAAGTACAAGGCCAGCTATGTCCGCAGTCGCTCCATCCGCTCAGTGGCCATCGAGGTGGACGGCAGGGT
GTACCACGTAGGCCTGGGTGATGCCGCCCAGCCCCGAAACCTCACCAAGCGGCACTGGCCAGGGGCCCCTGAGGA
CCAAGATGACAAGGATGGTGGGGACTTCAGTGGCACTGGAGGCCTTCCCGACTACTCAGCCGCCAACCCCATTAA
AGTGACACATCGGTGCTACATCCTAGAGAACGACACAGTCCAGTGTGACCTGGACCTGTACAAGTCCCTGCAGGC
CTGGAAAGACCACAAGCTGCACATCGACCACGAGATTGAAACCCTGCAGAACAAAATTAAGAACCTGAGGGAAGT
CCGAGGTCACCTGAAGAAAAAGCGGCCAGAAGAATGTGACTGTCACAAAATCAGCTACCACACCCAGCACAAAGG
CCGCCTCAAGCACAGAGGCTCCAGTCTGCATCCTTTCAGGAAGGGCCTGCAAGAGAAGGACAAGGTGTGGCTGTT
GCGGGAGCAGAAGCGCAAGAAGAAACTCCGCAAGCTGCTCAAGCGCCTGCAGAACAACGACACGTGCAGCATGCC
AGGCCTCACGTGCTTCACCCACGACAACCAGCACTGGCAGACGGCGCCTTTCTGGACACTGGGGCCTTTCTGTGC
CTGCACCAGCGCCAACAATAACACGTACTGGTGCATGAGGACCATCAATGAGACTCACAATTTCCTCTTCTGTGA
ATTTGCAACTGGCTTCCTAGAGTACTTTGATCTCAACACAGACCCCTACCAGCTGATGAATGCAGTGAACACACT
GGACAGGGATGTCCTCAACCAGCTACACGTACAGCTCATGGAGCTGAGGAGCTGCAAGGGTTACAAGCAGTGTAA
CCCCCGGACTCGAAACATGGACCTGGATGGAGGAAGCTATGAGCAATACAGGCAGTTTCAGCGTCGAAAGTGGCC
AGAAATGAAGAGACCTTCTTCCAAATCACTGGGACAACTGTGGGAAGGCTGGGAAGGT**TAA**GAAACAACAGAGGT
GGACCTCCAAAAACATAGAGGCATCACCTGACTGCACAGGCAATGAAAAACCATGTGGGTGATTTCCAGCAGACC
TGTGCTATTGGCCAGGAGGCCTGAGAAAGCAAGCACGCACTCTCAGTCAACATGACAGATTCTGGAGGATAACCA
GCAGGAGCAGAGATAACTTCAGGAAGTCCATTTTTGCCCCTGCTTTTGCTTTGGATTATACCTCACCAGCTGCAC
AAAATGCATTTTTTCGTATCAAAAAGTCACCACTAACCCTCCCCCAGAAGCTCACAAAGGAAAACGGAGAGAGCG
AGCGAGAGAGATTTCCTTGGAAATTTCTCCCAAGGGCGAAAGTCATTGGAATTTTTAAATCATAGGGGAAAAGCA
GTCCTGTTCTAAATCCTCTTATTCTTTTGGTTTGTCACAAAGAAGGAACTAAGAAGCAGGACAGAGGCAACGTGG
AGAGGCTGAAAACAGTGCAGAGACGTTTGACAATGAGTCAGTAGCACAAAAGAGATGACATTTACCTAGCACTAT
AAACCCTGGTTGCCTCTGAAGAAACTGCCTTCATTGTATATATGTGACTATTTACATGTAATCAACATGGGAACT
TTTAGGGGAACCTAATAAGAAATCCCAATTTTCAGGAGTGGTGGTGTCAATAAACGCTCTGTGGCCAGTGTAAAA
GAAAAA

FIGURE 20

MGPPSLVLCLLSATVFSLLGGSSAFLSHHRLKGRFQRDRRNIRPNIILVLTDDQDVELGSMQV
MNKTRRIMEQGGAHFINAFVTTPMCCPSRSSILTGKYVHNHNTYTNNENCSSPSWQAQHESRT
FAVYLNSTGYRTAFFGKYLNEYNGSYVPPGWKEWVGLLKNSRFYNYTLCRNGVKEKHGSDYSK
DYLTDLITNDSVSFFRTSKKMYPHRPVLMVISHAAPHGPEDSAPQYSRLFPNASQHITPSYNY
APNPDKHWIMRYTGPMKPIHMEFTNMLQRKRLQTLMSVDDSMETIYNMLVETGELDNTYIVYT
ADHGYHIGQFGLVKGKSMPYEFDIRVPFYVRGPNVEAGCLNPHIVLNIDLAPTILDIAGLDIP
ADMDGKSILKLLDTERPVNRFHLKKKMRVWRDSFLVERGKLLHKRDNDKVDAQEENFLPKYQR
VKDLCQRAEYQTACEQLGQKWQCVEDATGKLKLHKCKGPMRLGGSRALSNLVPKYYGQGSEAC
TCDSGDYKLSLAGRRKKLFKKKYKASYVRSRSIRSVAIEVDGRVYHVGLGDAAQPRNLTKRHW
PGAPEDQDDKDGGDFSGTGGLPDYSAANPIKVTHRCYILENDTVQCDLDLYKSLQAWKDHKLH
IDHEIETLQNKIKNLREVRGHLKKKRPEECDCHKISYHTQHKGRLKHRGSSLHPFRKGLQEKD
KVWLLREQKRKKKLRKLLKRLQNNDTCSMPGLTCFTHDNQHWQTAPFWTLGPFCACTSANNNT
YWCMRTINETHNFLFCEFATGFLEYFDLNTDPYQLMNAVNTLDRDVLNQLHVQLMELRSCKGY
KQCNPRTRNMDLDGGSYEQYRQFQRRKWPEMKRPSSKSLGQLWEGWEG

Important features:

Signal peptide:

amino acids 1-17

Sulfatases signature 1.

amino acids 86-99

Homologous region to sulfatase:

amino acids 87-106, 133-146, 216-229, 291-320, 365-375

N-glycosylation sites.

amino acids 65-69, 112-116, 132-136, 149-153, 171-175, 198-202, 241-245, 561-565, 608-612, 717-721, 754-758, 764-768

FIGURE 21

GGGCGCGCGAGAGCTGCTAGGGCGGTTTCTCTGCCTCGGGCCTGTTGGGCAGGGCCGGCT
AAGGTGCGCGTGCTCGCTGGTTCTAACCCTTCTGTTGGGCGTTTCTGCTGAGAGGCGGGA
GGCGCTGAGAGTCTGTGCGGAGGTCCGTGGACAGACTGCTTTGCTCGTTGTTGCTCTTCG
GAGGCGGCGATCCCCGAAGGCGAGCTGAAATACGGCTGCAGGCTACAATTTGCAGCCGAC
GATTATGGAAGACGGAAGCGGGAGAGGTGGCCCACCCTC**ATG**GAGCGCTTGTGCTCGGAT
GGCTTCGCATTTCCCCAATACCCCATTAAACCGTATCATCTGAAGAGGATCCACAGAGCT
GTCTTACATGGTAATCTAGAGAAACTGAAGTACCTTCTGCTCACGTATTATGACGCCAAT
AAGAGAGACAGGAAGGAAAGGACCGCCCTACATTTGGCCTGTGCCACTGGCCAACCGGAA
ATGGTACATCTCCTGGTGTCCAGAAGATGTGAGCTTAACCTCTGCGACCGTGAAGACAGG
ACACCTCTGATCAAGGCTGTACAACTGAGGCAGGAGGCTTGTGCAACTCTTCTGCTGCAA
AATGGCGCCAATCCAAATATTACGGATTTCTTTGGAAGGACTGCTCTGCACTACGCTGTG
TATAATGAAGATACATCCATGATAGAAAAACTTCTTTCACATGGTACAAATATTGAAGAA
TGCAGCAAGGTA**TAG**GTCAACCAATGTTATTTTCAAACTATCTGAAATGAATTTATTTTA
ACATTGACACATGTAAGGGTCAATTTTTCATATTTGGAAGCTCAAACATTCCTTGAATGA
AAATATTTTGAAATGCCTTAACTGTCTAAGATTTTACTTTAAATATTGGAACTTTTAAAG
AAGCATTATAGGGAACAGCCTTTTTTCATGCACTTATGGTAAATAACTATAAAAACAAAT
GAATTACAATAAATTTATAATTCATGACAACTGAATTTGGGAAAGGTAATAGTTAAGTGT
TTTTCCACTAAATTACTTTTT

FIGURE 22

MERLCSDGFAFPQYPIKPYHLKRIHRAVLHGNLEKLKYLLLTYYDANKRDRKERTALHLACAT
GQPEMVHLLVSRRCELNLCDREDRTPLIKAVQLRQEACATLLLQNGANPNITDFFGRTALHYA
VYNEDTSMIEKLLSHGTNIEECSKV

Important features of the protein:

N-glycosylation site.

amino acids 113-117

N-myristoylation site.

amino acids 109-115

Microbodies C-terminal targeting signal.

amino acids 149-153

FIGURE 23

GAGGCAGAAAGGCAGAAAGGAGAAAATTCAGGATAACTCTCCTGAGGGGTGAGCCAAGCCCTG
CCATGTAGTGCACGCAGGACATCAACAAACACAGATAACAGGAAATGATCCATTCCCTGTGGT
CACTTATTCTAAAGGCCCCAACCTTCAAAGTTCAAGTAGTGAT**ATG**GATGACTCCACAGAAAG
GGAGCAGTCACGCCTTACTTCTTGCCTTAAGAAAAGAGAAGAAATGAAACTGAAGGAGTGTGT
TTCCATCCTCCCACGGAAGGAAAGCCCCTCTGTCCGATCCTCCAAAGACGGAAAGCTGCTGGC
TGCAACCTTGCTGCTGGCACTGCTGTCTTGCTGCCTCACGGTGGTGTCTTTCTACCAGGTGGC
CGCCCTGCAAGGGGACCTGGCCAGCCTCCGGGCAGAGCTGCAGGGCCACCACGCGGAGAAGCT
GCCAGCAGGAGCAGGAGCCCCCAAGGCCGGCCTGGAGGAAGCTCCAGCTGTCACCGCGGGACT
GAAAATCTTTGAACCACCAGCTCCAGGAGAAGGCAACTCCAGTCAGAACAGCAGAAATAAGCG
TGCCGTTCAGGGTCCAGAAGAAACAGTCACTCAAGACTGCTTGCAACTGATTGCAGACAGTGA
AACACCAACTATACAAAAAGGATCTTACACATTTGTTCCATGGCTTCTCAGCTTTAAAAGGGG
AAGTGCCCTAGAAGAAAAAGAGAATAAAATATTGGTCAAAGAAACTGGTTACTTTTTTATATA
TGGTCAGGTTTTATATACTGATAAGACCTACGCCATGGGACATCTAATTCAGAGGAAGAAGGT
CCATGTCTTTGGGGATGAATTGAGTCTGGTGACTTTGTTTCGATGTATTCAAAATATGCCTGA
AACACTACCCAATAATTCCTGCTATTCAGCTGGCATTGCAAAACTGGAAGAAGGAGATGAACT
CCAACTTGCAATACCAAGAGAAAATGCACAAATATCACTGGATGGAGATGTCACATTTTTTGG
TGCATTGAAACTGCTG**TGA**CCTACTTACACCATGTCTGTAGCTATTTTCCTCCCTTTCTCTGT
ACCTCTAAGAAGAAAGAATCTAACTGAAAATACCAAAAAAAAAAAAAAAAA

FIGURE 24

MDDSTEREQSRLTSCLKKREEMKLKECVSILPRKESPSVRSSKDGKLLAATLLLALLSCCLTV
VSFYQVAALQGDLASLRAELQGHHAEKLPAGAGAPKAGLEEAPAVTAGLKIFEPPAPGEGNSS
QNSRNKRAVQGPEETVTQDCLQLIADSETPTIQKGSYTFVPWLLSFKRGSALEEKENKILVKE
TGYFFIYGQVLYTDKTYAMGHLIQRKKVHVFGDELSLVTLFRCIQNMPETLPNNSCYSAGIAK
LEEGDELQLAIPRENAQISLDGDVTFFGALKLL

Transmembrane domain:

amino acids 47-72

N-glycosylation site.

amino acids 124-127, 242-245

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 33-36, 173-176

N-myristoylation site.

amino acids 96-101

TNF family proteins.

amino acids 172-206

FIGURE 25

CTGCTTGGATACCTCCAGTCCCCAAACTGTGTTCCAGGAGTTTTCTTGGCCGAAGCTGCCCGA
TGTTTGAGCCTTTTCTTCCCAGAGAAGAAGATGGACTGAAAGCTGCCAGTTGGGGACTTTTTG
TGATCACGGCGTTGCAGCGTTTTAAAGGAGGTGATGGGGCTTGCGCTGGCTTGTCTTCCCACC
CAAGTGAAGAGTTGATGTTCACTGGTTATGCTTAGACAATGTGCAGTTTGTGTTAATTTAAAA
TTTTGGGTGGGATAGGGGCATAGGCTTGTGAAGGGCAGTCCGGATCCGGAGGAACTCGTCTTT
GTCCCTGGTAGGAGAGACACCCCCAGTCTATCCTCGATGCCGTCAGCCTTGGCCATCTTCACT
TGCCGCCCGAACTCGCACCCGTTTCAGGAGCGTCATGTCTACCTGGACGAGCCCATCAAAATC
GGCCGCTCAGTGGCCCGCTGTCGACCAGCGCAGAATAATGCCACTTTTGATTGCAAAGTGCTA
TCAAGGAACCACGCTCTCGTCTGGTTTGATCACAAGACGGGCAAGTTTTATCTTCAAGACACT
AAAAGTAGTAATGGTACTTTTATAAATAGCCAGAGATTGAGTCGAGGCTCTGAAGAAAGTCCA
CCATGTGAAATTCTTTCCGGTGACATTATCCAGTTTGGAGTAGACGTGACAGAGAATACACGG
AAAGTTACCCATGGGTGTATTGTTTCCACAATAAAACTTTTTCTACCAGATGGT**ATG**GAAGCC
CGGCTCCGCTCAGATGTCATCCATGCACCATTACCAAGTCCTGTTGACAAAGTTGCTGCTAAC
ACTCCAAGTATGTACTCTCAGGAACTATTCCAGCTTTCTCAGTATCTACAGGAGGCCTTACAT
CGGGAACAAATGTTGGAACAGAAGTTAGCCACGCTTCAGCGGCTACTAGCCATCACCCAAGAG
GCTTCAGATACCAGTTGGCAGGCTTTAATAGATGAAGATAGACTCTTATCACGGTTAGAAGTT
ATGGGAAACCAATTACAGGCATGCTCCAAAAATCAAACAGAAGATAGTTTACGAAAGGAACTT
ATAGCATTACAAGAGGATAAACATAACTATGAGACAACAGCCAAAGAGTCCCTGAGGCGGGTT
CTTCAGGAGAAAATTGAAGTGGTTAGAAAACTTTCAGAAGTTGAGCGAAGTCTGAGTAATACT
GAAGATGAATGTACCCATCTGAAAGAAATGAATGAAAGGACTCAGGAAGAATTAAGAGAATTA
GCCAACAAATATAATGGAGCAGTTAATGAGATTAAAGATTTATCTGATAAATTAAAGGTAGCA
GAGGGAAAACAAGAGGAAATCCAACAGAAGGGACAGGCTGAGAAAAAAGAATTACAACATAAA
ATAGATGAAATGGAAGAAAAAGAACAGGAGCTCCAGGCAAAAATAGAAGCTTTGCAAGCTGAT
AATGATTTCACCAATGAAAGGCTAACAGCTTTACAAGTACGGTTAGAACATCTTCAGGAGAAA
ACTCTTAAAGAATGCAGCAGCTTGGCTGATCGTCGAAGGGCATCTAACCAAAGCGGTAGAAGA
AACAAAGCTTTCAAAAGGTTTGTTTTCTGTTTTTCTATGTTTTTTGACAGTTCTTTTGGA**TAA**
TGAAGGTTAGTGTATATTTTCAAGGTTATAGTATTTTAACCATCAGTTTACTTCTTATAGCTC
ACAAAATAGCAAGCCAGTAACAGTATCAGATAATATATAAAATAATCAGACTTCTGTTTTAAG
AAGGGTATCGTAACTGGAATGTGTCTTTTTAAGTGGATGTATATTTATGGTTTTTTGAATGTT
AGTACTTGATATAGGTTTCTTTAGGTATTAAAGATTTGTTGCAATCTCTGTCATTCCCAGCAT
TAATTTCAGCTTTGATCTCAAATTTTAATCAAACACAATGTAAGTCGTTTGTGATACAACTTA
AGTGAAACATGCTTGCACTTCTATTTTGGGGGTTACAGTACCTTTAAAATCTCTTATGATGTT
TAATATTTCCTTAATTTTTGGCATCTCAGTTTGATTTAAACAAAATTAATGACTTTTGTGAAT
GTAGAATCTTCTTATATTTTATGAGTAGTCCAGTAATTGCCCAAAGTAGTTTATTGTGTTAAT
TCTGTTACAGTTGTCAGAGAAGAAAAGTGAGTTTTAAAGCACCATATTGTCAAGTCACTTTTA
TACATAGGGAAATTAGGCAAATAAATTTGGTGGCATGTGTTTATCATAGTAGAACTTTCATTA
GACTATACCAGTATAAAATTTAAAACTAGATTCACAGTCCTTTTGGCCAATTAAAACATTGAG
TTACAAAAGTTTGAGATACTTAATTTTAGTACATTCTATTTTATTAAAGTAACTGGATTCATT
TGACTTTTTTTAACCATGTAAGAGGATGGTGTTATTTCAAATATCTCGTGGTTTCCATTCTGAA
TTTTGTGCACGGCAGATGCCATATTTGGGGAAAAAATGCATAGAATATGCATCATTAATATTG
TTTTGGCAAACAGGCATTGAGTTTCAGAACAGTGAACTATTTTTAGTACATATGGCAATTTTT
TTCACCTTATTAAAGTGAGATGAGAACAGACCTTAAAATAGCTTTTACCTCACCATCCAAATA
CCTATTCAGATTAGTTGGTTGAATAGCCAGCACTTTGAAGTAGAGCCTTAGG

FIGURE 26

MEARLRSDVIHAPLPSPVDKVAANTPSMYSQELFQLSQYLQEALHREQMLEQKLATLQRLLAI
TQEASDTSWQALIDEDRLLSRLEVMGNQLQACSKNQTEDSLRKELIALQEDKHNYETTAKESL
RRVLQEKIEVVRKLSEVERSLSNTEDECTHLKEMNERTQEELRELANKYNGAVNEIKDLSDKL
KVAEGKQEEIQQKGQAEKKELQHKIDEMEEKEQELQAKIEALQADNDFTNERLTALQVRLEHL
QEKTLKECSSLADRRRASNQSGRRNKAFKRFVFCFSMFFDSSFG

Important features of the protein:

N-glycosylation sites.

amino acids 98-102, 271-275

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 138-142, 267-271

Amidation site.

amino acids 273-277

Tropomyosins proteins.

amino acids 169-217

FIGURE 27

GAACCTGGCGCCGCCGGAACTGATCGCGGCCTAGTCCCGACGCGTGTGTGCTAGTGAGCCGGA
GCCGGCGACGGCGGCAGTGGCGGCCCGGCCTGCAGGAGCCCGACGGGGTCTCTGCCATGGGGG
AGTGACGCGCCTGCACCCGCTGTTCCGCGGCAGCGGCGAGACATGAGGAGACCCCGCGACAGG
GGCAGCGGCGGCGGCTCGTGAGCCCCGGG**ATG**GAGGAGAAATACGGCGGGGACGTGCTGGCCG
GCCCCGGCGGCGGCGGCGGCCTTGGGCCGGTGGACGTACCCAGCGCTCGATTAACAAAATATA
TTGTGTTACTATGTTTCACTAAATTTTTGAAGGCTGTGGGACTTTTCGAATCATATGATCTCC
TAAAAGCTGTTCACATTGTTCAGTTCATTTTTATATTAAAACTTGGGACTGCATTTTTTATGG
TTTTGTTTCAAAAGCCATTTTCTTCTGGGAAAACTATTACCAAACACCAGTGGATCAAAATAT
TTAAACATGCAGTTGCTGGGTGTATTATTTCACTCTTGTGGTTTTTTGGCCTCACTCTTTGTG
GACCACTAAGGACTTTGCTGCTATTTGAGCACAGTGATATTGTTGTCATTTCACTACTCAGTG
TTTTGTTCACCAGTTCTGGAGGAGGACCAGCAAAGACAAGGGGAGCTGCTTTTTTCATTATTG
CTGTGATCTGTTTATTGCTTTTTGACAATGATGATCTCATGGCTAAAATGGCTGAACACCCTG
AAGGACATCATGACAGTGCTCTAACTCATATGCTTTACACAGCCATTGCCTTCTTAGGTGTGG
CAGATCACAAGGGTGGAGTATTATTGCTAGTACTGGCTTTGTGTTGTAAAGTTGGTTTTCATA
CAGCTTCCAGAAAGCTCTCTGTCGACGTTGGTGGAGCTAAACGTCTTCAAGCTTTATCTCATC
TTGTTTCTGTGCTTCTCTTGTGCCCATGGGTCATTGTTCTTTCTGTGACAACTGAGAGTAAAG
TGGAGTCTTGGTTTTCTCTCATTATGCCTTTTGCAACGGTTATCTTTTTTTGTCATGATCCTGG
ATTTCTACGTGGATTCCATTTGTTCAGTCAAAATGGAAGTTTCCAAATGTGCTCGTTATGGAT
CCTTTCCCATTTTTATTAGTGCTCTCCTTTTTGGAAATTTTTGGACACATCCAATAACAGACC
AGCTTCGGGCTATGAACAAAGCAGCACACCAGGAGAGCACTGAACACGTCCTGTCTGGAGGAG
TGGTAGTGAGTGCTATATTCTTCATTTTGTCTGCCAATATCTTATCATCTCCCTCTAAGAGAG
GACAAAAAGGTACCCTTATTGGATATTCTCCTGAAGGAACACCTCTTTATAACTTCATGGGTG
ATGCTTTTCAGCATAGCTCTCAATCGATCCCTAGGTTTATTAAGGAATCACTAAAACAAATTC
TTGAGGAGAGTGACTCTAGGCAGATCTTTTACTTCTTGTGCTTGAATCTGCTTTTTACCTTTG
TGGAATTATTCTATGGCGTGCTGACCAATAGTCTGGGCCTGATCTCGGATGGATTCCACATGC
TTTTTGACTGCTCTGCTTTAGTCATGGGACTTTTTGCTGCCCTGATGAGTAGGTGGAAAGCCA
CTCGGATTTTCTCCTATGGGTACGGCCGAATAGAAATTCTGTCTGGATTTATTAATGGACTTT
TTCTAATAGTAATAGCGTTTTTTGTGTTTATGGAGTCAGTGGCTAGATTGATTGATCCTCCAG
AATTAGACACTCACATGTTAACACCAGTCTCAGTTGGAGGGCTGATAGTAAACCTTATTGGTA
TCTGTGCCTTTAGCCATGCCCATAGCCATGCCCATGGAGCTTCTCAAGGAAGCTGTCACTCAT
CTGATCACAGCCATTCACACCATATGCATGGACACAGTGACCATGGGCATGGTCACAGCCACG
GATCTGCGGGTGGAGGCATGAATGCTAACATGAGGGGTGTATTTCTACATGTTTTGGCAGATA
CACTTGGCAGCATTGGTGTGATCGTATCCACAGTTCTTATAGAGCAGTTTGGATGGTTCATCG
CTGACCCACTCTGTTCTCTTTCTACTGCTATATTAATATTTCTCAGTGTTGTTCCACTGATTA
AAGATGCCTGCCAGGTTCTACTCCTGAGATTGCCACCAGAATATGAAAAAGAACTACATATTG
CTTTAGAAAAGATACAGAAAATTGAAGGATTAATATCATACCGAGACCCTCATTTTTGGCGTC
ATTCTGCTAGTATTGTGGCAGGAACAATTCATATACAGGTGACATCTGATGTGCTAGAACAAA
GAATAGTACAGCAGGTTACAGGAATACTTAAAGATGCTGGAGTAAACAATTTAACAATTCAAG
TGGAAAAGGAGGCATACTTTCAACATATGTCTGGCCTAAGTACTGGATTTCATGATGTTCTGG
CTATGACAAAACAAATGGAATCCATGAAATACTGCAAAGATGGTACTTACATCATG**TGA**GATA
ACTCAAGAATTACCCCTGGAGAATAAACAATGAAGATTAAATGACTCAGTATTTGTAATATTG
CCAGAAGGATAAAAATTACACATTAACTGTACAGAAACAGAGTTCCCTACTACTGGATCAAGG
AATCTTTCTTGAAGGAAATTTAAATACAGAATGAAACATTAATGGTAAAAAAAA

FIGURE 28

MEEKYGGDVLAGPGGGGGLGPVDVPSARLTKYIVLLCFTKFLKAVGLFESYDLLKAVHIVQFI
FILKLGTAFFMVLFQKPFSSGKTITKHQWIKIFKHAVAGCIISLLWFFGLTLCGPLRTLLLFE
HSDIVVISLLSVLFTSSGGGPAKTRGAAFFIIAVICLLLFDNDDLMAKMAEHPEGHHDSALTH
MLYTAIAFLGVADHKGGVLLLVLALCCKVGFHTASRKLSVDVGGAKRLQALSHLVSVLLLCPW
VIVLSVTTESKVESWFSLIMPFATVIFFVMILDFYVDSICSVKMEVSKCARYGSFPIFISALL
FGNFWTHPITDQLRAMNKAAHQESTEHVLSGGVVVSAIFFILSANILSSPSKRGQKGTLIGYS
PEGTPLYNFMGDAFQHSSQSIPRFIKESLKQILEESDSRQIFYFLCLNLLFTFVELFYGVLTN
SLGLISDGFHMLFDCSALVMGLFAALMSRWKATRIFSYGYGRIEILSGFINGLFLIVIAFFVF
MESVARLIDPPELDTHMLTPVSVGGLIVNLIGICAFSHAHSHAHGASQGSCHSSDHSHSHHMH
GHSDHGHGHSHGSAGGGMNANMRGVFLHVLADTLGSIGVIVSTVLIEQFGWFIADPLCSLSTA
ILIFLSVVPLIKDACQVLLLRLPPEYEKELHIALEKIQKIEGLISYRDPHFWRHSASIVAGTI
HIQVTSDVLEQRIVQQVTGILKDAGVNNLTIQVEKEAYFQHMSGLSTGFHDVLAMTKQMESMK
YCKDGTYIM

Important features of the protein:

Signal peptide:

amino acids 1-46

Transmembrane domains:

amino acids 59-77, 101-119, 150-167, 205-223, 239-258, 267-284, 305-324, 343-360, 421-440, 452-469, 486-505, 522-539, 592-612, 621-641

N-glycosylation site.

amino acids 721-725

Glycosaminoglycan attachment site.

amino acids 143-147

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 225-229

Tyrosine kinase phosphorylation sites.

amino acids 750-758, 756-764

N-myristoylation sites.

amino acids 14-20, 46-52, 102-108, 112-118, 144-150, 317-323, 347-353, 369-375, 372-378, 437-443, 462-468, 529-535, 549-555, 553-559, 579-585, 582-588, 583-589, 584-590, 605-611, 737-743

Multicopper oxidases protein:

amino acids 561-569

FIGURE 29

GGCACGAGGGCAGGATATTAGAA**ATG**GCTACTCCCCAGTCAATTTTCATCTTTGCAATCTGCA
TTTTAATGATAACAGAATTAATTCTGGCCTCAAAAAGCTACTATGATATCTTAGGTGTGCCAA
AATCGGCATCAGAGCGCCAAATCAAGAAGGCCTTTCACAAGTTGGCCATGAAGTACCACCCTG
ACAAAAATAAGAGCCCGGATGCTGAAGCAAAATTCAGAGAGATTGCAGAAGCATATGAAACAC
TCTCAGATGCTAATAGACGAAAAGAGTATGATACACTTGGACACAGTGCTTTTACTAGTGGTA
AAGGACAAAGAGGTAGTGGAAGTTCTTTTGAGCAGTCATTTAACTTCAATTTTGATGACTTAT
TTAAAGACTTTGGCTTTTTTTGGTCAAAACCAAAAACACTGGATCCAAGAAGCGTTTTGAAAATC
ATTTCCAGACACGCCAGGATGGTGGTTCCAGTAGACAAAGGCATCATTTCCAAGAATTTTCTT
TTGGAGGTGGATTATTTGATGACATGTTTGAAGATATGGAGAAAATGTTTTCTTTTAGTGGTT
TTGACTCTACCAATCAGCATACAGTACAGACTGAAAATAGATTTCATGGATCTAGCAAGCACT
GCAGGACTGTCACTCAACGAAGAGGAAATATGGTTACTACATACACTGACTGTTCAGGACAG**T**
AGTTCTTATTCTATTCTCACTAAATCCAACTGGTTGACTCTTCCTCATTATCTTTGATGCTAA
ACAATTTTCTGTGAACTATTTTGACAAGTGCATGATTTCACTTTAAACAATTTGATATAGCTA
TTAAATATATTTAAGGGTTTTTTTTTTTGACAAATTCAACATTCAACGAGTAGACAAAATGCT
AATTATTTCCCTGATTAGGAAAGTTTCTTTAAAAAACACGTAATTTTGCCTAGTGCTTTTTCT
CTACCTGCCCTTGGGCTCACTAATATCACCAGTATTATTACCAAGAAAATATTGAGTTTACCT
GATTAAACTTTAAAAGTTAATTGTAGATTTAAATTGTGTGAACCTAATGATTTTTGCAGTGAA
ACCTTTACTAATTCAAAGTTGCATGTTCTATGACATCTGTGACTTGCGTTGCAGAGTGTACAT
GAAACTGTATAATTGAGTCATTCAGTAAAGGAGAACAGTATCTTGGTTAATTGCTACTGAAAG
GTTGAGAAAGGAATGGTTTGATATTTACCACAGCGCTGTGCCTTTCTACAGTAGAACTGGGGT
AAAGGAAATGGTTTTATTGCCCATAGTCATTTAGGCTGGAAAAAAGTTGAAAACTTAACGAAA
TATTGCCAAGAGATTGTTATGTGTTTGGTTCCAGCCTAAAAATGATTTTGTAGTGTTGAAATC
ATAGCTACTTACATAGCTTTTTCATATTTCTTTCTTAGTTGTTGGCACTCTTAGGTCTTAGTA
TGGATTTATGTGTTTGTGTGTGTGTAGTTTATCCTCTCTCTCATCTTTATCTAGAGATTGACT
GATACCTCATTCTGTTTGTAAAACCAGCCAGTAATTTCTGTGCAACCTTACTATGTGCAATAT
TTTTAAATCCTGAGAAATGTGTGCTTTTGTTTTCGGATAGACTTATTTCTTTAGTTCTGCACT
TTTCCACATTATACTCCATATGAGTATTAATCCTATGGATACATATTAAAACAAGTGTCTCAT

FIGURE 30

MATPQSIFIFAICILMITELILASKSYYDILGVPKSASERQIKKAFHKLAMKYHPDKNKSPDA
EAKFREIAEAYETLSDANRRKEYDTLGHSAFTSGKGQRGSGSSFEQSFNFNFDDLFKDFGFFG
QNQNTGSKKRFENHFQTRQDGGSSRQRHHFQEFSFGGGLFDDMFEDMEKMFSFSGFDSTNQHT
VQTENRFHGSSKHCRTVTQRRGNMVTTYTDCSGQ

Important features of the protein:

Signal peptide:

amino acids 1-23

Nt-dnaJ domain signature.

amino acids 27-59, 66-90

Glycosaminoglycan attachment site.

amino acids 96-100

N-myristoylation sites.

amino acids 32-38, 99-105, 102-108, 126-132, 211-217

FIGURE 31

AAAGTTACATTTTCTCTGGAACTCTCCTAGGCCACTCCCTGCTGATGCAACATCTGGGTTTGG
GCAGAAAGGAGGGTGCTTCGGAGCCCGCCCTTTCTGAGCTTCCTGGGCCGGCTCTAGAACAAT
TCAGGCTTCGCTGCGACTCAGACCTCAGCTCCAACATATGCATTCTGAAGAAAGATGGCTGAG
ATGGACAGAATGCTTTATTTTGGAAAGAAACAATGTTCTAGGTCAAACTGAGTCTACCAA**ATG**
CAGACTTTCACAATGGTTCTAGAAGAAATCTGGACAAGTCTTTTCATGTGGTTTTTCTACGCA
TTGATTCCATGTTTGCTCACAGATGAAGTGGCCATTCTGCCTGCCCCTCAGAACCTCTCTGTA
CTCTCAACCAACATGAAGCATCTCTTGATGTGGAGCCCAGTGATCGCGCCTGGAGAAACAGTG
TACTATTCTGTCGAATACCAGGGGGAGTACGAGAGCCTGTACACGAGCCACATCTGGATCCCC
AGCAGCTGGTGCTCACTCACTGAAGGTCCTGAGTGTGATGTCACTGATGACATCACGGCCACT
GTGCCATACAACCTTCGTGTCAGGGCCACATTGGGCTCACAGACCTCAGCCTGGAGCATCCTG
AAGCATCCCTTTAATAGAAACTCAACCATCCTTACCCGACCTGGGATGGAGATCACCAAAGAT
GGCTTCCACCTGGTTATTGAGCTGGAGGACCTGGGGCCCCAGTTTGAGTTCCTTGTGGCCTAC
TGGAGGAGGGAGCCTGGTGCCGAGGAACATGTCAAAATGGTGAGGAGTGGGGGTATTCCAGTG
CACCTAGAAACCATGGAGCCAGGGGCTGCATACTGTGTGAAGGCCCAGACATTCGTGAAGGCC
ATTGGGAGGTACAGCGCCTTCAGCCAGACAGAATGTGTGGAGGTGCAAGGAGAGGCCATTCCC
CTGGTACTGGCCCTGTTTGCCTTTGTTGGCTTCATGCTGATCCTTGTGGTCGTGCCACTGTTC
GTCTGGAAAATGGGCCGGCTGCTCCAGTACTCCTGTTGCCCCGTGGTGGTCCTCCCAGACACC
TTGAAAATAACCAATTCACCCCAGAAGTTAATCAGCTGCAGAAGGGAGGAGGTGGATGCCTGT
GCCACGGCTGTGATGTCTCCTGAGGAACTCCTCAGGGCCTGGATCTCA**TAG**GTTTGCGGAAGG
GCCCAGGTGAAGCCGAGAACCTGGTCTGCATGACATGGAAACCATGAGGGGACAAGTTGTGTT
TCTGTTTTCCGCCACGGACAAGGGATGAGAGAAGTAGGAAGAGCCTGTTGTCTACAAGTCTAG
AAGCAACCATCAGAGGCAGGGTGGTTTGTCTAACAGAACACTGACTGAGGCTTAGGGGATGTG
ACCTCTAGACTGGGGGCTGCCACTTGCTGGCTGAGCAACCCTGGGAAAAGTGACTTCATCCCT
TCGGTCCTAAGTTTTCTCATCTGTAATGGGGGAATTACCTACACACCTGCTAAACACACACAC
ACAGAGTCTCTCTCTATATATACACACGTACACATAAATACACCCAGCACTTGCAAGGCTAGA
GGGAAACTGGTGACACTCTACAGTCTGACTGATTCAGTGTTTCTGGAGAGCAGGACATAAATG
TATGATGAGAATGATCAAGGACTCTACACACTGGGTGGCTTGGAGAGCCCACTTTCCCAGAAT
AATCCTTGAGAGAAAAGGAATCATGGGAGCAATGGTGTTGAGTTCACTTCAAGCCCAATGCCG
GTGCAGAGGGGAATGGCTTAGCGAGCTCTACAGTAGGTGACCTGGAGGAAGGTCACAGCCACA
CTGAAAATGGGATGTGCATGAACACGGAGGATCCATGAACTACTGTAAAGTGTTGACAGTGTG
TGCACACTGCAGACAGCAGGTGAAATGTATGTGTGCAATGCGACGAGAATGCAGAAGTCAGTA
ACATGTGCATGTTTGTTGTGCTCCTTTTTTCTGTTGGTAAAGTACAGAATTCAGCAAATAAAA
AGGGCCACCCTGGCCAAAAGCGGTAAAAAAAAAAAAAAAA

FIGURE 32

MQTFTMVLEEIWTSLFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLLMWSPVIAPGET
VYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTSAWSI
LKHPFNRNSTILTRPGMEITKDGFHLVIELEDLGPQFEFLVAYWRREPGAEEHVKMVRSGGIP
VHLETMEPGAAYCVKAQTFVKAIGRYSAFSQTECVEVQGEAIPLVLALFAFVGFMLILVVVPL
FVWKMGRLLQYSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVMSPEELLRAWIS

Important features:

Signal peptide:

amino acids 1-29

Transmembrane domain:

amino acids 230-255

N-glycosylation sites.

amino acids 40-44, 134-138

Tissue factor proteins.

amino acids 92-120

Integrins alpha chain proteins.

amino acids 232-263

FIGURE 33

GAGACACGCGAGCGGGGAGACCTCCAAGGCAGCGAGGCATCGGACATGTGTCAGCACATCTGG
GGCGCACATCCGTCGAGCCCGAGGGGAGATTTGCCGGAACAATTCAAACTGCGATATTGATCT
TGGGGGTGACTGTCCCTGGCCGGCTGTCGGGTGGGAGTGCGAGTGTGCACTCGCTCGGAAGTG
TGTGCGAGTGTGTATGTGTGTGTGCCGTGTCGGGCTCCCCCCTTCCCCCCGTTTTCCCGTCGA
GTGATGCACTTGGAATGAGAATCAGAGG**ATG**GAAATAGTCTGGGAGGTGCTTTTTCTTCTTCA
AGCCAATTTCATCGTCTGCATATCAGCTCAACAGAATTCACCAAAAATCCATGAAGGCTGGTG
GGCATACAAGGAGGTGGTCCAGGGAAGCTTTGTTCCAGTTCCTTCTTTCTGGGGATTGGTGAA
CTCAGCTTGGAATCTTTGCTCTGTGGGGAAACGGCAGTCGCCAGTCAACATAGAGACCAGTCA
CATGATCTTCGACCCCTTTCTGACACCTCTTCGCATCAACACGGGGGGCAGGAAGGTCAGTGG
GACCATGTACAACACTGGAAGACACGTATCCCTTCGCCTGGACAAGGAGCACTTGGTCAACAT
ATCTGGAGGGCCCATGACATACAGCCACCGGCTGGAGGAGATCCGACTACACTTTGGGAGTGA
GGACAGCCAAGGGTCGGAGCACCTCCTCAATGGACAGGCCTTCTCTGGGGAGGTGCAGCTCAT
CCACTATAACCATGAGCTATATACGAATGTCACAGAAGCTGCAAAGAGTCCAAATGGATTGGT
GGTAGTTTCTATATTTATAAAAGTTTCTGATTCATCAAACCCATTTCTTAATCGAATGCTCAA
CAGAGATACTATCACAAGAATAACATATAAAAATGATGCATATTTACTACAGGGGCTTAATAT
AGAGGAACTATATCCAGAGACCTCTAGTTTCATCACTTACGATGGGTCGATGACTATCCCACC
CTGCTATGAGACAGCAAGTTGGATCATAATGAACAAACCTGTCTATATAACCAGGATGCAGAT
GCATTCCTTGCGCCTGCTCAGCCAGAACCAGCCATCTCAGATCTTTCTGAGCATGAGTGACAA
CTTCAGGCCTGTCCAGCCACTCAACAACCGCTGCATCCGCACCAATATCAACTTCAGTTTACA
GGGGAAGGACTGTCCAAACAACCGAGCCCAGAAGCTTCAGTATAGAGTAAATGAATGGCTCCT
CAAG**TAG**GAACAAAGCCAAGAAGAATCCCACCTCAGTGAAATGCTACAACTGTGAATTGACG
TAACCTAGAATGTCCCCCTTCTTGCTTCTCTCTCCTTCTTTCCCCCAAGCCTCATTCATTCTT
GGGATTGGCCCTTTCTTCATGAAAAGTGTCTGCGAAACCATGGCAGAGGAATACATCTCTCAC
ACATACTCACAAACACACACACAAGCACTTGCACATACATACAAACACATGCAAACATACCTA
CACACACACACTCTCTTACAACCTCCATCATGGGAAGTCAAGTTTCAGAAACAAAAGTCTCAT
TCATAAGAGGTCTTAGAAGAAAATAACCAGTTAACCTGATTTCAATTTTGATACCGTTTTCCT
GAACTAATAAATCTACCCAATGAGACTTTTCAGCCTTTGTACATACAAAATTCTTCCAAAAGA
GAGAGGAGAAAATACAGCTCTGATGGCATCAAACGGACTTTGCATCAAGTAATTTCAGATAGT
GTCCTAGGATCCTTTGAGGGTGCTGGTAGCAGGTGAGCAGGACAAAGTTGACCAAGGACACTT
ATTTCTAGATTATGATTCTTCTGTTTACTCAACAATTTACAAAGAAAAAAAAGGACAGACATTG
AAGAGCTACACATTGTATATATATCACCACAGACTATAAGGAAATGGAATTATTTCCCTCTTT
GTCACATATCTGTAGTAGGATTTGCCAAGATCAGAAATGATCCATTTGCTGTTTCTTGTTTTC
CAAAGGTCATACATTGTGTTTGGTTATTGTTACCAGCTCAATAAATGTGTTTAACGAGTTAAT
TTCATTTTTCTGGCTTTGGTCTGTTCTCCTTCCTTACAGGCTAAGCCCTGGCTCCATGCAACT
GCATTCTTTGATTTCACTTGTTCCTTCATCTACATGTTTTGTTCATTTGCAGCCAGTTTTTAC
TGAGTTTGTGGCAATCAGGAATGCATTTGCTAAGCAAGTATGACTTTAATTCCACTCCATGGC
TCAATCATTCACATGAGGTGAGCTTCAGCCTGAGATAGCAGGCGACAGACTTCTTGCGTTTCA
AAACTGCCATGCCCCCCTGTGATGCTCCCGTGAAGGAATGCACTTTGCCTTGTAAGTTCCTGG
GAAAGGGGTATGTTTTCTCTCCAGGTGCAGCCAGATCTCACAAAGTACAAAACGAATGCCTTT
CTTTTCTTGTTTATAATGGTCACTCACTGTGTTTGGTTACTGTCAAGAAATCAATAAATGTGT
TTAACAAGTTA

FIGURE 34

MEIVWEVLFLLQANFIVCISAQQNSPKIHEGWWAYKEVVQGSFVPVPSFWGLVNSAWNLCSVG
KRQSPVNIETSHMIFDPFLTPLRINTGGRKVSGTMYNTGRHVSLRLDKEHLVNISGGPMTYSH
RLEEIRLHFGSEDSQGSEHLLNGQAFSGEVQLIHYNHELYTNVTEAAKSPNGLVVVSIFIKVS
DSSNPFLNRMLNRDTITRITYKNDAYLLQGLNIEELYPETSSFITYDGSMTIPPCYETASWII
MNKPVYITRMQMHSLRLLSQNQPSQIFLSMSDNFRPVQPLNNRCIRTNINFSLQGKDCPNNRA
QKLQYRVNEWLLK

Important features:

Signal peptide:

amino acids 1-20

Eukaryotic-type carbonic anhydrases proteins.

amino acids 126-162, 220-269, 43-91

N-glycosylation sites.

amino acids 116-119, 168-171, 302-305

FIGURE 35

GTCGGAACCCCCTCAGGCCACCCTCGGGAGTCCTGGGGTCCAGAGGGGTGTCCCTGTACCCCTTGCAC
ACAGGACCCTCACTCTGCAGGGATAAGCCAGCTGCGCCTGCAGCCTAGGGTGCCAAGGAGGCTGCTGA
TTGTGGCCCACAGCCTCATCTGAACGCCAGGAGACCAGGATACCGAGGCACCGGATCCCCTCTCTGTG
CCCTGGGGAGCCCCAGTGCTGCCCAGTCACCCCAGGGCTGAGGTCTGCGTCCCTAGTGGTGCAAGGCC
TGGTAGGACCACGGGGCAGGGAATGTGAGCGCCATCCGAGCTCACGGTGTCCTGAGTCGCGGCTTCGT
GACTTTGGCAGGGGCCTCCGGACCAGTGACCCCAGTCAAACCCAGAGGGTCTTGGGCGGCAGCGACGA
AGGAGGTATTCAGGCTCCAGGCCAGGTGGGGCCGGACGCCCCCAGCCATCCACC**ATG**GTGGTGGCACA
CCCCACCGCCACTGCCACCACCACGCCCACTGCCACTGTCACGGCCACCGTTGTGATGACCACGGCCA
CCATGGACCTGCGGGACTGGCTGTTCCTCTGCTACGGGCTCATCGCCTTCCTGACGGAGGTCATCGAC
AGCACCACCTGCCCCTCGGTGTGCCGCTGCGACAACGGCTTCATCTACTGCAACGACCGGGGACTCAC
ATCCATCCCCGCAGATATCCCTGATGACGCCACCACCCTCTACCTGCAGAACAACCAGATCAACAACG
CCGGCATCCCCCAGGACCTCAAGACCAAGGTCAACGTGCAGGTCATCTACCTATACGAGAATGACCTG
GATGAGTTCCCCATCAACCTGCCCCGCTCCCTCCGGGAGCTGCACCTGCAGGACAACAATGTGCGCAC
CATTGCCAGGGACTCGCTGGCCCGCATCCCGCTGCTGGAGAAGCTGCACCTGGATGACAACTCCGTGT
CCACCGTCAGCATTGAGGAGGACGCCTTCGCCGACAGCAAACAGCTCAAGCTGCTCTTCCTGAGCCGG
AACCACCTGAGCAGCATCCCCTCGGGGCTGCCGCACACGCTGGAGGAGCTGCGGCTGGATGACAACCG
CATCTCCACCATCCCGCTGCATGCCTTCAAGGGCCTCAACAGCCTGCGGCGCCTGGTGCTGGACGGTA
ACCTGCTGGCCAACCAGCGCATCGCCGACGACACCTTCAGCCGCCTACAGAACCTCACAGAGCTCTCG
CTGGTGCGCAATTCGCTGGCCGCGCCACCCCTCAACCTGCCCAGCGCCCACCTGCAGAAGCTCTACCT
GCAGGACAATGCCATCAGCCACATCCCCTACAACACGCTGGCCAAGATGCGTGAGCTGGAGCGGCTGG
ACCTGTCCAACAACAACCTGACCACGCTGCCCCGCGGCCTGTTCGACGACCTGGGGAACCTGGCCCAG
CTGCTGCTCAGGAACAACCCTTGGTTTTGTGGCTGCAACCTCATGTGGCTGCGGGACTGGGTGAAGGC
ACGGGCGGCCGTGGTCAACGTGCGGGGCCTCATGTGCCAGGGCCCTGAGAAGGTCCGGGGCATGGCCA
TCAAGGACATTACCAGCGAGATGGACGAGTGTTTTGAGACGGGGCCGCAGGGCGGCGTGGCCAATGCG
GCTGCCAAGACCACGGCCAGCAACCACGCCTCTGCCACCACGCCCCAGGGTTCCCTGTTTACCCTCAA
GGCCAAAAGGCCAGGGCTGCGCCTCCCCGACTCCAACATTGACTACCCCATGGCCACGGGTGATGGCG
CCAAGACCCTGGCCATCCACGTGAAGGCCCTGACGGCAGACTCCATCCGCATCACGTGGAAGGCCACG
CTCCCCGCCTCCTCTTTCCGGCTCAGTTGGCTGCGCCTGGGCCACAGCCCAGCCGTGGGCTCCATCAC
GGAGACCTTGGTGCAGGGGGACAAGACAGAGTACCTGCTGACAGCCCTGGAGCCCAAGTCCACCTACA
TCATCTGCATGGTCACCATGGAGACCAGCAATGCCTATGTAGCTGATGAGACACCCGTGTGTGCCAAG
GCAGAGACAGCCGACAGCTATGGCCCTACCACCACACTCAACCAGGAGCAGAACGCTGGCCCCATGGC
GAGCCTGCCCCTGGCGGGCATCATCGGCGGGGCAGTGGCTCTGGTCTTCCTCTTCCTGGTCCTGGGGG
CCATCTGCTGGTACGTGCACCAGGCTGGCGAGCTGCTGACCCGGGAGAGGGCCTACAACCGGGGCAGC
AGGAAAAAGGATGACTATATGGAGTCAGGGACCAAGAAGGATAACTCCATCCTGGAAATCCGCGGCCC
TGGGCTGCAGATGCTGCCCATCAACCCGTACCGCGCCAAAGAGGAGTACGTGGTCCACACTATCTTCC
CCTCCAACGGCAGCAGCCTCTGCAAGGCCACACACACCATTGGCTACGGCACCACGCGGGGCTACCGG
GACGGCGGCATCCCCGACATAGACTACTCCTACACA**TGA**TGCCCGCCCACCCGGGCTGCCCCGCCTCA
GCCCCAGCTGCCCTGGCGTGGCCATGTGGCTTTGCCCAGCCTGCTGCAATCCAAGAGAGCAAGGAAGA
GAAATTCCATGGGTGACTTTCCTCCGCAGAAAGCAAAGTTTGGGGAGGGCTGACGATTTTGTAGAACA
CAACAGTGACAATTTTTTTTAAAAGAATAGAAGGCAGGAGGGGGAATTCGACATTGTTGAAGACATAA
TTTATACCAAGTTATGCCAGTTGGGGAGGGAAGGACTAAAAATAATATTGCAGGCAGGGCTGGGTTGG
GTTTTTTTTTTTTCCCCCCCTGAACTGGAAGGATACTACCTGTACAACATCTGTGGACACCTCATGCTCT
GTTCAAGGCCATCACAAAGGAACCGCCAGGGAGAAGCAGCCGGCTCTCAAAGCTCCCACGCAGCTCTC
CCGCCACTGGCCACTCGCTGGCGACCCGATGGAAGGTTTTCAGGCTCCTCACAAAGGAGAGAGGGAAG
AAAAGATCTTTTGCCCTGGAGATATGGTCCTGAAATCTCTCCCCTGGCTTATTCCATACCATTTCCCT
TGCAGATTTGCAGAAACATGGCATCTTTCACTGCATTCTTTGAACAATCATGTAGTCGATTAAAAAAA
AAAACAAACTTTTTTTTCCTAGGCTGAAGCCCTCTTCAGTTCCATGCACCACGCTCCGTAGAAGCCCC
GGCGGAAGCCGTAGCTTTCCCTGCCACCTGGAGGTGCATCTGTCTGCCTGTCTATCCCTGTCGCGGTG
TCTCTAAGTACAGATGGGTAGATAGAGCCACATGCACGGTCCTTACCGTTCTTCTTGGGTCAGTTCTT
ACCATTTCCTGAACAATAGAATTGTGAAAGTGTTAAAAA

FIGURE 36

MVVAHPTATATTTPTATVTATVVMTTATMDLRDWLFLCYGLIAFLTEVIDSTTCPSVCRCDNG
FIYCNDRGLTSIPADIPDDATTLYLQNNQINNAGIPQDLKTKVNVQVIYLYENDLDEFPINLP
RSLRELHLQDNNVRTIARDSLARIPLLEKLHLDDNSVSTVSIEEDAFADSKQLKLLFLSRNHL
SSIPSGLPHTLEELRLDDNRISTIPLHAFKGLNSLRRLVLDGNLLANQRIADDTFSRLQNLTE
LSLVRNSLAAPPLNLPSAHLQKLYLQDNAISHIPYNTLAKMRELERLDLSNNNLTTLPRGLFD
DLGNLAQLLLRNNPWFCGCNLMWLRDWVKARAAVVNVRGLMCQGPEKVRGMAIKDITSEMDEC
FETGPQGGVANAAAKTTASNHASATTPQGSLFTLKAKRPGLRLPDSNIDYPMATGDGAKTLAI
HVKALTADSIRITWKATLPASSFRLSWLRLGHSPAVGSITETLVQGDKTEYLLTALEPKSTYI
ICMVTMETSNAYVADETPVCAKAETADSYGPTTTLNQEQNAGPMASLPLAGIIGGAVALVFLF
LVLGAICWYVHQAGELLTRERAYNRGSRKKDDYMESGTKKDNSILEIRGPGLQMLPINPYRAK
EEYVVHTIFPSNGSSLCKATHTIGYGTTRGYRDGGIPDIDYSYT

Important features of the protein:

Transmembrane domain:
amino acids 552-573

N-glycosylation sites.
amino acids 249-252, 305-308, 642-645

Leucine zipper pattern.
amino acids 182-203, 299-320

Phospholipase A2 aspartic acid active site.
amino acids 57-67

FIGURE 37

GGTGACTGAAGCGAGCCTGGCCTCTTGCATCCTCCGCCTGTGTACCTCCCTCCCCTTTTTTTCCGCCT
TCTGCCAGCAGAAGCAGCAGCCGCAGCACCTGAGCCGCTACTGCCGCTCACTCAGGACAACGCT**ATG**G
CTGAGCCTGGGCACAGCCACCATCTCTCCGCCAGAGTCAGGAGAAGAACTGAGAGGCGCATACCCCGG
CTGTGGCGGCTGCTGCTCTGGGCTGGGACCGCCTTCCAGGTGACCCAGGGAACGGGACCGGAGCTTCA
TGCCTGCAAAGAGTCTGAGTACCACTATGAGTACACGGCGTGTGACAGCACGGGTTCCAGGTGGAGGG
TCGCCGTGCCGCATACCCCGGGCCTGTGCACCAGCCTGTCTGACCCCGTCAAGGGCACCGAGTGCTCC
TTCTCCTGCAACGCCGGGGAGTTTCTGGATATGAAGGACCAGTCATGTAAGCCATGCGCTGAGGGCCG
CTACTCCCTCGGCACAGGCATTCGGTTTGATGAGTGGGATGAGCTGCCCCATGGCTTTGCCAGCCTCT
CAGCCAACATGGAGCTGGATGACAGTGCTGCTGAGTCCACCGGGAACTGTACTTCGTCCAAGTGGGTT
CCCCGGGGCGACTACATCGCCTCCAACACGGACGAATGCACAGCCACACTGATGTACGCCGTCAACCT
GAAGCAATCTGGCACCGTTAACTTCGAATACTACTATCCAGACTCCAGCATCATCTTTGAGTTTTTCG
TTCAGAATGACCAGTGCCAGCCCAATGCAGATGACTCCAGGTGGATGAAGACCACAGAGAAAGGATGG
GAATTCCACAGTGTGGAGCTAAATCGAGGCAATAATGTCCTCTATTGGAGAACCACAGCCTTCTCAGT
ATGGACCAAAGTACCCAAGCCTGTGCTGGTGAGAAACATTGCCATAACAGGGGTGGCCTACACTTCAG
AATGCTTCCCCTGCAAACCTGGCACGTATGCAGACAAGCAGGGCTCCTCTTTCTGCAAACTTTGCCCA
GCCAACTCTTATTCAAATAAAGGAGAAACTTCTTGCCACCAGTGTGACCCTGACAAATACTCAGAGAA
AGGATCTTCTTCCTGTAACGTGCGCCCAGCTTGCACAGACAAAGATTATTTCTACACACACACGGCCT
GCGATGCCAACGGAGAGACACAACTCATGTACAAATGGGCCAAGCCGAAAATCTGTAGCGAGGACCTT
GAGGGGGCAGTGAAGCTGCCTGCCTCTGGTGTGAAGACCCACTGCCCACCCTGCAACCCAGGCTTCTT
CAAAACCAACAACAGCACCTGCCAGCCCTGCCCATATGGTTCCTACTCCAATGGCTCAGACTGTACCC
GCTGCCCTGCAGGGACTGAACCTGCTGTGGGATTTGAATACAAATGGTGGAACACGCTGCCCACAAAC
ATGGAAACGACCGTTCTCAGTGGGATCAACTTCGAGTACAAGGGCATGACAGGCTGGGAGGTGGCTGG
TGATCACATTTACACAGCTGCTGGAGCCTCAGACAATGACTTCATGATTCTCACTCTGGTTGTGCCAG
GATTTAGACCTCCGCAGTCGGTGATGGCAGACACAGAGAATAAAGAGGTGGCCAGAATCACATTTGTC
TTTGAGACCCTCTGTTCTGTGAACTGTGAGCTCTACTTCATGGTGGGTGTGAATTCTAGGACCAACAC
TCCTGTGGAGACGTGGAAAGGTTCCAAAGGCAAACAGTCCTATACCTACATCATTGAGGAGAACACTA
CCACGAGCTTCACCTGGGCCTTCCAGAGGACCACTTTTCATGAGGCAAGCAGGAAGTACACCAATGAC
GTTGCCAAGATCTACTCCATCAATGTCACCAATGTTATGAATGGCGTGGCCTCCTACTGCCGTCCCTG
TGCCCTAGAAGCCTCTGATGTGGGCTCCTCCTGCACCTCTTGTCCTGCTGGTTACTATATTGACCGAG
ATTCAGGAACCTGCCACTCCTGCCCCCCTAACACAATTCTGAAAGCCCACCAGCCTTATGGTGTCCAG
GCCTGTGTGCCCTGTGGTCCAGGGACCAAGAACAACAAGATCCACTCTCTGTGCTACAATGATTGCAC
CTTCTCACGCAACACTCCAACCAGGACTTTCAACTACAACTTCTCCGCTTTGGCAAACACCGTCACTC
TTGCTGGAGGGCCAAGCTTCACTTCCAAAGGGTTGAAATACTTCCATCACTTTACCCTCAGTCTCTGT
GGAAACCAGGGTAGGAAAATGTCTGTGTGCACCGACAATGTCACTGACCTCCGGATTCCTGAGGGTGA
GTCAGGGTTCTCCAAATCTATCACAGCCTACGTCTGCCAGGCAGTCATCATCCCCCCAGAGGTGACAG
GCTACAAGGCCGGGGTTTCCTCACAGCCTGTCAGCCTTGCTGATCGACTTATTGGGGTGACAACAGAT
ATGACTCTGGATGGAATCACCTCCCCAGCTGAACTTTTCCACCTGGAGTCCTTGGGAATACCGGACGT
GATCTTCTTTTATAGGTCCAATGATGTGACCCAGTCCTGCAGTTCTGGGAGATCAACCACCATCCGCG
TCAGGTGCAGTCCACAGAAAACTGTCCCTGGAAGTTTGCTGCTGCCAGGAACGTGCTCAGATGGGACC
TGTGATGGCTGCAACTTCCACTTCCTGTGGGAGAGCGCGGCTGCTTGCCCGCTCTGCTCAGTGGCTGA
CTACCATGCTATCGTCAGCAGCTGTGTGGCTGGGATCCAGANGACTACTTACGTGTGNCGAGAACCCA
AGCTATGCTCTGGTGGCATTTCTCTGCCTGAGCAGAGAGTCACCATCTGCAAAACCATAGATTTCTGG
CTGAAAGTGGGCATCTCTGCAGGCACCTGTACTGCCATCCTGCTCACCGTCTTGACCTGCTACTTTTG
GAAAAAGAATCAAAAACTAGAGTACAAGTACTCCAAGCTGGTGATGAATGCTACTCTCAAGGACTGTG
ACCTGCCAGCAGCTGACAGCTGCGCCATCATGGAAGGCGAGGATGTAGAGGACGACCTCATCTTTACC
AGCAAGAAGTCACTTTTTGGGAAGATCAAATCATTTACCTCCAAGAGGACTCCTGATGGATTTGACTC
AGTGCCGCTGAAGACATCCTCAGGAGGCCCAGACATGGACCTG**TGA**GAGGCACTGCCTGCCTCACCTG
CCTCCTCACCTTGCATAGCACCTTTGCAAGCCTGCGGCGATTTGGGTGCCAGCATCCTGCAACACCCA
CTGCTGGAAATCTCTTCATTGTGGCCTTATCAGATGTTTGAATTTCAGATCTTTTTTTATAGAGTACC
CAAACCCTCCTTTCTGCTTGCCTCAAACCTGCCAAATATACCCACATTTTTTTTTAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 38

MAEPGHSHHLSARVRRRTERRIPRLWRLLLWAGTAFQVTQGTGPELHACKESEYHYEYTACDS
TGSRWRVAVPHTPGLCTSLSDPVKGTECSFSCNAGEFLDMKDQSCKPCAEGRYSLGTGIRFDE
WDELPHGFASLSANMELDDSAAESTGNCTSSKWVPRGDYIASNTDECTATLMYAVNLKQSGTV
NFEYYYPDSSIIFEFFVQNDQCQPNADDSRWMKTTEKGWEFHSVELNRGNNVLYWRTTAFSVW
TKVPKPVLVRNIAITGVAYTSECFPCKPGTYADKQGSSFCKLCPANSYSNKGETSCHQCDPDK
YSEKGSSSCNVRPACTDKDYFYTHTACDANGETQLMYKWAKPKICSEDLEGAVKLPASGVKTH
CPPCNPGFFKTNNSTCQPCPYGSYSNGSDCTRCPAGTEPAVGFEYKWWNTLPTNMETTVLSGI
NFEYKGMTGWEVAGDHIYTAAGASDNDFMILTLVVPGFRPPQSVMADTENKEVARITFVFETL
CSVNCELYFMVGVNSRTNTPVETWKGSKGKQSYTYIIEENTTTSFTWAFQRTTFHEASRKYTN
DVAKIYSINVTNVMNGVASYCRPCALEASDVGSSCTSCPAGYYIDRDSGTCHSCPPNTILKAH
QPYGVQACVPCGPGTKNNKIHSLCYNDCTFSRNTPTRTFNYNFSALANTVTLAGGPSFTSKGL
KYFHHFTLSLCGNQGRKMSVCTDNVTDLRIPEGESGFSKSITAYVCQAVIIPPEVTGYKAGVS
SQPVSLADRLIGVTTDMTLDGITSPAELFHLESLGIPDVIFFYRSNDVTQSCSSGRSTTIRVR
CSPQKTVPGSLLLPGTCSDGTCDGCNFHFLWESAAACPLCSVADYHAIVSSCVAGIQXTTYVX
REPKLCSGGISLPEQRVTICKTIDFWLKVGISAGTCTAILLTVLTCYFWKKNQKLEYKYSKLV
MNATLKDCDLPAADSCAIMEGEDVEDDLIFTSKKSLFGKIKSFTSKRTPDGFDSVPLKTSSGG
PDMDL

Important features of the protein:

N-glycosylation sites:

amino acids 153-156, 390-393, 391-394, 404-407, 544-547, 576-579, 672-675, 717-720, 947-950

cAMP- and cGMP-dependent protein kinase phosphorylation sites:

amino acids 15-18, 563-566, 709-712

Casein kinase II phosphorylation sites:

amino acids 42-45, 59-62, 81-84, 146-149, 168-171, 282-285, 331-334, 340-343, 431-434, 449-452, 465-468, 523-526, 557-560, 761-764, 780-783, 835-838, 860-863, 893-896, 949-952

Tyrosine kinase phosphorylation sites:

amino acids 50-56, 109-116

N-myristoylation sites:

amino acids 77-82, 88-93, 152-157, 268-273, 288-293, 320-325, 400-405, 405-410, 414-419, 463-468, 599-604, 616-621, 634-639, 644-649, 839-844, 874-879, 912-917, 916-921

Amidation site:

amino acids 707-710

Cell attachment sequence:

amino acids 162-164

FIGURE 39

GGGAAGGGGTTCTGGGCTGCCGCAGGCACACAGGCCAGAGCTTCGTGGATACCTGCAGGGCCC
AAAGGTCCCTCCCTGTTTTGAAGAGTGAGTGATGGCTATGAGGTAGCGGCCAGGCTGATCACC
CCTGCGTTGGCTGGAGGCAGAATTCTGTAAATCCTCGCCAAGTCTTTCTCCAGGCCACTGGTT
AGCTCATCTCAGCCTCCTCTGGGAGCATCAACACCAACATGGCACAGGGGACTGCAGTGGTGT
GCTTTGGACCTGTGTACCCACCCAAGGCTAAAGGCAGAGCCAGGTGACTTTGCGGGGGTCTCT
TCTCTAGGATTATCTGTACTTCCCCTCTGTCCTCTTTTACTACGGGAGATCGAGCTAGCTATA
ACCCACCTTCTTTCATGAGAACCACACTAAATTGCAAAAATTATCCCAGTGCTGGAGGAGGGC
AGCAGGTTGAGATTATGTTGGCAGGAAGAATGTTGGCATTGATTGGCACGCAGGGGACGAGAG
CTGCTTTGTGCTTTAAAGGAGCCAAGTTACACCCTGTTTAACCCTGCCTTCAAAGGGACGACT
CTGTAAGATTCTCTGCTACTTATTCAAGTTGACACG**ATG**CCCTTCACACTCCACCTGAGGTCC
CGCCTTCCCTCTGCCATAAGGAGTTTGATTCTACAAAAGAAACCAAACATCAGAAATACATCC
AGCATGGCTGGAGAGCTCCGACCAGCCAGCCTGGTGGTCCTGCCCAGGTCCCTTGCTCCAGCT
TTTGAAAGATTCTGCCAGGTCAACACTGGTCCTCTACCCCTGCTGGGCCAGAGTGAGCCAGAA
AAGTGGATGCTGCCCCCTCAAGGTGCTATCTCAGAGACCAGGATGGGCCATCCCCAGTTCTGG
AAATACGAGTTCGGTGCCTGCACCGGTAGCCTGGCTTCGCTGGAGCAGTACTCGGAGCAGCTG
AAGGACATGGTGGCCTTCTTCCTGGGCTGCAGCTTCTCCCTGGAGGAGGCCTTGGAGAAAGCG
GGGCTCCCCAGAAGAGACCCAGCAGGTCACAGCCAGGCGGGTGCATACAAGACAACAGTGCCT
TGTGTTACCCATGCTGGCTTCTGCTGCCCTCTGGTGGTCACGATGAGGCCCATTCCCAAGGAC
AAGCTGGAAGGGCTGGTGCGGGCCTGCTGCTCCCTCGGAGGTGAGCAGGGGCAACCTGTTCAC
ATGGGCGACCCAGAACTGTTGGGAATCAAAGAGCTTTCCAAACCTGCCTACGGGGATGCCATG
GTGTGTCCCCCAGGGGAGGTTCCAGTGTTCTGGCCTTCTCCGCTGACCAGTCTCGGAGCTGTC
AGCAGCTGTGAGACCCCACTGGCTTTTGCCAGCATCCCAGGCTGCACAGTTATGACTGACCTG
AAGGATGCAAAGGCTCCACCTGGTTGTCTCACCCCAGAGAGAATTCCAGAGGTCCATCACATT
TCCCAAGATCCTCTGCACTACAGCATCGCGTCAGTCTCTGCTTCTCAGAAGATCAGAGAACTA
GAGTCTATGATCGGCATAGACCCAGGGAACCGGGGGATTGGGCACCTGCTCTGTAAAGATGAG
CTGCTGAAGGCCTCTCTCTCGCTGTCCCATGCCCGCTCAGTGCTCATCACCACTGGGTTCCCC
ACACATTTCAATCATGAGCCTCCAGAAGAGACAGATGGCCCACCAGGAGCTGTTGCTCTGGTT
GCCTTCCTGCAGGCCTTGGAGAAGGAGGTCGCCATAATCGTTGACCAGAGAGCCTGGAACTTG
CACCAGAAGATTGTTGAAGATGCTGTTGAGCAAGGTGTTCTGAAGACGCAGATCCCGATATTA
ACTTACCAAGGTGGATCAGTGGAAGCTGCTCAGGCATTCCTGTGCAAAAATGGGGACCCGCAG
ACACCTAGATTTGACCACCTGGTGGCCATAGAGCGTGCCGGAAGAGCTGCTGATGGCAATTAC
TACAATGCAAGGAAGATGAACATCAAGCACTTGGTTGACCCCATTGACGATCTTTTTCTTGCT
GCGAAGAAGATTCCTGGAATCTCATCAACTGGAGTCGGTGATGGAGGCAACGAGCTTGGGATG
GGTAAAGTCAAGGAGGCTGTGAGGAGGCACATACGGCACGGGGATGTCATCGCCTGCGACGTG
GAGGCTGACTTTGCCGTCATTGCTGGTGTTTCTAACTGGGGAGGCTATGCCCTGGCCTGCGCA
CTCTACATCCTGTACTCATGTGCTGTCCACAGTCAGTACCTGAGGAAAGCAGTCGGACCCTCC
AGGGCACCTGGAGATCAGGCCTGGACTCAGGCCCTCCCGTCGGTCATTAAGGAAGAAAAAATG
CTGGGCATCTTGGTGCAGCACAAAGTCCGGAGTGGCGTCTCGGGCATCGTGGGCATGGAGGTG
GATGGGCTGCCCTTCCACAACACCCACGCCGAGATGATCCAGAAGCTGGTGGACGTCACCACG
GCACAGGTG**TAA**CCGTCCATGTTCCGTGTGAGCAGAGTCCCTACCAACGGGCAGGTCTGCATC
CGGGGAGAATGCAGCTGCTTCTGGCGACAATCCTGCTAGTAAACACTGGTCTTCGGTGAGCAA
CGAACACTCGCCTGGCCTGGGAAACTGCATGCCCACTTTCTGGGAGGGGTTAGTGCAGGTGCC
GTGGACAAAGGACAACATTTCTCTGGGGCTTTTTAACTTTTATTCCTAAGACTCTAAAGGCGT
TGATTTCAACCCTCCTTCACTCTGGCTTCTTCAGGCAACCCACGTGGTCTCCTATGAGAATCT
TCTCGACAGTTACTTATGGGGACACTTGTGAACAATTAACTGCCAGGGCAGAGCATGAGAACA
AACATTCCCAGGCCATGTAGGATAGGATACTCCAGACTCCAGTCATCCTCCCCCATCCATGGT
TTCTGTTACTCATGGTTTCAGTTACTCATAGCCAACTGCAGACCGAAAATACTAAATGAAAAA
TTTCAGAAATAAACAACTCTTAAGTTTTAAAAAAAAA

FIGURE 40

MPFTLHLRSRLPSAIRSLILQKKPNIRNTSSMAGELRPASLVVLPRSLAPAFERFCQVNTGPL
PLLGQSEPEKWMLPPQGAISETRMGHPQFWKYEFGACTGSLASLEQYSEQLKDMVAFFLGCSF
SLEEALEKAGLPRRDPAGHSQAGAYKTTVPCVTHAGFCCPLVVTMRPIPKDKLEGLVRACCSL
GGEQGQPVHMGDPELLGIKELSKPAYGDAMVCPPGEVPVFWPSPLTSLGAVSSCETPLAFASI
PGCTVMTDLKDAKAPPGCLTPERIPEVHHISQDPLHYSIASVSASQKIRELESMIGIDPGNRG
IGHLLCKDELLKASLSLSHARSVLITTGFPTHFNHEPPEETDGPPGAVALVAFLQALEKEVAI
IVDQRAWNLHQKIVEDAVEQGVLKTQIPILTYQGGSVEAAQAFLCKNGDPQTPRFDHLVAIER
AGRAADGNYYNARKMNIKHLVDPIDDLFLAAKKIPGISSTGVGDGGNELGMGKVKEAVRRHIR
HGDVIACDVEADFAVIAGVSNWGGYALACALYILYSCAVHSQYLRKAVGPSRAPGDQAWTQAL
PSVIKEEKMLGILVQHKVRSGVSGIVGMEVDGLPFHNTHAEMIQKLVDVTTAQV

Signal peptide:

amino acids 1-17

Transmembrane domain:

amino acids 358-378, 517-539

N-glycosylation site.

amino acids 28-32

Tyrosine kinase phosphorylation site.

amino acids 444-452

N-myristoylation site.

amino acids 98-104, 102-108, 123-129, 149-155, 181-187, 190-196, 238-244, 308-314, 399-405, 413-419, 448-454, 477-483, 482-488, 487-493

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 233-244, 531-542

FIGURE 41

CTTTCCTGTTTTATCCGCAGCCCTTTTCTTCTTTGAGTTAGTAAAGATTTATTCTGTAACCTG
ACACTCATCTGGCCCTTTGCAGTTTGCCAGCCATATTCCCATGTGATTTCCCACTGGATCCAG
GCCCCCATCCGGCTGGCAGGAGGGGGCTCTGACGTACAGGTTGGAAATCAGAAGTCTGTGAGA
GCGCGGGAGTGCATGGCAGCTCTGGGTCCCAGACCTGGCCCGACCCCTCTGCTTCACCTCCAG
CTCTGCTGCTCCTCTACTCTTGGGTCGAGATCCCTTTGGAGCCACAGCGAGGAACCCTGTGGT
CCTCAGGCAGGTGTACCTTGAGTCAGCCAGGAGCCCTCTTTTCCTGTGTCAAAGCCTGCCCTC
GGGCTCTGCTCACCTCTGGTGACCCTCCAAGATGCCCCTGCCCTCAGTTTCCCCTCATGATCT
GGCCTCTGCCCCCTTCTCTAGCCACAGCCTCTAGTACACTTTAGCAATACCACCAGACTAGTT
AGAGTTCCCCACTCACCAAGCAAGAC**ATG**CAGTTTCATGCCTCTGTGCCTTCGCTCATGCTGT
TTCTTCCGACTGGAATGCCTTCCCCTGCTCCTCCTGCCTTGTCTGCCTGGCAAGTTCATCTCT
CACGATCCCCTCAAAGGCCCCCTCCTCCAGGAAGGCAACCCCTGTGCCCCTCCCCTCCAGGCT
ACCTCTGCACTTTGTCAATGCTTCTCTTGTGGCACTTATCACACTGTATTTTACTTGTTTACA
TGTTTGTCTCCCCTTCTAGACTG**TGA**ATCCTTAAGGGCATGGACTGTATCTTATGCATCTCTG
TATTTCTGCGCCTAGCACGGTGCCTAGCACACAGTAGGCGCTCAATAAATGTTGAATGAATGA
ATGATTT

FIGURE 42

MQFHASVPSLMLFLPTGMPSPAPPALSAWQVHLSRSPQRPPPPGRQPLCPSPPGYLCTLSMLL
LWHLSHCILLVYMFVSPSRL

Important features of the protein:

Signal peptide:

amino acids 1-22

Microbodies C-terminal targeting signal.

amino acids 81-83

FIGURE 43

GTTTCCAACAAGGATGATATGAAGACTTCCCTGAAGAAAGTTGTGAAGGGACCTCCTACGAG**A**

TGATGATGCAGTGTGTGTCCCGCATGTTGGCCCACCCCCTGCATGTCATCTCAATGCGCTGCA

TGGTCCAGTTTGTGGGACGGGAGGCCAAGTACAGTGGTGTGCTGAGCTCCATTGGGAAGATTT

TCAAAGAGGAAGGGCTGCTGGGATTCTTCGTTGGATTAATCCCTCACCTCCTGGGCGATGTGG

TTTTCTTGTGGGGCTGTAACCTGCTGGCCCACTTCATCAATGCCTACCTGGTGGATGACAGCT

TCAGCCAGGCCCTGGCCATCCGGAGCTATACCAAGTTCGTGATGGGGATTGCAGTGAGCATGC

TGACCTACCCCTTCCTGCTAGTTGGCGACCTCATGGCTGTGAACAACTGCGGGCTGCAAGCTG

GGCTCCCCCCTTACTCCCCAGTGTTCAAATCCTGGATTCACTGCTGGAAGTACCTGAGTGTGC

AGGGCCAGCTCTTCCGAGGCTCCAGCCTGCTTTTCCGCCGGGTGTCATCAGGATCATGCTTTG

CCCTGGAG**TAA**CCTGAATCATCTAAAAAACACGGTCTCAACCTGGCCACTGTGGGTGAGGCCT

GACCACCTTGGGACACCTGCAAGACGACTCCAACCCAACAACAACCAGATGTGCTCCAGCCCA

GCCGGGCTTCAGTTCCATATTTGCCATGTGTCTGTCCAGATGTGGGGTTGAGCGGGGGTGGGG

CTGCACCCAGTGGATTGGGTCACCCGGCAGACCTAGGGAAGGTGAGGCGAGGTGGGGAGTTGG

CAGAATCCCCATACCTCGCAGATTTGCTGAGTCTGTCTTGTGCAGAGGGCCAGAGAATGGCTT

ATGGGGGCCCAGGTTGGATGGGGAAAGGCTAATGGGGTCAGACCCCACCCCGTCTACCCCTCC

AGTCAGCCCAGCGCCCATCCTGCAGCTCAGCTGGGAGCATCATTCTCCTGCTTTGTACATAGG

GTGTGGTCCCCTGGCACGTGGCCACCATCATGTCTAGGCCTATGCTAGGAGGCAAATGGCCAG

GCTCTGCCTGTGTTTTTCTCAACACTACTTTTCTGATATGAGGGCAGCACCTGCCTCTGAATG

GGAAATCATGCAACTACTCAGAATGTGTCCTCCTCATCTAATGCTCATCTGTTTAATGGTGAT

GCCTCGCGTACAGGATCTGGTTACCTGTGCAGTTGTGAATACCCAGAGGTTGGGCAGATCAGT

GTCTCTAGTCCTACCCAGTTTTAAAGTTCATGGTAAGATTTGACCTCATCTCCCGCAAATAAA

TGTATTGGTGATTTGGAAAAAAAAAAAAAAAA

FIGURE 44

MMMQCVSRMLAHPLHVISMRCMVQFVGREAKYSGVLSSIGKIFKEEGLLGFFVGLIPHLLGDV
VFLWGCNLLAHFINAYLVDDSFSQALAIRSYTKFVMGIAVSMLTYPFLLVGDLMAVNNCGLQA
GLPPYSPVFKSWIHCWKYLSVQGQLFRGSSLLFRRVSSGSCFALE

Important features of the protein:

Signal peptide:

amino acids 1-18

Transmembrane domains:

amino acids 51-72, 97-114

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 160-163

N-myristoylation sites.

amino acids 34-39, 100-105, 123-128, 165-170

FIGURE 45

GCTCACTCTTTGGGTCCACACTGCCTTTATGAGCTGTAACACTCACTGGGAATGTCTGCAGCT
TCACTCCTGAAGCCAGCGAGACCACGAACCCACCAGGAGGAACAAACAACTCCAGACGCGCAG
CCTTAAGAGCTGTAACACTCACCGCGAAGGTCTGCAGCTTCACTCCTGAGCCAGCCAGACCAC
GAACCCACCAGAAGGAAGAAACTCCAAACACATCCGAACATCAGAAGGAGCAAACTCGTGACA
CGCCACCTTTAAGAACCGTGACACTCAACGCTAGGGTCCGCGGCTTCATTCTTGAAGTCAGTG
AGACCAAGAACCCACCAATTCCGGACACGGCAAAGTAACATCCTAGAC**ATG**GCTTTAGAGATC
CACATGTCAGACCCCATGTGCCTCATCGAGAACTTTAATGAGCAGCTGAAGGTTAATCAGGAA
GCTTTGGAGATCCTGTCTGCCATTACGCAACCTGTAGTTGTGGTAGCGATTGTGGGCCTCTAT
CGCACTGGCAAATCCTACCTGATGAACAAGCTGGCTGGGAAGAACAAGGGCTTCTCTGTTGCA
TCTACGGTGCAGTCTCACACCAAGGGAATTTGGATATGGTGTGTGCCTCATCCCAACTGGCCA
AATCACACATTAGTTCTGCTTGACACCGAGGGCCTGGGAGATGTAGAGAAGGCTGACAACAAG
AATGATATCCAGATCTTTGCACTGGCACTCTTACTGAGCAGCACCTTTGTGTACAATACTGTG
AACAAAATTGATCAGGGTGCTATCGACCTACTGCACAATGTGACAGAACTGACAGATCTGCTC
AAGGCAAGAAACTCACCTGACCTTGACAGGGTTGAAGATCCTGCTGACTCTGCGAGCTTCTTC
CCAGACTTAGTGTGGACTCTGAGAGATTTCTGCTTAGGCCTGGAAATAGATGGGCAACTTGTC
ACACCAGATGAATACCTGGAGAATTCCCTAAGGCCAAAGCAAGGTAGTGATCAAAGAGTTCAA
AATTTCAATTTGCCCCGTCTGTGTATACAGAAGTTCTTTCCAAAAAAGAAATGCTTTATCTTT
GACTTACCTGCTCACCAAAAAAAGCTTGCCCAACTTGAAACACTGCCTGATGATGAGCTAGAG
CCTGAATTTGTGCAACAAGTGACAGAATTCTGTTCCTACATCTTTAGCCATTCTATGACCAAG
ACTCTTCCAGGTGGCATCATGGTCAATGGATCTCGTCTAAAGAACCTGGTGCTGACCTATGTC
AATGCCATCAGCAGTGGGGATCTGCCTTGCATAGAGAATGCAGTCCTGGCCTTGGCTCAGAGA
GAGAACTCAGCTGCAGTGCAAAAGGCCATTGCCCACTATGACCAGCAAATGGGCCAGAAAGTG
CAGCTGCCCATGGAAACCCTCCAGGAGCTGCTGGACCTGCACAGGACCAGTGAGAGGGAGGCC
ATTGAAGTCTTCATGAAAAACTCTTTCAAGGATGTAGACCAAAGTTTCCAGAAAGAATTGGAG
ACTCTACTAGATGCAAAACAGAATGACATTTGTAAACGGAACCTGGAAGCATCCTCGGATTAT
TGCTCGGCTTTACTTAAGGATATTTTTGGTCCTCTAGAAGAAGCAGTGAAGCAGGGAATTTAT
TCTAAGCCAGGAGGCCATAATCTCTTCATTCAGAAAACAGAAGAACTGAAGGCAAAGTACTAT
CGGGAGCCTCGGAAAGGAATACAGGCTGAAGAAGTTCTGCAGAAATATTTAAAGTCCAAGGAG
TCTGTGAGTCATGCAATATTACAGACTGACCAGGCTCTCACAGAGACGGAAAAAAAGAAGAAA
GAGGCACAAGTGAAAGCAGAAGCTGAAAAGGCTGAAGCGCAAAGGTTGGCGGCGATTCAAAGG
CAGAACGAGCAAATGATGCAGGAGAGGGAGAGACTCCATCAGGAACAAGTGAGACAAATGGAG
ATAGCCAAACAAAATTGGCTGGCAGAGCAACAGAAAATGCAGGAACAACAGATGCAGGAACAG
GCTGCACAGCTCAGCACAACATTCCAAGCTCAAAATAGAAGCCTTCTCAGTGAGCTCCAGCAC
GCCCAGAGGGCTGTTAATAACGATGATCCATGTGTTTTACTC**TAA**AGTGCTAAATATGGGAGT
TTCCTTTTTTTACTCTTTGTCACTGATGACACAACAGAAAAGAAACTGTAGACCTTGGGACAA
TCAACATTTAAATAAACTTTATAATTATTAAA

FIGURE 46

MALEIHMSDPMCLIENFNEQLKVNQEALEILSAITQPVVVVAIVGLYRTGKSYLMNKLAGKNK
GFSVASTVQSHTKGIWIWCVPHPNWPNHTLVLLDTEGLGDVEKADNKNDIQIFALALLLSSTF
VYNTVNKIDQGAIDLLHNVTELTDLLKARNSPDLDRVEDPADSASFFPDLVWTLRDFCLGLEI
DGQLVTPDEYLENSLRPKQGSDQRVQNFNLPRLCIQKFFPKKKCFIFDLPAHQKKLAQLETLP
DDELEPEFVQQVTEFCSYIFSHSMTKTLPGGIMVNGSRLKNLVLTYVNAISSGDLPCIENAVL
ALAQRENSAAVQKAIAHYDQQMGQKVQLPMETLQELLDLHRTSEREAIEVFMKNSFKDVDQSF
QKELETLLDAKQNDICKRNLEASSDYCSALLKDIFGPLEEAVKQGIYSKPGGHNLFIQKTEEL
KAKYYREPRKGIQAEEVLQKYLKSKESVSHAILQTDQALTETEKKKKEAQVKAEAEKAEAQRL
AAIQRQNEQMMQERERLHQEQVRQMEIAKQNWLAEQQKMQEQQMQEQAAQLSTTFQAQNRSLL
SELQHAQRAVNNDDPCVLL

Important features of the protein:

Transmembrane domains:

amino acids 31-49, 114-131

N-glycosylation sites.

amino acids 90-94, 144-148, 287-291, 563-567

N-myristoylation sites.

amino acids 45-51, 283-289

Prenyl group binding site.

amino acids 583-588

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

amino acids 45-53

FIGURE 47

CACTCATTCATTCCAAAGGGTCTCTCAAGGCAATGGTAATGTGCAAGGAGGTGATACCTAAAT
GAATGACCAAAAGAACATGCTTCTGCTTTTGTGTGTCTCCTACATTTTAGACATTTGTTTGTT
TCTCTTGGTAGCCTTTAAATTCCTTGAAGCCCAGGACCATGTCTCACTTACCTTTGTGTTTCC
ACTAACTAGTCTACCTCCTGGAATTGGCAGATACTCAGTGAAAGCCTGTGAAATAAGTGATGT
CTATTTCTAGCATATTATTCTGAGATTTAATGATAGATTTAGTGATTGAATGAGATTTCCATT
TTCAAATACAGCAAAAGCATAACTATTTTCATTCATTCATATTCATTCAACTTCATTCTCAAA
ATTAGGTCCTGAGTTAACTAATAATTACCTTTGAAATGTGTGGGTTATTTGAGGCAATCAGGT
GGTGACATTGAGCTCTCAGCCAGAGTTTGTTTCTGGAATTGATTCAGTTCCATTGCATTGATT
TTTGTTCTCAGAAGCCAAGGTTTCCCATGAAAAATCATTCCCACTTGAATTGGGCTGTGATTC
TTGCTGCGTTTAAGTAAAGGAAGCCTCTTGGTTCTAGTTCTGCAAACTTACACACTGAACTGG
GACAAGTTTTTGTTTAGAGTAATGGCTGGGAAAAGAGGAACCTTTCATTTTATTCAGAAGTCA
AAAACAAAGGCCTCCCAGCCACCTGGAGATGTTTTGTTGCAGACACCAGCCTGGCTCTGTCTT
TATGCCTAACAATTGAGCATCCAGTCTTCTTTGTGCTGGGACCATTGCTCAGCTCTGCAAGGG
GAAAAGAGGGAGAAAGCCAGAGCTGCCAGGCTTCTTGCACTGGGGCCGGGGGAGGGTTCCTGG
GAAGCAGGTGCTCTCTGGCTTCTTGGTACGTGAGGCTCTCGGAGCTGCCTCTCCTCTGACCCT
CAGGTCCTCACCGAGTTTGCTCCAGGAGTATATTGAAAACATACCCAGTGCTCTCTCAAGCAC
CCACTGCTTAGAGGGCCCAGATTTCTTTTCCTTCTTTCCCTTGCAGAGCTGGAGACTGCATCG
GGCATCTGGTGTTTAAACTAAACAGGAAAACTGACTAAAGGTCCACAGTGCTCATTGTGTAGA
CTAGCTGCCCTCCG**ATG**GGTGCTCTGATTATCAGTGGTTCCAGTGCAGGGCCTGTCACTAAAC
AGGCCTCACTTCCTCCTTGGGGGCTTTCCCATGGGAGGTGTGGCTTTTTACTCTACATGGAAA
TGACTCTCTGCAGCCACAGAACACAGTCATTTTCTGAATTATCCCAGTCTCTCATGCGCCCTG
GATTCCTCCAGATGCCTTATATCTCTTGTGCAAAGTTGTCTAAAATTTGGTTCCCAGCTTCCA
AGCCTTGCCTTTTGGCCTTCCTGGAAGTATTTTTGTTGATGAGTCGTCTGTCATTATTCTCTA
AAATGATTTGCTTTTTGTTTCTTTCATTCCTATTTCCACCCCACATATACACACATGCTTCT**T**
AACTTAGGGGATTACATGCCAATAAATCTATTGTTGAAAATGCACTAATACTATCGCAAAGAC
GAAAATTCACAGGCTGAACCGTTGTAAGTCCATATGCTCCTCAACTTACATGTGTGATGGAGT
TATGCCCAAATAAGTCCATCGTCAAGTTGAAAAATCAAAATCAAGCCATCTTAGGTTGAGGAC
CATTTGTTTGTACCTCCAAAGATGTCATATCTTTAAACATACTCCCTAGCTTTTCTTTTTACT
TTTTATTTTGAAGTAATTATAGAATCACAGAAAGTTGCAAAAAA

FIGURE 48

MGALIISGSSAGPVTKQASLPPWGLSHGRCGFLLYMEMTLCSHRTQSFSELSQSLMRPGFLQM

PYISCAKLSKIWFPASKPCLLAFLEVFLLMSRLSLFSKMICFLFLSFLFPPHIYTHAS

Important features of the protein:

Signal peptide:

amino acids 1-41

Transmembrane domain:

amino acids 88-107

Casein kinase II phosphorylation site.

amino acids 47-50

N-myristoylation site.

amino acids 24-29

FIGURE 49

GGCTTCTACAGTCCACAACACCCACCAGCCCCAGGCCCAGCAGAATGAGCCCAGTGAGTGCCGGGGCTCCCAGTT
TGGCTGTTGCTATGACAACGTGGCCACTGCAGCCGGTCCTCTTGGGGAAGGCTGTGTGGGCCAGCCCAGCCATGC
CTACCCCGTGCGGTGCCTGCTGCCCAGTGCCCATGGCTCTTGTGCAGACTGGGCTGCCCGCTGGTACTTCGTTGC
CTCTGTGGGCCAATGTAACCGCTTCTGGTATGGCGGCTGCCATGGCAATGCCAATAACTTTGCCTCGGAGCAAGA
GTGCATGAGCAGCTGCCAGGGATCTCTCC**ATG**GGCCCCGTCGTCCCCAGCCTGGGGCTTCTGGAAGGAGCACCCA
CACGGATGGTGGCGGCAGCAGTCCTGCAGGCGAGCAGGAACCCAGCCAGCACAGGACAGGGGCCGCGGTGCAGAG
AAAGCCCTGGCCTTCTGGTGGTCTCTGGCGGCAAGACCAACAGCCTGGGCCAGGGGAGGCCCCCCACACCCAGGC
CTTTGGAGAATGGCCATGGGGGCAGGAGCTTGGGTCCAGGGCCCCTGGACTGGGTGGAGATGCCGGATCACCAGC
GCCACCCTTCCACAGCTCCTCCTACAGATCTCACTTCCCACCTCTCCAGGATTAGCTTGGCAGGTGTGGAGCCCT
CGTTGGTGCAGGCAGCCCTGGGGCAGTTGGTGCGGCTCTCCTGCTCAGACGACACTGCCCCGGAATCCCAGGCTG
CCTGGCAGAAAGATGGCCAGCCCATCTCCTCTGACAGGCACAGGCTGCAGTTCGACGGATCCCTGATCATCCACC
CCCTGCAGGCAGAGGACGCGGGCACCTACAGCTGTGGCAGCACCCGGCCAGGCCGCGACTCCCAGAAGATCCAAC
TCCGCATTATAGGGGGTGACATGGCCGTGCTGTCTGAGGCTGAGCTGAGCCGCTTCCCTCAGCCCAGGGACCCAG
CTCAGGACTTTGGCCAAGCGGGGGCTGCTGGGCCCCTGGGGGCCATCCCCTCTTCACACCCACAGCCTGCAAACA
GGCTGCGTTTGGACCAGAACCAGCCCCGGGTGGTGGATGCCAGTCCAGGCCAGCGGATCCGGATGACCTGCCGTG
CCGAAGGCTTCCCGCCCCCAGCCATCGAGTGGCAGAGAGATGGGCAGCCTGTCTCTTCTCCCAGACACCAGCTGC
AGCCTGATGGCTCCCTGGTCATTAGCCGAGTGGCTGTAGAAGATGGCGGCTTCTACACCTGTGTCGCTTTCAATG
GGCAGGACCGAGACCAGCGATGGGTCCAGCTCAGAGTTCTGGGGGAGCTGACAATCTCAGGACTGCCCCCTACTG
TGACAGTGCCAGAGGGTGATACGGCCAGGCTATTGTGTGTGGTAGCAGGAGAAAGTGTGAACATCAGGTGGTCCA
GGAACGGGCTACCTGTGCAGGCTGATGGCCACCGTGTCCACCAGTCCCCAGATGGCACGCTGCTCATTTACAACT
TGCGGGCCAGGGATGAGGGCTCCTACATGTGCAGTGCCTACCAGGGGAGCCAGGCAGTCAGCCGCAGCACCGAGG
TGAAGGTGGTCTCACCAGCACCCACCGCCCAGCCCAGGGACCCTGGCAGGGACTGCGTCGACCAGCCAGAGCTGG
CCAACTGTGATTTGATCCTGCAGGCCCAGCTTTGTGGCAATGAGTATTACTCCAGCTTCTGCTGTGCCAGCTGTT
CACGTTTCCAGCCTCACGCTCAGCCCATCTGGCAG**TAG**GGATGAAGGCTAGTTCCAGCCCCAGTCCAAAATAGTT
CATAGGGCTAGGGAGAAAGGAAGATGGACTCTTGGCTTCCTCTCTCTGGCTGGCAAAGGGAGTTATCTTCTGGAA
TACATTAGCTCTTTCAAAAACCCACCCAGTGTTTAGCCTCAACGGCAGCCAGTTACCAGCTTCTCTCTGTAGCCT
TCAGCAGTGTTTGCATCTCTGACATAACCACAGGCTGCTGTTTTCAAGAAGAGCAATCTGTTTGGATAAGAAAAA
CCTTTACTTTACAGCTTCCCTTTATAATTTGTTACACAGGAATAGTTAAATGCATTTGTTTGTTTGTTTTTTGAG
ACGGAGTTTCACTCTTGTTGCCCAGGCTGGAGGGCAATGGCGCGATCTCAGCTCACTGCAACCTCCGTCTCCTGG
GTTCTTGATTCTCCTGTGTCAGCCTTCTGAGTAGCTGGGATTACAGATGCCTATCACCATGCCTGGGTAATTTTT
GTATTTTTAGTTGAGATGGGGTTTCGCCATGTTGGCCAGGCTGGTCTCGAACTTCTGACCTCAGATGATCTGCCC
GCCTCAGCCTCCCAAAGTGCTGGGATTACAGGCATGAGCCACCACGCCCAGCCATCAATGCATTTTTTTTATTTT
TTTTTTGAGACAGAGTTTCGCACTTCTTGCCCAGGCTGGAGTACAATGGTGCGATCTTGGCTCACTGCAACCTCC
ACCTCCTGGGTTCAAGCGCTTCTCCAGCCTCAGCCTCCTGAGTAGCTGGGATTACAGGTATGTGCCACCATGCCT
GGCTAATTTTGTATTTTTGGTGGAGACGGGGTTTCTCCATGTTGGTCAGACTGGTCTTGAACTCCCGACCTCAGG
TAATCCGCCCGCCTCCGCCTCCCAAAATGCTGGGATTAGAGGTGTGAGCCACTGTGCCCAGCCCATCAATGTGTT
TTAAAGCTAGCTGTCAGGGTTCCACTTAATTTAAAGCTGGGCAGGGAGATGTGTAATGATTTCAAAGTTAACACC
TGTTTGTTTTCTAAAGGGCATGCCAAGTCCTGCTGTATCAGGGAAGTATTCTGTGCTAAAATCAGCGATGGTTCA
TTGCTCTAGTCTCTCTCACCCTTCTAGGCAGTGCATCAGTCAGCTCTAAATCTGGTGCAGAGGGTTAACAGCATA
ACCCTTGTTGGCAAAATGGAATAGATGTTAAGACCTCAAATAGGGATTTGGGATGAAACAGCTGCAGTTAGCACT
GTTATCTGAGCATGAAAGAACTGGAAACGCTCCTTACGTCGAGATGTTGGACCTTGAAGCCCTCCTGAGGCCAAC
ATGCAAATCTGGCTGTGACGGTTCATCTGACACCTGTGTAAAGCTGACCAGCCTGCTCTGTACAGTGACAATGAG
GAGCCCCTCTCTTCCTTAAGTAGGAATCTGTGAAGCAAAATGTTTGCTGCCAAAGACAAATCAGACTGTCAGTCA
TTAAAAACAGCATTAGCAGGATGAGGATAGCAATGGGGAAGGGTTGTGGGCAATGCAGTAACAGGGAAATGGCTT
CAGAAATGGTTTGAGTTGGAAGACAACATTCTTCATCTCTCAGGACTTCTAATTCCTTGATGCTAAAAGAAGAGG
CATGGATTCTATGAGCTTCCAAGTCCCTTTCCACTTTAACCTTCTACAAATCTTTCAGAGGACTGCCTAGTAGCA
AAGGTTATTCCTGGACACAGGAAAGACGGGCATTACAGGGACCAAAGCTCTGAAAGGTGACTTTTATTACCAACA
CACTGGCTGGAAAAGGGACAAACCACATCACGGGTGAGTGATACTTCTCAGTCTTCTCTACTCATTCAACAAAGG
AAATGTGGGCTGGGGCAGAGGTCTTTTTTCATTTAATACTGGAAAAATATTGAAGAGCATCCATGTTCACTTATG
GCTGGTTTTGCTATAGAAATTGGAAAATAAAGGCCACTTTTTTG

FIGURE 50

MGPVVPSLGLLEGAPTRMVAAAVLQASRNPASTGQGPRCRESPGLLVVSGGKTNSLGQGRPPT
PRPLENGHGGRSLGPGPLDWVEMPDHQRHPSTAPPTDLTSHLSRISLAGVEPSLVQAALGQLV
RLSCSDDTAPESQAAWQKDGQPISSDRHRLQFDGSLIIHPLQAEDAGTYSCGSTRPGRDSQKI
QLRIIGGDMAVLSEAELSRFPQPRDPAQDFGQAGAAGPLGAIPSSHPQPANRLRLDQNQPRVV
DASPGQRIRMTCRAEGFPPPAIEWQRDGQPVSSPRHQLQPDGSLVISRVAVEDGGFYTCVAFN
GQDRDQRWVQLRVLGELTISGLPPTVTVPEGDTARLLCVVAGESVNIRWSRNGLPVQADGHRV
HQSPDGTLLIYNLRARDEGSYMCSAYQGSQAVSRSTEVKVVSPAPTAQPRDPGRDCVDQPELA
NCDLILQAQLCGNEYYSSFCCASCSRFQPHAQPIWQ

Important features of the protein:

Signal peptide:

amino acids 1-16

Tyrosine kinase phosphorylation site.

amino acids 392-400

N-myristoylation sites.

amino acids 9-15, 50-56, 112-118, 146-152, 173-179, 195-201, 220-226, 229-235, 280-286, 306-312, 336-342, 397-403

Myelin P0 protein.

amino acids 153-182

FIGURE 51

CAGGCAGAAGCGAACAAAGACCCAGCAAGAGAAGGCAGAGGCTAAGACCCATCCCGTATCTGC

TCTCCTGAAATAATTCTGGAGTC**ATG**CCTGAAATGCCAGAGGACATGGAGCAGGAGGAAGTTA

ACATCCCTAATAGGAGGGTTCTGGTTACTGGTGCCACTGGGCTTCTTGGCAGAGCTGTACACA

AAGAATTTCAGCAGAATAATTGGCATGCAGTTGGCTGTGGTTTCAGAAGAGCAAGACCAAAAT

TTGAACAGGTTAATCTGTTGGATTCTAATGCAGTTCATCACATCATTCATGATTTTCAGCCCC

ATGTTATAGTACATTGTGCAGCAGAGAAGACCAGATGTTGTAGAAAATCAGCCAGATGCTG

CCTCTCAACTTAATGTGGATGCTTCTGGGAATTTAGCAAAGGAAGCAGCTGCTGTTGGAGCAT

TTCTCATCTACATTAGCTCAGATTATGTATTTGATGGAACAAATCCACCTTACAGAGAGGAAG

ACATACCAGCTCCCCTAAATTTGTATGGCAAAACAAAATTAGATGGAGAAAAGGCTGTCCTGG

AGAACAATCTAGGAGCTGCTGTTTTGAGGATTCCTATTCTGTATGGGGAAGTTGAAAAGCTCG

AAGAAAGTGCTGTGACTGTTATGTTTGATAAAGTGCAGTTCAGCAACAAGTCAGCAAACATGG

ATCACTGGCAGCAGAGGTTCCCCACACATGTCAAAGATGTGGCCACTGTGTGCCGGCAGCTAG

CAGAGAAGAGAATGCTGGATCCATCAATTAAGGGAACCTTTCACTGGTCTGGCAATGAACAGA

TGACTAAGTATGAAATGGCATGTGCAATTGCAGATGCCTTCAACCTCCCCAGCAGTCACTTAA

GACCTATTACTGACAGCCCTGTCCTAGGAGCACAACGTCCGAGAAATGCTCAGCTTGACTGCT

CCAAATTGGAGACCTTGGGCATTGGCCAACGAACACCATTTCGAATTGGAATCAAAGAATCAC

TTTGGCCTTTCCTCATTGACAAGAGATGGAGACAAACGGTCTTTCAT**TAG**TTTATTTGTGTTG

GGTTCTTTTTTTTTTTAAATGAAAAGTATAGTATGTGGCACTTTTTAAAGAACAAAGGAAATA

GTTTTGTATGAGTACTTTAATTGTGACTCTTAGGATCTTTCAGGTAAATGATGCTCTTGCACT

AGTGAAATTGTCTAAAGAAACTAAAGGGCAGTCATGCCCTGTTTGCAGTAATTTTTCTTTTTA

TCATTTTGTTTGTCCTGGCTAAACTTGGAGTTTGAGTATAGTAAATTATGATCCTTAAATATT

TGAGAGTCAGGATGAAGCAGATCTGCTGTAGACTTTTCAGATGAAATTGTTCATTCTCGTAAC

CTCCATATTTTCAGGATTTTTGAAGCTGTTGACCTTTTCATGTTGATTATTTTAAATTGTGTG

AAATAGTATAAAAATCATTGGTGTTCATTATTTGCTTTGCCTGAGCTCAGATCAAAATGTTTG

AAGAAAGGAACTTTATTTTTGCAAGTTACGTACAGTTTTTATGCTTGAGATATTTCAACATGT

TATGTATATTGGAACTTCTACAGCTTGATGCCTCCTGCTTTTATAGCAGTTTATGGGGAGCAC

TTGAAAGAGCGTGTGTACATGTATTTTTTTTCTAGGCAAACATTGAATGCAAACGTGTATTTT

TTTAATATAAATATATAACTGTCCTTTTCATCCCATGTTGCCGCTAAGTGATATTTCATATGT

GTGGTTATACTCATAATAATGGGCCTTGTAAGTCTTTTCACCATTCATGAATAATAATAAATA

TGTACTGCTGGCATGTAATGCTTAGTTTTCTTGTATTTACTTCTTTTTTTTAAATGTAAGGACC

AAACTTCTAAACTAATTGTTCTTTTGTTGCTTTAATTTTTAAAAATTACATTCTTCTGATGTA

ACATGTGATACATACAAAAGAATATAGTTTAATATGTATTGAAATAAAACACAATAAAATT

FIGURE 52

MPEMPEDMEQEEVNIPNRRVLVTGATGLLGRAVHKEFQQNNWHAVGCGFRRARPKFEQVNLLD
SNAVHHIIHDFQPHVIVHCAAERRPDVVENQPDAASQLNVDASGNLAKEAAAVGAFLIYISSD
YVFDGTNPPYREEDIPAPLNLYGKTKLDGEKAVLENNLGAAVLRIPILYGEVEKLEESAVTVM
FDKVQFSNKSANMDHWQQRFPTHVKDVATVCRQLAEKRMLDPSIKGTFHWSGNEQMTKYEMAC
AIADAFNLPSSHLRPITDSPVLGAQRPRNAQLDCSKLETLGIGQRTPFRIGIKESLWPFLIDK
RWRQTVFH

Signal peptide:

amino acids 1-30

Transmembrane domain:

amino acids 105-127

N-glycosylation site.

amino acids 197-201

N-myristoylation site.

amino acids 303-309

Short-chain dehydrogenases/reductases family proteins.

amino acids 18-30

FIGURE 53

TGGGCTCCCTCCAGCACTGCTGTTGCCTGCTGCCTAAGATGGGTGACACTTGGGCCCAGCTTCCCTGGCCTGGGC
CACCCCACCCAGCA**ATG**CTGCTGATCTCCCTCCTCTTGGCAGCCGGGTTGATGCACTCGGATGCCGGCACCAGCT
GCCCCGTCCTTTGCACATGCCGTAACCAGGTGGTGGATTGTAGCAGCCAGCGGCTATTCTCCGTGCCCCCAGACC
TGCCAATGGACACCCGAAACCTCAGCCTGGCCCACAACCGCATCACAGCAGTGCCGCCTGGCTACCTCACATGCT
ACATGGAGCTCCAGGTGCTGGATTTGCACAACAACTCCTTAATGGAGCTGCCCCGGGGCCTCTTCCTCCATGCCA
AGCGCTTGGCACACTTGGACCTGAGCTACAACAATTTCAGCCATGTGCCAGCCGACATGTTCCAGGAGGCCCATG
GGCTAGTCCACATCGACCTGAGCCACAACCCCTGGCTGCGGAGGGTGCATCCCCAGGCCTTTCAGGGCCTCATGC
AGCTCCGAGACCTGGACCTCAGTTATGGGGGCCTGGCCTTCCTCAGCCTGGAGGCTCTTGAGGGCCTACCGGGGC
TGGTGACCCTGCAGATCGGTGGCAATCCCTGGGTGTGTGGCTGCACCATGGAACCCCTGCTGAAGTGGCTGCGAA
ACCGGATCCAGCGCTGTACAGCAGATTCTCAGCTGGCTGAGTGCCGGGGCCCTCCTGAAGTCGAGGGCGCCCCGC
TCTTCTCACTCACTGAGGAGAGCTTCAAGGCCTGCCACCTGACCCTGACCCTGGATGATTACCTATTCATTGCGT
TCGTGGGCTTCGTGGTCTCCATTGCTTCTGTGGCCACCAACTTCCTCCTGGGCATCACTGCCAACTGCTGCCACC
GCTGGAGCAAGGCCAGTGAAGAGGAAGAGATC**TGA**CATGCCTGCCTCTCATCCCTCCATGCTGCTGACCGCCACA
GCTGCTGGCCACCAGACGCCCTCCCTGATTGCTCACTCTGGTTCCATGGTGACCTGGCTGCCTCAGTCATGGTTC
AAGCAAGGTGGGGACACTCATTTTGTATGAGCATCTGCTTTGGGCCAGGCGGCACGCTAGGAATTGGGAACATCA
GATGAACTGACTCAGTCCCTGCCCTCAAGGCACTTCCCTCTGGTCAAGGAGAGAGATCCAAAAACTATTCCCTTT
AAGACTATATGTCAGGACTCTGAGCACGTCATTATGGAGGCCCAGAGGAGGAGCCATCATCTGTATCTAGCAATG
TCCATGAGAATTATAAGATTAGAGTGATTTGTGAACTGGGTCATCAGGAAATATCTACTTTGTCAGGTAGGCAAA
GAAGGGTGTCTGCACATGGCAGAGGCCAGAATATGCATAGTGTGCTGTGTTGAGAAGAGTGAACAGTTCCTGGTC
ACTTACTTGTATAGAGGGGGTGTGGCACAGAACTCAAACCTACCCCTCACCTCCTGACACCAAAACTGTCAGCTC
TCAGCAATGCCAGCCACTGCCTACAGGGAGTAAGAACACCTCTATGACAGCCCCTGGCCTCCTTCCACCAGCAGC
TACCAGGTGAGACCACCTCCCAGTGACTGCCCCCATATGACCAAATGTCACCAGTTGGTGAGGTCCCAGGCAGCA
GGCTGAGGATGGACACTTTCAATGCCCTTGCTCCTGCCTCTCACTCAAGTTTTGCTTCAGAAGAGAGAGGCAGGA
GGCCCAGCAACTGGGGCAGCAAGAGTCCTGGCACCTTGGGATCCTAATCATGTGACTGTTCTTGCCACAGTGCTC
ATGCCACAGGGTCTCACCAGGAAAGTGCACTGTGGGCCACAGACCCACAGCCTGGCAGCACCCAGAGCTAAAAGG
GGACAAAGGCAGCACAGTTATGACCATATGAGGCTTTGCATTTTCTTCTAAGCAACTTACCCACGTTAAGCATGA
GGGTGAGAGAGCTATTAAATACTAAGCCCTTGCCAGTGTCAGGTACTTTGAAAAGCTCTCTGCACAAACCATTCC
CTTTGACACACACACACACAAATCTTTTGAGGTGAACGCTGTTGTTCCCATTTTACGGATGAGGCAACTAAGGCT
CAGAGAGGTTAAAGTCACATGCCACTATGAGCAAGATAAAGTCTGTGCTCTTTCTACTGCCCCATCCAAGTTGGG
GAACATCACCATTCCCTCTAGAGTTATATAAATTCAAATTCAACTAGAGCTGACAAAGTTCCTCATAAGGTCCAG
GCACTCCTCTGGGCACTTTTATATCTATTGACTCACTTCTTTCAATTCTCACAGCAACACTGCCTGGTGGTTTTT
ATTATCCCCATTTGACAGATGAATTAATCGTAGAGAGTTGAGTGACTTACCCAAGGTTGTCTGGATAAGCCCTAG
AAGGAAGGCGGTAGGCAGCTCCATTCAGGGAAACTGCATCTAATCAGTCAGTCAAAAATCAAGTAACTTTACGAG
CAAAGCACAATTATCATCATCGTGGTCTTCTTCATCAGTTTCGTCAGCAGCATCATTATCTTCCCTCTATTTGTT
CAGCACCGGATAGTTCATGAGTATTTTTGCATCATTCTCCTTGACTTTTCACATCCCTGTGCAGGAGGTAAATCA
AACATCAGTAATCCTGTTTTACAGATGGGGAAAAAAGTCTCAAGGTTGGATATGACTTGCTATGTGGCAAGGTTG
GGGCTCAACCCTAACACAGTTCTCTTTCCAGTGCTTTCTCAAGTGCTTGGGGAAGAGAATGCCTCAGAAGGCTGG
GTAGTGGGGCCCTGGAATTCAGCATCCATGAATGTGCTAGTGGATAAGCTAAATAGAAGGCAGCCAAACCCATCT
GCTGTACAGATTGAACTATGCTCACGGTAGGGCAAATTGCAGGCTCTGAAACAGAGACTACACAGGTAACACCTG
AATAGGAGACTCCTGCTTTACAATGTGTAGATAAAACATCAGCAATGGTGGCCATGGTGGCAGTCATGTGAAAAG
TAAGATCTTTGGGAATCAAGAAAGGAAGCTGTGTTAACCACTCCTGCTCAAGCCCTGCTGCGTGTGTTGCAAGAG
ATACTAAGAGAGCAAGAAAGCTATAGGTGAGAACCTCTGCAGTTTAGGAGAAGAACATCAAGGCACAGTCCAACA
TGCTGATAAGTCTGGCCAGGAGGAGAATTAAAACAGGGGCTTTCCACACCTCCCTTGCCCCAAGCTCCAGCGGTA
TTCTATCAGCCCATCCTCCTGGAAAGCCTGAAAGGAATGAAGGAGGCTAATAAGTCATCTTCCAGGAAGGCATCC
CTCACTCGTGCTTCCCTGAGCTAGTCAACCAAAAGAGTCTTCAGAAACTTTGCTAGACCTGAAGTACTTGAACCT
GTGTCCCCTGAATCTTTCTTACAACATCTGGGACAAATCCCTGGTCCTGTGACATCCGAAGCAGAACTGTGCCCT
GCTCTCTCCTTCTGTGATGACCAAGGATGGTGAACTCAAGTTGTTCTCTACAAGCCAGGCCAGCAACCTAAATAC
TTGGAGAGGAACTTTTAGAAACTATAATCCTGACAAAATAGAAAAGTTTCCCATAGGGGCATACCATAATACTAT
AATAACCTCCCAGGAACTATTGTTTGCCAAAATGTAGTTAATATATTTTAAGATATATGCTTTTTTGCATAGGAC
TAGAACCAGAAAAGACACCAAATGCCCCCTTGACATCAATGTCCTTTCTAGTGGGACAATTTGGTCTCCATTAAT
GCCAAACCTTTCTGAACAGGATACATGGCTTTTAAAGGACAGATGTTTCTCCTGCTGCTAGAAGTTCCTCAGTTT
ACTAGAGCACAATGAGGAAAGTATTCAACCTCCCTACTGCCAAGGAATTCCCTGCTTCTCCCCCACCGCCATCAT
CTTGTCCAAGCTATCAGAAGCAACCTTCTAGAGATAATCTAACAATCCTGATTAGAATTGCTCCCATATCCCTGG
TGACCACAGGCTTCATTCAAATTGTCCAAACTGGTTAACATGTATGTGATGGGGTATCTCTGCATCTGTATGTCT
GTCTGCGAGGTTCCTTGTATATTGGCTGTCCGCTGACTTGGGACAGATCTCTCTAGAACTTGGGTTCAGTTCTCT
GACATAGTCCACTCAGCCATAGGCTGAGTGGCTAAATATGCATAAATAAGCATGCCTAAATAGGCATATATAGGT
TGGTGCAAAAGTAATTGCGGTTTTTGCCATTAAAAATGATGGCAAAAATCCCAATTACTTTTGCGTCAATCTAAT
ATTACATTGCTTGATAGATTAAGATGGAATCCCACCAGGTTTAGGGTAGGACTGGATGCTCAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAA

FIGURE 54

MLLISLLLAAGLMHSDAGTSCPVLCTCRNQVVDCSSQRLFSVPPDLPMDTRNLSLAHNRITAV
PPGYLTCYMELQVLDLHNNSLMELPRGLFLHAKRLAHLDLSYNNFSHVPADMFQEAHGLVHID
LSHNPWLRRVHPQAFQGLMQLRDLDLSYGGLAFLSLEALEGLPGLVTLQIGGNPWVCGCTMEP
LLKWLRNRIQRCTADSQLAECRGPPEVEGAPLFSLTEESFKACHLTLTLDDYLFIAFVGFVVS
IASVATNFLLGITANCCHRWSKASEEEEI

Important features of the protein:

Signal peptide:

amino acids 1-17

Transmembrane domain:

amino acids 241-260

N-glycosylation sites.

amino acids 52-55, 81-84, 107-110

Tyrosine kinase phosphorylation site.

amino acids 148-154

N-myristoylation sites.

amino acids 11-15, 263-268

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 175-185

Leucine zipper pattern.

amino acids 77-98

FIGURE 55

GGCTGCGCCCAGGCCGGCGGGCCCAGCAGCTGCGAACCGCCGGCGCACCACCTGTTTCCGCGC
CCGGGGACTTCCCCGGCGGGGCTCAGAAGTGTGGGGTCGGTCGCTTGGCTTCCCCTGGCGTCA
GCGACCCAGGGTAACCTCCTCCACTGCTGCGTGCCGTGCAGGCCTGCCTGTGTGAGAGCCACG
TGTGCCGCGCTCTGGGCACAGCCTTGGAAAGTCAGGACCGCGACGGCAGCAGAGCAGAAACCT
TACAGAAACATGAAGCCCTCAACCATCTGCTACTCAGTTATTCGGGGCTGACGGCGGCTTCTA
GAACATCCAGGTGTTCTGCAGATGCGAGAACTCATCCTGTAGTCACCAGATGGAGTCCCAAAC
AGCCAAGCAGATGTAAGGCCTGTGCTGTGGCTCTGAGGCCCTGAATACAGAAGGGTCACTTTC
TTAGTGGCCAAAGAGCAGTTGTTGACATTGATGTCTAATTATTGAACACGACCAGTCATTTTA
CTGAGCTGCAGTGAGGAAACACTGACCATAGAAGATCAAGCCAAATGAGGGATTGCAAATTTC
CTGATTCTTTTGAATTAGGATTCCAGATGGGGGCCTCATTTCTACAGCCCCCAACATTCCTAT
AGCCGTTATCACTGCCATCACCACTGCCACCAGCATCTTCTTGCAGATTCCACCCCTGCTCCC
CAGAGACTTCCTGCTTTGAAAGTGAGCAGAAAGGAAGCTCTCAGAAAAATCTCTAGTGGTGGC
TGCCGTCGCTCCAGACAATCGGAATCCTGCCTTCACCACC**ATG**GGCTGGCTTTTTCTAAAGGT
TTTGTTGGCGGGAGTGAGTTTCTCAGGATTTCTTTATCCTCTTGTGGATTTTTGCATCAGTGG
GAAAACAAGAGGACAGAAGCCAAACTTTGTGATTATTTTGGCCGATGACATGGGGTGGGGTGA
CCTGGGAGCAAACTGGGCAGAAACAAAGGACACTGCCAACCTTGATAAGATGGCTTCGGAGGG
AATGAGGTTTGTGGATTTCCATGCAGCTGCCTCCACCTGCTCACCCTCCCGGGCTTCCTTGCT
CACCGGCCGGCTTGGCCTTCGCAATGGAGTCACACGCAACTTTGCAGTCACTTCTGTGGGAGG
CCTTCCGCTCAACGAGACCACCTTGGCAGAGGTGCTGCAGCAGGCGGGTTACGTCACTGGGAT
AATAGGCAAATGGCATCTTGGACACCACGGCTCTTATCACCCCAACTTCCGTGGTTTTGATTA
CTACTTTGGAATCCCATATAGCCATGATATGGGCTGTACTGATACTCCAGGCTACAACCACCC
TCCTTGTCCAGCGTGTCCACAGGGTGATGGACCATCAAGGAACCTTCAAAGAGACTGTTACAC
TGACGTGGCCCTCCCTCTTTATGAAAACCTCAACATTGTGGAGCAGCCGGTGAACTTGAGCAG
CCTTGCCCAGAAGTATGCTGAGAAAGCAACCCAGTTCATCCAGCGTGCAAGCACCAGCGGGAG
GCCCTTCCTGCTCTATGTGGCTCTGGCCCACATGCACGTGCCCTTACCTGTGACTCAGCTACC
AGCAGCGCCACGGGGCAGAAGCCTGTATGGTGCAGGGCTCTGGGAGATGGACAGTCTGGTGGG
CCAGATCAAGGACAAAGTTGACCACACAGTGAAGGAAAACACATTCCTCTGGTTTACAGGAGA
CAATGGCCCGTGGGCTCAGAAGTGTGAGCTAGCGGGCAGTGTGGGTCCCTTCACTGGATTTTG
GCAAACTCGTCAAGGGGGAAGTCCAGCCAAGCAGACGACCTGGGAAGGAGGGCACCGGGTCCC
AGCACTGGCTTACTGGCCTGGCAGAGTTCCAGTTAATGTCACCAGCACTGCCTTGTTAAGCGT
GCTGGACATTTTTCCAACTGTGGTAGCCCTGGCCCAGGCCAGCTTACCTCAAGGACGGCGCTT
TGATGGTGTGGACGTCTCCGAGGTGCTCTTTGGCCGGTCACAGCCTGGGCACAGGGTGCTGTT
CCACCCCAACAGCGGGGCAGCTGGAGAGTTTGGAGCCCTGCAGACTGTCCGCCTGGAGCGTTA
CAAGGCCTTCTACATTACCGGTGGAGCCAGGGCGTGTGATGGGAGCATGGTGCCTGAGCTGCA
GCATAAGTTTCCTCTGATTTTCAACCTGGAAGACGATACCGCAGAAGCTGTGCCCCTAGAAAG
AGGTGGTGCGGAGTACCAGGCTGTGCTGCCCGAGGTCAGAAAGGTTCTTGCAGACGTCCTCCA
AGACATTGCCAACGACAACATCTCCAGCGCAGATTACACTCAGGACCCTTCAGTAACTCCCTG
CTGTAATCCCTACCAAATTGCCTGCCGCTGTCAAGCCGCA**TAA**CAGACCAATTTTTATTCCAC
GAGGAGGAGTACCTGGAAATTAGGCAAGTTTGCTTCCAAATTTCATTTTTACCCTCTTTACAA
ACACACGCTTTAGTTTAGTCTTGGAGTTTAGTTTTGGAGTTAGCCTTGCATATCCCTTCTGTA
TCCTGTCCCCCCTCCACGCCGACCCGAGAGCAGCTGAGCTGCGCTGGCTCTGGGCAGGGAGTG
TGCCTTAATGGGAAGCACACGGGCTTTGGAGTCAGGCACAGGTGCCAGCTCCAGCTTTTGAAC
TTGGGCAATTGTTTAACCTAACCTGCAAGTTGATTTTGAGGGTTAAATAAAGGCATACATGAA
AATGCCTGGCAACTTTAAAAAAAAAAAA

FIGURE 56

MGWLFLKVLLAGVSFSGFLYPLVDFCISGKTRGQKPNFVIILADDMGWGDLGANWAETKDTAN
LDKMASEGMRFVDFHAAASTCSPSRASLLTGRLGLRNGVTRNFAVTSVGGLPLNETTLAEVLQ
QAGYVTGIIGKWHLGHHGSYHPNFRGFDYYFGIPYSHDMGCTDTPGYNHPPCPACPQGDGPSR
NLQRDCYTDVALPLYENLNIVEQPVNLSSLAQKYAEKATQFIQRASTSGRPFLLYVALAHMHV
PLPVTQLPAAPRGRSLYGAGLWEMDSLVGQIKDKVDHTVKENTFLWFTGDNGPWAQKCELAGS
VGPFTGFWQTRQGGSPAKQTTWEGGHRVPALAYWPGRVPVNVTSTALLSVLDIFPTVVALAQA
SLPQGRRFDGVDVSEVLFGRSQPGHRVLFHPNSGAAGEFGALQTVRLERYKAFYITGGARACD
GSMVPELQHKFPLIFNLEDDTAEAVPLERGGAEYQAVLPEVRKVLADVLQDIANDNISSADYT
QDPSVTPCCNPYQIACRCQAA

Important features of the protein:

Signal peptide:

amino acids 1-16

Transmembrane domain:

amino acids 353-373

N-glycosylation sites.

amino acids 117-120, 215-218, 356-359, 397-500

N-myristoylation sites.

amino acids 12-17, 33-38, 52-57, 97-102, 101-106, 113-118, 158-163, 328-333, 388-393, 418-423, 435-440, 436-441

Amidation site.

amino acids 382-385

Sulfatases signature 2.

amino acids 129-138

FIGURE 57

TGGACAAGACACCTCCAGGAGCCCAGCTCACAGCCACCGGTACCTTCTTCCAGGACAAGCTGG
GGGCCTCCATGGGCGCCTGAGGGCCAGGCGCCAGGGCCGTGGGCACGAGT**ATG**GTGAGACACC
AGCCCCTGCAGTACTACGAGCCACAGCTGTGCCTCTCCTGCCTCACGGGCATCTACGGCTGCC
GTTGGAAGCGCTACCAGCGCTCCCATGATGATACCACACCGGGCACAGCGCCATTCCTGCATG
TGGGGGCTGTGGCAGCAGTCACCATGCTCTCCTGGATCGTGGCAGGACAGTTCGCCCGTGCAG
AGCGGACCTCCTCCCAGGTGACCATTCTCTGTACCTTCTTCACCGTGGTGTTTGCCCTCTACC
TGGCCCCTCTCACCATCTCCTCTCCCTGCATCATGGAGAAGAAAGACCTCGGCCCCAAGCCTG
CTCTCATTGGCCACCGCGGGGCCCCCATGCTGGCTCCAGAGCACACGCTCATGTCCTTCCGGA
AGGCCCTCGAGCAGAAGCTGTACGGGCTCCAGGCTGACATTACCATCAGCCTGGACGGCGTGC
CCTTCCTCATGCATGACACCACCCTGCGGCGCACCACCAACGTGGAGGAGGAGTTCCCGGAGC
TGGCCCGCAGGCCTGCCTCCATGCTTAACTGGACCACCCTGCAGAGACTCAACGCTGGCCAGT
GGTTCCTGAAGACTGACCCCTTCTGGACAGCCAGCTCCCTGTCACCCTCCGACCACAGAGAGG
CCCAGAACCAGTCCATCTGCAGCCTGGCAGAGCTCCTGGAGCTGGCCAAGGGCAATGCCACAC
TGCTGCTCAACCTGCGTGACCCGCCCCGGGAGCACCCCTACCGCAGCAGTTTTATCAACGTGA
CTCTGGAGGCCGTGCTGCACTCCGGCTTCCCCCAGCACCAGGTCATGTGGCTGCCTAGCAGGC
AGAGGCCCCTGGTGCGGAAGGTGGCTCCCGGCTTCCAACAGACATCAGGCTCCAAGGAGGCAG
TCGCCAGCCTGCGGAGAGGCCACATCCAGCGGCTGAACCTGCGCTACACTCAGGTGTCCCGCC
AGGAGCTCAGGGACTACGCGTCCTGGAACCTGAGTGTGAACCTCTACACAGTCAACGCACCGT
GGCTCTTCTCCCTGCTGTGGTGTGCGGGGGTCCCATCCGTCACCTCTGACAACTCCCACACCC
TGTCCCAGGTGCCTTCCCCCCTCTGGATCATGCCCCCGGACGAGTACTGTCTCATGTGGGTCA
CTGCCGACCTGGTCTCCTTCACCCTCATCGTGGGCATCTTCGTGCTCCAGAAGTGGCGCCTGG
GTGGCATACGGAGCTACAACCCTGAGCAGATCATGCTGAGTGCTGCGGTGCGCCGGACCAGCC
GGGACGTCAGCATCATGAAGGAGAAGCTTATTTTCTCAGAGATCAGCGATGGTGTAGAGGTCT
CCGATGTGCTCTCCGTATGTTCAGACAACAGTTATGACACATATGCCAACAGCACCGCCACCC
CTGTGGGCCCCCGAGGGGGTGGCAGCCACACCAAGACCCTCATAGAGCGGAGTGGGCGT**TAG**C
TGAAGACATGTCTGTCCCACCTGTACCTGACACAGAAGCTGGGGAGCCTAGGAGAGCTGGTGG
AAGTGTGTCTGAACTCGGAGTGCTCTGGGAGCGGGCTCCACAGCCTCCTTGTGGGCTCCAGCC
CCTTGTCAGCCGCAGCCTCTCTTGAGGGGACTCCCTGTCTCCTGAGGCCCAGCTGGGCCAGG
ACTCCATCCTTTCAGATGCCCCTGCAGGCCTGGGGCTCCTTCTGGGAAGTATGGGGCCTAGGG
CTTGGTCCCCCTCTTCTGAGGCCCTCTCCTGTATCCCGACCTGGAAGCTTTGATGGGTCATGG
GCCATGCCATACCCCCTGTGGCAATGGAGTGTGTGGATGCTCACCTGTGCCATCTGTCCTCCT
GTCTGTGCCAGGAGGCACCTGAGTTCTCTGCTGTTATCCTGCCCCAAGGGCCTGGGCCGAGCC
TCTACCTGAAGCAACTCTGCTCTTCCTGTCAGTCTCAAAGCACAAGGAGGTTCAGCCCAGGAG
GAAGCCAGCTGCAATGTGGAGACACGTCCTCCTCCCCAACCCACCTCATGCCACCGCCAACCC
CCTGCCCCAGGAGCGGGCCTGAGCCACGTCCCCTAGGAGCAGCTGGAGATGGCCAAAAGAGTG
AGCTCAGGACTACTGGATCCCATGCCCAGGTGTCCAGCAGACCTCAAGGCAGAAGGGTCACCT
AACCCAGGAGTCCACAGACTGATGTGACCTCAGGTTCCCACATCAGTGGCCACAGGGCAGGGC
CCACCTGGTAGAAGTGTTCTGGATATGGCCAGGGTGGGTGTGTGGCTAAGTGGGCCTGAACAG
AGGGAACCTAGGGCCCTTGGCCAATGTGATTAAAGCTGCCATCTTGAAA

FIGURE 58

MVRHQPLQYYEPQLCLSCLTGIYGCRWKRYQRSHDDTTPGTAPFLHVGAVAAVTMLSWIVAGQ
FARAERTSSQVTILCTFFTVVFALYLAPLTISSPCIMEKKDLGPKPALIGHRGAPMLAPEHTL
MSFRKALEQKLYGLQADITISLDGVPFLMHDTTLRRTTNVEEEFPELARRPASMLNWTTLQRL
NAGQWFLKTDPFWTASSLSPSDHREAQNQSICSLAELLELAKGNATLLLNLRDPPREHPYRSS
FINVTLEAVLHSGFPQHQVMWLPSRQRPLVRKVAPGFQQTSGSKEAVASLRRGHIQRLNLRYT
QVSRQELRDYASWNLSVNLYTVNAPWLFSLLWCAGVPSVTSDNSHTLSQVPSPLWIMPPDEYC
LMWVTADLVSFTLIVGIFVLQKWRLGGIRSYNPEQIMLSAAVRRTSRDVSIMKEKLIFSEISD
GVEVSDVLSVCSDNSYDTYANSTATPVGPRGGGSHTKTLIERSGR

Important features of the protein:

Signal peptide:

amino acids 1-24

Transmembrane domains:

amino acids 47-61, 77-93, 335-350, 380-399

N-glycosylation sites.

amino acids 182-186, 217-221, 233-237, 255-259, 329-333, 462-466

Tyrosine kinase phosphorylation site.

amino acids 130-139

N-myristoylation sites.

amino acids 21-27, 48-54, 294-300, 404-410, 442-448, 473-479

FIGURE 59

CCTGAGCAAACACAGCAGCCCGAGTGTTCCCAAGGCCAAA**ATG**CTGAGAACGTCCACTCCTAA
TCTGTGTGGTGGTCTGCATTGCCGGGCCCCCTGGCTCTCTTCTGGCATTCTCTGCCTCTGCCT
CATATTCTTGTTAGGCCAGGTGGGCTTGCTGCAGGGACACCCCCAGTGCCTGGATTACGGGCC
CCCTTTCCAGCCCCCTCTGCACCTTGAGTTTTGCTCTGACTATGAGTCCTTCGGCTGCTGTGA
TCAGCACAAGGACCGCCGCATCGCTGCCCGGTACTGGGACATCATGGAATATTTTGATCTGAA
GAGACATGAGCTGTGTGGAGATTACATTAAAGACATCCTTTGCCAGGAGTGCTCGCCCTACGC
AGCCCACCTCTACGACGCCGAAAACACCCAGACGCCTCTCCGGAATCTCCCGGGCCTCTGCTC
TGATTACTGCTCTGCCTTCCATTCTAACTGTCACTCAGCCATTTCCCTGCTGACCAATGACCG
CGGCCTCCAGGAGTCTCATGGAAGGGACGGTACCCGCTTCTGCCACCTCCTGGACCTTCCTGA
CAAGGACTATTGCTTCCCTAATGTCCTGAGGAACGACTATCTCAACCGCCACCTGGGCATGGT
GGCCCAAGATCCTCAGGGCTGCCTGCAGCTCTGCCTGAGCGAGGTGGCCAACGGGCTGAGGAA
CCCCGTCTCCATGGTCCATGCTGGGGACGGCACCCATCGCTTCTTTGTTGCCGAGCAGGTAGG
AGTGGTGTGGGTCTACCTCCCTGATGGGAGTCGCCTGGAGCAACCCTTCCTGGACCTCAAGAA
CATCGTGTTGACCACCCCATGGATCGGGGATGAGAGAGGCTTCTTGGGGTTGGCTTTTCACCC
CAAATTCCGCCACAATCGCAAGTTCTATATTTATTATTCGTGCCTGGACAAGAAGAAGGTAGA
AAAGATCCGAATTAGTGAGATGAAGGTTTCTCGGGCTGATCCTAACAAAGCTGACCTGAAATC
AGAGAGGGTCATCTTGGAGATTGAAGAACCAGCCTCAAACCATAATGGCGGACAACTTCTTTT
TGGCCTGGATGGCTATATGTACATATTCACTGGGGACGGGGGACAGGCTGGAGATCCCTTTGG
CCTGTTTGGAAATGCTCAGAACAAAAGTTCCCTGCTGGGAAAAGTTTTAAGGATCGATGTGAA
CAGGGCAGGCTCACATGGCAAGCGGTACCGAGTCCCCTCGGACAATCCATTTGTTTCTGAGCC
AGGGGCCCACCCCGCCATCTATGCCTATGGGATCAGGAACATGTGGCGTTGTGCTGTGGACCG
AGGGGACCCCATCACGCGCCAGGGCCGAGGCCGGATATTCTGTGGGGACGTGGGCCAGAACAG
GTTTGAAGAGGTTGACCTCATTTTGAAAGGTGGAAACTATGGCTGGAGAGCAAAGGAAGGGTT
TGCATGTTATGACAAAAAACTTTGTCACAATGCCTCTTTGGATGATGTTCTGCCAATCTATGC
TTATGGCCATGCAGTGGGGAAGTCAGTCACTGGAGGTTATGTCTATCGTGGTTGTGAATCCCC
AAATCTCAATGGCCTGTATATCTTTGGAGACTTCATGAGTGGTCGACTTATGGCTTTGCAGGA
AGATAGAAAAAACAAGAAATGGAAGAAGCAGGATCTTTGCCTGGGCAGCACCACGTCCTGTGC
CTTCCCAGGGCTGATCAGCACCCATAGCAAGTTCATCATCTCCTTTGCTGAAGATGAAGCAGG
GGAGCTGTATTTCCTGGCGACCTCTTACCCAAGTGCCTATGCACCACGTGGATCTATTTACAA
GTTTGTTGACCCCTCAAGGCGAGCACCCCCAGGCAAGTGCAAATACAAGCCAGTGCCCGTGAG
AACCAAGAGTAAGCGGATCCCGTTCAGACCACTCGCCAAGACAGTCTTGGACTTGCTAAAGGA
ACAATCAGAGAAAGCTGCTAGAAAATCTTCCAGTGCAACCTTAGCTTCTGGCCCAGCCCAGGG
TTTGTCTGAGAAAGGCTCCTCCAAGAAGCTGGCTTCTCCTACAAGCAGCAAGAATACATTGCG
AGGGCCTGGTACAAAGAAGAAAGCCAGAGTGGGGCCCCACGTCCGCCAGGGCAAGAGGAGGAA
GAGCCTGAAAAGCCACAGTGGCAGGATGAGGCCATCAGCAGAGCAGAAGCGAGCTGGCAGAAG
TCTCCCT**TGA**CCTATTGGTCAAGGTGGCCGACAGGGTGACGTGAGAGAGGAGAGCCACCTCAT
CAAATGAAAGTCACTGCTGAATAAAGACCTTAGAAGTCTGGGAAGCCAGGGTAGAGGTGGGGC
AGGGCGGTTTTCCTCTCCCTGGGAAATCTTGCTGTCTACTGAATAAATAAATGCACCTTCTCT
GTATGCAGTGCTTCTGTGGGAGACCATATCCCAGATTGCTGGTGCACCTGGGTTATGGTAAGC
ACTAGTCCATGAGCCTGCTTGGAATCACACTGGATGTCTCCGTTTTGTCTTGTAAATGCCTAC
AACCTGAGGTAATAAATCAACATTTGCTCA

FIGURE 60

MLRTSTPNLCGGLHCRAPWLSSGILCLCLIFLLGQVGLLQGHPQCLDYGPPFQPPLHLEFCSD
YESFGCCDQHKDRRIAARYWDIMEYFDLKRHELCGDYIKDILCQECSPYAAHLYDAENTQTPL
RNLPGLCSDYCSAFHSNCHSAISLLTNDRGLQESHGRDGTRFCHLLDLPDKDYCFPNVLRNDY
LNRHLGMVAQDPQGCLQLCLSEVANGLRNPVSMVHAGDGTHRFFVAEQVGVVWVYLPDGSRLE
QPFLDLKNIVLTTPWIGDERGFLGLAFHPKFRHNRKFYIYYSCLDKKKVEKIRISEMKVSRAD
PNKADLKSERVILEIEEPASNHNGGQLLFGLDGYMYIFTGDGGQAGDPFGLFGNAQNKSSLLG
KVLRIDVNRAGSHGKRYRVPSDNPFVSEPGAHPAIYAYGIRNMWRCAVDRGDPITRQGRGRIF
CGDVGQNRFEEVDLILKGGNYGWRAKEGFACYDKKLCHNASLDDVLPIYAYGHAVGKSVTGGY
VYRGCESPNLNGLYIFGDFMSGRLMALQEDRKNKKWKKQDLCLGSTTSCAFPGLISTHSKFII
SFAEDEAGELYFLATSYPSAYAPRGSIYKFVDPSRRAPPGKCKYKPVPVRTKSKRIPFRPLAK
TVLDLLKEQSEKAARKSSSATLASGPAQGLSEKGSSKKLASPTSSKNTLRGPGTKKKARVGPH
VRQGKRRKSLKSHSGRMRPSAEQKRAGRSLP

Important features of the protein:

Signal peptide:

amino acids 1-41

Transmembrane domain:

amino acids 17-36

N-glycosylation sites.

amino acids 372-376, 480-484

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 645-649, 699-703

Tyrosine kinase phosphorylation site.

amino acids 81-89

N-myristoylation sites.

amino acids 11-17, 37-43, 156-162, 165-171, 357-363, 365-371, 368-374, 408-414, 459-465, 548-554, 557-563

Amidation sites.

amino acids 391-395, 696-700

Cell attachment sequence.

amino acids 428-431

Leucine zipper pattern.

amino acids 25-47

FIGURE 61

CTCCATTAAACCACCACCAGCTCCCCAAGCCACCCCTTCAGCC**ATG**AAGTTCCTGCTCCTGGT
CTTGGCAGCCCTCGGATTCCTGACCCAGGTGATCCCAGCCAGTGCAGGTGGGTCAAAATGTGT
GAGTAACACCCCAGGATACTGCAGGACATGTTGCCACTGGGGGGAGACAGCATTGTTCATGTG
CAACGCTTCCAGAAAATGCTGCATCAGCTACTCCTTCCTGCCGAAGCCTGACCTACCACAGCT
CATCGGTAACCACTGGCAATCAAGGAGAAGAAACACACAAAGGAAAGACAAGAAGCAACAAAC
GACCGTAACATCA**TAA**TAACCACTGCTATCGCCTCCACCAACTCAGAGAAATATCATTTCCAC
AGTTCCAATTCCTCCTACATTGCTGAGTACTAGCCAAGGCTCCTCTTTATGGGGCAGATATCT
ATAGCCAACCCCAAAACTTCTGTCTTCTATCATTCTGTCATTCATCTAGTAACTAATTTGGAG
TTTGTATCTATCTTACGAGAACAATCATCATGCAGATTCGTCCACAGGGGATCTGTCAGTTTG
GGTCCTCCAAATGAAAAATGTCAAGACAGAATTGGACATGCAAAAGATTGACTGGGAGAACAC
ACCTCTGATGGACAAAGGTGAGACAGAGCAGCCACAGGCAGGGAGAGCCTTCAGACTGCAACG
CTGGCCTGATACGTGTCAAAGGAGAGAGGGATAGAGGAGGATTGAATAGAAGGAGACTAAGAC
TGCAGCTCTAAGAAAGTCTCAGCCAAACAGATGGGGAGGCCCAAAGCAAGGCTTGCCCCTCAG
AGGAGCTCACGCAGGGCAGGAATAGCCAGGTTCTCATATCCCAGGGGTTCAGACTTGGCTGAG
AACAGCCCCTGGAGAACATGGGGTGACTGCTACCATAGGTCTGGAAGTATGAGGCTGTCCACC
AACTATCCCCTTGAAGCAAGTTCTCTTGAAAGGAAATCTAAACAGTGCACCCCCATGGCTGCC
ACGGAGTATAAGGAGGGAGAGAAAGGAGCTGAAAGTCTAGGTTTGGCCAGCTAGGTAGACTGA
CTTGTGAGGTATTTATTTATTCATTTGAGTAACAAAGCAGACAGAATACATAGCCACCATTGG
TAGTACACCCCAAAAGCAAGGATGGCATGATGCTGGTGACTCAAACGTGCCTACTCATGGTGT
CAAATTGGCATAATCCTCTTGGGAAGCTGTGTGGAAATAAGCACAGAGAAGCAGAACTCTAAT
TGCTTAATCCACTAAACATTACTTCTGGGAATTGGCTCATCATAAATTATCCAAGAGAAAGCA
CAAAGTTATGGGCACAAAGGTTTTCCATATAATATTATTTAAAATGCTGAGAAAATGAAAAAA
TCTAAATGGTGAAATATATACTAATGCCATCTATAAATACAAACAAATAGAATGTTTATAGAA
TAATGGAACATAATAACATTATTCAAAATTGCATTTATGCTATAGTTGTCAAAATTGTCTCCT
TATATGATACAAAACTCATGAAAATTATGACTTTTTTGTTTGGTTGGAAAGCAGAATTATGCA
TAAATTTCCTCTTACAGTTCGATGCCCATTAGTTTTATATAACATTTATTTGACACGTACTGA
CTTCTATCTGAGAAGAACAAACCAAAACACTCAGGCCTAAATAATTAAAAACGGTCCTAAAAA
CTAGCAAACCAGATAAGAAAAGATGTTAATGCCCATTCCCTAACTTATGTCTTAGACCAAAAT
TAATTCTAGATGGTTTTAAAATGACAGTGTAAAAGTAAAGTATTAAAAGATTGTGTGGTCAAA
TATTCAATTTAAGAGCAAGGAAATTCTTATAAATATAACAATAGAGGCAGAACTCATGTAAGA
ATAAATTGATTAGGTGGTATTAAATATTAAGTTCTTATGTATGTCAAAAGATATCATTTTGAA
ATTCATCCATCTTATTGGGTATTGCAGGAGTTCATTCCTTTTTGTTTATAAATACTCTTCCGT
CATATGAATAGTATTCATTTGTATACTGGTTTGTTGATGGACATTTGGGTTGTTCCCAGTTTA
TGGCTATTACAAATAAAGCTTCTATGAACATTTATGTACA

FIGURE 62

MKFLLLVLAALGFLTQVIPASAGGSKCVSNTPGYCRTCCHWGETALFMCNASRKCCISYSFLP
KPDLPQLIGNHWQSRRRNTQRKDKKQQTTVTS

Important features of the protein:

Signal peptide:

amino acids 1-16

Transmembrane domain:

amino acids 1-22

N-glycosylation site.

amino acids 50-53

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 79-82

N-myristoylation site.

amino acids 23-28

FIGURE 63

GCGGAGCGCCTGGGAGAGGAGAAGGAGCCGACCTGCCGAG**ATG**GAGGCGACCGGCACCTGGGC
GCTGCTGCTGGCGCTGGCGCTGCTCCTGCTGCTGACGCTGGCGCTGTCCGGGACCAGGGCCCG
AGGCCACCTGCCCCCCGGGCCCACGCCGCTACCACTGCTGGGAAACCTCCTGCAGCTACGGCC
CGGGGCGCTGTATTCAGGGCTCATGCGGCTGAGTAAGAAGTACGGACCGGTGTTCACCATCTA
CCTGGGACCCTGGCGGCCTGTGGTGGTCCTGGTTGGGCAGGAGGCTGTGCGGGAGGCCCTGGG
AGGTCAGGCTGAGGAGTTCAGCGGCCGGGGAACCGTAGCGATGCTGGAAGGGACTTTTGATGG
CCATGGGGTTTTCTTCTCCAACGGGGAGCGGTGGAGGCAGCTGAGGAAGTTTACCATGCTTGC
TCTGCGGGACCTGGGCATGGGGAAGCGAGAAGGCGAGGAGCTGATCCAGGCGGAGGCCCGGTG
TCTGGTGGAGACATTCCAGGGGACAGAAGGACGCCCATTCGATCCCTCCCTGCTGCTGGCCCA
GGCCACCTCCAACGTAGTCTGCTCCCTCCTCTTTGGCCTCCGCTTCTCCTATGAGGATAAGGA
GTTCCAGGCCGTGGTCCGGGCAGCTGGTGGTACCCTGCTGGGAGTCAGCTCCCAGGGGGGTCA
GACCTACGAGATGTTCTCCTGGTTCCTGCGGCCCCTGCCAGGCCCCCACAAGCAGCTCCTCCA
CCACGTCAGCACCTTGGCTGCCTTCACAGTCCGGCAGGTGCAGCAGCACCAGGGGAACCTGGA
TGCTTCGGGCCCCGCACGTGACCTTGTCGATGCCTTCCTGCTGAAGATGGCACAGGAGGAACA
AAACCCAGGCACAGAATTCACCAACAAGAACATGCTGATGACAGTCATTTATTTGCTGTTTGC
TGGGACGATGACGGTCAGCACCACGGTCGGCTATACCCTCCTGCTCCTGATGAAATACCCTCA
TGTCCAAAAGTGGGTACGTGAGGAGCTGAATCGGGAGCTGGGGGCTGGCCAGGCACCAAGCCT
AGGGGACCGTACCCGCCTCCCTTACACCGACGCGGTTCTGCATGAGGCGCAGCGGCTGCTGGC
GCTGGTGCCCATGGGAATACCCCGCACCCTCATGCGGACCACCCGCTTCCGAGGGTACACCCT
GCCCCAGGGCACGGAGGTCTTCCCCCTCCTTGGCTCCATCCTGCATGACCCCAACATCTTCAA
GCACCCAGAAGAGTTCAACCCAGACCGTTTCCTGGATGCAGATGGACGGTTCAGGAAGCATGA
GGCGTTCCTGCCCTTCTCCTTAGGGAAGCGTGTCTGCCTTGGAGAGGGCCTGGCAAAAGCGGA
GCTCTTCCTCTTCTTCACCACCATCCTACAAGCCTTCTCCCTGGAGAGCCCGTGCCCGCCGGA
CACCCTGAGCCTCAAGCCCACCGTCAGTGGCCTTTTCAACATTCCCCCAGCCTTCCAGCTGCA
AGTCCGTCCCACTGACCTTCACTCCACCACGCAGACCAGA**TGA**AGGAAGGCAACTTGGAAGTG
GTGGGTGCCCAGGACGGTGCCTCCAGCCTCAACAGTGGGCATGGACAGGGTTAATGTCTCCAG
AGTGTACACTGCAGGCAGCCACATTTACACGCCTGCAGTTGTTTTCCGGAGTCTGTCCCACGG
CCCACACGCTCACTTGACTCATGCTGCTAAGATGCACAACCGCACACCCATACACAACTACAA
GGGCCACAAAGCAACTGCTGGGTTAGCTTTCCACAGACATAAATATAGTCCATCTGCAATCAC
AAGCACATAGCCAGGTAACCCACCAACTCCCCTGGATCTGCAGCCCACACGTGGGAGTCTGGC
TGTCACCTTCACAAGCCACAGAAACGGCCACACATGTTCACAGCTCACACGCCCTCTCCATTC
ATCGAACTTCTCAGTGTCCCTGTCCCTGGTGCCTGGCACAGGGAACAGCATGCCCCCTCCGGG
GTCATGCCACCCAGAGACTGTCGCTGTCTATGGCCCCAACTCATGCTCCCTCTCTTGGCTACA
CCACTCTCCCAGCCTGTGACCACCGATGTCCACACACCCCCAACCACTTGTCCACACAGCTAC
CCACGTACAACATCGTCCTGGCTCCCCAGAGTATCTTCCCACTGAGACACGCCGCCCCCACAG
AGGCACAGTCCCCAGCCACCTCTGCAACTGCAGCCCTCAGTCACCCCTTTTTAAGCACCCTGA
TTCTACCAAATGCAAACACATCTGGGTCTGCGATTATGCACAGAGACTTTGGACATACGAGGA
CCCTCAGACCGGAGGAACACCTGCCCAACCCCAACACGTGCTTATGTAACCACGTGGAAAGCG
GCCCCTGCTGCCCCTCCACACACACATACACACTCACTGATCTACAGCCCCTGTTCGGCGTCA
GAGTCCCCACTAGACCCAGTGGAAGGGGTTAGAGACCAAGTAGGGGCCAGTTTCCAATTCACC
CTGTCAGGGAGTGAGCCGGATCTGACGTTCCTTGTGACTTAAGGGTCCGGCTTGGGAATTAAA
GTTTGTTTCTGGCCTTTAGCCTAAAAAAAAAAAAAAAAAA

FIGURE 64

MEATGTWALLLALALLLLLTLALSGTRARGHLPPGPTPLPLLGNLLQLRPGALYSGLMRLSKK
YGPVFTIYLGPWRPVVVLVGQEAVREALGGQAEEFSGRGTVAMLEGTFDGHGVFFSNGERWRQ
LRKFTMLALRDLGMGKREGEELIQAEARCLVETFQGTEGRPFDPSLLLAQATSNVVCSLLFGL
RFSYEDKEFQAVVRAAGGTLLGVSSQGGQTYEMFSWFLRPLPGPHKQLLHHVSTLAAFTVRQV
QQHQGNLDASGPARDLVDAFLLKMAQEEQNPGTEFTNKNMLMTVIYLLFAGTMTVSTTVGYTL
LLLMKYPHVQKWVREELNRELGAGQAPSLGDRTRLPYTDAVLHEAQRLLALVPMGIPRTLMRT
TRFRGYTLPQGTEVFPLLGSILHDPNIFKHPEEFNPDRFLDADGRFRKHEAFLPFSLGKRVCL
GEGLAKAELFLFFTTILQAFSLESPCPPDTLSLKPTVSGLFNIPPAFQLQVRPTDLHSTTQTR

Important features of the protein:

Signal peptide:

amino acids 1-28

Transmembrane domain:

amino acids 294-313

Glycosaminoglycan attachment site.

amino acids 99-103

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 128-132

N-myristoylation sites.

amino acids 51-57, 109-115, 115-121, 188-194, 207-213, 257-263, 284-290, 339-345, 370-376, 444-450

Amidation sites.

amino acids 140-144, 435-439

Leucine zipper pattern.

amino acids 32-54, 39-61

Cytochrome P450 cysteine heme-iron ligand signature.

amino acids 433-443

FIGURE 65

CGGACGCGTGGGGCCGT**ATG**CGCGGCTCTGTGGAGTGCACCTGGGGTTGGGGGCACTGTGCCC
CCAGCCCCCTGCTCCTTTGGACTCTACTTCTGTTTGCAGCCCCATTTGGCCTGCTGGGGGAGA
AGACCCGCCAGGTGTCTCTGGAGGTCATCCCTAACTGGCTGGGCCCCCTGCAGAACCTGCTTC
ATATACGGGCAGTGGGCACCAATTCCACACTGCACTATGTGTGGAGCAGCCTGGGGCCTCTGG
CAGTGGTAATGGTGGCCACCAACACCCCCCACAGCACCCTGAGCATCAACTGGAGCCTCCTGC
TATCCCCTGAGCCCGATGGGGGCCTGATGGTGCTCCCTAAGGACAGCATTCAGTTTTCTTCTG
CCCTTGTTTTTACCAGGCTGCTTGAGTTTGACAGCACCAACGTGTCCGATACGGCAGCAAAGC
CTTTGGGAAGACCATATCCTCCATACTCCTTGGCCGATTTCTCTTGGAACAACATCACTGATT
CATTGGATCCTGCCACCCTGAGTGCCACATTTCAAGGCCACCCCATGAACGACCCTACCAGGA
CTTTTGCCAATGGCAGCCTGGCCTTCAGGGTCCAGGCCTTTTCCAGGTCCAGCCGACCAGCCC
AACCCCCTCGCCTCCTGCACACAGCAGACACCTGTCAGCTAGAGGTGGCCCTGATTGGAGCCT
CTCCCCGGGGAAACCGTTCCCTGTTTGGGCTGGAGGTAGCCACATTGGGCCAGGGCCCTGACT
GCCCCTCAATGCAGGAGCAGCACTCCATCGACGATGAATATGCACCGGCCGTCTTCCAGTTGG
ACCAGCTACTGTGGGGCTCCCTCCCATCAGGCTTTGCACAGTGGCGACCAGTGGCTTACTCCC
AGAAGCCGGGGGGCCGAGAATCAGCCCTGCCCTGCCAAGCTTCCCCTCTTCATCCTGCCTTAG
CATACTCTCTTCCCCAGTCACCCATTGTCCGAGCCTTCTTTGGGTCCCAGAATAACTTCTGTG
CCTTCAATCTGACGTTCGGGGCTTCCACAGGCCCTGGCTATTGGGACCAACACTACCTCAGCT
GGTCGATGCTCCTGGGTGTGGGCTTCCCTCCAGTGGACGGCTTGTCCCCACTAGTCCTGGGCA
TCATGGCAGTGGCCCTGGGTGCCCCAGGGCTCATGCTGCTAGGGGGCGGCTTGGTTCTGCTGC
TGCACCACAAGAAGTACTCAGAGTACCAGTCCATAAAT**TAA**GGCCCGCTCTCTGGAGGGAAGG
ACATTACTGAACCTGTCTTGCTGTGCCTCGAAACTCTGGAGGTTGGAGCATCAAGTTCCAGCC
GGCCCCTTCACTCCCCCATCTTGCTTTTCTGTGGAACCTCAGAGGCCAGCCTCGACTTCCTGG
AGACCCCCAGGTGGGGCTTCCTTCATACTTTGTTGGGGGACTTTGGAGGCGGGCAGGGGACAG
GGCTATTGATAAGGTCCCCTTGGTGTTGCCTTCTTGCATCTCCACACATTTCCCTTGGATGGG
ACTTGCAGGCCTAAATGAGAGGCATTCTGACTGGTTGGCTGCCCTGGAAGGCAAGAAAATAGA
TTTATTTTTTTTCACAGGGAAAAAAAAAAAA

FIGURE 66

MRGSVECTWGWGHCAPSPLLLWTLLLFAAPFGLLGEKTRQVSLEVIPNWLGPLQNLLHIRAVG
TNSTLHYVWSSLGPLAVVMVATNTPHSTLSINWSLLLSPEPDGGLMVLPKDSIQFSSALVFTR
LLEFDSTNVSDTAAKPLGRPYPPYSLADFSWNNITDSLDPATLSATFQGHPMNDPTRTFANGS
LAFRVQAFSRSSRPAQPPRLLHTADTCQLEVALIGASPRGNRSLFGLEVATLGQGPDCPSMQE
QHSIDDEYAPAVFQLDQLLWGSLPSGFAQWRPVAYSQKPGGRESALPCQASPLHPALAYSLPQ
SPIVRAFFGSQNNFCAFNLTFGASTGPGYWDQHYLSWSMLLGVGFPPVDGLSPLVLGIMAVAL
GAPGLMLLGGGLVLLLHHKKYSEYQSIN

N-glycosylation sites:

amino acids 65-69, 95-99, 134-138, 159-163, 187-191, 230-234, 333-337

cAMP- and cGMP-dependent protein kinase phosphorylation site:

amino acids 397-401

Casein kinase II phosphorylation sites:

amino acids 151-155, 249-253, 255-259

N-myristoylation sites:

amino acids 3-9, 63-69, 235-241, 273-279, 292-298, 324-330

Leucine zipper pattern.

amino acids 371-393

FIGURE 67

CGGGACAGGCGCGTGAGGCCACAACACATGCGTGTATCTTGCTTGGGCTATCTTCCCTGCTCTGCCACGCCGGGT
CTGGAGAAGGGGTTTCAGCCCCAGGACATTTACTGAGAGTCGGCGAATATTGGGAGCCGCG**ATG**TTCCCCCTTCG
GGCCCTGTGGTTGGTCTGGGCGCTTCTAGGAGTGGCCGGATCATGCCCGGAGCCGTGCGCCTGCGTGGACAAGTA
CGCTCACCAGTTCGCGGACTGCGCTTACAAAGAGTTGCGTGAGGTGCCGGAAGGACTGCCTGCCAACGTGACGAC
GCTTAGTCTGTCCGCGAACAAGATCACTGTGCTGCGGCGCGGGGCCTTCGCCGACGTCACACAGGTCACGTCGCT
GTGGCTGGCGCACAATGAGGTGCGCACCGTGGAGCCAGGCGCACTGGCCGTGCTGAGTCAGCTCAAGAACCTCGA
TCTGAGCCACAACTTCATATCCAGCTTTCCGTGGAGCGACCTGCGCAACCTGAGCGCGCTGCAGCTGCTCAAAAT
GAACCACAACCGCCTGGGCTCTCTGCCCCGGGACGCACTCGGTGCGCTACCCGACCTGCGTTCCCTGCGCATCAA
CAACAACCGGCTGCGTACGCTGGCGCCTGGCACCTTCGACGCGCTTAGCGCGCTGTCACACTTGCAACTCTATCA
CAATCCCTTCCACTGCGGCTGCGGCCTTGTGTGGCTGCAGGCCTGGGCCGCGAGCACCCGGGTGTCCTTACCCGA
GCCCGACTCCATTGCTTGTGCCTCGCCTCCCGCGCTGCAGGGGGTGCCGGTGTACCGCCTGCCCGCCCTGCCCTG
TGCACCGCCCAGCGTGCATCTGAGTGCCGAGCCACCGCTTGAAGCACCCGGCACCCCACTGCGCGCAGGACTGGC
GTTCGTGTTACACTGCATCGCCGACGGCCACCCTACGCCTCGCCTGCAATGGCAACTTCAGATCCCCGGTGGCAC
CGTAGTCTTAGAGCCACCGGTTCTGAGCGGGGAGGACGACGGGGTTGGGGCGGAGGAAGGAGAGGGAGAAGGAGA
TGGGGATTTGCTGACGCAGACCCAAGCCCAAACGCCGACTCCAGCACCCGCTTGGCCGGCGCCCCCAGCCACACC
GCGCTTCCTGGCCCTCGCAAATGGCTCCCTGTTGGTGCCCCTCCTGAGTGCCAAGGAGGCGGGCGTCTACACTTG
CCGTGCACACAATGAGCTGGGCGCCAACTCTACGTCAATACGCGTGGCGGTGGCAGCAACCGGGCCCCCAAAACA
CGCGCCTGGCGCCGGGGGAGAACCCGACGGACAGGCCCCGACCTCTGAGCGCAAGTCCACAGCCAAGGGCCGGGG
CAACAGCGTCCTGCCTTCCAAACCCGAGGGCAAAATCAAAGGCCAAGGCCTGGCCAAGGTCAGCATTCTCGGGGA
GACCGAGACGGAGCCGGAGGAGGACACAAGTGAGGGAGAGGAGGCCGAAGACCAGATCCTCGCGGACCCGGCGGA
GGAGCAGCGCTGTGGCAACGGGGACCCCTCTCGGTACGTTTCTAACCACGCGTTCAACCAGAGCGCAGAGCTCAA
GCCGCACGTCTTCGAGCTGGGCGTCATCGCGCTGGATGTGGCGGAGCGCGAGGCGCGGGTGCAGCTGACTCCGCT
GGCTGCGCGCTGGGGCCCTGGGCCCGGCGGGGCTGGCGGAGCCCCGCGACCCGGGCGGCGACCCCTGCGCCTACT
CTATCTGTGTCCAGCGGGGGGCGGCGCGGCAGTGCAGTGGTCCCGCGTAGAGGAAGGCGTCAACGCCTACTGGTT
CCGCGGCCTGCGGCCGGGTACCAACTACTCCGTGTGCCTGGCGCTGGCGGGCGAAGCCTGCCACGTGCAAGTGGT
GTTTTCCACCAAGAAGGAGCTCCCATCGCTGCTGGTCATAGTGGCAGTGAGCGTATTCCTCCTGGTGCTGGCCAC
AGTGCCCCTTCTGGGCGCCGCCTGCTGCCATCTGCTGGCTAAACACCCGGGCAAGCCCTACCGTCTGATCCTGCG
GCCTCAGGCCCCTGACCCTATGGAGAAGCGCATCGCCGCAGACTTCGACCCGCGTGCTTCGTACCTCGAGTCCGA
GAAAAGCTACCCGGCAGGCGGCGAGGCGGGCGGCGAGGAGCCAGAGGACGTGCAGGGGGAGGGCCTTGATGAAGA
CGCGGAGCAGGGAGACCCAAGTGGGGACCTGCAGAGAGAGGAGAGCCTGGCGGCCTGCTCACTGGTGGAGTCCCA
GTCCAAGGCCAACCAAGAGGAGTTCGAGGCGGGCTCTGAGTACAGCGATCGGCTGCCCCTGGGCGCCGAGGCGGT
CAACATCGCCCAGGAGATTAATGGCAACTACAGGCAGACGGCAGGC**TGA**ACCTCCGCCCGTCCGGCCCGCCCATT
CCCGACCTCCACCTAGGGTGCCTGGGAGCAGCAGTCTAGGGCTGGCAGGACTTATGTCCCCCGTCCCCAACCTTC
ACCTACTCCTCCCCCTTACTACTCCCCAACCTTGACTACCAGGGACTTCTATTAGGGAGTGGGCCGATTTCACCA
GTCCCTGCTACCCACGGCTGCCATTCTCCCTGCGGGCTGAATCCCCTTCCCCGCCAAGCACAGTGTTTATCTTAC
CCCATGCAAGACTCCACCCGCAGACGGTGGGCGATATCTATGTCCCTCCATTCCCGTCGCGATTATCTGCGAAAT
CCACCCCCGCAGCCCGCCCCACCGTGGGCTCTGGAGCCAGAGGAAACGAGCGAAGACTTTGGAAACCTCGCGGTAA
CGCGGTGGTTTCGGGGGCCAGCCAAGGCCAGTGGAGTGCTGTGGGGTCCCACCTCGACCCCTCCTCCTCCCTTTC
TTTCTTTCCTTTTTTTTTATTTTTTAATTTTATTTATTTATTTATTTATTTTTTGACGGAGTCTTGGTCTGTCGC
CAGGCTGGAGTGCAGTGGCGCGATCTCGGCTCACTGCATCTTCCGCCTCCCGGGTTCAAGCGATTCTCCTGCCTC
AGCCTGCCTAGTAGCTGGGACTACAGGCGCGCGCCACCACGACCAGCTAATTTCTTCTATTTTTAGTAGAGACGG
GGTTTCACCATGTTGGCCAGGATGGTCTGGATCTCTTGACCTCAGGTGATCCATCTGCCTCGGCCTCTCAAAGTG
CTGGGATTACAGGCGTGAGGCACCGCGCCCGGCCCCTCCTCCCTTTCAATCCCTACTCCCAGAAGCCGGGATTCG
TGGCAACCCCTAGTTTTTAGTTCCAAAGCCTCCTGCCGGCAGGGAACCAAATCCTTCTGTCCTCCCACCCCCACC
CCACTTCTGGCCAGTTGGAGTCCAGCCCGGTGCCTGGGGCGCCTTTCAGCTCCGCGCTCAGATTTTCCTGTTTTC
GTTGTTTTCAAAGACAGCGACATTTCGGGTCTGGTGCTAACACCCCCTTCCCAGCCTCTGGGAAAATCGAGTGTG
TGTGTCGGGGGGTAGGGAGGGAATGCGTTTTCTGTCGTCTCTCTCCTAACTTAAAGCGCCGCAGGACCGCGCGCC
CCTTGGCGGCTGAGCCTGTGGACTTGGTCGCGGGCCAATTTCGTTGTCCGTGTGTTGGGCTTTCCGGAGGTCTGT
GCGCCCAACAGCGCCGCTCCCGCGGCTCCACCCGACCCAGACCCTAGCTGGAAAGCGCCGGAGGCGGAGGAAGCT
GACTGTGGCCTCCCGGGCCGCGGCTCTCTGGAGGGCTCGCGCCCTAGTTCGCACAAAGCCTGCTCGTGACTGTGC
GACTGTGCGACGGGATCCGGATGGAGCCGAGCCCCTCCGTCCTCGCGTCTCGGTCCTCGCGTCGCCCCGCCCCAC
CCGCCCCTGCTTCGGCGGGAATCGTGTTTGCCCGGCGTGTAGTCCCTGACAAGCGTGCCCTGTAGGAGAAAAGTC
TGTGTCCTGTGAAGTGTGACCGTGTAGTGTAGGGGGGCGGGCGGGGGGGCGGATGGGCGGGGAGGGAGGGAAGGG
GAGGGGCGCGGCGCGGCGACTCGGGGCGGGGTTCTTTTTTCCATTTTGAAAGAAAGCGTCGGGGTTGGGGTGGGG
GGAGTTTCAGTCCTCGGGATCAGCCCTCTCCGCGAAGCGCAGCACAAGCGCGGGCCTGGGACGGAGTAGCCCCCC
GGAGCCCGTGCCCTTTTCTAAACGCGTCTGTATGCAGTCAATAAAACAATCGATTTGAAA

FIGURE 68

MFPLRALWLVWALLGVAGSCPEPCACVDKYAHQFADCAYKELREVPEGLPANVTTLSLSANKI
TVLRRGAFADVTQVTSLWLAHNEVRTVEPGALAVLSQLKNLDLSHNFISSFPWSDLRNLSALQ
LLKMNHNRLGSLPRDALGALPDLRSLRINNNRLRTLAPGTFDALSALSHLQLYHNPFHCGCGL
VWLQAWAASTRVSLPEPDSIACASPPALQGVPVYRLPALPCAPPSVHLSAEPPLEAPGTPLRA
GLAFVLHCIADGHPTPRLQWQLQIPGGTVVLEPPVLSGEDDGVGAEEGEGEGDGDLLTQTQAQ
TPTPAPAWPAPPATPRFLALANGSLLVPLLSAKEAGVYTCRAHNELGANSTSIRVAVAATGPP
KHAPGAGGEPDGQAPTSERKSTAKGRGNSVLPSKPEGKIKGQGLAKVSILGETETEPEEDTSE
GEEAEDQILADPAEEQRCGNGDPSRYVSNHAFNQSAELKPHVFELGVIALDVAEREARVQLTP
LAARWGPGPGGAGGAPRPGRRPLRLLYLCPAGGAAVQWSRVEEGVNAYWFRGLRPGTNYSVC
LALAGEACHVQVVFSTKKELPSLLVIVAVSVFLLVLATVPLLGAACCHLLAKHPGKPYRLILR
PQAPDPMEKRIAADFDPRASYLESEKSYPAGGEAGGEEPEDVQGEGLDEDAEQGDPSGDLQRE
ESLAACSLVESQSKANQEEFEAGSEYSDRLPLGAEAVNIAQEINGNYRQTAG

Important features of the protein:

Signal peptide:

amino acids 1-19

Transmembrane domain:

amino acids 587-610

N-glycosylation sites.

amino acids 52-55, 121-124, 337-340, 364-367, 474-477, 563-566

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 397-400

Casein kinase II phosphorylation sites.

amino acids 19-23, 202-205, 289-292, 246-249, 411-414, 431-434, 433-436, 440-443, 544-547, 583-586, 650-653, 700-703

N-myristoylation sites.

amino acids 15-20, 48-53, 165-170, 296-301, 351-356, 362-367, 390-395, 419-424, 514-519, 536-541, 557-562, 561-566, 610-615, 661-666, 716-721

Amidation site.

amino acids 522-525

Prokaryotic membrane lipoprotein lipid attachment sites.

amino acids 10-20, 603-613

FIGURE 69

GGCGGCGGGAGCAGCGAAGGGGGCGGCAGGGATCCTCCAGGCTGCCGGCTGGGAAGGCGTGGG
CGACCCGGTGTGTGGCGCGCCCAGAGCCCCGCGTTTCAGCCCTAGGGAAGGAAGCCAGTTGAG
GGAAGTTCTCCATGAATGTACGTCACA**ATG**ATGATGACCGACCAAATCCCTCTGGAACTGCCA
CCATTGCTGAACGGAGAGGTAGCCATGATGCCCCACTTGGTGAATGGAGATGCAGCTCAGCAT
GTTATTCTCGTTCAAGTTAATCCAGGTGAGACTTTCACAATAAGAGCAGAGGATGGAACACTT
CAGTGCATTCAAGGACCTGCTGAAGTTCCCATGATGTCACCCAATGGATCCATTCCTCCCATT
CATGTGCCTCCAGGTTATATCTCACAGGTGATTGAAGATAGTACTGGAGTCCGCCGGGTGGTG
GTCACACCCCAGTCTCCTGAGTGTTATCCCCCAAGCTACCCCTCAGCCATGTCTCCAACCCAT
CATCTCCCTCCCTATCTGACTCACCATCCACATTTTATTCATAACTCACACACGGCTTACTAC
CCACCTGTTACCGGACCTGGAGATATGCCGCCTCAGTTTTTTCCCCAGCATCATCTTCCCCAC
ACAATATATGGTGAGCAAGAAATTATACCATTTTATGGAATGTCAAGCTACATCACCCGAGAA
GACCAGTACAGCAAGCCTCCGCACAAAAAACTGAAAGACCGCCAGATCGATCGCCAGAACCGC
CTCAACAGCCCTCCTTCTTCTATCTACAAAAGCAGCTGCACAACAGTATACAATGGCTATGGG
AAGGGCCATAGTGGTGGAAGTGGCGGAGGCGGCAGCGGTAGTGGTCCCGGAATTAAGAAAACA
GAGCGACGAGCAAGAAGCAGCCCAAAGTCGAATGATTCAGACTTGCAAGAATATGAGTTGGAA
GTAAAGAGGGTGCAAGACATTCTTTCGGGAATAGAGAAACCACAGGTTTCTAATATTCAGGCA
AGAGCAGTTGTGTTGTCCTGGGCTCCCCCTGTTGGACTTTCCTGTGGACCCCACAGTGGTCTT
TCCTTCCCCTACAGTTACGAGGTGGCCTTATCAGACAAAGGACGAGATGGAAAATACAAGATA
ATTTACAGTGGAGAAGAATTAGAATGTAACCTGAAAGATCTTAGACCAGCAACAGATTATCAT
GTGAGGGTGTATGCCATGTACAATTCCGTAAAGGGATCCTGCTCCGAGCCTGTTAGCTTCACC
ACCCACAGCTGTGCACCCGAGTGTCCTTTCCCCCCTAAGCTGGCACATAGGAGCAAAAGTTCA
CTAACCCTGCAGTGGAAGGCACCAATTGACAACGGTTCAAAAATCACCAACTACCTTTTAGAG
TGGGATGAGGGAAAAAGAAATAGTGGTTTCAGACAGTGCTTCTTCGGGAGCCAGAAGCACTGC
AAGTTGACAAAGCTTTGTCCGGCAATGGGGTACACATTCAGGCTGGCCGCTCGAAACGACATT
GGCACCAGTGGTTATAGCCAAGAGGTGGTGTGCTACACATTAGGAAATATCCCTCAGATGCCT
TCTGCACCAAGGCTGGTTCGAGCTGGCATCACATGGGTCACGTTGCAGTGGAGTAAGCCAGAA
GGCTGTTCACCCGAGGAAGTGATCACCTACACCTTGGAAATTCAGGAGGATGAAAATGATAAC
CTTTTCCACCCAAAATACACTGGAGAGGATTTAACCTGTACTGTGAAAAATCTCAAAAGAAGC
ACACAGTATAAATTCAGGCTGACTGCTTCTAATACGGAAGGAAAAAGCTGTCCAAGCGAAGTT
CTTGTTTGTACGACGAGTCCTGACAGGCCTGGACCTCCTACCAGACCGCTTGTCAAAGGCCCA
GTTACATCTCATGGCTTTAGTGTCAAATGGGATCCCCCTAAGGACAATGGTGGTTCAGAAATC
CTCAAGTACTTGCTAGAGATTACTGATGGAAATTCTGAAGGTGAAGTTTTTGGCAATTGTTTT
ATTCAAATCCAA**TAG**CAAGCTCTGTTTTCTAATATAGTAAATGTCTTTATAGTAATAGTGAGT
AATCATTAATTCTAAAGATAGAATTATTATTACAATAAACAAACTTTAGTCACATATTGGCAG
TTTTTCTATTTCAAACACAGCACCAGAGATCAGAGTCTACTTGAAACTTACATTTGTGTTATT
TAACAATTTTTCTGTATCTTTTTCATTGGTGTTTTGTTTTGTTTATCTTTTGTTTTTGTTTCT
TTGGTTTGGTTTGTTTTTGTTTTGTTTTTTGAGATACGATCTCTGTCACACAGGCTGGAGGGC
AGTGGCACAGACATGGCCCATTGCAGTCTCAGACTCCTGGGCTTAAGTGACTCTTCTGCCACA
GAAGATGAGGAAGAATACATTTTTCATAGTGATGGGGTCTCACTATGTTATCTAGGCTGGTCT
CAAACTCCTGGCCTCAAGCAACCCTCCACCTTGGCCTCCCAAAGTGCTGGGACTATAGACATG
AATCACCACACTCAGCTTCCATGTCTTTTTATGAACTAGGGTTCCTAATTAATCAGATAAATT
TGGTATTTTCATCTCCTAACTTGCCATATGTTTTCTGGAAATTCTTATAAGCAGCCGAGAGTG
GTGGCTCACGCTGTAGTCCCAGCACTTTGGGAGGCTGAGGTGGGTGGTCAGGAGATCAAGACC
ATCCTGGCCAACATGGTGAAACCCCGTCTCTACTAAAAATACAAAAATTAGCTGGGTGTGGTG
GCAGGCACCTGTAGTCCCAGCTACTTGGGAGGCTGAGGCAGAAGAATTGCTTGAACCCAGCAG
GCGGAGGTTGCAGTGAGCTGAGATTGCACCACTGCACTCCAGCCTGGTGACAGAGTGAGACTC
TGTCTCAAAAAAAAAAAA

FIGURE 70

MMMTDQIPLELPPLLNGEVAMMPHLVNGDAAQHVILVQVNPGETFTIRAEDGTLQCIQGPAEV
PMMSPNGSIPPIHVPPGYISQVIEDSTGVRRVVVTPQSPECYPPSYPSAMSPTHHLPPYLTHH
PHFIHNSHTAYYPPVTGPGDMPPQFFPQHHLPHTIYGEQEIIPFYGMSSYITREDQYSKPPHK
KLKDRQIDRQNRLNSPPSSIYKSSCTTVYNGYGKGHSGGSGGGGSGSGPGIKKTERRARSSPK
SNDSDLQEYELEVKRVQDILSGIEKPQVSNIQARAVVLSWAPPVGLSCGPHSGLSFPYSYEVA
LSDKGRDGKYKIIYSGEELECNLKDLRPATDYHVRVYAMYNSVKGSCSEPVSFTTHSCAPECP
FPPKLAHRSKSSLTLQWKAPIDNGSKITNYLLEWDEGKRNSGFRQCFFGSQKHCKLTKLCPAM
GYTFRLAARNDIGTSGYSQEVVCYTLGNIPQMPSAPRLVRAGITWVTLQWSKPEGCSPEEVIT
YTLEIQEDENDNLFHPKYTGEDLTCTVKNLKRSTQYKFRLTASNTEGKSCPSEVLVCTTSPDR
PGPPTRPLVKGPVTSHGFSVKWDPPKDNGGSEILKYLLEITDGNSEGEVFGNCFIQIQ

Important features of the protein:

N-glycosylation sites.

amino acids 69-73, 254-258, 401-405

Glycosaminoglycan attachment sites.

amino acids 229-233, 234-238, 236-240

cAMP- and cGMP-dependent protein kinase phosphorylation sites.

amino acids 416-420, 535-539

Tyrosine kinase phosphorylation site.

amino acids 319-326

N-myristoylation sites.

amino acids 52-58, 227-233, 228-234, 230-236, 231-237, 232-238, 235-241, 239-245, 402-408, 610-616

Amidation site.

amino acids 414-418

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 290-301

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

amino acids 546-554

CUB domain proteins profile.

amino acids 294-301

FIGURE 71

AAGTCATTCAGTGGATGTGATCTTGGCTCACAGGGGACG**ATG**TCAAGCTCTTCCTGGCTCCTTCTCAGCCTTGTT
GCTGTAACTGCTGCTCAGTCCACCATTGAGGAACAGGCCAAGACATTTTTGGACAAGTTTAACCACGAAGCCGAA
GACCTGTTCTATCAAAGTTCACTTGCTTCTTGGAATTATAACACCAATATTACTGAAGAGAATGTCCAAAACATG
AATAATGCTGGGGACAAATGGTCTGCCTTTTTAAAGGAACAGTCCACACTTGCCCAAATGTATCCACTACAAGAA
ATTCAGAATCTCACAGTCAAGCTTCAGCTGCAGGCTCTTCAGCAAAATGGGTCTTCAGTGCTCTCAGAAGACAAG
AGCAAACGGTTGAACACAATTCTAAATACAATGAGCACCATCTACAGTACTGGAAAAGTTTGTAACCCAGATAAT
CCACAAGAATGCTTATTACTTGAACCAGGTTTGAATGAAATAATGGCAAACAGTTTAGACTACAATGAGAGGCTC
TGGGCTTGGGAAAGCTGGAGATCTGAGGTCGGCAAGCAGCTGAGGCCATTATATGAAGAGTATGTGGTCTTGAAA
AATGAGATGGCAAGAGCAAATCATTATGAGGACTATGGGGATTATTGGAGAGGAGACTATGAAGTAAATGGGGTA
GATGGCTATGACTACAGCCGCGGCCAGTTGATTGAAGATGTGGAACATACCTTTGAAGAGATTAAACCATTATAT
GAACATCTTCATGCCTATGTGAGGGCAAAGTTGATGAATGCCTATCCTTCCTATATCAGTCCAATTGGATGCCTC
CCTGCTCATTTGCTTGGTGATATGTGGGGTAGATTTTGGACAAATCTGTACTCTTTGACAGTTCCCTTTGGACAG
AAACCAAACATAGATGTTACTGATGCAATGGTGGACCAGGCCTGGGATGCACAGAGAATATTCAAGGAGGCCGAG
AAGTTCTTTGTATCTGTTGGTCTTCCTAATATGACTCAAGGATTCTGGGAAAATTCCATGCTAACGGACCCAGGA
AATGTTCAGAAAGCAGTCTGCCATCCCACAGCTTGGGACCTGGGGAAGGGCGACTTCAGGATCCTTATGTGCACA
AAGGTGACAATGGACGACTTCCTGACAGCTCATCATGAGATGGGGCATATCCAGTATGATATGGCATATGCTGCA
CAACCTTTTCTGCTAAGAAATGGAGCTAATGAAGGATTCCATGAAGCTGTTGGGGAAATCATGTCACTTTCTGCA
GCCACACCTAAGCATTTAAAATCCATTGGTCTTCTGTCACCCGATTTTCAAGAAGACAATGAAACAGAAATAAAC
TTCCTGCTCAAACAAGCACTCACGATTGTTGGGACTCTGCCATTTACTTACATGTTAGAGAAGTGGAGGTGGATG
GTCTTTAAAGGGGAAATTCCCAAAGACCAGTGGATGAAAAAGTGGTGGGAGATGAAGCGAGAGATAGTTGGGGTG
GTGGAACCTGTGCCCCATGATGAAACATACTGTGACCCCGCATCTCTGTTCCATGTTTCTGATGATTACTCATTC
ATTCGATATTACACAAGGACCCTTTACCAATTCCAGTTTCAAGAAGCACTTTGTCAAGCAGCTAAACATGAAGGC
CCTCTGCACAAATGTGACATCTCAAACTCTACAGAAGCTGGACAGAAACTGTTG**TAA**GAAATACCTCAAAATGTT
GAACCTCTCCTAGTATTCAGTATTACTCATTTCCATGCCTAGGTTTGTATTTGATTTCTTTGTTCTAAAAAGAAA
ATTTTATGGCCTCAAAATGTCCTCATTTACAAACCAAACATTTAATTTGTGGTCAGACAGGAACCTAGACCATAC
AACAATTGGGTGGGCCACCTCTTTTCTCCCTATCATAACTACAGCCCTCTCTTCCTGGTAATTGGAAGGAAAGAG
CGGTTTAGGGTGGAATATATCTGTTAATATGCATTCTTTTCTTATCTGCCAGAAGCAAATTTAGCCAAGTCAAAG
AGAAGAAACCATAGATCATAGATGTAAATATATGTACATCTGGAACCCCTCAAAAGGCCCTGAACCCCCTTTTTT
TGTGTAGCAATATGCTGAGGCTTGGAAAATCAGAACCCTGGACCCTAGCATTGGAAAATGTTGTAGGAGCAAGAA
CATGAATGTAAGGCCACTGCTCAACTACTTTGAGCCCTTATTTACCTGGCTGAAAGACCAGAACAAGAATTCTTT
TGTGGGATGGAGTACCGACTGGAGTCCATATGCAGACCCAAAGCATCAAAGTGAGGATAAGCCTAAAATCAGCTC
TTGGAGATAAAGCATATGAATGGAACGACAATGAAATGTACCTGTTCCGATCATCTGTTGCATATGCTATGAGGC
AGTACTTTTTAAAAGTAAAAAATCAGATGATTCTTTTTGGGGAGGAGGATGTGCGAGTGGCTAATTTGAAACCAA
GAATCTCCTTTAATTTCTTTGTCACTGCACCTAAAAATGTGTCTGATATCATTCCTAGAACTGAAGTTGAAAAGG
CCATCAGGATGTCCCGGAGCCGTATCAATGATGCTTTCCGTCTGAATGACAACAGCCTAGAGTTTCTGGGGATAC
AGCCAACACTTGGACCTCCTAACCAGCCCCCTGTTTCCATATGGCTGATTGTTTTTTGGAGTTGTGATGGGAGTGA
TAGTGGTTGGCATTGTCATCCTGATCTTCACTGGGATCAGAGATCGGAAGAAGAAAAATAAAGCAAGAAGTGGAG
AAAATCCTTATGCCTCCATCGATATTAGCAAAGGAGAAAATAATCCAGGATTCCAAAACACTGATGATGTTCAGA
CCTCCTTTTAGAAAAATCTATGTTTTTCCTCTTGAGGTGATTTTGTTGTATGTAAATGTTAATTTCATGGTATAG
AAAATATAAGATGATAAAGATATCATTAAATGTCAAAACTATGACTCTGTTCAGAAAAAAAATTGTCCAAAGACA
ACATGGCCAAGGAGAGAGCATCTTCATTGACATTGCTTTCAGTATTTATTTCTGTCTCTGGATTTGACTTCTGTT
CTGTTTCTTAATAAGGATTTTGTATTAGAGTATATTAGGGAAAGTGTGTATTTGGTCTCACAGGCTGTTCAGGGA
TAATCTAAATGTAAATGTCTGTTGAATTTCTGAAGTTGAAAACAAGGATATATCATTGGAGCAAGTGTTGGATCT
TGTATGGAATATGGATGGATCACTTGTAAGGACAGTGCCTGGGAACTGGTGTAGCTGCAAGGATTGAGAATGGCA
TGCATTAGCTCACTTTCATTTAATCCATTGTCAAGGATGACATGCTTTCTTCACAGTAACTCAGTTCAAGTACTA
TGGTGATTTGCCTACAGTGATGTTTGGAATCGATCATGCTTTCTTCAAGGTGACAGGTCTAAAGAGAGAAGAATC
CAGGGAACAGGTAGAGGACATTGCTTTTTCACTTCCAAGGTGCTTGATCAACATCTCCCTGACAACACAAAACTA
GAGCCAGGGGCCTCCGTGAACTCCCCAGAGCATGCCTGATAGAAACTCATTTCTACTGTTCTCTAACTGTGGAGT
GAATGGAAATTCCAACTGTATGTTCACCCTCTGAAGTGGGTACCCAGTCTCTTAAATCTTTTGTATTTGCTCACA
GTGTTTGAGCAGTGCTGAGCACAAAGCAGACACTCAATAAATGCTAGATTTACAAAA

FIGURE 72

MSSSSWLLLSLVAVTAAQSTIEEQAKTFLDKFNHEAEDLFYQSSLASWNYNTNITEENVQNMN
NAGDKWSAFLKEQSTLAQMYPLQEIQNLTVKLQLQALQQNGSSVLSEDKSKRLNTILNTMSTI
YSTGKVCNPDNPQECLLLEPGLNEIMANSLDYNERLWAWESWRSEVGKQLRPLYEEYVVLKNE
MARANHYEDYGDYWRGDYEVNGVDGYDYSRGQLIEDVEHTFEEIKPLYEHLHAYVRAKLMNAY
PSYISPIGCLPAHLLGDMWGRFWTNLYSLTVPFGQKPNIDVTDAMVDQAWDAQRIFKEAEKFF
VSVGLPNMTQGFWENSMLTDPGNVQKAVCHPTAWDLGKGDFRILMCTKVTMDDFLTAHHEMGH
IQYDMAYAAQPFLLRNGANEGFHEAVGEIMSLSAATPKHLKSIGLLSPDFQEDNETEINFLLK
QALTIVGTLPFTYMLEKWRWMVFKGEIPKDQWMKKWWEMKREIVGVVEPVPHDETYCDPASLF
HVSDDYSFIRYYTRTLYQFQFQEALCQAAKHEGPLHKCDISNSTEAGQKLL

Important features of the protein:

Signal peptide:

amino acids 1-17

N-glycosylation sites.

amino acids 53-57, 90-94, 103-107, 322-326, 432-438, 546-550

N-myristoylation sites.

amino acids 260-266, 286-292, 395-401

Cell attachment sequence.

amino acids 204-207

Neutral zinc metallopeptidases, zinc-binding region signature.

amino acids 371-381

FIGURE 73

CCCACGCGTCCGAGCGGGGTGGACAAGTGGCGTGTGTGCTGCGACCCCGAGGGAAG**ATG**AACG

GGACGCGGAACTGGTGTACCCTGGTGGACGTGCACCCAGAGGACCAGGCGGCGGCGGGCAGGA

AGACCTATGCCATGGTGTCCAGCCACTCAGCTGGTCATTCTCTGGCTTCAGAACTGGTGGAGT

CCCATGATGGACATGAGGAGATCATTAAGGTGTACTTGAAGGGGAGGTCTGGAGACAAGATGA

TTCACGAGAAGAATATTAACCAGCTGAAGAGTGAGGTCCAGTACATCCAGGAGGCCAGGAACT

GCCTACAGAAGCTCCGGGAGGATATAAGTAGCAAGCTTGACAGGAACCTAGGAGATTCTCTCC

ATCGACAGGAGATACAGGTGGTGCTAGAAAAGCCAAATGGCTTTAGTCAGAGTCCCACAGCCC

TGTACAGCAGCCCACCTGAGGTGGACACCTGTATAAATGAGGATGTTGAGAGCTTGAGGAAGA

CGGTGCAGGACTTGCTGGCCAAGCTTCAGGAGGCCAAGCGGCAACACCAGTCAGACTGTGTGG

CTTTTGAGGTCACACTCAGCCGGTACCAGAGGGAAGCAGAACAAAGTAATGTGGCCCTTCAGA

GAGAGGAGGACAGATGTCCAGAG**TGA**TTGGAGAATGTCCTGGGGGAATGAAGTTCCTTCCACA

AACACAGCTCAGTTCTTAGCAACAAACTGTTTGTTTTTCTACTTGCTCCATCTGCAGCCTACG

CTGCCCTGGCCTCCTGCAGACAGATAGTGGGGTTACCTGGCAAGGCCTGGTGAGAGCCAGTGA

ACCTAAGCTTTGACTGGGTGGCCTTGTCTTTCTGGGGAGGAGGGAATGTACATTCAGGGAGTA

GCCTTTTGCGGAAAAATTCTCTAGGGCTACAGACAGTCATGTGTGACTTCTCTCTGCTGTGAA

AACTCCCAGAGTCTCTTTAGGGATTTTCCCTAAGGTGTACCACCAGGCACACCTCAGTCTTCT

TGACCCAGAGCCTGAAAACTGTTTTCACTGGGTTCCACCAGTCCCAGCAAAATCCTCTTTGTA

TTTATTTTGCTAAGTTATTGGTGGTTTTGCTTACATCTCATGATTGATATAATACCAAAGTTC

TATAGCCTTCTCTTGCAGTATTTGGATTTGCTTGAAACCGGGAAAACTGTTCCCATTAGGCTT

GTTAATGTCAGAGTGACACTATTATGAATCTTTCTCTCCCTTTCCTCTGCCTGTTTCTTCTCT

CTTTCTCCTTCAAACTTGCTCTGCAGCTAAGGAAGGTGAGTCTACTTTCCCTGAGGCTTTGGG

GTCAGAGTATATGTTGTTTGGAGAAAGAGGGCAATCAGGACTCTTCTGGGACCCAGATGAGTT

CTTCACTAGCCCTTCTGAACCCCTTGCTCCATAATTGGTCTTTTATCCTGGCTCTGAATGACC

CTGCAGGTCATCATGGTTTTCTTTTTTTATTGTTTTTTTTTTTTTTCTGAGACAGAGTCTCACT

CTGTCACCCAGGCTGGAGTGCAGTGGCGCGATCTCAGCTCACTGCAACCTCTGCCTCCCGGAT

TTAAGCGATTCTTCTGCCTCAGCCTCCCGAGTAGCTGGGACTACAGGTGTGCCACCACGCCTG

GCTGATTTTTGTATTTTTAGTAGAGATGGGGTTTCACCATACTGGCTAGGCTGGTCTCGAATT

CCTGACCTCAGGTGATCCACCCACCTCGGCTTCCCAAAGTGCTAGGATTATAGGCTTGAGCTA

CTGCGCCCGGCCCATGGTGTTTTTCTTTAGGGCTCTTCCTACAGCCTTGAGAAGTAGATAGGC

ATCAGAGTATGGTACTATAGGAATCAGAAAAATTCAAAACAAATGTGGATTAAGTGTTTAGGC

TCTATGTGGCTCACGCAGCCAGAATCCTTAAGTCTGTGTGTTTCTGTGTCTCAAGACTGGGCT

CACATTCTGGCTTTGTCCATAACAATGCTCTGGGATTTCAGGGAGTTCCCTCATTTGTAAAAT

GAGGGGGTCAGAGCAGGTGATATCCATGTTTCTTCCCTTTCTGATATTGTTGTCTGTGGCATA

TTCTTTGTATGGCGAATTTAATAAATTATATTAATGTGTCA

FIGURE 74

MNGTRNWCTLVDVHPEDQAAAGRKTYAMVSSHSAGHSLASELVESHDGHEEIIKVYLKGRSGD
KMIHEKNINQLKSEVQYIQEARNCLQKLREDISSKLDRNLGDSLHRQEIQVVLEKPNGFSQSP
TALYSSPPEVDTCINEDVESLRKTVQDLLAKLQEAKRQHQSDCVAFEVTLSRYQREAEQSNVA
LQREEDRCPE

Important features of the protein:

Signal peptide:

amino acids 1-39

N-glycosylation site.

amino acids 2-6

Amidation site.

amino acids 21-25

FIGURE 75

GCTTGCACACATGGCTCCGGAGGCTCCGGTTGCCCATCCGAGCCCCTGCCAGGCTCTAACGTTCCCAACTGACAA
CACCAGTAACTAAATATAGGAGCAGATGGTGGGGACGGGCTGTCGCAGCGGCTCCTTTGCAGAGGTCTCCGGACT
GCAGATAAGGCTCAGGCCCTTTTGTGAGAAGCAGACCAGCCTGGGGGCTGGCGGCAGGACACCTGTGTCTGC**ATG**
CTGAAGAAGATGGGTGAGGCCGTGGCCAGAGTAGCAAGGAAGGTCAACGAGACGGTGGAGAGCGGCTCTGACACT
CTGGACCTGGCCGAGTGCAAGCTGGTCTCCTTTCCCATTGGCATCTACAAGGTCCTGCGGAATGTCTCTGGCCAG
ATCCACCTCATCACCCTGGCTAACAACGAGCTTAAGTCCCTCACCAGCAAGTTCATGACCACATTCAGTCAGCTC
CGAGAGCTCCACCTGGAGGGGAACTTCCTACACCGCCTCCCCAGCGAGGTCAGTGCCCTGCAGCACCTCAAGGCC
ATTGACCTGTCCCGGAACCAGTTCCAGGACTTCCCTGAGCAGCTTACCGCCCTGCCGGCGCTGGAGACCATCAAC
CTGGAGGAGAACGAGATCGTAGATGTGCCCGTGGAGAAGCTGGCCGCCATGCCAGCCTTGCGCAGCATCAACCTC
CGCTTCAACCCACTCAACGCCGAGGTGCGCGTGATCGCCCCGCCGCTCATCAAGTTTGACATGCTCATGTCTCCG
GAAGGCGCAAGAGCCCCCCTACCT**TAG**GCCACCCTCCTCATGCCCACCCAGCAAGGGACAGAGGCCACAGGCCTG
GAACCCTGGAAGGGAGGGAGGCCCATGGGAGGCCAAGCCTGGGGGCTGGGGGCGGGTGGGCCGAGCAGCACGTGG
TGGGTGGGGTGCAGCTGGTCTGGATAGATAGCTTACAGCAGTAGTGGGCTCTGGAATGCCCAAGGGAAGAGGCAA
GGTGGGGCCTGCAGCCTGGACTCGGCACTCACAGCTGCTGTGCAAACTCAGGCAGATCTCCTGCCCTCTCTGAGC
CTTGTCACTTGAAAAAAACAGGACCCTTTCCCTCCTTTGGGCTCCCTGGAGGTTTTTAAGCAGTACGTGCCTCCA
AGTTACCTCCAGATCAGCAGGCACAGGTGGGCATTGCCAGGTATTTTCTGAGCCCCTGCGGGTTTGAGGCCTTGT
TTTTAGTGCTGAGAGCCAGTTGCTGCCCTGAGAAGAGAAGACAACCTCCATCTATTTATTGCTTCCTGAGAACTG
ACCTGGATGCGGCCCTCTGCAGGGCCCAGTCTTCAGTCCTGTGGTCCCTGGACTGGTGGGAACCTGAACTAGGAG
TCCTGGGAGAGCTGTGGTGGGAATATGGGCTGGCACTGCTGCAGGGCAAGAACATTCATGTAGGAGCCCGAGGAC
CANCANGCTGGGAATGGGGAGCAAGTCACGTCAGCTCTGTCATTCCCCACAGTTAACAAATTGGCGGGGTGGGAA
GTCCTGAGTGCTCCGTCCCTCTAGCATCACTCCTGAGCTGCGGGAGAGGTGGCCCAGAGAACAGCAGAGTCAGTT
ACACCTGCAGCTCTTGTCTAAAGTGATTAGATGGCCACCCTCACCACTGTCCAGTCCAGCAGCAGCCTGGCTGCC
TTGTCATGGCCTCCTGGGGGCAGAAGGCGATGTGGACCACGGGATTTGTAGCCAGCCAGCTCCCAGGCCAACGCC
CAAAGCCCTGATGACCTGGTTCTTCTGAGGCCCTCAACCTGGCATCTTAGGGTATGGTCAGGCAACAGGGTGACC
AGCTGTCCTGGTTTCCCAGGACATGGAACTTTCAATGCTAAAACTGGGACATTACCCAGCAAGTGGGGATGGTTG
GTCCCCTACCAGGAGAGGCCTGGGGCTCTTGCTTCCCGAGAACGCCTGTGGCTTGAAGAACCTTGACTGCTTGG
TCCTCAGGTATCTACCTCCCACCTTCTCCTCATCTGTGGAGCAAGCCAACTCAGTGCCCCAGACCCCACCTGATC
TGCATCTTTGTTTGCTCCAGAGACACCTGAGGCCCCAGAGCTTGAGGCAAAGCCAGGCCGTCCAAATCCTGTGTG
CCGTGGACGAGTGGCCACTTTACTACTCCTAAGGCTAAGATGTTGAGAGCTCAGACCACTGCTCAGAGCAGTAAT
CCCTGCTCAGAATGCTCCCAGTTCCCTCGTCCCTGCCCAGGTCTCTTGTCTCTTGGGAAGGAACTGATAGGTCGG
GCCATTGTTGGGCCATCACTGAGCGCTCAGTATCTCAAGAGACTCTGTTCATTCTGCTCGTATCCCAAGGCCTGG
TTGGTCAAACTCTGGGCAAAGGGTTTTCAGGATGAGGAGGTCAAGACAGGATGTCCAGAGCTACCGAGTTCATCT
GTGGGTGTTGGGGGCAAGTGGGGGCTGAAGTCCTGTGCAGGCTGCGCTGGCCCCACCTGCCTTGTGCCCTGGAGT
GGGGTTTCTCCTTGTTGAAGAAGAGGCATCCTTCTCTGATGTGCACAAACACAATGTATGACCAGAGCCTTGCAA
CTCAAAGTGTGGTCTGTGGACCAGCAGCGGCAGTGACACCTGGGAGCTTGTTAGGAATGCAGAGTCTAGGCCTCA
CCCTATACCTCCCGACTCAGACCCTGCATTTTAGCAAGACCCCCAGCTGATTCCTATAAGCACTTTAGAGTTTGA
GAAGCAAGGACCTAGGCTGGGGATGTCCTCCGAGCAGAGGGTGAAGTTTCTCTCAGTTCTCTCCCTGCCACTTCC
AGGGATCTGAGCCTGTGTTCAGCCTCCTCCCTAACCCACCCTGGGAGACACTTGGCCTGTTAGATTGTTCCAGAG
TCTGCATGGCACTCCTGAAGAAGGGAGTGTGACCTGCAGTCACCAGGAGATGAGGGTTAGGTGTGCCCAGCCCTC
CAGACCCGGCCTTTCTGGTTAACCCCTGCATGCCAAGCTGCCTGCTGCCCCAGGTCCTCACCTCAGGCCTTTGAA
GGGGCAGCTTCTGGAAGTTGTTTTCTCCTCTGCTTGGAGAGTTTGCCCTTGTCTGTCTTGGAAAGTGTGGGCAGC
CACAGATGCCCCCAAATCAGAGCTCACAGTGAGTGAGCCCCTAAGCTTCAGTCTGCAATAAAGAATGCATTGGTT
TCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 76

MLKKMGEAVARVARKVNETVESGSDTLDLAECKLVSFPIGIYKVLRNVSGQIHLITLANNELK
SLTSKFMTTFSQLRELHLEGNFLHRLPSEVSALQHLKAIDLSRNQFQDFPEQLTALPALETIN
LEENEIVDVPVEKLAAMPALRSINLRFNPLNAEVRVIAPPLIKFDMLMSPEGARAPLP

Important features of the protein:

N-glycosylation sites.

amino acids 17-21, 47-51

FIGURE 77

CACCAACAAGCAATCGTTCATGAGAAAGCCGTGCACCCGCTGCAGTTGGGCCATGTGGTCCGCATCGTATTCCAC
TAGGTCCCCATTGTACACCAAGTACTGTCCCGGCGTCTCCAGCAGATGCCTGCAGCCTTCCACCTTCTCAAGCAG
GGTGGTGTGAGTGCGCTGCTTTCCTTCCTCGCCTGGACCGGAGCCGTCGCGGGAGGCACCCCCGGGGGTGGAGAA
AAAGCCGGCCTGGCCTCGGAGGTGGTCTCGGCCCCCCGCCCCACCGACTCCCTCCTCCCCTCCAGAGGCGGCGGC
GGCTCCGGCGGCAGCAGCGGCAGGCAGCAACGTAAGCGGGATGCTCTCCAGGCTGCTTTTCTGCTCGGTCAGCAA
ATGGCTGAGCTGGTACATCTCGCTCTCCAGGTAGGAGATCTCGCGGGCCGTCTCTATGAACTGCCGGTAGTTCTG
GTAGACGTTGCGCTTCAGGTTCTGCGCCGTCTCCTCCGCCAGCGCCTGGATGCGCTGCCGGTGCTCCTGGAGGTC
CCGGTCCCCATCCGACTGCTGCGAGAGCTGCTTCACGTACAGCCGCGCCTCAAAACCCCCTGACTCCAGCTGCCG
ACGCAGGCGGCTCGCCCCACTGTCCGACATCGCCATCGCCATTTCTCTCCGGGTCTCACGCACTCACTGTCACTA
TCGGCGCCGCAGCCGCCGCGGCTGTCTAGACCCACCCAAGGCCAACCGAGCTCCTGGGCTGAGGAAGCAGGAATG
GGAACGAGACGAGTACGCCTGCGCCGGGTCTGAGCGTCAGACACTGCGCCTGCGCAAGTGGGCCGAGCGCAGACA
TTGCGCCTGCGCAGCAATGCCATCGGTTAAAGCGCATGCGCAAGATGAGCTATTGCGGAAGTGAGGGGAGGGAGA
GGCCGAGAGAAATTTCGGTACTGCGCATGAACCGAGCGTGACGTTGAGGTTTGAAATAACCGGCAAAGAGTAAAG
GCTGAAACTAGCTTCCTGAAAGCTTCGTAGGGCCCGAGCCCTGTGAGCCCAGGTTCTGCGCCCACTAGGAGGTGT
CATGCTGACTGCTTTTTTTAAAGCCCTAGAATCCTTGGCTTCGGCGTTTGGGGTAAGCTCCGTTCTCGTTCTCAA
GCGCGTTTCCGCGAACTCTCGCGGGATTGACGGGCCGTCTCGAGAGCCGGCATCTCCTAGGAGCTAGTCCTGGTC
CTCGGCTAGGCGGCTTGGGGTCGCGGCGTAACTGGGGAGCCAGCCTGACGCCGGCGGACCCCGCCTGTGATCCTG
GCAACG**ATG**GATGATGACTTGATGTTGGCACTGCGGCTTCAGGAGGAGTGGAACTTGCAGGAGGCGGAGCGCGAT
CATGCCCAGGAGTCCCTGTCGCTAGTGGACGCGTCGTGGGAGTTGGTGGACCCCACACCGGACTTGCAGGCACTG
TTTGTTCAGTTTAACGACCAATTCTTCTGGGGCCAGCTGGAGGCCGTCGAGGTGAAGTGGAGCGTGCGAATGACC
CTGTGTGCTGGGATATGCAGCTATGAAGGGAAGGGTGGAATGTGTTCCATCCGTCTCAGCGAACCCCTTTTGAAG
TTGAGGCCAAGAAAGGATCTTGTAGAGACCCTCCTGCATGAAATGATACATGCCTATTTATTTGTCACTAATAAC
GACAAAGACCGAGAAGGGCATGGTCCAGAATTTTGTAAACATATGCATCGCATCAACAGCCTGACTGGAGCCAAT
ATAACGGTATACCATACTTTTCACGATGAGGTGGATGAGTATCGGCGACACTGGTGGCGCTGCAATGGGCCGTGC
CAGCACAGGCCACCGTATTACGGCTATGTCAAACGAGCTACTAACAGGGAACCCTCTGCTCATGACTATTGGTGG
GCTGAGCACCAGAAAACCTGTGGAGGCACTTACATAAAAATCAAGGAACCAGAGAATTACTCAAAAAAAGGCAAA
GGAAAGGCAAAACTAGGAAAGGAACCAGTATTGGCCGCAGAGAATAAAGGTACCTTCGTGTATATTCTTCTGATT
TTTATG**TGA**CCATAGCTATGATGTAAAGACAATACTGTCCTTCAGAGAACTGGTATTAAGATAAACTTAAGGATC
GTTTCTGGTGTAGAAGTCTTCAAGTGTAGACTTAAGGAAAAAATCCCACTGTCCATGAAATGATGGTAGGAAAAC
AGACTTTGCTCTGTACAGAAGTAAGTAAAAGTAGGAATAGTTTCCATGGATATTTTTATTTTTATTAACTTTTTT
CAGTTTCTTTTTATTCAAAGAAACAAAATTCAATCTCTGATAATATTTGAGGTAAAGTTCCTTTCCCTATCTTGA
CTCACTGAGTTATTAGGAAACAGAAGGCAAAAAGATTGTCAAAATAAAAACAATAATTCAAGTAACAATGCCCGG
AATATACGTCCTAACTACACCCCTTCCTATCAGCTGGATTCTATCCAAGTGACTCTATTGATGTATGTATGTTCA
TTCAAAGAATGGGAAAAGGATATGACATATATTTGCCAGTACTTCATCTTCAAGATTTACCCTTTTCCTGTGAAG
TTCAGAGTTACTGAAGATGCTTCTTCCCTTGGGAAGTTGTTGACCCAAGAACATAGGTTATATTTCCCAAATCTT
TAATTATTGAGTGAAAGAGCTATAGATGAATTGATATGGAAAGACCGTATCTTCATTTTCGTGAGTAGAAGGAAA
GATAAGAATGAGGCAGCAGATTTTCCCTCCTGGAATTACACATAAAGGACACTAAGCAATTTTCAAGGTAAATGT
TGCCTTGTTGTTGGTCTTTGGCATGATAAGATTCTTTATTTAAATATGAGAGAATTTTTTTTTATCCTTTATATT
CTCTCAATATCAGAACTCCTGAATTCTGAAGATTGCCCTCCTCCCATTAATAGGATTGTATGGATGTAAGATGGA
ATAAAATACTAGTTCTTCATTTTGAGAAAACTGTACATTAGTTTAATGTTTGTTACTGTATTTCTTTTGAGTTGA
GGCACTTACATAACAATCTTCTTTGCTTTTTTGGCAGATAAACCCAACAGAGGTGAGGCCCAGCTAGTAATCCCT
TTTAGTGGGAAAGGATATGTTCTAGGAGAAACAAGCAATTTACCTTCACCTGGGAAACTGATCACTTCACATGCC
ATTAATAAAACCCAAGATCTTTTAAATCAAAACCATTCAGCAAATGCTGTAAGACCTAATTCTAAAATCAAGGTG
AAATTTGAACAGAATGGTTCAAGTAAAAATTCTCATCTGGTCTCCCCTGCTGTTAGTAACAGTCACCAAAATGTT
CTAAGCAACTACTTTCCTAGAGTATCATTTGCCAACCAAAAGGCTTTCAGAGGTGTGAATGGATCTCCAAGGATA
AGTGTAACAGTTGGCAACATCCCTAAAAACTCAGTCTCTTCTAGTTCTCAGAGAAGGGTTTCATCTTCTAAGATA
TCCCTAAGAAATTCTTCAAAAGTAACGGAATCAGCATCTGTGATGCCATCCCAGGATGTGAGTGGGTCTGAAGAT
ACATTCCCAAATAAACGACCTAGGCTAGAAGATAAAAAAAAA

FIGURE 78

MDDDLMLALRLQEEWNLQEAERDHAQESLSLVDASWELVDPTPDLQALFVQFNDQFFWGQLEA
VEVKWSVRMTLCAGICSYEGKGGMCSIRLSEPLLKLRPRKDLVETLLHEMIHAYLFVTNNDKD
REGHGPEFCKHMHRINSLTGANITVYHTFHDEVDEYRRHWWRCNGPCQHRPPYYGYVKRATNR
EPSAHDYWWAEHQKTCGGTYIKIKEPENYSKKGKGKAKLGKEPVLAAENKGTFVYILLIFM

Important features of the protein:

Signal peptide:

amino acids 1-41

N-glycosylation sites.

amino acids 148-151, 217-220

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 184-187

Casein kinase II phosphorylation sites.

amino acids 30-33, 121-124, 154-157, 187-190, 192-195

Tyrosine kinase phosphorylation site.

amino acids 211-218

N-myristoylation sites.

amino acids 59-64, 85-90, 146-151

Neutral zinc metallopeptidases, zinc-binding region signature.

amino acids 108-117

FIGURE 79

CGGACGCGTGGGTGGCAACCAGGAGAAGCCAAACTTGGTCCCCCGGCTCGCGGAGTGCCTGCG
AGCGGTGCTC**ATG**GCGCTCTATGAGGTCTTCTCTCACCCGGTCGAGCGCAGTTACCGCGCGGG
GCTCTGCTCCAAAGCCGCGCTGTTCCTGCTGCTGGCCGCTGCGCTCACGTACATCCCGCCGCT
GCTGGTGGCCTTCCGGAGCCACGGGTTTTGGCTGAAGCGGAGCAGCTACGAGGAGCAGCCGAC
CGTGCGCTTCCAACACCAGGTGCTGCTCGTGGCCCTGCTCGGACCCGAAAGCGACGGGTTCCT
CGCCTGGAGCACGTTCCCCGCCTTCAACCGGCTGCAAGGGGATCGCCTGCGCGTCCCGCTCGT
TTCGACTAGAGAAGAAGACAGGAACCAGGATGGGAAGACGGACATGTTACATTTTAAGCTGGA
GCTTCCCCTGCAGTCCACGGAGCACGTTCTCGGTGTGCAGCTCATCCTGACTTTCTCCTATCG
ATTACACAGGATGGCGACCCTCGTGATGCAGAGCATGGCGTTTCTCCAGTCCTCCTTTCCTGT
CCCGGGATCCCAGTTATACGTGAACGGAGACCTGAGGCTGCAGCAGAAGCAGCCGCTGAGCTG
TGGTGGCCTAGATGCCCGATACAACATATCCGTGATCAACGGGACCAGCCCCTTTGCCTATGA
CTACGACCTCACCCATATTGTTGCTGCCTACCAGGAGAGGAACGTTACCACCGTCCTGAATGA
TCCCAACCCCATCTGGCTGGTGGGCAGGGCCGCAGATGCTCCATTTGTGATTAATGCTATCAT
CCGATACCCTGTGGAAGTCATTTCTTATCAGCCAGGATTCTGGGAGATGGTAAAGTTCGCCTG
GGTACAGTATGTCAGCATCCTGCTTATCTTCCTCTGGGTGTTTGAAAGAATCAAGATCTTCGT
GTTTCAGAATCAGGTGGTGACCACCATTCCTGTGACAGTGACGCCCCGGGGAGACTTGTGTAA
GGAGCACTTATCC**TAG**AAAGGCCATTTCTGAAGACTCAGCAGGACCGTGGCTGCCTCATTGTC
ATCTTCTGGGAACATCTTAGGACCTTTTGAAAGAGCCCAGCGGACACCTGCGGGCTTGTGTGC
TTTTCCCTCAGAGACAACGGTTCTTTCCGGTTTTGCTCTACACAGTTCCGTATCTTCAGAGCT
CCTGCAGAATTGTCAGGGACTAGTTTGTGGAAAGGTCTGAGAGTTCCTGGAGGCTATAATTAG
CTTTTTGGGTTTTCCTTCTTTGCCTTAGCGTTGAATTTCAGGAGAAAATTGCAGTCAGTTCAG
ACATCTTGGAAAGAGTCCCATCTCTGGTCAAGCAGAGACTTTTCCTCTGTTGAACTGAGGAAC
ACACTGTGCATTTCTTCCTTCTGTTGTGAGCCACTCTTACTCTTTTCAGGGCTCTCTTGTGAC
AAACATGCCAATCACTAGCACTTTGCACCCCTGGGCTTCTCCATTTCCCATTCACAGCTTTGA
TTTCCAGAGCTGAGGCCTTTAACTGGAGACCTGGAGGGGCAGGGCCCAAGGGCAAGGGCCGCA
TTAGCACAGGCAATCAGGGAGGGCCGCTGAAGGACACTTGGACCGTCCACCTGCCCCAGCCCA
ACAGTCAGTCATCTGTCATCAGCTCAGCTGAGCAGCCCTGGATCTTTGCCGTACTGTGACTGG
GCTCTTTGCCCTATTTTTCCCTCTGTCTGTGCCCCTGGATGGCAGGCTGAAGTCAGAGGGGCT
GTTTCATTCTCAGCCCCCTCAGCAGCACTGGGGGAAGAAAGCATTGTCACAACAGGTTCTTTC
TGGCCCTCACCCAACAGCCTGGGCACTTGGCCCTCCTCCTCCTTGACAGCCCTCCCCCTTCCT
GCAAAGGACAGGGGCGACAGGGGTTGGTGTTGGGATTGGCTCCCGCTGCCTGACAACCACAAG
TTTATTTGGAAGGCTAGCGGGAAGCCCAGCGGCTGGCGTTTCCCTTGACTAAGGAACAGGGTG
CCCATCAGAGTGGGGCGGGCAGCTTTGGGAAGGACACAAGAAGCAGTAAGAGTGTAAAGAGGA
TGCTGGCCTGGGCAGGCCAGTCCAGCCTGGCCACTAGCAGAATACCAAGCAGTCCAGTGGATT
ACCCTCGTGGCTAAGCAAGTGTCTGCAGGAGCAGAGATGGCTGGAAGGGGCCTCTGCACACGG
AAGATGGCTTGTTCAGCCCATTCACCTCCTGAGGATGTGGGCAGTCTCCTCCAAGAACACATG
GAGCTGCTTCCTGATCCCAAGCAGGTCATTGCCACTGGAAGGACATGGCCCCGGTGATCCATG
CTTCATGCCCACCCAGAAACACACCCCTCAGTGTGTGCCTCAGTTTACTTTGGAGATCAGTTG
TCGTTTTTAGTGCTCCTTTAGGCTTACTAAAACAGTTTTGGAAACAAAGCTATTTTGAAGTAT
TCAAGCAGAGGAATTCCCTAACACTGACCCCCTTGTCTTTTTTTTAATATTCAGGCTGTTTTAT
ATGCCTAAATTTTTTTCTTAAGATCTAAACGAAAAATAGTTTCTTGTTTAAATTCACATAAGG
CAATGAGATATGGAAAGATGACAAGATACGTATAAACATTGGTTTGCATCTTATTAAATTATT
CTAATGCAAATCTTGTATAAAGAACCCATGATGTTTTGTAACTTTCTAATTAAAATGTTCAAA
ATGAG

FIGURE 80

MALYEVFSHPVERSYRAGLCSKAALFLLLAAALTYIPPLLVAFRSHGFWLKRSSYEEQPTVRF
QHQVLLVALLGPESDGFLAWSTFPAFNRLQGDRLRVPLVSTREEDRNQDGKTDMLHFKLELPL
QSTEHVLGVQLILTFSYRLHRMATLVMQSMAFLQSSFPVPGSQLYVNGDLRLQQKQPLSCGGL
DARYNISVINGTSPFAYDYDLTHIVAAYQERNVTTVLNDPNPIWLVGRAADAPFVINAIIRYP
VEVISYQPGFWEMVKFAWVQYVSILLIFLWVFERIKIFVFQNQVVTTIPVTVTPRGDLCKEHLS

Important features of the protein:

Signal peptide:

amino acids 1-34

Transmembrane domain:

amino acids 268-284

N-glycosylation sites.

amino acids 194-198, 199-203, 221-225

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 51-55

Tyrosine kinase phosphorylation site.

amino acids 250-259

N-myristoylation site.

amino acids 187-193

Cell attachment sequence.

amino acids 307-310

FIGURE 81

GCCGGGAGCTTCCCTG**ATG**GTGCCGCCGCCTCCGAGCCGGGGAGGAGCTGCCAGGGGCCAGCTGGGCAGGAGCCT
GGGTCCGCTGCTGCTGCTCCTGGCGTTGGGACACACGTGGACCTACAGAGAGGAGCCGGAGGACGGCGACAGAGA
AATCTGCTCAGAGAGCAAAATCGCGACGACTAAATACCCGTGTCTGAAGTCTTCAGGCGAGCTCACCACATGCTA
CAGGAAAAAGTGCTGCAAAGGATATAAATTTGTTCTTGGACAATGCATCCCAGAAGATTACGACGTTTGTGCCGA
GGCTCCCTGTGAACAGCAGTGCACGGACAACTTTGGCCGAGTGCTGTGTACTTGTTATCCGGGATACCGATATGA
CCGGGAGAGACACCGGAAGCGGGAGAAGCCATACTGTCTGGATATTGATGAGTGTGCCAGCAGCAATGGGACGCT
GTGTGCCCACATCTGCATCAATACCTTGGGCAGCTACCGCTGCGAGTGCCGGGAAGGCTACATCCGGGAAGATGA
TGGGAAGACATGTACCAGGGGAGACAAATATCCCAATGACACTGGCCATGAGAAGTCTGAGAACATGGTGAAAGC
CGGAACTTGCTGTGCCACATGCAAGGAGTTCTACCAGATGAAGCAGACCGTGCTGCAGCTGAAGCAAAAGATTGC
TCTGCTCCCCAACAATGCAGCTGACCTGGGCAAGTATATCACTGGTGACAAGGTGCTGGCCTCAAACACCTACCT
TCCAGGACCTCCTGGCCTGCCTGGGGGCCAGGGCCCTCCCGGCTCACCAGGACCAAAGGGAAGCCCAGGCTTCCC
CGGTATGCCAGGCCCTCCTGGGCAGCCCGGCCCACGGGGCTCAATGGGACCCATGGGACCATCTCCTGATCTGTC
CCACATTAAGCAAGGCCGGAGGGGCCCTGTGGGTCCACCAGGGGCACCAGGAAGAGATGGTTCTAAGGGGGAGAG
AGGAGCGCCTGGGCCCAGAGGGTCTCCAGGACCCCCTGGTTCTTTCGACTTCCTGCTACTTATGCTGGCTGACAT
CCGCAATGACATCACTGAGCTGCAGGAAAAGGTGTTCGGGCACCGGACTCACTCTTCAGCAGAGGAGTTCCCTTT
ACCTCAGGAATTTCCCAGCTACCCAGAAGCCATGGACCTGGGCTCTGGAGATGACCATCCAAGAAGAACTGAGAC
AAGAGACTTGAGAGCCCCCAGAGACTTCTACCCA**TAG**CACATCCCAACACCGTCACGCCAAAGGAAGAGAAAGAT
CAACTCACCTGCAGTTAAACCATCTAAAGAGAAGAAAGACCACTGGAGACCTAGAAAACATACATTTTTCTCTTC
TCTTCTCCTGACGTCTCTCCACTCCTCTTCTTCCAAATACGATGCTATTTTCAGAGTCCCCTCCTAGGCCTGCAG
ACATGAGGGAGTGAATGATTGATTTACCTGCTTCTCACTAAGAGTCCATTGGGGTGGTTTGCATTGTAACTTTTC
TTTTACATCCTATTTTTCCAGGAACTTTGGATTTAAGTACTCTCACAGTGTCTTAAATCATAAATTCTTGAAGTT
AAATTTGGCAGAGTATCAAAAGGGGGAAAATGACAAAGTGAGCTCTAAGAAAATGTGAGGCTACTTCTAAGATGT
GTGTTCACAATAGACCATAACTCCTCTAGTATCAAAATTGGGGCTCTTCAGTTAAAAAGGGGTGGGGAGGACAAA
CGTGTCGATGTGCTTTGGTGGAGAATTTTTTCCTTGTGCTTCTAGTAGACTTTAAATATTGTATCCCTTTGTCAA
ACCTTGTTTCCCAAATTCAATTAAAGAGAGGAGAGAATTGAATGGCGTTTAGAGAAGATAGAAAAGAATCACAGT
CATATATTTACTGTTATATAGATTGCCACATTCTAAAATTCAAATACGGTGCTTAAGGTTTCATGCCATGCTTAT
CTGTAAGTATCCTATTTAGGGAAGAAGATTAAACTCTCTTTTCAAAAAAACAAAGTGAAATGCCTGGATTCACAT
TAAAACAATGGGCTCTCGTTTGCTATAATATTTTAAAGCTGTTTAATCAACAGTGGAGTCTGCTCTATAAATATA
GATTATTTGTTCAATAAACTGGCTGAGCTTAGAGAGAGGTGCAGAATTCCTGGTTCTGAGCAGGTGCCCAGAAGG
TACCATTAGGTGCCATGATCCAGGCTGAACCAATATACAGTGGGGCTGAAGTCTGCAAGGAGGTTGCTGGCTTGG
GCTGACCTCACTAATGCCATCAGCAGCGGTAGGTAAATTTTTTCTCCTTGGGTATTACAAGTTTTTGTCTGGAGC
CAACCAAGCTTGCCACCAACATATTGAGAGTAATACACTATTGAAAGTTATCTTGGATGGGGAGAAAAAAAAATA
GTGGTTTTCCTTGTTTGCAAAAACTTCCTTCCTATTCTCATTTTTTCTTAATTTTCTTTAATTTAGTCCAAGTTC
CAGTTCTTTTAGGCCTTCTCTTTGATTTATTTTCCCCTGCATGTGAGAAGCAGTTCAGAAAAAGGTCTATATCTC
CACCTCCTAGTGAGTTAGAGTGTTTTCTCAGAGCACCTCTGGGTGGCAAAGGGAAGCATGTTCCTGCCAAGGTTT
GCTGTGGATTCAGAAGCACCAGGAGCAAGAGACCAGAAGGATGATCTGCTCCTTTGTAACGTTGTTGAGGGCCCT
CTTGTTTCCAATGAGCAGCTTATAGGTTACTCACAGTCCACTTTCTCACTGGACACACAAAGTGGCTCTTTATCT
ACCTTTGCGGGAGATTTTCACTCTCCTGCAAATGATCGTTCTCACACTCATATTAGCTCATGTTGGAATTTCCCA
TCCTGCCATGTCCTTTCCCATTTCTTTTTGGCTTTTTTGCCTCCACCTTTTAGCCCACATCATTTAACTCCACTA
CTGTGAAAGCTTGCTTAAAGAAAATCCCTCTTGGCCGGGTGTGGTAGCCCACGCCTCTAATCCCAGCACTTTGGG
AGGCTGAGGCGGGGAGATCACAAGGTCAGGAGATCGAGACCAGCCTGACCAACATGGTGAAACCCTGTCTCTACT
AAAAATACAAAAATTAGCTGGGCGTGTTGGCACACACCTGTAATCCCAGCTACTCAGGAGGCTGAGGCAGGAGAA
TTACTTTAACCTGCGGGGGGAGCCTAGATTGCGCTACTGCACTCCAGCCTAGGCAACAGAGGGAGACTCTGTCTC
ATTAAAAA

FIGURE 82

MVPPPPSRGGAARGQLGRSLGPLLLLLALGHTWTYREEPEDGDREICSESKIATTKYPCLKSS
GELTTCYRKKCCKGYKFVLGQCIPEDYDVCAEAPCEQQCTDNFGRVLCTCYPGYRYDRERHRK
REKPYCLDIDECASSNGTLCAHICINTLGSYRCECREGYIREDDGKTCTRGDKYPNDTGHEKS
ENMVKAGTCCATCKEFYQMKQTVLQLKQKIALLPNNAADLGKYITGDKVLASNTYLPGPPGLP
GGQGPPGSPGPKGSPGFPGMPGPPGQPGPRGSMGPMGPSPDLSHIKQGRRGPVGPPGAPGRDG
SKGERGAPGPRGSPGPPGSFDFLLLMLADIRNDITELQEKVFGHRTHSSAEEFPLPQEFPSYP
EAMDLGSGDDHPRRTETRDLRAPRDFYP

Important features of the protein:

Signal peptide:

amino acids 1-34

N-glycosylation sites.

amino acids 142-148, 182-188

Tyrosine kinase phosphorylation site.

amino acids 125-132

N-myristoylation sites.

amino acids 10-16, 143-149, 155-161, 196-202, 250-256

Amidation site.

amino acids 299-303

Aspartic acid and asparagine hydroxylation site.

amino acids 150-162

Cell attachment sequence.

amino acids 176-179

C1q domain proteins.

amino acids 247-280

Calcium-binding EGF-like domain proteins pattern proteins.

amino acids 144-165

FIGURE 83

ATCTGAGTGAGCTAACTGACACA**ATG**AAACTGTCAGGCATGTTTCTGCTCCTCTCTCTGGCTC
TTTTCTGCTTTTTAACAGGTGTCTTCAGTCAGGGAGGACAGGTTGACTGTGGTGAGTTCCAGG
ACCCCAAGGTCTACTGCACTCGGGAATCTAACCCACACTGTGGCTCTGATGGCCAGACATATG
GCAATAAATGTGCCTTCTGTAAGGCCATAGTGAAAAGTGGTGGAAAGATTAGCCTAAAGCATC
CTGGAAAATGC**TGA**GTTAAAGCCAATGTTTCTTGGTGACTTGCCAGCTTTTGCAGCCTTCTTT
TCTCACTTCTGCTTATACTTTTGCTGGTGGATTCCTTTAATTCATAAAGACATACCTACTCTG
CCTGGGTCTTGAGGAGTTCAATGTATGTCTATTTCTCTTGATTCACTTGTCAATAAAGTACATTC
TGCAAAAGCAAAAA

FIGURE 84

MKLSGMFLLLSLALFCFLTGVFSQGGQVDCGEFQDPKVYCTRESNPHCGSDGQTYGNKCAFCK
AIVKSGGKISLKHPGKC

Important features of the protein:

Signal peptide:

amino acids 1-23

N-myristoylation sites.

amino acids 26-32, 52-58, 56-62, 69-75

Kazal serine protease inhibitors family signature.

amino acids 40-63

FIGURE 85

GGAGCAGACACACAGACCCGGGCCGGAGGCCCCTCTTCTAGCCCTGCGGGAACCGGACAGTTC
CCCAACTGGGGACTCTGGAACCACAGCTCCTAAATCATCAAATTCTCAAGCTTTTTTTTTCCC
TCTCTTCGTCCCAGCCATCCCAGTCTTCTTCTTCTTTTTTTTTTTTTTTAACTTATTGTTTTTT
TCGCTCCTGTCATTATGAAAGTGGTCACGCCATTCAATATTAAGACTTGGAGGGAATTGGGGA
AAGAAAAGAAAGAATCTAAAAGAAGAGAAGCGACCGGTGCTTTTAAGGGTGTCTAATTTTCAA
AAGAGACGTCTGGGAGTATTTTGCTCTGGGCGTTTGGAGCAACTTCGCGGACAGCGGAGCTCG
CCCAGCATGGATGTTCCAGGTTCACAGGCGCCTTTCTTCTGAGAACGACCCTGGCCTTGAACG
TCAGAGCCGGGGACGAAGGCCCCCGGAGGCTGCTGCGAGCTCCGCGCGTTCCTTCGCGCCCTT
CCGCGCCGCTCGCGCCGGCGCCGGCCTCCACCCCCGCGCGCCGCCTCCCACCAGTCCCG**ATG**C
AGGCGCCCGGCCGGGGGCCACTCGGGCTGCGGCTGATGATGCCCGGGCGCCGGGGGGCGCTGC
GCGAGCCTGGCGGCTGCGGATCCTGCCTGGGGGTGGCGCTGGCCCTGCTGTTGCTGCTACTGC
CCGCCTGCTGCCCCGTGCGGGCGCAGAACGACACGGAGCCCATCGTGCTGGAGGGCAAGTGCC
TGGTGGTGTGCGACTCCAGCCCGTCGGCGGACGGCGCCGTCACCTCCTCCCTAGGCATCTCCG
TGCGCTCCGGCAGCGCCAAGGTGGCCTTCTCCGCCACGCGGAGCACCAACCACGAGCCGTCCG
AGATGAGCAACCGCACCATGACCATCTATTTCGACCAGGTATTAGTAAATATTGGCAACCACT
TTGATCTTGCTTCCAGTATATTTGTAGCACCGAGAAAAGGGATTTATAGCTTCAGCTTCCACG
TGGTCAAAGTGTATAACAGACAAACCATCCAGGTCAGTTTAATGCAGAATGGCTACCCAGTGA
TCTCGGCCTTTGCAGGAGACCAGGATGTCACCAGAGAAGCTGCTAGCAATGGCGTGCTGCTGC
TCATGGAAAGGGAAGACAAAGTGCATCTCAAACTTGAGAGAGGCAACCTCATGGGGGGCTGGA
AATACTCCACATTCTCGGGCTTCTTGGTGTTTCCTCTA**TAA**ACACAGAGCCCCCTAGATGGTG
GGGGAATGGCAAACTGGACCCAGGACTCCGCCCTTTAAAACACCCTGAACTTACTGGAATTGG
ACACCTTGTTTCCAACCTCCGTCAGACTGTTGCAGTAGAAGAATGATTTCCTTTGAAACCTCC
AGTACTTTTGTTTTTGTTTTTTGGAATACTGACAATTCCTCGGGAACCTGGCCTCTAATTAGT
TTTAGATGACAAGGTCTTAAGGAGAAATGAAATTATCGATTTGAGCAATTTGTACCTGTGATT
GTAAAGTCAATATCGGATTTTATTGTTGGGACCATGGACCTCTTTTGTTTGTATGTTGTATTG
TCGTCCCAACGGAAGGAGAGCTCCTGACTCCAGGATGGGCTGCAGGTTGCAGTCAGGGCTTGA
AGTAGGAGCCCAGCAAAGAACCACCTGCTGGACAGTCCTTGACATGTGTTCTGTGTGTGTCTG
TATAGCCTTAAGAAAAAGAATGGCTTCACTTTCATTCTGTATTCTTCCCCCCACCATGTGGCT
GGGAGGACTTGGGAGGGGGATGGGGACATTGGGAACCTGTCAAGAAGTGCTTTATCCAGAGAA
GCAAATTTTGCACGATTGGACTGCAATTTTTGTTTTGTATTGTTTGTGTTTTTTCTTGAAAAG
CTTTACTTTTCTTTCCACACTCAGCTCTCCCTCCTCAACCCCACTTTTATTTTTCTTGCTGGG
GTTGAGGAGAGAAAATATAGAATTCCTGGATAAGACCAAACAAAACAAAACATTAAAATACCT
GTATGTTTTGTTTTAGACGAGACCAAACTAAACAAAAAGTATCTGTTTATCAAAGTAAAAGTA
ACACAATGGACAATTCTGCTTATTCTCTCAAAGAGATTCTAAGATGCACCTTTAGAACTATTA
ATAGCAACCTGCATTTTTTTTTAATTTATACTTCAGAATCCTTTAAGAACCTGGTGTTCCTGA
GTGGTCCTGAATCATATAAGTTGGTAATGGAAGCTGTAATGACCAAGTCCCCTAAACATACTA
TGTCTTTGCCACGTGTGCTGTGACTTCTCTGTGGGTGATTTAATTTATTTGGATCCACCTCTG
AGTGAGCGCACAGTGATCAGGTGCTTCAAAGCCAACAGACCAGCTCCTCTTCCTCCGGATCCT
CTTTTGATCTGCCCAGGAAAGGGATGCATTGACACTCTCCTGCATGCACCTGGCGAGAAGCCA
CCTGAAAGTCACTGTGGTTAAAGATATTGGTGGAGGTACCCCAGGAGCACTGTTACAAATCCT
TCTTGTTTTGGCATCTCGTACAACATTATTAAGACACAGCTGAGAGTTGATGGGTGTGTAATG
CATATGCCAAGGAAATGTCACTAATCCCAAAGCAATCAAAAAGGAGACCTCAAACCAGATGTT
AATTTGTTCTTTGTGTAACAATGTAACCAAAATATTGATGATAAAAGTCATAATTTAAGATTC
AGAATAAATGGGTTTGATGTCTGGCAAAAAAAAAAAAAAAA

FIGURE 86

MQAPGRGPLGLRLMMPGRRGALREPGGCGSCLGVALALLLLLLPACCPVRAQNDTEPIVLEGK
CLVVCDSSPSADGAVTSSLGISVRSGSAKVAFSATRSTNHEPSEMSNRTMTIYFDQVLVNIGN
HFDLASSIFVAPRKGIYSFSFHVVKVYNRQTIQVSLMQNGYPVISAFAGDQDVTREAASNGVL
LLMEREDKVHLKLERGNLMGGWKYSTFSGFLVFPL

Important features of the protein:

Signal peptide:

amino acids 1-48

N-glycosylation sites.

amino acids 53-57, 110-114

N-myristoylation sites.

amino acids 26-32, 27-33, 29-35, 33-39, 76-82, 205-211

Amidation site.

amino acids 16-20

C1q domain signature.

amino acids 117-148

C1q domain proteins.

amino acids 115-149

FIGURE 87

AGGGCCCGCGGGTGGAGAGAGCGACGCCCGAGGGG**ATG**GCGGCAGCGTCCCGGAGCGCCTCTG
GCTGGGCGCTACTGCTGCTGGTGGCACTTTGGCAGCAGCGCGCGGCCGGCTCCGGCGTCTTCC
AGCTGCAGCTGCAGGAGTTCATCAACGAGCGCGGCGTACTGGCCAGTGGGCGGCCTTGCGAGC
CCGGCTGCCGGACTTTCTTCCGCGTCTGCCTTAAGCACTTCCAGGCGGTCGTCTCGCCCGGAC
CCTGCACCTTCGGGACCGTCTCCACGCCGGTATTGGGCACCAACTCCTTCGCTGTCCGGGACG
ACAGTAGCGGCGGGGGGCGCAACCCTCTCCAACTGCCCTTCAATTTCACCTGGCCGGGTACCT
TCTCGCTCATCATCGAAGCTTGGCACGCGCCAGGAGACGACCTGCGGCCAGAGGCCTTGCCAC
CAGATGCACTCATCAGCAAGATCGCCATCCAGGGCTCCCTAGCTGTGGGTCAGAACTGGTTAT
TGGATGAGCAAACCAGCACCCTCACAAGGCTGCGCTACTCTTACCGGGTCATCTGCAGTGACA
ACTACTATGGAGACAACTGCTCCCGCCTGTGCAAGAAGCGCAATGACCACTTCGGCCACTATG
TGTGCCAGCCAGATGGCAACTTGTCCTGCCTGCCCGGTTGGACTGGGGAATATTGCCAACAGC
CTATCTGTCTTTCGGGCTGTCATGAACAGAATGGCTACTGCAGCAAGCCAGCAGAGTGCCTCT
GCCGCCCAGGCTGGCAGGGCCGGCTGTGTAACGAATGCATCCCCCACAATGGCTGTCGCCACG
GCACCTGCAGCACTCCCTGGCAATGTACTTGTGATGAGGGCTGGGGAGGCCTGTTTTGTGACC
AAGATCTCAACTACTGCACCCACCACTCCCCATGCAAGAATGGGGCAACGTGCTCCAACAGTG
GGCAGCGAAGCTACACCTGCACCTGTCGCCCAGGCTACACTGGTGTGGACTGTGAGCTGGAGC
TCAGCGAGTGTGACAGCAACCCCTGTCGCAATGGAGGCAGCTGTAAGGACCAGGAGGATGGCT
ACCACTGCCTGTGTCCTCCGGGCTACTATGGCCTGCACTGTGAACACAGCACCTTGAGCTGCG
CCGACTCCCCCTGCTTCAATGGGGGCTCCTGCCGGGAGCGCAACCAGGGGGCCAACTATGCTT
GTGAATGTCCCCCCAACTTCACCGGCTCCAACTGCGAGAAGAAAGTGGACAGGTGCACCAGCA
ACCCCTGTGCCAACGGGGGACAGTGCCTGAACCGAGGTCCAAGCCGCATGTGCCGCTGCCGTC
CTGGATTCACGGGCACCTACTGTGAACTCCACGTCAGCGACTGTGCCCGTAACCCTTGCGCCC
ACGGTGGCACTTGCCATGACCTGGAGAATGGGCTCATGTGCACCTGCCCTGCCGGCTTCTCTG
GCCGACGCTGTGAGGTGCGGACATCCATCGATGCCTGTGCCTCGAGTCCCTGCTTCAACAGGG
CCACCTGCTACACCGACCTCTCCACAGACACCTTTGTGTGCAACTGCCCTTATGGCTTTGTGG
GCAGCCGCTGCGAGTTCCCCGTGGGCTTGCCGCCCAGCTTCCCCTGGGTGGCCGTCTCGCTGG
GTGTGGGGCTGGCAGTGCTGCTGGTACTGCTGGGCATGGTGGCAGTGGCTGTGCGGCAGCTGC
GGCTTCGACGGCCGGACGACGGCAGCAGGGAAGCCATGAACAACTTGTCGGACTTCCAGAAGG
ACAACCTGATTCCTGCCGCCCAGCTTAAAAACACAAACCAGAAGAAGGAGCTGGAAGTGGACT
GTGGCCTGGACAAGTCCAACTGTGGCAAACAGCAAAACCACACATTGGACTATAATCTGGCCC
CAGGGCCCCTGGGGCGGGGGACCATGCCAGGAAAGTTTCCCCACAGTGACAAGAGCTTAGGAG
AGAAGGCGCCACTGCGGTTACACAGTGAAAAGCCAGAGTGTCGGATATCAGCGATATGCTCCC
CCAGGGACTCCATGTACCAGTCTGTGTGTTTGATATCAGAGGAGAGGAATGAATGTGTCATTG
CCACGGAGGTA**TAA**GGCAGGAGCCTACCTGGACATCCCTGCTCAGCCCCGCGGCTGGACCTTC
CTTCTGCATTGTTTACA

FIGURE 88

MAAASRSASGWALLLLVALWQQRAAGSGVFQLQLQEFINERGVLASGRPCEPGCRTFFRVCLK
HFQAVVSPGPCTFGTVSTPVLGTNSFAVRDDSSGGGRNPLQLPFNFTWPGTFSLIIEAWHAPG
DDLRPEALPPDALISKIAIQGSLAVGQNWLLDEQTSTLTRLRYSYRVICSDNYYGDNCSRLCK
KRNDHFGHYVCQPDGNLSCLPGWTGEYCQQPICLSGCHEQNGYCSKPAECLCRPGWQGRLCNE
CIPHNGCRHGTCSTPWQCTCDEGWGGLFCDQDLNYCTHHSPCKNGATCSNSGQRSYTCTCRPG
YTGVDCELELSECDSNPCRNGGSCKDQEDGYHCLCPPGYYGLHCEHSTLSCADSPCFNGGSCR
ERNQGANYACECPPNFTGSNCEKKVDRCTSNPCANGGQCLNRGPSRMCRCRPGFTGTYCELHV
SDCARNPCAHGGTCHDLENGLMCTCPAGFSGRRCEVRTSIDACASSPCFNRATCYTDLSTDTF
VCNCPYGFVGSRCEFPVGLPPSFPWVAVSLGVGLAVLLVLLGMVAVAVRQLRLRRPDDGSREA
MNNLSDFQKDNLIPAAQLKNTNQKKELEVDCGLDKSNCGKQQNHTLDYNLAPGPLGRGTMPGK
FPHSDKSLGEKAPLRLHSEKPECRISAICSPRDSMYQSVCLISEERNECVIATEV

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 89

GTCTCCGCGTCACAGGAACTTCAGCACCCACAGGGCGGACAGCGCTCCCCTCTACCTGGAGAC
TTGACTCCCGCGCGCCCCAACCCTGCTTATCCCTTGACCGTCGAGTGTCAGAGATCCTGCAGC
CGCCCAGTCCCGGCCCCTCTCCCGCCCCACACCCACCCTCCTGGCTCTTCCTGTTTTTACTCC
TCCTTTTCATTCATAACAAAAGCTACAGCTCCAGGAGCCCAGCGCCGGGCTGTGACCCAAGCC
GAGCGTGGAAGA**ATG**GGGTTCCTCGGGACCGGCACTTGGATTCTGGTGTTAGTGCTCCCGATT
CAAGCTTTCCCCAAACCTGGAGGAAGCCAAGACAAATCTCTACATAATAGAGAATTAAGTGCA
GAAAGACCTTTGAATGAACAGATTGCTGAAGCAGAAGAAGACAAGATTAAAAAAACATATCCT
CCAGAAAACAAGCCAGGTCAGAGCAACTATTCTTTTGTTGATAACTTGAACCTGCTAAAGGCA
ATAACAGAAAAGGAAAAAATTGAGAAAGAAAGACAATCTATAAGAAGCTCCCCACTTGATAAT
AAGTTGAATGTGGAAGATGTTGATTCAACCAAGAATCGAAAACTGATCGATGATTATGACTCT
ACTAAGAGTGGATTGGATCATAAATTTCAAGATGATCCAGATGGTCTTCATCAACTAGACGGG
ACTCCTTTAACCGCTGAAGACATTGTCCATAAAATCGCTGCCAGGATTTATGAAGAAAATGAC
AGAGCCGTGTTTGACAAGATTGTTTCTAAACTACTTAATCTCGGCCTTATCACAGAAAGCCAA
GCACATACACTGGAAGATGAAGTAGCAGAGGTTTTACAAAAATTAATCTCAAAGGAAGCCAAC
AATTATGAGGAGGATCCCAATAAGCCCACAAGCTGGACTGAGAATCAGGCTGGAAAAATACCA
GAGAAAGTGACTCCAATGGCAGCAATTCAAGATGGTCTTGCTAAGGGAGAAAACGATGAAACA
GTATCTAACACATTAACCTTGACAAATGGCTTGGAAAGGAGAACTAAAACCTACAGTGAAGAC
AACTTTGAGGAACTCCAATATTTCCCAAATTTCTATGCGCTACTGAAAAGTATTGATTCAGAA
AAAGAAGCAAAAGAGAAAGAAACACTGATTACTATCATGAAAACACTGATTGACTTTGTGAAG
ATGATGGTGAAATATGGAACAATATCTCCAGAAGAAGGTGTTTCCTACCTTGAAAACTTGGAT
GAAATGATTGCTCTTCAGACCAAAAACAAGCTAGAAAAAAATGCTACTGACAATATAAGCAAG
CTTTTCCCAGCACCATCAGAGAAGAGTCATGAAGAAACAGACAGTACCAAGGAAGAAGCAGCT
AAGATGGAAAAGGAATATGGAAGCTTGAAGGATTCCACAAAAGATGATAACTCCAACCCAGGA
GGAAAGACAGATGAACCCAAAGGAAAAACAGAAGCCTATTTGGAAGCCATCAGAAAAAATATT
GAATGGTTGAAGAAACATGACAAAAAGGGAAATAAAGAAGATTATGACCTTTCAAAGATGAGA
GACTTCATCAATAAACAAGCTGATGCTTATGTGGAGAAAGGCATCCTTGACAAGGAAGAAGCC
GAGGCCATCAAGCGCATTTATAGCAGCCTG**TAA**AAATGGCAAAAGATCCAGGAGTCTTTCAAC
TGTTTCAGAAAACATAATATAGCTTAAAACACTTCTAATTCTGTGATTAAAATTTTTTGACCC
AAGGGTTATTAGAAAGTGCTGAATTTACAGTAGTTAACCTTTTACAAGTGGTTAAAACATAGC
TTTCTTCCCGTAAAAACTATCTGAAAGTAAAGTTGTATGTAAGCTGAAAAAAAAAAAAAAAAA
AAA

FIGURE 90

MGFLGTGTWILVLVLPIQAFPKPGGSQDKSLHNRELSAERPLNEQIAEAEEDKIKKTYPPENK
PGQSNYSFVDNLNLLKAITEKEKIEKERQSIRSSPLDNKLNVEDVDSTKNRKLIDDYDSTKSG
LDHKFQDDPDGLHQLDGTPLTAEDIVHKIAARIYEENDRAVFDKIVSKLLNLGLITESQAHTL
EDEVAEVLQKLISKEANNYEEDPNKPTSWTENQAGKIPEKVTPMAAIQDGLAKGENDETVSNT
LTLTNGLERRTKTYSEDNFEELQYFPNFYALLKSIDSEKEAKEKETLITIMKTLIDFVKMMVK
YGTISPEEGVSYLENLDEMIALQTKNKLEKNATDNISKLFPAPSEKSHEETDSTKEEAAKMEK
EYGSLKDSTKDDNSNPGGKTDEPKGKTEAYLEAIRKNIEWLKKHDKKGNKEDYDLSKMRDFIN
KQADAYVEKGILDKEEAEAIKRIYSSL

Important features:

N-glycosylation sites:

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

Casein kinase II phosphorylation site:

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

N-myristoylation sites:

amino acids 143-148, 239-244

FIGURE 91

TGCATCAGTGCCCAGGCAAGCCCAGGAGTTGACATTTCTCTGCCCAGCC**ATG**GGCCTCACCCT
GCTCTTGCTGCTGCTCCTGGGACTAGAAGGTCAGGGCATAGTTGGCAGCCTCCCTGAGGTGCT
GCAGGCACCCGTGGGAAGCTCCATTCTGGTGCAGTGCCACTACAGGCTCCAGGATGTCAAAGC
TCAGAAGGTGTGGTGCCGGTTCTTGCCGGAGGGGTGCCAGCCCCTGGTGTCCTCAGCTGTGGA
TCGCAGAGCTCCAGCGGGCAGGCGTACGTTTCTCACAGACCTGGGTGGGGGCCTGCTGCAGGT
GGAAATGGTTACCCTGCAGGAAGAGGATGCTGGCGAGTATGGCTGCATGGTGGATGGGGCCAG
GGGGCCCCAGATTTTGCACAGAGTCTCTCTGAACATACTGCCCCCAGAGGAAGAAGAAGAGAC
CCATAAGATTGGCAGTCTGGCTGAGAACGCATTCTCAGACCCTGCAGGCAGTGCCAACCCTTT
GGAACCCAGCCAGGATGAGAAGAGCATCCCCTTGATCTGGGGTGCTGTGCTCCTGGTAGGTCT
GCTGGTGGCAGCGGTGGTGCTGTTTGCTGTGATGGCCAAGAGGAAACAAGAATCCCTCCTCAG
TGGTCCACCACGTCAG**TGA**CTCTGGACCGGCTGCTGAATTGCCTTTGGATGTACCACACATTA
GGCTTGACTCACCACCTTCATTTGACAATACCACCTACACCAGCCTACCTCTTGATTCCCCAT
CAGGAAAACCTTCACTCCCAGCTCCATCCTCATTGCCCCCTCTACCTCCTAAGGTCCTGGTCT
GCTCCAAGCCTGTGACATATGCCACAGTAATCTTCCCGGGAGGGAACAAGGGTGGAGGGACCT
CGTGTGGGCCAGCCCAGAATCCACCTAACAATCAGACTCCATCCAGCTAAGCTGCTCATCACA
CTTTAAACTCATGAGGACCATCCCTAGGGGTTCTGTGCATCCATCCAGCCAGCTCATGCCCTA
GGATCCTTAGGATATCTGAGCAACCAGGGACTTTAAGATCTAATCCAATGTCCTAACTTTACT
AGGGAAAGTGACGCTCAGACATGACTGAGATGTCTTGGGGAAGACCTCCCTGCACCCAACTCC
CCCACTGGTTCTTCTACCATTACACACTGGGCTAAATAAACCCTAATAATGATGTGCAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 92

MGLTLLLLLLLLGLEGQGIVGSLPEVLQAPVGSSILVQCHYRLQDVKAQKVWCRFLPEGCQPLV
SSAVDRRAPAGRRTFLTDLGGGLLQVEMVTLQEEDAGEYGCMVDGARGPQILHRVSLNILPPE
EEEETHKIGSLAENAFSDPAGSANPLEPSQDEKSIPLIWGAVLLVGLLVAAVVLFAVMAKRKQ
ESLLSGPPRQ

Important features of the protein:

Signal peptide:

amino acids 1-15

Transmembrane domain:

amino acids 161-181

N-myristoylation sites.

amino acids 17-23, 172-178

Amidation site.

amino acids 73-79

FIGURE 93

GGCGGCGTTGCCGGGCTCTCCGGAAGGAGACGTGGCGGCGGTTGGGCCGGTGATACCCGGGCG
CTTTATAGTCCCGCCGCCTCCTCCTCCACCTCCTCCTCCTCCTCCTCTCCTCCTGGGGCAGAG
GAGGTTGTGGCGGTGGCTGGAGAAAGCGGCGGCGGAGG**ATG**GAGGAAGGAGGCGGCGGCGTAC
GGAGTCTGGTCCCGGGCGGGCCGGTGTTACTGGTCCTCTGCGGCCTCCTGGAGGCGTCCGGCG
GCGGCCGAGCCCTTCCTCAACTCAGCGATGACATCCCTTTCCGAGTCAACTGGCCCGGCACCG
AGTTCTCTCTGCCCACAACTGGAGTTTTATATAAAGAAGATAATTATGTCATCATGACAACTG
CACATAAAGAAAAATATAAATGCATACTTCCCCTTGTGACAAGTGGGGATGAGGAAGAAGAAA
AGGATTATAAAGGCCCTAATCCAAGAGAGCTTTTGGAGCCACTATTTAAACAAAGCAGTTGTT
CCTACAGAATTGAGTCTTATTGGACTTACGAAGTATGTCATGGAAAACACATTCGGCAGTACC
ATGAAGAGAAAGAAACTGGTCAGAAAATAAATATTCACGAGTACTACCTTGGGAATATGTTGG
CCAAGAACCTTCTATTTGAAAAAGAACGAGAAGCAGAAGAAAAGGAAAAATCAAATGAGATTC
CCACTAAAAATATCGAAGGTCAGATGACACCATACTATCCTGTGGGAATGGGAAATGGTACAC
CTTGTAGTTTGAAACAGAACCGGCCCAGATCAAGTACTGTGATGTACATATGTCATCCTGAAT
CTAAGCATGAAATTCTTTCAGTAGCTGAAGTTACAACTTGTGAATATGAAGTTGTCATTTTGA
CACCACTCTTGTGCAGTCATCCTAAATATAGGTTCAGAGCATCTCCTGTGAATGACATATTTT
GTCAATCACTGCCAGGATCTCCATTTAAGCCCCTCACCCTGAGGCAGCTGGAGCAGCAGGAAG
AAATACTAAGGGTGCCTTTTAGGAGAAATAAAGAGGGTGTCGGTTGGTGGAAATATGAATTCT
GCTATGGCAAACATGTACATCAATACCATGAGGACAAGGATAGTGGGAAAACCTCTGTGGTTG
TCGGGACATGGAACCAAGAAGAGCATATTGAATGGGCTAAGAAGAATACTGCTAGAGCTTATC
ATCTTCAAGACGATGGTACCCAGACAGTCAGGATGGTGTCACATTTTTATGGAAATGGAGATA
TTTGTGATATAACTGACAAACCAAGACAGGTGACTGTAAAACTAAAGTGCAAAGAATCAGATT
CACCTCATGCTGTTACTGTATATATGCTAGAGCCTCACTCCTGTCAATATATTCTTGGGGTTG
AATCTCCAGTGATCTGTAAAATCTTAGATACAGCAGATGAAAATGGACTTCTTTCTCTCCCCA
AC**TAA**AGGATATTAAAGTTAGGGGAAAGAAAAGATCATTGAAAGTCATGATAATTTCTGTCCC
ACTGTGTCTCATTATAGAGTTCTCAGCCATTGGACCTCTTCTAAAGGATGGTATAAAATGACT
CTCAACCACTTTGTGAATACATATGTGTATATAAGAGGTTATTGATAAACTTCTGAGGCAGAC
ATTTGTCTCGCTTTTTTTCATTTTTGTTGTGTCTTATAAACTGACTGTTTTTCTTTGCTTGGA
TACTGTGATTCCAAAATAAATCTCATCCAAGCAAGTTAGAGTCCAGCCTAATCAAATGTCATA
ATTGTTGTACCTATTGAAAGTTTTTAAATAATAGATTTATTATGTAAATTATAGTATATGTAA
GTAGCTAATGAAGTAAAGATCATGAAGAAAGAAATTGATAGGTGTAAATGAGAGACCATGTAA
AATATGTAAATTCTAGTACCTGAAATCCTTTCAACAGATTTTTATATAGCAACTGCTCTCTGC
AAGTAGTTAAACTAGAAACTGGGCACATGGTAGAGGCTCACATGGGAGTTGTCCTCACCCTTG
TTAATCTCAAGAAACTCTTATTTATAATAGGTTGCTTCTCTCTCAGAACTTTTATCTATTACT
TTTTTCTTCTTATGAGTATGTTTACTCTCAGAGTATCTATCTGATGTAGACAGTTGGTGATGC
TTCTGAGACTCAGAATGGTTTACTCTAACAAAACACTGTGCTGTCTATCCCTTGTACTTGCCT
ACTGTAATATGGATTTCACTTCTGAACAGTTTACAGCACAATATTTATTTTAAAGTGAATAAA
ATGTCCACAAGCAAAAA

FIGURE 94

MEEGGGGVRSLVPGGPVLLVLCGLLEASGGGRALPQLSDDIPFRVNWPGTEFSLPTTGVLYKE
DNYVIMTTAHKEKYKCILPLVTSGDEEEEKDYKGPNPRELLEPLFKQSSCSYRIESYWTYEVC
HGKHIRQYHEEKETGQKINIHEYYLGNMLAKNLLFEKEREAEEKEKSNEIPTKNIEGQMTPYY
PVGMGNGTPCSLKQNRPRSSTVMYICHPESKHEILSVAEVTTCEYEVVILTPLLCSHPKYRFR
ASPVNDIFCQSLPGSPFKPLTLRQLEQQEEILRVPFRRNKEGVGWWKYEFCYGKHVHQYHEDK
DSGKTSVVVGTWNQEEHIEWAKKNTARAYHLQDDGTQTVRMVSHFYGNGDICDITDKPRQVTV
KLKCKESDSPHAVTVYMLEPHSCQYILGVESPVICKILDTADENGLLSLPN

Important features of the protein:

Signal peptide:

amino acids 1-30

Glycosaminoglycan attachment site.

amino acids 28-32

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 337-341

N-myristoylation sites.

amino acids 6-12, 23-29, 29-35, 49-55, 141-147, 152-158, 192-198, 196-202

Gram-positive cocci surface proteins 'anchoring' hexapeptide.

amino acids 54-60

FIGURE 95

TTCCGTTTCTGGGAGGAGTGAGGGGCAACGGGTCGGAGAAAAAGGAAAAAAGAAGGGCTCAGC
GCCTCCCCGCCGGGCCGTGGACAGAGGGGCACAGTTTCGGCAGGCGGGTGAGGTCGCTGAGGG
CCCGCCGGAG**ATG**TTTTCCTTGTCGAGCACGGTGCAACCCCAGGTTACAGTTCCTCTGAGTCA
TCTCATCAATGCCTTCCATACACCAAAAAACACTTCTGTTTCTCTCAGTGGAGTGTCAGTTTC
TCAAAACCAGCATCGAGATGTAGTTCCTGAGCATGAGGCTCCCAGCAGTGAGCCTTCACTTAA
CTTAAGGGACCTTGGATTATCTGAACTAAAAATTGGACAGATTGATCAGCTGGTAGAAAATCT
ACTTCCTGGATTTTGTAAAGGCAAAAACATTTCTTCCCATTGGCATACATCCCATGTCTCTGC
ACAATCCTTCTTTGAAAATAAATATGGTAACTTAGATATATTTAGTACATTACGTTCCTCTTG
CTTGTATCGACATCATTCAAGAGCTCTTCAAAGCATTTGTTCAGATCTTCAGTACTGGCCAGT
TTTCATACAGTCTCGGGGTTTTAAAACTTTGAAATCAAGGACACGACGTCTCCAGTCTACCTC
CGAGAGATTAGCTGAAACACAGAATATAGCGCCATCATTCGTGAAGGGGTTTCTTTTGCGGGA
CAGAGGATCAGATGTTGAGAGTTTGGACAAACTCATGAAAACCAAAAATATACCTGAAGCTCA
CCAAGATGCATTTAAAACTGGTTTTGCGGAAGGTTTTCTGAAAGCTCAAGCACTCACACAAAA
AACCAATGATTCCCTAAGGCGAACCCGTCTGATTCTCTTCGTTCTGCTGCTATTCGGCATTTA
TGGACTTCTAAAAAACCCATTTTTATCTGTCCGCTTCCGGACAACAACAGGGCTTGATTCTGC
AGTAGATCCTGTCCAGATGAAAAATGTCACCTTTGAACATGTTAAAGGGGTGGAGGAAGCTAA
ACAAGAATTACAGGAAGTTGTTGAATTCTTGAAAAATCCACAAAAATTTACTATTCTTGGAGG
TAAACTTCCAAAAGGAATTCTTTTAGTTGGACCCCCAGGGACTGGAAAGACACTTCTTGCCCG
AGCTGTGGCGGGAGAAGCTGATGTTCCTTTTTATTATGCTTCTGGATCCGAATTTGATGAGAT
GTTTGTGGGTGTGGGAGCCAGCCGTATCAGAAATCTTTTTAGGGAAGCAAAGGCGAATGCTCC
TTGTGTTATATTTATTGATGAATTAGATTCTGTTGGTGGGAAGAGAATTGAATCTCCAATGCA
TCCATATTCAAGGCAGACCATAAATCAACTTCTTGCTGAAATGGATGGTTTTAAACCCAATGA
AGGAGTTATCATAATAGGAGCCACAAACTTCCCAGAGGCATTAGATAATGCCTTAATACGTCC
TGGTCGTTTTGACATGCAAGTTACAGTTCCAAGGCCAGATGTAAAAGGTCGAACAGAAATTTT
GAAATGGTATCTCAATAAAATAAAGTTTGATCAATCCGTTGATCCAGAAATTATAGCTCGAGG
TACTGTTGGCTTTTCCGGAGCAGAGTTGGAGAATCTTGTGAACCAGGCTGCATTAAAAGCAGC
TGTTGATGGAAAAGAAATGGTTACCATGAAGGAGCTGGAGTTTTCCAAAGACAAAATTCTAAT
GGGGCCTGAAAGAAGAAGTGTGGAAATTGATAACAAAAACAAAACCATCACAGCATATCATGA
ATCTGGTCATGCCATTATTGCATATTACACAAAAGATGCAATGCCTATCAACAAAGCTACAAT
CATGCCACGGGGGCCAACACTTGGACATGTGTCCCTGTTACCTGAGAATGACAGATGGAATGA
AACTAGAGCCCAGCTGCTTGCACAAATGGATGTTAGTATGGGAGGAAGAGTGGCAGAGGAGCT
TATATTTGGAACCGACCATATTACAACAGGTGCTTCCAGTGATTTTGATAATGCCACTAAAAT
AGCAAAGCGGATGGTTACCAAATTTGGAATGAGTGAAAAGCTTGGAGTTATGACCTACAGTGA
TACAGGGAAACTAAGTCCAGAAACCCAATCTGCCATCGAACAAGAAATAAGAATCCTTCTAAG
GGACTCATATGAACGAGCAAAACATATCTTGAAAACTCATGCAAAGGAGCATAAGAATCTCGC
AGAAGCTTTATTGACCTATGAGACTTTGGATGCCAAAGAGATTCAAATTGTTCTTGAGGGGAA
AAAGTTGGAAGTGAGA**TGA**TAACTCTCTTGATATGGATGCTTGCTGGTTTTATTGCAAGAATA
TAAGTAGCATTGCAGTAGTCTACTTTTACAACGCTTTCCCCTCATTCTTGATGTGGTGTAATT
GAAGGGTGTGAAATGCTTTGTCAATCATTTGTCACATTTATCCAGTTTGGGTTATTCTCATTA
TGACACCTATTGCAAATTAGCATCCCATGGCAAATATATTTTGAAAAAATAAAGAACTATCAG
GATTGAAAACAAAAAAAAAAAA

FIGURE 96

MFSLSSTVQPQVTVPLSHLINAFHTPKNTSVSLSGVSVSQNQHRDVVPEHEAPSSEPSLNLRD
LGLSELKIGQIDQLVENLLPGFCKGKNISSHWHTSHVSAQSFFENKYGNLDIFSTLRSSCLYR
HHSRALQSICSDLQYWPVFIQSRGFKTLKSRTRRLQSTSERLAETQNIAPSFVKGFLLRDRGS
DVESLDKLMKTKNIPEAHQDAFKTGFAEGFLKAQALTQKTNDSLRRTRLILFVLLLFGIYGLL
KNPFLSVRFRTTTGLDSAVDPVQMKNVTFEHVKGVEEAKQELQEVVEFLKNPQKFTILGGKLP
KGILLVGPPGTGKTLLARAVAGEADVPFYYASGSEFDEMFVGVGASRIRNLFREAKANAPCVI
FIDELDSVGGKRIESPMHPYSRQTINQLLAEMDGFKPNEGVIIIGATNFPEALDNALIRPGRF
DMQVTVPRPDVKGRTEILKWYLNKIKFDQSVDPEIIARGTVGFSGAELENLVNQAALKAAVDG
KEMVTMKELEFSKDKILMGPERRSVEIDNKNKTITAYHESGHAIIAYYTKDAMPINKATIMPR
GPTLGHVSLLPENDRWNETRAQLLAQMDVSMGGRVAEELIFGTDHITTGASSDFDNATKIAKR
MVTKFGMSEKLGVMTYSDTGKLSPETQSAIEQEIRILLRDSYERAKHILKTHAKEHKNLAEAL
LTYETLDAKEIQIVLEGKKLEVR

Important features of the protein:

Transmembrane domain:
amino acids 238-259

N-glycosylation sites.
amino acids 28-32, 90-94, 230-234, 278-282, 535-539, 584-588, 623-627

N-myristoylation sites.
amino acids 35-41, 266-272, 286-292, 325-331, 357-363, 599-605

Amidation site.
amino acids 387-393, 709-713

ATP/GTP-binding site motif A (P-loop).
amino acids 322-330

AAA-protein family proteins
amino acids 315-336, 343-386, 405-451

FIGURE 97

GATGGCGCAGCCACAGCTTCTGTGAGATTCGATTTCTCCCCAGTTCCCCTGTGGGTCTGAGGG
GACCAGAAGGGTGAGCTACGTTGGCTTTCTGGAAGGGGAGGCTATATGCGTCAATTCCCCAAA
ACAAGTTTTGACATTTCCCCTGAAATGTCATTCTCTATCTATTCACTGCAAGTGCCTGCTGTT
CCAGGCCTTACCTGCTGGGCACTAACGGCGGAGCCAGGATGGGGACAGAATAAAGGAGCCACG
ACCTGTGCCACCAACTCGCACTCAGACTCTGAACTCAGACCTGAAATCTTCTCTTCACGGGAG
GCTTGGCAGTTTTTCTTACTCCTGTGGTCTCCAGATTTCAGGCCTAAG**ATG**AAAGCCTCTAGT
CTTGCCTTCAGCCTTCTCTCTGCTGCGTTTTATCTCCTATGGACTCCTTCCACTGGACTGAAG
ACACTCAATTTGGGAAGCTGTGTGATCGCCACAAACCTTCAGGAAATACGAAATGGATTTTCT
GAGATACGGGGCAGTGTGCAAGCCAAAGATGGAAACATTGACATCAGAATCTTAAGGAGGACT
GAGTCTTTGCAAGACACAAAGCCTGCGAATCGATGCTGCCTCCTGCGCCATTTGCTAAGACTC
TATCTGGACAGGGTATTTAAAAACTACCAGACCCCTGACCATTATACTCTCCGGAAGATCAGC
AGCCTCGCCAATTCCTTTCTTACCATCAAGAAGGACCTCCGGCTCTCTCATGCCCACATGACA
TGCCATTGTGGGGAGGAAGCAATGAAGAAATACAGCCAGATTCTGAGTCACTTTGAAAAGCTG
GAACCTCAGGCAGCAGTTGTGAAGGCTTTGGGGGAACTAGACATTCTTCTGCAATGGATGGAG
GAGACAGAA**TAG**GAGGAAAGTGATGCTGCTGCTAAGAATATTCGAGGTCAAGAGCTCCAGTCT
TCAATACCTGCAGAGGAGGCATGACCCCAAACCACCATCTCTTTACTGTACTAGTCTTGTGCT
GGTCACAGTGTATCTTATTTATGCATTACTTGCTTCCTTGCATGATTGTCTTTATGCATCCCC
AATCTTAATTGAGACCATACTTGTATAAGATTTTTGTAATATCTTTCTGCTATTGGATATATT
TATTAGTTAATATATTTATTTATTTTTTGCTATTTAATGTATTTATTTTTTTACTTGGACATG
AAACTTTAAAAAAATTCACAGATTATATTTATAACCTGACTAGAGCAGGTGATGTATTTTTAT
ACAGTAAAAAAAAAAAACCTTGTAAATTCTAGAAGAGTGGCTAGGGGGGTTATTCATTTGTAT
TCAACTAAGGACATATTTACTCATGCTGATGCTCTGTGAGATATTTGAAATTGAACCAATGAC
TACTTAGGATGGGTTGTGGAATAAGTTTTGATGTGGAATTGCACATCTACCTTACAATTACTG
ACCATCCCCAGTAGACTCCCCAGTCCCATAATTGTGTATCTTCCAGCCAGGAATCCTACACGG
CCAGCATGTATTTCTACAAATAAAGTTTTCTTTGCATACCAAAAAAAAAAAAAAAAAAAA

FIGURE 98

MKASSLAFSLLSAAFYLLWTPSTGLKTLNLGSCVIATNLQEIRNGFSEIRGSVQAKDGNIDIR
ILRRTESLQDTKPANRCCLLRHLLRLYLDRVFKNYQTPDHYTLRKISSLANSFLTIKKDLRLC
HAHMTCHCGEEAMKKYSQILSHFEKLEPQAAVVKALGELDILLQWMEETE

Signal sequence:

amino acids 1-24

cAMP- and cGMP-dependent protein kinase phosphorylation sites.

amino acids 107-110, 140-143

N-myristoylation site.

amino acids 51-56

Interleukin 10:

amino acids 9-176

FIGURE 99

GCGCCGGCTCCGCGCCTCGCGCCCAGTCCGCGGGCCGCGCCGCCGCTCCCGCCGCTCCCGCCG

CTCCCGCAGCCGCCCCGCCGCCCGCCCGGAGCCCCGCGTCCCTAGGCCTGGCTCCCGCCTGCC

CGAGACCCGCCCAGCCTGCCCCGCTCAGCCGCCAGAGAAG**ATG**CGGCTGCTCCCGGAATGGTT

CCTCTTGCTCTTTGGCCCGTGGCTCCTTAGGAAGGCCGTCAGTGCCCAGATACCAGAGTCCGG

AAGGCCGCAGTACCTGGGGCTGCGCCCCGCCGCGGCCGGAGCGGGTGCCCCCGGCCAGCAGCT

CCCAGAGCCAAGGTCTTCGGACGGCCTAGGCGTGGGCCGCGCCTGGAGCTGGGCCTGGCCGAC

CAACCACACGGGGGCGCTGGCCCGGGCAGGGGCAGCCGGGGCGTTGCCCGCGCAGCGCACCAA

GAGGAAGCCGTCCATCAAGGCGGCGCGCGCCAAAAAGATCTTCGGCTGGGGGGACTTCTACTT

TCGGGTGCATACCCTCAAGTTTTCGCTGCTGGTGACCGGCAAGATCGTGGACCATGTGAACGG

TACCTTCAGTGTGTATTTCCGCCACAACTCGTCCAGCCTGGGCAACCTCAGTGTCAGCATCGT

GCCGCCCTCCAAGCGTGTCGAGTTCGGAGGAGTCTGGCTGCCCGGGCCTGTCCCCCACCCTCT

GCAGTCTACGCTCGCCCTGGAGGGGGTGCTTCCTGGGCTGGGGCCCCCGCTGGGGATGGCAGC

AGCAGCGGCGGGGCCGGGGCTTGGGGGCTCCCTCGGGGGCGCACTGGCGGGGCCGCTTGGGGG

CGCGTTGGGAGTGCCTGGGGCCAAAGAGTCACGCGCTTTCAATTGCCACGTGGAGTATGAGAA

GACAAACCGCGCGCGCAAGCACCGACCGTGCCTGTACGACCCGTCGCAGGTGTGTTTCACCGA

GCACACGCAGAGCCAGGCCGCCTGGCTCTGTGCCAAGCCCTTCAAAGTCATCTGTATCTTCGT

CTCTTTCCTCAGCTTTGACTACAAACTGGTGCAGAAGGTGTGCCCAGACTATAACTTCCAGAG

TGAGCACCCCTACTTCGGA**TAG**CGCCCCTCCCCAGCCAGTCCTGAGCCTCCCGCCAAATCCCA

GCCTCACTAGGTGGGACCCCCTTCCCAGTGTTCTGCCGCTCCTGTGGCCATGTCGCCCACTCC

TTCCACTCTGGGGGCGGAGGGGAATGGCTTCTCGGGACCCTCAGCTAGCGTGGGTGCCCTTTT

CCTTATGCGGAGTGCCCGCAAGGCTGGGGTAGCCCCCTCCAGTACACCCCAAAGTGAAAGGGA

TAAGAGTGCAGCCCCAGAATAGGCGGGGCTTGGAGGCGGTCCCAATGTCCCCTGGGTCCACAG

TGGGTCCCCTTTTCACCCTTGGCGCTAGGCTGCGCACTCCCTTTCCCCGCAGCTTTAATAACT

CCTGGCCTGGCACCCTCACCCCACCCTGACTTTCCCATCCCCCAGCGCTTGTCCTGCTTCACC

ATACCCCGCCTAAGACTGTAAAGGCCTAAAAACCTCGGCCTGTCCTCCCACCATTCTGCCTGC

CATATGCCTGTCCCCTTTTCCTCCAAACCCTATTAGGGTACCGGAAGCAGAACCCCTGGGCTG

AGGCCCTGGCCCTGCCCCCGGCCCCTGCCCCTGCCCGCCCCCCTCCAGTCCAGGCAGTCGAGC

TCCACCTGCCCTCTCCTGCTGCTTCCTCTCGGTGATATTTTTTCTACGCCAAAACAGACGGGA

AAGGGAACAAAATAAAGTGAAATCCCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

AAAAAAAAAAAAAA

FIGURE 100

MRLLPEWFLLLFGPWLLRKAVSAQIPESGRPQYLGLRPAAAGAGAPGQQLPEPRSSDGLGVGR
AWSWAWPTNHTGALARAGAAGALPAQRTKRKPSIKAARAKKIFGWGDFYFRVHTLKFSLLVTG
KIVDHVNGTFSVYFRHNSSSLGNLSVSIVPPSKRVEFGGVWLPGPVPHPLQSTLALEGVLPGL
GPPLGMAAAAAGPGLGGSLGGALAGPLGGALGVPGAKESRAFNCHVEYEKTNRARKHRPCLYD
PSQVCFTEHTQSQAAWLCAKPFKVICIFVSFLSFDYKLVQKVCPDYNFQSEHPYFG

Important features of the protein:

Signal peptide:

amino acids 1-22

Transmembrane domain:

amino acids 273-288

N-glycosylation sites.

amino acids 72-76, 133-137, 143-147, 149-153

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 93-97

N-myristoylation sites.

amino acids 35-41, 58-64, 60-66, 81-87, 84-90, 184-190, 194-200, 203-209, 205-211, 206-212, 209-215, 217-223, 221-227, 224-230

Cytochrome b/b6 Qo site signature.

amino acids 5-11

FIGURE 101

AATGCCCC**ATG**CGCACCCCACAGCTCGCGCTCCTGCAAGTGTTCTTTCTGGTGTTCCCCGATG
GCGTCCGGCCTCAGCCCTCTTCCTCCCCATCAGGGGCAGTGCCCACGTCTTTGGAGCTGCAGC
GAGGGACGGATGGCGGAACCCTCCAGTCCCCTTCAGAGGCGACTGCAACTCGCCCGGCCGTGC
CTGGACTCCCTACAGTGGTCCCTACTCTCGTGACTCCCTCGGCCCCTGGGAATAGGACTGTGG
ACCTCTTCCCAGTCTTACCGATCTGTGTCTGTGACTTGACTCCTGGAGCCTGCGATATAAATT
GCTGCTGCGACAGGGACTGCTATCTTCTCCATCCGAGGACAGTTTTCTCCTTCTGCCTTCCAG
GCAGCGTAAGGTCTTCAAGCTGGGTTTGTGTAGACAACTCTGTTATCTTCAGGAGTAATTCCC
CGTTTCCTTCAAGAGTTTTCATGGATTCTAATGGAATCAGGCAGTTTTGTGTCCATGTGAACA
ACTCAAACTTAAACTATTTCCAGAAGCTTCAAAAGGTCAATGCAACCAACTTCCAGGCCCTGG
CTGCAGAGTTTGGAGGCGAATCATTCACTTCAACATTCCAAACTCAATCACCACCATCTTTTT
ACAGGGCTGGGGACCCCATTCTTACTTACTTCCCCAAGTGGTCTGTAATAAGCTTGCTGAGAC
AACCTGCAGGAGTTGGAGCTGGGGGACTCTGTGCTGAAAGCAATCCTGCAGGTTTCCTAGAGA
GTAAAAGTACAACTTGCACTCGTTTTTTCAAGAACCTGGCTAGTAGCTGTACCTTGGATTCAG
CCCTCAATGCTGCCTCTTACTATAACTTCACAGTCTTAAAGGTTCCAAGAAGCATGACTGATC
CACAGAATATGGAGTTCCAGGTTCCTGTAATACTTACCTCACAGGCTAATGCTCCTCTGTTGG
CTGGAAACACTTGTCAGAATGTAGTTTCTCAGGTCACCTATGAGATAGAGACCAATGGGACTT
TTGGAATCCAGAAAGTTTCTGTCAGTTTGGGACAAACCAACCTGACTGTTGAGCCAGGCGCTT
CCTTACAGCAACACTTCATCCTTCGCTTCAGGGCTTTTCAACAGAGCACAGCTGCTTCTCTCA
CCAGTCCTAGAAGTGGGAATCCTGGCTATATAGTTGGGAAGCCACTCTTGGCTCTGACTGATG
ATATAAGTTACTCAATGACCCTCTTACAGAGCCAGGGTAATGGAAGTTGCTCTGTTAAAAGAC
ATGAAGTGCAGTTTGGAGTGAATGCAATATCTGGATGCAAGCTCAGGTTGAAGAAGGCAGACT
GCAGCCACTTGCAGCAGGAGATTTATCAGACTCTTCATGGAAGGCCCAGACCAGAGTATGTTG
CCATCTTTGGTAATGCTGACCCAGCCCAGAAAGGAGGGTGGACCAGGATCCTCAACAGGCACT
GCAGCATTTCAGCTATAAACTGTACTTCCTGCTGTCTCATACCAGTTTCCCTGGAGATCCAGG
TATTGTGGGCATATGTAGGTCTCCTGTCCAACCCGCAAGCTCATGTATCAGGAGTTCGATTCC
TATACCAGTGCCAGTCTATACAGGATTCTCAGCAAGTTACAGAAGTATCTTTGACAACTCTTG
TGAACTTTGTGGACATTACCCAGAAGCCACAGCCTCCAAGGGGCCAACCCAAAATGGACTGGA
AATGGCCATTCGACTTCTTTCCCTTCAAAGTGGCATTCAGCAGAGGAGTATTCTCTCAAAAAT
GCTCAGTCTCTCCCATCCTTATCCTGTGCCTCTTACTACTTGGAGTTCTCAACCTAGAGACTA
TG**TGA**AGAAAAGAAAATAATCAGATTTCAGTTTTCCCTATGAGAAACTCTGAGGCAGCCACTT
ATCTTGGCTAAATAGAACCTCACCTGCTCATGACCAGAGAGCATTTAGGATAATAGATGACCT
AACTGAAGGAATCCTTGTATATGAAAGGAGTTATTTTAGAAAAGCAATAAAAATATTTTATTC
ATCNTAAAAAAAAAA

FIGURE 102

MRTPQLALLQVFFLVFPDGVRPQPSSSPSGAVPTSLELQRGTDGGTLQSPSEATATRPAVPGL
PTVVPTLVTPSAPGNRTVDLFPVLPICVCDLTPGACDINCCCDRDCYLLHPRTVFSFCLPGSV
RSSSWVCVDNSVIFRSNSPFPSRVFMDSNGIRQFCVHVNNSNLNYFQKLQKVNATNFQALAAE
FGGESFTSTFQTQSPPSFYRAGDPILTYFPKWSVISLLRQPAGVGAGGLCAESNPAGFLESKS
TTCTRFFKNLASSCTLDSALNAASYYNFTVLKVPRSMTDPQNMEFQVPVILTSQANAPLLAGN
TCQNVVSQVTYEIETNGTFGIQKVSVSLGQTNLTVEPGASLQQHFILRFRAFQQSTAASLTSP
RSGNPGYIVGKPLLALTDDISYSMTLLQSQGNGSCSVKRHEVQFGVNAISGCKLRLKKADCSH
LQQEIYQTLHGRPRPEYVAIFGNADPAQKGGWTRILNRHCSISAINCTSCCLIPVSLEIQVLW
AYVGLLSNPQAHVSGVRFLYQCQSIQDSQQVTEVSLTTLVNFVDITQKPQPPRGQPKMDWKWP
FDFFPFKVAFSRGVFSQKCSVSPILILCLLLLGVLNLETM

Important features of the protein:

Signal peptide:

amino acids 1-22

Transmembrane domains:

amino acids 484-505, 581-600

N-glycosylation sites.

amino acids 78-82, 165-169, 179-185, 279-285, 331-337, 347-351, 410-414, 487-491

N-myristoylation sites.

amino acids 30-36, 41-47, 124-130, 232-238, 236-242, 409-415

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 420-431

FIGURE 103

CCTAATTCTCAAGGTGATGCTATTTAGGAAGTCATAACTCATGTGAGTGGAGCCATGTGGGAT
TAAGAAGTGATAGGAGAGCTTGCTGTCTGTCTCTGCTCTCCACTGTGTGAGGATACAACAGGA
AGACAGCCATCTGGTGAGGAAGAGAGGGCCCTCGCCAGATACCGGACCTGCTGACACCTTGAT
CTTGGACTTCCCATCTTCCAGGAAGGCCTGACCTCAGTTGTTCCAGGGTAAAGAATTTGGGCA
GTGCCCACACCCACGCTGTTGGATAACATTTCTTCACCATACCAGTGAGGGTGAATGTGTACA
CGCCCAGCTTCCTGCCTGTTACTCTCCACAGT**ATG**CGAAGAATATCCCTGACTTCTAGCCCTG
TGCGCCTTCTTTTGTTTCTGCTGTTGCTACTAATAGCCTTGGAGATCATGGTTGGTGGTCACT
CTCTTTGCTTCAACTTCACTATAAAATCATTGTCCAGACCTGGACAGCCCTGGTGTGAAGCGC
AGGTCTTCTTGAATAAAAATCTTTTCCTTCAGTACAACAGTGACAACAACATGGTCAAACCTC
TGGGCCTCCTGGGGAAGAAGGTATATGCCACCAGCACTTGGGGAGAATTGACCCAAACGCTGG
GAGAAGTGGGGCGAGACCTCAGGATGCTCCTTTGTGACATCAAACCCCAGATAAAGACCAGTG
ATCCTTCCACTCTGCAAGTCGAGATGTTTTGTCAACGTGAAGCAGAACGGTGCACTGGTGCAT
CCTGGCAGTTCGCCACCAATGGAGAGAAATCCCTCCTCTTTGACGCAATGAACATGACCTGGA
CAGTAATTAATCATGAAGCCAGTAAGATCAAGGAGACATGGAAGAAAGACAGAGGGCTGGAAA
AGTATTTCAGGAAGCTCTCAAAGGGAGACTGCGATCACTGGCTCAGGGAATTCTTAGGGCACT
GGGAGGCAATGCCAGAACCGACAGGCAGAAGATCCACC**TAG**AGGTGATACCACGGCGGCGCAG
AGTTGTTCACCTGTGGTCCTCGATCGCTGACAGCCTTGGCTCCCACTGCTGTGTGTTCCCTGA
GTCAAGTGGAGGCGGAGCCTGCAATGAGCGGAGATCGCGCCTCTGCATTCCAGTCTTGGCAAC
AGAGCAAGACTCCGTCTCAAAAAAAAAAAATTTTTTTTCAGTACATATTTTTTAAAAGATAGG
GCTGGGCACAGCAGCTCACATCTATAATCCCAACACTTTGGGAGGCCTAGGCAGGAGGATCAC
TTGAGCCCAGGAATCTGAAGCTGCAGTGAGCCTTTGCTCGTGAGATTGTGGACCTATGATCCT
ACCACCAGCCCACCTGGTTCTAACACCCCCTCCTCTATGTGTGAGAGGGAGAGAAGAAAAGTG
AGGGAGAAAAGAGAGATAAGCAAAGAACAGAGAGGAAAAATGGAAAATAAGAGGAAATTGGGG
GAATTAAACAGAGGGGAGGGCATGGATCCCCGGGAGTTAGAAGAGTAGCAGCTTGTGGATTAC
TACGCAGTGGAGGAAGAAGAGTTGTTGGAAATTATTTGAGAGGTAGTATAATCATTTGTGAGG
CAGTTTTCTGCATTCACCATTTCTCACAGACTAAGTTACTCATAAGCAAACGTGCAATTCACA
TTACACTGAAATTCTTCCCTAATACATCATTTGCATTGGAATAAAGTACGGTTTTCAAACAAC
CTGATATAGCAGAACTGACTGTATAAATTATGTGAGCACAGTGCAAGTAATTCTTTGTTTGTT
TGTTTGTTTTTTTGAGACAGAGTCTCACTCTATCTCCCAGGCTGGAGTGTAGTGGTGCGATCC
CGGCTCACTGCAACCTCGATCTCCCAGGCTCAAGCGATTCCCCTGCCTCAGCCTCCTGAGTAG
CTGGGATTACAGGCATGAGCCACCACGCCCGGCTAATTTTTGTATTTTTAGTAGAGACGGGGT
TTCACCCTGTTGGCCAGGCTGGTCTCGAACTACGGACCTCAGGTGATCTGCCCCCCTCAGCCT
CTCAAAGTGCTGGGATTATAGCATGAGCCACTGAGCCCAGACACAAGTAGTTCTTTCTGATAA
ACACTTTAACACTGAATGCA

FIGURE 104

MRRISLTSSPVRLLLFLLLLLIALEIMVGGHSLCFNFTIKSLSRPGQPWCEAQVFLNKNLFLQ
YNSDNNMVKPLGLLGKKVYATSTWGELTQTLGEVGRDLRMLLCDIKPQIKTSDPSTLQVEMFC
QREAERCTGASWQFATNGEKSLLFDAMNMTWTVINHEASKIKETWKKDRGLEKYFRKLSKGDC
DHWLREFLGHWEAMPEPTGRRST

Important features of the protein:

Signal peptide:

amino acids 1-23

Transmembrane domain:

amino acids 11-30(possible type II protein)

N-glycosylation site.

amino acids 36-39, 154-157

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 2-5, 182-185, 209-212

Casein kinase II phosphorylation site.

amino acids 86-89, 93-96, 142-145, 185-188

N-myristoylation site.

amino acids 46-51

Amidation site.

amino acids 77-80, 207-210

FIGURE 105

TTTTCCGAGTGACCTTCTTG**ATG**CTGGCTGTTTCTCTCACCGTTCCCCTGCTTGGAGCCATGA
TGCTGCTGGAATCTCCTATAGATCCACAGCCTCTCAGCTTCAAAGAACCCCCGCTCTTGCTTG
GTGTTCTGCATCCAAATACGAAGCTGCGACAGGCAGAAAGGCTGTTTGAAAATCAACTTGTTG
GACCGGAGTCCATAGCACATATTGGGGATGTGATGTTTACTGGGACAGCAGATGGCCGGGTCG
TAAAACTTGAAAATGGTGAAATAGAGACCATTGCCCGGTTTGGTTCGGGCCCTTGCAAAACCC
GAGATGATGAGCCTGTGTGTGGGAGACCCCTGGGTATCCGTGCAGGGCCCAATGGGACTCTCT
TTGTGGCCGATGCATACAAGGGACTATTTGAAGTAAATCCCTGGAAACGTGAAGTGAAACTGC
TGCTGTCCTCCGAGACACCCATTGAGGGGAAGAACATGTCCTTTGTGAATGATCTTACAGTCA
CTCAGGATGGGAGGAAGATTTATTTCACCGATTCTAGCAGCAAATGGCAAAGACGAGACTACC
TGCTTCTGGTGATGGAGGGCACAGATGACGGGCGCCTGCTGGAGTATGATACTGTGACCAGGG
AAGTAAAAGTTTTATTGGACCAGCTGCGGTTCCCGAATGGAGTCCAGCTGTCTCCTGCAGAAG
ACTTTGTCCTGGTGGCAGAAACAACCATGGCCAGGATACGAAGAGTCTACGTTTCTGGCCTGA
TGAAGGGCGGGGCTGATCTGTTTGTGGAGAACATGCCTGGATTTCCAGACAACATCCGGCCCA
GCAGCTCTGGGGGGTACTGGGTGGGCATGTCGACCATCCGCCCTAACCCTGGGTTTTCCATGC
TGGATTTCTTATCTGAGAGACCCTGGATTAAAAGGATGATTTTTAAGCTCTTTAGTCAAGAGA
CGGTGATGAAGTTTGTGCCGCGGTACAGCCTCGTCCTAGAACTCAGCGACAGCGGTGCCTTCC
GGAGAAGCCTGCATGATCCCGATGGGCTGGTGGCCACCTACATCAGCGAGGTGCACGAACACG
ATGGGCACCTGTACCTGGGCTCTTTCAGGTCCCCCTTCCTCTGCAGACTCAGCCTCCAGGCTG
TT**TAG**CCCTCCCAGATAGCTGCCCCTGCCACGCAGGCCAGGAGTCTTCACACTCAGGCACCAG
GCCTGGTCCAGGAGGAGCTGTGGACACAGTCGTGGTTCAAGTGTCCACATGCACCTGTTAGTC
CCTGAGAGGTGGTGGGAATGGCTGCTTCATTCCTCGAGGATGCCCGGGCCCCACCTGGGCTTG
TCTTTCTGTTTAGAGGGAAGTGTAACATATCTGCCATGAGGAACATAAATTCATGTAAAGCCA
TTTTCTCTTAAACAAAACAAAACTTTCTAAGTACAATCATTCTCTAGGATTTGGGAAGCTCCT
TGCACTTGGAACAGGGCTCAGGTGGGTGGAGCAGTAAGGCACTACCCAGAGAGCTTGCTGCTG
CGGCCCTGTCCTGCGGCCTCAAAGTTCTTCTTTACTATATATAACGTGCGGTCATACCTTTCT
TCGTTGTGGTGGGGATGGAAGAGCAGAGGGAGCATGGCCCAGGGGTGTTGAGGCCAGCGGTGA
GAGCCGTGTTAGCCAAGACATGGAACTGTGTTCTCAAGGGTTATGTGGGGCGTGGGCTCTCCA
TAGTGTGTATGAAAAGCTTGTTGACTCTAGCGGCTCAGAGAGGACTTTGCTGGGTTTCTTTCT
GTGAATATCTCCGTGCTGACCATGCTGGAATTGGATGATTCTGCAATTCGGGACCTACTGCAG
GGGTCCGTTTAGTAACGTCTTGTCTGTGATCTTTGTTCTTGACCTCTAGACCCCAAGATGTGA
ACAGTGCACGTGTTAATGTCATCTTTGCTCATGTGTTATAAGCCCCAAGTTGCTGTATATTTT
CACAAGTATGTCTACACACTGG

FIGURE 106

MLAVSLTVPLLGAMMLLESPIDPQPLSFKEPPLLLGVLHPNTKLRQAERLFENQLVGPESIAH
IGDVMFTGTADGRVVKLENGEIETIARFGSGPCKTRDDEPVCGRPLGIRAGPNGTLFVADAYK
GLFEVNPWKREVKLLLSSETPIEGKNMSFVNDLTVTQDGRKIYFTDSSSKWQRRDYLLLVMEG
TDDGRLLEYDTVTREVKVLLDQLRFPNGVQLSPAEDFVLVAETTMARIRRVYVSGLMKGGADL
FVENMPGFPDNIRPSSSGGYWVGMSTIRPNPGFSMLDFLSERPWIKRMIFKLFSQETVMKFVP
RYSLVLELSDSGAFRRSLHDPDGLVATYISEVHEHDGHLYLGSFRSPFLCRLSLQAV

Important features of the protein:

Signal peptide:

amino acids 1-13

Transmembrane domain:

amino acids 1-21 (possible type II)

N-glycosylation sites.

amino acids 116-119, 152-155

Casein kinase II phosphorylation sites.

amino acids 19-22, 27-30, 98-101, 146-149, 221-224, 286-289, 332-335

N-myristoylation sites.

amino acids 71-76, 92-97, 189-194, 244-249, 338-343

Amidation site.

amino acids 164-167

FIGURE 107

AACGAAGCGTGCGCGCTTTGGTAACCGGCTAGAAATCCCGCACGCGCGCCTGCCTCCTCTCCC
CAGGCCTGAGCTGCCCCTCCCACTGCCTTTCCTTCTTCCCGCGAGTCAGAAGCTTCGCGAGGG
CCCAGAGAGGCGGTGGGGTGGGCGACCCTACGCCAGCTCCGGGCGGGAGAAAGCCCACCCTCT
CCCGCGCCCCAGGAAACCGCCGGCGTTCGGCGCTGCGCAGAGCC**ATG**GAATTCTCCTGGCTGG
AGACGCGCTGGGCGCGGCCCTTTTACCTGGCGTTCGTGTTCTGCCTGGCCCTGGGGCTGCTGC
AGGCCATTAAGCTGTACCTGCGGAGGCAGCGGCTGCTGCGGGACCTGCGCCCCTTCCCAGCGC
CCCCCACCCACTGGTTCCTTGGGCACCAGAAGTTTATTCAGGATGATAACATGGAGAAGCTTG
AGGAAATTATTGAAAAATACCCTCGTGCCTTCCCTTTCTGGATTGGGCCCTTTCAGGCATTTT
TCTGTATCTATGACCCAGACTATGCAAAGACACTTCTGAGCAGAACAGATCCCAAGTCCCAGT
ACCTGCAGAAATTCTCACCTCCACTTCTTGGAAAAGGACTAGCGGCTCTAGACGGACCCAAGT
GGTTCCAGCATCGTCGCCTACTAACTCCTGGATTCCATTTTAACATCCTGAAAGCATACATTG
AGGTGATGGCTCATTCTGTGAAAATGATGCTGGATAAGTGGGAGAAGATTTGCAGCACTCAGG
ACACAAGCGTGGAGGTCTATGAGCACATCAACTCGATGTCTCTGGATATAATCATGAAATGCG
CTTTCAGCAAGGAGACCAACTGCCAGACAAACAGCACCCATGATCCTTATGCAAAAGCCATAT
TTGAACTCAGCAAAATCATATTTCACCGCTTGTACAGTTTGTTGTATCACAGTGACATAATTT
TCAAACTCAGCCCTCAGGGCTACCGCTTCCAGAAGTTAAGCCGAGTGTTGAATCAGTACACAG
ATACAATAATCCAGGAAAGAAAGAAATCCCTCCAGGCTGGGGTAAAGCAGGATAACACTCCGA
AGAGGAAGTACCAGGATTTTCTGGATATTGTCCTTTCTGCCAAGGATGAAAGTGGTAGCAGCT
TCTCAGATATTGATGTACACTCTGAAGTGAGCACATTCCTGTTGGCAGGACATGACACCTTGG
CAGCAAGCATCTCCTGGATCCTTTACTGCCTGGCTCTGAACCCTGAGCATCAAGAGAGATGCC
GGGAGGAGGTCAGGGGCATCCTGGGGGATGGGTCTTCTATCACTTGGGACCAGCTGGGTGAGA
TGTCGTACACCACAATGTGCATCAAGGAGACGTGCCGATTGATTCCTGCAGTCCCGTCCATTT
CCAGAGATCTCAGCAAGCCACTTACCTTCCCAGATGGATGCACATTGCCTGCAGGGATCACCG
TGGTTCTTAGTATTTGGGGTCTTCACCACAACCCTGCTGTCTGGAAAAACCCAAAGGTCTTTG
ACCCCTTGAGGTTCTCTCAGGAGAATTCTGATCAGAGACACCCCTATGCCTACTTACCATTCT
CAGCTGGATCAAGGAACTGCATTGGGCAGGAGTTTGCCATGATTGAGTTAAAGGTAACCATTG
CCTTGATTCTGCTCCACTTCAGAGTGACTCCAGACCCCACCAGGCCTCTTACTTTCCCCAACC
ATTTTATCCTCAAGCCCAAGAATGGGATGTATTTGCACCTGAAGAAACTCTCTGAATGT**TAG**A
TCTCAGGGTACAATGATTAAACGTACTTTGTTTTTCGAAGTTAAATTTACAGCTAATGATCCA
AGCAGATAGAAAGGGATCAATGTATGGTGGGAGGATTGGAGGTTGGTGGGATAGGGGTCTCTG
TGAAGAGATCCAAAATCATTTCTAGGTACACAGTGTGTCAGCTAGATCTGTTTCTATATAACT
TTGGGAGATTTTCAGATCTTTTCTGTTAAACTTTCACTACTATTAATGCTGTATACACCAATA
GACTTTCATATATTTTCTGTTGTTTTTAAAATAGTTTTCAGAATTATGCAAGTAATAAGTGCA
TGTATGCTCACTGTCAAAAATTCCCAACACTAGAAAATCATGTAGAATAAAAATTTTAAATCT
CACTTCACTTAGCCGACATTCCATGCCCTGACCAATCCTACTGCTTTTCCTAAAAACAGAATA
ATTTGGTGTGCATTCTTTCAGACTTTTTCCTATACATTTTATATGTAGAAATGTAGCAATGTA
TTTGTATAGATGTGATCATTCCTATATTGTTATTGATTTTTTTCACTTAATAAAAATTCACCT
TATTCCTTAAAA

FIGURE 108

MEFSWLETRWARPFYLAFVFCLALGLLQAIKLYLRRQRLLRDLRPFPAPPTHWFLGHQKFIQD
DNMEKLEEIIEKYPRAFPFWIGPFQAFFCIYDPDYAKTLLSRTDPKSQYLQKFSPPLLGKGLA
ALDGPKWFQHRRLLTPGFHFNILKAYIEVMAHSVKMMLDKWEKICSTQDTSVEVYEHINSMSL
DIIMKCAFSKETNCQTNSTHDPYAKAIFELSKIIFHRLYSLLYHSDIIFKLSPQGYRFQKLSR
VLNQYTDTIIQERKKSLQAGVKQDNTPKRKYQDFLDIVLSAKDESGSSFSDIDVHSEVSTFLL
AGHDTLAASISWILYCLALNPEHQERCREEVRGILGDGSSITWDQLGEMSYTTMCIKETCRLI
PAVPSISRDLSKPLTFPDGCTLPAGITVVLSIWGLHHNPAVWKNPKVFDPLRFSQENSDQRHP
YAYLPFSAGSRNCIGQEFAMIELKVTIALILLHFRVTPDPTRPLTFPNHFILKPKNGMYLHLK
KLSEC

Important features of the protein:

Signal peptide:

amino acids 1-29

Transmembrane domains:

amino acids 310-330, 397-413, 459-473

N-glycosylation site.

amino acids 206-210

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 265-269, 504-520

N-myristoylation sites.

amino acids 25-31, 298-304, 353-359, 450-456, 456-462

Cytochrome P450 cysteine heme-iron ligand signature.

amino acids 447-457

Cytochrome P450 cysteine heme-iron ligand proteins.

amino acids 444-475

FIGURE 109

GGCGTTCCGGGCCTCAACTTTGGCGTCGTGAGATTCTTGTGAGGCGTCTGCCTGGAAGCCGGC
AGCAATTTTGCTTCTTTAAAGAGAAAAAGAAGGCTAGGGACTCAGATTCCTGGATTCTGAGAT
CCAGACCAGCTCCTCCCAGACCTCTCCAGAAGAAGCC**ATG**GGAACCCCTCGTATCCAGCATTT
GCTGATCCTCCTGGTCCTAGGAGCCTCCCTCCTGACCTCGGGCCTAGAGCTGTATTGTCAAAA
GGGTCTGTCCATGACTGTGGAAGCAGATCCAGCCAATATGTTTAACTGGACCACAGAGGAAGT
GGAGACTTGTGACAAAGGGGCACTTTGCCAGGAAACCATACTAATAATTAAAGCAGGGACTGA
GACAGCCATTTTGGCCACGAAGGGCTGCATCCCGGAAGGGGAGGAGGCCATAACAATTGTCCA
GCACTCTTCACCTCCCGGCCTGATCGTGACCTCCTACAGTAACTACTGTGAGGATTCCTTCTG
TAATGACAAAGACAGCCTGTCTCAGTTTTGGGAGTTCAGTGAGACCACAGCTTCCACTGTGTC
AACAACCCTCCATTGTCCAACCTGTGTGGCTTTGGGGACCTGTTTCAGTGCTCCTTCTCTTCC
CTGTCCCAATGGTACAACTCGATGCTATCAAGGAAAACTTGAGATCACTGGAGGTGGCATTGA
GTCGTCTGTGGAGGTCAAAGGCTGTACAGCCATGATTGGCTGCAGGCTGATGTCTGGAATCTT
AGCAGTAGGACCCATGTTTGTGAGGGAAGCGTGCCCACATCAGCTGCTCACTCAACCTCGAAA
GACTGAAAATGGGGCCACCTGTCTTCCCATTCCTGTTTGGGGGTTACAGCTACTGCTGCCATT
GCTGCTGCCATCATTTATTCACTTTTCC**TAA**GAAGGCACTTCTGGGCCTGGGTCTGAGGACAT
CTTTTTTGACTGGGAGCCTTCTTACTGTTGAGGTTCAACAAGCTGAGGAGTAGATGGGAATTT
GAGGGAGAATACAGAGATACTATGAACGTATTTGACATTTTTAATACAATTTCTGCTATAATT
TTTGTATGCAGTAGGCGTTACTAATAAACATTTCTGCTGTGA

FIGURE 110

MGTPRIQHLLILLVLGASLLTSGLELYCQKGLSMTVEADPANMFNWTTEEVETCDKGALCQET
ILIIKAGTETAILATKGCIPEGEEAITIVQHSSPPGLIVTSYSNYCEDSFCNDKDSLSQFWEF
SETTASTVSTTLHCPTCVALGTCFSAPSLPCPNGTTRCYQGKLEITGGGIESSVEVKGCTAMI
GCRLMSGILAVGPMFVREACPHQLLTQPRKTENGATCLPIPVWGLQLLLPLLLPSFIHFS

Important features of the protein:

Signal peptide:

amino acids 1-23

Transmembrane domain:

amino acids 184-201

N-glycosylation sites.

amino acids 45-49, 159-163

N-myristoylation sites.

amino acids 31-37, 70-76, 99-105, 147-153, 160-166, 174-180, 175-181

FIGURE 111

CGAGAAGAGGACAGAGGAGACTGAGCAAAGGGGGGTGGGCTCCAGGCGACCCCTAGCCCAATTCTGCCCCTCCAT
CCCAAGGGGCAGAGAAATTGTCTTTCTTTGCTGACTCCTACGAGGAAAAAAAAAAAAAAAAAAAAACCATTTAA
AGGGAAAGATAAACGGAGACGGAGGAAAGGTGGCAGCCAGATTACTTAGAGAGGCACAGAGGAGAGAGATCGGGG
TGAGTCGCC**ATG**GGGACTCCCAGGGCCCAGCACCCGCCGCCTCCCCAGCTGCTGTTCCTAATTCTGCTGAGCTGT
CCCTGGATCCAGGGTCTGCCCCTGAAGGAGGAGGAGATATTGCCAGAGCCTGGAAGTGAGACCCCCACGGTGGCC
TCTGAGGCCCTGGCTGAACTGCTTCATGGGGCCCTGCTGAGGAGGGGCCCAGAGATGGGCTACCTGCCAGGATCT
GATCCGGACCCCACGCTAGCCACCCCTCCGGCCGGCCAGACTCTCGCAGTGCCCTCCCTGCCACGGGCCACTGAG
CCGGGGACAGGGCCTCTGACAACAGCCGTCACCCCTAACGGGGTCAGGGGGGCAGGCCCCACTGCGCCAGAACTG
CTGACCCCGCCCCCAGGAACCACAGCCCCACCCCCACCCAGCCCTGCCTCCCCAGGGCCTCCCCTTGGGCCTGAG
GGAGGAGAGGAGGAGACGACGACCACCATCATCACCACGACAACTGTTACCACTACGGTGACCAGCCCAGTTCTG
TGTAATAACAACATCTCCGAGGGCGAAGGGTATGTGGAGTCTCCAGATCTGGGGAGCCCCGTCAGCCGCACCCTG
GGGCTCCTGGACTGCACTTACAGCATCCATGTCTACCCTGGCTACGGCATTGAGATCCAGGTGCAGACGCTGAAC
CTGTCACAGGAAGAGGAGCTCCTGGTGCTGGCTGGTGGGGGATCCCCAGGCCTGGCCCCCCGACTCCTGGCCAAC
TCATCCATGCTTGGAGAAGGACAAGTCCTTCGGAGCCCAACCAACCGGCTGCTTCTGCACTTCCAGAGCCCACGG
GTCCCAAGGGGCGGTGGCTTCAGGATCCACTATCAGGCCTACCTCCTGAGCTGTGGCTTCCCTCCCCGGCCGGCC
CATGGGGACGTGAGTGTGACGGACCTGCACCCTGGGGGCACTGCCACCTTTCACTGTGATTCGGGCTACCAGCTG
CAGGGAGAGGAGACCCTCATCTGCCTCAATGGCACCCGGCCATCCTGGAACGGTGAAACCCCCAGCTGCATGGCA
TCCTGTGGTGGCACCATCCACAATGCCACCCTGGGCCGCATCGTGTCCCCAGAGCCTGGGGGAGCCGTAGGGCCC
AACCTCACCTGCCGTTGGGTCATTGAAGCAGCTGAGGGGCGCCGGCTGCACCTGCACTTTGAAAGGGTCTCGCTG
GATGAGGACAATGACCGGCTGATGGTGCGCTCAGGGGGCAGCCCCCTATCCCCCGTGATCTATGATTCGGACATG
GACGATGTCCCCGAGCGGGGTCTCATCAGTGACGCCCAGTCCCTCTACGTGGAGCTGCTGTCAGAGACACCTGCC
AATCCCCTGCTGTTAAGCCTTCGATTTGAAGCCTTTGAGGAGGATCGCTGCTTCGCCCCCTTCCTGGCACATGGA
AATGTCACTACCACGGACCCTGAGTATCGCCCAGGGGCACTGGCAACCTTCTCGTGCCTCCCAGGATATGCCCTG
GAGCCCCCTGGGCCCCCCAATGCCATCGAATGTGTGGATCCCACAGAACCCCACTGGAACGACACAGAGCCGGCC
TGCAAAGCCATGTGTGGAGGGGAGCTGTCGGAACCAGCTGGCGTGGTCCTCTCTCCCGACTGGCCCCAGAGCTAT
AGCCCGGGCCAAGACTGCGTGTGGGGCGTGCACGTCCAGGAAGAGAAGCGCATCTTGCTCCAAGTTGAGATATTG
AATGTGCGGGAAGGGGACATGCTGACGCTGTTCGACGGGGACGGTCCCAGCGCCCGAGTCTTGGCCCAGCTGCGG
GGACCTCAGCCGCGCCGCCGCCTTCTCTCCTCTGGGCCCGACCTCACACTGCAGTTTCAGGCACCGCCCGGGCCC
CCAAATCCAGGCCTGGGCCAGGGCTTCGTATTGCACTTCAAAGAGGTCCCGAGGAACGACACGTGCCCCGAGCTG
CCACCTCCGGAGTGGGGCTGGAGAACGGCATCCCACGGGGACCTGATCCGGGGCACGGTGCTCACCTACCAGTGC
GAGCCTGGCTACGAGCTGCTAGGCTCCGACATTCTCACTTGCCAGTGGGACCTGTCTTGGAGCGCCGCGCCGCCC
GCCTGCCAAAAGATCATGACTTGTGCTGACCCTGGCGAGATTGCCAACGGGCACCGCACCGCCTCGGACGCCGGC
TTCCCCGTTGGCTCCCACGTCCAGTACCGCTGCCTGCCAGGGTACAGCCTCGAGGGGGCAGCCATGCTCACCTGC
TACAGCCGGGACACAGGCACACCCAAGTGGAGCGATAGGGTCCCCAAATGCGCCTTGAAGTACGAGCCGTGCCTG
AACCCGGGGGTTCCCGAGAATGGCTACCAGACGCTGTACAAGCACCACTACCAGGCGGGCGAGTCTCTGCGCTTC
TTCTGCTATGAGGGCTTTGAGCTTATCGGCGAGGTCACCATCACCTGTGTGCCCGGCCACCCCTCCCAGTGGACC
AGCCAGCCCCCACTCTGCAAAGTGACCCAGACCACAGATCCATCACGGCAGCTGGAAGGGGGGAACCTGGCCCTG
GCCATCCTGCTGCCTCTAGGCTTGGTCATTGTCCTCGGCAGTGGCGTTTACATCTACTACACCAAGCTTCAGGGA
AAGTCCCTTTTCGGCTTCTCGGGCTCCCACTCCTACAGCCCCATCACCGTGGAGTCGGACTTCAGCAACCCGCTG
TATGAAGCTGGGGATACGCGGGAGTATGAAGTTTCCATC**TGA**ACCCCAAGACTACAGCTGCAGGACCCAGGACGC
CCCTCCCCTCCTCATTCGGGCAGAGGGAAATACGGGACCCGGTCTCTGCCTCCTGGCTGCCCTCCTCCCTGGCTG
TGTAAATAGTCTCCCTATCCCACGAGGGGGCTTTGATGGCCCTGGAGATCCTACAGTAAATAAACCAGCATCCTG
CCGCCCAAAAAA

FIGURE 112

MGTPRAQHPPPPQLLFLILLSCPWIQGLPLKEEEILPEPGSETPTVASEALAELLHGALLRRG
PEMGYLPGSDPDPTLATPPAGQTLAVPSLPRATEPGTGPLTTAVTPNGVRGAGPTAPELLTPP
PGTTAPPPPSPASPGPPLGPEGGEEETTTTIITTTTTVTTTVTSPVLCNNNISEGEGYVESPDL
GSPVSRTLGLLDCTYSIHVYPGYGIEIQVQTLNLSQEEELLVLAGGGSPGLAPRLLANSSMLG
EGQVLRSPTNRLLLHFQSPRVPRGGGFRIHYQAYLLSCGFPPRPAHGDVSVTDLHPGGTATFH
CDSGYQLQGEETLICLNGTRPSWNGETPSCMASCGGTIHNATLGRIVSPEPGGAVGPNLTCRW
VIEAAEGRRLHLHFERVSLDEDNDRLMVRSGGSPLSPVIYDSDMDDVPERGLISDAQSLYVEL
LSETPANPLLLSLRFEAFEEDRCFAPFLAHGNVTTTDPEYRPGALATFSCLPGYALEPPGPPN
AIECVDPTEPHWNDTEPACKAMCGGELSEPAGVVLSPDWPQSYSPGQDCVWGVHVQEEKRILL
QVEILNVREGDMLTLFDGDGPSARVLAQLRGPQPRRRLLSSGPDLTLQFQAPPGPPNPGLGQG
FVLHFKEVPRNDTCPELPPPEWGWRTASHGDLIRGTVLTYQCEPGYELLGSDILTCQWDLSWS
AAPPACQKIMTCADPGEIANGHRTASDAGFPVGSHVQYRCLPGYSLEGAAMLTCYSRDTGTPK
WSDRVPKCALKYEPCLNPGVPENGYQTLYKHHYQAGESLRFFCYEGFELIGEVTITCVPGHPS
QWTSQPPLCKVTQTTDPSRQLEGGNLALAILLPLGLVIVLGSGVYIYYTKLQGKSLFGFSGSH
SYSPITVESDFSNPLYEAGDTREYEVSI

Important features of the protein:

Signal peptide:

amino acids 1-27

Transmembrane domain:

amino acids 842-864

N-glycosylation sites.

amino acids 176-180, 222-226, 247-251, 332-336, 355-359, 373-377, 473-477, 517-521, 641-645

Tyrosine kinase phosphorylation site.

amino acids 61-69

N-myristoylation sites.

amino acids 2-8, 84-90, 111-117, 114-120, 190-196, 198-204, 235-241, 309-315, 333-339, 351-357, 472-478, 484-490, 528-534, 626-632, 665-671, 775-781, 842-848

Amidation site.

amino acids 384-388

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 12-23

CUB domain proteins profile.

amino acids 202-218, 376-392, 553-569

FIGURE 113

GCCGCGGGCGGAGCTGCCTGCCGGTCCCGCGCCGCGCGTCCGCACTCCTCGGCCCTCGGGCGGTCGATGGGACGG
GGCGCCGCGGAGCAGGAGGCGGCGCCCGTCGGGGTGCTCGGGCCGCGCGGGAGCCCACTGTGGGGCTCGGGCATG
GCGGGCCGCAGGACCTGAGCTCTCCTCAGGGGAGCGGGGAGGCAGCTGCTGGCCGGCGATGGGGACGGAGTGGGG
CCGTCGCCGCCGCGCCGAGCCGTGAGCGCCGAGCCACCGCCGCCGCTACCTCAGCCCTTCGCGAAGCGCCGGGCA
GCTCGGGAAC**ATG**GCCCTGGAGCGGCTCTGCTCGGTCCTCAAAGTGTTGTTAATAACAGTACTGGTAGTGGAAGG
GATTGCCGTGGCCCAAAAAACCCAAGATGGACAAAATATTGGAATCAAGCATATTCCTGCAACCCAGTGTGGCAT
TTGGGTTCGAACCAGCAATGGAGGTCATTTTGCTTCGCCAAATTATCCTGACTCATATCCACCAAACAAGGAGTG
TATCTACATTTTGGAAGCTGCTCCACGTCAAAGAATAGAGTTGACCTTTGATGAACATTATTATATAGAACCATC
ATTTGAGTGTCGGTTTGATCACTTGGAAGTTCGAGATGGGCCATTTGGTTTCTCTCCTCTTATAGATCGTTACTG
TGGCGTGAAAAGCCCTCCATTAATTAGATCAACAGGGAGATTCATGTGGATTAAGTTTAGTTCTGATGAAGAGCT
TGAAGGACTGGGATTTCGAGCAAAATATTCATTTATTCCAGATCCAGACTTTACTTACCTAGGAGGTATTTTAAA
TCCCATTCCAGATTGTCAGTTCGAGCTCTCGGGAGCTGATGGAATAGTGCGCTCTAGTCAGGTAGAACAAGAGGA
GAAAACAAAACCAGGCCAAGCCGTTGATTGCATCTGGACCATTAAAGCCACTCCAAAAGCTAAGATTTATTTGAG
GTTCCTAGATTATCAAATGGAGCACTCAAATGAATGCAAGAGAAACTTCGTTGCAGTCTATGATGGAAGCAGTTC
TATTGAAAACCTGAAGGCCAAGTTTTGCAGCACTGTGGCCAATGATGTAATGCTTAAAACAGGAATTGGAGTGAT
TCGAATGTGGGCAGATGAAGGTAGTCGGCTTAGCAGGTTTCGAATGCTCTTTACTTCCTTTGTGGAGCCTCCCTG
CACAAGCAGCACTTTCTTTTGCCATAGCAACATGTGCATCAATAATTCTTTAGTCTGTAATGGTGTCCAAAATTG
TGCATACCCTTGGGATGAAAATCATTGTAAAGAAAAGAAAAAAGCAGGAGTATTTGAACAAATCACTAAGACTCA
TGGAACAATTATTGGCATTACTTCAGGGATTGTCTTGGTCCTTCTCATTATTTCTATTTTAGTACAAGTGAAACA
GCCTCGAAAAAAGGTCATGGCTTGCAAAACCGCTTTTAATAAAACCGGGTTCCAAGAAGTGTTTGATCCTCCTCA
TTATGAACTGTTTTCACTAAGGGACAAAGAGATTTCTGCAGACCTGGCAGACTTGTCGGAAGAATTGGACAACTA
CCAGAAGATGCGGCGCTCCTCCACCGCCTCCCGCTGCATCCACGACCACCACTGTGGGTCGCAGGCCTCCAGCGT
CAAACAAAGCAGGACCAACCTCAGTTCCATGGAACTTCCTTTCCGAAATGACTTTGCACAACCACAGCCAATGAA
AACATTTAATAGCACCTTCAAGAAAAGTAGTTACACTTTCAAACAGGGACATGAGTGCCCTGAGCAGGCCCTGGA
AGACCGAGTAATGGAGGAGATTCCCTGTGAAATTTATGTCAGGGGGCGAGAAGATTCTGCACAAGCATCCATATC
CATTGACTTC**TAA**TCTTCTGCTAATGGTGATGTGAATTCTTAGGGTGTGTACGTACGCAGCCTCCAGGGCACCAT
ACTGTTTCCAGCAGCCAACCCTTTTCTCCCATCACAACTACGAAGACCTTGATTTACCGTTAACCTATTGTATGG
TGATGTTTTTATTCTCTCAGGCAGTCTATATATGTTAAACCAATCAAGGAACTTACTCTATTCAGTGGAAACAAT
AATCATCTCTATTGCTTGGTGTCATTTATAGGAAGCACTGCCAGTTAAAGAGCATTAGAAGAGGTGGTTGGATGG
AGCCAGGCTCAGGCTGCCTCTTCGTTTTAGCAACAAGAAGACTGCTCTTGACTGATAACAGCTCTGTCAATATTT
TGATGCCACAATAAACTTGATTTTTTTTTACATTCCTTTTATTTTTCCTTTCTCTAAATTTAATTTGTTTTATAA
GCCTATCGTTTTACCATTTCATTTTCTTACATAAGTACAAGTGGTTAATGTACCACATACTTCAGTATAGGCATT
TGTTCTTGAGTGTGTCAAAATACAGCTAGTTACTGTGCCAATTAAGACCCAGTTGTATTTCACCCATCTGTTTCT
TCTTGGCTAATCTCTGTACTTCTGCCTTTTAATTACTGGGCCCTTATTCCTTATTTTCTGTGAGAAATAATAGAT
GATATGATTTATTACCTTTCAATTATATTTTTCTCAGTTATACTAGAAAATTTCATAATCCTGGGATATATGTAC
CATTGTCAGCTATGACTAAAAATTTGAAAAAGATAAAAATTTCTAGCAAGCCTTTGAAGTTTACCAAGTATAGTC
ACATTCAGTGACAGCCCATTCATTCCAGTAAAGAATCATTTCATTCACTTTGGGAGAGGCCTATAATTACATTTA
TTTGCAATGTTTCTCTTCGCTAGATTGTTACATAGCTCCCATTCTGTTGGTTTTGCTTACAGCATATGGTAACCA
AGGTTAGATGCCAGTTAAAATTCCTTAGAAATTGGATGAGCCTTGAGATTGCTTCTTAACTGGGACATGACATTT
TTCTAGCTCTTATCAAGAATAACAACTTCCACTTTTTTTTTAAACTGCACTTTTGACTTTTTTTTATGGTATAAAAA
CAATAATTTATAAACATAAAAGCTCATTGTGTTTTTTAGACTTTTGATATTATTTGATACTGTACAAACTTTATT
AAATCAAGATGAAAGACCTACAGGACAGATTCCTTTCAGTGTTCACATCAGTGGCTTTGTATGCAAATATGCTGT
GTTGGACCTGGACGCTATAACTTATTGTAAAGACCTTGGAAATGTGGACATAAGCTCTTTCTTTCCTTTTGTTAC
TGTATTTAGTTTGTGATAAATTTTTCACTGTGTGATATTTATGCTCTAAATCACTACACAAATCCCATATTAAAA
TATACATTGTACCTGAAAAAAAA

FIGURE 114

MALERLCSVLKVLLITVLVVEGIAVAQKTQDGQNIGIKHIPATQCGIWVRTSNGGHFASPNYP
DSYPPNKECIYILEAAPRQRIELTFDEHYYIEPSFECRFDHLEVRDGPFGFSPLIDRYCGVKS
PPLIRSTGRFMWIKFSSDEELEGLGFRAKYSFIPDPDFTYLGGILNPIPDCQFELSGADGIVR
SSQVEQEEKTKPGQAVDCIWTIKATPKAKIYLRFLDYQMEHSNECKRNFVAVYDGSSSIENLK
AKFCSTVANDVMLKTGIGVIRMWADEGSRLSRFRMLFTSFVEPPCTSSTFFCHSNMCINNSLV
CNGVQNCAYPWDENHCKEKKKAGVFEQITKTHGTIIGITSGIVLVLLIISILVQVKQPRKKVM
ACKTAFNKTGFQEVFDPPHYELFSLRDKEISADLADLSEELDNYQKMRRSSTASRCIHDHHCG
SQASSVKQSRTNLSSMELPFRNDFAQPQPMKTFNSTFKKSSYTFKQGHECPEQALEDRVMEEI
PCEIYVRGREDSAQASISIDF

Important features of the protein:

Signal peptide:

amino acids 1-22

Transmembrane domain:

amino acids 348-369

N-glycosylation sites.

amino acids 311-315, 385-389, 453-457, 475-479

cAMP- and cGMP-dependent protein kinase phosphorylation sites.

amino acids 426-430, 479-483

N-myristoylation sites.

amino acids 22-28, 32-38, 54-60, 186-192, 279-285, 318-324, 348-354, 352-358, 441-447

FIGURE 115

GGTCTCTGTCCTTGGCTGTGGCTCCTGCGCTCTGGCTGAGCC**ATG**TTCCTTCTCCTCGCCCTC
CTCACTGAGCTTGGAAGACTGCAAGCCCACGAAGGTTCTGAAGGAATATTTCTGCATGTCACA
GTTCCACGGAAGATTAAGTCAAATGACAGTGAAGTTTCAGAGAGGAAGATGATTTACATCATT
ACAATTGATGGACAACCTTACACTCTACATCTCGGAAAACAATCATTCTTACCCCAGAACTTT
TTGGTTTATACATATAATGAAACTGGATCTTTGCATTCTGTGTCTCCATATTTTATGATGCAT
TGCCATTACCAAGGATATGCTGCCGAATTTCCAAATTCATTTGTGACACTCAGTATATGTTCT
GGTCTCAGGGGATTTCTCCAGTTTGAAAATATCAGTTATGGAATTGAACCAGTAGAATCTTCA
GCAAGATTTGAGCATATAATTTATCAAATGAAAAATAATGATCCAAATGTATCCATTTTAGCA
GTAAATTACAGTCATATTTGGCAGAAAGACCAGCCCTACAAAGTTCCTTTAAACTCACAGATA
AAAAATCTTTCAAAACTATTACCCCAATATCTGGAAATATACATTATAGTGGAAAAAGCTTTG
ATGTTTACCCAGTTCAAATTGACTGTTATACTGTCTTCCTTGGAATTGTGGTCAAATGAAAAC
CAGATTTCCACCAGTGGGGATGCTGATGATATATTACAAAGATTTTTGGCATGGAAACGGGAC
TATCTCATCCTACGGCCCCATGACATAGCATACTTACTTGTTTACAGGAAACATCCTAAATAT
GTGGGAGCAACATTTCCTGGCACCGTATGCAATAAAAGCTATGATGCAGGTATTGCTATGTAT
CCAGATGCAATAGGTTTGGAGGGATTTTCGGTTATTATAGCTCAACTGCTTGGCCTTAATGTA
GGATTAACATATGATGACATCACTCAGTGTTTCTGTCTGAGAGCTACATGCATCATGAATCAT
GAAGCAGTGAGTGCCAGTGGTAGAAAGATTTTTAGCAACTGCAGCATGCACGACTATAGATAT
TTTGTTTCAAAATTTGAGACTAAATGCCTTCAGAAGCTTTCAAATTTGCAACCATTACATCAA
AATCAACCAGTGTGTGGTAATGGGATTTTGGAATCCAATGAAGAATGTGACTGTGGTAATAAA
AATGAATGTCAATTTAAGAAGTGCTGTGATTATAACACATGTAAACTGAAGGGCTCAGTAAAA
TGTGGTTCTGGACCATGTTGTACATCAAAGTGTGAGTTGTCAATAGCAGGCACTCCATGTAGA
AAGAGTATTGATCCAGAGTGTGATTTTACAGAGTACTGCAATGGAACCTCTAGTAATTGTGTT
CCTGACACTTATGCACTGAATGGCCGTTTGTGCAAGTTGGGAACTGCCTATTGCTATAACGGA
CAATGTCAAACTACTGATAACCAGTGTGCCAAGATATTTGGAAAAGGTGCTCAAGGTGCTCCA
TTTGCCTGTTTTAAAGAAGTTAATTCTCTGCATGAAAGATCTGAAAACTGTGGTTTTAAAAAT
TCACAACCATTACCTTGTGAACGGAAGGATGTTCTCTGTGGAAAATTAGCTTGTGTTCAGCCA
CATAAAAATGCTAATAAAAGTGACGCTCAATCTACAGTTTATTCATATATTCAAGACCATGTA
TGTGTATCTATAGCCACTGGTTCCTCCATGAGATCAGATGGAACAGACAATGCCTATGTGGCT
GATGGCACCATGTGTGGTCCAGAAATGTACTGTGTAAATAAAACCTGCAGAAAAGTTCATTTA
ATGGGATATAACTGTAATGCCACCACAAAATGCAAAGGGAAAGGGATATGTAATAATTTTGGT
AATTGTCAATGCTTCCCTGGACATAGACCTCCAGATTGTAAATTCCAGTTTGGTTCCCCAGGG
GGTAGTATTGATGATGGAAATTTTCAGAAATCTGGTGACTTTTATACTGAAAAAGGCTACAAT
ACACACTGGAACAACTGGTTTATTCTGAGTTTCTGCATTTTTCTGCCGTTTTTCATAGTTTTC
ACCACTGTGATCTTTAAAAGAAATGAAATAAGTAAATCATGTAACAGAGAGAATGCAGAGTAT
AATCGTAATTCATCCGTTGTATCAGAAAGCGATGACGTGGGACAT**TAA**TATTGCACAGAACTT
CCATAGCAAATAACCTAAAGGAACGAATGTGCTTTATTTATAACCTTACGTTATCCCCAATGC
ATTGTAAATGTCAAACTTTTGGAAAATAAAGCCTGCGTGCCCTCCC

FIGURE 116

MFLLLALLTELGRLQAHEGSEGIFLHVTVPRKIKSNDSEVSERKMIYIITIDGQPYTLHLGKQ
SFLPQNFLVYTYNETGSLHSVSPYFMMHCHYQGYAAEFPNSFVTLSICSGLRGFLQFENISYG
IEPVESSARFEHIIYQMKNNDPNVSILAVNYSHIWQKDQPYKVPLNSQIKNLSKLLPQYLEIY
IIVEKALMFTQFKLTVILSSLELWSNENQISTSGDADDILQRFLAWKRDYLILRPHDIAYLLV
YRKHPKYVGATFPGTVCNKSYDAGIAMYPDAIGLEGFSVIIAQLLGLNVGLTYDDITQCFCLR
ATCIMNHEAVSASGRKIFSNCSMHDYRYFVSKFETKCLQKLSNLQPLHQNQPVCGNGILESNE
ECDCGNKNECQFKKCCDYNTCKLKGSVKCGSGPCCTSKCELSIAGTPCRKSIDPECDFTEYCN
GTSSNCVPDTYALNGRLCKLGTAYCYNGQCQTTDNQCAKIFGKGAQGAPFACFKEVNSLHERS
ENCGFKNSQPLPCERKDVLCGKLACVQPHKNANKSDAQSTVYSYIQDHVCVSIATGSSMRSDG
TDNAYVADGTMCGPEMYCVNKTCRKVHLMGYNCNATTKCKGKGICNNFGNCQCFPGHRPPDCK
FQFGSPGGSIDDGNFQKSGDFYTEKGYNTHWNNWFILSFCIFLPFFIVFTTVIFKRNEISKSC
NRENAEYNRNSSVVSESDDVGH

Important features of the protein:

Signal peptide:

amino acids 1-16

Transmembrane domain:

amino acids 665-684

N-glycosylation sites.

amino acids 36-39, 76-79, 122-125, 149-152, 156-159, 177-180, 270-273, 335-338, 441-444, 537-540, 587-590, 601-604, 703-706

Casein kinase II phosphorylation sites.

amino acids 74-77, 208-211, 221-224, 304-307, 337-340, 346-349, 376-380, 415-418, 499-502, 639-642, 708-711

Tyrosine kinase phosphorylation site.

amino acids 243-249

N-myristoylation sites.

amino acids 53-58, 79-84, 266-271, 298-303, 372-377, 403-408, 408-413, 442-447, 462-467, 469-474, 488-493, 567-572, 610-615, 616-621, 634-639

Amidation site.

amino acids 328-331

FIGURE 117

CCCACGCGTCCGCGGACGCGTGGGGCTCAGTGGGCGTCGCGCGAAGGCTAAGGGAGTGTGGCG

GGCGGCTCCGGGAGCCAAC**ATG**CCTCGGTATGCGCAGCTGGTCATGGGCCCCGCGGGCAGCGG

GAAGAGCACCTACTGTGCCACCATGGTCCAGCACTGTGAAGCCCTCAACCGGTCTGTCCAAGT

TGTAAACCTGGATCCAGCAGCAGAACACTTCAACTACTCCGTGATGGCTGACATCCGGGAACT

GATCGAGGTGGATGATGTAATGGAGGATGATTCTCTGCGATTCGGTCCCAACGGAGGATTGGT

ATTTTGCATGGAGTACTTTGCCAATAATTTTGACTGGCTGGAGAACTGTCTTGGCCATGTAGA

GGACGACTATATCCTTTTTGATTGTCCAGGTCAGATTGAGTTGTACACTCACCTGCCTGTGAT

GAAACATCTGGTCCAGCAGCTCGAGCAGTGGGAGTTCCGAGTCTGTGGAGTTTTTCTTGTTGA

TTCTCAGTTCATGGTGGAGTCATTCAAGTTTATTTCTGGCATCTTGGCAGCCCTGAGTGCCAT

GATCTCTCTAGAAATTCCGCAAGTCAACATCATGACAAAAATGGATCTGCTGAGTAAAAAAGC

AAAAAAGGAAATTGAGAAATTTTTAGATCCAGACATGTATTCTTTATTAGAAGATTCTACAAG

TGACTTAAGAAGCAAAAAATTCAAGAAACTGACTAAAGCTATATGTGGACTGATTGATGACTA

CAGCATGGTTCGATTTTTACCTTACGATCAGTCAGATGAAGAAAGCATGAACATTGTATTGCA

GCATATTGATTTTGCCATTCAATATGGAGAAGACCTAGAATTTAAAGAACCAAAGGAACGTGA

AGATGAGTCTTCCTCTATGTTTGACGAATATTTTCAAGAATGCCAGGATGAA**TGA**AGAGTTTA

CTAAAAGTAACCATCTAAAGAGCTTGTGGCCAAACCAGCAGAACATTCTTCTCTTCAAAGGAT

GCAATAGTAGAAAGCTACTTATTTTAATGAAAAAAAGTAAAACTTCGTTCTTTATCAGCCTCA

TGCCTGAATCAAATTTTTAATTATTCTGAAACTGCTGCTGTTTAAAGTGGAATCTTTTAGTAT

TATAACAGCATCACTTTAGATTTTGTAAGTCAAAATTGAAATGAATGCACATAGATTTATATA

TAAATTAGCACCTGAGCTAAGGTTAAGGCCGGTCTAAACTTATTTTCACTTTTTGTATTATTT

TTGAGATGCAGGAATTACTGTAACAAAATATGTATGTCCGAAGGGAAAAAGCTGCAAGGATAT

ATATAAGACCACTGCTTATCTGTATCTTCCCATTTTCCTATATTGAAAATGTATATTATTTAT

ATAACTTAAAAAGTAAAAATAACTATGTTTTGAGAT

FIGURE 118

MPRYAQLVMGPAGSGKSTYCATMVQHCEALNRSVQVVNLDPAAEHFNYSVMADIRELIEVDDV
MEDDSLRFGPNGGLVFCMEYFANNFDWLENCLGHVEDDYILFDCPGQIELYTHLPVMKHLVQQ
LEQWEFRVCGVFLVDSQFMVESFKFISGILAALSAMISLEIPQVNIMTKMDLLSKKAKKEIEK
FLDPDMYSLLEDSTSDLRSKKFKKLTKAICGLIDDYSMVRFLPYDQSDEESMNIVLQHIDFAI
QYGEDLEFKEPKEREDESSSMFDEYFQECQDE

Important features of the protein:

Signal peptide:

amino acids 1-29

Transmembrane domain:

amino acids 151-170

N-glycosylation sites.

amino acids 31-35, 47-51

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 212-216

Tyrosine kinase phosphorylation site.

amino acids 189-197

N-myristoylation sites.

amino acids 13-19, 76-82, 154-160

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

amino acids 10-18

FIGURE 119

GGGCGCTGGGAGACACCGGACGCCCGCTCGGCTGCGCTGCGGCTCAGGCCCCCGCTCGGGCCC
GACCCGCTCGGTCACCGCCGGCTCGGGCGCGCACCTGCCGGCTGCGGCCCCAGGGCCATGCGG
AGGCCCACGAGGAGGCCGGCGGCCACGCGCATCCCGTAGCCCAGGTGGCCCAGGTCTGCACCG
CGGCGGCCTCGGCGCC**ATG**GAGCCCCCGTATTCGCTGACGGCGCACTACGATGAGTTCCAAGA
GGTCAAGTACGTGAGCCGCTGCGGCGCGGGGGGCGCGCGCGGGGCCTCCCTGCCCCCGGGCTT
CCCGTTGGGCGCTGCGCGCAGCGTCACCGGGGCCCGGTCCGGGCTGCCGCGCTGGAACCGGCG
CGAGGTGTGCCTGCTGTCGGGGCTGGTGTTCGCCGCCGGCCTCTGCGCCATTCTGGCGGCTAT
GCTGGCCCTCAAGTACCTGGGCCCGGTCGCGGCCGGCGGCGGCGCCTGTCCCGAGGGCTGCCC
TGAGCGCAAGGCCTTCGCGCGCCGCTCGCTTCCTGGCCGCCAACCTGGACGCCAGCATCGA
CCCATGCCAGGACTTCTACTCGTTCGCCTGCGGCGGTTGGCTGCGGCGCCACGCCATCCCCGA
CGACAAGCTCACCTATGGCACCATCGCGGCCATCGGCGAGCAAAACGAGGAGCGCCTACGGCG
CCTGCTGGCGCGGCCCGGGGGTGGGCCTGGCGGCGCGGCCCAGCGCAAGGTGCGCGCCTTCTT
CCGCTCGTGCCTCGACATGCGCGAGATCGAGCGACTGGGCCCGCGACCCATGCTAGAGGTCAT
CGAGGACTGCGGGGGCTGGGACCTGGGCGGCGCGGAGGAGCGTCCGGGGGTCGCGGCGCGATG
GGACCTCAACCGGCTGCTGTACAAGGCGCAGGGCGTGTACAGCGCCGCCGCGCTCTTCTCGCT
CACGGTCAGCCTGGACGACAGGAACTCCTCGCGCTACGTCATCCGCATTGACCAGGATGGGCT
CACCCTGCCAGAGAGGACCCTGTACCTCGCTCAGGATGAGGACAGTGAGAAGATCCTGGCAGC
ATACAGGGTGTTCATGGAGCGAGTGCTCAGCCTCCTGGGTGCAGACGCTGTGGAACAGAAGGC
CCAAGAGATCCTGCAAGTGGAGCAGCAGCTGGCCAACATCACTGTGTCAGAGTATGACGACCT
ACGGCGAGATGTCAGCTCCATGTACAACAAGGTGACGCTGGGGCAGCTGCAGAAGATCACCCC
CCACTTGCGGTGGAAGTGGCTGCTAGACCAGATCTTCCAGGAGGACTTCTCAGAGGAAGAGGA
GGTGGTGCTGCTGGCGACAGACTACATGCAGCAGGTGTCGCAGCTCATCCGCTCCACACCCCA
CCGGGTCCTGCACAACTACCTGGTGTGGCGCGTGGTGGTGGTCCTGAGTGAACACCTGTCCCC
GCCATTCCGTGAGGCACTGCACGAGCTGGCACAGGAGATGGAGGGCAGCGACAAGCCACAGGA
GCTGGCCCGGGTCTGCTTGGGCCAGGCCAATCGCCACTTTGGCATGGCGCTTGGCGCCCTCTT
TGTACATGAGCACTTCTCAGCCGCCAGCAAAGCCAAGGTGCAGCAGCTAGTGGAAGACATCAA
GTACATCCTGGGCCAGCGCCTGGAGGAGCTGGACTGGATGGACGCCGAGACCAGGGCTGCTGC
TCGGGCCAAGCTCCAGTACATGATGGTGATGGTCGGCTACCCGGACTTCCTGCTGAAACCCGA
TGCTGTGGACAAGGAGTATGAGTTTGAGGTCCATGAGAAGACCTACTTCAAGAACATCTTGAA
CAGCATCCCCTTCAGCATCCAGCTCTCAGTTAAGAAGATTCGGCAGGAGGTGGACAAGTCCAC
GTGGCTGCTCCCCCCACAGGCGCTCAATGCCTACTATCTACCCAACAAGAACCAGATGGTGTT
CCCCGCGGGCATCCTGCAGCCCACCCTGTACGACCCTGACTTCCCACAGTCTCTCAACTACGG
GGGCATCGGCACCATCATTGGACATGAGCTGACCCACGGCTACGACGACTGGGGGGGCCAGTA
TGACCGCTCAGGGAACCTGCTGCACTGGTGGACGGAGGCCTCCTACAGCCGCTTCCTGCGAAA
GGCTGAGTGCATCGTCCGTCTCTATGACAACTTCACTGTCTACAACCAGCGGGTGAACGGGAA
ACACACGCTTGGGGAGAACATCGCAGATATGGGCGTCCTCAAGCTGGCCTACCACGCCTATCA
GAAGTGGGTGCGGGAGCACGGCCCAGAGCACCCACTTCCCCGGCTCAAGTACACACATGACCA
GCTCTTCTTCATTGCCTTTGCCCAGAACTGGTGCATCAAGCGGCGGTCGCAGTCCATCTACCT
GCAGGTGCTGACTGACAAGCATGCCCCTGAGCACTACAGGGTGCTGGGCAGTGTGTCCCAGTT
TGAGGAGTTTGGCCGGGCTTTCCACTGTCCCAAGGACTCACCCATGAACCCTGCCCACAAGTG
TTCCGTGTGG**TGA**GCCTGGCTGCCCGCCTGCACGCCCCCACTGCCCCCGCACGAATCACCTCC
TGCTGGCTACCGGGGCAGGCATGCACCCGGTGCCAGCCCCGCTCTGGGCACCACCTGCCTTCC
AGCCCCTCCAGGACCCGGTCCCCCTGCTGCCCCTCACTTCAGGAGGGGCCTGGAGCAGGGTGA
GGCTGGACTTTGGGGGGCTGTGAGGGAAATATACTGGGGTCCCCAGATTCTGCTCTAAGGGGG
CCAGACCCTCTGCCAGGCTGGATTGTACGGGCCCCACCTTCGCTGTGTTCTTGCTGCAAAGTC
TGGTCAATAAATCACTGCACTGTTAAAAAAAAA

FIGURE 120

MEPPYSLTAHYDEFQEVKYVSRCGAGGARGASLPPGFPLGAARSVTGARSGLPRWNRREVCLL
SGLVFAAGLCAILAAMLALKYLGPVAAGGGACPEGCPERKAFARAARFLAANLDASIDPCQDF
YSFACGGWLRRHAIPDDKLTYGTIAAIGEQNEERLRRLLARPGGGPGGAAQRKVRAFFRSCLD
MREIERLGPRPMLEVIEDCGGWDLGGAEERPGVAARWDLNRLLYKAQGVYSAAALFSLTVSLD
DRNSSRYVIRIDQDGLTLPERTLYLAQDEDSEKILAAYRVFMERVLSLLGADAVEQKAQEILQ
VEQQLANITVSEYDDLRRDVSSMYNKVTLGQLQKITPHLRWKWLLDQIFQEDFSEEEEVVLLA
TDYMQQVSQLIRSTPHRVLHNYLVWRVVVVLSEHLSPPFREALHELAQEMEGSDKPQELARVC
LGQANRHFGMALGALFVHEHFSAASKAKVQQLVEDIKYILGQRLEELDWMDAETRAAARAKLQ
YMMVMVGYPDFLLKPDAVDKEYEFEVHEKTYFKNILNSIPFSIQLSVKKIRQEVDKSTWLLPP
QALNAYYLPNKNQMVFPAGILQPTLYDPDFPQSLNYGGIGTIIGHELTHGYDDWGGQYDRSGN
LLHWWTEASYSRFLRKAECIVRLYDNFTVYNQRVNGKHTLGENIADMGVLKLAYHAYQKWVRE
HGPEHPLPRLKYTHDQLFFIAFAQNWCIKRRSQSIYLQVLTDKHAPEHYRVLGSVSQFEEFGR
AFHCPKDSPMNPAHKCSVW

Important features of the protein:

Transmembrane domain:

amino acids 64-88

N-glycosylation sites.

amino acids 255-259, 322-326, 656-660

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 722-726

N-myristoylation site.

amino acids 24-30, 26-32, 27-33, 40-46, 47-53, 65-71, 148-154, 169-175, 170-176, 237-243, 450-456, 604-610, 607-613

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 85-96

Prenyl group binding site.

amino acids 772-777

Neutral zinc metallopeptidases, zinc-binding region signature.

amino acids 609-619

Neutral zinc metallopeptidases, zinc-binding region proteins.

amino acids 609-619

FIGURE 121

CGGACTGCCCCGGACCGCGCG**ATG**GAGTCGACCGGCAGCGTCGGGGAGGCCCCGGGCGGACCCC
GGGTGCTGGTGGTGGGCGGCGGCATCGCGGGGCTGGGCGCGGCGCAGAGGCTCTGCGGCCACT
CCGCCTTCCCGCACCTGCGGGTCCTGGAGGCCACGGCCCGCGCCGGGGGCCGCATCCGCTCGG
AGCGCTGCTTCGGTGGCGTGGTGGAGGTGGGCGCGCACTGGATCCATGGGCCCTCCCGGGGTA
ACCCCGTCTTCCAGCTGGCTGCTGAGTACGGGCTGCTGGGGGAGAAGGAGCTGTCCCAGGAGA
ACCAGCTGGTGGAGACCGGGGGTCACGTGGGCCTGCCCTCCGTGAGCTACGCCAGCTCCGGGG
CCAGCGTGAGCCTCCAGCTGGTGGCGGAGATGGCGACTCTGTTCTACGGCCTGATAGACCAGA
CCCGGGAGTTCCTGCACGCTGCAGAGACCCCGGTGCCCAGCGTCGGGGAGTACCTCAAGAAGG
AGATTGGCCAGCACGTGGCCGGCTGGACAGAGGATGAGGAGACCAGGAAGCTGAAGCTGGCCG
TCCTGAACTCCTTCTTCAACCTGGAATGCTGTGTGAGCGGCACCCACAGCATGGACCTGGTGG
CCCTGGCACCCTTTGGGGAGTATACCGTGCTGCCGGGGCTGGACTGCACCTTTTCTAAGGGCT
ATCAAGGACTCACAAACTGCATGATGGCCGCCCTGCCGGAGGACACTGTAGTTTTTGAGAAGC
CTGTGAAGACCATCCACTGGAACGGGTCCTTCCAGGAGGCAGCCTTTCCCGGGGAGACCTTTC
CAGTGTCGGTAGAGTGTGAGGATGGAGACCGGTTCCCGGCGCACCATGTCATCGTCACCGTGC
CCTTAGGTTTTCTTAGGGAACATTTGGACACCTTCTTTGACCCTCCCCTGCCGGCTGAGAAGG
CAGAAGCAATCAGGAAGATAGGCTTTGGGACCAACAACAAAATCTTCCTGGAGTTTGAGGAGC
CCTTCTGGGAGCCAGACTGCCAGCTGATCCAGCTGGTGTGGGAGGACACGTCGCCCCTGGAGG
ATGCTGCCCCTGAGCTACAGGACGCCTGGTTCCGGAAGCTCATTGGCTTTGTGGTCCTGCCTG
CCTTTGCGTCTGTCCACGTTCTCTGTGGGTTCATTGCCGGACTTGAGTCTGAGTTCATGGAGA
CTCTGTCGGATGAAGAAGTACTTCTGTGTCTCACCCAAGTGCTCCGGAGAGTGACAGGAAACC
CACGGCTCCCCGCGCCCAAGAGCGTCCTGCGGTCTCGCTGGCACAGCGCCCCGTACACTAGGG
GGTCCTACAGCTACGTGGCCGTGGGCAGTACTGGGGGCGACCTGGACCTGCTGGCTCAGCCCC
TCCCTGCAGACGGCGCCGGCGCCCAGCTCCAGATCCTGTTTGCGGGGGAAGCCACACATCGCA
CGTTTTACTCCACGACGCACGGGGCTCTGCTGTCGGGATGGAGGGAGGCCGACCGCCTCCTCA
GTCTGTGGGCCCCGCAGGTGCAGCAGCCCAGGCCGAGGCTC**TAG**CTGGGCCCAGCCTACTCTG
TTCCACCCGTGTCGGGGGTAGGCTGGGACCGTCATTTCTTCTGACAGATTTCAGTCTGGCTTG
AAATTTGGGGATGTTAATGAGGGTCCTCTGGTTTTTGGTAACCAGGGCCACCTTCTCAGTTCT
TGTGTCTGTTATTGGAGTCTGGCCAGGGTTGACTTGAGCTGAGACACCAGATGCTCACGGAGA
TGCTGGACACATAAAGCAAGTTACAGCCACAAAAAAAAAAAA

FIGURE 122

MESTGSVGEAPGGPRVLVVGGGIAGLGAAQRLCGHSAFPHLRVLEATARAGGRIRSERCFGGV
VEVGAHWIHGPSRGNPVFQLAAEYGLLGEKELSQENQLVETGGHVGLPSVSYASSGASVSLQL
VAEMATLFYGLIDQTREFLHAAETPVPSVGEYLKKEIGQHVAGWTEDEETRKLKLAVLNSFFN
LECCVSGTHSMDLVALAPFGEYTVLPGLDCTFSKGYQGLTNCMMAALPEDTVVFEKPVKTIHW
NGSFQEAAFPGETFPVSVECEDGDRFPAHHVIVTVPLGFLREHLDTFFDPPLPAEKAEAIRKI
GFGTNNKIFLEFEEPFWEPDCQLIQLVWEDTSPLEDAAPELQDAWFRKLIGFVVLPAFASVHV
LCGFIAGLESEFMETLSDEEVLLCLTQVLRRVTGNPRLPAPKSVLRSRWHSAPYTRGSYSYVA
VGSTGGDLDLLAQPLPADGAGAQLQILFAGEATHRTFYSTTHGALLSGWREADRLLSLWAPQV
QQPRPRL

Signal peptide:

amino acids 1-28

Transmembrane domain:

amino acids 364-385

N-glycosylation site.

amino acids 253-257

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 408-412

N-myristoylation sites.

amino acids 20-26, 21-27, 25-31, 105-111, 119-125, 164-170, 216-222, 227-233, 443-449, 484-490

Aminooxidase Flavin containing amine oxidase:

amino acids 23-497

FIGURE 123

CGGACGCGTGGGGGAAGATGGATAAATAATTCTGTCACACGTGCCCTGGCCTCTGGAGCTCAGCTGCCAGTCCAC
GTCTAGGGAATCTTAGCATCTGGGACCAAGACACTTTACAGCAATCATCACCCTTTGCAGAGGAGGTGAGCTCAC
CAGGACTCATCTGCCATTTCAGACCTTTTGCTGCTACCTGCCAGGTGGCCCCCACTGCTGACGAGAG**ATG**GTGGA
TCTCTCAGTCTCCCCGGACTCCTTGAAGCCAGTATCGCTGACCAGCAGTCTTGTCTTCCTCATGCACCTCCTCCT
CCTTCAGCCTGGGGAGCCGAGCTCAGAGGTCAAGGTGCTAGGCCCTGAGTATCCCATCCTGGCCCTCGTCGGGGA
GGAGGTGGAGTTCCCGTGCCACCTATGGCCACAGCTGGATGCCCAGCAAATGGAGATCCGCTGGTTCCGGAGTCA
GACCTTCAATGTGGTACACCTGTACCAGGAGCAGCAGGAGCTCCCTGGCAGGCAGATGCCGGCGTTCCGGAACAG
GACCAAGTTGGTCAAGGACGACATCGCCTATGGCAGCGTGGTCCTGCAGCTTCACAGCATCATCCCCTCTGACAA
GGGCACATATGGCTGCCGCTTCCACTCCGACAACTTCTCTGGCGAAGCTCTCTGGGAACTGGAGGTAGCAGGGCT
GGGCTCAGACCCTCACCTCTCCCTTGAGGGCTTCAAGGAAGGAGGCATTCAGCTGAGGCTCAGATCCAGTGGCTG
GTACCCCAAGCCTAAGGTTCAGTGGAGAGACCACCAGGGACAGTGCCTGCCTCCAGAGTTTGAAGCCATCGTCTG
GGATGCCCAGGACCTGTTCAGTCTGGAAACATCTGTGGTTGTCCGAGCGGGAGCCCTCAGCAATGTGTCCGTCTC
CATCCAGAATCTCCTCTTGAGCCAGAAGAAAGAGTTGGTGGTCCAGATAGCAGACGTGTTCGTACCCGGAGCCTC
TGCGTGGAAGAGCGCGTTCGTCGCGACCCTGCCGCTGCTGTTGGTCCTCGCGGCGCTGGCGCTGGGCGTCCTCCG
GAAGCAGCGGAGAAGCCGAGAAAAGCTGAGGAAGCAGGCGGAGAAGAGACAAGAGAAACTCACTGCAGAGCTGGA
AAAGCTTCAGACAGAGCTTGACTGGAGACGGGCTGAAGGCCAGGCTGAGTGGAGAGCAGCCCAAAAATATGCAGT
GGATGTGACGCTGGACCCGGCCTCGGCGCACCCCAGCCTGGAGGTGTCGGAGGATGGCAAGAGCGTGTCTTCCCG
CGGGGCGCCGCCAGGCCCGGCGCCTGGCCACCCGCAGCGGTTCTCGGAGCAGACGTGCGCGCTGAGCCTGGAGCG
GTTCTCCGCCGGCCGCCACTACTGGGAGGTGCACGTGGGCCGCCGCAGCCGCTGGTTCCTGGGCGCCTGCCTGGC
CGCGGTGCCGCGCGCGGGGCCTGCGCGCCTGAGCCCTGCGGCCGGCTACTGGGTGCTGGGGCTGTGGAACGGCTG
CGAGTACTTCGTCCTGGCCCCGCACCGCGTCGCGCTCACCCTGCGCGTGCCCCCGCGGCGCCTGGGCGTCTTCCT
GGACTACGAGGCCGGAGAGCTGTCCTTCTTCAACGTGTCCGACGGCTCCCACATCTTCACCTTCCACGACACCTT
CTCGGGCGCGCTCTGTGCGTACTTCAGGCCCAGGGCCCACGACGGCGGCGAACATCCGGATCCCCTGACCATCTG
CCCGCTGCCGGTTAGAGGGACGGGCGTCCCCGAAGAGAACGACAGTGACACCTGGCTACAGCCCTATGAGCCCGC
GGACCCCGCCCTGGACTGGTGG**TGA**GGCGCCCTCGTGGCCGCGGGACTGGCCCCGGGGGGCCCCCTGGATCCCAG
GCCAGCGCTTTGCTCTCCTGCTCCGTCTGAAGGGAGCAGGTGCACCAGCCAAAATGTCAGCGAGGGGGACAAAGA
GAGGGACCTTTGCCTACGTAGATGTGTATGTGTAGTGCGATTTTCTTCAAGGAAAGGAGACAAGTCCAAAGCTCG
TTTGTGGATTGTGGGACTGAGCGAAGGAGTACAAATATATCCACGTCGCTCAGAGCTGGGGTGCTCACGGTGGGC
GGTGGGCAAGAAGCCAGCATGGAAGAAAGAAGGGAGAAAACTTTGGTGACTGCCTTAGAGGGATCAGTTAATTTG
TATAGTTTTATATTTTTTGTATATGTTTGCTAGCTCTAAAAAGGTCGAGATGCAATAACACTTCGTAAGCAACGA
GTTCACCTAAGTAAGGCTCAGATCCTAGTTTTAAAAACCATTTCCCATTAAAATGAAGTTGGAGGAACAGCTGCT
TCTGAGCCGGGGCAAAAATTTCAAGGTGAGCCTGGAGCATTGTGTGTGGTGAAGTAAAATAAAGGCTCAAAACGT
GACGGCAACCCGGCAAAAGGGTAGGGAGCCAGGCCGAAGGGGCCTCACTGACCAATTGTGGGACAATTTGAACAT
CAGGATGAATAATGACAGGAGAGATTATAACACACTGAATAAAAACATAATCCATGAGTTCATGCTGATACTCAA
ATTTCTTTTTAAAAAGGAGAAACAGGAAGGTTTCTTTTGGAGGTGAAATCTAATTATTGGTGAGAGTCTTGGAGA
ACAGGCTGTTTCCAGTCTCAAAGCAGTAACCTTATACACTACTTATAAGTTTGAAAGGGGAAAGGTTACCTTTAC
AATGGAGACATCTACCAGATCATCCAAGTGATTAAATTTAACATCATCAATGATGGGACCAAGGACATTATTAGT
TTGACAACTGGGGAAAGAAGTGTTCTTCACCCCCTACCCCCAAGACATTCTCTCTGTCGGCCAGGCTGGAGTGCA
GCCTCAACCTCCTGGGCCCAAGTGATCCTCCCACCTCAGCACACAACACCATGCCCAATTTTAAGTGCGTTATAG
AGACGGGGGTCTCACTTTGTTACCCAGGCTGGTCTCAAACTCCTGCGCTCAAGCAATCCTCCCACCTGGGCCTCC
CAAAATGCTGGGTGTACAGGCATGAGCCGCTGTGCCTGGCTTCATTTTCAGAGTGAGACATTTGTACTGTGGCTA
TGTAGGAGAACATTCTTGTTCTTAGCAAACATACTGAAGTTTTTAGATATTAATTACCACAGTGTCTGCCACTGA
ATTTCCAGTGACTAAGTGGAAAAATATAAAACATATGAATATAAAGAAAGAAAGAGACAAGTCAAATGTAGTAAA
ATGACAACACTTGGTGACTCTAGGTGACTGGTCGACAGATGTTCATTGTACTATCAATGTGGCTTTGCTGTGGGT
TTGAAATTTTGCAAACTAAGAGTTGGGTGGCGGGGAGAAGGATACACCAAAAAACTAAGTGATTATCTTTGGATG
GGAAAATGTTTGGTAATTGCATTCTTAAAATGTCTTCTTTGTATTTTTTAATGTTCAATAATGTATATGTATCAG
TTCTGTAATAAAGGGGAAAACACTTTTCA

FIGURE 124

MVDLSVSPDSLKPVSLTSSLVFLMHLLLLQPGEPSSEVKVLGPEYPILALVGEEVEFPCHLWP
QLDAQQMEIRWFRSQTFNVVHLYQEQQELPGRQMPAFRNRTKLVKDDIAYGSVVLQLHSIIPS
DKGTYGCRFHSDNFSGEALWELEVAGLGSDPHLSLEGFKEGGIQLRLRSSGWYPKPKVQWRDH
QGQCLPPEFEAIVWDAQDLFSLETSVVVRAGALSNVSVSIQNLLLSQKKELVVQIADVFVPGA
SAWKSAFVATLPLLLVLAALALGVLRKQRRSREKLRKQAEKRQEKLTAELEKLQTELDWRRAE
GQAEWRAAQKYAVDVTLDPASAHPSLEVSEDGKSVSSRGAPPGPAPGHPQRFSEQTCALSLER
FSAGRHYWEVHVGRRSRWFLGACLAAVPRAGPARLSPAAGYWVLGLWNGCEYFVLAPHRVALT
LRVPPRRLGVFLDYEAGELSFFNVSDGSHIFTFHDTFSGALCAYFRPRAHDGGEHPDPLTICP
LPVRGTGVPEENDSDTWLQPYEPADPALDWW

Important features of the protein:

Signal peptide:

amino acids 1-34

Transmembrane domain:

amino acids 247-272

N-glycosylation sites.

amino acids 102-106, 139-143, 224-228, 464-468, 516-520

Tyrosine kinase phosphorylation site.

amino acids 105-114

N-myristoylation sites.

amino acids 129-135, 220-226, 399-405, 423-429, 480-486

Amidation site.

amino acids 390-394

FIGURE 125

TATAGTCCCAGCTACTCATGGGGCTGATGCAGGTTGAGGCAGGAGGTTCATGAGCCCAGGAGGTTGGAGCTGTAA
TGAGCTAGGATTCTGCCTCTGCACTCCTAGCTGGATGACAGAGCAAGACCCTGTCTCAAAAAAGAAAAAAAAAAA
AAAAAGAATGCATGAACCAGACATGACAGTTCCTGGCCTCAAAGATCTTCCAAAGGAAATGATTTTTTTTTAACC
ACCAATGCTGCAGGAAAAAGCAACATATTTAAGTTATCCAATAACACCTATCCAATAATTGTAAATCATTATCAT
GAC**ATG**GTAGAGTTGTTTATATTTCTTTTCCTTTTAGGTGAAACACCATTCAAAGTCGTAGTCAAATCTCTTTCA
CCTAAAGAGTTGGTCCGGATACATGTCCCTAAACCTTTGGACAGGAATGATGGAACATTTTTGATGAGATATAGG
ATGTATGAAACTGTCGATGAAGGCCTGAAGATAGAGGTCCTTTATGGTGATGAACATGTGGCTCAGTCTCCCTAT
ATTTTGAAAGGACCAGTGTACCATGAGTACTGTGAGTGTCCGGAAGATCCTCAGGCCTGGCAGAAGACTCTTTCT
TGTCCAACCAAGGAACCACAGATTGCAAAAGATTTTGCTTCCTTTCCCAGCATCAATCTCCAGCAAATGCTAAAA
GAAGTCCCCAAAAGGTTTGGGGATGAGAGAGGTGCCATTGTTCATTACACGATTCTCAATAACCATGTTTACCGG
AGATCTTTAGGGAAATACACAGACTTCAAGATGTTCTCTGATGAGATTTTGTTATCATTGACAAGAAAGGTCCTT
CTCCCAGATTTAGAATTTTATGTTAATCTTGGAGATTGGCCCTTGGAGCATCGAAAAGTCAATGGAACCCCTAGC
CCCATACCTATCATTTCATGGTGTGGCTCTCTGGATTCAAGAGATGTTGTCCTTCCAACGTATGACATCACCCAC
TCCATGCTTGAAGCCATGCGGGGTGTTACAAATGATCTCCTCTCTATTCAGGGAAATACAGGGCCTTCCTGGATC
AATAAAACAGAGAGAGCTTTCTTCAGAGGTAGAGACAGCCGAGAGGAGAGGCTCCAGTTGGTACAGCTGTCCAAA
GAAAATCCTCAGCTACTAGATGCAGGAATTACAGGATATTTCTTTTTCCAAGAGAAAGAAAAGGAGCTTGGAAAA
GCCAAGTTGATGGGTTTCTTTGATTTCTTTAAGTACAAGTATCAAGTAAATGTGGATGGGACCGTGGCTGCTTAC
AGATATCCATATCTCATGCTGGGCGACAGTCTGGTTTTAAAGCAGGACTCGCCATATTATGAACATTTCTACATG
GCACTAGAACCTTGGAAGCATTATGTTCCAATTAAAAGAAATCTGAGTGATTTATTAGAGAAAGTTAAATGGGCT
AAGGAAAATGATGAAGAAGCCAAGAAGATTGCAAAAGAAGGACAGTTGATGGCTAGGGACCTACTACAGCCACAC
AGGCTTTACTGCTACTATTACCAAGTACTGCAGAAATATGCCGAGCGCCAGTCCAGCAAACCCGAAGTACGTGAT
GGAATGGAACTTGTTCCTCAGCCAGAAGATAGCACAGCCATCTGCCAGTGCCACAGGAAAAAGCCTTCAAGAGAA
GAACTT**TGA**GTCAGCCCAGAATCACACTCCTGTGTATCCCGGCTACACTTTAAGGAAAGATTGAATCTAAGCTGT
GAAGGACAGTATAGAAGACTGCACCAAGTGGACTAGTTCTCCCGGTGGCTTTATATATGTAGATGGATATAGCAG
TACTGGTTGAGTATCCCTCATCTGAAATGCTTAGGACCAGGAGTGTTTCAGGCTTCAGATTTTTTAAGATTTGGG
AATATTTGCATGTACATAATGAGGTATCTTGGGGATGAGATCCAAGTCTAAACACAAAATTCATTTATATTTTAT
ATATACCTTGTTCACATACCCTGAAGGTAATTTTATATAATATTTTTAATAATTTGTGCATGAAACAAAGTTTGT
ATACATTGAACTGTCAGAAAGCAAAGGTGTCACTATCTTAGCGACCCAAGTGGTGGTGTCAGCACTCAAAAAGTT
TTGGATTTTGGGGTATTTCAGATTTTAGATTTTTGTATGAGGAATGTTCAACCTGTATTTGAACAAGCATTACCA
AATATCATTGAATATTAATATCTTTTGCGTAAAAACTGCTATTATCAGCATCATAGTTTCTCTAAAAAGAAAACT
TGGGGATCATAGCCGATAGAGAGACTTGCTAAAATATAAATCAGCCTCTGCAAAACTGTTTACATATTTATTGGT
TTACATATTTTATTGGTTTATTTCTATCCCCTGTTCACTTTTTCTCTTCCACTTCCAATTATGAAGAGAAAATAT
TTGTTCAGGGTTGTCCCCCCGCCCCCCGTCACTGCATAATTTCTCCTCTTACAAGCTGCTTTTGGCTTTCATTAA
TAACAGCTTCCTTTTAGAAGGTCTGATAAGGATATTTAAGGAAGAAGAGAATGACTCTGTTATTAAAGGTGGCAT
GGAGACTGTGGAGGGAATATTTTTTAAAGCACTACTCATATCCTTTAAACTAAATTTTGCCAAAGCCCGAGACAA
CATTAAGGAGAAATTGTACCTTAAGTTAGTAATTCCAAATCTATCTGAGTTGTATACCCATCAAAGACAATACAG
TTATTAACATAGATGAAGGTATGCTATAGGCATCATTCATTATCTCTATATTGAATAGGTGAAAGATAACTGTAG
TCAGGTGAAAGGCATTCATCATTTTTAAGCTGAAAAGGGGATCCTTGAAAACACTGAAAACCTCTACAACAATCT
TCAGGAAGCCTGCTATCTTGGGATTCACTAATAATAGGCCAAGAACAAAGGCAAGCATCCATTCCTCACTCCACC
ACTTTTCTATTTCAGTGGGTGTCATTGCTACGATGAAGACTTTGGAAATTTCCTTTCTCTTTTAGGACAGGGTCA
GGATTTAGGACTCATAGCCTGAAAGCTCATTACATACTCCTTGTAACCATCAGTCCAAGGTTCAGTTCACTAAAG
TGCATGTTCTAAAACAAGAGCTATCCTCATTCCAAATTTTAAAATATGTACTCTGGCCGGTTGCAGTGGCTCACG
CCTGTAATCCCAGCACTTTGGCAGGCCGAGATGGGCGGATCTTTTGAGGTCAGGAGTTTGAGACCAGCCTGGCCA
ACATGGTGAAACCCCGTCTCTACTAAAAATACAAAAATTAGCCAGGCATGGTGGCATTTGCCTGTAATCCCAGCT
ACTCGGGAGGCTGAGGCAGGAGAATCACTTGAACCTGGGAGGCAGAGGTTGCAGTGAGCTGAGATTACACCACTG
CACTCCAGCCTGGGTGACAGAGTGAGACTCCATCTCAAAAACTGAAAATAAAAATAAAAATATGTATTCTCCTAA
CTGAAATATTTACTTAATCTGGAAAACAATGTAACTATTTTTAAAGTGGTTACATCTATTCTTGCTGAAGAACAA
TAAACAGAATTTTTTGACTAAGCATAACCAAATTTCAGAACAGTCTAATCAATGCCAAGTATCCAAGGCAAACTC
TAATACCCATCCATTGTGCAAAACCACAAGCACGCAAGTATTAAATAAGAGCAAGCTGTCCTGAGCCCATACCTA
ATGAATTTGTGTCTTAAATATTGTACATTGTGTTTGAGGCTTGTCAAAACTGGGATTATGGCAAGAAAGGTTGCC
TAACTCATACCTTTCTGCCTCAAATTCCAGGTGCTAAAGGCTAATGGCATTTTAAACATCTTACATTTTTAAAAA
TTTATATTGCCTCTGCCAAACAGGCCTAATAGTTAAAAGCAAGTTGAGACAAACCAGGCAGATTCAGTGTGTGGA
ACAGGAAGGATGTGCTTTAAAAAAAGGTGGAATCCCTCAAAAAATTCTATAGGGAGACAGCAGCCTTAATCTACA
TAATTCTTCATCTCGCCAATTCAGCCGCAGCCTTTAAAGAGTTAGTGTTAATGGCTTTCTGGTTTGAAAACAAAA
ATGCATCTATGTGGTTGAAAGTTTGGGAGGAGATTCACCAATATCTGAGGAGAAGATGGAGTGAAGGGAATTCTT
ACTTTTTGCTTTATACCTTTCTATAATATTTAGATTTTTTTTTTACTGTAAGTATGGATCAAATTGCAAAATAAAG
AAAAATGCCAACCTTAGAAAAGACAATAAATGCACAAAAGATATAAACAGGAACAGCAAATATTTATATTTTTTC
CATTTTGCTCTTTTTAAATCTATGTTTAGAACTTTATATCTTGGGACTTATGTATATATATACCTTTTAAATAAA
ATAAATTTTCTAAATAAAAAGTTG

FIGURE 126

MVELFIFLFLLGETPFKVVVKSLSPKELVRIHVPKPLDRNDGTFLMRYRMYETVDEGLKIEVL
YGDEHVAQSPYILKGPVYHEYCECPEDPQAWQKTLSCPTKEPQIAKDFASFPSINLQQMLKEV
PKRFGDERGAIVHYTILNNHVYRRSLGKYTDFKMFSDEILLSLTRKVLLPDLEFYVNLGDWPL
EHRKVNGTPSPIPIISWCGSLDSRDVVLPTYDITHSMLEAMRGVTNDLLSIQGNTGPSWINKT
ERAFFRGRDSREERLQLVQLSKENPQLLDAGITGYFFFQEKEKELGKAKLMGFFDFFKYKYQV
NVDGTVAAYRYPYLMLGDSLVLKQDSPYYEHFYMALEPWKHYVPIKRNLSDLLEKVKWAKEND
EEAKKIAKEGQLMARDLLQPHRLYCYYYQVLQKYAERQSSKPEVRDGMELVPQPEDSTAICQC
HRKKPSREEL

Important features of the protein:

Signal peptide:

amino acids 1-16

N-glycosylation sites.

amino acids 250-254, 363-367

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 444-448

N-myristoylation site.

amino acids 208-214, 319-325, 388-394

Endoplasmic reticulum targeting sequence.

amino acids 448-453

Mitochondrial energy transfer proteins signature.

amino acids 25-34

FIGURE 127

AGCCGTCGGAGGGAGCCGGAGCGCTTCTCCCGAGTTGGTGATAGATTGGTGGTCATCCAACAT
GCAGAAATGAATGAGCAGTGAAAAGCAGCAGAGCCGATGGGTCATGAGGATGTAAGTGCGTTT
GAAGGCTTCCACACCCTCTACTCCAGGAATCATGAATAAACTGGAGGATAAGCAGGACCAGAT
GATACC**ATG**AAGAGAAGTTTACAGGCCCTCTATTGCCAACTGTTAAGTTTCCTGCTGATCTTG
GCACTGACCGAAGCGCTGGCATTTGCCATCCAGGAACCATCTCCCAGGGAATCTCTTCAGGTC
CTCCCTTCAGGCACTCCCCCGGGAACCATGGTGACAGCACCCCACAGCTCTACCAGACATACT
TCTGTGGTGATGCTGACCCCCAATCCCGATGGACCCCCCTCACAGGCTGCAGCTCCCATGGCA
ACACTGACACCCCGTGCAGAGGGGCACCCTCCTACGCACACCATCTCCACCATCGCTGCGACA
GTAACCGCCCCCTATTCTGAAAGCTCCCTGTCCACAGGGCCCGCTCCAGCAGCCATGGCAACC
ACATCCTCCAAGCCAGAGGGCCGCCCTCGAGGGCAGGCTGCCCCCACCATCCTGCTGACAAAG
CCACCGGGGGCCACCAGCCGCCCCACCACAGCGCCCCCCCGCACTACCACACGCAGGCCCCCC
AGGCCCCCAGGCTCTTCCCGAAAAGGGGCTGGTAATTCATCACGCCCTGTCCCGCCTGCACCT
GGTGGCCACTCCAGGAGTAAAGAAGGACAGCGAGGACGAAATCCAAGCTCCACACCTCTGGGG
CAGAAGCGGCCCCTGGGGAAAATCTTTCAGATCTACAAGGGCAACTTCACAGGGTCTGTGGAA
CCAGAGCCCTCTACCCTCACCCCCAGGACCCCACTCTGGGGCTACTCCTCTTCACCACAGCCC
CAGACAGTGGCTGCGACCACAGTGCCCAGCAATACCTCATGGGCACCCACCACCACCTCCCTG
GGGCCTGCAAAGGACAAGCCAGGCCTTCGCAGAGCAGCCCAGGGGGGTGGTTCTACCTTCACC
AGCCAAGGAGGGACACCAGATGCCACAGCAGCCTCAGGTGCCCCTGTCAGTCCACAAGCTGCC
CCAGTGCCTTCTCAGCGCCCCCACCACGGTGACCCACAGGATGGCCCCAGCCATAGTGACTCT
TGGCTTACTGTTACCCCTGGCACCAGCAGACCTCTGTCTACCAGCTCTGGGGTCTTCACGGCT
GCCACGGGGCCCACCCCAGCTGCCTTCGATACCAGTGTCTCAGCCCCTTCCCAGGGGATTCCT
CAGGGAGCATCCACAACCCCACAAGCTCCAACCCATCCCTCCAGGGTCTCAGAAAGCACTATT
TCTGGAGCCAAGGAGGAGACTGTGGCCACCCTCACCATGACCGACCGGGTGCCCAGTCCTCTC
TCCACAGTGGTATCCACAGCCACAGGCAATTTCCTCAACCGCCTGGTCCCCGCCGGGACCTGG
AAGCCTGGGACAGCAGGGAACATCTCCCATGTGGCCGAGGGGGACAAACCGCAGCACAGAGCC
ACCATCTGCCTGAGCAAGATGGATATCGCCTGGGTGATCCTGGCCATCAGCGTGCCCATCTCC
TCCTGCTCTGTCCTGCTGACGGTGTGCTGCATGAAGAGGAAGAAGAAGACCGCCAACCCGGAG
AACAACCTGAGCTACTGGAACAACACCATCACCATGGACTACTTCAACAGGCATGCTGTGGAG
CTGCCCAGGGAGATCCAGTCCCTTGAAACCTCTGAGGACCAGCTCTCAGAGCCCCGCTCCCCA
GCCAATGGCGACTATAGAGACACTGGGATGGTCCTTGTTAACCCCTTCTGTCAAGAAACACTG
TTTGTGGGAAACGATCAAGTATCTGAGATC**TAA**CTACAGCAGGCATCACTTTGCCATTCCGTA
TTTTTCGTCTCTAAATTATAAATATACAAATATATATATTATAAATATAACCTTGTGTAACCC
TGACTTAATGAGAAACATTTTCAGCTTTTTTTCCTATGAATTGTCAACATCTTTTTTACAAGT
GTGGTTTAAAAAAAAAAAAACTTTACAGAATGATCTGTGGCTTTATAAAATAAAGGTATTTCT
AAGCAAAAAAAAAAAAAAAA

FIGURE 128

MKRSLQALYCQLLSFLLILALTEALAFAIQEPSPRESLQVLPSGTPPGTMVTAPHSSTRHTSV
VMLTPNPDGPPSQAAAPMATLTPRAEGHPPTHTISTIAATVTAPYSESSLSTGPAPAAMATTS
SKPEGRPRGQAAPTILLTKPPGATSRPTTAPPRTTTRRPPRPPGSSRKGAGNSSRPVPPAPGG
HSRSKEGQRGRNPSSTPLGQKRPLGKIFQIYKGNFTGSVEPEPSTLTPRTPLWGYSSSPQPQT
VAATTVPSNTSWAPTTTSLGPAKDKPGLRRAAQGGGSTFTSQGGTPDATAASGAPVSPQAAPV
PSQRPHHGDPQDGPSHSDSWLTVTPGTSRPLSTSSGVFTAATGPTPAAFDTSVSAPSQGIPQG
ASTTPQAPTHPSRVSESTISGAKEETVATLTMTDRVPSPLSTVVSTATGNFLNRLVPAGTWKP
GTAGNISHVAEGDKPQHRATICLSKMDIAWVILAISVPISSCSVLLTVCCMKRKKKTANPENN
LSYWNNTITMDYFNRHAVELPREIQSLETSEDQLSEPRSPANGDYRDTGMVLVNPFCQETLFV
GNDQVSEI

Important features of the protein:

Signal peptide:

amino acids 1-28

Transmembrane domain:

amino acids 469-487

N-glycosylation sites.

amino acids 178-182, 223-227, 261-265, 446-450, 504-508, 509-513

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 495-499

N-myristoylation sites.

amino acids 44-50, 48-54, 175-181, 222-228, 279-285, 286-292, 288-294, 296-302, 351-357, 374-380, 427-433, 442-448

TonB-dependent receptor proteins signature 1.

amino acids 1-44

FIGURE 129

AGGCGAGGCGCGGCGCCGCTGCACACACGCACACGGAGCT**ATG**GGGTGCCATGTTGCCACCAG
CTGCCACGTGGCCTGGCTTTTGGTGCTGATCTCTGGATGCTGGGGCCAGGTGAACCGGCTGCC
CTTCTTCACCAACCACTTCTTTGATACATACCTGCTGATCAGCGAGGACACGCCTGTGGGTTC
TTCTGTGACCCAGTTGCTGGCCCAAGACATGGACAATGACCCCCTGGTGTTTGGCGTGTCTGG
GGAGGAGGCCTCTCGCTTCTTTGCAGTGGAGCCTGACACTGGCGTGGTGTGGCTCCGGCAGCC
ACTGGACAGAGAGACCAAGTCAGAGTTCACCGTGGAGTTCTCTGTCAGCGACCACCAGGGGGT
GATCACACGGAAGGTGAACATCCAGGTCGGGGATGTGAATGACAACGCGCCCACATTTCACAA
TCAGCCCTACAGCGTCCGCATCCCTGAGAATACACCAGTGGGGACGCCCATCTTCATCGTGAA
TGCCACAGACCCCGACTTGGGGGCAGGGGGCAGCGTCCTCTACTCCTTCCAGCCCCCCTCCCA
ATTCTTCGCCATTGACAGCGCCCGCGGTATCGTCACAGTGATCCGGGAGCTGGACTACGAGAC
CACACAGGCCTACCAGCTCACGGTCAACGCCACAGATCAAGACAAGACCAGGCCTCTGTCCAC
CCTGGCCAACTTGGCCATCATCATCACAGATGTCCAGGACATGGACCCCATCTTCATCAACCT
GCCTTACAGCACCAACATCTACGAGCATTCTCCTCCGGGCACGACGGTGCGCATCATCACCGC
CATAGACCAGGATAAAGGACGTCCCCGGGGCATTGGCTACACCATCGTTTCAGGGAATACCAA
CAGCATCTTTGCCCTGGACTACATCAGCGGAGTGCTGACCTTGAATGGCCTGCTGGACCGGGA
GAACCCCCTGTACAGCCATGGCTTCATCCTGACTGTGAAGGGCACGGAGCTGAACGATGACCG
CACCCCATCTGACGCTACAGTCACCACGACCTTCAATATCCTGGTTATTGACATCAATGACAA
TGCCCCGGAGTTCAACAGCTCCGAGTACAGCGTGGCCATCACTGAGCTGGCACAGGTCGGCTT
TGCCCTTCCACTCTTCATCCAGGTGGTGGACAAGGATGAGAATTTGGGCCTGAACAGCATGTT
TGAGGTGTACTTGGTGGGGAACAACTCCCACCACTTCATCATCTCCCCGACCTCCGTCCAGGG
GAAGGCGGACATTCGTATTCGGGTGGCCATCCCACTGGACTACGAGACCGTGGACCGCTACGA
CTTTGATCTCTTTGCCAATGAGAGTGTGCCTGACCATGTGGGCTATGCCAAGGTGAAGATCAC
TCTCATCAATGAAAATGACAACCGGCCCATCTTCAGCCAGCCACTGTACAACATCAGCCTGTA
CGAGAACGTCACCGTGGGGACCTCTGTGCTGACAGTCCTGGTGAGTCCCCGCTTCACTGCAGG
GCCACTGAGCTCTCCAGGGCCGACTGTGGTGAGGCACCCAGAGGGATTTTGTCCAAGGGACCT
CAGCAATCAGGGAAGGAGGCACCCCCAAATCCCTGAGCTGTGTTTGTTGGTGTAT**TAA**ATAAA
GTTTTTGGACTCTTCAGGAAGGGGCTCCCTTGACCTAGGTTGCAATATGGAAAAGGAGCCAAC
CTGAGGGGTGACGAGACTGAGCTGAGGACACTGGTTTTCTGCCTTTCCCTGAGAGAGACTCAG
TGAGGGTGGGCTGGGAGCCCTGGAAGCCCCCTCAAATGGGTGGGAAGGTGCCAGCCATCCTTG
AGAAGGGCAACCCTCTCCATGTGAGCACAGGCACCAGAGAGGGGCAGGCGCCTGGAGGGTACC
GGGGCACCCCCAGCTGCCCATGGCTGGACTTGCCCTTTGACAAGGGGCCCTCCCAGTGTCATT
TGTATCTGTCAGTACTCTTGGTTGCAAGGGACAGAAACCCTTAAGTAGTTCAAGCAAAAAAGG
ATTGGCTCATGTAACTCAAAAGTATAAGTGATTTCAGGCCGGGCTCGGTGGCTCACGCCTGTC
ATCCAACACCTTGAGAAAGCCGAGGTGGGCGGATCACTTGAGGTCGGGAGTTTGAGACCAGCC
TGGCCAACATGGCAAAACCCCGTCTCTACTAAAAATACAAAAATTAGCCGGGTGTGGTGGCAC
ACGCCTGTAGTCCCAGCTACTAGGGAGGCTGAGGCAGGAGAATCGCTTGAACCCAGGAGGCGG
AGGTTGCAGTGAGCCGAGATTGTGTCACTGCCCTCCAGCCTGGGCGACAGAGCCAGATTCTGT
CTC

FIGURE 130

MGCHVATSCHVAWLLVLISGCWGQVNRLPFFTNHFFDTYLLISEDTPVGSSVTQLLAQDMDND
PLVFGVSGEEASRFFAVEPDTGVVWLRQPLDRETKSEFTVEFSVSDHQGVITRKVNIQVGDVN
DNAPTFHNQPYSVRIPENTPVGTPIFIVNATDPDLGAGGSVLYSFQPPSQFFAIDSARGIVTV
IRELDYETTQAYQLTVNATDQDKTRPLSTLANLAIIITDVQDMDPIFINLPYSTNIYEHSPPG
TTVRIITAIDQDKGRPRGIGYTIVSGNTNSIFALDYISGVLTLNGLLDRENPLYSHGFILTVK
GTELNDDRTPSDATVTTTFNILVIDINDNAPEFNSSEYSVAITELAQVGFALPLFIQVVDKDE
NLGLNSMFEVYLVGNNSHHFIISPTSVQGKADIRIRVAIPLDYETVDRYDFDLFANESVPDHV
GYAKVKITLINENDNRPIFSQPLYNISLYENVTVGTSVLTVLVSPRFTAGPLSSPGPTVVRHP
EGFCPRDLSNQGRRHPQIPELCLLVY

Important features of the protein:

Signal peptide:

amino acids 1-23

Transmembrane domain:

amino acids 355-374

N-glycosylation sites.

amino acids 155-159, 206-210, 349-353, 393-397, 434-438, 466-470, 472-476

N-myristoylation sites.

amino acids 2-8, 49-55, 162-168, 270-276, 278-284, 316-322

Amidation site.

amino acids 515-519

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 11-22

Leucine zipper pattern.

amino acids 298-320

PTS HPR component serine phosphorylation site signature.

amino acids 377-393

Cadherins extracellular repeated domain signature.

amino acids 120-131, 336-347

Cadherins extracellular

amino acids 120-144, 336-360

FIGURE 131

GTGGGCCGCCCCTGCTGCTGCCGTCC**ATG**CTGATGTTTGCGGTGATCGTGGCCTCCAGCGGGC

TGCTGCTCATGATCGAGCGGGGCATCCTGGCCGAGATGAAGCCCCTGCCCCTGCACCCGCCCG

GCCGCGAGGGCACAGCCTGGCGCGGGAAAGCCCCCAAGCCTGGGGGCCTGTCCCTCAGGGCTG

GGGACGCGGACTTGCAAGTGCGGCAGGACGTCCGGAACAGGACCCTGCGGGCGGTGTGCGGAC

AGCCAGGCATGCCCCGGGACCCCTGGGACTTGCCGGTGGGGCAGCGGCGCACCCTGCTGCGCC

ACATCCTCGTAAGTGACCGTTACCGCTTCCTCTACTGCTACGTCCCCAAGGTGGCCTGCTCTA

ACTGGAAGCGGGTGATGAAGGTGCTGGCAGGCGTCCTGGACAGCGTGGACGTCCGCCTCAAGA

TGGACCACCGCAGTGACCTGGTGTTCCTGGCCGACCTGCGGCCTGAGGAGATTCGCTACCGCC

TGCAGCACTACTTTAAGTTCCTGTTTGTGCGGGAGCCCTTGGAACGCCTCCTCTCTGCCTACC

GCAACAAGTTTGGCGAGATCCGAGAGTACCAGCAACGCTATGGGGCTGAGATAGTGAGGCGGT

ACAGGGCTGGAGCGGGGCCCAGCCCTGCAGGCGACGATGTCACATTCCCCGAGTTCCTGAGAT

ACCTGGTGGATGAGGACCCTGAGCGCATGAATGAGCATTGGATGCCCGTGTACCACCTGTGCC

AGCCTTGTGCCGTGCACTATGACTTTGTGGGCTCCTATGAGAGGCTGGAGGCTGATGCAAATC

AGGTGCTGGAGTGGGTACGGGCACCACCTCACGTCCGATTTCCAGCTCGCCAGGCCTGGTACC

GGCCAGCCAGCCCCGAAAGCCTGCATTACCACTTGTGCAGTGCCCCCCGGGCCCTGCTGCAGG

ATGTGCTGCCTAAGTATATCCTGGACTTCTCCCTCTTTGCCTACCCACTGCCTAATGTCACCA

AGGAGGCGTGTCAGCAG**TGA**CCATGGGTGTGGGGCCAGCAGCTGGTGGGGACTGGTTTCAACG

CCAGCTTTCTGTGCTTCTGCCTGTCATTCGGAGAAACTCTGGCTCTGGGGCTTGGGGCTTCTC

AGGATCCTGGATGGCAGAGACTGCCCTCAGAAGTTCCTTGTCCAGGGTGGGCACCCACAGTGA

CTCAGAGGACAGGGCTAGGCAGGAGACCTGCTGCTCCTCATTGGGGGGATCTCTTGGGGGGCA

GACACCAGTTTGCCAATGAAGCAACACATCTGATCTAAAGACTGGCTCCAGACCCCGGGCTGC

CAGGATTATGCAGTCCACTTGGTCTACCTTAATTTAACCTGTGGCCAAACTCAGAGATGGTAC

CAGCCAGGGGCAAGCATGACCAGAGCCAGGGACCCTGTGGCTCTGATCCCCCATTTATCCACC

CCATGTGCCTCAGGACTAGAGTGAGCAATCATACCTTATAAATGACTTTTGTGCCTTTCTGCT

CCAGTCTCAAAATTTCCTACACCTGCCAGTTCTTTACATTTTTCCAAGGAAAGGAAAACGGAA

GCAGGGTTCTTGCCTGGTAGCTCCAGGACCCAGCTCTGCAGGCACCCAAAGACCCTCTGTGCC

CAGCCTCTTCCTTGAGTTCTCGGAACCTCCTCCCTAATTCTCCCTTCCTTCCCCACAAGGCCT

TTGAGGTTGTGACTGTGGCTGGTATATCTGGCTGCCATTTTTCTGATGCATTTATTTAAAATT

TGTACTTTTTGATAGAACCCTTGTAAGGGCTTTGTTTTCCTAATAGCTGACTTTTTAATAAAG

CAGTTTTATATAT

FIGURE 132

MLMFAVIVASSGLLLMIERGILAEMKPLPLHPPGREGTAWRGKAPKPGGLSLRAGDADLQVRQ
DVRNRTLRAVCGQPGMPRDPWDLPVGQRRTLLRHILVSDRYRFLYCYVPKVACSNWKRVMKVL
AGVLDSVDVRLKMDHRSDLVFLADLRPEEIRYRLQHYFKFLFVREPLERLLSAYRNKFGEIRE
YQQRYGAEIVRRYRAGAGPSPAGDDVTFPEFLRYLVDEDPERMNEHWMPVYHLCQPCAVHYDF
VGSYERLEADANQVLEWVRAPPHVRFPARQAWYRPASPESLHYHLCSAPRALLQDVLPKYILD
FSLFAYPLPNVTKEACQQ

Important features of the protein:

Signal peptide:

amino acids 1-23

N-glycosylation sites.

amino acids 67-71, 325-329

Tyrosine kinase phosphorylation sites.

amino acids 152-159, 183-183

N-myristoylation sites.

amino acids 89-95, 128-134

FIGURE 133

CGGCAGTTCTGGCCCCTGCAGCTGGAGGTACCCTGAGTTCTGAGGGTCGTAGTGCTGTTTCTG
GTATTCTCATCGCGGTCACCTCTACCGGTGTGGACAAGTAAAGTTTGAATCAGCTTCTCCATG
GCCTGGGCACCAGTTCCCGGCTGAGCCATTTTCCTTTTGGCTAAAAGTCCCCGCCCAGAGGCC
AATTCGTCGCGGCGGCGGTGGAGATCGCAGGTCGCTCAGGCTTGCAG**ATG**GGTCAAGGGTTGT
GGAGAGTGGTCAGAAACCAGCAGCTGCAACAAGAAGGCTACAGTGAGCAAGGCTACCTCACCA
GAGAGCAGAGCAGGAGAATGGATGCGAGCAACATTTCTAACACCAATCATCGTAAACAAGTCC
AAGGAGGCATTGACATATATCATCTTTTGAAGGCAAGGAAATCGAAAGAACAGGAAGGATTCA
TTAATTTGGAAATGTTGCCTCCTGAGCTAAGCTTTACCATCTTGTCCTACCTGAATGCAACTG
ACCTTTGCTTGGCTTCATGTGTTTGGCAGGACCTTGCGAATGATGAACTTCTCTGGCAAGGGT
TGTGCAAATCCACTTGGGGTCACTGTTCCATATACAATAAGAACCCACCTTTAGGATTTTCTT
TTAGAAAATTGTATATGCAGCTGGATGAAGGCAGCCTCACCTTTAATGCCAACCCAGATGAGG
GAGTGAACTACTTTATGTCCAAGGGTATCCTGGATGATTCGCCAAAGGAAATAGCAAAGTTTA
TCTTCTGTACAAGAACACTAAATTGGAAAAAACTGAGAATCTATCTTGATGAAAGGAGAGATG
TCTTGGATGACCTTGTAACATTGCATAATTTTAGAAATCAGTTCTTGCCAAATGCACTGAGAG
AATTTTTTCGTCATATCCATGCCCCTGAAGAGCGTGGAGAGTATCTTGAAACTCTTATAACAA
AGTTCTCACATAGATTCTGTGCTTGCAACCCTGATTTAATGCGAGAACTTGGCCTTAGTCCTG
ATGCTGTCTATGTACTGTGCTACTCTTTGATTCTACTTTCCATTGACCTCACTAGCCCTCATG
TGAAGAATAAAATGTCAAAAAGGGAATTTATTCGAAATACCCGTCGCGCTGCTCAAAATATTA
GTGAAGATTTTGTAGGGCATCTTTATGACAATATCTACCTTATTGGCCATGTGGCTGCA**TAA**A
AAGCACAATTGCTAGGACTTCAGTTTTTACTTCAGACTAAAGCTACCCAAGGACTTAGCAGAT
ATGGGGGTTACATCAGTGCTGGTCATTGTAGCCTGAGTATACAATCAAGCTTCAGTGTGCAAC
CTTTTTTTCTTTTGCCATTTTCTATTTTAGTAATTTCCTTGGGGAACTAAATAATTTTGCAGA
ATTTTTCCTAATTTTGTTTATCACGTTTTGCACAAAGCAGAGCCACTGTCTAACACAGCTGTT
AACGAATGATAAACTGACATTATACTCTAAAAGATGGTGTATTTGTGCATTAGATTTGCCTGA
AAAACTTTATCCATTTCCATTCTTTATACAAATACCATGTAATGTGTACATATTTAACTAAAG
AGATTTATAGTCATAATTATTTTATTGTAAAGATTTTAACTAAAGTTTTTCCTTTTCTCTC

FIGURE 134

MGQGLWRVVRNQQLQQEGYSEQGYLTREQSRRMDASNISNTNHRKQVQGGIDIYHLLKARKSK
EQEGFINLEMLPPELSFTILSYLNATDLCLASCVWQDLANDELLWQGLCKSTWGHCSIYNKNP
PLGFSFRKLYMQLDEGSLTFNANPDEGVNYFMSKGILDDSPKEIAKFIFCTRTLNWKKLRIYL
DERRDVLDDLVTLHNFRNQFLPNALREFFRHIHAPEERGEYLETLITKFSHRFCACNPDLMRE
LGLSPDAVYVLCYSLILLSIDLTSPHVKNKMSKREFIRNTRRAAQNISEDFVGHLYDNIYLIG
HVAA

Important features of the protein:

Transmembrane domain:

amino acids 253-272

N-glycosylation sites.

amino acids 37-41, 87-91, 298-302

N-myristoylation site.

amino acids 110-116

FIGURE 135

GGCACGAGGGAGCCTCCGTTAGGGGGTGGGAAAGGACTTTGCCATAGGTCGCTGAGGCCACCA
TCTGCTCTCTTACTGGCCAAGGGCGTAAAAAGATAGTCTTCCCATTAGCTAGAGAGCAAACCC
CAGAAAGCCTATTGGCTGCGCCGTCCGCGGGCCTTGGTCCGCTTTGAAGGCGGGCTGCGGCTG
CGAGAGGAGGGCGGGCGGGAGGCTAGCTGTTGTCGTGGTTGCTCGGAGGCACGTGTGCAGTCC
CGGAAGCGGCGAGGGGAAACTGCTCCGCGCGCGCCGCGGGAGGAGGAACCGCCCGGTCCTTTA
GGGTCCGGGCCCGGCCGGGCC**ATG**GATTCAATGCCTGAGCCCGCGTCCCGCTGTCTTCTGCTT
CTTCCCTTGCTGCTGCTGCTGCTGCTGCTGCTGCCGGCCCCGGAGCTGGGCCCGAGCCAGGCC
GGAGCTGAGGAGAACGACTGGGTTCGCCTGCCCAGCAAATGCGAAGTGTGTAAATATGTTGCT
GTGGAGCTGAAGTCAGCCTTTGAGGAAACCGGCAAGACCAAGGAGGTGATTGGCACGGGCTAT
GGCATCCTGGACCAGAAGGCCTCTGGAGTCAAATACACCAAGTCGGACTTGCGGTTAATCGAA
GTCACTGAGACCATTTGCAAGAGGCTCCTGGATTATAGCCTGCACAAGGAGAGGACCGGCAGC
AATCGATTTGCCAAGGGCATGTCAGAGACCTTTGAGACATTACACAACCTGGTACACAAAGGG
GTCAAGGTGGTGATGGACATCCCCTATGAGCTGTGGAACGAGACTTCTGCAGAGGTGGCTGAC
CTCAAGAAGCAGTGTGATGTGCTGGTGGAAGAGTTTGAGGAGGTGATCGAGGACTGGTACAGG
AACCACCAGGAGGAAGACCTGACTGAATTCCTCTGCGCCAACCACGTGCTGAAGGGAAAAGAC
ACCAGTTGCCTGGCAGAGCAGTGGTCCGGCAAGAAGGGAGACACAGCTGCCCTGGGAGGGAAG
AAGTCCAAGAAGAAGAGCAGCAGGGCCAAGGCAGCAGGCGGCAGGAGTAGCAGCAGCAAACAA
AGGAAGGAGCTGGGTGGCCTTGAGGGAGACCCCAGCCCCGAGGAGGATGAGGGCATCCAGAAG
GCATCCCCTCTCACACACAGCCCCCCTGATGAGCTC**TGA**GCCCACCCAGCATCCTCTGTCCTG
AGACCCCTGATTTTGAAGCTGAGGAGTCAGGGGCATGGCTCTGGCAGGCCGGGATGGCCCCGC
AGCCTTCAGCCCCTCCTTGCCTTGGCTGTGCCCTCTTCTGCCAAGGAAAGACACAAGCCCCAG
GAAGAACTCAGAGCCGTCATGGGTAGCCCACGCCGTCCTTTCCCCTCCCCAAGTGTTTCTCTC
CTGACCCAGGGTTCAGGCAGGCCTTGTGGTTTCAGGACTGCAAGGACTCCAGTGTGAACTCAG
GAGGGGCAGGTGTCAGAACTGGGCACCAGGACTGGAGCCCCCTCCGGAGACCAAACTCACCAT
CCCTCAGTCCTCCCCAACAGGGTACTAGGACTGCAGCCCCCTGTAGCTCCTCTCTGCTTACCC
CTCCTGTGGACACCTTGCACTCTGCCTGGCCCTTCCCAGAGCCCAAAGAGTAAAAATGTTCTG
GTTCTGATTTCTGAAAAAAAAAAAAAAAAAAATTCCT

FIGURE 136

MDSMPEPASRCLLLLPLLLLLLLLLLPAPELGPSQAGAEENDWVRLPSKCEVCKYVAVELKSAF
EETGKTKEVIGTGYGILDQKASGVKYTKSDLRLIEVTETICKRLLDYSLHKERTGSNRFAKGM
SETFETLHNLVHKGVKVVMDIPYELWNETSAEVADLKKQCDVLVEEFEEVIEDWYRNHQEEDL
TEFLCANHVLKGKDTSCLAEQWSGKKGDTAALGGKKSKKKSSRAKAAGGRSSSSKQRKELGGL
EGDPSPEEDEGIQKASPLTHSPPDEL

Important features of the protein:

Signal peptide:

amino acids 1-26

N-glycosylation site.

amino acids 153-157

cAMP- and cGMP-dependent protein kinase phosphorylation sites.

amino acids 227-231, 228-232

Tyrosine kinase phosphorylation site.

amino acids 142-150

N-myristoylation sites.

amino acids 36-42, 74-80, 86-92, 125-131, 222-228, 237-243, 250-256, 263-269

Amidation sites.

amino acids 212-216, 222-226

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

amino acids 62-70

FIGURE 137

CACGCCTCCCGCTGCCAGCCCGGCACCGGGATCTTAATCAGTCACTATGAAAACTCATTAGCT
CCACAGCA**ATG**AGTCCTCCACTGCTGAAGCTTGGCGCTGTGCTTAGTACCATGGCAATGATCT
CAAACTGGATGTCCCAAACTCTCCCATCCTTGGTGGGACTGAACACCACGAGGCTGTCGACTC
CGGATACCTTAACTCAGATTAGTCCTAAAGAAGGGTGGCAGGTGTACAGCTCAGCTCAGGATC
CTGATGGGCGGTGCATTTGCACAGTTGTTGCTCCAGAACAAAACCTGTGTTCCCGGGATGCCA
AAAGCAGGCAACTTCGCCAACTACTGGAAAAGGTTCAGAACATGTCCCAGTCTATTGAAGTCT
TAAACTTGAGAACTCAGAGAGATTTCCAATATGTTTTAAAAATGGAAACCCAAATGAAAGGGC
TGAAGGCAAAATTTCGGCAGATTGAAGATGATCGAAAGACACTTATGACCAAGCATTTTCAGG
AGTTGAAAGAGAAAATGGACGAGCTCCTGCCTTTGATCCCCGTGCTGGAACAGTACAAAACAG
ATGCTAAGTTAATCACCCAGTTCAAGGAGGAAATAAGGAATCTGTCTGCTGTCCTCACTGGTA
TTCAGGAGGAAATTGGTGCCTATGACTACGAGGAACTACACCAAAGAGTGCTGAGCTTGGAAA
CAAGACTTCGTGACTGCATGAAAAAGCTAACATGTGGCAAACTGATGAAAATCACAGGCCCAG
TTACAGTCAAGACATCTGGAACCCGATTTGGTGCTTGGATGACAGACCCTTTAGCATCTGAGA
AAAACAACAGAGTCTGGTACATGGACAGTTATACTAACAATAAAATTGTTCGTGAATACAAAT
CAATTGCAGACTTTGTCAGTGGGGCTGAATCAAGGACATACAACCTTCCTTTCAAGTGGGCAG
GAACTAACCATGTTGTCTACAATGGCTCACTCTATTTTAACAAGTATCAGAGTAATATCATCA
TCAAATACAGCTTTGATATGGGGAGAGTGCTTGCCCAACGAAGCCTGGAGTATGCTGGTTTTC
ATAATGTTTACCCCTACACATGGGGTGGATTCTCTGACATCGACCTAATGGCTGATGAAATCG
GGCTGTGGGCTGTGTATGCAACTAACCAGAATGCAGGCAATATTGTCATCAGCCAACTTAACC
AAGATACCTTGGAGGTGATGAAGAGCTGGAGCACTGGCTACCCCAAGAGAAGTGCAGGGGAAT
CTTTCATGATCTGTGGGACACTGTATGTCACCAACTCCCACTTAACTGGAGCCAAGGTGTATT
ATTCCTATTCCACCAAAACCTCCACATATGAGTACACAGACATTCCCTTCCATAACCAATACT
TTCACATATCCATGCTTGACTACAATGCAAGAGATCGAGCTCTCTATGCCTGGAACAATGGCC
ACCAGGTGCTGTTCAATGTCACCCTTTTCCATATCATCAAGACAGAGGATGACACA**TAG**GCAA
ATGTGACATGTTTTCATTGATTTAAACAGTGTGATTTGTGATAAACTCTATAAGACCCCTTCC
GTTTTTTTCTTCACTATTATTTTTCATCATTTCTCCAAAGCAAAGCATTTTTATTGTAAAGTT
GGTGTTTCAAAAACATAGCTGAGCTTGTCTAACTTACCATGTTGGAAACACATCTTAACTTCT
AAATTTACAAGGCCTATCATGTCCTTGTCATGAAAAGCACTAAAAAAAAAAAAAGAGTTTAAGT
GGCTAAAGTCATAGTTTTGCAAGAGATTAATGATCTGCCTTATATTAGAGTCAGAGACTAATG
GTGGCTTAAATGCACGAATGTCTTTTTTTTTTAAAACTGTCATTTTTTACTGTCTTTTGCTCCA
TCTCAGGAAATATTTTGGTAGGAATTAGGAGAACAAAAAGCACTTTTATCCCATTTATTTCTT
TAAAAAATGTAAGGATTTCATTTATATTGAAAAATAATATTAATCATTTTGCTGTTAACACAA
TTCTCTGATGCGGTGCTGTACAGTCATTTTTAAATCTCTTGCTAACATTTTATTGGCAGTATG
TATTTCTACCATTGTAACCACCATTGTGCTATTGTATCTCTTCACTTCTGTGAAAGTAATATT
TTTTATAAAANACACTGNAATTTTAAAAAAAAAAAAAAAAAACAAAAAAAAAAAAAAAAAAAA

FIGURE 138

MSPPLLKLGAVLSTMAMISNWMSQTLPSLVGLNTTRLSTPDTLTQISPKEGWQVYSSAQDPDG
RCICTVVAPEQNLCSRDAKSRQLRQLLEKVQNMSQSIEVLNLRTQRDFQYVLKMETQMKGLKA
KFRQIEDDRKTLMTKHFQELKEKMDELLPLIPVLEQYKTDAKLITQFKEEIRNLSAVLTGIQE
EIGAYDYEELHQRVLSLETRLRDCMKKLTCGKLMKITGPVTVKTSGTRFGAWMTDPLASEKNN
RVWYMDSYTNNKIVREYKSIADFVSGAESRTYNLPFKWAGTNHVVYNGSLYFNKYQSNIIIKY
SFDMGRVLAQRSLEYAGFHNVYPYTWGGFSDIDLMADEIGLWAVYATNQNAGNIVISQLNQDT
LEVMKSWSTGYPKRSAGESFMICGTLYVTNSHLTGAKVYYSYSTKTSTYEYTDIPFHNQYFHI
SMLDYNARDRALYAWNNGHQVLFNVTLFHIIKTEDDT

Important features of the protein:

Signal peptide:

amino acids 1-16

N-glycosylation sites.

amino acids 33-37, 95-99, 179-183, 299-303, 465-469

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 215-219

Tyrosine kinase phosphorylation site.

amino acids 106-114

N-myristoylation sites.

amino acids 9-15, 31-37, 235-241, 239-245

FIGURE 139

GAAGCAGTGCAGAGAGGAGAGCGGAGCGGAGCTGCCGCTGAGCAAAGGCCTTCACC**ATG**GCCG
AGTCCCCCGGCTGCTGCTCCGTCTGGGCCCGCTGCCTCCACTGCCTGTATAGCTGCCACTGGA
GGAAATGCCCCAGAGAGAGGATGCAAACCAGCAAGTGCGACTGTATCTGGTTTGGCCTGCTCT
TCCTCACCTTCCTCCTTTCCCTGAGCTGGCTGTACATCGGGCTCGTCCTTCTCAATGACCTGC
ACAACTTCAATGAATTCCTCTTCCGCCGCTGGGGACACTGGATGGACTGGTCCCTGGCATTCC
TGCTGGTCATCTCTCTACTGGTCACATATGCATCCTTGCTATTGGTCCTGGCCCTGCTCCTGC
GGCTTTGTAGACAGCCCCTGCATCTGCACAGCCTCCACAAGGTGCTGCTGCTCCTCATTATGC
TGCTTGTGGCGGCTGGCCTTGTGGGACTGGACATCCAATGGCAGCAGGAGTGGCATAGCTTGC
GTGTGTCACTGCAGGCCACAGCCCCATTCCTTCATATTGGAGCAGCCGCTGGAATTGCCCTCC
TGGCCTGGCCTGTGGCTGATACCTTCTACCGTATCCACCGAAGAGGTCCCAAGATTCTGCTAC
TGCTCCTATTTTTTGGAGTTGTCCTGGTCATCTACTTGGCCCCCCTATGCATCTCCTCACCCT
GCATCATGGAACCCAGAGACTTACCACCCAAGCCTGGGCTGGTGGGACACCGAGGGGCCCCCA
TGCTGGCTCCCGAGAACACCCTGATGTCCTTGCGGAAGACAGCTGAATGCGGAGCTACTGTGT
TTGAGACTGATGTGATGGTCAGCTCCGATGGGGTCCCCTTCCTCATGCATGATGAGCACCTCA
GCAGGACCACGAATGTAGCCTCTGTATTCCCAACCCGAATCACAGCCCACAGCAGTGACTTCT
CCTGGACTGAACTGAAGAGACTCAATGCTGGATCCTGGTTCCTAGAGAGGCGACCCTTCTGGG
GGGCCAAACCGCTGGCAGGCCCTGATCAGAAAGAGGCTGAGAGTCAGACGGTACCAGCATTAG
AAGAGCTATTGGAGGAAGCTGCAGCCCTCAACCTTTCCATCATGTTCGACTTGCGCCGACCCC
CACAGAACCACACATACTATGACACTTTTGTGATCCAGACATTGGAGACTGTGCTGAATGCAA
GGGTGCCCCAAGCCATGGTCTTTTGGCTACCAGATGAAGATCGGGCTAATGTCCAACGACGGG
CACCTGGAATGCGCCAGATATATGGACGTCAGGGAGGCAACAGAACGGAGAGGCCCCAGTTTC
TTAACCTCCCCTATCAAGATCTGCCACTATTGGATATCAAGGCATTGCATAAGGATAATGTCT
CGGTGAACCTATTTGTAGTGAACAAGCCCTGGCTCTTCTCTCTGCTTTGGTGTGCAGGGGTGG
ATTCGGTCACCACCAACGACTGCCAGCTGCTGCAGCAGATGCGTTACCCTATCTGGCTTATTA
CCCCTCAAACCTACCTAATCATATGGGTCATTACCAATTGTGTTTCCACCATGCTGCTTTTGT
GGACCTTCCTCCTCCAAAGGAGATTTGTTAAGAAGAGAGGGAAAACTGGCTTAGAAACAGCAG
TGCTGCTGACAAGGATCAACAATTTCATGATGGAG**TGA**ATGCCCTGCCCTGCTTCCCCACCCA
AGCCAGTCTACATTGCCCAAACAGCAAGGGTTGGAGAGTGGCTTAAGTGGAATGCTTCAGGGG
TGGTGGGTTGCAAGTGGGGGGAGCTTTGCCAACAGGAGGTTTTGAACCATGAGGGCCCTCTGC
CCAGGTGATGGGCATTCCCTAAGCTGCTATGGAATCTGCTCCCTTTGGGGTTTTGACCTGAGA
TGTTTGGGAAGAGAGTGAGTAATGAGAAGTTTCTCCTCAAATGAAACTAGAACAGAGGAAGTA
AAAGGGAGATTGCTCGGA

FIGURE 140

MAESPGCCSVWARCLHCLYSCHWRKCPRERMQTSKCDCIWFGLLFLTFLLSLSWLYIGLVLLN
DLHNFNEFLFRRWGHWMDWSLAFLLVISLLVTYASLLLVLALLLRLCRQPLHLHSLHKVLLLL
IMLLVAAGLVGLDIQWQQEWHSLRVSLQATAPFLHIGAAAGIALLAWPVADTFYRIHRRGPKI
LLLLLFFGVVLVIYLAPLCISSPCIMEPRDLPPKPGLVGHRGAPMLAPENTLMSLRKTAECGA
TVFETDVMVSSDGVPFLMHDEHLSRTTNVASVFPTRITAHSSDFSWTELKRLNAGSWFLERRP
FWGAKPLAGPDQKEAESQTVPALEELLEEAAALNLSIMFDLRRPPQNHTYYDTFVIQTLETVL
NARVPQAMVFWLPDEDRANVQRRAPGMRQIYGRQGGNRTERPQFLNLPYQDLPLLDIKALHKD
NVSVNLFVVNKPWLFSLLWCAGVDSVTTNDCQLLQQMRYPIWLITPQTYLIIWVITNCVSTML
LLWTFLLQRRFVKKRGKTGLETAVLLTRINNFMME

Important features of the protein:

Transmembrane domains:

amino acids 38-60, 83-107, 122-138, 156-173, 189-210, 484-506

N-glycosylation sites.

amino acids 349-353, 362-366, 415-419, 442-446

N-myristoylation sites.

amino acids 163-169, 413-419, 523-529

Leucine zipper pattern.

amino acids 93-115, 109-131

Glutamine amidotransferases class-II active site.

amino acids 1-13

FIGURE 141

GCCGCCGGCCCGGGCTGGAGCCGAGCGCAGCAGCCACCGCCGCCGCCGCGCCAGAAGTTTGGGTTGAACCGGAGC
TGCCGGGAGGAAACTTTTTTCTTTTTTCCCCCTCCCTCCCGGGAGGAGGAGGAGGAGGAGGAGGGGAAGCTGCCG
CCGGCGCCAAGGCTCGTGGGCTCGGGGTCGGCGCGGCCCGCAGAAGGGGCGGGGGCCTCGCCCCGCGAGGGGAGG
CGCGCCCCGGGGGCCCCGAGAGGGGCGGTGAGGACCGCGGGCTGCTGGTGCGGCGGCGGCGGCGCGTGTGCCCCG
CGCAGGGGAGGGCGCCCGCCCCGCTCCCGGCCCGGCTGCGAGGAGGAGGCGGCGGCGGCGCAGGAGG**ATG**TACTT
GGTGGCGGGGGACAGGGGGTTGGCCGGCTGCGGGCACCTCCTGGTCTCGCTGCTGGGGCTGCTGCTGCTGCTGGC
GCGCTCCGGCACCCGGGCGCTGGTCTGCCTGCCCTGTGACGAGTCCAAGTGCGAGGAGCCCAGGAACTGCCCGGG
GAGCATCGTGCAGGGCGTCTGCGGCTGCTGCTACACGTGCGCCAGCCAGAGGAACGAGAGCTGCGGCGGCACCTT
CGGGATTTACGGAACCTGCGACCGGGGGCTGCGTTGTGTCATCCGCCCCCCGCTCAATGGCGACTCCCTCACCGA
GTACGAAGCGGGCGTTTGCGAAGATGAGAACTGGACTGATGACCAACTGCTTGGTTTTAAACCATGCAATGAAAA
CCTTATTGCTGGCTGCAATATAATCAATGGGAAATGTGAATGTAACACCATTCGAACCTGCAGCAATCCCTTTGA
GTTTCCAAGTCAGGATATGTGCCTTTCAGCTTTAAAGAGAATTGAAGAAGAGAAGCCAGATTGCTCCAAGGCCCG
CTGTGAAGTCCAGTTCTCTCCACGTTGTCCTGAAGATTCTGTTCTGATCGAGGGTTATGCTCCTCCTGGGGAGTG
CTGTCCCTTACCCAGCCGCTGCGTGTGCAACCCCGCAGGCTGTCTGCGCAAAGTCTGCCAGCCGGGAAACCTGAA
CATACTAGTGTCAAAAGCCTCAGGGAAGCCGGGAGAGTGCTGTGACCTCTATGAGTGCAAACCAGTTTTCGGCGT
GGACTGCAGGACTGTGGAATGCCCTCCTGTTCAGCAGACCGCGTGTCCCCCGGACAGCTATGAAACTCAAGTCAG
ACTAACTGCAGATGGTTGCTGTACTTTGCCAACAAGATGCGAGTGTCTCTCTGGCTTATGTGGTTTCCCCGTGTG
TGAGGTGGGATCCACTCCCCGCATAGTCTCTCGTGGCGATGGGACACCTGGAAAGTGCTGTGATGTCTTTGAATG
TGTTAATGATACAAAGCCAGCCTGCGTATTTAACAATGTGGAATATTATGATGGAGACATGTTTCGAATGGACAA
CTGTCGGTTCTGTCGATGCCAAGGGGGCGTTGCCATCTGCTTCACTGCCCAGTGTGGTGAGATAAACTGCGAGAG
GTACTACGTGCCCGAAGGAGAGTGCTGCCCAGTGTGTGAAGATCCAGTGTATCCTTTTAATAATCCCGCTGGCTG
CTATGCCAATGGCCTGATCCTTGCCCACGGAGACCGGTGGCGGGAAGACGACTGCACATTCTGCCAGTGCGTCAA
CGGTGAACGCCACTGCGTTGCGACCGTCTGCGGACAGACCTGCACAAACCCTGTGAAAGTGCCTGGGGAGTGTTG
CCCTGTGTGCGAAGAACCAACCATCATCACAGTTGATCCACCTGCATGTGGGGAGTTATCAAACTGCACTCTGAC
AGGGAAGGACTGCATTAATGGTTTCAAACGCGATCACAATGGTTGTCGGACCTGTCAGTGCATAAACACCGAGGA
ACTATGTTCAGAACGTAAACAAGGCTGCACCTTGAACTGTCCCTTCGGTTTCCTTACTGATGCCCAAAACTGTGA
GATCTGTGAGTGCCGCCCAAGGCCCAAGAAGTGCAGACCCATAATCTGTGACAAGTATTGTCCACTTGGATTGCT
GAAGAATAAGCACGGCTGTGACATCTGTCGCTGTAAGAAATGTCCAGAGCTCTCATGCAGTAAGATCTGCCCCTT
GGGTTTCCAGCAGGACAGTCACGGCTGTCTTATCTGCAAGTGCAGAGAGGCCTCTGCTTCAGCTGGGCCACCCAT
CCTGTCGGGCACTTGTCTCACCGTGGATGGTCATCATCATAAAAATGAGGAGAGCTGGCACGATGGGTGCCGGGA
ATGCTACTGTCTCAATGGACGGGAAATGTGTGCCCTGATCACCTGCCCGGTGCCTGCCTGTGGCAACCCCACCAT
TCACCCTGGACAGTGCTGCCCATCATGTGCAGATGACTTTGTGGTGCAGAAGCCAGAGCTCAGTACTCCCTCCAT
TTGCCACGCCCCTGGAGGAGAATACTTTGTGGAAGGAGAAACGTGGAACATTGACTCCTGTACTCAGTGCACCTG
CCACAGCGGACGGGTGCTGTGTGAGACAGAGGTGTGCCCACCGCTGCTCTGCCAGAACCCCTCACGCACCCAGGA
TTCCTGCTGCCCACAGTGTACAGATCAACCTTTTCGGCCTTCCTTGTCCCGCAATAACAGCGTACCTAATTACTG
CAAAAATGATGAAGGGGATATATTCCTGGCAGCTGAGTCCTGGAAGCCTGACGTTTGTACCAGCTGCATCTGCAT
TGATAGCGTAATTAGCTGTTTCTCTGAGTCCTGCCCTTCTGTATCCTGTGAAAGACCTGTCTTGAGAAAAGGCCA
GTGTTGTCCCTACTGCATAGAAGACACAATTCCAAAGAAGGTGGTGTGCCACTTCAGTGGGAAGGCCTATGCCGA
CGAGGAGCGGTGGGACCTTGACAGCTGCACCCACTGCTACTGCCTGCAGGGCCAGACCCTCTGCTCGACCGTCAG
CTGCCCCCCTCTGCCCTGTGTTGAGCCCATCAACGTGGAAGGAAGTTGCTGCCCAATGTGTCCAGAAATGTATGT
CCCAGAACCAACCAATATACCCATTGAGAAGACAAACCATCGAGGAGAGGTTGACCTGGAGGTTCCCCTGTGGCC
CACGCCTAGTGAAAATGATATCGTCCATCTCCCTAGAGATATGGGTCACCTCCAGGTAGATTACAGAGATAACAG
GCTGCACCCAAGTGAAGATTCTTCACTGGACTCCATTGCCTCAGTTGTGGTTCCCATAATTATATGCCTCTCTAT
TATAATAGCATTCCTATTCATCAATCAGAAGAAACAGTGGATACCACTGCTTTGCTGGTATCGAACACCAACTAA
GCCTTCTTCCTTAAATAATCAGCTAGTATCTGTGGACTGCAAGAAAGGAACCAGAGTCCAGGTGGACAGTTCCCA
GAGAATGCTAAGAATTGCAGAACCAGATGCAAGATTCAGTGGCTTCTACAGCATGCAAAAACAGAACCATCTACA
GGCAGACAATTTCTACCAAACAGTG**TGA**AGAAAGGCAACTAGGATGAGGTTTCAAAAGACGGAAGACGACTAAAT
CTGCTCTAAAAAGTAAACTAGAATTTGTGCACTTGCTTAGTGGATTGTATTGGATTGTGACTTGATGTACAGCGC
TAAGACCTTACTGGGATGGGCTCTGTCTACAGCAATGTGCAGAACAAGCATTCCCACTTTTCCTCAAAAAA

FIGURE 142

MYLVAGDRGLAGCGHLLVSLLGLLLLLARSGTRALVCLPCDESKCEEPRNCPGSIVQGVCGCC
YTCASQRNESCGGTFGIYGTCDRGLRCVIRPPLNGDSLTEYEAGVCEDENWTDDQLLGFKPCN
ENLIAGCNIINGKCECNTIRTCSNPFEFPSQDMCLSALKRIEEEKPDCSKARCEVQFSPRCPE
DSVLIEGYAPPGECCPLPSRCVCNPAGCLRKVCQPGNLNILVSKASGKPGECCDLYECKPVFG
VDCRTVECPPVQQTACPPDSYETQVRLTADGCCTLPTRCECLSGLCGFPVCEVGSTPRIVSRG
DGTPGKCCDVFECVNDTKPACVFNNVEYYDGDMFRMDNCRFCRCQGGVAICFTAQCGEINCER
YYVPEGECCPVCEDPVYPFNNPAGCYANGLILAHGDRWREDDCTFCQCVNGERHCVATVCGQT
CTNPVKVPGECCPVCEEPTIITVDPPACGELSNCTLTGKDCINGFKRDHNGCRTCQCINTEEL
CSERKQGCTLNCPFGFLTDAQNCEICECRPRPKKCRPIICDKYCPLGLLKNKHGCDICRCKKC
PELSCSKICPLGFQQDSHGCLICKCREASASAGPPILSGTCLTVDGHHHKNEESWHDGCRECY
CLNGREMCALITCPVPACGNPTIHPGQCCPSCADDFVVQKPELSTPSICHAPGGEYFVEGETW
NIDSCTQCTCHSGRVLCETEVCPPLLCQNPSRTQDSCCPQCTDQPFRPSLSRNNSVPNYCKND
EGDIFLAAESWKPDVCTSCICIDSVISCFSESCPSVSCERPVLRKGQCCPYCIEDTIPKKVVC
HFSGKAYADEERWDLDSCTHCYCLQGQTLCSTVSCPPLPCVEPINVEGSCCPMCPEMYVPEPT
NIPIEKTNHRGEVDLEVPLWPTPSENDIVHLPRDMGHLQVDYRDNRLHPSEDSSLDSIASVVV
PIIICLSIIIAFLFINQKKQWIPLLCWYRTPTKPSSLNNQLVSVDCKKGTRVQVDSSQRMLRI
AEPDARFSGFYSMQKQNHLQADNFYQTV

Important features of the protein:

Signal peptide:

amino acids 1-34

Transmembrane domain:

amino acids 940-962

N-glycosylation sites.

amino acids 71-75, 113-117, 330-334, 474-478, 746-750

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 992-996

N-myristoylation site.

amino acids 9-15, 58-64, 61-67, 75-81, 79-85, 362-368, 402-408, 407-413, 439-445, 492-498, 511-517, 551-557, 558-564, 586-592, 606-612, 625-631, 845-851

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 52-63, 844-855

Cell attachment sequence.

amino acids 314-317

Leucine zipper pattern.

amino acids 3-25

Eukaryotic thiol (cysteine) proteases cysteine active site.

amino acids 57-69

VWFC domain proteins.

amino acids 448-456, 382-390

C-terminal cystine knot proteins

amino acids 60-86

FIGURE 143

GACGTCTGGCCGGCTCCCGGCGAAGGGCAGCGGAGGAGCGGCCCAGAGCGCGCAGCTAGGGCA
CTGGCGAAACCCCGGGACAGTCCCTCTCCGTGCGGGGGCGGCGCAGAGCAGTCCCATCCCCGG
GGTCCCGGGCGCGGCTGACTGCCGGCTGGTTCCCTGCGCGCAGTAGCTCCCCGAGCCGGGCTG
CACCGGAGGCGGCGAG**ATG**GTCGCGCGCGTCGGCCTCCTGCTGCGCGCCCTGCAGCTGCTACT
GTGGGGCCACCTGGACGCCCAGCCCGCGGAGCGCGGAGGCCAGGAGCTGCGCAAGGAGGCGGA
GGCATTCCTAGAGAAGTACGGATACCTCAATGAACAGGTCCCCAAAGCTCCCACCTCCACTCG
ATTCAGCGATGCCATCAGAGCGTTTCAGTGGGTGTCCCAGCTACCTGTCAGCGGCGTGTTGGA
CCGCGCCACCCTGCGCCAGATGACTCGTCCCCGCTGCGGGGTTACAGATACCAACAGTTATGC
GGCCTGGGCTGAGAGGATCAGTGACTTGTTTGCTAGACACCGGACCAAAATGAGGCGTAAGAA
ACGCTTTGCAAAGCAAGGTAACAAATGGTACAAGCAGCACCTCTCCTACCGCCTGGTGAACTG
GCCTGAGCATCTGCCGGAGCCGGCAGTTCGGGGCGCCGTGCGCGCCGCCTTCCAGTTGTGGAG
CAACGTCTCAGCGCTGGAGTTCTGGGAGGCCCCAGCCACAGGCCCCGCTGACATCCGGCTCAC
CTTCTTCCAAGGGGACCACAACGATGGGCTGGGCAATGCCTTTGATGGCCCAGGGGGCGCCCT
GGCGCACGCCTTCCTGCCCCGCCGCGGCGAAGCGCACTTCGACCAAGATGAGCGCTGGTCCCT
GAGCCGCCGCCGCGGGCGCAACCTGTTCGTGGTGCTGGCGCACGAGATCGGTCACACGCTTGG
CCTCACCCACTCGCCCGCGCCGCGCGCTCATGGCGCCCTACTACAAGAGGCTGGGCCGCGA
CGCGCTGCTCAGCTGGGACGACGTGCTGGCCGTGCAGAGCCTGTATGGGAAGCCCCTAGGGGG
CTCAGTGGCCGTCCAGCTCCCAGGAAAGCTGTTCACTGACTTTGAGACCTGGGACTCCTACAG
CCCCCAAGGAAGGCGCCCTGAAACGCAGGGCCCTAAATACTGCCACTCTTCCTTCGATGCCAT
CACTGTAGACAGGCAACAGCAACTGTACATTTTTAAAGGGAGCCATTTCTGGGAGGTGGCAGC
TGATGGCAACGTCTCAGAGCCCCGTCCACTGCAGGAAAGATGGGTCGGGCTGCCCCCCAACAT
TGAGGCTGCGGCAGTGTCATTGAATGATGGAGATTTCTACTTCTTCAAAGGGGGTCGATGCTG
GAGGTTCCGGGGCCCCAAGCCAGTGTGGGGTCTCCCACAGCTGTGCCGGGCAGGGGGCCTGCC
CCGCCATCCTGACGCCGCCCTCTTCTTCCCTCCTCTGCGCCGCCTCATCCTCTTCAAGGGTGC
CCGCTACTACGTGCTGGCCCGAGGGGGACTGCAAGTGGAGCCCTACTACCCCCGAAGTCTGCA
GGACTGGGGAGGCATCCCTGAGGAGGTCAGCGGCGCCCTGCCGAGGCCCGATGGCTCCATCAT
CTTCTTCCGAGATGACCGCTACTGGCGCCTCGACCAGGCCAAACTGCAGGCAACCACCTCGGG
CCGCTGGGCCACCGAGCTGCCCTGGATGGGCTGCTGGCATGCCAACTCGGGGAGCGCCCTGTT
C**TGA**AGGCACCTCCTCACCTCAGAAACTGGTGGTGCTCTCAGGGCAAAATCATGTTCCCCACC
CCCGGGGCAGAACCCCTCTTAGAAGCCTCTGAGTCCCTCTGCAGAAGACCGGGCAGCAAAGCC
TCCATCTGGAAGTCTGTCTGCCTTTGTTCCTTGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 144

MVARVGLLLRALQLLLWGHLDAQPAERGGQELRKEAEAFLEKYGYLNEQVPKAPTSTRFSDAI
RAFQWVSQLPVSGVLDRATLRQMTRPRCGVTDTNSYAAWAERISDLFARHRTKMRRKKRFAKQ
GNKWYKQHLSYRLVNWPEHLPEPAVRGAVRAAFQLWSNVSALEFWEAPATGPADIRLTFFQGD
HNDGLGNAFDGPGGALAHAFLPRRGEAHFDQDERWSLSRRRGRNLFVVLAHEIGHTLGLTHSP
APRALMAPYYKRLGRDALLSWDDVLAVQSLYGKPLGGSVAVQLPGKLFTDFETWDSYSPQGRR
PETQGPKYCHSSFDAITVDRQQQLYIFKGSHFWEVAADGNVSEPRPLQERWVGLPPNIEAAAV
SLNDGDFYFFKGGRCWRFRGPKPVWGLPQLCRAGGLPRHPDAALFFPPLRRLILFKGARYYVL
ARGGLQVEPYYPRSLQDWGGIPEEVSGALPRPDGSIIFFRDDRYWRLDQAKLQATTSGRWATE
LPWMGCWHANSGSALF

Important features of the protein:

Signal peptide:

amino acids 1-22

N-glycosylation sites.

amino acids 164-168, 355-359

N-myristoylation sites.

amino acids 92-98, 153-159, 193-199, 202-208, 288-294, 368-374, 509-515

Amidation site.

amino acids 312-316

Neutral zinc metallopeptidases, zinc-binding region signature.

amino acids 237-247

Matrixins cysteine switch

amino acids 231-262, 271-284

Hemopexin domain protein

amino acids 66-108, 231-262

FIGURE 145

GCCGGCTAGGGCGCCGGAGCCGCACGCAGCCGCGGGGCTCCGAGAGGCGCGCACTGGGGCTGGGACTGCGCGGCG
CCGCCGCTGCGAGCGCCACTGAGCGGTCGCGCAACTTCGGAGGCACAGCGCCGGAGCCAGGCGAGCGCTCAGAGA
CCCGGAGCCAGAGGGGCGCGCCGGAGCCTCGTTCGAGAGCCGGCGCCAGGCACCCACCGCGCTCCGAGTGCCAGG
CGGCCCTCCGCGCAGCGTGGCTTCCGCTGCCCCCACGGAAGGCACGGGCTGGCGCTGCCGGGCGCCGGGGAGGAC
GGCGAGGAGGAGGCGGCGGCGGCGGAGACGGCGGCGGCGAGACTGGGGCCAGGGAGACAGCCCTGGGGGAGAGGC
GCCCGAACCAGGCCGCGGGAGC**ATG**GGGGCCCGGAGCGGAGCTCGGGGCGCGCTGCTGCTGGCACTGCTGCTCTG
CTGGGACCCGAGGCTGAGCCAAGCAGGCACTGATTCTGGCAGCGAGGTGCTCCCTGACTCCTTCCCGTCAGCGCC
AGCAGAGCCGCTGCCCTACTTCCTGCAGGAGCCACAGGACGCCTACATTGTGAAGAACAAGCCTGTGGAGCTCCG
CTGCCGCGCCTTCCCCGCCACACAGATCTACTTCAAGTGCAACGGCGAGTGGGTCAGCCAGAACGACCACGTCAC
ACAGGAAGGCCTGGATGAGGCCACCGGCCTGCGGGTGCGCGAGGTGCAGATCGAGGTGTCGCGGCAGCAGGTGGA
GGAGCTCTTTGGGCTGGAGGATTACTGGTGCCAGTGCGTGGCCTGGAGCTCCGCAGGCACCACCAAGAGTCGCCG
AGCCTACGTCCGCATCGCCTACCTGCGCAAGAACTTCGATCAGGAGCCTCTGGGCAAGGAGGTGCCCCTGGACCA
TGAGGTTCTCCTGCAGTGCCGCCCGCCGGAGGGGGTGCCTGTGGCCGAGGTGGAATGGCTCAAGAATGAGGATGT
CATCGACCCCACCCAGGACACCAACTTCCTGCTCACCATCGACCACAACCTCATCATCCGCCAGGCCCGCCTGTC
GGACACTGCCAACTATACCTGCGTGGCCAAGAACATCGTGGCCAAACGCCGGAGCACCACTGCCACCGTCATCGT
CTACGTGAATGGCGGCTGGTCCAGCTGGGCAGAGTGGTCACCCTGCTCCAACCGCTGTGGCCGAGGCTGGCAGAA
GCGCACCCGGACCTGCACCAACCCCGCTCCACTCAACGGAGGGGCCTTCTGCGAGGGCCAGGCATTCCAGAAGAC
CGCCTGCACCACCATCTGCCCAGTCGATGGGGCGTGGACGGAGTGGAGCAAGTGGTCAGCCTGCAGCACTGAGTG
TGCCCACTGGCGTAGCCGCGAGTGCATGGCGCCCCCACCCCAGAACGGAGGCCGTGACTGCAGCGGGACGCTGCT
CGACTCTAAGAACTGCACAGATGGGCTGTGCATGCAAAATAAGAAAACTCTAAGCGACCCCAACAGCCACCTGCT
GGAGGCCTCAGGGGATGCGGCGCTGTATGCGGGGCTCGTGGTGGCCATCTTCGTGGTCGTGGCAATCCTCATGGC
GGTGGGGGTGGTGGTGTACCGCCGCAACTGCCGTGACTTCGACACAGACATCACTGACTCATCTGCTGCCCTGAC
TGGTGGTTTCCACCCCGTCAACTTTAAGACGGCAAGGCCCAGCAACCCGCAGCTCCTACACCCCTCTGTGCCTCC
TGACCTGACAGCCAGCGCCGGCATCTACCGCGGACCCGTGTATGCCCTGCAGGACTCCACCGACAAAATCCCCAT
GACCAACTCTCCTCTGCTGGACCCCTTACCCAGCCTTAAGGTCAAGGTCTACAGCTCCAGCACCACGGGCTCTGG
GCCAGGCCTGGCAGATGGGGCTGACCTGCTGGGGGTCTTGCCGCCTGGCACATACCCTAGCGATTTCGCCCGGGA
CACCCACTTCCTGCACCTGCGCAGCGCCAGCCTCGGTTCCCAGCAGCTCTTGGGCCTGCCCCGAGACCCAGGGAG
CAGCGTCAGCGGCACCTTTGGCTGCCTGGGTGGGAGGCTCAGCATCCCCGGCACAGGGGTCAGCTTGCTGGTGCC
CAATGGAGCCATTCCCCAGGGCAAGTTCTACGAGATGTATCTACTCATCAACAAGGCAGAAAGTACCCTCCCGCT
TTCAGAAGGGACCCAGACAGTATTGAGCCCCTCGGTGACCTGTGGACCCACAGGCCTCCTGCTGTGCCGCCCCGT
CATCCTCACCATGCCCCACTGTGCCGAAGTCAGTGCCCGTGACTGGATCTTTCAGCTCAAGACCCAGGCCCACCA
GGGCCACTGGGAGGAGGTGGTGACCCTGGATGAGGAGACCCTGAACACACCCTGCTACTGCCAGCTGGAGCCCAG
GGCCTGTCACATCCTGCTGGACCAGCTGGGCACCTACGTGTTCACGGGCGAGTCCTATTCCCGCTCAGCAGTCAA
GCGGCTCCAGCTGGCCGTCTTCGCCCCCGCCCTCTGCACCTCCCTGGAGTACAGCCTCCGGGTCTACTGCCTGGA
GGACACGCCTGTAGCACTGAAGGAGGTGCTGGAGCTGGAGCGGACTCTGGGCGGATACTTGGTGGAGGAGCCGAA
ACCGCTAATGTTCAAGGACAGTTACCACAACCTGCGCCTCTCCCTCCATGACCTCCCCCATGCCCATTGGAGGAG
CAAGCTGCTGGCCAAATACCAGGAGATCCCCTTCTATCACATTTGGAGTGGCAGCCAGAAGGCCCTCCACTGCAC
TTTCACCCTGGAGAGGCACAGCTTGGCCTCCACAGAGCTCACCTGCAAGATCTGCGTGCGGCAAGTGGAAGGGGA
GGGCCAGATATTCCAGCTGCATACCACTCTGGCAGAGACACCTGCTGGCTCCCTGGACACTCTCTGCTCTGCCCC
TGGCAGCACTGTCACCACCCAGCTGGGACCTTATGCCTTCAAGATCCCACTGTCCATCCGCCAGAAGATATGCAA
CAGCCTAGATGCCCCCAACTCACGGGGCAATGACTGGCGGATGTTAGCACAGAAGCTCTCTATGGACCGGTACCT
GAATTACTTTGCCACCAAAGCGAGCCCCACGGGTGTGATCCTGGACCTCTGGGAAGCTCTGCAGCAGGACGATGG
GGACCTCAACAGCCTGGCGAGTGCCTTGGAGGAGATGGGCAAGAGTGAGATGCTGGTGGCTGTGGCCACCGACGG
GGACTGC**TGA**GCCTCCTGGGACAGCGGGCTGGCAGGGACTGGCAGGAGGCAGGTGCAGGGAGGCCTGGGGCAGCC
TCCTGATGGGGATGTTTGGCCTCTGCTTCCTCCCAGTTCACAGCCAGAGTTGCCTCTCCTCCTCCTCTTCCCCAA
CCCCCAGACCATGACCAGCCTTAGAAAATCCATGTACTCTGTTGTTAGAGGGCCCAGAGTTCCTTCTCCACCCCC
GCTCTCTCTCTCTTGGCCTGAGATCTCTGTGCAGGAACCAAGATGGGGCTGAAGCCTCTGGAGGCAGTTGGTTGG
GGGCGGGCAGGCAGGAGGCCCTCCCTCCACCCCCCCACCCTCAGCCCGGCAACTTCTGGGTTCCGTGGGTTTTAG
TTCCGTTCTTCGTTTTCTTCCTCCGTTATTGATTTCTCCTTTCTCCCTAAGCCCCCTTCTGCTTCCACGCCCTTT
TCCTCTTTGAAGAGTCAAGTACAATTCAGACAAACTGCTTTCTCCTGTCCAAAAGCAAAAAGGCAAAGGAAAGAA
AGAAAGCTTCAGACCGCTAGTAAGGCTCAAAGAAGAAGAAAAACACCAAAACCACAAGGGAAAAGAAAAACCCAG
TTTCTTAGGAAACGCAAACGATTTATTATCCAGATTATTTGGATAAGTCCTTTTTAAAA

FIGURE 146

MGARSGARGALLLALLLCWDPRLSQAGTDSGSEVLPDSFPSAPAEPLPYFLQEPQDAYIVKNK
PVELRCRAFPATQIYFKCNGEWVSQNDHVTQEGLDEATGLRVREVQIEVSRQQVEELFGLEDY
WCQCVAWSSAGTTKSRRAYVRIAYLRKNFDQEPLGKEVPLDHEVLLQCRPPEGVPVAEVEWLK
NEDVIDPTQDTNFLLTIDHNLIIRQARLSDTANYTCVAKNIVAKRRSTTATVIVYVNGGWSSW
AEWSPCSNRCGRGWQKRTRTCTNPAPLNGGAFCEGQAFQKTACTTICPVDGAWTEWSKWSACS
TECAHWRSRECMAPPPQNGGRDCSGTLLDSKNCTDGLCMQNKKTLSDPNSHLLEASGDAALYA
GLVVAIFVVVAILMAVGVVVYRRNCRDFDTDITDSSAALTGGFHPVNFKTARPSNPQLLHPSV
PPDLTASAGIYRGPVYALQDSTDKIPMTNSPLLDPLPSLKVKVYSSSTTGSGPGLADGADLLG
VLPPGTYPSDFARDTHFLHLRSASLGSQQLLGLPRDPGSSVSGTFGCLGGRLSIPGTGVSLLV
PNGAIPQGKFYEMYLLINKAESTLPLSEGTQTVLSPSVTCGPTGLLLCRPVILTMPHCAEVSA
RDWIFQLKTQAHQGHWEEVVTLDEETLNTPCYCQLEPRACHILLDQLGTYVFTGESYSRSAVK
RLQLAVFAPALCTSLEYSLRVYCLEDTPVALKEVLELERTLGGYLVEEPKPLMFKDSYHNLRL
SLHDLPHAHWRSKLLAKYQEIPFYHIWSGSQKALHCTFTLERHSLASTELTCKICVRQVEGEG
QIFQLHTTLAETPAGSLDTLCSAPGSTVTTQLGPYAFKIPLSIRQKICNSLDAPNSRGNDWRM
LAQKLSMDRYLNYFATKASPTGVILDLWEALQQDDGDLNSLASALEEMGKSEMLVAVATDGDC

Important features of the protein:

Signal peptide:

amino acids 1-26

Transmembrane domain:

amino acids 374-395

N-glycosylation sites.

amino acids 222-225, 347-350

Glycosaminoglycan attachment site.

amino acids 492-495

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 233-236, 234-237

Casein kinase II phosphorylation sites.

amino acids 30-33, 87-90, 251-254, 341-344, 359-362, 629-632, 651-654, 706-709, 757-760, 827-830, 925-928, 941-944

Tyrosine kinase phosphorylation sites.

amino acids 216-223, 773-780

N-myristoylation sites.

amino acids 2-7, 6-11, 27-32, 96-101, 137-142, 179-184, 247-252, 281-286, 334-339, 379-384, 491-496, 495-500, 509-514, 542-547, 547-552, 550-555, 553-558, 560-565, 611-616, 785-790, 834-839, 844-849

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 541-551

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

amino acids 926-933

Growth factor and cytokines receptors family signature 2.

amino acids 306-312

FIGURE 147

GAGAGGGACAGAGGCTGGAGAAGGATGTATGGCCTGCCCTGGGCTTGTCTGTTCCCTCCTGAGCCTGAGCCCCTT
ACCTTCCTGACCCC**ATG**AAGCACACACTGGCTCTGCTGGCTCCCCTGCTGGGCCTGGGCCTGGGGCTGGCCCTGA
GTCAGCTGGCTGCAGGGGCCACAGACTGCAAGTTCCTTGGCCCGGCAGAGCACCTGACATTCACCCCAGCAGCCA
GGGCCCGGTGGCTGGCCCCTCGAGTTCGTGCGCCAGGACTCCTGGACTCCCTCTATGGCACCGTGCGCCGCTTCC
TCTCGGTGGTGCAGCTCAATCCTTTCCCTTCAGAGTTGGTAAAGGCCCTACTGAATGAGCTGGCCTCCGTGAAGG
TGAATGAGGTGGTGCGGTACGAGGCGGGCTACGTGGTATGCGCTGTGATCGCGGGCCTCTACCTGCTGCTGGTGC
CCACTGCCGGGCTTTGCTTCTGCTGCTGCCGCTGCCACCGGCGCTGCGGGGGACGAGTGAAGACAGAGCACAAGG
CGCTGGCCTGTGAGCGCGCGGCCCTCATGGTCTTCCTGCTGCTGACCACCCTCTTGCTGCTGATTGGTGTGGTCT
GTGCCTTTGTCACCAACCAGCGCACGCATGAACAGATGGGCCCCAGCATCGAGGCCATGCCTGAGACCCTGCTCA
GCCTCTGGGGCCTGGTCTCTGATGTCCCCCAAGAGCTGCAGGCCGTGGCACAGCAATTCTCCCTGCCCCAGGAGC
AAGTCTCAGAGGAGCTGGATGGTGTTGGTGTGAGCATTGGGAGCGCGATCCACACTCAGCTCAGGAGCTCCGTGT
ACCCCTTGCTGGCGGCCGTGGGCAGTTTGGGCCAGGTCCTGCAGGTCTCCGTGCACCACCTGCAAACCTTGAATG
CTACAGTGGTAGAGCTGCAGGCCGGGCAGCAGGACCTGGAGCCAGCCATCCGGGAACACCGGGACCGCCTCCTTG
AGCTGCTGCAGGAGGCCAGGTGCCAGGGAGATTGTGCAGGGGCCCTGAGCTGGGCCCGCACCCTGGAGCTGGGTG
CTGACTTCAGCCAGGTGCCCTCTGTGGACCATGTCCTGCACCAGCTAAAAGGTGTCCCCGAGGCCAACTTCTCCA
GCATGGTCCAGGAGGAGAACAGCACCTTCAACGCCCTTCCAGCCCTGGCTGCCATGCAGACATCCAGCGTGGTGC
AAGAGCTGAAGAAGGCAGTGGCCCAGCAGCCGGAAGGGGTGAGGACACTGGCTGAAGGGTTCCCGGGCTTGGAGG
CAGCTTCCCGCTGGGCCCAGGCACTGCAGGAGGTGGAGGAGAGCAGCCGCCCCTACCTGCAGGAGGTGCAGAGAT
ACGAGACCTACAGGTGGATCGTGGGCTGCGTGCTGTGCTCCGTGGTCCTATTCGTGGTGCTCTGCAACCTGCTGG
GCCTCAATCTGGGCATCTGGGGCCTGTCTGCCAGGGACGACCCCAGCCACCCAGAAGCCAAGGGCGAGGCTGGAG
CCCGCTTCCTCATGGCAGGTGTGGGCCTCAGCTTCCTCTTTGCTGCACCCCTCATCCTCCTGGTGTTCGCCACCT
TCCTGGTGGGTGGCAACGTGCAGACGCTGGTGTGCCGGAGCTGGGAGAACGGCGAGCTCTTTGAGTTTGCAGACA
CCCCAGGGAACCTGCCCCCGTCCATGAACCTGTCGCAACTTCTTGGCCTGAGGAAGAACATCAGCATCCACCAAG
CCTATCAGCAGTGCAAGGAAGGGGCAGCGCTCTGGACAGTCCTGCAGCTCAACGACTCCTACGACCTGGAGGAGC
ACCTGGATATCAACCAGTATACCAACAAGCTACGGCAGGAGTTGCAGAGCCTGAAAGTAGACACACAGAGCCTGG
ACCTGCTGAGCTCAGCCGCCCGCCGGGACCTGGAGGCCCTGCAGAGCAGTGGGCTTCAGCGCATCCACTACCCCG
ACTTCCTCGTTCAGATCCAGAGGCCCGTGGTGAAGACCAGCATGGAGCAGCTGGCCCAGGAGCTGCAAGGACTGG
CCCAGGCCCAAGACAATTCTGTGCTGGGGCAGCGGCTGCAGGAGGAGGCCCAAGGACTCAGAAACCTTCACCAGG
AGAAGGTCGTCCCCCAGCAGAGCCTTGTGGCAAAGCTCAACCTCAGCGTCAGGGCCCTGGAGTCCTCTGCCCCGA
ATCTCCAGCTGGAGACCTCAGATGTCCTAGCCAATGTCACCTACCTGAAAGGAGAGCTGCCTGCCTGGGCAGCCA
GGATCCTGAGGAATGTGAGTGAGTGTTTCCTGGCCCGGGAGATGGGCTACTTCTCCCAGTACGTGGCCTGGGTGA
GAGAGGAGGTGACTCAGCGCATTGCCACCTGCCAGCCCCTCTCCGGAGCCCTGGACAACAGCCGTGTGATCCTGT
GTGACATGATGGCTGACCCCTGGAATGCCTTCTGGTTCTGCCTGGCATGGTGCACCTTCTTCCTGATCCCCAGCA
TCATCTTTGCCGTCAAGACCTCCAAATACTTCCGTCCTATCCGGAAACGCCTCAGCTCCACCAGCTCTGAGGAGA
CTCAGCTCTTCCACATCCCCCGGGTTACCTCCCTGAAGCTG**TAG**GGCCTTGTGGGGTGAGGTGACCCTGAGGCTG
CCTGTCCTCCCCTTTGATTTAGCCTGGGCCACAGGACTTCGGTAGCTCTTGCCCCAGAGCCCAGGCTGGCATCCA
GGCCTGGACTGTCCCCAGTTCCGGCTTACCTGGCCCCACCTTGCCTGCTCCTTTCCACCCCTTTCTGCTCACGAC
CCCCATCATTCACGCTCAGAATCACATGGGACTTCTGTGCAGCTGCAGAGCCAGCAAGTCCCTACAGGTGTCACC
CGTTACCCCCATGCTGGTGGCATCCTCACAGGAAGAGCCTGTTCTCCACCTGCTGGAGCCTGGACCCTGGGGTGG
GACAGAGGCCTCGTCCAACCCCACTCCCCTTCCCGTGTGTCTTCCCCCTGCCAAGCCTCCCCCTGCCAAGCCTCC
CCCTGCCCCTCTCTGAGCCCCTCGCCCCCCACACCGTCCTCATCTGGCCTCCCCCCTGGCCCCCACTTCCCTCTT
ATGCCCTTCCTGGCCCTTTGCTTCCTCCCTTAGTCCCCTCTTCACCATATCTCCACTGCTACCTTGCTGGCCCCA
GAGACCACCCTGCCCAACCAAACCACTCAGGTAACGCCACTAATCAGGCAGGGGCCACCATGGCCTAGGTCTGGG
CTGGCTGCAGGCCCTGCCTCATGGCCTCTGAGCCCTCCACTGCCCCAGGGCCTTGGGCCCTCTGCAGATCTCATC
CAGGATTTATTGTTGTCCAGTGGGGTGAGGGAGGCCTGTCTGAAGGCCGAGCCTCCCTGCCTGCACCCAAGTTAG
AAATGGGGGTACCAGCACTTAGCTTCTCTCTGAGTGCTGGCTCCCAAGGAAGGGACCTGGGACCTGGGCCACAGT
GGGGGCTTGCCCTTACCTCTTCAGAAGGAAGCATCTTCCACAGCCCCCACCCAACTTTCTTAGGAGTGATCTGGT
GGCCAGAACAGGATTTTGCACGGCCCCTTTTATCCTGCGCATGTGGCCTAGGGTCATCCCCAGCCCATCCCTGTG
TCAGCCCTGAGTGCTGGACACTGCGTTCCAGAAATGAGGAAGAGGAGAGAGAAGAGATGGACAGACCTCAGATCC
ATTAAAGTGTTCTCACTTCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 148

MKHTLALLAPLLGLGLGLALSQLAAGATDCKFLGPAEHLTFTPAARARWLAPRVRAPGLL
DSLYGTVRRFLSVVQLNPFPSELVKALLNELASVKVNEVVRYEAGYVVCAVIAGLYLLLV
PTAGLCFCCCRCHRRCGGRVKTEHKALACERAALMVFLLLTTLLLLIGVVCAFVTNQRTH
EQMGPSIEAMPETLLSLWGLVSDVPQELQAVAQQFSLPQEQVSEELDGVGVSIGSAIHTQ
LRSSVYPLLAAVGSLGQVLQVSVHHLQTLNATVVELQAGQQDLEPAIREHRDRLLELLQE
ARCQGDCAGALSWARTLELGADFSQVPSVDHVLHQLKGVPEANFSSMVQEENSTFNALPA
LAAMQTSSVVQELKKAVAQQPEGVRTLAEGFPGLEAASRWAQALQEVEESSRPYLQEVQR
YETYRWIVGCVLCSVVLFVVLCNLLGLNLGIWGLSARDDPSHPEAKGEAGARTLMAGVGL
SFLFAAPLILLVFATFLVGGNVQTLVCRSWENGELFEFADTPGNLPPSMNLSQLLGLRKN
ISIHQAYQQCKEGAALWTVLQLNDSYDLEEHLDINQYTNKLRQELQSLKVDTQSLDLLSS
AARRDLEALQSSGLQRIHYPDFLVQIQRPVVKTSMEQLAQELQGLAQAQDNSVLGQRLQE
EAQGLRNLHQEKVVPQQSLVAKLNLSVRALESSAPNLQLETSDVLANVTYLKGELPAWAA
RILRNVSECFLAREMGYFSQYVAWVREEVTQRIATCQPLSGALDNSRVILCDMMADPWNA
FWFCLAWCTFFLIPSIIFAVKTSKYFRPIRKRLSSTSSEETQLFHIPRVTSLKL

Signal peptide:

amino acids 1-17

Transmembrane domain:

amino acids 105-125, 153-173, 428-449, 476-500, 778-797

N-glycosylation sites:

amino acids 270-273, 343-347, 352-356, 530-534, 540-546, 563-567, 684-688, 707-711, 725-729

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 811-815

Tyrosine kinase phosphorylation site.

amino acids 95-103

N-myristoylation sites.

amino acids 13-19, 15-21, 17-23, 26-32, 58-64, 124-130, 168-174, 228-234, 230-236, 320-326, 338-344, 393-399, 429-435, 446-452, 477-483, 500-506, 536-542, 644-650, 761-767

Phospholipase A2 histidine active site.

aminop acids 129-137

4Fe-4S ferredoxins, iron-sulfur binding region signature.

amino acids 126-138

Mitochondrial energy transfer proteins signature.

amino acids 80-89

FIGURE 149

CACAGCTCCCTTCCCAGGACGTGAAAATCTGCCTTCTCACC**ATG**AGGCTTCTAGTCCTTTCCA

GCCTGCTCTGTATCCTGCTTCTCTGCTTCTCCATCTTCTCCACAGAAGGGAAGAGGCGTCCTG

CCAAGGCCTGGTCAGGCAGGAGAACCAGGCTCTGCTGCCACCGAGTCCCTAGCCCCAACTCAA

CAAACCTGAAAGGACATCATGTGAGGCTCTGTAAACCATGCAAGCTTGAGCCAGAGCCCCGCC

TTTGGGTGGTGCCTGGGGCACTCCCACAGGTG**TAG**CACTCCCAAAGCAAGACTCCAGACAGCG

GAGAACCTCATGCCTGGCACCTGAGGTACCCAGCAGCCTCCTGTCTCCCCTTTCAGCCTTCAC

AGCAGTGAGCTGCAATGTTGGAGGGCTTCATCTCGGGCTGCAAGGACCCTGGGAAAGTTCCAG

AACTCCACGTCCTTGTCTCAATTGTGCCATCAACTTTCAGAGCTATCATGAGCCAACCTCACC

CCACAGGGCCTCAGTCGCCACCATGTGGGCCTCTCCAGTGCAAACCACCGAGCATTCCACCAT

GACCGGTCACAGCTACAAATCCAGAGACCATCAATCCTGCTAGAGTGCAGGGTGGCAAGCACC

CAAGGGTGGCTGACCAAGACTGCAGAGTCTCCTCCATCTTCAGGTCCATTCAGCCTCCTGGCA

TTTAACTACCAGCATCCAGTGGTCCCCAAGGAATCCCTTCCTAGCCTCCTGACATGAGTCTGC

TGGAAAGAGCATCCAAACAAACAAGTAATAAATAAATAAATAAACTCA

FIGURE 150

MRLLVLSSLLCILLLCFSIFSTEGKRRPAKAWSGRRTRLCCHRVPSPNSTNLKGHHVRLCKPC
KLEPEPRLWVVPGALPQV

Important features of the protein:

Signal peptide:

amino acids 1-21

N-glycosylation site.

amino acids 48-52

Amidation sites.

amino acids 23-27, 33-37

FIGURE 151

CACCGGAGGGCACGCAGCTGACGGAGCTGCGCTGCGTTCGCCTCGTTTGCCTCGCGCCCTCCA
CTGGAGCTGTTCGCGCCTCCCGGCTCCCACCGCAGCCCACCCGGCAGAGGAGTCGCTACCAGC
GCCCAGTGCGCTCTGTCAGTCCGCAAACTCCTTGCCGCCCGCCCCGGGCTGGGCACCAAATAC
CAGGCTACC**ATG**GTCTACAAGACTCTCTTCGCTCTTTGCATCTTAACTGCAGGATGGAGGGTA
CAGAGTCTGCCTACATCAGCTCCTTTGTCTGTTTCTCTTCCGACAAACATTGTACCACCGACC
ACCATCTGGACTAGCTCTCCACAAAACACTGATGCAGACACTGCCTCCCCATCCAACGGCACT
CACAACAACTCGGTGCTCCCAGTTACAGCATCAGCCCCAACATCTCTGCTTCCTAAGAACATT
TCCATAGAGTCCAGAGAAGAGGAGATCACCAGCCCAGGTTCGAATTGGGAAGGCACAAACACA
GACCCCTCACCTTCTGGGTTCTCGTCAACAAGCGGTGGAGTCCACTTAACAACCACGTTGGAG
GAACACAGCTCGGGCACTCCTGAAGCAGGCGTGGCAGCTACACTGTCGCAGTCCGCTGCTGAG
CCTCCCACACTCATCTCCCCTCAAGCTCCAGCCTCATCACCCTCATCCCTATCAACCTCACCA
CCTGAGGTCTTTTCTGCCTCCGTTACTACCAACCATAGCTCCACTGTGACCAGCACCCAACCC
ACTGGAGCTCCAACTGCACCAGAGTCCCCGACAGAGGAGTCCAGCTCTGACCACACACCCACT
TCACATGCCACAGCTGAGCCAGTGCCCCAGGAGAAAACACCCCCAACAACTGTGTCAGGCAAA
GTGATGTGTGAGCTCATAGACATGGAGACCACCACCACCTTTCCCAGGGTGATCATGCAGGAA
GTAGAACATGCATTAAGTTCAGGCAGCATCGCCGCCATTACCGTGACAGTCATTGCCGTGGTG
CTGCTGGTGTTTGGAGTTGCAGCCTACCTAAAAATCAGGCATTCCTCCTATGGAAGACTTTTG
GACGACCATGACTACGGGTCCTGGGGAAACTACAACAACCCTCTGTACGATGACTCC**TAA**CAA
TGGAATATGGCCTGGGATGAGGATTAACTGTTCTTTATTTATAAGTGCTTATCCAGTAGAATT
AATAAGTACCTGATGCGCATTGAACGACAATCTTAAGCCCTGTTTTGTTGGTATGGTTGTTTT
TGTTTTCCTCCCTCTCCTCTGGCTGCTACAACTTCCCCTTTCTGGTACAAGAAGAACCATTCT
TTAAAGGTGAGTGGAGGCTGATTTGCAGCTGAAGTGGGCCAGCCTTGCACCAGCCAGGCCAGA
CCACCATGGTGAAGGCTTCTTTCCCCACTGCAGGACCCACTTTGAGAAGGATCGAGGAGGAGG
ATTTGGGTTGTTTTGTTAGGGGTTACTTTCAGGGGAACATTTCATTTGTGTTATTTCTTAAAC
TTCTATTTAGGAAATTACATTAAGTATTAATGAGGGGAAAGGAAATGAGCTCTACGAGGATTT
CACCTTGCATGGGAGAGAGCAGGGTTTTCTCAGATTCCTTTTTTAATCTCTATTTATCTGGTTG
TTTCTGACAGGATGCTGCCTGCTTGGCTCTACGAGCTGGAAAGCAGCTTCTTAGCTGCCTAAT
TAATGAAAGATGAAAATAGGAAGTGCCCTGGAGGGGGCCAGCAGGTCACGGGGCAGAATCTCT
CAGGTTGCTGTGGGATCTCAGTGTGCCCCTACCTGTTCTCCCCTCCAGGCCACCTGTCTCTGT
AAAGGATGTCTGCTCTGTTCAAAAGGCAGCTGGGATCCCAGCCCACAAGTGATCAGCAGAGTT
GCATTTCCAAAGAAAAAGGCTATGAGATGAGCTGAGTTATAGAGAGAAAGGGAGAGGCATGTA
CGGTGTGGGGAAGTGGAAGAGAAGCTGGCGGGGGAGAAGGAGGCTAACCTGCACTGAGTACTT
CATTAGGACAAGTGAGAATCAGCTATTGATAATGGCCAGAGATATCCACAGCTTGGAGGAGCC
CAGAGACTGTTTGCTTTATACCCACACAGCAACTGGTCCACTGCTTTACTGTCTGTTGGATAA
TGGCTGTAAAATGTTTAAAAAC

FIGURE 152

MVYKTLFALCILTAGWRVQSLPTSAPLSVSLPTNIVPPTTIWTSSPQNTDADTASPSNGTHNN
SVLPVTASAPTSLLPKNISIESREEEITSPGSNWEGTNTDPSPSGFSSTSGGVHLTTTLEEHS
SGTPEAGVAATLSQSAAEPPTLISPQAPASSPSSLSTSPPEVFSASVTTNHSSTVTSTQPTGA
PTAPESPTEESSSDHTPTSHATAEPVPQEKTPPTTVSGKVMCELIDMETTTTFPRVIMQEVEH
ALSSGSIAAITVTVIAVVLLVFGVAAYLKIRHSSYGRLLDDHDYGSWGNYNNPLYDDS

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 153

ACGTCACTGTCTTGAAGCAGCAGTAGCCTGGGAAGTGAGGCAGGAGGAATTGAGAGGCAGGAA

GGGNGCTGGAGACACAGCTGAGCCTGGAAATGAGAGTGGGCATCGCCGTGGTCATCATGACTC

CTCTGCGGCGTGGTCACC**ATG**TTGGTTCACTGTGTTGGGCTCTTATTGACGGGTCTCCTGCTA

GGCCTGACCTTGGGTGCCGGAGCCCTGCTGGCTTCTGAGCCTATCTACCAACCACCTTCAGCC

TGGGTGCCAGCTGGGGGGCTGGTGGGGCTGGCGCTGCTGGGAGCCCTGCTCACACTTCGGTGG

CCACGTCCATTCACAGTTCTGGGCACAACCCTGCTGGGTTCTGCAGTGCTTGTGGCCTGTGTT

GACTACTTCCTGGAGGGGCTGGCACTGGGGAGTTGGCTGGGCCAACGCCTGCAGACACTTCCA

GCCTTGCCTTCTCTCTGC**TGA**TATAGCTGGGTCTTACTGGGGATCTGGCCAGCCTTGGGGGCC

CTTGGAGCCCTGGCCCAGTGGAAGCTCGTGCCTGAGGAACATGGAGGCCACGCTAATGGGTCT

GTTCCTGGTTTCCCAGATGCATAAAGGAAGACATATCCCTCCCCTGGGCAGCAAGGCTACAAT

GGGAGGGAGGGAGAACATGGGAGCATGTGAATAAAATGGCATTAAATACTGAAAAAAAAAAAA

AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 154

MLVHCVGLLLTGLLLGLTLGAGALLASEPIYQPPSAWVPAGGLVGLALLGALLTLRWPRPFTV
LGTTLLGSAVLVACVDYFLEGLALGSWLGQRLQTLPALPSLC

Signal peptide:

amino acids 1-20

Transmembrane domain:

amino acids 38-55, 60-78

N-myristoylation sites.

amino acids 7-13, 12-18, 16-22, 22-28, 41-47, 50-56, 84-90, 88-94

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 67-78

FIGURE 155

TGCAATTAAAGGAGTCGGGTCTCTAACTGTTGATCTGTTTTTTTCCCTTCTGAGCA**ATG**GAGC

TTACCATCTTTATCCTGAGACTGGCCATTTACATCCTGACATTTCCCTTGTACCTGCTGAACT

TTCTGGGCTTGTGGAGCTGGATATGCAAAAAATGGTTCCCCTACTTCTTGGTGAGGTTCACTG

TGATATACAACGAACAGATGGCAAGCAAGAAGCGGGAGCTCTTCAGTAACCTGCAGGAGTTTG

CGGGCCCCTCCGGGAAACTCTCCCTGCTGGAAGTGGGCTGTGGCACGGGGGCCAACTTCAAGT

TCTACCCACCTGGGTGCAGGGTGACCTGTATTGACCCCAACCCCAACTTTGAGAAGTTTTTGA

TCAAGAGCATTGCAGAGAACCGACACCTGCAGTTTGAGCGCTTTGTGGTAGCTGCCGGGGAGA

ACATGCACCAGGTGGCTGATGGCTCTGTGGATGTGGTGGTCTGCACCCTGGTGCTGTGCTCTG

TGAAGAACCAGGAGCGGATTCTCCGCGAGGTGTGCAGAGTGCTGAGACCGGGAGGGGCTTTCT

ATTTCATGGAGCATGTGGCAGCTGAGTGTTCGACTTGGAATTACTTCTGGCAACAAGTCCTGG

ATCCTGCCTGGCACCTTCTGTTTGATGGGTGCAACCTGACCAGAGAGAGCTGGAAGGCCCTGG

AGCGGGCCAGCTTCTCTAAGCTGAAGCTGCAGCACATCCAGGCCCCACTGTCCTGGGAGTTGG

TGCGCCCTCATATCTATGGATATGCTGTGAAA**TAG**TGTGAGCTGGCAGTTAAGAGCTGAATGG

CTCAAAGAATTTAAAGCTTCAGTTTTACATTTAAAATGCTAAGTGGGAGAAGAGAAACCTTTT

TTTTGGGGGGCGGTTTTTTTGGTTTGTTGTTGGTTTTTTTTTTTTTTTTGGCAGGAGAATCTC

TTGAACCCAGAAGGCGAAGGTTGCAGTGAACCGAGATCATGCCATTGTACTCTAGCCTGGGTG

ACAAGAGCAAGACTCCGTCTCAAAAAAAAAAAAAAAAAAAAAAAGAAGTAGAGACAGGGAGAC

GGGGTCTCACTGTGTTGCCTAGGCCGGTCTTGAACTCCTGGGCTCAAGTGATTCTCCCACCTT

GACCTCCTAAATTGTTGGGATTACAGGTGTGAGACAGTGCACCTGGCCGAAATAGCTCAAGTT

TCTGAAAAACAAATCTGAATCTATTTGTTATTCTTAGCGTCACTGGTCTGGCTTTCAGAATTA

ACATACAAGGTTGCCACACCTAGTTCTGCCCAGCTTTATGTCTTTTATTCCAGTATTCCACCA

AAGTTTGTTTTCCTGCATTCCAGTTCTCAAGTCTTAAGATAAAGATTGTACTTGACAGTTTAG

TATATCCATAAAACTATTTGAGGTGGTTAAGGTTCTTGGGTTCATTTTCCTTAATACTTTGCT

GAATATTGTAGATTGTAGGCAATGAAAAAGTCTACTAAATTAGGAAAACCTTGAATAATTAGG

TATCCTAGGTAAGAGCCCCTAAACATCAAGCAATCTGTGAGTCTGTAAAGAAATAAATATTTT

TTGGATTATTCTTATCTAATTCCACCCCTGTTGGAAGATGATTTCTTTGTTCTTTGCAACTAT

GGAAGCTGTGAAAATCATCACAAGTGCCTCTGAAAGCGAGTGTTAGGTTGGTTAGAGGGTTTA

ATATTTTCTGCAATGGTTTGTAGGAATTTTAATAAATGTAGTATATTTTCTGAGATGATTTTG

TAAAAGTACTATTTTAAATATCAAATCAACCAATAAATTCACATTTGTGTTAGGAACAAAA

FIGURE 156

MELTIFILRLAIYILTFPLYLLNFLGLWSWICKKWFPYFLVRFTVIYNEQMASKKRELFSNLQ
EFAGPSGKLSLLEVGCGTGANFKFYPPGCRVTCIDPNPNFEKFLIKSIAENRHLQFERFVVAA
GENMHQVADGSVDVVVCTLVLCSVKNQERILREVCRVLRPGGAFYFMEHVAAECSTWNYFWQQ
VLDPAWHLLFDGCNLTRESWKALERASFSKLKLQHIQAPLSWELVRPHIYGYAVK

Signal peptide:

amino acids 1-29

N-glycosylation site.

amino acids 203-207

N-myristoylation sites.

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

FIGURE 157

CCGCTGAGATGTACGAACTTCCGGTTCTCCGGGCAGCTGCCACTGCTGTAGCTTCTGCCACCT
GCCACGACCGGGCCTCTCCCTGGCGTTTGGTCACCTCTGCTTCATTCTCCACCGCGCCTATGG
TCCCTCTTGGAGCCAGCGTGGCGGGCCTGGCGGCTCCCGGGTGGTGAGAGAGCGGTCCGGGAA
CG**ATG**AAGGCCTCGCAGTGCTGCTGCTGTCTCAGCCACCTCTTGGCTTCCGTCCTCCTCCTGC
TGTTGCTGCCTGAACTAAGCGGGCCCCTGGCAGTCCTGCTGCAGGCAGCCGAGGCCGCGCCAG
GTCTTGGGCCTCCTGACCCTAGACCACGGACATTACCGCCGCTGCCACCGGGCCCTACCCCTG
CCCAGCAGCCGGGCCGTGGTCTGGCTGAAGCTGCGGGGCCGCGGGGCTCCGAGGGAGGCAATG
GCAGCAACCCTGTGGCCGGGCTTGAGACGGACGATCACGGAGGGAAGGCCGGGGAAGGCTCGG
TGGGTGGCGGCCTTGCTGTGAGCCCCAACCCTGGCGACAAGCCCATGACCCAGCGGGCCCTGA
CCGTGTTGATGGTGGTGAGCGGCGCGGTGCTGGTGTACTTCGTGGTCAGGACGGTCAGGATGA
GAAGAAGAAACCGAAAGACTAGGAGATATGGAGTTTTGGACACTAACATAGAAAATATGGAAT
TGACACCTTTAGAACAGGATGATGAGGATGATGACAACACGTTGTTTGATGCCAATCATCCTC
GAAGA**TAA**GAATGTGCCTTTTGATGAAAGAACTTTATCTTTCTACAATGAAGAGTGGAATTTC
TATGTTTAAGGAATAAGAAGCCACTATATCAATGTTGGGGGGGTATTTAAGTTACATATATTT
TAACAACCTTTAATTTGCTGTTGCAATAAATACCGTATCCTTTTATTATATCTTTATATGTAT
AGAAGTACTCTATTAATGGGCTCAGAGATGTTGGGGATAAAGTATACTGTAATAATTTATCTG
TTTGAAAATTACTATAAAACGGTGTTTTCTGGTCGGTTTTTGTTTCCTGCTTACCATATGATT
GTAAATTGTTTTATGTATTAATCAGTTAATGCTAATTATTTTTGCTGATGTCATATGTTAAAG
AGCTATAAATTCCAACAACCAACTGGTGTGTAAAAATAATTTAAAATTTCCTTTACTGAAAGG
TATTTCCCATTTTTGTGGGGAAAAGAAGCCAAATTTATTACTTTGTGTTGGGGTTTTTAAAAT
ATTAAGAAATGTCTAAGTTATTGTTTGCAAAACAATAAATATGATTTTAAATTCTCTTAAAAA
AAAAA

FIGURE 158

MKASQCCCCLSHLLASVLLLLLLPELSGPLAVLLQAAEAAPGLGPPDPRPRTLPPLPPGPTPA
QQPGRGLAEAAGPRGSEGGNGSNPVAGLETDDHGGKAGEGSVGGGLAVSPNPGDKPMTQRALT
VLMVVSGAVLVYFVVRTVRMRRRNRKTRRYGVLDTNIENMELTPLEQDDEDDDNTLFDANHPRR

Signal peptide:

amino acids 1-28

Transmembrane domain:

amino acids 124-140

N-glycosylation site.

amino acids 83-87

N-myristoylation sites.

amino acids 69-75, 78-84, 81-87, 97-103, 103-109, 106-112, 157-160

FIGURE 159

GCTGCAGGCGGCGACGGCTACACC**ATG**GGCCGGCTGCTGCGGGCCGCCCGGCTGCCGCCGCTG
CTTTCGCCGCTGCTGCTTCTGCTGGTTGGGGGAGCGTTCCTGGGTGCCTGTGTGGCTGGGTCT
GATGAGCCTGGCCCAGAGGGCCTCACCTCCACCTCCCTGCTAGACCTCCTGCTGCCCACTGGC
TTGGAGCCACTGGACTCAGAGGAGCCTAGTGAGACCATGGGCCTGGGAGCTGGGCTGGGAGCC
TCTGGCTCAGGCTTCCCCAGCGAAGAGAATGAAGAGTCTCGGATTCTGCAGCCACCACAGTAC
TTCTGGGAAGAGGAGGAAGAGCTGAATGACTCAAGTCTGGACCTGGGACCCACTGCAGATTAT
GTTTTTCCTGACTTAACTGAGAAGGCAGGTTCCATTGAAGACACTAGCCAGGCTCAAGAGCTG
CCAAACCTCCCCTCTCCCTTGCCCAAGATGAATCTGGTTGAGCCTCCCTGGCATATGCCTCCC
AGAGAGGAGGAAGAAGAGGAAGAGGAAGAGGAGGAGAGGGAGAAGGAAGAGGTAGAGAAACAA
GAGGAGGAGGAAGAGGAGGAGCTGCTCCCTGTGAATGGATCCCAAGAAGAAGCCAAGCCTCAG
GTCCGTGACTTTTCTCTCACCAGCAGCAGCCAGACCCCAGGGGCCACCAAAAGCAGGCATGAA
GACTCCGGGGACCAGGCCTCATCAGGTGTGGAGGTGGAGAGCAGCATGGGGCCCAGCTTGCTG
CTGCCTTCAGTCACCCCAACTACAGTGACTCCGGGGGACCAGGACTCCACCAGCCAAGAGGCA
GAGGCCACAGTGCTGCCAGCTGCAGGGCTTGGGGTAGAGTTCGAGGCTCCTCAGGAAGCAAGC
GAGGAAGCCACTGCAGGAGCAGCTGGTTTGTCTGGCCAGCACGAGGAGGTGCCGGCCTTGCCT
TCATTCCCTCAAACCACAGCTCCCAGTGGGGCCGAGCACCCAGATGAAGATCCCCTTGGCTCT
AGAACCTCAGCCTCTTCCCCACTGGCCCCTGGAGACATGGAACTGACACCTTCCTCTGCTACC
TTGGGACAAGAAGATCTCAACCAGCAGCTCCTAGAAGGGCAGGCAGCTGAAGCTCAATCCAGG
ATACCCTGGGATTCTACGCAGGTGATCTGCAAGGACTGGAGCAATCTGGCTGGGAAAAACTAC
ATCATTCTGAACATGACAGAGAACATAGACTGTGAGGTGTTCCGGCAGCACCGGGGGCCACAG
CTCCTGGCCCTGGTGGAAGAGGTGCTGCCCCGCCATGGCAGTGGCCACCATGGGGCCTGGCAC
ATCTCTCTGAGCAAGCCCAGCGAGAAGGAGCAGCACCTTCTCATGACACTGGTGGGCGAGCAG
GGGGTGGTGCCCACTCAAGATGTCCTTTCCATGCTGGGTGACATCCGCAGGAGCCTGGAGGAG
ATTGGCATCCAGAACTATTCCACAACCAGCAGCTGCCAGGCGCGGGCCAGCCAGGTGCGCAGC
GACTACGGCACGCTCTTCGTGGTGCTGGTGGTCATTGGGGCCATCTGCATCATCATCATTGCG
CTTGGCCTGCTCTACAACTGCTGGCAGCGCCGGCTGCCCAAGCTCAAGCACGTGTCGCACGGC
GAGGAGCTGCGCTTCGTGGAGAACGGCTGCCACGACAACCCCCACGCTGGACGTGGCCAGCGAC
AGCCAGTCGGAGATGCAGGAGAAGCACCCCAGCCTGAACGGCGGCGGGGCCCTCAACGGCCCG
GGGAGCTGGGGGGCGCTCATGGGGGGCAAGCGGGACCCCGAGGACTCGGACGTGTTCGAGGAG
GACACGCACCTG**TGA**GCGCAGCCGAGGCGCAGGCCGAGTGGGCCGCCAGGACCAAGCGAGGTG
GACCCCGAAACGGACGGCCCGGAGCCCGCACCAGCCCCGCGCCTACCCGGGCCGCCCCCGCGG
CCTGGCCCTCGGCGCGGGCTCCTTCCCGCTTCCCCCGACTTCACACGGCGGCTTCGGACCAAC
TCCCTCACTCCCGCCCGAGGGGCAGGCCTCAAAGCCCGCCTTGGCCCCGCTTTCCCGCCCCTG
AACCCCGGCCCCGCGGGCGGCGGGCGGCGCTTCCTGCGCCCCGGGACTCAATTAAACCCGCCC
GGAGACCACGCCGGGCCCAGCAAAA

FIGURE 160

MGRLLRAARLPPLLSPLLLLLVGGAFLGACVAGSDEPGPEGLTSTSLLDLLLPTGLEPLDSEE
PSETMGLGAGLGASGSGFPSEENEESRILQPPQYFWEEEEELNDSSLDLGPTADYVFPDLTEK
AGSIEDTSQAQELPNLPSPLPKMNLVEPPWHMPPREEEEEEEEEEEREKEEVEKQEEEEEEEL
LPVNGSQEEAKPQVRDFSLTSSSQTPGATKSRHEDSGDQASSGVEVESSMGPSLLLPSVTPTT
VTPGDQDSTSQEAEATVLPAAGLGVEFEAPQEASEEATAGAAGLSGQHEEVPALPSFPQTTAP
SGAEHPDEDPLGSRTSASSPLAPGDMELTPSSATLGQEDLNQQLLEGQAAEAQSRIPWDSTQV
ICKDWSNLAGKNYIILNMTENIDCEVFRQHRGPQLLALVEEVLPRHGSGHHGAWHISLSKPSE
KEQHLLMTLVGEQGVVPTQDVLSMLGDIRRSLEEIGIQNYSTTSSCQARASQVRSDYGTLFVV
LVVIGAICIIIIALGLLYNCWQRRLPKLKHVSHGEELRFVENGCHDNPTLDVASDSQSEMQEK
HPSLNGGGALNGPGSWGALMGGKRDPEDSDVFEEDTHL

Signal peptide:

amino acids 1-29

Transmembrane domain:

amino acids 499-521

N-glycosylation sites.

amino acids 106-110, 193-197, 395-399, 480-484

Glycosaminoglycan attachment site.

amino acids 77-81

N-myristoylation sites.

amino acids 24-30, 28-34, 41-47, 69-75, 71-77, 73-79, 75-81, 216-222, 327-333, 455-461, 519-525, 574-580, 581-587, 584-590

Amidation site.

amino acids 588-592

FIGURE 161

CCAGGGCGGAGCGCAGCTGCGCCGGGCTTGGGCGCCTGGGGCCGCCGCTCCCCACCGTCGTTT

TCCCCACCGAGGCCGAGGCGTCCCGGAGTC**ATG**GCCGGCCTGAACTGCGGGGTCTCTATCGCA

CTGCTAGGGGTTCTGCTGCTGGGTGCGGCGCGCCTGCCGCGCGGGGCAGAAGCTTTTGAGATT

GCTCTGCCACGAGAAAGCAACATTACAGTTCTCATAAAGCTGGGGACCCCGACTCTGCTGGCA

AAACCCTGTTACATCGTCATTTCTAAAAGACATATAACCATGTTGTCCATCAAGTCTGGAGAA

AGAATAGTCTTTACCTTTAGCTGCCAGAGTCCTGAGAATCACTTTGTCATAGAGATCCAGAAA

AATATTGACTGTATGTCAGGCCCATGTCCTTTTGGGGAGGTTCAGCTTCAGCCCTCGACATCG

TTGTTGCCTACCCTCAACAGAACTTTCATCTGGGATGTCAAAGCTCATAAGAGCATCGGTTTA

GAGCTGCAGTTTTCCATCCCTCGCCTGAGGCAGATCGGTCCGGGTGAGAGCTGCCCAGACGGA

GTCACTCACTCCATCAGCGGCCGAATCGATGCCACCGTGGTCAGGATCGGAACCTTCTGCAGC

AATGGCACTGTGTCCCGGATCAAGATGCAAGAAGGAGTGAAAATGGCCTTACACCTCCCATGG

TTCCACCCCAGAAATGTCTCCGGCTTCAGCATTGCAAACCGCTCATCTATAAAACGTCTGTGC

ATCATCGAGTCTGTGTTTGAGGGTGAAGGCTCAGCAACCCTGATGTCTGCCAACTACCCAGAA

GGCTTCCCTGAGGATGAGCTCATGACGTGGCAGTTTGTCGTTCCTGCACACCTGCGGGCCAGC

GTCTCCTTCCTCAACTTCAACCTCTCCAACTGTGAGAGGAAGGAGGAGCGGGTTGAATACTAC

ATCCCGGGCTCCACCACCAACCCCGAGGTGTTCAAGCTGGAGGACAAGCAGCCTGGGAACATG

GCGGGGAACTTCAACCTCTCTCTGCAAGGCTGTGACCAAGATGCCCAAAGTCCAGGGATCCTC

CGGCTGCAGTTCCAAGTTTTGGTCCAACATCCACAAAATGAAAGCAGTGAG**TGA**GCCCCACTT

TCCTTTTTCTTCCTCCTCCAGCACCTTCGTTGTTTCCTGGGTAGTCTGCCTGGGTGAGGCTCC

CTTCCTGTTTCTCATCTGTGGCTTCTGAAACACTTAGACTCTGGACCCAGCAAGAGTTTCAGG

AAGTGGGTTGCTAGGCAGTTAGACAGGCTTGTTGGTGAACACCCGGTATGTAGTTCCATTTCA

GCACAATAAAAAGAAATCTTGCATTCAAGATGCTAAATTGTTTTTAACGAAAA

FIGURE 162

MAGLNCGVSIALLGVLLLGAARLPRGAEAFEIALPRESNITVLIKLGTPTLLAKPCYIVISKR
HITMLSIKSGERIVFTFSCQSPENHFVIEIQKNIDCMSGPCPFGEVQLQPSTSLLPTLNRTFI
WDVKAHKSIGLELQFSIPRLRQIGPGESCPDGVTHSISGRIDATVVRIGTFCSNGTVSRIKMQ
EGVKMALHLPWFHPRNVSGFSIANRSSIKRLCIIESVFEGEGSATLMSANYPEGFPEDELMTW
QFVVPAHLRASVSFLNFNLSNCERKEERVEYYIPGSTTNPEVFKLEDKQPGNMAGNFNLSLQG
CDQDAQSPGILRLQFQVLVQHPQNESSE

Signal peptide:

amino acids 1-29

N-glycosylation sites.

amino acids 39-43, 122-126, 180-184, 205-209, 213-217, 270-274, 310-314, 339-343

Tyrosine kinase phosphorylation site.

amino acids 276-284

N-myristoylation sites.

amino acids 3-9, 7-13, 158-164, 175-181, 191-197, 303-309

FIGURE 163

CAACCACACACCTGGGGAATTGCTGGCCTGACTTCTGACCCCTGACTCCTCATACCCTTCCTC
CAGAGCATGACATTTGACCACCAACTGAAACCTGACCTCTGACCCCAGACCACTGGCCCTTCC
CCCGCCCTGTGGTGACTTCATAAAGGTTACTAGCTTCTCCCCTGGCCTTGAGACCCACACG**AT**
GGCCCTGCTGGCTCTGGCCAGTGCCGTCCCCTCTGCCCTGCTGGCCCTGGCTGTCTTCAGGGT
GCCCGCCTGGGCCTGTCTCCTCTGCTTCACAACCTACTCTGAGCGCCTCCGCATCTGCCAGAT
GTTTGTTGGGATGCGGAGCCCCAAGCTTGAAGAGTGTGAGGAGGCCTTCACGGCCGCCTTCCA
GGGCCTCTCTGACACCGAAATCAGTGAGGAGACCATCCACACTTCATCAGTGTCCTGGGGAAG
GTGCAGAGGGAGGGCAGGAGAGGCCCAGAGGGTCAGGCTGAGGGACAGACAGAGAGAAACAGT
CAGAGGAGAAAGGCTCAAAGACCATGAGAACAACAGAGACTTAGGGACAGAGAGACACAGACA
GGGGAAGACAGCAGGGCAAAGACTCAGAGAGGGGAGGATGGAGAGTCAGAGAGGGGAAGATGG
AGACTCAGAGAGAGGGGAGGATGGAGACTCAGAGAGAGAGGAAGATGGAGACTCAGAGGGAAA
GATGGAGACTCAGGAGTATGGAGAGTCAGAGAGGGGAGGATGGACACTCAGGGGAGGATGGAG
AGTCAGGAGGATGGAGACTCATAGAAAGGGGAGGATGGAGAGTCAGGAGAGGTTGGAGACTGG
AGAGGGAATAGAGACCCAGAAAGGGGAGGATGGAGACTCAGAGGGTGGAAGATGGAGACTCAA
AGAGGATGGAAACCCAGAGAGAGGAGGACAGAGA**TGA**GGCAGAGACTAGGGGAAGCAGGATAG
CGACTGGTCGGGGGCAGAGACTCAGGGAGGATAGAGACTCACAGAGAGGTGAGGATAGAGACT
TGGGAGGGACTCAGGAAGCATAGCGACTGTGGGGCAAAGAGTCAGAGAGGGGAGGATACAGAC
TTGGGAGGGCAGAGACTCAGAAACAGAATGTTCGCATTAGGGACATGGTGTTGCGGGGAGCTG
CCTCCCCCAGCCCCTGCTCCCTCCCTCACCGCCAGACTATGATGAGAGAAGCCACCTGCATGA
CACCTTCACCCAGATGACCCATGCCCTGCAGGAGCTGGCTGCTGCCCAGGGATCCTTTGAGGT
TGCCTTCCCTGATGCTGCAGAGAAAATGAAGAAGGTCATTACACAGCTTAAAGAAGCCCAGGC
TTGCATCCCTCCCTGCGGTCTCCAGGAGTTCGCCCGGCGTTTCCTCTGCAGCGGGTGCTACTC
TAGGGTCTGCGACCTCCCGCTGGACTGCCCAGTTCAGGATGTGACAGTGACTCGGGGCGACCA
GGCTATGTTTTCTTGCATCGTAAACTTCCAGCTGCCAAAGGAGGAGATCACCTATTCCTGGAA
GTTCGCAGGAGGAGGTCTCCGGACTCAGGACTTGTCCTATTTCCGAGATATGCCGCGGGCCGA
AGGATACCTGGCGCGGATCCGGCCGGCTCAGCTCACGCACCGCGGGACGTTCTCCTGCGTGAT
CAAGCAAGACCAGCGCCCCCTGGCCCGGCTCTACTTCTTTCTTAACGTCCTCGGGGCCCTCGC
ATCAGCGAGTGCGACAGTGTTGGCGTGGTGAGTTCTGGGGACTCCGGAGCCCCAGCATCTAGC
TCCCCGCTGTCTCAGATCCCACCGAGAAGTCTGGGTTCCCAGCAACCTCCAACCCAGGAGGAT
GTTCTTTCGATGGTACTGCAGTGGCAACTAACAAAGGTATCTTTCCTCCTTCCCTATCCTATT
TCCATCCTGAAAATAAAGAATATATTTCAACTCTAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAA

FIGURE 164

MALLALASAVPSALLALAVFRVPAWACLLCFTTYSERLRICQMFVGMRSPKLEECEEAFTAAF
QGLSDTEISEETIHTSSVSWGRCRGRAGEAQRVRLRDRQRETVRGERLKDHENNRDLGTERHR
QGKTAGQRLREGRMESQRGEDGDSERGEDGDSEREEDGDSEGKMETQEYGESERGGWTLRGGW
RVRRMETHRKGRMESQERLETGEGIETQKGEDGDSEGGRWRLKEDGNPERGGQR

Signal peptide:

amino acids 1-26

N-myristoylation site.

amino acids 65-71

FIGURE 165

CAGAATCGCAGATTGCCAGCCCTTTTCCCGACCCCTACGGAAAGACGAGTCCAGGGGCCGTCC

TGGCGAGGTCAAAACATTTAGTCTGGTCTTTTCAGCGTGGACCCTGCCAGCAGCCAGGCC**ATG**

GAGCTCTCTGATGTCACCCTCATTGAGGGTGTGGGTAATGAGGTGATGGTGGTGGCAGGTGTG

GTGGTGCTGATTCTAGCCTTGGTCCTAGCTTGGCTCTCTACCTACGTAGCAGACAGCGGTAGC

AACCAGCTCCTGGGCGCTATTGTGTCAGCAGGCGACACATCCGTCCTCCACCTGGGGCATGTG

GACCACCTGGTGGCAGGCCAAGGCAACCCCGAGCCAACTGAACTCCCCCATCCATCAGAGGGT

AATGATGAGAAGGCTGAAGAGGCGGGTGAAGGTCGGGGAGACTCCACTGGGGAGGCTGGAGCT

GGGGGTGGTGTTGAGCCCAGCCTTGAGCATCTCCTTGACATCCAAGGCCTGCCCAAAAGACAA

GCAGGTGCAGGCAGCAGCAGTCCAGAGGCCCCCCTGAGATCTGAGGATAGCACCTGCCTCCCT

CCCAGCCCTGGCCTCATCACTGTGCGGCTCAAATTCCTCAATGATACCGAGGAGCTGGCTGTG

GCTAGGCCAGAGGATACCGTGGGTGCCCTGAAGAGCAAATACTTCCCTGGACAAGAAAGCCAG

ATGAAACTGATCTACCAGGGCCGCCTGCTACAAGACCCAGCCCGCACACTGCGTTCTCTGAAC

ATTACCGACAACTGTGTGATTCACTGCCACCGCTCACCCCCAGGGTCAGCTGTTCCAGGCCCC

TCAGCCTCCTTGGCCCCCTCGGCCACTGAGCCACCCAGCCTTGGTGTCAATGTGGGCAGCCTC

ATGGTGCCTGTCTTTGTGGTGCTGTTGGGTGTGGTCTGGTACTTCCGAATCAATTACCGCCAA

TTCTTCACAGCACCTGCCACTGTCTCCCTGGTGGGAGTCACCGTCTTCTTCAGCTTCCTAGTA

TTTGGGATGTATGGACGA**TAA**GGACATAGGAAGAAAATGAAAGGCATGGTCTTTCTCCTTTAT

GGCCTCCCCACTTTTCCTGGCCAGAGCTGGGCCCAAGGGCCGGGGAGGGAGGGGTGGAAAGGA

TGTGATGGAAATCTCCTCCATAGGACACAGGAGGCAAGTATGCGGCCTCCCCTTCTCATCCAC

AGGAGTACAGATGTCCCTCCCGTGCGAGCACAACTCAGGTAGAAATGAGGATGTCATCTTCCT

TCACTTTTAGGGTCCTCTGAAGGAGTTCAAAGCTGCTGGCCAAGCTCAGTGGGGAGCCTGGGC

TCTGAGATTCCCTCCCACCTGTGGTTCTGACTCTTCCCAGTGTCCTGCATGTCTGCCCCCAGC

ACCCAGGGCTGCCTGCAAGGGCAGCTCAGCATGGCCCCAGCACAACTCCGTAGGGAGCCTGGA

GTATCCTTCCATTTCTCAGCCAAATACTCATCTTTTGAGACTGAAATCACACTGGCGGGAATG

AAGATTGTGCCAGCCTTCTCTTATGGGCACCTAGCCGCCTTCACCTTCTTCCTCTACCCCTTA

GCAGGAATAGGGTGTCCTCCCTTCTTTCAAAGCACTTTGCTTGCATTTTATTTTATTTTTTTA

AGAGTCCTTCATAGAGCTCAGTCAGGAAGGGGATGGGGCACCAAGCCAAGCCCCCAGCATTGG

GAGCGGCCAGGCCACAGCTGCTGCTCCCGTAGTCCTCAGGCTGTAAGCAAGAGACAGCACTGG

CCCTTGGCCAGCGTCCTACCCTGCCCAACTCCAAGGACTGGGTATGGATCGCTGGGCCCTAGG

CTCTTGCTTCTGGGGCTATTGGAGGGTCAGTGTCTGTGACTGAATAAAGTTCCATTTTGTGGA

AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 166

MELSDVTLIEGVGNEVMVVAGVVVLILALVLAWLSTYVADSGSNQLLGAIVSAGDTSVLHLGH
VDHLVAGQGNPEPTELPHPSEGNDEKAEEAGEGRGDSTGEAGAGGGVEPSLEHLLDIQGLPKR
QAGAGSSSPEAPLRSEDSTCLPPSPGLITVRLKFLNDTEELAVARPEDTVGALKSKYFPGQES
QMKLIYQGRLLQDPARTLRSLNITDNCVIHCHRSPPGSAVPGPSASLAPSATEPPSLGVNVGS
LMVPVFVVLLGVVWYFRINYRQFFTAPATVSLVGVTVFFSFLVFGMYGR

Signal peptide:

amino acids 1-36

Transmembrane domains:

amino acids 246-267, 275-301

N-glycosylation sites.

amino acids 162-166, 211-215

N-myristoylation sites.

amino acids 48-54, 105-111, 109-115, 129-135, 177-183, 247-253

Cell attachment sequence.

amino acids 97-100

FIGURE 167

GGCGGCTGTGTGTCGCCGGAGCCGAAGCGCGCAGGCCCGTCCCGGTGGCCGGGGAGCGGGCGGGTGGGGGCGCC**A**
TGTGGTTCATGTACCTGCTGAGCTGGCTGTCGCTCTTCATCCAGGTGGCCTTCATCACGCTGGCTGTCGCGGCTG
GACTCTATTACCTGGCAGAACTGATAGAAGAATACACAGTGGCCACCAGCAGGATCATAAAATACATGATCTGGT
TCTCCACCGCTGTACTGATTGGCCTCTACGTCTTTGAGCGCTTCCCCACCAGCATGATTGGAGTGGGCCTATTCA
CCAACCTCGTCTACTTTGGCCTCCTCCAGACCTTCCCCTTCATCATGCTGACCTCGCCTAACTTCATCCTGTCGT
GTGGACTAGTGGTGGTGAATCATTACCTAGCATTTCAGTTTTTTGCAGAAGAATATTATCCCTTCTCAGAGGTCC
TGGCCTATTTCACTTTCTGCCTGTGGATAATTCCGTTTGCGTTTTTTGTGTCACTTTCGGCCGGGGAGAACGTCC
TGCCCTCTACCATGCAGCCAGGAGATGATGTCGTCTCCAATTATTTCACCAAAGGCAAGCGGGGCAAACGCTTAG
GGATCCTGGTTGTCTTCTCCTTCATCAAAGAGGCCATTCTACCCAGTCGTCAGAAGATATAC**TGA**CCCCCATGCA
GGCAGGATGTGGGGGGCAAGATCAGGAGAGTCAGGCCCCTGGGCCTCTATGCCAGGTGGGGACCAGAAGTCGGGA
AGGCACCTACCACCTGCCCTGGCTTTCTTCCCCTCAACTCTGGAGCCCCATCCCCACCCTCCTTGGGGGGCTCAG
CTTGGCTCAGATCTGATGCTTCAAGAGGCTGTAACCTCAGAGGGCACCAAGGAGGGTGGCAGAGCCTGCTTAGCC
AGGAGGCCGAGGTCCCTCAGTCCTCCCCCTGTCCCTTCCAAGGTGGGTCAGGAGGTTCTGGCCCCGCTGGGGCAGG
CAGGGCAGGGTCTGTGAAGCTTAAGAGCAGATGGTGACAAGTTCTCTGGGCAGGTGGCCATGGGGAGGGGCCATG
GCTTGGCATGTCCAACAGAAATAGTTTTTGCTGTTGAACGGTGATTTCTGTCCAAGTGCAGATTTCCGTTTGAAT
AAAGCTTCGCTTCTAGGTGGCACTGTTTGCCTTAATACCCTGACAGTTCATCTTCCTTTCTTCCTGCTAACCTTC
TGCTCTGGACTGGACTCACTTTTCTGCTCCAGGGACTCCTTTTCTGGGTTTGGGTCTTGCCCTTCCCAAGGGACT
GTTCTTGTGGCCCTTAATGGGAAGGGGGCAGGGGTGAGGAGCTGAGCCTGCTCAAGGAGTGGGAAGTGGGGCTAT
AGGCAGCCTCTCTGATGCACTCTCTTCCATCTCTTTCCCCAAGGCTCCGTGACTGTCAAACTGGGAGTAGGAGAG
GGGACAATTTAGGACTGGGCTAGATTTTCAGAAGAACATCTACAATATCCTATTTATAAATCTTCCTCTGGGAAA
AGGAGTGGTTTCTGGCTGAATACTATCTTAGGCTCAAGGAGAAACAAAATAAAAATTAGCTTCCAGGCAGCCTGT
TTTTAAAGAAATGGGACTAATGGGAGAAGCTGTTTGTCACTCTAAGAGCATCCAAGCCCTGGCCCGTCTGTGCAC
TCTTGGCTCCTGGGGAGATATATCTGCCTTCTAAGAAGGCAGGCCAGGTCTTGGGCACAGACCTGCATTTGTTGA
CCTTGCACTCCAACTATAGTGCCTTGCAAGTGCTCAACAGTACATATTGGAATGAAGTCCCTATGAGAGCCATTT
CTGGCCATGTTCTATACCTCAAAGTGAGGCTGGCAGGTACAGAGATGAACTGTACACATGTGATACATTTAAGCC
ACTGGAAAAACCCCTGTGCTTGAAAATATTTCCTCTATATCATGCCTGGAGTTCCATCATAGCCCTTCATTTCCT
TGGCTTTAGCATTTACCTTCTCTTAAGAATACCAGCTTTCCCCTTTCCCTGAGAGGAAGAGCACATGTTGGTCTC
CTCTTAGTGTGAACGAGATTGCCAGGCCCTTTTCTCCTATGCACACCAGGATAGACAAGGCAGGGGATACTGGCA
GCCTGCATCATCCTCCCATTGGGCTGACAGCTGGCCCTACTTTCCTCCCTCTGCTGCTTGGTCCCTCACCTTGAT
GATGTGGCTTCGCCCCCTCCACTCTACTGCCAGTGTTCTCCCAGGGGTTGCTAAATCCAGCAGACCCCTTTCCTG
TCTTACTAGATCTGGGCAGCATTTGACATGGCTGATCACCCCTTGCTTCTTGGATGGCACTTCCCTGGCACCTCT
GTGGCTAGTTGTCCTACCTCCCTGGCTGTTCCTTTCAGGCTTCCGTGCAGGCTTCTCCACTTGCCCATGCACAGT
AGGGTCTTTCAGGGTTCTGCTGTGGGCTCCCTAGGGAAGCCCATCCATCTGGATGGTTTCAAGGATGGTGAGGAA
TTTAGAGTTGACCTCCAGCCCCAACATCCTTCCTGATCACCTGAACCACAGTTTTGCTGCCCTCTAGGTGCACAG
ACAATTCAGGTCCATGGCCCAGATGGTACTTGCTGTCTTCTGCAAACCTGCCCCTTCTGGGTACTTCCCTTGACC
CCGAGATCACTCAGGAGCCAGACAGGAAACTTATTCTATTCCTGTTTTCTCTTTCTGCCCACCACATCCAATCTC
TCAAAACGGTCAGGTCTACCTTAACATCTCTTGATTTGAGCCACTCCCACTGTCATCAGCTTTCACCTGGATTAT
CGTGACAGCCTCCTACTGCTTCTCTATCATGTGGCCAGAGCTATCTTCCTAAAATGCATTGCATAGTTGATCAAG
TCACTCTCTGGCCTAAAACCTTCCTTGGCTCCCTGCTGCCCTCAGGATAAAGTCTGGACCCCTCAGCATGGCTTG
TGAGACTCATGGTGTCCTTGTCCCTGCTCACCTCTCTGGTCTCATCACTTGCCTTCTTGCATTCTGGGTCCCAGC
CTCCTGTATCCAGAGATGCAGTGGCTCTCCATTGCCACTCTGATTCCTCCTTTCTTTTGGTCACAGAGAAAGGGT
ACTTTCTCTGTCAAATCTCAACTTAGACTTGACTTCCTCCAAGGAGCTTTGGCTATACTCTCTCCTCCCGACCCC
CACCCTGGCATACTACACAGATCACTCTGGGCTCACTTGCCTGCCTAATGGTCATCTCCCCAGTAGACTGTAAGC
TCCTTGAGGGCAAGGATTGTGTTGGAATTTTTGTATTAACAGTGCCTGGCTTGGTGCCTGGCACCTAGAAAGCAC
TCAATAAATGTTTGTTTAATGAA

FIGURE 168

MWFMYLLSWLSLFIQVAFITLAVAAGLYYLAELIEEYTVATSRIIKYMIWFSTAVLIGLYVFE
RFPTSMIGVGLFTNLVYFGLLQTFPFIMLTSPNFILSCGLVVVNHYLAFQFFAEEYYPFSEVL
AYFTFCLWIIPFAFFVSLSAGENVLPSTMQPGDDVVSNYFTKGKRGKRLGILVVFSFIKEAIL
PSRQKIY

Signal peptide:

amino acids 1-25

Transmembrane domain:

amino acids 126-146

Casein kinase II phosphorylation site.

amino acids 145-148

N-myristoylation sites.

amino acids 73-78, 82-87

Amidation sites.

amino acids 168-171, 171-174

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 91-101

FIGURE 169

CAAAGCCCTACCCTCACCATTCACCAGGTCCTGTGGGAAGAGCAGCGTGGAGGTGGGCTGAGG
TTAGAAGGTGCAGAGCGTGGAAGAAGATTGTGAGCTGAGTATTGGACATCTGTTCTTGAATAG
TCCCTGGGCCTGCCATAGGAAAGGAAGTTCTCCAGGGTTACAGTTCTTATCCGCGTGAATACA
C**ATG**GCTCTGTTACGAAAAATTAATCAGGTGCTGCTGTTCCTTCTGATCGTGACCCTCTGTGT
GATTCTGTATAAGAAAGTTCATAAGGGGACTGTGCCCAAGAATGACGCAGATGATGAATCCGA
GACTCCTGAAGAACTGGAAGAAGAGATTCCTGTGGTGATTTGTGCTGCAGCAGGGAGGATGGG
TGCCACTATGGCTGCCATCAATAGCATCTACAGCAACACTGACGCCAACATCTTGTTCTATGT
AGTGGGACTCCGGAATACTCTGACTCGAATACGAAAATGGATTGAACATTCCAAACTGAGAGA
AATAAACTTTAAAATCGTGGAATTCAACCCGATGGTCCTCAAAGGGAAGATCAGACCAGACTC
ATCGAGGCCTGAATTGCTCCAGCCTCTGAACTTTGTTCGATTTTATCTCCCTCTACTTATCCA
CCAACACGAGAAAGTCATCTATTTGGACGATGATGTAATTGTACAAGGTGATATCCAAGAACT
GTATGACACCACCTTGGCCCTGGGCCACGCGGCGGCTTTCTCAGATGACTGCGATTTGCCCTC
TGCTCAGGACATAAACAGACTCGTGGGACTTCAGAACACATATATGGGCTATCTGGACTACCG
GAAGAAGGCCATCAAGGACCTTGGCATCAGCCCCAGCACCTGCTCTTTCAATCCTGGTGTGAT
TGTTGCCAACATGACAGAATGGAAGCACCAGCGCATCACCAAGCAATTGGAGAAATGGATGCA
AAAGAATGTGGAGGAAAACCTCTATAGCAGCTCCCTGGGAGGAGGGGTGGCCACCTCCCCAAT
GCTGATTGTGTTTCATGGGAAATATTCCACAATTAACCCCCTGTGGCACATAAGGCACCTGGG
CTGGAATCCAGATGCCAGATATTCGGAGCATTTTCTGCAGGAAGCTAAATTACTCCACTGGAA
TGGAAGACATAAACCTTGGGACTTCCCTAGTGTTCACAACGACTTATGGGAAAGCTGGTTTGT
TCCTGACCCTGCAGGGATATTTAAACTCAATCACCATAGC**TGA**TATAACTCTACCCTTAAAAT
ATTCCCTGTATAGAAATGTGGAATTGTCCCTTTGTAGCCAACTATAACATTGTTCTTTATGAA
TATTACCTTTGATACATATGATCCACAATATAAAAACCAAAAACTACTGTGTGCAAATTATAC
CTTGGACCATATAGGCATTGATTAACTTCTTTAAGTACATGTGATAACTATGGAAATCAAGAT
TATGTGACTGAAAAACATAAAGGAAGAGACCCATCTAGATAACAGCAATCAACCTGCTTAATT
CTGAATGACAATTATATCCACAAATTTTTAAAACTTCTACATGTATTTTTCACATGAAGATCT
CCTTAACAGGTTGCCAACCTTTTCTTTTATAAAACTATTACATTTAAAATATGGACGTCTGAA
AAATAAAATATTCATCATTTTTAAAA

FIGURE 170

MALLRKINQVLLFLLIVTLCVILYKKVHKGTVPKNDADDESETPEELEEEIPVVICAAAGRMG
ATMAAINSIYSNTDANILFYVVGLRNTLTRIRKWIEHSKLREINFKIVEFNPMVLKGKIRPDS
SRPELLQPLNFVRFYLPLLIHQHEKVIYLDDDVIVQGDIQELYDTTLALGHAAAFSDDCDLPS
AQDINRLVGLQNTYMGYLDYRKKAIKDLGISPSTCSFNPGVIVANMTEWKHQRITKQLEKWMQ
KNVEENLYSSSLGGGVATSPMLIVFHGKYSTINPLWHIRHLGWNPDARYSEHFLQEAKLLHWN
GRHKPWDFPSVHNDLWESWFVPDPAGIFKLNHHS

Signal peptide:

amino acids 1-20

N-glycosylation site.

amino acids 234-238

Tyrosine kinase phosphorylation site.

amino acids 253-261

N-myristoylation sites.

amino acids 63-69, 86-92, 198-204, 218-224, 229-235, 265-271, 266-272

FIGURE 171

GCCAGAGGCTGCAGCTGGAGCCCAGAGCCCAAG**ATG**GAGCCCCAGCTGGGGCCTGAGGCTGCC

GCCCTCCGCCCTGGCTGGCTGGCCCTGCTGCTGTGGGTCTCAGCCCTGAGCTGTTCTTTCTCC

TTGCCAGCTTCTTCCCTTTCTTCTCTGGTGCCCCAAGTCAGAACCAGCTACAATTTTGGAAGG

ACTTTCCTCGGTCTTGATAAATGCAATGCCTGCATCGGGACATCTATTTGCAAGAAGTTCTTT

AAAGAAGAAATAAGATCTGACAACTGGCTGGCTTCCCACCTTGGACTGCCTCCCGATTCCTTG

CTTTCTTATCCTGCAAATTACTCAGATGATTCCAAAATCTGGCGCCCTGTGGAGATCTTTAGA

CTGGTCAGCAAATATCAAAACGAGATCTCAGACAGGAGAATCTGTGCCTCTGCATCAGCCCCA

AAGACCTGCAGCATTGAGCGTGTCCTGCGGAAAACAGAGAGGTTCCAGAAATGGCTGCAGGCC

AAGCGCCTCACGCCGGACCTGGTGCAGGACTGTCACCAGGGCCAGAGAGAACTAAAGTTCCTG

TGTATGCTGAGA**TAA**CACCAGTGAAAAAGCCTGGCATGGAGCCCAGCACTGAGAACTTCCAGA

AAGTGTTAGCCTTCTCCCAACTGTGTTATACCAACCACATTTTCAAATAGTAATCATTAAAGA

GGCTTCTGCATCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 172

MEPQLGPEAAALRPGWLALLLWVSALSCSFSLPASSLSSLVPQVRTSYNFGRTFLGLDKCNAC
IGTSICKKFFKEEIRSDNWLASHLGLPPDSLLSYPANYSDDSKIWRPVEIFRLVSKYQNEISD
RRICASASAPKTCSIERVLRKTERFQKWLQAKRLTPDLVQDCHQGQRELKFLCMLR

Signal peptide:
amino acids 1-28

N-glycosylation site.
amino acids 100-103

cAMP- and cGMP-dependent protein kinase phosphorylation site.
amino acids 158-161

N-myristoylation sites.
amino acids 56-61, 65-70

Prokaryotic membrane lipoprotein lipid attachment site.
amino acids 18-28

Prenyl group binding site (CAAX box).
amino acids 179-182

Leucine zipper pattern.
amino acids 5-26

FIGURE 173

GCTGGACTGCTCGCTGGCCGGCAGCGCACCGTTTTGAAGGTCCTAGCCCACCTGGGCTGGCTC
ACGCGCACGACTAGCCGCTCCCATACAGCACGCCCGGACTCTGTCGTCGCTTAAGGCCACTCC
TATTCTACGGCTGACCCCTGGTGGTCACGTGGATCTGTTCGCCACGCAAGTCTGGGTCCTTCG
GCGATTGACCGGGGTCCTTGCTGTTCGGGAGCCTCTCCTAAGCTGCCTGTTCGCGCGAGAGTT
TGGAGGGGCGGGTTTGGGGTCGGTGTCTGATTGGGGCTCGCACCGCAGCACGCTGGAGTCCCG
CTTAGGTACCAGTTAGCGTCAGGGGAGCTGGGTCAGGCGGTCGCCGGGACACCCCGTGTGTGG
CAGGCGGCGAAGCGCTCTGGAGAATCCCGGACAGCCCTGCTCCCTGCAGCCAGGTGTAGTTTC
GGGAGCCACTGGGGCCAAAGTGAGAGTCCAGCGGTCTTCCAGCGCTTGGGCCACGGCGGCGGC
CCTGGGAGCAGAGGTGGAGCGACCCCATTACGCTAAAG**ATG**AAAGGCTGGGGTTGGCTGGCCC
TGCTTCTGGGGGCCCTGCTGGGAACCGCCTGGGCTCGGAGGAGCCAGGATCTCCACTGTGGAG
CATGCAGGGCTCTGGTGGATGAACTAGAATGGGAAATTGCCCAGGTGGACCCCAAGAAGACCA
TTCAGATGGGATCTTTCCGGATCAATCCAGATGGCAGCCAGTCAGTGGTGGAGGTGCCTTATG
CCCGCTCAGAGGCCCACCTCACAGAGCTGCTGGAGGAGATATGTGACCGGATGAAGGAGTATG
GGGAACAGATTGATCCTTCCACCCATCGCAAGAACTACGTACGTGTAGTGGGCCGGAATGGAG
AATCCAGTGAACTGGACCTACAAGGCATCCGAATCGACTCAGATATTAGCGGCACCCTCAAGT
TTGCGTGTGAGAGCATTGTGGAGGAATACGAGGATGAACTCATTGAATTCTTTTCCCGAGAGG
CTGACAATGTTAAAGACAAACTTTGCAGTAAGCGAACAGATCTTTGTGACCATGCCCTGCACA
TATCGCATGATGAGCTA**TGA**ACCACTGGAGCAGCCCACACTGGCTTGATGGATCACCCCCAGG
AGGGGAAAATGGTGGCAATGCCTTTTATATATTATGTTTTTACTGAAATTAACTGAAAAAATA
TGAAACCAAAAGT

FIGURE 174

MKGWGWLALLLGALLGTAWARRSQDLHCGACRALVDELEWEIAQVDPKKTIQMGSFRINPDGS
QSVVEVPYARSEAHLTELLEEICDRMKEYGEQIDPSTHRKNYVRVVGRNGESSELDLQGIRID
SDISGTLKFACESIVEEYEDELIEFFSREADNVKDKLCSKRTDLCDHALHISHDEL

Signal peptide:

amino acids 1-20

N-myristoylation sites.

amino acids 12-18, 16-22, 29-35

Endoplasmic reticulum targeting sequence.

amino acids 179-184

FIGURE 175

CGCAGCGCGGCAGTCCTG**ATG**GCCCGGCATGGGTTACCGCTGCTGCCCCTGCTGTCGCTCCTG
GTCGGCGCGTGGCTCAAGCTAGGAAATGGACAGGCTACTAGCATGGTCCAACTGCAGGGTGGG
AGATTCCTGATGGGAACAAATTCTCCAGACAGCAGAGATGGTGAAGGGCCTGTGCGGGAGGCG
ACAGTGAAACCCTTTGCCATCGACATATTTCCTGTCACCAACAAAGATTTCAGGGATTTTGTC
AGGGAGAAAAAGTATCGGACAGAAGCTGAGATGTTTGGATGGAGCTTTGTCTTTGAGGACTTT
GTCTCTGATGAGCTGAGAAACAAAGCCACCCAGCCAATGAAGTCTGTACTCTGGTGGCTTCCA
GTGGAAAAGGCATTTTGGAGGCAGCCTGCAGGTCCTGGCTCTGGCATCCGAGAGAGACTGGAG
CACCCAGTGTTACACGTGAGCTGGAATGACGCCCGTGCCTACTGTGCTTGGCGGGGAAAACGA
CTGCCCACGGAGGAAGAGTGGGAGTTTGCCGCCCGAGGGGCTTGAAGGGTCAAGTTTACCCA
TGGGGGAACTGGTTCCAGCCAAACCGCACCAACCTGTGGCAGGGAAAGTTCCCCAAGGGAGAC
AAAGCTGAGGATGGCTTCCATGGAGTCTCCCCAGTGAATGCTTTCCCCGCCCAGAACAACTAC
GGGCTCTATGACCTCCTGGGGAACGTGTGGGAGTGGACAGCATCACCGTACCAGGCTGCTGAG
CAGGACATGCGCGTCCTCCGGGGGGCATCCTGGATCGACACAGCTGATGGCTCTGCCAATCAC
CGGGCCCGGGTCACCACCAGGATGGGCAACACTCCAGATTCAGCCTCAGACAACCTCGGTTTC
CGCTGTGCTGCAGACGCAGGCCGGCCGCCAGGGGAGCTG**TAA**GCAGCCGGGTGGTGACAAGGA
GAAAAGCCTTCTAGGGTCACTGTCATTCCCTGGCCATGTTGCAAACAGCGCAATTCCAAGCTC
GAGAGCTTCAGCCTCAGGAAAGAACTTCCCCTTCCCTGTCTCCCATCCCTCTGTGGCAGGCGC
CTCTCACCAGGGCAGGAGAGGACTCAGCCTCCTGTGTTTTGGAGAAGGGGCCCAATGTGTGTT
GACGATGGCTGGGGGCCAGGTGTTTCTGTTAGAGGCCAAGTATTATTGACACAGGATTGCAAA
CACACAAACAGTTGGAACAGAGCACTCTGAAAGGCCATTTTTTAAGCATTTTAAAATCTATTC
TCTCCCCCTTTCTCCCTGGATGATTCAGGAAGCTGACATTGTTTCCTCAAGGCAGAATTTTCC
TGGTTCTGTTTTCTCAGCCAGTTGCTGTGGAAGGAGAATGCTTTCTTTGTGGCCTCATCTGTG
GTTTCGTGTCCCTCTGAAGGAAACTAGTTTCCACTGTGTAACAGGCAGACATGTAACTATTTA
AAGCACAGTTCAGTCCTAAAAGGGTCTGGGAGAACCAGATGATGTACTAGGTGAAGCATTGCA
TTGTGGGAATCACAAAGCAAATAGTACTCCAGAAAGACAAATATCAGAAGCTTCCTATTCTTT
TTTTTTTTTTTTTTTTTTTTTTGAGACAGGGTCTTTCTCTGTTGCCCAGGCTAGAGTGCACTG
GTGATCACGGCTCACTCTAGCCTTGAATTCCTGGGCCCAAGCAATTCTCCCACCTCAGCCTCC
TGAGTAGCTGGGACTACAAGTGTGCACCACCATGCCTGGCTAATTTTTTGAATTTTTGTAGTG
ATGGGATCTCGCTCTGTTGCCCAGGGTGGTCTCGAACTCCTGGCCTCAAGCGATCCTCCCACC
TCGACCTCCCAAAGTGCTGGGATTACAGGTGTGAGCCACCTCGCCTGGGCCCCCTTCTCCATA
TGCCTCCAAAAACATGTCCCTGGAGAGTAGCCTGCTCCCACACTGTCACTGGATGTCATGGGG
CCAATAAAATCTCCTGCAATTGTGTATCTCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAA

FIGURE 176

MARHGLPLLPLLSLLVGAWLKLGNGQATSMVQLQGGRFLMGTNSPDSRDGEGPVREATVKPFA
IDIFPVTNKDFRDFVREKKYRTEAEMFGWSFVFEDFVSDELRNKATQPMKSVLWWLPVEKAFW
RQPAGPGSGIRERLEHPVLHVSWNDARAYCAWRGKRLPTEEEWEFAARGGLKGQVYPWGNWFQ
PNRTNLWQGKFPKGDKAEDGFHGVSPVNAFPAQNNYGLYDLLGNVWEWTASPYQAAEQDMRVL
RGASWIDTADGSANHRARVTTRMGNTPDSASDNLGFRCAADAGRPPGEL

Signal peptide:

amino acids 1-20

N-glycosylation site.

amino acids 191-195

N-myristoylation sites.

amino acids 23-29, 25-31, 175-181

Amidation site.

amino acids 159-163

FIGURE 177

GCCTTCTCGCGCCTGACCATGCACCCCTGCATCTTCCTGCTGGGCCACAGGCGAGCGCTTTAT
TTCTGGAGCTGAGGGCTAAAACTTTTTTGACTTTTCTTCTCCTCAACATCTGAATC**ATG**CCAT
GTGCCCAGAGGAGCTGGCTTGCAAACCTTTCCGTGGTGGCTCAGCTCCTTAACTTTGGGGCGC
TTTGCTATGGGAGACAGCCTCAGCCAGGCCCGGTTCGCTTCCCGGACAGGAGGCAAGAGCATT
TTATCAAGGGCCTGCCAGAATACCACGTGGTGGGTCCAGTCCGAGTAGATGCCAGTGGGCATT
TTTTGTCATATGGCTTGCACTATCCCATCACGAGCAGCAGGAGGAAGAGAGATTTGGATGGCT
CAGAGGACTGGGTGTACTACAGAATTTCTCACGAGGAGAAGGACCTGTTTTTTTAACTTGACGG
TCAATCAAGGATTTCTTTCCAATAGCTACATCATGGAGAAGAGATATGGGAACCTCTCCCATG
TTAAGATGATGGCTTCCTCTGCCCCCCTCTGCCATCTCAGTGGCACGGTTCTACAGCAGGGCA
CCAGAGTTGGGACGGCAGCCCTCAGTGCCTGCCATGGACTGACTGGATTTTTCCAACTACCAC
ATGGAGACTTTTTCATTGAACCCGTGAAGAAGCATCCACTGGTTGAGGGAGGGTACCACCCGC
ACATCGTTTACAGGAGGCAGAAAGTTCCAGAAACCAAGGAGCCAACCTGTGGATTAAAGGGTA
TTGTGACTCACATGTCCTCCTGGGTTGAAGAATCTGTTTTGTTCTTTTGG**TAG**TTTTATTAAA
ACATGACCTATTCTTACTCAAGTCTCTTATCTCCTCTGTATTCTTTTTTTTTTAATATCTTCA
TGACATTCAAATCTCTTCTGTATTCTCTTGCCAGAAAGTGTACATTCTTTTTGCTTGTATAAA
CCCTTTCACTTGTC

FIGURE 178

MPCAQRSWLANLSVVAQLLNFGALCYGRQPQPGPVRFPDRRQEHFIKGLPEYHVVGPVRVDAS
GHFLSYGLHYPITSSRRKRDLDGSEDWVYYRISHEEKDLFFNLTVNQGFLSNSYIMEKRYGNL
SHVKMMASSAPLCHLSGTVLQQGTRVGTAALSACHGLTGFFQLPHGDFFIEPVKKHPLVEGGY
HPHIVYRRQKVPETKEPTCGLKGIVTHMSSWVEESVLFFW

Signal peptide:

amino acids 1-27

N-glycosylation sites.

amino acids 11-15, 105-109, 125-129

N-myristoylation site.

amino acids 149-155

FIGURE 179

CAGATTTAAAAAGAAAACCTTTACTGAATCAGCTGAGTGTTAATAATACGAATTTCCTTTTCT
TGCCAATTCTGATCTGAACAGAAAATCCAAGAACAGGGAT**ATG**TGTGGATTACAGTTTTCTCT
GCCTTGCCTACGACTGTTTCTGGTTGTTACCTGTTATCTTTTATTATTACTCCACAAAGAAAT
ACTTGGATGTTCGTCTGTTTGTCAGCTCTGCACTGGGAGACAAATTAACTGCCGTAACTTAGG
CCTTTCGAGTATTCCTAAGAATTTTCCTGAAAGTACAGTTTTTCTGTATCTGACTGGGAATAA
TATATCTTATATAAATGAAAGTGAATTAACAGGACTTCATTCTCTTGTAGCATTGTATTTGGA
TAATTCTAACATTCTGTATGTATATCCAAAAGCCTTTGTTCAATTGAGGCATCTATATTTTCT
ATTTCTAAATAATAATTTCATCAAACGCTTAGATCCTGGAATATTTAAGGGACTTTTAAATCT
TCGTAATTTATATTTACAGTATAATCAGGTATCTTTTGTTCCGAGAGGAGTATTTAATGATCT
AGTTTCAGTTCAGTACTTAAATCTACAAAGGAATCGCCTCACTGTCCTTGGGAGTGGTACCTT
TGTTGGTATGGTTGCTCTTCGGATACTTGATTTATCAAACAATAACATTTTGAGGATATCAGA
ATCAGGCTTTCAACATCTTGAAAACCTTGCTTGTTTGTATTTAGGAAGTAATAATTTAACAAA
AGTACCATCAAATGCCTTTGAAGTACTTAAAAGTCTTAGAAGACTTTCTTTGTCTCATAATCC
TATTGAAGCAATACAGCCCTTTGCATTTAAAGGACTTGCCAATCTGGAATACCTCCTCCTGAA
AAATTCAAGAATTAGGAATGTTACTAGGGATGGGTTTAGTGGAATTAATAATCTTAAACATTT
GATCTTAAGTCATAATGATTTAGAGAATTTAAATTCTGACACATTCAGTTTGTTAAAGAATTT
AATTTACCTTAAGTTAGATAGAAACAGAATAATTAGCATTGATAATGATACATTTGAAAATAT
GGGAGCATCTTTGAAGATCCTTAATCTGTCATTTAATAATCTTACAGCCTTGCATCCAAGGGT
CCTTAAGCCGTTGTCTTCATTGATTCATCTTCAGGCAAATTCTAATCCTTGGGAATGTAACTG
CAAACTTTTGGGCCTTCGAGACTGGCTAGCATCTTCAGCCATTACTCTAAACATCTATTGTCA
GAATCCCCCATCCATGCGTGGCAGAGCATTACGTTATATTAACATTACAAATTGTGTTACATC
TTCAATAAATGTATCCAGAGCTTGGGCTGTTGTAAAATCTCCTCATATTCATCACAAGACTAC
TGCGCTAATGATGGCCTGGCATAAAGTAACCACAAATGGCAGTCCTCTGGAAAATACTGAGAC
TGAGAACATTACTTTCTGGGAACGAATTCCTACTTCACCTGCTGGTAGATTTTTTCAAGAGAA
TGCCTTTGGTAATCCATTAGAGACTACAGCAGTGTTACCTGTGCAAATACAACTTACTACTTC
TGTTACCTTGAACTTGGAAAAAAACAGTGCTCTACCGAATGATGCTGCTTCAATGTCAGGGAA
AACATCTCTAATTTGTACACAAGAAGTTGAGAAGTTGAATGAGGCTTTTGACATTTTGCTAGC
TTTTTTCATCTTAGCTTGTGTTTTAATCATTTTTTTGATCTACAAAGTTGTTCAGTTTAAACA
AAAACTAAAGGCATCAGAAAACTCAAGGGAAAATAGACTTGAATACTACAGCTTTTATCAGTC
AGCAAGGTATAATGTAACTGCCTCAATTTGTAACACTTCCCCAAATTCTCTAGAAAGTCCTGG
CTTGGAGCAGATTCGACTTCATAAACAAATTGTTCCTGAAAATGAGGCACAGGTCATTCTTTT
TGAACATTCTGCTTTA**TAA**CTCAACTAAATATTGTCTATAAGAAACTTCAGTGCCATGGACAT
GATTTAAACTGAAACCTCCTTATATAATTATATACTTTAGTTGGAAATATAATGAATTATATG
AGGTTAGCATTATTAAAATATGTTTTTTNTTAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 180

MCGLQFSLPCLRLFLVVTCYLLLLLHKEILGCSSVCQLCTGRQINCRNLGLSSIPKNFPESTV
FLYLTGNNISYINESELTGLHSLVALYLDNSNILYVYPKAFVQLRHLYFLFLNNNFIKRLDPG
IFKGLLNLRNLYLQYNQVSFVPRGVFNDLVSVQYLNLQRNRLTVLGSGTFVGMVALRILDLSN
NNILRISESGFQHLENLACLYLGSNNLTKVPSNAFEVLKSLRRLSLSHNPIEAIQPFAFKGLA
NLEYLLLKNSRIRNVTRDGFSGINNLKHLILSHNDLENLNSDTFSLLKNLIYLKLDRNRIISI
DNDTFENMGASLKILNLSFNNLTALHPRVLKPLSSLIHLQANSNPWECNCKLLGLRDWLASSA
ITLNIYCQNPPSMRGRALRYINITNCVTSSINVSRAWAVVKSPHIHHKTTALMMAWHKVTTNG
SPLENTETENITFWERIPTSPAGRFFQENAFGNPLETTAVLPVQIQLTTSVTLNLEKNSALPN
DAASMSGKTSLICTQEVEKLNEAFDILLAFFILACVLIIFLIYKVVQFKQKLKASENSRENRL
EYYSFYQSARYNVTASICNTSPNSLESPGLEQIRLHKQIVPENEAQVILFEHSAL

Signal peptide:

amino acids 1-41

Transmembrane domain:

amino acids 530-547

N-glycosylation sites.

amino acids 71-75, 76-80, 215-219, 266-270, 317-321, 331-335, 336-340, 400-404, 410-414, 451-455, 579-583

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 231-235

N-myristoylation sites.

amino acids 3-9, 69-75, 126-132, 174-180

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

amino acids 506-514

FIGURE 181

GGCCTGGCGCGGCGCTCCGGTAAGGCGTGTGTGCGGCAGGGCGGGGACAGAACCGTCCTCTCG

GGCTCTGGGCGTGTCCGAGACCGCGCTCCCCGCCGAAATCAAGCTCCGAGTCATCCGTGTGGG

GCATTCGTCCCCCCTGGCACAGTTGGCCTCTTTCCAGAAGCCCGTTTTGTTTGTTTTACGTCT

AAATTCGCGTCGGTTCTTATTTCTCTCCCTGGCAAGGTCTGAAGACGGGTAGGAGAATAACCT

GTGTCAGCGTGTT**ATG**ATGCCGTCCCGTACCAACCTGGCTACTGGAATCCCCAGTAGTAAAGT

GAAATATTCAAGGCTCTCCAGCACAGACGATGGCTACATTGACCTTCAGTTTAAGAAAACCCC

TCCTAAGATCCCTTATAAGGCCATCGCACTTGCCACTGTGCTGTTTTTGATTGGCGCCTTTCT

CATTATTATAGGCTCCCTCCTGCTGTCAGGCTACATCAGCAAAGGGGGGGCAGACCGGGCCGT

TCCAGTGCTGATCATTGGCATTCTGGTGTTCCTACCCGGATTTTACCACCTGCGCATCGCTTA

CTATGCATCCAAAGGCTACCGTGGTTACTCCTATGATGACATTCCAGACTTTGATGAC**TAG**CA

CCCACCCCATAGCTGAGGAGGAGTCACAGTGGAACTGTCCCAGCTTTAAGATATCTAGCAGAA

ACTATAGCTGAGGACTAAGGAATTCTGCAGCTTGCAGATGTTTAAGAAAATAATGGCCAGATT

TTTTGGGTCCTTCCCAAAGATGTTAAGTGAACCTACAGTTAGCTAATTAGGACAAGCTCTATT

TTTCATCCCTGGGCCCTGACAAGTTTTTCCACAGGAATATGTATCATGGAAGAATAGAGGTTA

TTCTGTAATGGAAAAGTGTTGCCTGCCACCACCCTCTGTAGAGCTGAGCATTTCTTTTAAATA

GTCTTCATTGCCAATTTGTTCTTGTAGCAAATGGAACAATGTGGTATGGCTAATTTCTTATTA

TTAAGTAGTTTATTTTAAAAATATCTGAGTATATTATCCTGTACACTTATCCCTACCTTCATG

TTCCAGTGGAAGACCTTAGTAAAATCAAAGATCAGTGAGTTCATCTGTAATATTTTTTTTACT

TGCTTTCTTACTGACAGCAACCAGGAATTTTTTTATCCTGCAGAGCAAGTTTTCAAAATGTAA

ATACTTCCTCTGTTTAACAGTCCTTGGACCATTCTGATCCAGTTCACCAGTAGGTTGGACAGC

ATATAATTTGCATCATTTTGTCCCTTGTAAATCAAGATGTTCTGCAGATTATTCCTTTAACGG

CCGGACTTTTGGCTGTTTCCTAATGAAACATGTAGTGGTTATTATTTAGAGTTTATAGCCGTA

TTGCTAGCACCTTGTAGTATGTCATCATTCTGCTCATGATTCCAAGGATCAGCCTGGATGCCT

AGAGGACTAGATCACCTTAGTTTGATTCTATTTTTTAGCTTGCAAAAAGTGACTTATATTCCA

AAGAAATTAAAATGTTGAAATCCAAATCCTAGAAATAAAATGAGTTTNNTTCCAAAAAAAAAA

AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 182

MMPSRTNLATGIPSSKVKYSRLSSTDDGYIDLQFKKTPPKIPYKAIALATVLFLIGAFLIIIG
SLLLSGYISKGGADRAVPVLIIGILVFLPGFYHLRIAYYASKGYRGYSYDDIPDFDD

Transmembrane domains:

amino acids 45-66, 79-95

N-myristoylation sites.

amino acids 11-17, 75-81

FIGURE 183

CTAAAAAATACAAAAATTAGCTGGGCGTGGTGTCATGTACCTGTAATCCCAGCTACTCAAGAGGCTGAGGCAGGA
GAATCGCTTGAACCCAGGAGGCAGAGGTTGCAGTGAGCCAAGATTAAGTCACTGCACTCCAGCCTGGGTGACAGA
GCAAGACTCTGTATCAAAATAAATAAATAAAGTACAACTCTGGATGGGCATGGTGGCTTATGTCTGTAATCCCAG
CACTTTGGGAACTTGAGGCGGGTAGATTGCTTGAGTCCGGGAGTTTGAGACCAGTCTGGGTAATATGGTAACCCT
GTCTACCAAAAATACAGGTATTAGCCAGTCTCATAACTCGGTCTCAAAATAAATAAATACATACATACATAGATG
AAAATTTAAAAAATAAAGTCCAACTCAGCGGTTTTCAGCATATTTACAGAGTTGTACAATCTTCACCACTATCTA
ATTTCAGAACATTTTCATCACCCCCAAAAGAAACCTAACCCATTGACTATCTCTCCATTTCCTCCCTCTCCCTAG
CCTCTGGCAACCACTAATCTCTTTTTTGTCTCTATAGATTTGCCTATTTTGGACAGTTCATATACAAGGAATCAT
ACCACATGTAGCCTTTTGTGTCCGGCTTCTTTGATTAATAGAATGTTTTCAAGGCTCATCTATGCTGTAGCCTGT
ATCAGCACTTCATTCCTTTCTATGGCTGAATAATAGTCCACTGTAGGGATGTGCCATGTTTTTCCACTAGCTGAT
GGACATTTGGGTTGTTTCCACCTTCTGGCTATTATAAATATTGCTGCTATAAATATTCACTTACAAGTTTTTGTG
TGGACATATGTTTTTATTTCTTCTGGTATATCCTTCGGAGTGGAACTGCTGGATCAGGTGGTAACTCTAGGTCTA
ACCTGGCAGTTAAACAGAATCCTATGCATGCTGTAGTCCATGAGTTGAAATAAACACTTGACCCATAGTAAGTGC
CAGATCATCTTCATTTCACAGCAACCAGTAATTTCACAGATGAGGAAATGAAGGCTCCCAGAGGTGAACTGGCTT
TTCCCATTTGAGCAGTTCCAAGTCAGACAGTTAAAAAGTGGCAGGACCTGGAAGAGAAGCTAGTTCTTTCACCCT
GGCATTCAGGGCTGCCTCCTGGGCTACGGGGCTGGCATTTAGAATAGAGCTAAGGTCTGCTGCCAAGGCAGGTGC
CCCAGTCTGCCTCCTCTGTGTCCTTATTCCACTTTCTCTGCAGCCCTCCAGGGGACCCCTCTCTCAGCCACCCTC
TCTCTGGTG**ATG**TCACAGTGCTGCCGGAAGATCAAAGATACGGTGCAGAAACTGGCTTCGGACCATAAGGACATT
CACAGCAGTGTATCCCGAGTGGGCAAAGCCATTGACAGGAACTTCGACTCTGAGATCTGTGGTGTTGTGTCAGAT
GCGGTGTGGGACGCGCGGGAACAGCAGCAGCAGATCCTGCAGATGGCCATCGTGGAACACCTGTATCAGCAGGGC
ATGCTCAGCGTGGCCGAGGAGCTGTGCCAGGAATCAACGCTGAATGTGGACTTGGATTTCAAGCAGCCTTTCCTA
GAGTTGAATCGAATCCTGGAAGCCCTGCACGAACAAGACCTGGGTCCTGCGTTGGAATGGGCCGTCTCCCACAGG
CAGCGCCTGCTGGAACTCAACAGCTCCCTGGAGTTCAAGCTGCACCGACTGCACTTCATCCGCCTCTTGGCAGGA
GGCCCCGCGAAGCAGCTGGAGGCCCTCAGCTATGCTCGGCACTTCCAGCCCTTTGCTCGGCTGCACCAGCGGGAG
ATCCAGGTGATGATGGGCAGCCTGGTGTACCTGCGGCTGGGCTTGGAGAAGTCACCCTACTGCCACCTGCTGGAC
AGCAGCCACTGGGCAGAGATCTGTGAGACCTTTACCCGGGACGCCTGTTCCCTGCTGGGGCTTTCTGTGGAGTCC
CCCCTTAGCGTCAGCTTTGCCTCTGGCTGTGTGGCGCTGCCTGTGTTGATGAACATCAAGGCTGTGATTGAGCAG
CGGCAGTGCACTGGGGTCTGGAATCACAAGGACGAGTTACCGATTGAGATTGAACTAGGCATGAAGTGCTGGTAC
GCTCATCTGTGGCCATGTTATCTCCCGAGATGCACTCAATAAGCTCATTAATGGAGGAAACACTCCGTGTTCGCT
TGCCCCATCCTCCGCCAGCAGACGTCAGATTCCAACCCTCCCATCAAGCTGAAGTGTCCCTACTGTCCCATGGAG
CAGAACCCGGCAGATGGGAAACGCATCATATTC**TGA**TTCCTACCTGGAAGGAATTTTGTTGAAAGGGGTTTTCAC
CTGTGAGCCTTGGTCTGTCTCGGTAGGGTGGTCAACTTCAGTGGACTGTGGTTGGTTTCAGAGCGCCTGGCTGAG
GAGTTCCACTGAGGGGAGCACTGGAGCAGCCCTTTGGCAGAGGCTGAGGAGGGAGATGGACCAGCCCACGCCTGG
CACCTGGCTCCATGGCATAAGGAAAGGGAGATGCTGGCCTCTGTGCTCCTGCTGTCTTTTCCTGTTTCTGTTTGC
GTTTGACTTAGTAGCAACCGACAGAGTGGCAAGGGATTTGGTCTTCAGCAGTAGACATCCTTCCACCCCTGCCCT
CAGCCAAGTCTCTTGCTGCCATGCCAATGCTATGTCCACCCTTGCCCCTCGGCCCAAGAGTGTCCAGCGGTGGCC
CACCTCTTCCTCCCACTACAGCCTCAACAGTATGTACCATCTCCCACTGTAAATAGTCCCAGTTAGAACGGAATG
CCGTTGTTTTATAACTTTGAACAAATGTATTTACTGCCCTTCTCAAAA

FIGURE 184

QCCRKIKDTVQKLASDHKDIHSSVSRVGKAIDRNFDSEICGVVSDAVWDAREQQQQILQMAIV
EHLYQQGMLSVAEELCQESTLNVDLDFKQPFLELNRILEALHEQDLGPALEWAVSHRQRLLEL
NSSLEFKLHRLHFIRLLAGGPAKQLEALSYARHFQPFARLHQREIQVMMGSLVYLRLGLEKSP
YCHLLDSSHWAEICETFTRDACSLLGLSVESPLSVSFASGCVALPVLMNIKAVIEQRQCTGVW
NHKDELPIEIELGMKCWYHSVFACPILRQQTSDSNPPIKLICGHVISRDALNKLINGGKLKCP
YCPMEQNPADGKRIIF

Transmembrane domain:

amino acids 222-241

N-glycosylation site.

amino acids 129-133

Tyrosine kinase phosphorylation site.

amino acids 151-159, 184-193

Amidation site.

amino acids 327-331

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 222-233

FIGURE 185

GAGCGACGCTGTCTCTAGTCGCTGATCCCAA**ATG**CACCGGCTCATCTTTGTCTACACTCTAAT
CTGCGCAAACTTTTGCAGCTGTCGGGACACTTCTGCAACCCCGCAGAGCGCATCCATCAAAGC
TTTGCGCAACGCCAACCTCAGGCGAGATGACTTGTACCGAAGAGATGAGACCATCCAGGTGAA
AGGAAACGGCTACGTGCAGAGTCCTAGATTCCCGAACAGCTACCCCAGGAACCTGCTCCTGAC
ATGGCGGCTTCACTCTCAGGAGAATACACGGATACAGCTAGTGTTTGACAATCAGTTTGGATT
AGAGGAAGCAGAAAATGATATCTGTAGGTATGATTTTGTGGAAGTTGAAGATATATCCGAAAC
CAGTACCATTATTAGAGGACGATGGTGTGGACACAAGGAAGTTCCTCCAAGGATAAAATCAAG
AACGAACCAAATTAAAATCACATTCAAGTCCGATGACTACTTTGTGGCTAAACCTGGATTCAA
GATTTATTATTCTTTGCTGGAAGATTTCCAACCCGCAGCAGCTTCAGAGACCAACTGGGAATC
TGTCACAAGCTCTATTTCAGGGGTATCCTATAACTCTCCATCAGTAACGGATCCCACTCTGAT
TGCGGATGCTCTGGACAAAAAAAATTGCAGAATTTGATACAGTGGAAGATCTGCTCAAGTACTT
CAATCCAGAGTCATGGCAAGAAGATCTTGAGAATATGTATCTGGACACCCCTCGGTATCGAGG
CAGGTCATACCATGACCGGAAGTCAAAAGTTGACCTGGATAGGCTCAATGATGATGCCAAGCG
TTACAGTTGCACTCCCAGGAATTACTCGGTCAATATAAGAGAAGAGCTGAAGTTGGCCAATGT
GGTCTTCTTTCCACGTTGCCTCCTCGTGCAGCGCTGTGGAGGAAATTGTGGCTGTGGAACTGT
CAACTGGAGGTCCTGCACATGCAATTCAGGGAAAACCGTGAAAAAGTATCATGAGGTATTACA
GTTTGAGCCTGGCCACATCAAGAGGAGGGGTAGAGCTAAGACCATGGCTCTAGTTGACATCCA
GTTGGATCACCATGAACGATGCGATTGTATCTGCAGCTCAAGACCACCTCGA**TAA**GAGAATGT
GCACATCCTTACATTAAGCCTGAGAGAA

FIGURE 186

MHRLIFVYTLICANFCSCRDTSATPQSASIKALRNANLRRDDLYRRDETIQVKGNGYVQSPRF
PNSYPRNLLLTWRLHSQENTRIQLVFDNQFGLEEAENDICRYDFVEVEDISETSTIIRGRWCG
HKEVPPRIKSRTNQIKITFKSDDYFVAKPGFKIYYSLLEDFQPAAASETNWESVTSSISGVSY
NSPSVTDPTLIADALDKKIAEFDTVEDLLKYFNPESWQEDLENMYLDTPRYRGRSYHDRKSKV
DLDRLNDDAKRYSCTPRNYSVNIREELKLANVVFFPRCLLVQRCGGNCGCGTVNWRSCTCNSG
KTVKKYHEVLQFEPGHIKRRGRAKTMALVDIQLDHHERCDCICSSRPPR

Signal peptide:

amino acids 1-18

N-glycosylation site.

amino acids 270-274

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 262-266

Tyrosine kinase phosphorylation site.

amino acids 256-265

N-myristoylation sites.

amino acids 94-100, 186-192, 297-303, 298-304

TonB-dependent receptor proteins signature 1.

amino acids 1-56

FIGURE 187

C**ATG**CCGCTGCCGCCGCTGCTGCTGTTGCTCCTGGCGGCGCCTTGGGGACGGGCAGTTCCCTG
TGTCTCTGGTGGTTTGCCTAAACCTGCAAACATCACCTTCTTATCCATCAACATGAAGAATGT
CCTACAATGGACTCCACCAGAGGGTCTTCAAGGAGTTAAAGTTACTTACACTGTGCAGTATTT
CATATATGGGCAAAAGAAATGGCTGAATAAATCAGAATGCAGAAATATCAATAGAACCTACTG
TGATCTTTCTGCTGAAACTTCTGACTACGAACACCAGTATTATGCCAAAGTTAAGGCCATTTG
GGGAACAAAGTGTTCCAAATGGGCTGAAAGTGGACGGTTCTATCCTTTTTTAGAAACACAAAT
TGGCCCACCAGAGGTGGCACTGACTACAGATGAGAAGTCCATTTCTGTTGTCCTGACAGCTCC
AGAGAAGTGGAAGAGAAATCCAGAAGACCTTCCTGTTTCCATGCAACAAATATACTCCAATCT
GAAGTATAACGTGTCTGTGTTGAATACTAAATCAAACAGAACGTGGTCCCAGTGTGTGACCAA
CCACACGCTGGTGCTCACCTGGCTGGAGCCGAACACTCTTTACTGCGTACACGTGGAGTCCTT
CGTCCCAGGGCCCCCTCGCCGTGCTCAGCCTTCTGAGAAGCAGTGTGCCAGGACTTTGAAAGA
TCAATCATCAGAGTTCAAGGCTAAAATCATCTTCTGGTATGTTTTGCCCATATCTATTACCGT
GTTTCTTTTTTCTGTGATGGGCTATTCCATCTACCGATATATCCACGTTGGCAAAGAGAAACA
CCCAGCAAATTTGATTTTGATTTATGGAAATGAATTTGACAAAAGATTCTTTGTGCCTGCTGA
AAAAATCGTGATTAACTTTATCACCCTCAATATCTCGGATGATTCTAAAATTTCTCATCAGGA
TATGAGTTTACTGGGAAAAAGCAGTGATGTATCCAGCCTTAATGATCCTCAGCCCAGCGGGAA
CCTGAGGCCCCCTCAGGAGGAAGAGGAGGTGAAACATTTAGGGTATGCTTCGCATTTGATGGA
AATTTTTTGTGACTCTGAAGAAAACACGGAAGGTACTTCTCTCACCCAGCAAGAGTCCCTCAG
CAGAACAATACCCCCGGATAAAACAGTCATTGAATATGAATATGATGTCAGAACCACTGACAT
TTGTGCGGGGCCTGAAGAGCAGGAGCTCAGTTTGCAGGAGGAGGTGTCCACACAAGGAACATT
ATTGGAGTCGCAGGCAGCGTTGGCAGTCTTGGGCCCGCAAACGTTACAGTACTCATACACCCC
TCAGCTCCAAGACTTAGACCCCCTGGCGCAGGAGCACACAGACTCGGAGGAGGGGCCGGAGGA
AGAGCCATCGACGACCCTGGTCGACTGGGATCCCCAAACTGGCAGGCTGTGTATTCCTTCGCT
GTCCAGCTTCGACCAGGATTCAGAGGGCTGCGAGCCTTCTGAGGGGGATGGGCTCGGAGAGGA
GGGTCTTCTATCTAGACTCTATGAGGAGCCGGCTCCAGACAGGCCACCAGGAGAAAATGAAAC
CTATCTCATGCAATTCATGGAGGAATGGGGGTTATATGTGCAGATGGAAAAC**TGA**TGCCAACA
CTTCCTTTTGCCTTTTGTTTCCTGTGCAAACAAGTGAGTCACCCCTTTGATCCCAGCCATAAA
GTACCTGGGATGAAAGAAGTTTTTTCCAGTTTGTCAGTGTCTGTGAGAA

FIGURE 188

MPLPPLLLLLLAAPWGRAVPCVSGGLPKPANITFLSINMKNVLQWTPPEGLQGVKVTYTVQYF
IYGQKKWLNKSECRNINRTYCDLSAETSDYEHQYYAKVKAIWGTKCSKWAESGRFYPFLETQI
GPPEVALTTDEKSISVVLTAPEKWKRNPEDLPVSMQQIYSNLKYNVSVLNTKSNRTWSQCVTN
HTLVLTWLEPNTLYCVHVESFVPGPPRRAQPSEKQCARTLKDQSSEFKAKIIFWYVLPISITV
FLFSVMGYSIYRYIHVGKEKHPANLILIYGNEFDKRFFVPAEKIVINFITLNISDDSKISHQD
MSLLGKSSDVSSLNDPQPSGNLRPPQEEEEVKHLGYASHLMEIFCDSEENTEGTSLTQQESLS
RTIPPDKTVIEYEYDVRTTDICAGPEEQELSLQEEVSTQGTLLESQAALAVLGPQTLQYSYTP
QLQDLDPLAQEHTDSEEGPEEEPSTTLVDWDPQTGRLCIPSLSSFDQDSEGCEPSEGDGLGEE
GLLSRLYEEPAPDRPPGENETYLMQFMEEWGLYVQMEN

Signal sequence:

amino acids 1-18

Transmembrane domain:

amino acids 240-260

N-glycosylation sites.

amino acids 31-34, 72-75, 80-83, 171-174, 180-183, 189-192, 304-307, 523-526

Tyrosine kinase phosphorylation site.

amino acids 385-392, 518-526

N-myristoylation sites.

amino acids 53-58, 106-111, 368-373, 492-497

Tissue factor

amino acids 1-278

FIGURE 189

ATGTGCTGCTGGCCGCTGCTCCTGCTGTGGGGGCTGCTCCCCGGGACGGCGGCGGGGGGCTCG
GGCCGAACCTATCCGCACCGGACCCTCCTGGACTCGGAGGGCAAGTACTGGCTGGGCTGGAGC
CAGCGGGGCAGCCAGATCGCCTTCCGCCTCCAGGTGCGCACTGCAGGCTACGTGGGCTTCGGC
TTCTCGCCCACCGGGGCCATGGCGTCCGCCGACATCGTCGTGGGCGGGGTGGCCCACGGGCGG
CCCTACCTCCAGGATTATTTTACAAATGCAAATAGAGAGTTGAAAAAAGATGCTCAGCAAGAT
TACCATCTAGAATATGCCATGGAAAATAGCACACACACAATAATTGAATTTACCAGAGAGCTG
CATACATGTGACATAAATGACAAGAGTATAACGGATAGCACTGTGAGAGTGATCTGGGCCTAC
CACCATGAAGATGCAGGAGAAGCTGGTCCCAAGTACCATGACTCCAATAGGGGCACCAAGAGT
TTGCGGTTATTGAATCCTGAGAAAACTAGTGTGCTATCTACAGCCTTACCATACTTTGATCTG
GTAAATCAGGACGTCCCCATCCCAAACAAAGATACAACATATTGGTGCCAAATGTTTAAGATT
CCTGTGTTCCAAGAAAAGCATCATGTAATAAAGGTTGAGCCAGTGATACAGAGAGGCCATGAG
AGTCTGGTGCACCACATCCTGCTCTATCAGTGCAGCAACAACTTTAACGACAGCGTTCTGGAG
TCCGGCCACGAGTGCTATCACCCCAACATGCCCGATGCATTCCTCACCTGTGAAACTGTGATT
TTTGCCTGGGCTATTGGTGGAGAGGGCTTTTCTTATCCACCTCATGTTGGATTATCCCTTGGC
ACTCCATTAGATCCGCATTATGTGCTCCTAGAAGTCCATTATGATAATCCCACTTATGAGGAA
GGCTTAATAGATAATTCTGGACTGAGGTTATTTTACACAATGGATATAAGGAAATATGATGCT
GGGGTGATTGAGGCTGGCCTCTGGGTGAGCCTCTTCCATACCATCCCTCCAGGGATGCCTGAG
TTCCAGTCTGAGGGTCACTGCACTTTGGAGTGCCTGGAAGAGGCTCTGGAAGCCGAAAAGCCA
AGTGGAATTCATGTGTTTGCTGTTCTTCTCCATGCTCACCTGGCTGGCAGAGGCATCAGGCTG
CGTCATTTTCGAAAAGGGAAGGAAATGAAATTACTTGCCTATGATGATGATTTTGACTTCAAT
TTCCAGGAGTTTCAGTATCTAAAGGAAGAACAAACAATCTTACCAGGAGATAACCTAATTACT
GAGTGTCGCTACAACACGAAAGATAGAGCTGAGATGACTTGGGGAGGACTAAGCACCAGGAGT
GAAATGTGTCTCTCATACCTTCTTTATTACCCAAGAATTAATCTTACTCGATGTGCAAGTATT
CCAGACATTATGGAACAACTTCAGTTCATTGGGGTTAAGGAGATCTACAGACCAGTCACGACC
TGGCCTTTCATTATCAAAAGTCCCAAGCAATATAAAAACCTTTCTTTCATGGATGCTATGAAT
AAGTTTAAATGGACTAAAAAGGAAGGTCTCTCCTTCAACAAGCTGGTCCTCAGCCTGCCAGTG
AATGTGAGATGTTCCAAGACAGACAATGCTGAGTGGTCGATTCAAGGAATGACAGCATTACCT
CCAGATATAGAAAGACCCTATAAAGCAGAACCTTTGGTGTGTGGCACGTCTTCTTCCTCTTCC
CTGCACAGAGATTTCTCCATCAACTTGCTTGTTTGCCTTCTGCTACTCAGCTGCACGCTGAGC
ACCAAGAGCTTG**TGA**TCAAAATTCTGTTGGACTTGACAATGTTTTCTATGATCTGAACCTGTC
ATTTGAAGTACAGGTTAAAGACTGTGTCCACTTTGGGCATGAAGAGTGTGGAGACTTTTCTTC
CCCATTTTCCCTCCCTCCTTTTTCCTTTCCATGTTACATGAGAGACATCAATCAGGTTCTCTT
CTCTTTCTTAGAAATACCTGATGTTATATATACATGGTCAATAAAATAAAACTGGCCTGACTT
AAGATAACCATTTTAAAAAATTGGGCTGTCATGTGGGAATAAAAGAATTCTTTCTTTCCTAAA
AAAAAAAA

FIGURE 190

MCCWPLLLLWGLLPGTAAGGSGRTYPHRTLLDSEGKYWLGWSQRGSQIAFRLQVRTAGYVGFG
FSPTGAMASADIVVGGVAHGRPYLQDYFTNANRELKKDAQQDYHLEYAMENSTHTIIEFTREL
HTCDINDKSITDSTVRVIWAYHHEDAGEAGPKYHDSNRGTKSLRLLNPEKTSVLSTALPYFDL
VNQDVPIPNKDTTYWCQMFKIPVFQEKHHVIKVEPVIQRGHESLVHHILLYQCSNNFNDSVLE
SGHECYHPNMPDAFLTCETVIFAWAIGGEGFSYPPHVGLSLGTPLDPHYVLLEVHYDNPTYEE
GLIDNSGLRLFYTMDIRKYDAGVIEAGLWVSLFHTIPPGMPEFQSEGHCTLECLEEALEAEKP
SGIHVFAVLLHAHLAGRGIRLRHFRKGKEMKLLAYDDDFDFNFQEFQYLKEEQTILPGDNLIT
ECRYNTKDRAEMTWGGLSTRSEMCLSYLLYYPRINLTRCASIPDIMEQLQFIGVKEIYRPVTT
WPFIIKSPKQYKNLSFMDAMNKFKWTKKEGLSFNKLVLSLPVNVRCSKTDNAEWSIQGMTALP
PDIERPYKAEPLVCGTSSSSSLHRDFSINLLVCLLLLSCTLSTKSL

Signal peptide:

amino acids 1-18

Transmembrane domains:

amino acids 56-73, 378-393, 583-602

N-glycosylation sites.

amino acids 114-118, 247-251, 476-480, 517-521

N-myristoylation sites.

amino acids 11-17, 15-21, 20-26, 45-51, 68-74, 79-85, 290-296, 316-322, 337-343, 342-348, 456-462, 534-540, 582-588

Copper type II, ascorbate-dependent monooxygenases proteins.

amino acids 271-321, 422-474

FIGURE 191

GCTTCAGCTGAAGAAAGAGAGGA**ATG**AAGCGCCTTCTGCTTCTGTTTTTGTTCTTTATAACAT
TTTCTTCTGCATTTCCCTTAGTCCGGATGACGGAAAATGAAGAAAATATGCAACTGGCTCAGG
CATATCTCAACCAGTTCTACTCTCTTGAAATAGAAGGGAATCATCTTGTTCAAAGCAAGAATA
GGAGTCTCATAGATGACAAAATTCGGGAAATGCAAGCATTTTTTGGATTGACAGTGACTGGAA
AACTGGACTCAAACACCCTTGAGATCATGAAGACACCCAGGTGTGGGGTGCCTGATGTGGGCC
AGTATGGCTACACCCTCCCTGGGTGGAGAAAATACAACCTCACCTACAGAATAATAAACTATA
CTCCGGATATGGCACGAGCTGCTGTGGATGAGGCTATCCAAGAAGGTTTAGAAGTGTGGAGCA
AAGTCACTCCACTAAAATTCACCAAGATTTCAAAGGGGATTGCAGACATCATGATTGCCTTTA
GGACTCGAGTCCATGGTCGGTGTCCTCGCTATTTTGATGGTCCCTTGGGAGTGCTTGGCCATG
CCTTTCCTCCTGGTCCGGGTCTGGGTGGTGACACTCATTTTGATGAGGATGAAAACTGGACCA
AGGATGGAGCAGGATTCAACTTGTTTCTTGTGGCTGCTCATGAATTTGGTCATGCACTGGGGC
TCTCTCACTCCAATGATCAAACAGCCTTGATGTTCCCAAATTATGTCTCCCTGGATCCCAGAA
AATACCCACTTTCTCAGGATGATATCAATGGAATCCAGTCCATCTATGGAGGTCTGCCTAAGG
TACCTGCTAAGCCAAAGGAACCCACTATACCCCATGCCTGTGACCCTGACTTGACTTTTGACG
CTATCACAACTTTCCGCAGAGAAGTAATGTTCTTTAAAGGCAGGCACCTATGGAGGATCTATT
ATGATATCACGGATGTTGAGTTTGAATTAATTGCTTCATTCTGGCCATCTCTGCCAGCTGATC
TGCAAGCTGCATACGAGAACCCCAGAGATAAGATTCTGGTTTTTAAAGATGAAAACTTCTGGA
TGATCAGAGGATATGCTGTCTTGCCAGATTATCCCAAATCCATCCATACATTAGGTTTTCCAG
GACGTGTGAAGAAAATAGATGCAGCCGTCTGTGATAAGACCACAAGAAAAACCTACTTCTTTG
TGGGCATTTGGTGCTGGAGGTTTGATGAAATGACCCAAACCATGGACAAAGGATTCCCGCAGA
GAGTGGTAAAACACTTTCCTGGAATCAGTATCCGTGTTGATGCTGCTTTCCAGTACAAAGGAT
TCTTCTTTTTCAGCCGTGGATCAAAGCAATTTGAATACAACATTAAGACAAAGAATATTACCC
GAATCATGAGAACTAATACTTGGTTTCAATGCAAAGAACCAAAGAACTCCTCATTTGGTTTTG
ATATCAACAAGGAAAAAGCACATTCAGGAGGCATAAAGATATTGTATCATAAGAGTTTAAGCT
TGTTTATTTTTGGTATTGTTCATTTGCTGAAAAACACTTCTATTTATCAA**TAA**ATTCATAGAC
CTAAAATAAACCTCAACAGGTCTTTTAATATAAATTCTGCTTCAAAATAGAATAAAACCATTC
TTTAACAAC

FIGURE 192

MKRLLLLFLFFITFSSAFPLVRMTENEENMQLAQAYLNQFYSLEIEGNHLVQSKNRSLIDDKI
REMQAFFGLTVTGKLDSNTLEIMKTPRCGVPDVGQYGYTLPGWRKYNLTYRIINYTPDMARAA
VDEAIQEGLEVWSKVTPLKFTKISKGIADIMIAFRTRVHGRCPRYFDGPLGVLGHAFPPGPGL
GGDTHFDEDENWTKDGAGFNLFLVAAHEFGHALGLSHSNDQTALMFPNYVSLDPRKYPLSQDD
INGIQSIYGGLPKVPAKPKEPTIPHACDPDLTFDAITTFRREVMFFKGRHLWRIYYDITDVEF
ELIASFWPSLPADLQAAYENPRDKILVFKDENFWMIRGYAVLPDYPKSIHTLGFPGRVKKIDA
AVCDKTTRKTYFFVGIWCWRFDEMTQTMDKGFPQRVVKHFPGISIRVDAAFQYKGFFFFSRGS
KQFEYNIKTKNITRIMRTNTWFQCKEPKNSSFGFDINKEKAHSGGIKILYHKSLSLFIFGIVH
LLKNTSIYQ

Signal peptide:

amino acids 1-17

N-glycosylation sites.

amino acids 55-59, 110-114, 200-204, 452-456, 470-474, 508-512

N-myristoylation site.

amino acids 71-77, 205-211, 223-229

Hemopexin domain signature.

amino acids 171-202, 207-238, 318-334

Neutral zinc metallopeptidases, zinc-binding region signature.

amino acids 213-223

Matrixins cysteine switch.

amino acids 89-97, 207-238

FIGURE 193

CACAATCAGGTCCCATTCTATAGATGGGGAAACTGAGGCTTGAGGTCACATAGGCGTCGTTCA

AGGCTGGTATACCTGCACCCTCTCCCATGTGAACAAC**ATG**GTTCTGGGTAATGGGGGCTGTCA

TCCAGTCTCCTCCCTGCCCCTGCTGGTGCACTTCCTGCCTCTGCTGGTGCACTTTCTGCCCCT

ACTGGTATATTTGCTGCCTCTGCTGGGGCGCTTCCTGCCTCGGCTGGTGTATCTCCTGCCCCT

GCTGGTGCACTTTCTGCCCCCGCTGATGCACTTCCTGCCTCTGCTGGTGCACTTCCTGGCTCT

GCTGGCACACTTCCTGCCTCTGCTGGTGCACTTCCTGGCTCTGCTGGCGCACTTTCCTGCCCC

TGCTGGTGTATTTCCTGCCCCTGCTGGTGTACTTCCTTCCCCTGCTGGTGCACTTCCTGCCTC

TGCTGGCGCACTTCTTGCCTCTCCAGGCCCTACC**TAG**CCTCTCCCTCTTATATATGGAAGTCT

TCCCAGTTCACTGACACTGGTAACAGGGACTCTGCTCTTGGTGTTGCTGTCTGCCCTGGGGAT

GGGCATCTGTGTCTTCCTTTACTACTGCTGGCTCAGGACCCAGAGCTTTGAAGCATGTCCAGA

TGCAGGTCCGGGCACCAGAGTCTAAGGAGCCCCTACACCCACCAGGATTTTCCAATAAAGAGA

TGTTCACCA

FIGURE 194

MVLGNGGCHPVSSLPLLVHFLPLLVHFLPLLVYLLPLLGRFLPRLVYLLPLLVHFLPPLMHFL

PLLVHFLALLAHFLPLLVHFLALLAHFPAPAGVFPAPAGVLPSPAGALPASAGALLASPGPT

Signal peptide:

amino acids 1-39

N-myristoylation sites.

amino acids 4-10, 109-115, 116-122

Leucine zipper pattern.

amino acids 14-36, 16-38, 17-39, 21-43, 24-46, 28-50, 31-53, 35-57, 38-60, 42-64, 45-67, 49-71, 52-74, 56-78, 59-81, 63-85, 65-87, 66-88

FIGURE 195

GGCAAGGCGGCGGCGGCGGCGGCGGCAGCCGCGGTGGCGGCGTGGGGAACATCTCGGCAGCCA
CCGCGCTTCTCCCGCTGGAGCGGGCGTCCAGCTTGGCTGCCCTCGGTCCTTCCCTGCCACGTT
TCGGGTCGCCCTGCACCCCCCACCCAGGCTCGCTTCTCTTCGAAGCGGGAAGGGCGCCTTGCA
GGATCCTGCCGCCCCTCCAACCGGATCCTGGGTCTAGAGCTCCCCAGAGCGAGGCGCTCGCCA
GGACTCCTGCCCCGCCAACCCTGACCGCCGGGGGGTGCCCCCGGGACGTAGCGCCGCGGAGAG
GAAGCGGCAAAGGGGACC**ATG**CGGCGCCTGACTCGTCGGCTGGTTCTGCCAGTCTTCGGGGTG
CTCTGGATCACGGTGCTGCTGTTCTTCTGGGTAACCAAGAGGAAGTTGGAGGTGCCGACGGGA
CCTGAAGTGCAGACCCCTAAGCCTTCGGACGCTGACTGGGACGACCTGTGGGACCAGTTTGAT
GAGCGGCGGTATCTGAATGCCAAAAAGTGGCGCGTTGGTGACGACCCCTATAAGCTGTATGCT
TTCAACCAGCGGGAGAGTGAGCGGATCTCCAGCAATCGGGCCATCCCGGACACTCGCCATCTG
AGATGCACACTGCTGGTGTATTGCACGGACCTTCCACCCACTAGCATCATCATCACCTTCCAC
AACGAGGCCCGCTCCACGCTGCTCAGGACCATCCGCAGTGTATTAAACCGCACCCCTACGCAT
CTGATCCGGGAAATCATATTAGTGGATGACTTCAGCAATGACCCTGATGACTGTAAACAGCTC
ATCAAGTTGCCCAAGGTGAAATGCTTGCGCAATAATGAACGGCAAGGTCTGGTCCGGTCCCGG
ATTCGGGGCGCTGACATCGCCCAGGGCACCACTCTGACTTTCCTCGACAGCCACTGTGAGGTG
AACAGGGACTGGCTCCAGCCTCTGTTGCACAGGGTCAAAGAGGACTACACGCGGGTGGTGTGC
CCTGTGATCGATATCATTAACCTGGACACCTTCACCTACATCGAGTCTGCCTCGGAGCTCAGA
GGGGGGTTTGACTGGAGCCTCCACTTCCAGTGGGAGCAGCTCTCCCCAGAGCAGAAGGCTCGG
CGCCTGGACCCCACGGAGCCCATCAGGACTCCTATCATAGCTGGAGGGCTCTTCGTGATCGAC
AAAGCTTGGTTTGATTACCTGGGGAAATATGATATGGACATGGACATCTGGGGTGGGGAGAAC
TTTGAAATCTCCTTCCGAGTGTGGATGTGCGGGGGCAGCCTAGAGATCGTCCCCTGCAGCCGA
GTGGGGCACGTCTTCCGGAAGAAGCACCCCTACGTTTTCCCTGATGGAAATGCCAACACGTAT
ATAAAGAACACCAAGCGGACAGCTGAAGTGTGGATGGATGAATACAAGCAATACTATTACGCT
GCCCGGCCATTCGCCCTGGAGAGGCCCTTCGGGAATGTTGAGAGCAGATTGGACCTGAGGAAG
AATCTGCGCTGCCAGAGCTTCAAGTGGTACCTGGAGAATATCTACCCTGAACTCAGCATCCCC
AAGGAGTCCTCCATCCAGAAGGGCAATATCCGACAGAGACAGAAGTGCCTGGAATCTCAAAGG
CAGAACAACCAAGAAACCCCAAACCTAAAGTTGAGCCCCTGTGCCAAGGTCAAAGGCGAAGAT
GCAAAGTCCCAGGTATGGGCCTTCACATACACCCAGCAGATCCTCCAGGAGGAGCTGTGCCTG
TCAGTCATCACCTTGTTCCCTGGCGCCCCAGTGGTTCTTGTCCTTTGCAAGAATGGAGATGAC
CGACAGCAATGGACCAAAACTGGTTCCCACATCGAGCACATAGCATCCCACCTCTGCCTCGAT
ACAGATATGTTCGGTGATGGCACCGAGAACGGCAAGGAAATCGTCGTCAACCCATGTGAGTCC
TCACTCATGAGCCAGCACTGGGACATGGTGAGCTCT**TGA**GGACCCCTGCCAGAAGCAGCAAGG
GCCATGGGGTGGTGCTTCCCTGGACCAGAACAGACTGGAAACTGGGCAGCAAGCAGCCTGCAA
CCACCTCAGACATCCTGGACTGGGAGGTGGAGGCAGAGCCCCCCAGGACAGGAGCAACTGTCT
CAGGGAGGACAGAGGAAAACATCACAAGCCAATGGGCTCAAAGACAAATCCCACATGTTCTCA
AGGCCGTTAAGTTCCAGTCCTGGCCAGTCATTCCCTGATTGGTATCTGGAGACAGAAACCTAA
TGGGAAGTGTTTATTGTTCCTTTTCCTACAAAGGAAGCAGTCTCTGGAGGCCAGAAAGAAAAG
CCTTCTTTTTCACTAGGCCAGGACTACATTGAGAGATGAAGAATGGAGGTTGTTTCCAAAAGA
AATAAAGAGAAACTTAGAAGTTGTCTCTGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAA

FIGURE 196

MRRLTRRLVLPVFGVLWITVLLFFWVTKRKLEVPTGPEVQTPKPSDADWDDLWDQFDERRYLN
AKKWRVGDDPYKLYAFNQRESERISSNRAIPDTRHLRCTLLVYCTDLPPTSIIITFHNEARST
LLRTIRSVLNRTPTHLIREIILVDDFSNDPDDCKQLIKLPKVKCLRNNERQGLVRSRIRGADI
AQGTTLTFLDSHCEVNRDWLQPLLHRVKEDYTRVVCPVIDIINLDTFTYIESASELRGGFDWS
LHFQWEQLSPEQKARRLDPTEPIRTPIIAGGLFVIDKAWFDYLGKYDMDMDIWGGENFEISFR
VWMCGGSLEIVPCSRVGHVFRKKHPYVFPDGNANTYIKNTKRTAEVWMDEYKQYYYAARPFAL
ERPFGNVESRLDLRKNLRCQSFKWYLENIYPELSIPKESSIQKGNIRQRQKCLESQRQNNQET
PNLKLSPCAKVKGEDAKSQVWAFTYTQQILQEELCLSVITLFPGAPVVLVLCKNGDDRQQWTK
TGSHIEHIASHLCLDTDMFGDGTENGKEIVVNPCESSLMSQHWDMVSS

Transmembrane domain:

amino acids 475-493

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 2-6

Tyrosine kinase phosphorylation sites.

amino acids 68-75, 401-409

N-myristoylation sites.

amino acids 178-184, 186-192, 192-198, 346-352, 383-389, 526-532

FIGURE 197

GCAGCTCACCCTTCGCAGCCGCG**ATG**GGGGAAGACGACGCCGCGCTTCGGGCTGGCAGCAGGGGGCTCTCCGACC
CGTGGGCAGACTCAGTGGGAGTGCGACCCCGCACCACGGAGCGCCACATCGCCGTACACAAGCGGCTTGTGCTGG
CCTTCGCTGTGTCCCTCGTGGCATTGCTCGCGGTCACAATGCTCGCTGTGCTGCTCAGCCTGCGCTTCGACGAGT
GCGGGGCGAGTGCCACGCCAGGCGCCGACGGTGGCCCCTCAGGCTTTCCGGAGCGCGGCGGCAACGGGAGCCTCC
CTGGATCGGCCCGGCGCAACCACCACGCAGGCGGGGACTCCTGGCAGCCCGAGGCGGGTGGGGTGGCCAGTCCGG
GGACCACGTCGGCCCAGCCGCCGTCGGAGGAGGAGCGGGAGCCGTGGGAGCCGTGGACGCAGCTGCGCCTGTCGG
GCCACCTGAAGCCGCTGCACTACAATCTGATGCTCACCGCCTTCATGGAGAACTTCACCTTCTCCGGGGAGGTCA
ACGTGGAGATCGCGTGCCGGAACGCCACCCGCTACGTAGTGCTGCACGCTTCCCGAGTGGCGGTGGAGAAAGTGC
AGCTGGCCGAGGACCGGGCGTTCGGGGCTGTCCCTGTAGCCGGTTTTTTCCTCTACCCGCAAACCCAGGTCTTAG
TGGTGGTGCTGAATAGGACACTGGACGCGCAGAGGAATTACAATCTGAAGATTATCTACAACGCGCTCATCGAGA
ATGAGCTCCTGGGCTTCTTCCGCAGCTCCTATGTGCTCCACGGGGAGAGAAGATTCCTTGGTGTTACTCAGTTTT
CGCCTACACATGCCAGAAAGGCATTTCCTTGTTTTGATGAGCCAATCTACAAGGCTACTTTCAAAATCAGCATCA
AGCATCAAGCAACCTATTTATCTTTATCTAATATGCCAGTGGAAACTTCCGTGTTTGAGGAAGATGGATGGGTTA
CGGATCACTTTTCACAGACCCCTCTCATGTCCACATATTATTTAGCCTGGGCAATTTGCAACTTCACATACAGAG
AAACTACCACCAAGAGTGGGGTTGTAGTACGATTATATGCAAGACCTGATGCTATCAGAAGAGGATCCGGGGACT
ATGCTCTCCATATAACAAAGAGATTAATAGAATTTTATGAAGACTACTTTAAAGTGCCCTATTCCTTGCCAAAAC
TAGATCTTTTAGCTGTGCCTAAGCATCCGTATGCTGCTATGGAGAACTGGGGACTAAGTATTTTTGTGGAACAAA
GAATACTGCTGGATCCCAGTGTTTCATCTATTTCTTATTTGCTGGATGTCACCATGGTCATTGTTCATGAGATAT
GTCACCAGTGGTTTGGTGACCTTGTGACGCCTGTGTGGTGGGAAGACGTGTGGCTGAAGGAAGGGTTTGCTCACT
ACTTTGAATTTGTTGGTACAGACTACCTCTATCCTGGCTGGAACATGGAAAAGCAGAGGTTTCTGACCGATGTTC
TGCATGAAGTGATGCTGCTGGACGGTTTGGCCAGTTCCCATCCAGTATCACAGGAAGTGCTGCAGGCAACAGATA
TTGACAGGGTGTTTGACTGGATCGCATATAAAAAGGGTGCTGCTTTAATAAGAATGCTGGCTAATTTTATGGGCC
ATTCAGTTTTCCAGAGGGGTTTGCAAGATTATTTAACCATTCATAAGTATGGTAATGCAGCCAGAAATGATCTCT
GGAATACATTATCGGAGGCTTTAAAAAGAAATGGGAAATATGTAAATATACAAGAAGTAATGGATCAGTGGACAC
TCCAGATGGGTTATCCTGTTATCACCATCTTGGGAAACACAACAGCAGAAAATAGAATAATAATTACCCAACAGC
ATTTTATCTATGATATCAGTGCTAAAACTAAAGCACTTAAACTTCAGAATAACAGTTACCTGTGGCAGATTCCAT
TAACTATTGTGGTAGGAAATAGAAGCCATGTGTCTTCAGAAGCAATTATTTGGGTGTCTAACAAATCAGAGCACC
ACAGAATAACTTATTTGGACAAAGGAAGCTGGCTGCTGGGGAACATCAATCAAACTGGCTATTTTAGAGTCAACT
ATGACCTAAGGAACTGGAGATTATTAATTGATCAATTAATCCGGAATCATGAGGTTCTTTCTGTCAGTAACCGAG
CGGGCTTGATCGATGATGCCTTCAGCCTAGCCAGGGCTGGCTATTTGCCTCAGAATATTCCTCTGGAGATTATCA
GATACCTGTCTGAGGAGAAGGATTTTCTTCCTTGGCATGCTGCCAGCCGAGCTCTTTATCCTCTAGATAAATTAC
TGGACCGCATGGAAAACTACAACATTTTCAATGAATATATTTTAAAGCAAGTTGCAACAACATATATCAAGCTTG
GGTGGCCGAAAAATAATTTTAATGGATCTCTTGTTCAAGCATCCTACCAACATGAAGAACTACGTAGAGAAGTTA
TAATGCTGGCCTGCAGTTTTGGCAACAAGCACTGTCACCAACAGGCATCAACACTTATTTCAGATTGGATTTCCA
GCAACAGGAACAGAATACCACTAAATGTTAGAGACATCGTATACTGTACAGGAGTGTCACTACTGGATGAGGATG
TCTGGGAATTCATATGGATGAAATTCCATTCCACCACAGCAGTTTCTGAGAAGAAAATATTATTGGAAGCCTTAA
CTTGCAGTGATGACAGGAATTTATTAAACAGGCTTCTAAATCTGTCACTGAATTCTGAGGTGGTGCTGGATCAAG
ATGCAATTGATGTCATAATCCATGTAGCTCGAAATCCACATGGTCGAGACCTTGCCTGGAAGTTTTTCAGGGATA
AATGGAAGATATTAAATACCAGGTATGGAGAAGCATTGTTTATGTATTCCAAACTCATCAGTGGTGTCACAGAAT
TTCTTAATACTGAAGGTGAACTCAAAGAGCTCAAGAACTTCATGAAAAACTATGATGGGGTAGCTGCTGCTTCTT
TCTCACGAGCTGTGGAAACTGTCGAAGCCAATGTGCGCTGGAAAATGCTTTACCAAGACGAGCTTTTCCAATGGT
TAGGAAAAGCTCTAAGACAC**TAA**TATATGTATCTTATAAACAAACAATTCAACTCAGAAGTTTATGAGAAGACAC
GCTTTTTGTGGAATGAGGAAAATGTACTACCTAGAAAATGGCCAGATTTTCAGTGTTAACGTGTGGGAGGAATTT
TTTTTTTTAGTTTTTATTTTTTGGTTTTGGGGGATATTTTTTATTTGTTTCATTCATTCTGTTCTGTTTCTCTAC
TGGGTGTTCCTCTCTAAAGAAACTCTTGCAAGTGAAACTAGCCATGATTGCTTCAGCTGTACATTCCTTGCTGTA
CAGGACCAAATATGATAGTGATGCATGTTGATGTTACAGTCAATTTGGAAAAACATATTCAGAATATCTGTGCAT
GGATATATTGTCCTGCCTGTGTTCCAGCATGCTTATTTCAAACGTCCAGTGTTGTGTGTGAATATGTGTTACACC
TAGGATGGGCATTATGCAAAAGCACAAAGATTATATATGACAATCAGTATTGCAATGAAAGAAAAACTAAAAACA
GAAATGATATTCTCAATTTTGGGCAATGTGAGAGGTAAAATAGCCCTTGACATGATGAACATCACTTATTTCAGC
ACTTGGATTGTCTGGCAATGATTACTGTGTTGCTAACTCATTTTCTTTGAGTTAAAGCTGTGTATACATTTTAAA
AGGCATATAGATAGTGTATGCATATGTATATGTACATAGGGAAGCCCCATATGTATATAGTATGTTGTACACTGC
ACATGTACAAAGAATGTCTTCAGATCAAAGAAAATTTATCTCTTTTTATAAACTTAAGGACAGTTGCAAAAGGCT
TCAAGGAATTTATCTCAACATTATTCTTTCTATGTCCTAACTAAATTTCTCAACTGTTATGAATTTTTCATCTAC
TTCTTGAACAGTGGTCTATTCTGCTACATGAAGATGAATACAAACAAAATTTTTGTATAAACTCCCAAAAAAAAA
AAAAAAAAAA

FIGURE 198

MGEDDAALRAGSRGLSDPWADSVGVRPRTTERHIAVHKRLVLAFAVSLVALLAVTMLAVLLSL
RFDECGASATPGADGGPSGFPERGGNGSLPGSARRNHHAGGDSWQPEAGGVASPGTTSAQPPS
EEEREPWEPWTQLRLSGHLKPLHYNLMLTAFMENFTFSGEVNVEIACRNATRYVVLHASRVAV
EKVQLAEDRAFGAVPVAGFFLYPQTQVLVVVLNRTLDAQRNYNLKIIYNALIENELLGFFRSS
YVLHGERRFLGVTQFSPTHARKAFPCFDEPIYKATFKISIKHQATYLSLSNMPVETSVFEEDG
WVTDHFSQTPLMSTYYLAWAICNFTYRETTTKSGVVVRLYARPDAIRRGSGDYALHITKRLIE
FYEDYFKVPYSLPKLDLLAVPKHPYAAMENWGLSIFVEQRILLDPSVSSISYLLDVTMVIVHE
ICHQWFGDLVTPVWWEDVWLKEGFAHYFEFVGTDYLYPGWNMEKQRFLTDVLHEVMLLDGLAS
SHPVSQEVLQATDIDRVFDWIAYKKGAALIRMLANFMGHSVFQRGLQDYLTIHKYGNAARNDL
WNTLSEALKRNGKYVNIQEVMDQWTLQMGYPVITILGNTTAENRIIITQQHFIYDISAKTKAL
KLQNNSYLWQIPLTIVVGNRSHVSSEAIIWVSNKSEHHRITYLDKGSWLLGNINQTGYFRVNY
DLRNWRLLIDQLIRNHEVLSVSNRAGLIDDAFSLARAGYLPQNIPLEIIRYLSEEKDFLPWHA
ASRALYPLDKLLDRMENYNIFNEYILKQVATTYIKLGWPKNNFNGSLVQASYQHEELRREVIM
LACSFGNKHCHQQASTLISDWISSNRNRIPLNVRDIVYCTGVSLLDEDVWEFIWMKFHSTTAV
SEKKILLEALTCSDDRNLLNRLLNLSLNSEVVLDQDAIDVIIHVARNPHGRDLAWKFFRDKWK
ILNTRYGEALFMYSKLISGVTEFLNTEGELKELKNFMKNYDGVAAASFSRAVETVEANVRWKM
LYQDELFQWLGKALRH

Transmembrane domain:

amino acids 44-63

N-glycosylation sites.

amino acids 89-93, 160-164, 175-179, 222-226, 338-342, 605-609, 634-638, 649-653, 663-667, 684-688, 800-804, 906-910

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 362-366

Tyrosine kinase phosphorylation site.

amino acids 520-528

N-myristoylation sites.

amino acids 78-84, 87-93, 90-96, 118-124, 501-507, 604-610, 825-831, 987-993

Neutral zinc metallopeptidases, zinc-binding region signature.

amino acids 437-447

FIGURE 199

GCGCCCGGCGCAGCTCGGCCAGAGCGACCGCGGGGCTGAGCGCGCGTCCGCCCAGGGGGCTCCGGAAGCTGCCCC
GGCCCGCGGCCTCCTCCCTCGCTCCCGCTTCCCCTTTCTCGCTCACCGCCGCCCTCCTTCCCCAGCTCCCTCGCC
GTCCGCCCGCCCCACAGCCAGCGGCTCCGCGCCCCCTGCAGCCACG**ATG**CCCGCGGCCCGGCCGCCCGCCGCGGG
ACTCCGCGGGATCTCGCTGTTCCTCGCTCTGCTCCTGGGGAGCCCGGCGGCAGCGCTGGAGCGAGATGCTCTTCC
CGAGGGAGATGCTAGCCCTTTGGGTCCTTACCTCCTGCCCTCAGGAGCCCCGGAGAGAGGCAGTCCTGGCAAAGA
GCACCCTGAAGAGAGAGTGGTAACAGCGCCCCCCAGTTCCTCACAGTCGGCGGAAGTGCTGGGCGAGCTGGTGCT
GGATGGGACCGCACCCTCTGCACATCACGACATCCCAGCCCTGTCACCGCTGCTTCCAGAGGAGGCCCGCCCCAA
GCACGCCTTGCCCCCCAAGAAGAAACTGCCTTCGCTCAAGCAGGTGAACTCTGCCAGGAAGCAGCTGAGGCCCAA
GGCCACCTCCGCAGCCACTGTCCAAAGGGCAGGGTCCCAGCCAGCGTCCCAGGGCCTAGATCTCCTCTCCTCCTC
CACGGAGAAGCCTGGCCCACCGGGGGACCCGGACCCCATCGTGGCCTCCGAGGAGGCATCAGAAGTGCCCCTTTG
GCTGGATCGAAAGGAGAGTGCGGTCCCTACAACACCCGCACCCCTGCAAATCTCCCCCTTCACTTCGCAGCCCTA
TGTGGCCCACACACTCCCCCAGAGGCCAGAACCCGGGGAGCCTGGGCCTGACATGGCCCAGGAGGCCCCCCAGGA
GGACACCAGCCCCATGGCCCTGATGGACAAAGGTGAGAATGAGCTGACTGGGTCAGCCTCAGAGGAGAGCCAGGA
GACCACTACCTCCACCATTATCACCACCACGGTCATCACCACCGAGCAAGCACCAGCTCTCTGCAGTGTGAGCTT
CTCCAATCCTGAGGGGTACATTGACTCCAGCGACTACCCACTGCTGCCCCTCAACAACTTTCTGGAGTGCACATA
CAACGTGACAGTCTACACTGGCTATGGGGTGGAGCTCCAGGTGAAGAGTGTGAACCTGTCCGATGGGGAACTGCT
CTCCATCCGCGGGGTGGACGGCCCTACCCTGACCGTCCTGGCCAACCAGACACTCCTGGTGGAGGGGCAGGTAAT
CCGAAGCCCCACCAACACCATCTCCGTCTACTTCCGGACCTTCCAGGACGACGGCCTTGGGACCTTCCAGCTTCA
CTACCAGGCCTTCATGCTGAGCTGCAACTTTCCCCGCCGGCCTGACTCTGGGGATGTCACGGTGATGGACCTGCA
CTCAGGTGGGGTGGCCCACTTTCACTGCCACCTGGGCTATGAGCTCCAGGGCGCTAAGATGCTGACATGCATCAA
TGCCTCCAAGCCGCACTGGAGCAGCCAGGAGCCCATCTGCTCAGCTCCTTGTGGAGGGGCAGTGCACAATGCCAC
CATCGGCCGCGTCCTCTCCCCAAGTTACCCTGAAAACACAAATGGGAGCCAATTCTGCATCTGGACGATTGAAGC
TCCAGAGGGCCAGAAGCTGCACCTGCACTTTGAGAGGCTGTTGCTGCATGACAAGGACAGGATGACGGTTCACAG
CGGGCAGACCAACAAGTCAGCTCTTCTCTACGACTCCCTTCAAACCGAGAGTGTCCCTTTTGAGGGCCTGCTGAG
CGAAGGCAACACCATCCGCATCGAGTTCACGTCCGACCAGGCCCGGGCGGCCTCCACCTTCAACATCCGATTTGA
AGCGTTTGAGAAAGGCCACTGCTATGAGCCCTACATCCAGAATGGGAACTTCACTACATCCGACCCGACCTATAA
CATTGGGACTATAGTGGAGTTCACCTGCGACCCCGGCCACTCCCTGGAGCAGGGCCCGGCCATCATCGAATGCAT
CAATGTGCGGGACCCATACTGGAATGACACAGAGCCCCTGTGCAGAGCCATGTGTGGTGGGGAGCTCTCTGCTGT
GGCTGGGGTGGTATTGTCCCCAAACTGGCCCGAGCCCTACGTGGAAGGTGAAGATTGTATCTGGAAGATCCACGT
GGGAGAAGAGAAACGGATCTTCTTAGATATCCAGTTCCTGAATCTGAGCAACAGTGACATCTTGACCATCTACGA
TGGCGACGAGGTCATGCCCCACATCTTGGGGCAGTACCTTGGGAACAGTGGCCCCCAGAAACTGTACTCCTCCAC
GCCAGACTTAACCATCCAGTTCCATTCGGACCCTGCTGGCCTCATCTTTGGAAAGGGCCAGGGATTTATCATGAA
CTACATAGAGGTATCAAGGAATGACTCCTGCTCGGATTTACCCGAGATCCAGAATGGCTGGAAAACCACTTCTCA
CACGGAGTTGGTGCGGGGAGCCAGAATCACCTACCAGTGTGACCCCGGCTATGACATCGTGGGGAGTGACACCCT
CACCTGCCAGTGGGACCTCAGCTGGAGCAGCGACCCCCCATTTTGTGAGAAAATTATGTACTGCACCGACCCCGG
AGAGGTGGATCACTCGACCCGCTTAATTTCGGATCCTGTGCTGCTGGTGGGGACCACCATCCAATACACCTGCAA
CCCCGGTTTTGTGCTTGAAGGGAGTTCTCTTCTGACCTGCTACAGCCGTGAAACAGGGACTCCCATCTGGACGTC
TCGCCTGCCCCACTGCGTTTCGGAGGAGTCCCTGGCATGTGACAACCCAGGGCTGCCTGAAAATGGATACCAAAT
CCTGTACAAGCGACTCTACCTGCCAGGAGAGTCCCTCACCTTCATGTGCTACGAAGGCTTTGAGCTCATGGGTGA
AGTGACCATCCGCTGCATCCTGGGACAGCCATCCCACTGGAACGGGCCCCTGCCCGTGTGTAAAGTTAATCAAGA
CAGTTTTGAACATGCTTTAGAAGCAGAAGCGGCAGCAGAGACGTCGCTGGAAGGGGGGAACATGGCCCTGGCTAT
CTTCATCCCGGTCCTCATCATCTCCTTACTGCTGGGAGGAGCCTACATTTACATCACAAGATGTCGCTACTATTC
CAACCTCCGCCTGCCTCTGATGTACTCCCACCCCTACAGCCAGATCACCGTGGAAACCGAGTTTGACAACCCCAT
TTACGAGACAGGGGAAACCAGAGAGTATGAGGTTTCTATC**TAA**AGAGAGCTACACTTGAGAAGGGGACTTGTGAA
CTCAACCACAATCTCCTCGAGACATTCATCCAGAGACCATGTGGCACTTGATTGAAACCCCAGAATGTCGACTGT
CTTTTGTTTAGACTCTTTATCAAAGGTTTACTGTTTTCTTCCCTGTATTTATTATATTTAAAAGTGAAAAAAAAA
AAAAAAAAAAA

FIGURE 200

MPAARPPAAGLRGISLFLALLLGSPAAALERDALPEGDASPLGPYLLPSGAPERGSPGKEHPE
ERVVTAPPSSSQSAEVLGELVLDGTAPSAHHDIPALSPLLPEEARPKHALPPKKKLPSLKQVN
SARKQLRPKATSAATVQRAGSQPASQGLDLLSSSTEKPGPPGDPDPIVASEEASEVPLWLDRK
ESAVPTTPAPLQISPFTSQPYVAHTLPQRPEPGEPGPDMAQEAPQEDTSPMALMDKGENELTG
SASEESQETTTSTIITTTVITTEQAPALCSVSFSNPEGYIDSSDYPLLPLNNFLECTYNVTVY
TGYGVELQVKSVNLSDGELLSIRGVDGPTLTVLANQTLLVEGQVIRSPTNTISVYFRTFQDDG
LGTFQLHYQAFMLSCNFPRRPDSGDVTVMDLHSGGVAHFHCHLGYELQGAKMLTCINASKPHW
SSQEPICSAPCGGAVHNATIGRVLSPSYPENTNGSQFCIWTIEAPEGQKLHLHFERLLLHDKD
RMTVHSGQTNKSALLYDSLQTESVPFEGLLSEGNTIRIEFTSDQARAASTFNIRFEAFEKGHC
YEPYIQNGNFTTSDPTYNIGTIVEFTCDPGHSLEQGPAIIECINVRDPYWNDTEPLCRAMCGG
ELSAVAGVVLSPNWPEPYVEGEDCIWKIHVGEEKRIFLDIQFLNLSNSDILTIYDGDEVMPHI
LGQYLGNSGPQKLYSSTPDLTIQFHSDPAGLIFGKGQGFIMNYIEVSRNDSCSDLPEIQNGWK
TTSHTELVRGARITYQCDPGYDIVGSDTLTCQWDLSWSSDPPFCEKIMYCTDPGEVDHSTRLI
SDPVLLVGTTIQYTCNPGFVLEGSSLLTCYSRETGTPIWTSRLPHCVSEESLACDNPGLPENG
YQILYKRLYLPGESLTFMCYEGFELMGEVTIRCILGQPSHWNGPLPVCKVNQDSFEHALEAEA
AAETSLEGGNMALAIFIPVLIISLLLGGAYIYITRCRYYSNLRLPLMYSHPYSQITVETEFDN-
PIYETGETREYEVSI

Signal peptide:

amino acids 1-28

Transmembrane domain:

amino acids 893-915

N-glycosylation sites.

amino acids 311-315, 328-332, 350-354, 435-439, 458-462, 474-478, 514-518, 576-580, 618-622, 674-678, 742-746

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 188-192

N-myristoylation sites.

amino acids 23-29, 87-93, 146-152, 454-460, 475-481, 575-581, 629-635, 695-701, 723-729, 766-772, 877-883, 953-959

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 383-394

FIGURE 201

G**ATG**GCTACGGCAGGGGGTGGCTCTGGGGCTGACCCGGGAAGTCGGGGTCTCCTTCGCCTTCT
GTCTTTCTGCGTCCTACTAGCAGGTTTGTGCAGGGGAAACTCAGTGGAGAGGAAGATATATAT
CCCCTTAAATAAAACAGCTCCCTGTGTTCGCCTGCTCAACGCCACTCATCAGATTGGCTGCCA
GTCTTCAATTAGTGGAGACACAGGGGTTATCCACGTAGTAGAGAAAGAGGAGGACCTACAGTG
GGTATTGACTGATGGCCCCAACCCCCCTTACATGGTTCTGCTGGAGAGCAAGCATTTTACCAG
GGATTTAATGGAGAAGCTGAAAGGGAGAACCAGCCGAATTGCTGGTCTTGCAGTGTCCTTGAC
CAAGCCCAGTCCTGCCTCAGGCTTCTCTCCTAGTGTACAGTGCCCAAATGATGGGTTTGGTGT
TTACTCCAATTCCTATGGGCCAGAGTTTGCTCACTGCAGAGAAATACAGTGGAATTCGCTGGG
CAATGGTTTGGCTTATGAAGACTTTAGTTTCCCCATCTTTCTTCTTGAAGATGAAAATGAAAC
CAAAGTCATCAAGCAGTGCTATCAAGATCACAACCTGAGTCAGAATGGCTCAGCACCAACCTT
CCCACTATGTGCCATGCAGCTCTTTTCACACATGCATGCTGTCATCAGCACTGCCACCTGCAT
GCGGCGCAGCTCCATCCAAAGCACCTTCAGCATCAACCCAGAAATCGTCTGTGACCCCCTGTC
TGATTACAATGTGTGGAGCATGCTAAAGCCTATAAATACAACTGGGACATTAAAGCCTGACGA
CAGGGTTGTGGTTGCTGCCACCCGGCTGGATAGTCGTTCCTTTTTCTGGAATGTGGCCCCAGG
GGCTGAAAGCGCAGTGGCTTCCTTTGTCACCCAGCTGGCTGCTGCTGAAGCTTTGCAAAAGGC
ACCTGATGTGACCACCCTGCCCCGCAATGTCATGTTTGTCTTCTTTCAAGGGGAAACTTTTGA
CTACATTGGCAGCTCGAGGATGGTCTACGATATGGAGAAGGGCAAGTTTCCCGTGCAGTTAGA
GAATGTTGACTCATTTGTGGAGCTGGGACAGGTGGCCTTAAGAACTTCATTAGAGCTTTGGAT
GCACACAGATCCTGTTTCTCAGAAAAATGAGTCTGTACGGAACCAGGTGGAGGATCTCCTGGC
CACATTGGAGAAGAGTGGTGCTGGTGTCCCTGCTGTCATCCTCAGGAGGCCAAATCAGTCCCA
GCCTCTCCCACCATCTTCCCTGCAGCGATTTCTTCGAGCTCGAAACATCTCTGGCGTTGTTCT
GGCTGACCACTCTGGTGCCTTCCATAACAAATATTACCAGAGTATTTACGACACTGCTGAGAA
CATTAATGTGAGCTATCCCGAATGGCTGAGCCCTGAAGAGGACCTGAACTTTGTAACAGACAC
TGCCAAGGCCCTGGCAGATGTGGCCACGGTGCTGGGACGTGCTCTGTATGAGCTTGCAGGAGG
AACCAACTTCAGCGACACAGTTCAGGCTGATCCCCAAACGGTTACCCGCCTGCTCTATGGGTT
CCTGATTAAAGCCAACAACTCATGGTTCCAGTCTATCCTCAGGCAGGACCTAAGGTCCTACTT
GGGTGACGGGCCTCTTCAACATTACATCGCTGTCTCCAGCCCCACCAACACCACTTATGTTGT
ACAGTATGCCTTGGCAAATTTGACTGGCACAGTGGTCAACCTCACCCGAGAGCAGTGCCAGGA
TCCAAGTAAAGTCCCAAGTGAAAACAAGGATCTGTATGAGTACTCATGGGTCCAGGGCCCTTT
GCATTCTAATGAGACGGACCGACTCCCCCGGTGTGTGCGTTCTACTGCACGATTAGCCAGGGC
CTTGTCTCCTGCCTTTGAACTGAGTCAGTGGAGCTCTACTGAATACTCTACATGGACTGAGAG
CCGCTGGAAAGATATCCGTGCCCGGATATTTCTCATCGCCAGCAAAGAGCTTGAGTTGATCAC
CCTGACAGTGGGCTTCGGCATCCTCATCTTCTCCCTCATCGTCACCTACTGCATCAATGCCAA
AGCTGATGTCCTTTTCATTGCTCCCCGGGAGCCAGGAGCTGTGTCATAC**TGA**GGAGGACCCCA
GCTTTTCTTGCCAGNTCAGCAGTTCACTTCCTAGAGCATCTGTCCCACTGGGACACAACCACT
AATTTGTCACTGGAACCTCCCTGGGCCTGTCTCAGATTGGGATTAACATAAAAGAGTGGAACT
ATCCAAAAGAGACAGGGAGAAATAAATAAATTGCCTCCCTTCCTCCGCTCCCCTTTCCCATCA
CCCCTTCCCCATTTCCTCTTCCTTCTCTACTCATGCCAGATTTTGGGATTACAAATAGAAGCT
TCTTGCTCCTGTTTAACTCCCTAGTTACCCACCCTAATTTGCCCTTCAGGACCCTTCTACTTT
TTCCTTCCTGCCCTGTACCTCTCTCTGCTCCTCACCCCCACCCCTGTACCCAGCCACCTTCCT
GACTGGGAAGGACATAAAAGGTTTAATGTCAGGGTCAAACTACATTGAGCCCCTGAGGACAGG
GGCATCTCTGGGCTGAGCCTACTGTCTCCTTCCCACTGTCCTTTCTCCAGGCCCTCAGATGGC
ACATTAGGGTGGGCGTGCTGCGGGTGGGTATCCCACCTCCAGCCCACAGTGCTCAGTTGTACT
TTTTATTAAGCTGTAATATCTATTTTTGTTTTTGTCTTTTTCCTTTATTCTTTTTGTAAATAT
ATATATAATGAGTTTCATTAAAATAGATTATCCC

FIGURE 202

MATAGGGSGADPGSRGLLRLLSFCVLLAGLCRGNSVERKIYIPLNKTAPCVRLLNATHQIGCQ
SSISGDTGVIHVVEKEEDLQWVLTDGPNPPYMVLLESKHFTRDLMEKLKGRTSRIAGLAVSLT
KPSPASGFSPSVQCPNDGFGVYSNSYGPEFAHCREIQWNSLGNGLAYEDFSFPIFLLEDENET
KVIKQCYQDHNLSQNGSAPTFPLCAMQLFSHMHAVISTATCMRRSSIQSTFSINPEIVCDPLS
DYNVWSMLKPINTTGTLKPDDRVVVAATRLDSRSFFWNVAPGAESAVASFVTQLAAAEALQKA
PDVTTLPRNVMFVFFQGETFDYIGSSRMVYDMEKGKFPVQLENVDSFVELGQVALRTSLELWM
HTDPVSQKNESVRNQVEDLLATLEKSGAGVPAVILRRPNQSQPLPPSSLQRFLRARNISGVVL
ADHSGAFHNKYYQSIYDTAENINVSYPEWLSPEEDLNFVTDTAKALADVATVLGRALYELAGG
TNFSDTVQADPQTVTRLLYGFLIKANNSWFQSILRQDLRSYLGDGPLQHYIAVSSPTNTTYVV
QYALANLTGTVVNLTREQCQDPSKVPSENKDLYEYSWVQGPLHSNETDRLPRCVRSTARLARA
LSPAFELSQWSSTEYSTWTESRWKDIRARIFLIASKELELITLTVGFGILIFSLIVTYCINAK
ADVLFIAPREPGAVSY

Signal peptide:

amino acids 1-33

Transmembrane domain:

amino acids 671-692

N-glycosylation sites.

amino acids 45-49, 55-59, 187-191, 200-204, 204-208, 264-268, 387-391, 417-421, 435-439, 464-468, 506-510, 530-534, 562-566, 573-577, 580-584, 612-616

Glycosaminoglycan attachment site.

amino acids 404-408

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 232-236

N-myristoylation site.

amino acids 5-11, 6-12, 9-15, 29-35, 61-67, 120-126, 146-152, 168-174, 205-211, 294-300, 438-444, 446-452, 504-510, 576-582

FIGURE 203

GCTAGACCGAGCCCTGGGAGGCTACGGGCTCCCCCGGAAACCCTGCCAGGGGAGCCGGGTTTT
GAGCTCAGGCGCCTCTAGCGGCGGCCCCCAGAAATCTGACTCGCGAGGCCAGAGTTGCAGGGA
CTGAATAGCAAACTGAGGCTGAGTAGGGAACAGACC**ATG**AGGTCAGTGCAGATCTTCCTCTCC
CAATGCCGTTTGCTCCTTCTACTAGTTCCGACAATGCTCCTTAAGTCTCTTGGCGAAGATGTA
ATTTTTCACCCTGAAGGGGAGTTTGACTCGTATGAAGTCACCATTCCTGAGAAGCTGAGCTTC
CGGGGAGAGGTGCAGGGTGTGGTCAGTCCCGTGTCCTACCTACTGCAGTTAAAAGGCAAGAAG
CACGTCCTCCATTTGTGGCCCAAGAGACTTCTGTTGCCCCGACATCTGCGCGTTTTCTCCTTC
ACAGAACATGGGGAACTGCTGGAGGATCATCCTTACATACCAAAGGACTGCAACTACATGGGC
TCCGTGAAAGAGTCTCTGGACTCTAAAGCTACTATAAGCACATGCATGGGGGGTCTCCGAGGT
GTATTTAACATTGATGCCAAACATTACCAAATTGAGCCCCTCAAGGCCTCTCCCAGTTTTGAA
CATGTCGTCTATCTCCTGAAGAAAGAGCAGTTTGGGAATCAGGTTTGTGGCTTAAGTGATGAT
GAAATAGAATGGCAGATGGCCCCTTATGAGAATAAGGCGAGGCTAAGGGACTTTCCTGGATCC
TATAAACACCCAAAGTACTTGGAATTGATCCTACTCTTTGATCAAAGTAGGTATAGGTTTGTG
AACAACAATCTTTCTCAAGTCATACATGATGCCATTCTTTTGACTGGGATTATGGACACCTAC
TTTCAAGATGTTCGTATGAGGATACACTTAAAGGCTCTTGAAGTATGGACAGATTTTAACAAA
ATACGCGTTGGATATCCAGAGTTAGCTGAAGTTTTAGGCAGATTTGTAATATATAAAAAAAGT
GTATTAAATGCTCGCCTGTCATCAGATTGGGCACATTTATATCTTCAAAGAAAATATAATGAT
GCTCTTGCATGGTCGTTTGGAAAAGTGTGTTCTCTAGAATATGCTGGATCAGTGAGTACTTTA
CTAGATACAAATATCCTTGCCCCTGCTACCTGGTCTGCTCATGAGCTGGGTCATGCTGTAGGA
ATGTCACATGATGAACAATACTGCCAATGTAGGGGTAGGCTTAATTGCATCATGGGCTCAGGA
CGCACTGGGTTTAGCAATTGCAGTTATATCTCTTTTTTTAAACATATCTCTTCGGGAGCAACA
TGTCTAAATAATATCCCAGGACTAGGTTATGTGCTTAAGAGATGTGGAAACAAAATTGTGGAG
GACAATGAGGAATGTGACTGTGGTTCCACAGAGGAGTGTCAGAAAGATCGGTGTTGCCAATCA
AATTGTAAGTTGCAACCAGGTGCCAACTGTAGCATTGGACTTTGCTGTCATGATTGTCGGTTT
CGTCCATCTGGATACGTGTGTAGGCAGGAAGGAAATGAATGTGACCTTGCAGAGTACTGCGAC
GGGAATTCAAGTTCCTGCCCAAATGACGTTTATAAGCAGGATGGAACCCCTTGCAAGTATGAA
GGCCGTTGTTTCAGGAAGGGGTGCAGATCCAGATATATGCAGTGCCAAAGCATTTTTGGACCT
GATGCCATGGAGGCTCCTAGTGAGTGCTATGATGCAGTTAACTTAATAGGTGATCAATTTGGT
AACTGTGAGATTACAGGAATTCGAAATTTTAAAAAGTGTGAAAGTGCAAATTCAATATGTGGC
AGGCTACAGTGTATAAATGTTGAAACCATCCCTGATTTGCCAGAGCATACGACTATAATTTCT
ACTCATTTACAGGCAGAAAATCTCATGTGCTGGGGCACAGGCTATCATCTATCCATGAAACCC
ATGGGAATACCTGACCTAGGTATGATAAATGATGGCACCTCCTGTGGAGAAGGCCGGGTATGT
TTTAAAAAAAATTGCGTCAATAGCTCAGTCCTGCAGTTTGACTGTTTGCCTGAGAAATGCAAT
ACCCGGGGTGTTTGCAACAACAGAAAAAACTGCCACTGCATGTATGGGTGGGCACCTCCATTC
TGTGAGGAAGTGGGGTATGGAGGAAGCATTGACAGTGGGCCTCCAGGACTGCTCAGAGGGGCG
ATTCCCTCGTCAATTTGGGTTGTGTCCATCATAATGTTTCGCCTTATTTTATTAATCCTTTCA
GTGGTTTTTGTGTTTTTCCGGCAAGTGATAGGAAACCACTTAAAACCCAAACAGGAAAAAATG
CCACTATCCAAAGCAAAAACTGAACAGGAAGAATCTAAAACAAAAACTGTACAGGAAGAATCT
AAAACAAAAACTGGACAGGAAGAATCTGAAGCAAAAACTGGACAGGAAGAATCTAAAGCAAAA
ACTGGACAGGAAGAATCTAAAGCAAACATTGAAAGTAAACGACCCAAAGCAAAGAGTGTCAAG
AAACAAAAAAAAG**TAA**CCGGGCAATCCATACTCATTCAGTAACACAGGCTCATTTATTTAACCA
GCTAATCATTTATCCAAAGGCTTTCCATTCTTCTCCCAATATTTTTTTACTTTAATTTTTCCC
ACAAGTTTTGATCAGCAAATAAACAGCATTCTTGTTTTGGAAACAAAAA

FIGURE 204

MRSVQIFLSQCRLLLLLVPTMLLKSLGEDVIFHPEGEFDSYEVTIPEKLSFRGEVQGVVSPVS
YLLQLKGKKHVLHLWPKRLLLPRHLRVFSFTEHGELLEDHPYIPKDCNYMGSVKESLDSKATI
STCMGGLRGVFNIDAKHYQIEPLKASPSFEHVVYLLKKEQFGNQVCGLSDDEIEWQMAPYENK
ARLRDFPGSYKHPKYLELILLFDQSRYRFVNNNLSQVIHDAILLTGIMDTYFQDVRMRIHLKA
LEVWTDFNKIRVGYPELAEVLGRFVIYKKSVLNARLSSDWAHLYLQRKYNDALAWSFGKVCSL
EYAGSVSTLLDTNILAPATWSAHELGHAVGMSHDEQYCQCRGRLNCIMGSGRTGFSNCSYISF
FKHISSGATCLNNIPGLGYVLKRCGNKIVEDNEECDCGSTEECQKDRCCQSNCKLQPGANCSI
GLCCHDCRFRPSGYVCRQEGNECDLAEYCDGNSSSCPNDVYKQDGTPCKYEGRCFRKGCRSRY
MQCQSIFGPDAMEAPSECYDAVNLIGDQFGNCEITGIRNFKKCESANSICGRLQCINVETIPD
LPEHTTIISTHLQAENLMCWGTGYHLSMKPMGIPDLGMINDGTSCGEGRVCFKKNCVNSSVLQ
FDCLPEKCNTRGVCNNRKNCHCMYGWAPPFCEEVGYGGSIDSGPPGLLRGAIPSSIWVVSIIM
FRLILLILSVVFVFFRQVIGNHLKPKQEKMPLSKAKTEQEESKTKTVQEESKTKTGQEESEAK
TGQEESKAKTGQEESKANIESKRPKAKSVKKQKK

Signal peptide:

amino acids 1-27

Transmembrane domain:

amino acids 684-705

N-glycosylation sites.

amino acids 222-226, 372-376, 438-442, 473-477, 625-629

N-myristoylation sites.

amino acids 131-137, 168-174, 235-241, 319-325, 364-370, 436-442, 472-478, 609-615, 642-648, 668-674, 676-680, 680-686, 749-755, 758-764, 767-773

Amidation site.

amino acids 69-73

Disintegrins proteins

amino acids 429-479

EGF-like domain proteins

amino acids 650-662

Neutral zinc metallopeptidases, zinc-binding region proteins

amino acids 335-345

FIGURE 205

CGGACGCGTGGGCGGACGCGTGGGCGGACGCGTGGGGGAAGGTTGAATGGGGTAGAAGGCCTG
TTGTGGAGGGAAACCACCCATCCTCCTGCCTCCCACCACCACCATCATCCTGGCTGGACGGAG
AGGGTGACGGGGGCTGGGAAGGGGCAGCTCATGTTCAGGTTTCCAGGAGGGGCTACCTGTTGA
CTGTCTTTGCAGGAAGAAGAAAACACCTGAGTGACCAGATGTCCCAGCTCCAGGTGCCTTGCC
AGATGGCCAGAACCACACCTCTTGAAGAGTGACAGTGCTGTGGAGCATGGTTTCTGCACACCT
GGAATGACTGGAACCCCAAAGACTCAAGAAGGAGCTAAAGATCTTGAAGTAGACATGAATAAA
ACAGAAGGCTGTGGACCACCTGTCGAGATGGAGAAGTCCTTCTGAGGCTATCCAAACACGGAC
CAGGCCATGAGACCCCG**ATG**ACCATCCCTGAATTTTTTCGAGAGTCAGTCAACCGATTTGGAA
CTTATCCAGCCCTCCCATCCAAGAATGGCAAAAAGTGGGAAATTCTGAATTTCAACCAGTACT
ATGAGGCTTGTCGGAAGGCTGCAAAATCCTTGATCAAGCTGGGTTTGGAGCGTTTCCACGGAG
TTGGTATCCTGGGGTTTAACTCTGCAGAGTGGTTTATCACTGCTGTTGGTGCCATCCTAGCCG
GGGGTCTTTGTGTTGGTATTTATGCCACCAACTCTGCCGAGGCTTGTCAATATGTCATCACTC
ATGCCAAAGTGAACATCTTGCTGGTTGAGAATGATCAACAGTTACAGAAAATCCTTTCGATTC
CACAGAGCAGCCTAGAGCCCCTAAAAGCGATCATCCAGTACAGACTGCCAATGAAGAAGAACA
ACAACTTGTACTCTTGGGATGATTTCATGGAACTTGGCAGAAGTATCCCTGACACCCAACTGG
AGCAGGTCATCGAGAGCCAGAAGGCGAATCAATGCGCAGTGCTCATCTACACTTCAGGGACCA
CAGGCATACCCAAGGGAGTGATGCTCAGTCATGACAACATCACGTGGATTGCAGGAGCAGTGA
CAAAGGACTTTAAACTGACAGACAAGCATGAGACGGTGGTTAGCTACCTCCCACTCAGCCATA
TTGCAGCACAGATGATGGACATCTGGGTACCCATAAAGATTGGGGCGCTCACATACTTTGCTC
AAGCAGATGCTCTCAAGGGCACCTTGGTAAGTACTCTAAAGGAGGTAAAACCTACTGTCTTCA
TTGGAGTGCCTCAAATTTGGGAGAAGATACATGAGATGGTGAAGAAAAATAGTGCCAAGTCCA
TGGGCTTGAAGAAGAAGGCATTCGTGTGGGCAAGAAACATTGGCTTCAAGGTCAACTCAAAAA
AGATGTTGGGGAAATATAATACTCCCGTGAGCTACCGCATGGCTAAGACTCTCGTGTTCAGCA
AAGTCAAGACATCCCTTGGCTTGGATCACTGTCACTCTTTTATCAGTGGGACTGCGCCCCTCA
ACCAAGAGACTGCCGAGTTCTTTCTAAGCTTGGACATACCTATAGGCGAGTTGTATGGGTTGA
GTGAGAGCTCGGGACCCCACACGATATCCAACCAGAATAACTACAGGCTTCTAAGCTGTGGCA
AGATCTTGACTGGGTGTAAGAATATGCTGTTCCAGCAGAACAAGGATGGCATTGGGGAGATCT
GCCTCTGGGGTAGGCACATCTTCATGGGCTATCTGGAAAGTGAGACTGAAACTACAGAGGCCA
TCGATGATGAAGGCTGGCTACACTCTGGGGATCTGGGCCAGCTGGACGGTCTGGGTTTCCTCT
ATGTCACCGGCCACATCAAAGAAATCCTTATCACTGCTGGTGGTGAAAATGTGCCCCCCATTC
CTGTTGAGACCTTGGTTAAGAAGAAGATCCCCATCATCAGTAACGCCATGTTAGTAGGAGATA
AACTGAAGTTTCTGAGCATGTTGCTGACGCTGAAGTGTGAGATGAATCAGATGAGCGGAGAAC
CTCTGGACAAGCTGAACTTCGAGGCCATCAACTTCTGTCGGGGTCTGGGCAGCCAGGCATCCA
CCGTGACTGAGATTGTGAAGCAGCAAGACCCCCTGGTCTACAAGGCCATCCAGCAAGGCATCA
ATGCTGTGAACCAGGAAGCCATGAACAATGCACAGAGGATTGAAAAGTGGGTCATCTTGGAGA
AGGACTTTTCCATCTATGGTGGAGAGCTAGGTCCAATGATGAAACTTAAGAGACATTTTGTAG
CCCAGAAATACAAAAAACAAATTGATCACATGTACCAC**TGA**CTGCTTTGATGGAGCTGCTCTC
AGCTGTTCTGATGCCTTCAGCAGGAAGACCTCATTGCAATAAGTGAAATGCTGCTCTAGGTAG
AAGCTCTCCCTGCTGTTTTTAAGAAGCCACATTCCTCATTGGTCAGTTTCTTGATTGTTCGTC
TGTTGGAGAGGTGCTCCCTAGAAGAACCTGCCATACGTTTCAAAGCAATAAAATCACTGTATA
TCTTTCTAAGGACCTTCAAGTCATGACTCCAGGGAAGCCTATTGGGAAGTCTACTAAAAACTG
CCTGATTTACAAGAAAGACCTGAACTTGTGGGCTCCCATTTGATTTTTTTCTCCTCAGGGGAC
TCAGACATTAGAAAGAAAAAGCCTCACAGATTTGAAGAACTGGACCCCCAAATCAACTCACCT
GCCTGGAAGCAACTGGGAAACCCTTCCAATAAGTCCTGATAATAAAGCACTTCAGGGTCCCAA
AAAAAAAAAA

FIGURE 206

MTIPEFFRESVNRFGTYPALPSKNGKKWEILNFNQYYEACRKAAKSLIKLGLERFHGVGILGF
NSAEWFITAVGAILAGGLCVGIYATNSAEACQYVITHAKVNILLVENDQQLQKILSIPQSSLE
PLKAIIQYRLPMKKNNNLYSWDDFMELGRSIPDTQLEQVIESQKANQCAVLIYTSGTTGIPKG
VMLSHDNITWIAGAVTKDFKLTDKHETVVSYLPLSHIAAQMMDIWVPIKIGALTYFAQADALK
GTLVSTLKEVKPTVFIGVPQIWEKIHEMVKKNSAKSMGLKKKAFVWARNIGFKVNSKKMLGKY
NTPVSYRMAKTLVFSKVKTSLGLDHCHSFISGTAPLNQETAEFFLSLDIPIGELYGLSESSGP
HTISNQNNYRLLSCGKILTGCKNMLFQQNKDGIGEICLWGRHIFMGYLESETETTEAIDDEGW
LHSGDLGQLDGLGFLYVTGHIKEILITAGGENVPPIPVETLVKKKIPIISNAMLVGDKLKFLS
MLLTLKCEMNQMSGEPLDKLNFEAINFCRGLGSQASTVTEIVKQQDPLVYKAIQQGINAVNQE
AMNNAQRIEKWVILEKDFSIYGGELGPMMKLKRHFVAQKYKKQIDHMYH

Signal peptide:

amino acids 1-22

Transmembrane domain:

amino acids 65-86

N-glycosylation site.

amino acids 196-200

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 282-286

Tyrosine kinase phosphorylation sites.

amino acids 547-555, 608-616

N-myristoylation sites.

amino acids 15-21, 74-80, 80-86, 84-90, 185-191, 189-195, 253-259, 337-343, 371-377, 448-454, 536-542

Amidation site.

amino acids 24-28

Putative AMP-binding domain signature.

amino acids 177-189

Putative AMP-binding domain proteins.

amino acids 173-190

FIGURE 207

CCCACGCGTCCGCCCACGCGTCCGCGGACGCGTGGGGCCAGATCGCGGCCGGCGCCAGCGCCA
CCGTCCGGTCCACCCGCCAGCCCGCACAGCCGCGCCGCCGCCGAGCGTTTCGTGAGCGGCGCT
CCGAGGATCAGGAATGGGGCTTCGGGCGCTGGGCGCGCTCCGAACCCGGCGCACGTAAGAGCC
TGGGAGCGCCCGAGCCGCCCGGCTGCCCGGAGCCCCATCGCCTAGGACCGGGAGATGCTGGAA
ATGCAACCGCCTGTTCCCCGAGGAGCCGCTGCCCCCGGGACCCCCTGGCACTGTGCGCACCCT
GGTCAGCAGCCCCCGGAGAAGACGGCGCCCCCAACGCCCGACCCGCGTGGCCGTGGCAGCGCC
ACGCGAGCCCTCTAGGCGACCGCAGGGCCACAGCAGCTCAGCCGCCGGTGCCCCCTCGGAAAC
CATGACCCCCGGCGCGGGCCCATGGAGCC**ATG**GCCTATAGGGTCCTGGGCCGCGCGGGGCCAC
CTCAGCCGCGGAGGGCGCGCAGGCTGCTCTTCGCCTTCACGCTCTCGCTCTCCTGCACTTACC
TGTGTTACAGCTTCCTGTGCTGCTGCGACGACCTGGGTCGGAGCCGCCTCCTCGGCGCGCCTC
GCTGCCTCCGCGGCCCCAGCGCGGGCGGCCAGAAACTTCTCCAGAAGTCCCGCCCCTGTGATC
CCTCCGGGCCGACGCCCAGCGAGCCCAGCGCTCCCAGCGCGCCCGCCGCCGCCGTGCCCGCCC
CTCGCCTCTCCGGTTCCAACCACTCCGGCTCACCCAAGCTGGGTACCAAGCGGTTGCCCCAAG
CCCTCATTGTGGGCGTGAAGAAGGGGGGCACCCGGGCCGTGCTGGAGTTTATCCGAGTACACC
CGGACGTGCGGGCCTTGGGCACGGAACCCCACTTCTTTGACAGGAACTACGGCCGCGGGCTGG
ATTGGTACAGGAGCCTGATGCCCAGGACCCTCGAGAGCCAGATCACGCTGGAGAAGACGCCCA
GCTACTTTGTCACTCAAGAGGCTCCTCGACGCATCTTCAACATGTCCCGAGACACCAAGCTGA
TCGTGGTTGTGCGGAACCCTGTGACCCGTGCCATCTCTGATTACACGCAGACACTCTCCAAGA
AGCCCGACATCCCGACCTTTGAGGGCCTCTCCTTCCGCAACCGCACCCTGGGCCTGGTGGACG
TGTCATGGAACGCCATCCGCATCGGCATGTACGTGCTGCACCTGGAGAGCTGGCTGCAGTACT
TCCCGCTAGCTCAGATTCACTTCGTCAGTGGCGAGCGACTCATCACTGACCCGGCCGGCGAGA
TGGGGCGAGTCCAGGACTTCCTGGGCATTAAGAGATTCATCACGGACAAGCACTTCTATTTCA
ACAAGACCAAAGGATTCCCTTGCTTGAAAAAAACAGAATCGAGCCTCCTGCCTCGATGCTTGG
GCAAATCAAAAGGGAGAACTCATGTACAGATTGATCCTGAAGTGATAGACCAGCTCCGAGAAT
TTTATAGACCGTATAATATCAAATTTTATGAAACCGTTGGGCAGGACTTCAGGTGGGAA**TAA**G
CCCACGAAAGGAAAGGGCTCTCAAGGGCTCTTCTGCTCATCTCTTCCGTGAGATTTGCTCCCA
GACCCTCTGATCTCCCTCCAACAAACCCTGGCTCCAGCCCCCTTTCCCAACTTGAGTTGCATC
ATCTTGGAACCAGGAAGCCCAGCTAAAGCCAAGAGACCAGAGAGTCCCTGCCACTAGTTTTCA
TCAGTCTGTTCAAGCAAAGTTGATCTGCTCCTGGCACGTCCAGTAAATTCCAGAATCATTCTC
CTTTCTGCCCATAAAGGGCCTTGGAGAATTGCTTTAAGAAGAGTGAATGTTCCAATGATGATA
GATATTATAAGCGATGATGGTTCTGTTGCTATGAACACAGCAGTCGGTCCCTGTCATTGTCCA
CCCAGGAGTGGCCTTGTTAATTCCAAGTGGCATGTATCTTCCCTCTGAGCTTCATTTCTTCAA
GATGCTCTGGGTGGTGGGATGGGAGACCATCCTCAGCCCTCCTCAGACCTTATCAATTCATTG
AGAGATTGCAAAGCTGAAAGCACCTCCGGCCACTCCTGGGAGACAGACCCTTTGGTGATGAAA
TAAACCAGTGACTTCAGAGCCTATGGTCTCAACTGTGCTTGAAAAACACTGTCTCTGAAAACA
ACTTTGTGATTCTCCCTGCTCCCTGTGGACAAAAGCACATAATTCTGCTGTTACGGGTACTTT
GCTCATACGAGCTTTCATGTTCAGCATGCAATGGAATCATGCTTGTCCATGTGAAATAAATAT
GGCTCTCTCGTGTCCTTAATGCTGGGCTTTTCTCTGTAAGCTGGTTCTGCAGCACAATTCATT
AATTAAACTTCTCCCAGTGCAAGAAGGCAGCTGGTGCTGGGGGTGGTCTGGGGGGTCAGGGAG
GAGGGCAAGGACTACATGGGGCAGAGGCAAGGCGGTGGTGGAGATGAGGAAAGAAGTTCTTCT
TGGCAGAAGCTGGGGCAGAAAGATCACATGAGATCTGTGGGGACACCCTCTATCTGAAACATA
AGTCTGTGTTCATTCTCTGCTTAGAAATTTTAGATCTGAAGTGCTACACTGAAGGTCCGAAGG
TTGATGGGGCATCAGATATCTTTTTGGTTGGCCAGCATGATATTTTGAAATAACTGTCAACAG
TTAGAAACTGGGAGCATTCATATGTAAAAAATATGGATTTTCAGCTTCTTCTTAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAA

FIGURE 208

MAYRVLGRAGPPQPRRARRLLFAFTLSLSCTYLCYSFLCCCDDLGRSRLLGAPRCLRGPSAGG
QKLLQKSRPCDPSGPTPSEPSAPSAPAAAVPAPRLSGSNHSGSPKLGTKRLPQALIVGVKKGG
TRAVLEFIRVHPDVRALGTEPHFFDRNYGRGLDWYRSLMPRTLESQITLEKTPSYFVTQEAPR
RIFNMSRDTKLIVVVRNPVTRAISDYTQTLSKKPDIPTFEGLSFRNRTLGLVDVSWNAIRIGM
YVLHLESWLQYFPLAQIHFVSGERLITDPAGEMGRVQDFLGIKRFITDKHFYFNKTKGFPCLK
KTESSLLPRCLGKSKGRTHVQIDPEVIDQLREFYRPYNIKFYETVGQDFRWE

Signal peptide:

amino acids 1-33

N-glycosylation sites.

amino acids 102-106, 193-197, 235-239, 306-310

Tyrosine kinase phosphorylation site.

amino acids 296-305

N-myristoylation sites.

amino acids 51-57, 100-106, 121-127, 125-131

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 20-31

FIGURE 209

CTTTCCTTATCTGTGTGTACTCTTATCTCACTGTTCTATTTTTTCTCCTCATTTATATTAACT
CTTTCTTACCTTTTTTTCTGAACTTCTAGGCCTTCTCTTTCCAGAACTGGTGGAAGACAAATG
AAACGGCCAAGATGGTAAGAAACAAGCCGCATTTCTCCTTGGGGAGACTGATAATTTAAAAGG
TTTGTTGTGTCAGAAACATTCCCAGCTTCATCACCAACCCTTTCCTTCCACCTCTGCCCACTG
GAGACCACTTACATCCCGAAGCGGACGCGGCAGCTGAAGTCAGGAAACCATGCATCACATTAG
CAGGAGCCAACTGCAGACTTTAAACTCCGTTCAACATGTGGATGCGGCAGAGAA**ATG**ACCTGT
CCAGACAAGCCGGGGCAGCTCATAAACTGGTTCATCTGCTCCCTGTGCGTCCCGCGGGTGCGT
AAGCTCTGGAGCAGCCGGCGTCCAAGGACCCGGAGAAACCTTCTGCTGGGCACTGCGTGTGCC
ATCTACTTGGGCTTCCTGGTGAGCCAGGTGGGGAGGGCCTCTCTCCAGCATGGACAGGCGGCT
GAGAAGGGGCCACATCGCAGCCGCGACACCGCCGAGCCATCCTTCCCTGAGATACCCCTGGAT
GGTACCCTGGCCCCTCCAGAGTCCCAGGGCAATGGGTCCACTCTGCAGCCCAATGTGGTGTAC
ATTACCCTACGCTCCAAGCGCAGCAAGCCGGCCAATATCCGTGGCACCGTGAAGCCCAAGCGC
AGGAAAAAGCATGCAGTGGCATCGGCTGCCCCAGGGCAGGAGGCTTTGGTCGGACCATCCCTT
CAGCCGCAGGAAGCGGCAAGGGAAGCTGATGCTGTAGCACCTGGGTACGCTCAGGGAGCAAAC
CTGGTTAAGATTGGAGAGCGACCCTGGAGGTTGGTGCGGGGTCCGGGAGTGCGAGCCGGGGGC
CCAGACTTCCTGCAGCCCAGCTCCAGGGAGAGCAACATTAGGATCTACAGCGAGAGCGCCCCC
TCCTGGCTGAGCAAAGATGACATCCGAAGAATGCGACTCTTGGCGGACAGCGCAGTGGCAGGG
CTCCGGCCTGTGTCCTCTAGGAGCGGAGCCCGTTTGCTGGTGCTGGAGGGGGGCGCACCTGGC
GCTGTGCTCCGCTGTGGCCCTAGCCCCTGTGGGCTTCTCAAGCAGCCCTTGGACATGAGTGAG
GTGTTTGCCTTCCACCTAGACAGGATCCTGGGGCTCAACAGGACCCTGCCGTCTGTGAGCAGG
AAAGCAGAGTTCATCCAAGATGGCCGCCCATGCCCCATCATTCTTTGGGATGCATCTTTATCT
TCAGCAAGTAATGACACCCATTCTTCTGTTAAGCTCACCTGGGGAACTTATCAGCAGTTGCTG
AAACAGAAATGCTGGCAGAATGGCCGAGTACCCAAGCCTGAATCAGGTTGTACTGAAATACAT
CATCATGAGTGGTCCAAGATGGCACTCTTTGATTTTTTGTTACAGATTTATAATCGCTTAGAT
ACAAATTGCTGTGGATTCAGACCTCGCAAGGAAGATGCCTGTGTACAGAATGGATTGAGGCCA
AAATGTGATGACCAAGGTTCTGCGGCTCTAGCACACATTATCCAGCGAAAGCATGACCCAAGG
CATTTGGTTTTTATAGACAACAAGGGTTTCTTTGACAGGAGTGAAGATAACTTAAACTTCAAA
TTGTTAGAAGGCATCAAAGAGTTTCCAGCTTCTGCAGTTTCTGTTTTGAAGAGCCAGCACTTA
CGGCAGAAACTTCTTCAGTCTCTGTTTCTTGATAAAGTGTATTGGGAAAGTCAAGGAGGTAGA
CAAGGAATTGAAAAGCTTATCGATGTAATAGAACACAGAGCCAAAATTCTTATCACCTATATC
AATGCACACGGGGTCAAAGTATTACCTATGAATGAA**TGA**CAAAAGAATCTTCTGGCTAGGGTG
TTAGATATATTTATGCATTTTTGGTTTTGTTTTTAAATCAAGCACATCAACCTCAAGCCCGTT
TAGCAATGAGGCAGTGTAGATGAATACGTAAAATAAATGACTTTAACCAAGTAGCTATAAAGG
GACTTAGCACTGTATGCATACTTAAAAAGGTTTTGAAAAACAAACTACTTGAGAAATATTTGT
TTATATTTTTCTCTAACATCATGCTATGTGTCAGTCTGAACATCTGACAACAGAAATTTCAGT
TATTATTCTAGCTAAGTTTTGAAAACATTTGTCATGCTGTTTAATAGAAAACTGCAAACCAGA
GATACTGACTCCATTAATAAACCATATTTTGTGCCGTTTTGACTGTTCTGACCAAATACTAAT
GGGAACAATTCTTGACGTTTTTCTGTTGCTGATTGTTAACATAGAGCAGTCTCTACACTACCC
TGAGGCAACTCTACATTGGAACACTGAGGCTTACAGCCTGCAAGAGCATCAGAGCTGACCATA
CATTTAAACAGAAATGCTGGTTTATTTGCAAAATCACCAGTATATTTTCTATTGTGTCTATAA
AAAATCAGTCATTTAAGTACAAGAATCATATTTTCCATTCCTTTTTAGAAATTTATTTTGTTG
TCCCTATGGAAATCATTCACATCTGACAATTTATATGTTAAAGAGTTTTACTCTCTCTATTTT
GGTCCAATTTGTATCTAGTGGCTGAGAAATTAAATAATTCTAAAGTATGAAGTTACCTATCTG
AAAATGTACTTACAGAGTATCATTTTAAAATGGATGTCTCTTTAAAAATTTTGTTACTTTTAC
CAACAATGTAATATAATTTATGTATATTTTATTAATAATAGTGAATTCCTTAAAATTTGTTCT
ATGTACTTATATTTAATTTGATTTAATGGTTACTGCCCAGATATTGAGAAATGGTTCAAATAT
TGAGTGTGTTTCAATAA

FIGURE 210

MTCPDKPGQLINWFICSLCVPRVRKLWSSRRPRTRRNLLLGTACAIYLGFLVSQVGRASLQHG
QAAEKGPHRSRDTAEPSFPEIPLDGTLAPPESQGNGSTLQPNVVYITLRSKRSKPANIRGTVK
PKRRKKHAVASAAPGQEALVGPSLQPQEAAREADAVAPGYAQGANLVKIGERPWRLVRGPGVR
AGGPDFLQPSSRESNIRIYSESAPSWLSKDDIRRMRLLADSAVAGLRPVSSRSGARLLVLEGG
APGAVLRCGPSPCGLLKQPLDMSEVFAFHLDRILGLNRTLPSVSRKAEFIQDGRPCPIILWDA
SLSSASNDTHSSVKLTWGTYQQLLKQKCWQNGRVPKPESGCTEIHHHEWSKMALFDFLLQIYN
RLDTNCCGFRPRKEDACVQNGLRPKCDDQGSAALAHIIQRKHDPRHLVFIDNKGFFDRSEDNL
NFKLLEGIKEFPASAVSVLKSQHLRQKLLQSLFLDKVYWESQGGRQGIEKLIDVIEHRAKILI
TYINAHGVKVLPMNE

Transmembrane domain:

amino acids 40-56

N-glycosylation sites.

amino acids 98-102, 289-293, 322-326

N-myristoylation sites.

amino acids 8-14, 41-47, 97-103, 187-193, 251-257, 252-258, 287-293, 484-490

FIGURE 211

GTGGGGTGGTGAGCGCAGCGCCGAGG**ATG**AGGAGGTGCAACAGCGGCTCCGGGCCGCCGCCGTCGCTGCTGCTGC
TGCTGCTGTGGCTGCTCGCGGTTCCCGGCGCTAACGCGGCCCCGCGGTCGGCGCTCTATTCGCCTTCCGACCCGC
TGACGCTGCTGCAGGCGGACACGGTGCGCGGCGCGGTGCTGGGCTCCCGCAGCGCCTGGGCCGTGGAGTTCTTCG
CCTCCTGGTGCGGCCACTGCATCGCCTTCGCCCCGACGTGGAAGGCGCTGGCCGAAGACGTCAAAGCCTGGAGGC
CGGCCCTGTATCTCGCCGCCCTGGACTGTGCTGAGGAGACCAACAGTGCAGTCTGCAGAGACTTCAACATCCCTG
GCTTCCCGACTGTGAGGTTCTTCAAGGCCTTTACCAAGAACGGCTCGGGAGCAGTATTTCCAGTGGCTGGTGCTG
ACGTGCAGACGCTGCGGGAGAGGCTCATTGACGCCCTGGAGTCCCATCATGACACGTGGCCCCCAGCCTGTCCCC
CACTGGAGCCTGCCAAGCTGGAGGAGATTGATGGATTCTTTGCGAGAAATAACGAAGAGTACCTGGCTCTGATCT
TTGAAAAGGGAGGCTCCTACCTGGGTAGAGAGGTGGCTCTGGACCTGTCCCAGCACAAAGGCGTGGCGGTGCGCA
GGGTGCTGAACACAGAGGCCAATGTGGTGAGAAAGTTTGGTGTCACCGACTTCCCCTCTTGCTACCTGCTGTTCC
GGAATGGCTCTGTCTCCCGAGTCCCCGTGCTCATGGAATCCAGGTCCTTCTATACCGCTTACCTGCAGAGACTCT
CTGGGCTCACCAGGGAGGCTGCCCAGACCACAGTTGCACCAACCACTGCTAACAAGATAGCTCCCACTGTTTGGA
AATTGGCAGATCGCTCCAAGATCTACATGGCTGACCTGGAATCTGCACTGCACTACATCCTGCGGATAGAAGTGG
GCAGGTTCCCGGTCCTGGAAGGGCAGCGCCTGGTGGCCCTGAAAAAGTTTGTGGCAGTGCTGGCCAAGTATTTCC
CTGGCCGGCCCTTAGTCCAGAACTTCCTGCACTCCGTGAATGAATGGCTCAAGAGGCAGAAGAGAAATAAAATTC
CCTACAGTTTCTTTAAAACTGCCCTGGACGACAGGAAAGAGGGTGCCGTTCTTGCCAAGAAGGTGAACTGGATTG
GCTGCCAGGGGAGTGAGCCGCATTTCCGGGGCTTTCCCTGCTCCCTGTGGGTCCTCTTCCACTTCTTGACTGTGC
AGGCAGCTCGGCAAAATGTAGACCACTCACAGGAAGCAGCCAAGGCCAAGGAGGTCCTCCCAGCCATCCGAGGCT
ACGTGCACTACTTCTTCGGCTGCCGAGACTGCGCTAGCCACTTCGAGCAGATGGCTGCTGCCTCCATGCACCGGG
TGGGGAGTCCCAACGCCGCTGTCCTCTGGCTCTGGTCTAGCCACAACAGGGTCAATGCTCGCCTTGCAGGTGCCC
CCAGCGAGGACCCCCAGTTCCCCAAGGTGCAGTGGCCACCCCGTGAACTTTGTTCTGCCTGCCACAATGAACGCC
TGGATGTGCCCGTGTGGGACGTGGAAGCCACCCTCAACTTCCTCAAGGCCCACTTCTCCCCAAGCAACATCATCC
TGGACTTCCCTGCAGCTGGGTCAGCTGCCCGGAGGGATGTGCAGAATGTGGCAGCCGCCCCAGAGCTGGCGATGG
GAGCCCTGGAGCTGGAAAGCCGGAATTCAACTCTGGACCCTGGGAAGCCTGAGATGATGAAGTCCCCCACAAACA
CCACCCCACATGTGCCGGCTGAGGGACCTGAGGCAAGTCGACCCCCGAAGCTGCACCCTGGCCTCAGAGCTGCAC
CAGGCCAGGAGCCTCCTGAGCACATGGCAGAGCTTCAGAGGAATGAGCAGGAGCAGCCGCTTGGGCAGTGGCACT
TGAGCAAGCGAGACACAGGGGCTGCATTGCTGGCTGAGTCCAGGGCTGAGAAGAACCGCCTCTGGGGCCCTTTGG
AGGTCAGGCGCGTGGGCCGCAGCTCCAAGCAGCTGGTCGACATCCCTGAGGGCCAGCTGGAGGCCCGAGCTGGAC
GGGGCCGAGGCCAGTGGCTGCAGGTGCTGGGAGGGGGCTTCTCTTACCTGGACATCAGCCTCTGTGTGGGGCTCT
ATTCCCTGTCCTTCATGGGCCTGCTGGCCATGTACACCTACTTCCAGGCCAAGATAAGGGCCCTGAAGGGCCATG
CTGGCCACCCTGCAGCC**TGA**ACCACCTGGGGAGGAGGCGGGAGAGGGAGCTGCCATCTCTAGGCACCTCAAGCCC
CCTGACCCCATTCCCTCCCCTCCCACCCCTTGCTCCTTGTCTGGCCTAGAAGTGTGGGAAATTCAGGAAAACGAG
TTGCTCCAGTGAAGCTTCTTGGGGTTGCTAGGACAGAGAGCTCCTTTGACACAAAAGACAGGAGCAGGGTCCAGG
TTCCCCTGCTGTGCAGGGAGGGCAGCCCCGGGCAGTGGGCATAGGGCAGCTCAGTCCCTGGCCTCTTAGCACCAC
ATTCCTGTTTTTCAGCTTATTTGAAGTCCTGCCTCATTCTCACTGGAGCCTCAGTCTCTCCTGCTTGGTCTTGGC
CCTCAACTGGGGCAAGTGAAGCCAGAGGAGGGTCCCCCAGCTGGGTGGGCTGGAATGGAACTCCTCACTAGCTGC
TGGGGCTCCGCCCACCCTGCTCCCTTCCGGACAATGAAGAAGCCTTTGCACCCTGGGAGGAAGGACCACCCCGGG
CCCTCTATGCCTGGCCAGCCTCCAGCTCCTCAGACCTCCTGGGTGGGGTTTGGCTTCAGGGTGGGGTTTGGAAGC
TTCTGGAAGTCGTGCTGGTCTCCCAGGTGAGGCAAGCCATGGTTGCTGGGCTGTAGGGTGAGTGGCTTGCTTGGT
GGGACCTGACGAGTTGGTGGCATGGGAAGGATGTGGGTCTCTAGTGCCTTGCCCTGGCTTAGCTGCAGGAGAAGA
TGGCTGCTTTCACTTCCCCCCATTGAGCTCTGCTCCCTCTGAGCCTGGTCTTTTGTCCTTTTTTATTTTGGTCTC
CAAGATGAATGCTCATCTTTGGAGGGTGCCAGGTAGAAGCTAGGGAGGGGAGTGTCTTCTCTCTCCAGGTTTCAC
CTTCCAGTGTGCAGAAGTTAGAAGGGTCTGGCGGGGGCAGTGCCTTACACATGCTTGATTCCCACGCTACCCCCT
GCCTTGGGAGGTGTGTGGAATAAATTATTTTTGTTAAGGCA

FIGURE 212

MRRCNSGSGPPPSLLLLLLWLLAVPGANAAPRSALYSPSDPLTLLQADTVRGAVLGSRSAWAV
EFFASWCGHCIAFAPTWKALAEDVKAWRPALYLAALDCAEETNSAVCRDFNIPGFPTVRFFKA
FTKNGSGAVFPVAGADVQTLRERLIDALESHHDTWPPACPPLEPAKLEEIDGFFARNNEEYLA
LIFEKGGSYLGREVALDLSQHKGVAVRRVLNTEANVVRKFGVTDFPSCYLLFRNGSVSRVPVL
MESRSFYTAYLQRLSGLTREAAQTTVAPTTANKIAPTVWKLADRSKIYMADLESALHYILRIE
VGRFPVLEGQRLVALKKFVAVLAKYFPGRPLVQNFLHSVNEWLKRQKRNKIPYSFFKTALDDR
KEGAVLAKKVNWIGCQGSEPHFRGFPCSLWVLFHFLTVQAARQNVDHSQEAAKAKEVLPAIRG
YVHYFFGCRDCASHFEQMAAASMHRVGSPNAAVLWLWSSHNRVNARLAGAPSEDPQFPKVQWP
PRELCSACHNERLDVPVWDVEATLNFLKAHFSPSNIILDFPAAGSAARRDVQNVAAAPELAMG
ALELESRNSTLDPGKPEMMKSPTNTTPHVPAEGPEASRPPKLHPGLRAAPGQEPPEHMAELQR
NEQEQPLGQWHLSKRDTGAALLAESRAEKNRLWGPLEVRRVGRSSKQLVDIPEGQLEARAGRG
RGQWLQVLGGGFSYLDISLCVGLYSLSFMGLLAMYTYFQAKIRALKGHAGHPAA

Signal peptide:

amino acids 1-29

Transmembrane domain:

amino acids 705-728

N-glycosylation sites.

amino acids 130-134, 243-247, 575-579

Glycosaminoglycan attachment site.

amino acids 6-10

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 644-648

N-myristoylation sites.

amino acids 52-58, 56-62, 196-202, 381-387, 392-398, 448-454, 468-474, 684-690, 702-708

Cytochrome c family heme-binding site signature.

amino acids 509-515

Thioredoxin family proteins

amino acids 62-78

FIGURE 213

GCACGAGGCCGACTTCCAGACCATCTACAACTGCACGGCCTGGAACAGCTTCGGCTCCGACAC
TGAGATCATCCGGCTCAAGGAGCAAGGTTCGGAAATGAAGTCGGGAGCCGGGCTGGAAGCAGA
GTCTGTGCCG**ATG**GCCGTCATCATTGGGGTGGCCGTAGGAGCTGGTGTGGCCTTCCTCGTCCT
TATGGCAACCATCGTGGCGTTCTGCTGTGCCCGTTCCCAGAGAAATCTCAAAGGTGTTGTGTC
AGCCAAAAATGATATCCGAGTGGAAATTGTCCACAAGGAACCAGCCTCTGGTCGGGAGGGTGA
GGAGCACTCCACCATCAAGCAGCTGATGATGGACCGGGGTGAATTCCAGCAAGACTCAGTCCT
GAAACAGCTGGAGGTCCTCAAAGAAGAGGAGAAAGAGTTTCAGAACCTGAAGGACCCCACCAA
TGGCTACTACAGCGTCAACACCTTCAAAGAGCACCACTCAACCCCGACCATCTCCCTCTCCAG
CTGCCAGCCCGACCTGCGTCCTGCGGGTAAGCAGCGTGTGCCCACAGGCATGTCCTTCACCAA
CATCTACAGCACCCTGAGCGGCCAGGGCCGCCTCTACGACTACGGGCAGCGGTTTGTGCTGGG
CATGGGCAGCTCGTCCATCGAGCTTTGTGAGCGGGAGTTCCAGAGAGGCTCCCTCAGCGACAG
CAGCTCCTTCCTGGACACGCAGTGTGACAGCAGCGTCAGCAGCAGCGGCAAGCAGGATGGCTA
TGTGCAGTTCGACAAGGCCAGCAAGGCTTCTGCTTCCTCCTCCCACCACTCCCAGTCCTCGTC
CCAGAACTCTGACCCCAGTCGACCCCTGCAGCGGCGGATGCAGACTCACGTC**TAA**GGATCACA
CACCGCGGGTGGGGACGGGCCAGGGAAGAGGTCAGGGCACGTTCTGGTTGTCCAGGGACGAGG
GGTACTTTGCAGAGGACACCAGAATTGGCCACTTCCAGGACAGCCTCCCAGCGCCTCTGCCAC
TGCCTTCCTTCGAAGCTCTGATCAAGCACAAATCTGGGTCCCCAGGTGCTGTGTGCCAGAGGT
GGGCGGGTGGGGAGACAGACAGAGGCTGCGGCTGAGTGCGCTGTGCTTAGTGCTGGACACCCG
TGTCCCCGGCCCTTTCCTGGAGGCCCCTCTACCACCTGCTCTGCCCACAGGCACAAGTGGCAG
CTATAACTCTGCTTTCATGAAACTGCGGTCCACTCTCTGGTCTCTCTGTGGGCTCTACCCCTC
ACTGACCACAAGCTCTACCTACCCCTGTGCCTGTGCTCCCATACAGCCCTGGGGAGAAGGGGA
TGACGTCTTCCCAGCACTGAGCTGCCCCAGAAACCCCGGCTCCCCACTGCTGCTCATAGCCCA
TACCCTGGAGGCTGACAAGCCAGAAATGGCCTTGGCTAAAGGAGCCTCTCTCTCACCAGGCTG
GCCGGGAGCCCACCCCCAATTTGTTTGGTGTTTTGTGTCCATACTCTTGCAGTTCTGTCCTTG
GACTTGATGCCGCTGAACTCTGCGGTGGGACCGGTCCCGTCAGAGCCTGGTGTACTGGGGGGA
GGGAGGGAGGAGGGAGCCTGTGCTGACGGAGCACCTCGCCGGGTGTGCCCCTCCTGGGCTGTG
TGACCCCAGCCTCCCCACCCACCTCCTGCTTTGTGTACTCCTCCCCTCCCCCTCAGCACAATC
GGAGTTCATATAAGAAGTGCGGGAGCTTCTCTGGTCAGGGTTCTCTGAACACTTATGGAGAGA
GTGCTTCCTGGGAAGTGTGGCGTTTGAAGGGGCTGGAGGGCAGGTCTTTAAGATGGCGAGACT
GCCCTTCTCAGCTGATAAACACAAGAACGGCGATCCTGTCTTCAGTAAGGCTCCACGAGAAGA
GAGGAAGTATATCTACACCTCAACCCTCCTAGTCACCACCTGAAATAAATGTTAGGGAAAAAAAA

FIGURE 214

MAVIIGVAVGAGVAFLVLMATIVAFCCARSQRNLKGVVSAKNDIRVEIVHKEPASGREGEEHS
TIKQLMMDRGEFQQDSVLKQLEVLKEEEKEFQNLKDPTNGYYSVNTFKEHHSTPTISLSSCQP
DLRPAGKQRVPTGMSFTNIYSTLSGQGRLYDYGQRFVLGMGSSSIELCEREFQRGSLSDSSSF
LDTQCDSSVSSSGKQDGYVQFDKASKASASSSHHSQSSSQNSDPSRPLQRRMQTHV

Signal peptide:

amino acids 1-28

Glycosaminoglycan attachment site.

amino acids 150-154

N-myristoylation sites.

amino acids 6-12, 10-16, 36-42, 139-145, 165-171

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 114-125

FIGURE 215

CAGCCTTCCTCCCCCAGCCTGAGTGACTACTCTATTCCTTGGTCCCTGCTATTGTCGGGGACG

ATTGC**ATG**GGCTACGCCAGGAAAGTAGGCTGGGTGACCGCAGGCCTGGTGATTGGGGCTGGCG

CCTGCTATTGCATTTATAGACTGACTAGGGGAAGAAAACAGAACAAGGAAAAAATGGCTGAGG

GTGGATCTGGGGATGTGGATGATGCTGGGGACTGTTCTGGGGCCAGGTATAATGACTGGTCTG

ATGATGATGATGACAGCAATGAGAGCAAGAGTATAGTATGGTACCCACCTTGGGCTCGGATTG

GGACTGAAGCTGGAACCAGAGCTAGGGCCAGGGCAAGGGCCAGGGCTACCCGGGCACGTCGGG

CTGTCCAGAAACGGGCTTCCCCCAATTCAGATGATACCGTTTTGTCCCCTCAAGAGCTACAAA

AGGTTCTTTGCTTGGTTGAGATGTCTGAAAAGCCTTATATTCTTGAAGCAGCTTTAATTGCTC

TGGGTAACAATGCTGCTTATGCATTTAACAGAGATATTATTCGTGATCTGGGTGGTCTCCCAA

TTGTCGCAAAGATTCTCAATACTCGGGATCCCATAGTTAAGGAAAAGGCTTTAATTGTCCTGA

ATAACTTGAGTGTGAATGCTGAAAATCAGCGCAGGCTTAAAGTATACATGAATCAAGTGTGTG

ATGACACAATCACTTCTCGCTTGAACTCATCTGTGCAGCTTGCTGGACTGAGATTGCTTACAA

ATATGACTGTTACTAATGAGTATCAGCACATGCTTGCTAATTCCATTTCTGACTTTTTTCGTT

TATTTTCAGCGGGAAATGAAGAAACCAAACTTCAGGTTCTGAAACTCCTTTTGAATTTGGCTG

AAAATCCAGCCATGACTAGGGAACTGCTCAGGGCCCAAGTACCATCTTCACTGGGCTCCCTCT

TTAATAAGAAGGAGAACAAAGAAGTTATTCTTAAACTTCTGGTCATATTTGAGAACATAAATG

ATAATTTCAAATGGGAAGAAAATGAACCTACTCAGAATCAATTCGGTGAAGGTTCACTTTTTT

TCTTTTTAAAAGAATTTCAAGTGTGTGCTGATAAGGTTCTGGGAATAGAAAGTCACCATGATT

TTTTGGTGAAAGTAAAAGTTGGAAAATTCATGGCCAAACTTGCTGAACATATGTTCCCAAAGA

GCCAGGAA**TAA**CACCTTGATTTTGTAATTTAGAAGCAACACACATTGTAAACTATTCATTTTC

TCCACCTTGTTTATATGGTAAAGGAATCCTTTCAGCTGCCAGTTTTGAATAATGAATATCATA

TTGTATCATCAATGCTGATATTTAACTGAGTTGGTCTTTAGGTTTAAGATGGATAAATGAATA

TCACTACTTGTTCTGAAAACATGTTTGTTGCTTTTTATCTCGCTGCCTAGATTGAAATATTTT

GCTATTTCTTCTGCATAAGTGACAGTGAACCAATTCATCATGAGTAAGCTCCCTTCTGTCATT

TTCATTGATTTAATTTGTGTATCATCAATAAAATTGTATGTTAATGCTGGAAAGA

FIGURE 216

MGYARKVGWVTAGLVIGAGACYCIYRLTRGRKQNKEKMAEGGSGDVDDAGDCSGARYNDWSDD
DDDSNESKSIVWYPPWARIGTEAGTRARARARARATRARRAVQKRASPNSDDTVLSPQELQKV
LCLVEMSEKPYILEAALIALGNNAAYAFNRDIIRDLGGLPIVAKILNTRDPIVKEKALIVLNN
LSVNAENQRRLKVYMNQVCDDTITSRLNSSVQLAGLRLLTNMTVTNEYQHMLANSISDFFRLF
SAGNEETKLQVLKLLLNLAENPAMTRELLRAQVPSSLGSLFNKKENKEVILKLLVIFENINDN
FKWEENEPTQNQFGEGSLFFFLKEFQVCADKVLGIESHHDFLVKVKVGKFMAKLAEHMFPKSQE

Signal peptide:

amino acids 1-20

N-glycosylation sites.

amino acids 68-72, 189-193, 217-221, 230-234

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 107-111

N-myristoylation sites.

amino acids 13-19, 17-23, 19-25, 54-60, 83-89, 147-153, 255-261, 290-296

Amidation site.

amino acids 29-33

FIGURE 217

GAGACACAAAGGCAGGCGGGATGCGGGAGCAGGCAAAGGGAAAGCGAAAGCCGCGCGCCCGGC

CGGTGACTGGGTGAAGGCGCCGCGCAGCTTTCCCGACGCCGGCTGTACCCGGACCTCCTGGTC

GAGCCTGGCGCGCCGCAGCC**ATG**GCCATCGCTCAACTGGCCACGGAGTACGTGTTCTCGGATT

TCTTGCTGAAGGAGCCCACGGAGCCCAAGTTCAAGGGGCTGCGACTGGAGCTGGCTGTGGACA

AGATGGTCACGTGCATTGCGGTGGGGCTGCCCCTGCTGCTCATCTCGCTGGCCTTCGCGCAGG

AGATCTCGATTGGTACACAGATAAGCTGTTTCTCTCCAAGTTCTTTCTCCTGGCGTCAGGCTG

CCTTTGTGGATTCATATTGCTGGGCGGCTGTTCAGCAGAAGAACTCACTGCAGAGCGAGTCTG

GAAACCTCCCACTGTGGCTGCATAAGTTTTTCCCCTACATCCTGCTGCTCTTTGCGATCCTCC

TGTACCTGCCCCCGCTGTTCTGGCGTTTCGCAGCTGCTCCTCATATTTGCTCAGACTTGAAGT

TTATCATGGAAGAACTTGACAAAGTTTACAACCGTGCAATTAAGGCTGCAAAGAGTGCGCGTG

ACCTTGACATGAGAGATGGAGCCTGCTCAGTTCCAGGTGTTACCGAGAACTTAGGGCAAAGTT

TGTGGGAGGTATCTGAAAGCCACTTCAAGTACCCAATTGTGGAGCAGTACTTGAAGACAAAGA

AAAATTCTAATAATTTAATCATCAAGTACATTAGCTGCCGCCTGCTGACACTCATCATTATAC

TGTTAGCGTGTATCTACCTGGGCTATTACTTCAGCCTCTCCTCACTCTCAGACGAGTTTGTGT

GCAGCATCAAATCAGGGATCCTGAGAAACGACAGCACCGTGCCCGATCAGTTTCAGTGCAAAC

TCATTGCCGTGGGCATCTTCCAGTTGCTCAGTGTCATTAACCTTGTGGTTTATGTCCTGCTGG

CTCCCGTGGTTGTCTACACGCTGTTTGTTCCATTCCGACAGAAGACAGATGTTCTCAAAGTGT

ACGAAATCCTCCCCACTTTTGATGTTCTGCATTTCAAATCTGAAGGGTACAACGATTTGAGCC

TCTACAATCTCTTCTTGGAGGAAAATATAAGTGAGGTCAAGTCATACAAGTGTCTTAAGGTAC

TGGAGAATATTAAGAGCAGTGGTCAGGGGATCGACCCAATGCTACTCCTGACAAACCTTGGCA

TGATCAAGATGGATGTTGTTGATGGCAAAACTCCCATGTCTGCAGAGATGAGAGAGGAGCAGG

GGAACCAGACGGCAGAGCTCCAAGGTATGAACATAGACAGTGAAACTAAAGCAAATAATGGAG

AGAAGAATGCCCGACAGAGACTTCTGGATTCTTCTTGC**TGA**TGATTTTTTTTCCTTGAGCTGT

AAATCTGTGACTTCTGCGACATGGGATTTAATTTGGCTAAAGCACCCCTGTTGGTTTCACAGC

TGGTTTGCAATAAATGGTTCTTGGTGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 218

MAIAQLATEYVFSDFLLKEPTEPKFKGLRLELAVDKMVTCIAVGLPLLLISLAFAQEISIGTQ
ISCFSPSSFSWRQAAFVDSYCWAAVQQKNSLQSESGNLPLWLHKFFPYILLLFAILLYLPPLF
WRFAAAPHICSDLKFIMEELDKVYNRAIKAAKSARDLDMRDGACSVPGVTENLGQSLWEVSES
HFKYPIVEQYLKTKKNSNNLIIKYISCRLLTLIIILLACIYLGYYFSLSSLSDEFVCSIKSGI
LRNDSTVPDQFQCKLIAVGIFQLLSVINLVVYVLLAPVVVYTLFVPFRQKTDVLKVYEILPTF
DVLHFKSEGYNDLSLYNLFLEENISEVKSYKCLKVLENIKSSGQGIDPMLLLTNLGMIKMDVV
DGKTPMSAEMREEQGNQTAELQGMNIDSETKANNGEKNARQRLLDSSC

Transmembrane domains:

amino acids 37-55, 108-126, 216-232, 273-290

N-glycosylation sites.

amino acids 255-259, 338-342, 394-398

Glycosaminoglycan attachment site.

amino acids 357-361

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 203-207

N-myristoylation sites.

amino acids 61-67, 174-180, 251-257, 393-399

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 218-229

FIGURE 219

CTGTGAGTGACACACGCTGAGTGGGGTGAAGGGAA**ATG**CTGGTGAATTTCATTTTGAGGTGTG
GGTTGCTGTTAGTCACTCTGTCTCTTGCCATTGCCAAGCACAAGCAATCTTCCTTCACCAAAA
GTTGTTACCCAAGGGGAACATTGTCCCAAGCTGTTGACGCTCTCTATATCAAAGCAGCATGGC
TCAAAGCAACGATTCCAGAAGACCGCATAAAAAATATACGATTATTAAAAAAGAAAACAAAAA
AGCAGTTTATGAAAAACTGTCAATTTCAAGAACAGCTTCTGTCCTTCTTCATGGAAGACGTTT
TTGGTCAACTGCAATTGCAAGGCTGCAAGAAAATACGCTTTGTGGAGGACTTTCATAGCCTTA
GGCAGAAATTGAGCCACTGTATTTCCTGTGCTTCATCAGCTAGAGAGATGAAATCCATTACCA
GGATGAAAAGAATATTTTATAGGATTGGAAACAAAGGAATCTACAAAGCCATCAGTGAACTGG
ATATTCTTCTTTCCTGGATTAAAAAATTATTGGAAAGCAGTCAG**TAA**ACCAAAGCCAAGTACA
TTGATTTTACAGTTATTTTGAAATACAATAAGAACTGCTAGAAATATGTTTATAACAGTCTAT
TTCTTTTAAAAACTTTTTAACATAATACTGACGGCATGTTAGGTGATTCAGAATAGACAAGAA
GGATTTAGTAAATTAACGTTTTGGATATAAGTTGTCACTAATTTGCACATTTTCTGTGTTTTC
AAATAATGTTTCCATTCTGAACATGTTTTGTCATTCACAAGTACATTGTGTCAACTTAATTTA
AAGTATGTAACCTGAATTAACTCGTGTAATATTTGTGTGTGGAGTGGGATGTGGGGGGTGGAG
GGGGAATGACAGATTTCTGGAATGCAATGTAATGTTACTGAGACTTAAATAGATGTTATGTAT
ATGATTGTCTGTTTAAGTGTTTGAAAATTGTTAATTATGCCCAGTGTGAACTTAGTACTTAAC
ACATTTTGATTTTAATTAAATAAATTGGGTTTCCTTCTCAAAAAAAAAAAAAAAAAAAAAAAA
AAAAA

FIGURE 220

MLVNFILRCGLLLVTLSLAIAKHKQSSFTKSCYPRGTLSQAVDALYIKAAWLKATIPEDRIKN
IRLLKKKTKKQFMKNCQFQEQLLSFFMEDVFGQLQLQGCKKIRFVEDFHSLRQKLSHCISCAS
SAREMKSITRMKRIFYRIGNKGIYKAISELDILLSWIKKLLESSQ

Signal sequence:

amino acids 1-21

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 68-71

N-myristoylation site.

amino acids 148-153

Interleukin-10 proteins.

amino acids 58-94, 74-102, 128-170

FIGURE 221

GACCACGGCCCTGCGCCCCAGCCAGGCCTGAGGAC**ATG**AGGCGGCCGGCGGCGGTGCCGCTCC

TGCTGCTGCTGTGTTTTGGGTCTCAGAGGGCCAAGGCAGCAACAGCCTGTGGTCGCCCCAGGA

TGCTGAACCGAATGGTGGGCGGGCAGGACACGCAGGAGGGCGAGTGGCCCTGGCAAGTCAGCA

TCCAGCGCAACGGAAGCCACTTCTGCGGGGGCAGCCTCATCGCGGAGCAGTGGGTCCTGACGG

CTGCGCACTGCTTCCGCAACACCTCTGAGACGTCCCTGTACCAGGTCCTGCTGGGGGCAAGGC

AGCTAGTGCAGCCGGGACCACACGCTATGTATGCCCGGGTGAGGCAGGTGGAGAGCAACCCCC

TGTACCAGGGCACGGCCTCCAGCGCTGACGTGGCCCTGGTGGAGCTGGAGGCACCAGTGCCCT

TCACCAATTACATCCTCCCCGTGTGCCTGCCTGACCCCTCGGTGATCTTTGAGACGGGCATGA

ACTGCTGGGTCACTGGCTGGGGCAGCCCCAGTGAGGAAGACCTCCTGCCCGAACCGCGGATCC

TGCAGAAACTCGCTGTGCCCATCATCGACACACCCAAGTGCAACCTGCTCTACAGCAAAGACA

CCGAGTTTGGCTACCAACCCAAAACCATCAAGAATGACATGCTGTGCGCCGGCTTCGAGGAGG

GCAAGAAGGATGCCTGCAAGGGCGACTCGGGCGGCCCCCTGGTGTGCCTCGTGGGTCAGTCGT

GGCTGCAGGCGGGGGTGATCAGCTGGGGTGAGGGCTGTGCCCGCCAGAACCGCCCAGGTGTCT

ACATCCGTGTCACCGCCCACCACAACTGGATCCATCGGATCATCCCCAAACTGCAGTTCCAGC

CAGCGAGGTTGGGCGGCCAGAAG**TGA**GACCCCCGGGGCCAGGAGCCCCTTGAGCAGAGCTCTG

CACCCAGCCTGCCCGCCCACACCATCCTGCTGGTCCTCCCAGCGCTGCTGTTGCACCTGTGAG

CCCCACCAGACTCATTTGTAAATAGCGCTCCTTCCTCCCCTCTCAAATACCCTTATTTTATTT

ATGTTTCTCCCAATAAAAACCCAGCCTGTGTGCCAGCTGAAAAAAAAAAAAAAAAAAA

FIGURE 222

MRRPAAVPLLLLLCFGSQRAKAATACGRPRMLNRMVGGQDTQEGEWPWQVSIQRNGSHFCGGS
LIAEQWVLTAAHCFRNTSETSLYQVLLGARQLVQPGPHAMYARVRQVESNPLYQGTASSADVA
LVELEAPVPFTNYILPVCLPDPSVIFETGMNCWVTGWGSPSEEDLLPEPRILQKLAVPIIDTP
KCNLLYSKDTEFGYQPKTIKNDMLCAGFEEGKKDACKGDSGGPLVCLVGQSWLQAGVISWGEG
CARQNRPGVYIRVTAHHNWIHRIIPKLQFQPARLGGQK

Important features of the protein:

Signal peptide:

amino acids 1-22

N-glycosylation sites.

amino acids 55-58, 79-82

Casein kinase II phosphorylation sites.

amino acids 121-124, 165-168, 167-170, 248-251

Tyrosine kinase phosphorylation sites.

amino acids 78-86, 197-203

N-myristoylation sites.

amino acids 16-21, 37-42, 56-61, 62-67, 118-123

Amidation site.

amino acids 219-222

Serine proteases, trypsin family, histidine active site.

amino acids 71-76

FIGURE 223

CAAG**ATG**TGGACAGCTCTTGTGCTCATTTGGATTTTCTCCTTGTCCTTATCTGAAAGCCATGC
GGCATCCAACGATCCACGCAACTTTGTCCCTAACAAAATGTGGAAGGGATTAGTCAAGAGGAA
TGCATCTGTGGAAACAGTTGATAATAAAACGTCTGAGGATGTAACCATGGCAGCAGCTTCTCC
TGTCACATTGACCAAAGGGACTTCGGCAGCCCACCTCAACTCTATGGAAGTCACAACAGAGGA
CACAAGCAGGACAGATGTGAGTGAACCAGCAACTTCAGGAGTTGCAGCTGATGGTGTGACCTC
CATTGCTCCCACGGCTGTGGCCTCCAGTACGACTGCGGCCTCCATTACGACTGCGGCCTCCAG
TATGACTGTGGCCTCCAGTGCTCCCACGACTGCAGCCTCCAGTACAACTGTGGCCTCCATTGC
TCCCACGACTGCAGCCTCCAGTATGACTGCGGCCTCCAGCACTCCCATGACACTTGCACTCCC
CGCGCCCACGTCCACTTCCACAGGGCGGACCCCGTCCACTACCGCCACTGGGCATCCATCTCT
CAGCACAGCCCTCGCACAAGTGCCAAAGAGCAGCGCGTTGCCAAGAACAGCAACCCTGGCCAC
ATTGGCCACACGTGCTCAGACTGTAGCGACCACAGCAAACACAAGCAGCCCCATGAGCACTCG
TCCAAGTCCTTCCAAGCACATGCCCAGTGACACCGCGGCAAGCCCTGTACCCCCTATGCGTCC
CCAAGCACAAGGTCCCATTAGCCAGGTGTCAGTGGACCAGCCTGTGGTTAACACAACAAATAA
ATCCACACCCATGCCCTCAAACACAACCCCAGAGCCCGCCCCCACCCCCACAGTGGTGACCAC
CACCAAGGCACAAGCCAGGGAGCCAACTGCCAGCCCAGTGCCAGTACCTCACACCAGCCCAAT
CCCTGAGATGGAGGCCATGTCCCCCACGACACAGCCAAGCCCCATGCCATATACCCAGAGGGC
CGCTGGGCCAGGCACATCCCAGGCACCGGAGCAGGTAGAGACTGAAGCCACACCAGGTACTGA
TTCCACTGGGCCAACACCCAGGAGCTCAGGGGGCACTAAGATGCCAGCCACGGACTCGTGCCA
GCCCAGCACCCAAGGCCAGTACATGGTGGTCACCACTGAGCCCCTCACCCAGGCCGTGGTAGA
CAAAACTCTCCTTCTGGTGGTGCTGTTACTCGGGGTGACCCTTTTCATCACAGTCTTGGTTTT
GTTTGCCCTGCAGGCCTATGAGAGCTACAAGAAGAAGGACTACACCCAGGTGGACTACTTAAT
CAACGGGATGTATGCGGACTCAGAAATG**TGA**GGGGGGCGGGGGCCTGGCGGGAGGCCTGGCCC
CTTCCTCGTCCTTTCCTTTTGCCTTTGAGACCAAACCAAGTGCTTCCAAATTCTTTTGGTGCA
ATTGAGGAGATATGCCAGATGCTTAAACACATTTAATTGCTGTCAGATTAATTCCATGATCAC
TAAAGAGTTGCTGCTTTTTTCATATTTATTTTTGTAAATGATTCTGTGCCCAGGAGCAGCTGG
GGGTTCCACCTCAGGGTGGGGCGGGCAGGACCCCGTCTCCCCAGGTGTCGGAGCCTGACCTGA
ATTAAAGTACTGACTGCTCGCCA

FIGURE 224

MWTALVLIWIFSLSLSESHAASNDPRNFVPNKMWKGLVKRNASVETVDNKTSEDVTMAAASPV
TLTKGTSAAHLNSMEVTTEDTSRTDVSEPATSGVAADGVTSIAPTAVASSTTAASITTAASSM
TVASSAPTTAASSTTVASIAPTTAASSMTAASSTPMTLALPAPTSTSTGRTPSTTATGHPSLS
TALAQVPKSSALPRTATLATLATRAQTVATTANTSSPMSTRPSPSKHMPSDTAASPVPPMRPQ
AQGPISQVSVDQPVVNTTNKSTPMPSNTTPEPAPTPTVVTTTKAQAREPTASPVPVPHTSPIP
EMEAMSPTTQPSPMPYTQRAAGPGTSQAPEQVETEATPGTDSTGPTPRSSGGTKMPATDSCQP
STQGQYMVVTTEPLTQAVVDKTLLLVVLLLGVTLFITVLVLFALQAYESYKKKDYTQVDYLIN
GMYADSEM

Signal peptide:

amino acids 1-20

Transmembrane domain:

amino acids 396-420

N-glycosylation sites.

amino acids 41-44, 49-52, 222-225, 268-271, 271-274

Casein kinase II phosphorylation sites.

amino acids 14-17, 51-54, 80-83, 85-88, 280-283, 434-437

N-myristoylation sites.

amino acids 68-73, 354-359

Aldo/keto reductase family putative active site signature.

amino acids 195-210

FIGURE 225

GGAAGGCGCTCAAGGTGCGCGGCCCGGGGCGCGCTACTGGGGGCGCCCTCCGCGGTGGGCAGC

GCGCCAGGGATCGGCCTGGGCAGCCGCGGGGCGCGCGAAGGCTGCGCTTTCCCTACGGCCCCC

CTCGCTTCCTCCGGCACGGCGGCAACGGAGATTTCCTCTCGGGGAAACTACGCGGATCCTTTT

CGGGGATCCTCGCCCCGCCCCAGTTCTCCGCCCCCTCCCCTTTGCTGGGGCGCCTGGGCTGGC

CCGCGCAGGGGAGGAGGCTCTGGCAGCCTGGGCAGGGAGGCGGCGGGGGGCCGCGGAGCCGCT

GGCCATCGATTCTCCCCGCCATGTGACGCCGTCCTTAGCCCTGCGACCCCCAGCGCGTCCCGG

GCCTGCGCCTCCGCCCCGCCGCGCAGCGCACG**ATG**CTTCTGCCGGGACGCGCACGCCAACCGC

CGACGCCCCAGCCCGTGCAGCATCCCGGCCTCCGCCGGCAGGTAGAGCCGCCGGGGCAGCTCC

TGCGCCTCTTCTACTGCACTGTCCTGGTCTGCTCCAAAGAGATCTCAGCGCTCACCGACTTCT

CTGGTTACCTAACCAAACTCCTGCAAAACCACACCACCTATGCCTGTGATGGGGACTATTTGA

ATCTACAGTGCCCTCGGCATTCTACGATAAGTGTCCAATCGGCATTTTATGGGCAAGATTACC

AAATGTGTAGTTCCCAGAAGCCTGCCTCCCAGAGGGAAGACAGCTTAACCTGTGTGGCAGCCA

CCACCTTCCAGAAGGTGCTGGACGAATGCCAGAACCAGCGGGCCTGCCACCTCCTGGTCAATA

GCCGTGTTTTTGGACCTGACCTTTGTCCAGGAAGCAGTAAATACCTCCTGGTCTCCTTTAAAT

GCCAACCTAATGAATTAAAAAACAAAACCGTGTGTGAAGACCAGGAGCTGAAACTGCACTGCC

ATGAATCCAAGTTCCTCAACATCTACTCTGCGACCTACGGCAGGAGGACCCAGGAAAGGGACA

TCTGCTCCTCCAAGGCAGAGCGGCTCCCCCCTTTCGATTGCTTGTCTTACTCAGCTTTGCAAG

TCCTATCCCGAAGGTGCTATGGGAAGCAGAGATGCAAAATCATCGTCAACAATCACCATTTTG

GAAGCCCCTGTTTGCCAGGCGTGAAAAAATACCTCACTGTGACCTACGCATGTGTTCCCAAGA

ACATACTCACAGCGATTGATCCAGCCATTGCTAATCTAAAACCTTCTTTGAAGCAGAAAGATG

GTGAATATGGTATAAACTTCGACCCAAGCGGATCGAAGGTTCTGAGGAAAGATGGAATTCTTG

TTAGCAACTCTCTGGCAGCCTTTGCTTACATTAGAGCCCACCCAGAGAGAGCTGCCCTGCTGT

TCGTGTCCAGTGTCTGCATCGGCCTGGCCCTCACACTGTGCGCCCTGGTCATCAGAGAGTCCT

GTGCCAAGGACTTCCGCGACTTGCAGCTGGGGAGGGAGCAGCTGGTGCCAGGAAGTGACAAGG

TCGAGGAGGACAGCGAGGATGAAGAAGAGGAGGAGGACCCCTCTGAGTCTGATTTCCCAGGGG

AACTGTCGGGGTTCTGTAGGACTTCATATCCTATATACAGTTCCATAGAAGCTGCAGAGCTCG

CAGAAAGGATTGAGCGCAGGGAGCAAATCATTCAGGAAATATGGATGAACAGTGGTTTGGACA

CCTCGCTCCCAAGAAACATGGGCCAGTTCTAC**TGA**AAACCACATGCATCTTGATGCGATCGCA

CTTTCTGAAGAAGGAAGGATCCCAAATGCCCCTCCAGTTCTGGTTCACCTGTACCTTCTATGA

AGGAGAATTCGTCATGTCATTCAACACTCGTGAGGCCAGGAAGCTATTAAAGGGATGTTTCAA

GCTGTTTCTAGCACATTCCAAAATAAATGAGGAGGGAGGAAAAAAAAAAAAAAAAAAAAAAAA

AAAAAAAAAAAAAAAAAA

FIGURE 226

MLLPGRARQPPTPQPVQHPGLRRQVEPPGQLLRLFYCTVLVCSKEISALTDFSGYLTKLLQNH
TTYACDGDYLNLQCPRHSTISVQSAFYGQDYQMCSSQKPASQREDSLTCVAATTFQKVLDECQ
NQRACHLLVNSRVFGPDLCPGSSKYLLVSFKCQPNELKNKTVCEDQELKLHCHESKFLNIYSA
TYGRRTQERDICSSKAERLPPFDCLSYSALQVLSRRCYGKQRCKIIVNNHHFGSPCLPGVKKY
LTVTYACVPKNILTAIDPAIANLKPSLKQKDGEYGINFDPSGSKVLRKDGILVSNSLAAFAYI
RAHPERAALLFVSSVCIGLALTLCALVIRESCAKDFRDLQLGREQLVPGSDKVEEDSEDEEEE
EDPSESDFPGELSGFCRTSYPIYSSIEAAELAERIERREQIIQEIWMNSGLDTSLPRNMGQFY

Transmembrane domains:

amino acids 32-49, 322-343

N-glycosylation sites.

amino acids 62-66, 165-169

Tyrosine kinase phosphorylation site.

amino acids 280-287

N-myristoylation site.

amino acids 302-308, 333-339, 428-434

Amidation site.

amino acids 191-195

FIGURE 227

GGCACGAGGTGGAAGGGCTTTTACAAACAGATTGCTGGCCCCACCCCCCAGAATTTCTCATCA

GGAGTGGGCAAGACCAATCATTTGCATTTCTGACAAGTTCCCAGGAGCTGCAGCTGCTGGCCC

TGGAACCACACTTTGAGAACCACTGCTTTAGACCAAACACCAAAGGAAGATGCAGCCACCCTC

CTTTACATGTCACAACGCTCAGGGTCCATGAGTACCTCAGGCTGTCCAGCTGAGCTCCACCTG

CAGCAGCCGAGATTCCCGACTCGCTCCACCATTGGGGGCTAGGAGTGAAGCGTGTCACC**ATG**G

TCAGCTCATGGCCAGCCAGGAAAGCCTCTCTGCTGTGCGTCTGTGCAGTTCTTGTTCTTCCCT

GGAGGACTCTTGGATCGCCTGTGATCTTGGCCAGGAGACCAGGTGCCTGGGTCCCTTCCTGGA

AGGGGACAAGTTACACACCCCAGCCCCATTTTCCCACCAACTTCTACATGCCTTGGGAGAACC

TTCTACATGTTGGCTGCCCCCTTCCCCTATTTCAGCAGTGCCCAGTCCTGCTTATAAACCTGA

GGCCTGCTCCCCATACCTTCCCTGTGCAAGTGCCAGCCGTTATTCCAGGCAGCCCAATGTTGT

TGAGGCCAGATGGATTCCTGGAAGCAGCTGGCCCATGGATG**TGA**GTCATCACAGTATTCTAGA

AACAGAGAAGAGGTCTTAACCTAATGCGCATAGAGAAATTGTTCTCATTGTAAACATACCCCT

GTCCTTAGCTGATCTAGGTGGAAGCCCAGCTTCATGTGCTAGGGGGCATGATAATGATAATAA

AGGAATTGTATCTAGGACTAA

FIGURE 228

MVSSWPARKASLLCVCAVLVLPWRTLGSPVILARRPGAWVPSWKGTSYTPQPHFPTNFYMPWE

NLLHVGCPLPLFQQCPVLLINLRPAPHTFPVQVPAVIPGSPMLLRPDGFLEAAGPWM

Signal peptide:

amino acids 1-27

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 8-12

FIGURE 229

GGGAAGGGATGCAAGGAAGCCCTCCGGCGCTGCGCTCCGAGGCGGGAGACAGCGTCCCGCTGA
AAATGTGTGTCTGACATGCAAGCTCAGTGGGGCAGAGACCCGTGGATTGCTGTGCCCTGCCCT
CCGGACCTGGATC**ATG**AAGGTGTTGGGAAGAAGCTTCTTCTGGGTGCTGTTTCCCGTCCTTCC
CTGGGCGGTGCAGGCTGTGGAGCACGAGGAGGTGGCGCAGCGTGTGATCAAACTGCACCGCGG
GCGAGGGGTGGCTGCCATGCAGAGCCGGCAGTGGGTCCGGGACAGCTGCAGGAAGCTCTCAGG
GCTTCTCCGCCAGAAGAATGCAGTTCTGAACAAACTGAAAACTGCAATTGGAGCAGTGGAGAA
AGACGTGGGCCTGTCGGATGAAGAGAAACTGTTTCAGGTGCACACGTTTGAAATTTTCCAGAA
AGAGCTGAATGAAAGTGAAAATTCCGTTTTCCAAGCTGTCTACGGACTGCAGAGAGCCCTGCA
GGGGGATTACAAAGATGTCGTGAACATGAAGGAGAGCAGCCGGCAGCGCCTGGAGGCCCTGAG
AGAGGCTGCAATAAAGGAAGAAACAGAATATATGGAACTTCTGGCAGCAGAAAAACATCAAGT
TGAAGCCCTTAAAAATATGCAACATCAAAACCAAAGTTTATCCATGCTTGACGAGATTCTTGA
AGATGTAAGAAAGGCAGCGGATCGTCTGGAGGAAGAGATAGAGGAACATGCTTTTGACGACAA
TAAATCAGTCAAGGGGGTCAATTTTGAGGCAGTTCTGAGGGTGGAGGAAGAAGAGGCCAATTC
TAAGCAAAATATAACAAAACGAGAAGTGGAGGATGACTTGGGTCTTAGCATGCTGATTGACTC
CCAGAACAACCAGTATATTTTGACCAAGCCCAGAGATTCAACCATCCCACGTGCAGATCACCA
CTTTATAAAGGACATTGTTACCATAGGAATGCTGTCCTTGCCTTGTGGCTGGCTATGTACAGC
CATAGGATTGCCTACAATGTTTGGTTATATTATTTGTGGTGTACTTCTGGGACCTTCAGGACT
AAATAGTATTAAGTCTATTGTGCAAGTGGAGACATTAGGAGAATTTGGGGTGTTTTTTACTCT
TTTTCTTGTTGGCTTAGAATTTTCTCCAGAAAAGCTAAGAAAGGTGTGGAAGATTTCCTTACA
AGGGCCGTGTTACATGACACTGTTAATGATTGCATTTGGCTTGCTGTGGGGGCATCTCTTGCG
GATCAAACCCACGCAGAGCGTCTTCATTTCCACGTGTCTGTCCTTGTCAAGCACACCCCTCGT
GTCCAGGTTCCTCATGGGCAGTGCTCGGGGTGACAAAGAAGGCGACATTGACTACAGCACCGT
GCTCCTCGGCATGCTGGTGACGCAGGACGTGCAGCTCGGGCTCTTCATGGCCGTCATGCCGAC
TCTCATACAGGCGGGCGCCAGTGCATCTTCTAGCATTGTCGTGGAAGTTCTCCGAATCCTGGT
TTTGATTGGTCAGATTCTTTTTTCACTAGCGGCGGTTTTTCTTTTATGTCTTGTTATAAAGAA
GTATCTCATTGGACCCTATTATCGGAAGCTGCACATGGAAAGCAAGGGGAACAAAGAAATCCT
GATCTTGGGAATATCTGCCTTTATCTTCTTAATGTTAACGGTCACGGAGCTGCTGGACGTCTC
CATGGAGCTGGGCTGTTTCCTGGCTGGAGCGCTCGTCTCCTCTCAGGGCCCCGTGGTCACCGA
GGAGATCGCCACCTCCATCGAACCCATCCGCGACTTCCTGGCCATCGTTTTCTTCGCCTCCAT
AGGGCTCCACGTGTTCCCCACGTTTGTGGCGTACGAGCTCACGGTGCTGGTGTTCCTCACCTT
GTCAGTGGTGGTGATGAAGTTTCTCCTGGCGGCGCTGGTCCTGTCTCTCATTCTGCCGAGGAG
CAGCCAGTACATCAAGTGGATCGTCTCTGCGGGGCTTGCCCAGGTCAGCGAGTTTTCCTTTGT
CCTGGGGAGCCGGGCGCGAAGAGCGGGCGTCATCTCTCGGGAGGTGTACCTCCTTATACTGAG
TGTGACCACGCTCAGCCTCTTGCTCGCCCCGGTGCTGTGGAGAGCTGCAATCACGAGGTGTGT
GCCCAGACCGGAGAGACGGTCCAGCCTC**TGA**TGGCTCGGAGATGATGGACCGTGGAAGGGAAG
CGTCTGTGGGGAGTGAGCGCTTAGATGGCCAGCAGCTGCTCCTTCTGGGAAGCTCGCACCTTG
GCAACAGAACAGCCCTCTAGCAGAGCGTCAGTGCAGTCGTGTTATCCCGGCTTTTACAGAATA
TTCTTGTCCTATTTTAGAATTTTCCGGAGTAGTTTATTTGCAGTCTGTTGATTATGTGCAGTA
GACCCGGGACACTGCGTTTTACCGATCACCTTGAATGTGGTGCCTGGATGTGCCTTTTTTTTT
TTTCCCTGAAATTATTATTAATTTTCTATTGTGAGTTCATCAGTTCATAGTTTTTTTAGTAAA
GAAGCAAAATTAAAAGGCTTTTAAAAATGTACAACTTCAGAATTATAATCTGTTAGTCAAATA
TTTGTTATTAAACATTTCTGTAATATGAAGTTGTAATCCTGGCCGTGAGCTTGGAAGCTTACT
TTTGATTCTTAAAGCCTATGTTTTCTAAAATGAGACAAATACGGATGTCTATTTGCCTTTTAT
TGTAACTTTTAAATGAAATAATTTCATGTCAATTTCTATTAGATATATCACTTAAAATATTTG
GTTTTAAATCACAAGAATATGTATTCTTTAATAAAGATAATTTATGATCATGGTAAAAAAAAAA

FIGURE 230

MKVLGRSFFWVLFPVLPWAVQAVEHEEVAQRVIKLHRGRGVAAMQSRQWVRDSCRKLSGLLRQ
KNAVLNKLKTAIGAVEKDVGLSDEEKLFQVHTFEIFQKELNESENSVFQAVYGLQRALQGDYK
DVVNMKESSRQRLEALREAAIKEETEYMELLAAEKHQVEALKNMQHQNQSLSMLDEILEDVRK
AADRLEEEIEEHAFDDNKSVKGVNFEAVLRVEEEEANSKQNITKREVEDDLGLSMLIDSQNNQ
YILTKPRDSTIPRADHHFIKDIVTIGMLSLPCGWLCTAIGLPTMFGYIICGVLLGPSGLNSIK
SIVQVETLGEFGVFFTLFLVGLEFSPEKLRKVWKISLQGPCYMTLLMIAFGLLWGHLLRIKPT
QSVFISTCLSLSSTPLVSRFLMGSARGDKEGDIDYSTVLLGMLVTQDVQLGLFMAVMPTLIQA
GASASSSIVVEVLRILVLIGQILFSLAAVFLLCLVIKKYLIGPYYRKLHMESKGNKEILILGI
SAFIFLMLTVTELLDVSMELGCFLAGALVSSQGPVVTEEIATSIEPIRDFLAIVFFASIGLHV
FPTFVAYELTVLVFLTLSVVVMKFLLAALVLSLILPRSSQYIKWIVSAGLAQVSEFSFVLGSR
ARRAGVISREVYLLILSVTTLSLLLAPVLWRAAITRCVPRPERRSSL

Signal peptide:

amino acids 1-22

Transmembrane domains:

amino acids 282-304, 322-337, 354-370, 379-395, 445-474, 501-520, 576-598, 641-660

N-glycosylation sites.

amino acids 104-108, 174-178, 206-210, 230-234

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 55-59, 673-677

Tyrosine kinase phosphorylation site.

amino acids 407-414

N-myristoylation sites.

amino acids 116-122, 327-333, 366-372, 401-407, 419-425, 429-435, 442-448, 525-531, 530-536

Cell attachment sequence.

amino acids 404-407

FIGURE 231

GAGAAAAACAACAGGAAGCAGCTTACAAACTCGGTGAACAACTGAGGGAACCAAACCAGAGAC

GCGCTGAACAGAGAGAATCAGGCTCAAAGCAAGTGGAAGTGGGCAGAGATTCCACCAGGACTG

GTGCAAGGCGCAGAGCCAGCCAGATTTGAGAAGAAGGCAAAAAG**ATG**CTGGGGAGCAGAGCTG

TAATGCTGCTGTTGCTGCTGCCCTGGACAGCTCAGGGCAGAGCTGTGCCTGGGGGCAGCAGCC

CTGCCTGGACTCAGTGCCAGCAGCTTTCACAGAAGCTCTGCACACTGGCCTGGAGTGCACATC

CACTAGTGGGACACATGGATCTAAGAGAAGAGGGAGATGAAGAGACTACAAATGATGTTCCCC

ATATCCAGTGTGGAGATGGCTGTGACCCCCAAGGACTCAGGGACAACAGTCAGTTCTGCTTGC

AAAGGATCCACCAGGGTCTGATTTTTTATGAGAAGCTGCTAGGATCGGATATTTTCACAGGGG

AGCCTTCTCTGCTCCCTGATAGCCCTGTGGGCCAGCTTCATGCCTCCCTACTGGGCCTCAGCC

AACTCCTGCAGCCTGAGGGTCACCACTGGGAGACTCAGCAGATTCCAAGCCTCAGTCCCAGCC

AGCCATGGCAGCGTCTCCTTCTCCGCTTCAAAATCCTTCGCAGCCTCCAGGCCTTTGTGGCTG

TAGCCGCCCGGGTCTTTGCCCATGGAGCAGCAACCCTGAGTCCC**TAA**AGGCAGCAGCTCAAGG

ATGGCACTCAGATCTCCATGGCCCAGCAAGGCCAAGATAAATCTACCACCCCAGGCACCTGTG

AGCCAACAGGTTAATTAGTCCATTAATTTTAGTGGGACCTGCATATGTTGAAAATTACCAATA

CTGACTGACATGTGATGCTGACCTATGATAAGGTTGAGTATTTATTAGATGGGAAGGGAAATT

TGGGGATTATTTATCCTCCTGGGGACAGTTTGGGGAGGATTATTTATTGTATTTATATTGAAT

TATGTACTTTTTTCAATAAAGTCTTATTTTTGTGGCTAAAAAAAAAAAAA

FIGURE 232

MLGSRAVMLLLLLPWTAQGRAVPGGSSPAWTQCQQLSQKLCTLAWSAHPLVGHMDLREEGDEE
TTNDVPHIQCGDGCDPQGLRDNSQFCLQRIHQGLIFYEKLLGSDIFTGEPSLLPDSPVGQLHA
SLLGLSQLLQPEGHHWETQQIPSLSPSQPWQRLLLRFKILRSLQAFVAVAARVFAHGAATLSP

Important features of the protein:

Signal peptide:

amino acids 1-21

Casein kinase II phosphorylation site.

amino acids 64-67

N-myristoylation sites.

amino acids 25-30, 81-86, 122-127

FIGURE 233

CCCACGCGTCCGGCCCTGTAACCAAGATACTGACTGAACATGGCTGGCGGACTCAGGCTGGGGTCTGCAGTGCAG
CATTAATGGGCCGCTGACATGAATATGGAGTAGTTTTCTCTAGCAAAGAGTA**ATG**TGGGCCATGGAGTCAGGCCA
CCTCCTCTGGGCTCTGCTGTTCATGCAGTCCTTGTGGCCTCAACTGACTGATGGAGCCACTCGAGTCTACTACCT
GGGCATCCGGGATGTGCAGTGGAACTATGCTCCCAAGGGAAGAAATGTCATCACGAACCAGCCTCTGGACAGTGA
CATAGTGGCTTCCAGCTTCTTAAAGTCTGACAAGAACCGGATAGGGGGAACCTACAAGAAGACCATCTATAAAGA
ATACAAGGATGACTCATACACAGATGAAGTGGCCCAGCCTGCCTGGTTGGGCTTCCTGGGGCCAGTGTTGCAGGC
TGAAGTGGGGGATGTCATTCTTATTCACCTGAAGAATTTTGCCACTCGTCCCTATACCATCCACCCTCATGGTGT
CTTCTACGAGAAGGACTCTGAAGGTTCCCTATACCCAGATGGCTCCTCTGGGCCACTGAAAGCTGATGACTCTGT
TCCCCCGGGGGGCAGCCATATCTACAACTGGACCATTCCAGAAGGCCATGCACCCACCGATGCTGACCCAGCGTG
CCTCACCTGGATCTACCATTCTCATGTAGATGCTCCACGAGACATTGCAACTGGCCTAATTGGGCCTCTCATCAC
CTGTAAAAGAGGAGCCCTGGATGGGAACTCCCCTCCTCAACGCCAGGATGTAGACCATGATTTCTTCCTCCTCTT
CAGTGTGGTAGATGAGAACCTCAGCTGGCATCTCAATGAGAACATTGCCACTTACTGCTCAGATCCTGCTTCAGT
GGACAAAGAAGATGAGACATTTCAGGAGAGCAATAGGATGCATGCAATCAATGGCTTTGTTTTTGGGAATTTACC
TGAGCTGAACATGTGTGCACAGAAACGTGTGGCCTGGCACTTGTTTGGCATGGGCAATGAAATTGATGTCCACAC
AGCATTTTTCCATGGACAGATGCTGACTACCCGTGGACACCACACTGATGTGGCTAACATCTTTCCAGCCACCTT
TGTGACTGCTGAGATGGTGCCCTGGGAACCTGGTACCTGGTTAATTAGCTGCCAAGTGAACAGTCACTTTCGAGA
TGGCATGCAGGCACTCTACAAGGTCAAGTCTTGCTCCATGGCCCCTCCTGTGGACCTGCTCACAGGCAAAGTTCG
ACAGTACTTCATTGAGGCCCATGAGATTCAATGGGACTATGGCCCGATGGGGCATGATGGGAGTACTGGGAAGAA
TTTGAGAGAGCCAGGCAGTATCTCAGATAAGTTTTTCCAGAAGAGCTCCAGCCGAATTGGGGGCACTTACTGGAA
AGTGCGATATGAAGCCTTTCAAGATGAGACATTCCAAGAGAAGATGCATTTGGAGGAAGATAGGCATCTTGGAAT
CCTGGGGCCAGTGATCCGGGCTGAGGTGGGTGACACCATTCAGGTGGTCTTCTACAACCGTGCCTCCCAGCCATT
CAGCATGCAGCCCCATGGGGTCTTTTATGAGAAAGACTATGAAGGCACTGTGTACAATGATGGCTCATCTTACCC
TGGCTTGGTTGCCAAGCCCTTTGAGAAAGTAACATACCGCTGGACAGTCCCCCCTCATGCCGGTCCCACTGCTCA
GGATCCTGCTTGTCTCACTTGGATGTACTTCTCTGCTGCAGATCCCATAAGAGACACAAATTCTGGCCTGGTGGG
CCCGCTGCTGGTGTGCAGGGCTGGTGCCTTGGGTGCAGATGGCAAGCAGAAAGGGGTGGATAAAGAATTCTTTCT
TCTCTTCACTGTGTTGGATGAGAACAAGAGCTGGTACAGCAATGCCAATCAAGCAGCTGCTATGTTGGATTTCCG
ACTGCTTTCAGAGGATATTGAGGGCTTCCAAGACTCCAATCGGATGCATGCCATTAATGGGTTTCTGTTCTCTAA
CCTGCCCAGGCTGGACATGTGCAAGGGTGACACAGTGGCCTGGCACCTGCTCGGCCTGGGCACAGAGACTGATGT
GCATGGAGTCATGTTCCAGGGCAACACTGTGCAGCTTCAGGGCATGAGGAAGGGTGCAGCTATGCTCTTTCCTCA
TACCTTTGTCATGGCCATCATGCAGCCTGACAACCTTGGGACATTTGAGATTTATTGCCAGGCAGGCAGCCATCG
AGAAGCAGGGATGAGGGCAATCTATAATGTCTCCCAGTGTCCTGGCCACCAAGCCACCCCTCGCCAACGCTACCA
AGCTGCAAGAATCTACTATATCATGGCAGAAGAAGTAGAGTGGGACTATTGCCCTGACCGGAGCTGGGAACGGGA
ATGGCACAACCAGTCTGAGAAGGACAGTTATGGTTACATTTTCCTGAGCAACAAGGATGGGCTCCTGGGTTCCAG
ATACAAGAAAGCTGTATTCAGGGAATACACTGATGGTACATTCAGGATCCCTCGGCCAAGGACTGGACCAGAAGA
ACACTTGGGAATCTTGGGTCCACTTATCAAAGGTGAAGTTGGTGATATCCTGACTGTGGTATTCAAGAATAATGC
CAGCCGCCCCTACTCTGTGCATGCTCATGGAGTGCTAGAATCTACTACTGTCTGGCCACTGGCTGCTGAGCCTGG
TGAGGTGGTCACTTATCAGTGGAACATCCCAGAGAGGTCTGGCCCTGGGCCCAATGACTCTGCTTGTGTTTCCTG
GATCTATTATTCTGCAGTGGATCCCATCAAGGACATGTATAGTGGCCTGGTGGGGCCCTTGGCTATCTGCCAAAA
GGGCATCCTGGAGCCCCATGGAGGACGGAGTGACATGGATCGGGAATTTGCATTGTTGTTCTTGATTTTTGATGA
AAATAAGTCTTGGTATTTGGAGGAAAATGTGGCAACCCATGGGTCCCAGGATCCAGGCAGTATTAACCTACAGGA
TGAAACTTTCTTGGAGAGCAATAAAATGCATGCAATCAATGGGAAACTCTATGCCAACCTTAGGGGTCTTACCAT
GTACCAAGGAGAACGAGTGGCCTGGTACATGCTGGCCATGGGCCAAGATGTGGATCTACACACCATCCACTTTCA
TGCAGAGAGCTTCCTCTATCGGAATGGCGAGAACTACCGGGCAGATGTGGTGGATCTGTTCCCAGGGACTTTTGA
GGTTGTGGAGATGGTGGCCAGCAACCCTGGGACATGGCTGATGCACTGCCATGTGACTGACCATGTCCATGCTGG
CATGGAGACCCTCTTCACTGTTTTTTCTCGAACAGAACACTTAAGCCCTCTCACCGTCATCACCAAAGAGACTGA
AAAAGTGCCCCCCAGAGACATTGAAGAAGGCAATGTGAAGATGCTGGGCATGCAGATCCCCATAAAGAATGTTGA
GATGCTGGCCTCTGTTTTGGTTGCCATTAGTGTCACCCTTCTGCTCGTTGTTCTGGCTCTTGGTGGAGTGGTTTG
GTACCAACATCGACAGAGAAAGCTACGACGCAATAGGAGGTCCATCCTGGATGACAGCTTCAAGCTTCTGTCTTT
CAAACAG**TAA**CATCTGGAGCCTGGAGATATCCTCAGGAAGCACATCTGTAGTGCACTCCCAGCAGGCCATGGACT
AGTCACTAACCCCACACTCAAAGGGGCATGGGTGGTGGAGAAGCAGAAGGAGCAATCAAGCTTATCTGGATATTT
CTTTCTTTATTTATTTTACATGGAAATAATATGATTTCACTTTTTCTTTAGTTTCTTTGCTCTACGTGGGCACCT
GGCACTAAGGGAGTACCTTATTATCCTACATCGCAAATTTCAACAGCTACATTATATTTCCTTCTGACACTTGGA
AGGTATTGAAATTTCTAGAAATGTATCCTTCTCACAAAGTAGAGACCAAGAGAAAAACTCATTGATTGGGTTTCT
ACTTCTTTCAAGGACTCAGGAAATTTCACTTTGAACTGAGGCCAAGTGAGCTGTTAAGATAACCCACACTTAAAC
TAAAGGCTAAGAATATAGGCTTGATGGGAAATTGAAGGTAGGCTGAGTATTGGGAATCCAAATTGAATTTTGATT
CTCCTTGGCAGTGAACTACTTTGAAGAAGTGGTCAATGGGTTGTTGCTGCCATGAGCATGTACAACCTCTGGAGC
TAGAAGCTCCTCAGGAAAGCCAGTTCTCCAAGTTCTTAACCTGTGGCACTGAAAGGAATGTTGAGTTACCTCTTC
ATGTTTTAGACAGCAAACCCTATCCATTAAAGTACTTGTTAGACCAAAAAAAAAAAAA

FIGURE 234

MWAMESGHLLWALLFMQSLWPQLTDGATRVYYLGIRDVQWNYAPKGRNVITNQPLDSDIVASS
FLKSDKNRIGGTYKKTIYKEYKDDSYTDEVAQPAWLGFLGPVLQAEVGDVILIHLKNFATRPY
TIHPHGVFYEKDSEGSLYPDGSSGPLKADDSVPPGGSHIYNWTIPEGHAPTDADPACLTWIYH
SHVDAPRDIATGLIGPLITCKRGALDGNSPPQRQDVDHDFFLLFSVVDENLSWHLNENIATYC
SDPASVDKEDETFQESNRMHAINGFVFGNLPELNMCAQKRVAWHLFGMGNEIDVHTAFFHGQM
LTTRGHHTDVANIFPATFVTAEMVPWEPGTWLISCQVNSHFRDGMQALYKVKSCSMAPPVDLL
TGKVRQYFIEAHEIQWDYGPMGHDGSTGKNLREPGSISDKFFQKSSSRIGGTYWKVRYEAFQD
ETFQEKMHLEEDRHLGILGPVIRAEVGDTIQVVFYNRASQPFSMQPHGVFYEKDYEGTVYNDG
SSYPGLVAKPFEKVTYRWTVPPHAGPTAQDPACLTWMYFSAADPIRDTNSGLVGPLLVCRAGA
LGADGKQKGVDKEFFLLFTVLDENKSWYSNANQAAAMLDFRLLSEDIEGFQDSNRMHAINGFL
FSNLPRLDMCKGDTVAWHLLGLGTETDVHGVMFQGNTVQLQGMRKGAAMLFPHTFVMAIMQPD
NLGTFEIYCQAGSHREAGMRAIYNVSQCPGHQATPRQRYQAARIYYIMAEEVEWDYCPDRSWE
REWHNQSEKDSYGYIFLSNKDGLLGSRYKKAVFREYTDGTFRIPRPRTGPEEHLGILGPLIKG
EVGDILTVVFKNNASRPYSVHAHGVLESTTVWPLAAEPGEVVTYQWNIPERSGPGPNDSACVS
WIYYSAVDPIKDMYSGLVGPLAICQKGILEPHGGRSDMDREFALLFLIFDENKSWYLEENVAT
HGSQDPGSINLQDETFLESNKMHAINGKLYANLRGLTMYQGERVAWYMLAMGQDVDLHTIHFH
AESFLYRNGENYRADVVDLFPGTFEVVEMVASNPGTWLMHCHVTDHVHAGMETLFTVFSRTEH
LSPLTVITKETEKVPPRDIEEGNVKMLGMQIPIKNVEMLASVLVAISVTLLLVVLALGGVVWY
QHRQRKLRRNRRSILDDSFKLLSFKQ

Signal peptide:

amino acids 1-21

Transmembrane domain:

amino acids 1109-1130

N-glycosylation sites.

amino acids 167-171, 239-243, 591-595, 717-721, 761-765, 832-836, 876-880, 934-938

Glycosaminoglycan attachment site.

amino acids 871-875

Tyrosine kinase phosphorylation sites.

amino acids 82-90, 137-145, 494-502, 513-521

N-myristoylation sites.

amino acids 212-218, 313-319, 498-504, 566-572, 672-678, 778-784, 843-849

Multicopper oxidases signature 1.

amino acids 344-365, 696-717, 1043-1064

Multicopper oxidases signature 2.

amino acids 1048-1060

FIGURE 235

GGAAAGAGTGCTGGTACTACAACCAGGAAGTGACAGATAATGTGCTTTAAACTACATTAGAAAAGCTTCTCATAG
CAAAACTGAGAGATTGAAGCAGTGATTATTTTTACATAGTTGTCATTAAATATTTGGAGCTCTGCTGTGCATAGA
GATGGCAACATACTTAGAATACACAGCTTTCTGGGCCAGAAATTGATCTTCTGACTTTTGAGCCTTATCTGATTA
CTGCTTGGTTCATCTTTATTTTGTTAAACTACTCTGTAGGCTGAAAGGGAGAGACTCTCCTTGGTTTGCAGAGCC
TGACTAGACAGGAATTCTGGCAACTGCTCCAGCAGAACTATGGCACTGAGCTAGGTTTAAATGCTGAGGAG**ATG**G
AAAACTTGTCACTGTCGATTGAGGATGTGCAGCCAAGAAGTCCAGGAAGAAGCAGCTTGGATGACTCTGGGGAGA
GAGATGAAAAATTATCCAAGTCAATCAGTTTTACCAGTGAATCAATTAGTCGGGTTTCAGAAACAGAGTCATTCG
ATGGAAATTCATCAAAAGGAGGATTAGGCAAAGAGGAGTCCCAAAATGAGAAACAGACCAAAAAGAGTCTCTTAC
CAACTTTGGAAAAGAAGTTAACTAGAGTGCCATCAAAGTCACTGGACTTGAATAAAAATGAATATCTTTCTCTGG
ACAAAAGCAGCACTTCAGATTCTGTTGATGAAGAAAATGTTCCTGAGAAAGATCTTCATGGAAGACTTTTTATCA
ACCGTATTTTTCATATCAGTGCTGACAGAATGTTTGAATTGCTCTTTACCAGTTCACGCTTTATGCAGAAATTTG
CCAGTTCTAGAAATATAATAGATGTAGTATCTACCCCTTGGACTGCAGAACTTGGAGGTGATCAGCTGAGAACGA
TGACCTACACTATAGTCCTTAATAGTCCACTTACTGGAAAATGCACTGCTGCCACTGAAAAGCAGACACTGTATA
AAGAAAGTCGGGAAGCACGATTTTATTTGGTAGATTCAGAAGTACTGACACATGATGTCCCCTACCATGATTACT
TCTATACCGTGAACAGATACTGTATCATCCGATCTTCAAAACAGAAATGCAGGCTAAGAGTTTCCACAGATTTGA
AATACAGAAAACAGCCATGGGGCCTTGTCAAATCTTTAATTGAAAAGAATTCCTGGAGTTCTTTGGAGGACTATT
TCAAACAGCTTGAATCAGATTTGTTAATTGAAGAATCTGTATTAAATCAGGCCATTGAAGACCCTGGAAAACTTA
CTGGCCTACGAAGGAGAAGGCGAACCTTCAACCGAACAGCAGAAACAGTTCCTAAACTTTCCTCTCAGCATTCCT
CTGGAGATGTGGGCTTAGGTGCCAAAGGGGATATTACAGGAAAGAAAAAGGAAATGGAAAACTATAACGTCACTC
TTATTGTGGTAATGAGTATTTTTGTGTTGTTATTAGTTTTGTTGAATGTGACACTGTTTCTGAAGCTGTCAAAGA
TAGAACATGCTGCTCAGTCCTTTTACCGTCTCCGCCTCCAAGAAGAGAAATCTTTAAATTTAGCCTCTGATATGG
TGTCAAGAGCAGAAACTATTCAGAAGAATAAAGATCAGGCCCATCGTTTAAAGGGAGTGCTCCGAGACTCCATAG
TGATGCTTGAACAGCTGAAGAGCTCACTCATTATGCTTCAGAAAACGTTTGATCTACTAAATAAGAATAAGACTG
GCATGGCTGTTGAAAGC**TAG**TGATCTGAAGGACTAAAACCGCAGAGATACTTGGAACTTAAAGAAAATACCTGGA
AGAAAACCAGACGAATGAAGGATTTTGGCATAGAACATTTCTATGTTTTTTCATTATTGAGATTTCTAATATGAA
CATTTCTTTCAGTAACATTTATTTGATAATTAGTTTCTGCTGGCCTTAATAATCCATCCTTTCACTTCTTATAGA
TATTTTTAAGCTGTGAATTTCTTCAGTGAACCATGAAATATATTATAGAACTGAATTTCTCTGATACAAAAAGAA
AATGACACACCCTGAATTGAGTGGTATGGTCTCATTTCTACAGTGAAGTCTGATGCTTTGTTAGCACAGAATCCG
TACATGTCCAATAGGTCGCTTTTGTAACTGAGATAAGACCAAGAGGATAAACAGGACAATATAAGAAGAAACCTC
TATGTCATTACTGATTTTAAAGGTTCTGTTTTCAGGCATATAACATTTCCAGGTTTGTGTACTGTAAAGATTATA
ATGTCTTCATTTATTTAGCATGCAAATTTAATAGTCAAACTTTTTGAATCTGCATGTTGATGATGATTATCAGAA
AGGGTCTTCTGCCATGCTGTATCTTTATGAAAGAAATAGTTGTTTTTTCTTAAGGTAACTATCAGAGGTGGGATT
ATCTTGCCTCCTCACTTAGAATACCAACAGTCAAAAGGAAGAACCATCCTCTGAGTTTTAAAAACCAGAAGGTTA
TGTTAAAATCTGGGCATTTAGTGACAGATCAAATGCATACTTGAACTAAGATTGGCTTCAGCTTAGCAGTCTTTC
ATGGTGGAAGTGACACATCTGGTTGAAAATAATTTGTGTATTTTCAGTAACCATGTATGGCTTCCTTCTTTATGT
ATGTGTGTGACTTGTTTTAATTGGTAAGTTATAAGCCAGACATAGATTTTAGCTCTTTAATAAAAACTTCAGGGG
CACGTATGTCCCAGTACAAGTGTACTGACTATCAAGTTTTAACTCAGATGCAAGCTTTGGCTCTTTCATAAAAAG
TTTTTATGCATATGTGTCTCCATACAAGTGGCTCATTAAAATAAGAACTTTGTAAACTGACTTAAAATCAGATAT
TTTTTCAAGAGTTAGGGAAAGTTGAAGTGTTTTACTGTTTTGTCTCTTGAGCCCTTTCTCTGGGGAAAAAATACA
TATCCATCTATCTATCTATATATAAACTGTGTATACATTCTTACTGTTTGAACAACTATTGCCTTTAATTAAATG
TTTCATTTTTCTCCAGAGTCCCCAAAGCCACATGGCATTATTATAGTCATTTTTGAGATGCCTGTAGAGAATGAA
AGTATTGACTCCGTTAGAGGGAAAATGGGTTTCTCTGGGTGAATTCCAACGAAGCATACCTAGGGGTAACAGTGA
ACCTACCTGGGTTTGTTTTGTTTTGGTAAGGATTTATGTAGTGTCTGGCTGTAAGCAAGAATGAGTGGATTATAA
ACTTGAAGATTTCTCTGTTAAAGTCACAAAAATGATCGACAAACAATATTTTTGTGATGTTTATTTAAACGTTGT
ATTTTATAACATACTTCAAGGAAGAGTATCGAAGTAAGTTGCTTTATAAATTAAGACTAAATTCGTATGGATGCA
GAATTCAATTAATAAAATTTGAGCCTGTTACGTAAATTGAATATTAATAAAATTGAAAATTTCAAAA

FIGURE 236

MENLSLSIEDVQPRSPGRSSLDDSGERDEKLSKSISFTSESISRVSETESFDGNSSKGGLGKE
ESQNEKQTKKSLLPTLEKKLTRVPSKSLDLNKNEYLSLDKSSTSDSVDEENVPEKDLHGRLFI
NRIFHISADRMFELLFTSSRFMQKFASSRNIIDVVSTPWTAELGGDQLRTMTYTIVLNSPLTG
KCTAATEKQTLYKESREARFYLVDSEVLTHDVPYHDYFYTVNRYCIIRSSKQKCRLRVSTDLK
YRKQPWGLVKSLIEKNSWSSLEDYFKQLESDLLIEESVLNQAIEDPGKLTGLRRRRRTFNRTA
ETVPKLSSQHSSGDVGLGAKGDITGKKKEMENYNVTLIVVMSIFVLLLVLLNVTLFLKLSKIE
HAAQSFYRLRLQEEKSLNLASDMVSRAETIQKNKDQAHRLKGVLRDSIVMLEQLKSSLIMLQK
TFDLLNKNKTGMAVES

Transmembrane domain:

amino acids 352-371

N-glycosylation sites.

amino acids 3-7, 54-58, 312-316, 349-353, 367-371, 449-453

cAMP- and cGMP-dependent protein kinase phosphorylation sites.

amino acids 81-85, 307-311

Tyrosine kinase phosphorylation sites.

amino acids 202-211, 246-254, 341-349

N-myristoylation site.

amino acids 259-265

Amidation site.

amino acids 339-343

FIGURE 237

CAGGGGCTGGAGGGCAGGGGAGGGG**ATG**ATGTCATTCCTGCTCGGCGCAATCCTGACCCTGCT
CTGGGCGCCCACGGCTCAGGCTGAGGTTCTGCTGCAGCCTGACTTCAATGCTGAAAAGTTCTC
AGGCCTCTGGTACGTGGTCTCCATGGCATCTGACTGCAGGGTCTTCCTGGGCAAGAAGGACCA
CCTGTCCATGTCCACCAGGGCCATCAGGCCCACAGAGGAGGGCGGCCTCCACGTCCACATGGA
GTTCCCGGGGGCGGACGGCTGTAACCAGGTGGATGCCGAGTACCTGAAGGTGGGCTCCGAGGG
ACACTTCAGAGTCCCGGCCTTGGGCTACCTGGACGTGCGCATCGTGGACACAGACTACAGCTC
CTTCGCCGTCCTTTACATCTACAAGGAGCTGGAGGGGGCCCTCAGCACCATGGTGCAGCTCTA
CAGCCGGACCCAGGATGTGAGTCCCCAGGCTCTGAAGTCCTTCCAGGACTTCTACCCGACCCT
GGGGCTCCCCAAGGACATGATGGTCATGCTGCCCCAGTCAGATGCATGCAACCCTGAGAGCAA
GGAGGCGCCC**TGA**CACCTCCGGAGCCCCACCCCCGCCCTTCCCAGGTGGAGCCAAAGCAGCAG
GCGCCTTTGCCCCTGGAGTCAAGACCCACAGCCCTCGGGGACCACCTGGAGTCTCTCCATCCT
CCACCCCCCGCCTGTGGGATGCCTTGTGGGACGTCTCTTTCTATTCAATAAACAGATGCTGCA
GCCTCA

FIGURE 238

MMSFLLGAILTLLWAPTAQAEVLLQPDFNAEKFSGLWYVVSMASDCRVFLGKKDHLSMSTRAI
RPTEEGGLHVHMEFPGADGCNQVDAEYLKVGSEGHFRVPALGYLDVRIVDTDYSSFAVLYIYK
ELEGALSTMVQLYSRTQDVSPQALKSFQDFYPTLGLPKDMMVMLPQSDACNPESKEAP

Signal peptide:

amino acids 1-20

Tyrosine kinase phosphorylation site.

amino acids 110-117

N-myristoylation sites.

amino acids 7-13, 79-85, 130-136

Amidation site.

amino acids 50-54

FIGURE 239

GGCGCGCTGGTCCAGGTGAGCGGGCGCGTCCCCGCGACGGCGCTGCCTGCCCGAGGCGGTTCA
CGTAAAGACAGCGAGATCCTGAGGGCCAGCCGGGAAGGAGGCGTGGATATGGAGCTGGCTGCT
GCCAAGTCCGGGGCCCGCGCCGCTGCCTAGCGCGTCCTGGGGACTCTGTGGGGACGCGCCCCG
CGCCGCGGCTCGGGGACCCGTAGAGCCCGGCGCTGCGCGC**ATG**GCCCTGCTCTCGCGCCCCGC
GCTCACCCTCCTGCTCCTCCTCATGGCCGCTGTTGTCAGGTGCCAGGAGCAGGCCCAGACCAC
CGACTGGAGAGCCACCCTGAAGACCATCCGGAACGGCGTTCATAAGATAGACACGTACCTGAA
CGCCGCCTTGGACCTCCTGGGAGGCGAGGACGGTCTCTGCCAGTATAAATGCAGTGACGGATC
TAAGCCTTTCCCACGTTATGGTTATAAACCCTCCCCACCGAATGGATGTGGCTCTCCACTGTT
TGGTGTTCATCTTAACATTGGTATCCCTTCCCTGACAAAGTGTTGCAACCAACACGACAGGTG
CTATGAGACCTGTGGCAAAAGCAAGAATGACTGTGATGAAGAATTCCAGTATTGCCTCTCCAA
GATCTGCCGAGATGTACAGAAAACACTAGGACTAACTCAGCATGTTCAGGCATGTGAAACAAC
AGTGGAGCTCTTGTTTGACAGTGTTATACATTTAGGTTGTAAACCATATCTGGACAGCCAACG
AGCCGCATGCAGGTGTCATTATGAAGAAAAAACTGATCTT**TAA**AGGAGATGCCGACAGCTAGT
GACAGATGAAGATGGAAGAACATAACCTTTGACAAATAACTAATGTTTTTACAACATAAAACT
GTCTTATTTTTGTGAAAGGATTATTTTGAGACCTTAAAATAATTTATATCTTGATGTTAAAAC
CTCAAAGCAAAAAAAGTGAGGGAGATAGTGAGGGGAGGGCACGCTTGTCTTCTCAGGTATCTT
CCCCAGCATTGCTCCCTTACTTAGTATGCCAAATGTCTTGACCAATATCAAAAACAAGTGCTT
GTTTAGCGGAGAATTTTGAAAAGAGGAATATATAACTCAATTTTCACAACCACATTTACCAAA
AAAAGAGATCAAATATAAAATTCATCATAATGTCTGTTCAACATTATCTTATTTGGAAAATGG
GGAAATTATCACTTACAAGTATTTGTTTACTATGAAATTTTAAATACACATTTATGCCTAGAA
GGAACGGACTTTTTTTTTCTATTTTAATTACACATAATATGTAATTAAAGTACAACATAATAT
GTTGTTTCTCTGTAGCCCGTTGAGCATATGAGTAAGTCACATTTCTATTAGGACTACTTACAA
GGACAAGGTTTCCATTTTTCCAGTTGTAAAATTGGAACCATCAGCTGATAACCTCGTAGGGAG
CAACCCCAGGATAGCTAAGTGTTATGTAATATGCCTAGAAGGTGATGTGAATGCGATTCAGAA
GCATAGCCACTCCCATTTTATGAGCTACTCACATGACAAATGTCATCTTTTGCTATAACCTTT
GCCAAGTTAGAGAAAAGATGGATTTAATGAGATAAATGAAAAGATATTTAACCTAAAAAAAAA
AAAAAAAAAAAAAAAAAAA

FIGURE 240

MALLSRPALTLLLLLMAAVVRCQEQAQTTDWRATLKTIRNGVHKIDTYLNAALDLLGGEDGLC
QYKCSDGSKPFPRYGYKPSPPNGCGSPLFGVHLNIGIPSLTKCCNQHDRCYETCGKSKNDCDE
EFQYCLSKICRDVQKTLGLTQHVQACETTVELLFDSVIHLGCKPYLDSQRAACRCHYEEKTDL

Important features:

Signal peptide:

amino acids 1-22

N-myristoylation sites:

amino acids 57-63,93-99

Phospholipase A2 histidine active site:

amino acids 106-114

Neuraxin and MAP1B proteins repeat proteins Block:

amino acids 109-137

FIGURE 241

GATTCCGAGCGCCTCCACTGCTGGTCCGTTGGCCAGATCAACTCGCCGCGTGGGCCGGCCGTT
CCCTGAGAGTCTGAGCGCTCGCCGCACCCCCTTCCGAGCTTCTATTGGCCGTAGCAGACGTCC
GTCTGCCGCTATCTCCGCCCCAATACGGAAGCGGCCTAGTCCTCCGGCTCCGACAGCTGGGTG
TCCAGGCC**ATG**GGGCAGCCCTGGGCGGCTGGGAGCACGGACGGGGCGCCCGCGCAGCTGCCTC
TCGTGCTCACCGCGCTGTGGGCCGCGGCCGTGGGCCTGGAGCTGGCTTACGTGCTGGTGCTCG
GTCCCGGGCCGCCGCCGCTGGGACCCCTGGCCCGGGCCTTGCAGCTGGCGCTGGCCGCCTTCC
AGCTGCTCAACCTGCTGGGCAACGTGGGGCTCTTCCTGCGCTCGGATCCCAGCATCCGTGGCG
TGATGCTGGCCGGCCGCGGTCTGGGCCAGGGCTGGGCTTACTGCTACCAATGCCAAAGCCAGG
TGCCGCCACGCAGCGGACACTGCTCTGCCTGCCGCGTCTGCATCCTGCGTCGGGACCACCACT
GCCGCCTGCTGGGCCGCTGCGTGGGCTTCGGCAACTACCGGCCCTTCCTGTGCCTGCTGCTTC
ATGCCGCCGGCGTCCTGCTCCACGTCTCTGTGCTGCTGGGCCCTGCACTGTCGGCCCTGCTGC
GAGCCCACACGCCCCTCCACATGGCTGCCCTCCTCCTGCTTCCCTGGCTCATGTTGCTCACAG
GCAGAGTGTCTCTGGCACAGTTTGCCTTGGCCTTCGTGACGGACACGTGCGTGGCGGGTGCGC
TGCTGTGCGGGGCTGGGCTGCTCTTCCATGGGATGCTGCTGCTGCGGGGCCAGACCACATGGG
AGTGGGCTCGGGGCCAGCACTCCTATGACCTGGGTCCCTGCCACAACCTGCAGGCAGCCCTGG
GGCCCCGCTGGGCCCTCGTCTGGCTCTGGCCCTTCCTGGCCTCCCCATTGCCTGGGGATGGGA
TCACCTTCCAGACCACAGCAGATGTGGGACACACAGCCTCC**TGA**CTCCAGGAAGAGCCAGAGC
TGTGCAGGGAGGAAGGGGTGAGAGGGGGGCCCCCACACCTAGACTCAGTAAGGAAGTCGGGTT
GGACCTTAACATCTGCATTGGACAACTCCACCCCTTCCTTGGCCTTGCCCCTGCCCGCCTACA
CTCCTACGTGTCCAGGGCTTGGGCCGTGACTTAGGCAGAGGAGTGCAGAGGAGGGTCTGGCAG
GGGCTGCTCAGGCCGCCTAGCTGCCCCTTTGCCAGGTTAATAAAGCACTGACTTGTTAA

FIGURE 242

MGQPWAAGSTDGAPAQLPLVLTALWAAAVGLELAYVLVLGPGPPPLGPLARALQLALAAFQLL
NLLGNVGLFLRSDPSIRGVMLAGRGLGQGWAYCYQCQSQVPPRSGHCSACRVCILRRDHHCRL
LGRCVGFGNYRPFLCLLLHAAGVLLHVSVLLGPALSALLRAHTPLHMAALLLLPWLMLLTGRV
SLAQFALAFVTDTCVAGALLCGAGLLFHGMLLLRGQTTWEWARGQHSYDLGPCHNLQAALGPR
WALVWLWPFLASPLPGDGITFQTTADVGHTAS

Important features:

Signal peptide:

amino acids 1-30

Transmembrane domain:

amino acids 51-66,143-160,174-191,198-214

N-myristoylation sites:

amino acids 2-8,8-14,30-36,81-87,88-94,90-96,206-212

Leucine zipper pattern:

amino acids 143-165,150-172,157-179,164-186

FIGURE 243

CTTGTCTTTGTGTCGGTTGTGATTTTCCTAATCTCTGATTTTCCTTTTCTCTCGGACGCTCTC
CCTCTTCGGACCCATTTTCTCCCGTGCTTCATGCCCTGATAGCCTGGCCCCTTCCCGGCTTCC
TTCGCTACCGGGGACGCCTCTAGTTTTTCTGAATTTCTGGCTGGCTCCACCCTCCGCGTTCAT
CTTCCTCAAGAGTTCGCCCCTCTGGGGGCTCCTCTGTGTAATCGTCGCCTTCTCTGGGTATTT
CTGTGAACTCCGTCTCACACCATCCCGCCATCTTCTCTGCCTTGGCCCCTTTTCTCTGTACAG
CCAGCTCTGTGTCCTTTTCTTCTCCCCCTCTAAAATCGACTCCTCTTCTCCCTGAGAGCCCCA
CCTTTGTGCCCCACTCCTCATTTTCCTACGCCTCCCTCTCTCTGCTGGTCCTCTCTCTCCCTG
CAAGGTTCCATTCCATCAATTTGTTTGTCTTTTGTAGGGGTGGCATCCCCTCTGACTACTGCT
CCATCCTTTTTTTTTTTTTTTTTTTTTTTTTTTGCTTGAGGATTTCACTTCAATCTTTTCTGGT
TGCGTCTCCACTTGTACTCAGCTTGTTAGGTCCAGGTCCAGTTGTTCTGCATCTGAGGCTGGC
GTGTGCTGTCTTCTCTGATTGGCCTAATCTCCCTCACCCCCGTGAGATCTGTTGTCAGCCTTC
GTTTCTCTTTCCTGTGTCCCAGCTTTTCTGCGGGTCTTGGCACCTTTCTTGGCCACAGATTTC
TGGGTTACAGAGCATGTGTGTCTGAGGCATTGCAGGCAGAAAAGGGTGGCCGACGTGACCTCT
AGCTGGACTGCTGGGCAGGGGAGCTGTCCTAGATAAAATTGGAAAGAAACAGTGACCCAGAGA
CAGGTGGACAAAGAATTCGGGGACTGATGGGAACTGAGCTTGGGATCCAGACTGAAACTGATT
CCAGACTGACCTCTAGCACCCAGGACCCAGACACAGGGCC**ATG**GGACCCCAGCATTTGAGACT
TGTGCAGCTGTTCTGCCTTCTAGGGGCCATCCCCACTCTGCCTCGGGCTGGAGCTCTTTTGTG
CTATGAAGCAACAGCCTCAAGATTCAGAGCTGTTGCTTTCCATAACTGGAAGTGGCTTCTGAT
GAGGAACATGGTGTGTAAGCTGCAAGAGGGCTGCGAGGAGACGCTAGTGTTCATTGAGACAGG
GACTGCAAGGGGAGTTGTGGGCTTTAAAGGCTGCAGCTCGTCTTCGTCTTACCCTGCGCAAAT
CTCCTACCTTGTTTCCCCACCCGGAGTGTCCATTGCCTCCTACAGTCGCGTCTGCCGGTCTTA
TCTCTGCAACAACCTCACCAATTTGGAGCCTTTTGTGAAACTCAAGGCCAGCACTCCTAAGTC
TATCACATCTGCGTCCTGTAGCTGCCCGACCTGTGTGGGCGAGCACATGAAGGATTGCCTCCC
AAATTTTGTCACCACTAATTCTTGCCCCTTGGCTGCTTCTACGTGTTACAGTTCCACCTTAAA
ATTTCAGGCAGGGTTTCTCAATACCACCTTCCTCCTCATGGGGTGTGCTCGTGAACATAACCA
GCTTTTAGCAGATTTTCATCATATTGGGAGCATCAAAGTGACTGAGGTCCTCAACATCTTAGA
GAAGTCTCAGATTGTTGGTGCAGCATCCTCCAGGCAAGATCCTGCTTGGGGTGTCGTCTTAGG
CCTCCTGTTTGCCTTCAGGGAC**TGA**CCATCTAGCTGCACCCGACAAGCACCCAGACTCTTTCA
CATAACAAATAAAATAGCAGAGTTCCCTTAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAA

FIGURE 244

MGPQHLRLVQLFCLLGAIPTLPRAGALLCYEATASRFRAVAFHNWKWLLMRNMVCKLQEGCEE
TLVFIETGTARGVVGFKGCSSSSSYPAQISYLVSPPGVSIASYSRVCRSYLCNNLTNLEPFVK
LKASTPKSITSASCSCPTCVGEHMKDCLPNFVTTNSCPLAASTCYSSTLKFQAGFLNTTFLLM
GCAREHNQLLADFHHIGSIKVTEVLNILEKSQIVGAASSRQDPAWGVVLGLLFAFRD

Important features:

Signal peptide:

amino acids 1-20

N-glycosylation sites:

amino acids 117-121,183-187

N-myristoylation sites:

amino acids 16-22,25-31,60-66,71-77,81-87,100-106,224-230,
235-241,239-245

Prokaryotic membrane lipoprotein lipid attachment site:

amino acids 181-192

FIGURE 245

GTGGAGTTGGGTGGTGTCGGGAGCCTCTCCCTGAGGGGCACCGCGTCTTCAGGAGCTGGGCCTCCAGTGCGGCGC
GATGTCAGGCGCGGTGACAGCTCTGTGAGTCCGAGGCCGCGGCCGTGGCGCTGGGCGGCTGCGGGGCCTGACCGG
TCCGCTC**ATG**GTGCCGCCACGACGCCATCGCGGGGCAGGAAGGCCAGGGGTGCTGAGTTCTTCACCTCCTTTTAG
ACTGAGATCTGCCAAGTTTTCCGGCATTGCTCTTGAGGATCTCAGAAGGGCTCTTAAGACAAGACTGCAAATGGT
GTGTGTATTTGTCATGAACCGAATGAATTCCCAGAACAGTGGTTTCACTCAGCGCAGGCGAATGGCTCTTGGGAT
TGTTATTCTTCTGCTTGTTGATGTGATATGGGTTGCTTCCTCTGAACTTACTTCGTATGTTTTTACCCAGTACAA
CAAACCATTCTTCAGCACCTTTGCAAAAACATCTATGTTTGTTTTGTACCTTTTGGGCTTTATTATTTGGAAGCC
ATGGAGACAACAGTGTACAAGAGGACTTCGCGGAAAGCATGCTGCTTTTTTTGCAGATGCTGAAGGTTACTTTGC
TGCTTGCACAACAGATACAACTATGAATAGTTCTTTGAGTGAACCTCTGTATGTGCCTGTGAAATTCCATGATCT
TCCAAGTGAAAAACCTGAGAGCACAAACATTGATACTGAAAAAACCCCCAAAAAGTCTCGTGTGAGGTTCAGTAA
TATCATGGAGATTCGACAGCTTCCGTCAAGTCATGCATTGGAAGCAAAGTTGTCTCGCATGTCATATCCTGTGAA
AGAACAAGAATCCATACTGAAAACTGTGGGGAAACTTACTGCAACTCAAGTAGCGAAAATTAGCTTTTTTTTTTG
CTTTGTGTGGTTTTTGGCAAATTTGTCATATCAAGAAGCACTTTCAGACACACAAGTTGCTATAGTTAATATTTT
ATCTTCAACTTCCGGACTTTTTACCTTAATCCTTGCTGCAGTATTTCCAAGTAACAGTGGAGATAGATTTACCCT
TTCTAAACTATTAGCTGTAATTTTAAGCATTGGAGGCGTTGTACTGGTAAACCTGGCAGGGTCTGAAAAACCTGC
TGGAAGAGACACAGTAGGTTCCATTTGGTCTCTTGCTGGAGCCATGCTCTATGCTGTCTATATTGTTATGATTAA
GAGAAAAGTAGATAGAGAAGACAAGTTGGATATTCCAATGTTCTTTGGTTTTGTAGGTTTGTTTAATCTGCTGCT
CTTATGGCCAGGTTTCTTTTTACTTCATTATACTGGATTTGAGGACTTCGAGTTTCCCAATAAAGTAGTATTAAT
GTGCATTATCATTAATGGCCTTATTGGAACAGTACTCTCAGAGTTCCTGTGGTTGTGGGGCTGCTTTCTTACCTC
ATCATTGATAGGCACACTTGCACTAAGCCTTACAATACCTCTGTCCATAATAGCTGACATGTGTATGCAAAAGGT
GCAGTTTTCTTGGTTATTTTTTGCAGGAGCTATCCCTGTATTTTTTTCATTTTTTATTGTAACTCTCCTATGCCA
TTATAATAATTGGGATCCTGTGATGGTGGGAATCAGAAGAATATTTGCTTTTATATGCAGAAAACATCGAATTCA
GAGAGTTCCAGAAGACAGCGAACAGTGTGAGAGTCTCATTTCTATGCACAGTGTTTCTCAGGAGGATGGAGCTAG
T**TAG**CTGTCTGTTGTCTGTAGCCCAGCTTGATAATGGAACTATACAGCGAAGAGACAATCTCTGGCAAGTTTTTG
TAGAAAAAATGTTTCAGTGCCTAGTCTGAAAAATAACAGTTTGAGTTCTTTGAAACTCTAAAATATATTTTTCTC
ATACCTGTTTTCTTCATTTTCATAATGAAGCACTTTGCTATGTAGCTGTGTACATATCACTACAGTTATAGGAAG
TTTCAGTCTACAGTCCATCCAAAGGACCAACCTGCCTTACACATCTCAAGGAATTCAGCTGTTGAAATCATTTGA
ACTAATCAAGGAATAAATCCTAATGTTCTGGGACTTTATTTTCACATGTTAAATGCTGGAATATATTATGAAAAT
GTTTTCAAGAAATCACTTAAGTGTTCATAGACCAGTATTTCTGACAGGTAAAATGCTAAAATAAGCTACCTGTAA
TAAGTGTGGATTATATTTTTGGGTTTTGTAGAATATTGCAAATTAACCACACAAAAAATGTTTAATTTATGCAAC
AAGCATGTTTGTGCAAATTTCATGGGACTTTAAAAAGAATAAGTATTTGAGAAAATATCTGGTTCACTTACACTA
CATTTACTGTATTATTCTTTTATAGCATTAGGTGCCTTGTATTTTAAATCTGTGACAAACCATGGCAAATTTTTA
AAGGGGAAGTATTATTATAAAATGAAGAAATATGTATTTCTAAAGGCTATATTGCTGTAAACTTAATTGATAAAG
CTCTGTTTAATTTAGAGTTTTGAAGAAATAGTCTCCCTTCAATTAAGAAATTTTCATAATGGAATGATTTAAATT
GAAGTGACAAAGAGTATTATTAAAATACAATGTTTATAAAAAAA

FIGURE 246

MVPPRRHRGAGRPGVLSSSPPFRLRSAKFSGIALEDLRRALKTRLQMVCVFVMNRMNSQNSGF
TQRRRMALGIVILLLVDVIWVASSELTSYVFTQYNKPFFSTFAKTSMFVLYLLGFIIWKPWRQ
QCTRGLRGKHAAFFADAEGYFAACTTDTTMNSSLSEPLYVPVKFHDLPSEKPESTNIDTEKTP
KKSRVRFSNIMEIRQLPSSHALEAKLSRMSYPVKEQESILKTVGKLTATQVAKISFFFCFVWF
LANLSYQEALSDTQVAIVNILSSTSGLFTLILAAVFPSNSGDRFTLSKLLAVILSIGGVVLVN
LAGSEKPAGRDTVGSIWSLAGAMLYAVYIVMIKRKVDREDKLDIPMFFGFVGLFNLLLLWPGF
FLLHYTGFEDFEFPNKVVLMCIIINGLIGTVLSEFLWLWGCFLTSSLIGTLALSLTIPLSIIA
DMCMQKVQFSWLFFAGAIPVFFSFFIVTLLCHYNNWDPVMVGIRRIFAFICRKHRIQRVPEDS
EQCESLISMHSVSQEDGAS

Important features:

Transmembrane domain:

amino acids 69-87,105-118,237-256,266-285,300-316,332-346,
364-379,399-419,453-472

N-glycosylation sites:

amino acids 157-161,255-259

N-myristoylation sites:

amino acids 14-20,329-335,404-410,407-413,418-424

FIGURE 247

CGTCTGTAGAGATATCATGAACTTCAACTTAGCTTTGGTACTTTCTTCCCTGAAGACAGAGGG
CAGAACTCTGAGTTCCAGAACCATTTTCAACTGTATTGGGGACCAATCACTTGACTCTATTCT
TGTCTCTCTGACAGATGACGCTACACTCTCCTCTGAATAATGGACACCATTTCTAAAACTGAA
TCCTGCTACTAAAATAATTCAGATGATATATTTTTCCAATTCTACAATCTTGCTTTGTTTTAT
TTAGTTGTTTTCTCTCTCTCTTCCCAGTTTTCCAGAGACTGGAGCTAAACTGGGCTTTCAACA
TCATC**ATG**AAGTTTATCCTCCTCTGGGCCCTCTTGAATCTGACTGTTGCTTTGGCCTTTAATC
CAGATTACACAGTCAGCTCCACTCCCCCTTACTTGGTCTATTTGAAATCTGACTACTTGCCCT
GCGCTGGAGTCCTGATCCACCCGCTTTGGGTGATCACAGCTGCACACTGCAATTTACCAAAGC
TTCGGGTGATATTGGGGGTTACAATCCCAGCAGACTCTAATGAAAAGCATCTGCAAGTGATTG
GCTATGAGAAGATGATTCATCATCCACACTTCTCAGTCACTTCTATTGATCATGACATCATGC
TAATCAAGCTGAAAACAGAGGCTGAACTCAATGACTATGTGAAATTAGCCAACCTGCCCTACC
AAACTATCTCTGAAAATACCATGTGCTCTGTCTCTACCTGGAGCTACAATGTGTGTGATATCT
ACAAAGAGCCCGATTCACTGCAAACTGTGAACATCTCTGTAATCTCCAAGCCTCAGTGTCGCG
ATGCCTATAAAACCTACAACATCACGGAAAATATGCTGTGTGTGGGCATTGTGCCAGGAAGGA
GGCAGCCCTGCAAGGAAGTTTCTGCTGCCCCGGCAATCTGCAATGGGATGCTTCAAGGAATCC
TGTCTTTTGCGGATGGATGTGTTTTGAGAGCCGATGTTGGCATCTATGCCAAAATTTTTTACT
ATATACCCTGGATTGAAAATGTAATCCAAAATAAC**TGA**GCTGTGGCAGTTGTGGACCATATGA
CACAGCTTGTCCCCATCGTTCACCTTTAGAATTAAATATAAATTAACTCCTC

FIGURE 248

MKFILLWALLNLTVALAFNPDYTVSSTPPYLVYLKSDYLPCAGVLIHPLWVITAAHCNLPKLR
VILGVTIPADSNEKHLQVIGYEKMIHHPHFSVTSIDHDIMLIKLKTEAELNDYVKLANLPYQT
ISENTMCSVSTWSYNVCDIYKEPDSLQTVNISVISKPQCRDAYKTYNITENMLCVGIVPGRRQ
PCKEVSAAPAICNGMLQGILSFADGCVLRADVGIYAKIFYYIPWIENVIQNN

Important features:

Signal peptide:

amino acids 1-17

N-glycosylation sites:

amino acids 11-15,156-160,173-177

Tyrosine kinase phosphorylation site:

amino acids 108-117

N-myristoylation sites:

amino acids 182-188,203-209

Amidation site:

amino acids 185-189

Serine proteases, trypsin family, histidine active site:

amino acids 52-58

FIGURE 249

GCGAGGCGGCCGCTGTCTTCTGCTGCGGCTTCCGCGACCACAAGTACTGCTGCGACGACCCGC

ACAGCTTCTTCCCCTACGAGCACAGCTAC**ATG**TGGTGGCTCAGCATTGGCGCTCTCATAGGCC

TGTCCGTAGCAGCAGTGGTTCTTCTCGCCTTCATTGTTACCGCCTGTGTGCTCTGCTACCTGT

TCATCAGCTCTAAGCCCCACACAAAGTTGGACCTGGGCTTGAGCTTACAGACAGCAGGCCCTG

AGGAGGTTTCTCCTGACTGCCAAGGTGTGAACACAGGCATGGCGGCAGAAGTGCCAAAAGTGA

GCCCTCTCCAGCAGAGTTACTCCTGCTTGAACCCGCAGCTGGAGAGCAATGAGGGGCAGGCTG

TGAACTCCAAACGCCTCCTCCATCATTGCTTCATGGCCACAGTGACCACCAGTGACATTCCAG

GCAGCCCTGAGGAAGCCTCTGTACCCAACCCTGACCTATGTGGACCAGTCCCA**TAA**ACATTCA

ATAAATGTCTCCATACCATCAA

FIGURE 250

MWWLSIGALIGLSVAAVVLLAFIVTACVLCYLFISSKPHTKLDLGLSLQTAGPEEVSPDCQGV
NTGMAAEVPKVSPLQQSYSCLNPQLESNEGQAVNSKRLLHHCFMATVTTSDIPGSPEEASVPN
PDLCGPVP

Important features:

Signal peptide:

Amino acids 1-26

N-myristoylation sites:

Amino acids 7-13,11-17,62-68,93-99

FIGURE 251

GTGGTTTGGATTGAGCCGGGCCCGGCCGGGGCGCCGAGTCGGAGGGGGTGGCAGTGAGCGGCG

GCAGAGGCTACGGGGCTCGGTTTGGCTGACTGGGGAGTCGGCAGGCGGCAGGAACC**ATG**CGAG

GCCAGCGGAGCCTGCTGCTGGGCCCGGCCCGCCTCTGCCTCCGCCTCCTTCTGCTGCTGGGTT

ACAGGCGCCGCTGTCCACCTCTACTCCGGGGTCTAGTACAGCGCTGGCGCTACGGCAAGGTCT

GCCTGCGCTCCCTGCTCTACAACTCCTTTGGGGGCAGTGACACCGCTGTTGATGCTGCCTTTG

AGCCTGTCTACTGGCTGGTAGACAACGTGATCCGCTGGTTTGGAGTGGTGTTCGTGGTCCTGG

TGATCGTGCTGACAGGCTCCATTGTAGCTATCGCCTACCTGTGTGTCCTGCCTCTCATCCTCC

GAACCTACTCAGTGCCACGACTCTGCTGGCATTTCTTCTATAGCCACTGGAATCTGATCCTGA

TTGTCTTCCACTACTACCAGGCCATCACCACTCCGCCTGGGTACCCACCCCAGGGCAGGAATG

ATATCGCCACCGTCTCCATCTGTAAGAAGTGCATTTACCCCAAGCCAGCCCGAACACACCACT

GCAGCATCTGCAACAGGTGTGTGCTGAAGATGGATCACCACTGCCCCTGGCTAAACAATTGTG

TGGGCCACTATAACCATCGGTACTTCTTCTCTTTCTGCTTTTTCATGACTCTGGGCTGTGTCT

ACTGCAGCTATGGAAGTTGGGACCTTTTCCGGGAGGCTTATGCTGCCATTGAGACTTATCACC

AGACCCCACCACCCACCTTCTCCTTTCGAGAAAGGATGACTCACAAGAGTCTTGTCTACCTCT

GGTTCCTGTGCAGTTCTGTGGCACTTGCCCTGGGTGCCCTAACTGTATGGCATGCTGTTCTCA

TCAGTCGAGGTGAGACTAGCATCGAAAGGCACATCAACAAGAAGGAGAGACGTCGGCTACAGG

CCAAGGGCAGAGTATTTAGGAATCCTTACAACTACGGCTGCTTGGACAACTGGAAGGTATTCC

TGGGTGTGGATACAGGAAGGCACTGGCTTACTCGGGTGCTCTTACCTTCTAGTCACTTGCCCC

ATGGGAATGGAATGAGCTGGGAGCCCCCTCCCTGGGTGACTGCTCACTCAGCCTCTGTGATGG

CAGTG**TGA**GCTGGACTGTGTCAGCCACGACTCGAGCACTCATTCTGCTCCCTATGTTATTTCA

AGGGCCTCCAAGGGCAGCTTTTCTCAGAATCCTTGATCAAAAAGAGCCAGTGGGCCTGCCTTA

GGGTACCATGCAGGACAATTCAAGGACCAGCCTTTTTACCACTGCAGAAGAAAGACACAATGT

GGAGAAATCTTAGGACTGACATCCCTTTACTCAGGCAAACAGAAGTTCCAACCCCAGACTAGG

GGTCAGGCAGCTAGCTACCTACCTTGCCCAGTGCTGACCCGGACCTCCTCCAGGATACAGCAC

TGGAGTTGGCCACCACCTCTTCTACTTGCTGTCTGAAAAAACACCTGACTAGTACAGCTGAGA

TCTTGGCTTCTCAACAGGGCAAAGATACCAGGCCTGCTGCTGAGGTCACTGCCACTTCTCACA

TGCTGCTTAAGGGAGCACAAATAAAGGTATTCGATTTTTAAAAAAAAAAAAAAAAAAAAAAAA

AAAAAAAAAAAAA

FIGURE 252

MRGQRSLLLGPARLCLRLLLLLGYRRRCPPLLRGLVQRWRYGKVCLRSLLYNSFGGSDTAVDA
AFEPVYWLVDNVIRWFGVVFVVLVIVLTGSIVAIAYLCVLPLILRTYSVPRLCWHFFYSHWNL
ILIVFHYYQAITTPPGYPPQGRNDIATVSICKKCIYPKPARTHHCSICNRCVLKMDHHCPWLN
NCVGHYNHRYFFSFCFFMTLGCVYCSYGSWDLFREAYAAIETYHQTPPPTFSFRERMTHKSLV
YLWFLCSSVALALGALTVWHAVLISRGETSIERHINKKERRRLQAKGRVFRNPYNYGCLDNWK
VFLGVDTGRHWLTRVLLPSSHLPHGNGMSWEPPPWVTAHSASVMAV

Important features:

Transmembrane domain:

amino acids 88-100,202-216,254-274

N-myristoylation sites:

amino acids 55-61,56-62,92-98,210-216,309-315,319-325,340-346

Prokaryotic membrane lipoprotein lipid attachment site:

amino acids 201-212

FIGURE 253

GATCAAGCGCCTTCCTTTCCCTTCCTCTCCCTACTTGGCCTTTGCCCTAAGCCAAGACCTGGCCATCAGCCTGGC
TGCAGGGGCCTGCAGAGCCAGCTGCACTTTTTCAGGTATGGGGGAGGGCCAGGCACC**ATG**AAGCCAGTGTGGGTC
GCCACCCTTCTGTGGATGCTACTGCTGGTGCCCAGGCTGGGGGCCGCCCGGAAGGGGTCCCCAGAAGAGGCCTCC
TTCTACTATGGAACCTTCCCTCTTGGCTTCTCCTGGGGCGTGGGCAGTTCTGCCTACCAGACGGAGGGCGCCTGG
GACCAGGACGGGAAAGGGCCTAGCATCTGGGACGTCTTCACACACAGTGGGAAGGGGAAAGTGCTTGGGAATGAG
ACGGCAGATGTAGCCTGTGACGGCTACTACAAGGTCCAGGAGGACATCATTCTGCTGAGGGAACTGCACGTCAAC
CACTACCGATTCTCCCTGTCTTGGCCCCGGCTCCTGCCCACAGGCATCCGAGCCGAGCAGGTGAACAAGAAGGGA
ATCGAATTCTACAGTGATCTTATCGATGCCCTTCTGAGCAGCAACATCACTCCCATCGTGACCTTGCACCACTGG
GATCTGCCACAGCTGCTCCAGGTCAAATACGGTGGGTGGCAGAATGTGAGCATGGCCAACTACTTCAGAGACTAC
GCCAACCTGTGCTTTGAGGCCTTTGGGGACCGTGTGAAGCACTGGATCACGTTCAGTGATCCTCGGGCAATGGCA
GAAAAAGGCTATGAGACGGGCCACCATGCGCCGGGCCTGAAGCTCCGCGGCACCGGCCTGTACAAGGCAGCACAC
CACATCATTAAGGCCCACGCCAAAACCTGGCATTCTTATAACACCACGTGGCGCAGCAAGCAGCAAGGTCTGGTG
GGAATTTCACTGAACTGTGACTGGGGGGAACCTGTGGACATTAGTAACCCCAAGGACCTAGAGGCTGCCGAGAGA
TACCTACAGTTCTGTCTGGGCTGGTTTGCCAACCCCATTTATGCCGGTGACTACCCCCAAGTCATGAAGGACTAC
ATTGGAAGAAAGAGTGCAGAGCAAGGCCTGGAGATGTCGAGGTTACCGGTGTTCTCACTCCAGGAGAAGAGCTAC
ATTAAAGGCACATCCGATTTCTTGGGATTAGGTCATTTTACTACTCGGTACATCACGGAAAGGAACTACCCCTCC
CGCCAGGGGCCCAGCTACCAGAACGATCGTGACTTGATAGAGCTGGTTGACCCAAACTGGCCAGATCTGGGGTCT
AAATGGCTATATTCTGTGCCATGGGGATTTAGGAGGCTCCTTAACTTTGCTCAGACTCAATACGGTGATCCTCCC
ATATATGTGATGGAAAATGGAGCATCTCAAAAATTCCACTGTACTCAATTATGTGATGAGTGGAGAATTCAATAC
CTTAAAGGATACATAAATGAAATGCTAAAAGCTATAAAAGATGGTGCTAATATAAAGGGGTATACTTCCTGGTCT
CTGTTGGATAAGTTTGAATGGGAGAAAGGATACTCAGATAGATATGGATTCTACTATGTTGAATTTAACGACAGA
AATAAGCCTCGCTATCCAAAGGCTTCAGTTCAATATTACAAGAAGATTATCATTGCCAATGGGTTTCCCAATCCA
AGAGAGGTGGAAAGTTGGTACCTCAAAGCTTTGGAAACTTGCTCTATCAACAATCAGATGCTTGCTGCAGAGCCT
TTGCTAAGTCACATGCAAATGGTTACGGAGATCGTGGTACCCACTGTCTGCTCCCTCTGTGTCCTCATCACTGCT
GTTCTACTAATGCTCCTCCTGAGGAGGCAGAGC**TGA**GACAGGATTATCAATTTTGGAGCTTCATAAGAGAATCTT
CAGGATCTTCCTCCCTTTTCTGCTTTGAGGGTTTCCATACATTGCTGTTTTCAGGTTCTACAATAATTACCTTTT
TTTCTCTTTCTCTTTTTGGCTTGTGCTGGGATTTAAGAATTAGAAAATAAAAATAAGCAGAAATTA

FIGURE 254

MKPVWVATLLWMLLLVPRLGAARKGSPEEASFYYGTFPLGFSWGVGSSAYQTEGAWDQDGKGPSIWDVFTHSGKG
KVLGNETADVACDGYYKVQEDIILLRELHVNHYRFSLSWPRLLPTGIRAEQVNKKGIEFYSDLIDALLSSNITPI
VTLHHWDLPQLLQVKYGGWQNVSMANYFRDYANLCFEAFGDRVKHWITFSDPRAMAEKGYETGHHAPGLKLRGTG
LYKAAHHIIKAHAKTWHSYNTTWRSKQQGLVGISLNCDWGEPVDISNPKDLEAAERYLQFCLGWFANPIYAGDYP
QVMKDYIGRKSAEQGLEMSRLPVFSLQEKSYIKGTSDFLGLGHFTTRYITERNYPSRQGPSYQNDRDLIELVDPN
WPDLGSKWLYSVPWGFRRLLNFAQTQYGDPPIYVMENGASQKFHCTQLCDEWRIQYLKGYINEMLKAIKDGANIK
GYTSWSLLDKFEWEKGYSDRYGFYYVEFNDRNKPRYPKASVQYYKKIIIANGFPNPREVESWYLKALETCSINNQ
MLAAEPLLSHMQMVTEIVVPTVCSLCVLITAVLLMLLLRRQS

Important features:
Signal peptide:
amino acids 1-21

Transmembrane domain:
amino acids 541-558

N-glycosylation sites:
amino acids 80-84,171-175,245-249

Glycosaminoglycan attachment site:
amino acids 72-76

cAMP- and cGMP-dependent protein kinase phosphorylation sites:
amino acids 23-27,564-568

Tyrosine kinase phosphorylation sites:
amino acids 203-211,347-355,460-468,507-514

N-myristoylation sites:
amino acids 44-50,79-85,167-173,225-231,257-263,315-321

Amidation site:
amino acids 307-311

Glycosyl hydrolases family 1 active site:
amino acids 407-416

Glycosyl hydrolases family 1 N-terminal signature:
amino acids 41-56

Motif name Glycosyl hydrolases family:
amino acids 37- 67

FIGURE 255

CGCGAAG**ATG**CGAAAGGTGGTTTTGATCACCGGGGCTAGCAGTGGCATTGGCCTGGCCCTCTG

CAAGCGGCTGCTGGCGGAAGATGATGAGCTTCATCTGTGTTTGGCGTGCAGGAACATGAGCAA

GGCAGAAGCTGTCTGTGCTGCTCTGCTGGCCTCTCACCCCACTGCTGAGGTCACCATTGTCCA

GGTGGATGTCAGCAACCTGCAGTCGGTCTTCCGGGCCTCCAAGGAACTTAAGCAAAGGTTTCA

GAGATTAGACTGTATATATCTAAATGCTGGGATCATGCCTAATCCACAACTAAATATCAAAGC

ACTTTTCTTTGGCCTCTTTTCAAGAAAAGTGATTCATATGTTCTCCACAGCTGAAGGCCTGCT

GACCCAGGGTGATAAGATCACTGCTGATGGACTTCAGGAGGTGTTTGAGACCAATGTCTTTGG

CCATTTTATCCTGATTCGGGAACTGGAGCCTCTCCTCTGTCACAGTGACAATCCATCTCAGCT

CATCTGGACATCATCTCGCAGTGCAAGGAAATCTAATTTCAGCCTCGAGGACTTCCAGCACAG

CAAAGGCAAGGAACCCTACAGCTCTTCCAAATATGCCACTGACCTTTTGAGTGTGGCTTTGAA

CAGGAACTTCAACCAGCAGGGTCTCTATTCCAATGTGGCCTGTCCAGGTACAGCATTGACCAA

TTTGACATATGGAATTCTGCCTCCGTTTATATGGACGCTGTTGATGCCGGCAATATTGCTACT

TCGCTTTTTTGCAAATGCATTCACTTTGACACCATATAATGGAACAGAAGCTCTGGTATGGCT

TTTCCACCAAAAGCCTGAATCTCTCAATCCTCTGATCAAATATCTGAGTGCCACCACTGGCTT

TGGAAGAAATTATATTATGACCCAGAAGATGGACCTAGATGAAGACACTGCTGAAAAATTTTA

TCAAAAGTTACTGGAACTGGAAAAGCACATTAGGGTCACTATTCAAAAAACAGATAATCAGGC

CAGGCTCAGTGGCTCATGCCTA**TAA**TTCCAGCACTTTGGGAGGCCAAGGCAGAAGGATCACTT

GAGACCAGGAGTTCAAGACCAGCCTGAGAAACATAGTGAGCCCTTGTCTCTACAAAAAGAAAT

AAAAATAATAGCTGGGTGTGGTGGCATGCGCATGTAGTCCCAGCTACTCAGAAGGATGAGGTG

GGAGGATCTCTTGAGGCTGGGAGGCAGAGGTTGCAGTGAGCTGAGATTGTGCCACTGCACTCC

AGCCTGGGTGACAGCGAGACCCTGTCTCAAAATATGTATATATTTAATATATATATATAAAACCA

GAGCTGACAATGACACTCTGGAACATTGCATACCTTCTGTACATTCTGGGGTACATGGATTTC

TACTGAGTTGGATAATATGCATTTGTAATAAACTATGAACTATGAA

FIGURE 256

MRKVVLITGASSGIGLALCKRLLAEDDELHLCLACRNMSKAEAVCAALLASHPTAEVTIVQVD
VSNLQSVFRASKELKQRFQRLDCIYLNAGIMPNPQLNIKALFFGLFSRKVIHMFSTAEGLLTQ
GDKITADGLQEVFETNVFGHFILIRELEPLLCHSDNPSQLIWTSSRSARKSNFSLEDFQHSKG
KEPYSSSKYATDLLSVALNRNFNQQGLYSNVACPGTALTNLTYGILPPFIWTLLMPAILLLRF
FANAFTLTPYNGTEALVWLFHQKPESLNPLIKYLSATTGFGRNYIMTQKMDLDEDTAEKFYQK
LLELEKHIRVTIQKTDNQARLSGSCL

Important features:

Transmembrane domain:

amino acids 234-254

N-glycosylation sites:

amino acids 37-41,178-182,229-233,263-267

Glycosaminoglycan attachment site:

amino acids 12-16

N-myristoylation sites:

amino acids 9-15,13-19,15-21,215-221,224-230

FIGURE 257

CGGACGCGTGGGGCCGT**ATG**CGCGGCTCTGTGGAGTGCACCTGGGGTTGGGGGCACTGTGCCC
CCAGCCCCCTGCTCCTTTGGACTCTACTTCTGTTTGCAGCCCCATTTGGCCTGCTGGGGGAGA
AGACCCGCCAGGTGTCTCTGGAGGTCATCCCTAACTGGCTGGGCCCCCTGCAGAACCTGCTTC
ATATACGGGCAGTGGGCACCAATTCCACACTGCACTATGTGTGGAGCAGCCTGGGGCCTCTGG
CAGTGGTAATGGTGGCCACCAACACCCCCCACAGCACCCTGAGCATCAACTGGAGCCTCCTGC
TATCCCCTGAGCCCGATGGGGGCCTGATGGTGCTCCCTAAGGACAGCATTCAGTTTTCTTCTG
CCCTTGTTTTTACCAGGCTGCTTGAGTTTGACAGCACCAACGTGTCCGATACGGCAGCAAAGC
CTTTGGGAAGACCATATCCTCCATACTCCTTGGCCGATTTCTCTTGGAACAACATCACTGATT
CATTGGATCCTGCCACCCTGAGTGCCACATTTCAAGGCCACCCCATGAACGACCCTACCAGGA
CTTTTGCCAATGGCAGCCTGGCCTTCAGGGTCCAGGCCTTTTCCAGGTCCAGCCGACCAGCCC
AACCCCCTCGCCTCCTGCACACAGCAGACACCTGTCAGCTAGAGGTGGCCCTGATTGGAGCCT
CTCCCCGGGGAAACCGTTCCCTGTTTGGGCTGGAGGTAGCCACATTGGGCCAGGGCCCTGACT
GCCCCTCAATGCAGGAGCAGCACTCCATCGACGATGAATATGCACCGGCCGTCTTCCAGTTGG
ACCAGCTACTGTGGGGCTCCCTCCCATCAGGCTTTGCACAGTGGCGACCAGTGGCTTACTCCC
AGAAGCCGGGGGGCCGAGAATCAGCCCTGCCCTGCCAAGCTTCCCCTCTTCATCCTGCCTTAG
CATACTCTCTTCCCCAGTCACCCATTGTCCGAGCCTTCTTTGGGTCCCAGAATAACTTCTGTG
CCTTCAATCTGACGTTCGGGGCTTCCACAGGCCCTGGCTATTGGGACCAACACTACCTCAGCT
GGTCGATGCTCCTGGGTGTGGGCTTCCCTCCAGTGGACGGCTTGTCCCCACTAGTCCTGGGCA
TCATGGCAGTGGCCCTGGGTGCCCCAGGGCTCATGCTGCTAGGGGGCGGCTTGGTTCTGCTGC
TGCACCACAAGAAGTACTCAGAGTACCAGTCCATAAAT**TAA**GGCCCGCTCTCTGGAGGGAAGG
ACATTACTGAACCTGTCTTGCTGTGCCTCGAAACTCTGGAGGTTGGAGCATCAAGTTCCAGCC
GGCCCCTTCACTCCCCCATCTTGCTTTTCTGTGGAACCTCAGAGGCCAGCCTCGACTTCCTGG
AGACCCCCAGGTGGGGCTTCCTTCATACTTTGTTGGGGGACTTTGGAGGCGGGCAGGGGACAG
GGCTATTGATAAGGTCCCCTTGGTGTTGCCTTCTTGCATCTCCACACATTTCCCTTGGATGGG
ACTTGCAGGCCTAAATGAGAGGCATTCTGACTGGTTGGCTGCCCTGGAAGGCAAGAAAATAGA
TTTATTTTTTTTCACAGGGAAAAAAAAAAAA

FIGURE 258

MRGSVECTWGWGHCAPSPLLLWTLLLFAAPFGLLGEKTRQVSLEVIPNWLGPLQNLLHIRAVG
TNSTLHYVWSSLGPLAVVMVATNTPHSTLSINWSLLLSPEPDGGLMVLPKDSIQFSSALVFTR
LLEFDSTNVSDTAAKPLGRPYPPYSLADFSWNNITDSLDPATLSATFQGHPMNDPTRTFANGS
LAFRVQAFSRSSRPAQPPRLLHTADTCQLEVALIGASPRGNRSLFGLEVATLGQGPDCPSMQE
QHSIDDEYAPAVFQLDQLLWGSLPSGFAQWRPVAYSQKPGGRESALPCQASPLHPALAYSLPQ
SPIVRAFFGSQNNFCAFNLTFGASTGPGYWDQHYLSWSMLLGVGFPPVDGLSPLVLGIMAVAL
GAPGLMLLGGGLVLLLHHKKYSEYQSIN

Important features:

Signal peptide:

amino acids 1-35

Transmembrane domain:

amino acids 365-386

N-glycosylation sites:

amino acids 65-69,95-99,134-138,159-163,187-191,230-234,333-337

cAMP- and cGMP-dependent protein kinase phosphorylation site:

amino acids 397-401

N-myristoylation sites:

amino acids 3-9,63-69,235-241,273-279,292-298,324-330

Leucine zipper pattern:

amino acids 371-393

FIGURE 259

CAGGCGGGCCCCCGCGCGGCAGGGCCCTGGACCCGCGCGGCTCCCGGGG**ATG**GTGAGCAAGGCGCTGCTGCGCCT
CGTGTCTGCCGTCAACCGCAGGAGGATGAAGCTGCTGCTGGGCATCGCCTTGCTGGCCTACGTCGCCTCTGTTTG
GGGCAACTTCGTTAATATGAGGTCTATCCAGGAAAATGGTGAACTAAAAATTGAAAGCAAGATTGAAGAGATGGT
TGAACCACTAAGAGAGAAAATCAGAGATTTAGAAAAAAGCTTTACCCAGAAATACCCACCAGTAAAGTTTTTATC
AGAAAAGGATCGGAAAAGAATTTTGATAACAGGAGGCGCAGGGTTCGTGGGCTCCCATCTAACTGACAAACTCAT
GATGGACGGCCACGAGGTGACCGTGGTGGACAATTTCTTCACGGGCAGGAAGAGAAACGTGGAGCACTGGATCGG
ACATGAGAACTTCGAGTTGATTAACCACGACGTGGTGGAGCCCCTCTACATCGAGGTTGACCAGATATACCATCT
GGCATCTCCAGCCTCCCCTCCAAACTACATGTATAATCCTATCAAGACATTAAAGACCAATACGATTGGGACATT
AAACATGTTGGGGCTGGCAAAACGAGTCGGTGCCCGTCTGCTCCTGGCCTCCACATCGGAGGTGTATGGAGATCC
TGAAGTCCACCCTCAAAGTGAGGATTACTGGGGCCACGTGAATCCAATAGGACCTCGGGCCTGCTACGATGAAGG
CAAACGTGTTGCAGAGACCATGTGCTATGCCTACATGAAGCAGGAAGGCGTGGAAGTGCGAGTGGCCAGAATCTT
CAACACCTTTGGGCCACGCATGCACATGAACGATGGGCGAGTAGTCAGCAACTTCATCCTGCAGGCGCTCCAGGG
GGAGCCACTCACGGTATACGGATCCGGGTCTCAGACAAGGGCGTTCCAGTACGTCAGCGATCTAGTGAATGGCCT
CGTGGCTCTCATGAACAGCAACGTCAGCAGCCCGGTCAACCTGGGGAACCCAGAAGAACACACAATCCTAGAATT
TGCTCAGTTAATTAAAAACCTTGTTGGTAGCGGAAGTGAAATTCAGTTTCTCTCCGAAGCCCAGGATGACCCACA
GAAAAGAAAACCAGACATCAAAAAAGCAAAGCTGATGCTGGGGTGGGAGCCCGTGGTCCCGCTGGAGGAAGGTTT
AAACAAAGCAATTCACTACTTCCGTAAAGAACTCGAGTACCAGGCAAATAATCAGTACATCCCCAAACCAAAGCC
TGCCAGAATAAAGAAAGGACGGACTCGCCACAGC**TGA**ACTCCTCACTTTTAGGACACAAGACTACCATTGTACAC
TTGATGGGATGTATTTTTGGCTTTTTTTTTGTTGTCGTTTAAAGAAAGACTTTAACAGGTGTCATGAAGAACAAAC
TGGAATTTCATTCTGAAGCTTGCTTTAATGAAATGGATGTGCCTAAAAGCTCCCCTCAAAAAACTGCAGATTTTG
CCTTGCACTTTTTTGAATCTCTCTTTTTTATGTAAAATAGCGTAGATGCATCTCTGCGTATTTTCAAGTTTTTTTAT
CTTGCTGTGAGAGCATATGTTGTGACTGTCGTTGACAGTTTTATTTACTGGTTTCTTTGTGAAGCTGAAAAGGAA
CATTAAGCGGGACAAAAAATGCCGATTTTATTTATAAAAGTGGGTACTTAATAAATGAGTCGTTATACTATGCAT
AAAGAAAAATCCTAGCAGTATTGTCAGGTGGTGGTGCGCCGGCATTGATTTTAGGGCAGATAAAAGAATTCTGTG
TGAGAGCTTTATGTTTCTCTTTTAATTCAGAGTTTTTCCAAGGTCTACTTTTGAGTTGCAAACTTGACTTTGAAA
TATTCCTGTTGGTCATGATCAAGGATATTTGAAATCACTACTGTGTTTTGCTGCGTATCTGGGGCGGGGGCAGGT
TGGGGGGCACAAAGTTAACATATTCTTGGTTAACCATGGTTAAATATGCTATTTTAATAAAATATTGAAACTCA

FIGURE 260

MVSKALLRLVSAVNRRRMKLLLGIALLAYVASVWGNFVNMRSIQENGELKIESKIEEMVEPLR
EKIRDLEKSFTQKYPPVKFLSEKDRKRILITGGAGFVGSHLTDKLMMDGHEVTVVDNFFTGRK
RNVEHWIGHENFELINHDVVEPLYIEVDQIYHLASPASPPNYMYNPIKTLKTNTIGTLNMLGL
AKRVGARLLLASTSEVYGDPEVHPQSEDYWGHVNPIGPRACYDEGKRVAETMCYAYMKQEGVE
VRVARIFNTFGPRMHMNDGRVVSNFILQALQGEPLTVYGSGSQTRAFQYVSDLVNGLVALMNS
NVSSPVNLGNPEEHTILEFAQLIKNLVGSGSEIQFLSEAQDDPQKRKPDIKKAKLMLGWEPVV
PLEEGLNKAIHYFRKELEYQANNQYIPKPKPARIKKGRTRHS

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 261

GCGTGGTGCGGGGGCGTGGGGAAATCGGGTTGCCCCAGCCGTTACTGGTCCGCGCAGTCAGGG

CATCCTCCGCATCCTCCACATCCTTCC**ATG**GCTCTGAAGAATAAATTCAGTTGTTTATGGATC

TTGGGTCTGTGTTTGGTAGCCACTACATCTTCCAAAATCCCATCCATCACTGACCCACACTTT

ATAGACAACTGCATAGAAGCCCACAACGAATGGCGTGGCAAAGTCAACCCTCCCGCGGCCGAC

ATGAAATACATGATTTGGGATAAAGGTTTAGCAAAGATGGCTAAAGCATGGGCAAACCAGTGC

AAATTTGAACATAATGACTGTTTGGATAAATCATATAAATGCTATGCAGCTTTTGAATATGTT

GGAGAAAATATCTGGTTAGGTGGAATAAAGTCATTCACACCAAGACATGCCATTACGGCTTGG

TATAATGAAACCCAATTTTATGATTTTGATAGTCTATCATGCTCCAGAGTCTGTGGCCATTAT

ACACAGTTAGTTTGGGCCAATTCATTTTATGTCGGTTGTGCAGTTGCAATGTGTCCTAACCTT

GGGGGAGCTTCAACTGCAATATTTGTATGCAACTACGGACCTGCAGGAAATTTTGCAAATATG

CCTCCTTACGCAAGAGGAGAATCTTGCTCTCTCTGCTCAAAAGAAGAGAAATGTGTAAAGAAC

CTCTGCAGGACTCCACAACTTATTATACCTAACCAAAATCCATTTCTGAAGCCAACGGGGAGA

GCACCTCAGCAGACAGCCTTTAATCCATTCAGCTTAGGTTTTCTTCTTCTGAGAATCTTT**TAA**

TGTCATTTATATACAAAAGAAATTCTCAAATGTTAAAATAAAGGAATAGTTTATTGCTTAATA

FIGURE 262

MALKNKFSCLWILGLCLVATTSSKIPSITDPHFIDNCIEAHNEWRGKVNPPAADMKYMIWDKG
LAKMAKAWANQCKFEHNDCLDKSYKCYAAFEYVGENIWLGGIKSFTPRHAITAWYNETQFYDF
DSLSCSRVCGHYTQLVWANSFYVGCAVAMCPNLGGASTAIFVCNYGPAGNFANMPPYARGESC
SLCSKEEKCVKNLCRTPQLIIPNQNPFLKPTGRAPQQTAFNPFSLGFLLLRIF

Important features:

Signal peptide:

amino acids 1-23

N-glycosylation site:

amino acids 119-123

N-myristoylation sites:

amino acids 103-109,150-156,160-166,161-167,175-181

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

amino acids 136-156

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

amino acids 166-178

FIGURE 263

CGCCCTCCGACCCGCCCCGCGGCGCATTGTGGGATCTGTCGGCTTGTCAGGTGGTGGAGGAAA

AGGCGCTCCGTC**ATG**GGGATCCAGACGAGCCCCGTCCTGCTGGCCTCCCTGGGGGTGGGGCTG

GTCACTCTGCTCGGCCTGGCTGTGGGCTCCTACTTGGTTCGGAGGTCCCGCCGGCCTCAGGTC

ACTCTCCTGGACCCCAATGAAAAGTACCTGCTACGACTGCTAGACAAGACGACTGTGAGCCAC

AACACCAAGAGGTTCCGCTTTGCCCTGCCCACCGCCCACCACACTCTGGGGCTGCCTGTGGGC

AAACATATCTACCTCTCCACCCGAATTGATGGCAGCCTGGTCATCAGGCCATACACTCCTGTC

ACCAGTGATGAGGATCAAGGCTATGTGGATCTTGTCATCAAGGTCTACCTGAAGGGTGTGCAC

CCCAAATTTCCTGAGGGAGGGAAGATGTCTCAGTACCTGGATAGCCTGAAGGTTGGGGATGTG

GTGGAGTTTCGGGGGCCAAGCGGGTTGCTCACTTACACTGGAAAAGGGCATTTTAACATTCAG

CCCAACAAGAAATCTCCACCAGAACCCCGAGTGGCGAAGAAACTGGGAATGATTGCCGGCGGG

ACAGGAATCACCCCAATGCTACAGCTGATCCGGGCCATCCTGAAAGTCCCTGAAGATCCAACC

CAGTGCTTTCTGCTTTTTGCCAACCAGACAGAAAAGGATATCATCTTGCGGGAGGACTTAGAG

GAACTGCAGGCCCGCTATCCCAATCGCTTTAAGCTCTGGTTCACTCTGGATCATCCCCCAAAA

GATTGGGCCTACAGCAAGGGCTTTGTGACTGCCGACATGATCCGGGAACACCTGCCCGCTCCA

GGGGATGATGTGCTGGTACTGCTTTGTGGGCCACCCCCAATGGTGCAGCTGGCCTGCCATCCC

AACTTGGACAAACTGGGCTACTCACAAAAGATGCGATTCACCTAC**TGA**GCATCCTCCAGCTTC

CCTGGTGCTGTTCGCTGCAGTTGTTCCCCATCAGTACTCAAGCACTATAAGCCTTAGATTCCT

TTCCTCAGAGTTTCAGGTTTTTTCAGTTACATCTAGAGCTGAAATCTGGATAGTACCTGCAGG

AACAATATTCCTGTAGCCATGGAAGAGGGCAAGGCTCAGTCACTCCTTGGATGGCCTCCTAAA

TCTCCCCCGTGGCAACAGGTCCAGGAGAGGCCCATGGAGCAGTCTCTTCCATGGAGTAAGAAGG

AAGGGAGCATGTACGCTTGGTCCAAGATTGGCTAGTTCCTTGATAGCATCTTACTCTCACCTT

CTTTGTGTCTGTGATGAAAGGAACAGTCTGTGCAATGGGTTTTACTTAAACTTCACTGTTCAA

CCTATGAGCAAATCTGTATGTGTGAGTATAAGTTGAGCATAGCATACTTCCAGAGGTGGTNTT

ATGGAGATGGCAAGAAAGGAGGAAATGATTTCTTCAGATNTCAAAGGAGTCTGAAATATCATA

TTTCTGTGTGTGTCTCTCTCAGCCCCTGCCCAGGCTAGAGGGAAACAGCTACTGATAATCGAA

AACTGCTGTTTGTGGCANGAACCCCTGGCTGTGCAAATAAATGGGGCTGAGGCCCCTGTGTGA

TATTGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAGA

FIGURE 264

MGIQTSPVLLASLGVGLVTLLGLAVGSYLVRRSRRPQVTLLDPNEKYLLRLLDKTTVSHNTKR
FRFALPTAHHTLGLPVGKHIYLSTRIDGSLVIRPYTPVTSDEDQGYVDLVIKVYLKGVHPKFP
EGGKMSQYLDSLKVGDVVEFRGPSGLLTYTGKGHFNIQPNKKSPPEPRVAKKLGMIAGGTGIT
PMLQLIRAILKVPEDPTQCFLLFANQTEKDIILREDLEELQARYPNRFKLWFTLDHPPKDWAY
SKGFVTADMIREHLPAPGDDVLVLLCGPPPMVQLACHPNLDKLGYSQKMRFTY

Important features:

Signal peptide:

amino acids 1-26

N-glycosylation site:

amino acids 214-218

N-myristoylation sites:

amino acids 22-28,76-82,128-134,180-186

FIGURE 265

CCCGTGCCAAGAGTGACGTAAGTACCGCCTATAGAGTCTATAGGCCCACTTGGCTTCGTTAGA
ACGCGGCTACAATTAATACATAACCTTATGTATCATACACATACGATTTAGGTGACACTATAG
AATAACATCCACTTTGCCTTTCTCTCCACAGGTGTCCACTCCCAGGTCCAACTGCACCTCGGT
TCTATCGATAATCTCAGCACCAGCCACTCAGAGCAGGGCACG**ATG**TTGGGGGCCCGCCTCAGG
CTCTGGGTCTGTGCCTTGTGCAGCGTCTGCAGCATGAGCGTCCTCAGAGCCTATCCCAATGCC
TCCCCACTGCTCGGCTCCAGCTGGGGTGGCCTGATCCACCTGTACACAGCCACAGCCAGGAAC
AGCTACCACCTGCAGATCCACAAGAATGGCCATGTGGATGGCGCACCCCATCAGACCATCTAC
AGTGCCCTGATGATCAGATCAGAGGATGCTGGCTTTGTGGTGATTACAGGTGTGATGAGCAGA
AGATACCTCTGCATGGATTTCAGAGGCAACATTTTTGGATCACACTATTTCGACCCGGAGAAC
TGCAGGTTCCAACACCAGACGCTGGAAAACGGGTACGACGTCTACCACTCTCCTCAGTATCAC
TTCCTGGTCAGTCTGGGCCGGGCGAAGAGAGCCTTCCTGCCAGGCATGAACCCACCCCCGTAC
TCCCAGTTCCTGTCCCGGAGGAACGAGATCCCCCTAATTCACTTCAACACCCCCATACCACGG
CGGCACACCCGGAGCGCCGAGGACGACTCGGAGCGGGACCCCCTGAACGTGCTGAAGCCCCGG
GCCCGGATGACCCCGGCCCCGGCCTCCTGTTCACAGGAGCTCCCGAGCGCCGAGGACAACAGC
CCGATGGCCAGTGACCCATTAGGGGTGGTCAGGGGCGGTCGAGTGAACACGCACGCTGGGGGA
ACGGGCCCGGAAGGCTGCCGCCCCTTCGCCAAGTTCATC**TAG**GGTCGCTGG

FIGURE 266

MLGARLRLWVCALCSVCSMSVLRAYPNASPLLGSSWGGLIHLYTATARNSYHLQIHKNGHVDG
APHQTIYSALMIRSEDAGFVVITGVMSRRYLCMDFRGNIFGSHYFDPENCRFQHQTLENGYDV
YHSPQYHFLVSLGRAKRAFLPGMNPPPYSQFLSRRNEIPLIHFNTPIPRRHTRSAEDDSERDP
LNVLKPRARMTPAPASCSQELPSAEDNSPMASDPLGVVRGGRVNTHAGGTGPEGCRPFAKFI

Important features:

Signal peptide:

amino acids 1-24

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 175-179

N-myristoylation site.

amino acids 33-39, 100-106, 225-231, 229-235

HBGF/FGF family proteins

amino acids 73-124

FIGURE 267

GGCTGAGGGGAGGCCCGGAGCCTTTCTGGGGCCTGGGGGATCCTCTTGCACTGGTGGGTGGAGAGAAGCGCCTGC
AGCCAACCAGGGTCAGGCTGTGCTCACAGTTTCCTCTGGCGGCATGTAAAGGCTCCACAAAGGAGTTGGGAGTTC
AAATGAGGCTGCTGCGGACGGCCTGAGGATGGACCCCAAGCCCTGGACCTGCCGAGCGTGGCACTGAGGCAGCGG
CTGACGCTACTGTGAGGGAAAGAAGGTTGTGAGCAGCCCCGCAGGACCCCTGGCCAGCCCTGGCCCCAGCCTCTG
CCGGAGCCCTCTGTGGAGGCAGAGCCAGTGGAGCCCAGTGAGGCAGGGCTGCTTGGCAGCCACCGGCCTGCAACT
CAGGAACCCCTCCAGAGGCCATGGACAGGCTGCCCCGCTGACGGCCAGGGTGAAGCATGTGAGGAGCCGCCCCGG
AGCCAAGCAGGAGGGAAGAGGCTTTCATAGATTCTATTCACAAAGAATAACCACCATTTTGCAAGGACC**ATG**AGG
CCACTGTGCGTGACATGCTGGTGGCTCGGACTGCTGGCTGCCATGGGAGCTGTTGCAGGCCAGGAGGACGGTTTT
GAGGGCACTGAGGAGGGCTCGCCAAGAGAGTTCATTTACCTAAACAGGTACAAGCGGGCGGGCGAGTCCCAGGAC
AAGTGCACCTACACCTTCATTGTGCCCCAGCAGCGGGTCACGGGTGCCATCTGCGTCAACTCCAAGGAGCCTGAG
GTGCTTCTGGAGAACCGAGTGCATAAGCAGGAGCTAGAGCTGCTCAACAATGAGCTGCTCAAGCAGAAGCGGCAG
ATCGAGACGCTGCAGCAGCTGGTGGAGGTGGACGGCGGCATTGTGAGCGAGGTGAAGCTGCTGCGCAAGGAGAGC
CGCAACATGAACTCGCGGGTCACGCAGCTCTACATGCAGCTCCTGCACGAGATCATCCGCAAGCGGGACAACGCG
TTGGAGCTCTCCCAGCTGGAGAACAGGATCCTGAACCAGACAGCCGACATGCTGCAGCTGGCCAGCAAGTACAAG
GACCTGGAGCACAAGTACCAGCACCTGGCCACACTGGCCCACAACCAATCAGAGATCATCGCGCAGCTTGAGGAG
CACTGCCAGAGGGTGCCCTCGGCCAGGCCCGTCCCCCAGCCACCCCCCGCTGCCCCGCCCCGGGTCTACCAACCA
CCCACCTACAACCGCATCATCAACCAGATCTCTACCAACGAGATCCAGAGTGACCAGAACCTGAAGGTGCTGCCA
CCCCCTCTGCCCACTATGCCCACTCTCACCAGCCTCCCATCTTCCACCGACAAGCCGTCGGGCCCATGGAGAGAC
TGCCTGCAGGCCCTGGAGGATGGCCACGACACCAGCTCCATCTACCTGGTGAAGCCGGAGAACACCAACCGCCTC
ATGCAGGTGTGGTGCGACCAGAGACACGACCCCGGGGGCTGGACCGTCATCCAGAGACGCCTGGATGGCTCTGTT
AACTTCTTCAGGAACTGGGAGACGTACAAGCAAGGGTTTGGGAACATTGACGGCGAATACTGGCTGGGCCTGGAG
AACATTTACTGGCTGACGAACCAAGGCAACTACAAACTCCTGGTGACCATGGAGGACTGGTCCGGCCGCAAAGTC
TTTGCAGAATACGCCAGTTTCCGCCTGGAACCTGAGAGCGAGTATTATAAGCTGCGGCTGGGGCGCTACCATGGC
AATGCGGGTGACTCCTTTACATGGCACAACGGCAAGCAGTTCACCACCCTGGACAGAGATCATGATGTCTACACA
GGAAACTGTGCCCACTACCAGAAGGGAGGCTGGTGGTATAACGCCTGTGCCCACTCCAACCTCAACGGGGTCTGG
TACCGCGGGGGCCATTACCGGAGCCGCTACCAGGACGGAGTCTACTGGGCTGAGTTCCGAGGAGGCTCTTACTCA
CTCAAGAAAGTGGTGATGATGATCCGACCGAACCCCAACACCTTCCAC**TAA**GCCAGCTCCCCCTCCTGACCTCTC
GTGGCCATTGCCAGGAGCCCACCCTGGTCACGCTGGCCACAGCACAAAGAACAACTCCTCACCAGTTCATCCTGA
GGCTGGGAGGACCGGGATGCTGGATTCTGTTTTCCGAAGTCACTGCAGCGGATGATGGAACTGAATCGATACGGT
GTTTTCTGTCCCTCCTACTTTCCTTCACACCAGACAGCCCCTCATGTCTCCAGGACAGGACAGGACTACAGACAA
CTCTTTCTTTAAATAAATTAAGTCTCTACAATAAAAAAAA

FIGURE 268

MRPLCVTCWWLGLLAAMGAVAGQEDGFEGTEEGSPREFIYLNRYKRAGESQDKCTYTFIVPQQ
RVTGAICVNSKEPEVLLENRVHKQELELLNNELLKQKRQIETLQQLVEVDGGIVSEVKLLRKE
SRNMNSRVTQLYMQLLHEIIRKRDNALELSQLENRILNQTADMLQLASKYKDLEHKYQHLATL
AHNQSEIIAQLEEHCQRVPSARPVPQPPPAAPPRVYQPPTYNRIINQISTNEIQSDQNLKVLP
PPLPTMPTLTSLPSSTDKPSGPWRDCLQALEDGHDTSSIYLVKPENTNRLMQVWCDQRHDPGG
WTVIQRRLDGSVNFFRNWETYKQGFGNIDGEYWLGLENIYWLTNQGNYKLLVTMEDWSGRKVF
AEYASFRLEPESEYYKLRLGRYHGNAGDSFTWHNGKQFTTLDRDHDVYTGNCAHYQKGGWWYN
ACAHSNLNGVWYRGGHYRSRYQDGVYWAEFRGGSYSLKKVVMMIRPNPNTFH

Important features:

Signal peptide:
amino acids 1-22

N-glycosylation sites:
amino acids 164-168,192-196

cAMP- and cGMP-dependent protein kinase phosphorylation site:
amino acids 124-128

Tyrosine kinase phosphorylation sites:
amino acids 177-184,385-393,385-394,461-468

N-myristoylation sites:
amino acids 12-18,18-24,22-28,29-35,114-120,341-347,465-471,
473-479

Amidation site:
amino acids 373-377

Fibrinogen beta and gamma chains C-terminal domain signature:
amino acids 438-451

Fibrinogen beta and gamma chains C-terminal domain proteins:
amino acids 305-343, 365-402, 411-424, 428-458

Trehalase proteins:
amino acids 275-292

FIGURE 269

GCCGAGCTGAGCGGATCCTCAC**ATG**ACTGTGATCCGATTCTTTCCAGCGGCTTCTGCAACCAA
GCGGGTCTTACCCCCGGTCCTCCGCGTCTCCAGTCCTCGCACCTGGAACCCCAACGTCCCCGA
GAGTCCCCGAATCCCCGCTCCCAGGCTACCTAAGAGGATGAGCGGTGCTCCGACGGCCGGGGC
AGCCCTGATGCTCTGCGCCGCCACCGCCGTGCTACTGAGCGCTCAGGGCGGACCCGTGCAGTC
CAAGTCGCCGCGCTTTGCGTCCTGGGACGAGATGAATGTCCTGGCGCACGGACTCCTGCAGCT
CGGCCAGGGGCTGCGCGAACACGCGGAGCGCACCCGCAGTCAGCTGAGCGCGCTGGAGCGGCG
CCTGAGCGCGTGCGGGTCCGCCTGTCAGGGAACCGAGGGGTCCACCGACCTCCCGTTAGCCCC
TGAGAGCCGGGTGGACCCTGAGGTCCTTCACAGCCTGCAGACACAACTCAAGGCTCAGAACAG
CAGGATCCAGCAACTCTTCCACAAGGTGGCCCAGCAGCAGCGGCACCTGGAGAAGCAGCACCT
GCGAATTCAGCATCTGCAAAGCCAGTTTGGCCTCCTGGACCACAAGCACCTAGACCATGAGGT
GGCCAAGCCTGCCCGAAGAAAGAGGCTGCCCGAGATGGCCCAGCCAGTTGACCCGGCTCACAA
TGTCAGCCGCCTGCACCGGCTGCCCAGGGATTGCCAGGAGCTGTTCCAGGTTGGGGAGAGGCA
GAGTGGACTATTTGAAATCCAGCCTCAGGGGTCTCCGCCATTTTTGGTGAACTGCAAGATGAC
CTCAGATGGAGGCTGGACAGTAATTCAGAGGCGCCACGATGGCTCAGTGGACTTCAACCGGCC
CTGGGAAGCCTACAAGGCGGGGTTTGGGGATCCCCACGGCGAGTTCTGGCTGGGTCTGGAGAA
GGTGCATAGCATCACGGGGGACCGCAACAGCCGCCTGGCCGTGCAGCTGCGGGACTGGGATGG
CAACGCCGAGTTGCTGCAGTTCTCCGTGCACCTGGGTGGCGAGGACACGGCCTATAGCCTGCA
GCTCACTGCACCCGTGGCCGGCCAGCTGGGCGCCACCACCGTCCCACCCAGCGGCCTCTCCGT
ACCCTTCTCCACTTGGGACCAGGATCACGACCTCCGCAGGGACAAGAACTGCGCCAAGAGCCT
CTCTGGAGGCTGGTGGTTTGGCACCTGCAGCCATTCCAACCTCAACGGCCAGTACTTCCGCTC
CATCCCACAGCAGCGGCAGAAGCTTAAGAAGGGAATCTTCTGGAAGACCTGGCGGGGCCGCTA
CTACCCGCTGCAGGCCACCACCATGTTGATCCAGCCCATGGCAGCAGAGGCAGCCTCC**TAG**CG
TCCTGGCTGGGCCTGGTCCCAGGCCCACGAAAGACGGTGACTCTTGGCTCTGCCCGAGGATGT
GGCCGTTCCCTGCCTGGGCAGGGGCTCCAAGGAGGGGCCATCTGGAAACTTGTGGACAGAGAA
GAAGACCACGACTGGAGAAGCCCCCTTTCTGAGTGCAGGGGGGCTGCATGCGTTGCCTCCTGA
GATCGAGGCTGCAGGATATGCTCAGACTCTAGAGGCGTGGACCAAGGGGCATGGAGCTTCACT
CCTTGCTGGCCAGGGAGTTGGGGACTCAGAGGGACCACTTGGGGCCAGCCAGACTGGCCTCAA
TGGCGGACTCAGTCACATTGACTGACGGGGACCAGGGCTTGTGTGGGTCGAGAGCGCCCTCAT
GGTGCTGGTGCTGTTGTGTGTAGGTCCCCTGGGGACACAAGCAGGCGCCAATGGTATCTGGGC
GGAGCTCACAGAGTTCTTGGAATAAAAGCAACCTCAGAACAC

FIGURE 270

MTVIRFFPAASATKRVLPPVLRVSSPRTWNPNVPESPRIPAPRLPKRMSGAPTAGAALMLCAA
TAVLLSAQGGPVQSKSPRFASWDEMNVLAHGLLQLGQGLREHAERTRSQLSALERRLSACGSA
CQGTEGSTDLPLAPESRVDPEVLHSLQTQLKAQNSRIQQLFHKVAQQQRHLEKQHLRIQHLQS
QFGLLDHKHLDHEVAKPARRKRLPEMAQPVDPAHNVSRLHRLPRDCQELFQVGERQSGLFEIQ
PQGSPPFLVNCKMTSDGGWTVIQRRHDGSVDFNRPWEAYKAGFGDPHGEFWLGLEKVHSITGD
RNSRLAVQLRDWDGNAELLQFSVHLGGEDTAYSLQLTAPVAGQLGATTVPPSGLSVPFSTWDQ
DHDLRRDKNCAKSLSGGWWFGTCSHSNLNGQYFRSIPQQRQKLKKGIFWKTWRGRYYPLQATT
MLIQPMAAEAAS

Important features:
Signal peptide:
Amino acids 1-13

Transmembrane domain:
Amino acids 53-70

N-glycosylation site:
Amino acids 224-228

cAMP- and cGMP-dependent protein kinase phosphorylation sites:
Amino acids 46-50;118-122

N-myristoylation sites:
Amino acids 50-56;129-135;341-347;357-363

Fibrinogen beta and gamma chains C-terminal domain signature:
Amino acids 396-409

FIGURE 271

CGGACGCGTGGGGGAAACCCTTCCGAGAAAACAGCAACAAGCTGAGCTGCTGTGACAGAGGGG

AACAAG**ATG**GCGGCGCCGAAGGGGAGCCTCTGGGTGAGGACCCAACTGGGGCTCCCGCCGCTG

CTGCTGCTGACCATGGCCTTGGCCGGAGGTTCGGGGACCGCTTCGGCTGAAGCATTTGACTCG

GTCTTGGGTGATACGGCGTCTTGCCACCGGGCCTGTCAGTTGACCTACCCCTTGCACACCTAC

CCTAAGGAAGAGGAGTTGTACGCATGTCAGAGAGGTTGCAGGCTGTTTTCAATTTGTCAGTTT

GTGGATGATGGAATTGACTTAAATCGAACTAAATTGGAATGTGAATCTGCATGTACAGAAGCA

TATTCCCAATCTGATGAGCAATATGCTTGCCATCTTGGTTGCCAGAATCAGCTGCCATTCGCT

GAACTGAGACAAGAACAACTTATGTCCCTGATGCCAAAAATGCACCTACTCTTTCCTCTAACT

CTGGTGAGGTCATTCTGGAGTGACATGATGGACTCCGCACAGAGCTTCATAACCTCTTCATGG

ACTTTTTATCTTCAAGCCGATGACGGAAAAATAGTTATATTCCAGTCTAAGCCAGAAATCCAG

TACGCACCACATTTGGAGCAGGAGCCTACAAATTTGAGAGAATCATCTCTAAGCAAAATGTCC

TATCTGCAAATGAGAAATTCACAAGCGCACAGGAATTTTCTTGAAGATGGAGAAAGTGATGGC

TTTTTAAGATGCCTCTCTCTTAACTCTGGGTGGATTTTAACTACAACTCTTGTCCTCTCGGTG

ATGGTATTGCTTTGGATTTGTTGTGCAACTGTTGCTACAGCTGTGGAGCAGTATGTTCCCTCT

GAGAAGCTGAGTATCTATGGTGACTTGGAGTTTATGAATGAACAAAAGCTAAACAGATATCCA

GCTTCTTCTCTTGTGGTTGTTAGATCTAAAACTGAAGATCATGAAGAAGCAGGGCCTCTACCT

ACAAAAGTGAATCTTGCTCATTCTGAAATT**TAA**GCATTTTTCTTTTAAAAGACAAGTGTAATA

GACATCTAAAATTCCACTCCTCATAGAGCTTTTAAAATGGTTTCATTGGATATAGGCCTTAAG

AAATCACTATAAAATGCAAATAAAGTTACTCAAATCTGTG

FIGURE 272

MAAPKGSLWVRTQLGLPPLLLLTMALAGGSGTASAEAFDSVLGDTASCHRACQLTYPLHTYPK
EEELYACQRGCRLFSICQFVDDGIDLNRTKLECESACTEAYSQSDEQYACHLGCQNQLPFAEL
RQEQLMSLMPKMHLLFPLTLVRSFWSDMMDSAQSFITSSWTFYLQADDGKIVIFQSKPEIQYA
PHLEQEPTNLRESSLSKMSYLQMRNSQAHRNFLEDGESDGFLRCLSLNSGWILTTTLVLSVMV
LLWICCATVATAVEQYVPSEKLSIYGDLEFMNEQKLNRYPASSLVVVRSKTEDHEEAGPLPTK
VNLAHSEI

Important features:

Signal peptide:

amino acids 1-31

Transmembrane domain:

amino acids 241-260

N-glycosylation site:

amino acids 90-94

N-myristoylation sites:

amino acids 28-34,29-35,31-37,86-92

FIGURE 273

CCCACGCGTCCGAACCTCTCCAGCG**ATG**GGAGCCGCCCGCCTGCTGCCCAACCTCACTCTGTG
CTTACAGCTGCTGATTCTCTGCTGTCAAACTCAGTACGTGAGGGACCAGGGCGCCATGACCGA
CCAGCTGAGCAGGCGGCAGATCCGCGAGTACCAACTCTACAGCAGGACCAGTGGCAAGCACGT
GCAGGTCACCGGGCGTCGCATCTCCGCCACCGCCGAGGACGGCAACAAGTTTGCCAAGCTCAT
AGTGGAGACGGACACGTTTGGCAGCCGGGTTCGCATCAAAGGGGCTGAGAGTGAGAAGTACAT
CTGTATGAACAAGAGGGGCAAGCTCATCGGGAAGCCCAGCGGGAAGAGCAAAGACTGCGTGTT
CACGGAGATCGTGCTGGAGAACAACTATACGGCCTTCCAGAACGCCCGGCACGAGGGCTGGTT
CATGGCCTTCACGCGGCAGGGGCGGCCCCGCCAGGCTTCCCGCAGCCGCCAGAACCAGCGCGA
GGCCCACTTCATCAAGCGCCTCTACCAAGGCCAGCTGCCCTTCCCCAACCACGCCGAGAAGCA
GAAGCAGTTCGAGTTTGTGGGCTCCGCCCCCACCCGCCGGACCAAGCGCACACGGCGGCCCCA
GCCCCTCACG**TAG**TCTGGGAGGCAGGGGGCAGCAGCCCCTGGGCCGCCTCCCCACCCCTTTCC
CTTCTTAATCCAAGGACTGGGCTGGGGTGGCGGGAGGGGAGCCAGATCCCCGAGGGAGGACCC
TGAGGGCCGCGAAGCATCCGAGCCCCCAGCTGGGAAGGGGCAGGCCGGTGCCCCAGGGGCGGC
TGGCACAGTGCCCCCTTCCCGGACGGGTGGCAGGCCCTGGAGAGGAACTGAGTGTCACCCTGA
TCTCAGGCCACCAGCCTCTGCCGGCCTCCCAGCCGGGCTCCTGAAGCCCGCTGAAAGGTCAGC
GACTGAAGGCCTTGCAGACAACCGTCTGGAGGTGGCTGTCCTCAAAATCTGCTTCTCGGATCT
CCCTCAGTCTGCCCCCAGCCCCCAAACTCCTCCTGGCTAGACTGTAGGAAGGGACTTTTGTTT
GTTTGTTTGTTTCAGGAAAAAAGAAAGGGAGAGAGAGGAAAATAGAGGGTTGTCCACTCCTCA
CATTCCACGACCCAGGCCTGCACCCCACCCCCAACTCCCAGCCCCGGAATAAAACCATTTTCC
TGC

FIGURE 274

MGAARLLPNLTLCLQLLILCCQTQYVRDQGAMTDQLSRRQIREYQLYSRTSGKHVQVTGRRIS
ATAEDGNKFAKLIVETDTFGSRVRIKGAESEKYICMNKRGKLIGKPSGKSKDCVFTEIVLENN
YTAFQNARHEGWFMAFTRQGRPRQASRSRQNQREAHFIKRLYQGQLPFPNHAEKQKQFEFVGS
APTRRTKRTRRPQPLT

Important features:

Signal peptide:

Amino acids 1-22

N-glycosylation site.

amino acids 9-13, 126-130

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 60-64

Casein kinase II phosphorylation site.

amino acids 65-69

Tyrosine kinase phosphorylation site.

amino acids 39-48, 89-97

N-myristoylation site.

amino acids 69-75, 188-194

Amidation site.

amino acids 58-62

HBGF/FGF family signature.

amino acids 103-128

FIGURE 275

TATTTACCATATCAGATTCACATTCAGTCCTCAGCAAA**ATG**AAGGGCTCCATTTTCACTCTGT
TTTTATTCTCTGTCCTATTTGCCATCTCAGAAGTGCGGAGCAAGGAGTCTGTGAGACTCTGTG
GGCTAGAATACATACGGACAGTCATCTATATCTGTGCTAGCTCCAGGTGGAGAAGGCATCTGG
AGGGGATCCCTCAAGCTCAGCAAGCTGAGACAGGAAACTCCTTCCAGCTCCCACATAAACGTG
AGTTTTCTGAGGAAAATCCAGCGCAAAACCTTCCGAAGGTGGATGCCTCAGGGGAAGACCGTC
TTTGGGGTGGACAGATGCCCACTGAAGAGCTTTGGAAGTCAAAGAAGCATTCAGTGATGTCAA
GACAAGATTTACAAACTTTGTGTTGCACTGATGGCTGTTCCATGACTGATTTGAGTGCTCTTT
GC**TAA**GACAAGAGCAAATACCCAATGGGTGGCAGAGCTTTATCACATGTTTAATTACAGTGTT
TTACTGCCTGGTAGAACACTAATATTGTGTTATTAAAATGATGGCTTTTGGGTAGGCAAAACT
TCTTTTCTAAAAGGTATAGCTGAGCGGTTGAAACCACAGTGATCTCTATTTTCTCCCTTTGCC
AAGGTTAATGAACTGTTCTTTTCAAATTCTACTAATGCTTTGAAATTTCAAATGCTGCGCAAA
ATTGCAATAAAAATGCTATAAA

FIGURE 276

MKGSIFTLFLFSVLFAISEVRSKESVRLCGLEYIRTVIYICASSRWRRHLEGIPQAQQAETGN
SFQLPHKREFSEENPAQNLPKVDASGEDRLWGGQMPTEELWKSKKHSVMSRQDLQTLCCTDGC
SMTDLSALC

Important features:

Signal sequence:

amino acids 1-18

cAMP- and cGMP-dependent protein kinase phosphorylation site:

amino acids 107-111

N-myristoylation sites:

amino acids 3-9,52-58,96-102,125-131

Insulin family signature:

amino acids 121-136

Insulin family proteins:

amino acids 28-46

FIGURE 277

GCAGCTGGTTACTGCATTTCTCCATGTGGCAGACAGAGCAAAGCCACAACGCTTTCTCTGCTGGATTAAAGACGG
CCCACAGACCAGAACTTCCACTATACTACTTAAAATTACATAGGTGGCTTGTCAAATTCAATTGATTAGTATTGT
AAAAGGAAAAAGAAGTTCCTTCTTACAGCTTGGATTCAACGGTCCAAAACAAAAATGCAGCTGCCATTAAAGTCT
CAGATGAACAAACTTCTACACTGATTTTTAAAATCAAGAATAAGGGCAGCAAGTTTCTGGATTCACTGAATCAAC
AGACACAAAAAGCTGGCAATATAGCAACTATGAAGAGAAAAGCTACTAATAAAATTAACCCAACGCATAGAAGAC
TTTTTTTTCTCTTCTAAAAACAACTAAGTAAAGACTTAAATTTAAACACATCATTTTACAACCTCATTTCAAA**AT**
GAAGACTTTTACCTGGACCCTAGGTGTGCTATTCTTCCTACTAGTGGACACTGGACATTGCAGAGGTGGACAATT
CAAAATTAAAAAAATAAACCAGAGAAGATACCCTCGTGCCACAGATGGTAAAGAGGAAGCAAAGAAATGTGCATA
CACATTCCTGGTACCTGAACAAAGAATAACAGGGCCAATCTGTGTCAACACCAAGGGGCAAGATGCAAGTACCAT
TAAAGACATGATCACCAGGATGGACCTTGAAAACCTGAAGGATGTGCTCTCCAGGCAGAAGCGGGAGATAGATGT
TCTGCAACTGGTGGTGGATGTAGATGGAAACATTGTGAATGAGGTAAAGCTGCTGAGAAAGGAAAGCCGTAACAT
GAACTCTCGTGTTACTCAACTCTATATGCAATTATTACATGAGATTATCCGTAAGAGGGATAATTCACTTGAACT
TTCCCAACTGGAAAACAAAATCCTCAATGTCACCACAGAAATGTTGAAGATGGCAACAAGATACAGGGAACTAGA
GGTGAAATACGCTTCCTTGACTGATCTTGTCAATAACCAATCTGTGATGATCACTTTGTTGGAAGAACAGTGCTT
GAGGATATTTTCCCGACAAGACACCCATGTGTCTCCCCCACTTGTCCAGGTGGTGCCACAACATATTCCTAACAG
CCAACAGTATACTCCTGGTCTGCTGGGAGGTAACGAGATTCAGAGGGATCCAGGTTATCCCAGAGATTTAATGCC
ACCACCTGATCTGGCAACTTCTCCCACCAAAAGCCCTTTCAAGATACCACCGGTAACTTTCATCAATGAAGGACC
ATTCAAAGACTGTCAGCAAGCAAAAGAAGCTGGGCATTCGGTCAGTGGGATTTATATGATTAAACCTGAAAACAG
CAATGGACCAATGCAGTTATGGTGTGAAAACAGTTTGGACCCTGGGGGTTGGACTGTTATTCAGAAAAGAACAGA
CGGCTCTGTCAACTTCTTCAGAAATTGGGAAAATTATAAGAAAGGGTTTGGAAACATTGACGGAGAATACTGGCT
TGGACTGGAAAATATCTATATGCTTAGCAATCAAGATAATTACAAGTTATTGATTGAATTAGAAGACTGGAGTGA
TAAAAAAGTCTATGCAGAATACAGCAGCTTTCGTCTGGAACCTGAAAGTGAATTCTATAGACTGCGCCTGGGAAC
TTACCAGGGAAATGCAGGGGATTCTATGATGTGGCATAATGGTAAACAATTCACCACACTGGACAGAGATAAAGA
TATGTATGCAGGAAACTGCGCCCACTTTCATAAAGGAGGCTGGTGGTACAATGCCTGTGCACATTCTAACCTAAA
TGGAGTATGGTACAGAGGAGGCCATTACAGAAGCAAGCACCAAGATGGAATTTTCTGGGCCGAATACAGAGGCGG
GTCATACTCCTTAAGAGCAGTTCAGATGATGATCAAGCCTATTGAC**TGA**AGAGAGACACTCGCCAATTTAAATGA
CACAGAACTTTGTACTTTTCAGCTCTTAAAAATGTAAATGTTACATGTATATTACTTGGCACAATTTATTTCTAC
ACAGAAAGTTTTTAAAATGAATTTTACCGTAACTATAAAAGGGAACCTATAAATGTAGTTTCATCTGTCGTCAAT
TACTGCAGAAAATTATGTGTATCCACAACCTAGTTATTTTAAAAATTATGTTGACTAAATACAAAGTTTGTTTTC
TAAAATGTAAATATTTGCCACAATGTAAAGCAAATCTTAGCTATATTTTAAATCATAAATAACATGTTCAAGATA
CTTAACAATTTATTTAAAATCTAAGATTGCTCTAACGTCTAGTGAAAAAAATATTTTTTAAATTTCAGCCAAATA
ATGCATTTTATTTTATAAAAATACAGACAGAAAATTAGGGAGAAACTTCTAGTTTTGCCAATAGAAAATGTTCTT
CCATTGAATAAAAGTTATTTCAAATTGAATTTGTGCCTTTCACACGTAATGATTAAATCTGAATTCTTAATAATA
TATCCTATGCTGATTTTCCCAAAACATGACCCATAGTATTAAATACATATCATTTTTAAAAATAAAAAAAAACCC
AAAAATAATGCATGCATAATTTAAATGGTCAATTTATAAAGACAAATCTATGAATGAATTTTTCAGTGTTATCTT
CATATGATATGCTGAACACCAAAATCTCCAGAAATGCATTTTATGTAGTTCTAAAATCAGCAAAATATTGGTATT
ACAAAAATGCAGAATATTTAGTGTGCTACAGATCTGAATTATAGTTCTAATTTATTATTACTTTTTTTCTAATTT
ACTGATCTTACTACTACAAAGAAAAAAAAACCCAACCCATCTGCAATTCAAATCAGAAAGTTTGGACAGCTTTAC
AAGTATTAGTGCATGCTCAGAACAGGTGGGACTAAAACAAACTCAAGGAACTGTTGGCTGTTTTCCCGATACTGA
GAATTCAACAGCTCCAGAGCAGAAGCCACAGGGGCATAGCTTAGTCCAAACTGCTAATTTCATTTTACAGTGTAT
GTAACGCTTAGTCTCACAGTGTCTTTAACTCATCTTTGCAATCAACAACTTTACTAGTGACTTTCTGGAACAATT
TCCTTTCAGGAATACATATTCACTGCTTAGAGGTGACCTTGCCTTAATATATTTGTGAAGTTAAAATTTTAAAGA
TAGCTCATGAAACTTTTGCTTAAGCAAAAAGAAAACCTCGAATTGAAATGTGTGAGGCAAACTATGCATGGGAAT
AGCTTAATGTGAAGATAATCATTTGGACAACTCAAATCCATCAACATGACCAATGTTTTTCATCTGCCACATCTC
AAAATAAAACTTCTGGTGAAACAAATTAAACAAAATATCCAAACCTCAAAAAAAA

FIGURE 278

MKTFTWTLGVLFFLLVDTGHCRGGQFKIKKINQRRYPRATDGKEEAKKCAYTFLVPEQRITGP
ICVNTKGQDASTIKDMITRMDLENLKDVLSRQKREIDVLQLVVDVDGNIVNEVKLLRKESRNM
NSRVTQLYMQLLHEIIRKRDNSLELSQLENKILNVTTEMLKMATRYRELEVKYASLTDLVNNQ
SVMITLLEEQCLRIFSRQDTHVSPPLVQVVPQHIPNSQQYTPGLLGGNEIQRDPGYPRDLMPP
PDLATSPTKSPFKIPPVTFINEGPFKDCQQAKEAGHSVSGIYMIKPENSNGPMQLWCENSLDP
GGWTVIQKRTDGSVNFFRNWENYKKGFGNIDGEYWLGLENIYMLSNQDNYKLLIELEDWSDKK
VYAEYSSFRLEPESEFYRLRLGTYQGNAGDSMMWHNGKQFTTLDRDKDMYAGNCAHFHKGGWW
YNACAHSNLNGVWYRGGHYRSKHQDGIFWAEYRGGSYSLRAVQMMIKPID

Important features:

Signal sequence:

Amino acids 1-23

N-glycosylation sites:

Amino acids 160-164;188-192

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 120-124

Tyrosine kinase phosphorylation sites:

Amino acids 173-180;387-396

N-myristoylation sites:

Amino acids 70-76;110-116;232-238,343-349;400-406;467-473;
475-487

Fibrinogen beta and gamma chains C-terminal domain signature:

Amino acids 440-453

FIGURE 279

CCCACGCGTCCGCGCAGTCGCGCAGTTCTGCCTCCGCCTGCCAGTCTCGCCCGCGATCCCGGC
CCGGGGCTGTGGCGTCGACTCCGACCCAGGCAGCCAGCAGCCCGCGCGGGAGCCGGACCGCCG
CCGGAGGAGCTCGGACGGCATGCTGAGCCCCCTCCTTTGCTGAAGCCCGAGTGCGGAGAAGCC
CGGGCAAACGCAGGCTAAGGAGACCAAAGCGGCGAAGTCGCGAGACAGCGGACAAGCAGCGGA
GGAGAAGGAGGAGGAGGCGAACCCAGAGAGGGGCAGCAAAAGAAGCGGTGGTGGTGGGCGTCG
TGGCC**ATG**GCGGCGGCTATCGCCAGCTCGCTCATCCGTCAGAAGAGGCAAGCCCGCGAGCGCG
AGAAATCCAACGCCTGCAAGTGTGTCAGCAGCCCCAGCAAAGGCAAGACCAGCTGCGACAAAA
ACAAGTTAAATGTCTTTTCCCGGGTCAAACTCTTCGGCTCCAAGAAGAGGCGCAGAAGAAGAC
CAGAGCCTCAGCTTAAGGGTATAGTTACCAAGCTATACAGCCGACAAGGCTACCACTTGCAGC
TGCAGGCGGATGGAACCATTGATGGCACCAAAGATGAGGACAGCACTTACACTCTGTTTAACC
TCATCCCTGTGGGTCTGCGAGTGGTGGCTATCCAAGGAGTTCAAACCAAGCTGTACTTGGCAA
TGAACAGTGAGGGATACTTGTACACCTCGGAACTTTTCACACCTGAGTGCAAATTCAAAGAAT
CAGTGTTTGAAAATTATTATGTGACATATTCATCAATGATATACCGTCAGCAGCAGTCAGGCC
GAGGGTGGTATCTGGGTCTGAACAAAGAAGGAGAGATCATGAAAGGCAACCATGTGAAGAAGA
ACAAGCCTGCAGCTCATTTTCTGCCTAAACCACTGAAAGTGGCCATGTACAAGGAGCCATCAC
TGCACGATCTCACGGAGTTCTCCCGATCTGGAAGCGGGACCCCAACCAAGAGCAGAAGTGTCT
CTGGCGTGCTGAACGGAGGCAAATCCATGAGCCACAATGAATCAACG**TAG**CCAGTGAGGGCAA
AAGAAGGGCTCTGTAACAGAACCTTACCTCCAGGTGCTGTTGAATTCTTCTAGCAGTCCTTCA
CCCAAAAGTTCAAATTTGTCAGTGACATTTACCAAACAAACAGGCAGAGTTCACTATTCTATC
TGCCATTAGACCTTCTTATCATCCATACTAAAGC

FIGURE 280

MAAAIASSLIRQKRQARE REKSNACKCVSSPSKGKTSCDKNKLNVFSRVKLFGSKKRRRRRPE
PQLKGIVTKLYSRQGYHLQLQADGTIDGTKDEDSTYTLFNLIPVGLRVVAIQGVQTKLYLAMN
SEGYLYTSELFTPECKFKESVFENYYVTYSSMIYRQQQSGRGWYLGLNKEGEIMKGNHVKKNK
PAAHFLPKPLKVAMYKEPSLHDLTEFSRSGSGTPTKSRSVSGVLNGGKSMSHNEST

Important Features:

N-glycosylation site:

Amino acids 242-246

Glycosaminoglycan attachment sites:

Amino acids 165-169, 218-222

Tyrosine kinase phosphorylation site:

Amino acids 93-100

N-myristoylation sites:

Amino acids 87-93, 231-237

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

Amino acids 231-239

HBGF/FGF family proteins:

Amino acids 78-94, 102-153

FIGURE 281

CCAGGATGGAGCTGGGGCCTGTATAGCCATATTATTGTTCTATGCTACTAGACATGGGGGGGA
CTTGGTGAAAAAGGTATTATCCAGCCAGAGGGTCTGGGAGCCCTGTCTTACTGAACCTGGGCA
ACCTGGATATTCTGAGACATATTTTGGGGGGATTTCAGTGAAAAAAGTGGGGGATCCCCTCCA
TTTAGAGTGTAGCAAAGGAAAAAACACCAAGGTTGGGTTCCTTCCTGACATTGGCAGTGCCCC
AGTAGGGGTGGGATGAGCGAATATTCCCAAAGCTAAAGTCCCACACCCTGTAGATTACAAGAG
TGGATTTGGCAGGAGTGTGCCCCAAAATACAGTGGAAAGGTGCCTGAAGATATTTAAACCACG
TCTTGGAAATTTAGTGGGTCTTGGCTTTGGGATAGGTGAAGTGAGGACAGACACTGGAGAGGA
GGGAAAGGGGACGTTTTCAATAGGAGGCAAAACTCGAGGGTGGGATCCACTGAGGAGTACATA
GGCTGCTGGATCTGGTGGAGCCAGCACTGGGCCCACGGGTGGTAACTGGCTGCTGTGGAGGGG
GGTACGTGAGGGGGGGGTCTGGGGCTTATCCTCAGGTCCTGTGGGTGGGGCAGCGAGTCGGGG
CCTGAGCGTCAAGAGCATGCCCTAGTGAGCGGGCTCCTCTGGGGGAGCCCAGCGCGCTCCGGG
CGCCTGCCGGTTTGGGGGTGTCTCCTCCCGGGGCGCT**ATG**GCGGCGCTGGCCAGTAGCCTGAT
CCGGCAGAAGCGGGAGGTCCGCGAGCCCGGGGGCAGCCGGCCGGTGTCGGCGCAGCGGCGCGT
GTGTCCCCGCGGCACCAAGTCCCTTTGCCAGAAGCAGCTCCTCATCCTGCTGTCCAAGGTGCG
ACTGTGCGGGGGGCGGCCCGCGCGGCCGGACCGCGGCCCGGAGCCTCAGCTCAAAGGCATCGT
CACCAAACTGTTCTGCCGCCAGGGTTTCTACCTCCAGGCGAATCCCGACGGAAGCATCCAGGG
CACCCCAGAGGATACCAGCTCCTTCACCCACTTCAACCTGATCCCTGTGGGCCTCCGTGTGGT
CACCATCCAGAGCGCCAAGCTGGGTCACTACATGGCCATGAATGCTGAGGGACTGCTCTACAG
TTCGCCGCATTTCACAGCTGAGTGTCGCTTTAAGGAGTGTGTCTTTGAGAATTACTACGTCCT
GTACGCCTCTGCTCTCTACCGCCAGCGTCGTTCTGGCCGGGCCTGGTACCTCGGCCTGGACAA
GGAGGGCCAGGTCATGAAGGGAAACCGAGTTAAGAAGACCAAGGCAGCTGCCCACTTTCTGCC
CAAGCTCCTGGAGGTGGCCATGTACCAGGAGCCTTCTCTCCACAGTGTCCCCGAGGCCTCCCC
TTCCAGTCCCCCTGCCCCC**TGA**AATGTAGTCCCTGGACTGGAGGTTCCCTGCACTCCCAGTGA
GCCAGCCACCACCACAACCTGT

FIGURE 282

MAALASSLIRQKREVREPGGSRPVSAQRRVCPRGTKSLCQKQLLILLSKVRLCGGRPARPDRG
PEPQLKGIVTKLFCRQGFYLQANPDGSIQGTPEDTSSFTHFNLIPVGLRVVTIQSAKLGHYMA
MNAEGLLYSSPHFTAECRFKECVFENYYVLYASALYRQRRSGRAWYLGLDKEGQVMKGNRVKK
TKAAAHFLPKLLEVAMYQEPSLHSVPEASPSSPPAP

Important features:

Tyrosine kinase phosphorylation site:

Amino acids 199-207

N-myristoylation sites:

Amino acids 54-60; 89-95; 131-137

HBGF/FGF family signature:

Amino acids 131-155

FIGURE 283

ATGGCCGCGGCCATCGCTAGCGGCTTGATCCGCCAGAAGCGGCAGGCGCGGGAGCAGCACTGG
GACCGGCCGTCTGCCAGCAGGAGGCGGAGCAGCCCCAGCAAGAACCGCGGGCTCTGCAACGGC
AACCTGGTGGATATCTTCTCCAAAGTGCGCATCTTCGGCCTCAAGAAGCGCAGGTTGCGGCGC
CAAGATCCCCAGCTCAAGGGTATAGTGACCAGGTTATATTGCAGGCAAGGCTACTACTTGCAA
ATGCACCCCGATGGAGCTCTCGATGGAACCAAGGATGACAGCACTAATTCTACACTCTTCAAC
CTCATACCAGTGGGACTACGTGTTGTTGCCATCCAGGGAGTGAAAACAGGGTTGTATATAGCC
ATGAATGGAGAAGGTTACCTCTACCCATCAGAACTTTTTACCCCTGAATGCAAGTTTAAAGAA
TCTGTTTTTGAAAATTATTATGTAATCTACTCATCCATGTTGTACAGACAACAGGAATCTGGT
AGAGCCTGGTTTTTGGGATTAAATAAGGAAGGGCAAGCTATGAAAGGGAACAGAGTAAAGAAA
ACCAAACCAGCAGCTCATTTTCTACCCAAGCCATTGGAAGTTGCCATGTACCGAGAACCATCT
TTGCATGATGTTGGGGAAACGGTCCCGAAGCCTGGGGTGACGCCAAGTAAAAGCACAAGTGCG
TCTGCAATAATGAATGGAGGCAAACCAGTCAACAAGAGTAAGACAACA**TAG**

FIGURE 284

MAAAIASGLIRQKRQAREQHWDRPSASRRRSSPSKNRGLCNGNLVDIFSKVRIFGLKKRRLRR
QDPQLKGIVTRLYCRQGYYLQMHPDGALDGTKDDSTNSTLFNLIPVGLRVVAIQGVKTGLYIA
MNGEGYLYPSELFTPECKFKESVFENYYVIYSSMLYRQQESGRAWFLGLNKEGQAMKGNRVKK
TKPAAHFLPKPLEVAMYREPSLHDVGETVPKPGVTPSKSTSASAIMNGGKPVNKSKTT

Important features:

N-glycosylation sites:

Amino acids 100-104, 242-246

cAMP- and cGMP-dependent protein kinase phosphorylation sites:

Amino acids 28-32, 29-33

Tyrosine kinase phosphorylation site:

Amino acids 199-207

N-myristoylation sites:

Amino acids 38-44, 89-95, 118-124, 122-128, 222-228

HBGF/FGF family proteins:

Amino acids 104-155, 171-198

FIGURE 285

CGGACGCGTGGGCGGACGCGTGGGCGGACGCGTGGGCGGACGCGTGGGCTGGTTCAGGTCCAGGTTTTGCTTTGA
TCCTTTTCAAAAACTGGAGACACAGAAGAGGGCTCTAGGAAAAAGTTTTGGATGGGATTATGTGGAAACTACCCT
GCGATTCTCTGCTGCCAGAGCAGGCTCGGCGCTTCCACCCCAGTGCAGCCTTCCCCTGGCGGTGGTGAAAGAGAC
TCGGGAGTCGCTGCTTCCAAAGTGCCCGCCGTGAGTGAGCTCTCACCCCAGTCAGCCAA**ATG**AGCCTCTTCGGGC
TTCTCCTGCTGACATCTGCCCTGGCCGGCCAGAGACAGGGGACTCAGGCGGAATCCAACCTGAGTAGTAAATTCC
AGTTTTCCAGCAACAAGGAACAGAACGGAGTACAAGATCCTCAGCATGAGAGAATTATTACTGTGTCTACTAATG
GAAGTATTCACAGCCCAAGGTTTCCTCATACTTATCCAAGAAATACGGTCTTGGTATGGAGATTAGTAGCAGTAG
AGGAAAATGTATGGATACAACTTACGTTTGATGAAAGATTTGGGCTTGAAGACCCAGAAGATGACATATGCAAGT
ATGATTTTGTAGAAGTTGAGGAACCCAGTGATGGAACTATATTAGGGCGCTGGTGTGGTTCTGGTACTGTACCAG
GAAAACAGATTTCTAAAGGAAATCAAATTAGGATAAGATTTGTATCTGATGAATATTTTCCTTCTGAACCAGGGT
TCTGCATCCACTACAACATTGTCATGCCACAATTCACAGAAGCTGTGAGTCCTTCAGTGCTACCCCCTTCAGCTT
TGCCACTGGACCTGCTTAATAATGCTATAACTGCCTTTAGTACCTTGGAAGACCTTATTCGATATCTTGAACCAG
AGAGATGGCAGTTGGACTTAGAAGATCTATATAGGCCAACTTGGCAACTTCTTGGCAAGGCTTTTGTTTTTGGAA
GAAAATCCAGAGTGGTGGATCTGAACCTTCTAACAGAGGAGGTAAGATTATACAGCTGCACACCTCGTAACTTCT
CAGTGTCCATAAGGGAAGAACTAAAGAGAACCGATACCATTTTCTGGCCAGGTTGTCTCCTGGTTAAACGCTGTG
GTGGGAACTGTGCCTGTTGTCTCCACAATTGCAATGAATGTCAATGTGTCCCAAGCAAAGTTACTAAAAAATACC
ACGAGGTCCTTCAGTTGAGACCAAAGACCGGTGTCAGGGGATTGCACAAATCACTCACCGACGTGGCCCTGGAGC
ACCATGAGGAGTGTGACTGTGTGTGCAGAGGGAGCACAGGAGGA**TAG**CCGCATCACCACCAGCAGCTCTTGCCCA
GAGCTGTGCAGTGCAGTGGCTGATTCTATTAGAGAACGTATGCGTTATCTCCATCCTTAATCTCAGTTGTTTGCT
TCAAGGACCTTTCATCTTCAGGATTTACAGTGCATTCTGAAAGAGGAGACATCAAACAGAATTAGGAGTTGTGCA
ACAGCTCTTTTGAGAGGAGGCCTAAAGGACAGGAGAAAAGGTCTTCAATCGTGGAAAGAAAATTAAATGTTGTAT
TAAATAGATCACCAGCTAGTTTCAGAGTTACCATGTACGTATTCCACTAGCTGGGTTCTGTATTTCAGTTCTTTC
GATACGGCTTAGGGTAATGTCAGTACAGGAAAAAAACTGTGCAAGTGAGCACCTGATTCCGTTGCCTTGCTTAAC
TCTAAAGCTCCATGTCCTGGGCCTAAAATCGTATAAAATCTGGATTTTTTTTTTTTTTTTTGCTCATATTCACAT
ATGTAAACCAGAACATTCTATGTACTACAAACCTGGTTTTTAAAAAGGAACTATGTTGCTATGAATTAAACTTGT
GTCATGCTGATAGGACAGACTGGATTTTTCATATTTCTTATTAAAATTTCTGCCATTTAGAAGAAGAGAACTACA
TTCATGGTTTGGAAGAGATAAACCTGAAAAGAAGAGTGGCCTTATCTTCACTTTATCGATAAGTCAGTTTATTTG
TTTCATTGTGTACATTTTTATATTCTCCTTTTGACATTATAACTGTTGGCTTTTCTAATCTTGTTAAATATATCT
ATTTTTACCAAAGGTATTTAATATTCTTTTTTATGACAACTTAGATCAACTATTTTTAGCTTGGTAAATTTTTCT
AAACACAATTGTTATAGCCAGAGGAACAAAGATGATATAAAATATTGTTGCTCTGACAAAAATACATGTATTTCA
TTCTCGTATGGTGCTAGAGTTAGATTAATCTGCATTTTAAAAAACTGAATTGGAATAGAATTGGTAAGTTGCAAA
GACTTTTTGAAAATAATTAAATTATCATATCTTCCATTCCTGTTATTGGAGATGAAAATAAAAAGCAACTTATGA
AAGTAGACATTCAGATCCAGCCATTACTAACCTATTCCTTTTTTGGGGAAATCTGAGCCTAGCTCAGAAAAACAT
AAAGCACCTTGAAAAAGACTTGGCAGCTTCCTGATAAAGCGTGCTGTGCTGTGCAGTAGGAACACATCCTATTTA
TTGTGATGTTGTGGTTTTATTATCTTAAACTCTGTTCCATACACTTGTATAAATACATGGATATTTTTATGTACA
GAAGTATGTCTCTTAACCAGTTCACTTATTGTACTCTGGCAATTTAAAAGAAAATCAGTAAAATATTTTGCTTGT
AAAATGCTTAATATNGTGCCTAGGTTATGTGGTGACTATTTGAATCAAAAATGTATTGAATCATCAAATAAAAGA
ATGTGGCTATTTTGGGGAGAAAATTAAAAAAAAAAAAAAAAAAAAAAGGTTTAGGGATAACAGGGTAATGCGGCC

FIGURE 286

MSLFGLLLLTSALAGQRQGTQAESNLSSKFQFSSNKEQNGVQDPQHERIITVSTNGSIHSPRF
PHTYPRNTVLVWRLVAVEENVWIQLTFDERFGLEDPEDDICKYDFVEVEEPSDGTILGRWCGS
GTVPGKQISKGNQIRIRFVSDEYFPSEPGFCIHYNIVMPQFTEAVSPSVLPPSALPLDLLNNA
ITAFSTLEDLIRYLEPERWQLDLEDLYRPTWQLLGKAFVFGRKSRVVDLNLLTEEVRLYSCTP
RNFSVSIREELKRTDTIFWPGCLLVKRCGGNCACCLHNCNECQCVPSKVTKKYHEVLQLRPKT
GVRGLHKSLTDVALEHHEECDCVCRGSTGG

Important features:

signal sequence:

Amino acids 1-14

N-glycosylation sites:

Amino acids 25-29;55-59;254-258

N-myristoylation sites:

Amino acids 15-21;117-123;127-133;281-287;282-288;319-325

Amidation site:

Amino acids 229-233

FIGURE 287

CAGCGCTGACTGCGCCGCGGAGAAAGCCAGTGGGAACCCAGACCCATAGGAGACCCGCGTCCC

CGCTCGGCCTGGCCAGGCCCCGCGCT**ATG**GAGTTCCTCTGGGCCCCTCTCTTGGGTCTGTGCT

GCAGTCTGGCCGCTGCTGATCGCCACACCGTCTTCTGGAACAGTTCAAATCCCAAGTTCCGGA

ATGAGGACTACACCATACATGTGCAGCTGAATGACTACGTGGACATCATCTGTCCGCACTATG

AAGATCACTCTGTGGCAGACGCTGCCATGGAGCAGTACATACTGTACCTGGTGGAGCATGAGG

AGTACCAGCTGTGCCAGCCCCAGTCCAAGGACCAAGTCCGCTGGCAGTGCAACCGGCCCAGTG

CCAAGCATGGCCCGGAGAAGCTGTCTGAGAAGTTCCAGCGCTTCACACCTTTCACCCTGGGCA

AGGAGTTCAAAGAAGGACACAGCTACTACTACATCTCCAAACCCATCCACCAGCATGAAGACC

GCTGCTTGAGGTTGAAGGTGACTGTCAGTGGCAAAATCACTCACAGTCCTCAGGCCCATGACA

ATCCACAGGAGAAGAGACTTGCAGCAGATGACCCAGAGGTGCGGGTTCTACATAGCATCGGTC

ACAGTGCTGCCCCACGCCTCTTCCCACTTGCCTGGACTGTGCTGCTCCTTCCACTTCTGCTGC

TGCAAACCCCG**TGA**AGGTGTGTGCCACACCTGGCCTTAAAGAGGGACAGGCTGAAGAGAGGGA

CAGGCACTCCAAACCTGTCTTGGGGCCACTTTCAGAGCCCCCAGCCCTGGGAACCACTCCCAC

CACAGGCATAAGCTATCACCTAGCAGCCTCAAAACGGGTCAATATTAAGGTTTTCAACCGGAA

GGAGGCCAACCAGCCCGACAGTGCCATCCCCACCTTCACCTCGGAGGGATGGAGAAAGAAGTG

GAGACAGTCCTTTCCCACCATTCCTGCCTTTAAGCCAAAGAAACAAGCTGTGCAGGCATGGTC

CCTTAAGGCACAGTGGGAGCTGAGCTGGAAGGGGCCACGTGGATGGGCAAAGCTTGTCAAAGA

TGCCCCCTTCAGGAGAGAGCCAGGATGCCCAGATGAACTGACTGAAGGAAAAGCAAGAAACAG

TTTCTTGCTTGGAAGCCAGGTACAGGAGAGGCAGCATGCTTGGGCTGACCCAGCATCTCCCAG

CAAGACCTCATCTGTGGAGCTGCCACAGAGAAGTTTGTAGCCAGGTACTGCATTCTCTCCCAT

CCTGGGGCAGCACTCCCCAGAGCTGTGCCAGCAGGGGGGCTGTGCCAACCTGTTCTTAGAGTG

TAGCTGTAAGGGCAGTGCCCATGTGTACATTCTGCCTAGAGTGTAGCCTAAAGGGCAGGGCCC

ACGTGTATAGTATCTGTATATAAGTTGCTGTGTGTCTGTCCTGATTTCTACAACTGGAGTTTT

TTTATACAATGTTCTTTGTCTCAAAATAAAGCAATGTGTTTTTTCGG

FIGURE 288

MEFLWAPLLGLCCSLAAADRHTVFWNSSNPKFRNEDYTIHVQLNDYVDIICPHYEDHSADAAM
EQYILYLVEHEEYQLCQPQSKDQVRWQCNRPSAKHGPEKLSEKFQRFTPFTLGKEFKEGHSYY
YISKPIHQHEDRCLRLKVTVSGKITHSPQAHDNPQEKRLAADDPEVRVLHSIGHSAAPRLFPL
AWTVLLLPLLLLQTP

Important features:

Signal sequence:

Amino acids 1-17

N-glycosylation site:

Amino acids 26-30

Tyrosine kinase phosphorylation site:

Amino acids 118-127

N-myristoylation site:

Amino acids 10-16

FIGURE 289

CGGACGCGTGGGCGGACGCGTGGGCGGCCCACGGCGCCCGCGGGCTGGGGCGGTCGCTTCTTC

CTTCTCCGTGGCCTACGAGGGTCCCCAGCCTGGGTAAAG**ATG**GCCCCATGGCCCCCGAAGGGC

CTAGTCCCAGCTGTGCTCTGGGGCCTCAGCCTCTTCCTCAACCTCCCAGGACCTATCTGGCTC

CAGCCCTCTCCACCTCCCCAGTCTTCTCCCCCCGCCTCAGCCCCATCCGTGTCATACCTGCCGG

GGACTGGTTGACAGCTTTAACAAGGGCCTGGAGAGAACCATCCGGGACAACTTTGGAGGTGGA

AACACTGCCTGGGAGGAAGAGAATTTGTCCAAATACAAAGACAGTGAGACCCGCCTGGTAGAG

GTGCTGGAGGGTGTGTGCAGCAAGTCAGACTTCGAGTGCCACCGCCTGCTGGAGCTGAGTGAG

GAGCTGGTGGAGAGCTGGTGGTTTCACAAGCAGCAGGAGGCCCCGGACCTCTTCCAGTGGCTG

TGCTCAGATTCCCTGAAGCTCTGCTGCCCCGCAGGCACCTTCGGGCCCTCCTGCCTTCCCTGT

CCTGGGGGAACAGAGAGGCCCTGCGGTGGCTACGGGCAGTGTGAAGGAGAAGGGACACGAGGG

GGCAGCGGGCACTGTGACTGCCAAGCCGGCTACGGGGGTGAGGCCTGTGGCCAGTGTGGCCTT

GGCTACTTTGAGGCAGAACGCAACGCCAGCCATCTGGTATGTTCGGCTTGTTTTGGCCCCTGT

GCCCGATGCTCAGGACCTGAGGAATCAAACTGTTTGCAATGCAAGAAGGGCTGGGCCCTGCAT

CACCTCAAGTGTGTAGACATTGATGAGTGTGGCACAGAGGGAGCCAACTGTGGAGCTGACCAA

TTCTGCGTGAACACTGAGGGCTCCTATGAGTGCCGAGACTGTGCCAAGGCCTGCCTAGGCTGC

ATGGGGGCAGGGCCAGGTCGCTGTAAGAAGTGTAGCCCTGGCTATCAGCAGGTGGGCTCCAAG

TGTCTCGATGTGGATGAGTGTGAGACAGAGGTGTGTCCGGGAGAGAACAAGCAGTGTGAAAAC

ACCGAGGGCGGTTATCGCTGCATCTGTGCCGAGGGCTACAAGCAGATGGAAGGCATCTGTGTG

AAGGAGCAGATCCCAGAGTCAGCAGGCTTCTTCTCAGAGATGACAGAAGACGAGTTGGTGGTG

CTGCAGCAGATGTTCTTTGGCATCATCATCTGTGCACTGGCCACGCTGGCTGCTAAGGGCGAC

TTGGTGTTCACCGCCATCTTCATTGGGGCTGTGGCGGCCATGACTGGCTACTGGTTGTCAGAG

CGCAGTGACCGTGTGCTGGAGGGCTTCATCAAGGGCAGA**TAA**TCGCGGCCACCACCTGTAGGA

CCTCCTCCCACCCACGCTGCCCCCAGAGCTTGGGCTGCCCTCCTGCTGGACACTCAGGACAGC

TTGGTTTATTTTTGAGAGTGGGGTAAGCACCCCTACCTGCCTTACAGAGCAGCCCAGGTACCC

AGGCCCGGGCAGACAAGGCCCCTGGGGTAAAAAGTAGCCCTGAAGGTGGATACCATGAGCTCT

TCACCTGGCGGGGACTGGCAGGCTTCACAATGTGTGAATTTCAAAAGTTTTTCCTTAATGGTG

GCTGCTAGAGCTTTGGCCCCTGCTTAGGATTAGGTGGTCCTCACAGGGGTGGGGCCATCACAG

CTCCCTCCTGCCAGCTGCATGCTGCCAGTTCCTGTTCTGTGTTCACCACATCCCCACACCCCA

TTGCCACTTATTTATTCATCTCAGGAAATAAAGAAAGGTCTTGGAAAGTTAAAAAAAAAAAAA

AAAAAAAAAAA

FIGURE 290

MAPWPPKGLVPAVLWGLSLFLNLPGPIWLQPSPPPQSSPPPQPHPCHTCRGLVDSFNKGLERT
IRDNFGGGNTAWEEENLSKYKDSETRLVEVLEGVCSKSDFECHRLLELSEELVESWWFHKQQE
APDLFQWLCSDSLKLCCPAGTFGPSCLPCPGGTERPCGGYGQCEGEGTRGGSGHCDCQAGYGG
EACGQCGLGYFEAERNASHLVCSACFGPCARCSGPEESNCLQCKKGWALHHLKCVDIDECGTE
GANCGADQFCVNTEGSYECRDCAKACLGCMGAGPGRCKKCSPGYQQVGSKCLDVDECETEVCP
GENKQCENTEGGYRCICAEGYKQMEGICVKEQIPESAGFFSEMTEDELVVLQQMFFGIIICAL
ATLAAKGDLVFTAIFIGAVAAMTGYWLSERSDRVLEGFIKGR

Important features:

Signal sequence:

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 291

CAGGTCCAACTGCACCTCGGTTCTATCGATTGAATTCCCCGGGGATCCTCTAGAGATCCCTCGACCTCGACCCAC
GCGTCCGAACACAGGTCCTTGTTGCTGCAGAGAAGCAGTTGTTTTGCTGGAAGGAGGGAGTGCGCGGGCTGCCCC
GGGCTCCTCCCTGCCGCCTCCTCTCAGTGGATGGTTCCAGGCACCCTGTCTGGGGCAGGGAGGGCACAGGCCTGC
ACATCGAAGGTGGGGTGGGACCAGGCTGCCCCTCGCCCCAGCATCCAAGTCCTCCCTTGGGCGCCCGTGGCCCTG
CAGACTCTCAGGGCTAAGGTCCTCTGTTGCTTTTTGGTTCCACCTTAGAAGAGGCTCCGCTTGACTAAGAGTAGC
TTGAAGGAGGCACC**ATG**CAGGAGCTGCATCTGCTCTGGTGGGCGCTTCTCCTGGGCCTGGCTCAGGCCTGCCCTG
AGCCCTGCGACTGTGGGGAAAAGTATGGCTTCCAGATCGCCGACTGTGCCTACCGCGACCTAGAATCCGTGCCGC
CTGGCTTCCCGGCCAATGTGACTACACTGAGCCTGTCAGCCAACCGGCTGCCAGGCTTGCCGGAGGGTGCCTTCA
GGGAGGTGCCCCTGCTGCAGTCGCTGTGGCTGGCACACAATGAGATCCGCACGGTGGCCGCCGGAGCCCTGGCCT
CTCTGAGCCATCTCAAGAGCCTGGACCTCAGCCACAATCTCATCTCTGACTTTGCCTGGAGCGACCTGCACAACC
TCAGTGCCCTCCAATTGCTCAAGATGGACAGCAACGAGCTGACCTTCATCCCCCGCGACGCCTTCCGCAGCCTCC
GTGCTCTGCGCTCGCTGCAACTCAACCACAACCGCTTGCACACATTGGCCGAGGGCACCTTCACCCCGCTCACCG
CGCTGTCCCACCTGCAGATCAACGAGAACCCCTTCGACTGCACCTGCGGCATCGTGTGGCTCAAGACATGGGCCC
TGACCACGGCCGTGTCCATCCCGGAGCAGGACAACATCGCCTGCACCTCACCCCATGTGCTCAAGGGTACACCGC
TGAGCCGCCTGCCGCCACTGCCATGCTCGGCGCCCTCAGTGCAGCTCAGCTACCAACCCAGCCAGGATGGTGCCG
AGCTGCGGCCTGGTTTTGTGCTGGCACTGCACTGTGATGTGGACGGGCAGCCGGCCCCTCAGCTTCACTGGCACA
TCCAGATACCCAGTGGCATTGTGGAGATCACCAGCCCCAACGTGGGCACTGATGGGCGTGCCCTGCCTGGCACCC
CTGTGGCCAGCTCCCAGCCGCGCTTCCAGGCCTTTGCCAATGGCAGCCTGCTTATCCCCGACTTTGGCAAGCTGG
AGGAAGGCACCTACAGCTGCCTGGCCACCAATGAGCTGGGCAGTGCTGAGAGCTCAGTGGACGTGGCACTGGCCA
CGCCCGGTGAGGGTGGTGAGGACACACTGGGGCGCAGGTTCCATGGCAAAGCGGTTGAGGGAAAGGGCTGCTATA
CGGTTGACAACGAGGTGCAGCCATCAGGGCCGGAGGACAATGTGGTCATCATCTACCTCAGCCGTGCTGGGAACC
CTGAGGCTGCAGTCGCAGAAGGGGTCCCTGGGCAGCTGCCCCCAGGCCTGCTCCTGCTGGGCCAAAGCCTCCTCC
TCTTCTTCTTCCTCACCTCCTTC**TAG**CCCCACCCAGGGCTTCCCTAACTCCTCCCCTTGCCCCTACCAATGCCCC
TTTAAGTGCTGCAGGGGTCTGGGGTTGGCAACTCCTGAGGCCTGCATGGGTGACTTCACATTTTCCTACCTCTCC
TTCTAATCTCTTCTAGAGCACCTGCTATCCCCAACTTCTAGACCTGCTCCAAACTAGTGACTAGGATAGAATTTG
ATCCCCTAACTCACTGTCTGCGGTGCTCATTGCTGCTAACAGCATTGCCTGTGCTCTCCTCTCAGGGGCAGCATG
CTAACGGGGCGACGTCCTAATCCAACTGGGAGAAGCCTCAGTGGTGGAATTCCAGGCACTGTGACTGTCAAGCTG
GCAAGGGCCAGGATTGGGGGAATGGAGCTGGGGCTTAGCTGGGAGGTGGTCTGAAGCAGACAGGGAATGGGAGAG
GAGGATGGGAAGTAGACAGTGGCTGGTATGGCTCTGAGGCTCCCTGGGGCCTGCTCAAGCTCCTCCTGCTCCTTG
CTGTTTTCTGATGATTTGGGGGCTTGGGAGTCCCTTTGTCCTCATCTGAGACTGAAATGTGGGGATCCAGGATGG
CCTTCCTTCCTCTTACCCTTCCTCCCTCAGCCTGCAACCTCTATCCTGGAACCTGTCCTCCCTTTCTCCCCAACT
ATGCATCTGTTGTCTGCTCCTCTGCAAAGGCCAGCCAGCTTGGGAGCAGCAGAGAAATAAACAGCATTTCTGATG
CCAAAAAAAAAAAAAAAAAAGGGCGGCCGCGACTCTAGAGTCGACCT

FIGURE 292

MQELHLLWWALLLGLAQACPEPCDCGEKYGFQIADCAYRDLESVPPGFPANVTTLSLSANRLP
GLPEGAFREVPLLQSLWLAHNEIRTVAAGALASLSHLKSLDLSHNLISDFAWSDLHNLSALQL
LKMDSNELTFIPRDAFRSLRALRSLQLNHNRLHTLAEGTFTPLTALSHLQINENPFDCTCGIV
WLKTWALTTAVSIPEQDNIACTSPHVLKGTPLSRLPPLPCSAPSVQLSYQPSQDGAELRPGFV
LALHCDVDGQPAPQLHWHIQIPSGIVEITSPNVGTDGRALPGTPVASSQPRFQAFANGSLLIP
DFGKLEEGTYSCLATNELGSAESSVDVALATPGEGGEDTLGRRFHGKAVEGKGCYTVDNEVQP
SGPEDNVVIIYLSRAGNPEAAVAEGVPGQLPPGLLLLGQSLLLFFFLTSF

Important features:

Signal peptide:
amino acids 1-18

Transmembrane domain:
amino acids 403-418

N-glycosylation sites:
Amino acids 51-55,120-124,309-313

Tyrosine kinase phosphorylation site:
amino acids 319-326

N-myristoylation sites:
amino acids 14-20,64-70,92-98,218-224,294-300,323-329,334-340,
350-356,394-400

Amidation site:
amino acids 355-359

Leucine Rich Repeat:
amino acids 51-74,75-98, 99-122,123-146,147-170

Leucine rich repeat C-terminal domain:
amino acids 180-230

FIGURE 293

ACTTGGAGCAAGCGGCGGCGGCGGAGACAGAGGCAGAGGCAGAAGCTGGGGCTCCGTCCTCGCCTCCCACGAGCG
ATCCCCGAGGAGAGCCGCGGCCCTCGGCGAGGCGAAGAGGCCGACGAGGAAGACCCGGGTGGCTGCGCCCCTGCC
TCGCTTCCCAGGCGCCGGCGGCTGCAGCCTTGCCCCTCTTGCTCGCCTTGAAA**ATG**GAAAAGATGCTCGCAGGCT
GCTTTCTGCTGATCCTCGGACAGATCGTCCTCCTCCCTGCCGAGGCCAGGGAGCGGTCACGTGGGAGGTCCATCT
CTAGGGGCAGACACGCTCGGACCCACCCGCAGACGGCCCTTCTGGAGAGTTCCTGTGAGAACAAGCGGGCAGACC
TGGTTTTCATCATTGACAGCTCTCGCAGTGTCAACACCCATGACTATGCAAAGGTCAAGGAGTTCATCGTGGACA
TCTTGCAATTCTTGGACATTGGTCCTGATGTCACCCGAGTGGGCCTGCTCCAATATGGCAGCACTGTCAAGAATG
AGTTCTCCCTCAAGACCTTCAAGAGGAAGTCCGAGGTGGAGCGTGCTGTCAAGAGGATGCGGCATCTGTCCACGG
GCACCATGACTGGGCTGGCCATCCAGTATGCCCTGAACATCGCATTCTCAGAAGCAGAGGGGGCCCGGCCCCTGA
GGGAGAATGTGCCACGGGTCATAATGATCGTGACAGATGGGAGACCTCAGGACTCCGTGGCCGAGGTGGCTGCTA
AGGCACGGGACACGGGCATCCTAATCTTTGCCATTGGTGTGGGCCAGGTAGACTTCAACACCTTGAAGTCCATTG
GGAGTGAGCCCCATGAGGACCATGTCTTCCTTGTGGCCAATTTCAGCCAGATTGAGACGCTGACCTCCGTGTTCC
AGAAGAAGTTGTGCACGGCCCACATGTGCAGCACCCTGGAGCATAACTGTGCCCACTTCTGCATCAACATCCCTG
GCTCATACGTCTGCAGGTGCAAACAAGGCTACATTCTCAACTCGGATCAGACGACTTGCAGAATCCAGGATCTGT
GTGCCATGGAGGACCACAACTGTGAGCAGCTCTGTGTGAATGTGCCGGGCTCCTTCGTCTGCCAGTGCTACAGTG
GCTACGCCCTGGCTGAGGATGGGAAGAGGTGTGTGGCTGTGGACTACTGTGCCTCAGAAAACCACGGATGTGAAC
ATGAGTGTGTAAATGCTGATGGCTCCTACCTTTGCCAGTGCCATGAAGGATTTGCTCTTAACCCAGATGAAAAAA
CGTGCACAAGGATCAACTACTGTGCACTGAACAAACCGGGCTGTGAGCATGAGTGCGTCAACATGGAGGAGAGCT
ACTACTGCCGCTGCCACCGTGGCTACACTCTGGACCCCAATGGCAAAACCTGCAGCCGAGTGGACCACTGTGCAC
AGCAGGACCATGGCTGTGAGCAGCTGTGTCTGAACACGGAGGATTCCTTCGTCTGCCAGTGCTCAGAAGGCTTCC
TCATCAACGAGGACCTCAAGACCTGCTCCCGGGTGGATTACTGCCTGCTGAGTGACCATGGTTGTGAATACTCCT
GTGTCAACATGGACAGATCCTTTGCCTGTCAGTGTCCTGAGGGACACGTGCTCCGCAGCGATGGGAAGACGTGTG
CAAAATTGGACTCTTGTGCTCTGGGGGACCACGGTTGTGAACATTCGTGTGTAAGCAGTGAAGATTCGTTTGTGT
GCCAGTGCTTTGAAGGTTATATACTCCGTGAAGATGGAAAAACCTGCAGAAGGAAAGATGTCTGCCAAGCTATAG
ACCATGGCTGTGAACACATTTGTGTGAACAGTGACGACTCATACACGTGCGAGTGCTTGGAGGGATTCCGGCTCG
CTGAGGATGGGAAACGCTGCCGAAGGAAGGATGTCTGCAAATCAACCCACCATGGCTGCGAACACATTTGTGTTA
ATAATGGGAATTCCTACATCTGCAAATGCTCAGAGGGATTTGTTCTAGCTGAGGACGGAAGACGGTGCAAGAAAT
GCACTGAAGGCCCAATTGACCTGGTCTTTGTGATCGATGGATCCAAGAGTCTTGGAGAAGAGAATTTTGAGGTCG
TGAAGCAGTTTGTCACTGGAATTATAGATTCCTTGACAATTTCCCCCAAAGCCGCTCGAGTGGGGCTGCTCCAGT
ATTCCACACAGGTCCACACAGAGTTCACTCTGAGAAACTTCAACTCAGCCAAAGACATGAAAAAAGCCGTGGCCC
ACATGAAATACATGGGAAAGGGCTCTATGACTGGGCTGGCCCTGAAACACATGTTTGAGAGAAGTTTTACCCAAG
GAGAAGGGGCCAGGCCCCTTTCCACAAGGGTGCCCAGAGCAGCCATTGTGTTCACCGACGGACGGGCTCAGGATG
ACGTCTCCGAGTGGGCCAGTAAAGCCAAGGCCAATGGTATCACTATGTATGCTGTTGGGGTAGGAAAAGCCATTG
AGGAGGAACTACAAGAGATTGCCTCTGAGCCCACAAACAAGCATCTCTTCTATGCCGAAGACTTCAGCACAATGG
ATGAGATAAGTGAAAAACTCAAGAAAGGCATCTGTGAAGCTCTAGAAGACTCCGATGGAAGACAGGACTCTCCAG
CAGGGGAACTGCCAAAAACGGTCCAACAGCCAACAGAATCTGAGCCAGTCACCATAAATATCCAAGACCTACTTT
CCTGTTCTAATTTTGCAGTGCAACACAGATATCTGTTTGAAGAAGACAATCTTTTACGGTCTACACAAAAGCTTT
CCCATTCAACAAAACCTTCAGGAAGCCCTTTGGAAGAAAAACACGATCAATGCAAATGTGAAAACCTTATAATGT
TCCAGAACCTTGCAAACGAAGAAGTAAGAAAATTAACACAGCGCTTAGAAGAAATGACACAGAGAATGGAAGCCC
TGGAAAATCGCCTGAGATACAGA**TGA**AGATTAGAAATCGCGACACATTTGTAGTCATTGTATCACGGATTACAAT
GAACGCAGTGCAGAGCCCCAAAGCTCAGGCTATTGTTAAATCAATAATGTTGTGAAGTAAAACAATCAGTACTGA
GAAACCTGGTTTGCCACAGAACAAAGACAAGAAGTATACACTAACTTGTATAAATTTATCTAGGAAAAAAATCCT
TCAGAATTCTAAGATGAATTTACCAGGTGAGAATGAATAAGCTATGCAAGGTATTTTGTAATATACTGTGGACAC
AACTTGCTTCTGCCTCATCCTGCCTTAGTGTGCAATCTCATTTGACTATACGATAAAGTTTGCACAGTCTTACTT
CTGTAGAACACTGGCCATAGGAAATGCTGTTTTTTTGTACTGGACTTTACCTTGATATATGTATATGGATGTATG
CATAAAATCATAGGACATATGTACTTGTGGAACAAGTTGGATTTTTTATACAATATTAAAATTCACCACTTCAG

FIGURE 294

MEKMLAGCFLLILGQIVLLPAEARERSRGRSISRGRHARTHPQTALLESSCENKRADLVFIID
SSRSVNTHDYAKVKEFIVDILQFLDIGPDVTRVGLLQYGSTVKNEFSLKTFKRKSEVERAVKR
MRHLSTGTMTGLAIQYALNIAFSEAEGARPLRENVPRVIMIVTDGRPQDSVAEVAAKARDTGI
LIFAIGVGQVDFNTLKSIGSEPHEDHVFLVANFSQIETLTSVFQKKLCTAHMCSTLEHNCAHF
CINIPGSYVCRCKQGYILNSDQTTCRIQDLCAMEDHNCEQLCVNVPGSFVCQCYSGYALAEDG
KRCVAVDYCASENHGCEHECVNADGSYLCQCHEGFALNPDEKTCTRINYCALNKPGCEHECVN
MEESYYCRCHRGYTLDPNGKTCSRVDHCAQQDHGCEQLCLNTEDSFVCQCSEGFLINEDLKTC
SRVDYCLLSDHGCEYSCVNMDRSFACQCPEGHVLRSDGKTCAKLDSCALGDHGCEHSCVSSED
SFVCQCFEGYILREDGKTCRRKDVCQAIDHGCEHICVNSDDSYTCECLEGFRLAEDGKRCRRK
DVCKSTHHGCEHICVNNGNSYICKCSEGFVLAEDGRRCKKCTEGPIDLVFVIDGSKSLGEENF
EVVKQFVTGIIDSLTISPKAARVGLLQYSTQVHTEFTLRNFNSAKDMKKAVAHMKYMGKGSMT
GLALKHMFERSFTQGEGARPLSTRVPRAAIVFTDGRAQDDVSEWASKAKANGITMYAVGVGKA
IEEELQEIASEPTNKHLFYAEDFSTMDEISEKLKKGICEALEDSDGRQDSPAGELPKTVQQPT
ESEPVTINIQDLLSCSNFAVQHRYLFEEDNLLRSTQKLSHSTKPSGSPLEEKHDQCKCENLIM
FQNLANEEVRKLTQRLEEMTQRMEALENRLRYR

Important features:

Signal sequence:
Amino acids 1-23

N-glycosylation site:
Amino acids 221-225

cAMP- and cGMP-dependent protein kinase phosphorylation sites:
Amino acids 115-119;606-610;892-896

N-myristoylation sites:
Amino acids 133-139;258-264;299-305;340-346;453-459;494-500;
639-645;690-694;
752-758;792-798

Amidation sites:
Amino acids 314-318;560-564;601-605

Aspartic acid and asparagine hydroxylation sites:
Amino acids 253-265;294-306;335-347;376-388;417-429;
458-470;540-552;581-593

FIGURE 295

GGCCGGAGCAGCACGGCCGCAGGACCTGGAGCTCCGGCTGCGTCTTCCCGCAGCGCTACCCGC

C**ATG**CGCCTGCCGCGCCGGGCCGCGCTGGGGCTCCTGCCGCTTCTGCTGCTGCTGCCGCCCGC

GCCGGAGGCCGCCAAGAAGCCGACGCCCTGCCACCGGTGCCGGGGGCTGGTGGACAAGTTTAA

CCAGGGGATGGTGGACACCGCAAAGAAGAACTTTGGCGGCGGGAACACGGCTTGGGAGGAAAA

GACGCTGTCCAAGTACGAGTCCAGCGAGATTCGCCTGCTGGAGATCCTGGAGGGGCTGTGCGA

GAGCAGCGACTTCGAATGCAATCAGATGCTAGAGGCGCAGGAGGAGCACCTGGAGGCCTGGTG

GCTGCAGCTGAAGAGCGAATATCCTGACTTATTCGAGTGGTTTTGTGTGAAGACACTGAAAGT

GTGCTGCTCTCCAGGAACCTACGGTCCCGACTGTCTCGCATGCCAGGGCGGATCCCAGAGGCC

CTGCAGCGGGAATGGCCACTGCAGCGGAGATGGGAGCAGACAGGGCGACGGGTCCTGCCGGTG

CCACATGGGGTACCAGGGCCCGCTGTGCACTGACTGCATGGACGGCTACTTCAGCTCGCTCCG

GAACGAGACCCACAGCATCTGCACAGCCTGTGACGAGTCCTGCAAGACGTGCTCGGGCCTGAC

CAACAGAGACTGCGGCGAGTGTGAAGTGGGCTGGGTGCTGGACGAGGGCGCCTGTGTGGATGT

GGACGAGTGTGCGGCCGAGCCGCCTCCCTGCAGCGCTGCGCAGTTCTGTAAGAACGCCAACGG

CTCCTACACGTGCGAAGAGTGTGACTCCAGCTGTGTGGGCTGCACAGGGGAAGGCCCAGGAAA

CTGTAAAGAGTGTATCTCTGGCTACGCGAGGGAGCACGGACAGTGTGCAGATGTGGACGAGTG

CTCACTAGCAGAAAAAACCTGTGTGAGGAAAAACGAAAACTGCTACAATACTCCAGGGAGCTA

CGTCTGTGTGTGTCCTGACGGCTTCGAAGAAACGGAAGATGCCTGTGTGCCGCCGGCAGAGGC

TGAAGCCACAGAAGGAGAAAGCCCGACACAGCTGCCCTCCCGCGAAGACCTG**TAA**TGTGCCGG

ACTTACCCTTTAAATTATTCAGAAGGATGTCCCGTGGAAAATGTGGCCCTGAGGATGCCGTCT

CCTGCAGTGGACAGCGGCGGGGAGAGGCTGCCTGCTCTCTAACGGTTGATTCTCATTTGTCCC

TTAAACAGCTGCATTTCTTGGTTGTTCTTAAACAGACTTGTATATTTTGATACAGTTCTTTGT

AATAAAATTGACCATTGTAGGTAATCAGGAGGAAAAAAAAA

FIGURE 296

MRLPRRAALGLLPLLLLLPPAPEAAKKPTPCHRCRGLVDKFNQGMVDTAKKNFGGGNTAWEEK
TLSKYESSEIRLLEILEGLCESSDFECNQMLEAQEEHLEAWWLQLKSEYPDLFEWFCVKTLKV
CCSPGTYGPDCLACQGGSQRPCSGNGHCSGDGSRQGDGSCRCHMGYQGPLCTDCMDGYFSSLR
NETHSICTACDESCKTCSGLTNRDCGECEVGWVLDEGACVDVDECAAEPPPCSAAQFCKNANG
SYTCEECDSSCVGCTGEGPGNCKECISGYAREHGQCADVDECSLAEKTCVRKNENCYNTPGSY
VCVCPDGFEETEDACVPPAEAEATEGESPTQLPSREDL

Important features:

Signal peptide:
Amino acids 1-24

N-glycosylation sites:
Amino acids 190-194;251-255

Glycosaminoglycan attachment sites:
Amino acids 149-153;155-159

cAMP- and cGMP-dependent protein kinase phosphorylation site:
Amino acids 26-30

Tyrosine kinase phosphorylation site:
Amino acids 303-310

N-myristoylation sites:
Amino acids 44-50;54-60;55-61;81-87;150-156;158-164;164-170;
252-258;313-319

Aspartic acid and asparagine hydroxylation site:
Amino acids 308-320

EGF-like domain cysteine pattern signature:
Amino acids 166-178

Leucine zipper pattern:
Amino acids 94-116

FIGURE 297

GACATCGGAGGTGGGCTAGCACTGAAACTGCTTTTCAAGACGAGGAAGAGGAGGAGAAAGAGAAAGAAGAGGAAG
ATGTTGGGCAACATTTATTTAACATGCTCCACAGCCCGGACCCTGGCATCATGCTGCTATTCCTGCAAATACTGA
AGAAGCATGGGATTTAAATATTTTACTTCTAAATAAATGAATTACTCAATCTCCTATGACCATCTATACATACTC
CACCTTCAAAAAGTACATCAATATTATATCATTAAGGAAATAGTAACCTTCTCTTCTCCAATATGCATGACATTT
TTGGACAATGCAATTGTGGCACTGGCACTTATTTCAGTGAAGAAAAACTTTGTGGTTCTATGGCATTCATCATTT
GACAAATGCAAGCATCTTCCTTATCAATCAGCTCCTATTGAACTTACTAGCACTGACTGTGGAATCCTTAAGGGC
CCATTACATTTCTGAAGAAGAAAGCTAAG**ATG**AAGGACATGCCACTCCGAATTCATGTGCTACTTGGCCTAGCTA
TCACTACACTAGTACAAGCTGTAGATAAAAAAGTGGATTGTCCACGGTTATGTACGTGTGAAATCAGGCCTTGGT
TTACACCCAGATCCATTTATATGGAAGCATCTACAGTGGATTGTAATGATTTAGGTCTTTTAACTTTCCCAGCCA
GATTGCCAGCTAACACACAGATTCTTCTCCTACAGACTAACAATATTGCAAAAATTGAATACTCCACAGACTTTC
CAGTAAACCTTACTGGCCTGGATTTATCTCAAAACAATTTATCTTCAGTCACCAATATTAATGTAAAAAAGATGC
CTCAGCTCCTTTCTGTGTACCTAGAGGAAAACAAACTTACTGAACTGCCTGAAAAATGTCTGTCCGAACTGAGCA
ACTTACAAGAACTCTATATTAATCACAACTTGCTTTCTACAATTTCACCTGGAGCCTTTATTGGCCTACATAATC
TTCTTCGACTTCATCTCAATTCAAATAGATTGCAGATGATCAACAGTAAGTGGTTTGATGCTCTTCCAAATCTAG
AGATTCTGATGATTGGGGAAAATCCAATTATCAGAATCAAAGACATGAACTTTAAGCCTCTTATCAATCTTCGCA
GCCTGGTTATAGCTGGTATAAACCTCACAGAAATACCAGATAACGCCTTGGTTGGACTGGAAAACTTAGAAAGCA
TCTCTTTTTTACGATAACAGGCTTATTAAAGTACCCCATGTTGCTCTTCAAAAAGTTGTAAATCTCAAATTTTTGG
ATCTAAATAAAAATCCTATTAATAGAATACGAAGGGGTGATTTTAGCAATATGCTACACTTAAAAGAGTTGGGGA
TAAATAATATGCCTGAGCTGATTTCCATCGATAGTCTTGCTGTGGATAACCTGCCAGATTTAAGAAAAATAGAAG
CTACTAACAACCCTAGATTGTCTTACATTCACCCCAATGCATTTTTCAGACTCCCCAAGCTGGAATCACTCATGC
TGAACAGCAATGCTCTCAGTGCCCTGTACCATGGTACCATTGAGTCTCTGCCAAACCTCAAGGAAATCAGCATAC
ACAGTAACCCCATCAGGTGTGACTGTGTCATCCGTTGGATGAACATGAACAAAACCAACATTCGATTCATGGAGC
CAGATTCACTGTTTTGCGTGGACCCACCTGAATTCCAAGGTCAGAATGTTCGGCAAGTGCATTTCAGGGACATGA
TGGAAATTTGTCTCCCTCTTATAGCTCCTGAGAGCTTTCCTTCTAATCTAAATGTAGAAGCTGGGAGCTATGTTT
CCTTTCACTGTAGAGCTACTGCAGAACCACAGCCTGAAATCTACTGGATAACACCTTCTGGTCAAAAACTCTTGC
CTAATACCCTGACAGACAAGTTCTATGTCCATTCTGAGGGAACACTAGATATAAATGGCGTAACTCCCAAAGAAG
GGGGTTTATATACTTGTATAGCAACTAACCTAGTTGGCGCTGACTTGAAGTCTGTTATGATCAAAGTGGATGGAT
CTTTTCCACAAGATAACAATGGCTCTTTGAATATTAAAATAAGAGATATTCAGGCCAATTCAGTTTTGGTGTCCT
GGAAAGCAAGTTCTAAAATTCTCAAATCTAGTGTTAAATGGACAGCCTTTGTCAAGACTGAAAATTCTCATGCTG
CGCAAAGTGCTCGAATACCATCTGATGTCAAGGTATATAATCTTACTCATCTGAATCCATCAACTGAGTATAAAA
TTTGTATTGATATTCCCACCATCTATCAGAAAAACAGAAAAAAATGTGTAAATGTCACCACCAAAGGTTTGCACC
CTGATCAAAAAGAGTATGAAAAGAATAATACCACAACACTTATGGCCTGTCTTGGAGGCCTTCTGGGGATTATTG
GTGTGATATGTCTTATCAGCTGCCTCTCTCCAGAAATGAACTGTGATGGTGGACACAGCTATGTGAGGAATTACT
TACAGAAACCAACCTTTGCATTAGGTGAGCTTTATCCTCCTCTGATAAATCTCTGGGAAGCAGGAAAAGAAAAAA
GTACATCACTGAAAGTAAAAGCAACTGTTATAGGTTTACCAACAAATATGTCC**TAA**AAACCACCAAGGAAACCTA
CTCCAAAAATGAAC

FIGURE 298

MKDMPLRIHVLLGLAITTLVQAVDKKVDCPRLCTCEIRPWFTPRSIYMEASTVDCNDLGLLTF
PARLPANTQILLLQTNNIAKIEYSTDFPVNLTGLDLSQNNLSSVTNINVKKMPQLLSVYLEEN
KLTELPEKCLSELSNLQELYINHNLLSTISPGAFIGLHNLLRLHLNSNRLQMINSKWFDALPN
LEILMIGENPIIRIKDMNFKPLINLRSLVIAGINLTEIPDNALVGLENLESISFYDNRLIKVP
HVALQKVVNLKFLDLNKNPINRIRRGDFSNMLHLKELGINNMPELISIDSLAVDNLPDLRKIE
ATNNPRLSYIHPNAFFRLPKLESLMLNSNALSALYHGTIESLPNLKEISIHSNPIRCDCVIRW
MNMNKTNIRFMEPDSLFCVDPPEFQGQNVRQVHFRDMMEICLPLIAPESFPSNLNVEAGSYVS
FHCRATAEPQPEIYWITPSGQKLLPNTLTDKFYVHSEGTLDINGVTPKEGGLYTCIATNLVGA
DLKSVMIKVDGSFPQDNNGSLNIKIRDIQANSVLVSWKASSKILKSSVKWTAFVKTENSHAAQ
SARIPSDVKVYNLTHLNPSTEYKICIDIPTIYQKNRKKCVNVTTKGLHPDQKEYEKNNTTTLM
ACLGGLLGIIGVICLISCLSPEMNCDGGHSYVRNYLQKPTFALGELYPPLINLWEAGKEKSTS
LKVKATVIGLPTNMS

Important features:

Signal sequence:
amino acids 1-22

Transmembrane domain:
amino acids 633-650

N-glycosylation site.
amino acids 93-97, 103-107, 223-227, 382-386, 522-526, 579-583, 608-612, 624-628, 625-629

Casein kinase II phosphorylation site.
amino acids 51-55, 95-99, 242-246, 468-472, 487-491

Tyrosine kinase phosphorylation site.
amino acids 570-579

N-myristoylation site.
amino acids 13-19, 96-102, 158-164, 221-227, 352-358, 437-443, 491-497, 492-498, 634-640, 702-708

Cell attachment sequence.
amino acids 277-280

FIGURE 299

GCTGTGGGAACCTCTCCACGCGCACGAACTCAGCCAACGATTTCTGATAGATTTTTGGGAGTT
TGACCAGAGATGCAAGGGGTGAAGGAGCGCTTCCTACCGTTAGGGAACTCTGGGGACAGAGCG
CCCCGGCCGCCTGATGGCCGAGGCAGGGTGCGACCCAGGACCCAGGACGGCGTCGGGAACCAT
ACC**ATG**GCCCGGATCCCCAAGACCCTAAAGTTCGTCGTCGTCATCGTCGCGGTCCTGCTGCCA
GTCCTAGCTTACTCTGCCACCACTGCCCGGCAGGAGGAAGTTCCCCAGCAGACAGTGGCCCCA
CAGCAACAGAGGCACAGCTTCAAGGGGGAGGAGTGTCCAGCAGGATCTCATAGATCAGAACAT
ACTGGAGCCTGTAACCCGTGCACAGAGGGTGTGGATTACACCAACGCTTCCAACAATGAACCT
TCTTGCTTCCCATGTACAGTTTGTAAATCAGATCAAAAACATAAAAGTTCCTGCACCATGACC
AGAGACACAGTGTGTCAGTGTAAAGAAGGCACCTTCCGGAATGAAAACTCCCCAGAGATGTGC
CGGAAGTGTAGCAGGTGCCCTAGTGGGGAAGTCCAAGTCAGTAATTGTACGTCCTGGGATGAT
ATCCAGTGTGTTGAAGAATTTGGTGCCAATGCCACTGTGGAAACCCCAGCTGCTGAAGAGACA
ATGAACACCAGCCCGGGGACTCCTGCCCCAGCTGCTGAAGAGACAATGAACACCAGCCCAGGG
ACTCCTGCCCCAGCTGCTGAAGAGACAATGACCACCAGCCCGGGGACTCCTGCCCCAGCTGCT
GAAGAGACAATGACCACCAGCCCGGGGACTCCTGCCCCAGCTGCTGAAGAGACAATGACCACC
AGCCCGGGGACTCCTGCCTCTTCTCATTACCTCTCATGCACCATCGTAGGGATCATAGTTCTA
ATTGTGCTTCTGATTGTGTTTGTT**TGA**AAGACTTCACTGTGGAAGAAATTCCTTCCTTACCTG
AAAGGTTCAGGTAGGCGCTGGCTGAGGGCGGGGGGCGCTGGACACTCTCTGCCCTGCCTCCCT
CTGCTGTGTTCCCACAGACAGAAACGCCTGC

FIGURE 300

MARIPKTLKFVVVIVAVLLPVLAYSATTARQEEVPQQTVAPQQQRHSFKGEECPAGSHRSEHT
GACNPCTEGVDYTNASNNEPSCFPCTVCKSDQKHKSSCTMTRDTVCQCKEGTFRNENSPEMCR
KCSRCPSGEVQVSNCTSWDDIQCVEEFGANATVETPAAEETMNTSPGTPAPAAEETMNTSPGT
PAPAAEETMTTSPGTPAPAAEETMTTSPGTPAPAAEETMTTSPGTPASSHYLSCTIVGIIVLI
VLLIVFV

Important features:

Signal peptide:

Amino acids 1-29

Transmembrane domain:

Amino acids 240-259

N-glycosylation site:

Amino acids 77-81;140-144;156-160

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 126-130

N-myristoylation sites:

Amino acids 56-62;72-78;114-120;154-160;233-239

FIGURE 301

CACAAGCATCTTAATTTGAATCCACAAAGTTTCATGTAATGAAAAGAAATACATAATTTTAAT
TCAACCCGAGTGTTTTCCAAGAAGATTGTATTTGCTTAAATTGCTACAGTAATTCAAGAGACA
GCCCTGTCTGGACACAGAGTTACTGTGGATTTTTAAGAGACTCAGTTAAAGAATTTAGGAATT
TCTGATTCATTTAAAGGATTTACAAATTCATCAACCCCTGAAAACTAAAGCAAATTGAACAGG
AAAAAAAAAAAGAAG**ATG**GGTTTTTTAAGTCCAATATATGTTATTTTCTTCTTTTTTGGAGTC
AAAGTACATTGCCAATATGAAACTTATCAGTGGGATGAAGACTATGACCAAGAGCCAGATGAT
GATTACCAAACAGGATTCCCATTTCGTCAAAATGTAGACTACGGAGTTCCTTTTCATCAGTAT
ACTTTAGGCTGTGTCAGTGAATGCTTCTGTCCAACTAACTTTCCATCATCAATGTACTGTGAT
AATCGCAAACTCAAGACTATCCCAAATATTCCGATGCACATTCAGCAACTCTACCTTCAGTTC
AATGAAATTGAGGCTGTGACTGCAAATTCATTCATCAATGCAACTCATCTTAAAGAAATTAAC
CTCAGCCACAACAAAATTAAATCTCAAAAGATTGATTATGGTGTGTTTGCTAAGCTTCCAAAT
CTACTACAACTTCATCTAGAGCATAATAATTTAGAAGAATTTCCATTTCCTCTTCCTAAATCT
CTGGAAAGACTCCTTCTTGGTTACAATGAAATCTCCAAACTGCAGACAAATGCTATGGATGGG
CTAGTAAACTTGACCATGCTTGATCTCTGTTATAATTATCTTCATGATTCTCTGCTAAAAGAC
AAAATCTTTGCCAAAATGGAAAAACTAATGCAGCTCAACCTCTGCAGTAACAGATTAGAATCA
ATGCCTCCTGGTTTGCCTTCTTCACTTATGTATCTGTCTTTAGAAAATAATTCAATTTCTTCT
ATACCCGAAAAATACTTCGACAAACTTCCAAAACTTCATACTCTAAGAATGTCACACAACAAA
CTACAAGACATCCCATATAATATTTTTAATCTTCCCAACATTGTAGAACTCAGTGTTGGACAC
AACAAATTGAAGCAAGCATTCTATATTCCAAGAAATTTGGAACACCTATACCTACAAAATAAT
GAAATAGAAAAGATGAATCTTACAGTGATGTGTCCTTCTATTGACCCACTACATTACCACCAT
TTAACATACATTCGTGTGGACCAAAATAAACTAAAAGAACCAATAAGCTCATACATCTTCTTC
TGCTTCCCTCATATACACACTATTTATTATGGTGAACAACGAAGCACTAATGGTCAAACAATA
CAACTAAAGACACAAGTTTTCAGGAGATTTCCAGATGATGATGATGAAAGTGAAGATCACGAT
GATCCTGACAATGCTCATGAGAGCCCAGAACAAGAAGGAGCAGAAGGGCACTTTGACCTTCAT
TATTATGAAAATCAAGAA**TAG**CAAGAAACTATATAGGTATACACTTACGACTTCACAAAACCTA
TACTTAATATAGTAAATCTAAGTAAACATGTATTACTCAAAGTAATATATTTAGAATTATGTA
TTAGTATAAGATCAGAATTGAATTTAAGTTGTTGGTGACATCTGCATCATTTCATAGGATTAG
AACTTACTCAAAATAATGTAAATCTTTAAAAATATAAATTAGAATGACAAGTGGGAATCATAA
ATTAAACGTTAATGGTTTCTTATGCTCTTTTTAAATATAGAAATATCATGTTAAAGAAAAAAA
AAAAAAA

FIGURE 302

MGFLSPIYVIFFFFGVKVHCQYETYQWDEDYDQEPDDDYQTGFPFRQNVDYGVPFHQYTLGCV
SECFCPTNFPSSMYCDNRKLKTIPNIPMHIQQLYLQFNEIEAVTANSFINATHLKEINLSHNK
IKSQKIDYGVFAKLPNLLQLHLEHNNLEEFPFPLPKSLERLLLGYNEISKLQTNAMDGLVNLT
MLDLCYNYLHDSLLKDKIFAKMEKLMQLNLCSNRLESMPPGLPSSLMYLSLENNSISSIPEKY
FDKLPKLHTLRMSHNKLQDIPYNIFNLPNIVELSVGHNKLKQAFYIPRNLEHLYLQNNEIEKM
NLTVMCPSIDPLHYHHLTYIRVDQNKLKEPISSYIFFCFPHIHTIYYGEQRSTNGQTIQLKTQ
VFRRFPDDDDESEDHDDPDNAHESPEQEGAEGHFDLHYYENQE

Important feastures:

N-glycosylation sites:

Amino acids 113-117;121-125; 187-191;242-246;316-320

Tyrosine kinase phosphorylation sites:

Amino acids 268-275;300-307

N-myristoylation site:

Amino acids 230-236

Leucine zipper patterns:

Amino acids 146-168;217-239

FIGURE 303

GCCCGGGACTGGCGCAAGGTGCCCAAGCAAGGAAAGAAATAATGAAGAGACACATGTGTTAGC
TGCAGCCTTTTGAAACACGCAAGAAGGAAATCAATAGTGTGGACAGGGCTGGAACCTTTACCA
CGCTTGTTGGAGTAGATGAGGAATGGGCTCGTGATTATGCTGACATTCCAGC**ATG**AATCTGGT
AGACCTGTGGTTAACCCGTTCCCTCTCCATGTGTCTCCTCCTACAAAGTTTTGTTCTTATGAT
ACTGTGCTTTCATTCTGCCAGTATGTGTCCCAAGGGCTGTCTTTGTTCTTCCTCTGGGGGTTT
AAATGTCACCTGTAGCAATGCAAATCTCAAGGAAATACCTAGAGATCTTCCTCCTGAAACAGT
CTTACTGTATCTGGACTCCAATCAGATCACATCTATTCCCAATGAAATTTTTAAGGACCTCCA
TCAACTGAGAGTTCTCAACCTGTCCAAAAATGGCATTGAGTTTATCGATGAGCATGCCTTCAA
AGGAGTAGCTGAAACCTTGCAGACTCTGGACTTGTCCGACAATCGGATTCAAAGTGTGCACAA
AAATGCCTTCAATAACCTGAAGGCCAGGGCCAGAATTGCCAACAACCCCTGGCACTGCGACTG
TACTCTACAGCAAGTTCTGAGGAGCATGGCGTCCAATCATGAGACAGCCCACAACGTGATCTG
TAAAACGTCCGTGTTGGATGAACATGCTGGCAGACCATTCCTCAATGCTGCCAACGACGCTGA
CCTTTGTAACCTCCCTAAAAAAACTACCGATTATGCCATGCTGGTCACCATGTTTGGCTGGTT
CACTATGGTGATCTCATATGTGGTATATTATGTGAGGCAAAATCAGGAGGATGCCCGGAGACA
CCTCGAATACTTGAAATCCCTGCCAAGCAGGCAGAAGAAAGCAGATGAACCTGATGATATTAG
CACTGTGGTA**TAG**TGTCCAAACTGACTGTCATTGAGAAAGAAAGAAAGTAGTTTGCGATTGCA
GTAGAAATAAGTGGTTTACTTCTCCCATCCATTGTAAACATTTGAAACTTTGTATTTCAGTTT
TTTTTGAATTATGCCACTGCTGAACTTTTAACAAACACTACAACATAAATAATTTGAGTTTAG
GTGATCCACCCCTTAATTGTACCCCCGATGGTATATTTCTGAGTAAGCTACTATCTGAACATT
AGTTAGATCCATCTCACTATTTAATAATGAAATTTATTTTTTTAATTTAAAAGCAAATAAAAG
CTTAACTTTGAACCATGGGAAAAAAAAAAAAAAAAAAAAAAACA

FIGURE 304

MNLVDLWLTRSLSMCLLLQSFVLMILCFHSASMCPKGCLCSSSGGLNVTCSNANLKEIPRDLP
PETVLLYLDSNQITSIPNEIFKDLHQLRVLNLSKNGIEFIDEHAFKGVAETLQTLDLSDNRIQ
SVHKNAFNNLKARARIANNPWHCDCTLQQVLRSMASNHETAHNVICKTSVLDEHAGRPFLNAA
NDADLCNLPKKTTDYAMLVTMFGWFTMVISYVVYYVRQNQEDARRHLEYLKSLPSRQKKADEP
DDISTVV

Important features:

Signal sequence:

Amino acids 1-33

Transmembrane domain:

Amino acids 204-219

N-glycosylation sites:

Amino acids 47-51;94-98

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 199-203

Casein kinase II phosphorylation site.

amino acids 162-166, 175-179

N-myristoylation sites:

Amino acids 37-43;45-51;110-116

FIGURE 305

CGCCACCACTGCGGCCACCGCCA**ATG**AAACGCCTCCCGCTCCTAGTGGTTTTTTCCACTTTGTTGAATTGTTCCT
ATACTCAAAATTGCACCAAGACACCTTGTCTCCCAAATGCAAAATGTGAAATACGCAATGGAATTGAAGCCTGCT
ATTGCAACATGGGATTTTCAGGAAATGGTGTCACAATTTGTGAAGATGATAATGAATGTGGAAATTTAACTCAGT
CCTGTGGCGAAAATGCTAATTGCACTAACACAGAAGGAAGTTATTATTGTATGTGTGTACCTGGCTTCAGATCCA
GCAGTAACCAAGACAGGTTTATCACTAATGATGGAACCGTCTGTATAGAAAATGTGAATGCAAACTGCCATTTAG
ATAATGTCTGTATAGCTGCAAATATTAATAAAACTTTAACAAAAATCAGATCCATAAAAGAACCTGTGGCTTTGC
TACAAGAAGTCTATAGAAATTCTGTGACAGATCTTTCACCAACAGATATAATTACATATATAGAAATATTAGCTG
AATCATCTTCATTACTAGGTTACAAGAACAACACTATCTCAGCCAAGGACACCCTTTCTAACTCAACTCTTACTG
AATTTGTAAAAACCGTGAATAATTTTGTTCAAAGGGATACATTTGTAGTTTGGGACAAGTTATCTGTGAATCATA
GGAGAACACATCTTACAAAACTCATGCACACTGTTGAACAAGCTACTTTAAGGATATCCCAGAGCTTCCAAAAGA
CCACAGAGTTTGATACAAATTCAACGGATATAGCTCTCAAAGTTTTCTTTTTTGATTCATATAACATGAAACATA
TTCATCCTCATATGAATATGGATGGAGACTACATAAATATATTTCCAAAGAGAAAAGCTGCATATGATTCAAATG
GCAATGTTGCAGTTGCATTTTTATATTATAAGAGTATTGGTCCTTTGCTTTCATCATCTGACAACTTCTTATTGA
AACCTCAAAATTATGATAATTCTGAAGAGGAGGAAAGAGTCATATCTTCAGTAATTTCAGTCTCAATGAGCTCAA
ACCCACCCACATTATATGAACTTGAAAAAATAACATTTACATTAAGTCATCGAAAGGTCACAGATAGGTATAGGA
GTCTATGTGCATTTTGGAATTACTCACCTGATACCATGAATGGCAGCTGGTCTTCAGAGGGCTGTGAGCTGACAT
ACTCAAATGAGACCCACACCTCATGCCGCTGTAATCACCTGACACATTTTGCAATTTTGATGTCCTCTGGTCCTT
CCATTGGTATTAAAGATTATAATATTCTTACAAGGATCACTCAACTAGGAATAATTATTTCACTGATTTGTCTTG
CCATATGCATTTTTACCTTCTGGTTCTTCAGTGAAATTCAAAGCACCAGGACAACAATTCACAAAAATCTTTGCT
GTAGCCTATTTCTTGCTGAACTTGTTTTTCTTGTTGGGATCAATACAAATACTAATAAGCTCTTCTGTTCAATCA
TTGCCGGACTGCTACACTACTTCTTTTTAGCTGCTTTTGCATGGATGTGCATTGAAGGCATACATCTCTATCTCA
TTGTTGTGGGTGTCATCTACAACAAGGGATTTTTGCACAAGAATTTTTATATCTTTGGCTATCTAAGCCCAGCCG
TGGTAGTTGGATTTTCGGCAGCACTAGGATACAGATATTATGGCACAACCAAAGTATGTTGGCTTAGCACCGAAA
ACAACTTTATTTGGAGTTTTATAGGACCAGCATGCCTAATCATTCTTGTTAATCTCTTGGCTTTTGGAGTCATCA
TATACAAAGTTTTTCGTCACACTGCAGGGTTGAAACCAGAAGTTAGTTGCTTTGAGAACATAAGGTCTTGTGCAA
GAGGAGCCCTCGCTCTTCTGTTCCTTCTCGGCACCACCTGGATCTTTGGGGTTCTCCATGTTGTGCACGCATCAG
TGGTTACAGCTTACCTCTTCACAGTCAGCAATGCTTTCCAGGGGATGTTCATTTTTTTATTCCTGTGTGTTTTAT
CTAGAAAGATTCAAGAAGAATATTACAGATTGTTCAAAAATGTCCCCTGTTGTTTTGGATGTTTAAGG**TAA**ACAT
AGAGAATGGTGGATAATTACAACTGCACAAAAATAAAAATTCCAAGCTGTGGATGACCAATGTATAAAAATGACT
CATCAAATTATCCAATTATTAACTACTAGACAAAAAGTATTTTAAATCAGTTTTTCTGTTTATGCTATAGGAACT
GTAGATAATAAGGTAAAATTATGTATCATATAGATATACTATGTTTTTCTATGTGAAATAGTTCTGTCAAAAATA
GTATTGCAGATATTTGGAAAGTAATTGGTTTCTCAGGAGTGATATCACTGCACCCAAGGAAAGATTTTCTTTCTA
ACACGAGAAGTATATGAATGTCCTGAAGGAAACCACTGGCTTGATATTTCTGTGACTCGTGTTGCCTTTGAAACT
AGTCCCCTACCACCTCGGTAATGAGCTCCATTACAGAAAGTGGAACATAAGAGAATGAAGGGGCAGAATATCAAA
CAGTGAAAAGGGAATGATAAGATGTATTTTGAATGAACTGTTTTTTCTGTAGACTAGCTGAGAAATTGTTGACAT
AAAATAAAGAATTGAAGAAACACATTTTACCATTTTGTGAATTGTTCTGAACTTAAATGTCCACTAAAACAACTT
AGACTTCTGTTTGCTAAATCTGTTTCTTTTTCTAATATTCTAAAAAAAAAAAAAAAGGTTTACCTCCACAAATTGA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 306

MKRLPLLVVFSTLLNCSYTQNCTKTPCLPNAKCEIRNGIEACYCNMGFSGNGVTICEDDNECGNLTQSCGENANC
TNTEGSYYCMCVPGFRSSSNQDRFITNDGTVCIENVNANCHLDNVCIAANINKTLTKIRSIKEPVALLQEVYRNS
VTDLSPTDIITYIEILAESSSLLGYKNNTISAKDTLSNSTLTEFVKTVNNFVQRDTFVVWDKLSVNHRRTHLTKL
MHTVEQATLRISQSFQKTTEFDTNSTDIALKVFFFDSYNMKHIHPHMNMDGDYINIFPKRKAAYDSNGNVAVAFL
YYKSIGPLLSSSDNFLLKPQNYDNSEEEERVISSVISVSMSSNPPTLYELEKITFTLSHRKVTDRYRSLCAFWNY
SPDTMNGSWSSEGCELTYSNETHTSCRCNHLTHFAILMSSGPSIGIKDYNILTRITQLGIIISLICLAICIFTFW
FFSEIQSTRTTIHKNLCCSLFLAELVFLVGINTNTNKLFCSIIAGLLHYFFLAAFAWMCIEGIHLYLIVVGVIYN
KGFLHKNFYIFGYLSPAVVVGFSAALGYRYYGTTKVCWLSTENNFIWSFIGPACLIILVNLLAFGVIIYKVFRHT
AGLKPEVSCFENIRSCARGALALLFLLGTTWIFGVLHVVHASVVTAYLFTVSNAFQGMFIFLFLCVLSRKIQEEY
YRLFKNVPCCFGCLR

Important features:

Signal peptide:

Amino acids 1-19

Transmembrane domain:

Amino acids 431-450;494-515;573-594;619-636;646-664

N-glycosylation sites:

Amino acids 15-19;21-25;64-68;74-78;127-131;177-181;
188-192;249-253;381-385;395-399

Glycosaminoglycan attachment site:

Amino acids 49-53

cAMP- and cGMP-dependent protein kinase phosphorylation site:

Amino acids 360-364

Tyrosine kinase phosphorylation sites:

Amino acids 36-44;670-677

N-myristoylation sites:

Amino acids 38-44;50-56;52-58;80-86;382-388;388-394;
434-440;480-486;521-527

Aspartic acid and asparagine hydroxylation site:

Amino acids 75-87

FIGURE 307

CCAGGCCGGGAGGCGACGCGCCCAGCCGTCTAAACGGGAACAGCCCTGGCTGAGGGAGCTGCAGCGCAGCAGAGT
ATCTGACGGCGCCAGGTTGCGTAGGTGCGGCACGAGGAGTTTTCCCGGCAGCGAGGAGGTCCTGAGCAGC**ATG**GC
CCGGAGGAGCGCCTTCCCTGCCGCCGCGCTCTGGCTCTGGAGCATCCTCCTGTGCCTGCTGGCACTGCGGGCGGA
GGCCGGGCCGCCGCAGGAGGAGAGCCTGTACCTATGGATCGATGCTCACCAGGCAAGAGTACTCATAGGATTTGA
AGAAGATATCCTGATTGTTTCAGAGGGGAAAATGGCACCTTTTACACATGATTTCAGAAAAGCGCAACAGAGAAT
GCCAGCTATTCCTGTCAATATCCATTCCATGAATTTTACCTGGCAAGCTGCAGGGCAGGCAGAATACTTCTATGA
ATTCCTGTCCTTGCGCTCCCTGGATAAAGGCATCATGGCAGATCCAACCGTCAATGTCCCTCTGCTGGGAACAGT
GCCTCACAAGGCATCAGTTGTTCAAGTTGGTTTCCCATGTCTTGGAAAACAGGATGGGGTGGCAGCATTTGAAGT
GGATGTGATTGTTATGAATTCTGAAGGCAACACCATTCTCCAAACACCTCAAAATGCTATCTTCTTTAAAACATG
TCAACAAGCTGAGTGCCCAGGCGGGTGCCGAAATGGAGGCTTTTGTAATGAAAGACGCATCTGCGAGTGTCCTGA
TGGGTTCCACGGACCTCACTGTGAGAAAGCCCTTTGTACCCCACGATGTATGAATGGTGGACTTTGTGTGACTCC
TGGTTTCTGCATCTGCCCACCTGGATTCTATGGAGTGAACTGTGACAAAGCAAACTGCTCAACCACCTGCTTTAA
TGGAGGGACCTGTTTCTACCCTGGAAAATGTATTTGCCCTCCAGGACTAGAGGGAGAGCAGTGTGAAATCAGCAA
ATGCCCACAACCCTGTCGAAATGGAGGTAAATGCATTGGTAAAAGCAAATGTAAGTGTTCCAAAGGTTACCAGGG
AGACCTCTGTTCAAAGCCTGTCTGCGAGCCTGGCTGTGGTGCACATGGAACCTGCCATGAACCCAACAAATGCCA
ATGTCAAGAAGGTTGGCATGGAAGACACTGCAATAAAAGGTACGAAGCCAGCCTCATACATGCCCTGAGGCCAGC
AGGCGCCCAGCTCAGGCAGCACACGCCTTCACTTAAAAAGGCCGAGGAGCGGCGGGATCCACCTGAATCCAATTA
CATCTGG**TGA**ACTCCGACATCTGAAACGTTTTAAGTTACACCAAGTTCATAGCCTTTGTTAACCTTTCATGTGTT
GAATGTTCAAATAATGTTCATTACACTTAAGAATACTGGCCTGAATTTTATTAGCTTCATTATAAATCACTGAGC
TGATATTTACTCTTCCTTTTAAGTTTTCTAAGTACGTCTGTAGCATGATGGTATAGATTTTCTTGTTTCAGTGCT
TTGGGACAGATTTTATATTATGTCAATTGATCAGGTTAAAATTTTCAGTGTGTAGTTGGCAGATATTTTCAAAAT
TACAATGCATTTATGGTGTCTGGGGGCAGGGGAACATCAGAAAGGTTAAATTGGGCAAAAATGCGTAAGTCACAA
GAATTTGGATGGTGCAGTTAATGTTGAAGTTACAGCATTTCAGATTTTATTGTCAGATATTTAGATGTTTGTTAC
ATTTTTAAAAATTGCTCTTAATTTTTAAACTCTCAATACAATATATTTTGACCTTACCATTATTCCAGAGATTCA
GTATTAAAAAAAAAAAAATTACACTGTGGTAGTGGCATTTAAACAATATAATATATTCTAAACACAATGAAATAG
GGAATATAATGTATGAACTTTTTGCATTGGCTTGAAGCAATATAATATATTGTAAACAAAACACAGCTCTTACCT
AATAAACATTTTATACTGTTTGTATGTATAAAATAAAGGTGCTGCTTTAGTTTTTTGGAAAAAAAAAAAAAAAAA
AAAAAAAA

FIGURE 308

MARRSAFPAAALWLWSILLCLLALRAEAGPPQEESLYLWIDAHQARVLIGFEEDILIVSEGKM
APFTHDFRKAQQRMPAIPVNIHSMNFTWQAAGQAEYFYEFLSLRSLDKGIMADPTVNVPLLGT
VPHKASVVQVGFPCLGKQDGVAAFEVDVIVMNSEGNTILQTPQNAIFFKTCQQAECPGGCRNG
GFCNERRICECPDGFHGPHCEKALCTPRCMNGGLCVTPGFCICPPGFYGVNCDKANCSTTCFN
GGTCFYPGKCICPPGLEGEQCEISKCPQPCRNGGKCIGKSKCKCSKGYQGDLCSKPVCEPGCG
AHGTCHEPNKCQCQEGWHGRHCNKRYEASLIHALRPAGAQLRQHTPSLKKAEERRDPPESNYIW

Important features:

Signal sequence:

Amino acids 1-28

N-glycosylation sites:

Amino acids 88-92;245-249

Tyrosine kinase phosphorylation site:

Amino acids 370-378

N-myristoylation sites:

Amino acids 184-190;185-191;189-195;315-321

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

Amino acids 285-293

EGF-like domain cysteine pattern signatures:

Amino acids 198-210;230-242;262-274;294-306;326-338

FIGURE 309

CCCACGCGTCCGGTCTCGCTCGCTCGCGCAGCGGCGGCAGCAGAGGTCGCGCACAGATGCGGG
TTAGACTGGCGGGGGGAGGAGGCGGAGGAGGGAAGGAAGCTGCATGCATGAGACCCACAGACT
CTTGCAAGCTGGATGCCCTCTGTGGATGAAAG**ATG**TATCATGGAATGAACCCGAGCAATGGAG
ATGGATTTCTAGAGCAGCAGCAGCAGCAGCAGCAACCTCAGTCCCCCCAGAGACTCTTGGCCG
TGATCCTGTGGTTTCAGCTGGCGCTGTGCTTCGGCCCTGCACAGCTCACGGGCGGGTTCGATG
ACCTTCAAGTGTGTGCTGACCCCGGCATTCCCGAGAATGGCTTCAGGACCCCCAGCGGAGGGG
TTTTCTTTGAAGGCTCTGTAGCCCGATTTCACTGCCAAGACGGATTCAAGCTGAAGGGCGCTA
CAAAGAGACTGTGTTTGAAGCATTTTAATGGAACCCTAGGCTGGATCCCAAGTGATAATTCCA
TCTGTGTGCAAGAAGATTGCCGTATCCCTCAAATCGAAGATGCTGAGATTCATAACAAGACAT
ATAGACATGGAGAGAAGCTAATCATCACTTGTCATGAAGGATTCAAGATCCGGTACCCCGACC
TACACAATATGGTTTCATTATGTCGCGATGATGGAACGTGGAATAATCTGCCCATCTGTCAAG
GCTGCCTGAGACCTCTAGCCTCTTCTAATGGCTATGTAAACATCTCTGAGCTCCAGACCTCCT
TCCCGGTGGGGACTGTGATCTCCTATCGCTGCTTTCCCGGATTTAAACTTGATGGGTCTGCGT
ATCTTGAGTGCTTACAAAACCTTATCTGGTCGTCCAGCCCACCCCGGTGCCTTGCTCTGGAAG
CCCAAGTCTGTCCACTACCTCCAATGGTGAGTCACGGAGATTTCGTCTGCCACCCGCGGCCTT
GTGAGCGCTACAACCACGGAACTGTGGTGGAGTTTTACTGCGATCCTGGCTACAGCCTCACCA
GCGACTACAAGTACATCACCTGCCAGTATGGAGAGTGGTTTCCTTCTTATCAAGTCTACTGCA
TCAAATCAGAGCAAACGTGGCCCAGCACCCATGAGACCCTCCTGACCACGTGGAAGATTGTGG
CGTTCACGGCAACCAGTGTGCTGCTGGTGCTGCTGCTCGTCATCCTGGCCAGGATGTTCCAGA
CCAAGTTCAAGGCCCACTTTCCCCCCAGGGGCCTCCCCGGAGTTCCAGCAGTGACCCTGACT
TTGTGGTGGTAGACGGCGTGCCCGTCATGCTCCCGTCCTATGACGAAGCTGTGAGTGGCGGCT
TGAGTGCCTTAGGCCCCGGGTACATGGCCTCTGTGGGCCAGGGCTGCCCCTTACCCGTGGACG
ACCAGAGCCCCCCAGCATACCCCGGCTCAGGGGACACGGACACAGGCCCAGGGGAGTCAGAAA
CCTGTGACAGCGTCTCAGGCTCTTCTGAGCTGCTCCAAAGTCTGTATTCACCTCCCAGGTGCC
AAGAGAGCACCCACCCTGCTTCGGACAACCCTGACATAATTGCCAGCACGGCAGAGGAGGTGG
CATCCACCAGCCCAGGCATCCATCATGCCCACTGGGTGTTGTTCCTAAGAAAC**TGA**TTGATTA
AAAAATTTCCCAAAGTGTCCTGAAGTGTCTCTTCAAATACATGTTGATCTGTGGAGTTGATTC
CTTTCCTTCTCTTGGTTTTAGACAAATGTAAACAAAGCTCTGATCCTTAAAATTGCTATGCTG
ATAGAGTGGTGAGGGCTGGAAGCTTGATCAAGTCCTGTTTCTTCTTGACACAGACTGATTAAA
AATTAAAAGNAAAAAA

FIGURE 310

MYHGMNPSNGDGFLEQQQQQQQPQSPQRLLAVILWFQLALCFGPAQLTGGFDDLQVCADPGIP
ENGFRTPSGGVFFEGSVARFHCQDGFKLKGATKRLCLKHFNGTLGWIPSDNSICVQEDCRIPQ
IEDAEIHNKTYRHGEKLIITCHEGFKIRYPDLHNMVSLCRDDGTWNNLPICQGCLRPLASSNG
YVNISELQTSFPVGTVISYRCFPGFKLDGSAYLECLQNLIWSSSPPRCLALEAQVCPLPPMVS
HGDFVCHPRPCERYNHGTVVEFYCDPGYSLTSDYKYITCQYGEWFPSYQVYCIKSEQTWPSTH
ETLLTTWKIVAFTATSVLLVLLLVILARMFQTKFKAHFPPRGPPRSSSSDPDFVVVDGVPVML
PSYDEAVSGGLSALGPGYMASVGQGCPLPVDDQSPPAYPGSGDTDTGPGESETCDSVSGSSEL
LQSLYSPPRCQESTHPASDNPDIIASTAEEVASTSPGIHHAHWVLFLRN

Important features:

Signal sequence:

amino acids 1-41

Transmembrane domain:

amino acids 325-344

N-glycosylation site.

amino acids 104-108, 134-138, 192-196

Casein kinase II phosphorylation site.

amino acids 8-12, 146-150, 252-256, 270-274, 313-317, 362-366, 364-368, 380-384, 467-471, 468-472

N-myristoylation site.

amino acids 4-10, 61-67, 169-175, 203-209, 387-393, 418-424, 478-484

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 394-405

FIGURE 311

CAGCGCGTGGCCGGCGCCGCTGTGGGGACAGC**ATG**AGCGGCGGTTGGATGGCGCAGGTTGGAG
CGTGGCGAACAGGGGCTCTGGGCCTGGCGCTGCTGCTGCTGCTCGGCCTCGGACTAGGCCTGG
AGGCCGCCGCGAGCCCGCTTTCCACCCCGACCTCTGCCCAGGCCGCAGGCCCCAGCTCAGGCT
CGTGCCCACCCACCAAGTTCCAGTGCCGCACCAGTGGCTTATGCGTGCCCCTCACCTGGCGCT
GCGACAGGGACTTGGACTGCAGCGATGGCAGCGATGAGGAGGAGTGCAGGATTGAGCCATGTA
CCCAGAAAGGGCAATGCCCACCGCCCCCTGGCCTCCCCTGCCCCTGCACCGGCGTCAGTGACT
GCTCTGGGGGAACTGACAAGAAACTGCGCAACTGCAGCCGCCTGGCCTGCCTAGCAGGCGAGC
TCCGTTGCACGCTGAGCGATGACTGCATTCCACTCACGTGGCGCTGCGACGGCCACCCAGACT
GTCCCGACTCCAGCGACGAGCTCGGCTGTGGAACCAATGAGATCCTCCCGGAAGGGGATGCCA
CAACCATGGGGCCCCCTGTGACCCTGGAGAGTGTCACCTCTCTCAGGAATGCCACAACCATGG
GGCCCCCTGTGACCCTGGAGAGTGTCCCCTCTGTCGGGAATGCCACATCCTCCTCTGCCGGAG
ACCAGTCTGGAAGCCCAACTGCCTATGGGGTTATTGCAGCTGCTGCGGTGCTCAGTGCAAGCC
TGGTCACCGCCACCCTCCTCCTTTTGTCCTGGCTCCGAGCCCAGGAGCGCCTCCGCCCACTGG
GGTTACTGGTGGCCATGAAGGAGTCCCTGCTGCTGTCAGAACAGAAGACCTCGCTGCCC**TGA**G
GACAAGCACTTGCCACCACCGTCACTCAGCCCTGGGCGTAGCCGGACAGGAGGAGAGCAGTGA
TGCGGATGGGTACCCGGGCACACCAGCCCTCAGAGACCTGAGTTCTTCTGGCCACGTGGAACC
TCGAACCCGAGCTCCTGCAGAAGTGGCCCTGGAGATTGAGGGTCCCTGGACACTCCCTATGGA
GATCCGGGGAGCTAGGATGGGGAACCTGCCACAGCCAGAACTGAGGGGCTGGCCCCAGGCAGC
TCCCAGGGGGTAGAACGGCCCTGTGCTTAAGACACTCCCTGCTGCCCCGTCTGAGGGTGGCGA
TTAAAGTTGCTTC

FIGURE 312

MSGGWMAQVGAWRTGALGLALLLLLGLGLGLEAAASPLSTPTSAQAAGPSSGSCPPTKFQCRT
SGLCVPLTWRCDRDLDCSDGSDEEECRIEPCTQKGQCPPPPGLPCPCTGVSDCSGGTDKKLRN
CSRLACLAGELRCTLSDDCIPLTWRCDGHPDCPDSSDELGCGTNEILPEGDATTMGPPVTLES
VTSLRNATTMGPPVTLESVPSVGNATSSSAGDQSGSPTAYGVIAAAAVLSASLVTATLLLLSW
LRAQERLRPLGLLVAMKESLLLSEQKTSLP

Important features:

Signal sequence:

Amino acids 1-30

Transmembrane domain:

Amino acids 231-248

N-glycosylation sites:

Amino acids 126-130;195-199;213-217

Casein kinase II phosphorylation site.

amino acids 84-88, 140-144, 161-165, 218-222

N-myristoylation sites:

Amino acids 3-9;10-16;26-32;30-36;112-118;166-172;212-218;
224-230;230-236;263-269

Prokaryotic membrane lipoprotein lipid attachment site:

Amino acids 44-55

Leucine zipper pattern:

Amino acids 17-39

FIGURE 313

CGGACGCGTGGGCGTCCGGCGGTCGCAGAGCCAGGAGGCGGAGGCGCGCGGGCCAGCCTGGGCCCCAGCCCACAC
CTTCACCAGGGCCCAGGAGCCACC**ATG**TGGCGATGTCCACTGGGGCTACTGCTGTTGCTGCCGCTGGCTGGCCAC
TTGGCTCTGGGTGCCCAGCAGGGTCGTGGGCGCCGGGAGCTAGCACCGGGTCTGCACCTGCGGGGCATCCGGGAC
GCGGGAGGCCGGTACTGCCAGGAGCAGGACCTGTGCTGCCGCGGCCGTGCCGACGACTGTGCCCTGCCCTACCTG
GGCGCCATCTGTTACTGTGACCTCTTCTGCAACCGCACGGTCTCCGACTGCTGCCCTGACTTCTGGGACTTCTGC
CTCGGCGTGCCACCCCCTTTTCCCCCGATCCAAGGATGTATGCATGGAGGTCGTATCTATCCAGTCTTGGGAACG
TACTGGGACAACTGTAACCGTTGCACCTGCCAGGAGAACAGGCAGTGGCATGGTGGATCCAGACATGATCAAAGC
CATCAACCAGGGCAACTATGGCTGGCAGGCTGGGAACCACAGCGCCTTCTGGGGCATGACCCTGGA**TGA**GGGCAT
TCGCTACCGCCTGGGCACCATCCGCCCATCTTCCTCGGTCATGAACATGCATGAAATTTATACAGTGCTGAACCC
AGGGGAGGTGCTTCCCACAGCCTTCGAGGCCTCTGAGAAGTGGCCCAACCTGATTCATGAGCCTCTTGACCAAGG
CAACTGTGCAGGCTCCTGGGCCTTCTCCACAGCAGCTGTGGCATCCGATCGTGTCTCAATCCATTCTCTGGGACA
CATGACGCCTGTCCTGTCGCCCCAGAACCTGCTGTCTTGTGACACCCACCAGCAGCAGGGCTGCCGCGGTGGGCG
TCTCGATGGTGCCTGGTGGTTCCTGCGTCGCCGAGGGGTGGTGTCTGACCACTGCTACCCCTTCTCGGGCCGTGA
ACGAGACGAGGCTGGCCCTGCGCCCCCCTGTATGATGCACAGCCGAGCCATGGGTCGGGGCAAGCGCCAGGCCAC
TGCCCACTGCCCCAACAGCTATGTTAATAACAATGACATCTACCAGGTCACTCCTGTCTACCGCCTCGGCTCCAA
CGACAAGGAGATCATGAAGGAGCTGATGGAGAATGGCCCTGTCCAAGCCCTCATGGAGGTGCATGAGGACTTCTT
CCTATACAAGGGAGGCATCTACAGCCACACGCCAGTGAGCCTTGGGAGGCCAGAGAGATACCGCCGGCATGGGAC
CCACTCAGTCAAGATCACAGGATGGGGAGAGGAGACGCTGCCAGATGGAAGGACGCTCAAATACTGGACTGCGGC
CAACTCCTGGGGCCCAGCCTGGGGCGAGAGGGGCCACTTCCGCATCGTGCGCGGCGTCAATGAGTGCGACATCGA
GAGCTTCGTGCTGGGCGTCTGGGGCCGCGTGGGCATGGAGGACATGGGTCATCACTGAGGCTGCGGGCACCACGC
GGGGTCCGGCCTGGGATCCAGGCTAAGGGCCGGCGGAAGAGGCCCCAATGGGGCGGTGACCCCAGCCTCGCCCGA
CAGAGCCCGGGGCGCAGGCGGGCGCCAGGGCGCTAATCCCGGCGCGGGTTCCGCTGACGCAGCGCCCCGCCTGGG
AGCCGCGGGCAGGCGAGACTGGCGGAGCCCCCAGACCTCCCAGTGGGGACGGGGCAGGGCCTGGCCTGGGAAGAG
CACAGCTGCAGATCCCAGGCCTCTGGCGCCCCCACTCAAGACTACCAAAGCCAGGACACCTCAAGTCTCCAGCCC
CAATACCCCACCCCAATCCCGTATTCTTTTTTTTTTTTTTTAGACAGGGTCTTGCTCCGTTGCCCAGGTTGGAG
TGCAGTGGCCCATCAGGGCTCACTGTAACCTCCGACTCCTGGGTTCAAGTGACCCTCCCACCTCAGCCTCTCAAG
TAGCTGGGACTACAGGTGCACCACCACACCTGGCTAATTTTTGTATTTTTTGTAAAGAGGGGGGTCTCACTGTGT
TGCCCAGGCTGGTTTCGAACTCCTGGGCTCAAGCGGTCCACCTGCCTCCGCCTCCCAAAGTGCTGGGATTGCAGG
CATGAGCCACTGCACCCAGCCCTGTATTCTTATTCTTCAGATATTTATTTTTCTTTTCACTGTTTTAAAATAAAA
CCAAAGTATTGATAAAAAAAAA

FIGURE 314

MWRCPLGLLLLLPLAGHLALGAQQGRGRRELAPGLHLRGIRDAGGRYCQEQDLCCRGRADDCA
LPYLGAICYCDLFCNRTVSDCCPDFWDFCLGVPPPFPPIQGCMHGGRIYPVLGTYWDNCNRCT
CQENRQWHGGSRHDQSHQPGQLWLAGWEPQRLLGHDPG

Important features:

N-glycosylation site.

amino acids 78-82, 161-165

Casein kinase II phosphorylation site.

amino acids 80-84, 117-121, 126-130, 169-173, 205-209, 296-300, 411-415

N-myristoylation site.

amino acids 21-27, 39-45, 44-50, 104-110, 160-164, 224-230, 269-275, 378-384, 442-448

Amidation site.

amino acids 26-30, 318-322

Eukaryotic thiol (cysteine) proteases histidine active site.

amino acids 398-409

FIGURE 315

CGGACGCGTGGGCCCCTGGTGGGCCCAGCAAG**ATG**GATCTACTGTGGATCCTGCCCTCCCTGT
GGCTTCTCCTGCTTGGGGGGCCTGCCTGCCTGAAGACCCAGGAACACCCCAGCTGCCCAGGAC
CCAGGGAACTGGAAGCCAGCAAAGTTGTCCTCCTGCCCAGTTGTCCCGGAGCTCCAGGAAGTC
CTGGGGAGAAGGGAGCCCCAGGTCCTCAAGGGCCACCTGGACCACCAGGCAAGATGGGCCCCA
AGGGTGAGCCAGGCCCCAGAAACTGCCGGGAGCTGTTGAGCCAGGGCGCCACCTTGAGCGGCT
GGTACCATCTGTGCCTACCTGAGGGCAGGGCCCTCCCAGTCTTTTGTGACATGGACACCGAGG
GGGGCGGCTGGCTGGTGTTTCAGAGGCGCCAGGATGGTTCTGTGGATTTCTTCCGCTCTTGGT
CCTCCTACAGAGCAGGTTTTGGGAACCAAGAGTCTGAATTCTGGCTGGGAAATGAGAATTTGC
ACCAGCTTACTCTCCAGGGTAACTGGGAGCTGCGGGTAGAGCTGGAAGACTTTAATGGTAACC
GTACTTTCGCCCACTATGCGACCTTCCGCCTCCTCGGTGAGGTAGACCACTACCAGCTGGCAC
TGGGCAAGTTCTCAGAGGGCACTGCAGGGGATTCCCTGAGCCTCCACAGTGGGAGGCCCTTTA
CCACCTATGACGCTGACCACGATTCAAGCAACAGCAACTGTGCAGTGATTGTCCACGGTGCCT
GGTGGTATGCATCCTGTTACCGATCAAATCTCAATGGTCGCTATGCAGTGTCTGAGGCTGCCG
CCCACAAATATGGCATTGACTGGGCCTCAGGCCGTGGTGTGGGCCACCCCTACCGCAGGGTTC
GGATGATGCTTCGA**TAG**GGCACTCTGGCAGCCAGTGCCCTTATCTCTCCTGTACAGCTTCCGG
ATCGTCAGCCACCTTGCCTTTGCCAACCACCTCTGCTTGCCTGTCCACATTTAAAAATAAAAT
CATTTTAGCCCTTTCA

FIGURE 316

MDLLWILPSLWLLLLGGPACLKTQEHPSCPGPRELEASKVVLLPSCPGAPGSPGEKGAPGPQG
PPGPPGKMGPKGEPGPRNCRELLSQGATLSGWYHLCLPEGRALPVFCDMDTEGGGWLVFQRRQ
DGSVDFFRSWSSYRAGFGNQESEFWLGNENLHQLTLQGNWELRVELEDFNGNRTFAHYATFRL
LGEVDHYQLALGKFSEGTAGDSLSLHSGRPFTTYDADHDSSNSNCAVIVHGAWWYASCYRSNL
NGRYAVSEAAAHKYGIDWASGRGVGHPYRRVRMMLR

Important features:

Signal peptide:

Amino acids 1-16

N-glycosylation site:

Amino acids 178-182

Glycosaminoglycan attachment site:

Amino acids 272-276

Tyrosine kinase phosphorylation site:

Amino acids 188-197

N-myristoylation sites:

Amino acids 16-22;89-95;144-150;267-273

Fibrinogen beta and gamma chains C-terminal domain signature:

Amino acids 242-255

FIGURE 317

CCCAAGCCAGCCGAGCCGCCAGAGCCGCGGGCCGCGGGGGTGTCGCGGGCCCAACCCCAGGATG
CTCCCCTGCGCCTCCTGCCTACCCGGGTCTCTACTGCTCTGGGCGCTGCTACTGTTGCTCTTGGG
ATCAGCTTCTCCTCAGGATTCTGAAGAGCCCGACAGCTACACGGAATGCACAGATGGCTATGAG
TGGGACCCAGACAGCCAGCACTGCCGGGATGTCAACGAGTGTCTGACCATCCCTGAGGCCTGC
AAGGGGGAAATGAAGTGCATCAACCACTACGGGGGCTACTTGTGCCTGCCCCGCTCCGCTGC
CGTCATCAACGACCTACATGGCGAGGGACCCCCGCCACCAGTGCCTCCCGCTCAACACCCCA
ACCCCCTGCCCACCAGGCTATGAGCCCGACGATCAGGACAGCTGTGTGGATGTGGACGAGTGT
GCCCAGGCCCTGCACGACTGTCGCCCCAGCCAGGACTGCCATAACTTGCCTGGCTCCTATCAG
TGCACCTGCCCTGATGGTTACCGCAAGATCGGGCCCGAGTGTGTGGACATAGACGAGTGCCGC
TACCGCTACTGCCAGCACCGCTGCGTGAACCTGCCTGGCTCCTTCCGCTGCCAGTGCGAGCCG
GGCTTCCAGCTGGGGCCTAACAACCGCTCCTGTGTTGATGTGAACGAGTGTGACATGGGGGCC
CATGCGAGCAGCGCTGCTTCAACTCCTATGGGACCTTCCTGTGTCGCTGCCACCAGGGCTAT
GAGCTGCATCGGGATGGCTTCTCCTGCAGTGATATTGATGAGTGTAGCTACTCCAGCTACCTC
TGTCAGTACCGCTGCGTCAACGAGCCAGGCCGTTTCTCCTGCCACTGCCCACAGGGTTACCAG
CTGCTGGCCACACGCCTCTGCCAAGACATTGATGAGTGTGAGTCTGGTGCGCACCAGTGCTCC
GAGGCCCAAACCTGTGTCAACTTCCATGGGGGCTACCGCTGCGTGGACACCAACCGCTGCGTG
GAGCCCTACATCCAGGTCTCTGAGAACCGCTGTCTCTGCCCGGCCTCCAACCCTCTATGTCGA
GAGCAGCCTTCATCCATTGTGCACCGCTACATGACCATCACCTCGGAGCGGAGCGTGCCCGCT
GACGTGTTCCAGATCCAGGCGACCTCCGTCTACCCCGGTGCCTACAATGCCTTTCAGATCCGT
GCTGGAAACTCGCAGGGGGACTTTTACATTAGGCAAATCAACAACGTCAGCGCCATGCTGGTC
CTCGCCCGGCCGGTGACGGGCCCCCGGGAGTACGTGCTGGACCTGGAGATGGTCACCATGAAT
TCCCTCATGAGCTACCGGGCCAGCTCTGTACTGAGGCTCACCGTCTTTGTAGGGGCCTACACC
TTCTGAGGAGCAGGAGGGAGCCACCCTCCCTGCAGCTACCCTAGCTGAGGAGCCTGTTGTGAG
GGGCAGAATGAGAAAGGCAATAAAGGGAGAAAGAAAGTCCTGGTGGCTGAGGTGGGCGGGTCA
CACTGCAGGAAGCCTCAGGCTGGGGCAGGGTGGCACTTGGGGGGGCAGGCCAAGTTCACCTAA
TGGGGGTCTCTATATGTTCAGGCCCAGGGGCCCCCATTGACAGGAGCTGGGAGCTCTGCACC
GAGCTTCAGTCACCCCGAGAGGAGAGGAGGTAACGAGGAGGGCGGACTCCAGGCCCCGGCC
AGAGATTTGGACTTGGCTGGCTTGCAGGGGTCCTAAGAAACTCCACTCTGGACAGCGCCAGG
AGGCCCTGGGTTCCATTCCTAACTCTGCCTCAAACTGTACATTTGGATAAGCCCTAGTAGTTC
CTGGGCCTGTTTTTCTATAAAACGAGGCAACTGGAAAAAAAAAAAA

FIGURE 318

MLPCASCLPGSLLLWALLLLLLLGSASPQDSEEPDSYTECTDGYEWDPDSQHCRDVNECLTIPE
ACKGEMKCINHYGGYLCLPRSAAVINDLHGEGPPPPVPPAQHPNPCPPGYEPDDQDSCVDVDE
CAQALHDCRPSQDCHNLPGSYQCTCPDGYRKIGPECVDIDECRYRYCQHRCVNLPGSFRCQCE
PGFQLGPNNRSCVDVNECDMGAPCEQRCFNSYGTFLCRCHQGYELHRDGFSCSDIDECSYSSY
LCQYRCVNEPGRFSCHCPQGYQLLATRLCQDIDECESGAHQCSEAQTCVNFHGGYRCVDTNRC
VEPYIQVSENRCLCPASNPLCREQPSSIVHRYMTITSERSVPADVFQIQATSVYPGAYNAFQI
RAGNSQGDFYIRQINNVSAMLVLARPVTGPREYVLDLEMVTMNSLMSYRASSVLRLTVFVGAYTF

Important features:

Signal sequence:

Amino acids 1-25

N-glycosylation sites:

Amino acids 198-202;394-398

N-myristoylation sites:

Amino acids 76-82;145-151;182-188;222-228;290-296;305-311;
371-377;381-387

Aspartic acid and asparagine hydroxylation sites:

amino acids 140-152;177-189;217-229;258-270

FIGURE 319

GCTGGGGAC**ATG**AGAGGCACACCGAAGACCCACCTCCTGGCCTTCTCCCTCCTCTGCCTCCTC

TCAAAGGTGCGTACCCAGCTGTGCCCGACACCATGTACCTGCCCCTGGCCACCTCCCCGATGC

CCGCTGGGAGTACCCCTGGTGCTGGATGGCTGTGGCTGCTGCCGGGTATGTGCACGGCGGCTG

GGGGAGCCCTGCGACCAACTCCACGTCTGCGACGCCAGCCAGGGCCTGGTCTGCCAGCCCGGG

GCAGGACCCGGTGGCCGGGGGGCCCTGTGCCTCTTGGCAGAGGACGACAGCAGCTGTGAGGTG

AACGGCCGCCTGTATCGGGAAGGGGAGACCTTCCAGCCCCACTGCAGCATCCGCTGCCGCTGC

GAGGACGGCGGCTTCACCTGCGTGCCGCTGTGCAGCGAGGATGTGCGGCTGCCCAGCTGGGAC

TGCCCCCACCCCAGGAGGGTCGAGGTCCTGGGCAAGTGCTGCCCTGAGTGGGTGTGCGGCCAA

GGAGGGGGACTGGGGACCCAGCCCCTTCCAGCCCAAGGACCCCAGTTTTCTGGCCTTGTCTCT

TCCCTGCCCCCTGGTGTCCCCTGCCCAGAATGGAGCACGGCCTGGGGACCCTGCTCGACCACC

TGTGGGCTGGGCATGGCCACCCGGGTGTCCAACCAGAACCGCTTCTGCCGACTGGAGACCCAG

CGCCGCCTGTGCCTGTCCAGGCCCTGCCCACCCTCCAGGGGTCGCAGTCCACAAAACAGTGCC

TTC**TAG**AGCCGGGCTGGGAATGGGGACACGGTGTCCACCATCCCCAGCTGGTGGCCCTGTGCC

TGGGCCCTGGGCTGATGGAAGATGGTCCGTGCCCAGGCCCTTGGCTGCAGGCAACACTTTAGC

TTGGGTCCACCATGCAGAACACCAATATTAACACGCTGCCTGGTCTGTCTGGATCCCGAGGTA

TGGCAGAGGTGCAAGACCTAGTCCCCTTTCCTCTAACTCACTGCCTAGGAGGCTGGCCAAGGT

GTCCAGGGTCCTCTAGCCCACTCCCTGCCTACACACACAGCCTATATCAAACATGCACACGGG

CGAGCTTTCTCTCCGACTTCCCCTGGGCAAGAGATGGGACAAGCAGTCCCTTAATATTGAGGC

TGCAGCAGGTGCTGGGCTGGACTGGCCATTTTTCTGGGGGTAGGATGAAGAGAAGGCACACAG

AGATTCTGGATCTCCTGCTGCCTTTTCTGGAGTTTGTAAAATTGTTCCTGAATACAAGCCTAT

GCGTGA

FIGURE 320

MRGTPKTHLLAFSLLCLLSKVRTQLCPTPCTCPWPPPRCPLGVPLVLDGCGCCRVCARRLGEP
CDQLHVCDASQGLVCQPGAGPGGRGALCLLAEDDSSCEVNGRLYREGETFQPHCSIRCRCEDG
GFTCVPLCSEDVRLPSWDCPHPRRVEVLGKCCPEWVCGQGGGLGTQPLPAQGPQFSGLVSSLP
PGVPCPEWSTAWGPCSTTCGLGMATRVSNQNRFCRLETQRRLCLSRPCPPSRGRSPQNSAF

Important features:

Signal sequence:

Amino acids 1-23

N-myristoylation sites:

Amino acids 3-9;49-55;81-87;85-91;126-132;164-170;166-172;
167-173;183-189;209-215

Insulin-like growth factor binding proteins signature:

Amino acids 49-65

von Willebrand C1 domain:

Amino acids 107-124

Thrombospondin 1 Homology Block:

Amino acids 201-216

IGF binding protein site:

Amino acids 49-58

FIGURE 321

AGAACCTCAGAAATGTGAGTTATTTGGGAATGGCTGTTTGTAAATGTCCTTACGTAAGCCAAG
AGGAGGTCTTGACTTGGGGTCCCAGGGGTACCGCAGATCCCAGGGACTGGAGCAGCACTAGCA
AGCTCTGGAGGATGAGCCAGGAGTCTGGAATTGAGGCTGAGCCAAAGACCCCAGGGCCGTCTC
AGTCTCATAAAAGGGGATCAGGCAGGAGGAGTTTGGGAGAAACCTGAGAAGGGCCTGATTTGC
AGCATC**ATG**ATGGGCCTCTCCTTGGCCTCTGCTGTGCTCCTGGCCTCCCTCCTGAGTCTCCAC
CTTGGAACTGCCACACGTGGGAGTGACATATCCAAGACCTGCTGCTTCCAATACAGCCACAAG
CCCCTTCCCTGGACCTGGGTGCGAAGCTATGAATTCACCAGTAACAGCTGCTCCCAGCGGGCT
GTGATATTCACTACCAAAAGAGGCAAGAAAGTCTGTACCCATCCAAGGAAAAAATGGGTGCAA
AAATACATTTCTTTACTGAAAACTCCGAAACAATTG**TGA**CTCAGCTGAATTTTCATCCGAGGA
CGCTTGGACCCCGCTCTTGGCTCTGCAGCCCTCTGGGGAGCCTGCGGAATCTTTTCTGAAGGC
TACATGGACCCGCTGGGGAGGAGAGGGTGTTTCCTCCCAGAGTTACTTTAATAAAGGTTGTTC
ATAGAGTTGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 322

MMGLSLASAVLLASLLSLHLGTATRGSDISKTCCFQYSHKPLPWTWVRSYEFTSNSCSQRAVI

FTTKRGKKVCTHPRKKWVQKYISLLKTPKQL

Important features:

Signal peptide:

amino acids 1-23

N-myristoylation sites.

amino acids 3-9, 26-32

Amidation site.

amino acids 68-72

Small cytokines (intecrine/chemokine).

amino acids 23-88

FIGURE 323

ACCGAGCCGAGCGGACCGAAGGCGCGCCCGAG**ATG**CAGGTGAGCAAGAGGATGCTGGCGGGGGGCGTGAGGAGCA
TGCCCAGCCCCCTCCTGGCCTGCTGGCAGCCCATCCTCCTGCTGGTGCTGGGCTCAGTGCTGTCAGGCTCGGCCA
CGGGCTGCCCGCCCCGCTGCGAGTGCTCCGCCCAGGACCGCGCTGTGCTGTGCCACCGCAAGTGCTTTGTGGCAG
TCCCCGAGGGCATCCCCACCGAGACGCGCCTGCTGGACCTAGGCAAGAACCGCATCAAAACGCTCAACCAGGACG
AGTTCGCCAGCTTCCCGCACCTGGAGGAGCTGGAGCTCAACGAGAACATCGTGAGCGCCGTGGAGCCCGGCGCCT
TCAACAACCTCTTCAACCTCCGGACGCTGGGTCTCCGCAGCAACCGCCTGAAGCTCATCCCGCTAGGCGTCTTCA
CTGGCCTCAGCAACCTGACCAAGCAGGACATCAGCGAGAACAAGATCGTTATCCTACTGGACTACATGTTTCAGG
ACCTGTACAACCTCAAGTCACTGGAGGTTGGCGACAATGACCTCGTCTACATCTCTCACCGCGCCTTCAGCGGCC
TCAACAGCCTGGAGCAGCTGACGCTGGAGAAATGCAACCTGACCTCCATCCCCACCGAGGCGCTGTCCCACCTGC
ACGGCCTCATCGTCCTGAGGCTCCGGCACCTCAACATCAATGCCATCCGGGACTACTCCTTCAAGAGGCTGTACC
GACTCAAGGTCTTGGAGATCTCCCACTGGCCCTACTTGGACACCATGACACCCAACTGCCTCTACGGCCTCAACC
TGACGTCCCTGTCCATCACACACTGCAATCTGACCGCTGTGCCCTACCTGGCCGTCCGCCACCTAGTCTATCTCC
GCTTCCTCAACCTCTCCTACAACCCCATCAGCACCATTGAGGGCTCCATGTTGCATGAGCTGCTCCGGCTGCAGG
AGATCCAGCTGGTGGGCGGGCAGCTGGCCGTGGTGGAGCCCTATGCCTTCCGCGGCCTCAACTACCTGCGCGTGC
TCAATGTCTCTGGCAACCAGCTGACCACACTGGAGGAATCAGTCTTCCACTCGGTGGGCAACCTGGAGACACTCA
TCCTGGACTCCAACCCGCTGGCCTGCGACTGTCGGCTCCTGTGGGTGTTCCGGCGCCGCTGGCGGCTCAACTTCA
ACCGGCAGCAGCCCACGTGCGCCACGCCCGAGTTTGTCCAGGGCAAGGAGTTCAAGGACTTCCCTGATGTGCTAC
TGCCCAACTACTTCACCTGCCGCCGCGCCCGCATCCGGGACCGCAAGGCCCAGCAGGTGTTTGTGGACGAGGGCC
ACACGGTGCAGTTTGTGTGCCGGGCCGATGGCGACCCGCCGCCCGCCATCCTCTGGCTCTCACCCCGAAAGCACC
TGGTCTCAGCCAAGAGCAATGGGCGGCTCACAGTCTTCCCTGATGGCACGCTGGAGGTGCGCTACGCCCAGGTAC
AGGACAACGGCACGTACCTGTGCATCGCGGCCAACGCGGGCGGCAACGACTCCATGCCCGCCCACCTGCATGTGC
GCAGCTACTCGCCCGACTGGCCCCATCAGCCCAACAAGACCTTCGCTTTCATCTCCAACCAGCCGGGCGAGGGAG
AGGCCAACAGCACCCGCGCCACTGTGCCTTTCCCCTTCGACATCAAGACCCTCATCATCGCCACCACCATGGGCT
TCATCTCTTTCCTGGGCGTCGTCCTCTTCTGCCTGGTGCTGCTGTTTCTCTGGAGCCGGGGCAAGGGCAACACAA
AGCACAACATCGAGATCGAGTATGTGCCCCGAAAGTCGGACGCAGGCATCAGCTCCGCCGACGCGCCCCGCAAGT
TCAACATGAAGATGATA**TGA**GGCCGGGGCGGGGGGCAGGGACCCCCGGGCGGCCGGGCAGGGGAAGGGGCCTGGT
CGCCACCTGCTCACTCTCCAGTCCTTCCCACCTCCTCCCTACCCTTCTACACACGTTCTCTTTCTCCCTCCCGCC
TCCGTCCCCTGCTGCCCCCCGCCAGCCCTCACCACCTGCCCTCCTTCTACCAGGACCTCAGAAGCCCAGACCTGG
GGACCCCACCTACACAGGGGCATTGACAGACTGGAGTTGAAAGCCGACGAACCGACACGCGGCAGAGTCAATAAT
TCAATAAAAAAGTTACGAACTTTCTCTGTAACTTGGGTTTCAATAATTATGGATTTTTATGAAAACTTGAAATAA
TAAAAAGAGAAAAAAACTAAAAAAAAAAAAAAAAAAAAAA

FIGURE 324

MQVSKRMLAGGVRSMPSPLLACWQPILLLVLGSVLSGSATGCPPRCECSAQDRAVLCHRKCFVAVPEGIPTETRL
LDLGKNRIKTLNQDEFASFPHLEELELNENIVSAVEPGAFNNLFNLRTLGLRSNRLKLIPLGVFTGLSNLTKQDI
SENKIVILLDYMFQDLYNLKSLEVGDNDLVYISHRAFSGLNSLEQLTLEKCNLTSIPTEALSHLHGLIVLRLRHL
NINAIRDYSFKRLYRLKVLEISHWPYLDTMTPNCLYGLNLTSLSITHCNLTAVPYLAVRHLVYLRFLNLSYNPIS
TIEGSMLHELLRLQEIQLVGGQLAVVEPYAFRGLNYLRVLNVSGNQLTTLEESVFHSVGNLETLILDSNPLACDC
RLLWVFRRRWRLNFNRQQPTCATPEFVQGKEFKDFPDVLLPNYFTCRRARIRDRKAQQVFVDEGHTVQFVCRADG
DPPPAILWLSPRKHLVSAKSNGRLTVFPDGTLEVRYAQVQDNGTYLCIAANAGGNDSMPAHLHVRSYSPDWPHQP
NKTFAFISNQPGEGEANSTRATVPFPFDIKTLIIATTMGFISFLGVVLFCLVLLFLWSRGKGNTKHNIEIEYVPR
KSDAGISSADAPRKFNMKMI

Important features:

Signal sequence:

amino acids 1-41

Transmembrane domain:

amino acids 556-578

N-glycosylation site.

amino acids 144-148, 202-206, 264-268, 274-278, 293-297, 341-345, 492-496, 505-509, 526-530, 542-546

Casein kinase II phosphorylation site.

amino acids 49-53, 108-112, 146-150, 300-304, 348-352, 349-353, 607-611

Tyrosine kinase phosphorylation site.

amino acids 590-598

N-myristoylation site.

amino acids 10-16, 32-38, 37-43, 113-119, 125-131, 137-143, 262-268, 320-326, 344-350, 359-365, 493-499, 503-509, 605-611

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 32-43

FIGURE 325

CCCACGCGTCCGCCCACGCGTCCGAGGGACAAGAGAGAAGAGAGACTGAAACAGGGAGAAGAG
GCAGGAGAGGAGGAGGTGGGGAGAGCACGAAGCTGGAGGCCGACACTGAGGGAGGGCGGGAGG
AGGTGAAGAAGGAGAGAGGGGAGAAGAGGCAGGAGCTGGAAAGGAGAGAGGGAGGAGGAGGAG
GAGATGCGGGATGGAGACCTGGAGTTAGGTGGCTTGGGAGAGCTTAATGAAAAGAGAACGGAG
AGGAGGTGTGGGTTAGGAACCAAGAGGTAGCCCTGTGGGCAGCAGAAGGCTGAGAGGAGTAGG
AAGATCAGGAGCTAGAGGGAGACTGGAGGGTTCCGGGAAAAGAGCAGAGGAAAGAGGAAAGAC
ACAGAGAGACGGGAGAGAGAAGAAGAGTGGGTTTGAAGGGCGGATCTCAGTCCCTGGCTGCTT
TGGCATTTGGGGAACTGGGACTCCCTGTGGGGAGGAGAGGAAAGCTGGAAGTCCTGGAGGGAC
AGGGTCCCAGAAGGAGGGGACAGAGGAGCTGAGAGAGGGGGGCAGGGCGTTGGGCAGGGGTCC
CTCGGAGGCCTCCTGGGG**ATG**GGGGCTGCAGCTCGTCTGAGCGCCCCTCGAGCGCTGGTACTC
TGGGCTGCACTGGGGGCAGCAGCTCACATCGGACCAGCACCTGACCCCGAGGACTGGTGGAGC
TACAAGGATAATCTCCAGGGAAACTTCGTGCCAGGGCCTCCTTTCTGGGGCCTGGTGAATGCA
GCGTGGAGTCTGTGTGCTGTGGGGAAGCGGCAGAGCCCCGTGGATGTGGAGCTGAAGAGGGTT
CTTTATGACCCCTTTCTGCCCCCATTAAGGCTCAGCACTGGAGGAGAAGCTCCGGGGAACC
TTGTACAACACCGGCCGACATGTCTCCTTCCTGCCTGCACCCCGACCTGTGGTCAATGTGTCT
GGAGGTCCCCTCCTTTACAGCCACCGACTCAGTGAACTGCGGCTGCTGTTTGGAGCTCGCGAC
GGAGCCGGCTCGGAACATCAGATCAACCACCAGGGCTTCTCTGCTGAGGTGCAGCTCATTCAC
TTCAACCAGGAACTCTACGGGAATTTCAGCGCTGCCTCCCGCGGCCCCAATGGCCTGGCCATT
CTCAGCCTCTTTGTCAACGTTGCCAGTACCTCTAACCCATTCCTCAGTCGCCTCCTTAACCGC
GACACCATCACTCGCATCTCCTACAAGAATGATGCCTACTTTCTTCAAGACCTGAGCCTGGAG
CTCCTGTTCCCTGAATCCTTCGGCTTCATCACCTATCAGGGCTCTCTCAGCACCCCGCCCTGC
TCCGAGACTGTCACCTGGATCCTCATTGACCGGGCCCTCAATATCACCTCCCTTCAGATGCAC
TCCCTGAGACTCCTGAGCCAGAATCCTCCATCTCAGATCTTCCAGAGCCTCAGCGGTAACAGC
CGGCCCCTGCAGCCCTTGGCCCACAGGGCACTGAGGGGCAACAGGGACCCCCGGCACCCCGAG
AGGCGCTGCCGAGGCCCCAACTACCGCCTGCATGTGGATGGTGTCCCCCATGGTCGC**TGA**GAC
TCCCCTTCGAGGATTGCACCCGCCCGTCCTAAGCCTCCCCACAAGGCGAGGGGAGTTACCCCT
AAAACAAAGCTATTAAAGGGACAGAATACTTA

FIGURE 326

MGAAARLSAPRALVLWAALGAAAHIGPAPDPEDWWSYKDNLQGNFVPGPPFWGLVNAAWSLCA
VGKRQSPVDVELKRVLYDPFLPPLRLSTGGEKLRGTLYNTGRHVSFLPAPRPVVNVSGGPLLY
SHRLSELRLLFGARDGAGSEHQINHQGFSAEVQLIHFNQELYGNFSAASRGPNGLAILSLFVN
VASTSNPFLSRLLNRDTITRISYKNDAYFLQDLSLELLFPESFGFITYQGSLSTPPCSETVTW
ILIDRALNITSLQMHSLRLLSQNPPSQIFQSLSGNSRPLQPLAHRALRGNRDPRHPERRCRGP
NYRLHVDGVPHGR

Important features:

Signal peptide:

Amino acids 1-23

Transmembrane domain:

Amino acids 177-199

N-glycosylation sites:

Amino acids 118-122;170-174;260-264

Eukaryotic-type carbonic anhydrases proteins:

Amino acids 222-271;128-165;45-93

FIGURE 327

GGACTAATCTGTGGGAGCAGTTTATTCCAGTATCACCCAGGGTGCAGCCACACCAGGACTGTGTTGAAGGGTGTT
TTTTTTCTTTTAAATGTAATACCTCCTCATCTTTTCTTCTTACACAGTGTCTGAGAACATTTACATTATAGATAA
GTAGTACATGGTGGATAACTTCTACTTTTAGGAGGACTACTCTCTTCTGACAGTCCTAGACTGGTCTTCTACACT
AAGACACC**ATG**AAGGAGTATGTGCTCCTATTATTCCTGGCTTTGTGCTCTGCCAAACCCTTCTTTAGCCCTTCAC
ACATCGCACTGAAGAATATGATGCTGAAGGATATGGAAGACACAGATGATGATGATGATGATGATGATGATGATG
ATGATGATGAGGACAACTCTCTTTTTCCAACAAGAGAGCCAAGAAGCCATTTTTTTCCATTTGATCTGTTTCCAA
TGTGTCCATTTGGATGTCAGTGCTATTCACGAGTTGTACATTGCTCAGATTTAGGTTTGACCTCAGTCCCAACCA
ACATTCCATTTGATACTCGAATGCTTGATCTTCAAAACAATAAAATTAAGGAAATCAAAGAAAATGATTTTAAAG
GACTCACTTCACTTTATGGTCTGATCCTGAACAACAACAAGCTAACGAAGATTCACCCAAAAGCCTTTCTAACCA
CAAAGAAGTTGCGAAGGCTGTATCTGTCCCACAATCAACTAAGTGAAATACCACTTAATCTTCCCAAATCATTAG
CAGAACTCAGAATTCATGAAAATAAAGTTAAGAAAATACAAAAGGACACATTCAAAGGAATGAATGCTTTACACG
TTTTGGAAATGAGTGCAAACCCTCTTGATAATAATGGGATAGAGCCAGGGGCATTTGAAGGGGTGACGGTGTTCC
ATATCAGAATTGCAGAAGCAAAACTGACCTCAGTTCCTAAAGGCTTACCACCAACTTTATTGGAGCTTCACTTAG
ATTATAATAAAATTTCAACAGTGGAACTTGAGGATTTTAAACGATACAAAGAACTACAAAGGCTGGGCCTAGGAA
ACAACAAAATCACAGATATCGAAAATGGGAGTCTTGCTAACATACCACGTGTGAGAGAAATACATTTGGAAAACA
ATAAACTAAAAAAAATCCCTTCAGGATTACCAGAGTTGAAATACCTCCAGATAATCTTCCTTCATTCTAATTCAA
TTGCAAGAGTGGGAGTAAATGACTTCTGTCCAACAGTGCCAAAGATGAAGAAATCTTTATACAGTGCAATAAGTT
TATTCAACAACCCGGTGAAATACTGGGAAATGCAACCTGCAACATTTCGTTGTGTTTTGAGCAGAATGAGTGTTC
AGCTTGGGAACTTTGGAATG**TAA**TAATTAGTAATTGGTAATGTCCATTTAATATAAGATTCAAAAATCCCTACAT
TTGGAATACTTGAACTCTATTAATAATGGTAGTATTATATATACAAGCAAATATCTATTCTCAAGTGGTAAGTCC
ACTGACTTATTTTATGACAAGAAATTTCAACGGAATTTTGCCAAACTATTGATACATAAGGGGTTGAGAGAAACA
AGCATCTATTGCAGTTTCCTTTTTGCGTACAAATGATCTTACATAAATCTCATGCTTGACCATTCCTTTCTTCAT
AACAAAAAAGTAAGATATTCGGTATTTAACACTTTGTTATCAAGCACATTTTAAAAAGAACTGTACTGTAAATGG
AATGCTTGACTTAGCAAAATTTGTGCTCTTTCATTTGCTGTTAGAAAAACAGAATTAACAAAGACAGTAATGTGA
AGAGTGCATTACACTATTCTTATTCTTTAGTAACTTGGGTAGTACTGTAATATTTTTAATCATCTTAAAGTATGA
TTTGATATAATCTTATTGAAATTACCTTATCATGTCTTAGAGCCCGTCTTTATGTTTAAAACTAATTTCTTAAAA
TAAAGCCTTCAGTAAATGTTCATTACCAACTTGATAAATGCTACTCATAAGAGCTGGTTTGGGGCTATAGCATAT
GCTTTTTTTTTTTTAATTATTACCTGATTTAAAAATCTCTGTAAAAACGTGTAGTGTTTCATAAAATCTGTAACT
CGCATTTTAATGATCCGCTATTATAAGCTTTTAATAGCATGAAAATTGTTAGGCTATATAACATTGCCACTTCAA
CTCTAAGGAATATTTTTGAGATATCCCTTTGGAAGACCTTGCTTGGAAGAGCCTGGACACTAACAATTCTACACC
AAATTGTCTCTTCAAATACGTATGGACTGGATAACTCTGAGAAACACATCTAGTATAACTGAATAAGCAGAGCAT
CAAATTAAACAGACAGAAACCGAAAGCTCTATATAAATGCTCAGAGTTCTTTATGTATTTCTTATTGGCATTCAA
CATATGTAAAATCAGAAAACAGGGAAATTTTCATTAAAAATATTGGTTTGAAAT

FIGURE 328

MKEYVLLLFLALCSAKPFFSPSHIALKNMMLKDMEDTDDDDDDDDDDDDDEDNSLFPTREPRS
HFFPFDLFPMCPFGCQCYSRVVHCSDLGLTSVPTNIPFDTRMLDLQNNKIKEIKENDFKGLTS
LYGLILNNNKLTKIHPKAFLTTKKLRRLYLSHNQLSEIPLNLPKSLAELRIHENKVKKIQKDT
FKGMNALHVLEMSANPLDNNGIEPGAFEGVTVFHIRIAEAKLTSVPKGLPPTLLELHLDYNKI
STVELEDFKRYKELQRLGLGNNKITDIENGSLANIPRVREIHLENNKLKKIPSGLPELKYLQI
IFLHSNSIARVGVNDFCPTVPKMKKSLYSAISLFNNPVKYWEMQPATFRCVLSRMSVQLGNFGM

Important features:

Signal sequence.

amino acids 1-15

N-glycosylation site.

amino acids 281-285

N-myristoylation sites.

amino acids 129-135, 210-216, 214-220, 237-243, 270-276, 282-288

Leucine zipper pattern.

amino acids 154-176

FIGURE 329

GGGGTCTCCCTCAGGGCCGGGAGGCACAGCGGTCCCTGCTTGCTGAAGGGCTGGATGTACGCA
TCCGCAGGTTCCCGCGGACTTGGGGGCGCCCGCTGAGCCCCGGCGCCCGCAGAAGACTTGTGT
TTGCCTCCTGCAGCCTCAACCCGGAGGGCAGCGAGGGCCTACCACC**ATG**ATCACTGGTGTGTT
CAGCATGCGCTTGTGGACCCCAGTGGGCGTCCTGACCTCGCTGGCGTACTGCCTGCACCAGCG
GCGGGTGGCCCTGGCCGAGCTGCAGGAGGCCGATGGCCAGTGTCCGGTCGACCGCAGCCTGCT
GAAGTTGAAAATGGTGCAGGTCGTGTTTCGACACGGGGCTCGGAGTCCTCTCAAGCCGCTCCC
GCTGGAGGAGCAGGTAGAGTGGAACCCCCAGCTATTAGAGGTCCCACCCCAAACTCAGTTTGA
TTACACAGTCACCAATCTAGCTGGTGGTCCGAAACCATATTCTCCTTACGACTCTCAATACCA
TGAGACCACCCTGAAGGGGGGCATGTTTGCTGGGCAGCTGACCAAGGTGGGCATGCAGCAAAT
GTTTGCCTTGGGAGAGAGACTGAGGAAGAACTATGTGGAAGACATTCCCTTTCTTTCACCAAC
CTTCAACCCACAGGAGGTCTTTATTCGTTCCACTAACATTTTTCGGAATCTGGAGTCCACCCG
TTGTTTGCTGGCTGGGCTTTTCCAGTGTCAGAAAGAAGGACCCATCATCATCCACACTGATGA
AGCAGATTCAGAAGTCTTGTATCCCAACTACCAAAGCTGCTGGAGCCTGAGGCAGAGAACCAG
AGGCCGGAGGCAGACTGCCTCTTTACAGCCAGGAATCTCAGAGGATTTGAAAAAGGTGAAGGA
CAGGATGGGCATTGACAGTAGTGATAAAGTGGACTTCTTCATCCTCCTGGACAACGTGGCTGC
CGAGCAGGCACACAACCTCCCAAGCTGCCCCATGCTGAAGAGATTTGCACGGATGATCGAACA
GAGAGCTGTGGACACATCCTTGTACATACTGCCCAAGGAAGACAGGGAAAGTCTTCAGATGGC
AGTAGGCCCATTCCTCCACATCCTAGAGAGCAACCTGCTGAAAGCCATGGACTCTGCCACTGC
CCCCGACAAGATCAGAAAGCTGTATCTCTATGCGGCTCATGATGTGACCTTCATACCGCTCTT
AATGACCCTGGGGATTTTTGACCACAAATGGCCACCGTTTGCTGTTGACCTGACCATGGAACT
TTACCAGCACCTGGAATCTAAGGAGTGGTTTGTGCAGCTCTATTACCACGGGAAGGAGCAGGT
GCCGAGAGGTTGCCCTGATGGGCTCTGCCCGCTGGACATGTTCTTGAATGCCATGTCAGTTTA
TACCTTAAGCCCAGAAAAATACCATGCACTCTGCTCTCAAACTCAGGTGATGGAAGTTGGAAA
TGAAGAG**TAA**CTGATTTATAAAAGCAGGATGTGTTGATTTTAAAATAAAGTGCCTTTATACAATG

FIGURE 330

MITGVFSMRLWTPVGVLTSLAYCLHQRRVALAELQEADGQCPVDRSLLKLKMVQVVFRHGARSPLKPLPLEEQVE
WNPQLLEVPPQTQFDYTVTNLAGGPKPYSPYDSQYHETTLKGGMFAGQLTKVGMQQMFALGERLRKNYVEDIPFL
SPTFNPQEVFIRSTNIFRNLESTRCLLAGLFQCQKEGPIIIHTDEADSEVLYPNYQSCWSLRQRTRGRRQTASLQ
PGISEDLKKVKDRMGIDSSDKVDFFILLDNVAAEQAHNLPSCPMLKRFARMIEQRAVDTSLYILPKEDRESLQMA
VGPFLHILESNLLKAMDSATAPDKIRKLYLYAAHDVTFIPLLMTLGIFDHKWPPFAVDLTMELYQHLESKEWFVQ
LYYHGKEQVPRGCPDGLCPLDMFLNAMSVYTLSPEKYHALCSQTQVMEVGNEE

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 331

CGAGGGCTTTTCCGGCTCCGGAATGGCACATGTGGGAATCCCAGTCTTGTTGGCTACAACATTTTTCCCTTTCCT
AACAAGTTCTAACAGCTGTTCTAACAGCTAGTGATCAGGGGTTCTTCTTGCTGGAGAAGAAAGGGCTGAGGGCAG
AGCAGGGCACTCTCACTCAGGGTGACCAGCTCCTTGCCTCTCTGTGGATAACAGAGCATGAGAAAGTGAAGAGAT
GCAGCGGAGTGAGGTGATGGAAGTCTAAAATAGGAAGGAATTTTGTGTGCAATATCAGACTCTGGGAGCAGTTGA
CCTGGAGAGCCTGGGGGAGGGCCTGCCTAACAAGCTTTCAAAAAACAGGAGCGACTTCCACTGGGCTGGGATAAG
ACGTGCCGGTAGGATAGGGAAGACTGGGTTTAGTCCTAATATCAAATTGACTGGCTGGGTGAACTTCAACAGCCT
TTTAACCTCTCTGGGAGATGAAAACGATGGCTTAAGGGGCCAGAAATAGAGATGCTTTGTAAAATAAAATTTTAA
AAAAAGCAAGTATTTTATAGCATAAAGGCTAGAGACCAAAATAGATAACAGGATTCCCTGAACATTCCTAAGAGG
GAGAAAGTATGTTAAAAATAGAAAAACCAAAATGCAGAAGGAGGAGACTCACAGAGCTAAACCAGG**ATG**GGGACC
CTGGGTCAGGCCAGCCTCTTTGCTCCTCCCGGAAATTATTTTTGGTCTGACCACTCTGCCTTGTGTTTTGCAGAA
TCATGTGAGGGCCAACCGGGGAAGGTGGAGCAGATGAGCACACACAGGAGCCGTCTCCTCACCGCCGCCCCTCTC
AGCATGGAACAGAGGCAGCCCTGGCCCCGGGCCCTGGAGGTGGACAGCCGCTCTGTGGTCCTGCTCTCAGTGGTC
TGGGTGCTGCTGGCCCCCCCAGCAGCCGGCATGCCTCAGTTCAGCACCTTCCACTCTGAGAATCGTGACTGGACC
TTCAACCACTTGACCGTCCACCAAGGGACGGGGGCCGTCTATGTGGGGGCCATCAACCGGGTCTATAAGCTGACA
GGCAACCTGACCATCCAGGTGGCTCATAAGACAGGGCCAGAAGAGGACAACAAGTCTCGTTACCCGCCCCTCATC
GTGCAGCCCTGCAGCGAAGTGCTCACCCTCACCAACAATGTCAACAAGCTGCTCATCATTGACTACTCTGAGAAC
CGCCTGCTGGCCTGTGGGAGCCTCTACCAGGGGGTCTGCAAGCTGCTGCGGCTGGATGACCTCTTCATCCTGGTG
GAGCCATCCCACAAGAAGGAGCACTACCTGTCCAGTGTCAACAAGACGGGCACCATGTACGGGGTGATTGTGCGC
TCTGAGGGTGAGGATGGCAAGCTCTTCATCGGCACGGCTGTGGATGGGAAGCAGGATTACTTCCCGACCCTGTCC
AGCCGGAAGCTGCCCCGAGACCCTGAGTCCTCAGCCATGCTCGACTATGAGCTACACAGCGATTTTGTCTCCTCT
CTCATCAAGATCCCTTCAGACACCCTGGCCCTGGTCTCCCACTTTGACATCTTCTACATCTACGGCTTTGCTAGT
GGGGGCTTTGTCTACTTTCTCACTGTCCAGCCCGAGACCCCTGAGGGTGTGGCCATCAACTCCGCTGGAGACCTC
TTCTACACCTCACGCATCGTGCGGCTCTGCAAGGATGACCCCAAGTTCCACTCATACGTGTCCCTGCCCTTCGGC
TGCACCCGGGCCGGGGTGGAATACCGCCTCCTGCAGGCTGCTTACCTGGCCAAGCCTGGGGACTCACTGGCCCAG
GCCTTCAATATCACCAGCCAGGACGATGTACTCTTTGCCATCTTCTCCAAAGGGCAGAAGCAGTATCACCACCCG
CCCGATGACTCTGCCCTGTGTGCCTTCCCTATCCGGGCCATCAACTTGCAGATCAAGGAGCGCCTGCAGTCCTGC
TACCAGGGCGAGGGCAACCTGGAGCTCAACTGGCTGCTGGGGAAGGACGTCCAGTGCACGAAGGCGCCTGTCCCC
ATCGATGATAACTTCTGTGGACTGGACATCAACCAGCCCCTGGGAGGCTCAACTCCAGTGGAGGGCCTGACCCTG
TACACCACCAGCAGGGACCGCATGACCTCTGTGGCCTCCTACGTTTACAACGGCTACAGCGTGGTTTTTGTGGGG
ACTAAGAGTGGCAAGCTGAAAAAGGTAAGAGTCTATGAGTTCAGATGCTCCAATGCCATTCACCTCCTCAGCAAA
GAGTCCCTCTTGGAAGGTAGCTATTGGTGGAGATTTAACTATAGGCAACTTTATTTTCTTGGGGAACAAAGG**TGA**
AATGGGGAGGTAAGAAGGGGTTAATTTTGTGACTTAGCTTCTAGCTACTTCCTCCAGCCATCAGTCATTGGGTAT
GTAAGGAATGCAAGCGTATTTCAATATTTCCCAAACTTTAAGAAAAAACTTTAAGAAGGTACATCTGCAAAAGCAAA

FIGURE 332

MGTLGQASLFAPPGNYFWSDHSALCFAESCEGQPGKVEQMSTHRSRLLTAAPLSMEQRQPWPR
ALEVDSRSVVLLSVVWVLLAPPAAGMPQFSTFHSENRDWTFNHLTVHQGTGAVYVGAINRVYK
LTGNLTIQVAHKTGPEEDNKSRYPPLIVQPCSEVLTLTNNVNKLLIIDYSENRLLACGSLYQG
VCKLLRLDDLFILVEPSHKKEHYLSSVNKTGTMYGVIVRSEGEDGKLFIGTAVDGKQDYFPTL
SSRKLPRDPESSAMLDYELHSDFVSSLIKIPSDTLALVSHFDIFYIYGFASGGFVYFLTVQPE
TPEGVAINSAGDLFYTSRIVRLCKDDPKFHSYVSLPFGCTRAGVEYRLLQAAYLAKPGDSLAQ
AFNITSQDDVLFAIFSKGQKQYHHPPDDSALCAFPIRAINLQIKERLQSCYQGEGNLELNWLL
GKDVQCTKAPVPIDDNFCGLDINQPLGGSTPVEGLTLYTTSRDRMTSVASYVYNGYSVVFVGT
KSGKLKKVRVYEFRCSNAIHLLSKESLLEGSYWWRFNYRQLYFLGEQR

Important features:

Signal sequence:

amino acids 1-32

Transmembrane domain:

amino acids 71-87

N-glycosylation site.

amino acids 130-134, 145-149, 217-221, 381-385

Casein kinase II phosphorylation site.

amino acids 139-143, 229-233, 240-244, 291-295, 324-328, 383-387, 384-388, 471-475, 481-485, 530-534

N-myristoylation site.

amino acids 220-226, 319-325, 353-359, 460-466, 503-509

FIGURE 333

GCTGAGTCTGCTGCTCCTGCTGCTGCTGCTCCAGCCTGTAACCTGTGCCTACACCACGCCAGG

CCCCCCCAGAGCCCTCACCACGCTGGGCGCCCCCAGAGCCCACACC**ATG**CCGGGCACCTACGC

TCCCTCGACCACACTCAGTAGTCCCAGCACCCAGGGCCTGCAAGAGCAGGCACGGGCCCTGAT

GCGGGACTTCCCGCTCGTGGACGGCCACAACGACCTGCCCCTGGTCCTAAGGCAGGTTTACCA

GAAAGGGCTACAGGATGTTAACCTGCGCAATTTCAGCTACGGCCAGACCAGCCTGGACAGGCT

TAGAGATGGCCTCGTGGGCGCCCAGTTCTGGTCAGCCTATGTGCCATGCCAGACCCAGGACCG

GGATGCCCTGCGCCTCACCCTGGAGCAGATTGACCTCATACGCCGCATGTGTGCCTCCTATTC

TGAGCTGGAGCTTGTGACCTCGGCTAAAGCTCTGAACGACACTCAGAAATTGGCCTGCCTCAT

CGGTGTAGAGGGTGGCCACTCGCTGGACAATAGCCTCTCCATCTTACGTACCTTCTACATGCT

GGGAGTGCGCTACCTGACGCTCACCCACACCTGCAACACACCCTGGGCAGAGAGCTCCGCTAA

GGGCGTCCACTCCTTCTACAACAACATCAGCGGGCTGACTGACTTTGGTGAGAAGGTGGTGGC

AGAAATGAACCGCCTGGGCATGATGGTAGACTTATCCCATGTCTCAGATGCTGTGGCACGGCG

GGCCCTGGAAGTGTCACAGGCACCTGTGATCTTCTCCCACTCGGCTGCCCGGGGTGTGTGCAA

CAGTGCTCGGAATGTTCCTGATGACATCCTGCAGCTTCTGAAGAAGAACGGTGGCGTCGTGAT

GGTGTCTTTGTCCATGGGAGTAATACAGTGCAACCCATCAGCCAATGTGTCCACTGTGGCAGA

TCACTTCGACCACATCAAGGCTGTCATTGGATCCAAGTTCATCGGGATTGGTGGAGATTATGA

TGGGGCCGGCAAATTCCCTCAGGGGCTGGAAGACGTGTCCACATACCCGGTCCTGATAGAGGA

GTTGCTGAGTCGTGGCTGGAGTGAGGAAGAGCTTCAGGGTGTCCTTCGTGGAAACCTGCTGCG

GGTCTTCAGACAAGTGGAAAAGGTACAGGAAGAAAACAAATGGCAAAGCCCCTTGGAGGACAA

GTTCCCGGATGAGCAGCTGAGCAGTTCCTGCCACTCCGACCTCTCACGTCTGCGTCAGAGACA

GAGTCTGACTTCAGGCCAGGAACTCACTGAGATTCCCATACACTGGACAGCCAAGTTACCAGC

CAAGTGGTCAGTCTCAGAGTCCTCCCCCCACATGGCCCCAGTCCTTGCAGTTGTGGCCACCTT

CCCAGTCCTTATTCTGTGGCTC**TGA**TGACCCAGTTAGTCCTGCCAGATGTCACTGTAGCAAGC

CACAGACACCCCACAAAGTTCCCCTGTTGTGCAGGCACAAATATTTCCTGAAATAAATGTTTT

GGACATAG

FIGURE 334

MPGTYAPSTTLSSPSTQGLQEQARALMRDFPLVDGHNDLPLVLRQVYQKGLQDVNLRNFSYGQ
TSLDRLRDGLVGAQFWSAYVPCQTQDRDALRLTLEQIDLIRRMCASYSELELVTSAKALNDTQ
KLACLIGVEGGHSLDNSLSILRTFYMLGVRYLTLTHTCNTPWAESSAKGVHSFYNNISGLTDF
GEKVVAEMNRLGMMVDLSHVSDAVARRALEVSQAPVIFSHSAARGVCNSARNVPDDILQLLKK
NGGVVMVSLSMGVIQCNPSANVSTVADHFDHIKAVIGSKFIGIGGDYDGAGKFPQGLEDVSTY
PVLIEELLSRGWSEEELQGVLRGNLLRVFRQVEKVQEENKWQSPLEDKFPDEQLSSSCHSDLS
RLRQRQSLTSGQELTEIPIHWTAKLPAKWSVSESSPHMAPVLAVVATFPVLILWL

Important features:

N-glycosylation sites.

amino acids 58-62, 123-127, 182-186, 273-277

N-myristoylation sites.

amino acids 72-78, 133-139, 234-240, 264-270, 334-340, 389-395

Renal dipeptidase active site.

amino acids 134-157

FIGURE 335

CCCAGAAGTTCAAGGGCCCCCGGCCTCCTGCGCTCCTGCCGCCGGGACCCTCGACCTCCTCAG

AGCAGCCGGCTGCCGCCCCGGGAAG**ATG**GCGAGGAGGAGCCGCCACCGCCTCCTCCTGCTGCT

GCTGCGCTACCTGGTGGTCGCCCTGGGCTATCATAAGGCCTATGGGTTTTCTGCCCCAAAAGA

CCAACAAGTAGTCACAGCAGTAGAGTACCAAGAGGCTATTTTAGCCTGCAAAACCCCAAAGAA

GACTGTTTCCTCCAGATTAGAGTGGAAGAAACTGGGTCGGAGTGTCTCCTTTGTCTACTATCA

ACAGACTCTTCAAGGTGATTTTAAAAATCGAGCTGAGATGATAGATTTCAATATCCGGATCAA

AAATGTGACAAGAAGTGATGCGGGGAAATATCGTTGTGAAGTTAGTGCCCCATCTGAGCAAGG

CCAAAACCTGGAAGAGGATACAGTCACTCTGGAAGTATTAGTGGCTCCAGCAGTTCCATCATG

TGAAGTACCCTCTTCTGCTCTGAGTGGAACTGTGGTAGAGCTACGATGTCAAGACAAAGAAGG

GAATCCAGCTCCTGAATACACATGGTTTAAGGATGGCATCCGTTTGCTAGAAAATCCCAGACT

TGGCTCCCAAAGCACCAACAGCTCATACACAATGAATACAAAAACTGGAACTCTGCAATTTAA

TACTGTTTCCAAACTGGACACTGGAGAATATTCCTGTGAAGCCCGCAATTCTGTTGGATATCG

CAGGTGTCCTGGGAAACGAATGCAAGTAGATGATCTCAACATAAGTGGCATCATAGCAGCCGT

AGTAGTTGTGGCCTTAGTGATTTCCGTTTGTGGCCTTGGTGTATGCTATGCTCAGAGGAAAGG

CTACTTTTCAAAAGAAACCTCCTTCCAGAAGAGTAATTCTTCATCTAAAGCCACGACAATGAG

TGAAAATGTGCAGTGGCTCACGCCTGTAATCCCAGCACTTTGGAAGGCCGCGGCGGGCGGATC

ACGAGGTCAGGAGTTC**TAG**ACCAGTCTGGCCAATATGGTGAAACCCCATCTCTACTAAAATAC

AAAAATTAGCTGGGCATGGTGGCATGTGCCTGCAGTTCCAGCTGCTTGGGAGACAGGAGAATC

ACTTGAACCCGGGAGGCGGAGGTTGCAGTGAGCTGAGATCACGCCACTGCAGTCCAGCCTGGG

TAACAGAGCAAGATTCCATCTCAAAAAATAAAATAAATAAATAAATAAATACTGGTTTTTACC

TGTAGAATTCTTACAATAAATATAGCTTGATATTC

FIGURE 336

MARRSRHRLLLLLLRYLVVALGYHKAYGFSAPKDQQVVTAVEYQEAILACKTPKKTVSSRLEW
KKLGRSVSFVYYQQTLQGDFKNRAEMIDFNIRIKNVTRSDAGKYRCEVSAPSEQGQNLEEDTV
TLEVLVAPAVPSCEVPSSALSGTVVELRCQDKEGNPAPEYTWFKDGIRLLENPRLGSQSTNSS
YTMNTKTGTLQFNTVSKLDTGEYSCEARNSVGYRRCPGKRMQVDDLNISGIIAAVVVVALVIS
VCGLGVCYAQRKGYFSKETSFQKSNSSSKATTMSENVQWLTPVIPALWKAAAGGSRGQEF

Important features:

Signal peptide:

amino acids 1-20

Transmembrane domain:

amino acids 130-144, 238-258

N-glycosylation site.

amino acids 98-102, 187-191, 236-240, 277-281

Casein kinase II phosphorylation site.

amino acids 39-43, 59-63, 100-104, 149-153, 205-209, 284-288

N-myristoylation site.

amino acids 182-188, 239-245, 255-261, 257-263, 305-311

Amidation site.

amino acids 226-230

FIGURE 337

GGAGCCGCCCTGGGTGTCAGCGGCTCGGCTCCCGCGCACGCTCCGGCCGTCGCGCAGCCTCGG

CACCTGCAGGTCCGTGCGTCCCGCGGCTGGCGCCCCTGACTCCGTCCCGGCCAGGGAGGGCC**A**

TGATTTCCCTCCCGGGGCCCCTGGTGACCAACTTGCTGCGGTTTTTGTTCCTGGGGCTGAGTG

CCCTCGCGCCCCCCTCGCGGGCCCAGCTGCAACTGCACTTGCCCGCCAACCGGTTGCAGGCGG

TGGAGGGAGGGGAAGTGGTGCTTCCAGCGTGGTACACCTTGCACGGGGAGGTGTCTTCATCCC

AGCCATGGGAGGTGCCCTTTGTGATGTGGTTCTTCAAACAGAAAGAAAAGGAGGATCAGGTGT

TGTCCTACATCAATGGGGTCACAACAAGCAAACCTGGAGTATCCTTGGTCTACTCCATGCCCT

CCCGGAACCTGTCCCTGCGGCTGGAGGGTCTCCAGGAGAAAGACTCTGGCCCCTACAGCTGCT

CCGTGAATGTGCAAGACAAACAAGGCAAATCTAGGGGCCACAGCATCAAAACCTTAGAACTCA

ATGTACTGGTTCCTCCAGCTCCTCCATCCTGCCGTCTCCAGGGTGTGCCCCATGTGGGGGCAA

ACGTGACCCTGAGCTGCCAGTCTCCAAGGAGTAAGCCCGCTGTCCAATACCAGTGGGATCGGC

AGCTTCCATCCTTCCAGACTTTCTTTGCACCAGCATTAGATGTCATCCGTGGGTCTTTAAGCC

TCACCAACCTTTCGTCTTCCATGGCTGGAGTCTATGTCTGCAAGGCCCACAATGAGGTGGGCA

CTGCCCAATGTAATGTGACGCTGGAAGTGAGCACAGGGCCTGGAGCTGCAGTGGTTGCTGGAG

CTGTTGTGGGTACCCTGGTTGGACTGGGGTTGCTGGCTGGGCTGGTCCTCTTGTACCACCGCC

GGGGCAAGGCCCTGGAGGAGCCAGCCAATGATATCAAGGAGGATGCCATTGCTCCCCGGACCC

TGCCCTGGCCCAAGAGCTCAGACACAATCTCCAAGAATGGGACCCTTTCCTCTGTCACCTCCG

CACGAGCCCTCCGGCCACCCCATGGCCCTCCCAGGCCTGGTGCATTGACCCCCACGCCCAGTC

TCTCCAGCCAGGCCCTGCCCTCACCAAGACTGCCCACGACAGATGGGGCCCACCCTCAACCAA

TATCCCCCATCCCTGGTGGGGTTTCTTCCTCTGGCTTGAGCCGCATGGGTGCTGTGCCTGTGA

TGGTGCCTGCCCAGAGTCAAGCTGGCTCTCTGGTA**TGA**TGACCCCACCACTCATTGGCTAAAG

GATTTGGGGTCTCTCCTTCCTATAAGGGTCACCTCTAGCACAGAGGCCTGAGTCATGGGAAAG

AGTCACACTCCTGACCCTTAGTACTCTGCCCCCACCTCTCTTTACTGTGGGAAAACCATCTCA

GTAAGACCTAAGTGTCCAGGAGACAGAAGGAGAAGAGGAAGTGGATCTGGAATTGGGAGGAGC

CTCCACCCACCCCTGACTCCTCCTTATGAAGCCAGCTGCTGAAATTAGCTACTCACCAAGAGT

GAGGGGCAGAGACTTCCAGTCACTGAGTCTCCCAGGCCCCCTTGATCTGTACCCCACCCCTAT

CTAACACCACCCTTGGCTCCCACTCCAGCTCCCTGTATTGATATAACCTGTCAGGCTGGCTTG

GTTAGGTTTTACTGGGGCAGAGGATAGGGAATCTCTTATTAAAACTAACATGAAATATGTGTT

GTTTTCATTTGCAAATTTAAATAAAGATACATAATGTTTGTATGAAAAA

FIGURE 338

MISLPGPLVTNLLRFLFLGLSALAPPSRAQLQLHLPANRLQAVEGGEVVLPAWYTLHGEVSSS
QPWEVPFVMWFFKQKEKEDQVLSYINGVTTSKPGVSLVYSMPSRNLSLRLEGLQEKDSGPYSC
SVNVQDKQGKSRGHSIKTLELNVLVPPAPPSCRLQGVPHVGANVTLSCQSPRSKPAVQYQWDR
QLPSFQTFFAPALDVIRGSLSLTNLSSSMAGVYVCKAHNEVGTAQCNVTLEVSTGPGAAVVAG
AVVGTLVGLGLLAGLVLLYHRRGKALEEPANDIKEDAIAPRTLPWPKSSDTISKNGTLSSVTS
ARALRPPHGPPRPGALTPTPSLSSQALPSPRLPTTDGAHPQPISPIPGGVSSSGLSRMGAVPV
MVPAQSQAGSLV

Important features:

Signal peptide:

amino acids 1-29

Transmembrane domain:

amino acids 245-267

N-glycosylation site.

amino acids 108-112, 169-173, 213-217, 236-240, 307-311

N-myristoylation site.

amino acids 90-96, 167-173, 220-226, 231-237, 252-258, 256-262, 262-268, 308-314, 363-369, 364-370

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 164-175

FIGURE 339

GCGAGAACCTTTGCACGCGCACAAACTACGGGGACGATTTCTGATTGATTTTTGGCGCTTTCGATCCACCCTCCT
CCCTTCTC**ATG**GGACTTTGGGGACAAAGCGTCCCGACCGCCTCGAGCGCTCGAGCAGGGCGCTATCCAGGAGCCA
GGACAGCGTCGGGAACCAGACCATGGCTCCTGGACCCCAAGATCCTTAAGTTCGTCGTCTTCATCGTCGCGGTTC
TGCTGCCGGTCCGGGTTGACTCTGCCACCATCCCCCGGCAGGACGAAGTTCCCCAGCAGACAGTGGCCCCACAGC
AACAGAGGCGCAGCCTCAAGGAGGAGGAGTGTCCAGCAGGATCTCATAGATCAGAATATACTGGAGCCTGTAACC
CGTGCACAGAGGGTGTGGATTACACCATTGCTTCCAACAATTTGCCTTCTTGCCTGCTATGTACAGTTTGTAAAT
CAGGTCAAACAAATAAAAGTTCCTGTACCACGACCAGAGACACCGTGTGTCAGTGTGAAAAAGGAAGCTTCCAGG
ATAAAAACTCCCCTGAGATGTGCCGGACGTGTAGAACAGGGTGTCCCAGAGGGATGGTCAAGGTCAGTAATTGTA
CGCCCCGGAGTGACATCAAGTGCAAAAATGAATCAGCTGCCAGTTCCACTGGGAAAACCCCAGCAGCGGAGGAGA
CAGTGACCACCATCCTGGGGATGCTTGCCTCTCCCTATCACTACCTTATCATCATAGTGGTTTTAGTCATCATTT
TAGCTGTGGTTGTGGTTGGCTTTTCATGTCGGAAGAAATTCATTTCTTACCTCAAAGGCATCTGCTCAGGTGGTG
GAGGAGGTCCCGAACGTGTGCACAGAGTCCTTTTCCGGCGGCGTTCATGTCCTTCACGAGTTCCTGGGGCGGAGG
ACAATGCCCGCAACGAGACCCTGAGTAACAGATACTTGCAGCCCACCCAGGTCTCTGAGCAGGAAATCCAAGGTC
AGGAGCTGGCAGAGCTAACAGGTGTGACTGTAGAGTCGCCAGAGGAGCCACAGCGTCTGCTGGAACAGGCAGAAG
CTGAAGGGTGTCAGAGGAGGAGGCTGCTGGTTCCAGTGAATGACGCTGACTCCGCTGACATCAGCACCTTGCTGG
ATGCCTCGGCAACACTGGAAGAAGGACATGCAAAGGAAACAATTCAGGACCAACTGGTGGGCTCCGAAAAGCTCT
TTTATGAAGAAGATGAGGCAGGCTCTGCTACGTCCTGCCTG**TGA**AAGAATCTCTTCAGGAAACCAGAGCTTCCCT
CATTTACCTTTTCTCCTACAAAGGGAAGCAGCCTGGAAGAAACAGTCCAGTACTTGACCCATGCCCCAACAAACT
CTACTATCCAATATGGGGCAGCTTACCAATGGTCCTAGAACTTTGTTAACGCACTTGGAGTAATTTTTATGAAAT
ACTGCGTGTGATAAGCAAACGGGAGAAATTTATATCAGATTCTTGGCTGCATAGTTATACGATTGTGTATTAAGG
GTCGTTTTAGGCCACATGCGGTGGCTCATGCCTGTAATCCCAGCACTTTGATAGGCTGAGGCAGGTGGATTGCTT
GAGCTCGGGAGTTTGAGACCAGCCTCATCAACACAGTGAAACTCCATCTCAATTTAAAAAGAAAAAAAGTGGTTT
TAGGATGTCATTCTTTGCAGTTCTTCATCATGAGACAAGTCTTTTTTTCTGCTTCTTATATTGCAAGCTCCATCT
CTACTGGTGTGTGCATTTAATGACATCTAACTACAGATGCCGCACAGCCACAATGCTTTGCCTTATAGTTTTTTA
ACTTTAGAACGGGATTATCTTGTTATTACCTGTATTTTCAGTTTCGGATATTTTTGACTTAATGATGAGATTATC
AAGACGTAGCCCTATGCTAAGTCATGAGCATATGGACTTACGAGGGTTCGACTTAGAGTTTTGAGCTTTAAGATA
GGATTATTGGGGCTTACCCCCACCTTAATTAGAGAAACATTTATATTGCTTACTACTGTAGGCTGTACATCTCTT
TTCCGATTTTTTGTATAATGATGTAAACATGGAAAAACTTTAGGAAATGCACTTATTAGGCTGTTTACATGGGTTG
CCTGGATACAAATCAGCAGTCAAAAATGACTAAAAATATAACTAGTGACGGAGGGAGAAATCCTCCCTCTGTGGG
AGGCACTTACTGCATTCCAGTTCTCCCTCCTGCGCCCTGAGACTGGACCAGGGTTTGATGGCTGGCAGCTTCTCA
AGGGGCAGCTTGTCTTACTTGTTAATTTTAGAGGTATATAGCCATATTTATTTATAAATAAATATTTATTTATTT
ATTTATAAGTAGATGTTTACATATGCCCAGGATTTTGAAGAGCCTGGTATCTTTGGGAAGCCATGTGTCTGGTTT
GTCGTGCTGGGACAGTCATGGGACTGCATCTTCCGACTTGTCCACAGCAGATGAGGACAGTGAGAATTAAGTTAG
ATCCGAGACTGCGAAGAGCTTCTCTTTCAAGCGCCATTACAGTTGAACGTTAGTGAATCTTGAGCCTCATTTGGG
CTCAGGGCAGAGCAGGTGTTTATCTGCCCCGGCATCTGCCATGGCATCAAGAGGGAAGAGTGGACGGTGCTTGGG
AATGGTGTGAAATGGTTGCCGACTCAGGCATGGATGGGCCCCTCTCGCTTCTGGTGGTCTGTGAACTGAGTCCCT
GGGATGCCTTTTAGGGCAGAGATTCCTGAGCTGCGTTTTAGGGTACAGATTCCCTGTTTGAGGAGCTTGGCCCCT
CTGTAAGCATCTGACTCATCTCAGAGATATCAATTCTTAAACACTGTGACAACGGGATCTAAAATGGCTGACACA
TTTGTCCTTGTGTCACGTTCCATTATTTTATTTAAAAACCTCAGTAATCGTTTTAGCTTCTTTCCAGCAAACTCT
TCTCCACAGTAGCCCAGTCGTGGTAGGATAAATTACGGATATAGTCATTCTAGGGGTTTCAGTCTTTTCCATCTC
AAGGCATTGTGTGTTTTGTTCCGGGACTGGTTTGGCTGGGACAAAGTTAGAACTGCCTGAAGTTCGCACATTCAG
ATTGTTGTGTCCATGGAGTTTTAGGAGGGGATGGCCTTTCCGGTCTTCGCACTTCCATCCTCTCCCACTTCCATC
TGGCGTCCCACACCTTGTCCCCTGCACTTCTGGATGACACAGGGTGCTGCTGCCTCCTAGTCTTTGCCTTTGCTG
GGCCTTCTGTGCAGGAGACTTGGTCTCAAAGCTCAGAGAGAGCCAGTCCGGTCCCAGCTCCTTTGTCCCTTCCTC
AGAGGCCTTCCTTGAAGATGCATCTAGACTACCAGCCTTATCAGTGTTTAAGCTTATTCCTTTAACATAAGCTTC
CTGACAACATGAAATTGTTGGGGTTTTTTGGCGTTGGTTGATTTGTTTAGGTTTTGCTTTATACCCGGGCCAAAT
AGCACATAACACCTGGTTATATATGAAATACTCATATGTTTATGACCAAAATAAATATGAAACCTCATRTTAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 340

MGLWGQSVPTASSARAGRYPGARTASGTRPWLLDPKILKFVVFIVAVLLPVRVDSATIPRQDEVPQQTVAPQQQR
RSLKEEECPAGSHRSEYTGACNPCTEGVDYTIASNNLPSCLLCTVCKSGQTNKSSCTTTRDTVCQCEKGSFQDKN
SPEMCRTCRTGCPRGMVKVSNCTPRSDIKCKNESAASSTGKTPAAEETVTTILGMLASPYHYLIIIVVLVIILAV
VVVGFSCRKKFISYLKGICSGGGGGPERVHRVLFRRRSCPSRVPGAEDNARNETLSNRYLQPTQVSEQEIQGQEL
AELTGVTVESPEEPQRLLEQAEAEGCQRRRLLVPVNDADSADISTLLDASATLEEGHAKETIQDQLVGSEKLFYE
EDEAGSATSCL

Important features:

Transmembrane domains:

amino acids 35-52, 208-230

N-glycosylation sites.

amino acids 127-131, 182-186, 277-281

Glycosaminoglycan attachment site.

amino acids 245-249

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 260-264

N-myristoylation sites.

amino acids 21-27, 86-92, 102-108, 161-167, 242-248, 270-276, 297-303, 380-386

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

amino acids 185-193

TNFR/NGFR cysteine-rich region.

amino acids 99-139

FIGURE 341

GCCTCTGAATTGTTGGGCAGTCTGGCAGTGGAGCTCTCCCCGGTCTGACAGCCACTCCAGAGG

CC**ATG**CTTCGTTTCTTGCCAGATTTGGCTTTCAGCTTCCTGTTAATTCTGGCTTTGGGCCAGG

CAGTCCAATTTCAAGAATATGTCTTTCTCCAATTTCTGGGCTTAGATAAGGCGCCTTCACCCC

AGAAGTTCCAACCTGTGCCTTATATCTTGAAGAAAATTTTCCAGGATCGCGAGGCAGCAGCGA

CCACTGGGGTCTCCCGAGACTTATGCTACGTAAAGGAGCTGGGCGTCCGCGGGAATGTACTTC

GCTTTCTCCCAGACCAAGGTTTCTTTCTTTACCCAAAGAAAATTTCCCAAGCTTCCTCCTGCC

TGCAGAAGCTCCTCTACTTTAACCTGTCTGCCATCAAAGAAAGGGAACAGTTGACATTGGCCC

AGCTGGGCCTGGACTTGGGGCCCAATTCTTACTATAACCTGGGACCAGAGCTGGAACTGGCTC

TGTTCCTGGTTCAGGAGCCTCATGTGTGGGGCCAGACCACCCCTAAGCCAGGTAAAATGTTTG

TGTTGCGGTCAGTCCCATGGCCACAAGGTGCTGTTCACTTCAACCTGCTGGATGTAGCTAAGG

ATTGGAATGACAACCCCCGGAAAAATTTCGGGTTATTCCTGGAGATACTGGTCAAAGAAGATA

GAGACTCAGGGGTGAATTTTCAGCCTGAAGACACCTGTGCCAGACTAAGATGCTCCCTTCATG

CTTCCCTGCTGGTGGTGACTCTCAACCCTGATCAGTGCCACCCTTCTCGGAAAAGGAGAGCAG

CCATCCCTGTCCCCAAGCTTTCTTGTAAGAACCTCTGCCACCGTCACCAGCTATTCATTAACT

TCCGGGACCTGGGTTGGCACAAGTGGATCATTGCCCCCAAGGGGTTCATGGCAAATTACTGCC

ATGGAGAGTGTCCCTTCTCACTGACCATCTCTCTCAACAGCTCCAATTATGCTTTCATGCAAG

CCCTGATGCATGCCGTTGACCCAGAGATCCCCCAGGCTGTGTGTATCCCCACCAAGCTGTCTC

CCATTTCCATGCTCTACCAGGACAATAATGACAATGTCATTCTACGACATTATGAAGACATGG

TAGTCGATGAATGTGGGTGTGGG**TAG**GATGTCAGAAATGGGAATAGAAGGAGTGTTCTTAGGG

TAAATCTTTTAATAAAACTACCTATCTGGTTTATGACCACTTAGATCGAAATGTC

FIGURE 342

MLRFLPDLAFSFLLILALGQAVQFQEYVFLQFLGLDKAPSPQKFQPVPYILKKIFQDREAAAT
TGVSRDLCYVKELGVRGNVLRFLPDQGFFLYPKKISQASSCLQKLLYFNLSAIKEREQLTLAQ
LGLDLGPNSYYNLGPELELALFLVQEPHVWGQTTPKPGKMFVLRSVPWPQGAVHFNLLDVAKD
WNDNPRKNFGLFLEILVKEDRDSGVNFQPEDTCARLRCSLHASLLVVTLNPDQCHPSRKRRAA
IPVPKLSCKNLCHRHQLFINFRDLGWHKWIIAPKGFMANYCHGECPFSLTISLNSSNYAFMQA
LMHAVDPEIPQAVCIPTKLSPISMLYQDNNDNVILRHYEDMVVDECGCG

Important features:

Signal peptide:

amino acids 1-21

N-glycosylation sites.

amino acids 112-116, 306-310

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 96-100

N-myristoylation site.

amino acids 77-83

TGF-beta family proteins.

amino acids 264-299, 327-341, 345-364

FIGURE 343

CCCACGCGTCCGGCCTTCTCTCTGGACTTTGCATTTCCATTCCTTTTCATTGACAAACTGACTTTTTTTATTTCT
TTTTTTCCATCTCTGGGCCAGCTTGGGATCCTAGGCCGCCCTGGGAAGACATTTGTGTTTTACACACATAAGGAT
CTGTGTTTGGGGTTTCTTCTTCCTCCCCTGACATTGGCATTGCTTAGTGGTTGTGTGGGGAGGGAGACCACGTGG
GCTCAGTGCTTGCTTGCACTTATCTGCCTAGGTACATCGAAGTCTTTTGACCTCCATACAGTGATTATGCCTGTC
ATCGCTGGTGGTATCCTGGCGGCCTTGCTCCTGCTGATAGTTGTCGTGCTCTGTCTTTACTTCAAAATACACAAC
GCGCTAAAAGCTGCAAAGGAACCTGAAGCTGTGGCTGTAAAAAATCACAACCCAGACAAGGTGTGGTGGGCCAAG
AACAGCCAGGCCAAAACCATTGCCACGGAGTCTTGTCCTGCCCTGCAGTGCTGTGAAGGATATAGAATGTGTGCC
AGTTTTGATTCCCTGCCACCTTGCTGTTGCGACATAAATGAGGGCCTCTGAGTTAGGAAAGGCTCCCTTCTCAAA
GCAGAGCCCTGAAGACTTCAATGATGTCAATGAGGCCACCTGTTTGTGATGTGCAGGCACAGAAGAAAGGCACAG
CTCCCCATCAGTTTCATGGAAAATAACTCAGTGCCTGCTGGGAACCAGCTGCTGGAGATCCCTACAGAGAGCTTC
CACTGGGGGCAACCCTTCCAGGAAGGAGTTGGGGAGAGAGAACCCTCACTGTGGGGAATGCTGATAAACCAGTCA
CACAGCTGCTCTATTCTCACACAAATCTACCCCTTGCGTGGCTGGAACTGACGTTTCCCTGGAGGTGTCCAGAAA
GCTGATGTAACACAGAGCCTATAAAAGCTGTCGGTCCTTAAGGCTGCCCAGCGCCTTGCCAAA**ATG**GAGCTTGTA
AGAAGGCTCATGCCATTGACCCTCTTAATTCTCTCCTGTTTGGCGGAGCTGACAATGGCGGAGGCTGAAGGCAAT
GCAAGCTGCACAGTCAGTCTAGGGGGTGCCAATATGGCAGAGACCCACAAAGCCATGATCCTGCAACTCAATCCC
AGTGAGAACTGCACCTGGACAATAGAAAGACCAGAAAACAAAAGCATCAGAATTATCTTTTCCTATGTCCAGCTT
GATCCAGATGGAAGCTGTGAAAGTGAAAACATTAAAGTCTTTGACGGAACCTCCAGCAATGGGCCTCTGCTAGGG
CAAGTCTGCAGTAAAAACGACTATGTTCCTGTATTTGAATCATCATCCAGTACATTGACGTTTCAAATAGTTACT
GACTCAGCAAGAATTCAAAGAACTGTCTTTGTCTTCTACTACTTCTTCTCTCCTAACATCTCTATTCCAAACTGT
GGCGGTTACCTGGATACCTTGGAAGGATCCTTCACCAGCCCCAATTACCCAAAGCCGCATCCTGAGCTGGCTTAT
TGTGTGTGGCACATACAAGTGGAGAAAGATTACAAGATAAAACTAAACTTCAAAGAGATTTTCCTAGAAATAGAC
AAACAGTGCAAATTTGATTTTCTTGCCATCTATGATGGCCCCTCCACCAACTCTGGCCTGATTGGACAAGTCTGT
GGCCGTGTGACTCCCACCTTCGAATCGTCATCAAACTCTCTGACTGTCGTGTTGTCTACAGATTATGCCAATTCT
TACCGGGGATTTTCTGCTTCCTACACCTCAATTTATGCAGAAAACATCAACACTACATCTTTAACTTGCTCTTCT
GACAGGATGAGAGTTATTATAAGCAAATCCTACCTAGAGGCTTTTAACTCTAATGGGAATAACTTGCAACTAAAA
GACCCAACTTGCAGACCAAAATTATCAAATGTTGTGGAATTTTCTGTCCCTCTTAATGGATGTGGTACAATCAGA
AAGGTAGAAGATCAGTCAATTACTTACACCAATATAATCACCTTTTCTGCATCCTCAACTTCTGAAGTGATCACC
CGTCAGAAACAACTCCAGATTATTGTGAAGTGTGAAATGGGACATAATTCTACAGTGGAGATAATATACATAACA
GAAGATGATGTAATACAAAGTCAAAATGCACTGGGCAAATATAACACCAGCATGGCTCTTTTTGAATCCAATTCA
TTTGAAAAGACTATACTTGAATCACCATATTATGTGGATTTGAACCAAACTCTTTTTGTTCAAGTTAGTCTGCAC
ACCTCAGATCCAAATTTGGTGGTGTTTCTTGATACCTGTAGAGCCTCTCCCACCTCTGACTTTGCATCTCCAACC
TACGACCTAATCAAGAGTGGATGTAGTCGAGATGAAACTTGTAAGGTGTATCCCTTATTTGGACACTATGGGAGA
TTCCAGTTTAATGCCTTTAAATTCTTGAGAAGTATGAGCTCTGTGTATCTGCAGTGTAAAGTTTTGATATGTGAT
AGCAGTGACCACCAGTCTCGCTGCAATCAAGGTTGTGTCTCCAGAAGCAAACGAGACATTTCTTCATATAAATGG
AAAACAGATTCCATCATAGGACCCATTCGTCTGAAAAGGGATCGAAGTGCAAGTGGCAATTCAGGATTTCAGCAT
GAAACACATGCGGAAGAAACTCCAAACCAGCCTTTCAACAGTGTGCATCTGTTTTCCTTCATGGTTCTAGCTCTG
AATGTGGTGACTGTAGCGACAATCACAGTGAGGCATTTTGTAAATCAACGGGCAGACTACAAATACCAGAAGCTG
CAGAACTAT**TAA**CTAACAGGTCCAACCCTAAGTGAGACATGTTTCTCCAGGATGCCAAAGGAAATGCTACCTCGT
GGCTACACATATTATGAATAAATGAGGAAGGGCCTGAAAGTGACACACAGGCCTGCATGTAAAAAAA

DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 2
CONTENANT LES PAGES 1 À 343

NOTE : Pour les tomes additionels, veuillez contacter le Bureau canadien des brevets

JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

THIS IS VOLUME 1 OF 2
CONTAINING PAGES 1 TO 343

NOTE: For additional volumes, please contact the Canadian Patent Office

NOM DU FICHIER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

MSTMFADTLLIVFISVCTALLAEGITWVLVYRTDKYKRLKAEVEKQSKKLEKKKETITESAGR
QQKKKIERQEEKLKNNNRDLSMVRMKSMFAIGFCFTALMGMFNSIFDGRVVAKLPFTPLSYIQ
GLSHRNLLGDDTTDCSFIFLYILCTMSIRQNIQKILGLAPSRAATKQAGGFLGPPPPSGKFS

Important features:

Signal peptide:

amino acids 1-22

N-myristoylation sites.

amino acids 103-109, 163-169

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 53-57