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- (54) **CANINE IL-13 IMMUNOREGULATORY PROTEINS AND USES THEREOF**
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See application file for complete search history.

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(57) **ABSTRACT**

The present invention relates to canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, and/or feline GM-CSF proteins; to canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, and/or feline GM-CSF nucleic acid molecules, including those that encode canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, and/or feline GM-CSF proteins, respectively; to antibodies raised against such proteins; and to inhibitory compounds that regulate such proteins. The present invention also includes methods to identify and obtain such proteins, nucleic acid molecules, antibodies, and inhibitory compounds. Also included in the present invention are therapeutic compositions comprising such proteins, nucleic acid molecules, antibodies and/or inhibitory compounds as well as the use of such therapeutic compositions to regulate an immune response in an animal.

**12 Claims, No Drawings**

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## CANINE IL-13 IMMUNOREGULATORY PROTEINS AND USES THEREOF

**Matter enclosed in heavy brackets [ ] appears in the original patent but forms no part of this reissue specification; matter printed in italics indicates the additions made by reissue.**

### CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of U.S. patent application Ser. No. 09/322,409, filed May 28, 1999, entitled "CANINE AND FELINE IMMUNOREGULATORY PROTEINS, NUCLEIC ACID MOLECULES, AND USES THEREOF"; which claims priority to U.S. Provisional Patent Application Ser. No. 60/087,306, filed May 29, 1998, entitled "CANINE INTERLEUKIN-4 AND FLT-3 LIGAND PROTEINS, NUCLEIC ACID MOLECULES, AND USES THEREOF"; each of which is incorporated herein by reference in its entirety.

### FIELD OF THE INVENTION

The present invention relates to canine interleukin-4, canine or feline Flt-3 ligand, canine and feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecules, proteins encoded by such nucleic acid molecules, antibodies raised against such proteins and/or inhibitors of such proteins or nucleic acid molecules. The present invention also includes therapeutic compositions comprising such nucleic acid molecules, proteins, antibodies and/or inhibitors, as well as their use to regulate an immune response in an animal.

### BACKGROUND OF THE INVENTION

Regulating immune responses in animals is important in disease management. Immune responses can be regulated by modifying the activity of immunoregulatory molecules and immune cells.

Several immunoregulatory molecules have been found in humans and other mammal species. Interleukin-4, produced by activated type 2 helper cells ( $T_H2$  cells), has a number of functions. These functions include promotion of naive T cells and B cells to differentiate and proliferate. IL-4 promotes  $T_H2$  differentiation and inhibits  $T_H1$  development. FMS-like tyrosine kinase 3, (Flt-3 ligand) stimulates the expansion and mobilization of hematopoietic precursor cell stimulating activity. CD40 is a type I transmembrane protein expressed on antigen presenting cells, such as B lymphocytes, and other types of cells such as endothelial cells, epithelial cells, and fibroblasts. CD40 ligand (also known as CD154) is a type II transmembrane protein that is preferentially expressed on activated T lymphocytes. The CD40-CD154 interaction regulates diverse pathways of the immune system, including B cell proliferation, immunoglobulin production and class switching by B cells, activation and clonal expansion of T cells, activity of antigen presenting cells, growth and differentiation of epithelial cells, and regulation of inflammatory responses at mucosal and cutaneous sites. Interleukin-5 is produced by activated type 2 helper cells ( $T_H2$ ), mast cells, and eosinophils. Its main functions include promotion of growth and differentiation of eosinophils and generation of cytotoxic T cells from thymocytes. Interleukin-13 is produced by  $T_H1$  and  $T_H2$  cells, and promotes growth and differentiations of B cells, up-regulation of MHC class II and CD23 expression on

monocytes/macrophages and B cells; and inhibition of production of inflammatory cytokines such as IL-1 $\alpha$ , IL-1 $\beta$ , IL-6, IL-8, IL-10, IL-12, among others. Interferon alpha is an antiviral protein that has three major functions: it inhibits viral replication by activating cellular genes that destroy mRNA and inhibit protein translation, it induces MHC class I expression in non virally-infected cells, increasing resistance to NK cells, and can activate NK cells. GM-CSF, (granulocyte-macrophage colony-stimulating factor) stimulates the production of granulocytes and macrophages.

Prior investigators have disclosed sequences encoding feline IL-4 (Lerner et al., Genbank Accession No. U39634); porcine L-4 (Zhou et al., Genbank Accession No. L12991); bovine IL-4 (Heussler, V.T., et al., Gene. vol. 114, pp. 273-278, 1992); ovine IL-4 (Seow, H.-F., et al., Gene, vol. 124, pp. 291-293, 1993); human IL-4 (Yokota, T., et al., Proc. Natl. Acad. Sci. U.S.A., vol. 83(16), pp. 5894-5898, 1986); and murine IL-4 (Sideras, P., et al., Adv. Exp. Med. Biol., vol. 213, pp. 227-236, 1987). Prior investigators have disclosed sequences encoding murine Flt-3 ligand (McClanahan et al., Genbank Accession No. U44024); and human Flt-3 ligand (Lyman et al., Blood, vol. 83, pp. 2795-2801, 1994). Prior investigators have disclosed sequences encoding human CD40 (Stamenkovic et al., EMBO J., vol. 8:1403-1410, 1989, GenBank Accession No. X60592), bovine CD40 (Hirano et al., Immunology, vol. 90, pp. 294-300, 1997), GenBank Accession No. U57745), and murine CD40 (Grimaldi et al., J. Immunol., vol. 143, pp.3921-3926, 1992; Torres and Clark, J. Immunol., vol. 148, pp. 620-626, 1992, GenBank Accession No. M83312). Prior investigators have disclosed sequences encoding human CD154 (Graf et al., Eur. J. Immunol., vol. 22, pp. 3191-3194, 1992; Hollenbaugh, et al., EMBO J., vol. 11:4313-4321, 1992; Gauchat et al., FEBS lett., vol., 315, pp. 259-266, 1993; GenBank Accession Nos L07414, X68550, Z15017, X67878, respectively); bovine CD154 (Mertens et al., Immunogenetics, vol. 42, pp. 430-431, GenBank Accession No. Z48468); and murine CD154 (Armitage et al., Nature, vol. 357, pp. 80-82; 1992, GenBank Accession No. X65453). Prior investigators have disclosed sequences encoding feline interleukin-5 (Padrid et al., Am. J. Vet. Res., vol. 59, pp. 1263-1269, 1998, GenBank Accession No. AF025436) and human interleukin-5 (Azuma et al., Nucleic Acids Res., vol. 14, pp. 9149-9158, 1986, GenBank Accession No. X04688). Prior investigators have disclosed sequences encoding human interleukin-13 (McKenzie et al., Proc. Natl Acad. Sci. USA, vol. 90, pp. 3735-3739, 1993; Minty et al., Nature, vol. 362, pp. 248-250, 1993, GenBank Accession Nos L06801 and X69079, respectively); murine interleukin-13 (Brown et al., J. Immunol., vol. 142, pp. 679-687, 1989, GenBank Accession No M23504); and rat interleukin-13 (Lakkis et al., Biochem. Biophys. Res. Commun., Vol. 197, pp. 612-618, 1993, GenBank Accession No. L26913). Prior investigators have disclosed sequences encoding feline interferon (Nakamura, N., Sudo, T., Matsuda, S., Yanai, A., Biosci. Biotechnol. Biochem. (1992) Vol: 56 pp 211-214, GenBank accession # E02521). Prior investigators have also disclosed sequences encoding feline GM-CSF (direct submission to GenBank, Accession No. AF053007)

There remains a need for compounds and methods to regulate an immune response by manipulation of the function of canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF.

### SUMMARY OF THE INVENTION

The present invention relates to canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine

or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecules, proteins encoded by such nucleic acid molecules, antibodies raised against such proteins and/or inhibitors of such proteins or nucleic acid molecules. Identification of the nucleic acid molecules of the present invention is unexpected because initial attempts to obtain nucleic acid molecules using PCR were unsuccessful. After numerous attempts, the inventors discovered specific primers that were useful for isolating such nucleic acid molecules.

One embodiment of the present invention is an isolated nucleic acid molecule selected from the group consisting of: (a) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, and/or SEQ ID NO:21 or a homolog thereof, wherein said homolog has an at least about 50 contiguous nucleotide region identical in sequence to a 50 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, and/or SEQ ID NO:21; (b) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and/or SEQ ID NO:37 or a homolog thereof, wherein said homolog has an at least 40 contiguous nucleotide region identical in sequence to a 40 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and/or SEQ ID NO:37; (c) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and/or SEQ ID NO:50, and/or a homolog thereof, wherein said homolog has an at least 30 contiguous nucleotide region identical in sequence to a 30 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and/or SEQ ID NO:50; (d) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and/or SEQ ID NO:59, and/or a homolog thereof, wherein said homolog has an at least 40 contiguous nucleotide region identical in sequence to a 40 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and/or SEQ ID NO:59; (e) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:60 and/or SEQ ID NO:62, and/or a homolog thereof, wherein said homolog has an at least 30 contiguous nucleotide region identical in sequence to a 30 contiguous nucleotide region of a nucleic acid molecule having a 3 nucleic acid sequence selected from the group consisting of SEQ ID NO:60 and/or SEQ ID NO:62; (f) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of

SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69 and/or SEQ ID NO:71, and/or a homolog thereof, wherein said homolog has an at least 45 contiguous nucleotide region identical in sequence to a 45 nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69 and/or SEQ ID NO:71; (g) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and/or SEQ ID NO:79, and/or a homolog thereof, wherein said homolog has an at least 35 contiguous nucleotide region identical in sequence to a 35 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and/or SEQ ID NO:79; (h) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and/or SEQ ID NO:87, and/or a homolog thereof, wherein said homolog has an at least 45 contiguous nucleotide region identical in sequence to a 45 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and/or SEQ ID NO:87; (i) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and/or SEQ ID NO:106, and/or a homolog thereof, wherein said homolog has an at least 15 contiguous nucleotide region identical to a 15 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and/or SEQ ID NO:106; (j) an isolated nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:155, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:172; and/or (k) an isolated nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:126.

Another embodiment of the present invention is an isolated nucleic acid molecule selected from the group consisting of: (a) a nucleic acid molecule having a nucleic acid sequence that is at least about 92 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, and/or SEQ ID NO:21; (b) a nucleic acid molecule having a nucleic acid sequence that is at least about 75 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24,

SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and/or SEQ ID NO:37; (c) a nucleic acid molecule having a nucleic acid sequence that is at least about 75 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and/or SEQ ID NO:50; (d) a nucleic acid molecule having a nucleic acid sequence that is at least about 70 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and/or SEQ ID NO:59; (e) a nucleic acid molecule having a nucleic acid sequence that is at least about 70 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:60 and/or SEQ ID NO:62; (f) a nucleic acid molecule having a nucleic acid sequence that is at least about 85 percent identical to a nucleic acid sequences selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, and/or SEQ ID NO:71; (g) a nucleic acid molecule having a nucleic acid sequence that is at least about 91 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and/or SEQ ID NO:79; (h) a nucleic acid molecule having a nucleic acid sequence that is at least about 90 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and/or SEQ ID NO:87; (i) a nucleic acid molecule having a nucleic acid sequence that is at least about 65 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and/or SEQ ID NO:106; (j) a nucleic acid molecule having a nucleic acid sequence that is selected from the group consisting of SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:155, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:169, SEQ ID NO:170 and/or SEQ ID NO:172; and/or (k) a nucleic acid molecule having a nucleic acid sequence that is selected from the group consisting of SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, and/or SEQ ID NO:126.

Yet another embodiment of the present invention is an isolated nucleic acid molecule selected from the group consisting of: (a) a nucleic acid molecule having a nucleic acid sequence encoding an IL-4 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:2 and/or SEQ ID NO:20 and/or (ii) a protein comprising a fragment of at least 20 amino acids of an amino acid sequences selected from the group consisting of SEQ ID NO:2 and/or SEQ ID NO:20; (b) a nucleic acid molecule having a nucleic acid sequence encoding a Flt-3 ligand protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 75 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ

ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34 and/or (ii) a protein comprising a fragment of at least 25 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34; (c) a nucleic acid molecule having a nucleic acid sequence encoding a Flt-3 ligand protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 75 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:44 and/or SEQ ID NO:49 and/or (ii) a protein comprising a fragment of at least 25 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:44 and/or SEQ ID NO:49; (d) a nucleic acid molecule having a nucleic acid sequence encoding a CD40 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 70 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:53 and/or SEQ ID NO:58 and/or (ii) a protein comprising a fragment of at least 30 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:53 and/or SEQ ID NO:58; (e) a nucleic acid molecule having a nucleic acid sequence encoding a CD40 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 60 percent identical to an amino acid sequence comprising SEQ ID NO:61 and/or (ii) a protein comprising a fragment of at least 20 amino acids of an amino acid sequence comprising SEQ ID NO:61; (f) a nucleic acid molecule having a nucleic acid sequence encoding a CD154 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 80 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:65 and/or SEQ ID NO:70, and/or (ii) a protein comprising a fragment of at least 35 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:65 and/or SEQ ID NO:70; (g) a nucleic acid molecule having a nucleic acid sequence encoding a CD154 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:73 and/or SEQ ID NO:78, and/or (ii) a protein comprising a fragment of at least 50 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:73 and/or SEQ ID NO:78; (h) a nucleic acid molecule having a nucleic acid sequence encoding an IL-5 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:81 and/or SEQ ID NO:86 and/or (ii) a protein comprising a fragment of at least 20 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:81 and/or SEQ ID NO:86; (i) a nucleic acid molecule having a nucleic acid sequence encoding an IL-13 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 70 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and/or SEQ ID NO:105 and/or (ii) a protein comprising a fragment of at least 15 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and/or SEQ ID NO:105; (j) a nucleic acid molecule having a nucleic acid sequence encoding an interferon alpha protein having an amino acid sequence that is selected from the group consisting of amino acid sequence SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID

NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and/or SEQ ID NO:171; (k) a nucleic acid molecule having a nucleic acid sequence encoding a GMCSF protein having an amino acid sequence that is selected from the group consisting of amino acid sequence SEQ ID NO:120, SEQ ID NO:125, and/or (l) a nucleic acid molecule comprising a complement of any of said nucleic acid molecules as set forth in (a), (b), (c), (d), (e), (f), (g), (h), (i), (j), (k), wherein said IL-4 protein elicits an immune response against an IL-4 protein selected from the group consisting of SEQ ID NO:2 and/or SEQ ID NO:20 and/or is a protein with interleukin-4 activity, said Flt-3 ligand protein elicits an immune response against a Flt-3 ligand protein selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:44, and/or SEQ ID NO:49 and/or is a protein with Flt-3 ligand activity, said CD40 protein elicits an immune response against a CD40 protein selected from the group consisting of SEQ ID NO:53, SEQ ID NO:58, and/or SEQ ID NO:61 and/or is a protein with CD40 activity, said CD154 protein elicits an immune response against a CD154 protein selected from the group consisting of SEQ ID NO:65, SEQ ID NO:70, SEQ ID NO:73, and/or SEQ ID NO:78 and/or is a protein with CD154 activity, said IL-5 protein elicits an immune response against a IL-5 protein selected from the group consisting of SEQ ID NO:81 and/or SEQ ID NO:86 and/or is a protein with IL-5 activity, said IL-13 protein elicits an immune response against an IL-13 protein selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and/or SEQ ID NO:105 and/or is a protein with IL-13 activity, said interferon alpha protein elicits an immune response against an interferon alpha protein selected from the group consisting of SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and/or SEQ ID NO:171 and/or is a protein with interferon alpha activity, and/or said GMCSF protein elicits an immune response against a GMCSF protein selected from the group consisting of SEQ ID NO:120 and/or SEQ ID NO:125 and/or is a protein with GM-CSF activity.

The present invention also includes methods to produce any of the proteins of the present invention using nucleic acid molecules of the present invention and recombinantly using such nucleic acid molecules.

The present invention also includes an isolated protein selected from the group consisting of: (a) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:4, and/or SEQ ID NO:19; and/or (ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:2 and/or SEQ ID NO:20, wherein said isolated protein elicits an immune response against a canine IL-4 protein and/or has IL-4 activity; (b) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:9, SEQ ID NO:22, SEQ ID NO:25, SEQ ID NO:28,

SEQ ID NO:30, SEQ ID NO:33, and/or SEQ ID NO:36; and/or (ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34, wherein said isolated protein is capable of eliciting an immune response against a canine Flt-3 ligand protein and/or has Flt-3 activity; (c) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:46, and/or SEQ ID NO:48; and/or (ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:44 and/or SEQ ID NO:49, wherein said isolated protein is capable of eliciting an immune response against a feline Flt-3 ligand protein and/or has Flt-3 activity; (d) (i) an isolated protein of at least about 30 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 90 contiguous nucleotide region identical in sequence to a 90 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:55, and/or SEQ ID NO:57; and/or (ii) an isolated protein of at least about 30 amino acids in length, wherein said protein has an at least 30 contiguous amino acid region identical in sequence to a 30 contiguous amino acid region selected from the group consisting of SEQ ID NO:53, SEQ ID NO:58, wherein said isolated protein is capable of eliciting an immune response against a canine CD40 protein and/or has CD40 activity; (e) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence comprising SEQ ID NO:60; and/or (ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region comprising the amino acid sequence SEQ ID NO:61, wherein said isolated protein is capable of eliciting an immune response against a feline CD40 protein and/or has CD40 activity; (f) (i) an isolated protein of at least about 35 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 105 contiguous nucleotide region identical in sequence to a 105 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:67, and/or SEQ ID NO:69; and/or (ii) an isolated protein of at least about 35 amino acids in length, wherein said protein has an at least 35 contiguous amino acid region identical in sequence to a 35 contiguous amino acid region selected from the group consisting of SEQ ID NO:65 and/or SEQ ID NO:70, wherein said isolated protein is capable of eliciting an immune response against a canine CD154 protein and/or has CD154 activity; (g) (i) an isolated protein of at least about 50 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 150 contiguous nucleotide region identical in sequence to a 150

contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:75, and/or SEQ ID NO:77; and/or (ii) an isolated protein of at least about 50 amino acids in length, wherein said protein has an at least 50 contiguous amino acid region identical in sequence to a 50 contiguous amino acid region selected from the group consisting of SEQ ID NO:73 and/or SEQ ID NO:78, wherein said isolated protein is capable of eliciting an immune response against a feline CD154 protein and/or has CD154 activity; (h)(i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:83, and/or SEQ ID NO:85; and/or (ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:81 and/or SEQ ID NO:86, wherein said isolated protein is capable of eliciting an immune response against a canine IL-5 protein and/or has IL-5 activity; (i)(i) an isolated protein of at least about 15 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 45 contiguous nucleotide region identical in sequence to a 45 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:99, SEQ ID NO:102, and/or SEQ ID NO:104; and/or (ii) an isolated protein of at least about 15 amino acids in length, wherein said protein has an at least 15 contiguous amino acid region identical in sequence to a 15 contiguous amino acid region selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and/or SEQ ID NO:105, wherein said isolated protein is capable of eliciting an immune response against a canine IL-13 protein and/or has IL-13 activity; (j) (i) an isolated protein encoded by a nucleic acid molecule selected from the group consisting of SEQ ID NO:107, SEQ ID NO:110, SEQ ID NO:113, SEQ ID NO:116, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:161, SEQ ID NO:164, SEQ ID NO:167, and/or SEQ ID NO:170, and/or (ii) an isolated protein selected from the group consisting of SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and/or SEQ ID NO:171, wherein said isolated protein is capable of eliciting an immune response against a feline interferon alpha protein and/or has interferon alpha activity; (k) (i) an isolated protein encoded by a nucleic acid molecule selected from the group consisting of SEQ ID NO:119, SEQ ID NO:122, and/or SEQ ID NO:124, and/or (ii) an isolated protein selected from the group consisting of SEQ ID NO:120 and/or SEQ ID NO:125, wherein said isolated protein is capable of eliciting an immune response against a feline GM-CSF and/or has GM-CSF activity.

The present invention also includes an isolated protein selected from the group consisting of: (a) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:2 and/or SEQ ID NO:20; (b) a protein having an amino acid sequence that is at least about 75 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34; (c) a

protein having an amino acid sequence that is at least about 75 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:44 and/or SEQ ID NO:49; (d) a protein having an amino acid sequence that is at least about 70 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:53 and/or SEQ ID NO:58; (e) a protein having an amino acid sequence that is at least about 60 percent identical to an amino acid sequence comprising SEQ ID NO:61; (f) a protein having an amino acid sequence that is at least about 80 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:65 and/or SEQ ID NO:70; (g) a protein having an amino acid sequence that is at least about 85 percent identical to the amino acid sequence SEQ ID NO:73 and/or SEQ ID NO:78; (h) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:81 and/or SEQ ID NO:86; (i) a protein having an amino acid sequence that is at least about 70 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and/or SEQ ID NO:105; (j) a protein having an amino acid sequence selected from the group consisting of SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and/or SEQ ID NO:171, and/or (k) a protein having an amino acid sequence selected from the group consisting of SEQ ID NO:120, and/or SEQ ID NO:125.

The present invention also includes isolated antibodies that selectively bind to a protein of the present invention.

One aspect of the present invention is a therapeutic composition that, when administered to an animal, regulates an immune response in said animal, said therapeutic composition comprising a therapeutic compound selected from the group consisting of: an immunoregulatory protein of the present invention; a mimotope of any of said immunoregulatory proteins; and a multimeric form of any of said immunoregulatory proteins; an isolated nucleic acid molecule of the present invention; an antibody that selectively binds to any of said immunoregulatory proteins; and/or an inhibitor of a immunoregulatory protein activity identified by its ability to inhibit the activity of any of said immunoregulatory proteins. Yet another aspect of the present invention is a method to regulate an immune response in an animal comprising administering to the animal a therapeutic composition of the present invention.

The present invention also includes a method to produce an immunoregulatory protein, said method comprising culturing a cell capable of expressing said protein, said protein being encoded by a nucleic acid molecule of the present invention.

One embodiment of the present invention is a method to identify a compound capable of regulating an immune response in an animal, said method comprising: (a) contacting an isolated canine IL-4 protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has T cell proliferation stimulating activity; and determining if said putative inhibitory compound inhibits said activity; (b) contacting an isolated canine Flt-3 ligand protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has dendritic precursor cell proliferation stimulating activity; and determining if said putative inhibitory compound inhibits said activity; (c) contacting an isolated feline Flt-3 ligand protein of the present invention with a putative

inhibitory compound under conditions in which, in the absence of said compound, said protein has dendritic precursor cell proliferation stimulating activity; and determining if said putative inhibitory compound inhibits said activity; (d) contacting an isolated canine CD40 protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has CD40 ligand binding activity; and determining if said putative inhibitory compound inhibits said activity; (e) contacting an isolated feline CD40 protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has CD40 ligand binding activity; and determining if said putative inhibitory compound inhibits said activity; (f) contacting an isolated canine CD154 protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has B cell proliferation activity; and determining if said putative inhibitory compound inhibits said activity; (g) contacting an isolated feline CD154 protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has B cell proliferation activity; and determining if said putative inhibitory compound inhibits said activity; (h) contacting an isolated canine IL-5 protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has TF-1 cell proliferation activity; and determining if said putative inhibitory compound inhibits said activity; (i) contacting an isolated canine IL-13 protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has TF-1 cell proliferation activity; and determining if said putative inhibitory compound inhibits said activity; (j) contacting an isolated feline IFN $\alpha$  protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has inhibition of proliferation of GM-CSF stimulated TF-1 cell activity; and determining if said putative inhibitory compound inhibits said activity; or (k) contacting an isolated feline GMCSF protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has TF-1 cell proliferation activity; and determining if said putative inhibitory compound inhibits said activity.

#### DETAILED DESCRIPTION OF THE INVENTION

The present invention provides for isolated canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF proteins, isolated canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecules, antibodies directed against canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF proteins, and compounds derived therefrom that regulate the immune response of an animal (e.g. inhibitors, antibodies and peptides).

Canine IL-4 protein can refer to a canine IL-4 protein, including homologs thereof. Canine Flt-3 ligand protein can refer to a canine Flt-3 ligand, including homologs thereof, and feline Flt-3 ligand can refer to feline Flt-3 ligand, including homologs thereof. Canine CD40 can refer to a

canine CD4-, including homologs thereof; feline CD40 can refer to a feline CD40, including homologs thereof. Canine CD154 can refer to a canine CD154, including homologs thereof; feline CD154 can refer to a feline CD154, including homolog thereof. Canine IL-5 can refer to canine IL-5, including homologs thereof; canine IL-13 can refer to canine IL-13, including homologs thereof. Feline IFN $\alpha$  can refer to a feline IFN $\alpha$ , including homologs thereof, and feline GM-CSF can refer to a feline GM-CSF, including homologs thereof. As used herein, the phrase "regulate an immune response" refers to modulating the activity of cells or molecules involved in an immune response. The term "regulate" can refer to increasing or decreasing an immune response. Regulation of an immune response can be determined using methods known in the art as well as methods disclosed herein. The term, "immunoregulatory protein" refers to a protein that can modulate the activity of cells or of molecules involved in an immune response. An immunoregulatory protein of the present invention refers to a canine IL-4, a canine and/or feline CD40, a canine and/or feline Flt3 ligand, a canine and/or feline CD154, a canine IL-5, a canine IL-13, a feline IFN $\alpha$  and/or a feline GM-CSF protein as described herein. As used herein, the terms isolated canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF proteins and/or isolated canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecules refer to canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF proteins and/or canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecules derived from mammals and, as such, can be obtained from their natural source, or can be produced using, for example, recombinant nucleic acid technology or chemical synthesis. Also included in the present invention is the use of these proteins, nucleic acid molecules, antibodies, and/or compounds derived therefrom as therapeutic compositions to regulate the immune response of an animal as well as in other applications, such as those disclosed below.

One embodiment of the present invention is an isolated protein that includes a canine IL-4 protein, a canine and/or feline Flt-3 ligand protein, a canine and/or feline CD40 protein, a canine and/or feline CD154 protein, a canine interleukin-5 protein, a canine interleukin-13 protein, a feline interferon alpha protein, and/or a feline GM-CSF protein. It is to be noted that the term "a" or "an" entity refers to one or more of that entity; for example, a protein refers to one or more proteins or at least one protein. As such, the terms "a" (or "an") , "one or more" and "at least one" can be used interchangeably herein. It is also to be noted that the terms "comprising", "including", and "having" can be used interchangeably. According to the present invention, an isolated, or biologically pure, protein, is a protein that has been removed from its natural milieu. As such, "isolated" and/or "biologically pure" do not necessarily reflect the extent to which the protein has been purified. An isolated protein of the present invention can be obtained from its natural source, can be produced using recombinant DNA technology, or can be produced by chemical synthesis. Nucleic acid molecules of the present invention of known

length isolated from *Canis familiaris* are denoted as follows: IL-4 is denoted as nCaIL-4<sub>x</sub>, for example, nCaIL-4<sub>549</sub>, wherein “#” refers to the number of nucleotides in that molecule; and in a similar fashion, Flt-3 ligand nucleic acid molecules are referred to as nCaFlt3L<sub>x</sub>; CD40, nCaCD40<sub>x</sub>; CD154, nCaCD154<sub>x</sub>; IL-5, nCaIL-5<sub>x</sub>; and IL-13, nCaIL-13<sub>x</sub>. In a similar fashion, Flt-3 ligand nucleic acid molecules of the present invention of known length isolated from *Felis catus* are denoted as nFeFlt3L<sub>x</sub>; CD40, nFeCD40<sub>x</sub>; CD154, nFeCD154<sub>x</sub>; IFN $\alpha$ , nFeIFN $\alpha$ <sub>x</sub>; and GM-CSF (also denoted GMCSF), nFeGM-CSF<sub>x</sub>. Similarly, proteins of the present invention of known length isolated from *Felis catus* are denoted as PFeFlt3L<sub>x</sub>; PFeCD40<sub>x</sub>; PFeCD154<sub>x</sub>; PFeIFN $\alpha$ <sub>x</sub>; and/or PFeGM-CSF<sub>x</sub>; and proteins of the present invention of known length isolated from *Canis familiaris* are denoted PCaIL-4<sub>x</sub>, PCaFlt3L<sub>x</sub>, PCaCD40<sub>x</sub>, PCaCD154<sub>x</sub>, PCaIL-5<sub>x</sub>, and/or PCaIL-13<sub>x</sub>.

As used herein, an isolated canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, and/or feline GM-CSF ligand protein of the present invention (i.e., an canine interleukin-4, canine or feline Flt-3 ligand canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein, respectively) can be a full-length protein or any homolog of such a protein. An isolated IL-4 protein of the present invention, including a homolog, can be identified in a straight-forward manner by the protein's ability to elicit an immune response against, (or to) an IL-4 protein, bind to an IL-4 receptor, stimulate B cell differentiation or activation or stimulate production of immunoglobulin by a B cell. An isolated Flt-3 ligand protein of the present invention, including a homolog, can be identified in a straight-forward manner by the protein's ability to elicit an immune response against a Flt-3 ligand protein, bind to Flt-3 receptor or stimulate Flt-3 receptor-bearing hematopoietic stem cells, early hematopoietic progenitor cells or immature lymphocytes. An isolated CD40 protein of the present invention, including a homolog, can be identified in a straight-forward manner by the protein's ability to elicit an immune response against a CD40 protein, bind to CD154 or stimulate CD154-bearing B cells, T-cells, and/or epithelial cells. An isolated CD154 protein of the present invention, including a homolog, can be identified in a straight-forward manner by the protein's ability to elicit an immune response to a CD154 protein, bind to CD40 or stimulate CD40-bearing B cells, T cells, and/or epithelial cells. An isolated IL-5 protein of the present invention, including a homolog, can be identified in a straight-forward manner by the protein's ability to elicit an immune response to an IL-5 protein, bind to an IL-5 receptor, and/or stimulate eosinophils and/or cause thymocytes to produce cytotoxic T cells. An isolated IL-13 protein of the present invention, including a homolog, can be identified in a straight-forward manner by the protein's ability to elicit an immune response to an IL-13 protein, bind to an IL-13 receptor, and/or stimulate B cells, up-regulate expression of MHC class II and/or CD23 on monocytes, macrophages and/or B cells; and/or inhibition of proinflammatory cytokines. An isolated interferon alpha protein of the present invention, including a homolog, can be identified in a straight-forward manner by the protein's ability to elicit an immune response to an interferon alpha protein, bind to an interferon alpha receptor, and/or activate NK cells and/or inhibit viral replication. An isolated GM-CSF proteins of the present invention, including a homolog, can be identified in a straight-forward manner by the protein's ability to elicit an immune response

to a GM-CSF protein, bind to a GM-CSF receptor, and/or activate granulocytes and/or macrophages. Examples of protein homologs of the present invention include immunoregulatory proteins of the present invention in which amino acids have been deleted (e.g., a truncated version of the protein, such as a peptide), inserted, inverted, substituted and/or derivatized (e.g., by glycosylation, phosphorylation, acetylation, myristoylation, prenylation, palmitoylation, amidation and/or addition of glycerophosphatidyl inositol) such that the protein homolog includes at least one epitope capable of eliciting an immune response against the parent protein, of binding to an antibody directed against the parent protein and/or of binding to the parent's receptor, where the term parent refers to the longer and/or full-length protein that the homolog is derived from. That is, when the homolog is administered to an animal as an immunogen, using techniques known to those skilled in the art, that animal will produce an immune response against at least one epitope of an immunoregulatory protein of the present invention, depending upon which protein is administered to an animal. The ability of a protein to effect an immune response can be measured using techniques known to those skilled in the art. As used herein, the term “epitope” refers to the smallest portion of a protein capable of selectively binding to the antigen binding site of an antibody. It is well accepted by those skilled in the art that the minimal size of a protein epitope capable of selectively binding to the antigen binding site of an antibody is about five or six to seven amino acids.

Homologs of immunoregulatory proteins of the present invention can be the result of natural allelic variation, including natural mutation. Protein homologs of the present invention can also be produced using techniques known in the art including, but not limited to, direct modifications to the protein and/or modifications to the gene encoding the protein using, for example, classic or recombinant DNA techniques to effect random or targeted mutagenesis.

Immunoregulatory proteins of the present invention include variants of a full-length protein of a protein of the present invention. Such variants include proteins that are less than full-length. As used herein, variant of the present invention refer to nucleic acid molecules that are naturally-occurring as defined below, and may result from alternative RNA splicing, alternative termination of an amino acid sequence or DNA recombination. Examples of variants include allelic variants as defined below. It is to be noted that a variant is an example of a homolog of the present invention.

Immunoregulatory proteins of the present invention are encoded by nucleic acid molecules of the present invention. As used herein, an IL-4 nucleic acid molecule includes nucleic acid sequences related to a natural canine IL-4 gene. As used herein, a Flt-3 ligand nucleic acid molecule includes nucleic acid sequences related to a natural canine Flt-3 ligand gene. As used herein, a CD40 nucleic acid molecule includes nucleic acid sequences related to a natural CD40 gene. As used herein, a CD154 nucleic acid molecule includes nucleic acid sequences related to a natural CD154 gene. As used herein, an IL-5 nucleic acid molecule includes nucleic acid sequences related to a natural IL-5 gene. As used herein, an IL-13 nucleic acid molecule includes nucleic acid sequences related to a natural IL-13 gene. As used herein, an IFN $\alpha$  nucleic acid molecule includes nucleic acid sequences related to a natural IFN $\alpha$  gene. As used herein, a GM-CSF nucleic acid molecule includes nucleic acid sequences related to a natural GM-CSF gene. As used herein, a canine IL-4, a canine and/or feline CD40, a canine and/or feline Flt3 ligand, a canine and/or feline CD154, a

canine IL-5, a canine IL-13, a feline IFN $\alpha$ , and/or a feline GM-CSF gene refers to the natural genomic elements that encode a canine IL-4, a canine and/or feline CD40, a canine and/or feline Flt3 ligand, a canine and/or feline CD154, a canine IL-5, a canine IL-13, a feline IFN $\alpha$ , and/or a feline GM-CSF proteins, respectively, and includes all regions such as regulatory regions that control production of the protein encoded by the gene (such as, but not limited to, transcription, translation or post-translation control regions) as well as the coding region itself, and any introns or non-translated coding regions. As used herein, a gene that “includes” or “comprises” a sequence may include that sequence in one contiguous array, or may include the sequence as fragmented exons. As used herein, the term “coding region” refers to a continuous linear array of nucleotides that translates into a protein. A full-length coding region is that region that is translated into a full-length, i.e., a complete, protein as would be initially translated in its natural milieu, prior to any post-translational modifications.

In one embodiment, an IL-4 gene of the present invention includes the nucleic acid sequence SEQ ID NO:1, as well as the complement of SEQ ID NO:1. Nucleic acid sequence SEQ ID NO:1 represents the deduced sequence of the coding strand of a cDNA (complementary DNA) denoted herein as nucleic acid molecule nCaIL-4<sub>549</sub>, the production of which is disclosed in the Examples. Nucleic acid molecule nCaIL-4<sub>549</sub> comprises an apparently full-length coding region of canine IL-4. The complement of SEQ ID NO:1 (represented herein by SEQ ID NO:3) refers to the nucleic acid sequence of the strand fully complementary to the strand having SEQ ID NO:1, which can easily be determined by those skilled in the art. Likewise, a nucleic acid sequence complement of any nucleic acid sequence of the present invention refers to the nucleic acid sequence of the nucleic acid strand that is fully complementary to (i.e., can form a double helix with) the strand for which the sequence is cited. It should be noted that since nucleic acid sequencing technology is not entirely error-free, SEQ ID NO:1 (as well as other nucleic acid and protein sequences presented herein) represents an apparent nucleic acid sequence of the nucleic acid molecule encoding an immunoregulatory protein of the present invention.

In another embodiment, a Flt-3 ligand gene of the present invention includes the nucleic acid sequence SEQ ID NO:6, as well as the complement represented by SEQ ID NO:8. Nucleic acid sequence SEQ ID NO:6 represents the deduced sequence of the coding strand of a cDNA denoted herein as nucleic acid molecule nCaFlt3L<sub>1013</sub>, the production of which is disclosed in the Examples. Nucleic acid molecule nCaFlt3L<sub>1013</sub> comprises an apparently full-length coding region of canine Flt-3 ligand.

In another embodiment, a Flt-3 ligand gene of the present invention includes the nucleic acid sequence SEQ ID NO:43, as well as the complement represented by SEQ ID NO:45. Nucleic acid sequence SEQ ID NO:43 represents the deduced sequence of the coding strand of a cDNA denoted herein as nucleic acid molecule nFeFlt3L<sub>942</sub>, the production of which is disclosed in the Examples. Nucleic acid molecule nFeFlt3L<sub>942</sub> comprises an apparently full-length coding region of feline Flt-3 ligand.

In another embodiment, a CD40 gene of the present invention includes the nucleic acid sequence SEQ ID NO:52, as well as the complement represented by SEQ ID NO:54. Nucleic acid sequence SEQ ID NO:52 represents the deduced sequence of the coding strand of a cDNA denoted herein as nucleic acid molecule nCaCD40<sub>1425</sub>, the production of which is disclosed in the Examples. Nucleic acid

molecule nCaCD40<sub>1425</sub> comprises an apparently full-length coding region of canine CD40.

In another embodiment, a CD40 gene of the present invention includes the nucleic acid sequence SEQ ID NO:60, as well as the complement represented by SEQ ID NO:62. Nucleic acid sequence SEQ ID NO:60 represents the deduced sequence of the coding strand of a cDNA denoted herein as nucleic acid molecule nFeCD40<sub>336</sub>, the production of which is disclosed in the Examples. Nucleic acid molecule nFeCD40<sub>336</sub> comprises an apparent portion of the coding region of feline CD40.

In another embodiment, a CD154 gene of the present invention includes the nucleic acid sequence SEQ ID NO:64, as well as the complement represented by SEQ ID NO:66. Nucleic acid sequence SEQ ID NO:64 represents the deduced sequence of the coding strand of a cDNA denoted herein as nucleic acid molecule nCaCD154<sub>1878</sub>, the production of which is disclosed in the Examples. Nucleic acid molecule nCaCD154<sub>1878</sub> comprises an apparently full-length coding region of canine CD154.

In another embodiment, a CD154 gene of the present invention includes the nucleic acid sequence SEQ ID NO:72, as well as the complement represented by SEQ ID NO:74. Nucleic acid sequence SEQ ID NO:72 represents the deduced sequence of the coding strand of a cDNA denoted herein as nucleic acid molecule nFeCD154<sub>885</sub>, the production of which is disclosed in the Examples. Nucleic acid molecule nFeCD154<sub>885</sub> comprises an apparently full-length coding region of feline CD154.

In another embodiment, an IL-5 gene of the present invention includes the nucleic acid sequence SEQ ID NO:80, as well as the complement represented by SEQ ID NO:82. Nucleic acid sequence SEQ ID NO:80 represents the deduced sequence of the coding strand of a cDNA denoted herein as nucleic acid molecule nCaIL-5<sub>610</sub>, the production of which is disclosed in the Examples. Nucleic acid molecule nCaIL-5<sub>610</sub> comprises an apparently full-length coding region of canine IL-5.

In another embodiment, an IL-13 gene of the present invention includes the nucleic acid sequence SEQ ID NO:91, as well as the complement represented by SEQ ID NO:93. Nucleic acid sequence SEQ ID NO:91 represents the deduced sequence of the coding strand of a cDNA denoted herein as nucleic acid molecule nCaIL-13<sub>1302</sub>, the production of which is disclosed in the Examples. Nucleic acid molecule nCaIL-13<sub>1302</sub> comprises an apparently full-length coding region of canine IL-13.

In another embodiment, an IFN $\alpha$  gene of the present invention includes the nucleic acid sequence SEQ ID NO:107, SEQ ID NO:110, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:161, SEQ ID NO:164, SEQ ID NO:167, or SEQ ID NO:170, as well as the complement represented by, respectively, SEQ ID NO:109, SEQ ID NO:112, SEQ ID NO:157, SEQ ID NO:160, SEQ ID NO:163, or SEQ ID NO:166, SEQ ID NO:169, and SEQ ID NO:172. Nucleic acid sequences SEQ ID NO:107, SEQ ID NO:110, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:161, SEQ ID NO:164, SEQ ID NO:167, and SEQ ID NO:170 represent the deduced sequences of the coding strands of cDNAs denoted herein as nucleic acid molecules nFeIFN $\alpha$ <sub>567a</sub>, nFeIFN $\alpha$ <sub>567b</sub>, nFeIFN $\alpha$ <sub>567c</sub>, nFeIFN $\alpha$ <sub>498c</sub>, nFeIFN $\alpha$ <sub>582d</sub>, nFeIFN $\alpha$ <sub>513d</sub>, nFeIFN $\alpha$ <sub>567e</sub> and nFeIFN $\alpha$ <sub>498e</sub>, respectively. Each of these nucleic acid molecules, the production of which is disclosed in the Examples, comprises an apparently full-length coding region of a feline IFN $\alpha$  protein.

In another embodiment, a GM-CSF gene of the present invention includes the nucleic acid sequence SEQ ID NO:119, as well as the complement represented by SEQ ID NO:121. Nucleic acid sequence SEQ ID NO:119 represents the deduced sequence of the coding strand of a cDNA denoted herein as nucleic acid molecule nFeGM-CSF<sub>444</sub>, the production of which is disclosed in the Examples. Nucleic acid molecule nFeGM-CSF<sub>444</sub> comprises an apparently full-length coding region of feline GM-CSF.

Additional immunoregulatory nucleic acid molecules and proteins of the present invention having specific sequence identifiers are described in Table 1.

TABLE 1

Sequence identification numbers (SEQ ID NOs) and their corresponding nucleic acid molecules or proteins.	
SEQ ID NO:	DESCRIPTION
1	nCaIL-4 <sub>549</sub> coding strand
2	PCaIL-4 <sub>132</sub>
3	nCaIL-4 <sub>549</sub> complementary strand
4	nCaIL-4 <sub>396</sub> coding strand
5	nCaIL-4 <sub>396</sub> complementary strand
6	nCaFlt3L <sub>1013</sub> coding strand
7	PCaFlt3L <sub>294</sub>
8	nCaFlt3L <sub>1013</sub> complementary strand
9	nCaFlt3L <sub>882</sub> coding strand
10	nCaFlt3L <sub>882</sub> complementary strand
19	nCaIL-4 <sub>324</sub> coding strand
20	PCaIL-4 <sub>108</sub>
21	nCaIL-3 <sub>24</sub> complementary strand
22	nCaFlt3L <sub>804</sub> coding strand
23	PCaFlt3L <sub>268</sub>
24	nCaFlt3L <sub>804</sub> complementary strand
25	nCaFlt3L <sub>985</sub> coding strand
26	PCaFlt3L <sub>276</sub>
27	nCaFlt3L <sub>985</sub> complementary strand
28	nCaFlt3L <sub>828</sub> coding strand
29	nCaFlt3L <sub>828</sub> complementary strand
30	nCaFlt3L <sub>750</sub> coding strand
31	PCaFlt3L <sub>250</sub>
32	nCaFlt3L <sub>750</sub> complementary strand
33	nCaFlt3L <sub>1019</sub> coding strand
34	PCaFlt3L <sub>31</sub>
35	nCaFlt3L <sub>1019</sub> complementary strand
36	nCaFlt3L <sub>93</sub> coding strand
37	nCaFlt3L <sub>93</sub> complementary strand
41	nFeFlt3L <sub>395</sub> coding strand
42	nFeFlt3L <sub>793</sub> coding strand
43	nFeFlt3L <sub>942</sub> coding strand
44	PFeFlt3L <sub>291</sub>
45	nFeFlt3L <sub>942</sub> complementary strand
46	nFeFlt3L <sub>873</sub> coding strand
47	nFeFlt3L <sub>873</sub> complementary strand
48	nFeFlt3L <sub>795</sub> coding strand
49	PFeFlt3L <sub>265</sub>
50	nFeFlt3L <sub>795</sub> complementary strand
51	nCaCD40 <sub>321</sub> coding strand
52	nCaCD40 <sub>1425</sub> coding strand
53	PCaCD40 <sub>274</sub>
54	nCaCD40 <sub>1425</sub> complementary strand
55	nCaCD40 <sub>822</sub> coding strand
56	nCaCD40 <sub>822</sub> complementary strand
57	nCaCD40 <sub>765</sub> coding strand
58	PCaCD40 <sub>255</sub>
59	nCaCD40 <sub>765</sub> complementary strand
60	nFeCD40 <sub>336</sub> coding strand
61	PFeCD40 <sub>112</sub>
62	nFeCD40 <sub>336</sub> complementary strand
63	nCaCD154 <sub>390</sub> coding strand
64	nCaCD154 <sub>1878</sub> coding strand
65	PCaCD154 <sub>260</sub>
66	nCaCD154 <sub>1878</sub> complementary strand
67	nCaCD154 <sub>780</sub> coding strand
68	nCaCD154 <sub>780</sub> complementary strand
69	nCaCD154 <sub>633</sub> coding strand
70	PCaCD154 <sub>211</sub>
71	nCaCD154 <sub>633</sub> complementary strand

TABLE 1-continued

Sequence identification numbers (SEQ ID NOs) and their corresponding nucleic acid molecules or proteins.	
SEQ ID NO:	DESCRIPTION
72	nFeCD154 <sub>885</sub> coding strand
73	PFeCD154 <sub>260</sub>
74	nFeCD154 <sub>885</sub> complementary strand
75	nFeCD154 <sub>780</sub> coding strand
76	nFeCD154 <sub>780</sub> complementary strand
77	nFeCD154 <sub>633</sub> coding strand
78	PFeCD154 <sub>211</sub>
79	nFeCD154 <sub>633</sub> complementary strand
80	nCaIL-5 <sub>610</sub> coding strand
81	PCaIL-5 <sub>134</sub>
82	nCaIL-5 <sub>610</sub> complementary strand
83	nCaIL-5 <sub>402</sub> coding strand
84	nIL-5 <sub>402</sub> complementary strand
85	nCaIL-5 <sub>345</sub> coding strand
86	PCaIL-5 <sub>115</sub>
87	nCaIL-5 <sub>345</sub> complementary strand
88	nCaIL-13 <sub>166</sub> coding strand
89	nCaIL-13 <sub>272</sub> coding strand
90	nCaIL-13 <sub>278</sub> coding strand
91	nCaIL-13 <sub>1302</sub> coding strand
92	PCaIL-13 <sub>131</sub>
93	nCaIL-13 <sub>1302</sub> complementary strand
94	nCaIL-13 <sub>393</sub> coding strand
95	nCaIL-13 <sub>393</sub> complementary strand
96	nCaIL-13 <sub>333</sub> coding strand
97	PaIL-13 <sub>111</sub>
98	nCaIL-13 <sub>333</sub> complementary strand
99	nCaIL-13 <sub>1269</sub> coding strand
100	PCaIL-13 <sub>130</sub>
101	nCaIL-13 <sub>1269</sub> complementary strand
102	nCaIL-13 <sub>390</sub> coding strand
103	nCaIL-13 <sub>390</sub> complementary strand
104	nCaIL-13 <sub>330</sub> coding strand
105	PCaIL-13 <sub>110</sub>
106	nCaIL-13 <sub>330</sub> complementary strand
107	nFeIFN $\alpha$ <sub>567a</sub> coding strand
108	PFeIFN $\alpha$ <sub>189a</sub>
109	nFeIFN $\alpha$ <sub>567a</sub> complementary strand
110	nFeIFN $\alpha$ <sub>567b</sub> coding strand
111	PFeIFN $\alpha$ <sub>189b</sub>
112	nFeIFN $\alpha$ <sub>567b</sub> complementary strand
113	nFeIFN $\alpha$ <sub>498a</sub> coding strand
114	PFeIFN $\alpha$ <sub>166a</sub>
115	nFeIFN $\alpha$ <sub>498a</sub> complementary strand
116	nFeIFN $\alpha$ <sub>498b</sub> coding strand
117	PFeIFN $\alpha$ <sub>166b</sub>
118	nFeIFN $\alpha$ <sub>498b</sub> complementary strand
119	nFeGMCSF <sub>444</sub> coding strand
120	PFeGMCSF <sub>144</sub>
121	nFeGMCSF <sub>444</sub> complementary strand
122	nFeGMCSF <sub>432</sub> coding strand
123	nFeGMCSF <sub>432</sub> complementary strand
124	nFeGMCSF <sub>381</sub> coding strand
125	PFeGMCSF <sub>127</sub>
126	nFeGMCSF <sub>381</sub> complementary strand
155	nFeIFN $\alpha$ <sub>567c</sub>
156	PFeIFN $\alpha$ <sub>189c</sub>
157	nFeIFN $\alpha$ <sub>567a</sub> complementary strand
158	nFeIFN $\alpha$ <sub>498c</sub>
159	PFeIFN $\alpha$ <sub>166c</sub>
160	nFeIFN $\alpha$ <sub>498c</sub> complementary strand
161	nFeIFN $\alpha$ <sub>582d</sub>
162	PFeIFN $\alpha$ <sub>194d</sub>
163	nFeIFN $\alpha$ <sub>582d</sub> complementary strand
164	nFeIFN $\alpha$ <sub>513d</sub>
165	PFeIFN $\alpha$ <sub>171d</sub>
166	nFeIFN $\alpha$ <sub>513d</sub> complementary strand
167	nFeIFN $\alpha$ <sub>567e</sub>
168	PFeIFN $\alpha$ <sub>189e</sub>
169	nFeIFN $\alpha$ <sub>567e</sub> complementary strand
170	nFeIFN $\alpha$ <sub>498e</sub>
171	PFeIFN $\alpha$ <sub>166e</sub>
172	nFeIFN $\alpha$ <sub>498e</sub> complementary strand

In another embodiment, an IL-4 gene or nucleic acid molecule can be an allelic variant that includes a similar but not identical sequence to SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, SEQ ID NO:2 1, and/or any other IL-4 nucleic acid sequence cited herein. In another embodiment, a Flt-3 ligand gene or nucleic acid molecule can be an allelic variant that includes a similar but not identical sequence to SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:50 and/or any other Flt-3 ligand nucleic acid sequence cited herein. In another embodiment, a CD40 gene or nucleic acid molecule can be an allelic variant that includes a similar but not identical sequence to SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62 and/or other CD40 nucleic acid sequence cited herein. In another embodiment, a CD154 gene or nucleic acid molecule can be an allelic variant that includes a similar but not identical sequence to SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79 and/or any other CD154 nucleic acid sequences cited herein. In another embodiment, an IL-5 gene or nucleic acid molecule can be an allelic variant that includes a similar but not identical sequence to SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:87 and/or any other IL-5 nucleic acid sequence cited herein. In another embodiment, an IL-13 gene or nucleic acid molecule can be an allelic variant that includes a similar but not identical sequence to SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:106 and/or any other IL-13 nucleic acid sequence cited herein. In another embodiment, an IFN $\alpha$  gene or nucleic acid molecule can be an allelic variant that includes a similar but not identical sequence to SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:155, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:169, SEQ ID NO:170 and/or SEQ ID NO:172, and/or any other IFN $\alpha$  nucleic acid sequence cited herein. In another embodiment, a GM-CSF gene or nucleic acid molecule can be an allelic variant that includes a similar but not identical sequence to SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, and/or SEQ ID NO:126 and/or any other GM-CSF nucleic acid cited herein. An allelic variant of a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF gene, including the particular SEQ ID NO's cited herein, is a gene that occurs at essentially the same locus (or loci) in the genome as the gene including the particular SEQ ID NO's cited herein, but which, due to natural variations caused by, for example, mutation or recombination, has a similar but not identical sequence. Also included in the term allelic variant are allelic variants of

cDNAs derived from such genes. Because natural selection typically selects against alterations that affect function, allelic variants usually encode proteins having similar activity to that of the protein encoded by the gene to which they are being compared. Allelic variants of genes or nucleic acid molecules can also comprise alterations in the 5' or 3' untranslated regions of the gene (e.g., in regulatory control regions), or can involve alternative splicing of a nascent transcript, thereby bringing alternative exons into juxtaposition. Allelic variants are well known to those skilled in the art and would be expected to be found within a given animal, since the respective genomes are diploid, and sexual reproduction will result in the reassortment of alleles.

The minimal size of an canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein homolog of the present invention is a size sufficient to be encoded by a nucleic acid molecule capable of forming a stable hybrid (i.e., hybridize under stringent hybridization conditions) with the complementary sequence of a nucleic acid molecule encoding the corresponding natural protein. Stringent hybridization conditions are determined based on defined physical properties of the gene to which the nucleic acid molecule is being hybridized, and can be defined mathematically. Stringent hybridization conditions are those experimental parameters that allow an individual skilled in the art to identify significant similarities between heterologous nucleic acid molecules. These conditions are well known to those skilled in the art. See, for example, Sambrook, et al., 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Labs Press, and Meinkoth, et al., 1984, *Anal. Biochem.* 138, 267-284, each of which is incorporated herein by this reference. As explained in detail in the cited references, the determination of hybridization conditions involves the manipulation of a set of variables including the ionic strength ( $M$ , in moles/liter), the hybridization temperature ( $^{\circ}C$ ), the concentration of nucleic acid helix destabilizing agents, such as formamide, the average length of the shortest hybrid duplex ( $n$ ), and the percent G+C composition of the fragment to which an unknown nucleic acid molecule is being hybridized. For nucleic acid molecules of at least about 150 nucleotides, these variables are inserted into a standard mathematical formula to calculate the melting temperature, or  $T_m$ , of a given nucleic acid molecule. As defined in the formula below,  $T_m$  is the temperature at which two complementary nucleic acid molecule strands will disassociate, assuming 100% complementarity between the two strands:

$$T_m = 81.5^{\circ}C + 16.6 \log M + 0.41(\%G+C) - 500/n - 0.61(\%formamide).$$

For nucleic acid molecules smaller than about 50 nucleotides, hybrid stability is defined by the dissociation temperature ( $T_d$ ), which is defined as the temperature at which 50% of the duplexes dissociate. For these smaller molecules, the stability at a standard ionic strength is defined by the following equation:

$$T_d = 4(G+C) + 2(A+T).$$

A temperature of  $5^{\circ}C$ . below  $T_d$  is used to detect hybridization between perfectly matched molecules.

Also well known to those skilled in the art is how base pair mismatch, i.e. differences between two nucleic acid molecules being compared, including non-complementarity of bases at a given location, and gaps due to insertion or deletion of one or more bases at a given location on either

of the nucleic acid molecules being compared, will affect  $T_m$  or  $T_d$  for nucleic acid molecules of different sizes. For example,  $T_m$  decreases about 1° C. for each 1% of mismatched base pairs for hybrids greater than about 150 bp, and  $T_d$  decreased about 5° C. for each mismatched base pair for hybrids below about 50 bp. Conditions for hybrids between about 50 and about 150 base pairs can be determined empirically and without undue experimentation using standard laboratory procedures well known to those skilled in the art. These simple procedures allow one skilled in the art to set the hybridization conditions, by altering, for example, the salt concentration, the formamide concentration or the temperature, so that only nucleic acid hybrids with greater than a specified % base pair mismatch will hybridize. Stringent hybridization conditions are commonly understood by those skilled in the art to be those experimental conditions that will allow about 30% base pair mismatch, i.e., about 70% identity. Because one skilled in the art can easily determine whether a given nucleic acid molecule to be tested is less than or greater than about 50 nucleotides, and can therefore choose the appropriate formula for determining hybridization conditions, he or she can determine whether the nucleic acid molecule will hybridize with a given gene or specified nucleic acid molecule under stringent hybridization conditions and similarly whether the nucleic acid molecule will hybridize under conditions designed to allow a desired amount of base pair mismatch.

Hybridization reactions are often carried out by attaching the nucleic acid molecule to be hybridized to a solid support such as a membrane, and then hybridizing with a labeled nucleic acid molecule, typically referred to as a probe, suspended in a hybridization solution. Examples of common hybridization reaction techniques include, but are not limited to, the well-known Southern and northern blotting procedures. Typically, the actual hybridization reaction is done under non-stringent conditions, i.e., at a lower temperature and/or a higher salt concentration, and then high stringency is achieved by washing the membrane in a solution with a higher temperature and/or lower salt concentration in order to achieve the desired stringency.

Preferred portions, or fragments, of a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF, protein of the present invention include at least 15 amino acids, at least 20 amino acids, at least 25 amino acids, at least 30 amino acids, at least 35 amino acids, at least 40 amino acids, at least 45 amino acids, at least 50 amino acids, at least 60 amino acids, at least 75 amino acids or at least 100 amino acids. An IL-4, IL-5, and/or IL-13 protein of the present invention can include at least a portion of an IL-4, IL-5, and/or IL-13 protein that is capable of binding to an IL-4, IL-5, and/or IL-13 receptor, respectively. IL4, IL-5, and IL-13 receptors are known to those of skill in the art, and are described in Janeway et al., in *Immunobiology, the Immune System in Health and Disease*, Garland Publishing, Inc., N.Y., 1996 (which is incorporated herein by this reference in its entirety). The IL-4, IL-5, and/or IL-13 receptor-binding protein of an IL-4, IL-5, and/or IL-13 protein, respectively, can be determined by incubating the protein with an isolated IL-4, IL-5, and/or IL-13 receptor, as appropriate, or a cell having an IL-4, IL-5, and/or IL-13 receptor on its surface, as appropriate. IL-4, IL-5, and/or IL-13 protein binding to purified IL-4, IL-5, and/or IL-13 receptor, respectively, can be determined using methods known in the art including Biacore® screening, confocal immunofluorescent microscopy, immunoprecipitation, gel chromatography,

determination of inhibition of binding of antibodies that bind specifically to the IL-4, IL-5, and/or IL-13 binding domain of an IL-4, IL-5, and/or IL-13 receptor, ELISA using an IL-4, IL-5, and/or IL-13 receptor, respectively, labeled with a detectable tag such as an enzyme or chemiluminescent tag or yeast-2 hybrid technology. A Flt-3 ligand protein of the present invention can include at least a portion of a Flt-3 ligand protein that is capable of binding to Flt-3 receptor or stimulating Flt-3 receptor-bearing hematopoietic stem cells, early hematopoietic progenitor cells or immature lymphocytes. Flt-3 receptors are known to those of skill in the art, and are described in Drexler, *Leukemia*, vol. 10, pp. 588-599, 1996 (which is incorporated herein in its entirety by this reference). The Flt-3 receptor-binding portion of a Flt-3 ligand protein can be determined by incubating the protein with isolated Flt-3 receptor or a cell having a Flt-3 receptor on its surface. Flt-3 ligand protein binding to purified Flt-3 receptor can be determined using methods known in the art including Biacore® screening, confocal immunofluorescent microscopy, immunoprecipitation, gel chromatography, determination of inhibition of binding of antibodies that bind specifically to the Flt-3 ligand binding domain of a Flt-3 receptor, ELISA using a Flt-3 receptor labeled with a detectable tag such as an enzyme or chemiluminescent tag or yeast-2 hybrid technology. A CD40 and/or CD154 protein of the present invention can include at least a portion of a CD40 and/or CD154 protein that is capable of binding to a CD40 and/or CD154 receptor, respectively, or stimulating CD40 and/or CD154 receptor-bearing hematopoietic stem cells, early hematopoietic progenitor cells or immature lymphocytes. The CD40 and/or CD154 receptor-binding portion of a CD40 and/or CD154 protein can be determined by incubating the protein with isolated CD40 and/or CD154 receptor, as appropriate, or a cell having a CD40 and/or CD154 receptor on its surface, as appropriate. CD40 and/or CD154 protein binding to CD154 and/or CD40, respectively, can be determined using methods known in the art including Biacore® screening, confocal immunofluorescent microscopy, immunoprecipitation, gel chromatography, determination of inhibition of binding of antibodies that bind specifically to the CD40 and/or CD154 binding domain of CD40 and/or CD154, as appropriate, ELISA using a CD40 and/or CD154 labeled with a detectable tag such as an enzyme or chemiluminescent tag or yeast-2 hybrid technology.

The present invention also includes mimetopes of canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF proteins of the present invention. As used herein, a mimetope of an immunoregulatory protein of the present invention refers to any compound that is able to mimic the activity of such a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein, respectively, often because the mimetope has a structure that mimics the particular protein. Mimetopes can be, but are not limited to: peptides that have been modified to decrease their susceptibility to degradation such as all-D retro peptides; anti-idiotypic and/or catalytic antibodies, or fragments thereof; non-proteinaceous immunogenic portions of an isolated protein (e.g., carbohydrate structures); and/or synthetic or natural organic molecules, including nucleic acids. Such mimetopes can be designed using computer-generated structures of proteins of the present invention. Mimetopes can also be obtained by generating random samples of molecules, such as

oligonucleotides, peptides or other organic molecules, and screening such samples by affinity chromatography techniques using the corresponding binding partner.

One embodiment of an immunoregulatory protein of the present invention is a fusion portion that includes either a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein-containing domain, each attached to one or more fusion segments. Suitable fusion segments for use with the present invention include, but are not limited to, segments that can: link two or more immunoregulatory proteins of the present invention, to form multimeric forms of an immunoregulatory protein of the present invention; enhance a protein's stability; act as an immunopotentiator to enhance an immune response against an canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein; and/or assist in purification of an canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein (e.g., by affinity chromatography). A suitable fusion segment can be a domain of any size that has the desired function (e.g., imparts increased stability, imparts increased immunogenicity to a protein, and/or simplifies purification of a protein). Fusion segments can be joined to amino and/or carboxyl termini of the IL-4-containing domain, or the Flt-3 ligand-containing domain, or the CD40-containing domain, or the CD154-containing domain, or the IL-5-containing domain, or the IL-3-containing domain, or the IFN $\alpha$ -containing domain, or GM-CSF-containing domain, of a protein and can be susceptible to cleavage in order to enable straightforward recovery of either canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein, respectively. Fusion proteins are preferably produced by culturing a recombinant cell transformed with a fusion nucleic acid molecule that encodes a protein including the fusion segment attached to either the carboxyl and/or amino terminal end of an canine interleukin-4-, canine or feline Flt-3 ligand-, canine or feline CD40-, canine or feline CD154-, canine interleukin-5-, canine interleukin-13-, feline interferon alpha-, or feline GM-CSF-containing domain. Preferred fusion segments include a metal binding domain (e.g., a poly-histidine segment); and immunoglobulin binding domain (e.g., Protein A; Protein G; T cell; B cell; Fc receptor or complement protein antibody-binding domains); a sugar binding domain (e.g., a maltose binding domain); and/or a "tag" domain (e.g., at least a portion of -galactosidase, a strep tag peptide, a T7 tag peptide, a Flag<sup>TM</sup> peptide, or other domains that can be purified using compounds that bind to the domain, such as monoclonal antibodies). More preferred fusion segments include metal binding domains, such as a poly-histidine segment; a maltose binding domain; a strep tag peptide, such as that available from Biometra in Tampa, Fla.; and an S10 peptide.

A suitable fusion segment that links one IL-4 protein to another IL-4 protein, or one Flt-3 ligand protein to another Flt-3 ligand protein, or one CD40 protein to another CD40 protein, or one CD154 protein to another CD154 protein, or one IL-5 protein to another IL-5 protein to another IL-5 protein, or one IL-13 protein to another IL-13 protein, or one IFN $\alpha$  protein to another IFN $\alpha$  protein, or one GM-CSF protein to another GM-CSF protein, includes any amino acid

sequence that enables such proteins to be linked while maintaining the biological function of either the canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF, proteins, respectively. Selection of a suitable linker is dependent upon how many proteins are to be linked to form one multimeric molecule and from where on either the canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF molecule the linker extends. Preferably, a linker fusion segment of the present invention comprises a peptide of from about 6 amino acid residues to about 40 residues, more preferably from about 6 residues to about 30 residues in length.

In another embodiment, an canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein of the present invention also includes at least one additional protein segment that is capable of targeting either canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein, respectively, to a desired cell or receptive molecule. Such a multivalent targeting protein can be produced by culturing a cell transformed with a nucleic acid molecule comprising two or more nucleic acid domains joined together in such a manner that the resulting nucleic acid molecule is expressed as a multivalent targeting protein containing a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein or portion thereof and/or at least one targeting compound capable of delivering the canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein, respectively, to a desired site in an animal.

Examples of multivalent targeting proteins include, but are not limited to, a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein of the present invention attached to one or more compounds that can bind to a receptive molecule on the surface of a cell located in an area of an animal where regulation of an immune response is desired. One of skill in the art can select appropriate targeting fusion segments depending upon the cell or receptive molecule being targeted.

Another example of a multivalent protein of the present invention includes, but is not limited to, a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein of the present invention attached to one or more proteins that are potentially antigenic in mammals. Thus, immunogenicity of the potentially antigenic protein could be enhanced by administering to a mammal together with an immunoregulatory protein of the present invention.

A naturally-occurring variant of a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein of the present invention is preferably isolated from (including isolation of the natural protein or production of the protein

by recombinant or synthetic techniques) from mammals, including but not limited to dogs (i.e., canids), cats (i.e., felids), horses (i.e., equids), humans, cattle, chinchillas, ferrets, goats, mice, minks, rabbits, raccoons, rats, sheep, squirrels, swine, chickens, ostriches, quail and/or turkeys as well as other furry animals, pets, zoo animals, work animals and/or food animals. Particularly preferred animals from which to isolate canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF proteins are dogs, cats, horses and/or humans.

A preferred isolated protein of the present invention is a protein encoded by at least one of the following nucleic acid molecules: nCaIL-4<sub>549</sub>, nCaIL-4<sub>396</sub>, nCaIL-4<sub>324</sub>, nCaFlt3L<sub>1013</sub>, nCaFlt3L<sub>882</sub>, nCaFlt3L<sub>804</sub>, nCaFlt3L<sub>828</sub>, nCaFlt3L<sub>985</sub>, nCaFlt3L<sub>1019</sub>, nCaFlt3L<sub>93</sub>, nCaFlt3L<sub>750</sub>, nFeFlt3L<sub>395</sub>, nFeFlt3L<sub>793</sub>, nFeFlt3L<sub>942</sub>, nFeFlt3L<sub>873</sub>, nFeFlt3L<sub>795</sub>, nCaCD40<sub>321</sub>, nCaCD40<sub>1425</sub>, nCaCD40<sub>822</sub>, nCaCD40<sub>765</sub>, nFeCD40<sub>336</sub>, nCaCD154<sub>390</sub>, nCaCD154<sub>1878</sub>, nCaCD154<sub>780</sub>, nCaCD154<sub>633</sub>, nFeCD154<sub>885</sub>, nFeCD154<sub>780</sub>, nFeCD154<sub>633</sub>, nCaIL-5<sub>610</sub>, nCaIL-5<sub>402</sub>, nCaIL-5<sub>345</sub>, nCaIL-13<sub>166</sub>, nCaIL-13<sub>272</sub>, nCaIL-13<sub>278</sub>, nCaIL-13<sub>1302</sub>, nCaIL-13<sub>393</sub>, nCaIL-13<sub>333</sub>, nCaIL-13<sub>1269</sub>, nCaIL-13<sub>390</sub>, nCaIL-13<sub>330</sub>, nFeIFN $\alpha$ <sub>567a</sub>, nFeIFN $\alpha$ <sub>567b</sub>, nFeIFN $\alpha$ <sub>567c</sub>, nFeIFN $\alpha$ <sub>498a</sub>, nFeIFN $\alpha$ <sub>498b</sub>, nFeIFN $\alpha$ <sub>498c</sub>, nFeIFN $\alpha$ <sub>582d</sub>, nFeIFN $\alpha$ <sub>513d</sub>, nFeIFN $\alpha$ <sub>567e</sub>, nFeIFN $\alpha$ <sub>498e</sub>, nFeGMCSF<sub>444</sub>, nFeGMCSF<sub>432</sub>, nFeGMCSF<sub>38</sub>, and/or allelic variants of any of these nucleic acid molecules. Also preferred is an isolated protein that is encoded by a nucleic acid molecule the having nucleic acid sequence SEQ ID NO:1, SEQ ID NO:4, SEQ ID NO:19, SEQ ID NO:6, SEQ ID NO:9, SEQ ID NO:22, SEQ ID NO:25, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:33, SEQ ID NO:36, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:55, SEQ ID NO:57, SEQ ID NO:60, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:72, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:80, SEQ ID NO:83, SEQ ID NO:85, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:99, SEQ ID NO:102, SEQ ID NO:104, SEQ ID NO:107, SEQ ID NO:110, SEQ ID NO:113, SEQ ID NO:116, SEQ ID NO:119, SEQ ID NO:122, SEQ ID NO:124, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:161, SEQ ID NO:164, SEQ ID NO:167, and SEQ ID NO:170; and/or an allelic variant of such a nucleic acid molecule.

Translation of SEQ ID NO:1, the coding strand of nCaIL-4<sub>549</sub>, yields a protein of about 132 amino acids, denoted herein as PCaIL-4<sub>132</sub>, the amino acid sequence of which is presented in SEQ ID NO:2, assuming an open reading frame having an initiation codon spanning from nucleotide 43 through nucleotide 45 of SEQ ID NO:1 and a stop codon spanning from nucleotide 439 through nucleotide 441 of SEQ ID NO:1.

Translation of SEQ ID NO:6, the coding strand of nCaFlt3L<sub>1013</sub>, yields a protein of about 294 amino acids, denoted herein as PCaFlt3L<sub>294</sub>, the amino acid sequence of which is presented in SEQ ID NO:7, assuming an open reading frame having an initiation codon spanning from nucleotide 35 through nucleotide 37 of SEQ ID NO:6 and a stop codon spanning from nucleotide 917 through nucleotide 919 of SEQ ID NO:6.

Translation of SEQ ID NO:43, the coding strand for nFeFlt3L<sub>942</sub>, yields a protein of about 291 amino acids, denoted herein as PFeFlt3L<sub>291</sub>, the amino acid sequence of

which is presented in SEQ ID NO:44, assuming an open reading frame having an initiation codon spanning from nucleotide 31 through nucleotide 33 of SEQ ID NO:43 and a stop codon spanning from nucleotide 904 through nucleotide 906 of SEQ ID NO:43.

Translation of SEQ ID NO:52, the coding strand for nCaCD40<sub>1425</sub>, yields a protein of about 274 amino acids, denoted herein as PCaCD40<sub>274</sub>, the amino acid sequence of which is presented in SEQ ID NO:53, assuming an open reading frame having an initiation codon spanning from nucleotide 196 through nucleotide 198 of SEQ ID NO:52 and a stop codon spanning from about nucleotide 1018 through nucleotide 1020 of SEQ ID NO:52.

Translation of SEQ ID NO:60, the coding strand for nFeCD40<sub>336</sub>, yields a protein of about 112 amino acids, denoted herein as PFeCD40<sub>112</sub>, the amino acid sequence of which is presented in SEQ ID NO:61, assuming an open reading frame having an initiation codon spanning from nucleotide 1 through nucleotide 3 of SEQ ID NO:60.

Translation of SEQ ID NO:64, the coding strand for nCaCD154<sub>1878</sub>, yields a protein of about 260 amino acids, denoted herein as PCaCD154<sub>260</sub>, the amino acid sequence of which is presented in SEQ ID NO:65, assuming an open reading frame having an initiation codon spanning from nucleotide 284 through nucleotide 286 of SEQ ID NO:64 and a stop codon spanning from nucleotide 1064 through nucleotide 1066 of SEQ ID NO:64.

Translation of SEQ ID NO:72, the coding strand for nFeCD154<sub>885</sub>, yields a protein of about 260 amino acids, denoted herein as PFeCD154<sub>260</sub>, the amino acid sequence of which is presented in SEQ ID NO:73, assuming an open reading frame having an initiation codon spanning from nucleotide 29 through nucleotide 31 of SEQ ID NO:72, and a stop codon spanning from nucleotide 809 through nucleotide 811 of SEQ ID NO:72.

Translation of SEQ ID NO:80, the coding strand for nCaIL-5<sub>610</sub>, yields a protein of about 134 amino acids, denoted herein as PCaIL-5<sub>134</sub>, the amino acid sequence of which is presented in SEQ ID NO:81, assuming an open reading frame having an initiation codon spanning from nucleotide 29 through nucleotide 31 of SEQ ID NO:80, and a stop codon spanning from nucleotide 431 through nucleotide 433 of SEQ ID NO:80.

Translation of SEQ ID NO:91, the coding stand for nCaIL-13<sub>1302</sub>, yields a protein of about 131 amino acids, denoted herein as PCaIL-13<sub>131</sub>, the amino acid sequence of which is presented in SEQ ID NO:92, assuming an open reading frame having an initiation codon spanning from nucleotide 52 through nucleotide 54 of SEQ ID NO:91 and a stop codon spanning from nucleotide 445 through nucleotide 447 of SEQ ID NO:91.

Translation of SEQ ID NO:107, the coding strand for nFeIFN $\alpha$ <sub>567a</sub>, yields a protein of about 189 amino acids, denoted herein as PFeIFN $\alpha$ <sub>189a</sub>, the amino acid sequence of which is presented in SEQ ID NO:108, assuming an open reading frame having an initiation codon spanning from nucleotide 1 through nucleotide 3 and a last codon prior to a stop codon spanning from nucleotide 565 through nucleotide 567 of SEQ ID NO:107.

Translation of SEQ ID NO:110, the coding strand for nFeIFN $\alpha$ <sub>567b</sub>, yields a protein of about 189 amino acids, denoted herein as PFeIFN $\alpha$ <sub>189b</sub>, the amino acids sequence of which is presented in SEQ ID NO:111, assuming an open reading frame having an initiation codon spanning from nucleotide 1 through nucleotide 3 and a last codon prior to a stop codon spanning from nucleotide 565 through nucleotide 567 of SEQ ID NO:110.

Translation of SEQ ID NO:155, the coding strand for nFeIFN $\alpha_{567c}$ , yields a protein of about 189 amino acids, denoted herein as PFeIFN $\alpha_{189c}$ , the amino acid sequence of which is presented in SEQ ID NO:156, assuming an open reading frame having an initiation codon spanning from nucleotide 1 through nucleotide 3 and a last codon prior to a stop codon spanning from nucleotide 565 through nucleotide 567 of SEQ ID NO:155.

Translation of SEQ ID NO:161, the coding strand for nFeIFN $\alpha_{582d}$ , yields a protein of about 194 amino acids, denoted herein as PFeIFN $\alpha_{194d}$ , the amino acid sequence of which is presented in SEQ ID NO:162, assuming an open reading frame having an initiation codon spanning from nucleotide 1 through nucleotide 3 and a last codon prior to a stop codon spanning from nucleotide 565 through nucleotide 567 of SEQ ID NO:161.

Translation of SEQ ID NO:167, the coding strand for nFeIFN $\alpha_{567e}$ , yields a protein of about 189 amino acids, denoted herein as PFeIFN $\alpha_{189e}$ , the amino acid sequence of which is presented in SEQ ID NO:168, assuming an open reading frame having an initiation codon spanning from nucleotide 1 through nucleotide 3 and a last codon prior to a stop codon spanning from nucleotide 565 through nucleotide 567 of SEQ ID NO:167.

Translation of SEQ ID NO:119, the coding strand for nFeGMCSF $_{444}$ , yields a protein of about 144 amino acids, denoted herein as PFeGMCSF $_{144}$ , the amino acid sequence of which is presented in SEQ ID NO:120, assuming an open reading frame having an initiation codon spanning from nucleotide 10 through nucleotide 12 of SEQ ID NO:119 and a stop codon spanning from nucleotide 442 through nucleotide 444 of SEQ ID NO:119.

Preferred IL-4 proteins of the present invention include proteins that are at least about 85%, preferably at least about 90%, and even more preferably at least about 95% identical to PCaIL-4 $_{132}$ , PCaIL-4 $_{108}$ , or fragments thereof. Preferred Flt-3 ligand proteins of the present invention include proteins that are at least about 75%, even more preferably at least about 80%, even more preferably at least about 90%, and even more preferably at least about 95% identical to PCaFlt3L $_{294}$ , PCaFlt3L $_{268}$ , PCaFlt3L $_{276}$ , PCaFlt3L $_{250}$ , PCaFlt3L $_{31}$ , and/or fragments thereof. Additional preferred Flt-3 ligand proteins of the present invention includes proteins that are at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to PFeFlt3L $_{291}$ , PFeFlt3L $_{265}$  and/or fragments thereof. Preferred CD40 proteins of the present invention includes proteins that are at least about 70%, preferably at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to PCaCD40 $_{274}$ , PCaCD40 $_{255}$  and/or fragments thereof. Additional preferred CD40 proteins of the present invention includes proteins that are at least about 60%, at least about 65%, preferably at least about 70%, preferably at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to PFeCD40 $_{112}$  and/or fragments thereof. Preferred CD154 proteins of the present invention includes proteins that are at least about 80% identical, preferably at least about 85% identical, even more preferably at least about 90%, and even more preferably at least about 95% identical to PCaCD154 $_{260}$ , PCaCD154 $_{211}$  and/or fragments thereof.

Additional preferred CD154 proteins of the present invention includes proteins that are at least about 85% identical, even more preferably at least about 90%, and even more preferably at least about 95% identical to PFeCD154 $_{260}$ , PFeCD154 $_{211}$  and/or fragments thereof. Preferred IL-5 proteins of the present invention includes proteins that are at least about 85% identical, even more preferably at least about 90%, and even more preferably at least about 95% identical to PCaIL-5 $_{134}$ , PCaIL-5 $_{115}$  and/or fragments thereof. Preferred IL-13 proteins of the present invention includes proteins that are at least about 70% identical, preferably at least about 75% identical, more preferably at least about 80% identical, more preferably at least about 85% identical, even more preferably at least about 90%, and even more preferably at least about 95% identical to PCaIL-13 $_{131}$ , PCaIL-13 $_{111}$ , PCaEL-13 $_{130}$ , PCaIL-13 $_{110}$ , and/or fragments thereof. Preferred IFN $\alpha$  proteins of the present invention include PFeIFN $\alpha_{189a}$ , PFeIFN $\alpha_{189b}$ , PFeIFN $\alpha_{189c}$ , PFeIFN $\alpha_{166a}$ , PFeIFN $\alpha_{166c}$ , PFeIFN $\alpha_{194d}$ , PFeIFN $\alpha_{171d}$ , PFeIFN $\alpha_{189e}$ , PFeIFN $\alpha_{166e}$ , and/or PFeIFN $\alpha_{166b}$ . Preferred GM-CSF proteins of the present invention include PFeGMCSF $_{144}$ , and/or PFeGMCSF $_{127}$ .

More preferred are IL-4 proteins comprising PCaIL-4 $_{132}$ , PCaIL-4 $_{108}$ , and/or proteins encoded by allelic variants of a nucleic acid molecule encoding proteins PCaIL-4 $_{132}$  and/or PCaEL-4 $_{108}$ . More preferred are Flt-3 ligand proteins comprising PCaFlt3L $_{294}$ , PCaFlt3L $_{268}$ , PCaFlt3L $_{276}$ , PCaFlt3L $_{250}$ , PCaFlt3L $_{31}$ , PFeFlt3L $_{291}$ , PFeFlt3L $_{265}$  and/or proteins encoded by allelic variants of a nucleic acid molecule encoding proteins PCaFlt3L $_{294}$ , PCaFlt3L $_{268}$ , PCaFlt3L $_{276}$ , PCaFlt3L $_{250}$ , PCaFlt3L $_{31}$ , PFeFlt3L $_{291}$ , and/or PFeFlt3L $_{265}$ . More preferred are CD40 proteins comprising PCaCD40 $_{274}$ , PCaCD40 $_{255}$ , and/or PFeCD40 $_{112}$  and/or proteins encoded by allelic variants of a nucleic acid molecule encoding proteins PCaCD40 $_{274}$ , PCaCD40 $_{255}$ , and/or PFeCD40 $_{112}$ . More preferred are CD154 proteins comprising PCaCD154 $_{260}$ , PCaCD154 $_{211}$ , PFeCD154 $_{260}$ , PFeCD154 $_{211}$ . More preferred are IL-5 proteins comprising PCaEL-5 $_{134}$ , PCaIL-5 $_{115}$  and/or proteins encoded by allelic variants of a nucleic acid molecule encoding one of the proteins PCaIL-5 $_{134}$  and/or PCaIL-5 $_{115}$ . More preferred are IL-13 proteins comprising PCaIL-13 $_{131}$ , PCaIL-13 $_{111}$ , PCaIL-13 $_{130}$ , PCaIL-13 $_{110}$ , and/or proteins encoded by allelic variants of a nucleic acid molecule encoding one of the proteins PCaIL-13 $_{131}$ , PCaIL-13 $_{111}$ , PCaIL-13 $_{130}$ , PCaIL-13 $_{110}$ .

Also preferred are IL-4 proteins of the present invention having amino acid sequences that are at least about 85%, preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:2, SEQ ID NO:20 and/or fragments thereof. Also preferred are Flt-3 ligand proteins of the present invention having amino acid sequences that are at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34 and/or fragments thereof. Additional preferred Flt-3 ligand proteins of the present invention includes proteins that are at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and/or even more preferably at least about 95% identical to SEQ ID NO:44, SEQ ID NO:49 and/or fragments thereof. Preferred CD40 proteins of the present invention includes proteins that are at

least about 70%, preferably at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and/or even more preferably at least about 95% identical to SEQ ID NO:53, SEQ ID NO:58 and/or fragments thereof. Additional preferred CD40 proteins of the present invention includes proteins that are at least about 60%, at least about 65%, preferably at least about 70%, preferably at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:61 and/or fragments thereof. Preferred CD154 proteins of the present invention includes proteins that are at least about 80% identical, preferably at least about 85% identical, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:65, SEQ ID NO:70 and/or fragments thereof. Additional preferred CD154 proteins of the present invention includes proteins that are at least about 85% identical, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:73, SEQ ID NO:78 and/or fragments thereof. Preferred IL-5 proteins of the present invention includes proteins that are at least about 85% identical, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:81, SEQ ID NO:86 and/or fragments thereof. Preferred IL-13 proteins of the present invention includes proteins that are at least about 70% identical, preferably at least about 75% identical, more preferably at least about 80% identical, more preferably at least about 85% identical, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, SEQ ID NO:105, and/or fragments thereof. Preferred IFN $\alpha$  proteins of the present invention include SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and SEQ ID NO:171. Preferred GM-CSF proteins of the present invention include SEQ ID NO:120, SEQ ID NO:125.

More preferred are IL-4 proteins comprising the amino acid sequence SEQ ID NO:2, SEQ ID NO:20; and/or L-4 proteins encoded by allelic variants of nucleic acid molecules encoding IL-4 proteins having the amino acid sequence SEQ ID NO:2, SEQ ID NO:20. More preferred are Flt-3 ligand proteins comprising SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34, SEQ ID NO:44, SEQ ID NO:49 and/or proteins encoded by allelic variants of a nucleic acid molecule encoding proteins SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:44, and/or SEQ ID NO:49. More preferred are CD40 proteins comprising SEQ ID NO:53, SEQ ID NO:58 SEQ ID NO:61 and/or proteins encoded by allelic variants of a nucleic acid molecule encoding proteins SEQ ID NO:53, SEQ ID NO:58 and/or SEQ ID NO:61. More preferred are CD154 proteins comprising SEQ ID NO:65, SEQ ID NO:70 SEQ ID NO:73, SEQ ID NO:78 and/or proteins encoded by allelic variants of a nucleic acid molecule encoding one of proteins SEQ ID NO:65, SEQ ID NO:70, SEQ ID NO:73, and/or SEQ ID NO:78. More preferred are IL-5 proteins comprising SEQ ID NO:81, SEQ ID NO:86 and/or proteins encoded by allelic variants of a nucleic acid molecule encoding one of the proteins SEQ ID NO:81, and/or SEQ ID NO:86. More preferred are IL-13 proteins comprising SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, SEQ ID NO:105, and/or proteins encoded by allelic variants of a nucleic acid mol-

ecule encoding one of the proteins SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and/or SEQ ID NO:105.

Percent identities between amino acid or nucleic acid sequences can be determined using standard methods known to those of skill in the art. It is known in the art that methods to determine the percentage identity and the number of gaps are substantially similar when different methods for determining sequence similarity are used and when the degree of similarity is greater than 30% amino acid identity, as described in Johnson et al., J. Mol. Biol., vol. 233, pages 716-738, 1993, and Feng et al., J. Mol. Evol., vol. 21, pages 112-125, 1985, which are incorporated by reference herein in their entirety. Preferred methods to determine percentage identities between amino acid sequences and between nucleic acid sequences include comparisons using various computer programs such as GCG™ program (available from Genetics Computer Group, Madison, Wis.), DNAsis™ program (available from Hitachi Software, San Bruno, Calif.) or the MacVector™ program (available from the Eastman Kodak Company, New Haven, Conn.). Preferred settings for sequence comparisons using the DNAsis™ computer program or the GAPGCG™ program are disclosed herein in the Examples section.

Additional preferred L-4 proteins of the present invention include proteins encoded by nucleic acid molecules comprising at least a portion of nCaIL-4<sub>549</sub>, nCaIL-4<sub>396</sub>, and/or nCaIL-4<sub>324</sub>, as well as IL-4 proteins encoded by allelic variants of such nucleic acid molecules. Additional preferred Flt-3 ligand proteins of the present invention include proteins encoded by nucleic acid molecules comprising at least a portion of nCaFlt3L<sub>1013</sub>, nCaFlt3L<sub>882</sub>, nCaFlt3L<sub>804</sub>, nCaFlt3L<sub>828</sub>, nCaFlt3L<sub>985</sub>, CaFlt3L<sub>109</sub>, nCaFlt3L<sub>93</sub>, nCaFlt3L<sub>750</sub>, nFeFlt3L<sub>395</sub>, nFeFlt3L<sub>793</sub>, nFeFlt3L<sub>942</sub>, nFeFlt3L<sub>873</sub>, and/or nFeFlt3L<sub>795</sub> as well as Flt-3 ligand proteins encoded by allelic variants of such nucleic acid molecules. Additional preferred CD40 proteins of the present invention include proteins encoded by nucleic acid molecules encoding at least a protein of nCaCD40<sub>321</sub>, nCaCD40<sub>1425</sub>, nCaCD40<sub>822</sub>, nCaCD40<sub>765</sub>, and/or nFeCD40<sub>336</sub> as well as CD40 proteins encoded by allelic variants of such nucleic acid molecules. Additional preferred CD154 proteins of the present invention include proteins encoded by nucleic acid molecules encoding at least a portion of nCaCD154<sub>390</sub>, nCaCD154<sub>878</sub>, nCaCD154<sub>780</sub>, nCaCD154<sub>633</sub>, nFeCD154<sub>885</sub>, nFeCD154<sub>780</sub>, and/or nFeCD154<sub>633</sub> as well as CD154 proteins encoded by allelic variants of such nucleic acid molecules. Additional preferred IL-5 proteins of the present invention include proteins encoded by nucleic acid molecules encoding at least a portion of nCaIL-5<sub>610</sub>, nCaIL-5<sub>402</sub>, and/or nCaIL-5<sub>345</sub> as well as IL-5 proteins encoded by allelic variants of such nucleic acid molecules. Additional preferred IL-13 proteins of the present invention include proteins encoded by nucleic acid molecules encoding at least a portion of nCaIL-5<sub>610</sub>, nCaIL-5<sub>402</sub>, and/or nCaIL-5<sub>345</sub> as well as IL-13 proteins encoded by allelic variants of such nucleic acid molecules.

Also preferred are IL-4 proteins encoded by nucleic acid molecules having nucleic acid sequences comprising at least a portion of SEQ ID NO:1, SEQ ID NO:4, and/or SEQ ID NO:19, as well as allelic variants of these nucleic acid molecules. Also preferred are Flt-3 ligand proteins encoded by nucleic acid molecules having nucleic acid sequences comprising at least a portion of SEQ ID NO:6, SEQ ID NO:9, SEQ ID NO:22, SEQ ID NO:25, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:33, SEQ ID NO:36, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:46, and/or SEQ ID NO:48, as well as allelic variants of these

nucleic acid molecules. Also preferred are CD40 proteins encoded by nucleic acid molecules having nucleic acid sequences comprising at least a portion of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:55, SEQ ID NO:57, and/or SEQ ID NO:60, as well as allelic variants of these nucleic acid molecules. Also preferred are CD154 proteins encoded by nucleic acid molecules having nucleic acid sequences comprising at least a portion of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:72, SEQ ID NO:75, and/or SEQ ID NO:77, as well as allelic variants of these nucleic acid molecules. Also preferred are IL-5 proteins encoded by nucleic acid molecules having nucleic acid sequences comprising at least a portion of SEQ ID NO:80, SEQ ID NO:83, and/or SEQ ID NO:85, as well as allelic variants of these nucleic acid molecules. Also preferred are EL-13 proteins encoded by nucleic acid molecules having nucleic acid sequences comprising at least a portion of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:99, SEQ ID NO:102, and/or SEQ ID NO:104, as well as allelic variants of these nucleic acid molecules.

Another embodiment of the present invention is a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecule that includes one or more regulatory regions, full-length or partial coding regions, or combinations thereof. The minimal size of a nucleic acid molecule of the present invention is a size sufficient to allow the formation of a stable hybrid (i.e., hybridization under stringent hybridization conditions) with the complementary sequence of another nucleic acid molecule. As such, the minimal size of a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecule of the present invention is from about 12 to about 18 nucleotides in length.

In accordance with the present invention, an isolated nucleic acid molecule is a nucleic acid molecule that has been removed from its natural milieu (i.e., that has been subjected to human manipulation) and can include DNA, RNA, or derivatives of either DNA or RNA. As such, "isolated" does not reflect the extent to which the nucleic acid molecule has been purified. An isolated canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecule of the present invention can be isolated from its natural source or produced using recombinant DNA technology (e.g., polymerase chain reaction (PCR) amplification or cloning) or chemical synthesis. Isolated canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, and/or feline GM-CSF, nucleic acid molecules can include, for example, natural allelic variants and/or nucleic acid molecules modified by nucleotide insertions, deletions, substitutions, and/or inversions in a manner such that the modifications do not substantially interfere with the nucleic acid molecule's ability to encode an canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, and/or feline GM-CSF protein of the present invention.

A canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha,

and/or feline GM-CSF ligand nucleic acid molecule homolog can be produced using a number of methods known to those skilled in the art, see, for example, Sambrook et al., 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Labs Press; Sambrook et al., *ibid.*, is incorporated by reference herein in its entirety. For example, nucleic acid molecules can be modified using a variety of techniques including, but not limited to, classic mutagenesis and recombinant DNA techniques such as site-directed mutagenesis, chemical treatment, restriction enzyme cleavage, ligation of nucleic acid fragments, PCR amplification, synthesis of oligonucleotide mixtures and ligation of mixture groups to "build" a mixture of nucleic acid molecules, and combinations thereof. Nucleic acid molecule homologs can be selected by hybridization with either a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecule or by screening the function of a protein encoded by the nucleic acid molecule (e.g., ability to elicit an immune response against at least one epitope of a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein, respectively).

An isolated nucleic acid molecule of the present invention can include a nucleic acid sequence that encodes at least one canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein of the present invention, examples of such proteins being disclosed herein. Although the phrase "nucleic acid molecule" primarily refers to the physical nucleic acid molecule and the phrase "nucleic acid sequence" primarily refers to the sequence of nucleotides on the nucleic acid molecule, the two phrases can be used interchangeably, especially with respect to a nucleic acid molecule, or a nucleic acid sequence, being capable of encoding a canine interleukin-4, canine or feline Flt3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF ligand protein.

A preferred nucleic acid molecule of the present invention, when administered to an animal, is capable of regulating an immune response in an animal. As will be disclosed in more detail below, such a nucleic acid molecule can be, or encode, an antisense RNA, a molecule capable of triple helix formation, a ribozyme, or other nucleic acid-based drug compound. In additional embodiments, a nucleic acid molecule of the present invention can encode an immunoregulatory protein (e.g., a cell-bound or soluble protein of the present invention), the nucleic acid molecule being delivered to the animal, for example, by direct injection (i.e., as a genetic vaccine) or in a vehicle such as a recombinant virus vaccine or a recombinant cell vaccine.

One embodiment of the present invention is an IL-4 nucleic acid molecule comprising all or part (i.e., a fragment of the IL-4 nucleic acid molecule) of nucleic acid molecules nCaIL-4<sub>549</sub>, nCaIL-4<sub>396</sub>, and/or nCaIL-4<sub>324</sub>, or allelic variants of these nucleic acid molecules. One embodiment of the present invention is a Flt-3 ligand nucleic acid molecule comprising all or part (i.e., a fragment of the Flt-3 ligand nucleic acid molecule) of nucleic acid molecules nCaFlt3L<sub>1013</sub>, nCaFlt3L<sub>882</sub>, nCaFlt3L<sub>804</sub>, nCaFlt3L<sub>828</sub>, nCaFlt3L<sub>985</sub>, nCaFlt3L<sub>1019</sub>, nCaFlt3L<sub>93</sub>, nCaFlt3L<sub>750</sub>, nFeFlt3L<sub>395</sub>, nFeFlt3L<sub>793</sub>, nFeFlt3L<sub>942</sub>, nFeFlt3L<sub>873</sub>, and/or nFeFlt3L<sub>795</sub>, and/or allelic variants of these nucleic acid

molecules. One embodiment of the present invention is a CD40 nucleic acid molecule comprising all or part (i.e. a fragment of the CD40 nucleic acid molecule) of nucleic acid molecules nCaCD40<sub>321</sub>, nCaCD40<sub>1425</sub>, nCaCD40<sub>822</sub>, nCaCD40<sub>765</sub>, and/or nFeCD40<sub>336</sub> and/or allelic variants of these nucleic acid molecules. One embodiment of the present invention is a CCD154 nucleic acid molecule comprising all or part of nucleic acid molecules nCaCD154<sub>390</sub>, nCaCD154<sub>1878</sub>, nCaCD154<sub>780</sub>, nCaCD154<sub>633</sub>, nFeCD154<sub>885</sub>, nFeCD154<sub>780</sub>, and/or nFeCD154<sub>633</sub>, and/or allelic variants of these nucleic acid molecules. One embodiment of the present invention is an IL-5 nucleic acid molecule comprising all or part of nucleic acid molecules nCaIL-5<sub>610</sub>, nCaIL-5<sub>402</sub>, and/or nCaIL-5<sub>345</sub>, and/or allelic variants of these nucleic acid molecules. One embodiment of the present invention is an IL-13 nucleic acid molecule comprising all or part of nucleic acid molecules nCaIL-13<sub>166</sub>, nCaIL-13<sub>272</sub>, nCaIL-13<sub>278</sub>, nCaIL-13<sub>1302</sub>, nCaIL-13<sub>393</sub>, nCaIL-13<sub>333</sub>, nCaIL-13<sub>1269</sub>, nCaIL-13<sub>390</sub>, and/or nCaIL-13<sub>330</sub>, and/or allelic variants of these nucleic acid molecules. Another preferred nucleic acid molecule of the present invention includes at least a portion of (i.e., a fragment of the nucleic acid molecule) nucleic acid sequence SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:126, SEQ ID NO:155, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:169, SEQ ID NO:170, and/or SEQ ID NO:172, as well as allelic variants of nucleic acid molecules having these nucleic acid sequences. Such nucleic acid molecules can include nucleotides in addition to those included in the SEQ ID NOs, such as, but not limited to, a full-length gene, a full-length coding region, a nucleic acid molecule encoding a fusion protein, and/or a nucleic acid molecule encoding a multivalent therapeutic compound.

One embodiment of an isolated nucleic acid molecule of the present invention is a nucleic acid molecule that can be any of the following: (a) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, and/or SEQ ID NO:21 and/or a homolog thereof, wherein said homolog has an at

least 50 contiguous nucleotide region identical in sequence to a 50 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, and/or SEQ ID NO:21; (b) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and/or SEQ ID NO:37, and/or a homolog thereof, wherein said homolog has an at least 40 contiguous nucleotide region identical in sequence to a 40 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and/or SEQ ID NO:37; (c) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and/or SEQ ID NO:50, and/or a homolog thereof, wherein said homolog has an at least 30 contiguous nucleotide region identical in sequence to a 30 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and/or SEQ ID NO:50; (d) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and/or SEQ ID NO:59, and/or a homolog thereof, wherein said homolog has an at least 40 contiguous nucleotide region identical in sequence to a 40 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and/or SEQ ID NO:59; (e) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:60 and/or SEQ ID NO:62, and/or a homolog thereof, wherein said homolog has an at least 30 contiguous nucleotide region identical in sequence to a 30 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:60 and/or SEQ ID NO:62; (f) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69 and/or SEQ ID NO:71, and/or a homolog thereof, wherein said homolog has an at least 45 contiguous nucleotide region identical in sequence to a 45 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, and/or SEQ ID NO:71; (g) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and/or SEQ ID NO:79, and/or a homolog thereof, wherein said homolog has an at least 35 contiguous nucleotide region identical in sequence to a 35 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from

the group consisting of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and/or SEQ ID NO:79; (h) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and/or SEQ ID NO:87, and/or a homolog thereof, wherein said homolog has an at least 45 contiguous nucleotide region identical in sequence to a 45 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and/or SEQ ID NO:87; (i) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and/or SEQ ID NO:106, and/or a homolog thereof, wherein said homolog has an at least 15 contiguous nucleotide region identical in sequence to a 15 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and/or SEQ ID NO:106; (j) an isolated nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:155, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:169, SEQ ID NO:170 and/or SEQ ID NO:172; and/or (k) an isolated nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, and/or SEQ ID NO:126. The phrase, a homolog having an at least "x" contiguous nucleotide region identical in sequence to an "x" contiguous nucleotide region of a nucleic acid molecule selected from the group consisting of SEQ ID NO:"y", refers to an "x"-nucleotide in length nucleic acid molecule that is identical in sequence to an "x"-nucleotide portion of SEQ ID NO:"y", as well as to nucleic acid molecules that are longer in length than "x". The additional length may be in the form of nucleotides that extend from either the 5' or the 3' end(s) of the contiguous identical "x"-nucleotide portion. The 5' and/or 3' extensions can include one or more extensions that have no identity to an immunoregulatory molecule of the present invention, as well as extensions that show similarity or identity to cited nucleic acids sequences or proteins thereof.

In another embodiment, an isolated nucleic acid molecule of the present invention can be any of the following: (a) a nucleic acid molecule having a nucleic acid sequence encoding an IL-4 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:2 and/or SEQ ID NO:20 and/or (ii) a protein comprising a fragment of at least 20 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:2 and/or SEQ ID NO:20; (b) a nucleic acid molecule having a nucleic acid sequence encoding a Flt-3 ligand protein selected from the group

consisting of (i) a protein having an amino acid sequence that is at least about 75 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34, and/or (ii) a protein comprising a fragment of at least 25 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34; (c) a nucleic acid molecule having a nucleic acid sequence encoding a Flt-3 ligand protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 75 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:44 and/or SEQ ID NO:49 and/or (ii) a protein comprising a fragment of at least 25 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:44 and/or SEQ ID NO:49; (d) a nucleic acid molecule having a nucleic acid sequence encoding a CD40 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 70 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:53 and/or SEQ ID NO:58 and/or (ii) a protein comprising a fragment of at least 30 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:53 and/or SEQ ID NO:58; (e) a nucleic acid molecule having a nucleic acid sequence encoding a CD40 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 60 percent identical to an amino acid sequence comprising SEQ ID NO:61 and/or (ii) a protein comprising a fragment of at least 20 amino acids of an amino acid sequence comprising SEQ ID NO:61; (f) a nucleic acid molecule having a nucleic acid sequence encoding a CD154 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 80 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:65 and/or SEQ ID NO:70, and/or (ii) a protein comprising a fragment of at least 35 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:65 and/or SEQ ID NO:70; (g) a nucleic acid molecule having a nucleic acid sequence encoding a CD154 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:73 and/or SEQ ID NO:78, and/or (ii) a protein comprising a fragment of at least 50 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:73 and/or SEQ ID NO:78; (h) a nucleic acid molecule having a nucleic acid sequence encoding an IL-5 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:81 and/or SEQ ID NO:86 and/or (ii) a protein comprising a fragment of at least 20 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:81 and/or SEQ ID NO:86; (i) a nucleic acid molecule having a nucleic acid sequence encoding an IL-13 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 70 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and/or SEQ ID NO:105 and/or (ii) a protein comprising a fragment of at least 15 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and/or SEQ ID NO:105; (j) a nucleic acid molecule having a nucleic acid

sequence encoding an interferon alpha protein having an amino acid sequence that is selected from the group consisting of amino acid sequence SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and/or SEQ ID NO:171; (k) a nucleic acid molecule having a nucleic acid sequence encoding a GMCSF protein having an amino acid sequence that is selected from the group consisting of amino acid sequence SEQ ID NO:120, SEQ ID NO:125, and/or (l) a nucleic acid molecule comprising a complement of any of the before-mentioned nucleic acid sequences; wherein said IL-4 protein elicits an immune response against an IL-4 protein selected from the group consisting of SEQ ID NO:2 and/or SEQ ID NO:20 and/or is a protein with interleukin-4 activity, said Flt-3 ligand protein elicits an immune response against a Flt-3 ligand protein selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:44, and/or SEQ ID NO:49 and/or is a protein with Flt-3 ligand activity, said CD40 protein elicits an immune response against a CD40 protein selected from the group consisting of SEQ ID NO:53, SEQ ID NO:58, and/or SEQ ID NO:61 and/or is a protein with CD40 activity, said CD154 protein elicits an immune response against a CD154 protein selected from the group consisting of SEQ ID NO:65, SEQ ID NO:70, SEQ ID NO:73, and/or SEQ ID NO:78 and/or is a protein with CD154 activity, said IL-5 protein elicits an immune response against a IL-5 protein selected from the group consisting of SEQ ID NO:81 and/or SEQ ID NO:86 and/or is a protein with IL-5 activity, said IL-13 protein elicits an immune response against an IL-13 protein selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and/or SEQ ID NO:105 and/or is a protein with IL-13 activity, said interferon alpha protein elicits an immune response against an interferon alpha protein selected from the group consisting of SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and/or SEQ ID NO:171 and/or is a protein with interferon alpha activity, and said GMCSF protein elicits an immune response against a GMCSF protein selected from the group consisting of SEQ ID NO:120 and/or SEQ ID NO:125 and/or is a protein with GM-CSF activity.

In one embodiment, an IL-4 nucleic acid molecule of the present invention encodes a protein that is at least about 85%, preferably at least about 90%, preferably at least about 92%, and even more preferably at least about 95% identical to PCaIL-4<sub>132</sub> and/or PCaIL-4<sub>108</sub>. In one embodiment, a Flt-3 ligand nucleic acid molecule of the present invention encodes a protein that is at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to PCaFlt3L<sub>294</sub>, PCaFlt3L<sub>268</sub>, PCaFlt3L<sub>276</sub>, PCaFlt3L<sub>250</sub>, and/or PCaFlt3L<sub>31</sub>. In one embodiment, a Flt-3 ligand nucleic acid molecule of the present invention encodes a protein that is at least about 75%, more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to PFeFlt3L<sub>291</sub>, and/or PFeFlt3L<sub>265</sub>. In one embodiment, a CD40 nucleic acid molecule of the present invention encodes a protein that is at least about PCaCD40<sub>274</sub>, and/or PCaCD40<sub>255</sub>. In one embodiment, a CD40 nucleic acid molecule of the present invention encodes a protein that is at least about 60%, preferably at

least about 65%, preferably at least about 70%, preferably at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to PFeCD40<sub>112</sub>. In one embodiment, a CD154 nucleic acid molecule of the present invention encodes a protein that is at least about 80%, at least about 85%, more preferably at least about 90%, and even more preferably at least about 95% identical to PCaCD154<sub>260</sub>, and/or PCaCD154<sub>211</sub>. In one embodiment, a CD154 nucleic acid molecule of the present invention encodes a protein that is at least about 85%, more preferably at least about 90%, and even more preferably at least about 95% identical to PFeCD154<sub>260</sub>, PFeCD154<sub>211</sub>. In one embodiment, an IL-5 nucleic acid molecule of the present invention encodes a protein that is at least about 85%, more preferably at least about 90%, and even more preferably at least about 95% identical to PCaIL-5<sub>134</sub>, and/or PCaIL-5<sub>115</sub>. In one embodiment, an IL-13 nucleic acid molecule of the present invention encodes a protein that is at least about 70%, at least about 75%, at least about 80%, preferably at least about 85%, more preferably at least about 90%, and even more preferably at least about 95% identical to PCaIL-13<sub>131</sub>, PCaIL-13<sub>111</sub>, PCaIL-13<sub>130</sub>, PCaIL-13<sub>110</sub>. Even more preferred is a nucleic acid molecule encoding PCaIL-4<sub>132</sub>, PCaIL-4<sub>108</sub>, PCaFlt3L<sub>294</sub>, PCaFlt3L<sub>268</sub>, PCaFlt3L<sub>276</sub>, PCaFlt3L<sub>250</sub>, PCaFlt3L<sub>31</sub>, PFeFlt3L<sub>291</sub>, PFeFlt3L<sub>265</sub>, PCaCD40<sub>274</sub>, PCaCD40<sub>255</sub>, PFeCD40<sub>112</sub>, PCaCD154<sub>260</sub>, PCaCD154<sub>211</sub>, PFeCD154<sub>260</sub>, PFeCD154<sub>211</sub>, PCaIL-5<sub>134</sub>, PCaIL-5<sub>115</sub>, PCaIL-13<sub>131</sub>, PCaIL-13<sub>111</sub>, PCaIL-13<sub>130</sub>, PCaIL-13<sub>110</sub> and/or an allelic variant of such a nucleic acid molecule.

In another embodiment, an IL-4 nucleic acid molecule of the present invention encodes a protein having an amino acid sequence that is at least about 85%, preferably at least about 90%, and even more preferably about at least about 95% identical to SEQ ID NO:2, SEQ ID NO:20. The present invention also includes an IL-4 nucleic acid molecule encoding a protein having at least a portion of SEQ ID NO:2, and/or SEQ ID NO:20, as well as allelic variants of an IL-4 nucleic acid molecule encoding a protein having these sequences, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In another embodiment, a Flt-3 ligand nucleic acid molecule of the present invention encodes a protein having an amino acid sequence that is at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34. The present invention also includes a Flt-3 ligand nucleic acid molecule encoding a protein having at least a portion of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34, as well as allelic variants of a Flt-3 ligand nucleic acid molecule encoding a protein having these sequences, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In another embodiment, a Flt-3 ligand nucleic acid molecule of the present invention encodes a protein having an amino acid sequence that is at least about 75%, more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID

NO:44, and/or SEQ ID NO:49. The present invention also includes a Flt-3 ligand nucleic acid molecule encoding a protein having at least a portion of SEQ ID NO:44, and/or SEQ ID NO:49, as well as allelic variants of a Flt-3 ligand nucleic acid molecule encoding a protein having these sequences, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In another embodiment, a CD40 nucleic acid molecule of the present invention encodes a protein having an amino acid sequence that is at least about 70%, preferably at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:53 and/or SEQ ID NO:58. The present invention also includes a CD40 nucleic acid molecule encoding a protein having at least a portion of SEQ ID NO:53 and/or SEQ ID NO:58, as well as allelic variants of a CD40 nucleic acid molecule encoding a protein having these sequences, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In another embodiment, a CD40 nucleic acid molecule of the present invention encodes a protein having an amino acid sequence that is at least about 60%, preferably at least about 65%, preferably at least about 70%, preferably at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:60. The present invention also includes a CD40 nucleic acid molecule encoding a protein having at least a portion of SEQ ID NO:60, as well as allelic variants of a CD40 nucleic acid molecule encoding a protein having these sequences, including nucleic acid molecules that have been modified to accommodate codon usage properties to the cells in which such nucleic acid molecules are to be expressed.

In another embodiment, a CD154 nucleic acid molecule of the present invention encodes a protein having an amino acid sequence that is at least about at least about 80%, at least about 85%, more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:67, and/or SEQ ID NO:69. The present invention also includes a CD154 nucleic acid molecule encoding a protein having at least a portion of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:67, and/or SEQ ID NO:69, as well as allelic variants of a CD154 nucleic acid molecule encoding a protein having these sequences, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In another embodiment, a CD154 nucleic acid molecule of the present invention encodes a protein having an amino acid sequence that is at least about at least about 85%, more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:72, SEQ ID NO:75, and/or SEQ ID NO:77. The present invention also includes a CD154 nucleic acid molecule encoding a protein having at least a portion of SEQ ID NO:72, SEQ ID NO:75, and/or SEQ ID NO:77, as well as allelic variants of a CD154 nucleic acid molecule encoding a protein having these sequences, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In another embodiment, an IL-5 nucleic acid molecule of the present invention encodes a protein having an amino acid sequence that is at least about at least about 85%, at least about 85%, more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:80, SEQ ID NO:83, and/or SEQ ID NO:85. The present invention also includes an IL-5 nucleic acid molecule encoding a protein having at least a portion of SEQ ID NO:80, SEQ ID NO:83, and/or SEQ ID NO:85, as well as allelic variants of an IL-5 nucleic acid molecule encoding a protein having these sequences, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In another embodiment, an IL-13 nucleic acid molecule of the present invention encodes a protein having an amino acid sequence that is at least about at least about 70%, at least about 75%, at least about 80%, preferably at least about 85%, more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:99, SEQ ID NO:102, and/or SEQ ID NO:104. The present invention also includes an IL-13 nucleic acid molecule encoding a protein having at least a portion of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:99, SEQ ID NO:102, and/or SEQ ID NO:104, as well as allelic variants of an IL-13 nucleic acid molecule encoding a protein having these sequences, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In one embodiment, an IL-4 nucleic acid molecule of the present invention is at least about 90%, and preferably at least about 95% identical to nCaIL-4<sub>549</sub>. Even more preferred is a nucleic acid molecule comprising nCaIL-4<sub>549</sub>, nCaIL-4<sub>396</sub>, nCaIL-4<sub>324</sub>, and/or an allelic variant of such a nucleic acid molecule. In another embodiment, a Flt-3 ligand nucleic acid molecule of the present invention is at least about 75%, more preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to nCaFlt3L<sub>1013</sub>. Even more preferred is a nucleic acid molecule comprising nCaFlt3L<sub>1013</sub>, nCaFlt3L<sub>882</sub>, nCaFlt3L<sub>804</sub>, nCaFlt3L<sub>828</sub>, nCaFlt3L<sub>985</sub>, nCaFlt3L<sub>1019</sub>, nCaFlt3L<sub>93</sub>, and/or nCaFlt3L<sub>750</sub>, and/or an allelic variant of such a nucleic acid molecule. In one embodiment, a Flt-3 ligand nucleic acid molecule of the present invention is at least about 75%, more preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to nFeFlt3L<sub>942</sub>. Even more preferred is a nucleic acid molecule comprising nFeFlt3L<sub>395</sub>, nFeFlt3L<sub>793</sub>, nFeFlt3L<sub>942</sub>, nFeFlt3L<sub>873</sub>, and/or nFeFlt3L<sub>795</sub>, and/or an allelic variant of such a nucleic acid molecule. In one embodiment, a CD40 nucleic acid molecule of the present invention is at least about 70%, at least about 75%, more preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to nCaCD40<sub>321</sub>, nCaCD40<sub>1425</sub>, nCaCD40<sub>822</sub>, and/or nCaCD40<sub>765</sub>, and/or an allelic variant of such a nucleic acid molecule. In one embodiment, a CD40 nucleic acid molecule of the present invention is at least about 70%, at least about 75%, more preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to nFeCD40<sub>336</sub>,

and/or an allelic variant of such a nucleic acid molecule. In one embodiment, a CD154 nucleic acid molecule of the present invention is at least about 85%, preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to nCaCD154<sub>390</sub>, nCaCD154<sub>878</sub>, nCaCD154<sub>780</sub>, and/or nCaCD154<sub>633</sub>, and/or an allelic variant of such a nucleic acid molecule. In one embodiment, a CD154 nucleic acid molecule of the present invention is at least about 91%, and preferably about 95% identical to nFeCD154<sub>885</sub>, nFeCD154<sub>780</sub>, and/or nFeCD154<sub>633</sub>, and/or an allelic variant of such a nucleic acid molecule. In one embodiment, an IL-5 molecule of the present invention is at least about 90% and preferably at least about 95% identical to nCaIL-5<sub>610</sub>, nCaIL-5<sub>402</sub>, and/or nCaIL-5<sub>345</sub>, and/or an allelic variant of such a nucleic acid molecule. In another embodiment, an IL-13 molecule of the present invention is at least about 65%, at least about 70%, preferably at least about 75%, more preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to nCaIL-13<sub>166</sub>, nCaIL-13<sub>272</sub>, nCaIL-13<sub>278</sub>, nCaIL-13<sub>1302</sub>, nCaIL-13<sub>393</sub>, nCaIL-13<sub>333</sub>, nCaIL-13<sub>1269</sub>, nCaIL-13<sub>390</sub>, and/or nCaIL-13<sub>330</sub>, and/or an allelic variant of such a nucleic acid molecule.

In another embodiment, an IL-4 nucleic acid molecule of the present invention comprises a nucleic acid sequence that is at least about 90%, and preferably at least about 95% identical to SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, and/or SEQ ID NO:21. The present invention also includes an IL-4 nucleic acid molecule comprising at least a portion of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, and/or SEQ ID NO:21, as well as allelic variants of such IL-4 nucleic acid molecules, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In another embodiment, a Flt-3 ligand nucleic acid molecule of the present invention comprises a nucleic acid sequence that is at least about 75%, preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and/or SEQ ID NO:37. The present invention also includes a Flt-3 ligand- nucleic acid molecule comprising at least a portion of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and/or SEQ ID NO:37, as well as allelic variants of such Flt-3 ligand nucleic acid molecules, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In one embodiment, a Flt-3 ligand nucleic acid molecule of the present invention comprises a nucleic acid sequence that is at least about 75%, more preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and/or SEQ ID NO:50. The present invention also

includes a Flt-3 ligand- nucleic acid molecule comprising at least a portion of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and/or SEQ ID NO:50, as well as allelic variants of such Flt-3 ligand nucleic acid molecules, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In one embodiment, a CD40 nucleic acid molecule of the present invention comprises a nucleic acid sequence that is at least about 70%, at least about 75%, more preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and/or SEQ ID NO:59. The present invention also includes a CD40 nucleic acid molecule comprising at least a portion of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and/or SEQ ID NO:59, as well as allelic variants of such CD40 nucleic acid molecules, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In one embodiment, a CD40 nucleic acid molecule of the present invention comprises a nucleic acid sequence that is at least about 70%, at least about 75%, more preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to SEQ ID NO:60 and/or SEQ ID NO:62. The present invention also includes a CD40 nucleic acid molecule comprising at least a portion of SEQ ID NO:60 and/or SEQ ID NO:62, as well as allelic variants of such CD40 nucleic acid molecules, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In one embodiment, a CD154 nucleic acid molecule of the present invention comprises a nucleic acid sequence that is at least about 85%, preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, and/or SEQ ID NO:71. The present invention also includes a CD154 nucleic acid molecule comprising at least a portion of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, and/or SEQ ID NO:71, as well as allelic variants of such CD154 nucleic acid molecules, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In one embodiment, a CD154 nucleic acid molecule of the present invention comprises a nucleic acid sequence that is at least about 91%, and preferably about 95% identical to SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and/or SEQ ID NO:79. The present invention also includes a CD154 nucleic acid molecule comprising at least a portion of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and/or SEQ ID NO:79, as well as allelic variants of such CD154 nucleic acid molecules, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In one embodiment, an IL-5 nucleic acid molecule of the present invention comprises a nucleic acid sequence that is

at least about 90% and preferably at least about 95% identical to SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and/or SEQ ID NO:87. The present invention also includes an IL-5 nucleic acid molecule comprising at least a portion of SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and/or SEQ ID NO:87, as well as allelic variants of such IL-5 nucleic acid molecules, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In one embodiment, an IL-13 nucleic acid molecule of the present invention comprises a nucleic acid sequence that is at least about 65%, at least about 70%, preferably at least about 75%, more preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and/or SEQ ID NO:106. The present invention also includes an IL-13 nucleic acid molecule comprising at least a portion of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and/or SEQ ID NO:106, as well as allelic variants of such IL-13 nucleic acid molecules, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In one embodiment, an IFN $\alpha$  nucleic acid molecule of the present invention is identical to SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:155, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:169, SEQ ID NO:170, and/or SEQ ID NO:172.

In another embodiment, a GM-CSF nucleic acid molecule of the present invention is identical to SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, and/or SEQ ID NO:126.

Knowing the nucleic acid sequences of certain immunoregulatory nucleic acid molecules of the present invention allows one skilled in the art to, for example, (a) make copies of those nucleic acid molecules, (b) obtain nucleic acid molecules including at least a portion of such nucleic acid molecules (e.g., nucleic acid molecules including full-length genes, full-length coding regions, regulatory control sequences, truncated coding regions), and/or (c) obtain other immunoregulatory nucleic acid molecules. Such nucleic acid molecules can be obtained in a variety of ways including screening appropriate expression libraries with antibodies of the present invention; traditional cloning techniques using oligonucleotide probes of the present invention to screen appropriate libraries; and PCR amplification of appropriate libraries or DNA using oligonucleotide primers of the present invention. Preferred libraries to screen or from which to amplify nucleic acid molecules include mammalian cDNA libraries as well as genomic DNA libraries. Similarly, preferred DNA sources from which to amplify nucleic acid molecules include mammalian cDNA and genomic DNA. Techniques to clone and amplify genes are disclosed, for example, in Sambrook et al., *ibid.*

The present invention also includes nucleic acid molecules that are oligonucleotides capable of hybridizing, under stringent hybridization conditions, with complementary regions of other, preferably longer, nucleic acid molecules of the present invention such as those comprising canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecules. Oligonucleotides of the present invention can be RNA, DNA, or derivatives of either. The minimum size of such oligonucleotides is the size required for formation of a stable hybrid between an oligonucleotide and a complementary sequence on a nucleic acid molecule of the present invention. A preferred oligonucleotide of the present invention has a maximum size of about 100 nucleotides. The present invention includes oligonucleotides that can be used as, for example, probes to identify nucleic acid molecules, primers to produce nucleic acid molecules, or therapeutic reagents to inhibit canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein production or activity (e.g., as antisense-, triplex formation-, ribozyme- and/or RNA drug-based reagents). The present invention also includes the use of such oligonucleotides to protect animals from disease using one or more of such technologies. Appropriate oligonucleotide-containing therapeutic compositions can be administered to an animal using techniques known to those skilled in the art.

One embodiment of the present invention includes a recombinant vector, which includes at least one isolated nucleic acid molecule of the present invention, inserted into any vector capable of delivering the nucleic acid molecule into a host cell. Such a vector contains heterologous nucleic acid sequences, that is nucleic acid sequences that are not naturally found adjacent to nucleic acid molecules of the present invention and that preferably are derived from a species other than the species from which the nucleic acid molecule(s) are derived. The vector can be either RNA or DNA, either prokaryotic or eukaryotic, and typically is a virus or a plasmid. Recombinant vectors can be used in the cloning, sequencing, and/or otherwise manipulating immunoregulatory nucleic acid molecules of the present invention.

One type of recombinant vector, referred to herein as a recombinant molecule, comprises a nucleic acid molecule of the present invention operatively linked to an expression vector. The phrase operatively linked refers to insertion of a nucleic acid molecule into an expression vector in a manner such that the molecule is able to be expressed when transformed into a host cell. As used herein, an expression vector is a DNA or RNA vector that is capable of transforming a host cell and of effecting expression of a specified nucleic acid molecule. Preferably, the expression vector is also capable of replicating within the host cell. Expression vectors can be either prokaryotic or eukaryotic, and are typically viruses or plasmids. Expression vectors of the present invention include any vectors that function (i.e., direct gene expression) in recombinant cells of the present invention, including in bacterial, fungal, parasite, insect, other animal, and plant cells. Preferred expression vectors of the present invention can direct gene expression in bacterial, yeast, insect and mammalian cells, and more preferably in the cell types disclosed herein, more preferably *in vivo*.

In particular, expression vectors of the present invention contain regulatory sequences such as transcription control sequences, translation control sequences, origins of

replication, and other regulatory sequences that are compatible with the recombinant cell and that control the expression of nucleic acid molecules of the present invention. In particular, recombinant molecules of the present invention include transcription control sequences. Transcription control sequences are sequences which control the initiation, elongation, and termination of transcription. Particularly important transcription control sequences are those which control transcription initiation, such as promoter, enhancer, operator and repressor sequences. Suitable transcription control sequences include any transcription control sequence that can function in at least one of the recombinant cells of the present invention. A variety of such transcription control sequences are known to those skilled in the art. Preferred transcription control sequences include those which function in bacterial, yeast, helminth and/or other endoparasite, insect and mammalian cells, such as, but not limited to, *tac*, *lac*, *trp*, *trc*, *oxy-pro*, *omp/lpp*, *rmB*, bacteriophage lambda (such as lambda  $p_L$  and lambda  $p_R$  and fusions that include such promoters), bacteriophage T7, T7lac, bacteriophage T3, bacteriophage SP6, bacteriophage SP01, metallothionein, alpha-mating factor, *Pichia* alcohol oxidase, alphavirus subgenomic promoter, antibiotic resistance gene, baculovirus, *Haliotis zea* insect virus, vaccinia virus, herpesvirus, raccoon poxvirus, other poxvirus, adenovirus, cytomegalovirus (such as immediate early promoter), simian virus 40, retrovirus, actin, retroviral long terminal repeat, Rous sarcoma virus, heat shock, phosphate and nitrate transcription control sequences as well as other sequences capable of controlling gene expression in prokaryotic or eukaryotic cells. Additional suitable transcription control sequences include tissue-specific promoters and enhancers as well as lymphokine-inducible promoters (e.g., promoters inducible by interferons or interleukins). Transcription control sequences of the present invention can also include naturally occurring transcription control sequences naturally associated with mammals, such as dog, cat, horse or human transcription control sequences.

Suitable and preferred nucleic acid molecules to include in recombinant vectors of the present invention are as disclosed herein. Preferred nucleic acid molecules to include in recombinant vectors, and particularly in recombinant molecules, include nCaIL-4<sub>549</sub>, nCaIL-4<sub>396</sub>, nCaIL-4<sub>324</sub>, nCaFlt3L<sub>1013</sub>, nCaFlt3L<sub>882</sub>, nCaFlt3L<sub>804</sub>, nCaFlt3L<sub>828</sub>, nCaFlt3L<sub>985</sub>, nCaFlt3L<sub>1019</sub>, nCaFlt3L<sub>93</sub>, nCaFlt3L<sub>750</sub>, nFeFlt3L<sub>395</sub>, nFeFlt3L<sub>793</sub>, nFeFlt3L<sub>942</sub>, nFeFlt3L<sub>873</sub>, nCaCD40<sub>321</sub>, nCaCD40<sub>1425</sub>, nCaCD40<sub>822</sub>, nCaCD40<sub>765</sub>, nFeCD40<sub>336</sub>, nCaCD154<sub>390</sub>, nCaCD154<sub>878</sub>, nCaCD154<sub>780</sub>, nCaCD154<sub>633</sub>, nFeCD154<sub>885</sub>, nFeCD154<sub>780</sub>, nFeCD154<sub>633</sub>, nCaIL-5<sub>610</sub>, nCaIL-5<sub>402</sub>, nCaIL-5<sub>345</sub>, nCaIL-13<sub>166</sub>, nCaIL-13<sub>272</sub>, nCaIL-13<sub>278</sub>, nCaIL-13<sub>1302</sub>, nCaIL-13<sub>393</sub>, nCaIL-13<sub>333</sub>, nCaIL-13<sub>1269</sub>, nCaIL-13<sub>390</sub>, nCaIL-13<sub>330</sub>, nFeIFN $\alpha$ <sub>567a</sub>, nFeIFN $\alpha$ <sub>567b</sub>, nFeIFN $\alpha$ <sub>567c</sub>, nFeIFN $\alpha$ <sub>498a</sub>, nFeIFN $\alpha$ <sub>498b</sub>, nFeIFN $\alpha$ <sub>498c</sub>, nFeIFN $\alpha$ <sub>582d</sub>, nFeIFN $\alpha$ <sub>513d</sub>, nFeIFN $\alpha$ <sub>567e</sub>, nFeIFN $\alpha$ <sub>498e</sub>, nFeGMCSF<sub>444</sub>, nFeGMCSF<sub>432</sub>, and/or nFeGMCSF<sub>381</sub>.

Recombinant molecules of the present invention may also (a) contain secretory signals (i.e., signal segment nucleic acid sequences) to enable an expressed parasitic helminth protein of the present invention to be secreted from the cell that produces the protein and/or (b) contain fusion sequences which lead to the expression of nucleic acid molecules of the present invention as fusion proteins. Examples of suitable signal segments include any signal segment capable of directing the secretion of a protein of the present invention. Preferred signal segments include, but are not limited to, tissue plasminogen activator (t-PA),

interferon, interleukin, growth hormone, histocompatibility and viral envelope glycoprotein signal segments. Suitable fusion segments encoded by fusion segment nucleic acids are disclosed herein. In addition, a nucleic acid molecule of the present invention can be joined to a fusion segment that directs the encoded protein to the proteasome, such as a ubiquitin fusion segment. Eukaryotic recombinant molecules may also include intervening and/or untranslated sequences surrounding and/or within the nucleic acid sequences of nucleic acid molecules of the present invention.

Another embodiment of the present invention includes a recombinant cell comprising a host cell transformed with one or more recombinant molecules of the present invention. Transformation of a nucleic acid molecule into a cell can be accomplished by any method by which a nucleic acid molecule can be inserted into the cell. Transformation techniques include, but are not limited to, transfection, electroporation, microinjection, lipofection, adsorption, and protoplast fusion. A recombinant cell may remain unicellular or may grow into a tissue, organ or a multicellular organism. Transformed nucleic acid molecules of the present invention can remain extrachromosomal or can integrate into one or more sites within a chromosome of the transformed (i.e., recombinant) cell in such a manner that their ability to be expressed is retained. Preferred nucleic acid molecules with which to transform a cell include immunoregulatory nucleic acid molecules of the present invention disclosed herein. Particularly preferred nucleic acid molecules with which to transform to cell include nCaIL-4<sub>549</sub>, nCaIL-4<sub>396</sub>, nCaIL-4<sub>324</sub>, nCaFlt3L<sub>1013</sub>, nCaFlt3L<sub>882</sub>, nCaFlt3L<sub>804</sub>, nCaFlt3L<sub>828</sub>, nCaFlt3L<sub>985</sub>, nCaFlt3L<sub>1019</sub>, nCaFlt3L<sub>93</sub>, nCaFlt3L<sub>750</sub>, nFeFlt3L<sub>395</sub>, nFeFlt3L<sub>793</sub>, nFeFlt3L<sub>942</sub>, nFeFlt3L<sub>873</sub>, nFeFlt3L<sub>795</sub>, nCaCD40<sub>321</sub>, nCaCD40<sub>1425</sub>, nCaCD40<sub>822</sub>, nCaCD40<sub>765</sub>, nFeCD40<sub>336</sub>, nCaCD154<sub>390</sub>, nCaCD154<sub>878</sub>, nCaCD154<sub>780</sub>, nCaCD154<sub>633</sub>, nFeCD154<sub>885</sub>, nFeCD154<sub>780</sub>, nFeCD154<sub>633</sub>, nCaIL-5<sub>610</sub>, nCaIL-5<sub>402</sub>, nCaIL-5<sub>345</sub>, nCaIL-13<sub>166</sub>, nCaIL-13<sub>272</sub>, nCaIL-13<sub>278</sub>, nCaIL-13<sub>1302</sub>, nCaIL-13<sub>393</sub>, nCaIL-13<sub>333</sub>, nCaIL-13<sub>1269</sub>, nCaIL-13<sub>390</sub>, nCaIL-13<sub>330</sub>, nFeIFN $\alpha$ <sub>567a</sub>, nFeIFN $\alpha$ <sub>567b</sub>, nFeIFN $\alpha$ <sub>567c</sub>, nFeIFN $\alpha$ <sub>498a</sub>, nFeIFN $\alpha$ <sub>498b</sub>, nFeIFN $\alpha$ <sub>498c</sub>, nFeIFN $\alpha$ <sub>528d</sub>, nFeIFN $\alpha$ <sub>513d</sub>, nFeIFN $\alpha$ <sub>567e</sub>, nFeIFN $\alpha$ <sub>498e</sub>, nFeGMCSF<sub>444</sub>, nFeGMCSF<sub>432</sub>, and/or nFeGMCSF<sub>381</sub>.

Suitable host cells to transform include any cell that can be transformed with a nucleic acid molecule of the present invention. Host cells can be either untransformed cells or cells that are already transformed with at least one nucleic acid molecule (e.g., nucleic acid molecules encoding one or more proteins of the present invention and/or other proteins useful in the production of multivalent vaccines). Host cells of the present invention either can be endogenously (i.e., naturally) capable of producing immunoregulatory proteins of the present invention or can be capable of producing such proteins after being transformed with at least one nucleic acid molecule of the present invention. Host cells of the present invention can be any cell capable of producing at least one protein of the present invention, and include bacterial, fungal (including yeast), parasite (including helminth, protozoa and endoparasite), other insect, other animal and plant cells. Preferred host cells include bacterial, mycobacterial, yeast, helminth, insect and mammalian cells. More preferred host cells include *Salmonella*, *Escherichia*, *Bacillus*, *Listeria*, *Saccharomyces*, *Spodoptera*, *Mycobacteria*, *Trichoplusia*, BHK (baby hamster kidney) cells, MDCK cells (Madin-Darby canine kidney cell line), CRFK cells (Crandell feline kidney cell line), CV-1 cells (African monkey kidney cell line used, for example, to

culture raccoon poxvirus), COS (e.g., COS-7) cells, chinese hamster ovary (CHO) cells, Ltk cells and Vero cells. Particularly preferred host cells are Escherichia coli, including E. coli K-12 derivatives; Salmonella typhi; Salmonella typhimurium, including attenuated strains such as UK-1<sub>o</sub>3987 and SR-11<sub>o</sub>4072; Spodoptera frugiperda; Trichoplasia ni; BHK cells; MDCK cells; CRFK cells; CV-1 cells; COS cells; Vero cells; and non-tumorigenic mouse myoblast G8 cells (e.g., ATCC CRL 1246). Additional appropriate mammalian cell hosts include other kidney cell lines, other fibroblast cell lines (e.g., human, murine or chicken embryo fibroblast cell lines), myeloma cell lines, Chinese hamster ovary cells, mouse NIH/3T3 cells, LMTK<sup>31</sup> cells and/or HeLa cells. In one embodiment, the proteins may be expressed as heterologous proteins in myeloma cell lines employing immunoglobulin promoters.

A recombinant cell is preferably produced by transforming a host cell with one or more recombinant molecules, each comprising one or more nucleic acid molecules of the present invention operatively linked to an expression vector containing one or more transcription control sequences, examples of which are disclosed herein.

A recombinant cell of the present invention includes any cell transformed with at least one of any nucleic acid molecule of the present invention. Suitable and preferred nucleic acid molecules as well as suitable and preferred recombinant molecules with which to transfer cells are disclosed herein.

Recombinant cells of the present invention can also be co-transformed with one or more recombinant molecules including any of canine interleukin-4, canine or feline Flt3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecule encoding one or more proteins of the present invention and/or one or more other nucleic acid molecules encoding other therapeutic compounds, as disclosed herein (e.g., to produce multivalent vaccines).

Recombinant DNA technologies can be used to improve expression of transformed nucleic acid molecules by manipulating, for example, the number of copies of the nucleic acid molecules within a host cell, the efficiency with which those nucleic acid molecules are transcribed, the efficiency with which the resultant transcripts are translated, and the efficiency of post-translational modifications. Recombinant techniques useful for increasing the expression of nucleic acid molecules of the present invention include, but are not limited to, operatively linking nucleic acid molecules to high-copy number plasmids, integration of the nucleic acid molecules into one or more host cell chromosomes, addition of vector stability sequences to plasmids, substitutions or modifications of transcription control signals (e.g., promoters, operators, enhancers), substitutions or modifications of translational control signals (e.g., ribosome binding sites, Shine-Dalgarno sequences), modification of nucleic acid molecules of the present invention to correspond to the codon usage of the host cell, deletion of sequences that destabilize transcripts, and use of control signals that temporally separate recombinant cell growth from recombinant enzyme production during fermentation. The activity of an expressed recombinant protein of the present invention may be improved by fragmenting, modifying, or derivatizing nucleic acid molecules encoding such a protein.

Isolated immunoregulatory proteins of the present invention can be produced in a variety of ways, including production and/or recovery of natural proteins, production

and/or recovery of recombinant proteins, and/or chemical synthesis of the proteins. In one embodiment, an isolated protein of the present invention is produced by culturing a cell capable of expressing the protein under conditions effective to produce the protein, and recovering the protein. A preferred cell to culture is a recombinant cell of the present invention. Effective culture conditions include, but are not limited to, effective media, bioreactor, temperature, pH and oxygen conditions that permit protein production. An effective medium refers to any medium in which a cell is cultured to produce an immunoregulatory protein of the present invention. Such medium typically comprises an aqueous medium having assimilable carbon, nitrogen and phosphate sources, and appropriate salts, minerals, metals and other nutrients, such as vitamins. Cells of the present invention can be cultured in conventional fermentation bioreactors, shake flasks, test tubes, microtiter dishes, and petri plates. Culturing can be carried out at a temperature, pH and oxygen content appropriate for a recombinant cell. Such culturing conditions are within the expertise of one of ordinary skill in the art.

Depending on the vector and host system used for production, resultant proteins of the present invention may either remain within the recombinant cell; be secreted into the fermentation medium; be secreted into a space between two cellular membranes, such as the periplasmic space in E. coli; or be retained on the outer surface of a cell or viral membrane.

The phrase "recovering the protein", as well as similar phrases, refers to collecting the whole fermentation medium containing the protein and need not imply additional steps of separation or purification. Proteins of the present invention can be purified using a variety of standard protein purification techniques, such as, but not limited to, affinity chromatography, ion exchange chromatography, filtration, electrophoresis, hydrophobic interaction chromatography, gel filtration chromatography, reverse phase chromatography, concanavalin A chromatography, chromatofocusing and/or differential solubilization. Proteins of the present invention are preferably retrieved in "substantially pure" form. As used herein, "substantially pure" refers to a purity that allows for the effective use of the protein as a therapeutic composition or diagnostic. A therapeutic composition for animals, for example, should exhibit no substantial toxicity and preferably should be capable of stimulating the production of antibodies in a treated animal.

The present invention also includes isolated (i.e., removed from their natural milieu) antibodies that selectively bind to an immunoregulatory protein of the present invention and/or a mimotope thereof (e.g., anti-IL-4 antibodies, anti-Flt-3 ligand antibodies, anti-CD40 antibodies, anti-CD154 antibodies, anti-IL-5 antibodies, anti-IL-13 antibodies, anti-IFN $\alpha$  antibodies, and/or anti-GM-CSF antibodies). As used herein, the term "selectively binds to" an immunoregulatory protein of the present invention, refers to the ability of antibodies of the present invention to preferentially bind to specified proteins and/or mimitopes thereof of the present invention. Binding can be measured using a variety of methods standard in the art including enzyme immunoassays (e.g., ELISA), immunoblot assays, etc.; see, for example, Sambrook et al., *ibid.*, and Harlow, et al., 1988, *Antibodies, a Laboratory Manual*, Cold Spring Harbor Labs Press; Harlow et al., *ibid.*, is incorporated by this reference herein in its entirety. An anti-IL-4 antibody of the present invention preferably selectively binds to an IL-4 protein in such a way as to inhibit the function of that protein. An anti-Flt-3 ligand antibody of the present invention preferably selectively

binds to a Flt-3 ligand- protein in such a way as to inhibit the function of that protein. An anti-CD40 antibody of the present invention preferably selectively binds to a CD40 protein in such a way as to inhibit the function of that protein. An anti-CD154 antibody of the present invention preferably selectively binds to a CD154 protein in such a way as to inhibit the function of that protein. An anti-IL-5 antibody of the present invention preferably selectively binds to an IL-5 protein in such a way as to inhibit the function of that protein. An anti-IL-13 antibody of the present invention preferably selectively binds to an IL-13 protein in such a way as to inhibit the function of that protein. An anti-IFN $\alpha$  antibody of the present invention preferably selectively binds to an IFN $\alpha$  protein in such a way as to inhibit the function of that protein. An anti-GM-CSF antibody of the present invention preferably selectively binds to a GM-CSF protein in such a way as to inhibit the function of that protein.

Isolated antibodies of the present invention can include antibodies in serum, or antibodies that have been purified to varying degrees. Antibodies of the present invention can be polyclonal or monoclonal, or can be functional equivalents such as antibody fragments and/or genetically-engineered antibodies, including single chain antibodies or chimeric antibodies that can bind to one or more epitopes.

A preferred method to produce antibodies of the present invention includes (a) administering to an animal an effective amount of a protein, peptide and/or mimotope thereof of the present invention to produce the antibodies and (b) recovering the antibodies. In another method, antibodies of the present invention are produced recombinantly using techniques as heretofore disclosed to produce any of the immunoregulatory proteins of the present invention. Antibodies raised against defined proteins or mimitopes can be advantageous because such antibodies are not substantially contaminated with antibodies against other substances that might otherwise cause interference in a diagnostic assay or side effects if used in a therapeutic composition.

Antibodies of the present invention have a variety of potential uses that are within the scope of the present invention. For example, such antibodies can be used (a) as reagents in assays to detect an immunoregulatory protein of the present invention, (b) as reagents in assays to modulate cellular activity through an immunoregulatory protein of the present invention (e.g., mimicking ligand binding to a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein, as appropriate), and/or (c) as tools to screen expression libraries and/or to recover desired proteins of the present invention from a mixture of proteins and other contaminants. Furthermore, antibodies of the present invention can be used to target compounds (e.g., nucleic acid molecules, drugs or proteins) to antigen presenting cells. Targeting can be accomplished by conjugating (i.e., stably joining) such antibodies to the compounds using techniques known to those skilled in the art. Suitable compounds are known to those skilled in the art.

One embodiment of the present invention is a therapeutic composition that, when administered to an animal in an effective manner, is capable of regulating an immune response in an animal. Therapeutic compositions of the present invention can include at least one of the following therapeutic compounds: an isolated IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF protein of the present invention and/or a mimotope thereof; an isolated IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13,

IFN $\alpha$ , and/or GM-CSF nucleic acid molecule of the present invention; an isolated antibody that selectively binds to an IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF protein of the present invention; an inhibitor of canine IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF function identified by its ability to bind to an IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF protein, respectively, of the present invention; such an inhibitor can inhibit binding of the respective immunoregulatory protein with its respective receptor, or inhibit the activity the respective protein. Methods to perform such assays to measure binding and/or activity of an immunoregulatory protein of the present invention are known to those of skill in the art, and are described, for example, in Janeway, et al., *ibid.* As used herein, a therapeutic compound refers to a compound that, when administered to an animal in an effective manner, is able to treat, ameliorate, and/or prevent a disease. Examples of proteins, nucleic acid molecules, antibodies and/or inhibitors of the present invention are disclosed herein.

The present invention also includes a therapeutic composition comprising at least one IL-4-, Flt-3 ligand-, CD40-, CD154-, IL-5-, IL-13-, IFN $\alpha$ -, and/or GM-CSF-based compound of the present invention in combination with at least one additional therapeutic compound. Examples of such compounds are disclosed herein.

Therapeutic compositions of the present invention can be administered to any animal susceptible to such therapy, preferably to mammals, and more preferably to dogs, cats, humans, ferrets, horses, cattle, sheep and/or other pets, economic food animals and/or zoo animals. Preferred animals include dogs, cats, horses and/or humans.

A therapeutic composition of the present invention is administered to an animal in an effective manner such that the composition is capable of regulating an immune response in that animal. Therapeutic compositions of the present invention can be administered to animals prior to onset of a disease (i.e., as a preventative vaccine) and/or can be administered to animals after onset of a disease in order to treat the disease (i.e., as a therapeutic vaccine). Preferred diseases to prevent and/or treat include autoimmune diseases, allergic reactions, infectious diseases, tumor development, inflammatory diseases and/or graft rejection. In one embodiment, a therapeutic composition of the present invention is administered with an antigen to enhance an immune response against that antigen.

Therapeutic compositions of the present invention can be formulated in an excipient that the animal to be treated can tolerate. Examples of such excipients include water, saline, Ringer's solution, dextrose solution, Hank's solution, and/or other aqueous physiologically balanced salt solutions. Non-aqueous vehicles, such as fixed oils, sesame oil, ethyl olate, or triglycerides may also be used. Other useful formulations include suspensions containing viscosity enhancing agents, such as sodium carboxymethylcellulose, sorbitol, or dextran. Excipients can also contain minor amounts of additives, such as substances that enhance isotonicity and chemical stability. Examples of buffers include phosphate buffer, bicarbonate buffer and/or Tris buffer, while examples of preservatives include thimerosal, o-cresol, formalin and/or benzyl alcohol. Standard formulations can either be liquid injectables or solids which can be taken up in a suitable liquid as a suspension or solution for injection. Thus, in a non-liquid formulation, the excipient can comprise dextrose, human serum albumin, preservative, etc., to which sterile water or saline can be added prior to administration.

In one embodiment of the present invention, a therapeutic composition can include an adjuvant. Adjuvants are agents

that are capable of enhancing the immune response of an animal to a specific antigen. Suitable adjuvants include, but are not limited to, cytokines, chemokines, and/or compounds that induce the production of cytokines and/or chemokines (e.g., granulocyte macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (G-CSF), macrophage colony stimulating factor (M-CSF), colony stimulating factor (CSF), erythropoietin (EPO), interleukin 2 (IL-2), interleukin-3 (IL-3), interleukin 5 (IL-5), interleukin 6 (IL-6), interleukin 7 (IL-7), interleukin 8 (IL-8), interleukin 10 (IL-10), interleukin 12 (IL-12), interferon gamma, interferon gamma inducing factor I (IGIF), transforming growth factor beta, RANTES (regulated upon activation, normal T cell expressed and presumably secreted), macrophage inflammatory proteins (e.g., MIP-1 alpha and MIP-1 beta), and Leishmania elongation initiating factor (LEIF)); bacterial components (e.g., endotoxins, in particular superantigens, exotoxins and cell wall components); aluminum-based salts; calcium-based salts; silica; polynucleotides, toxoids; serum proteins, viral coat proteins; block copolymer adjuvants (e.g., Hunter's Titermax™ adjuvant (Vaxcel™, Inc. Norcross, Ga.), Ribi adjuvants (Ribi ImmunoChem Research, Inc., Hamilton, Mont.); and saponins and their derivatives (e.g., Quil A (Superfos Biosector A/S, Denmark). Protein adjuvants of the present invention can be delivered in the form of the protein themselves or of nucleic acid molecules encoding such proteins using the methods described herein.

In one embodiment of the present invention, a therapeutic composition can include a carrier. Carriers include compounds that increase the half-life of a therapeutic composition in the treated animal. Suitable carriers include, but are not limited to, polymeric controlled release vehicles, biodegradable implants, liposomes, bacteria, viruses, other cells, oils, esters, and glycols.

One embodiment of the present invention is a controlled release formulation that is capable of slowly releasing a composition of the present invention into an animal. As used herein, a controlled release formulation comprises a composition of the present invention in a controlled release vehicle. Suitable controlled release vehicles include, but are not limited to, biocompatible polymers, other polymeric matrices, capsules, microcapsules, microparticles, bolus preparations, osmotic pumps, diffusion devices, liposomes, lipospheres, and transdermal delivery systems. Other controlled release formulations of the present invention include liquids that, upon administration to an animal, form a solid or a gel in situ. Preferred controlled release formulations are biodegradable (i.e., bioerodible).

A preferred controlled release formulation of the present invention is capable of releasing a composition of the present invention into the blood of the treated animal at a constant rate sufficient to attain therapeutic dose levels of the composition to regulate an immune response in an animal. The therapeutic composition is preferably released over a period of time ranging from about 1 to about 12 months. A controlled release formulation of the present invention is capable of effecting a treatment preferably for at least about 1 month, more preferably for at least about 3 months, even more preferably for at least about 6 months, even more preferably for at least about 9 months, and even more preferably for at least about 12 months.

Therapeutic compositions of the present invention can be administered to animals prior to and/or after onset of disease. Acceptable protocols to administer therapeutic compositions in an effective manner include individual dose size, number of doses, frequency of dose administration, and/or

mode of administration. Determination of such protocols can be accomplished by those skilled in the art. A suitable single dose is a dose that is capable of regulating the immune response in an animal when administered one or more times over a suitable time period. For example, a preferred single dose of a protein, mimotope or antibody therapeutic composition is from about 1 microgram ( $\mu\text{g}$ ) to about milligrams (mg) of the therapeutic composition per kilogram body weight of the animal. Booster vaccinations can be administered from about 2 weeks to several years after the original administration. Booster administrations preferably are administered when the immune response of the animal becomes insufficient to protect the animal from disease. A preferred administration schedule is one in which from about 10  $\mu\text{g}$  to about 1 mg of the therapeutic composition per kg body weight of the animal is administered from about one to about two times over a time period of from about 2 weeks to about 12 months. Modes of administration can include, but are not limited to, subcutaneous, intradermal, intravenous, intranasal, intraocular, oral, transdermal and/or intramuscular routes.

According to one embodiment, a nucleic acid molecule of the present invention can be administered to an animal in a fashion to enable expression of that nucleic acid molecule into a therapeutic protein or therapeutic RNA (e.g., antisense RNA, ribozyme, triple helix forms or RNA drug) in the animal. Nucleic acid molecules can be delivered to an animal in a variety of methods including, but not limited to, (a) administering a naked (i.e., not packaged in a viral coat or cellular membrane) nucleic acid as a genetic vaccine (e.g., as naked DNA or RNA molecules, such as is taught, for example in Wolff et al., 1990, Science 247, 1465-1468) or (b) administering a nucleic acid molecule packaged as a recombinant virus vaccine or as a recombinant cell vaccine (i.e., the nucleic acid molecule is delivered by a viral or cellular vehicle).

A genetic (i.e., naked nucleic acid) vaccine of the present invention includes a nucleic acid molecule of the present invention and preferably includes a recombinant molecule of the present invention that preferably is replication, or otherwise amplification, competent. A genetic vaccine of the present invention can comprise one or more nucleic acid molecules of the present invention in the form of, for example, a dicistronic recombinant molecule. Preferred genetic vaccines include at least a portion of a viral genome (i.e., a viral vector). Preferred viral vectors include those based on alphaviruses, poxviruses, adenoviruses, herpesviruses, picomaviruses, and/or retroviruses, with those based on alphaviruses (such as sindbis or SemlikiForest virus), species-specific herpesviruses and/or poxviruses being particularly preferred. Any suitable transcription control sequence can be used, including those disclosed as suitable for protein production. Particularly preferred transcription control sequences include cytomegalovirus immediate early (preferably in conjunction with Intron-A), Rous sarcoma virus long terminal repeat, and tissue-specific transcription control sequences, as well as transcription control sequences endogenous to viral vectors if viral vectors are used. The incorporation of a "strong" polyadenylation signal is also preferred.

Genetic vaccines of the present invention can be administered in a variety of ways, with intramuscular, subcutaneous, intradermal, transdermal, intranasal and/or oral routes of administration being preferred. A preferred single dose of a genetic vaccine ranges from about 1 nanogram (ng) to about 600  $\mu\text{g}$ , depending on the route of administration and/or method of delivery, as can be deter-

mined by those skilled in the art. Suitable delivery methods include, for example, by injection, as drops, aerosolized and/or topically. Genetic vaccines of the present invention can be contained in an aqueous excipient (e.g., phosphate buffered saline) alone or in a carrier (e.g., lipid-based vehicles).

A recombinant virus vaccine of the present invention includes a recombinant molecule of the present invention that is packaged in a viral coat and that can be expressed in an animal after administration. Preferably, the recombinant molecule is packaging- or replication-deficient and/or encodes an attenuated virus. A number of recombinant viruses can be used, including, but not limited to, those based on alphaviruses, poxviruses, adenoviruses, herpesviruses, picomaviruses, and/or retroviruses. Preferred recombinant virus vaccines are those based on alphaviruses (such as Sindbis virus), raccoon poxviruses, species-specific herpesviruses and/or species-specific poxviruses. An example of methods to produce and use alphavirus recombinant virus vaccines are disclosed in U.S. Pat. No. 5,766,602 by Xiong et al., issued Jun. 16, 1998, which is incorporated by this reference herein in its entirety.

When administered to an animal, a recombinant virus vaccine of the present invention infects cells within the immunized animal and directs the production of a therapeutic protein or RNA nucleic acid molecule that is capable of protecting the animal from disease caused by a parasitic helminth as disclosed herein. For example, a recombinant virus vaccine comprising an immunoregulatory nucleic acid molecule of the present invention is administered according to a protocol that results in the regulation of an immune response in an animal. A preferred single dose of a recombinant virus vaccine of the present invention is from about  $1 \times 10^4$  to about  $1 \times 10^8$  virus plaque forming units (pfu) per kilogram body weight of the animal. Administration protocols are similar to those described herein for protein-based vaccines, with subcutaneous, intramuscular, intranasal, intraocular and/or oral administration routes being preferred.

A recombinant cell vaccine of the present invention includes recombinant cells of the present invention that express at least one protein of the present invention. Preferred recombinant cells for this embodiment include *Salmonella*, *E. coli*, *Listeria*, *Mycobacterium*, *S. frugiperda*, yeast, (including *Saccharomyces cerevisiae* and *Pichia pastoris*), BHK, CV-1, myoblast G8, COS (e.g., COS-7), Vero, MDCK and CRFK recombinant cells. Recombinant cell vaccines of the present invention can be administered in a variety of ways but have the advantage that they can be administered orally, preferably at doses ranging from about  $10^8$  to about  $10^{12}$  cells per kilogram body weight. Administration protocols are similar to those described herein for protein-based vaccines. Recombinant cell vaccines can comprise whole cells, cells stripped of cell walls or cell lysates.

The efficacy of a therapeutic composition of the present invention to regulate the immune response in an animal can be tested in a variety of ways including, but not limited to, detection of cellular immunity within the treated animal, determining lymphocyte or dendritic cell activity, detection of immunoglobulin levels, determining hematopoietic stem cell or hematopoietic early progenitor cell development, determining dendritic cell development or challenge of the treated animal with an infectious agent to determine whether the treated animal is resistant to disease. In one embodiment, therapeutic compositions can be tested in animal models such as mice. Such techniques are known to those skilled in the art.

One embodiment of the present invention is an inhibitory compound. Preferably, such an inhibitory compound is derived from an IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF protein of the present invention. Examples of inhibitory compounds include an antibody of the present invention, that is administered to an animal in an effective manner (i.e., is administered in an amount so as to be present in the animal at a titer that is sufficient, upon interaction of that antibody with a native IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF protein, to decrease the activity of such proteins in an animal, at least temporarily). Oligonucleotide nucleic acid molecules of the present invention can also be administered in an effective manner, thereby reducing expression of either an IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF protein, in order to interfere with the protein activity targeted in accordance with the present invention. Peptides of an IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF protein of the present invention can also be administered in an effective manner, thereby reducing binding of IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF proteins to the appropriate receptor, in order to interfere with the protein activity targeted in accordance with the present invention. An inhibitory compound of an IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF function can be identified using IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF proteins of the present invention, respectively.

One embodiment of the present invention is a method to identify a compound capable of inhibiting IL-4 function. Such a method includes the steps of: (a) contacting (e.g., combining, mixing) an isolated IL-4 protein of the present invention, with a putative inhibitory compound under conditions in which, in the absence of the compound, the IL-4 protein binds to IL-4 receptor or stimulates T cells in a T cell proliferation assay, and (b) determining if the putative inhibitory compound inhibits the binding of IL-4 protein to IL-4 receptor or the stimulation of T cells in a T cell proliferation assay. Another embodiment of the present invention is a method to identify a compound capable of inhibiting Flt-3 ligand function. Such a method includes the steps of: (a) contacting an isolated Flt-3 ligand protein of the present invention, with a putative inhibitory compound under conditions in which, in the absence of the compound, the Flt-3 ligand protein binds to Flt-3 receptor or stimulates dendritic precursor cells in a proliferation assay, and (b) determining if the putative inhibitory compound inhibits the binding of Flt-3 ligand protein to Flt-3 receptor or the stimulation of dendritic precursor cells in a proliferation assay. Another embodiment of the present invention is a method to identify a compound capable of inhibiting CD40 function. Such a method includes the steps of (a) contacting an isolated CD40 protein of the present invention, with a putative inhibitory compound under conditions in which, in the absence of the compound, the CD40 protein binds to a CD40 binding partner (e.g., CD154) and (b) determining if the putative inhibitory compound inhibits the binding of CD40 protein to the CD40 binding partner. A CD40 binding partner is a molecule that selectively binds to CD40 protein. Likewise, a binding partner for any other immunoregulatory protein of the present invention includes molecules that selectively bind to that particular immunoregulatory protein. Another embodiment of the present invention is a method to identify a compound capable of inhibiting CD154 function. Such a method includes the steps of (a) contacting an isolated CD154 protein of the present invention, with a putative inhibitory compound under conditions in which, in

the absence of the compound, the CD154 protein binds to a CD154 binding partner (e.g., CD40) and (b) determining if the putative inhibitory compound inhibits the binding of CD154 protein to the CD154 binding partner. Yet another embodiment of the present invention is a method to identify a compound capable of inhibiting IL-5 function. Such a method includes the steps of: (a) contacting an isolated IL-5 protein of the present invention, with a putative inhibitory compound under conditions in which, in the absence of the compound, the IL-5 protein binds to IL-5 receptor or stimulates T cells in a T cell proliferation assay, and (b) determining if the putative inhibitory compound inhibits the binding of IL-5 protein to IL-5 receptor or the stimulation of T cells in a T cell proliferation assay. Another embodiment of the present invention is a method to identify a compound capable of inhibiting IL-13 function. Such a method includes the steps of: (a) contacting an isolated IL-13 protein of the present invention, with a putative inhibitory compound under conditions in which, in the absence of the compound, the IL-13 protein binds to IL-13 receptor or stimulates T cells in a T cell proliferation assay, and (b) determining if the putative inhibitory compound inhibits the binding of IL-13 protein to IL-13 receptor or the stimulation of T cells in a T cell proliferation assay. Another embodiment of the present invention is a method to identify a compound capable of inhibiting IFN $\alpha$  function. Such a method includes the steps of: (a) contacting an isolated IFN $\alpha$  protein of the present invention, with a putative inhibitory compound under conditions in which, in the absence of the compound; the IFN $\alpha$  protein binds to IFN $\alpha$  receptor or inhibits proliferation of GM-CSF stimulated TF-1 cells, and (b) determining if the putative inhibitory compound inhibits the binding of IFN $\alpha$  protein to IFN $\alpha$  receptor or inhibits proliferation of GM-CSF stimulated TF-1 cells. Another embodiment of the present invention is a method to identify a compound capable of inhibiting GM-CSF function. Such a method includes the steps of: (a) contacting an isolated GM-CSF protein of the present invention, with a putative inhibitory compound under conditions in which, in the absence of said compound, the GM-CSF protein binds to GM-CSF receptor or stimulates T cells in a T cell proliferation assay, and (b) determining if the putative inhibitory compound inhibits the binding of GM-CSF protein to GM-CSF receptor or the stimulation of T cells in a T cell proliferation assay.

Putative inhibitory compounds to screen include small organic molecules, antibodies (including mimetopes thereof), and/or ligand analogs. Such compounds are also screened to identify those that are substantially not toxic in host animals.

Preferred IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF, proteins in inhibit are those produced by dogs, cats, horses or humans, even more preferred IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF proteins to inhibit are those produced by domestic dogs or cats. A particularly preferred inhibitor of the present invention is capable of regulating an immune response in an animal. It is also within the scope of the present invention to use inhibitors of the present invention to target diseases involving undesired immune activity in animals. Compositions comprising inhibitors of IL4, Flt-3 ligand, CD40, CD154, IL-5, IL13, IFN $\alpha$ , and/or GM-CSF function can be administered to animals in an effective manner to regulate the immune response in the animals, and preferably to prevent autoimmune disease, allergy, infectious disease, inflammation or prevent graft rejection in animals, or to treat animals with such diseases. Effective amounts and/or dosing

regimens can be determined using techniques known to those skilled in the art.

It is also within the scope of the present invention to use isolated proteins, mimetopes, nucleic acid molecules and/or antibodies of the present invention as diagnostic reagents. Methods to use such diagnostic reagents are well known to those skilled in the art, see, for example, Janeway, et al., *ibid.*, and/or PCT Publication No. WO 98/23964, published Jun. 4, 1998.

The following examples are provided for the purposes of illustration and are not intended to limit the scope of the present invention.

## EXAMPLES

It is to be noted that the examples include a number of molecular biology, microbiology, immunology and biochemistry techniques considered to be familiar to those skilled in the art. Disclosure of such techniques can be found, for example, in Sambrook et al., *ibid.* and Ausubel, et al., 1993, *Current Protocols in Molecular Biology*, Greene/Wiley Interscience, New York, N.Y., and related references. Ausubel, et al, *ibid.* is incorporated by reference herein in its entirety.

### Example 1

This example describes the isolation and sequencing of canine interleukin-4 (IL-4) nucleic acid molecules of the present invention. This example also describes expression of recombinant canine IL-4 in *E. coli* and mammalian cells; development of monoclonal and polyclonal antibodies to *E. coli* expressed canine IL-4; and bioactivity of mammalian-expressed and *E. coli*-expressed canine IL-4.

#### A. Isolation and Sequencing of a Canine IL-4 Nucleic Acid Molecule.

Initial attempts to isolate a canine IL-4 nucleic acid molecule using various primers corresponding to putative conserved regions of IL-4 nucleic acid molecules failed. Forward and reverse primers were then designed using a sequence tag site (IL-4sts) described by Venta et al. in GenBank. The forward primer was designated as EL-4stsA, having the nucleic acid sequence 5' CTATTAATGG GTCTCACCTC CCAA CT 3', designated herein as SEQ ID NO:11. The reverse primer was designated as prIL-4stsB, having the nucleic acid sequence 5' TCAACTCGGT GCA-CAGAGTC TTGG 3', designated herein as SEQ ID NO:12. The primers were used to amplify PCR products from a *C. familiaris* mitogen activated PBMC cDNA library that was constructed in the Uni-ZAP $\text{\textcircled{R}}$  XR vector (available from Stratagene Cloning Systems, La Jolla, Calif.), using Stratagene's ZAP-cDNA $\text{\textcircled{R}}$  Synthesis Kit and the manufacturer's protocol. The mRNA was isolated from *C. familiaris* peripheral blood mononuclear cells about 4 hours after they were activated by a polyclonal activating agent in culture. Four PCR products were produced that had the expected size range. The PCR products were cloned and sequenced using standard techniques. A portion of one of the four products was found to be somewhat homologous with an IL-4 nucleic acid sequence reported in GenBank.

To identify a cDNA encoding a full-length canine IL-4 protein, the PCR product showing some homology with the IL-4 sequence reported in GenBank was used to generate an

about 549 base pair DNA fragment as follows. The PCR product was labeled with <sup>32</sup>P and used as a probe to screen the canine PBMC cDNA library. Hybridization was done at about 6×SSC, 5×Denhardt's solution, 0.5% SDS, 100 μg/ml of ssDNA and 100 μg/ml of tRNA, at about 68° C., for about 36 hr. (the compositions of SSC and Denhardt's are described in Sambrook et al., *ibid.*). The filters were washed 3 times, for about 30 minutes per wash, at about 55° C. in about 2×SSC, 0.2% SDS, followed by a final wash of about 30 minutes in the same buffer except using about 1×SSC. Positive clones were isolated and the cDNA inserts were sequenced for both strands using vector flanking primers and gene-specific internal primers. Sequence analysis was performed using the GAP program of GCG (available from the University of Wisconsin) using the alignment settings of: gap weight set at 50, length weight set at 3, and average match set at 10 for nucleic acid sequence comparisons; and gap weight set at 12, length weight set at 4, and average match set at 2.912 for amino acid sequence comparisons.

A cDNA nucleic acid molecule was isolated, referred to herein as nCaIL-4<sub>549</sub>, the coding strand of which was shown to have a nucleic acid sequence denoted herein as SEQ ID NO:1. The complement of SEQ ID NO:1 is represented herein by SEQ ID NO:3. Translation of SEQ ID NO:1 suggests that nucleic acid molecule nCaIL-4<sub>549</sub> encodes a full-length IL-4 protein of about 132 amino acids, denoted herein as PCaIL-4<sub>132</sub>, the amino acid sequence of which is presented in SEQ ID NO:2, assuming an open reading frame having an initiation codon spanning from nucleotide 43 through nucleotide 45 of SEQ ID NO:1 and a stop codon spanning from nucleotide 439 through nucleotide 441 of SEQ ID NO:1. The coding region encoding PCaIL-4<sub>132</sub> is presented herein as nCaIL-4<sub>396</sub>, which has the nucleotide sequence SEQ ID NO:4 (the coding strand) and SEQ ID NO:5 (the complementary strand). A putative signal sequence coding region extends from nucleotide 43 through nucleotide 114 of SEQ ID NO:1. The proposed mature protein (i.e., canine IL-4 protein from which the signal sequence has been cleaved), denoted herein as PCaIL-4<sub>108</sub>, contains about 108 amino acids, extending from residue 25 through residue 132 of SEQ ID NO:2; PCaIL-4<sub>108</sub> amino acid sequence is represented herein as SEQ ID NO:20. The nucleic acid molecule encoding PCaIL-4<sub>108</sub> is denoted herein as nCaIL-4<sub>324</sub>, extending from nucleotide 115 through nucleotide 438 of SEQ ID NO:1. nCaIL-4<sub>324</sub> has a coding sequence denoted SEQ ID NO:19 and a complementary sequence denoted SEQ ID NO:21.

Comparison of nucleic acid sequence SEQ ID NO:1 with nucleic acid sequences reported in GenBank indicates that SEQ ID NO:1 showed the most homology, i.e., about 89.3% identity, with a feline IL-4 gene. Comparison of amino acid sequence SEQ ID NO:2 with amino acid sequences reported in GenBank indicates that SEQ ID NO:2 showed the most homology, i.e., about 82.6% identity, with a feline IL-4 protein. Sequence analysis was performed using the GCG GAP program as described above.

B. Expression of Recombinant Canine L-4 in *E. coli* and Mammalian Cells

i. *E. coli* expression

A recombinant molecule capable of expressing the mature form of canine IL-4, denoted herein as pGEX-nCaIL-4<sub>327</sub>, was produced as follows. A 340-nucleotide fragment was PCR amplified from nucleic acid molecule nCaIL-4<sub>549</sub> (having coding strand SEQ ID NO:1) using the following primer sequences: positive strand 5' TGAATTCGGA CAT-  
AACTTCA ATATAC 3' (SEQ ID NO:38) (EcoRI site in bold) and 5' TCTCGAGATT CAGCTTCATG CCTGTA 3'

(SEQ ID NO:39) (XhoI site in bold). The resulting 340-base pair fragment was digested with EcoRI and XhoI restriction enzymes (available from New England Biolabs, Beverly, Mass.), according to the manufacturer's directions, and gel-purified using standard techniques. The digested 340-base pair fragment, now 327 base pairs, was then ligated into pGEX-6P-1 (available from Amersham Pharmacia, Piscataway, N.J.), which had been previously digested with EcoRI and XhoI and gel purified, to produce recombinant molecule pGEX-nCaIL-4<sub>327</sub>. Recombinant molecules of pGEX produce the protein of interest as a glutathione s-transferase (GST) fusion protein. The recombinant molecule pGEX-nCaIL-4<sub>327</sub> was transformed into DH5alpha cells (available from Life Technologies, Gaithersburg, Md.), a recombination deficient strain of *E. coli*, to produce recombinant cell DH5-pGEX-nCaIL-4<sub>327</sub>. The recombinant cells were screened for presence of insert by PCR and confirmed by enzyme restriction analysis and nucleic acid sequencing, using standard techniques. Several clonal recombinant molecules were transformed into BL21 cells (available from Amersham Pharmacia, Piscataway, N.J.), a protease deficient strain of *E. coli*, to produce recombinant cell BL21 -pGEX-nCaIL-4<sub>327</sub>. These recombinant cells were screened, and the clone with the highest level of protein yield was selected for scaling up for larger-scale protein production. The resultant recombinant protein is referred to herein as *E. coli*PCaIL-4<sub>109</sub>.

To produce and purify *E. coli*PCaIL-4<sub>109</sub>, bacterial cultures of recombinant cell BL21; pGEX-nCaIL-4<sub>327</sub> were grown in shake flasks at 37° C. and induced with 0.1 mM IPTG (isopropyl-β-D-thiogalactopyranoside), (available from Sigma Chemical Company, St. Louis, Mo.) when OD<sub>600nm</sub> reached about 0.8 units. Growth was allowed to continue for about 4 hours; then bacteria were harvested by centrifugation at 4000×g (times gravity) for 20 minutes. The bacterial pellet was washed and resuspended in phosphate buffered saline (PBS) (for recipe, see Sambrook et al. *ibid.*), then lysed by exposure to gaseous nitrogen pressure in a Parr pressure vessel (available from Parr Instrument Co., Moline, Ill.), according to the manufacturer's instructions. Cell debris was removed by centrifugation at 10,000×g for 20 minutes. The IL-4-GST fusion protein *E. coli*PCaIL-4<sub>109</sub> was purified from the supernatant by allowing incubation with glutathione-conjugated resin, removing unbound proteins and then removing the GST tag with PRESSION® protease; all reagents were available from Amersham Pharmacia and all were used according to the manufacturer's directions.

Concentration and purity of *E. coli*PCaIL-4<sub>109</sub> were estimated by BCA Protein Assay kit (available from Pierce, Rockford, Ill.) and SDS-PAGE followed by Coomassie staining, respectively. The purified material exhibited a single band of approximately 14 kilodaltons (kD) by Coomassie stained SDS-PAGE.

ii. CHO cell expression

A recombinant molecule denoted herein as pCMV-nCaIL-4<sub>399</sub>, capable of expressing a full length form of canine IL-4 (including signal sequence) was produced as follows. A 422-nucleotide fragment was PCR amplified from nucleic acid molecule nCaIL-4<sub>549</sub> using the following primers: 5' CCCAAGCTTA TGGGTCTCACC TCCCAAC (HindIII site in bold), denoted SEQ ID NO:40, and 3' CCTC-GAGATT CAGCTTCAATGCCTGTA (XhoI site in bold), denoted SEQ ID NO:127. The 422-base pair PCR product was digested with the restriction endonucleases HindIII and XhoI, both available from New England Biolabs. The resulting 399-base pair product encoding full-length canine IL-4

was gel purified using standard techniques and ligated into the cytomegalovirus (CMV) immediate-early transcription control region of the pCMV-Int A plasmid vector that had been digested with HindIII and XhoI (available from New England Biolabs), and gel purified, to produce the recombinant molecule pCMV-nCaIL-4<sub>399</sub>. The pCMV-Int A plasmid vector was generated as referenced by J. E. Osorio et al., 1999, Vaccine 17, 1109-1116. Briefly, vector pRc/RSV, (available from Invitrogen Corp., San Diego, Calif.) was cleaved with restriction enzyme PvuII (available from New England Biolabs), and the 2963-base pair PvuII fragment was gel purified. The fragment was self-ligated to form the vector pRc/RSV(Pvu), which contains a Rous Sarcoma Virus (RSV) long terminal repeat, a multiple cloning site, a bovine growth hormone polyadenylation sequence, a bacterial origin of replication, and an ampicillin resistance gene. Vector pRc/RSV(Pvu) was restriction enzyme digested using HindIII and NruI. A HindIII/SspI fragment containing the HCMV intermediate early promoter and first intron (i.e. intron A) was ligated into the digested pRc/RSV(Pvu) vector to produce the vector pCMV-Int A.

Stable expression of CaIL-4 in mammalian cells was carried out by transfecting the recombinant molecule pCMV-nCaIL-4<sub>399</sub> into Chinese Hamster Ovary cells, (CHO, available from ATCC) as follows. Six-well polystyrene tissue culture plates (available from Corning Costar, Acton, Mass.) were seeded with approximately  $5 \times 10^5$  cells/well in 2 milliliter (ml) cell culture media, consisting of Minimal Essential Media (MEM) supplemented with 100 mM L-glutamine, 100 mM gentamicin, and 10% fetal bovine serum (FBS), (all available from Life Technologies). Cells were grown to about 80% confluence (for about 18 hours) before transfection. The recombinant molecules to be transfected were purified using the Plasmid Midi Kit (available from Qiagen, Valencia, Calif.) and used according to the manufacture's instructions. The recombinant molecule pCMV-nCaIL-4<sub>399</sub> was linearized using the restriction enzyme PvuI (available from New England Biolabs). The plasmid pcDNA3, (available from Invitrogen), which contains the neomycin resistance gene, was linearized using the restriction enzyme EcoRI. Approximately 2  $\mu$ g of pCMV-nCaIL-4<sub>399</sub> was mixed with about 2 ng of linearized pcDNA3 in about 100  $\mu$ l OPTIMEM™ media, available from Life Technologies. About 10  $\mu$ l Lipofectamine, (available from Life Technologies) was mixed with 100  $\mu$ l OPTIMEM. The nucleic acid molecule-containing mixture was then added to the Lipofectamine mixture and incubated at room temperature for about 45 minutes. After incubation, about 0.8 ml OPTIMEM was added, and the mixture was overlaid onto the CHO cells which had been previously rinsed with OPTIMEM. Cells were incubated for about 5 hours at 37° C. 5% CO<sub>2</sub>, 95% relative humidity. Approximately 1 ml of cell culture media as described previously, with 20% FBS, was added and the cells were incubated overnight. The media was changed at 24 hours, and at 72 hours post transfection, the cells were split 1:4 and put into fresh cell culture media containing about 500  $\mu$ g/ml geneticin (G418, available from Life Technologies). The media was changed every 3-5 days. After several weeks, G418 resistant colonies were trypsinized using sterile filter papers, 5-6 mm in diameter that were soaked in trypsin, which were then placed over individual well of 24 well plates that contained separated widely spaced colonies of CHO cells. After 3 days, the papers were removed. The resulting recombinant cells are referred to herein as CHO-pCMV-nCaIL-4<sub>399</sub>. The recombinant cells were then expanded and tested for the presence of nIL-4<sub>399</sub> RNA by RT-PCR and

tested for the presence of pCaIL-4<sub>133</sub> protein by Western blot analysis. Westerns were developed with rabbit anti-E. coli pCaIL-4<sub>109</sub> serum and 607.1 monoclonal antibody, a monoclonal antibody that selectively binds to E. coli pCaIL-4<sub>109</sub> protein. See Example 1C for a description of how these antibodies were produced.

C. Monoclonal and Polyclonal Antibodies to Recombinant Canine IL-4 (i.e. Anti-canine IL-4 Antibodies)

The following describes the development of monoclonal and polyclonal antibodies that selectively bind to E. coli pCaIL-4<sub>109</sub>.

Female Balb/C mice, 6-8 weeks old, were injected subcutaneously, at about 4 sites, with a total of 25  $\mu$ g E. coli pCaIL-4<sub>109</sub> (produced as described in Example 1B) in Freund's Complete Adjuvant (day 0). Fourteen days later, the mice received an intraperitoneal boost of 25  $\mu$ g E. coli pCaIL-4<sub>109</sub> in Freund's Incomplete Adjuvant (day 14). Fourteen days later, serum was tested for antibody titer to E. coli pCaIL-4<sub>109</sub> by ELISA (day 28). Three days prior to fusion, mice were boosted intravenously with 20  $\mu$ g E. coli pCaIL-4<sub>109</sub> in PBS (day 35). Splenocytes were harvested from mice demonstrating the highest serum titer by ELISA and depleted of CD4+ and CD8+ cells. This depletion was achieved by incubation of the splenocytes with biotinylated rat anti-mouse CD4 and anti-mouse CD8 monoclonal antibodies, available from PharMingen, San Diego, Calif. Antibody-labeled cells were then removed by incubation with M-280 streptavidin coated magnetic beads, available from Dynal, Oslo, Norway. Depleted splenocytes were fused to SP2/0 cells (valuable from ATCC) using 50% polyethylene glycol in unsupplemented Iscove's Modified Dulbecco's Media (IMDM), following established protocols; see, for example, Harlow E., and Lane D., eds., 1995, Antibodies, A Laboratory Manual, Monoclonal Antibodies, Cold Spring Harbor Laboratories; Harlow et al, *ibid.*, is incorporated by reference herein in its entirety. Fused cells were plated in 96-well plates using IMDM cell culture media, (available from Life Technologies, Inc., Rockville, Md.), which was supplemented with 10% fetal bovine serum, 2 mM L-glutamine, 1 mM sodium pyruvate, 1 $\times$ nonessential amino acids, 1 $\times$ MEM amino acids, 0.05 mg/ml gentamicin, and 0.5 mM  $\beta$ -mercaptoethanol (all reagents available from Life Technologies). Additionally, 100  $\mu$ M hypoxanthine, 0.4  $\mu$ M aminopterin, and 16  $\mu$ M thymidine, all available from Sigma Chemical Corporation, St Louis, Mo., were added.

After about 7 days, wells positive for hybridoma growth were screened by ELISA to E. coli pCaIL-4<sub>109</sub>. Immulon II 96-well plates (available from VWR, Denver, Colo.) were coated, overnight, with 100 ng/ml E. coli pCaIL-4<sub>109</sub> in 0.1 M carbonate/bicarbonate buffer, Ph 9.6. After blocking the wells with 20% FBS in Tris buffered saline (TBS), culture supernatants were allowed to bind. Presence of anti-E. coli pCaIL-4<sub>109</sub> mouse antibody was detected with polyclonal goat anti-mouse IgG conjugated to horseradish peroxidase, (available from KPL, Gaithersburg, Md.), and color developed with 3,3',5,5' -tetramethylbenzidine dihydrochloride (TMB), available from Pierce, Rockford, Ill. Specificity of the ELISA reactivity was verified by Western blot analysis to E. coli pCaIL-4<sub>109</sub>, developed with polyclonal goat anti-mouse IgG conjugated to alkaline phosphatase and nitro-blue tetrazolium/5-bromo-4-chloro-3'-indolyphosphate p-toluidine salt substrate (NBT/BCIP, available from Sigma). Western blots exhibited a single band of approximately 14 kD. Immunoglobulin isotype of the monoclonal antibodies was determined using IsoStrips, available from Boehringer Mannheim, Indianapolis, Ind.

Twenty-three monoclonal antibodies were generated to *E. coli*PCaIL-4<sub>109</sub>, 22 of which were of the IgM isotype and one of which was IgG1, and is referred to herein as 607.1.

Polyclonal rabbit serum was produced by repeated immunization (over a 10 month period) of a male, New Zealand White rabbit 12-16 months old. Initial immunization was 50 µg *E. coli*PCaIL-4<sub>109</sub> (prepared as described in Example 1bi) in Freund's Complete Adjuvant, at several sites subcutaneously and intradermally. One month later, and at one month intervals thereafter, the rabbit was boosted intradermally with 50 µg *E. coli*PCaIL-4<sub>109</sub> in Freund's Incomplete Adjuvant. Serum was collected bi-weekly and titers monitored by ELISA and Western blot to *E. coli*PCaIL-4<sub>109</sub>. Serum that selectively bound to *E. coli*PCaIL-4<sub>109</sub> protein is referred to as anti-*E. coli*PCaIL-4<sub>109</sub> serum.

#### D. Bioactivity of Mammalian-Expressed Canine IL-4

The following describes a bioassay to detect the expression of canine IL-4 protein expressed in the supernatants from CHO-pCMV-nCaIL-4<sub>399</sub> recombinant cells by screening for production of CD23.

About 100 µl Ramos cells, available from ATCC, at a concentration of about  $3.5 \times 10^3$  cells/ml were seeded into 96-well flat bottom plates, available from Becton Dickinson, Franklin Lakes, N.J.). These cells were grown in RPMI media supplemented with 100 mM L-glutamine, gentamicin, and 10% FBS (called TCM). The Ramos cells were then treated in 5% CO<sub>2</sub> for 37° C. for approximately 48 h. with one of the following:

Group	Treatment
1	TCM
2	CHO-pCMV (a transfectant cell line containing the empty pCMV vector) supernatant (1:4 final dilution in TCM)
3	CHO-pCMV-nCaIL-4 <sub>399</sub> supernatant (1:10 final dilution in TCM)

Triplicate samples for each treatment group were pooled for staining to look for increased expression of CD23 (one of the reported effects of IL-4). Briefly,  $1 \times 10^5$  cells from each treatment group were incubated in phosphate buffered saline (PBS) containing 30% FBS for 15-30 min on ice. The cells were collected and incubated with the following:

Condition	Primary Incubation	Secondary Incubation
A	PBS	Goat anti mouse PE
B	Mouse anti human CD23	Goat anti mouse PE

Mouse anti-human CD23 monoclonal antibody, available from Pharmingen, was used at about 10 µg/ml. Goat (Fab'2) anti mouse IgG PE, available from Southern Biotechnologies was used at about 2.5 µg/ml. These reagents were diluted in PBS with 5% FBS. Primary incubations were performed for 30-60 minutes on ice, and secondary incubations were performed for 20-30 min on ice. Three washes of PBS/5% FBS were performed in between each incubation. Cells were then analyzed on a flow cytometer (e.g., MoFlow Desk Top System, available from Cytomation, Ft. Collins, Colo.) with the fluorescein gate set at 10<sup>1</sup>. The results are shown in Table 2.

TABLE 2

Incubation of CD23 on Ramos cells post-treatment with supernatants from CHO-pCMV-nCaIL-4 <sub>399</sub> .		
Treatment	Conditions	% positive
1	A	0
	B	1
2	A	8
	B	1
3	A	3
	B	99

Table 2 shows that the canine IL-4 expressed by the CHO transfectant CHO-pCMV-nCaIL-4<sub>399</sub> is biologically active, demonstrated by its ability to induce expression of CD23 in Ramos cells.

#### E. Bioactivity of *E. coli*-expressed Canine IL-4

The following describes a bioassay to detect the expression of canine IL-4 by stimulating the proliferation of TF-1 cells.

TF-1 cells (a human erythroleukaemia cell line, available from R&D Systems, Minneapolis, Minn.), were grown and maintained in TCM-TF-1 medium (RPMI-1640 media supplemented with 2 mM L-glutamine, 5 µg/ml gentamicin, 5% FBS and 2 ng/ml recombinant human GM-CSF (rhuGM-CSF, available from R&D Systems)) in 5% CO<sub>2</sub> at 37° C.

For assay, TF-1 cells were extensively washed to remove rhuGM-CSF, then added at approximately  $1 \times 10^4$  cells per well to 96-well flat bottom plates. Refolded and HPLC-purified *E. coli*-expressed PCaIL-4<sub>109</sub>, produced as described in Example 1Bi, was diluted to the appropriate concentration in TCM-TF-1 without rhuGM-CSF and filter sterilized. Cells and *E. coli*-expressed PCaIL-4<sub>109</sub> were incubated for 48 hours in 5% CO<sub>2</sub> at 37° C., then pulsed with 1 µCi/well tritiated thymidine (available from ICN Pharmaceuticals, Irvine, Calif.), and incubated for an additional 18 hours. Contents of the wells were harvested onto glass fiber filters and counted in a Wallace Trilux 1450 scintillation counter (available from Wallace Inc., Gaithersburg, Md.). The results are shown in Table 3.

TABLE 3

Stimulation of proliferation of TF-1 cells with <i>E. coli</i> -expressed PCaIL-4 <sub>109</sub>		
Concentration <i>E. coli</i> PCaIL-4 <sub>109</sub> (ng/ml)	Counts per minute	
1000	33,216	
500	26,297	
250	27,283	
125	23,804	
62.5	26,225	
31.3	19,803	
15.6	9,818	
7.8	6,475	
0	165	

Table 3 shows that canine IL-4 expressed by *E. coli* is biologically active, as demonstrated by its ability to stimulate proliferation of TF-1 cells.

#### Example 2

This example describes the isolation and sequencing of certain canine Flt-3 ligand and feline Flt-3 nucleic acid molecules and proteins of the present invention. The example also describes expression of a canine Flt-3 ligand

protein of the present invention in CHO cells, as well as detection of the expressed canine Flt-3 ligand protein.  
A. Canine Flt-3 Ligand Nucleic Acid Molecules and Proteins.

i. This example describes the isolation and sequencing of certain canine Flt-3 ligand nucleic acid molecules and proteins of the present invention.

A canine Flt-3 ligand nucleic acid molecule was produced as follows. A pair of primers was initially used to amplify DNA from the *C. familiaris* mitogen activated PBMC cDNA library described above in Example 1. A forward primer referred to as FLT3F1, having the nucleic acid sequence 5' CTGGCGCCAG CCTGGAGCCC 3', designated herein as SEQ ID NO:13 was used in combination with a reverse primer referred to herein as FLT3B1, having the nucleic acid sequence 5' GGGAGATGTT GGTCTGGACG 3', referred to herein as SEQ ID NO:14 to amplify Flt-3 ligand DNA from the cDNA library by polymerase chain reaction (PCR). The primers were designed using conserved regions of IL-4 cDNA sequences from other species in the public databases corresponding to the positions shown below:

Database	Accession number	Nucleotides	Animal
gb	U04806	102-121	human
gb	L23636	41-60	mouse
gb	U04806	77-458	human
gb	L23636	419-400	mouse

A 360-base pair (bp) PCR product was generated in the above reaction that was purified, radiolabeled and used as a probe to screen the cDNA library. Hybridization was performed in 6×SSC, 5×Denhardt's solution, 0.5% SDS, 100 μg/ml ssDNA and 100 μg/ml of tRNA, at 68° C., for about 36 hr. The filters were washed 3 times, for about 30 minutes per wash, at 55° C. in 2×SSC, 0.1% SDS, followed by a final wash in 0.25×SSC, for about 30 minutes, at 55° C. Several positive phage clones were identified and shown to produce PCR products when used as templates in combination with the FLT3F1 and FLT3B1 primers. The DNA inserts in the phage clones were sequenced using standard techniques and failed to yield any clones containing DNA inserts having a portion homologous to published Flt-3 ligand sequences. The 360-bp PCR fragment generated above was then cloned into the vector pcDNA 2.1 (available from Invitrogen Corp., San Diego, Calif.). Several independent colonies were generated and the sequences of their inserts determined. One clone was identified that which contained insert sequence having a portion that was somewhat homologous to published human or murine Flt-3 ligand sequence.

Two canine Flt-3 ligand-specific primers were then designed using the nucleic acid sequence obtained using the 360-bp PCR product described above.

Primer	Sequence	SEQ ID NO
DFLB1	5' GACCAGGCGCCAGAACGC 3'	SEQ ID NO: 15
DFLF1	5' CGGTCCACCATCCGCAAGC 3'	SEQ ID NO: 16

The 5' region of a Flt-3 ligand nucleic acid molecule was PCR amplified from the cDNA library using the DFLB1 primer in combination with the 5' T3 vector primer from the Uni-ZAP® XR vector (available from Stratagene). The 3' region of a Flt-3 ligand nucleic acid molecule was PCR amplified from the cDNA library using the DFLF1 in

combination with the 3' T7 primer from the Uni-ZAP® XR vector (available from Stratagene). A 855-bp PCR product was obtained representing the 5' region of a Flt-3 ligand nucleic acid molecule. A 265-bp PCR product was obtained representing the 3' region of a Flt-3 ligand nucleic acid molecule. Both the 855-bp PCR product and 265-bp PCR product were cloned and sequenced using standard methods. Additional canine Flt-3 ligand-specific primers were designed using the nucleic acid sequence obtained from the sequence of the 855-bp PCR product and 265-bp PCR products.

Primer	Sequence	SEQ ID NO
DFLB2	5' TGGCAAGGCAGTGGCCTC 3'	SEQ ID NO: 17
DFLF2	5' GCCGAGATGATAGTGCTGGC 3'	SEQ ID NO: 18

A 546-bp PCR product was generated using the primer DFLF2 in combination with the primer DFLB2 to amplify a PCR product from the cDNA library. The 546-bp PCR product was then purified, radiolabeled and used as a probe to screen the cDNA library. Hybridization was performed in 6×SSC, 5×Denhardt's solution, 0.5% SDS, 100 μg/ml of ssDNA, and 100 μg/ml of tRNA, at 68° C., for about 36 hr. The filters were washed in 1.25×SSC, for about 30 minutes, at 55° C. Four cDNA clones encoding full-length canine Flt-3 ligand were isolated. Nucleic acid sequence was obtained using standard techniques.

A Flt-3 ligand clone was isolated, referred to herein as nCaFlt3L<sub>1013</sub>, the coding strand of which was shown to have a nucleic acid sequence denoted herein as SEQ ID NO:6. The complement of SEQ ID NO:6 is represented herein by SEQ ID NO:8. Translation of SEQ ID NO:6 suggests that nucleic acid molecule nCaFlt3L<sub>1013</sub> encodes a full-length Flt-3 ligand protein of about 294 amino acids, denoted herein as PCaFlt3L<sub>294</sub>, the amino acid sequence of which is presented in SEQ ID NO:7, assuming an open reading frame having an initiation codon spanning from nucleotide 35 through nucleotide 37 of SEQ ID NO:6 and a stop codon spanning from nucleotide 917 through nucleotide 919 of SEQ ID NO:6. The coding region encoding PCaFlt3L<sub>294</sub> is presented herein as nCaFlt3L<sub>882</sub>, which has the nucleotide sequence SEQ ID NO:9 (the coding strand) and SEQ ID NO:10 (the complementary strand). A putative signal sequence coding region extends from nucleotide 35 through nucleotide 112 of SEQ ID NO:6. The proposed mature protein (i.e., canine Flt-3 ligand protein from which the signal sequence has been cleaved), denoted herein as PCaFlt3L<sub>268</sub> (SEQ ID NO:23), contains about 268 amino acids, extending from residue 27 through residue 294 of SEQ ID NO:7. The nucleic acid molecule encoding PCaFlt3L<sub>268</sub> is denoted herein as nCaFlt3L<sub>804</sub>, extending from nucleotide 113 through nucleotide 916 of SEQ ID NO:6. nCaFlt3L<sub>804</sub> has a coding sequence denoted SEQ ID NO:22 and a complementary sequence denoted SEQ ID NO:24.

Below is a description of the identification of alternatively spliced Canis Flt3 ligand transcripts. Besides cDNA clones such as nucleic acid molecule nCaFlt3L<sub>1013</sub> encoding the full-length canine Flt3 ligand protein, two splice variants of canine Flt3 ligand cDNA clones were also isolated, using the same hybridization conditions as mentioned previously in this Example. One such variant (Clone 1), denoted herein as nCaFlt3L<sub>985</sub>, has a coding strand the nucleic acid sequence of which is represented as SEQ ID NO:25. The complement of SEQ ID NO:25 is represented herein by SEQ ID NO:27.

Translation of SEQ ID NO:25 suggests that nucleic acid molecule nCaFlt3L<sub>985</sub> encodes a Flt-3 ligand protein of 276 amino acids, denoted herein as PCaFlt3L<sub>276</sub>, the amino acid sequence of which is represented by SEQ ID NO:26, assuming an open reading frame having an initiation codon spanning from nucleotide 74 through nucleotide 76 of SEQ ID NO:25 and a stop codon spanning from nucleotide 902 through nucleotide 904 of SEQ ID NO:25. The coding region encoding PCaFlt3L<sub>276</sub> is represented herein as nCaFlt3L<sub>828</sub>, which has the nucleotide sequence SEQ ID NO:28 (the coding strand) and SEQ ID NO:29 (the complementary strand). Alignment of nucleic acid molecules nCaFlt3L<sub>882</sub> and nCaFlt3L<sub>828</sub> indicates that the nucleic acid molecules are identical except for a deletion in nCaFlt3L<sub>828</sub>, which spans from nucleotide 343 through nucleotide 396 of nCaFlt3L<sub>882</sub>. Accordingly, nCaFlt3L<sub>828</sub> encodes 18 fewer amino acids than nCaFlt3L<sub>882</sub>. The deletion in PCaFlt3L<sub>276</sub>, which spans from residue 115 through residue 132 of PCaFlt3L<sub>294</sub>, occurs between helix III and helix IV of the canine Flt3 ligand protein inferred from alignment with the human and mouse Flt3 ligand protein (Lyman et al., Cell, vol. 75, pp. 1157-1167, 1993; Hannum et al., Nature, vol. 368, pp. 643-648, 1994; Lyamn et al., Blood, vol. 83, pp. 2795-2801, 1994). In addition, the alignment shows that there are 39 more nucleotides in the 5' untranslated region of nucleic acid molecule nCaFlt3L<sub>985</sub> (nucleotides 1 to 39) than nucleic acid molecule nCaFlt3L<sub>1013</sub> and there are 2 more nucleotides in the 3' untranslated region of nucleic acid molecule nCaFlt3L<sub>985</sub> (nucleotides 922 to 923) than nucleic acid molecule nCaFlt3L<sub>1013</sub>. The remaining sequences between nCaFlt3L<sub>985</sub> and nCaFlt3L<sub>1013</sub> are identical. A putative mature form of nCaFlt3L<sub>985</sub> (without the signal sequence) is predicted. The putative signal sequence coding region extends from nucleotide 74 to nucleotide 151 of SEQ ID NO:25. The proposed mature protein, denoted herein as PCaFlt3L<sub>250</sub>, represented by SEQ ID NO:31, contains about 250 amino acids, extending from residue 27 through residue 276 of SEQ ID NO:26. The nucleic acid molecule encoding PCaFlt3L<sub>250</sub>, extending from nucleotide 152 through nucleotide 901 of SEQ ID NO:6, denoted herein as nCaFlt3L<sub>750</sub>, is represented by SEQ ID NO:30 (the coding strand) and SEQ ID NO:32 (the complement strand).

A second variant (Clone 19) is represented by nucleic acid molecule nCaFlt3L<sub>1019</sub>, the coding strand of which is denoted herein as SEQ ID NO:33. The component of SEQ ID NO:33 is denoted herein as SEQ ID NO:35. Translation of SEQ ID NO:33 suggests that nCaFlt3L<sub>1019</sub> encodes a Flt-3 ligand protein of 31 amino acids, PCaFlt3L<sub>31</sub>, denoted SEQ ID NO:34, assuming an initiation codon spanning from nucleotide 74 through nucleotide 76 and a stop codon spanning nucleotide 167 through nucleotide 169 of SEQ ID NO:33. The coding region encoding PCaFlt3L<sub>31</sub> is represented herein as nCaFlt3L<sub>93</sub>, which has the nucleotide sequence SEQ ID NO:36 (the coding strand) and SEQ ID NO:37 (the complementary strand). Alignment of nucleic acid molecules nCaFlt3L<sub>985</sub> and nCaFlt3L<sub>1019</sub> indicates the presence of an insertion of 91 nucleotides in nCaFlt3L<sub>1019</sub>. The insertion spans nucleotide 107 through nucleotide 198 of nCaFlt3L<sub>1019</sub>. A stop codon is found in this insertion in frame with the predicted initiation codon, which span nucleotide 74 through nucleotide 76 of SEQ ID NO:6. Since this insertion (with an inframe stop codon) occurs in or close to the signal peptide, it is likely that nucleic acid molecule nCaFlt3L<sub>1019</sub> encodes a nonfunctional Flt-3 ligand protein.

Comparison of nucleic acid sequence SEQ ID NO:6 with nucleic acid sequences reported in GenBank indicates that SEQ ID NO:6 showed the most homology, i.e., about 69.8%

identity, with a human Flt-3 ligand gene. Comparison of amino acid sequence SEQ ID NO:7 with amino acid sequences reported in GenBank indicates that SEQ ID NO:7 showed the most homology, i.e. about 71% identity, with a human Flt-3 ligand protein. Sequence analysis was performed with DNAsis™ using the alignment settings of: gap penalty set at 5; number of top diagonals set at 5; fixed gap penalty set at 10; K-tuple set at 2; window size set at 5 and floating gap penalty set at 10.

ii. This example describes the production of a recombinant molecule encoding a full length canine Flt-3 ligand protein and expression of that protein by a recombinant cell of the present invention.

A recombinant molecule, denoted herein as pCMV-nCaFlt3L<sub>882</sub> and capable of expressing a full length form of Flt-3 ligand, was produced as follows. Nucleic acid molecule nCaFlt3L<sub>882</sub> was digested with the restriction endonucleases EcoRI and XbaI, gel purified and ligated into pCMV-Int A (prepared by methods described in Example 1) to produce recombinant molecule pCMV-nCaFlt3L<sub>882</sub>. Insert size and identity were confirmed by restriction digestion, PCR, and sequencing analyses.

Stable transfectants expressing the recombinant molecule pCMV-nCaFlt3L<sub>882</sub> were established in Chinese Hamster Ovary cells (CHO, available from ATCC) as follows. Briefly, six-well polystyrene tissue culture plates were seeded with approximately 4×10<sup>5</sup> cells per well in 2 ml of MEM (available from Life Technologies, Gaithersburg, Md.) supplemented with 100 mM L-glutamine, gentamicin, and 10% FBS (TCM). Cells were grown to about 80% confluence (about 18 hr). The recombinant molecule to be transfected was prepared using the Qiagen Endotoxin-Free Plasmid Maxi Kit as per the manufacturer's instructions. The recombinant molecule was linearized with the restriction enzyme PvuI, extracted with phenol, and precipitated with isopropanol. The plasmid pcDNA 3, available from Invitrogen, which contains the neomycin resistance gene, was linearized with the restriction enzyme EcoRI. Approximately 1 μg of recombinant plasmid DNA and 100 ng of pcDNA3 were mixed with about 100 μl OptiMEM medium, available from Life Technologies. About 10 μl Lipofectamine (available from Life Technologies) was mixed with 100 μl OptiMEM. The DNA-containing mixture was then added to the Lipofectamine mixture and incubated at room temperature for about 30 min. After incubation, about 800 μl of OptiMEM was added, and the entire mixture was overlaid onto the CHO cells that had been rinsed with OptiMEM. Cells were incubated for 6 hours at 37° C., 5% CO<sub>2</sub>, 95% relative humidity. Approximately 1 ml of TCM with 20% FBS was added, and the cells were incubated overnight. The media was changed after about 24 hr. About 72 hr post transfection, the cells were split 1:4 and put into selection TCM containing 500 μg/ml Geneticin (G418), available from Life Technologies. The medium was changed every 3-5 days. After several weeks, G418-resistant colonies were trypsinized, and the cells were plated into 24 well plates. The resulting recombinant cells are referred to herein as CHO-pCMV-nCaFlt3L<sub>882</sub>. The recombinant cells were then expanded for testing.

iii. The following describes the detection of expression of a canine Flt-3 ligand protein of the present invention by CHO-pCMV-nCaFlt3L<sub>882</sub>, a recombinant cell of the present invention.

Recombinant cells CHO-pCMV-nCaFlt3L<sub>882</sub>, produced as described in Example 2, part (B)(ii) above, were tested for surface expression of canine Flt-3 ligand using a cross-reactive goat anti-human Flt-3 ligand polyclonal antibody as

follows. Briefly,  $1 \times 10^5$  CHO-pCMV-nCaFlt3L<sub>882</sub> cells or CHO-pCMV cells (i.e., cells transfected with an empty vector as described in Example 1) were incubated in phosphate buffered saline (PBS) containing 30% fetal bovine serum (FBS) for about 30 min on ice. The cells were then spun down and treated with the following:

Condition	Primary Incubation	Secondary Incubation
1	PBS	Rabbit (Fab'2) anti sheep (H + L) FITC
2	Goat anti-human Flt3 ligand	Rabbit (Fab'2) anti sheep (H + L) FITC

Goat anti-human Flt3 ligand, available from R and D Systems, Minneapolis, Minn. was used at about 20  $\mu$ g/ml. Rabbit (Fab'2) anti sheep (H+L) FITC, available from Southern Biotechnology Associates, Inc., was used at about 10  $\mu$ g/ml. These reagents were diluted in PBS/5%FBS. All incubations were in 50  $\mu$ l for about 1 hr on ice with 2 washes of PBS/5% FBS in between each incubation. Cells were then analyzed on a flow cytometer (e.g., MoFlow Desk Top System, available from Cytomation, Ft. Collins, Colo.) with the fluorescein gate set at  $10^4$ . The results are shown below in Table 4.

TABLE 4

Cells	% positive	
	Condition 1	Condition 2
CHO-pCMV	1	1
CHO-pCMV nCaFlt3L <sub>882</sub>	2	48
CHO-pCMV nCaFlt3L <sub>882</sub>	1	20

Table 4 shows that canine Flt3 ligand is expressed on the surface of the CHO transfectants.

#### B. Feline Flt-3 Ligand Nucleic Acid Molecules and Proteins.

This example describes the production of certain feline Flt-3 ligand nucleic acid molecules and proteins of the present invention.

A nucleic acid molecule encoding a feline Flt 3 ligand was isolated from a feline PBMC cDNA library as follows. A *Felis catus* mitogen activated PBMC cDNA library was constructed in the Uni-Zap-R XR<sup>TM</sup> vector, available from Stratagene, La Jolla, Calif., using Stratagene's Zap-cDNA-R<sup>TM</sup> Synthesis Kit and the manufacturer's protocol using mRNA isolated from *F. catus* peripheral blood mononuclear cells about 4 hours after they were activated by a polyclonal activating agent in culture. PCR amplification to isolate a feline Flt 3 ligand nucleic acid molecule was conducted according to the following set of steps: one initial denaturation step at 95° C. for 3 minutes; then 35 cycles of the following: 94° C. for 30 seconds, 53.8° C. for 30 seconds, and 72° C. for 105 seconds; then one final extension step at 72° C. for 8 minutes. A 395-nucleotide cDNA fragment containing the 5' end of feline Flt3 ligand coding region, denoted c eFlt3L<sub>395</sub>, was amplified from the feline PBMC cDNA library using the following primers: vector primer T3 having nucleic acid sequence 5' AATTAACCTT CAC-TAAAGGG 3', (SEQ ID NO:142) (available from Stratagene) and the antisense primer having SEQ ID NO:14, described in Example 2A. The nucleic acid sequence of the coding strand of nFeFlt3L<sub>395</sub> is denoted SEQ ID NO:41. A 793-nucleotide cDNA fragment containing the 3' end of

feline Flt3 ligand coding region, denoted nFeFlt3L<sub>793</sub>, was isolated using sense primer 2 having the nucleic acid sequence 5' CACAGYCCCA TCTCCTCC 3', (where Y was either T or C) denoted herein as SEQ ID NO:151, in conjunction with vector primer T7 having the nucleic acid sequence 5' GTAATACGAC TCACTATAGG GC 3' (SEQ ID NO:152). The nucleic acid sequence of the coding strand of nFeFlt3L<sub>793</sub> is denoted SEQ ID NO:42. Nucleic acid molecules feFlt3L<sub>395</sub> and nFeFlt3L<sub>793</sub> overlap by 246 nucleotides and form a composite sequence encoding a Flt3 ligand protein that is similar in length to that of PCaFlt3L<sub>294</sub>. This composite feline Flt3 ligand cDNA is referred to herein as nFeFlt3L<sub>942</sub>, the coding strand of which was shown to have nucleic acid sequence SEQ ID NO:43. The reverse complement of SEQ ID NO:43 is referred to herein as SEQ ID NO:45. Translation of SEQ ID NO:43 suggests that nucleic acid molecule nFeFlt3L<sub>942</sub> encodes a Flt3 ligand protein of 291 amino acids, denoted herein as PeFlt3L<sub>291</sub>, the amino acid sequence of which is presented in SEQ ID NO:44, assuming an open reading frame having an initiation codon spanning from nucleotide 31 through nucleotide 33 of SEQ ID NO:43 and a stop codon spanning from nucleotide 904 through nucleotide 906 of SEQ ID NO:43. The coding region encoding PFeFlt3L<sub>291</sub>, not including the termination codon, is presented herein as nFeFlt3L<sub>873</sub>, which has the nucleotide sequence SEQ ID NO:46 (the coding strand) and SEQ ID NO:47 (the complementary strand). A putative signal sequence coding region extends from nucleotide 31 to nucleotide 108 of SEQ ID NO:43. The proposed mature protein, denoted herein as PFeFlt3L<sub>265</sub>, denoted SEQ ID NO:49, contains about 265 amino acids, extending from residue 27 through residue 291 of SEQ ID NO:44. The nucleic acid molecule encoding PFeFlt3L<sub>265</sub> is denoted herein as nFeFlt3L<sub>795</sub>, (SEQ ID NO:48) extending from nucleotide 109 through nucleotide 903 of SEQ ID NO:43. SEQ ID NO:48 has a complementary strand denoted SEQ ID NO:50.

Sequence alignment indicates that nucleic acid sequence SEQ ID NO:43 shares the highest (67.8%) identity with the nucleic acid sequence of human Flt-3 ligand (GenBank accession numbers U04806 and U03858). Amino acid sequence SEQ ID NO:44 shares the highest (70.2%) identity with human Flt-3 ligand protein (GenBank accession numbers U04806 and U03858).

#### Example 3

This example describes the isolation and sequencing of certain canine CD40 and feline CD40 nucleic acid molecules and proteins of the present invention.

##### A. Canine CD40 Nucleic Acid Molecules and Proteins

This example describes the production of certain canine CD40 nucleic acid molecules and proteins of the present invention.

A canine CD40 nucleic acid molecule of the present invention was produced by PCR amplification as follows. A 321-nucleotide canine CD40 nucleic acid molecule, denoted nCaCD40<sub>321</sub>, was amplified from a canine PBMC cDNA library, prepared as described in Example 1, using two degenerate oligonucleotide primers designed in accordance with conserved regions of human, bovine, rabbit, and mouse CD40 gene sequences available in GenBank; sense primer, 5' TGCCCRSTCG GCTTCTTCTC C 3', denoted herein as SEQ ID NO:128; and antisense primer, 5' CGACTCTCTT TRCCRTCCTC CTG 3', denoted herein as SEQ ID NO:129, where R was either A or G and S was either G or C. PCR conditions were as follows: one initial denaturation step at 95° C. for 3 minutes; then 35 cycles of the following: 94° C.

for 30 seconds, then 53° C. for 30 seconds, then 72° C. for 105 seconds; followed by one final extension at 72° C. for 5 minutes. The resulting PCR product, i.e., nCaCD40<sub>321</sub>, with a coding strand represented by SEQ ID NO:51, was radiolabeled using standard techniques and used to screen the canine PBMC cDNA library, under the following hybridization conditions: hybridized in 6×SSC, 5×Denhardt's solution, 0.5% SDS, 100 µg/ml single stranded DNA, 100 µg/ml tRNA for 36 hours at 68° C., followed by a wash of 0.1% SDS, 1×SSC at 55° C. for 60 minutes. A clone (Clone 18B) containing a 1425-nucleotide canine CD40 nucleic acid molecule, denoted nCaCD40<sub>1425</sub>, was obtained. The nucleic acid sequence of the coding strand of nCaCD40<sub>1425</sub> is represented as SEQ ID NO:52. The reverse complement of SEQ ID NO:52 is referred to herein as SEQ ID NO:54. Translation of SEQ ID NO:52 suggests that nucleic acid molecule nCaCD40<sub>1425</sub> encodes a canine CD40 protein of 274 amino acids, denoted herein as PCaCD40<sub>274</sub>, the amino acid sequence of which is presented in SEQ ID NO:53, assuming an open reading frame having an initiation codon spanning from nucleotide 196 through nucleotide 198 of SEQ ID NO:52 and a stop codon spanning from nucleotide 1018 through nucleotide 1020 of SEQ ID NO:52. The coding region encoding PCaCD40<sub>274</sub>, not including the termination codon, is presented herein as nCaCD40<sub>822</sub>, which has the nucleotide sequence SEQ ID NO:55 (the coding strand) and SEQ ID NO:56 (the complementary strand).

A putative signal sequence coding region extends from nucleotide 196 through nucleotide 252 of SEQ ID NO:52. The proposed mature protein, denoted herein as PCaCD40<sub>255</sub>, represented by SEQ ID NO:58, contains about 255 amino acids, extending from residue 20 through residue 274 of SEQ ID NO:53. The nucleotide sequence encoding PCaCD40<sub>255</sub>, which extends from nucleotide 253 through nucleotide 1017 of SEQ ID NO:52, is denoted herein as nucleic acid molecule nCaCD40<sub>765</sub>, represented by SEQ ID NO:57 (the coding strand) and SEQ ID NO:59 (the complement strand).

Sequence analysis was performed with DNAsis™ using the alignment settings of: gap penalty set at 5; number of top diagonals set at 5; fixed gap penalty set at 10; k-tuple set at 2; window size set at 5 and floating gap penalty set at 10. At the amino acid level, PCaCD40<sub>274</sub> shares 65.3%, 50.1%, and 42.3% identity with the CD40 proteins of human, bovine, and mouse, respectively (Stamenkovic et al., EMBO J., vol. 8:1403-1410, 1989; Hirano et al., Immunology, vol. 90, pp. 294-300, 1997; Grimaldi et al., J. Immunol., vol. 143, pp.3921-3926; Torres and Clark, J. Immuno., vol. 148, pp. 620-626). At the nucleotide level, nCaCD40<sub>1425</sub> shares 69.3%, 69.4%, and 40.4% identity with the cDNA sequences of human, bovine, and mouse CD40, respectively.

#### B. Feline CD40 Nucleic Acid Molecules and Proteins

This example describes the isolation and sequencing of certain nucleic acid molecules of the present invention that encode certain feline CD40 proteins of the present invention.

A 336-nucleotide feline CD40 nucleic acid molecule, denoted nFeCD40<sub>336</sub>, was amplified from a feline PBMC cDNA library, prepared as described in Example 2, using PCR conditions and primers as described in Example 3A, i.e., a sense primer having SEQ ID NO:128; and an antisense primer having SEQ ID NO:129. The resulting PCR product, i.e., nFeCD40<sub>336</sub>, was shown to have a coding strand the nucleic acid sequence of which is represented as SEQ ID NO:60. The reverse complement of SEQ ID NO:60 is referred to herein as SEQ ID NO:62. Translation of SEQ ID

NO:60 suggests that nucleic acid molecule nFeCD40<sub>336</sub> encodes a partial CD40 protein of 112 amino acids, denoted herein as PFeCD40<sub>112</sub>, the amino acid sequence of which is presented in SEQ ID NO:61, assuming an open reading frame spanning from nucleotide 1 through nucleotide 336 of SEQ ID NO:60.

Comparison of nucleic acid sequence SEQ ID NO:60 with nucleic acid molecules reported in GenBank indicates that SEQ ID NO:60 showed the most homology, i.e. 67.2% identity, with a human CD40 gene. Comparison of amino acid sequence SEQ ID NO:61 with amino acid sequences reported in GenBank indicates that SEQ ID NO:61 showed the most homology, i.e. about 54.4% identity, with a human CD40 protein. Sequence analysis was performed using the GCG GAP program as described above.

#### Example 4

This example describes the isolation and sequencing of certain canine CD154 (canine CD40 ligand) and feline CD154 (feline CD40 ligand) nucleic acid molecules and proteins of the present invention.

#### A. Canine CD154 (CD40 ligand) Nucleic Acid Molecules and Proteins

The following describes the isolation and sequencing of certain cDNA nucleic acid molecules encoding certain canine CD154 (CD40 ligand) protein of the present invention.

A canine CD154 nucleic acid molecule of the present invention was produced by PCR amplification as follows. A 390-nucleotide canine CD40 nucleic acid molecule, denoted nCaCD154<sub>390</sub>, was amplified from a canine PBMC cDNA library, prepared as described in Example 1, using two degenerate oligonucleotide primers designed in accordance with human CD154 gene sequences available in GenBank; sense primer, 5' CCTCAAATTG CGGCACATGT C 3', denoted herein as SEQ ID NO:130; and antisense primer, 5' CTGTTCAGAG TTTGAGTAAG CC 3', denoted herein as SEQ ID NO:131. PCR conditions used for canine CD154 cDNA amplification were standard conditions for PCR amplification (Sambrook, et al., *ibid.*). The resulting PCR product, i.e., nCaCD154<sub>390</sub>, with a coding strand represented by SEQ ID NO:63, was radiolabeled using standard techniques and used to screen the canine PBMC cDNA library, under the hybridization conditions described in Example 3. A clone containing a 1878-nucleotide canine CD154 nucleic acid molecule, denoted nCaCD154<sub>1878</sub>, was obtained. The nucleic acid sequence of the coding strand of nCaCD154<sub>1878</sub> is represented as SEQ ID NO:64. The reverse complement of SEQ ID NO:64 is referred to herein as SEQ ID NO:66. Translation of SEQ ID NO:64 suggests that nucleic acid molecule nCaCD154<sub>1878</sub> encodes a CD154 protein of 260 amino acids, denoted herein as PCaCD154<sub>260</sub>, the amino acid sequence of which is presented in SEQ ID NO:65, assuming an open reading frame having an initiation codon spanning from nucleotide 284 through nucleotide 286 of SEQ ID NO:64 and a stop codon spanning from nucleotide 1064 through nucleotide 1066 of SEQ ID NO:64. The coding region encoding PCaCD154<sub>260</sub>, not including the termination codon, is presented herein as nCaCD154<sub>780</sub>, which has the nucleotide sequence SEQ ID NO:67 (the coding strand) and SEQ ID NO:68 (the complementary strand).

A putative signal/membrane anchor sequence coding region extends from nucleotide 284 through nucleotide 430 of SEQ ID NO:64. The proposed soluble CD154 protein, denoted herein as PCaCD154<sub>211</sub>, represented by SEQ ID NO:70, contains about 211 amino acids, extending from

residue 50 though residue 260 of SEQ ID NO:65. The nucleotide sequence encoding PCaCD154<sub>211</sub>, which extends from nucleotide 431 through nucleotide 1063 of SEQ ID NO:64, is denoted herein as nucleic acid molecule nCaCD154<sub>633</sub>, represented by SEQ ID NO:69 (the coding strand) and SEQ ID NO:71 (the complement strand).

Sequence analysis was performed with DNAsis™ using the alignment settings of: gap penalty set at 5; number of top diagonals set at 5; fixed gap penalty set at 10; k-tuple set at 2; window size set at 5 and floating gap penalty set at 10. At the amino acid level, PCaCD154<sub>260</sub> shares 78.0%, 77.6%, and 67.6% identity with the CD154 proteins of human, bovine, and mouse, respectively (Graf et al., Eur. J. Immunol., vol. 22, pp. 3191-3194, 1992; Hollenbaugh, et al., EMBO J., vol. 11:4313-4321, 1992; Gauchat et al., FEBS Lett., vol. 315, pp. 259-266, 1993; Mertens et al., Immunogenetics, vol. 42, pp. 430-431; Armitage et al., Nature, vol. 357, pp. 80-82; 1992). At the nucleotide level, nCaCD154<sub>1878</sub> shares 81.1%, 81.5%, and 74.4% identity with the sequences of human, bovine, and mouse CD154 cDNAs, respectively.

B. Feline CD154 (CD40 ligand) Nucleic Acid Molecules and Proteins

This example describes the isolation and sequencing of certain nucleic acid molecules encoding certain feline CD154 (CD40 ligand) proteins of the present invention.

A feline CD154 nucleic acid molecule was isolated by PCR amplification from a feline PBMC cDNA library, prepared as described in Example 2, using Amplitaq DNA polymerase (available from PE Applied Biosystems Inc, Foster City, Calif.) under the following PCR protocol: one initial denaturation step at 95° C. for 5 minutes; then 40 cycles of the following: 94° C. for 45 seconds, then 48° C. for 45 seconds, then 72° C.; for 120 seconds; followed by a final extension at 72° C. for 7 minutes. The forward and reverse primers used were based on human CD154 cDNA sequences outside the open reading frame in the 5' and 3' untranslated regions, respectively, so that the open reading frame in the PCR product contained only feline sequences. The sequence of the forward primer was 5' GAAGATACCA TTTCAACTTT AACACAGC 3' SEQ ID NO:132, and that of the reverse primer was 5' TGCTGTATTG TGAA-GACTCC CAGC 3' SEQ ID NO:133. PCR products were cloned into the TA cloning vector (available from Invitrogen Corporation, Carlsbad, Calif.), and the resulting clones were sequenced using an ABI Prism™ Model 377 Automatic DNA Sequencer (available from PE Applied Biosystems Inc.). DNA sequencing reactions were performed using Prism™ dRhodamine Terminator Cycle Sequencing Ready Reaction kits (available from PE Applied Biosystems Inc.).

The PCR product was sequenced and found to contain 885 nucleotides, and is denoted as nFeCD154<sub>885</sub>. The nucleotide sequence of the coding strand of nFeCD154<sub>885</sub> is represented herein as SEQ ID NO:72, and its complement is denoted SEQ ID NO:74. Translation of the open reading frame in SEQ ID NO:72 suggests that nFeCD154<sub>885</sub> encodes a protein containing 260 amino acids, referred to herein as PFeCD154<sub>260</sub>, the amino acid sequence of which is presented as SEQ ID NO:73, assuming an open reading frame in which the first codon spans from nucleotide 29 through nucleotide 31 of SEQ ID NO:72, and the stop codon spans from nucleotide 809 through nucleotide 811 of SEQ ID NO:72. The encoded protein has a predicted molecular weight of 28.6 kDa for the precursor protein and 27.2 kDa for the mature protein. The coding region encoding PFeCD154<sub>260</sub>, not including the termination codon, is presented herein as nFeCD154780, which has the nucleotide

sequence SEQ ID NO:75 (the coding strand) and SEQ ID NO:76 (the complementary strand)

A putative signal/membrane anchor sequence coding region extends from nucleotide 29 through nucleotide 175 of SEQ ID NO:72. The proposed soluble feline CCD154 protein, denoted herein as PFeCD154<sub>211</sub>, represented by SEQ ID NO:78, contains about 211 amino acids, extending from residue 50 though residue 260 of SEQ ID NO:73. The nucleotide sequence encoding PFeCD154<sub>211</sub>, denoted herein as nFeCD154<sub>633</sub> which extends from nucleotide 176 through nucleotide 808 of SEQ ID NO:72, is represented herein by SEQ ID NO:77 (the coding strand) and SEQ ID NO:79 (the complementary strand).

Comparison of feline CD154 nucleotide and amino acid sequences with those of other species published in GenBank reveals that the feline CD154 nucleotide sequence SEQ ID NO:75 is 86%, 88% and 75% identical to the human, bovine and murine CD154 gene sequences, respectively (Genbank accession number L07414, Z48469 and X56453 respectively). At the amino acid sequence level, SEQ ID NO:73 is 81%, 82%, and 67% identical to the human, bovine and murine CD154 amino acid sequences, respectively. Hydrophobicity analysis of feline CD154 proteins results in a pattern similar to those of human, bovine and murine CD154 proteins. A putative N-glycosylation site was identified at position 239 in PFeCD154<sub>260</sub> that is conserved in the human, bovine and murine amino acid sequences. Five cysteine residues are present in the feline CD154 protein sequence SEQ ID NO:73. Four of the five residues, located at positions 72, 84, 177 and 217 of PFeCD154<sub>260</sub>, are conserved in all four species and are likely involved in disulfide bond formation. The cysteine residue located at position 193 of PFeCD154<sub>260</sub> is present in all but the murine sequence.

#### Example 5

This example describes the isolation and sequencing of certain canine IL-5 nucleic acid molecules and proteins of the present invention. This example also describes expression of canine IL-5 in a Pichia expression system and the bioactivity of such an expressed protein.

A. Isolation and Sequencing of Canine IL-5 Nucleic Acid Molecules and Proteins

A canine IL-5 cDNA nucleic acid molecule encoding a canine IL-5 protein was isolated by PCR amplification from a canine PBMC cDNA library (prepared as described in Example 1) using PCR conditions as described in Example 4B and the following primers. Degenerate oligonucleotide primers were designed in accordance with conserved regions of human and cat IL-5 gene sequences available in GenBank: sense primer, 5' ATGCACTTTC TTGCC 3', denoted herein as SEQ ID NO:134; antisense primer 1, 5' CTGGAG-GAAA AKACTTCRAT GATTCTGATA TCTGAAATAT AT 3', denoted herein as SEQ ID NO:135; and antisense primer 2, 5' CTGACYCTTK STGGSCCTC ATTCTCA 3', denoted herein as SEQ ID NO:136, where K was G or T, R was either A or G, S was either G or C, and Y was either T or C.

An about 610-nucleotide canine IL-5 nucleic acid molecule, denoted nCaIL-5<sub>610</sub>, was obtained using primers having SEQ ID NO:134 and SEQ ID NO:135, respectively. The sequence of the coding strand of nCaIL-5<sub>610</sub> is represented herein as SEQ ID NO:80. The reverse complement of SEQ ID NO:80 is referred to herein as SEQ ID NO:82. Translation of SEQ ID NO:80 suggests that nucleic acid molecule nCaIL-5<sub>610</sub> encodes an IL-5 protein of 134 amino acids, denoted herein as PCaIL-5<sub>134</sub>, the amino acid

sequence of which is presented in SEQ ID NO:81, assuming an open reading frame having an initiation codon spanning from nucleotide 29 through nucleotide 31 of SEQ ID NO:80 and a stop codon spanning from nucleotide 431 through nucleotide 433 of SEQ ID NO:80. The coding region encoding PCaIL-13<sub>134</sub>, not including the termination codon, is presented herein as nCaIL-5<sub>402</sub>, which has the nucleotide sequence SEQ ID NO:83 (the coding strand) and SEQ ID NO:84 (the complementary strand).

At about 488-nucleotide fragment, denoted herein as nCaIL-5<sub>488</sub>, isolated by PCR with primers having SEQ ID NO:134 and SEQ ID NO:136, respectively, corresponds to nucleotide 1 through nucleotide 488 of nCaIL-5<sub>610</sub>.

A putative signal sequence coding region extends from nucleotide 29 through nucleotide 85 of SEQ ID NO:80. The proposed mature protein, denoted herein as PCaIL-5<sub>115</sub>, represented by SEQ ID NO:86, contains about 115 amino acids, extending from residue 20 though residue 134 of SEQ ID NO:81. The nucleotide sequence encoding PCaIL-5<sub>115</sub>, which extends from nucleotide 86 through nucleotide 430 of SEQ ID NO:80, is denoted herein as nucleic acid molecule nCaIL-5<sub>345</sub>, represented by SEQ ID NO:85 (coding strand) and SEQ ID NO:87 (the complement strand).

Sequence analysis was performed with DNAsis™ using the alignment settings of: gap penalty set at 5; number of top diagonals set at 5; fixed gap penalty set at 10; k-tuple set at 2; window size set at 5 and floating gap penalty set at 10. At the amino acid level, PCaIL-5<sub>134</sub> shared 82.8% and 57.4% identity with feline and human IL-5 proteins, respectively (Padrid et al., Am. J. Vet. Res., vol. 59, pp. 1263-1269, 1998; Azuma et al., Nucleic Acids Res., vol. 14, pp. 9149-9158, 1986). At the nucleotide level, nCaIL-5<sub>610</sub> shared 81.7% and 75% identity with the cDNA sequences of the feline and human IL-5, respectively.

#### B. Expression of Canine IL-5 in Pichia

This example describes the expression in Pichia of a canine IL-5 cDNA fragment, namely a canine IL-5 nucleic acid molecule denoted nCaIL-5<sub>348</sub>, the coding strand of which consists of nucleotides 86-433 of SEQ ID NO:80, and as such, encodes a predicted mature canine IL-5 protein having SEQ ID NO:86. Nucleic acid molecule nCaIL-5<sub>348</sub>, was PCR amplified from nCaIL-5<sub>610</sub> using sense primer 5' GGGCTCGAGA AAAGATTTGC TGTAGAAAAT CCCATG 3' denoted herein as SEQ ID NO:137, with nucleotides 16-36 corresponding to nucleotides 86-106 of SEQ ID NO:80; and antisense primer 5' CCCGCGCCG CTCAACTTTC CGGTGTCCAC TC 3', denoted herein as SEQ ID NO:138, with nucleotides 12-32 corresponding to the reverse complement of nucleotides 413-433 of SEQ ID NO:80. To facilitate cloning, an XhoI site (shown in bold) was added to the sense primer and a NotI site (shown in bold) was added to the antisense primer. The PCR-amplified fragment was digested with restriction endonucleases XhoI and NotI, gel purified and ligated into pPICZαA plasmid vector, available from Invitrogen, that has been digested by Xho I and Not I and gel purified, to produce recombinant molecule pPICZαA-nCaIL-5<sub>348</sub>. The insert in the recombinant molecule was verified by DNA sequencing. The recombinant molecule was used to transform Pichia pastoris strain X-33 by electroporation to produce recombinant cell Pichia-pPICZαA-nCaIL-5<sub>348</sub>. Recombinant cell Pichia-pPICZαA-nCaIL-5<sub>348</sub> was cultured using techniques known to those skilled in the art and IL-5 expression was induced with methanol. The supernatant was recovered and submitted to SDS-PAGE. Silver staining of the resultant gel indicated a band of about 18 kDa only seen in the supernatant of Pichia transformed with recombinant molecule pPICZαA-nCaIL-5<sub>348</sub>.

#### C. Bioactivity of Pichia-expressed Canine IL-5

The following describes a bioassay to detect the expression of canine IL-5 by stimulating the proliferation of TF-1 cells.

TF-1 cells, grown and maintained as described in Example 1E, were extensively washed to remove rhuGM-CSF, and then added at approximately 1×10<sup>4</sup> cells per well to 96-well flat bottom plates. Pichia-expressed canine IL-5, produced as described in Example 5B, was dialyzed overnight at 4° C. against Phosphate Buffered Saline, diluted to the appropriate concentration in TCM-TF-1 without rhuGM-CSF and filter sterilized. Cells and Pichia-produced canine IL-5 were incubated for 48 hours in 5% CO<sub>2</sub> at 37° C., then pulsed, incubated, harvested and counted as described in Example 1E. The results are shown in Table 5.

TABLE 5

Stimulation of proliferation of TF-1 with Pichia-expressed canine IL-5	
1/dilution	Counts per minute
2	44,885
4	101,564
8	81,161
16	59,384
32	40,508
64	15,948
128	6,634
256	2,441
Media(noIL-5)	172

Table 5 shows that canine IL-5 expressed by Pichia is biologically active, as demonstrated by its ability to stimulate proliferation of TF-1 cells.

#### Example 6

This example describes the isolation and sequencing of certain canine IL-13 nucleic acid molecules and proteins of the present invention. This example also describes expression of canine IL-13 in E. coli and bioactivity of such an expressed protein.

#### A. Isolation and Sequencing of Canine IL-13 Nucleic Acid Molecules and Proteins

A canine IL-13 cDNA nucleic acid molecule encoding a canine IL-13 protein was isolated by PCR amplification from a canine PBMC cDNA library (prepared as described in Example 1) using the following primers and PCR conditions: Degenerate oligonucleotide primers were designed in accordance with conserved regions of human and cat IL-5 gene sequences available in GenBank: sense primer, 5' GTCMTKGCTC TYRCTTGCCT TGG 3', denoted herein as SEQ ID NO:139; antisense primer 1, 5' AAASGCGCY ACYTTCGATTT TGG 3', denoted herein as SEQ ID NO:140; antisense primer 2, 5' GTGATGTTGM YCAGCTCCTC 3', denoted herein as SEQ ID NO:141, where M was either A or C, K was G or T, R was either A or G, S was either G or C, and Y was either T or C. PCR conditions used were as follows: One initial denaturation step at 95° C. for 3 minutes; then 38 cycles of the following: 94° C. for 30 seconds, 51.8° C. for 45 seconds, then 72° C. for 105 seconds; then a final extension at 72° C. for 5 minutes.

An about 272-nucleotide canine IL-13 nucleic acid molecule, denoted nCaIL-13<sub>272</sub> and having a coding strand represented by SEQ ID NO:89, was PCR amplified using primers having nucleic acid sequences of SEQ ID NO:139 and SEQ ID NO:140, respectively. An about 166-nucleotide canine IL-13 nucleic acid molecule, denoted nCaIL-13<sub>166</sub>

and having a coding strand represented by SEQ ID NO:88, was isolated using primers nucleic acid sequences of SEQ ID NO:142 (see Example 2B) and SEQ ID NO:141, respectively. Nucleic acid molecules nCaIL-13<sub>272</sub> and nCaIL-13<sub>272</sub> form an overlapping composite fragment of 383 nucleotides, denoted nCaIL-13<sub>383</sub>. Two canine IL-13 specific primers (i.e., sense primer, 5' ATGGCGCTCT GGT-TGACTGT 3', denoted herein as SEQ ID NO:143; and antisense primer, 5' GGCTTTTGAG AGCACAGTGC 3', denoted herein as SEQ ID NO:144) were derived from nCaIL-13<sub>383</sub> and were used to isolate a 278-nucleotide fragment, denoted nCaIL-13<sub>278</sub> and having a coding strand represented by SEQ ID NO:90. Nucleic acid molecule nCaIL-13<sub>278</sub> was radiolabeled and used to screen the canine PBMC cDNA library under the following hybridization conditions: hybridization took place in 6×SSC, 5×Denhardt's solution, 0.5% SDS, 100 µg/ml single stranded DNA, 100 µg/ml tRNA, for 36 hours at 60° C.; the final wash solution was 0.1% SDS, 0.125×SSC at 60° C. for 30 minutes. Two clones were selected, namely clone 80 and clone 78.

Sequence analysis of Clone 80 indicated that the clone includes an about 1302-nucleotide canine IL-13 nucleic acid molecule referred to herein as nCaIL-13<sub>1302</sub>, the coding strand of which was shown to have nucleic acid sequence SEQ ID NO:91. The reverse complement of SEQ ID NO:91 is referred to herein as SEQ ID NO:93. Translation of SEQ ID NO:91 suggests that nucleic acid molecule nCaIL-13<sub>1302</sub> encodes an IL-13 protein of 131 amino acids, denoted herein as PCaIL-13<sub>131</sub>, the amino acid sequence of which is presented in SEQ ID NO:92, assuming an open reading frame having an initiation codon spanning from nucleotide 52 through nucleotide 54 of SEQ ID NO:91 and a stop codon spanning from nucleotide 445 through nucleotide 447 of SEQ ID NO:91. The coding region encoding PCaIL-13<sub>131</sub>, not including the termination codon, is presented herein as nCaIL-13<sub>393</sub>, which has the nucleotide sequence SEQ ID NO:94 (the coding strand) and SEQ ID NO:95 (the complementary strand).

A putative signal sequence coding region extends from nucleotide 52 to nucleotide 111 of SEQ ID NO:91. The proposed mature protein, denoted herein as PCaIL-13<sub>111</sub>, represented by SEQ ID NO:97, contains 111 amino acids, extending from residue 21 through residue 131 of SEQ ID NO:91. The nucleotide sequence encoding PCaIL-13<sub>111</sub>, which extends from nucleotide 112 through nucleotide 444 of SEQ ID NO:91, is denoted herein as nucleic acid molecule nCaIL-13<sub>333</sub>, represented by SEQ ID NO:96 (coding strand) and SEQ ID NO:98 (the complement strand).

Sequence analysis of Clone 78 indicated that the clone includes an about 1269-nucleotide canine IL-13 nucleic acid molecule referred to herein as nCaIL-13<sub>1269</sub>, the coding strand of which was shown to have nucleic acid sequence SEQ ID NO:99. The reverse complement of SEQ ID NO:99 is referred to herein as SEQ ID NO:101. Translation of SEQ ID NO:99 suggests that nucleic acid molecule nCaIL-13<sub>1269</sub> encodes an IL-13 protein of 130 amino acids, denoted herein as PCaIL-13<sub>130</sub>, the amino acid sequence of which is presented in SEQ ID NO:100, assuming an open reading frame having an initiation codon spanning from nucleotide 57 through nucleotide 59 of SEQ ID NO:99 and a stop codon spanning from nucleotide 447 through nucleotide 449 of SEQ ID NO:99. The coding region encoding PCaIL-13<sub>130</sub>, not including the termination codon, is represented herein as nCaIL-13<sub>390</sub>, which has the nucleotide sequence SEQ ID NO:102 (the coding strand) and SEQ ID NO:103 (the complementary strand). PCaIL-13<sub>130</sub> is missing one amino

acid compared to PCaIL-13<sub>133</sub>, namely amino acid position Q97 of PCaIL-13<sub>133</sub>.

A putative signal sequence coding region extends from nucleotide 57 to nucleotide 116 of SEQ ID NO:99. The proposed mature protein, denoted herein as PCaIL-13<sub>110</sub>, represented by SEQ ID NO:105, contains 110 amino acids, extending from residue 21 through residue 130 of SEQ ID NO:100. The nucleotide sequence encoding PCaIL-13<sub>110</sub>, which extends from nucleotide 117 through nucleotide 446 of SEQ ID NO:99, is denoted herein as nucleic acid molecule nCaIL-13<sub>330</sub>, represented by SEQ ID NO:104 (coding strand) and SEQ ID NO:106 (the complement strand).

Sequence analysis was performed with DNAsis™ using the alignment settings of: gap penalty set at 5; number of top diagonals set at 5; fixed gap penalty set at 10; k-tuple set at 2; window size set at 5 and floating gap penalty set at 10. At the amino acid level, PCaIL-13<sub>131</sub> shared 61.7%, 39.6%, 36.6% identity with the IL-13 proteins of human, mouse, and rat (Brown et al., J. Immunol., vol. 142, pp. 679-687, 1989; Lakkis et al., Biochem. Biophys. Res. Commun., Vol. 197, pp. 612-618, 1993; McKenzie et al., Proc. Natl Acad. Sci. USA, vol. 90, pp. 3735-3739, 1993; Minty et al., Nature, vol. 362, pp. 248-250, 1993), respectively. At the nucleotide level, nCaIL-13<sub>1302</sub> shared 56.0%, 57.1%, and 45.9% identity with the sequences of human, rat, and mouse IL-13 cDNAs, respectively.

#### B. Expression of Canine IL-13 in E. coli

This examples describes the expression in E. coli of a canine IL-13 cDNA fragment, namely a canine IL-13 nucleic acid molecule denoted nCaIL-13<sub>336</sub>, the coding strand of which consists of nucleotides 112-447 of SEQ ID NO:91, and as such, encodes a predicted mature canine IL-13 protein having SEQ ID NO:97. Nucleic acid molecule nCaIL-13<sub>336</sub> was PCR amplified from nCaIL-13<sub>1302</sub> using sense primer 5' CCCCATATGA GCCCTGTGAC TCCCTC-CCC 3' denoted herein as SEQ ID NO:145, with nucleotides 10-29 corresponding to nucleotides 112-1131 of SEQ ID NO:91; and antisense primer 5' GGGGAATTCT CATCT-GAAAT TTCCATGGCG 3', denoted herein as SEQ ID NO:146, with nucleotides 10-30 corresponding to the reverse complement of nucleotides 427-447 of SEQ ID NO:91. To facilitate cloning, an NdeI site (shown in bold) was added to the sense primer and an EcoRI site (shown in bold) was added to the antisense primer. The resulting PCR fragment was digested with restriction endonucleases NdeI and EcoRI, gel purified and ligated into λcro plasmid vector, the production of which is described in U.S. Pat. No. 5,569,603 by Tripp et al., issued Oct. 29, 1996, that had been digested by NdeI and EcoRI and gel purified to produce recombinant molecule pλcro-nCaIL-13<sub>336</sub>. The insert in the recombinant molecule was verified by DNA sequencing. Recombinant molecule pλcro-nCaIL-13<sub>336</sub> was used to transform E. coli strain HCE101 (BL21), thereby producing BL21-pλcro-nCaIL-13<sub>336</sub>. PCaIL-13<sub>111</sub> was produced under conditions as described in U.S. Pat. No. 5,569,603, *ibid.*, protein expression being induced by switching the fermentation temperature from 32° C. to 42° C. SDS-PAGE and Commassie blue staining analysis indicated that a band of about 11 kD was only produced by induced BL21-pλcro-nCaIL-13<sub>336</sub> recombinant cells. The 11-kD band showed a positive reaction with a rabbit polyclonal antibody against human IL-13 (available from PeproTech Inc, Rocky Hill, N.J.), indicating expression of canine IL-13 in E. coli.

#### C. Bioactivity of E. coli-expressed Canine IL-13

The following describes a bioassay to detect the expression of canine IL-13 by stimulating the proliferation of TF-1 cells.

TF-1 cells, grown and maintained as described in Example 1E, were extensively washed to remove rhuGM-CSF, and then added at approximately  $1 \times 10^4$  cells per well to 96-well flat bottom plates. *E. coli*-produced PCaIL-13<sub>111</sub>, produced as described in Example 6B, was dialyzed overnight at 4° C. against Phosphate Buffered Saline, diluted to the appropriate concentration in TCM-TF-1 without rhuGM-CSF and filter sterilized. Cells and *E. coli*-produced PCaIL-13<sub>111</sub> were incubated for 48 hours in 5% CO<sub>2</sub> at 37° C., then pulsed, incubated, harvested and counted as described in Example 1E. The results are shown in Table 6.

TABLE 6

Stimulation of proliferation of TF-1 cells with <i>E. coli</i> PCaIL-13 <sub>111</sub>	
Concentration <i>E. coli</i> PCaIL-13 <sub>111</sub> (ng/ml)	Counts per minute
1000	126,203
500	77,893
250	57,781
125	40,491
62.5	26,115
31.3	7,042
15.6	8,713
0	991

Table 6 shows that canine IL-13 expressed by *E. coli* is biologically active, as demonstrated by its ability to stimulate proliferation of TF-1 cells.

## Example 7

This example describes the isolation and sequencing of feline interferon alpha nucleic acid molecules and proteins of the present invention. This example also describes expression of feline interferon alpha proteins of the present invention in *E. coli* and mammalian cells as well as the bioactivities of the resulting proteins.

## A. Isolation and Sequencing of Feline IFN-alpha Nucleic Acids and Proteins

Feline IFN-alpha nucleic acid molecules were PCR amplified from a feline cDNA library as follows. Total RNA was isolated from cat (kitten) mesenteric lymph node cells stimulated with PMA (phorbol myristate acetate) for 48 hours using Tri Reagent™ (available from Molecular Research Center, Cincinnati, Ohio). cDNA was made from the RNA using the cDNA synthesis kit containing Ready to Go -You Prime First-Strand Beads™ (available from Amersham Pharmacia Biotech, Piscataway, N.J.). An aliquot of this cDNA was used as a template to isolate a feline IFN-alpha nucleic acid molecule by PCR amplification using Amplitaq DNA polymerase™ (available from PE Applied Biosystems Inc, Foster City, Calif.) and the following primers and conditions. The sequence of the forward primer was 5' ATGGCGCTGC CCTCTCCTT CTTG 3' (SEQ ID NO:143), and that of the reverse primer was 5' TCATTCTCG CTCCTAATC TTTTCTGC 3' (SEQ ID NO:148). The following PCR protocol was used: one initial denaturation step at 95° C. for 5 minutes; then 43 cycles of the following: 94° C. for 45 seconds, then 47° C. for 45 seconds, then 72° C. for 120 seconds; followed by a final extension at 72° C. for 7 minutes. PCR products were cloned into the TA cloning vector (available from Invitrogen Corporation) and the clones were sequenced using an ABI Prism™ Model 377 Automatic DNA Sequencer (available from PE Applied Biosystems Inc.). DNA sequencing reactions were performed using Prism™ dRhodamine Terminator Cycle Sequencing Ready Reaction kits (available from PE

Applied Biosystems Inc.). Five PCR products were generated and sequenced. These products were included, respectively, in Clones #1, #2, #3, #5, and #6.

Clone #2 includes a feline IFN-alpha nucleic acid molecule that is represented herein as nFeIFN $\alpha_{567a}$ , the coding strand of which was shown to have a nucleic acid sequence denoted herein as SEQ ID NO:107. The complement of SEQ ID NO:107 is represented herein by SEQ ID NO:109. Translation of SEQ ID NO:107 suggests that nFeIFN $\alpha_{567a}$  encodes a protein containing 189 amino acids, referred to herein as PFeIFN $\alpha_{189a}$ , with an amino acid sequence denoted SEQ ID NO:108. The open reading frame of SEQ ID NO:107 is assumed to be the following: the first codon spans from nucleotide 1 through nucleotide 3 and the last codon before the stop codon spans from nucleotide 565 to nucleotide 567 of SEQ ID NO:107. The encoded protein has a predicted molecular weight of 21 kDa. The putative signal peptide cleavage site occurs between amino acid positions 23 and 24, based on homology with the human and canine interferon-alpha proteins. The proposed mature protein (i.e. feline IFN $\alpha$  protein from which the signal sequence has been cleaved), denoted herein as PFeIFN $\alpha_{166a}$ , contains about 166 amino acids, extending from residue 24 to residue 166 of SEQ ID NO:108; the amino acid sequence is denoted herein as SEQ ID NO:114. The nucleic acid molecule encoding PFeIFN $\alpha_{166a}$  is denoted herein as nFeIFN $\alpha_{498a}$ , the coding strand of which is represented by SEQ ID NO:113, and the complementary strand of which is represented by SEQ ID NO:115. A putative N-glycosylation site and an interferon alpha-beta-delta family signature motif are present at amino acid positions 102 and 145, respectively, of PFeIFN $\alpha_{189a}$ .

Clone #3 includes a feline IFN-alpha nucleic acid molecule that is represented herein as nFeIFN $\alpha_{567b}$ , the coding strand of which was shown to have a nucleic acid sequence denoted herein as SEQ ID NO:110. The complement of SEQ ID NO:110 is represented herein by SEQ ID NO:112. Translation of SEQ ID NO:110 suggests that nFeIFN $\alpha_{567b}$  encodes a protein containing 189 amino acids, referred to herein as PFeIFN $\alpha_{189b}$ , with an amino acid sequence denoted SEQ ID NO:111. The open reading frame of SEQ ID NO:110 is assumed to be the following: the first codon spans from nucleotide 1 through nucleotide 3 and the last codon before the stop codon spans from nucleotide 565 through nucleotide 567 of SEQ ID NO:110. The encoded protein has a predicted molecular weight of 21 kDa. The putative signal peptide cleavage site occurs between amino acid positions 23 and 24, based on homology with the human and canine interferon-alpha proteins. The proposed mature protein (i.e. feline IFN $\alpha$  protein from which the signal sequence has been cleaved), denoted herein as PFeIFN $\alpha_{166b}$ , contains about 166 amino acids, extending from residue 24 to residue 166 of SEQ ID NO:111; the amino acid sequence is denoted herein as SEQ ID NO:117. The nucleic acid molecule encoding PFeIFN $\alpha_{166b}$  is denoted herein as nFeIFN $\alpha_{498b}$ , the coding strand of which is represented by SEQ ID NO:116, and complementary strand of which is represented by SEQ ID NO:118. A putative N-glycosylation site and an interferon alpha-beta-delta family signature motif are present at amino acid positions 102 and 145, respectively, of PFeIFN $\alpha_{189b}$ .

Clone #1 includes a feline IFN-alpha nucleic acid molecule that is represented herein as nFeIFN $\alpha_{567c}$ , the coding strand of which was shown to have a nucleic acid sequence denoted herein as SEQ ID NO:155. The complement of SEQ ID NO:155 is represented herein by SEQ ID NO:157. Translation of SEQ ID NO:155 suggests that nFeIFN $\alpha_{567c}$

encodes a protein containing 189 amino acids, referred to herein as PFeIFN $\alpha_{890c}$ , with an amino acid sequence denoted SEQ ID NO:156. The open reading frame of SEQ ID NO:155 is assumed to be the following: the first codon spans from nucleotide 1 through nucleotide 3 and the last codon before the stop codon spans from nucleotide 565 to nucleotide 567 of SEQ ID NO:155. The encoded protein has a predicted molecular weight of 21 kDa. The putative signal peptide cleavage site occurs between amino acid positions 23 and 24, based on homology with the human and canine interferon-alpha proteins. The proposed mature protein (i.e. feline IFN $\alpha$  protein from which the signal sequence has been cleaved), denoted herein as PFeIFN $\alpha_{166c}$ , contains about 166 amino acids, extending from residue 24 to residue 166 of SEQ ID NO:156; the amino acid sequence is denoted herein as SEQ ID NO:159. The nucleic acid molecule encoding PFeIFN $\alpha_{166c}$  is denoted herein as nFeIFN $\alpha_{498c}$ , the coding strand of which is represented by SEQ ID NO:158, and the complementary strand of which is represented by SEQ ID NO:160. A putative N-glycosylation site and an interferon alpha-beta-delta family signature motif are present at amino acid positions 102 and 145, respectively, of PFeIFN $\alpha_{189c}$ .

Clone #5 includes a feline IFN-alpha nucleic acid molecule that is represented herein as nFeIFN $\alpha_{582d}$ , the coding strand of which was shown to have a nucleic acid sequence denoted herein as SEQ ID NO:161. The complement of SEQ ID NO:161 is represented herein by SEQ ID NO:163. Translation of SEQ ID NO:161 suggests that nFeIFN $\alpha_{582d}$  encodes a protein containing 194 amino acids, referred to herein as PFeIFN $\alpha_{194d}$ , with an amino acid sequence denoted SEQ ID NO:162. The open reading frame of SEQ ID NO:161 is assumed to be the following: the first codon spans from nucleotide 1 through nucleotide 3 and the last codon before the stop codon spans from nucleotide 580 through nucleotide 582 of SEQ ID NO:161. The encoded protein has a predicted molecular weight of 21.5 kDa. The putative signal peptide cleavage site occurs between amino acid positions 23 and 24, based on homology with the human and canine interferon-alpha proteins. The proposed mature protein (i.e. feline IFN $\alpha$  protein from which the signal sequence has been cleaved), denoted herein as PFeIFN $\alpha_{171d}$ , contains about 171 amino acids, extending from residue 24 to residue 171 of SEQ ID NO:162; the amino acid sequence is denoted herein as SEQ ID NO:165. The nucleic acid molecule encoding PFeIFN $\alpha_{171d}$  is denoted herein as nFeIFN $\alpha_{513d}$ , the coding strand of which is represented by SEQ ID NO:164, and the complementary strand of which is represented by SEQ ID NO:166. A putative N-glycosylation site and an interferon alpha-beta-delta family signature motif are present at amino acid positions 102 and 145, respectively, of PFeIFN $\alpha_{194d}$ .

Clone #6 includes a feline IFN-alpha nucleic acid molecule that is represented herein as nFeIFN $\alpha_{567e}$ , the coding strand of which was shown to have a nucleic acid sequence denoted herein as SEQ ID NO:167. The complement of SEQ ID NO:167 is represented herein by SEQ ID NO:169. Translation of SEQ ID NO:167 suggests that nFeIFN $\alpha_{567e}$  encodes a protein containing 189 amino acids, referred to herein as PFeIFN $\alpha_{189e}$ , with an amino acid sequence denoted SEQ ID NO:168. The open reading frame of SEQ ID NO:167 is assumed to be the following: the first codon spans from nucleotide 1 through nucleotide 3 and the last codon before the stop codon spans from nucleotide 565 to nucleotide 567 of SEQ ID NO:167. The encoded protein has a predicted molecular weight of 21 kDa. The putative signal peptide cleavage site occurs between amino acid positions 23 and 24, based on homology with the human and canine

interferon-alpha proteins. The proposed mature protein (i.e. feline IFN $\alpha$  protein from which the signal sequence has been cleaved), denoted herein as PFeIFN $\alpha_{166e}$ , contains about 166 amino acids, extending from residue 24 to residue 166 of SEQ ID NO:167; the amino acid sequence is denoted herein as SEQ ID NO:171. The nucleic acid molecule encoding PFeIFN $\alpha_{166e}$  is denoted herein as nFeIFN $\alpha_{498e}$ , the coding strand of which is represented by SEQ ID NO:170, and the complementary strand of which is represented by SEQ ID NO:172. A putative N-glycosylation site and an interferon alpha-beta-delta family signature motif are present at amino acid positions 102 and 145, respectively, of PFeIFN $\alpha_{189e}$ .

Comparison of the nucleic acid sequences of the five feline IFN-alpha nucleic acid molecules of the present invention indicated that the sequences, while being very similar (i.e., encoded proteins sharing from about 96% to 99% identity), exhibited several differences. The differences in nucleic acid sequences and deduced amino acid sequences are summarized in Table 7. The left hand column indicates the change at the nucleotide or amino acid level, as appropriate, and the "X"s in the other columns indicate which clones include such changes. For example, feline IFN-alpha protein PFeIFN $\alpha_{194d}$  (having SEQ ID NO:161) has five extra amino acids (namely IHPED) inserted at position at 139 as compared to feline IFN-alpha proteins PFeIFN $\alpha_{189a}$  (SEQ ID NO:108), PFeIFN $\alpha_{189b}$  (SEQ ID NO:111), PFeIFN $\alpha_{189c}$  (SEQ ID NO:155) or PFeIFN $\alpha_{189e}$  (SEQ ID NO:167). Other variations, i.e., nucleotide substitutions, some of which lead to amino acid variations, are also indicated in Table 7.

TABLE 7

Comparison of feline IFN-alpha nucleic acid molecules and proteins

Amino acid Changes	Clone #1	Clone #2	Clone #3	Clone #5	Clone #6
5 amino acid deletion S <sub>18</sub> to S <sub>18</sub> (TCC to TCT)	X	X	X		X
C <sub>52</sub> to C <sub>52</sub> (TGT to TGC)					X
R <sub>56</sub> to R <sub>56</sub> (AGA to AGG)			X		
N <sub>57</sub> to S <sub>57</sub> (AAT to AGT)	X			X	
F <sub>66</sub> to F <sub>66</sub> (TTC to TTT)	X	X			
A <sub>74</sub> to A <sub>74</sub> (GCC to GCT)			X		
K <sub>86</sub> to E <sub>86</sub> (AAG to GAG)			X		
R <sub>115</sub> to W <sub>115</sub> (CGG to TGG)	X	X			
L <sub>125</sub> to V <sub>125</sub> (CTG to GTG)			X	X	X
L <sub>125</sub> to M <sub>125</sub> (CTG to ATG)	X	X			
L <sub>135</sub> to L <sub>135</sub> (CTG to CTC)	X	X	X		X
L <sub>141</sub> to L <sub>141</sub> (ATC to CTC)			X		

Feline IFN-alpha proteins of the present invention PFeIFN $\alpha_{189a}$ , PFeIFN $\alpha_{189b}$ , PFeIFN $\alpha_{189c}$ , and PFeIFN $\alpha_{189e}$  are five amino acids shorter than the GenBank entry for feline IFN-omega, accession #E02521, while IFN-alpha protein PFeIFN $\alpha_{194d}$  of the present invention has the same number of amino acids as the feline IFN-omega reported in GenBank. In addition, there are: 3 non-conservative and 2 conservative changes at the amino acid level between this GenBank entry and SEQ ID NO:108

(PfeIFN $\alpha_{189a}$ ); 4 non-conservative and 3 conservative changes at the amino acid level between this GenBank entry and SEQ ID NO:111 (PfeIFN $\alpha_{189b}$ ); 4 non-conservative and 3 conservative changes at the amino acid level between this GenBank entry and SEQ ID NO:156 (PfeIFN $\alpha_{189c}$ ); 2 non-conservative and 2 conservative changes at the amino acid level between this GenBank entry and SEQ ID NO:162 (PfeIFN $\alpha_{194d}$ ); and 1 non-conservative and 5 conservative changes at the amino acid level between this GenBank entry and SEQ ID NO:168 (PfeIFN $\alpha_{189e}$ ).

The lengths of SEQ ID NO:108 and SEQ ID NO:111, when compared with those of IFN-alpha proteins of other species, are two amino acids longer than published canine interferon-alpha subtype 1, 2 and 3 sequences, two amino acids longer than published human interferon-alpha type 1, B, D, F, and J sequences, three amino acids longer than the published human interferon-alpha sequence type A sequence and two amino acids longer than published murine interferon-alpha type B, 8, 7, 11, and 19 sequences. The lengths of SEQ ID NO:156 and SEQ ID NO:168, when compared with those of IFN-alpha proteins of other species, are two amino acids longer than published canine interferon-alpha subtype 1, 2 and 3 sequences, two amino acids longer than published human interferon-alpha type 1, B, D, F, and J sequences, three amino acids longer than the published human interferon-alpha sequence type A sequence and two amino acids longer than published murine interferon-alpha type B, 8, 7, 11, and 19 sequences. The length of SEQ ID NO:162, when compared with those of IFN-alpha proteins of other species, are seven amino acids longer than published canine interferon-alpha subtype 1, 2 and 3 sequences, seven amino acids longer than published human interferon-alpha type 1, B, D, F, and J sequences, eight amino acids longer than the published human interferon-alpha sequence type A sequence and seven amino acids longer than published murine interferon-alpha type B, 8, 7, 11, and 19 sequences.

#### B. Expression of Feline IFN-alpha Proteins in Mammalian Cells

This example describes the expression of the feline IFN-alpha proteins of the present invention in Chinese hamster ovary (CHO) cells.

Feline IFN-alpha nucleic acid molecule PCR products were amplified from nFeIFN $\alpha_{567a}$ , nFeIFN $\alpha_{567b}$ , nFeIFN $\alpha_{567c}$ , nFeIFN $\alpha_{582d}$ , and nFeIFN $\alpha_{567e}$  using Pfu DNA polymerase<sup>TM</sup> (available from Stratagene, La Jolla, Calif.) and the following primes and conditions. The sequence of the forward primer was 5' ATTAGGATCC ATGGCGCTGC CCTCTTCCT 3' (SEQ ID NO:173), and that of the reverse primer was 5' GCCTCTAGAC TGT-CATTCT CGCTCCTTAA TCTTTTCTGC 3' (SEQ ID NO:174). The following PCR protocol was used: one initial denaturation step at 95° C. for 5 minutes; then 30 cycles of the following: 94° C. for 30 seconds, then 50° C. for 30 seconds, then 72° C. for 90 seconds; followed by a final extension at 72° C. for 7 minutes.

Each of the five PCR products was ligated into a CMV-Int A-kan+(amp) expression vector using techniques similar to those described in Example 1Bii to produce recombinant molecules in which feline IFN-alpha nucleic acid molecules were operatively linked to transcription control sequences. It is to be noted that CMV-Int A-kan+(amp) vector is similar to the pCMV-Int A plasmid vector described in Example 1Bii except that the ampicillin resistance gene open reading frame has been disrupted by the insertion of the kanamycin resistance gene. The feline IFN-alpha nucleic acid molecules in the recombinant molecules were sequenced using

an ABI Prism<sup>TM</sup> Model 377 Automatic DNA Sequencer (available from PE Applied Biosystems Inc.). DNA sequencing reactions were performed using Prism<sup>TM</sup> dRhodamine Terminator Cycle Sequencing Ready Reaction kits (available from PE Applied Biosystems Inc.). The sequence data indicated that there was no changes introduced during the PCR amplification or ligation in any of the nucleic acid molecules.

Using techniques similar to those described elsewhere herein. CHO cells were transiently transfected with each of the five recombinant molecules encoding a subtype of feline IFN-alpha protein using Lipofectamine<sup>TM</sup> (available from Life technologies, Inc.) resulting in recombinant cells expressing feline IFN-alpha subtype proteins of the present invention. The cells and culture supernatants were harvested 48 hours later and Western analysis was done using both pellets and the supernatants from each transfection. The detecting antibody was an anti-human IFN-alpha-A antibody (available from Accurate Chemical and Scientific Corporation, Westbury, N.Y.). The Western analysis indicated that each of the five feline IFN-alpha nucleic acid molecule-containing recombinant cells expressed a corresponding feline IFN-alpha subtype protein which was secreted into the tissue culture supernatant and recognized by the antibody against human IFN-alpha-A. The migration patterns of each of the CHO cell-expressed feline IFN-alpha subtype proteins suggested that each of the proteins is glycosylated.

#### C. Bioactivity of Mammalian-expressed Feline-IFN Alpha Proteins

(i) The antiviral activity of the five CHO-expressed feline IFN-alpha subtype proteins, produced as described in Example 7B, was tested using the following protocol: Crandell feline kidney (CRFK) cells were treated for 24 hours, using procedures known to those skilled in the art, with or without IFN-alpha tissue culture supernatants, produced as described in Example 7B. The cells were then infected with feline calicivirus and cytopathic effects induced by the virus were assessed 12 to 14 hours later using techniques known to those skilled in the art. The cell layers were fixed in methanol, stained with crystal violet and examined under the microscope or processed for the MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) assay. The MTT assay was conducted as follows. After viral infection, the infected cells were washed with PBS. A volume of MTT stock solution (5 mg/ml in PBS) equal to one-tenth of the original culture volume was added to each well being assayed and incubated at 37° C. for 3 to 4 hr. The MTT solution was removed, and acidified isopropanol (1 N HCl in absolute isopropanol) was added to the wells to solubilize the converted dye. The absorbance of the converted dye was measured at 570 nm using a plate reader. Each of the five IFN-alpha subtype proteins demonstrated anti-viral activity. Pre-treatment with any of the subtypes of IFN-alpha proteins of the present invention resulted in significant reduction in the virus-induced cytopathic effect.

(ii) The CHO cell-expressed feline IFN-alpha subtype proteins were also tested for their ability to inhibit granulocyte-macrophage colony stimulating factor-induced proliferation of TF-1 cells using an assay similar to that described in Example 1E, but with the following modification: For the assay, the cells were washed and TCM-TF-1 medium containing a suboptimal amount of GM-CSF (i.e., 0.4 ng/ml) was added along with the appropriate dilutions of the designated IFN-alpha proteins. The results are shown in Table 8 for feline IFN-alpha proteins expressed as described in Example 7B, lanes labeled Clone #1, Clone #2, Clone #3,

Clone #5 and Clone #6, respectively; supernatant from a culture of CHO cells transfected with only the vector described in Example 7B, lane labeled vector; E. coli-expressed feline IFN-alpha protein PFeIFNa<sub>1,66c</sub> produced as described in Example 7D, lane labeled E. coli-expressed; and recombinant human IFN-alpha, lane labeled human IFN-alpha. Media alone gave a reading of 128 and recombinant GM-CSF alone gave a reading of 96080.

TABLE 8

Inhibition of TF-1 cell production by CHO cell-expressed feline IFN-alpha proteins								
Dilution	Clone #1	Clone #2	Clone #3	Clone #5	Clone #6	Vector	<i>E. coli</i> expressed	Human IFN alpha
2	15077	7914	21173	15218	13256	53585	19541	559
4	18318	23515	41488	43449	31618	64722	56315	10412
8	22484	25823	48487	40438	43896	83092	80646	21710
16	42138	34274	72145	66266	48775	102423	97255	23585
32	81248	52847	63264	95256				
64	74613	43848	58533	88172	70596	141821	129556	45907
128	59360	48901	48701	54623	90092	155960	151946	40402
256	75788	54017	37391	59849	83022	119491	123794	39299

Table 8 demonstrates that CHO cell-expressed and E. coli-expressed feline IFN-alpha subtype proteins inhibited granulocyte-macrophage colony stimulating factor-included proliferation of TF-1 cells.

#### D. Expression of Feline IFN-alpha in E. coli and Bioactivity Thereof

The nucleic acid molecule encoding the mature feline IFN-alpha protein having SEQ ID NO:171 was ligated into the  $\lambda$ cro plasmid vector, using techniques as described in Example 6B, to produce recombinant molecule p $\lambda$ cro-nFeIFNa<sub>498e</sub>. The recombinant molecule was transformed into E. coli, using techniques similar to those described in Example 6B to produce recombinant cell E. coli:p $\lambda$ cro-nFeIFNa<sub>498e</sub>. The recombinant cell was grown and induced as described in Example 6B. The resulting feline IFN-alpha protein, E. coli-expressed PFeIFNa<sub>1,66e</sub>, which was expressed as an insoluble form, was solubilized using urea and DTT and refolded using techniques known to those skilled in the art. The refolded E. coli-expressed feline IFN-alpha protein PFeIFNa<sub>1,66e</sub> when tested for antiviral activity as described in Example 7C was found to have significant antiviral activity.

#### Example 8

This example describes the isolation and sequencing of feline granulocyte-macrophage colony-stimulating factor (GMCSF) nucleic acid molecules and proteins of the present invention. This example also describes expression of a feline GMCSF protein of the present invention.

Nucleic acid molecules encoding feline GMCSF were isolated as follows. A cDNA library was prepared from feline PBMCs stimulated with Con A for 12 hours, as previously described in Example 2. An aliquot of this library was used as a template to amplify feline GMCSF nucleic acid molecules by PCR using Amplitaq DNA polymerase™ (PE Applied Biosystems Inc, Foster City, Calif.) and the following primers and conditions. The sequence of the forward primer was 5' CAGGGATCCA CCATGTGGCT GCA-GAACCTG CTTTCC 3' (SEQ ID NO:149), and that of the reverse primer was 5' TTACTTCTGG TCTGGTCCCC AGCAGTCAA GGGGTTGTTA AACAGAAAAT 3' (SEQ ID NO:150). The following PCR protocol was used: one initial denaturation step at 95° C. for 5 minutes; then 35 cycles of the following: 94° C. for 30 seconds, then 50° C. for 30 seconds, then 72° C. for 90 seconds; followed by a

final extension at 72° C. for 7 minutes. PCR products were cloned into the CMV-Intron A vector and the clones were sequenced as described in Example 7.

A PCR product was isolated, referred to herein as nFeGMCSF<sub>444</sub>, the coding strand of which is represented herein as SEQ ID NO:119, and its complement is denoted SEQ ID NO:121. Translation of the open reading frame in SEQ ID NO:119 suggests that nucleic acid molecule nFeGMCSF<sub>444</sub> encodes a protein containing 144 amino acids,

referred to herein as PFeGMCSF<sub>144</sub>, with an amino acid sequence denoted SEQ ID NO:120, assuming an open reading frame in which the first codon spans from nucleotide 10 through nucleotide 12 of SEQ ID NO:119, and the stop codon spans from nucleotide 442 through nucleotide 444 of SEQ ID NO:121. The encoded protein has a predicted molecular weight of 16 kDa. The coding region encoding PFeGMCSF<sub>144</sub> is presented herein as nFeGMCSF<sub>432</sub> which has the nucleotide sequence SEQ ID NO:122 (the coding strand) and SEQ ID NO:123 (the complementary strand). A putative signal peptide cleavage site is between amino acid positions 17 and 18, based on homology with human, mouse and bovine GMCSF proteins. The nucleic acid molecule encoding the proposed mature protein is denoted as nFeGMCSF<sub>381</sub> and has a nucleotide sequence represented herein as SEQ ID NO:124 and a complementary sequence represented herein as SEQ ID NO:126. The amino acid sequence of the putative mature protein, referred to herein as PFeGMCSF<sub>127</sub> has an amino acid sequence represented herein as SEQ ID NO:125. The number of amino acids in the feline GMCSF protein is the same compared to human, porcine, ovine and canine GMCSF proteins. The feline GMCSF protein is one amino acid longer than bovine GMCSF and three amino acids longer than murine GMCSF.

The deduced amino acid sequence of the full-length feline GMCSF protein of the present invention has four non-conservative changes and one conservative change compared to a GenBank entry for feline GMCSF (accession #AF053007). Amino acids asparagine, methionine, threonine, and lysine at positions 10, 36, 56 and 126 of the GenBank entry have been changed to glycine, isoleucine, alanine and asparagine, respectively, in PFeGMCSF<sub>144</sub>. PFeGMCSF<sub>144</sub>, containing the above-noted amino acid substitutions, appears to have GMCSF activity, as demonstrated by an experiment in which supernatant collected from Chinese Hamster Ovary (CHO) cells that were transiently transfected with a recombinant molecule encoding a feline GMCSF protein of the present invention was able to include proliferation of TF-1 cells.

While various embodiments of the present invention have been described in detail, it is apparent that modifications and adaptations of those embodiments will occur to those skilled in the art. It is to be expressly understood, however, that such modifications and adaptations are within the scope of the present invention, as set forth in the following claims.

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<400> SEQUENCE: 1

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  5                               10                               15                               20

ttt gtc cac gga cat aac ttc aat att act att aaa gag atc atc aaa      150
Phe Val His Gly His Asn Phe Asn Ile Thr Ile Lys Glu Ile Ile Lys
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atg ttg aac atc ctc aca gcg aga aac gac tcg tgc atg gag ctg act      198
Met Leu Asn Ile Leu Thr Ala Arg Asn Asp Ser Cys Met Glu Leu Thr
                               40                               45                               50

gtc aag gac gtc ttc act gct cca aag aac aca agc gat aag gaa atc      246
Val Lys Asp Val Phe Thr Ala Pro Lys Asn Thr Ser Asp Lys Glu Ile
                               55                               60                               65

ttc tgc aga gct gct act gta ctg cgg cag atc tat aca cac aac tgc      294
Phe Cys Arg Ala Ala Thr Val Leu Arg Gln Ile Tyr Thr His Asn Cys
                               70                               75                               80

tcc aac aga tat ctc aga gga ctc tac agg aac ctc agc agc atg gca      342
Ser Asn Arg Tyr Leu Arg Gly Leu Tyr Arg Asn Leu Ser Ser Met Ala
  85                               90                               95                               100

aac aag acc tgt tct atg aat gaa atc aag aag agt aca ctg aaa gac      390
Asn Lys Thr Cys Ser Met Asn Glu Ile Lys Lys Ser Thr Leu Lys Asp
                               105                              110                              115

ttc ttg gaa agg cta aaa gtg atc atg cag aag aaa tac tac agg cat      438
Phe Leu Glu Arg Leu Lys Val Ile Met Gln Lys Lys Tyr Tyr Arg His
                               120                              125                              130

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  20                               25                               30

Glu Ile Ile Lys Met Leu Asn Ile Leu Thr Ala Arg Asn Asp Ser Cys
  35                               40                               45

Met Glu Leu Thr Val Lys Asp Val Phe Thr Ala Pro Lys Asn Thr Ser
  50                               55                               60

Asp Lys Glu Ile Phe Cys Arg Ala Ala Thr Val Leu Arg Gln Ile Tyr
  65                               70                               75                               80

Thr His Asn Cys Ser Asn Arg Tyr Leu Arg Gly Leu Tyr Arg Asn Leu

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85					90					95					
Ser	Ser	Met	Ala	Asn	Lys	Thr	Cys	Ser	Met	Asn	Glu	Ile	Lys	Lys	Ser
			100					105					110		
Thr	Leu	Lys	Asp	Phe	Leu	Glu	Arg	Leu	Lys	Val	Ile	Met	Gln	Lys	Lys
		115					120				125				
Tyr	Tyr	Arg	His												
	130														

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<400> SEQUENCE: 3

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gtatttcttc tgcgatgatca cttttagcct ttccaagaag tctttcagtg tactctctct    180
gatttcattc atagaacagg tcttgtttgc catgctgctg aggttcctgt agagtcctct    240
gagatatctg ttggagcagt tgtgtgtata gatctgccgc agtacagtag cagctctgca    300
gaagatttcc ttatcgcttg tgttctttgg agcagtgaag acgtccttga cagtcagctc    360
catgcacgag tegtttctcg ctgtgaggat gttcaacatt ttgatgatct ctttaatagt    420
aatattgaag ttatgtccgt ggacaaaggt gctggtgagt gctagtaagc agaccagagt    480
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cctcgtgcc                                     549

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 <212> TYPE: DNA  
 <213> ORGANISM: Canis familiaris

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ctcacagcga gaaacgactc gtgcatggag ctgactgtca aggacgtctt cactgctcca    180
aagaacacaa gcgataagga aatcttctgc agagctgcta ctgtactgcg gcagatctat    240
acacacaact gctccaacag atatctcaga ggactctaca ggaacctcag cagcatggca    300
aacaagacct gttctatgaa tgaaatcaag aagagtacac tgaagactt cttggaagg    360
ctaaaagtga tcatgcagaa gaaatactac aggcatt                                     396

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gagtcctctg agatatctgt tggagcagtt gtgtgtatag atctgccgca gtacagtagc    180
agctctgcag aagatttctt tctcgtttgt gttctttgga gcagtgaaga cgtccttgac    240
agtcagctcc atgcacgagt cgtttctcgc tgtgaggatg ttcaacattt tgatgatctc    300

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ttaaataagta atattgaagt tatgtccgtg gacaaaggtg ctggtgagtg ctagtaagca 360
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<212> TYPE: DNA
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<222> LOCATION: (35)..(916)

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Met Ile Val Leu Ala Pro Ala
1 5

tgg agc cca act gcc tcc ctg ttg ctg ctg ctg ctg ctc agc ccc gcc 103
Trp Ser Pro Thr Ala Ser Leu Leu Leu Leu Leu Leu Ser Pro Gly
10 15 20

ctc cgc ggg acc ccc gac tgc tcc ttc agc cac agc ccc atc tcc tcc 151
Leu Arg Gly Thr Pro Asp Cys Ser Phe Ser His Ser Pro Ile Ser Ser
25 30 35

acc ttc gcg gtc acc atc cgc aag ctg tct gat tac ctg ctt cag gac 199
Thr Phe Ala Val Thr Ile Arg Lys Leu Ser Asp Tyr Leu Leu Gln Asp
40 45 50 55

tat cca gtc act gtc gcc tcc aac ctg cag gac gac gag ctc tgc ggg 247
Tyr Pro Val Thr Val Ala Ser Asn Leu Gln Asp Asp Glu Leu Cys Gly
60 65 70

gcg ttc tgg cgc ctg gtc ctg gcc cag cgc tgg atg gtg cgg ctc cag 295
Ala Phe Trp Arg Leu Val Leu Ala Gln Arg Trp Met Val Arg Leu Gln
75 80 85

gct gtg gct gga tcc caa atg caa atc ctg ctg gag gct gtc aac acg 343
Ala Val Ala Gly Ser Gln Met Gln Ile Leu Leu Glu Ala Val Asn Thr
90 95 100

gag ata cac ttt gtc acc ttc tgt gcc ttc cag ccc ctc ccc agc tgt 391
Glu Ile His Phe Val Thr Phe Cys Ala Phe Gln Pro Leu Pro Ser Cys
105 110 115

ctt cgc ttc gtc cag acc aac atc tcc cac ctc ctg cag gac acc tcc 439
Leu Arg Phe Val Gln Thr Asn Ile Ser His Leu Leu Gln Asp Thr Ser
120 125 130 135

cag cag ctg gcc gcc ctg aag ccc tgg atc acc cgc agg aat ttc tcc 487
Gln Gln Leu Ala Ala Leu Lys Pro Trp Ile Thr Arg Arg Asn Phe Ser
140 145 150

ggg tgc ctg gag ctg cag tgt cag ccc gac tcc tct aca ttg gtg ccc 535
Gly Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Val Pro
155 160 165

cca agg agc ccc ggg gcc ctg gag gcc act gcc ttg cca gcc cct cag 583
Pro Arg Ser Pro Gly Ala Leu Glu Ala Thr Ala Leu Pro Ala Pro Gln
170 175 180

gca cct cgg ctg ctc ctc ctg ctg ctg ctg ccc gtg gct ctc ctg ctg 631
Ala Pro Arg Leu Leu Leu Leu Leu Leu Leu Pro Val Ala Leu Leu Leu
185 190 195

atg tcc act gcc tgg tgc ctg cat tgg cga agg agg cgg cgg cgg agg 679
Met Ser Thr Ala Trp Cys Leu His Trp Arg Arg Arg Arg Arg Arg
200 205 210 215

tca ccc tac cct ggg gag cag agg aca ctg agg ccc agc gag cgg agc 727
Ser Pro Tyr Pro Gly Glu Gln Arg Thr Leu Arg Pro Ser Glu Arg Ser
220 225 230

cat ctg ccc gag gac aca gag ctg gga cct gga ggg agt cag cta gag 775
His Leu Pro Glu Asp Thr Glu Leu Gly Pro Gly Gly Ser Gln Leu Glu
235 240 245

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act ggt ccc ttc ctc gac cac gca gcc ccg ctc gct ccc tcc cca gga      823
Thr Gly Pro Phe Leu Asp His Ala Ala Pro Leu Ala Pro Ser Pro Gly
      250                255                260

tca agg caa cgc ccg ccc cca acg ccc cca aag cca gcc cca gcc cca      871
Ser Arg Gln Arg Pro Pro Pro Thr Pro Pro Lys Pro Ala Pro Ala Pro
      265                270                275

cct ctc ccc ctc tgt aca aag tcc ttg ccc cca aga aat tgt ata      916
Pro Leu Pro Leu Cys Thr Lys Ser Leu Pro Pro Arg Asn Cys Ile
      280                285                290

taaatcatcc ttttctacca aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa      976
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaa      1013

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Ser His Ser Pro Ile Ser Ser Thr Phe Ala Val Thr Ile Arg Lys Leu
      35                40                45

Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu
      50                55                60

Gln Asp Asp Glu Leu Cys Gly Ala Phe Trp Arg Leu Val Leu Ala Gln
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Arg Trp Met Val Arg Leu Gln Ala Val Ala Gly Ser Gln Met Gln Ile
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Leu Leu Glu Ala Val Asn Thr Glu Ile His Phe Val Thr Phe Cys Ala
      100                105                110

Phe Gln Pro Leu Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser
      115                120                125

His Leu Leu Gln Asp Thr Ser Gln Gln Leu Ala Ala Leu Lys Pro Trp
      130                135                140

Ile Thr Arg Arg Asn Phe Ser Gly Cys Leu Glu Leu Gln Cys Gln Pro
      145                150                155                160

Asp Ser Ser Thr Leu Val Pro Pro Arg Ser Pro Gly Ala Leu Glu Ala
      165                170                175

Thr Ala Leu Pro Ala Pro Gln Ala Pro Arg Leu Leu Leu Leu Leu Leu
      180                185                190

Leu Pro Val Ala Leu Leu Leu Met Ser Thr Ala Trp Cys Leu His Trp
      195                200                205

Arg Arg Arg Arg Arg Arg Arg Ser Pro Tyr Pro Gly Glu Gln Arg Thr
      210                215                220

Leu Arg Pro Ser Glu Arg Ser His Leu Pro Glu Asp Thr Glu Leu Gly
      225                230                235                240

Pro Gly Gly Ser Gln Leu Glu Thr Gly Pro Phe Leu Asp His Ala Ala
      245                250                255

Pro Leu Ala Pro Ser Pro Gly Ser Arg Gln Arg Pro Pro Pro Thr Pro
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Pro Pro Arg Asn Cys Ile

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290

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ggagccgcac catccagcgc tgggcccagga ccaggcgcga gaacgccccg cagagctcgt    780
cgtcctgcag gttggaggcg acagtgactg gatagtctcg aagcaggtaa tcagacagct    840
tgcggatggt gaccgcgaag gtggaggaga tggggctgtg gctgaaggag cagtcggggg    900
tcccgcggag gccggggctg agcagcagca gcagcaacag ggaggcagtt gggctccagg    960
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ttcgcggtca ccatccgcaa gctgtctgat tacctgcttc aggactatcc agtcaactgc    180
gcctccaacc tgcaggacga cgagctctgc ggggcgttct ggcgcctggt cctggcccag    240
cgctggatgg tgcggctcca ggctgtggct ggatcccaaa tgcaaatcct gctggaggct    300
gtcaaacacg agatacactt tgtcaccttc tgtgccttcc agccccctcc cagctgtctt    360
cgcttcgtcc agaccaacat ctcccacctc ctgcaggaca cctcccagca gctggccgcc    420
ctgaagccct ggatcaccgc caggaatttc tccgggtgcc tggagctgca gtgtcagccc    480
gactcctcta cattggtgcc cccaaggagc cccggggccc tggaggccac tgccttgcca    540
gcccctcagg cacctcggct gctcctcctg ctgctgctgc ccgtggctct cctgctgatg    600
tccactgcct ggtgcctgca ttggcgaagg aggcggcggc ggaggtcacc ctaccctggg    660
gagcagagga cactgaggcc cagcgagcgg agccatctgc ccgaggacac agagctggga    720
cctggagggg gtcagctaga gactggctcc ttcctcgacc acgcagcccc gctcgtccc    780
tcccaggat caaggcaacg cccgccccca acgcccccaa agccagcccc agccccacct    840

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ctccccctct gtacaaagtc cttgccccca agaaattgta ta 882

<210> SEQ ID NO 10  
 <211> LENGTH: 882  
 <212> TYPE: DNA  
 <213> ORGANISM: Canis familiaris

<400> SEQUENCE: 10

tatacaattt cttgggggca aggactttgt acagaggggg agaggtgggg ctggggctgg 60  
 ctttgggggc gttgggggag ggcgttgct tgatcctggg gagggagcga gcggggctgc 120  
 gtggtcaggg aagggaccag tctctagctg actccctcca ggtcccagct ctgtgtcttc 180  
 gggcagatgg ctccgctcgc tgggcctcag tgcctctgct tccccagggt aggggtgacct 240  
 ccgcgcgccg ctccctcgcc aatgcaggca ccaggcagtg gacatcagca ggagagccac 300  
 gggcagcagc agcaggagga gcagccgagg tgcctgaggg gctggcaagg cagtggcctc 360  
 cagggccccg gggctccttg ggggcaccaa tgtagaggag tcgggctgac actgcagctc 420  
 caggcacccg gagaaattcc tgcgggtgat ccagggcttc agggcgccca gctgctggga 480  
 ggtgtcctgc aggaggtggg agatgttggt ctggacgaag cgaagacagc tggggagggg 540  
 ctggaaggca cagaaggtga caaagtgtat ctccgtgttg acagcctcca gcaggatttg 600  
 catttgggat ccagccacag cctggagcgg caccatccag cgctggggcca ggaccaggeg 660  
 ccagaacgcc ccgcagagct cgtcgtcctg caggttgagg gcgacagtga ctggatagtc 720  
 ctgaagcagg taatcagaca gcttgccgat ggtgaccgag aaggtggagg agatggggct 780  
 gtggctgaag gagcagtcgg gggccccgag gaggccgggg ctgagcagca gcagcagcaa 840  
 cagggaggca gttgggctcc aggctggcgc cagcactatc at 882

<210> SEQ ID NO 11  
 <211> LENGTH: 26  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
 Primer

<400> SEQUENCE: 11

ctattaatgg gtctcacctc ccaact 26

<210> SEQ ID NO 12  
 <211> LENGTH: 24  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
 Primer

<400> SEQUENCE: 12

tcaactcggg gcacagagtc ttgg 24

<210> SEQ ID NO 13  
 <211> LENGTH: 20  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
 Primer

<400> SEQUENCE: 13

ctggcgccag cctggagccc 20

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<210> SEQ ID NO 14  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer  
  
<400> SEQUENCE: 14  
gggagatggt ggtctggacg 20

<210> SEQ ID NO 15  
<211> LENGTH: 18  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer  
  
<400> SEQUENCE: 15  
gaccaggcgc cagaacgc 18

<210> SEQ ID NO 16  
<211> LENGTH: 18  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer  
  
<400> SEQUENCE: 16  
cggtcacccat ccgcaagc 18

<210> SEQ ID NO 17  
<211> LENGTH: 18  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer  
  
<400> SEQUENCE: 17  
tggcaaggca gtggcctc 18

<210> SEQ ID NO 18  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer  
  
<400> SEQUENCE: 18  
gccgagatga tagtgctggc 20

<210> SEQ ID NO 19  
<211> LENGTH: 324  
<212> TYPE: DNA  
<213> ORGANISM: Canis familiaris  
<220> FEATURE:  
<221> NAME/KEY: CDS  
<222> LOCATION: (1)..(324)  
  
<400> SEQUENCE: 19  
cat aac ttc aat att act att aaa gag atc atc aaa atg ttg aac atc 48  
His Asn Phe Asn Ile Thr Ile Lys Glu Ile Ile Lys Met Leu Asn Ile

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1	5	10	15	
ctc aca gcg aga aac gac tcg tgc atg gag ctg act gtc aag gac gtc				96
Leu Thr Ala Arg Asn Asp Ser Cys Met Glu Leu Thr Val Lys Asp Val	20	25	30	
ttc act gct cca aag aac aca agc gat aag gaa atc ttc tgc aga gct				144
Phe Thr Ala Pro Lys Asn Thr Ser Asp Lys Glu Ile Phe Cys Arg Ala	35	40	45	
gct act gta ctg cgg cag atc tat aca cac aac tgc tcc aac aga tat				192
Ala Thr Val Leu Arg Gln Ile Tyr Thr His Asn Cys Ser Asn Arg Tyr	50	55	60	
ctc aga gga ctc tac agg aac ctc agc agc atg gca aac aag acc tgt				240
Leu Arg Gly Leu Tyr Arg Asn Leu Ser Ser Met Ala Asn Lys Thr Cys	65	70	75	80
tct atg aat gaa atc aag aag agt aca ctg aaa gac ttc ttg gaa agg				288
Ser Met Asn Glu Ile Lys Lys Ser Thr Leu Lys Asp Phe Leu Glu Arg	85	90	95	
cta aaa gtg atc atg cag aag aaa tac tac agg cat				324
Leu Lys Val Ile Met Gln Lys Lys Tyr Tyr Arg His	100	105		

<210> SEQ ID NO 20  
 <211> LENGTH: 108  
 <212> TYPE: PRT  
 <213> ORGANISM: Canis familiaris

<400> SEQUENCE: 20

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

<210> SEQ ID NO 21  
 <211> LENGTH: 324  
 <212> TYPE: DNA  
 <213> ORGANISM: Canis familiaris

<400> SEQUENCE: 21

atgctgtgtag tatttcttct gcatgatcac ttttagcctt tccaagaagt ctttcagtgt	60
actcttcttg atttcattca tagaacagggt cttgtttgcc atgctgctga ggttcctgta	120
gagtcctctg agatatctgt tggagcagtt gtgtgtatag atctgccgca gtacagtgc	180
agctctgcag aagatttctc tatcgtttgt gttctttgga gcagtgaaga cgtccttgac	240
agtcagctcc atgcacgagt cgtttctcgc tgtgaggatg ttcaacattt tgatgatctc	300
tttaatagta atattgaagt tatg	324

<210> SEQ ID NO 22  
 <211> LENGTH: 804  
 <212> TYPE: DNA

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&lt;213&gt; ORGANISM: Canis familiaris

&lt;220&gt; FEATURE:

&lt;221&gt; NAME/KEY: CDS

&lt;222&gt; LOCATION: (1)..(804)

&lt;400&gt; SEQUENCE: 22

acc ccc gac tgc tcc ttc agc cac agc ccc atc tcc tcc acc ttc gcg 48  
 Thr Pro Asp Cys Ser Phe Ser His Ser Pro Ile Ser Ser Thr Phe Ala  
 1 5 10 15

gtc acc atc cgc aag ctg tct gat tac ctg ctt cag gac tat cca gtc 96  
 Val Thr Ile Arg Lys Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val  
 20 25 30

act gtc gcc tcc aac ctg cag gac gac gag ctc tgc ggg gcg ttc tgg 144  
 Thr Val Ala Ser Asn Leu Gln Asp Asp Glu Leu Cys Gly Ala Phe Trp  
 35 40 45

cgc ctg gtc ctg gcc cag cgc tgg atg gtg cgg ctc cag gct gtg gct 192  
 Arg Leu Val Leu Ala Gln Arg Trp Met Val Arg Leu Gln Ala Val Ala  
 50 55 60

gga tcc caa atg caa atc ctg ctg gag gct gtc aac acg gag ata cac 240  
 Gly Ser Gln Met Gln Ile Leu Leu Glu Ala Val Asn Thr Glu Ile His  
 65 70 75 80

ttt gtc acc ttc tgt gcc ttc cag ccc ctc ccc agc tgt ctt cgc ttc 288  
 Phe Val Thr Phe Cys Ala Phe Gln Pro Leu Pro Ser Cys Leu Arg Phe  
 85 90 95

gtc cag acc aac atc tcc cac ctc ctg cag gac acc tcc cag cag ctg 336  
 Val Gln Thr Asn Ile Ser His Leu Leu Gln Asp Thr Ser Gln Gln Leu  
 100 105 110

gcc gcc ctg aag ccc tgg atc acc cgc agg aat ttc tcc ggg tgc ctg 384  
 Ala Ala Leu Lys Pro Trp Ile Thr Arg Arg Asn Phe Ser Gly Cys Leu  
 115 120 125

gag ctg cag tgt cag ccc gac tcc tct aca ttg gtg ccc cca agg agc 432  
 Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Val Pro Pro Arg Ser  
 130 135 140

ccc ggg gcc ctg gag gcc act gcc ttg cca gcc cct cag gca cct cgg 480  
 Pro Gly Ala Leu Glu Ala Thr Ala Leu Pro Ala Pro Gln Ala Pro Arg  
 145 150 155 160

ctg ctc ctc ctg ctg ctg ctg ccc gtg gct ctc ctg ctg atg tcc act 528  
 Leu Leu Leu Leu Leu Leu Leu Pro Val Ala Leu Leu Leu Met Ser Thr  
 165 170 175

gcc tgg tgc ctg cat tgg cga agg agg cgg cgg cgg agg tca ccc tac 576  
 Ala Trp Cys Leu His Trp Arg Arg Arg Arg Arg Ser Pro Tyr  
 180 185 190

cct ggg gag cag agg aca ctg agg ccc agc gag cgg agc cat ctg ccc 624  
 Pro Gly Glu Gln Arg Thr Leu Arg Pro Ser Glu Arg Ser His Leu Pro  
 195 200 205

gag gac aca gag ctg gga cct gga ggg agt cag cta gag act ggt ccc 672  
 Glu Asp Thr Glu Leu Gly Pro Gly Gly Ser Gln Leu Glu Thr Gly Pro  
 210 215 220

ttc ctc gac cac gca gcc ccg ctc gct ccc tcc cca gga tca agg caa 720  
 Phe Leu Asp His Ala Ala Pro Leu Ala Pro Ser Pro Gly Ser Arg Gln  
 225 230 235 240

cgc ccg ccc cca acg ccc cca aag cca gcc cca gcc cca cct ctc ccc 768  
 Arg Pro Pro Pro Thr Pro Pro Lys Pro Ala Pro Ala Pro Pro Leu Pro  
 245 250 255

ctc tgt aca aag tcc ttg ccc cca aga aat tgt ata 804  
 Leu Cys Thr Lys Ser Leu Pro Pro Arg Asn Cys Ile  
 260 265

&lt;210&gt; SEQ ID NO 23

&lt;211&gt; LENGTH: 268

&lt;212&gt; TYPE: PRT

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<213> ORGANISM: *Canis familiaris*

&lt;400&gt; SEQUENCE: 23

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

&lt;210&gt; SEQ ID NO 24

&lt;211&gt; LENGTH: 804

&lt;212&gt; TYPE: DNA

<213> ORGANISM: *Canis familiaris*

&lt;400&gt; SEQUENCE: 24

tatacaattt cttgggggca aggactttgt acagaggggg agaggtgggg ctggggctgg 60  
 ctttgggggc gttgggggcg ggcgttgctt tgatcctggg gagggagcga gcggggctgc 120  
 gtggtcgagg aagggaccag tctctagctg actcctcaca ggtccagct ctgtgtctc 180  
 gggcagatgg ctccgctcgc tgggcctcag tgtcctctgc tccccagggt aggggtgacct 240  
 ccgccgccgc ctcttcgcc aatgcaggca ccaggcagtg gacatcagca ggagagccac 300  
 gggcagcage agcaggagga gcagccgagg tgcctgaggg gctggcaagg cagtggcctc 360  
 cagggccccc gggctccttg ggggcaccaa tgtagaggag tccggctgac actgcagctc 420  
 caggcaccgc gagaaattcc tgcgggtgat ccagggcttc agggcgccca gctgctggga 480

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gggtgctctgc aggaggtggg agatgttggg ctggacgaag cgaagacagc tggggagggg 540
ctggaaggca cagaaggtga caaagtgtat ctccgtgttg acagcctcca gcaggatttg 600
catttgggat ccagccacag cctggagccg caccatccag cgctgggcca ggaccaggcg 660
ccagaacgcc ccgacagact cgctgctcctg caggttgag ggcacagtga ctggatagtc 720
ctgaagcagg taatcagaca gcttgccgat ggtgaccgag aaggtggagg agatggggct 780
gtggctgaag gagcagtcgg gggg 804

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<210> SEQ ID NO 25
<211> LENGTH: 985
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (74)..(901)

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<400> SEQUENCE: 25

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ccggcctggc cccttccaag cccagctggg gcaagcctga tctgaccata ggcattgagg 60
gcctccggcc gag atg ata gtg ctg gcg cca gcc tgg agc cca act gcc 109
      Met Ile Val Leu Ala Ala Pro Ala Trp Ser Pro Thr Ala
      1 5 10
tcc ctg ttg ctg ctg ctg ctg ctc agc ccc ggc ctc cgc ggg acc ccc 157
Ser Leu Leu Leu Leu Leu Leu Ser Pro Gly Leu Arg Gly Thr Pro
      15 20 25
gac tgc tcc ttc agc cac agc ccc atc tcc tcc acc ttc gcg gtc acc 205
Asp Cys Ser Phe Ser His Ser Pro Ile Ser Ser Thr Phe Ala Val Thr
      30 35 40
atc cgc aag ctg tct gat tac ctg ctt cag gac tat cca gtc act gtc 253
Ile Arg Lys Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val
      45 50 55 60
gcc tcc aac ctg cag gac gac gag ctc tgc ggg gcg ttc tgg cgc ctg 301
Ala Ser Asn Leu Gln Asp Asp Glu Leu Cys Gly Ala Phe Trp Arg Leu
      65 70 75
gtc ctg gcc cag cgc tgg atg gtg cgg ctc cag gct gtg gct gga tcc 349
Val Leu Ala Gln Arg Trp Met Val Arg Leu Gln Ala Val Ala Gly Ser
      80 85 90
caa atg caa atc ctg ctg gag gct gtc aac acg gag ata cac ttt gtc 397
Gln Met Ile Leu Leu Glu Ala Val Asn Thr Glu Ile His Phe Val
      95 100 105
acc ttc tgt gcc ttc cag gac acc tcc cag cag ctg gcc gcc ctg aag 445
Thr Phe Cys Ala Phe Gln Asp Thr Ser Gln Gln Leu Ala Ala Leu Lys
      110 115 120
ccc tgg atc acc cgc agg aat ttc tcc ggg tgc ctg gag ctg cag tgt 493
Pro Trp Ile Thr Arg Arg Asn Phe Ser Gly Cys Leu Glu Leu Gln Cys
      125 130 135 140
cag ccc gac tcc tct aca ttg gtg ccc cca agg agc ccc ggg gcc ctg 541
Gln Pro Asp Ser Ser Thr Leu Val Pro Pro Arg Ser Pro Gly Ala Leu
      145 150 155
gag gcc act gcc ttg cca gcc cct cag gca cct cgg ctg ctc ctc ctg 589
Glu Ala Thr Ala Leu Pro Ala Pro Gln Ala Pro Arg Leu Leu Leu Leu
      160 165 170
ctg ctg ctg ccc gtg gct ctc ctg ctg atg tcc act gcc tgg tgc ctg 637
Leu Leu Leu Pro Val Ala Leu Leu Leu Met Ser Thr Ala Trp Cys Leu
      175 180 185
cat tgg cga agg agg cgg cgg cgg agg tca ccc tac cct ggg gag cag 685
His Trp Arg Arg Arg Arg Arg Arg Ser Pro Tyr Pro Gly Glu Gln
      190 195 200
agg aca ctg agg ccc agc gag cgg agc cat ctg ccc gag gac aca gag 733
Arg Thr Leu Arg Pro Ser Glu Arg Ser His Leu Pro Glu Asp Thr Glu

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205	210	215	220	
ctg gga cct gga ggg agt cag cta gag act ggt ccc ttc ctc gac cac				781
Leu Gly Pro Gly Gly Ser Gln Leu Glu Thr Gly Pro Phe Leu Asp His	225	230	235	
gca gcc ccg ctc gct ccc tcc cca gga tca agg caa cgc ccg ccc cca				829
Ala Ala Pro Leu Ala Pro Ser Pro Gly Ser Arg Gln Arg Pro Pro Pro	240	245	250	
acg ccc cca aag cca gcc cca gcc cca cct ctc ccc ctc tgt aca aag				877
Thr Pro Pro Lys Pro Ala Pro Ala Pro Pro Leu Pro Leu Cys Thr Lys	255	260	265	
tcc ttg ccc cca aga aat tgt ata taaatcatcc ttttctacca gcaaaaaaaaa				931
Ser Leu Pro Pro Arg Asn Cys Ile	270	275		
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaa				985
<210> SEQ ID NO 26				
<211> LENGTH: 276				
<212> TYPE: PRT				
<213> ORGANISM: Canis familiaris				
<400> SEQUENCE: 26				
Met Ile Val Leu Ala Pro Ala Trp Ser Pro Thr Ala Ser Leu Leu Leu				
1	5	10	15	
Leu Leu Leu Leu Ser Pro Gly Leu Arg Gly Thr Pro Asp Cys Ser Phe				
	20	25	30	
Ser His Ser Pro Ile Ser Ser Thr Phe Ala Val Thr Ile Arg Lys Leu				
	35	40	45	
Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu				
	50	55	60	
Gln Asp Asp Glu Leu Cys Gly Ala Phe Trp Arg Leu Val Leu Ala Gln				
	65	70	75	80
Arg Trp Met Val Arg Leu Gln Ala Val Ala Gly Ser Gln Met Gln Ile				
	85	90	95	
Leu Leu Glu Ala Val Asn Thr Glu Ile His Phe Val Thr Phe Cys Ala				
	100	105	110	
Phe Gln Asp Thr Ser Gln Gln Leu Ala Ala Leu Lys Pro Trp Ile Thr				
	115	120	125	
Arg Arg Asn Phe Ser Gly Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser				
	130	135	140	
Ser Thr Leu Val Pro Pro Arg Ser Pro Gly Ala Leu Glu Ala Thr Ala				
	145	150	155	160
Leu Pro Ala Pro Gln Ala Pro Arg Leu Leu Leu Leu Leu Leu Pro				
	165	170	175	
Val Ala Leu Leu Leu Met Ser Thr Ala Trp Cys Leu His Trp Arg Arg				
	180	185	190	
Arg Arg Arg Arg Arg Ser Pro Tyr Pro Gly Glu Gln Arg Thr Leu Arg				
	195	200	205	
Pro Ser Glu Arg Ser His Leu Pro Glu Asp Thr Glu Leu Gly Pro Gly				
	210	215	220	
Gly Ser Gln Leu Glu Thr Gly Pro Phe Leu Asp His Ala Ala Pro Leu				
	225	230	235	240
Ala Pro Ser Pro Gly Ser Arg Gln Arg Pro Pro Thr Pro Pro Lys				
	245	250	255	
Pro Ala Pro Ala Pro Pro Leu Pro Leu Cys Thr Lys Ser Leu Pro Pro				
	260	265	270	

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 Arg Asn Cys Ile  
 275

<210> SEQ ID NO 27  
 <211> LENGTH: 985  
 <212> TYPE: DNA  
 <213> ORGANISM: *Canis familiaris*

<400> SEQUENCE: 27

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tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt    60
ttgctggtag aaaaggatga tttatataca atttcttggg ggcaaggact ttgtacagag    120
ggggagaggt ggggctgggg ctggctttgg gggcgttggg ggcgggctgt gccttgatcc    180
tggggagggg gcgagcgggg ctgctgtgtc gaggaaggga ccagtctcta gctgactccc    240
tccaggtccc agctctgtgt cctcgggcag atggctcgcg tcgctgggcc tcagtgtcct    300
ctgctcccca ggtaggggtg acctccggcg cgcctcctt cgccaatgca ggcaccaggc    360
agtggacatc agcaggagag ccacgggcag cagcagcagg aggagcagcc gaggtgcctg    420
aggggctggc aaggcagtgg cctccagggc cccggggctc cttgggggca ccaatgtaga    480
ggagtcgggc tgacctgca gctccaggca cccggagaaa ttcctgcggg tgatccaggg    540
cttcagggcg gccagctgct gggaggtgtc ctggaaggca cagaaggtag caaagtgtat    600
ctccgtgttg acagcctcca gcaggatttg catttgggat ccagccacag cctggagccg    660
caccatccag cgctgggcca ggaccaggcg ccagaacgcc ccgcagagct cgtcgtcctg    720
caggttgtag ggcacagtga ctggatagtc ctgaagcagg taatcagaca gcttgcggat    780
ggtgaccgcg aaggtggagg agatggggct gtggctgaag gagcagtcgg gggccccgcg    840
gaggccgggg ctgagcagca gcagcagcaa caggagggca gttgggctcc aggetggcgc    900
cagcactatc atctcggccg gagggcccctc atgcctatgg tcagatcagg cttgccccag    960
ctgggcgtgg aaggggccag gccgg                                     985
  
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<210> SEQ ID NO 28  
 <211> LENGTH: 828  
 <212> TYPE: DNA  
 <213> ORGANISM: *Canis familiaris*

<400> SEQUENCE: 28

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atgatagtgc tggcgccagc ctggagccca actgectccc tgttgctgct gctgctgctc    60
agccccggcc tccgcgggac ccccgactgc tccttcagcc acagccccat ctctccaacc    120
ttcgcggtea ccatccgcaa gctgtctgat tacctgcttc aggactatcc agtcaactgtc    180
gcctccaacc tgcaggacga cgagctctgc ggggcgttct ggcgcctggt cctggcccag    240
cgctggatgg tgcggctcca ggctgtggct ggatcccaaa tgcaaatcct gctggaggct    300
gtcaacacgg agatacactt tgtcaocttc tgtgccttcc aggacacctc ccagcagctg    360
gccgccctga agcctggat caccgcaggg aatttctccg ggtgcctgga gctgcagtgt    420
cagccccgact cctctacatt ggtgcccaca aggagcccgg gggccctgga ggccactgcc    480
ttgcagccc ctcaggcacc tcggctgctc ctctgctgct tgtgcccgtt ggtctctctg    540
ctgatgtcca ctgcctgggt cctgcattgg cgaaggaggc ggcggcggag gtcaccctac    600
cctgggggagc agaggacact gagggcccagc gagcggagcc atctgcccga ggacacagag    660
ctgggacctg gaggagctca gctagagact ggtcccttcc tcgaccaagc agccccgctc    720
gctccctccc caggatcaag gcaacgcccc cccccaacgc ccccaagcc agccccagcc    780
  
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ccacctctcc ccctctgtac aaagtctctg cccccaagaa attgtata 828

<210> SEQ ID NO 29  
 <211> LENGTH: 828  
 <212> TYPE: DNA  
 <213> ORGANISM: Canis familiaris

<400> SEQUENCE: 29

tatacaattt cttgggggca aggactttgt acagaggggg agaggtgggg ctggggctgg	60
ctttgggggg gttggggggc ggcgttgctt tgatcctggg gagggagcga gcggggctgc	120
gtggtcgagg aagggaccag tctctagctg actccctcca ggtcccagct ctgtgtcctc	180
gggcagatgg ctccgctcgc tgggcctcag tgctctctgc tccccagggt agggtgacct	240
ccgcgcccgc ctctctgcc aatgcaggca ccaggcagtg gacatcagca ggagagccac	300
gggcagcagc agcaggagga gcagccgagg tgcctgaggg gctggcaagg cagtggcctc	360
cagggccccc gggctctctg ggggcaccaa tgtagaggag tcgggctgac actgcagctc	420
caggcaccgc gagaaattcc tgcgggtgat ccagggcttc agggcggcca gctgctggga	480
ggtgtcctgg aaggcacaga aggtgacaaa gtgtatctcc gtgttgacag cctccagcag	540
gatttgattt tgggatccag ccacagcctg gagccgcacc atccagcgtt gggccaggac	600
caggcggcag aacgccccgc agagctcgtc gtctctcagg ttggaggcga cagtgactgg	660
atagtcctga agcaggtaat cagacagctt gcggatggtg accgcgaagg tggaggagat	720
ggggctgtgg ctgaaggagc agtcgggggt cccgcggagg cccgggctga gcagcagcag	780
cagcaacagg gaggcagttg ggctccagc tggcgcagc actatcat	828

<210> SEQ ID NO 30  
 <211> LENGTH: 750  
 <212> TYPE: DNA  
 <213> ORGANISM: Canis familiaris  
 <220> FEATURE:  
 <221> NAME/KEY: CDS  
 <222> LOCATION: (1)..(750)

<400> SEQUENCE: 30

acc ccc gac tgc tcc ttc agc cac agc ccc atc tcc tcc acc ttc gcg	48
Thr Pro Asp Cys Ser Phe Ser His Ser Pro Ile Ser Ser Thr Phe Ala	
1 5 10 15	
gtc acc atc cgc aag ctg tct gat tac ctg ctt cag gac tat cca gtc	96
Val Thr Ile Arg Lys Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val	
20 25 30	
act gtc gcc tcc aac ctg cag gac gac gag ctc tgc ggg gcg ttc tgg	144
Thr Val Ala Ser Asn Leu Gln Asp Asp Glu Leu Cys Gly Ala Phe Trp	
35 40 45	
cgc ctg gtc ctg gcc cag cgc tgg atg gtg cgg ctc cag gct gtg gct	192
Arg Leu Val Leu Ala Gln Arg Trp Met Val Arg Leu Gln Ala Val Ala	
50 55 60	
gga tcc caa atg caa atc ctg ctg gag gct gtc aac acg gag ata cac	240
Gly Ser Gln Met Gln Ile Leu Leu Glu Ala Val Asn Thr Glu Ile His	
65 70 75 80	
ttt gtc acc ttc tgt gcc ttc cag gac acc tcc cag cag ctg gcc gcc	288
Phe Val Thr Phe Cys Ala Phe Gln Asp Thr Ser Gln Gln Leu Ala Ala	
85 90 95	
ctg aag ccc tgg atc acc cgc agg aat ttc tcc ggg tgc ctg gag ctg	336
Leu Lys Pro Trp Ile Thr Arg Arg Asn Phe Ser Gly Cys Leu Glu Leu	
100 105 110	
cag tgt cag ccc gac tcc tct aca ttg gtg ccc cca agg agc ccc ggg	384
Gln Cys Gln Pro Asp Ser Ser Thr Leu Val Pro Pro Arg Ser Pro Gly	

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115	120	125	
gcc ctg gag gcc act gcc ttg cca gcc cct cag gca cct cgg ctg ctc Ala Leu Glu Ala Thr Ala Leu Pro Ala Pro Gln Ala Pro Arg Leu Leu 130 135 140			432
ctc ctg ctg ctg ctg ccc gtg gct ctc ctg ctg atg tcc act gcc tgg Leu Leu Leu Leu Leu Pro Val Ala Leu Leu Leu Met Ser Thr Ala Trp 145 150 155 160			480
tgc ctg cat tgg cga agg agg cgg cgg cgg agg tca ccc tac cct ggg Cys Leu His Trp Arg Arg Arg Arg Arg Arg Ser Pro Tyr Pro Gly 165 170 175			528
gag cag agg aca ctg agg ccc agc gag cgg agc cat ctg ccc gag gac Glu Gln Arg Thr Leu Arg Pro Ser Glu Arg Ser His Leu Pro Glu Asp 180 185 190			576
aca gag ctg gga cct gga ggg agt cag cta gag act ggt ccc ttc ctc Thr Glu Leu Gly Pro Gly Gly Ser Gln Leu Glu Thr Gly Pro Phe Leu 195 200 205			624
gac cac gca gcc cgg ctc gct ccc tcc cca gga tca agg caa cgc ccg Asp His Ala Ala Pro Leu Ala Pro Ser Pro Gly Ser Arg Gln Arg Pro 210 215 220			672
ccc cca acg ccc cca aag cca gcc cca gcc cca cct ctc ccc ctc tgt Pro Pro Thr Pro Pro Lys Pro Ala Pro Ala Pro Pro Leu Pro Leu Cys 225 230 235 240			720
aca aag tcc ttg ccc cca aga aat tgt ata Thr Lys Ser Leu Pro Pro Arg Asn Cys Ile 245 250			750

&lt;210&gt; SEQ ID NO 31

&lt;211&gt; LENGTH: 250

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Canis familiaris

&lt;400&gt; SEQUENCE: 31

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

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195	200	205	
Asp His Ala Ala Pro Leu Ala Pro Ser Pro Gly Ser Arg Gln Arg Pro 210	215	220	
Pro Pro Thr Pro Pro Lys Pro Ala Pro Ala Pro Pro Leu Pro Leu Cys 225	230	235	240
Thr Lys Ser Leu Pro Pro Arg Asn Cys Ile 245	250		
 <210> SEQ ID NO 32			
<211> LENGTH: 750			
<212> TYPE: DNA			
<213> ORGANISM: Canis familiaris			
 <400> SEQUENCE: 32			
tatacaattt cttgggggca aggactttgt acagaggggg agaggtgggg ctggggctgg			60
ctttgggggc gttgggggag ggcgttgctt tgatcctggg gagggagcga gcggggctgc			120
gtggtcgagg aagggaccag tctctagctg actccctcca ggtcccagct ctgtgtcctc			180
gggcagatgg ctccgctcgc tgggcctcag tgcctctgct tccccagggt agggtgacct			240
ccgccgccgc ctctctgcc aatgcaggca ccaggcagtg gacatcagca ggagagccac			300
gggcagcagc agcaggagga gcagccgagg tgcctgaggg gctggcaagg cagtggcctc			360
cagggccccc gggctccttg ggggcaccaa tgtagaggag tcgggctgac actgcagctc			420
caggcaccgc gagaaattcc tgcgggtgat ccagggcttc agggcggcca gctgctggga			480
ggtgtcctgg aaggcacaga aggtgacaaa gtgtatctcc gtgttgacag cctccagcag			540
gatttgcatt tgggatccag ccacagcctg gagccgcacc atccagcgtt gggccaggac			600
caggcgccag aacgccccgc agagctcgtc gtctctcagg ttggaggcga cagtgactgg			660
atagtctga agcaggtaat cagacagctt cgggatggtg accgcgaagg tggaggagat			720
ggggctgtgg ctgaaggagc agtcgggggt			750
 <210> SEQ ID NO 33			
<211> LENGTH: 1019			
<212> TYPE: DNA			
<213> ORGANISM: Canis familiaris			
<220> FEATURE:			
<221> NAME/KEY: CDS			
<222> LOCATION: (74)..(166)			
 <400> SEQUENCE: 33			
ccggcctggc cccttccacg cccagctggg gcaagcctga tctgaccata ggcattgagg			60
gcctccggcc gag atg ata gtg ctg gcg cca gcc tgg agc oca act gtg			109
Met Ile Val Leu Ala Pro Ala Trp Ser Pro Thr Val	1	5	10
cgt ata ccc ggg gga caa ggc ggg gga cag gca gag cgc tac cga gct			157
Arg Ile Pro Gly Gly Gln Gly Gly Gly Gln Ala Glu Arg Tyr Arg Ala	15	20	25
ggg cag agc tgagagagca gacggacaga ggctccctg ttgtctgtgc			206
Gly Gln Ser	30		
tgtgtctcag ccccgccctc cgcgggaccc ccgactgtct ctteagccac agccccatct			266
ctctccactt cgcggtcacc atccgcaagc tgtctgatta cctgcttcag gactatccag			326
tcactgtcgc ctccaacctg caggacgacg agctctgcgg ggcgttcttg cgctggctc			386
tggcccagcg ctggatggtg cggctccagg ctgtggctgg atcccaaatg caaatcctgc			446
tggaggctgt caacacggag atacactttg tcaccttctg tgccttccag gacacctccc			506

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agcagctggc cgccctgaag ccctggatca cccgcaggaa tttctccggg tgectggagc 566
tgcagtgtca gcccgactcc tctacattgg tgccccaag gagccccggg gcctggagg 626
ccactgcctt gccagccct caggcacctc ggctgctcct cctgctgctg ctgcccgtgg 686
ctctctgct gatgtccact gcctgggtgc tgcattggcg aaggaggcgg cggcggaggt 746
cacctaccc tggggagcag aggacactga ggcccagcga gcggagccat ctgcccgagg 806
acacagagct gggacctgga gggagtccgc tagagactgg tcccttcctc gaccacgcag 866
ccccgctgc tcctcccca ggatcaaggc aacgcccgcc cccaacgccc ccaagccag 926
ccccagcccc acctctccc ctctgtacaa agtccttgcc cccaagaaat tgtatataaa 986
tcatcctttt ctacaaaaa aaaaaaaaaa aaa 1019

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<210> SEQ ID NO 34
<211> LENGTH: 31
<212> TYPE: PRT
<213> ORGANISM: Canis familiaris

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<400> SEQUENCE: 34

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Met Ile Val Leu Ala Pro Ala Trp Ser Pro Thr Val Arg Ile Pro Gly
  1             5             10             15
Gly Gln Gly Gly Gly Gln Ala Glu Arg Tyr Arg Ala Gly Gln Ser
          20             25             30

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<210> SEQ ID NO 35
<211> LENGTH: 1019
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

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<400> SEQUENCE: 35

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ttttttttt ttttttttg tagaaaagga tgatttatat acaatttctt gggggcaagg 60
actttgtaca gagggggaga ggtggggctg gggctggctt tgggggcgtt gggggcgggc 120
gttgcttga tcctggggag ggagcagcgg gggctgcctg gtcgaggaag ggaccagtct 180
ctagctgact ccctccaggt ccagctctg tgcctcggg cagatggctc cgctcctgg 240
gcctcagtgt cctctgctcc ccagggtagg gtgacctcgg ccgccgctc cttcgccaat 300
gcaggcacca ggcagtggac atcagcagga gagccacggg cagcagcagc aggaggagca 360
gccgaggtgc ctgaggggct ggcaaggcag tggcctccag ggccccgggg ctcttgggg 420
gcaccaatgt agaggagtgc ggctgacct gcagctccag gcacccggag aaattcctgc 480
gggtgatcca gggcttcagg gcggccagct gctgggaggt gtcctggaag gcacagaagg 540
tgacaaagtg tatctcctg ttgacagcct ccagcaggat ttgcatttg gatccagcca 600
cagcctggag ccgcaccatc cagcgtggg ccaggaccag gcgccagaac gcccccaga 660
gctcgtcgtc ctgcaggttg gaggcagcag tgactggata gtcctgaagc aggtaatcag 720
acagcttgcg gatggtgacc gcgaagggtg aggagatggg gctgtggctg aaggagcagt 780
cgggggtccc gcggaggcgg gggctgagca gcagcagcag caacaggggag gcctctgtcc 840
gtctgctctc tcagctctgc ccagctcgtt agcgtctctc ctgtccccg ccttgtcccc 900
cgggtatacg cacagtggg ctccaggctg gcgccagcac tatcatctcg gccggaggcc 960
cctcatgcct atggteagat caggettgc ccagctgggc gtggaagggg ccaggccgg 1019

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<210> SEQ ID NO 36
<211> LENGTH: 93
<212> TYPE: DNA

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<213> ORGANISM: *Canis familiaris*

<400> SEQUENCE: 36

atgatagtgc tggcgccagc ctggagccca actgtgctga taccggggg acaaggcggg 60

ggacaggcag agcgtaccg agctgggcag agc 93

<210> SEQ ID NO 37

<211> LENGTH: 93

<212> TYPE: DNA

<213> ORGANISM: *Canis familiaris*

<400> SEQUENCE: 37

gctctgcccc gctcggtagc gctctgctg tccccgctt tgtcccccg gtatacgcac 60

agttgggctc caggtggcg ccagcactat cat 93

<210> SEQ ID NO 38

<211> LENGTH: 27

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer

<400> SEQUENCE: 38

tgaattcgga cataacttca atattac 27

<210> SEQ ID NO 39

<211> LENGTH: 27

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer

<400> SEQUENCE: 39

tctcgagatt cagcttcaat gcctgta 27

<210> SEQ ID NO 40

<211> LENGTH: 28

<212> TYPE: DNA

<213> ORGANISM: Artificial Sequence

<220> FEATURE:

<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer

<400> SEQUENCE: 40

cccaagctta tgggtctcac ctccaac 28

<210> SEQ ID NO 41

<211> LENGTH: 395

<212> TYPE: DNA

<213> ORGANISM: *Felis catus*

<400> SEQUENCE: 41

ggccataggc atgaaggcc tccggccgag atgatagtgc tggcgccagc ctggagccca 60

actacctccc tgctgtgct gctactgtgc agccctggcc tccgcggtc ccccgactgt 120

tccttcagcc acagcccat ctctccacc ttcaaggcca ccatccgaaa gctgtctgat 180

tacctgcttc aggattacc agtcaccgc gctccaacc tacaggacga cgagctctgt 240

gggcattct ggcacctgt cctggcccag cgctggatgg gtcggctcaa ggctgtggct 300

gggtcccaga tgcaaagcct gctggaggcg gtcaacacc agatacattt tgtcaccttg 360

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tgtgccttcc agccctccc cagctgtctt cgatt 395

<210> SEQ ID NO 42
<211> LENGTH: 793
<212> TYPE: DNA
<213> ORGANISM: Felis catus

<400> SEQUENCE: 42
cttcaaggtc accatccgaa agctgtctga ttacctgctt caggattacc cagtcaccgt 60
cgctccaac ctacaggacg acgagctctg tgggccattc tggcacctgg tcttggccca 120
gcgctggatg ggtcggctca aggctgtggc tgggtcccag atgcaaagcc tgctggaggc 180
ggtcaacacc gagatacatt ttgtcacctt gtgtgccttc cagcccctcc ccagctgtct 240
tcgattcgtc cagaccaaca tctcccacct cctgcaggac acctccgagc agctggcggc 300
cttgaagccc tggatcaccg gcaggaattt ctcggggtgc ctggagctac agtgcagcc 360
cgactcctcc acccactgc ccccaaggag ccccagggcc ttggaggcca cagccctgcc 420
agcccctcag gcccctctgc tctcctcctc gctgctgttg cctgtggctc tcttctgat 480
gtccgcgcgc tgggtcctgc actggcgaag aaggagatgg agaacgcctt accccagggg 540
gcagaggaag aactgaggc ccagagagag gaatcacctg cccgaggaca cagagccggg 600
actcggagaa agtcagctag agactggttc cttcctcgac cacgctgccc cgctcactct 660
ccccccggga tggaggcaac gccagcccc aacgccagcc ccagaccac ctatccccct 720
ctgtacaaag tctttgtcct caggaaattg tatataaatc atccttttct accaaaaaaaa 780
aaaaaaaaaa aaa 793

<210> SEQ ID NO 43
<211> LENGTH: 942
<212> TYPE: DNA
<213> ORGANISM: Felis catus
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (31)..(903)

<400> SEQUENCE: 43
ggccataggc atgaagggcc tccggccgag atg ata gtg ctg gcg cca gcc tgg 54
Met Ile Val Leu Ala Pro Ala Trp
1 5

agc cca act acc tcc ctg ctg ctg ctg cta ctg ctc agc cct ggc ctc 102
Ser Pro Thr Thr Ser Leu Leu Leu Leu Leu Leu Ser Pro Gly Leu
10 15 20

cgc ggg tcc ccc gac tgt tcc ttc agc cac agc ccc atc tcc tcc acc 150
Arg Gly Ser Pro Asp Cys Ser Phe Ser His Ser Pro Ile Ser Ser Thr
25 30 35 40

ttc aag gtc acc atc cga aag ctg tct gat tac ctg ctt cag gat tac 198
Phe Lys Val Thr Ile Arg Lys Leu Ser Asp Tyr Leu Leu Gln Asp Tyr
45 50 55

cca gtc acc gtc gcc tcc aac cta cag gac gac gag ctc tgt ggg cca 246
Pro Val Thr Val Ala Ser Asn Leu Gln Asp Asp Glu Leu Cys Gly Pro
60 65 70

ttc tgg cac ctg gtc ctg gcc cag cgc tgg atg ggt cgg ctc aag gct 294
Phe Trp His Leu Val Leu Ala Gln Arg Trp Met Gly Arg Leu Lys Ala
75 80 85

gtg gct ggg tcc cag atg caa agc ctg ctg gag gcg gtc aac acc gag 342
Val Ala Gly Ser Gln Met Gln Ser Leu Leu Glu Ala Val Asn Thr Glu
90 95 100

ata cat ttt gtc acc ttg tgt gcc ttc cag ccc ctc ccc agc tgt ctt 390
Ile His Phe Val Thr Leu Cys Ala Phe Gln Pro Leu Pro Ser Cys Leu

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105	110	115	120	
cga ttc gtc cag acc aac atc tcc cac ctc ctg cag gac acc tcc gag				438
Arg Phe Val Gln Thr Asn Ile Ser His Leu Leu Gln Asp Thr Ser Glu	125	130	135	
cag ctg gcg gcc ttg aag ccc tgg atc acc cgc agg aat ttc tcg ggg				486
Gln Leu Ala Ala Leu Lys Pro Trp Ile Thr Arg Arg Asn Phe Ser Gly	140	145	150	
tgc ctg gag cta cag tgt cag ccc gac tcc tcc acc cca ctg ccc cca				534
Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Pro Leu Pro Pro	155	160	165	
agg agc ccc agg gcc ttg gag gcc aca gcc ctg cca gcc cct cag gcc				582
Arg Ser Pro Arg Ala Leu Glu Ala Thr Ala Leu Pro Ala Pro Gln Ala	170	175	180	
cct ctg ctg ctc ctc ctg ctg ctg ttg cct gtg gct ctc ttg ctg atg				630
Pro Leu Leu Leu Leu Leu Leu Leu Leu Pro Val Ala Leu Leu Leu Met	185	190	195	200
tcc gcc gcc tgg tgc ctg cac tgg cga aga agg aga tgg aga acg ccc				678
Ser Ala Ala Trp Cys Leu His Trp Arg Arg Arg Trp Arg Thr Pro	205	210	215	
tac ccc agg gag cag agg aag aca ctg agg ccc aga gag agg aat cac				726
Tyr Pro Arg Glu Gln Arg Lys Thr Leu Arg Pro Arg Glu Arg Asn His	220	225	230	
ctg ccc gag gac aca gag ccg gga ctc gga gaa agt cag cta gag act				774
Leu Pro Glu Asp Thr Glu Pro Gly Leu Gly Glu Ser Gln Leu Glu Thr	235	240	245	
ggc tcc ttc ctc gac cac gct gcc ccg ctc act ctc ccc ccg gga tgg				822
Gly Ser Phe Leu Asp His Ala Ala Pro Leu Thr Leu Pro Pro Gly Trp	250	255	260	
agg caa cgc cag ccc cca acg cca gcc cca gac cca cct atc ccc ctc				870
Arg Gln Arg Gln Pro Pro Thr Pro Ala Pro Asp Pro Pro Ile Pro Leu	265	270	275	280
tgt aca aag tcc ttg tcc tca gga aat tgt ata taaatcatcc ttttctacca				923
Cys Thr Lys Ser Leu Ser Ser Gly Asn Cys Ile	285	290		
aaaaaaaaa aaaaaaaaaa				942

&lt;210&gt; SEQ ID NO 44

&lt;211&gt; LENGTH: 291

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Felis catus

&lt;400&gt; SEQUENCE: 44

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

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

&lt;210&gt; SEQ ID NO 45

&lt;211&gt; LENGTH: 942

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Felis catus

&lt;400&gt; SEQUENCE: 45

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ttttttttt ttttttttt ggtagaaaag gatgatttat atacaatttc ctgaggacaa      60
ggactttgta cagaggggga taggtgggtc tggggctggc gttgggggct ggcgttgcc      120
ccatcccggg gggagagtga gcggggcagc gtggtcgagg aaggaaccag tctctagctg      180
actttctccg agtcccggct ctgtgtcttc gggcaggtga ttcctctctc tgggectcag      240
tgtcttcttc tgetccctgg ggtagggcgt tctccatctc cttcttcgcc agtgcaggca      300
ccaggcggcg gacatcagca agagagccac aggcaacagc agcaggagga gcagcagagg      360
ggcctgaggg gctggcaggg ctgtggcctc caaggccttg gggctccttg ggggcagtgg      420
ggtggaggag tcgggctgac actgtagctc caggcacccc gagaaattcc tgcgggtgat      480
ccagggett c aaggccgcca gctgctcgga ggtgtcctgc aggaggtggg agatgttggt      540
ctggacgaat cgaagacagc tggggagggg ctggaaggca cacaaggtga caaaatgtat      600
ctcgggtgtg accgcctcca gcaggctttg catctgggac ccagccacag ccttgagccg      660
accatccag cgctgggcca ggaccaggtg ccagaatggc ccacagagct cgtcgtcctg      720
taggttgagg gcgacggtga ctgggtaatc ctgaagcagg taatcagaca gctttcggat      780
ggtgaccttg aaggtggagg agatggggct gtggctgaag gaacagtcgg gggaccgcg      840
gaggccaggg ctgagcagta gcagcagcag caggaggtga gttgggctcc aggctggcgc      900
cagcaactatc atctcgccg gaggcccttc atgcctatgg cc                               942

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&lt;210&gt; SEQ ID NO 46

&lt;211&gt; LENGTH: 873

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Felis catus

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&lt;400&gt; SEQUENCE: 46

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atgatagtgc tgggcccagc ctggagccca actacctccc tgetgctgct gctactgctc   60
agccctggcc tccgcggggtc ccccactgtt tccttcagcc acagcccatc ctctccacc   120
ttcaagggtca ccatccgaaa gctgtctgat tacctgcttc aggattaccc agtcaccgtc   180
gcctccaacc tacaggacga cgagctctgt gggccattct ggcacctggt cctggcccag   240
cgctggatgg gtcggctcaa ggctgtggct ggggccaga tgcaaagcct gctggaggcg   300
gtcaaacacc agatacattt tgtcaccttg tgtgccttcc agcccctccc cagctgtctt   360
cgattctgct agaccaacat ctcccactc ctgcaggaca cctccgagca gctggcggcc   420
ttgaagccct ggatcacccg caggaatttc tcgggggtgcc tggagctaca gtgtcagccc   480
gactcctcca cccactgccc cccaaggagc ccagggcctc tggaggccac agccctgcca   540
gcccctcagg cccctctgct gctcctctgt ctgctgttgc ctgtggtctc cttgctgatg   600
tccgcccctc ggtgcctgca ctggcgaaga aggagatgga gaacgcccta cccaggggag   660
cagaggaaga cactgaggcc cagagagagg aatcacctgc ccgaggacac agagccggga   720
ctcggagaaa gtcagctaga gactgggttc ttctcgacc acgctgcccc gctcaacttc   780
cccccgggat ggaggcaacg ccagccccc acgccagccc cagaccacc tatccccctc   840
tgtacaaagt ccttgtctc aggaaattgt ata                                     873

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&lt;210&gt; SEQ ID NO 47

&lt;211&gt; LENGTH: 873

&lt;212&gt; TYPE: DNA

<213> ORGANISM: *Felis catus*

&lt;400&gt; SEQUENCE: 47

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tatacaattt cctgaggaca aggactttgt acagaggggg ataggtgggt ctggggctgg   60
cgttgggggc tggcgttgcc tccatcccgg ggggagagtg agcggggcag cgtggtcgag   120
gaaggaacca gtctctagct gactttctcc gagtcccggc tctgtgtcct cgggcagggtg   180
attcctctct ctgggctca gtgtcttctc ctgctcctg gggtagggcg ttctccatct   240
ccttctctgc cagtgcaggc accaggcggc ggacatcagc aagagagcca caggcaacag   300
cagcaggagg agcagcagag gggcctgagg ggctggcagg gctgtggcct ccaaggccct   360
ggggctcctt gggggcagtg ggggtgagga gtcgggctga cactgtagct ccaggcacc   420
cgagaaatte ctgcccgtga tccagggcct caaggccgcc agctgctcgg aggtgtcctg   480
caggaggtgg gagatgttgg tctggacgaa tcgaagacag ctggggaggg gctggaaggc   540
acacaaggty acaaaatgta tctcgggtgt gaccgcctcc agcaggcttt gcatctggga   600
cccagccaca gccttgagcc gaccatcca gcgctgggccc aggaccaggt gccagaatgg   660
cccacagagc tcgtcgtcct gtaggttggg ggcgacggtg actgggtaat cctgaagcag   720
gtaatcagac agctttcgga tgggtacctt gaaggtggag gagatggggc tgtggctgaa   780
ggaaacagtc ggggaccgcc ggaggccagg gctgagcagt agcagcagca gcagggaggt   840
agttgggctc caggctggcg ccagcactat cat                                     873

```

&lt;210&gt; SEQ ID NO 48

&lt;211&gt; LENGTH: 795

&lt;212&gt; TYPE: DNA

<213> ORGANISM: *Felis catus*

&lt;220&gt; FEATURE:

&lt;221&gt; NAME/KEY: CDS

&lt;222&gt; LOCATION: (1)..(795)

-continued

&lt;400&gt; SEQUENCE: 48

```

tcc ccc gac tgt tcc ttc agc cac agc ccc atc tcc tcc acc ttc aag      48
Ser Pro Asp Cys Ser Phe Ser His Ser Pro Ile Ser Ser Thr Phe Lys
  1                    5                      10                    15

gtc acc atc cga aag ctg tct gat tac ctg ctt cag gat tac cca gtc      96
Val Thr Ile Arg Lys Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val
                20                      25                      30

acc gtc gcc tcc aac cta cag gac gac gag ctc tgt ggg cca ttc tgg      144
Thr Val Ala Ser Asn Leu Gln Asp Asp Glu Leu Cys Gly Pro Phe Trp
                35                      40                      45

cac ctg gtc ctg gcc cag cgc tgg atg ggt cgg ctc aag gct gtg gct      192
His Leu Val Leu Ala Gln Arg Trp Met Gly Arg Leu Lys Ala Val Ala
  50                    55                      60

ggg tcc cag atg caa agc ctg ctg gag gcg gtc aac acc gag ata cat      240
Gly Ser Gln Met Gln Ser Leu Leu Glu Ala Val Asn Thr Glu Ile His
  65                    70                      75                      80

ttt gtc acc ttg tgt gcc ttc cag ccc ctc ccc agc tgt ctt cga ttc      288
Phe Val Thr Leu Cys Ala Phe Gln Pro Leu Pro Ser Cys Leu Arg Phe
                85                      90                      95

gtc cag acc aac atc tcc cac ctc ctg cag gac acc tcc gag cag ctg      336
Val Gln Thr Asn Ile Ser His Leu Leu Gln Asp Thr Ser Glu Gln Leu
  100                   105                   110

gcg gcc ttg aag ccc tgg atc acc cgc agg aat ttc tcg ggg tgc ctg      384
Ala Ala Leu Lys Pro Trp Ile Thr Arg Arg Asn Phe Ser Gly Cys Leu
  115                   120                   125

gag cta cag tgt cag ccc gac tcc tcc acc cca ctg ccc cca agg agc      432
Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Pro Leu Pro Pro Arg Ser
  130                   135                   140

ccc agg gcc ttg gag gcc aca gcc ctg cca gcc cct cag gcc cct ctg      480
Pro Arg Ala Leu Glu Ala Thr Ala Leu Pro Ala Pro Gln Ala Pro Leu
  145                   150                   155                   160

ctg ctc ctc ctg ctg ctg ttg cct gtg gct ctc ttg ctg atg tcc gcc      528
Leu Leu Leu Leu Leu Leu Leu Pro Val Ala Leu Leu Leu Met Ser Ala
                165                   170                   175

gcc tgg tgc ctg cac tgg cga aga agg aga tgg aga acg ccc tac ccc      576
Ala Trp Cys Leu His Trp Arg Arg Arg Arg Trp Arg Thr Pro Tyr Pro
  180                   185                   190

agg gag cag agg aag aca ctg agg ccc aga gag agg aat cac ctg ccc      624
Arg Glu Gln Arg Lys Thr Leu Arg Pro Arg Glu Arg Asn His Leu Pro
  195                   200                   205

gag gac aca gag ccg gga ctc gga gaa agt cag cta gag act ggt tcc      672
Glu Asp Thr Glu Pro Gly Leu Gly Glu Ser Gln Leu Glu Thr Gly Ser
  210                   215                   220

ttc ctc gac cac gct gcc ccg ctc act ctc ccc ccg gga tgg agg caa      720
Phe Leu Asp His Ala Ala Pro Leu Thr Leu Pro Pro Gly Trp Arg Gln
  225                   230                   235                   240

cgc cag ccc cca acg cca gcc cca gac cca cct atc ccc ctc tgt aca      768
Arg Gln Pro Pro Thr Pro Ala Pro Asp Pro Pro Ile Pro Leu Cys Thr
  245                   250                   255

aag tcc ttg tcc tca gga aat tgt ata      795
Lys Ser Leu Ser Ser Gly Asn Cys Ile
                260                   265

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&lt;210&gt; SEQ ID NO 49

&lt;211&gt; LENGTH: 265

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Felis catus

&lt;400&gt; SEQUENCE: 49

-continued

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

&lt;210&gt; SEQ ID NO 50

&lt;211&gt; LENGTH: 795

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Felis catus

&lt;400&gt; SEQUENCE: 50

tatacaattt cctgaggaca aggactttgt acagaggggg ataggtgggt ctggggctgg	60
cgttgggggc tggcgttgcc tccatcccgg ggggagagtg agcggggcag cgtggtcgag	120
gaaggaacca gtctctagct gactttctcc gagtcccggc tctgtgtcct cgggcaggtg	180
attcctctct ctgggcctca gtgtcttctc ctgctccctg gggtagggcg ttctccatct	240
ccttcttcgc cagtgcaggc accaggcggc ggacatcagc aagagagcca caggcaacag	300
cagcaggagg agcagcagag gggcctgagg ggctggcagg gctgtggcct ccaaggccct	360
ggggctcctt gggggcagtg gggtgaggga gtcgggctga cactgtagct ccaggcaccc	420
cgagaaatte ctgcggtgta tccagggett caaggcggcc agctgctcgg aggtgtcctg	480
caggaggtgg gagatgttgg tctggacgaa tcgaagacag ctggggaggg gctggaaggc	540
acacaaggty acaaaatgta tctcgggtgt gaccgcctcc agcaggcttt gcattctggga	600

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cccagccaca gccttgagcc gacccatcca gcgctgggcc aggaccaggt gccagaatgg 660
cccacagagc tcgtcgtcct gtaggttggg ggcgacggtg actgggtaat cctgaagcag 720
gtaatcagac agctttcgga tggtgacctt gaaggtggag gagatggggc tgtggctgaa 780
ggaacagtcg gggga 795

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<210> SEQ ID NO 51
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

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<400> SEQUENCE: 51

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aatgtgtcct ctgctttgga aaagtgtcac ccttgacaa gctgtgaaac caaaggcctg 60
gtgaagggtc agcggggaac taacaagact gatgttatct gtgtcccca gcctcggtta 120
agagccctag tgggtgtccc catcattatg gggatcctgc ttgttgcct gttgggtgct 180
gcctgcatcc gaaaggtggt caagaagcca gagaataagg ttatgtatca ggaccctgtg 240
gaggacttgg aggaatttcc tatgccccg cactccattg ctccggtgca agagacctta 300
catgggtgcc agcccgtcac c 321

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<210> SEQ ID NO 52
<211> LENGTH: 1425
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (196)..(1017)

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<400> SEQUENCE: 52

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tagactcccc ggaatattca ggggaactcc cggcgctaag ggtctccagg agctccgccc 60
tgcccaacga agccggccac gatttggccc cgaagacccc gcccatctcc tggcgggggc 120
ggcggggggc aagggtggtg gagttactaa agacatcccc gcgcccctac tccgctgcct 180
getattcacc tcgcc atg gtt etc ctg cct ctg cgc tgt etc ttc tgg ggc 231
      Met Val Leu Leu Pro Leu Arg Cys Leu Phe Trp Gly
      1 5 10
tcc ttg ttg acc acc gtc tac cca gaa cca cgc act gca tgc aga gaa 279
Ser Leu Leu Thr Thr Val Tyr Pro Glu Pro Arg Thr Ala Cys Arg Glu
      15 20 25
aag caa tac cta gta gac agt cag tgc tgt aat atg tgc cca cca gga 327
Lys Gln Tyr Leu Val Asp Ser Gln Cys Cys Asn Met Cys Pro Pro Gly
      30 35 40
gag aaa ctg gtg aat gac tgc cta cat acc att gac acg gaa tgc act 375
Glu Lys Leu Val Asn Asp Cys Leu His Thr Ile Asp Thr Glu Cys Thr
      45 50 55 60
cgt tgc caa aca ggc gaa ttc cta gac act tgg aac gca gag aga cac 423
Arg Cys Gln Thr Gly Glu Phe Leu Asp Thr Trp Asn Ala Glu Arg His
      65 70 75
tgt cac cag cac aaa tac tgc gac ccc aac cta ggg ctc cat gtc gag 471
Cys His Gln His Lys Tyr Cys Asp Pro Asn Leu Gly Leu His Val Glu
      80 85 90
aag gag ggc acg tca gaa aca gac acc act tgc aca tgc gat gaa ggt 519
Lys Glu Gly Thr Ser Glu Thr Asp Thr Thr Cys Thr Cys Asp Glu Gly
      95 100 105
ctg cat tgt acc aac gct gcc tgt gag agc tgc acc atg cac agc ctg 567
Leu His Cys Thr Asn Ala Ala Cys Glu Ser Cys Thr Met His Ser Leu
      110 115 120
tgc ccc cct ggc ctg gga gtc aaa cag atc gct aca ggg att tct gat 615
Cys Pro Pro Gly Leu Gly Val Lys Gln Ile Ala Thr Gly Ile Ser Asp

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125	130	135	140	
acc atc tgc gat ccc tgc ccc atc ggc ttc ttc tcc aat gtg tct tct				663
Thr Ile Cys Asp Pro Cys Pro Ile Gly Phe Phe Ser Asn Val Ser Ser	145	150	155	
gct ttg gaa aag tgt cac cct tgg aca agc tgt gaa acc aaa ggc ctg				711
Ala Leu Glu Lys Cys His Pro Trp Thr Ser Cys Glu Thr Lys Gly Leu	160	165	170	
gtg aag gtt cag gcg gga act aac aag act gat gtt atc tgt ggt ccc				759
Val Lys Val Gln Ala Gly Thr Asn Lys Thr Asp Val Ile Cys Gly Pro	175	180	185	
cag cct cgg tta aga gcc cta gtg gtg gtc ccc atc att atg ggg atc				807
Gln Pro Arg Leu Arg Ala Leu Val Val Val Pro Ile Ile Met Gly Ile	190	195	200	
ctg ctt gtt gtc ctg ttg gtg tct gcc tgc atc cga aag gtg gtc aag				855
Leu Leu Val Val Leu Leu Val Ser Ala Cys Ile Arg Lys Val Val Lys	205	210	215	220
aag cca gag aat aag gtt atg tat cag gac cct gtg gag gac ttg gag				903
Lys Pro Glu Asn Lys Val Met Tyr Gln Asp Pro Val Glu Asp Leu Glu	225	230	235	
gaa ttt cct atg ccc ccg cac tcc att gct ccg gtg caa gag acc tta				951
Glu Phe Pro Met Pro Pro His Ser Ile Ala Pro Val Gln Glu Thr Leu	240	245	250	
cat ggg tgc cag ccc gtc acc cag gag gac ggc aaa gag agc cgc atc				999
His Gly Cys Gln Pro Val Thr Gln Glu Asp Gly Lys Glu Ser Arg Ile	255	260	265	
tcc gtg cag gag aga gtg tgaggcagcg tgtgccagg agtgtgacag				1047
Ser Val Gln Glu Arg Val	270			
cgtagggagag tgggcgcgtg gctggagagc ctggagctgc tggaggggca tgaaggggcg				1107
gtgctccct gctgcaacc ctgtgctgca gaaacagaga acctccacc ccaccctgg				1167
agccattcc acctcccaac ttgcttttaa agatggagat gaaacttttg gggggccaga				1227
tagtaatatc caccaacca gcatttcagg gccctgaggt gtatatcacg gtggtttcta				1287
cgagcccagg aagaccacag aagagccatt gtggcattgt ttgtgacagt ggacaactgg				1347
aggccactta gctgttcagc agcaggggac tggctaaata aaatttgtaa tatatttata				1407
aaaaaaaaa aaaaaaaaa				1425

&lt;210&gt; SEQ ID NO 53

&lt;211&gt; LENGTH: 274

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Canis familiaris

&lt;400&gt; SEQUENCE: 53

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

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100					105					110					
Asn	Ala	Ala	Cys	Glu	Ser	Cys	Thr	Met	His	Ser	Leu	Cys	Pro	Pro	Gly
			115				120					125			
Leu	Gly	Val	Lys	Gln	Ile	Ala	Thr	Gly	Ile	Ser	Asp	Thr	Ile	Cys	Asp
		130				135					140				
Pro	Cys	Pro	Ile	Gly	Phe	Phe	Ser	Asn	Val	Ser	Ser	Ala	Leu	Glu	Lys
	145					150					155				160
Cys	His	Pro	Trp	Thr	Ser	Cys	Glu	Thr	Lys	Gly	Leu	Val	Lys	Val	Gln
				165					170					175	
Ala	Gly	Thr	Asn	Lys	Thr	Asp	Val	Ile	Cys	Gly	Pro	Gln	Pro	Arg	Leu
			180					185					190		
Arg	Ala	Leu	Val	Val	Val	Pro	Ile	Ile	Met	Gly	Ile	Leu	Leu	Val	Val
		195				200						205			
Leu	Leu	Val	Ser	Ala	Cys	Ile	Arg	Lys	Val	Val	Lys	Lys	Pro	Glu	Asn
	210					215					220				
Lys	Val	Met	Tyr	Gln	Asp	Pro	Val	Glu	Asp	Leu	Glu	Glu	Phe	Pro	Met
	225					230					235				240
Pro	Pro	His	Ser	Ile	Ala	Pro	Val	Gln	Glu	Thr	Leu	His	Gly	Cys	Gln
				245					250					255	
Pro	Val	Thr	Gln	Glu	Asp	Gly	Lys	Glu	Ser	Arg	Ile	Ser	Val	Gln	Glu
			260					265					270		

Arg Val  
 <210> SEQ ID NO 54  
 <211> LENGTH: 1425  
 <212> TYPE: DNA  
 <213> ORGANISM: Canis familiaris

<400> SEQUENCE: 54  
 tttttttttt ttttttttta taaatatatt acaaatttta tttagccagt cccctgctgc 60  
 tgaacagcta agtggcctcc agttgtccac tgtcacaac aatgccaca tggtctctcg 120  
 tgggtcttcc tgggctcgta gaaaccaccg tgatatacac ctcagggccc tgaatgctg 180  
 ggttggtgga tattactatc tggccccca aaagtttcat ctccatcttt aaaagcaagt 240  
 tgggaggtgg aatgggctcc aggggtgggg tggaaggttc tctgtttctg cagcacaggg 300  
 gtgcaggcag gggagaccg ccccttcag cccctccagc agctccaggc tctccagcca 360  
 cgcgcccaact ctcccacgct gtcacactcc tgggcacacg ctgcctcaca ctctctctg 420  
 cacggagatg cggtctcttt tgccgtcttc ctgggtgacg ggctggcacc catgtaaggt 480  
 ctcttgcaac ggagcaatgg agtgccgggg cataggaat tcctccaagt cctccacagg 540  
 gtcctgatac ataaccttat tctctggctt cttgaccacc tttcggatgc aggcagacac 600  
 caacaggaca acaagcagga tccccataat gatggggacc accactaggg ctcttaaccg 660  
 aggctgggga ccacagataa catcagtctt gttagttccc gcctgaacct tcaccaggcc 720  
 tttgttttca cagcttctgc aagggtgaca cttttccaaa gcagaagaca cattggagaa 780  
 gaagccgatg gggcagggat cgcagatggt atcagaaatc cctgtagcga tctgtttgac 840  
 tcccaggcca ggggggcaca ggctgtgcat ggtgcagetc tcacaggcag cgttggtaca 900  
 atgcagacct tcatcgcgat tgcaagtggg gtctgtttct gacgtgccct ccttctcgac 960  
 atggagccct aggttggggg cgcagtatct gtgctggtga cagtgtctct ctgcgttcca 1020  
 agtgtctagg aattgcctcg tttggcaacg agtgcaatcc gtgtcaatgg tatgtaggca 1080  
 gtcattcacc agtttctctc ctgggtggga catattacag cactgactgt ctactaggtta 1140

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ttgcttttct ctgcatgcag tgcgtgggtc tgggtagacg gtggtcaaca aggagcccca 1200
gaagagacag cgcagaggca ggagaacat ggcgagggtga atagcaggca gcggagttag 1260
ggcgcgggga tgtctttagt aactccccag cccttgcccc cgcccccccc gcccaggaga 1320
tgggcgggggt ctteggggac caatcgtggc eggcttcgtt gggcagggcg gagctcctgg 1380
agacccttag cgccgggagt tcccctgaat attcccggga gtcta 1425

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<210> SEQ ID NO 55
<211> LENGTH: 822
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

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<400> SEQUENCE: 55

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atggttctcc tgcctctgag ctgtctcttc tggggctcct tgttgaccac cgtctacca 60
gaaccacgca ctgcatgcag agaaaagcaa tacctagtag acagtcaagt ctgtaatatg 120
tgcccaccag gagagaaact ggtgaatgac tgcctacata ccattgacac ggaatgcact 180
cgttgccaaa caggcgaatt cctagacact tggaacgcag agagacactg tcaccagcac 240
aaatactgag accccaacct agggctccat gtcgagaagg agggcacgtc agaaacagac 300
accacttgca catgcatgta aggtctgcat tgtaccaacg ctgcctgtga gagctgcacc 360
atgcacagcc tgtgcccccc tggcctggga gtcaaacaga tcgctacagg gatttctgat 420
accatctgag atccctgccc catcggtctc ttctccaatg tgtcttctgc tttgaaaag 480
tgtcacccct ggacaagctg tgaaacccaa ggccctgtga aggttcaggc gggaaactaac 540
aagactgatg ttatctgtgg tccccagcct eggtaagag ccctagtggg ggtcccctc 600
attatgggga tcctgcttgt tgtctgttg gtgtctgcct gcacccgaaa ggtggtaag 660
aagccagaga ataaggttat gtatcaggac cctgtggagg acttgagga atttcctatg 720
ccccgcact ccattgctcc ggtgcaagag acctacatg ggtgccagcc cgtcaccag 780
gaggacggca aagagagccg catctccgtg caggagagag tg 822

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<210> SEQ ID NO 56
<211> LENGTH: 822
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

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<400> SEQUENCE: 56

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cactctctcc tgcacggaga tgcggctctc tttgcccctc tcctgggtga cgggctggca 60
cccatgtaag gtctcttgca ccggagcaat ggagtgcggg ggcataggaa attcctccaa 120
gtctccaca gggctctgat acataacctt attctctggc ttcttgacca cctttcggat 180
gcaggcagac accaacagga caacaagcag gatccccata atgatgggga ccaccactag 240
ggctcttaac cgaggctggg gaccacagat aacatcagtc ttgttagttc ccgctgaac 300
cttcaccagg cctttggttt cacagcttgt ccaagggtga cacttttcca aagcagaaga 360
cacattggag aagaagccga tggggcaggg atcgcagatg gtatcagaaa tcctgtgagc 420
gatctgtttg actcccagc caggggggca caggctgtgc atggtgcagc tctcacaggc 480
agcgttggtg caatgcagac cttcatcgca tgtgcaagtg gtgtctgttt ctgacgtgcc 540
ctcctctctg acatggagcc ctaggttggg gtcgcagtat ttgtgctggg gacagtgtct 600
ctctgcgttc caagtgtcta ggaattcgcc tgtttggcaa cgagtgcatt ccgtgtcaat 660
ggatgtagg cagtcattca ccagtttctc tcctgggtggg cacatattac agcactgact 720

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gtctactagg tattgctttt ctctgcatgc agtgcgtggt tctgggtaga cggtggtcaa 780
caaggagccc cagaagagac agcgcagagg caggagaacc at 822

<210> SEQ ID NO 57
<211> LENGTH: 765
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (1)..(765)

<400> SEQUENCE: 57

cca gaa cca cgc act gca tgc aga gaa aag caa tac cta gta gac agt 48
Pro Glu Pro Arg Thr Ala Cys Arg Glu Lys Gln Tyr Leu Val Asp Ser
1 5 10 15

cag tgc tgt aat atg tgc cca cca gga gag aaa ctg gtg aat gac tgc 96
Gln Cys Cys Asn Met Cys Pro Pro Gly Glu Lys Leu Val Asn Asp Cys
20 25 30

cta cat acc att gac acg gaa tgc act cgt tgc caa aca ggc gaa ttc 144
Leu His Thr Ile Asp Thr Glu Cys Thr Arg Cys Gln Thr Gly Glu Phe
35 40 45

cta gac act tgg aac gca gag aga cac tgt cac cag cac aaa tac tgc 192
Leu Asp Thr Trp Asn Ala Glu Arg His Cys His Gln His Lys Tyr Cys
50 55 60

gac ccc aac cta ggg ctc cat gtc gag aag gag ggc acg tca gaa aca 240
Asp Pro Asn Leu Gly Leu His Val Glu Lys Glu Gly Thr Ser Glu Thr
65 70 75 80

gac acc act tgc aca tgc gat gaa ggt ctg cat tgt acc aac gct gcc 288
Asp Thr Thr Cys Thr Cys Asp Glu Gly Leu His Cys Thr Asn Ala Ala
85 90 95

tgt gag agc tgc acc atg cac agc ctg tgc ccc cct ggc ctg gga gtc 336
Cys Glu Ser Cys Thr Met His Ser Leu Cys Pro Pro Gly Leu Gly Val
100 105 110

aaa cag atc gct aca ggg att tct gat acc atc tgc gat ccc tgc ccc 384
Lys Gln Ile Ala Thr Gly Ile Ser Asp Thr Ile Cys Asp Pro Cys Pro
115 120 125

atc ggc ttc ttc tcc aat gtg tct tct gct ttg gaa aag tgt cac cct 432
Ile Gly Phe Phe Ser Asn Val Ser Ser Ala Leu Glu Lys Cys His Pro
130 135 140

tgg aca agc tgt gaa acc aaa ggc ctg gtg aag gtt cag gcg gga act 480
Trp Thr Ser Cys Glu Thr Lys Gly Leu Val Lys Val Gln Ala Gly Thr
145 150 155 160

aac aag act gat gtt atc tgt ggt ccc cag cct cgg tta aga gcc cta 528
Asn Lys Thr Asp Val Ile Cys Gly Pro Gln Pro Arg Leu Arg Ala Leu
165 170 175

gtg gtg gtc ccc atc att atg ggg atc ctg ctt gtt gtc ctg ttg gtg 576
Val Val Val Pro Ile Ile Met Gly Ile Leu Leu Val Val Leu Leu Val
180 185 190

tct gcc tgc atc cga aag gtg gtc aag aag cca gag aat aag gtt atg 624
Ser Ala Cys Ile Arg Lys Val Val Lys Lys Pro Glu Asn Lys Val Met
195 200 205

tat cag gac cct gtg gag gac ttg gag gaa ttt cct atg ccc ccg cac 672
Tyr Gln Asp Pro Val Glu Asp Leu Glu Glu Phe Pro Met Pro Pro His
210 215 220

tcc att gct ccg gtg caa gag acc tta cat ggg tgc cag ccc gtc acc 720
Ser Ile Ala Pro Val Gln Glu Thr Leu His Gly Cys Gln Pro Val Thr
225 230 235 240

cag gag gac ggc aaa gag agc cgc atc tcc gtg cag gag aga gtg 765
Gln Glu Asp Gly Lys Glu Ser Arg Ile Ser Val Gln Glu Arg Val
245 250 255

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<210> SEQ ID NO 58
<211> LENGTH: 255
<212> TYPE: PRT
<213> ORGANISM: Canis familiaris

<400> SEQUENCE: 58
Pro Glu Pro Arg Thr Ala Cys Arg Glu Lys Gln Tyr Leu Val Asp Ser
  1                               5                               10                               15
Gln Cys Cys Asn Met Cys Pro Pro Gly Glu Lys Leu Val Asn Asp Cys
  20                               25                               30
Leu His Thr Ile Asp Thr Glu Cys Thr Arg Cys Gln Thr Gly Glu Phe
  35                               40                               45
Leu Asp Thr Trp Asn Ala Glu Arg His Cys His Gln His Lys Tyr Cys
  50                               55                               60
Asp Pro Asn Leu Gly Leu His Val Glu Lys Glu Gly Thr Ser Glu Thr
  65                               70                               75                               80
Asp Thr Thr Cys Thr Cys Asp Glu Gly Leu His Cys Thr Asn Ala Ala
  85                               90                               95
Cys Glu Ser Cys Thr Met His Ser Leu Cys Pro Pro Gly Leu Gly Val
  100                              105                              110
Lys Gln Ile Ala Thr Gly Ile Ser Asp Thr Ile Cys Asp Pro Cys Pro
  115                              120                              125
Ile Gly Phe Phe Ser Asn Val Ser Ser Ala Leu Glu Lys Cys His Pro
  130                              135                              140
Trp Thr Ser Cys Glu Thr Lys Gly Leu Val Lys Val Gln Ala Gly Thr
  145                              150                              155                              160
Asn Lys Thr Asp Val Ile Cys Gly Pro Gln Pro Arg Leu Arg Ala Leu
  165                              170                              175
Val Val Val Pro Ile Ile Met Gly Ile Leu Leu Val Val Leu Leu Val
  180                              185                              190
Ser Ala Cys Ile Arg Lys Val Val Lys Lys Pro Glu Asn Lys Val Met
  195                              200                              205
Tyr Gln Asp Pro Val Glu Asp Leu Glu Glu Phe Pro Met Pro Pro His
  210                              215                              220
Ser Ile Ala Pro Val Gln Glu Thr Leu His Gly Cys Gln Pro Val Thr
  225                              230                              235                              240
Gln Glu Asp Gly Lys Glu Ser Arg Ile Ser Val Gln Glu Arg Val
  245                              250                              255

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<210> SEQ ID NO 59
<211> LENGTH: 765
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

<400> SEQUENCE: 59
cactctctcc tgcacggaga tgcggctctc tttgccgtcc tcctgggtga cgggctggca    60
cccatgtaag gtctcttgca cggagcaat ggagtgcggg ggcataggaa attcctccaa    120
gtctccaca gggctctgat acataacctt attctctggc ttcttgacca cctttcggat    180
gcaggcagac accaacagga caacaagcag gatccccata atgatgggga ccaccactag    240
ggctcttaac cgaggctggg gaccacagat aacatcagtc ttgttagttc cgectgaac    300
cttcaccagg cctttggttt cacagcttgt ccaagggtga cacttttcca aagcagaaga    360
cacattggag aagaagccga tggggcaggg atcgagatg gtatcagaaa tcctgtagc    420
gatctgtttg actcccagc caggggggca caggctgtgc atggtgcagc tctcacaggc    480

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agcgttggta caatgcagac cttcatcgca tgtgcaagtg gtgtctgttt ctgacgtgcc 540
ctccttctcg acatggagcc ctaggttggg gtcgcagtat ttgtgctggt gacagtgtct 600
ctctgcgttc caagtgtcta ggaattcgcc tgtttggcaa cgagtgcatt ccgtgtcaat 660
ggtatgtagg cagtcattca ccagtttctc tcttggtggg cacatattac agcactgact 720
gtctactagg tattgctttt ctctgcatgc agtgcgtggt tctgg 765

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<210> SEQ ID NO 60
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Felis catus
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (1)..(336)

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<400> SEQUENCE: 60

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aat gtg tca tct gct tcg gaa aag tgt cac cct tgg acg agg tgt gag 48
Asn Val Ser Ser Ala Ser Glu Lys Cys His Pro Trp Thr Arg Cys Glu
 1 5 10 15
acc aaa ggc ctg gtg gag ctt cag gcg ggg acc aac aag acg gat gcc 96
Thr Lys Gly Leu Val Glu Leu Gln Ala Gly Thr Asn Lys Thr Asp Ala
 20 25 30
gtc tgc ggt ttc cag gat cgg ata aga gcc ctg gtg gtg atc ccc atc 144
Val Cys Gly Phe Gln Asp Arg Ile Arg Ala Leu Val Val Ile Pro Ile
 35 40 45
acg atg gtg gtc ctg ctt gct gtc ttg ttg gtg tct gcg tat atc aga 192
Thr Met Val Val Leu Leu Ala Val Leu Leu Val Ser Ala Tyr Ile Arg
 50 55 60
aag gtg acc aag aag cca gag aat aag gtc ctc cag cct aag gct gtg 240
Lys Val Thr Lys Lys Pro Glu Asn Lys Val Leu Gln Pro Lys Ala Val
 65 70 75 80
tcg cag gac cct gtg gag gac ttg gag gtc ctt cct gtc ccc ctc cac 288
Ser Gln Asp Pro Val Glu Asp Leu Glu Val Leu Pro Val Pro Leu His
 85 90 95
ccc att gct ccg gtg cag gag acc tta cac ggg tgc cag ccg gtc acc 336
Pro Ile Ala Pro Val Gln Glu Thr Leu His Gly Cys Gln Pro Val Thr
 100 105 110

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<210> SEQ ID NO 61
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Felis catus

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<400> SEQUENCE: 61

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

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<210> SEQ ID NO 62
<211> LENGTH: 336
<212> TYPE: DNA
<213> ORGANISM: Felis catus

<400> SEQUENCE: 62
ggtgaccggc tggcaccctg gtaaggtctc ctgcaccgga gcaatggggg ggaggggggac   60
aggaaggacc tccaagtctc ccacagggtc ctgcgacaca gccttaggct ggaggacctt   120
attctctggc ttcttggtea cctttctgat atacgcagac accaacaaga cagcaagcag   180
gaccaccatc gtgatgggga tcaccaccag ggctcttata cgatcctgga aaccgcagac   240
ggcaccgctc ttgttggctc ccgcctgaag ctccaccagg cctttggctc cacacctcgt   300
ccaaggggta cacttttccg aagcagatga cacatt                                     336

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<210> SEQ ID NO 63
<211> LENGTH: 390
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

<400> SEQUENCE: 63
ataagtgagg ctagttagtaa cccagcgtcc gttctgcggt gggcgccaaa aggggtactac   60
accataagca gcaacctggt gagcctcgag aatgggaaac agttggccgt gaaaagacaa   120
ggactctatt acgtctatgc ccaagtcacc ttctgctcca atcgggcagc ttcgagtcaa   180
gtcccgttcg tcgccagcct atgcctccat tccccgagtg gaacggagag agtcttactc   240
cgcgcccgga gctcccggcg ctgctccaaa ccttgcggcc aacagtccat ccacttggga   300
ggagtatttg aattgcatcc aggtgcttcg gtgttcgtca acgtgactga tccaagccaa   360
gtgagccacg ggaccggctt cacgtctttt                                     390

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<210> SEQ ID NO 64
<211> LENGTH: 1878
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (284)..(1063)

<400> SEQUENCE: 64
aatgatgga agaagaaact tgtttcttct ttactaacia aagggaagc ctggaagtga   60
atgatatggg tataattaa aaaaaaaaaa aaaaaaaaaa aaaaccttta cgtaactttt   120
tttctgggga gagaagacta cgaagcacat tttccaggaa gtgtgggctg caacgattgt   180
gctgctctaa ctaactctga gtaaggtggc cactttgaca gtgttttcat gctgcctctg   240
ccaccttctc ggtctgaaga tatcatttca actctaacac agc atg atc gaa aca   295
Met Ile Glu Thr
1
tat agc caa act gct ccc cga tct gtg gcc act gga cca ccc gtc agt   343
Tyr Ser Gln Thr Ala Pro Arg Ser Val Ala Thr Gly Pro Pro Val Ser
5 10 15 20
atg aaa att ttt atg tat ttg ctt act gtt ttt ctc atc acc cag atg   391
Met Lys Ile Phe Met Tyr Leu Leu Thr Val Phe Leu Ile Thr Gln Met
25 30 35
att gga tcg gca ctc ttt gct gta tat ctt cac aga aga ttg gac aag   439
Ile Gly Ser Ala Leu Phe Ala Val Tyr Leu His Arg Arg Leu Asp Lys
40 45 50
ata gaa gat gaa agg aat ctt tat gaa gat ttt gtg ttc atg aaa acg   487
Ile Glu Asp Glu Arg Asn Leu Tyr Glu Asp Phe Val Phe Met Lys Thr

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55	60	65	
tta cag aaa tgc aac aaa ggg gag ggg tcc ttg tcc tta ctg aac tgt			535
Leu Gln Lys Cys Asn Lys Gly Glu Gly Ser Leu Ser Leu Leu Asn Cys			
70	75	80	
gag gaa att aaa agc caa ttt gaa gcc ttt ctc aag gag ata atg cta			583
Glu Glu Ile Lys Ser Gln Phe Glu Ala Phe Leu Lys Glu Ile Met Leu			
85	90	95	100
aac aac gaa atg aag aaa gaa gaa aac att gca atg caa aaa ggt gat			631
Asn Asn Glu Met Lys Lys Glu Glu Asn Ile Ala Met Gln Lys Gly Asp			
105	110	115	
cag gat cct cga att gca gcc cat gtc ata agt gag gct agt agt aac			679
Gln Asp Pro Arg Ile Ala Ala His Val Ile Ser Glu Ala Ser Ser Asn			
120	125	130	
cca gcg tcc gtt ctg cgg tgg gcg cca aaa ggg tac tac acc ata agc			727
Pro Ala Ser Val Leu Arg Trp Ala Pro Lys Gly Tyr Tyr Thr Ile Ser			
135	140	145	
agc aac ctg gtg agc ctc gag aat ggg aaa cag ttg gcc gtg aaa aga			775
Ser Asn Leu Val Ser Leu Glu Asn Gly Lys Gln Leu Ala Val Lys Arg			
150	155	160	
caa gga ctc tat tac gtc tat gcc caa gtc acc ttc tgc tcc aat cgg			823
Gln Gly Leu Tyr Tyr Val Tyr Ala Gln Val Thr Phe Cys Ser Asn Arg			
165	170	175	180
gca gct tcg agt caa gct ccg ttc gtc gcc agc cta tgc ctc cat tcc			871
Ala Ala Ser Ser Gln Ala Pro Phe Val Ala Ser Leu Cys Leu His Ser			
185	190	195	
ccg agt gga acg gag aga gtc tta ctc cgc gcc gcg agc tcc cgc ggc			919
Pro Ser Gly Thr Glu Arg Val Leu Leu Arg Ala Ala Ser Ser Arg Gly			
200	205	210	
tcg tcc aaa cct tgc ggc caa cag tcc atc cac ttg gga gga gta ttt			967
Ser Ser Lys Pro Cys Gly Gln Gln Ser Ile His Leu Gly Gly Val Phe			
215	220	225	
gaa ttg cat cca ggt gct tcg gtg ttc gtc aac gtg act gat cca agc			1015
Glu Leu His Pro Gly Ala Ser Val Phe Val Asn Val Thr Asp Pro Ser			
230	235	240	
caa gtg agc cac ggg acc ggc ttc acg tct ttt ggc tta ctc aaa ctc			1063
Gln Val Ser His Gly Thr Gly Phe Thr Ser Phe Gly Leu Leu Lys Leu			
245	250	255	260
tgagtgtggtg cacctcacag gctgcagctc agctcctggt ggtggtcttc gtaatacggc			1123
cgagcagtta agaccaccac cctgttgtaa ctgcctatatt ataaccctag gatcctctc			1183
gtggagaact atttattata caccocaggg cgtggagggc tgcaagaagg gaatgacagg			1243
gcgggggcag cgccaacagg ccccggtcgg taagagttga tattctgga gcagccgccc			1303
cactgatgca gacatccaga gagtcccatg aaaaagacga gactattatg cacagattga			1363
atcctcagta aacggcagat aattagtcca gtttcgtttt gtttctttgc atgcagtgtc			1423
tttcaactgga gaatgtactc gatttccccg cgaagatgct gaagggaac agggagcctc			1483
agctcacagt cagttacggt tgaccogggg tocccogggg cccgatggag gggacagget			1543
ccagaaagtc tgatggcgcg gagaactgga aaacctgccc cccaccagcc accctgacac			1603
tcattctctc cctcctccgc cccctcccc ccacagtcag gctggtgcta atcggttatc			1663
ttatttcaac cctgttgctc ctccaccagt gtaggcggga ggagagagca gaggctgccc			1723
actcctcctc ctgaaatgac tgtatttaaa ggaaatctct cctacctacc tgcagtctcc			1783
attgtttcca gagtgaactt gtgattatct tgttatttat tttttgaata ataaagcgc			1843
cttaacgtta aaaaaaaaaa aaaaaaaaaa aaaaa			1878

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<210> SEQ ID NO 65
<211> LENGTH: 260
<212> TYPE: PRT
<213> ORGANISM: Canis familiaris

<400> SEQUENCE: 65

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

Leu Leu Lys Leu
260

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<210> SEQ ID NO 66
<211> LENGTH: 1878
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

<400> SEQUENCE: 66

tttttttttt tttttttttt ttttttaacg ttaagggcgc tttattattc aaaaaataaa    60
taacaagata atcacaagtt cactctgtaa acaatggaga ctgcaggtag gtaggagaga    120
tttctttaa atacagtc atcaggagga ggagtgggca gcctctgctc tctctccc    180
cctacactgg tggagaggca acagggttga aataagataa cggattagca acagcctgac    240
tgtgggggga ggggggcgga ggaggagag aatgagtgtc aggggtgctg gtggggcag    300
ggttttccag ttctccgcgc catcagactt tctggagcct gtcccctcca tcggggcccc    360
ggggaccccc ggtcaacctg aactgactgt gagctgaggc tcctgtgtgc ccttcagcat    420

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cttcgcgggg aaatcgagta cattctccag tgaagacac tgcagcaaa gaaacaaaac 480
gaaactggac taattatctg ccgtttactg aggattcaat ctgtgcataa tagtctcgtc 540
tttttcatgg gactctctgg atgtctgcat cagtggggcg gctgcttcca gaatatcaac 600
tcttacgcac cggggcctgt tggcgctgcc cccgccctgt cattcccttc ttgcagccct 660
ccacgcctgg ggggtgataa taaatagttc tccacgagga ggatcctagg gttataaata 720
ggcagttcaa caggggtggt ggtcttaact gctcggccgt attacgaaga ccaccaacag 780
gagctgagct gcagcctgtg aggtgccagc actcagagtt tgagtaagcc aaaagacgtg 840
aagccggtcc cgtggctcac ttggcttggg tcagtcacgt tgacgaacac cgaagcacct 900
ggatgcaatt caaatactcc tcccagtggt atggactggt ggccgcaagg tttggacgag 960
ccgcggggagc tcgcggcgcg gagtaagact ctctccgttc cactcgggga atggaggcat 1020
aggctggcga cgaacgggagc ttgactcga gctgcccgat tggagcagaa ggtgacttgg 1080
gcatagacgt aatagagtcc ttgtcttttc acggccaact gtttccatt ctcgaggctc 1140
accagttgc tgcctatggt gtagtacct tttggcgccc accgcagaac ggacgctggg 1200
ttactactag cctcacttat gacatgggct gcaattcgag gatcctgac acctttttgc 1260
attgcaatgt tttctcttt ctctatttcg ttgtttagca ttatctcctt gagaaaggct 1320
tcaaattggc ttttaatttc ctcacagttc agtaaggaca aggaccctc ccctttgttg 1380
catttctgta acgttttcat gaacacaaaa tcttcataaa gattcctttc atcttctatc 1440
ttgtccaatc ttctgtgaag atatacagca aagagtgccg atccaatcat ctgggtgatg 1500
agaaaaacag taagcaata cataaaaatt ttcatactga cgggtggtcc agtggccaca 1560
gatcggggag cagtttgctt atatgtttcg atcatgctgt gttagagttg aatgatatc 1620
ttcagaccga gaaggtggca gaggcagcat gaaaacactg tcaaagtggc caccttactc 1680
aggattagtt aagagcgcac aatcgttgca gccacactt cctggaaaat gtgcttcgta 1740
gtcttctctc ccagcaaaaa aagttacgta aaggtttttt tttttttttt tttttttttt 1800
taattatacc catatcatc acttccagcg tttccctttt gttagtaaag aagaaacaag 1860
tttcttcttc catacatt 1878

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&lt;210&gt; SEQ ID NO 67

&lt;211&gt; LENGTH: 780

&lt;212&gt; TYPE: DNA

<213> ORGANISM: *Canis familiaris*

&lt;400&gt; SEQUENCE: 67

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atgatcgaaa catatagcca aactgctccc cgatctgtgg ccaactggacc acccgtcagt 60
atgaaaaatt ttatgtattt gcttactggt tttctcatca ccagatgat tggatcggca 120
ctctttgctg tatatcttca cagaagattg gacaagatag aagatgaaag gaatctttat 180
gaagattttg tgttcatgaa aacgttacag aatgcaaca aaggggaggg gtccttgtcc 240
ttactgaact gtgagaaaat taaaagccaa tttgaagcct ttctcaagga gataatgcta 300
aacaacgaaa tgaagaaaga agaaaacatt gcaatgcaaa aaggtgatca ggatcctcga 360
attgcagccc atgtcataag tgaggctagt agtaaccag cgtccgttct gcgggtggcg 420
ccaaaagggg actacaccat aagcagcaac ctggtgagcc tcgagaatgg gaaacagttg 480
gccgtgaaaa gacaaggact ctattacgtc tatgccaag tcacctctg ctccaatcg 540
gcagcttcga gtcaagctcc gttcgtcgcc agcctatgcc tccattcccc gagtgaacg 600

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gagagagtct tactccgcgc cgcgagctcc cgcggctcgt ccaaaccttg cggccaacag 660
tccatccact tgggaggagt atttgaattg catccaggtg cttcgggtgtt cgtcaacgtg 720
actgatccaa gccaagtgag ccacgggacc ggcttcacgt cttttggctt actcaaactc 780

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<210> SEQ ID NO 68
<211> LENGTH: 780
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

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<400> SEQUENCE: 68

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gagtttgagt aagccaaaag acgtgaagcc ggtcccgtgg ctcacttggc ttggatcagt 60
cacgttgacg aacaccgaag cacctggatg caattcaaat actcctccca agtggatgga 120
ctgttgcccg caaggtttgg acgagccgcg ggagctcgcg gcgaggagta agactctctc 180
cgttccactc ggggaatgga ggcataggct ggcgacgaac ggagcttgac tcgaagctgc 240
ccgattggag cagaaggtga cttgggcata gacgtaatag agtccttgtc ttttcacggc 300
caactgtttc ccattctcga ggctcaccag gttgctgctt atggtgtagt acccttttgg 360
cgcccaccgc agaacggacg ctgggttact actagcctca cttatgacat gggtgcgaat 420
tegaggatcc tgatecactt tttgcattgc aatgttttct tctttcttca tttcgttgtt 480
tagcattatc tccttgagaa aggcttcaaa ttggctttta atttctcac agttcagtaa 540
ggacaaggac ccctcccctt tgttgcattt ctgtaacggt ttcatgaaca caaaatcttc 600
ataaagattc ctttcatctt ctatcttgtc caatcttctg tgaagatata cagcaaagag 660
tgccgatcca atcatctggg tgatgagaaa aacagtaagc aaatacataa aaattttcat 720
actgacgggt ggtccagtgg ccacagatcg gggagcagtt tggctatatg tttcgatcat 780

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<210> SEQ ID NO 69
<211> LENGTH: 633
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (1)..(633)

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<400> SEQUENCE: 69

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```

ttg gac aag ata gaa gat gaa agg aat ctt tat gaa gat ttt gtg ttc 48
Leu Asp Lys Ile Glu Asp Glu Arg Asn Leu Tyr Glu Asp Phe Val Phe
1 5 10 15
atg aaa acg tta cag aaa tgc aac aaa ggg gag ggg tcc ttg tcc tta 96
Met Lys Thr Leu Gln Lys Cys Asn Lys Gly Glu Gly Ser Leu Ser Leu
20 25 30
ctg aac tgt gag gaa att aaa agc caa ttt gaa gcc ttt ctc aag gag 144
Leu Asn Cys Glu Glu Ile Lys Ser Gln Phe Glu Ala Phe Leu Lys Glu
35 40 45
ata atg cta aac aac gaa atg aag aaa gaa gaa aac att gca atg caa 192
Ile Met Leu Asn Asn Glu Met Lys Lys Glu Glu Asn Ile Ala Met Gln
50 55 60
aaa ggt gat cag gat cct cga att gca gcc cat gtc ata agt gag gct 240
Lys Gly Asp Gln Asp Pro Arg Ile Ala Ala His Val Ile Ser Glu Ala
65 70 75 80
agt agt aac cca gcg tcc gtt ctg cgg tgg gcg cca aaa ggg tac tac 288
Ser Ser Asn Pro Ala Ser Val Leu Arg Trp Ala Pro Lys Gly Tyr Tyr
85 90 95
acc ata agc agc aac ctg gtg agc ctc gag aat ggg aaa cag ttg gcc 336
Thr Ile Ser Ser Asn Leu Val Ser Leu Glu Asn Gly Lys Gln Leu Ala
100 105 110

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gtg aaa aga caa gga ctc tat tac gtc tat gcc caa gtc acc ttc tgc	384
Val Lys Arg Gln Gly Leu Tyr Tyr Val Tyr Ala Gln Val Thr Phe Cys	
115 120 125	
tcc aat cgg gca gct tcg agt caa gct cgg ttc gtc gcc agc cta tgc	432
Ser Asn Arg Ala Ala Ser Ser Gln Ala Pro Phe Val Ala Ser Leu Cys	
130 135 140	
ctc cat tcc cgg agt gga acg gag aga gtc tta ctc cgc gcc gcg agc	480
Leu His Ser Pro Ser Gly Thr Glu Arg Val Leu Leu Arg Ala Ala Ser	
145 150 155 160	
tcc cgc ggc tcg tcc aaa cct tgc ggc caa cag tcc atc cac ttg gga	528
Ser Arg Gly Ser Ser Lys Pro Cys Gly Gln Gln Ser Ile His Leu Gly	
165 170 175	
gga gta ttt gaa ttg cat cca ggt gct tcg gtg ttc gtc aac gtg act	576
Gly Val Phe Glu Leu His Pro Gly Ala Ser Val Phe Val Asn Val Thr	
180 185 190	
gat cca agc caa gtg agc cac ggg acc ggc ttc acg tct ttt ggc tta	624
Asp Pro Ser Gln Val Ser His Gly Thr Gly Phe Thr Ser Phe Gly Leu	
195 200 205	
ctc aaa ctc	633
Leu Lys Leu	
210	

&lt;210&gt; SEQ ID NO 70

&lt;211&gt; LENGTH: 211

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Canis familiaris

&lt;400&gt; SEQUENCE: 70

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

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<210> SEQ ID NO 71
<211> LENGTH: 633
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

<400> SEQUENCE: 71
gagtttgagt aagccaaaag acgtgaagcc ggtcccctgg ctcacttggc ttggatcagt      60
cacgttgacg aacaccgaag cacctggatg caattcaaat actcctccca agtggatgga      120
ctgttggccg caaggtttgg acgagccgcg ggagctcgcg gcgaggagta agactctctc      180
cgttccactc ggggaatgga ggcataggct ggcgacgaac ggagcttgac tcgaagctgc      240
ccgattggag cagaagtgta cttgggcata gacgtaatag agtccttgtc ttttcacggc      300
caactgtttc ccattctcga ggctcaccag gttgctgctt atggtgtagt acccttttgg      360
cgcccaccgc agaacggagc ctgggttact actagcctca cttatgacat gggctgcaat      420
tcgaggatcc tgatcacctt tttgcattgc aatgttttct tctttcttca tttcgttgtt      480
tagcattatc tccttgagaa aggcttcaaa ttggctttta attcctcac agttcagtaa      540
ggacaaggac cctcccctt tgttgcattt ctgtaacggt ttcatagaaca caaaatcttc      600
ataaagatcc ctttcatctt ctatcttctc caa                                     633

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<210> SEQ ID NO 72
<211> LENGTH: 885
<212> TYPE: DNA
<213> ORGANISM: Felis catus
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (29)..(808)

<400> SEQUENCE: 72
gaagatacca tttcaacttt aacacagc atg atc gaa aca tat agc caa act      52
                Met Ile Glu Thr Tyr Ser Gln Thr
                1                               5

gct ccc cgc tcc gtg gcc cct gga cca ccc gtc agt atg aaa att ttt      100
Ala Pro Arg Ser Val Ala Pro Gly Pro Pro Val Ser Met Lys Ile Phe
    10                15                20

atg tat tta ctt act gtg ttt ctc atc acc cag atg att ggg tca gca      148
Met Tyr Leu Leu Thr Val Phe Leu Ile Thr Gln Met Ile Gly Ser Ala
    25                30                35                40

ctc ttt gct gtg tat ctt cac aga aga ctg gac aag ata gaa gat gaa      196
Leu Phe Ala Val Tyr Leu His Arg Arg Leu Asp Lys Ile Glu Asp Glu
    45                50                55

agg aat ctt tat gaa gat ttt gtg ttc atg aaa aca tta cag aaa tgc      244
Arg Asn Leu Tyr Glu Asp Phe Val Phe Met Lys Thr Leu Gln Lys Cys
    60                65                70

aac aaa gga gag ggg gcc tta tcc tta ctg aac tgt gag gaa att aaa      292
Asn Lys Gly Glu Gly Ala Leu Ser Leu Leu Asn Cys Glu Glu Ile Lys
    75                80                85

agc cgg ttt gaa gcc ttt ctc aag gag ata atg cta aac aaa gaa acg      340
Ser Arg Phe Glu Ala Phe Leu Lys Glu Ile Met Leu Asn Lys Glu Thr
    90                95                100

aag aaa gaa aaa aat gtt gca atg caa aaa ggc gac cag gat cct cga      388
Lys Lys Glu Lys Asn Val Ala Met Gln Lys Gly Asp Gln Asp Pro Arg
    105                110                115                120

gtt gca gca cat gtc ata agt gag gcc agc agt agc aca gcg tct gtt      436
Val Ala Ala His Val Ile Ser Glu Ala Ser Ser Ser Thr Ala Ser Val
    125                130                135

ctc cag tgg gcc ccc aaa ggc tac tac acc ata agc agc aac ttg gtg      484
Leu Gln Trp Ala Pro Lys Gly Tyr Tyr Thr Ile Ser Ser Asn Leu Val
    140                145                150

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acc ctc gag aac ggg aag cag ctg gcc gtt aaa aga caa gga ctc tat      532
Thr Leu Glu Asn Gly Lys Gln Leu Ala Val Lys Arg Gln Gly Leu Tyr
      155                      160                      165

tat atc tac gcc caa gtc acc ttc tgt tcc aat cgg gaa gct tcg agt      580
Tyr Ile Tyr Ala Gln Val Thr Phe Cys Ser Asn Arg Glu Ala Ser Ser
      170                      175                      180

caa gct ccg ttc ata gcc agc ctc tgc ctg cat tcc ccg agt gga tcc      628
Gln Ala Pro Phe Ile Ala Ser Leu Cys Leu His Ser Pro Ser Gly Ser
      185                      190                      195                      200

gag aga gtc tta ctc aga gct gca aat gcc cgc agt tcc tcc aaa ccc      676
Glu Arg Val Leu Leu Arg Ala Ala Asn Ala Arg Ser Ser Ser Lys Pro
      205                      210                      215

tgt ggg cag caa tcc att cac ttg gga gga gtc ttc gaa ctg cat cca      724
Cys Gly Gln Gln Ser Ile His Leu Gly Gly Val Phe Glu Leu His Pro
      220                      225                      230

ggt gct tcg gtg ttc gtg aac gtg act gat ccg agc caa gtg agc cac      772
Gly Ala Ser Val Phe Val Asn Val Thr Asp Pro Ser Gln Val Ser His
      235                      240                      245

ggg acg ggc ttc acg tct ttt ggc ttg ctc aaa ctc tgaacactgg      818
Gly Thr Gly Phe Thr Ser Phe Gly Leu Leu Lys Leu
      250                      255                      260

cacctcgcag gccgcgaggc ctgcaggccg cggctgagct cacgctggga gtcttcacaa      878
tacagca                                                                885

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&lt;210&gt; SEQ ID NO 73

&lt;211&gt; LENGTH: 260

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Felis catus

&lt;400&gt; SEQUENCE: 73

```

Met Ile Glu Thr Tyr Ser Gln Thr Ala Pro Arg Ser Val Ala Pro Gly
  1                      5                      10                      15

Pro Pro Val Ser Met Lys Ile Phe Met Tyr Leu Leu Thr Val Phe Leu
      20                      25                      30

Ile Thr Gln Met Ile Gly Ser Ala Leu Phe Ala Val Tyr Leu His Arg
      35                      40                      45

Arg Leu Asp Lys Ile Glu Asp Glu Arg Asn Leu Tyr Glu Asp Phe Val
      50                      55                      60

Phe Met Lys Thr Leu Gln Lys Cys Asn Lys Gly Glu Gly Ala Leu Ser
      65                      70                      75                      80

Leu Leu Asn Cys Glu Glu Ile Lys Ser Arg Phe Glu Ala Phe Leu Lys
      85                      90                      95

Glu Ile Met Leu Asn Lys Glu Thr Lys Lys Glu Lys Asn Val Ala Met
      100                      105                      110

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

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

Tyr Thr Ile Ser Ser Asn Leu Val Thr Leu Glu Asn Gly Lys Gln Leu
      145                      150                      155                      160

Ala Val Lys Arg Gln Gly Leu Tyr Tyr Ile Tyr Ala Gln Val Thr Phe
      165                      170                      175

Cys Ser Asn Arg Glu Ala Ser Ser Gln Ala Pro Phe Ile Ala Ser Leu
      180                      185                      190

Cys Leu His Ser Pro Ser Gly Ser Glu Arg Val Leu Leu Arg Ala Ala
      195                      200                      205

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Asn Ala Arg Ser Ser Ser Lys Pro Cys Gly Gln Gln Ser Ile His Leu  
 210 215 220

Gly Gly Val Phe Glu Leu His Pro Gly Ala Ser Val Phe Val Asn Val  
 225 230 235 240

Thr Asp Pro Ser Gln Val Ser His Gly Thr Gly Phe Thr Ser Phe Gly  
 245 250 255

Leu Leu Lys Leu  
 260

<210> SEQ ID NO 74  
 <211> LENGTH: 885  
 <212> TYPE: DNA  
 <213> ORGANISM: Felis catus

<400> SEQUENCE: 74

```

tgctgtatta tgaagactcc cagcgtgagc tcagccgcgg cctgcaggcc tgcgggctcg      60
cgaggtgccca gtgttcagag tttgagcaag ccaaaagacg tgaagcccgt cccgtggctc     120
acttggtctcg gatcagctcac gttcacgaac accgaagcac ctggatgcag ttcgaagact     180
cctcccaagt gaatggattg ctgccacagc ggtttgaggg aactgcgggc atttgcagct     240
ctgagtaaga ctctctcgga tccactcggg gaatgcaggc agaggctggc tatgaacgga     300
gcttgactcg aagcttcccg attggaacag aaggtgactt gggcgtagat ataataagat     360
ccttgctctt taacggccag ctgcttcccg ttctcgaggg tcaccaagtt gctgcttatg     420
gtgtagtagc ctttgggggc ccaactggaga acagacgctg tgctactgct ggcctcactt     480
atgacatgtg ctgcaactcg aggatcctgg tcgccttttt gcattgcaac atttttttct     540
ttcttcgttt ctttgtttag cattatctcc ttgagaaagg cttcaaaccg gcttttaatt     600
tcctcacagt tcagtaagga taaggcccc tctcctttgt tgcattctcg taatgttttc     660
atgaacacaa aatcttcata aagattcctt tcactctteta tcttgtccag tcttctgtga     720
agatacacag caaagagtgc tgaccaatc atctgggtga tgagaaacac agtaagtaaa     780
tacataaaaa ttttcatact gacgggtggt ccaggggcca cggagcgggg agcagtttgg     840
ctatatgttt cgatcatgct gtgttaaagt tgaaatgta tcttc                          885

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<210> SEQ ID NO 75  
 <211> LENGTH: 780  
 <212> TYPE: DNA  
 <213> ORGANISM: Felis catus

<400> SEQUENCE: 75

```

atgatcgaaa catatagcca aactgctccc cgctccgtgg cccctggacc acccgctcagt      60
atgaaaaatt ttatgtattt acttactgtg tttctcatca occagatgat tgggtcagca     120
ctctttgctg tgtatcttca cagaagactg gacaagatag aagatgaaag gaatctttat     180
gaagattttg gtttcatgaa aacattacag aaatgcaaca aaggagaggg ggccttatcc     240
ttactgaact gtgagaaaat taaaagccgg tttgaagcct ttctcaagga gataatgcta     300
aacaagaaaa cgaagaaaga aaaaaatggt gcaatgcaaa aaggcgacca ggatcctcga     360
gttgacgac atgtcataag tgaggccacg agtagcacag cgtctgttct ccagtgggcc     420
cccaaaggct actacaccat aagcagcaac ttggtgacct tcgagaacgg gaagcagctg     480
gccgttaaaa gacaaggact ctattatctc tacgccaag tcacctctg ttccaatcgg     540
gaagcttcga gtcaagctcc gttcatagcc agcctctgcc tgcattcccc gagtggatcc     600

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gagagagtct tactcagagc tgcaaatgcc cgcagttcct ccaaacctcg tgggcagcaa 660
tccattcact tgggaggagt ctctgaactg catccagggtg cttcgggtgtt cgtgaactgt 720
actgatccga gccaagttag ccacgggacg ggcttcacgt cttttggctt gctcaaactc 780

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<210> SEQ ID NO 76
<211> LENGTH: 780
<212> TYPE: DNA
<213> ORGANISM: Felis catus

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<400> SEQUENCE: 76

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gagtttgagc aagccaaaag acgtgaagcc cgtcccgtgg ctcacttggc tcggatcagt 60
cacgttcacg aacaccgaag cacctggatg cagttcgaag actcctccca agtgaatgga 120
ttgtgcccc cagggtttgg aggaactgcg ggcatattgca gctctgagta agactctctc 180
ggatccactc ggggaatgca ggcagaggct ggctatgaac ggagcttgac tcgaagcttc 240
ccgattggaa cagaagggtga cttgggcgta gatataatag agtccttgtc ttttaacggc 300
cagctgcttc ccgttctcga gggtcaccaa gttgctgctt atggtgtagt agcctttggg 360
ggcccactgg agaacagacg ctgtgctact gctggcctca cttatgacat gtgctgcaac 420
tcgaggatcc tggtegccct tttgcattgc aacatttttt tctttcttcg tttctttgtt 480
tagcattatc tccttgagaa aggcttcaaa ccggctttta atttctcac agttcagtaa 540
ggataaggcc ccctctcctt tgttgcattt ctgtaatggt ttcatgaaca caaaatcttc 600
ataaagattc ctttcatctt ctatcttgtc cagtcttctg tgaagataca cagcaaagag 660
tgctgaccca atcatctggg tgatgagaaa cacagtaagt aaatacataa aaattttcat 720
actgacgggt ggtccagggg ccacggagcg gggagcagtt tggctatatg tttcgatcat 780

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<210> SEQ ID NO 77
<211> LENGTH: 633
<212> TYPE: DNA
<213> ORGANISM: Felis catus
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (1)..(633)

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<400> SEQUENCE: 77

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ctg gac aag ata gaa gat gaa agg aat ctt tat gaa gat ttt gtg ttc 48
Leu Asp Lys Ile Glu Asp Glu Arg Asn Leu Tyr Glu Asp Phe Val Phe
1 5 10 15
atg aaa aca tta cag aaa tgc aac aaa gga gag ggg gcc tta tcc tta 96
Met Lys Thr Leu Gln Lys Cys Asn Lys Gly Glu Gly Ala Leu Ser Leu
20 25 30
ctg aac tgt gag gaa att aaa agc cgg ttt gaa gcc ttt ctc aag gag 144
Leu Asn Cys Glu Glu Ile Lys Ser Arg Phe Glu Ala Phe Leu Lys Glu
35 40 45
ata atg cta aac aaa gaa acg aag aaa gaa aaa aat gtt gca atg caa 192
Ile Met Leu Asn Lys Glu Thr Lys Lys Glu Lys Asn Val Ala Met Gln
50 55 60
aaa ggc gac cag gat cct cga gtt gca gca cat gtc ata agt gag gcc 240
Lys Gly Asp Gln Asp Pro Arg Val Ala Ala His Val Ile Ser Glu Ala
65 70 75 80
agc agt agc aca gcg tct gtt ctc cag tgg gcc ccc aaa ggc tac tac 288
Ser Ser Ser Thr Ala Ser Val Leu Gln Trp Ala Pro Lys Gly Tyr Tyr
85 90 95
acc ata agc agc aac ttg gtg acc ctc gag aac ggg aag cag ctg gcc 336
Thr Ile Ser Ser Asn Leu Val Thr Leu Glu Asn Gly Lys Gln Leu Ala
100 105 110

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gtt aaa aga caa gga ctc tat tat atc tac gcc caa gtc acc ttc tgt	384
Val Lys Arg Gln Gly Leu Tyr Tyr Ile Tyr Ala Gln Val Thr Phe Cys	
115 120 125	
tcc aat cgg gaa gct tcg agt caa gct ccg ttc ata gcc agc ctc tgc	432
Ser Asn Arg Glu Ala Ser Ser Gln Ala Pro Phe Ile Ala Ser Leu Cys	
130 135 140	
ctg cat tcc ccg agt gga tcc gag aga gtc tta ctc aga gct gca aat	480
Leu His Ser Pro Ser Gly Ser Glu Arg Val Leu Leu Arg Ala Ala Asn	
145 150 155 160	
gcc cgc agt tcc tcc aaa ccc tgt ggg cag caa tcc att cac ttg gga	528
Ala Arg Ser Ser Ser Lys Pro Cys Gly Gln Gln Ser Ile His Leu Gly	
165 170 175	
gga gtc ttc gaa ctg cat cca ggt gct tcg gtg ttc gtg aac gtg act	576
Gly Val Phe Glu Leu His Pro Gly Ala Ser Val Phe Val Asn Val Thr	
180 185 190	
gat ccg agc caa gtg agc cac ggg acg ggc ttc acg tct ttt ggc ttg	624
Asp Pro Ser Gln Val Ser His Gly Thr Gly Phe Thr Ser Phe Gly Leu	
195 200 205	
ctc aaa ctc	633
Leu Lys Leu	
210	

&lt;210&gt; SEQ ID NO 78

&lt;211&gt; LENGTH: 211

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Felis catus

&lt;400&gt; SEQUENCE: 78

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

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<210> SEQ ID NO 79
<211> LENGTH: 633
<212> TYPE: DNA
<213> ORGANISM: Felis catus

<400> SEQUENCE: 79
gagtttgagc aagccaaaag acgtgaagcc cgtcccctgg ctcacttggc tcggatcagt      60
cacgttcacg aacaccgaag cacctggatg cagttcgaag actcctccca agtgaatgga      120
ttgctgcccc cagggtttgg aggaactgcg ggcatttgca gctctgagta agactctctc      180
ggatccactc ggggaatgca ggcagaggct ggctatgaac ggagcttgac tcgaagcttc      240
ccgattggaa cagaagtgta cttgggcgta gatataatag agtccttgtc ttttaacggc      300
cagctgcttc cegtctcga gggtcaccaa gttgctgctt atggtgtagt agcctttggg      360
ggcccactgg agaacagacg ctgtgctact gctggcctca cttatgacat gtgctgcaac      420
tcgaggatcc tggctgcctt tttgcattgc aacatttttt tctttcttcg tttctttggt      480
tagcattatc tccttgagaa aggcttcaaa ccggctttta attcctcac agttcagtaa      540
ggataaggcc cctctcctt tgttgcattt ctgtaatggt ttcataaaca caaaatcttc      600
ataaagatcc ctttcatctt ctatcttgtc cag                                     633

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<210> SEQ ID NO 80
<211> LENGTH: 610
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (29)..(430)

<400> SEQUENCE: 80
caaggcaaac actgaacatt tcagagct atg aga atg ctt ctg aat ttg agt      52
                Met Arg Met Leu Leu Asn Leu Ser
                1                5

ttg cta gct ctt ggg gct gcc tat gtt tct gcc ttt gct gta gaa aat      100
Leu Leu Ala Leu Gly Ala Ala Tyr Val Ser Ala Phe Ala Val Glu Asn
    10                15                20

ccc atg aat aga ctg gtg gca gag acc ttg aca ctg ctc tcc act cat      148
Pro Met Asn Arg Leu Val Ala Glu Thr Leu Thr Leu Leu Ser Thr His
    25                30                35                40

cga act tgg ctg ata ggc gat ggg aac ctg atg att cct act cct gaa      196
Arg Thr Trp Leu Ile Gly Asp Gly Asn Leu Met Ile Pro Thr Pro Glu
    45                50                55

aat aaa aat cac caa ctg tgc att aaa gaa gtt ttt cag ggt ata gac      244
Asn Lys Asn His Gln Leu Cys Ile Lys Glu Val Phe Gln Gly Ile Asp
    60                65                70

aca ttg aag aac caa act gcc cac ggg gag gct gtg gat aaa cta ttc      292
Thr Leu Lys Asn Gln Thr Ala His Gly Glu Ala Val Asp Lys Leu Phe
    75                80                85

caa aac ttg tct tta ata aaa gaa cac ata gag cgc caa aaa aaa agg      340
Gln Asn Leu Ser Leu Ile Lys Glu His Ile Glu Arg Gln Lys Lys Arg
    90                95                100

tgt gca gga gaa aga tgg aga gtg aca aag ttc cta gac tac ctg caa      388
Cys Ala Gly Glu Arg Trp Arg Val Thr Lys Phe Leu Asp Tyr Leu Gln
    105                110                115                120

gta ttt ctt ggt gta ata aac acc gag tgg aca ccg gaa agt      430
Val Phe Leu Gly Val Ile Asn Thr Glu Trp Thr Pro Glu Ser
    125                130

tgagaacaaa ccggttatt gtagtgaag attttgaga agaatggttt tttggcgatg      490
agaatgaggg ccaaccaaca gtagggactt aatggccagt ataactaagc ttcagagaca      550

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-continued

aagtaaataat ttcagcatc ctactacttt atcacttcac acagatgaaa tatatttgag 610

<210> SEQ ID NO 81  
 <211> LENGTH: 134  
 <212> TYPE: PRT  
 <213> ORGANISM: Canis familiaris

<400> SEQUENCE: 81

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

<210> SEQ ID NO 82  
 <211> LENGTH: 610  
 <212> TYPE: DNA  
 <213> ORGANISM: Canis familiaris

<400> SEQUENCE: 82

ctcaaatata tttcatctgt gtgaagtgat aaagtagtag gatgcctgaa atatttactt 60  
 tgtctctgaa gcttagttat actggccatt aagtcctac tgttggttg ccctcattct 120  
 catcgccaaa aaaccattct tctccaaaat cttccactac aataagccgg tttgttctca 180  
 actttccgggt gtccactcgg tgtttattac accaagaaat acttgcaggt agtctaggaa 240  
 ctttgtcact ctccatcttt ctctgcaca cctttttttt tggcgcctca tgtgttcttt 300  
 tattaagac aagttttgga atagtttacc cacagcctcc ccgtgggcag tttggttctt 360  
 caatgtgtct atacctgaa aaacttcttt aatgcacagt tggtgatttt tattttcagg 420  
 agtaggaatc atcaggttcc catcgctat cagccaagtt cgatgagtgg agagcagtg 480  
 caaggtctct gccaccagtc tattcatggg attttctaca gcaaaggcag aaacataggg 540  
 agccccaaga gctagcaaac tcaaattcag aagcattctc atagctctga aatgttcagt 600  
 gtttgccttg 610

<210> SEQ ID NO 83  
 <211> LENGTH: 402  
 <212> TYPE: DNA  
 <213> ORGANISM: Canis familiaris

<400> SEQUENCE: 83

atgagaatgc ttctgaattt gagtttgcta gctcttgggg ctgcctatgt ttctgccttt 60  
 gctgtagaaa atcccatgaa tagactggtg gcagagacct tgacactgct ctccactcat 120

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cgaacttggc tgataggcga tgggaacctg atgattccta ctctgaaaa taaaaatcac 180
caactgtgca ttaaagaagt ttttcagggg atagacacat tgaagaacca aactgcccac 240
ggggaggctg tggataaact attccaaaac ttgtctttaa taaagaaca catagagcgc 300
caaaaaaaaaa ggtgtgcagg agaaagatgg agagtgacaa agttcctaga ctacctgcaa 360
gtatttcttg gtgtaataaa caccgagtgg acaccggaaa gt 402

```

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<210> SEQ ID NO 84
<211> LENGTH: 402
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

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<400> SEQUENCE: 84

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actttccggt gtccactcgg tgtttattac accaagaaat acttgcaggt agtctaggaa 60
ctttgtcact ctccatcttt ctctgcaca cctttttttt tggcgcctca tgtgttcttt 120
tattaaagac aagttttgga atagtttacc cacagcctcc ccgtgggcag tttggttctt 180
caatgtgtct atacctgaa aaacttcttt aatgcacagt tgggtatttt tattttcagg 240
agtaggaate atcaggttcc catcgctat cagccaagtt cgatgagtgg agagcagtgt 300
caaggtctct gccaccagtc tattcatggg attttctaca gcaaaggcag aaacataggc 360
agccccaaga gctagcaaac tcaaattcag aagcattctc at 402

```

```

<210> SEQ ID NO 85
<211> LENGTH: 345
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (1)..(345)

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<400> SEQUENCE: 85

```

```

ttt gct gta gaa aat ccc atg aat aga ctg gtg gca gag acc ttg aca 48
Phe Ala Val Glu Asn Pro Met Asn Arg Leu Val Ala Glu Thr Leu Thr
  1          5          10          15
ctg ctc tcc act cat cga act tgg ctg ata ggc gat ggg aac ctg atg 96
Leu Leu Ser Thr His Arg Thr Trp Leu Ile Gly Asp Gly Asn Leu Met
  20          25          30
att cct act cct gaa aat aaa aat cac caa ctg tgc att aaa gaa gtt 144
Ile Pro Thr Pro Glu Asn Lys Asn His Gln Leu Cys Ile Lys Glu Val
  35          40          45
ttt cag ggt ata gac aca ttg aag aac caa act gcc cac ggg gag gct 192
Phe Gln Gly Ile Asp Thr Leu Lys Asn Gln Thr Ala His Gly Glu Ala
  50          55          60
gtg gat aaa cta ttc caa aac ttg tct tta ata aaa gaa cac ata gag 240
Val Asp Lys Leu Phe Gln Asn Leu Ser Leu Ile Lys Glu His Ile Glu
  65          70          75          80
cgc caa aaa aaa agg tgt gca gga gaa aga tgg aga gtg aca aag ttc 288
Arg Gln Lys Lys Arg Cys Ala Gly Glu Arg Trp Arg Val Thr Lys Phe
  85          90          95
cta gac tac ctg caa gta ttt ctt ggt gta ata aac acc gag tgg aca 336
Leu Asp Tyr Leu Gln Val Phe Leu Gly Val Ile Asn Thr Glu Trp Thr
  100          105          110
ccg gaa agt 345
Pro Glu Ser
  115

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```

<210> SEQ ID NO 86
<211> LENGTH: 115

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```

<212> TYPE: PRT
<213> ORGANISM: Canis familiaris

<400> SEQUENCE: 86

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

Pro Glu Ser
          115

```

```

<210> SEQ ID NO 87
<211> LENGTH: 345
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

<400> SEQUENCE: 87

actttccggt gtccactcgg tgtttattac accaagaaat acttgcaggt agtctaggaa      60
ctttgtcact ctccatcttt ctctgcaca cctttttttt tggcgcctcta tgtgttcttt    120
tattaaagac aagttttgga atagtttata cacagcctcc ccgtgggcag tttggttctt    180
caatgtgtct atacctgaa aaacttcttt aatgcacagt tggtgatttt tattttcagg    240
agtaggaatc atcaggttcc catcgctat cagccaagtt cgatgagtgg agagcagtgt    300
caaggtctct gccaccagtc tattcatggg attttctaca gcaaaa                    345

```

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<210> SEQ ID NO 88
<211> LENGTH: 166
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

<400> SEQUENCE: 88

ctcagcttag gccagcctac gacctgctg ctcttcctc gtcctcctg cattggctct      60
gggctccatg gcgctctggt tgactgtggt cattgctctc acctgcctcg gtggccttgc    120
ctccccgagc cctgtgactc cctcccacac cctcaaggag ctctatt                    166

```

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<210> SEQ ID NO 89
<211> LENGTH: 272
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

<400> SEQUENCE: 89

tggccttgcc tccccagacc ctgtgactcc ctcccccaacc ctcaaggagc tcattgagga      60
gctggtcaac atcaccacaga atcaggcatc cctctgcaac ggcagcatgg tgtggagcgt    120
caacctgacc gccggcatgt actgcgcagc tctagaatct ctgatcaatg tctccgactg    180
cagcgccatc caaaggaccc agaggatgct gaaagcactg tgctctcaaa agccccgggc    240

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agggcagatt tccagtgaac gcagccgaga ca                               272

<210> SEQ ID NO 90
<211> LENGTH: 278
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

<400> SEQUENCE: 90
atggcgctct ggttgactgt ggtcattgct ctcacctgcc tcggtggcct tgectccccg    60
agccctgtga ctccctcccc aacctcaag gagctcattg aggagctggt caacatcacc    120
cagaatcagg catccctctg caacggcagc atggtgtgga gcgtcaacct gaccgccggc    180
atgtactgcg cagctctaga atctctgac aatgtctcgg actgcagcgc catccaagg    240
accagagga tgctgaaagc actgtgctct caaaagcc                               278

<210> SEQ ID NO 91
<211> LENGTH: 1302
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (52)..(444)

<400> SEQUENCE: 91
ctacgacctg cctgctcttc cctegctcct cctgcattgg ctctgggctc c atg gcg    57
                                     Met Ala
                                     1
ctc tgg ttg act gtg gtc att gct ctc acc tgc ctc ggt ggc ctt gcc    105
Leu Trp Leu Thr Val Val Ile Ala Leu Thr Cys Leu Gly Gly Leu Ala
      5                10                15
tcc ccg agc cct gtg act ccc tcc cca acc ctc aag gag ctc att gag    153
Ser Pro Ser Pro Val Thr Pro Ser Pro Thr Leu Lys Glu Leu Ile Glu
  20                25                30
gag ctg gtc aac atc acc cag aat cag gca tcc ctc tgc aac ggc agc    201
Glu Leu Val Asn Ile Thr Gln Asn Gln Ala Ser Leu Cys Asn Gly Ser
  35                40                45                50
atg gtg tgg agc gtc aac ctg acc gcc ggc atg tac tgc gca gct cta    249
Met Val Trp Ser Val Asn Leu Thr Ala Gly Met Tyr Cys Ala Ala Leu
      55                60                65
gaa tct ctg atc aat gtc tcc gac tgc agc gcc atc caa agg acc cag    297
Glu Ser Leu Ile Asn Val Ser Asp Cys Ser Ala Ile Gln Arg Thr Gln
      70                75                80
agg atg ctg aaa gca ctg tgc tct caa aag ccc gcg gca ggg cag att    345
Arg Met Leu Lys Ala Leu Cys Ser Gln Lys Pro Ala Ala Gly Gln Ile
      85                90                95
tcc agt gaa cgc agc cga gac acc aaa att gaa gtg atc cag ttg gtg    393
Ser Ser Glu Arg Ser Arg Asp Thr Lys Ile Glu Val Ile Gln Leu Val
  100                105                110
aaa aac ctg ctc acc tat gta agg gga gtt tat cgc cat gga aat ttc    441
Lys Asn Leu Leu Thr Tyr Val Arg Gly Val Tyr Arg His Gly Asn Phe
  115                120                125                130
aga tgaagcatga aaacttagca tccttatctg tagaccaga cctgaccact    494
Arg
taagttccag attcattttt ctttcgacg tcacaaattt cttagggagg tggggggggg    554
ggagaaccat ttctcagct gggacctcag cctgcaccgc ctgcctccat ggagctgagc    614
ccagccaccc ctgccttggt gcatggggcc cagccgggtg gccctcctcc gtctgcactt    674
catcaacgct gagggaaagc actgcatccc atgactgtcc cctcctcaga gcaaagtgca    734
gcattacagt ggaggcagat atgtgtggga ggggtcttg ctgtacctgg gaggggcaca    794

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gacatgtttc ttcttagcct tatttattat tgtgtgttat ttaaacaagt gtctttgttt 854
gtgctgggga cagggagtggt cttggagctg ggggccagc gactcgggtt tagagagtcc 914
ctgggaataa gcaactgtgtg taaaattctg ctacctcact gggatcctgg ggcgacaca 974
ggggacagga gaaagggta gagatgctgc tcttgtctgc cactcagcag ctggccctca 1034
gcccaagcagt aatttattgt ttttccttgt atttaaagtt aagaataaaa atatgttacc 1094
aaagagttaa taatatatag aagagtagcc taaaaggctg catttggtgt ggtggccag 1154
gccggggcgg gtggggggga ggggtgttgc actgaatgtg ctctttcact gactttgtca 1214
aactggaagc cagaataaaa gatggtgaca agagaaaaaa aaaaaaaaaa aaaaaaaaaa 1274
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1302

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```

<210> SEQ ID NO 92
<211> LENGTH: 131
<212> TYPE: PRT
<213> ORGANISM: Canis familiaris

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<400> SEQUENCE: 92

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```

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

```

```

<210> SEQ ID NO 93
<211> LENGTH: 1302
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

```

```

<400> SEQUENCE: 93

```

```

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt ttttctcttg 60
tcaccatctt tttttctggc ttccagtttg acaaagtcag tgaaagagca cattcagtga 120
caacaccctc cccccaccg gccccggcct ggccacacac accaaatgca gccttttagg 180
ctactcttct atatattatt aactctttga taacatattt ttttcttaa ctttaaatac 240
aaggaaaaac aataaattac tgcttggtg agggccagct gctgagtggc agacaagagc 300
agcatctctg accctttctc ctgtcccttg tgtcgcccc aggatcccag tgaggtagca 360
gaattttaca cacagtgett attcccagg actctctaaa cccgagtcac tgggccccca 420
gctccaagcc actccctgtc cccagcaca acaagacac ttgtttaaat aacacacaat 480
aataaataag gctaagaaga aacatgtctg tgccactccc aggtacagca agacccttc 540

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ccacacatat ctgcctccac tgtaatgctg cactttgctc tgaggagggg acagtcgatgg 600
gatgcagtgc tttccctcag cgttgatgaa gtgcagacgg aggagggcca cccggctggg 660
ccccatgcac caaggcaggg gtggctgggc tcagctccat ggaggcaggg ggtgcaggct 720
gaggtcccag ctgaggaaat ggttctcccc cccccccacc tcctaagaa atttgtgacg 780
tcggaaagaa aatgaatct ggaacttaag tggtcaggtc tgggtctaca gataaggatg 840
ctaagttttc atgcttcacg tgaaatttcc atggcgataa actcccctta cataggtgag 900
caggtttttc accaactgga tcaactcaat tttgggtgtc cggtctcggt cactggaaat 960
ctgcctgcc gcgggctttt gagagcacag tgctttcagc atcctctggg tcctttggat 1020
ggcgctgcag tcggagacat tgatcagaga ttctagagct gcgcagtaca tgccggcggg 1080
caggttgacg ctccacacca tgctgccgtt gcagagggat gcctgattct gggatgatgt 1140
gaccagctcc tcaatgagct ccttgagggt tggggagggg gtcacagggc tcggggaggg 1200
aaggccaccg aggcaggtga gagcaatgac cacagtcaac cagagcgcca tggagcccag 1260
agccaatgca ggaggagcga gggaagagca ggcaggtcgt ag 1302

```

```

<210> SEQ ID NO 94
<211> LENGTH: 393
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

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<400> SEQUENCE: 94

```

```

atggcgctct ggttgactgt ggtcattgct ctcacctgcc tcggtggcct tgectccccg 60
agcctgtgta ctccctcccc aacctcaag gagctcattg aggagctggg caacatcacc 120
cagaatcagg catccctctg caacggcagc atggtgtgga gcgtcaacct gaccgccggc 180
atgtactgcg cagctctaga atctctgac aatgtctccg actgcagcgc catccaaagg 240
accagagga tgctgaaagc actgtgctct caaaagcccg cggcagggca gatttccagt 300
gaacgcagcc gagacaccaa aattgaagtg atccagttgg tgaaaaacct gctcacctat 360
gtaaggggag tttatcgcca tggaaatttc aga 393

```

```

<210> SEQ ID NO 95
<211> LENGTH: 393
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

```

```

<400> SEQUENCE: 95

```

```

tctgaaattt ccatggcgat aaactcccct tacataggtg agcaggtttt tcaccaactg 60
gatcacttca attttggtgt ctggctgctg ttcactggaa atctgccctg ccgcgggctt 120
ttgagagcac agtgctttca gcatcctctg ggtcctttgg atggcgctgc agtcggagac 180
attgatcaga gattctagag ctgcgcagta catgccggcg gtcaggttga cgctccacac 240
catgctgccg ttgcagaggg atgcctgatt ctgggtgatg ttgaccagct cctcaatgag 300
ctccttgagg gttggggagg gagtcacagg gctcggggag gcaaggccac cgaggcaggt 360
gagagcaatg accacagtca accagagcgc cat 393

```

```

<210> SEQ ID NO 96
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (1)..(333)

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&lt;400&gt; SEQUENCE: 96

```

agc cct gtg act ccc tcc cca acc ctc aag gag ctc att gag gag ctg      48
Ser Pro Val Thr Pro Ser Pro Thr Leu Lys Glu Leu Ile Glu Glu Leu
  1             5             10            15

gtc aac atc acc cag aat cag gca tcc ctc tgc aac ggc agc atg gtg      96
Val Asn Ile Thr Gln Asn Gln Ala Ser Leu Cys Asn Gly Ser Met Val
             20             25             30

tgg agc gtc aac ctg acc gcc ggc atg tac tgc gca gct cta gaa tct     144
Trp Ser Val Asn Leu Thr Ala Gly Met Tyr Cys Ala Ala Leu Glu Ser
             35             40             45

ctg atc aat gtc tcc gac tgc agc gcc atc caa agg acc cag agg atg     192
Leu Ile Asn Val Ser Asp Cys Ser Ala Ile Gln Arg Thr Gln Arg Met
             50             55             60

ctg aaa gca ctg tgc tct caa aag ccc gcg gca ggg cag att tcc agt     240
Leu Lys Ala Leu Cys Ser Gln Lys Pro Ala Ala Gly Gln Ile Ser Ser
             65             70             75

gaa cgc agc cga gac acc aaa att gaa gtg atc cag ttg gtg aaa aac     288
Glu Arg Ser Arg Asp Thr Lys Ile Glu Val Ile Gln Leu Val Lys Asn
             85             90             95

ctg ctc acc tat gta agg gga gtt tat cgc cat gga aat ttc aga     333
Leu Leu Thr Tyr Val Arg Gly Val Tyr Arg His Gly Asn Phe Arg
             100            105            110

```

&lt;210&gt; SEQ ID NO 97

&lt;211&gt; LENGTH: 111

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Canis familiaris

&lt;400&gt; SEQUENCE: 97

```

Ser Pro Val Thr Pro Ser Pro Thr Leu Lys Glu Leu Ile Glu Glu Leu
  1             5             10            15

Val Asn Ile Thr Gln Asn Gln Ala Ser Leu Cys Asn Gly Ser Met Val
             20             25             30

Trp Ser Val Asn Leu Thr Ala Gly Met Tyr Cys Ala Ala Leu Glu Ser
             35             40             45

Leu Ile Asn Val Ser Asp Cys Ser Ala Ile Gln Arg Thr Gln Arg Met
             50             55             60

Leu Lys Ala Leu Cys Ser Gln Lys Pro Ala Ala Gly Gln Ile Ser Ser
             65             70             75

Glu Arg Ser Arg Asp Thr Lys Ile Glu Val Ile Gln Leu Val Lys Asn
             85             90             95

Leu Leu Thr Tyr Val Arg Gly Val Tyr Arg His Gly Asn Phe Arg
             100            105            110

```

&lt;210&gt; SEQ ID NO 98

&lt;211&gt; LENGTH: 333

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Canis familiaris

&lt;400&gt; SEQUENCE: 98

```

tctgaaattt ccatggcgat aaactcccct tacatagggtg agcaggtttt tcaccaactg      60
gatcacttca attttgggtg ctgcgctgctg ttcactggaa atctgccctg cgcgggctt     120
ttgagagcac agtgcttca gcatcctctg ggtcctttgg atggcgctgc agtcggagac     180
attgatcaga gattctagag ctgcgcagta catgccggcg gtcaggttga cgtccacac     240
catgctgcgc ttgcagaggg atgctgatt ctgggtgatg ttgaccagct cctcaatgag     300
ctccttgagg gttggggagg gattcacagg gct                                     333

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<210> SEQ ID NO 99
<211> LENGTH: 1269
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (57)..(446)

<400> SEQUENCE: 99

ccagcctaag acctgctctg tcttcctctg ctctctctgc attggctctg ggctcc atg      59
                                         Met
                                         1

gcg ctc tgg ttg act gtg gtc att gct ctc acc tgc ctc ggt ggc ctt      107
Ala Leu Trp Leu Thr Val Val Ile Ala Leu Thr Cys Leu Gly Gly Leu
      5                10                15

gcc tcc ccg agc cct gtg act ccc tcc cca acc ctc aag gag ctc att      155
Ala Ser Pro Ser Pro Val Thr Pro Ser Pro Thr Leu Lys Glu Leu Ile
      20                25                30

gag gag ctg gtc aac atc acc cag aat cag gca tcc ctc tgc aac ggc      203
Glu Glu Leu Val Asn Ile Thr Gln Asn Gln Ala Ser Leu Cys Asn Gly
      35                40                45

agc atg gtg tgg agc gtc aac ctg acc gcc ggc atg tac tgc gca gct      251
Ser Met Val Trp Ser Val Asn Leu Thr Ala Gly Met Tyr Cys Ala Ala
      50                55                60                65

cta gaa tct ctg atc aat gtc tcc gac tgc agc gcc atc caa agg acc      299
Leu Glu Ser Leu Ile Asn Val Ser Asp Cys Ser Ala Ile Gln Arg Thr
      70                75                80

cag agg atg ctg aaa gca ctg tgc tct caa aag ccc gcg gca ggg att      347
Gln Arg Met Leu Lys Ala Leu Cys Ser Gln Lys Pro Ala Ala Gly Ile
      85                90                95

tcc agt gaa cgc agc cga gac acc aaa att gaa gtg atc cag ttg gtg      395
Ser Ser Glu Arg Ser Arg Asp Thr Lys Ile Glu Val Ile Gln Leu Val
      100               105               110

aaa aac ctg ctc acc tat gta agg gga gtt tat cgc cat gga aat ttc      443
Lys Asn Leu Leu Thr Tyr Val Arg Gly Val Tyr Arg His Gly Asn Phe
      115               120               125

aga tgaagcatga aaacttagca tcttatctg tagaccaga cctgaccact      496
Arg
130

taagttccag attcattttt ctttcgacg tcacaaattt cttagggagg tggggggggg      556

ggagaaccat ttctcagct gggacctcag cctgcaccgc ctgcctccat ggagctgagc      616

ccagccaccc ctgccttggt gcatggggcc cagccgggtg gccctcctcc gtctgcactt      676

catcaacgct gagggaaagc actgcatccc atgactgtcc cctcctcaga gcaaagtgca      736

gcattacagt ggaggcagat atgtgtggga ggggttcttg ctgtacctgg gagtggcaca      796

gacatgtttc ttcttagcct tatttattat tgtgtgttat ttaacaagt gtctttgttt      856

gtgctgggga cagggagtgg cttggagctg ggggcccagt gactcgggtt tagagagtcc      916

ctgggaataa gactgtgtg taaaattctg ctacctcact gggatcctgg ggcogacaca      976

ggggacagga gaaagggtca gagatgctgc tcttgtctgc cactcagcag ctggccctca      1036

gccaaagcagt aatttattgt ttttccttgt atttaaagtt aagaaataaa atatgttatc      1096

aaagagttaa taatatatag aagagtagcc taaaaggctg catttggtgt gtgtggccag      1156

gccggggcgg gtggggggga ggggtttgtc actgaatgtg ctctttcact gactttgtca      1216

aactggaagc cagaaataaa gatggtgaca agagaaaaaa aaaaaaaaaa aaa      1269

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<210> SEQ ID NO 100
<211> LENGTH: 130
<212> TYPE: PRT
<213> ORGANISM: Canis familiaris

<400> SEQUENCE: 100

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

Phe Arg
 130

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<210> SEQ ID NO 101
<211> LENGTH: 1269
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

<400> SEQUENCE: 101

tttttttttt ttttttttcc tcttgtcacc atctttatatt ctggettcca gtttgacaaa    60
gtcagtgaaa gagcacattc agtgacaaca ccttcccccc caccgcgccc ggccctggcca    120
cacacaccaa atgcagcctt ttaggctact cttctatata ttattaactc tttgataaca    180
tattttatatt cttaacttta aatacaagga aaaacaataa attactgctt ggctgagggc    240
cagctgctga gtggcagaca agagcagcat ctctgacctt ttctcctgtc cctgtgtctg    300
gccccaggat cccagtgagg tagcagaatt ttacacacag tgcttatccc cagggactct    360
ctaaaccgga gtcaactggg ccccagctcc aagccactcc ctgtccccag cacaaacaaa    420
gacacttggt taaataacac acaataataa ataaggctaa gaagaaacat gtctgtgcca    480
ctcccaggta cagcaagacc cctccocaca catatctgcc tccactgtaa tgctgcactt    540
tgctctgagg aggggacagt catgggatgc agtgctttcc ctcagcgttg atgaagtgca    600
gacggaggag ggccaccggt ctgggcccga tgcaccaagg caggggtggc tgggctcagc    660
tccatggagg cagggcgtgc aggctgaggt cccagctgag gaaatggttc tccccccccc    720
ccacctccct aagaaatttg tgacgtcgga aagaaaaatg aatctggaac ttaagtggtc    780
aggctctgggt ctacagataa ggatgctaag ttttcatgct tcatotgaaa tttccatggc    840
gataaactcc cttacatag gtgagcaggt ttttcaccaa ctggatcact tcaattttgg    900
tgtctcggct gcgttccact gaaatccctg ccgcgggctt ttgagagcac agtgctttca    960
gcatcctctg ggtccttttg atggcgctgc agtcggagac attgatcaga gattctagag    1020
ctgcgcagta catgcggcgt gtcaggttga cgctccacac catgctgccc ttgcagaggg    1080
atgctgatt ctgggtgatg ttgaccagct cctcaatgag ctccttgagg gttggggagg    1140

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gagtcacagg gctcggggag gcaaggccac cgaggcaggt gagagcaatg accacagtca 1200
accagagcgc catggagccc agagccaatg caggaggagc gagggaagag caggcaggtc 1260
gtaggctgg                                     1269

```

```

<210> SEQ ID NO 102
<211> LENGTH: 390
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

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<400> SEQUENCE: 102

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```

atggcgctct ggttgactgt ggtcattgct ctcacctgcc tcggtggcct tgcctccccg 60
agccctgtga ctccctcccc aacctcaag gagctcattg aggagctggt caacatcacc 120
cagaatcagg catccctctg caacggcagc atggtgtgga gcgtcaacct gaccgccggc 180
atgtactgcg cagctctaga atctctgac aatgtctccg actgcagcgc catccaaagg 240
acccagagga tgctgaaagc actgtgctct caaaagcccg cggcagggat tccagtgaa 300
cgcagccgag acacaaaat tgaagtgatc cagttggtga aaaacctgct cacctatgta 360
aggggagttt atcgccatgg aaatttcaga 390

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<210> SEQ ID NO 103
<211> LENGTH: 390
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

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<400> SEQUENCE: 103

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```

tctgaaattt ccatggcgat aaactccctt tacataggtg agcaggtttt tcaccaactg 60
gatcacttca attttggtgt ctggctgctg ttcactggaa atccctgccg cgggcttttg 120
agagcacagt gctttcagca tcctctgggt cctttggatg gcgctgcagt cggagacatt 180
gatcagagat tctagagctg cgcagtacat gccggcggtc aggttgacgc tccacaccat 240
gctgccgttg cagaggggat cctgattctg ggtgatgttg accagctcct caatgagctc 300
cttgagggtt ggggagggag tcacagggct cggggaggca aggccaccga ggcaggtgag 360
agcaatgacc acagtcaacc agagcgccat 390

```

```

<210> SEQ ID NO 104
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (1)..(330)

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<400> SEQUENCE: 104

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```

agc cct gtg act ccc tcc cca acc ctc aag gag ctc att gag gag ctg 48
Ser Pro Val Thr Pro Ser Pro Thr Leu Lys Glu Leu Ile Glu Glu Leu
  1          5          10          15
gtc aac atc acc cag aat cag gca tcc ctc tgc aac ggc agc atg gtg 96
Val Asn Ile Thr Gln Asn Gln Ala Ser Leu Cys Asn Gly Ser Met Val
  20          25          30
tgg agc gtc aac ctg acc gcc ggc atg tac tgc gca gct cta gaa tct 144
Trp Ser Val Asn Leu Thr Ala Gly Met Tyr Cys Ala Ala Leu Glu Ser
  35          40          45
ctg atc aat gtc tcc gac tgc agc gcc atc caa agg acc cag agg atg 192
Leu Ile Asn Val Ser Asp Cys Ser Ala Ile Gln Arg Thr Gln Arg Met
  50          55          60
ctg aaa gca ctg tgc tct caa aag ccc gcg gca ggg att tcc agt gaa 240

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Leu Lys Ala Leu Cys Ser Gln Lys Pro Ala Ala Gly Ile Ser Ser Glu
 65          70          75          80

cgc agc cga gac acc aaa att gaa gtg atc cag ttg gtg aaa aac ctg    288
Arg Ser Arg Asp Thr Lys Ile Glu Val Ile Gln Leu Val Lys Asn Leu
          85          90          95

ctc acc tat gta agg gga gtt tat cgc cat gga aat ttc aga    330
Leu Thr Tyr Val Arg Gly Val Tyr Arg His Gly Asn Phe Arg
          100          105          110

```

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<210> SEQ ID NO 105
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Canis familiaris

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<400> SEQUENCE: 105

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```

Ser Pro Val Thr Pro Ser Pro Thr Leu Lys Glu Leu Ile Glu Glu Leu
 1          5          10          15

Val Asn Ile Thr Gln Asn Gln Ala Ser Leu Cys Asn Gly Ser Met Val
          20          25          30

Trp Ser Val Asn Leu Thr Ala Gly Met Tyr Cys Ala Ala Leu Glu Ser
          35          40          45

Leu Ile Asn Val Ser Asp Cys Ser Ala Ile Gln Arg Thr Gln Arg Met
 50          55          60

Leu Lys Ala Leu Cys Ser Gln Lys Pro Ala Ala Gly Ile Ser Ser Glu
 65          70          75          80

Arg Ser Arg Asp Thr Lys Ile Glu Val Ile Gln Leu Val Lys Asn Leu
          85          90          95

Leu Thr Tyr Val Arg Gly Val Tyr Arg His Gly Asn Phe Arg
          100          105          110

```

```

<210> SEQ ID NO 106
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Canis familiaris

```

```

<400> SEQUENCE: 106

```

```

tctgaaattt ccatggcgat aaactcccct tacatagggtg agcagggtttt tcaccaactg    60
gatcacttca attttggtgt ctcggctgcg ttcactggaa atccctgccg cgggcttttg    120
agagcacagt gctttcagca tcctctgggt cctttggatg gcgctgcagt cggagacatt    180
gatcagagat tctagagctg cgcagtacat gccggcggtc aggttgacgc tccacaccat    240
gctgccgttg cagaggggatg cctgattctg ggtgatgttg accagctcct caatgagctc    300
cttgagggtt ggggaggag tcacagggt    330

```

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<210> SEQ ID NO 107
<211> LENGTH: 567
<212> TYPE: DNA
<213> ORGANISM: Felis catus
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (1)..(567)

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<400> SEQUENCE: 107

```

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atg gcg ctg ccc tct tcc ttc ttg gtg gcc ctg gtg gcg ctg ggc tgc    48
Met Ala Leu Pro Ser Ser Phe Leu Val Ala Leu Val Ala Leu Gly Cys
 1          5          10          15

aac tcc gtc tgc tct ctg ggc tgt gac ctg cct cag acc cac ggc ctg    96
Asn Ser Val Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Gly Leu
          20          25          30

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ctg aac agg agg gcc ttg acg ctc ctg gga caa atg agg aga ctc cct	144
Leu Asn Arg Arg Ala Leu Thr Leu Leu Gly Gln Met Arg Arg Leu Pro	
35 40 45	
gcc agc tcc tgt cag aag gac aga aat gac ttc gcc ttc ccc cag gac	192
Ala Ser Ser Cys Gln Lys Asp Arg Asn Asp Phe Ala Phe Pro Gln Asp	
50 55 60	
gtg ttt ggt gga gac cag tcc cac aag gcc caa gcc ctc tcg gtg gtg	240
Val Phe Gly Gly Asp Gln Ser His Lys Ala Gln Ala Leu Ser Val Val	
65 70 75 80	
cac gtg acg aac cag aag atc ttc cac ttc ttc tgc aca gag gcg tcc	288
His Val Thr Asn Gln Lys Ile Phe His Phe Phe Cys Thr Glu Ala Ser	
85 90 95	
tcg tct gct gct tgg aac acc acc ctc ctg gag gaa ttc tgc acg gga	336
Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Glu Glu Phe Cys Thr Gly	
100 105 110	
ctt gat tgg cag ctg acc cgc ctg gaa gcc tgt gtc atg cag gag gtg	384
Leu Asp Trp Gln Leu Thr Arg Leu Glu Ala Cys Val Met Gln Glu Val	
115 120 125	
ggg gag gga gag gct ccc ctc acg aac gag gac tcc atc ctg agg aac	432
Gly Glu Gly Glu Ala Pro Leu Thr Asn Glu Asp Ser Ile Leu Arg Asn	
130 135 140	
tac ttc caa aga ctc tcc ctc tac ctg caa gag aag aaa tac agc cct	480
Tyr Phe Gln Arg Leu Ser Leu Tyr Leu Gln Glu Lys Lys Tyr Ser Pro	
145 150 155 160	
tgt gcc tgg gag atc gtc aga gca gaa atc atg aga tcc ttg tat tat	528
Cys Ala Trp Glu Ile Val Arg Ala Glu Ile Met Arg Ser Leu Tyr Tyr	
165 170 175	
tca tca aca gcc ttg cag aaa aga tta agg agc gag aaa	567
Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser Glu Lys	
180 185	

&lt;210&gt; SEQ ID NO 108

&lt;211&gt; LENGTH: 189

&lt;212&gt; TYPE: PRP

&lt;213&gt; ORGANISM: Felis catus

&lt;400&gt; SEQUENCE: 108

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

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165	170	175	
Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser Glu Lys			
180	185		
<210> SEQ ID NO 109			
<211> LENGTH: 567			
<212> TYPE: DNA			
<213> ORGANISM: Felis catus			
<400> SEQUENCE: 109			
tttctcgctc cttaatcttt tctgcaaggc tgttgatgaa taatacaagg atctcatgat			60
ttctgctctg acgatctccc aggcacaagg gctgtatttc ttctcttgca ggtagagggga			120
gagtccttgg aagtagttcc tcaggatgga gtcctcgttc gtgaggggag cctctccctc			180
ccccactccc tgcattgacac aggcctccag gcgggtcagc tgccaatcaa gtcccgtgca			240
gaattcctcc aggaggggtgg tgttccaagc agcagacgag gacgcctctg tgcagaagaa			300
gtggaagatc ttctggttcg tcactgacac caccgagagg gcttgggctt tgtgggactg			360
gtctccacca aacacgtcct gggggaaggc gaagtcattt ctgtccttct gacaggagct			420
ggcagggagt ctctcattt gtcccaggag cgtcaaggcc ctctgttca gcaggccgtg			480
ggtctgaggc aggtcacagc ccagagagca gacggagtgg cagcccagcg ccaccagggc			540
caccaagaag gaagagggca gcgccat			567
<210> SEQ ID NO 110			
<211> LENGTH: 567			
<212> TYPE: DNA			
<213> ORGANISM: Felis catus			
<220> FEATURE:			
<221> NAME/KEY: CDS			
<222> LOCATION: (1)..(567)			
<400> SEQUENCE: 110			
atg gcg ctg ccc tct tcc ttc ttg gtg gcc ctg gtg gcg ctg ggc tgc			48
Met Ala Leu Pro Ser Ser Phe Leu Val Ala Leu Val Ala Leu Gly Cys			
1 5 10 15			
aac tcc gtc tgc tct ctg ggc tgt gac ctg cct cag acc cac ggc ctg			96
Asn Ser Val Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Gly Leu			
20 25 30			
ctg aac agg agg gcc ttg acg ctc ctg gga caa atg agg aga ctc cct			144
Leu Asn Arg Arg Ala Leu Thr Leu Leu Gly Gln Met Arg Arg Leu Pro			
35 40 45			
gcc agc tcc tgt cag aag gac agg aat gac ttc gcc ttc ccc cag gac			192
Ala Ser Ser Cys Gln Lys Asp Arg Asn Asp Phe Ala Phe Pro Gln Asp			
50 55 60			
gtg ttc ggt gga gac cag tcc cac aag gct caa gcc ctc tcg gtg gtg			240
Val Phe Gly Gly Asp Gln Ser His Lys Ala Gln Ala Leu Ser Val Val			
65 70 75 80			
cac gtg acg aac cag gag atc ttc cac ttc ttc tgc aca gag gcg tcc			288
His Val Thr Asn Gln Glu Ile Phe His Phe Phe Cys Thr Glu Ala Ser			
85 90 95			
tcg tct gct gct tgg aac acc acc ctc ctg gag gaa ttc tgc acg gga			336
Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Glu Glu Phe Cys Thr Gly			
100 105 110			
ctt gat cgg cag ctg acc cgc ctg gaa gcc tgt gtc gtg cag gag gtg			384
Leu Asp Arg Gln Leu Thr Arg Leu Glu Ala Cys Val Val Gln Glu Val			
115 120 125			
ggg gag gga gag gct ccc ctc acg aac gag gac tcc ctc ctg agg aac			432
Gly Glu Gly Glu Ala Pro Leu Thr Asn Glu Asp Ser Leu Leu Arg Asn			
130 135 140			

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tac ttc caa aga ctc tcc ctc tac ctg caa gag aag aaa tac agc cct 480  
 Tyr Phe Gln Arg Leu Ser Leu Tyr Leu Gln Glu Lys Lys Tyr Ser Pro  
 145 150 155 160

tgt gcc tgg gag atc gtc aga gca gaa atc atg aga tcc ttg tat tat 528  
 Cys Ala Trp Glu Ile Val Arg Ala Glu Ile Met Arg Ser Leu Tyr Tyr  
 165 170 175

tca tca aca gcc ttg caa aaa aga tta agg agc gag aaa 567  
 Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser Glu Lys  
 180 185

<210> SEQ ID NO 111  
 <211> LENGTH: 189  
 <212> TYPE: PRT  
 <213> ORGANISM: Felis catus

<400> SEQUENCE: 111

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

Asn Ser Val Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Gly Leu  
 20 25 30

Leu Asn Arg Arg Ala Leu Thr Leu Leu Gly Gln Met Arg Arg Leu Pro  
 35 40 45

Ala Ser Ser Cys Gln Lys Asp Arg Asn Asp Phe Ala Phe Pro Gln Asp  
 50 55 60

Val Phe Gly Gly Asp Gln Ser His Lys Ala Gln Ala Leu Ser Val Val  
 65 70 75 80

His Val Thr Asn Gln Glu Ile Phe His Phe Phe Cys Thr Glu Ala Ser  
 85 90 95

Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Glu Glu Phe Cys Thr Gly  
 100 105 110

Leu Asp Arg Gln Leu Thr Arg Leu Glu Ala Cys Val Val Gln Glu Val  
 115 120 125

Gly Glu Gly Glu Ala Pro Leu Thr Asn Glu Asp Ser Leu Leu Arg Asn  
 130 135 140

Tyr Phe Gln Arg Leu Ser Leu Tyr Leu Gln Glu Lys Lys Tyr Ser Pro  
 145 150 155 160

Cys Ala Trp Glu Ile Val Arg Ala Glu Ile Met Arg Ser Leu Tyr Tyr  
 165 170 175

Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser Glu Lys  
 180 185

<210> SEQ ID NO 112  
 <211> LENGTH: 567  
 <212> TYPE: DNA  
 <213> ORGANISM: Felis catus

<400> SEQUENCE: 112

tttctcgctc cttaatcttt tttgcaaggc tgttgatgaa taatacaagg atctcatgat 60

ttctgctctg acgatctccc aggcacaagg gctgtatttc ttctcttgca ggtagaggga 120

gagtcctttg aagtagttcc tcaggaggga gtcctcgttc gtgaggggag cctctcctc 180

ccccacctcc tgcacgacac aggcctccag gcgggtcagc tgccgatcaa gtcccgtgca 240

gaattctctc aggagggtgg tgttccaagc agcagacgag gacgcctctg tgcagaagaa 300

gtggaagatc tctgtgttcg tcactgtcac caccgagagg gcttgagcct tgtgggactg 360

gtctccaccg aacacgtcct gggggaaggc gaagtcattc ctgtccttct gacaggagct 420

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 ggcaggaggt ctctctcattt gtcccaggag cgtcaaggcc ctctctgttca gcaggccgtg 480

ggtctgagggc aggtcacagc ccagagagca gacggagtgtg cagcccagcg ccaccagggc 540

caccaagaag gaagagggca gcgccaat 567

&lt;210&gt; SEQ ID NO 113

&lt;211&gt; LENGTH: 498

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Felis catus

&lt;220&gt; FEATURE:

&lt;221&gt; NAME/KEY: CDS

&lt;222&gt; LOCATION: (1)..(498)

&lt;400&gt; SEQUENCE: 113

 tgt gac ctg cct cag acc cac ggc ctg ctg aac agg agg gcc ttg acg 48  
 Cys Asp Leu Pro Gln Thr His Gly Leu Leu Asn Arg Arg Ala Leu Thr  
 1 5 10 15

 ctc ctg gga caa atg agg aga ctc cct gcc agc tcc tgt cag aag gac 96  
 Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp  
 20 25 30

 aga aat gac ttc gcc ttc ccc cag gac gtg ttt ggt gga gac cag tcc 144  
 Arg Asn Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser  
 35 40 45

 cac aag gcc caa gcc ctc tcg gtg gtg cac gtg acg aac cag aag atc 192  
 His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Lys Ile  
 50 55 60

 ttc cac ttc ttc tgc aca gag gcg tcc tcg tct gct gct tgg aac acc 240  
 Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr  
 65 70 75 80

 acc ctc ctg gag gaa ttc tgc acg gga ctt gat tgg cag ctg acc cgc 288  
 Thr Leu Leu Glu Glu Phe Cys Thr Gly Leu Asp Trp Gln Leu Thr Arg  
 85 90 95

 ctg gaa gcc tgt gtc atg cag gag gtg ggg gag gga gag gct ccc ctc 336  
 Leu Glu Ala Cys Val Met Gln Glu Val Gly Glu Gly Glu Ala Pro Leu  
 100 105 110

 acg aac gag gac tcc atc ctg agg aac tac ttc caa aga ctc tcc ctc 384  
 Thr Asn Glu Asp Ser Ile Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu  
 115 120 125

 tac ctg caa gag aag aaa tac agc cct tgt gcc tgg gag atc gtc aga 432  
 Tyr Leu Gln Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Ile Val Arg  
 130 135 140

 gca gaa atc atg aga tcc ttg tat tat tca tca aca gcc ttg cag aaa 480  
 Ala Glu Ile Met Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys  
 145 150 155 160

 aga tta agg agc gag aaa 498  
 Arg Leu Arg Ser Glu Lys  
 165

&lt;210&gt; SEQ ID NO 114

&lt;211&gt; LENGTH: 166

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Felis catus

&lt;400&gt; SEQUENCE: 114

 Cys Asp Leu Pro Gln Thr His Gly Leu Leu Asn Arg Arg Ala Leu Thr  
 1 5 10 15

 Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp  
 20 25 30

 Arg Asn Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser  
 35 40 45

His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Lys Ile

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50	55	60	
Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr			
65	70	75	80
Thr Leu Leu Glu Glu Phe Cys Thr Gly Leu Asp Trp Gln Leu Thr Arg			
	85	90	95
Leu Glu Ala Cys Val Met Gln Glu Val Gly Glu Gly Glu Ala Pro Leu			
	100	105	110
Thr Asn Glu Asp Ser Ile Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu			
	115	120	125
Tyr Leu Gln Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Ile Val Arg			
	130	135	140
Ala Glu Ile Met Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys			
145	150	155	160
Arg Leu Arg Ser Glu Lys			
	165		
<210> SEQ ID NO 115			
<211> LENGTH: 498			
<212> TYPE: DNA			
<213> ORGANISM: Felis catus			
<400> SEQUENCE: 115			
tttctcgctc cttaatcttt tctgcaaggc tgttgatgaa taatacaagg atctcatgat			60
ttctgctctg acgatctccc aggcacaagg gctgtatttc ttctcttgca ggtagagggga			120
gagtccttgg aagtagttcc tcaggatgga gtcctcgttc gtgaggggag cctctcctc			180
ccccactcc tgcattgacac aggcctccag gcgggtcagc tgccaatcaa gtcccgtgca			240
gaattcctcc agggaggtgg tgttccaagc agcagacgag gacgcctctg tgcagaagaa			300
gtggaagatc ttctggttcg tcacgtgcac caccgagagg gcttgggect tgtgggactg			360
gtctccacca aacacgtcct gggggaaggc gaagtcattt ctgtccttct gacaggagct			420
ggcagggagt ctctcattt gtcccaggag cgtcaaggcc ctctgttca gcaggccgtg			480
ggtctgaggc aggtcaca			498
<210> SEQ ID NO 116			
<211> LENGTH: 498			
<212> TYPE: DNA			
<213> ORGANISM: Felis catus			
<220> FEATURE:			
<221> NAME/KEY: CDS			
<222> LOCATION: (1)..(498)			
<400> SEQUENCE: 116			
tgt gac ctg cct cag acc cac ggc ctg ctg aac agg agg gcc ttg acg			48
Cys Asp Leu Pro Gln Thr His Gly Leu Leu Asn Arg Arg Ala Leu Thr			
1	5	10	15
ctc ctg gga caa atg agg aga ctc cct gcc agc tcc tgt cag aag gac			96
Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp			
	20	25	30
agg aat gac ttc gcc ttc ccc cag gac gtg ttc ggt gga gac cag tcc			144
Arg Asn Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser			
	35	40	45
cac aag gct caa gcc ctc tcg gtg gtg cac gtg acg aac cag gag atc			192
His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Glu Ile			
	50	55	60
ttc cac ttc ttc tgc aca gag gcg tcc tcg tct gct gct tgg aac acc			240
Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr			
65	70	75	80

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acc ctc ctg gag gaa ttc tgc acg gga ctt gat cgg cag ctg acc cgc      288
Thr Leu Leu Glu Glu Phe Cys Thr Gly Leu Asp Arg Gln Leu Thr Arg
      85                      90                      95

ctg gaa gcc tgt gtc gtg cag gag gtg ggg gag gga gag gct ccc ctc      336
Leu Glu Ala Cys Val Val Gln Glu Val Gly Glu Gly Glu Ala Pro Leu
      100                      105                      110

acg aac gag gac tcc ctc ctg agg aac tac ttc caa aga ctc tcc ctc      384
Thr Asn Glu Asp Ser Leu Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu
      115                      120                      125

tac ctg caa gag aag aaa tac agc cct tgt gcc tgg gag atc gtc aga      432
Tyr Leu Gln Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Ile Val Arg
      130                      135                      140

gca gaa atc atg aga tcc ttg tat tat tca tca aca gcc ttg caa aaa      480
Ala Glu Ile Met Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys
      145                      150                      155                      160

aga tta agg agc gag aaa      498
Arg Leu Arg Ser Glu Lys
      165

```

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<210> SEQ ID NO 117
<211> LENGTH: 166
<212> TYPE: PRT
<213> ORGANISM: Felis catus

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<400> SEQUENCE: 117

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```

Cys Asp Leu Pro Gln Thr His Gly Leu Leu Asn Arg Arg Ala Leu Thr
  1          5          10          15

Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp
  20          25          30

Arg Asn Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser
  35          40          45

His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Glu Ile
  50          55          60

Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr
  65          70          75          80

Thr Leu Leu Glu Glu Phe Cys Thr Gly Leu Asp Arg Gln Leu Thr Arg
  85          90          95

Leu Glu Ala Cys Val Val Gln Glu Val Gly Glu Gly Glu Ala Pro Leu
  100         105         110

Thr Asn Glu Asp Ser Leu Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu
  115         120         125

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

Ala Glu Ile Met Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys
  145         150         155         160

Arg Leu Arg Ser Glu Lys
  165

```

```

<210> SEQ ID NO 118
<211> LENGTH: 498
<212> TYPE: DNA
<213> ORGANISM: Felis catus

```

```

<400> SEQUENCE: 118

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```

tttctcgctc cttaatcttt ttgcaaggc tgttgatgaa taatacaagg atctcatgat      60

ttctgctctg acgatctccc aggcacaagg gctgtatttc ttctcttgca ggtagaggga      120

gagtcctttgg aagtagttcc tcaggaggga gtcctcgttc gtgaggggag cctctccttc      180

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ccccacctcc tgcacgacac aggcttccag gcgggtcagc tgccgatcaa gtcccgtgca 240
gaattcctcc aggagggtgg tgttccaagc agcagacgag gacgcctctg tgcagaagaa 300
gtggaagatc tctgtgttcg tcacgtgcac caccgagagg gcttgagcct tgtgggactg 360
gtctccaccg aacacgtcct gggggaaggc gaagtcattc ctgtccttct gacaggagct 420
ggcagggagt ctctcattt gtcccaggag cgtcaaggcc ctctgttca gcaggccgtg 480
ggtctgaggc aggtcaca 498

```

```

<210> SEQ ID NO 119
<211> LENGTH: 444
<212> TYPE: DNA
<213> ORGANISM: Felis catus
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (10)..(441)

```

```

<400> SEQUENCE: 119

```

```

ggatccacc atg tgg ctg cag aac ctg ctt ttc ctg ggc act gtg gtc tgc 51
Met Trp Leu Gln Asn Leu Leu Phe Leu Gly Thr Val Val Cys
1 5 10
agc atc tct gca ccc acc agt tca ccc agc tct gtc act cgg ccc tgg 99
Ser Ile Ser Ala Pro Thr Ser Ser Pro Ser Ser Val Thr Arg Pro Trp
15 20 25 30
caa cac gtg gat gcc atc aag gag gcc ctg agc ctt ctg aac aac agt 147
Gln His Val Asp Ala Ile Lys Glu Ala Leu Ser Leu Leu Asn Asn Ser
35 40 45
agt gaa ata act gct gtg atg aat gaa gca gta gaa gtc gtc tct gaa 195
Ser Glu Ile Thr Ala Val Met Asn Glu Ala Val Glu Val Val Ser Glu
50 55 60
atg ttt gac cct gag gag ccg aaa tgc ctg cag act cac cta aag ctg 243
Met Phe Asp Pro Glu Glu Pro Lys Cys Leu Gln Thr His Leu Lys Leu
65 70 75
tac gag cag ggc cta cgg ggc agc ctc atc agc ctc aag gag cct ctg 291
Tyr Glu Gln Gly Leu Arg Gly Ser Leu Ile Ser Leu Lys Glu Pro Leu
80 85 90
aga atg atg gcc aac cat tac aag cag cac tgc ccc ctt act ccg gaa 339
Arg Met Met Ala Asn His Tyr Lys Gln His Cys Pro Leu Thr Pro Glu
95 100 105 110
acg ccc tgt gaa acc cag act atc acc ttc aaa aat ttc aaa gag aat 387
Thr Pro Cys Glu Thr Gln Thr Ile Thr Phe Lys Asn Phe Lys Glu Asn
115 120 125
ctg aag gat ttt ctg ttt aac aac ccc ttt gac tgc tgg gga cca gac 435
Leu Lys Asp Phe Leu Phe Asn Asn Pro Phe Asp Cys Trp Gly Pro Asp
130 135 140
cag aag taa 444
Gln Lys

```

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<210> SEQ ID NO 120
<211> LENGTH: 144
<212> TYPE: PRT
<213> ORGANISM: Felis catus

```

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<400> SEQUENCE: 120

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```

Met Trp Leu Gln Asn Leu Leu Phe Leu Gly Thr Val Val Cys Ser Ile
1 5 10 15
Ser Ala Pro Thr Ser Ser Pro Ser Ser Val Thr Arg Pro Trp Gln His
20 25 30
Val Asp Ala Ile Lys Glu Ala Leu Ser Leu Leu Asn Asn Ser Ser Glu
35 40 45

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Ile Thr Ala Val Met Asn Glu Ala Val Glu Val Val Ser Glu Met Phe  
 50 55 60

Asp Pro Glu Glu Pro Lys Cys Leu Gln Thr His Leu Lys Leu Tyr Glu  
 65 70 75 80

Gln Gly Leu Arg Gly Ser Leu Ile Ser Leu Lys Glu Pro Leu Arg Met  
 85 90 95

Met Ala Asn His Tyr Lys Gln His Cys Pro Leu Thr Pro Glu Thr Pro  
 100 105 110

Cys Glu Thr Gln Thr Ile Thr Phe Lys Asn Phe Lys Glu Asn Leu Lys  
 115 120 125

Asp Phe Leu Phe Asn Asn Pro Phe Asp Cys Trp Gly Pro Asp Gln Lys  
 130 135 140

<210> SEQ ID NO 121  
 <211> LENGTH: 444  
 <212> TYPE: DNA  
 <213> ORGANISM: Felis catus

<400> SEQUENCE: 121

```

ttacttctcg tctggtcccc agcagtc aaa ggggttg tta aacagaaaat ccttcagatt    60
ctctttgaaa tttttgaagg tgatagtctg ggtttcacag ggcgtttccg gagtaagggg    120
gcagtgctgc ttgtaatggt tggccatcat tctcagaggc tccttgaggc tgatgagget    180
gccccgtagg cctgtctcgt acagcttttag gtgagtctgc aggcatttcg gctcctcagg    240
gtcaaacatt tcagagacga ctttacttgc ttcattcatc acagcagtta tttcactact    300
gttgttcaga aggctcaggg cctccttgat ggcattccag tgttgccagg gccgagtgac    360
agagctgggt gaactgggtg gtgcagagat gctgcagacc acagtgccca ggaaaagcag    420
gttctgcagc cacatggtgg atcc                                           444

```

<210> SEQ ID NO 122  
 <211> LENGTH: 432  
 <212> TYPE: DNA  
 <213> ORGANISM: Felis catus

<400> SEQUENCE: 122

```

atgtggctgc agaacctgct tttctgggc actgtggtct gcagcatctc tgcaccacc    60
agttcacc ca gctctgtcac tcggcctcgg caacacgtgg atgccatcaa ggaggcctc    120
agccttctga acaacagttag tgaaataact gctgtgatga atgaagcagt agaagtctc    180
tctgaaatgt ttgaccctga ggagccgaaa tgctgcaga ctcacctaaa gctgtacgag    240
cagggcctac ggggcagcct catcagcctc aaggagcctc tgagaatgat ggccaaccat    300
tacaagcagc actgccccct tactcoggaa acgcccctgtg aaaccagac tatcaccctc    360
aaaaatttca aagagaatct gaaggatttt ctgtttaaca accccttga ctgctgggga    420
ccagaccaga ag                                           432

```

<210> SEQ ID NO 123  
 <211> LENGTH: 432  
 <212> TYPE: DNA  
 <213> ORGANISM: Felis catus

<400> SEQUENCE: 123

```

cttctggtct ggtccccagc agtcaaagg gttgttaaac agaaaatcct tcagattctc    60
tttgaattt ttgaaggta tagtctgggt ttcacagggc gtttccggag taagggggca    120

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gtgctgcttg taatggttg ccatcattct cagaggtcc ttgaggctga tgaggctgcc 180
ccgtaggccc tgctcgtaca gctttaggtg agtctgcagg catttcggct cctcagggtc 240
aaacatttca gagacgactt ctactgcttc attcatcaca gcagttatct cactactggt 300
gttcagaagg ctcagggtct ccttgatggc atccacgtgt tgccagggtc gagtgacaga 360
gctgggtgaa ctgggtgggtg cagagatgct gcagaccaca gtgcccagga aaagcaggtt 420
ctgcagccac at 432

```

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<210> SEQ ID NO 124
<211> LENGTH: 381
<212> TYPE: DNA
<213> ORGANISM: Felis catus
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (1)..(381)

```

```

<400> SEQUENCE: 124

```

```

gca ccc acc agt tca ccc agc tct gtc act cgg ccc tgg caa cac gtg 48
Ala Pro Thr Ser Ser Pro Ser Ser Val Thr Arg Pro Trp Gln His Val
 1 5 10 15
gat gcc atc aag gag gcc ctg agc ctt ctg aac aac agt agt gaa ata 96
Asp Ala Ile Lys Glu Ala Leu Ser Leu Leu Asn Asn Ser Ser Glu Ile
 20 25 30
act gct gtg atg aat gaa gca gta gaa gtc gtc tct gaa atg ttt gac 144
Thr Ala Val Met Asn Glu Ala Val Glu Val Val Ser Glu Met Phe Asp
 35 40 45
cct gag gag ccg aaa tgc ctg cag act cac cta aag ctg tac gag cag 192
Pro Glu Glu Pro Lys Cys Leu Gln Thr His Leu Lys Leu Tyr Glu Gln
 50 55 60
ggc cta cgg gcc agc ctc atc agc ctc aag gag cct ctg aga atg atg 240
Gly Leu Arg Gly Ser Leu Ile Ser Leu Lys Glu Pro Leu Arg Met Met
 65 70 75 80
gcc aac cat tac aag cag cac tgc ccc ctt act ccg gaa acg ccc tgt 288
Ala Asn His Tyr Lys Gln His Cys Pro Leu Thr Pro Glu Thr Pro Cys
 85 90 95
gaa acc cag act atc acc ttc aaa aat ttc aaa gag aat ctg aag gat 336
Glu Thr Gln Thr Ile Thr Phe Lys Asn Phe Lys Glu Asn Leu Lys Asp
 100 105 110
ttt ctg ttt aac aac ccc ttt gac tgc tgg gga cca gac cag aag 381
Phe Leu Phe Asn Asn Pro Phe Asp Cys Trp Gly Pro Asp Gln Lys
 115 120 125

```

```

<210> SEQ ID NO 125
<211> LENGTH: 127
<212> TYPE: PRT
<213> ORGANISM: Felis catus

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<400> SEQUENCE: 125

```

```

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

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85	90	95	
Glu Thr Gln Thr Ile Thr Phe Lys Asn Phe Lys Glu Asn Leu Lys Asp			
100	105	110	
Phe Leu Phe Asn Asn Pro Phe Asp Cys Trp Gly Pro Asp Gln Lys			
115	120	125	
<p>&lt;210&gt; SEQ ID NO 126            &lt;211&gt; LENGTH: 381            &lt;212&gt; TYPE: DNA            &lt;213&gt; ORGANISM: Felis catus</p>			
<400> SEQUENCE: 126			
cttctgggtct ggtccccagc agtcaaaggg gttgttaaac agaaaatcct tcagattctc			60
tttgaatttt ttgaagtgta tagtctgggt ttcacagggc gtttccggag taagggggca			120
gtgctgcttg taatggttg ccatcattct cagaggctcc ttgaggctga tgaggctgcc			180
ccgtagggccc tgctcgtaca gctttagggtg agtctgcagg catttcggct cctcagggtc			240
aaacatttca gagacgactt ctactgcttc attcatcaca gcagttattt cactactgtt			300
gttcagaagg ctccagggcct ccttgatggc atccacgtgt tgccagggcc gagtgacaga			360
gctgggtgaa ctgggtgggtg c			381
<p>&lt;210&gt; SEQ ID NO 127            &lt;211&gt; LENGTH: 28            &lt;212&gt; TYPE: DNA            &lt;213&gt; ORGANISM: Artificial Sequence            &lt;220&gt; FEATURE:            &lt;223&gt; OTHER INFORMATION: Description of Artificial Sequence: Synthetic            Primer</p>			
<400> SEQUENCE: 127			
cctcgagatt cagctttcaa tgcctgta			28
<p>&lt;210&gt; SEQ ID NO 128            &lt;211&gt; LENGTH: 21            &lt;212&gt; TYPE: DNA            &lt;213&gt; ORGANISM: Artificial Sequence            &lt;220&gt; FEATURE:            &lt;223&gt; OTHER INFORMATION: Description of Artificial Sequence: Synthetic            Primer</p>			
<400> SEQUENCE: 128			
tgcccrstcg gctttcttc c			21
<p>&lt;210&gt; SEQ ID NO 129            &lt;211&gt; LENGTH: 23            &lt;212&gt; TYPE: DNA            &lt;213&gt; ORGANISM: Artificial Sequence            &lt;220&gt; FEATURE:            &lt;223&gt; OTHER INFORMATION: Description of Artificial Sequence: Synthetic            Primer</p>			
<400> SEQUENCE: 129			
cgactctctt tccrctcctc ctg			23
<p>&lt;210&gt; SEQ ID NO 130            &lt;211&gt; LENGTH: 21            &lt;212&gt; TYPE: DNA            &lt;213&gt; ORGANISM: Artificial Sequence            &lt;220&gt; FEATURE:            &lt;223&gt; OTHER INFORMATION: Description of Artificial Sequence: Synthetic            Primer</p>			
<400> SEQUENCE: 130			

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cctcaaattg cggcacatgt c 21

<210> SEQ ID NO 131  
 <211> LENGTH: 22  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
 Primer

<400> SEQUENCE: 131

ctgttcagag ttgagtaag cc 22

<210> SEQ ID NO 132  
 <211> LENGTH: 28  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
 Primer

<400> SEQUENCE: 132

gaagatacca tttcaacttt aacacagc 28

<210> SEQ ID NO 133  
 <211> LENGTH: 24  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
 Primer

<400> SEQUENCE: 133

tgctgtattg tgaagactcc cagc 24

<210> SEQ ID NO 134  
 <211> LENGTH: 16  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
 Primer

<400> SEQUENCE: 134

atgcactttc tttgcc 16

<210> SEQ ID NO 135  
 <211> LENGTH: 42  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
 Primer

<400> SEQUENCE: 135

ctggaggaaa akacttcrat gattctgata tctgaaatat at 42

<210> SEQ ID NO 136  
 <211> LENGTH: 27  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
 Primer

<400> SEQUENCE: 136

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ctgacycttk sttggscctc attctca 27

<210> SEQ ID NO 137  
<211> LENGTH: 36  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer

<400> SEQUENCE: 137

gggctcgaga aaagatttgc tgtagaaaat cccatg 36

<210> SEQ ID NO 138  
<211> LENGTH: 32  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer

<400> SEQUENCE: 138

cccgcggccg ctcaactttc cgggtgccac tc 32

<210> SEQ ID NO 139  
<211> LENGTH: 23  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer

<400> SEQUENCE: 139

gtcmtggctc tyrcttgct tgg 23

<210> SEQ ID NO 140  
<211> LENGTH: 23  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer

<400> SEQUENCE: 140

aaastgggcy acytcgattt tgg 23

<210> SEQ ID NO 141  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer

<400> SEQUENCE: 141

gtgatgtgm ycagctcctc 20

<210> SEQ ID NO 142  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer

<400> SEQUENCE: 142

aattaaccct cactaaaggg 20

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<210> SEQ ID NO 143  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer  
  
<400> SEQUENCE: 143  
  
atggcgctct ggttgactgt 20

<210> SEQ ID NO 144  
<211> LENGTH: 20  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer  
  
<400> SEQUENCE: 144  
  
ggcttttgag agcacagtgc 20

<210> SEQ ID NO 145  
<211> LENGTH: 29  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer  
  
<400> SEQUENCE: 145  
  
ccccatatga gcctgtgac tccctcccc 29

<210> SEQ ID NO 146  
<211> LENGTH: 30  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer  
  
<400> SEQUENCE: 146  
  
ggggaattct catctgaaat ttccatggcg 30

<210> SEQ ID NO 147  
<211> LENGTH: 24  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer  
  
<400> SEQUENCE: 147  
  
atggcgctgc cctcttcctt cttg 24

<210> SEQ ID NO 148  
<211> LENGTH: 28  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer  
  
<400> SEQUENCE: 148  
  
tcatttctcg ctccttaac ttttctgc 28

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<210> SEQ ID NO 149  
<211> LENGTH: 37  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer  
  
<400> SEQUENCE: 149  
  
cagggatcca ccatgtggct gcagaacctg cttttcc 37

<210> SEQ ID NO 150  
<211> LENGTH: 50  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer  
  
<400> SEQUENCE: 150  
  
ttacttctgg tctggtcccc agcagtcaaa ggggttgta aacagaaaat 50

<210> SEQ ID NO 151  
<211> LENGTH: 18  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer  
  
<400> SEQUENCE: 151  
  
cacagyccca tctcctcc 18

<210> SEQ ID NO 152  
<211> LENGTH: 22  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer  
  
<400> SEQUENCE: 152  
  
gtaatacgac tcactatagg gc 22

<210> SEQ ID NO 153  
<211> LENGTH: 26  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer  
  
<400> SEQUENCE: 153  
  
acggaattcg agatgatagt gctggc 26

<210> SEQ ID NO 154  
<211> LENGTH: 28  
<212> TYPE: DNA  
<213> ORGANISM: Artificial Sequence  
<220> FEATURE:  
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
Primer  
  
<400> SEQUENCE: 154  
  
gtgtctagat ttggtagaaa aggatgat 28

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<210> SEQ ID NO 155
<211> LENGTH: 567
<212> TYPE: DNA
<213> ORGANISM: Felis catus
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (1)..(567)

<400> SEQUENCE: 155

atg gcg ctg ccc tct tcc ttc ttg gtg gcc ctg gtg gcg ctg ggc tgc      48
Met Ala Leu Pro Ser Ser Phe Leu Val Ala Leu Val Ala Leu Gly Cys
  1                               5                               10                               15

aac tcc gtc tgc tct ctg ggc tgt gac ctg cct cag acc cac ggc ctg      96
Asn Ser Val Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Gly Leu
                               20                               25                               30

ctg aac agg agg gcc ttg acg ctc ctg gga caa atg agg aga ctc cct     144
Leu Asn Arg Arg Ala Leu Thr Leu Leu Gly Gln Met Arg Arg Leu Pro
                               35                               40                               45

gcc agc tcc tgt cag aag gac aga agt gac ttc gcc ttc ccc cag gac     192
Ala Ser Ser Cys Gln Lys Asp Arg Ser Asp Phe Ala Phe Pro Gln Asp
                               50                               55                               60

gtg ttt ggt gga gac cag tcc cac aag gcc caa gcc ctc tcg gtg gtg     240
Val Phe Gly Gly Asp Gln Ser His Lys Ala Gln Ala Leu Ser Val Val
                               65                               70                               75                               80

cac gtg acg aac cag aag atc ttc cac ttc ttc tgc aca gag gcg tcc     288
His Val Thr Asn Gln Lys Ile Phe His Phe Phe Cys Thr Glu Ala Ser
                               85                               90                               95

tcg tct gct gct tgg aac acc acc ctc ctg gag gaa ttc tgc acg gga     336
Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Glu Glu Phe Cys Thr Gly
                               100                              105                              110

ctt gat tgg cag ctg acc cgc ctg gaa gcc tgt gtc atg cag gag gtg     384
Leu Asp Trp Gln Leu Thr Arg Leu Glu Ala Cys Val Met Gln Glu Val
                               115                              120                              125

ggg gag gga gag gct ccc ctc acg aac gag gac tcc atc ctg agg aac     432
Gly Glu Gly Glu Ala Pro Leu Thr Asn Glu Asp Ser Ile Leu Arg Asn
                               130                              135                              140

tac ttc caa aga ctc tcc ctc tac ctg caa gag aag aaa tac agc cct     480
Tyr Phe Gln Arg Leu Ser Leu Tyr Leu Gln Glu Lys Lys Tyr Ser Pro
                               145                              150                              155                              160

tgt gcc tgg gag atc gtc aga gca gaa atc atg aga tcc ttg tat tat     528
Cys Ala Trp Glu Ile Val Arg Ala Glu Ile Met Arg Ser Leu Tyr Tyr
                               165                              170                              175

tca tca aca gcc ttg cag aaa aga tta agg agc gag aaa                    567
Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser Glu Lys
                               180                              185

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<210> SEQ ID NO 156
<211> LENGTH: 189
<212> TYPE: PRT
<213> ORGANISM: Felis catus

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<400> SEQUENCE: 156

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

Asn Ser Val Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Gly Leu
                               20                               25                               30

Leu Asn Arg Arg Ala Leu Thr Leu Leu Gly Gln Met Arg Arg Leu Pro
                               35                               40                               45

Ala Ser Ser Cys Gln Lys Asp Arg Ser Asp Phe Ala Phe Pro Gln Asp
                               50                               55                               60

Val Phe Gly Gly Asp Gln Ser His Lys Ala Gln Ala Leu Ser Val Val

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-continued

65	70	75	80
His Val Thr Asn Gln Lys Ile Phe His Phe Phe Cys Thr Glu Ala Ser	85	90	95
Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Glu Glu Phe Cys Thr Gly	100	105	110
Leu Asp Trp Gln Leu Thr Arg Leu Glu Ala Cys Val Met Gln Glu Val	115	120	125
Gly Glu Gly Glu Ala Pro Leu Thr Asn Glu Asp Ser Ile Leu Arg Asn	130	135	140
Tyr Phe Gln Arg Leu Ser Leu Tyr Leu Gln Glu Lys Lys Tyr Ser Pro	145	150	155
Cys Ala Trp Glu Ile Val Arg Ala Glu Ile Met Arg Ser Leu Tyr Tyr	165	170	175
Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser Glu Lys	180	185	

<210> SEQ ID NO 157  
 <211> LENGTH: 567  
 <212> TYPE: DNA  
 <213> ORGANISM: Felis catus

<400> SEQUENCE: 157

```

tttctcgctc cttaatcttt tctgcaaggc tgttgatgaa taatacaagg atctcatgat      60
ttctgctctg acgatctccc aggcacaagg gctgtatttc ttctcttgca ggtagaggga      120
gagtctttgg aagtagttcc tcaggatgga gtcctcgttc gtgaggggag cctctcctc      180
ccccactcc tgcacacac aggcctccag gcgggtcagc tgccaatcaa gtcccgtgca      240
gaattcctcc aggaggggtg tgttccaagc agcagacgag gacgcctctg tgcagaagaa      300
gtggaagatc ttctggttcg tcacgtgcac caccgagagg gcttgggect tgtgggactg      360
gtctccacca aacacgtcct gggggaaggc gaagtcaact ctgtccttct gacaggagct      420
ggcagggagt ctctcattt gtcccaggag cgtcaaggcc ctctgttca gcaggccgtg      480
ggtctgaggc aggtcacagc ccagagagca gacggagtgg cagcccagcg ccaccagggc      540
caccaagaag gaagagggca ggcceat                                          567
    
```

<210> SEQ ID NO 158  
 <211> LENGTH: 498  
 <212> TYPE: DNA  
 <213> ORGANISM: Felis catus  
 <220> FEATURE:  
 <221> NAME/KEY: CDS  
 <222> LOCATION: (1)..(498)

<400> SEQUENCE: 158

```

tgt gac ctg cct cag acc cac ggc ctg ctg aac agg agg gcc ttg acg      48
Cys Asp Leu Pro Gln Thr His Gly Leu Leu Asn Arg Arg Ala Leu Thr
  1          5          10          15

ctc ctg gga caa atg agg aga ctc cct gcc agc tcc tgt cag aag gac      96
Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp
  20          25          30

aga agt gac ttc gcc ttc ccc cag gac gtg ttt ggt gga gac cag tcc      144
Arg Ser Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser
  35          40          45

cac aag gcc caa gcc ctc tcg gtg gtg cac gtg acg aac cag aag atc      192
His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Lys Ile
  50          55          60

ttc cac ttc ttc tgc aca gag gcg tcc tcg tct gct gct tgg aac acc      240
    
```

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Phe	His	Phe	Phe	Cys	Thr	Glu	Ala	Ser	Ser	Ser	Ala	Ala	Trp	Asn	Thr	
65					70					75					80	
acc	ctc	ctg	gag	gaa	ttc	tgc	acg	gga	ctt	gat	tgg	cag	ctg	acc	cgc	288
Thr	Leu	Leu	Glu	Glu	Phe	Cys	Thr	Gly	Leu	Asp	Trp	Gln	Leu	Thr	Arg	
			85					90						95		
ctg	gaa	gcc	tgt	gtc	atg	cag	gag	gtg	ggg	gag	gga	gag	gct	ccc	ctc	336
Leu	Glu	Ala	Cys	Val	Met	Gln	Glu	Val	Gly	Glu	Gly	Glu	Ala	Pro	Leu	
			100					105					110			
acg	aac	gag	gac	tcc	atc	ctg	agg	aac	tac	ttc	caa	aga	ctc	tcc	ctc	384
Thr	Asn	Glu	Asp	Ser	Ile	Leu	Arg	Asn	Tyr	Phe	Gln	Arg	Leu	Ser	Leu	
		115					120					125				
tac	ctg	caa	gag	aag	aaa	tac	agc	cct	tgt	gcc	tgg	gag	atc	gtc	aga	432
Tyr	Leu	Gln	Glu	Lys	Lys	Tyr	Ser	Pro	Cys	Ala	Trp	Glu	Ile	Val	Arg	
		130				135					140					
gca	gaa	atc	atg	aga	tcc	ttg	tat	tat	tca	tca	aca	gcc	ttg	cag	aaa	480
Ala	Glu	Ile	Met	Arg	Ser	Leu	Tyr	Tyr	Ser	Ser	Thr	Ala	Leu	Gln	Lys	
145					150					155					160	
aga	tta	agg	agc	gag	aaa											498
Arg	Leu	Arg	Ser	Glu	Lys											
				165												

&lt;210&gt; SEQ ID NO 159

&lt;211&gt; LENGTH: 166

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Felis catus

&lt;400&gt; SEQUENCE: 159

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

&lt;210&gt; SEQ ID NO 160

&lt;211&gt; LENGTH: 498

&lt;212&gt; TYPE: DNA

&lt;213&gt; ORGANISM: Felis catus

&lt;400&gt; SEQUENCE: 160

tttctcgctc	cttaatcttt	tctgcaaggc	tggtgatgaa	taatacaagg	atctcatgat	60
ttctgctctg	acgatctccc	aggcacaagg	gctgtatttc	ttctcttgca	ggtagagggga	120

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gagtctttgg aagtagttcc tcaggatgga gtcctcgttc gtgaggggag cctctcctc 180
ccccacctcc tgcattgacac aggcttccag gcgggtcagc tgccaatcaa gtcccgtgca 240
gaattcctcc aggagggtgg tgttccaagc agcagacgag gacgcctctg tgcagaagaa 300
gtggaagatc ttctggttcg tcacgtgcac caccgagagg gcttgggctt tgtgggactg 360
gtctccacca aacacgtcct gggggaagge gaagtcactt ctgtccttct gacaggagct 420
ggcagggagt ctctcattt gtcccaggag cgtcaaggcc ctctgttca gcaggccgtg 480
ggtctgagge aggtcaca 498

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<210> SEQ ID NO 161
<211> LENGTH: 582
<212> TYPE: DNA
<213> ORGANISM: Felis catus
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (1)..(582)

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<400> SEQUENCE: 161

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```

atg gcg ctg ccc tct tcc ttc ttg gtg gcc ctg gtg gcg ctg ggc tgc 48
Met Ala Leu Pro Ser Ser Phe Leu Val Ala Leu Val Ala Leu Gly Cys
  1 5 10 15
aac tcc gtc tgc tct ctg ggc tgt gat ctg cct cag acc cac ggc ctg 96
Asn Ser Val Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Gly Leu
  20 25 30
ctg aac agg agg gcc ttg acg ctc ctg gga caa atg agg aga ctc cct 144
Leu Asn Arg Arg Ala Leu Thr Leu Leu Gly Gln Met Arg Arg Leu Pro
  35 40 45
gcc agc tcc tgt cag aag gac aga agt gac ttc gcc ttc ccc cag gac 192
Ala Ser Ser Cys Gln Lys Asp Arg Ser Asp Phe Ala Phe Pro Gln Asp
  50 55 60
gtg ttc ggt gga gac cag tcc cac aag gcc caa gcc ctc tcg gtg gtg 240
Val Phe Gly Gly Asp Gln Ser His Lys Ala Gln Ala Leu Ser Val Val
  65 70 75 80
cac gtg acg aac cag aag atc ttc cac ttc ttc tgc aca gag gcg tcc 288
His Val Thr Asn Gln Lys Ile Phe His Phe Phe Cys Thr Glu Ala Ser
  85 90 95
tcg tct gct gct tgg aac acc acc ctc ctg gag gaa ttc tgc acg gga 336
Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Glu Glu Phe Cys Thr Gly
  100 105 110
ctt gat cgg cag ctg acc cgc ctg gaa gcc tgt gtc gtg cag gag gtg 384
Leu Asp Arg Gln Leu Thr Arg Leu Glu Ala Cys Val Val Gln Glu Val
  115 120 125
ggg gag gga gag gct ccc ctg acg aac gag gac att cat ccc gag gac 432
Gly Glu Gly Glu Ala Pro Leu Thr Asn Glu Asp Ile His Pro Glu Asp
  130 135 140
tcc atc ctg agg aac tac ttc caa aga ctc tcc ctc tac ctg caa gag 480
Ser Ile Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu Tyr Leu Gln Glu
  145 150 155 160
aag aaa tac agc cct tgt gcc tgg gag atc gtc aga gca gaa atc atg 528
Lys Lys Tyr Ser Pro Cys Ala Trp Glu Ile Val Arg Ala Glu Ile Met
  165 170 175
aga tcc ttg tat tat tca tca aca gcc ttg cag aaa aga tta agg agc 576
Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser
  180 185 190
gag aaa 582
Glu Lys

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<210> SEQ ID NO 162

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<211> LENGTH: 194
<212> TYPE: PRT
<213> ORGANISM: Felis catus

<400> SEQUENCE: 162

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

Asn Ser Val Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Gly Leu
  20          25          30

Leu Asn Arg Arg Ala Leu Thr Leu Leu Gly Gln Met Arg Arg Leu Pro
  35          40          45

Ala Ser Ser Cys Gln Lys Asp Arg Ser Asp Phe Ala Phe Pro Gln Asp
  50          55          60

Val Phe Gly Gly Asp Gln Ser His Lys Ala Gln Ala Leu Ser Val Val
  65          70          75          80

His Val Thr Asn Gln Lys Ile Phe His Phe Phe Cys Thr Glu Ala Ser
  85          90          95

Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Glu Glu Phe Cys Thr Gly
  100         105         110

Leu Asp Arg Gln Leu Thr Arg Leu Glu Ala Cys Val Val Gln Glu Val
  115         120         125

Gly Glu Gly Glu Ala Pro Leu Thr Asn Glu Asp Ile His Pro Glu Asp
  130         135         140

Ser Ile Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu Tyr Leu Gln Glu
  145         150         155         160

Lys Lys Tyr Ser Pro Cys Ala Trp Glu Ile Val Arg Ala Glu Ile Met
  165         170         175

Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser
  180         185         190

Glu Lys

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<210> SEQ ID NO 163
<211> LENGTH: 582
<212> TYPE: DNA
<213> ORGANISM: Felis catus

<400> SEQUENCE: 163

tttctcgctc cttaatcttt tctgcaaggc tgttgatgaa taatacaagg atctcatgat    60
ttctgctctg acgatctccc aggcacaagg gctgtatttc ttctcttga ggtagaggga    120
gagtccttgg aagtagttcc tcaggatgga gtcctcggga tgaatgtcct cgttcgtcag    180
gggagcctct cctccccca cctctgcac gacacaggct tccaggcggg tcagctgccc    240
atcaagtccc gtgcagaatt cctccaggag ggtggtgttc caagcagcag acgaggacgc    300
ctctgtgcag aagaagtgga agatcttctg gttcgtcacg tgcaccaccg agagggttg    360
ggccttgtag gactggtctc caccgaacac gtcctggggg aaggcgaagt cacttctgtc    420
cttctgacag gagctggcag ggagtctcct catttgtccc aggagcgtca aggcctcct    480
gttcagcagg ccgtgggtct gaggcagatc acagcccaga gagcagacgg agttgcagcc    540
cagcgccacc agggccacca agaaggaaga gggcagcgc at                          582

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<210> SEQ ID NO 164
<211> LENGTH: 513
<212> TYPE: DNA
<213> ORGANISM: Felis catus
<220> FEATURE:
<221> NAME/KEY: CDS

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-continued

&lt;222&gt; LOCATION: (1) .. (513)

&lt;400&gt; SEQUENCE: 164

```

tgt gat ctg cct cag acc cac ggc ctg ctg aac agg agg gcc ttg acg      48
Cys Asp Leu Pro Gln Thr His Gly Leu Leu Asn Arg Arg Ala Leu Thr
  1                               5                               10                               15

ctc ctg gga caa atg agg aga ctc cct gcc agc tcc tgt cag aag gac      96
Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp
                               20                               25                               30

aga agt gac ttc gcc ttc ccc cag gac gtg ttc ggt gga gac cag tcc     144
Arg Ser Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser
                               35                               40                               45

cac aag gcc caa gcc ctc tgc gtg gtg cac gtg acg aac cag aag atc     192
His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Lys Ile
  50                               55                               60

ttc cac ttc ttc tgc aca gag ggc tcc tgc tct gct gct tgg aac acc     240
Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr
  65                               70                               75                               80

acc ctc ctg gag gaa ttc tgc acg gga ctt gat cgg cag ctg acc cgc     288
Thr Leu Leu Glu Glu Phe Cys Thr Gly Leu Asp Arg Gln Leu Thr Arg
                               85                               90                               95

ctg gaa gcc tgt gtc gtg cag gag gtg ggg gag gga gag gct ccc ctg     336
Leu Glu Ala Cys Val Val Gln Glu Val Gly Glu Gly Glu Ala Pro Leu
  100                               105                               110

acg aac gag gac att cat ccc gag gac tcc atc ctg agg aac tac ttc     384
Thr Asn Glu Asp Ile His Pro Glu Asp Ser Ile Leu Arg Asn Tyr Phe
  115                               120                               125

caa aga ctc tcc ctc tac ctg caa gag aag aaa tac agc cct tgt gcc     432
Gln Arg Leu Ser Leu Tyr Leu Gln Glu Lys Lys Tyr Ser Pro Cys Ala
  130                               135                               140

tgg gag atc gtc aga gca gaa atc atg aga tcc ttg tat tat tca tca     480
Trp Glu Ile Val Arg Ala Glu Ile Met Arg Ser Leu Tyr Tyr Ser Ser
  145                               150                               155                               160

aca gcc ttg cag aaa aga tta agg agc gag aaa                          513
Thr Ala Leu Gln Lys Arg Leu Arg Ser Glu Lys
                               165                               170

```

&lt;210&gt; SEQ ID NO 165

&lt;211&gt; LENGTH: 171

&lt;212&gt; TYPE: PRT

&lt;213&gt; ORGANISM: Felis catus

&lt;400&gt; SEQUENCE: 165

```

Cys Asp Leu Pro Gln Thr His Gly Leu Leu Asn Arg Arg Ala Leu Thr
  1                               5                               10                               15

Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp
                               20                               25                               30

Arg Ser Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser
  35                               40                               45

His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Lys Ile
  50                               55                               60

Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr
  65                               70                               75                               80

Thr Leu Leu Glu Glu Phe Cys Thr Gly Leu Asp Arg Gln Leu Thr Arg
                               85                               90                               95

Leu Glu Ala Cys Val Val Gln Glu Val Gly Glu Gly Glu Ala Pro Leu
  100                               105                               110

Thr Asn Glu Asp Ile His Pro Glu Asp Ser Ile Leu Arg Asn Tyr Phe
  115                               120                               125

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-continued

Gln Arg Leu Ser Leu Tyr Leu Gln Glu Lys Lys Tyr Ser Pro Cys Ala  
 130 135 140

Trp Glu Ile Val Arg Ala Glu Ile Met Arg Ser Leu Tyr Tyr Ser Ser  
 145 150 155 160

Thr Ala Leu Gln Lys Arg Leu Arg Ser Glu Lys  
 165 170

<210> SEQ ID NO 166

<211> LENGTH: 513

<212> TYPE: DNA

<213> ORGANISM: Felis catus

<400> SEQUENCE: 166

ttctcgcctc cttaatcttt tctgcaaggc tgttgatgaa taatacaagg atctcatgat 60  
 ttctgctctg acgatctccc aggcacaagg gctgtatttc ttctcttgca ggtagagggga 120  
 gagtctttgg aagtagttcc tcaggatgga gtcctcggga tgaatgtcct cgttcgtcag 180  
 gggagcctct cctccccca cctcctgcac gacacaggct tccaggcggg tcagctgccg 240  
 atcaagtccc gtgcagaatt cctccaggag ggtgggtgttc caagcagcag acgaggacgc 300  
 ctctgtgcag aagaagtgga agatcttctg gttcgtcacg tgcaccaccg agagggcttg 360  
 ggccttggg gactggcttc caccgaacac gtctggggg aaggcgaagt cacttctgtc 420  
 cttctgacag gagctggcag ggagtctcct catttgtccc aggagcgtca aggccctcct 480  
 gttcagcagg ccgtgggtct gaggcagatc aca 513

<210> SEQ ID NO 167

<211> LENGTH: 567

<212> TYPE: DNA

<213> ORGANISM: Felis catus

<220> FEATURE:

<221> NAME/KEY: CDS

<222> LOCATION: (1)..(567)

<400> SEQUENCE: 167

atg gcg ctg ccc tct tcc ttc ttg gtg gcc ctg gtg gcg ctg ggc tgc 48  
 Met Ala Leu Pro Ser Ser Phe Leu Val Ala Leu Val Ala Leu Gly Cys  
 1 5 10 15  
 aac tct gtc tgc tct ctg ggc tgt gac ctg cct cag acc cac ggc ctg 96  
 Asn Ser Val Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Gly Leu  
 20 25 30  
 ctg aac agg agg gcc ttg acg ctc ctg gga caa atg agg aga ctc cct 144  
 Leu Asn Arg Arg Ala Leu Thr Leu Leu Gly Gln Met Arg Arg Leu Pro  
 35 40 45  
 gcc agc tcc tgc cag aag gac aga aat gac ttc gcc ttc ccc cag gac 192  
 Ala Ser Ser Cys Gln Lys Asp Arg Asn Asp Phe Ala Phe Pro Gln Asp  
 50 55 60  
 gtg ttc ggt gga gac cag tcc cac aag gcc caa gcc ctc tcg gtg gtg 240  
 Val Phe Gly Gly Asp Gln Ser His Lys Ala Gln Ala Leu Ser Val Val  
 65 70 75 80  
 cac gtg acg aac cag aag atc ttc cac ttc ttc tgc aca gag gcg tcc 288  
 His Val Thr Asn Gln Lys Ile Phe His Phe Phe Cys Thr Glu Ala Ser  
 85 90 95  
 tcg tct gct gct tgg aac acc acc ctc ctg gag gaa ttc tgc acg gga 336  
 Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Glu Glu Phe Cys Thr Gly  
 100 105 110  
 ctt gat cgg cag ctg acc cgc ctg gaa gcc tgt gtc gtg cag gag gtg 384  
 Leu Asp Arg Gln Leu Thr Arg Leu Glu Ala Cys Val Val Gln Glu Val  
 115 120 125

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ggg gag gga gag gct ccc ctc acg aac gag gac tcc atc ctg agg aac      432
Gly Glu Gly Glu Ala Pro Leu Thr Asn Glu Asp Ser Ile Leu Arg Asn
    130                               135                               140

tac ttc caa aga ctc tcc ctc tac ctg caa gag aag aaa tac agc cct      480
Tyr Phe Gln Arg Leu Ser Leu Tyr Leu Gln Glu Lys Lys Tyr Ser Pro
    145                               150                               155                               160

tgt gcc tgg gag atc gtc aga gca gaa atc atg aga tcc ttg tat tat      528
Cys Ala Trp Glu Ile Val Arg Ala Glu Ile Met Arg Ser Leu Tyr Tyr
    165                               170                               175

tca tca aca gcc ttg cag aaa aga tta agg agc gag aaa                  567
Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser Glu Lys
    180                               185
    
```

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<210> SEQ ID NO 168
<211> LENGTH: 189
<212> TYPE: PRT
<213> ORGANISM: Felis catus
    
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<400> SEQUENCE: 168

```

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

Asn Ser Val Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Gly Leu
    20          25          30

Leu Asn Arg Arg Ala Leu Thr Leu Leu Gly Gln Met Arg Arg Leu Pro
    35          40          45

Ala Ser Ser Cys Gln Lys Asp Arg Asn Asp Phe Ala Phe Pro Gln Asp
    50          55          60

Val Phe Gly Gly Asp Gln Ser His Lys Ala Gln Ala Leu Ser Val Val
    65          70          75          80

His Val Thr Asn Gln Lys Ile Phe His Phe Phe Cys Thr Glu Ala Ser
    85          90          95

Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Glu Glu Phe Cys Thr Gly
    100         105         110

Leu Asp Arg Gln Leu Thr Arg Leu Glu Ala Cys Val Val Gln Glu Val
    115         120         125

Gly Glu Gly Glu Ala Pro Leu Thr Asn Glu Asp Ser Ile Leu Arg Asn
    130         135         140

Tyr Phe Gln Arg Leu Ser Leu Tyr Leu Gln Glu Lys Lys Tyr Ser Pro
    145         150         155         160

Cys Ala Trp Glu Ile Val Arg Ala Glu Ile Met Arg Ser Leu Tyr Tyr
    165         170         175

Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser Glu Lys
    180         185
    
```

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<210> SEQ ID NO 169
<211> LENGTH: 567
<212> TYPE: DNA
<213> ORGANISM: Felis catus
    
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<400> SEQUENCE: 169

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tttctcgctc cttaatcttt tctgcaaggc tgttgatgaa taatacaagg atctcatgat      60

ttctgctctg acgatctccc aggcacaagg gctgtatttc ttctcttgca ggtagagggg      120

gagtcctttg aagtagttcc tcaggatgga gtcctcgttc gtgagggggag cctctcctc      180

ccccacctcc tgcacgacac aggcctccag gcgggtcagc tgccgatcaa gtcccgtgca      240

gaattctctc aggaggggtg tgttccaagc agcagacgag gacgcctctg tgcagaagaa      300

gtggaagatc ttctggttcg tcacgtgcac caccgagagg gcttgggctc tgtgggactg      360
    
```

-continued

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gtctccaccg aacacgtcct gggggaagcc gaagtcattt ctgtccttct ggcaggagct 420
ggcagggagt ctctcattt gtcccaggag cgtcaaggcc ctctgttca gcaggccgtg 480
ggtctgaggg aggtcacagc ccagagagca gacagagttg cagcccagcg ccaccagggc 540
caccaagaag gaagagggca gcgccaat 567

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<210> SEQ ID NO 170
<211> LENGTH: 498
<212> TYPE: DNA
<213> ORGANISM: Felis catus
<220> FEATURE:
<221> NAME/KEY: CDS
<222> LOCATION: (1)..(498)

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<400> SEQUENCE: 170

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tgt gac ctg cct cag acc cac ggc ctg ctg aac agg agg gcc ttg acg 48
Cys Asp Leu Pro Gln Thr His Gly Leu Leu Asn Arg Arg Ala Leu Thr
 1 5 10 15
ctc ctg gga caa atg agg aga ctc cct gcc agc tcc tgc cag aag gac 96
Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp
 20 25 30
aga aat gac ttc gcc ttc ccc cag gac gtg ttc ggt gga gac cag tcc 144
Arg Asn Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser
 35 40 45
cac aag gcc caa gcc ctc tcg gtg gtg cac gtg acg aac cag aag atc 192
His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Lys Ile
 50 55 60
ttc cac ttc ttc tgc aca gag gcg tcc tcg tct gct gct tgg aac acc 240
Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr
 65 70 75 80
acc ctc ctg gag gaa ttc tgc acg gga ctt gat cgg cag ctg acc cgc 288
Thr Leu Leu Glu Glu Phe Cys Thr Gly Leu Asp Arg Gln Leu Thr Arg
 85 90 95
ctg gaa gcc tgt gtc gtg cag gag gtg ggg gag gga gag gct ccc ctc 336
Leu Glu Ala Cys Val Val Gln Glu Val Gly Glu Gly Glu Ala Pro Leu
 100 105 110
acg aac gag gac tcc atc ctg agg aac tac ttc caa aga ctc tcc ctc 384
Thr Asn Glu Asp Ser Ile Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu
 115 120 125
tac ctg caa gag aag aaa tac agc cct tgt gcc tgg gag atc gtc aga 432
Tyr Leu Gln Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Ile Val Arg
 130 135 140
gca gaa atc atg aga tcc ttg tat tat tca tca aca gcc ttg cag aaa 480
Ala Glu Ile Met Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys
 145 150 155 160
aga tta agg agc gag aaa 498
Arg Leu Arg Ser Glu Lys
 165

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<210> SEQ ID NO 171
<211> LENGTH: 166
<212> TYPE: PRT
<213> ORGANISM: Felis catus

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<400> SEQUENCE: 171

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Cys Asp Leu Pro Gln Thr His Gly Leu Leu Asn Arg Arg Ala Leu Thr
 1 5 10 15
Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp
 20 25 30
Arg Asn Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser

```

-continued

35	40	45
His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Lys Ile 50 55 60		
Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr 65 70 75 80		
Thr Leu Leu Glu Glu Phe Cys Thr Gly Leu Asp Arg Gln Leu Thr Arg 85 90 95		
Leu Glu Ala Cys Val Val Gln Glu Val Gly Glu Gly Glu Ala Pro Leu 100 105 110		
Thr Asn Glu Asp Ser Ile Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu 115 120 125		
Tyr Leu Gln Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Ile Val Arg 130 135 140		
Ala Glu Ile Met Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys 145 150 155 160		
Arg Leu Arg Ser Glu Lys 165		

<210> SEQ ID NO 172  
 <211> LENGTH: 498  
 <212> TYPE: DNA  
 <213> ORGANISM: Felis catus

<400> SEQUENCE: 172

tttctcgctc cttaatcttt tctgcaagcc tgttgatgaa taatacaagg atctcatgat	60
ttctgctctg acgatctccc aggcacaagg gctgtatttc ttctcttga ggtagagggga	120
gagtccttgg aagtagttcc tcaggatgga gtcctcgttc gtgaggggag cctctcctc	180
ccccacctcc tgcaacgacac aggcctccag gcgggtcagc tgccgatcaa gtcccgtgca	240
gaattcctcc aggaggggtg tgttccaagc agcagacgag gacgcctctg tgcagaagaa	300
gtggaagatc ttctggttcg tcacgtgcac caccgagagg gcttgggect tgtgggactg	360
gtctccaccg aacacgtcct gggggaagcc gaagtcattt ctgtccttct ggcaggagct	420
ggcaggagct ctctcattt gtcccaggag cgtaaggcc ctctgttca gcaggccgtg	480
ggtctgagcc aggtcaca	498

<210> SEQ ID NO 173  
 <211> LENGTH: 29  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
 Primer

<400> SEQUENCE: 173

attaggatcc atggcgctgc cctcttct	29
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<210> SEQ ID NO 174  
 <211> LENGTH: 40  
 <212> TYPE: DNA  
 <213> ORGANISM: Artificial Sequence  
 <220> FEATURE:  
 <223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic  
 Primer

<400> SEQUENCE: 174

gcctctagac tgtcatttct cgctccttaa tctttctg	40
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241

What is claimed is:

1. An isolated protein selected from the group consisting of:

(a) an isolated protein of at least about 20 amino acids in length, wherein said 20 amino acids are encoded by a nucleic acid molecule that has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:99, SEQ ID NO:102, and SEQ ID NO:104; and

(b) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and SEQ ID NO:105,

wherein said isolated protein of (a) or (b) elicits an immune response against a canine IL-13 protein or has IL-13 activity.

2. The isolated protein of claim 1, wherein said protein has an amino acid sequence selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and SEQ ID NO:105.

3. The isolated protein of claim 2, wherein the protein has the amino acid sequence of SEQ ID NO:92.

242

4. The isolated protein of claim 2, wherein the protein has the amino acid sequence of SEQ ID NO:97.

5. The isolated protein of claim 2, wherein the protein has the amino acid sequence of SEQ ID NO:100.

6. The isolated protein of claim 2, wherein the protein has the amino acid sequence of SEQ ID NO:105.

7. An isolated protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and SEQ ID NO:105, wherein said isolated protein elicits an immune response against a canine IL-13 protein or has IL-13 activity.

8. A therapeutic composition comprising the isolated protein of claim 1.

9. The composition of claim 8, wherein said composition further comprises a component selected from the group consisting of an excipient, an adjuvant and a carrier.

10. A method to regulate an immune response in an animal comprising administering to the animal the therapeutic composition of claim 8.

11. The method of claim 10, wherein said animal is a canid.

12. The method of claim 10, wherein said composition further comprises a component selected from the group consisting of an excipient, an adjuvant and a carrier.

\* \* \* \* \*