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(57) Abrégé/Abstract:
The present invention relates to methods for enhancing the quality of life of a senior or super senior animal by feeding the animal a composition comprising at least one omega-3 polyunsaturated fatty acid and various combinations of amino acids, minerals, and antioxidants in amounts effective to enhance alertness, improve vitality, protect cartilage, maintain muscle mass, enhance digestibility, and improve skin and pelage quality. Beneficial changes in expression of genes associated with several biological pathways may be induced in an animal by feeding it said composition and are consistent with an enhancement in the quality of life of said animal.

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(54) **Title**: METHOD FOR ENHANCING THE QUALITY OF LIFE OF A SENIOR ANIMAL

(57) **Abstract**: The present invention relates to methods for enhancing the quality of life of a senior or super senior animal by feeding the animal a composition comprising at least one omega-3 polyunsaturated fatty acid and various combinations of amino acids, minerals, and antioxidants in amounts effective to enhance alertness, improve vitality, protect cartilage, maintain muscle mass, enhance digestibility, and improve skin and pelage quality. Beneficial changes in expression of genes associated with several biological pathways may be induced in an animal by feeding it said composition and are consistent with an enhancement in the quality of life of said animal.

# METHODS FOR ENHANCING THE QUALITY OF LIFE OF A SENIOR ANIMAL

## FIELD OF THE INVENTION

**[0001]** The present invention relates generally to methods for modulating biological functions associated with the aging process of an animal and particularly to using food compositions containing omega-3 polyunsaturated fatty acids for modulating biological functions associated with the aging process of a senior or super senior animal.

## BACKGROUND OF THE INVENTION

**[0002]** Companion animals such as dogs and cats frequently require differing diets depending on their life stage (age), size, body composition, and breed. Both dog and cat nutrient requirements can be separated into three different life-stages, based on age: growing dogs (or cats), adult dogs (or cats), and senior dogs (or cats). The latter category, senior dogs (or cats), can be further separated into two stages, which include senior (or mature adult) and super senior (or geriatric). Dogs are further separated into different categories for regular breed dogs versus large-breed dogs.

**[0003]** Essential fatty acids, consisting of omega-3 and omega-6 polyunsaturated fatty acids, are critical nutrients for the health of an animal. These nutrients, however, either cannot be made by animals or cannot be made in sufficient amounts to elicit benefits and therefore must be consumed in an animal's diet. See, e.g., Hornstra, G., et al., "Essential fatty acids in pregnancy and early human development", Eur. J. Obs. & Gyn. and Reprod. Biology, 61:57-62 (1995). It has previously been postulated that Docosahexaenoic Acid ("DHA"), an omega-3 polyunsaturated fatty acid, is effective in increasing the maze-learning ability and brain functions in aged mice. See, Lim, S.-Y., "Intakes of dietary docosahexaenoic acid ethyl ester and egg phosphatidylcholine improve maze-learning ability in young and old mice", J. Nutr., 130:1629-1632 (2000).

**[0004]** Rogers discusses the theory of the potential use of antioxidants to slow the deterioration of cognitive function, particularly in the elderly. See Rogers, P., "A healthy body,

a healthy mind: long-term impact of diet on mood and cognitive function", Proceedings of the Nutrition Society, 60:135-143 (2001).

**[0005]** Despite the studies and developments relating to improving cognitive abilities, there continues to be a need for methods for enhancing the quality of life of senior animals, as measured by, e.g., enhanced alertness, improved vitality, cartilage protection, maintenance of muscle mass, enhanced digestibility, and improved skin and pelage quality in senior and super senior animals.

**[0006]** As previously reported, the super senior pet food composition described herein may be administered to achieve this result. Additionally, we now report herein our surprising discovery that the enhanced quality of life of senior and super senior animals achieved by the administration of the pet food compositions disclosed herein is reflected at the genomic level. Specifically, as described in detail in the Examples below, gene chip data indicate that the expression of genes that encode proteins associated with several biological pathways such as blood clotting and platelet activation and aggregation, bone and muscle integrity, inflammatory responses, cartilage degradation and pain response, DNA damage and repair pathways, neural function, glycogen synthesis and degradation, glycolysis, gluconeogenesis, the pentose phosphate pathway,the aging process, and electron transport are modified, i.e., in general, the majority are beneficially altered through administration to the animal of the super senior pet food compositions described herein.

## SUMMARY OF THE INVENTION

**[0007]** The invention encompasses methods for improving or enhancing the quality of life of senior and super senior animals by feeding the animal a composition comprising at least about 9% by weight protein, at least about 5% by weight fat, and at least about 0.05% by weight of at least one omega-3 polyunsaturated fatty acid.

**[0008]** In one embodiment, the invention encompasses compositions effective to enhance an animal's quality of life, wherein enhanced quality of life is evidenced by improvement in one or more characteristics chosen from alertness, vitality, cartilage protection, muscle mass maintenance, digestibility, and skin and pelage quality.

**[0009]** In another embodiment, the invention encompasses compositions comprising at least one omega-3 polyunsaturated fatty acid chosen from docosahexaenoic acid ("DHA") and

eicosapentaenoic acid ("EPA"). In an additional embodiment, the method comprises feeding the animal a composition further comprising at least one antioxidant and at least one nutrient chosen from choline, manganese, methionine, cysteine, L-carnitine, lysine, and mixtures thereof.

**[0010]** In one embodiment, the invention encompasses compositions effective to improve or enhance the animal's quality of life, wherein enhanced quality of life is evidenced by improvement in one or more biological pathways chosen from blood clotting and platelet activation and aggregation, bone and muscle integrity, inflammatory responses, cartilage degradation and pain response, DNA damage and repair pathways, neural function, glycogen synthesis and degradation, glycolysis, gluconeogenesis, the pentose phosphate pathway, the aging process, and electron transport.

**[0011]** In another embodiment, the invention encompasses compositions effective to enhance the animal's quality of life, wherein enhanced quality of life is evidenced by a beneficial change in expression of one or more genes which encode proteins associated with or related to biological pathways chosen from blood clotting and platelet activation and aggregation, bone and muscle integrity, inflammatory responses, cartilage degradation and pain response, DNA damage and repair pathways, neural function, glycogen synthesis and degradation, glycolysis, gluconeogenesis, the pentose phosphate pathway, the aging process, and electron transport.

**[0012]** In yet another embodiment, the invention encompasses methods to treat an animal suffering from a disorder or disease associated with or related to a biological pathway chosen from blood clotting and platelet activation and aggregation, bone and muscle integrity, inflammatory responses, cartilage degradation and pain response, DNA damage and repair pathways, neural function, glycogen synthesis and degradation, glycolysis, gluconeogenesis, the pentose phosphate pathway, the aging process, and electron transport comprising administering to said animal an effective amount of a composition of the present invention. In one embodiment, the composition includes at least about 9% by weight protein, at least about 5% by weight fat, and at least about 0.05% by weight of at least one omega-3 polyunsaturated fatty acid. In a further embodiment said composition comprises at least one omega-3 polyunsaturated fatty acid chosen from docosahexaenoic acid ("DHA") and eicosapentaenoic acid ("EPA"). In yet an additional embodiment, the composition further comprises at least one

antioxidant and at least one nutrient chosen from choline, manganese, methionine, cysteine, L-carnitine, lysine, and mixtures thereof. In additional embodiments, the composition may comprise the components disclosed in Table 1 or Table 1A.

**[0013]** In another embodiment, the invention encompasses methods of measuring or characterizing the enhancement in the quality of life of an animal, particularly a senior or super senior animal, fed a composition described herein by quantitating the gene expression levels of one or more genes chosen from those disclosed in Tables 5-14 in said animal prior to and after feeding a composition disclosed herein and comparing said levels in the animal wherein an enhancement in the quality of life of said animal is reflected by a beneficial change in gene expression levels in said animal.

**[0014]** Another embodiment encompasses methods of altering the expression of at least one peptide in a mammal, the method comprising administering to the mammal a composition comprising at least about 9% by weight protein; at least about 5% by weight fat; and at least about 0.05% by weight of at least one omega-3 polyunsaturated fatty acid, wherein the at least one peptide is selected from the group consisting of X, Y and Z. With regard to the various embodiments presented herein, it is contemplated herein that the senior or super senior animal may be a senior or super senior large breed canine, regular breed canine, small breed canine or feline.

**[0015]** In another embodiment, the invention encompasses methods for screening one or more test compounds for its ability to alter the expression of at least one gene of interest in a mammal, the method comprising administering a control composition to a control group of mammals and determining the levels of expression of the at least one gene of interest, administering the one or more test compositions to an experimental group of mammals and determining the levels of expression of the least one gene of interest, wherein the test composition comprises at least about 9% by weight protein; at least about 5% by weight fat; and at least about 0.05% by weight of at least one omega-3 polyunsaturated fatty acid, and determining the differences in expression levels in the at least one gene of interest between the control and experimental groups of mammals after each group has been administered their respective compositions, wherein a difference in the expression levels of the at least one gene of interest indicates that the test composition is capable of altering the expression of the at least one gene of interest.

**[0016]** Another embodiment encompasses methods for screening one or more test compounds for its ability to alter the expression of at least one gene of interest in a mammal, the method comprising administering a control composition to a control group of mammals and determining the levels of expression of the at least one gene of interest, wherein the control composition comprises at least about 9% by weight protein; at least about 5% by weight fat; and at least about 0.05% by weight of at least one omega-3 polyunsaturated fatty acid, administering the one or more test compositions to an experimental group of mammals and determining the levels of expression of the least one gene of interest, and determining the differences in expression levels in the at least one gene of interest between the control and experimental groups of mammals after each group has been administered their respective compositions, wherein a difference in the expression levels of the at least one gene of interest indicates that the test composition is capable of altering the expression of the at least one gene of interest.

**[0016a]** Another embodiment relates to a composition comprising a) 20.1% crude protein, 16.5% fat, 0.7% calcium, 0.6% phosphorus, 0.3% eicosapentaenoic acid (EPA), 0.2% docosahexaenoic acid (DHA), 4% linoleic acid, 1.3% total omega-3 fatty acids, 4% total omega-6 fatty acids, 1400 ppm taurine, 314 ppm carnitine, 1% methionine, 0.3% cystine, 87 ppm manganese, and 1492 IU/kg vitamin E, 127 ppm Vitamin C and 101 ppm lipoic acid, or b) 19.3% crude protein, 16.9% fat, 0.7% calcium, 0.7% phosphorus, 0.3% eicosapentaenoic acid (EPA), 0.2% docosahexaenoic acid (DHA), 4% linoleic acid, 2.2% total omega-3 fatty acids, 4% total omega-6 fatty acids, 1525 ppm taurine, 337 ppm carnitine, 1.2% methionine, 0.2% cystine, 100 ppm manganese, and 1525 IU/kg vitamin E, 261 ppm Vitamin C and 135 ppm lipoic acid, or c) 35.7% crude protein, 22.5% fat, 0.9% calcium, 0.8% phosphorus, 0.2% eicosapentaenoic acid (EPA), 0.3% docosahexaenoic acid (DHA), 5.1% linoleic acid, 1.1% total omega-3 fatty acids, 5.1% total omega-6 fatty acids, 2100 ppm taurine, 367 ppm carnitine, 1.3% methionine, 0.5% cystine, 104 ppm manganese, and 1292 IU/kg vitamin E, and 141 ppm Vitamin C, for modulating biological functions associated with the aging process of a senior or super senior companion animal; wherein the modulation of biological functions comprises one or more of: improving blood clotting and platelet activation and aggregation, improving DNA damage and repair pathways, improving neural function,

improving glucose metabolism, and improving an aging process, wherein the improvement in the ageing process comprises an improvement in DNA repair, fat or cholesterol metabolism, and protein synthesis.

**[0016b]** Another embodiment relates to a composition for use in modulating biological functions associated with the aging process of a senior or super senior companion animal wherein the composition comprises: at least 9% by weight protein, at least about 5% by weight fat, and at least about 0.05% by weight of at least one omega-3 polyunsaturated fatty acid, wherein the modulation of biological functions comprises one or more of: improving blood clotting and platelet activation and aggregation; improving DNA damage and repair pathways, improving neural function, improving glucose metabolism, and improving an aging process, wherein the improvement in the ageing process comprises an improvement in DNA repair, fat or cholesterol metabolism, and protein synthesis, and wherein the composition is fed to the animal.

**[0017]** Other and further objects, features, and advantages of the present invention will be readily apparent to those skilled in the art.

## DETAILED DESCRIPTION OF THE INVENTION

### Definitions

**[0018]** It is contemplated that the invention described herein is not limited to the particular methodology, protocols, and reagents described as these may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to limit the scope of the present invention in any way.

**[0019]** Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art to which this invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the advantageous methods, devices and materials are now described. All publications mentioned herein are incorporated by reference for the purpose of describing and disclosing the materials and methodologies that are reported in the publication which might be used in connection with the invention.

**[0016b]** Another embodiment relates to a composition for use in modulating biological functions associated with the aging process of a senior or super senior companion animal wherein the composition comprises: at least 9% by weight protein, at least about 5% by weight fat, and at least about 0.05% by weight of at least one omega-3 polyunsaturated fatty acid, wherein the modulation of biological functions comprises one or more of: improving blood clotting and platelet activation and aggregation, improving muscle integrity; improving cartilage degradation and the pain response, improving DNA damage and repair pathways, improving neural function, improving glucose metabolism, and improving an aging process, wherein the improvement in the ageing process comprises an improvement in inflammation, DNA repair, fat or cholesterol metabolism, and protein synthesis, and wherein the composition is fed to the animal.

**[0017]** Other and further objects, features, and advantages of the present invention will be readily apparent to those skilled in the art.

## DETAILED DESCRIPTION OF THE INVENTION

### Definitions

**[0018]** It is contemplated that the invention described herein is not limited to the particular methodology, protocols, and reagents described as these may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to limit the scope of the present invention in any way.

**[0019]** Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art to which this invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the advantageous methods, devices and materials are now described. All publications mentioned herein are incorporated by reference for the purpose of describing and disclosing the materials and methodologies that are reported in the publication which might be used in connection with the invention.

**[0020]** In practicing the present invention, many conventional techniques in molecular biology may be used. These techniques are well known and are explained in, for example, F. M. Ausubel, Ed. *Current Protocols in Molecular Biology, Volumes I, II, and III*, (Wiley, New York), 1997 ; J. Sambrook, E. F. Fritsch, T. Maniatis, Eds., *Molecular Cloning: A Laboratory Manual* (Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1989).

**[0021]** As used herein and in the appended claims, the singular forms "a", "an", and "the" include plural reference unless the context clearly dictates otherwise.

**[0022]** The terms “senior” or “mature adult” refers to the life-stage of an animal. For small or regular breed canines, the “senior” life stage is about 7 to about 10 years of age. For felines, the “senior” life stage is about 7 to about 12 years of age. For large breed canines, over 5 years of age represents “super senior” as described below.

**[0023]** The terms “super senior” or “geriatric” refers to a specific life-stage of an animal. For small or regular breed canines, the super senior stage is any age greater than 10 years of age. For large breed canines, the super senior stage is any age greater than 5 years of age. For felines, the super senior stage is any age greater than 12 years of age.

**[0024]** The term “large breed” canine means a canine that normally weighs about 55 pounds or more when an adult.

**[0025]** The term “regular breed” canine means a canine that normally weighs less than about 55 pounds when an adult.

**[0026]** The term “small breed” canine means a canine that weighs less than about 20 pounds when an adult.

**[0027]** The term “super senior pet food composition” refers to any and all of the pet food compositions disclosed herein.

**[0028]** The term “carbohydrate” as used herein includes polysaccharides (e.g., starches and dextrins) and sugars (e.g. sucrose, lactose, maltose, glucose, and fructose) that are metabolized for energy when hydrolyzed. Examples of carbohydrates suitable for inclusion in the compositions disclosed herein include, but are not limited to, corn, grain sorghum, wheat, barley, and rice.

**[0029]** The term “antioxidant” means a substance that is capable of reacting with free radicals and neutralizing them. Illustrative examples of such substances include beta-carotene, selenium, coenzyme Q10 (ubiquinone), luetin, tocotrienols, soy isoflavones, S-

adenosylmethionine, glutathione, taurine, N-acetylcysteine, vitamin E, vitamin C, lipoic acid and L-carnitine. Examples of foods containing useful levels of one or more antioxidants include but are not limited to ginkgo biloba, green tea, broccoli, citrus pulp, grape pomace, tomato pomace, carrot spinach, and a wide variety of fruit meals and vegetable meals. It will be understood by one of skill in the art that while units of antioxidants may be provided herein as "ppm", appropriate amounts of antioxidants may also be provided as "IU/kg" where appropriate and customary for a given antioxidant such as, e.g., Vitamin E.

**[0030]** The terms "beneficial change" in gene expression, or gene expression may be "beneficially altered" and like terms refer to a modification in gene expression (e.g., up or down regulation of mRNA levels) such that levels of proteins or peptide chains encoded by the genes may be correspondingly modified such that an associated biological pathway may be more likely to function normally, such as in a healthy adult animal and with less tendency to reflect pathological changes in the pathway that, e.g., may be typical of a super senior or geriatric animal. Generally, beneficial changes in gene expression relate to improved health and/or reduced propensity for disease in an animal. As used herein, measuring differences in "gene expression" and like terms refer to, e.g., characterizing whether expression of a gene is up or down regulated in an animal compared to a control level. Gene expression levels can assessed by determining mRNA levels for a corresponding gene, or they may be inferred by determining protein or peptide chain levels. To be clear, determining "gene expression" or "gene expression levels" as used herein includes, but is not limited to, determining either corresponding RNA levels or peptide/protein levels or both. The invention is not limited to a particular method for determining protein or peptide or RNA levels, all of which are well known in the art. Moreover, gene expression and gene expression levels can be assessed in any cell or tissue that is appropriate for expression of the gene of interest. In one embodiment, gene expression is assessed in blood cells. In a more specific embodiment, the blood cells are lymphocytes. In an even more specific embodiment, the cells are T-lymphocytes. Other cell types include, but are not limited to, muscle cells, nerve cells, glial cells, endothelial cells, skin cells, liver cells, kidney cells, bone cells, other types of blood cells, such as but not limited to, macrophages. The cells may be primary cells, i.e., taken directly from an animal, such as cells isolated from recently drawn blood. The cells may also be non-primary, i.e. an established cell line through passage or even an immortalized cell line, such that the methods determining gene

expression levels can be performed on established animal cell lines, e.g., CHO cells, prior to administration of a composition to an animal.

**[0031]** As used herein, a "gene" is a DNA molecule where at least a portion of which is transcribed into an RNA molecule. The DNA molecule may or may not include non-transcribed regions and/or non-translated regions, such as but not limited to introns, promoters, enhancer regions, 5' untranslated regions.

**[0032]** The methods include the genes listed herein, as well as homologs. Thus, the methods of the present invention are not limited to the genes whose database accession numbers are disclosed herein and include homologs thereof. As used herein, a homolog of a gene listed herein means a gene whose coding or non-coding sequence may vary slightly from the reference sequence but also codes for the same or "equivalent" protein or peptide in a different organism. For example, the methods of the present invention relate to expression of phospholipase A2 in at least a canine. A homolog of the canine phospholipase A2 gene would include, but would not be limited to, the feline phospholipase A2 gene, the bovine phospholipase A2 gene, the porcine phospholipase A2 gene, the equine phospholipase A2 gene and the primate phospholipase A2 gene. Homologs also include variations in the coding or non-coding sequences that account for slight variations across species. For example, the present invention relates to the human phospholipase A2 gene, and a homolog thereof would include, but would not be limited to a monkey or chimpanzee phospholipase A2 gene.

**[0033]** As used herein, "improving" or "enhancing" the quality of life of an animal refers to as an improvement or enhancement in one or more characteristics chosen from alertness, vitality, protection of cartilage, maintenance of muscle mass, digestibility, and skin and pelage quality. Additionally, improvement/enhancement in blood clotting and platelet activation and aggregation, bone and muscle integrity, inflammatory responses, cartilage degradation and pain response, DNA damage and repair pathways, neural function, glycogen synthesis and degradation, glycolysis, gluconeogenesis, the pentose phosphate pathway, the aging process, and electron transport are also contemplated.

**[0034]** An "improvement" or an "enhancement" in a characteristic or biological pathway refers to a modification in said characteristic or biological pathway such that there is a tendency for the characteristic or pathway to appear and/or function normally and with less tendency to

reflect pathological changes in the characteristic or pathway that, e.g., may be typical of a super senior animal.

**[0035]** As used herein, methods to "treat" an animal suffering from a disease or disorder is also meant to encompass methods to prevent and/or to ameliorate the disease or disorder as well.

**[0036]** As used herein, "genes associated with the aging process" or "aging genes" or like terms refers to those genes which may be involved in the process of senescence in an animal. These genes may include, e.g., genes that encode for proteins that have a role in a number of biological functions such as inflammation, DNA repair or cell survival, fat or cholesterol metabolism, protein synthesis, immune regulation, cell growth and cell death.

**[0037]** Similarly, the "aging process", as the term is used herein, refers to the process of senescence in an animal and may include changes in biological functions such as, e.g., inflammation, DNA repair or cell survival, fat or cholesterol metabolism, protein synthesis, cell growth and cell death.

**[0038]** As used herein, the phrase "modulating biological functions associated with the aging process" refers to op-regulating or down-regulating genes, which may be involved in the process of senescence in an animal. These genes may include, e.g., genes that encode for proteins that have a role in a number of biological functions such as inflammation, DNA repair or cell survival, fat or cholesterol metabolism, protein synthesis, immune regulation, cell growth and cell death.

## The Invention

**[0039]** The present invention encompasses compositions and methods for improving or enhancing the quality of life of a senior or super senior animal. The methods comprise feeding the animal a composition comprising at least about 9% by weight protein, at least about 5% by weight fat, and at least about 0.05% by weight omega-3 polyunsaturated fatty acid. The methods are useful for enhancing alertness, improving vitality, protecting cartilage, maintaining muscle mass, enhancing digestibility, and improving skin and pelage quality in a senior or super senior animal. The methods are also useful for improving in an animal one or more biological pathways chosen from blood clotting and platelet activation and aggregation, bone and muscle integrity, inflammatory responses, cartilage degradation and pain response, DNA damage and repair pathways, neural function, glycogen synthesis and degradation, glycolysis,

gluconeogenesis, the pentose phosphate pathway, the aging process, and the electron transport pathway, such improvements also being reflected in overall beneficial changes at the genomic level. Methods for treating animals suffering from disorders or diseases associated with or related to these biological pathways comprising administering the compositions of the present invention are also contemplated herein.

**[0040]** Without being bound by theory, the benefits of the invention may be the result of physiological effects from the addition of omega-3 polyunsaturated fatty acids to a senior or super senior animal's diet. Similarly, the antioxidants, choline, and other nutrients may play a role in enhancing a senior or super senior animal's quality of life.

**[0041]** Although the methods of the present invention may improve an animal's quality of life by enhancing all of the above described characteristics or improving all of the described biological pathways, it is not necessary to demonstrate substantial improvements in each of the characteristics or pathways to achieve the "enhanced quality of life" as defined herein.

**[0042]** When the compositions are administered to a senior or super senior animal, the animal experiences an enhanced quality of life, e.g., exhibits or experiences one or more of enhanced alertness, improved vitality, protected cartilage, maintained muscle mass, enhanced digestibility, improved skin and pelage quality, as well as improvements in e.g., blood clotting and platelet activation and aggregation, bone and muscle integrity, inflammatory responses, cartilage degradation and pain response, DNA damage and repair pathways, neural function, glycogen synthesis and degradation, glycolysis, gluconeogenesis, the pentose phosphate pathway, the aging process and the electron transport pathway as indicated by overall beneficial changes at the genomic level. Methods for determining these measurements of quality of life are known to skilled artisans. For example, alertness can be measured by various means, including an analysis of metabolism and antioxidant markers, as well as through clinical studies with follow-up questions to participating pet owners. Potential metabolism markers may include ghrelin, GLP-1, thyroid hormone, and/or growth hormone. Potential markers of antioxidant status may include serum vitamin E, ORAC, glutathione peroxidase, alkanels, and/or cell damage indicators. Further, vitality can be measured by various means, including an analysis of metabolism and antioxidant markers, as well as through clinical studies with follow-up questions to participating pet owners. Similarly, cartilage protection can be measured by various means, including an analysis of arthritis biomarkers. Potential arthritis biomarkers may

include type II collagen synthesis, matrix metaloproteinase, osteocalcin, alkaline phosphatase activity, COMP, and fragments of cartilage damage. Muscle mass maintenance can be measured by various means, including an analysis of body composition and digestibility can be measured by various means, including clinical studies with follow-up questions to participating pet owners and animal feeding to determine the percentage of nutrients digested. Skin and pelage quality can be measured by various means, including clinical studies with follow-up questions to participating pet owners. Additionally, as discussed above, improvements in quality of life is also reflected at the genomic level, as evidenced by gene chip data which indicate beneficial changes on the expression of genes associated with various important biological pathways including blood clotting and platelet activation and aggregation, bone and muscle integrity, inflammatory responses, cartilage degradation and protection and pain response, DNA damage and repair pathways, neural function, glycogen synthesis and degradation, glycolysis, gluconeogenesis, the pentose phosphate pathway, the aging process, and the electron transport pathway. The identities of these genes are provided in the Examples below.

**[0043]** The methods of the invention are useful for enhancing the quality of life of humans and animals, including primates (e.g., monkeys, chimpanzees, etc.), companion animals (e.g., dogs, cats, horses, etc.), farm animals (e.g., goats, sheep, swine, cattle, etc.), laboratory animals (e.g., mice, rats, etc.), birds (e.g., domestic birds such as canaries, parrots, etc. and commercial birds such as chickens, ducks, turkeys, etc.), rodents (e.g., hamsters, guinea pigs, gerbils, rabbits, hedgehogs, ferrets, chinchillas, etc.), and wild, exotic, and zoo animals (e.g., wolves, bears, deer, etc.). In various embodiments, the animal is a cat, a dog, or a horse.

**[0044]** The compositions of the present invention are designed to enhance digestibility and improve chewability. Canine and feline foods are typically formulated based on life stage (age), size, body composition, and breed. Thus, some embodiments of the present invention include compositions that are formulated to address specific nutritional differences between regular or small breed dogs, large breed dogs, and cats.

**[0045]** The invention provides methods utilizing a variety of compositions containing at least one omega-3 polyunsaturated fatty acid. The compositions include foods, supplements, treats, and toys (typically chewable and consumable toys). The methods also provide the compositions to the designated animals over a period of time that is long enough to effectuate

the improved quality of life. In one embodiment, the method provides the animal with a composition for at least thirty days.

**[0046]** The compositions for use in the methods of the present invention generally have an omega-3 polyunsaturated fatty acid content of at least about 0.02% (or about 0.05 % to about 10%, or about 0.1% to about 6%) by weight on a dry matter basis. In some embodiments, the omega-3 polyunsaturated fatty acid is DHA. In other embodiments, the omega-3 polyunsaturated fatty acid is EPA. In still other embodiments, the omega-3 polyunsaturated fatty acid comprises a mixture of DHA and EPA.

**[0047]** In some embodiments, the composition containing omega-3 polyunsaturated fatty acid is a food. Although both liquid and solid foods are provided, solid foods are typically advantageous. Foods include both dry foods and wet foods. Some of the non-polyunsaturated fatty acid components of the food, and useful proportions, include those listed in Table 1.

Table 1

| **Component** | **Proportion of the composition (% of dry weight of composition or parts per million)** |
|---|---|
| Protein | about 9% to about 55%, or about 18% to about 30%, or about 33% to about 55% or about 18% to about 20% or about 33% to about 36% |
| Fat | about 7% to about 35%, or about 18% to about 35%, or about 7% to about 24%, or about 14% to about 24%, or about 14% to about 16% or about 18% to about 24% |
| Antioxidant | about 0 ppm to about 7500 ppm, or about 0.05 ppm to about 3600 ppm, or about 250 to about 3600, or about 250 ppm to about 1650 ppm, or about 5 ppm to about 225 ppm, or about 0.05 ppm to about 2.4 ppm |

**[0048]** In one embodiment, the methods of this invention comprise feeding a super senior animal a composition in an amount effective to enhance the animal's quality of life. Such compositions generally comprise:

(a) 0.02% (or about 0.05 % to about 10%, or about 0.1% to about 6%) of at least one omega-3 polyunsaturated fatty acid, and

(b) at least one of the following:

(i) about 10% to about 55% (or about 18% to about 30%, or about 33% to about 55% or about 18% to about 20% or about 33% to about 36%) protein,

(ii) about 7% to about 35% (or about 18% to about 35%, or about 7% to about 24%, or about 14% to about 24%, or about 14% to about 16% or about 18% to about 24%) fat, and

(iii) at least about .05 (or about 0.05 ppm or IU/kg to about 7500 ppm or IU/kg, or about 250 ppm or IU/kg to about 3600 ppm or IU/kg, or about 250 ppm or IU/kg to about 1650 ppm or IU/kg, or about 5 ppm or IU/kg to about 225 ppm or IU/kg, or about 0.05 ppm or IU/kg to about 2.4 ppm or IU/kg) antioxidant.

**[0049]** In another embodiment, the methods of this invention comprise feeding a super senior regular or small breed canine a composition in an amount effective to enhance the canine's quality of life. The composition generally comprises:

(a) at least one of the following:

(i) at least about 0.02% (or about 0.02% to about 0.3%, or about 0.05% to about 0.3%, or about 0.05% to about 0.2%) DHA, and

(ii) at least about 0.1% (or about 0.1% to about 0.5%, or about 0.2% to about 0.5%, or about 0.2% to about 0.3%) EPA,

(b) at least about 9% (or about 9% to about 30%, or about 18% to about 30%, or about 18% to about 20%) protein,

(c) at least about 7% (or about 7% to about 24%, or about 14% to about 24%, or about 14% to about 16%) fat, and

(d) at least one of the following:

(i) at least about 250 IU/kg (or about 250 IU/kg to about 1500 IU/kg, or about 500 IU/kg to about 1500 IU/kg, or about 500 IU/kg to about 1000 IU/kg) vitamin E,

(iv) at least about 50 ppm (or about 50 ppm to about 500 ppm, or about 100 ppm to about 500 ppm, or about 100 ppm to about 301 ppm) vitamin C,

(v) at least about 600 ppm (or about 600 ppm to about 2400 ppm, or about 1260 ppm to about 2400 ppm, or about 1260 ppm to about 1545 ppm) taurine,

(vi) at least about 50 ppm (or about 50 ppm to about 200 ppm, or about 100 to about 160, or about 100 to about 155) lipoic acid, and

(vii) at least about 50 ppm (or about 50 ppm to about 500 ppm, or about 200 ppm to about 500 ppm, or about 200 ppm to about 350 ppm) carnitine.

**[0050]** In another embodiment, the methods of this invention comprise feeding a super senior large breed canine a composition in an amount effective to enhance the canine's quality of life. The compositions generally comprise:

(a) at least one of the following:

(i) at least about 0.02% (or about 0.02% to about 0.3%, or about 0.05% to about 0.3%, or about 0.05% to about 0.2%) DHA, and

(ii) at least about 0.1% (or about 0.1% to about 0.5%, or about 0.2% to about 0.5%, or about 0.2% to about 0.3%) EPA,

(b) at least about 9% (or about 9% to about 30%, or about 18% to about 30%, or about 18% to about 20%) protein,

(c) at least about 7% (or about 7% to about 24%, or about 14% to about 24%, or about 14% to about 16%) fat, and

(d) at least one of the following:

(i) at least about 250 IU/kg (or about 250 IU/kg to about 1500 IU/kg, or about 500 IU/kg to about 1500 IU/kg, or about 500 IU/kg to about 1000 IU/kg) vitamin E ,

(viii) at least about 50 ppm (or about 50 ppm to about 500 ppm, or about 100 ppm to about 500 ppm, or about 100 ppm to about 301 ppm) vitamin C,

(ix) at least about 600 ppm (or about 600 ppm to about 2400 ppm, or about 1260 ppm to about 2400 ppm, or about 1260 ppm to about 1575 ppm) taurine, and

(x) at least about 50 ppm (or about 50 ppm to about 200 ppm, or about 100 to about 160, or about 100 to about 155) lipoic acid, and

(xi) at least about 50 ppm (or about 50 ppm to about 500 ppm, or about 200 ppm to about 500 ppm, or about 200 ppm to about 350 ppm) carnitine.

**[0051]** In another embodiment, the methods of this invention comprise feeding a super senior feline a composition in an amount effective to enhance the feline's quality of life. The compositions generally comprise:

(a) at least one of the following:

(i) at least about 0.05% (or about 0.05% to about 0.30%, or about 0.1% to about 0.30%, or about 0.1% to about 0.2%) DHA, and

(ii) at least about 0.1% (or about 0.1% to about 0.5%, or about 0.2% to about 0.5%, or about 0.2% to about 0.3%) EPA,

(b) at least about 15% (or about 15% to about 55%, or about 30% to about 55%, or about 33% to about 36%) protein,

(c) at least about 9% (or about 9% to about 35%, or about 18% to about 35%, or about 18% to about 24%) fat, and

(d) at least one of the following:

(i) at least about 250 IU/kg (or about 250 IU/kg to about 1500 IU/kg, or about 500 IU/kg to about 1500 IU/kg, or about 500 IU/kg to about 1100 IU/kg) vitamin E ,

(xii) at least about 50 ppm (or about 50 ppm to about 300 ppm, or about 100 ppm to about 300 ppm, or about 100 ppm to about 200 ppm) vitamin C,

(xiii) at least about 1100 ppm (or about 1100 ppm to about 3500 ppm, or about 2300 ppm to about 3500 ppm, or about 2300 ppm to about 2350 ppm) taurine, and

(xiv) at least about 200 ppm (or about 200 to about 750 ppm, or about 400 ppm to about 750 ppm, or about 400 to about 525 ppm) carnitine, and

(xv) at least about 0.05% (or about 0.05% to about 0.6%, or about 0.1% to about 0.6%, or about 0.1% to about 0.4%) cystine.

**[0052]** In another embodiment, the methods of this invention comprise feeding a super senior animal a composition in an amount effective to enhance the animal's alertness and vitality. The composition generally comprises:

(a) 0.02% (or about 0.05 % to about 10%, or about 0.1% to about 6%) at least one omega-3 polyunsaturated fatty acid, and

(b) at least one of the following:

(xvi) about 10% to about 55% (or about 18% to about 30%, or about 33% to about 55% or about 18% to about 20% or about 33% to about 36%) protein,

(xvii) about 7% to about 35% (or about 18% to about 35%, or about 7% to about 24%, or about 14% to about 24%, or about 14% to about 16% or about 18% to about 24%) fat,

(xviii) at least about .05 (or about 0.05 ppm to about 7500 ppm, or about 250 to about 3600, or about 250 ppm to about 1650 ppm, or about 5 ppm to about 225 ppm, or about 0.05 ppm to about 2.4 ppm) antioxidant, and

(xix) at least about 1000 ppm (or about 1000 ppm to about 5000 ppm, about 3300 ppm to about 5000 ppm, or about 2000 ppm to about 3000 ppm, or about 3000 ppm to about 4000 ppm) choline.

**[0053]** In another embodiment, the methods of this invention comprise feeding a super senior regular or small breed canine a composition in an amount effective to enhance the canine's alertness and vitality. The composition generally comprises:

(a) at least one of the following:

(i) at least about 0.02% (or about 0.02% to about 0.3%, or about 0.05% to about 0.3%, or about 0.05% to about 0.2%) DHA, and (ii) at least about 0.1% (or about 0.1% to about 0.5%, or about 0.2% to about 0.5%, or about 0.2% to about 0.3%) EPA,

(b) at least about 9% (or about 9% to about 30%, or about 18% to about 30%, or about 18% to about 20%) protein,

(c) at least about 7% (or about 7% to about 24%, or about 14% to about 24%, or about 14% to about 16%) fat,

(d) at least one of the following:

(i) at least about 250 IU/kg (or about 250 IU/kg to about 1500 IU/kg, or about 500 IU/kg to about 1500 IU/kg, or about 500 IU/kg to about 1000 IU/kg) vitamin E ,

(xx) at least about 50 ppm (or about 50 ppm to about 500 ppm, or about 100 ppm to about 500 ppm, or about 100 ppm to about 301 ppm) vitamin C,

(xxi) at least about 600 ppm (or about 600 ppm to about 2400 ppm, or about 1260 ppm to about 2400 ppm, or about 1260 ppm to about 1545 ppm) taurine, and

(xxii) at least about 50 ppm (or about 50 ppm to about 200 ppm, or about 100 to about 160, or about 100 to about 155) lipoic acid, and

(xxiii) at least about 50 ppm (or about 50 ppm to about 500 ppm, or about 200 ppm to about 500 ppm, or about 200 ppm to about 350 ppm) carnitine,

(e) at least about 1000 ppm (or about 1000 ppm to about 3200 ppm, or about 2000 ppm to about 3200 ppm, or about 2000 ppm to about 2500 ppm) choline,

(f) at least about 50 ppm (or about 50 ppm to about 150 ppm, or about 100 ppm to about 150 ppm, or about 100 ppm to about 110 ppm) manganese, and

(g) at least about 0.4% (or about 0.4% to about 2%, or about 0.9% to about 2%, or about 0.9% to about 1.2%) lysine, and

(h) at least about 0.4% to about 1.5% methionine.

**[0054]** In another embodiment, the methods of this invention comprise feeding a super senior large breed canine a composition in an amount effective to enhance the canine's alertness and vitality. The composition generally comprises:

(a) at least one of the following:

(i) at least about 0.02% (or about 0.02% to about 0.3%, or about 0.05% to about 0.3%, or about 0.05% to about 0.2%) DHA, and

(ii) at least about 0.1% (or about 0.1% to about 0.5%, or about 0.2% to about 0.5%, or about 0.2% to about 0.3%) EPA,

(b) at least about 9% (or about 9% to about 30%, or about 18% to about 30%, or about 18% to about 20%) protein,

(c) at least about 7% (or about 7% to about 24%, or about 14% to about 24%, or about 14% to about 16%) fat,

(d) at least one of the following:

(i) at least about 250 IU/kg (or about 250 IU/kg to about 1500 IU/kg, or about 500 IU/kg to about 1500 IU/kg, or about 500 IU/kg to about 1000 IU/kg) vitamin E ,

(xxiv) at least about 50 ppm (or about 50 ppm to about 500 ppm, or about 100 ppm to about 500 ppm, or about 100 ppm to about 301 ppm) vitamin C,

(xxv) at least about 600 ppm (or about 600 ppm to about 2400 ppm, or about 1260 ppm to about 2400 ppm, or about 1260 ppm to about 1575 ppm) taurine, and

(xxvi) at least about 50 ppm (or about 50 ppm to about 200 ppm, or about 100 to about 160, or about 100 to about 155) lipoic acid, and

(xxvii) at least about 50 ppm (or about 50 ppm to about 500 ppm, or about 200 ppm to about 500 ppm, or about 200 ppm to about 350 ppm) carnitine,

(e) at least about 1000 ppm (or about 1000 ppm to about 3200 ppm, or about 2000 ppm to about 3200 ppm, or about 2000 ppm to about 2500 ppm) choline,

(f) at least about 50 ppm (or about 50 ppm to about 150 ppm, or about 100 ppm to about 150 ppm, or about 100 ppm to about 110 ppm) manganese, and

(g) at least about 0.4% (or about 0.4% to about 2%, or about 0.9% to about 2%, or about 0.9% to about 1.2%) lysine, and

(h) at least about 0.4% to about 1.5% methionine.

**[0055]** In another embodiment, the methods of this invention comprise feeding a super senior feline a composition in an amount effective to enhance the feline's alertness and vitality. The composition generally comprises:

(a) at least one of the following:

(i) at least about 0.05% (or about 0.05% to about 0.30%, or about 0.1% to about 0.30%, or about 0.1% to about 0.2%) DHA, and

(ii) at least about 0.1% (or about 0.1% to about 0.5%, or about 0.2% to about 0.5%, or about 0.2% to about 0.3%) EPA,

(b) at least about 15% (or about 15% to about 55%, or about 30% to about 55%, or about 33% to about 36%) protein,

(c) at least about 9% (or about 9% to about 35%, or about 18% to about 35%, or about 18% to about 24%) fat,

(d) at least one of the following:

(i) at least about 250 IU/kg (or about 250 IU/kg to about 1500 IU/kg, or about 500 IU/kg to about 1500 IU/kg, or about 500 IU/kg to about 1100 IU/kg) vitamin E ,

(xxviii) at least about 50 ppm (or about 50 ppm to about 300 ppm, or about 100 ppm to about 300 ppm, or about 100 ppm to about 200 ppm) vitamin C,

(xxix) at least about 1100 ppm (or about 1100 ppm to about 3500 ppm, or about 2300 ppm to about 3500 ppm, or about 2300 ppm to about 2350 ppm) taurine, and

(xxx) at least about 200 ppm (or about 200 to about 750 ppm, or about 400 ppm to about 750 ppm, or about 400 to about 525 ppm) carnitine, and

(xxxi) at least about 0.05% (or about 0.05% to about 0.6%, or about 0.1% to about 0.6%, or about 0.1% to about 0.4%) cystine,

(e) at least about 1600 ppm (or about 1600 ppm to about 5000 ppm, or about 3300 ppm to about 5000 ppm, or about 3300 ppm to about 3400 ppm) choline,

(f) at least about 50 ppm (or about 50 ppm to about 150 ppm, or about 100 ppm to about 150 ppm, or about 100 ppm to about 110 ppm) manganese, and

(g) at least about 0.7% (or about 0.7% to about 3%, or about 1.4% to about 3%, or about 1.4% to about 1.7%) lysine, and

(h) at least about 0.4% to about 1.5% methionine.

**[0056]** In another embodiment, this invention provides a method for improving the quality of life of a senior or super senior small or regular breed canine. The method comprises feeding the canine a composition comprising:

about 60% to about 70% by weight carbohydrate;

about 15% to about 25% by weight protein chosen from animal protein and vegetable protein;

about 5% to about 7% by weight fat chosen from animal fat and vegetable fat;

about 2.5% to about 4% by weight of at least one omega-3 polyunsaturated fatty acids;

about 1% to about 4% by weight fiber;

about 1% to about 2% by weight minerals; and

about 0.5 to about 1.5% by weight vitamins.

**[0057]** In another embodiment, this invention provides a method for improving the quality of life of a senior or super senior large breed canine. The method comprises feeding the canine a composition comprising:

about 60% to about 70% by weight carbohydrate;

about 15% to about 25% by weight protein chosen from animal protein and vegetable protein;

about 5% to 10% by weight fat chosen from animal fat and vegetable fat;

about 3% to about 5% by weight of at least one omega-3 polyunsaturated fatty acids;

about 1% to about 4% by weight fiber;

about 0.5% to about 1% by weight minerals; and

about 0.75 to about 1.25% by weight vitamins.

**[0058]** In another embodiment, this invention provides a method for improving the quality of life of a senior or super senior feline. The method comprises feeding the feline a composition comprising:

about 30% to about 35% by weight carbohydrate;

about 35 % to about 50% by weight protein chosen from animal protein and vegetable protein;

about 12% to about 15% by weight fat chosen from animal fat and vegetable fat;
about 1% to about 2% by weight of at least one omega-3 polyunsaturated fatty acids;
about 1% to about 5% by weight fiber;
about 1% to about 2% by weight minerals; and
about 1% to about 2% by weight vitamins.

**[0059]** In a further embodiment, this invention provides a method for improving the quality of life of a senior or super senior animal comprising feeding the animal (e.g., small, regular or large breed canine or feline, as the case may be) a composition comprising the components as indicated in Table 1A below:

**Table 1A: Chemical composition of Super Senior Foods**

| Nutrient Component | Small/Regular Breed Canine | Large Breed Canine | Feline |
|---|---|---|---|
| Crude Protein, % | 20.1 | 19.34 | 35.73 |
| Fat, % | 16.45 | 16.92 | 22.47 |
| Calcium, % | 0.71 | 0.73 | 0.94 |
| Phosphorus, % | 0.61 | 0.68 | 0.77 |
| EPA, % | 0.32 | 0.32 | 0.23 |
| DHA, % | 0.22 | 0.22 | 0.32 |
| Linoleic Acid, % | 3.96 | 4.04 | 5.05 |
| Total N-3 fatty acids, % | 1.3 | 2.24 | 1.14 |
| Total N-6 fatty acids, % | 3.96 | 3.99 | 5.09 |
| Taurine, ppm | 1400 | 15.25 | 2100 |
| Carnitine, ppm | 314 | 337 | 367 |
| Methioinine, % | 1 | 1.19 | 1.32 |
| Cystine, % | 0.25 | 0.24 | 0.47 |
| Manganese, ppm | 87 | 100 | 104 |
| Vitamin E, IU/kg | 1492 | 1525 | 1292 |
| Vitamin C, ppm | 127 | 261 | 141 |
| Lipoic Acid, ppm* | 101 | 135 | |

* Lipoic acid based on formulated, not analyzed values.

**[0060]** The compositions for use in the methods of this invention further comprise at least one nutrient chosen from manganese, methionine, cysteine, mixtures of methionine and cysteine, L-carnitine, lysine, and arginine. Specific advantageous amounts for each component in a composition will depend on a variety of factors including, for example, the species of

animal consuming the composition; the particular components included in the composition; the age, weight, general health, sex, and diet of the animal; the animal's consumption rate, and the like. Thus, the component amounts may vary widely, and may even deviate from the proportions given herein.

**[0061]** The omega-3 fatty acids may be obtained from a variety of sources. One convenient source is fish oils from, for example, menhaden, mackerel, herring, anchovy, and salmon. DHA and EPA are typical fatty acids present in such fish oils, and, together often make up a significant portion of the oil, such as about 25% to about 38% of the oil.

**[0062]** When the composition is an animal food, vitamins and minerals preferably are included in amounts required to avoid deficiency and maintain health. These amounts are readily available in the art. The National Research Council (NRC), for example, provides recommended amounts of such ingredients for farm animals. See, e.g., Nutrient Requirements of Swine (10th Rev. Ed., Nat'l Academy Press, Wash. D.C., 197298), Nutrient Requirements of Poultry (9th Rev. Ed., Nat'l Academy Press, Wash. D.C., 1994), Nutrient Requirements of Horses (Fifth Rev. Ed., Nat'l Academy Press, Wash. D.C., 1989), Nutrient Requirements of Dogs and Cats (Nat'l Academy Press, Wash. D.C., 2006). The American Feed Control Officials (AAFCO), for example, provides recommended amounts of such ingredients for dogs and cats. See American Feed Control Officials, Inc., Official publication, pp. 126-140 (2003). Examples of vitamins useful as food additives include vitamin A, B1, B2, B6, B12, C, D, E, K, H (biotin), K, folic acid, inositol, niacin, and pantothenic acid. Examples of minerals and trace elements useful as food additives include calcium, phosphorus, sodium, potassium, magnesium, copper, zinc, chloride, and iron salts.

**[0063]** The methods of the present invention include compositions that may further contain other additives known in the art. Preferably, such additives are present in amounts that do not impair the purpose and effect provided by the invention. Examples of additives include, for example, substances with a stabilizing effect, processing aids, substances that enhance palatability, coloring substances, and substances that provide nutritional benefits.

**[0064]** Stabilizing substances include, for example, substances that tend to increase the shelf life of the composition. Potentially suitable examples of such substances include, for example, preservatives, antioxidants, synergists and sequestrants, packaging gases, stabilizers, emulsifiers, thickeners, gelling agents, and humectants. Examples of emulsifiers and/or

thickening agents include, for example, gelatin, cellulose ethers, starch, starch esters, starch ethers, and modified starches.

**[0065]** Additives for coloring, palatability ("pal enhancers"), and nutritional purposes include, for example, colorants (e.g., iron oxide, such as the red, yellow, or brown forms); sodium chloride, potassium citrate, potassium chloride, and other edible salts; vitamins; minerals; and flavoring. Such additives are known in the art. See, e.g., U.S. Patent No. 3,202,514. See also, U.S. Patent No. 4,997,671. Flavorants include, for example, dairy product flavorants (e.g., milk or cheese), meat flavorants (e.g., bacon, liver, beef, poultry, or fish), oleoresin, pinacol, and the various flavorants identified in the trade by a FEMA (Flavor Extract Manufacturers Association) number. Flavorants help provide additional palatability, and are known in the art. See, e.g., U.S. Patent No. 4,997,672. See also, U.S. Patent No. 5,004,624. See also, U.S. Patent No. 5,114,704. See also, U.S. Patent No. 5,532,010. See also, U.S. Patent No. 6,379,727. The concentration of such additives in the composition typically may be up to about 5% by weight. In some embodiments, the concentration of such additives (particularly where such additives are primarily nutritional balancing agents, such as vitamins and minerals) is about 0% to about 2.0% by weight. In some embodiments, the concentration of such additives (again, particularly where such additives are primarily nutritional balancing agents) is about 0% to about 1.0% by weight.

**[0066]** Supplements include, for example, a feed used with another feed to improve the nutritive balance or performance of the total. Supplements include compositions that are fed undiluted as a supplement to other feeds, offered free choice with other parts of an animal's ration that are separately available, or diluted and mixed with an animal's regular feed to produce a complete feed. The AAFCO, for example, provides a discussion relating to supplements in the American Feed Control Officials, Inc. Official Publication, p. 220 (2003). Supplements may be in various forms including, for example, powders, liquids, syrups, pills, encapsulated compositions, and the like.

**[0067]** Treats include, for example, compositions that are given to an animal to entice the animal to eat during a non-meal time. Treats for canines include, for example, dog bones. Treats may be nutritional, wherein the composition comprises one or more nutrients, and may, for example, have a composition as described above for food. Non-nutritional treats encompass any other treats that are non-toxic.

**[0068]** Toys include, for example, chewable toys. Toys for dogs include, for example, artificial bones. There is a wide range of suitable toys currently marketed. See, e.g.,, U.S. Pat. No. 5,339,771 (and references disclosed in U.S. Pat. No. 5,339,771). See also, e.g., U.S. Pat. No.5,419,283 (and references disclosed in U.S. Pat. No. 5,419,283). The invention provides both partially consumable toys (e.g., toys comprising plastic components) and fully consumable toys (e.g., rawhides and various artificial bones). It should be further recognized that this invention provides toys for both human and non-human use, particularly for companion, farm, and zoo animal use, and particularly for dog, cat, or bird use.

**[0069]** A "food" is a nutritionally complete diet for the intended recipient animal (e.g., domestic cat or domestic dog). A "nutritionally complete diet" is a diet that includes sufficient nutrients for maintenance of normal health of a healthy animal on the diet. The methods of this invention utilize compositions that are not intended to be restricted by any specific listing of proteinaceous or fat ingredients or product form. The compositions can be prepared in, for example, a dry, canned, wet, or intermediate moisture form using conventional pet food processes. In some embodiments, the moisture content is about 10% to about 90% of the total weight of the composition. In other embodiments, the moisture content is about 65% to about 75% of the total weight of the composition.

**[0070]** In preparing a composition for use with the methods of the present invention, any ingredient (e.g., fish oil) generally may, for example, be incorporated into the composition during the processing of the formulation, such as during and/or after mixing of other components of the composition. Distribution of these components into the composition can be accomplished by conventional means. In one embodiment, ground animal and poultry proteinaceous tissues are mixed with the other ingredients, including fish oils, cereal grains, other nutritionally balancing ingredients, special-purpose additives (e.g., vitamin and mineral mixtures, inorganic salts, cellulose and beet pulp, bulking agents, and the like); and water that is sufficient for processing is also added. These ingredients preferably are mixed in a vessel suitable for heating while blending the components. Heating of the mixture may be effected using any suitable manner, such as, for example, by direct steam injection or by using a vessel fitted with a heat exchanger. Following the addition of the last ingredient, the mixture is heated to a temperature range of about 50°F (10°C) to about 212°F (100°C). In some embodiments, the mixture is heated to a temperature range of about 70°F (21°C) to about 140°F (60°C).

Temperatures outside these ranges are generally acceptable, but may be commercially impractical without use of other processing aids. When heated to the appropriate temperature, the material will typically be in the form of a thick liquid. The thick liquid is filled into cans. A lid is applied, and the container is hermetically sealed. The sealed can is then placed into conventional equipment designed to sterilize the contents. This is usually accomplished by heating to temperatures of greater than about 230°F (110°C) for an appropriate time, which is dependent on, for example, the temperature used and the composition.

**[0071]** Methods of the present invention include utilizing compositions that can be prepared in a dry form using conventional processes. In one embodiment, dry ingredients, including, for example, animal protein sources, plant protein sources, grains, etc., are ground and mixed together. Moist or liquid ingredients, including fats, oils, animal protein sources, water, etc., are then added to and mixed with the dry mix. The mixture is then processed into kibbles or similar dry pieces. Kibble is often formed using an extrusion process in which the mixture of dry and wet ingredients is subjected to mechanical work at a high pressure and temperature, and forced through small openings and cut off into kibble by a rotating knife. The wet kibble is then dried and optionally coated with one or more topical coatings which may include, for example, flavors, fats, oils, powders, and the like. Kibble also can be made from the dough using a baking process, rather than extrusion, wherein the dough is placed into a mold before dry-heat processing.

**[0072]** The compositions are also designed to be easier to chew. Canine and feline foods are typically formulated based on life stage (age), size, body composition, and breed. In the methods of this invention, some embodiments of the compositions address specific nutritional differences between super senior regular or small breed dogs, large breed dogs, and cats.

**[0073]** All percentages expressed herein are on a weight by dry matter basis unless specifically stated otherwise.

**[0074]** As noted previously, this invention is directed, in part, to a method for enhancing the quality of life of an animal. The method comprises feeding a senior or super senior animal a composition in an amount effective to enhance alertness, improve vitality, protect cartilage, maintain muscle mass, enhance digestibility, and improve skin and pelage quality. Additionally, we now report herein our surprising discovery that the enhanced quality of life of an animal achieved by administration of the compositions of the present invention is reflected

at the genomic level. While it may be that a change in expression of any one gene disclosed in the tables presented below may result in beneficial or deleterious biological effects, the data presented herein indicate that, overall, the observed expression profiles are consistent with the beneficial biological effects seen in vivo after administration of the diets disclosed herein. Specifically, gene chip data indicate that the expression of genes that encode proteins associated with or related to several biological pathways such as blood clotting and platelet activation and aggregation, bone and muscle integrity, inflammatory responses, cartilage degradation and pain response, DNA damage and repair pathways, neural function, glycogen synthesis and degradation, glycolysis, gluconeogenesis, the pentose phosphate pathway, the aging process, and electron transport are, for the most part, beneficially altered through administration to the animal of compositions described herein. Thus, the invention also relates to methods of measuring or characterizing the enhancement in the quality of life of an animal, particularly a senior or super senior animal, fed a composition described herein by quantitating the gene expression levels of one or more genes chosen from those disclosed in Tables 5-14 in said animal prior to and after feeding a composition disclosed herein and comparing said levels in the animal wherein an enhancement in the quality of life of said animal is reflected by a beneficial change in gene expression levels in said animal.

**[0075]** Quantitation of gene expression may be carried out in numerous ways familiar to one of skill in the art and include such techniques as RT PCR as well as gene chip assays and Northern blotting. Thus, it is contemplated herein that the expression levels detected may be used, for example, in methods to measure enhancement in the quality of life of an animal as disclosed herein.

**[0076]** There are certain age-induced changes in gene expression patterns (see, for example, P. Tollet-Egnell et al., *Molecular Endocrinology*, 15(2):308-318(2001)). Without being bound by theory, such changes in gene expression patterns may be related to senescence, the aging mechanism. C-K Lee et al., *Science*, 285:1390-1393(1999) reported that alterations in the gene expression profile of the aging process in mice can be completely or partially prevented by caloric restriction. We have found that, surprisingly, the changes in expression of certain genes as an animal, such as a dog, ages from a healthy adult animal to a geriatric animal can be reversed by a diet of super senior dog food according to the present invention. Thus, comparing the gene expression pattern in a healthy adult dog to the gene expression pattern in a

geriatric dog, one finds certain genes expressed higher ("up") in the geriatric dog while other genes are expressed lower ("down"). Surprisingly, we have found that by feeding a diet of super senior dog food according to the present invention to a geriatric dog, the gene expression pattern can be reversed. That is, comparing the gene expression pattern in a geriatric dog fed a control diet to the gene expression pattern in a geriatric dog fed a diet of super senior dog food of the present invention, one finds that certain genes are expressed higher ("up") under the control dog food regimen, while other genes are expressed lower ("down") under the control dog food regimen. The result is that the geriatric dogs under the super senior dog food diet of the present invention had their gene expression profiles altered towards that of healthy adult dogs. Comparing the list of genes that correlate in the opposite sense to the healthy adult dog/geriatric dog expression pattern, we found genes provided in Tables 15-20 below that surprisingly demonstrate that the super senior dog food of the present invention can reverse the alteration in expression that certain genes undergo as a part of the aging process. Thus, the quality of life of geriatric animals can be benefited by modifying the aging process in that the gene expression pattern of certain genes are altered towards that of a healthy adult dog from the pattern of a geriatric dog.

**[0077]** Accordingly, this invention is directed, in part, to a method for enhancing the quality of life of an animal comprising feeding a senior or super senior animal a composition in an amount effective to alter the gene expression pattern of certain genes (provided on Tables 15-20 where the direction of adult vs geriatric is the same as the direction of super senior vs control) towards the pattern of a healthy adult dog form the pattern of a geriatric dog. The method enhances the quality of life of an animal by modifying the expression of genes associated with the aging process such that the gene expression pattern is altered towards that of a healthy adult animal from that of a geriatric animal.

**[0078]** In one aspect, this invention is directed to a method for improving the quality of life of a senior or super senior animal comprising feeding the animal a composition comprising at least about 9% by weight protein; at least about 5% by weight fat; and at least about 0.05% by weight of at least one omega-3 polyunsaturated fatty acid, wherein the method comprises feeding the animal the composition in an amount effective to enhance the animal's quality of life, wherein enhanced quality of life is evidenced by a change in expression of one or more genes which encode proteins associated with the aging process. As described herein, these

genes are generally referred to as genes associated with the aging process, however, it should be noted that these genes specifically may be related to biological pathways chosen from , e.g., inflammation, DNA repair, cell survival, fat or cholesterol metabolism, immune regulation, protein synthesis, cell growth and cell death.

**[0079]** In an embodiment of this aspect, the change in expression is of one or more genes listed on Tables 15-19 and wherein the change in expression is towards the expression level in a healthy adult animal as compared to the expression level in a geriatric animal.

**[0080]** In another embodiment of this aspect, the animal is a dog.

**[0081]** In another aspect, this invention is directed to a method for improving the quality of life of a senior or super senior animal comprising feeding the animal a composition comprising at least about 9% by weight protein; at least about 5% by weight fat; and at least about 0.05% by weight of at least one omega-3 polyunsaturated fatty acid, wherein the method comprises feeding the animal the composition in an amount effective to enhance the animal's quality of life, wherein enhanced quality of life is evidenced by a change in expression of one or more genes listed on Table 20 and wherein the change in expression is towards the expression level in a healthy adult animal as compared to the expression level in a geriatric animal.

**[0082]** In an embodiment of this aspect, the animal is a dog.

**[0083]** It is also contemplated herein that the invention relates to methods for treating an animal suffering from disorders or disease associated with or relating to any one of more of the following biological pathways: blood clotting and platelet activation and aggregation, bone and muscle integrity, inflammatory responses, cartilage degradation and pain response, DNA damage and repair pathways, neural function, glycogen synthesis and degradation, glycolysis, gluconeogenesis, the pentose phosphate pathway, the aging process, and electron transport comprising administering to the animal an effective amount of a food composition of the present invention.

**[0084]** This invention is not limited to the particular methodology, protocols, and reagents described herein because they may vary. Further, the terminology used herein is for the purpose of describing particular embodiments only and is not intended to limit the scope of the present invention. The terms "comprise", "comprises", and "comprising" are to be interpreted inclusively rather than exclusively.

**[0085]** Unless defined otherwise, all technical and scientific terms and any acronyms used herein have the same meanings as commonly understood by one of ordinary skill in the art in the field of the invention. Many modifications and variations of the present invention are possible in light of the above teachings. It is therefore to be understood that within the scope of the appended claims the invention may be practiced otherwise than as specifically described.

**[0086]** All patents, patent applications, and publications mentioned herein are incorporated herein by reference in their entirety. However, where there is a conflict between a definition in the present disclosure and that of a cited reference, the present disclosure controls.

## EXAMPLES

**[0087]** This invention can be further illustrated by the following examples, although it will be understood that these examples are included merely for purposes of illustration and are not intended to limit the scope of the invention unless otherwise specifically indicated.

### Example 1

**[0088]** A composition formulated for senior or super senior regular or small breed canines is described in Table 2.

**Table 2**

**Ingredient Composition for Canine Regular or Small Breed Super Senior**

| Ingredient | % of composition |
|---|---|
| Carbohydrate | 65.83 |
| Animal Protein | 14.31 |
| Vegetable Protein | 6.05 |
| Animal/Vegetable Fat | 6.60 |
| Omega Fat | 3.38 |
| Fiber | 1.42 |
| Minerals | 1.63 |
| Vitamins | 0.78 |

### Example 2

**[0089]** A composition formulated for senior or super senior large breed canines is described in Table 3.

**Table 3**

**Ingredient Composition for Canine Large Breed Super Senior**

| Ingredient | % of composition |
|---|---|
| Carbohydrate | 65.15 |
| Animal Protein | 14.79 |
| Vegetable Protein | 6.45 |
| Animal/Vegetable Fat | 6.23 |
| Omega Fat | 4.12 |
| Fiber | 1.30 |
| Minerals | 0.91 |
| Vitamins | 1.05 |

**Example 3**

**[0090]** A composition formulated for senior or super senior felines is described in Table 4.

**Table 4**

**Ingredient Composition for Feline Super Senior**

| Ingredient | % of composition |
|---|---|
| Carbohydrate | 31.47 |
| Animal Protein | 25.57 |
| Vegetable Protein | 20.14 |
| Animal/Vegetable Fat | 13.31 |
| Omega Fat | 1.61 |
| Fiber | 4.80 |
| Minerals | 1.77 |
| Vitamins | 1.34 |

**Example 4**

**Genomic Analysis of Control vs. Super Senior Pet Food**

**[0091]** To further characterize the nutritional benefits of the super senior pet food compositions of the present invention, gene expression profiles from animals fed the compositions compared to control animals are assayed and the results are described in detail below.

Materials and Methods:

**Study design:**

**[0092]** Blood samples are drawn from 9 Beagles according to conventional methods before and after feeding for 14 days on Super Senior K9 diet (a total of 18 samples). Each sample taken after the 14-day trial is compared to its own control.

**Isolation of Lymphocytes from Canine Blood**

**Reagents:**

**[0093]** 4ml canine blood, heparin or EDTA tubes, Hank's Balanced Salt Solution (Gibco 14175-095),HEPES buffer (Gibco 15630-080), Accu-Paque (Accurate Chemical & Scientific Corp AN3100).

**Materials/Equipment:**

**[0094]** Transfer pipettes (VWR 14670-147),14 ml centrifuge tubes w/ caps,9" Pasteur pipettes,1.5 ml microcentrifuge tubes (VWR 20170-038), centrifuge tube racks, microcentrifuge tube bale, waste container, Beckman Coulter Allegra 25R Centrifuge, SN AJC01J015Eppendorf Centrifuge, 5417C.

**Solutions:**

**[0095]** Hank's Balanced Salt Solution (HBSS) w/ 25 mM HEPES buffer solution is made by adding 12.8 ml of HEPES buffer solution to a 500 ml bottle of HBSS. Hank's Balanced Salt Solution and Accu-Paque need to be removed from the refrigerator and placed at room temperature at least 30 minutes before beginning the lymphocyte isolation. Both solutions should be place back in the refrigerator (4°C) immediately following their use.

**[0096]** **Procedure:**

**[0097]** 1. Measure 4 ml of HBSS w/ HEPES into the correct number of 14 ml centrifuge tubes (one tube for each 4 ml draw of blood)

**[0098]** 2. Using a transfer pipette, transfer 4 ml blood from the Vacutainer® tubes to the 14 ml centrifuge tube containing the HBSS w/ HEPES.

**[0099]** 3. Mix the sample well using the transfer pipette to pipette up and down for 30 seconds.

**[00100]** 4. Insert a 9" Pasteur pipette into each of the 14 ml centrifuge tubes. Make sure the bottom tip of the Pasteur pipette touches the bottom of the tube.

**[00101]** 5. Using a transfer pipette, slowly add 4 ml of Accu-Paque by running the liquid down the inside of the Pasteur pipette allowing gravity to layer the Accu-Paque under the diluted blood sample.

**[00102]** 6. Plug the top of the Pasteur pipette using your finger and gently remove the pipette.

**[00103]** 7. Centrifuge the tubes at 800 x g for 20 minutes at room temperature. For puppy blood a longer centrifugation of 45 minutes is necessary to allow for a good separation of RBC's from WBC's.

**[00104]** 8. Using a transfer pipette, carefully remove the top layer to within 0.5cm of the middle opaque layer and discard.

**[00105]** 9. Using a new transfer pipette, carefully remove the middle opaque layer and transfer to a 1.5 ml microcentrifuge tube. Be careful not to transfer any of the bottom layers.

**[00106]** 10. Centrifuge the microcentrifuge tubes at 13,200 rpm for 3.5 minutes at room temperature.

**[00107]** 11. Carefully remove the supernatant and flash freeze the remaining pellet (lymphocytes) in liquid nitrogen. Store the final samples at -80°C.

**RNA isolation:**
**Reagents:**

**[00108]** Deionized $H_2O$, Absolute ethanol (Sigma E7023), RNA Storage Solution (Ambion 7000), RNase Zap® (Ambion 9780), Buffer RLT, Buffer RW1 and Buffer RPE (provided in the RNeasy Mini Kit).

**Equipment/Materials:**

**[00109]** RNeasy Mini Kit (Qiagen 74104), QIAshredder spin columns (Qiagen 79656), P1000 Pipetman pipette (Rainin), P200 Pipetman pipette (Rainin), 100-100 µl filtered pipette tips (USA Scientific 1126-7810), 1-200 µl filtered pipette tips (USA Scientific 1120-8810), sterile transfer pipettes (VWR 14670-147), 55 ml sterile solution basin (VWR 21007-974), 2

waste containers (one for liquid, one for tips/pipettes), 1.5 ml sterile microcentrifuge tubes (VWR 20170-038), Microcentrifuge tube rack, permanent marker, Eppendorf Microcentrifuge, model #5417C.

**Procedure:**

**[00110]** 1. Loosen the pellet in the microcentrifuge tubes by thawing slightly and then flick the tube to dislodge the pellet.

**[00111]** 2. Add the appropriate volume of Buffer RLT (in this case use 600 µl). Vortex or pipette to mix.

**[00112]** 3. Transfer sample to a QIAshredder tube to homogenize the sample. Centrifuge for 2 minutes at 14,000 rpm. Discard spin column but keep the collection tube and its contents.

**[00113]** 4. Add one volume (600 µl) of 70% ethanol to the homogenized lysate and mix by pipetting.

**[00114]** 5. Apply a 600 µl aliquot of the sample to an RNeasy mini column placed in a 2ml collection tube. Close tube gently and centrifuge for 15 sec at 14,000 rpm. Discard the flow-through. Add the second 600 µl aliquot of the cell lysate to the same spin column and repeat. Discard flow-through.

**[00115]** 6. Reuse the collection tube from step 5. Add 700 µl Buffer RW1 to the column. Centrifuge for 15 sec at 14,000rpm. Discard the flow-through and collection tube.

**[00116]** 7. Transfer the column to a new 2 ml collection tube and pipette 500 µl Buffer RPE onto the column. Centrifuge for 15 sec at 14,000rpm to wash the column. Discard the flow-through but save the collection tube for step 8.

**[00117]** 8. Add another 500 ml Buffer RPE to the column. Centrifuge for 2 min at 14,000rpm to dry the membrane.

**[00118]** 9. Transfer the column to a new 1.5 ml collection tube. Pipette 10 µl of RNA Storage Solution directly onto the membrane. Centrifuge for 1min at 14,000 rpm to elute the RNA. Add a second volume of 5 µl of RNA Storage Solution directly to the membrane and spin for an additional minute. Store the final elution of RNA at -80°C.

**RNA probe preparation and hybridization.**
**Reagent:**
**[00119]** Ovation TM Biotin System v1.0 for probe preps.

**Protocol :**

**[00120]** User Guide (Cat#D01002, version 10/27/04, NuGEN Technologies, Inc). The experimental procedure is followed as described in the user guide. All probe preparation starts with 50 ng of total RNA.

**Gene chip Procedures:**

**[00121]** The Genechips used for the test is the Canine Genome 2.0 Array (Affymetrix). This Genechip contains 44,000 probe sets. Detailed sequence information for each unique probe identification number is available from the manufacturer.

**Gene expression analysis:**

**[00122]** Normalization is performed using MAS 5 provided in GCOS Affymetrix software (version 1.2). Expression levels for the genes analyzed are indicated on the tables included in the examples below, where an upward facing arrow refers to "up regulation" or increase and a downward facing arrow indicates "down regulation" in gene expression. Similarly, in some tables, upward or downward facing arrows also indicate increases or decreases in activity of certain proteins involved in a particular pathway, and are otherwise self explanatory.

**Gene list selection:**

**[00123]** 15,411 genes are chosen for further analysis based on their "present" calls in at least 9 out of 18 samples.

**[00124]** Results of the gene chip analysis indicate that 1088 genes are differentially expressed between the control and Super Senior diet treated groups. The expression levels of these 1088 genes are statistically significant when grouped by 'diet'; using a parametric test where the variances is not assumed to be equal (Welch t-test). The p-value cutoff is 0.01 with no multiple testing correction. Under those selection criteria only about 154 genes would be expected to pass the restriction by chance. The genomic data is discussed in detail below.

**Results:**

**Effect of nutrition on genes associated with pain and inflammation**

**[00125]** Based on an analysis of the gene chip data, at the $P < 0.01$ level, expression levels of 1,088 genes changed compared to control expression levels (10 were up regulated and the rest down regulated). At the $P < 0.001$ level, data indicate that expression in 35 genes is down

regulated in beagles fed the super senior food. Nine of these down regulated genes are identified as related to the inflammatory and pain response. Down regulation of these genes may be predicted to result in pain relief, cartilage protection (less damage) and reduction in inflammatory responses. The compositions disclosed herein may be part of a therapeutic regimen to treat animals suffering from pain and/or inflammatory diseases. These genes and their putative role in inflammation and pain response are provided below in Tables 5-6.

**Table 5: Genes involved in inflammation and pain response (P < 0.001)**

| Genes | Also Known As | Probe | Best Current BLAST Annotation | % match of probe sequence to BLAST hit | Probe Target Sequence |
|---|---|---|---|---|---|
| Phospholipase A2 | IPLA2GAMMA, IPLA2-2 | CfaAffx.6431.1.S1_s_at | PREDICTED: Canis familiaris similar to intracellular membrane-associated calcium-independent phospholipase A2 gamma; transcript variant 3 (LOC475880); mRNA | 100 | GGAGCCATGCATTT TATGACAGTCAAAC GTGGGAAAATATTC TTAAGGACAGAATG GGATCCTCGCTAAT GATTGAAACAGCAA GAAACCCTTCATGT CCTAAGGATGGAG GTTTGCTTCTGAAT AACCCTTCAGCGCT AGCAATGCACGAGT GCAAATGTCTTTGG CCTGACGTCCCATT AGAGTGCATTGTGT CCCTGGGCACCGG GCGTTATGAGAGTG ATGTGAGAAACTCT GTGACATCTACAAG CTTGAAAACCAAAC TGTCTAATGTCATT AACAGTGCTACAGA TACAGAAGAAGTCC ACGTAATGCTTGAT GGTCTTTTACCTCC TGACACCTATTTTA GAT |
| Dipeptidase 2 | Putative dipeptidase | CfaAffx.31124.1.S1_at | PREDICTED: Canis familiaris similar to dipeptidase 2 (LOC611083); mRNA | 82.197 | GTGCTGCAATGCAA CCTGTTAGCTAACG TGTCCACTGTGGCA GTTCCCACGCATCC CTGCCCTGGAAGC CCCACAGTGCTGAC TCTCCATCCCTCAG ATCACTTTGACTAC ATCAGGGCAGTCAT TGGATCCAAGTTCA TTGGAATTGGTGGA GATTATGATGGGGC CAGACGTTTCCCTC AGGGGCTGGAGGA TGTGTCCACATACC CAGTTCTGATAGAG GAGTTGCTGAGGC GTGGCTGGAGTAG GGAAGAGCTCCAG GGTGTCCTTCGAG |

| Genes | Also Known As | Probe | Best Current BLAST Annotation | % match of probe sequence to BLAST hit | Probe Target Sequence |
|---|---|---|---|---|---|
| | | | | | GAAACCTACTGCGG<br>GTCTTTGGACAGGT<br>GGAACAGGTACGG<br>GAGGCAAGCAAGG<br>GGCAAAGGCCCTT<br>GGAGGATGAGTTC<br>CCGGATGAGCAGC<br>TGAGCAGCTCTTGC<br>CGCTCCGTTCTCTC<br>ACGTCTGCATCAGA<br>CACAGTACCCTGCT<br>CCATACCAGAAACT<br>AACTGAGATTTCAC<br>CTGAGTGGTCCCCT<br>AAACAGTCATTGTC<br>AAAATCTCTCCCCA<br>TCATGGCCCCAGG<br>CCTCATAGTTATTG<br>CTGCTTGT |
| Thromboxane synthase | Thromboxane A synthase 1,<br><br>Thromboxane A synthase, Platelet,<br><br>Cytochrome P450, subfamily V,<br><br>CYP5, CYP5A1,<br>Thromboxane synthatase, TXA synthase, TXS | CfaAffx.6939.1.S1_s_at | PREDICTED: Canis familiaris similar to Thromboxane-A synthase (TXA synthase) (TXS) (LOC482771); mRNA | 100 | ATCGCTGGCTATGA<br>GATCATCACCAACA<br>CGCTCTCTTTTGCC<br>ACCTACCTCCTGGC<br>CACCAACCCTGACT<br>GCCAAGAGAAGCTT<br>CTGGCAGAGGTGG<br>ACAGCTTTAAGGAG<br>AAATATACGGCCCT<br>TGACTACTGCAGCC<br>TCCAGGAAGGCCT<br>GCCCTACCTGGACA<br>TGGTGATTGCGGA<br>GACCTTGAGGATCT<br>ACCCCCCGGCTTTC<br>AGGTTCACACGGG<br>AGGCGGCGCGGGA<br>CTGCGAGGTGCGG<br>GGACAGCGCATCC<br>CCGCGGGCGCCGT<br>GGTGGAGGTGGCC<br>GTGGGCGCCCTGC<br>ACCGTGACCCTGA<br>GTACTGGCCACAAC<br>CGGAGACCTTCAAC<br>CCCGAGAGGTTCAA<br>GGCCGAGGCGCAG<br>CGACGACAGCAAC<br>CCTTCACCTACCTG<br>CCGTTCGGCGCGG<br>GCCCCCGGAGCTG<br>CCTCGGGGTGCGG<br>CTGGGGCTGCTGG<br>AGGTCAAGCTGAC<br>GCTGCTGCAGGTC<br>CTGCACCAGTTCCG<br>GTTCGAGGCCTGC<br>CCGGAGACGCAGG<br>TACCACTGCAGCTA<br>GACTCCAAATCTGC<br>CCTAGGTCCAAAGA<br>ATGGCATCTACATC<br>AAGATTGTCTCCCG<br>CT |

| Genes | Also Known As | Probe | Best Current BLAST Annotation | % match of probe sequence to BLAST hit | Probe Target Sequence |
|---|---|---|---|---|---|
| Ubiquitin conjugating enzyme E2D 3 | Ubiquitin protein ligase, Ubiquitin carrier protein, E2(17)KB 3, Ubiquitin conjugating enzyme E2-17 kDa 3, UBC4/5, UBCH5C | CfaAffx.275.1.S1_s_at | PREDICTED: Pan troglodytes LOC461941 (LOC461941); mRNA | 97.19626 | GATTTGGCCCGTGA CCCTCCAGCACAAT GTTCTGCAGGTCCT GTTTGGGATGATAT GTTTCATTGGCAAG CCACAATTATAGGA CCTAATGACAGCCC ATATCAAGG |
| NEDD8 ultimate buster-1 | Neural precursor cell expressed, developmentally down regulated 8, Ubiquitin like protein NEDD8 | Cfa.12556.1.A1_s_at | PREDICTED: Canis familiaris similar to NEDD8 ultimate buster-1 (NY-REN-18 antigen) (LOC475542); mRNA | 99.12473 | GGAATGGGCTACTC TACTCATGCAGNCA AGCAGGNCCTGCA TCAGGCCAGTGGG AACCTGGACGAAG CCCTGAAGATTCTT CTCAGCAATCCTCA GATGTGGTGGTTAA ATGATTCAGATCCT GAAACGANCAACCA GCAAGAAAGTCCTT CCCAGGAAAACATT GACCAACTGGTGTA CATGGGCTTCGAC GCTGTGGTGGCTG ATGCTGCCTTGAGA GTGTTCAGGGGAAA CGTGCAGCTGGCA GCTCAGNCCCTCG CCCACAACGGAGG AACTCTTCCTCCTG ACCTGCAGCTCTTG GTGGAAGACTCTTC ATCAACGCCATCCA CGTCCCCTTCCGAC TCCGCAGGTACCTC TAGTGCCTCAACAG ATGAAGATATGGAA ACCGAAGCTGTCAA TGAAATACTGGAAG ATATTCCAGAACAT GAAGAAGATTATCT TGACTCAACACTGG AAG |
| Mitogen - activated protein kinase 14 (p38) | p38, Mitogen activated protein kinase 14, Cytokine suppressive antiinflammatory drug binding protein 1, CSBP1 , CSAID binding protein 1, Stress activated protein kinase 2A, SAPK2A , p38 MAP kinase, p38 alpha, RK, MXI2, Cytokine suppressive antiinflammatory drug binding protein 2, CSBP2 , CSAID binding | CfaAffx.2947.1.S1_at | Homo sapiens mitogen-activated protein kinase 14; transcript variant 2; mRNA (cDNA clone MGC:34610 IMAGE:5181064); complete cds | 97.84946 | GAGATGGAGTCCT GAGCACCTGGTTTC TGTTTTGTTGATCC CACTTCACTGTGAG GGGAAGGCCTTTTC ATGGGAACTCTCCA AATATCATTC |

| Genes | Also Known As | Probe | Best Current BLAST Annotation | % match of probe sequence to BLAST hit | Probe Target Sequence |
|---|---|---|---|---|---|
| | protein 2 | | | | |
| Matrix metalloproteinase 19 (MMP-19) | MMP 19 | Cfa.4573.1.A1_at | Homo sapiens cDNA FLJ38021 fis; clone CTONG2012847 | 48.93048 | GTAGTTGATTCCTG GTTCGCCTTTCCTC TTGGGTCCCATAGG TTCGAATCCCCTTC TACCTCAGTCGGGA GTACTGTCCTCCAT GGTGCTTCCCTTCC TCTCCTTAATGTGG GGAAGACCATGGG GCAATGCATGGCG CAGGACCTGCCTC CCCCAAAAGCAGTC TACTTGCTCCACGG AGAGAGAACTGGG TCCACGTGCCAGA GTCTTGCCCTTTGG CCCAGAGTAGCCT GGTCTTCATGGCTG TATGGGAGACAAGT GCCTTCTCTGCTTC TTGTTGTAGGTGAT GCTAATCTCCTTAA CCAAACCTTTGTCC CAGCCGCTAATCTG TTCTAACTCTCCCT CCTCNTGATTCTCC TGCTCAAAGTCTGT TC |
| Tissue Inhibitor of metalloproteinases (TIMP-1) | TIMP-1 | Cfa.3680.1.S1_s_at | Canis familiaris TIMP metallopeptidase inhibitor 1 (TIMP1); mRNA | 99.4 | AGATGTTCAAGGGT TTCAGCGCCTTGGG GAATGCCTCGGACA TCCGCTTCGTCGAC ACCCCCGCCCTGG AGAGCGTCTGCGG ATACTTGCACAGGT CCCAGAACCGCAG CGAGGAGTTTCTGG TCGCCGGAAACCT GCGGGACGGACAC TTGCAGATCAACAC CTGCAGTTTCGTGG CCCCGTGGAGCAG CCTGAGTACCGCTC AGCGCCGGGGCTT CACCAAGACCTATG CTGCTGGCTGTGA GGGGTGCACAGTG TTTACCTGTTCATC CATCCCCTGCAAAC TGCAGAGTGACACT CACTGCTTGTGGAC GGACCAGTTCCTCA CAGGCTCTGACAAG GGTTTCCAGAGCC GCCACCTGGCCTG CCTGCCAAGAGAG CCAGGGATATGCAC CTGGCAGTCCCTG CGGCCCCGGATGG CCTAAATCCTACTC CCCGTGGAAGCCA |

| Genes | Also Known As | Probe | Best Current BLAST Annotation | % match of probe sequence to BLAST hit | Probe Target Sequence |
|---|---|---|---|---|---|
| Fatty acid amide hydrolase (FAAH) | Oleamide hydrolase Anandamide amidohydrolase FAAH | CfaAffx.7308.1.S1_x_at | PREDICTED: Canis familiaris similar to Ubiquinol-cytochrome c reductase complex 11 kDa protein; mitochondrial precursor (Mitochondrial hinge protein) (Cytochrome C1; nonheme 11 kDa protein) (Complex III subunit VIII); transcript variant 2 (LOC608530); mRNA | 63.33333 | AAGCCTGCACAGTG TTCACCCCACTTCC CACTCCTGTCTTTC TTTATCCAAAA GAAGTGGAGTAGG TGCCGCTGTTGCTG CTGGTGTTGAATTC AGAACTGTAGCGG GACATGGGGCTGG AGGACGAGCAAAA GATGCTGACCGGG TCCGGAGATCCCAA GGAGGATCCCCTAA CAACAGTGAGAGA GCAATGCGAGCAG CTGGAGAAATGTGT AAAGGCTCGGGAG CGGCTAGAGCTCT GTGACCAGCGTGTA TCCTCCAGGTCACA GACAGAGGAGGAT TGCACAGAGGAGC TCTTTGACTTCCTG CATGCAAGGGACC ACTGTGTGGCCCAC AAACTCTTTAACAG CTTG |

**Table 6. Summary of down-regulated enzyme roles involved in the eicosanoid pathway (inflammatory response)**

| Gene | Gene Expression Compared to Control | Results in | Role |
|---|---|---|---|
| Phospholipase $A_2$ | ↓ | ↓ in arachidonic release from phospholipids | ↓ in 2-series inflammatory response |
| Thromboxane synthase | ↓ | ↓ Thromboxane $A_2$ | ↓ platelet aggregation, vasoconstriction, lymphocyte proliferation and bronchoconstriction |
| | ↓ | ↓ Thromboxane $B_2$ | ↓ vasoconstriction |
| Dipeptidase 2 | ↓ | ↓ Leukotriene $E_4$ | ↓ component of slow-reactive substance of anaphylaxis, microvascular vasoconstrictor and bronchoconstriction |
| Ubiquitin conjugating enzyme E2D 3 (and NEDD8 | ↓ | ↓ ubiquination or activation of TAK1, IRAK and TRAF | ↓ MMP Production |

| Gene | Gene Expression Compared to Control | Results in | Role |
|---|---|---|---|
| ultimate buster-1) Mitogen activated protein kinase 14 (p38) | ↓ | ↓ in c-Jun promotor | ↓ MMP Production |
| MMP-19 | ↓ | ↓ MMP-19 | ↓ in T-cell derived MMP-19 which has been implicated in rheumatoid arthritis |
| TIMP-1 | ↓ | ↓ TIMP-1 | Deactivates MMP's concentration is directly related to MMP concentration |
| Fatty acid amide hydrolase | ↓ | ↑ anandmide | ↓ pain response |

**Effect of nutrition on genes involved in heart health and blood coagulation**

**[00126]** At the $P < 0.001$ and $P < 0.01$ level, 12 genes are identified to be related to heart health through regulation of the eicosanoid pathway and blood coagulation pathway. The genes are responsible for blood coagulation through platelet activation and aggregation. The down regulation of these genes through nutrition can prevent inappropriate blood clotting which may result in heart or brain related disorders. The compositions of the present invention may be part of a therapeutic regimen to treat animals suffering from disorders or diseases of the blood, heart or brain. These genes and their putative role in vivo are described in Tables 7 and 8 below.

**Table 7. Genes involved in heart health and blood coagulation**

| Gene | Probe | P-value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Seq. |
|---|---|---|---|---|---|
| Glycoprotein Ib | Cfa.3503.1.S1_at | < 0.01 | Canis familiaris glycoprotein Ib mRNA; complete cds | 98.57143 | TGTGGGTCCGAGCTAACAGCTA<br>CGTGGGGCCTCTGATGGCAGG<br>ACGGCGGCCCTCTGCCCTGAG<br>CCTGGGTCGTGGGCAGGACCT<br>GCTAGGTACGGTGGGCGTTAG<br>GTACTCCAGCCACAGCCTCTGA<br>GGCGACGGTGGGCAGTTTGGG<br>GACCTTGAGAGGCTGTGATGG<br>GCCCTCCTATCAGGATCTTGCT<br>GGGGGTGGGTGGGCAGGGAG<br>CACAGGATTGGGGGGAGGCCT |

| Gene | Probe | P-value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Seq. |
|---|---|---|---|---|---|
| | | | | | TAAGCACCTTTTCTGGGTCAGA AGCCTCCTCTCCGCATTGCATG TGCAACCTCAGTGAAGCAGCAT GGGCAGGGGAGCCGGACGGG CCACCCAACAGAGCTCCTTATG CTGCAGGAGGGGTTCACAGAC CACTCGGACATCACCATCACCT TGGGGGGGGTGCTTGAGGGAA AAGCAAATTGAACAGAGCGTGA TTCTCACGTGCAGGTACCTAAG GGAACTGGGGAAGAGATGCAC CAAGACGAGAGCCCTCGTCATC CCTGGGGAGCCCAAGCCTAGG GGTTTTCTTCCTCTTCCCGTTTA GCATTTTCCACCATCGTATGTTA C |
| Platelet glycoprotein VI | CfaAffx.4809.1.S1_at | < 0.01 | PREDICTED: Canis familiaris similar to glycoprotein VI (platelet) (LOC484303); mRNA | 50 | AGTTTTGACCAATTCGCTCTGT ACAAGGAGGGGGACACTGAGC CCCACAAGCAATCTGCAGAACA GTACTGGGCCAATTTCCCCATC ACCGCAGTGACTGTTGCCCACA GTGGGATCTACCGATGCTATAG CTTTTCCAGCAAGTTCCCGTAC CTGTGGTCAGCCCCCAGCGAC CCCCTGGAGCTTGTGGTAACAG GTGAGGGAGATGCAGTCCAAG CCTTTCTTCTTCAGCTCTTGCAT ACTCTGGTGGAAGTTCCAGGG GAGGGGCCAACAGTGCCTTCT AGGACTATCACTGTCTCTCCAA AGGGGTCAGACTCTCCAACTG GTCTTGCTCACCAGCACTACAC CAAGGGCAATCTGGTCCGGATA TGCCTTGGAGCTGTGATTCTAA TACTCCTGGTGGGAATTCTGGC AGAAGATTGGCACAGCAGAAAG AAACCCCTGTTGCTCCGGGTCA GAGCTGTCCACAGGCCACTCC CACCCCTCCCACAGACCCAGAA ACCACACAGTCATCAGGATGGG GGTCGACCAGATGGCCATAAC CAT |
| Platelet glycoprotein IX precursor | CfaAffx.7430.1.S1_at | < 0.01 | PREDICTED: Canis familiaris similar to Platelet glycoprotein IX precursor (GPIX) (CD42A) (LOC609630); mRNA | 100 | TCTGGGCTGCCACGGAGGCCA CCAACGACTGCCCCGCAGAGT GCACCTGCCAGACCCTGGAGA CCATGGGGCTGTGGGTGGACT GCAGGGGGCGGGGACTCAAGG CCCTGCCCGCCCTGCCGGTCC ACACCCGCCACCTCCTGCTGG CCAATAACAGCCTCCGCTCCGT GCCCCCTGGTGCCTTCGACCA CCTGCCTGGGCTGCAGATCCT CGACGTGATGCACAACCCCTG GCACTGTGACTGCAGCCTCACC TACCTGCGTCTCTGGCTGGAG GACCACACGCCCGAGGCCTTG CTGCAGGTCCGCTGTGCCAGC CCCGCGCTGGCCACCACCCGG CCGCTGGGCTGGCTGACGGGC TACGAGCTGGGCAGCTGCGGC TGGCAGCTACAGGCACCCTGG ACCTA |

| Gene | Probe | P-value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Seq. |
|---|---|---|---|---|---|
| Coagulation factor XIII A chain precursor | CfaAffx.14964.1.S1_s_at | < 0.01 | PREDICTED: Canis familiaris similar to Coagulation factor XIII A chain precursor (Coagulation factor XIIIa) (Protein-glutamine gamma-glutamyltransferase A chain) (Transglutaminase A chain); transcript variant 1 (LOC478711); mRNA | 99.6008 | ATCTCTCAGGCAACATCGTCTT CTACACCGGGGTCTCCAAGAC GGAATTCAAGAAGGAGACATTT GAAGTGACACTGGAGCCCTTGT CTTTCAAGAGAGAGGAGGTGCT GATCAGAGCGGGCGAGTACAT GGGCCAGCTGCTAGAGCAAGC ATACCTGCACTTCTTTGTCACA GCGCGTGTCAATGAGTCCAAG GATATTCTGGCCAAGCAGAAGT CCACCGTGCTGACGATCCCCC AGCTCATCATCAAGGTCCGTGG CGCCAAGATGGTTGGTTCTGAC ATGGTGGTGACAGTTGAGTTCA CCAATCCCCTGAAAGAAACTCT GCGGAATGTGTGGATACACCTG GATGGTCCTGGAGTGATAAAGC CAATGAGGAAGATGTTCCGTGA AATCCAGCCCANTGCCACCATA CAATGGGAAGAAGTGTGTCGAC CCTGGGTGTCTGGCCCTCGGA AGCTGATAGCCAGCATGACGA GTGACTCCCTGAGACACGTGTA TG |
| Thromboxane synthase | CfaAffx.6939.1.S1_s_at | < 0.001 | PREDICTED: Canis familiaris similar to Thromboxane-A synthase (TXA synthase) (TXS) (LOC482771); mRNA | 100 | ATCGCTGGCTATGAGATCATCA CCAACACGCTCTCTTTTGCCAC CTACCTCCTGGCCACCAACCCT GACTGCCAAGAGAAGCTTCTGG CAGAGGTGGACAGCTTTAAGGA GAAATATACGGCCCTTGACTAC TGCAGCCTCCAGGAAGGCCTG CCCTACCTGGACATGGTGATTG CGGAGACCTTGAGGATCTACCC CCCGGCTTTCAGGTTCACACGG GAGGCGGCGCGGGACTGCGA GGTGCGGGGACAGCGCATCCC CGCGGGCGCCGTGGTGGAGGT GGCCGTGGGCGCCCTGCACCG TGACCCTGAGTACTGGCCACAA CCGGAGACCTTCAACCCCGAG AGGTTCAAGGCCGAGGCGCAG CGACGACAGCAACCCTTCACCT ACCTGCCGTTCGGCGCGGGCC CCCGGAGCTGCCTCGGGGTGC GGCTGGGGCTGCTGGAGGTCA AGCTGACGCTGCTGCAGGTCC TGCACCAGTTCCGGTTCGAGG CCTGCCCGGAGACGCAGGTAC CACTGCAGCTAGACTCCAAATC TGCCCTAGGTCCAAAGAATGGC ATCTACATCAAGATTGTCTCCC GCT |
| Dystrobrevin binding protein 1 isoform a | CfaAffx.15541.1.S1_s_at | < 0.01 | PREDICTED: Canis familiaris similar to dystrobrevin binding protein 1 isoform a (LOC610315); mRNA | 99.65986 | GGCAACATGTCGTCCATGGAG GTCAACATCGACATGCTGGAGC AGATGGACCTGATGGACATCTC TGACCAGGAGGCCCTGGACGT CTTCCTGAACTCCGGCGCTGAA GACAACACGGTGCCGTCTCCG GTCTCAGGGCCTGGCTCGGGG GACAGTCGGCAGGAAATCACG CTCCGGGTTCCAGATCCCGCC GAATCGCAAGCTGAGCCTCCTC CCTCGCCGTGTGCCTGTCCTGA |

| Gene | Probe | P-value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Seq. |
|---|---|---|---|---|---|
| | | | | | GCTGGCCGCCCCGGCCCCCGG<br>CGACGGTGAGGCCCCCGTGGT<br>CCAGTCTGACGAGGAG |
| Integrin beta-7 precursor | Cfa.11961.1.A1_s_at | < 0.01 | PREDICTED: Canis familiaris similar to Integrin beta-7 precursor (LOC477598); mRNA | 99.0909 | ATTACAACGTGACTCTGGCTTT<br>GGTCCCTGTCCTGGATGACGG<br>CTGGTGCAAAGAGAGGACCCT<br>AGACNAACCAGCTGCTGTTCTT<br>CCTGGTGGAGGAGGAANCCGG<br>AGGCATGGTTGTGTTGACAGTG<br>AGACCCCAAGAGAGAGGCGCG<br>GATCACACCCAGGCCATCGTG<br>CTGGGCTGTGTAGGGGGCATC<br>GTGGCAGTGGGGCTGGGGCTG<br>GTCCTGGCTTACCGGCTCTCTG<br>TGGAAATCTACGNCCGCCGAG<br>AATTTAGCCGCTTTGAGAAGGA<br>GCAGAAGCACCTCAACTGGAA<br>GCAGGAAAACAATCCTCTCTAC<br>AGAAGCGCC |
| integrin-linked kinase | Cfa.465.1.S1_s_at | < 0.01 | PREDICTED: Canis familiaris similar to integrin linked kinase; transcript variant 1 (LOC476836); mRNA | 100 | TGGGCGCATGTATGCACCTGC<br>CTGGGTGGCCCCTGAAGCTCT<br>GCAGAAGAAGCCTGAAGATACA<br>AACAGACGCTCAGCAGATATGT<br>GGAGTTTTGCAGTGCTTCTGTG<br>GGAACTGGTGACGAGGGAGGT<br>ACCCTTTGCTGACCTCTCCAAC<br>ATGGAGATTGGAATGAAGGTGG<br>CACTGGAAGGCCTTCGGCCTA<br>CTATCCCACCAGGCATTTCCCC<br>CCATGTGTGTAAGCTCATGAAG<br>ATCTGCATGAATGAAGACCCTG<br>CTAAGCGGCCCAAGTTTGACAT<br>GATTGTGCCTATCCTGGAGAAG<br>ATGCAGGACAAGTAGAGCTGG<br>AAAGCCCTTGCCTAAACTCCAG<br>AGGTGTCAGGACACGGTTAGG<br>GGAGTGTGTCTCCCCAAAGCA<br>GCAGGC |
| Thrombospondin 1 | Cfa.21204.1.S1_at | < 0.01 | PREDICTED: Canis familiaris similar to thrombospondin 1 precursor (LOC487486); mRNA | 54.83871 | ATACGAATGCAGAGATTCCTAA<br>TCAAACTGTTGATCAAAAGACT<br>GATCCTAACCAATGCTGGTGTT<br>GCACCTTCTGGAACCACGGGC<br>TTAAGAAAACCCCCAGGATCAC<br>TCCTCCCTGCCTTTTCTCTGCTT<br>GCATATCATTGTGGACACCTAG<br>AATACGGGACTTGCCTCGAGAC<br>CATGCNNNNNTCCAAATCAGAC<br>TNNNNNNGTAGCCTCTGAACGC<br>GAAGAGAATCTTCCAAGAGCAT<br>GAACAG |
| Thrombospondin repeat containing 1 | CfaAffx.18675.1.S1_s_at | < 0.01 | PREDICTED: Canis familiaris similar to extracellular matrix protein 1 isoform 1 precursor (LOC608791); mRNA | 100 | GAAGCCCTTGATGGATACTGTG<br>AACGGGAACAGGCTATAAAGAC<br>CCACCACCACTCCTGTTGCCAC<br>CACCCTCCTAGCCCTGCCCGC<br>GATGAGTGCTTTGCCCGTCAGG<br>CGCCATACCCCAACTATGACCG<br>GGACATCCTGACCCTTGATTTC<br>AGCCAAGTTACCCCCAACCTCA<br>TGCAACATCTCTGTGGAAATGG<br>AAGACTTCTCACCAAGCATAAA<br>CAGATTCCTGGGCTGATCCGGA |

| Gene | Probe | P-value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Seq. |
|---|---|---|---|---|---|
| Thrombospondin type 1 motif, 17 | CfaAffx.16694.1.S1_at | < 0.01 | PREDICTED: Canis familiaris similar to lines homolog 1 isoform 1 (LOC607902); mRNA | 98.13084 | ACATGACTGCCCACTGCTGTGA CCTGCCATTTCCAGAGCAGGCC TGCTGTGCTGAGGAGGAGAAAT CGGCCTTCATTGCAGACTTGTG TGGTTCCCGACGTAACTTCTGG CGAGACTCTGCCCTCTGCTGTA ACCTGAATCCTGGAGATGAACA GACCAACTGCTTCAACACTTAT TATCTGAGGAATGTGGCTCTAG TGGCTGGAGACAAT TGGTTGTAGCTCCTCACTTGTC CAAGACCGAAGCAGCAACCAAA CTGAACTTAGCCTTTGGGCTGC TCTTGGTAGTCACAGAAATGCC CACGCTTCAGTCCCCTGGGCTT CCAATGCTTCTGGACCTCTGAA CCAGCCTGTGATGTCCAAGGAA CCCCACGTCACGCTCCAGGCT GCTGCTGGTCTGTCTCCCCCAC AAGCTTCTCAAAGTCTGGTAGA TTATGACAGCTCTGATGATTCT GAAGTAGAAGTCACAGACCAGC ACTCAACAAACAGTAAACAAAC ATCTTTACAGCAAGAAGCAAAG AAGAAATTTCAGGACACAGTTA GAACAGGTCCAGATGAAAAAGA ACTTAGCATGGAGCCTCAATCA AGGCCTCTGGTTCCAGAACAAT CTAATATTAATATTCCCTTCTCT GTTGACTGTGACATCTCCAAAG TAGGAATATCTTACAGGACACT GAAGTGCTTTCAGGAGCTACAG GGTGCCATTTACCGTTTGCAGA AAAAAAATCTTTTCCCCTATAAT GCCACA |
| Angio-associated migratory cell protein (AAMP) | Cfa.8616.1.A1_s_at | <0.001 | Canis familiaris angio-associated migratory cell protein (AAMP) gene; complete cds | 64.77273 | GCGGACTGTGTTCCAACCCCTT CAGCCGACTTGCCCCCTCCGT CCCTTCTCTTAAGAGACCCATC CCTTGGCCCCCCACCCCACCC TCACCCAGACCTGCGGGTCCC TCAGAGGGGGGTCAGGCCTCT TTCTCTTTCACCTTCATTTGCTG GCGTGAGCTGCGGGGGTGTGT GTTTGTATGTGGGGAGTAGGTG TTTGAGGTTCCCGTTCTTTCCC TTCCCAAGTCTCTGGGGGTGGA AAGGAGGAAGAGATATTAGTTA CAGA |

**Table 8: Summary of down regulated enzyme roles involved in heart health and blood coagulation**

| Gene | Gene Expression compared to Control | Role |
|---|---|---|
| Glycoprotein Ib | ↓ | GP-Ib, a surface membrane protein of platelets, participates in the formation |

| Gene | Gene Expression compared to Control | Role |
|---|---|---|
| | | of platelet plugs by binding to the A1 domain of von Willebrand factor, which is already bound to the subendothelium. |
| Platelet glycoprotein VI | ↓ | Collagen receptor belonging to the immunoglobulin-like protein family that is essential for platelet interactions with collagen |
| Platelet glycoprotein IX precursor | ↓ | The GPIb-V-IX complex functions as the von Willebrand factor receptor and mediates von Willebrand factor-dependent platelet adhesion to blood vessels. The adhesion of platelets to injured vascular surfaces in the arterial circulation is a critical initiating event in hemostasis |
| Coagulation factor XIII A chain precursor | ↓ | Factor XIII is activated by thrombin and calcium ion to a transglutaminase that catalyzes the formation of gamma-glutamyl- epsilon-lysine cross-links between fibrin chains, thus stabilizing the fibrin clot. |
| Thromboxane synthase | ↓ | ↓ platelet aggregation, vasoconstriction, lymphocyte proliferation and bronchoconstriction |
| Angio-associated migratory cell protein (AAMP) | ↓ | contains a heparin-binding domain (dissociation constant, 14 pmol) and mediates heparin-sensitive cell adhesion |
| Dystrobrevin binding protein 1 isoform a | ↓ | Plays a role in the biogenesis of lysosome-related organelles such as platelet dense |

| Gene | Gene Expression compared to Control | Role |
|---|---|---|
| | | granule and melanosomes |
| Thrombospondin 1 | ↓ | Adhesive glycoprotein that mediates cell-to-cell and cell-to-matrix interactions. Can bind to fibrinogen, fibronectin, laminin, type V collagen and integrins alpha-V/beta-1, alpha-V/beta-3 and alpha-IIb/beta-3. |
| Thrombospondin type 1 motif, 17 | ↓ | Metalloprotease activity |
| Thrombospondin repeat containing 1 | ↓ | |
| Integrin beta-7 precursor | ↓ | Integrin alpha-4/beta-7 (Peyer's patches-specific homing receptor LPAM-1) is expected to play a role in adhesive interactions of leukocytes. It is a receptor for fibronectin and recognizes one or more domains within the alternatively spliced CS-1 region of fibronectin. Integrin alpha-4/beta-7 is also a receptor for MADCAM1 and VCAM1. It recognizes the sequence L-D-T in MADCAM1. Integrin alpha-E/beta-7 (HML-1) is a receptor for E- cadherin. |
| Integrin linked kinase | ↓ | Receptor-proximal protein kinase regulating integrin-mediated signal transduction. May act as a mediator of inside-out integrin signaling. Focal adhesion protein part of the complex ILK-PINCH. This complex is considered to be one of the convergence points of integrin- and |

| Gene | Gene Expression compared to Control | Role |
|---|---|---|
| | | growth factor-signaling pathway. Could be implicated in mediating cell architecture, adhesion to integrin substrates and anchorage-dependent growth in epithelial cells. Phosphorylates beta-1 and beta-3 integrin subunit on serine and threonine residues, but also AKT1 and GSK3B. |

**Effect of nutrition on genes involved with muscle and bone regulation**

**[00127]** Ten down regulated genes are identified as related to body composition through regulation of bone and muscle. The genes spare muscle and bone deterioration by reducing nitric oxide production and glucocorticoid degradation of muscle. Down regulation of these genes results in a decrease in nitric oxide production and glucocorticoid response. The compositions disclosed herein may be part of a therapeutic regimen to treat animals suffering from diseases or disorders associated with or relating to muscle or bone. These genes and their putative role in muscle and bone regulation are detailed in Tables 9 and 10 below.

**Table 9. Genes involved in muscle and bone regulation**

| Gene | Probe | P- value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Sequence |
|---|---|---|---|---|---|
| Capping Protein | Cfa.1044.1.S1_at | 0.001 | PREDICTED: Canis familiaris similar to F-actin capping protein beta subunit (LOC478209); mRNA | 44.87179 | AGGTCCCGTAACACCGGCAT CGCGACCGCACAGCGCCAT CTCCCCAGAATAAAGCCCAG TAAACACCCCTGNNNNNNAN NNNNANNNNNCACCACGTTT TGCTATCAGAACTCTCCTTGT TTCCAGAGCCCGTGTGCTTT TGTTTGCCCCAGCCCC |
| Calmodulin | Cfa.4168.1.S1_at | 0.01 | PREDICTED: Canis familiaris similar to calmodulin 1; transcript variant 3 (LOC480416); mRNA | 52.54237 | CCACCCATGGTGACGATGAC ACACATCCTGGTGGCATGCG TGTGTTGGTTTAGCGTTGTCT GCGTTGTACTAGAGCGAAAA TGGGTGTCAGGCTTGTCACC ATTCACACAGAAATTTAAAAA AAAAAAAAAAANNNNGANAA AAAACCTTTACCAAGGGAGC |

| Gene | Probe | P- value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Sequence |
|---|---|---|---|---|---|
| | | | | | ATCTTTGGACTCTCTGTTTTT AAAACCTCCTGAACCATGAC TTGGAGCCAGCAGATTAGGC TGTGGCTGTGGACTTCAGCA CAACCATCAACATTGCTGATC AAGAAATTACAATATACGTCC ATTCCAAGTT |
| Dynein | Cfa.4942.1.A1_s_at | 0.001 | PREDICTED: Canis familiaris similar to dynein; cytoplasmic; heavy polypeptide 2; transcript variant 2 (LOC479461); mRNA | 99.6016 | ATACCTCAGAGGTCTCGTAG CTCGTGCCCTTGCCATCCAG AGCTGGGTGGNAGAGAGCT GAGAAGCAGGCTCTTTTCTC TGATACACTCGACCTGTCAG AACTCTTCCACCCAGACACA TTTCTCAATGCTCTTCGCCAG GAAACAGCAAGGGTGATGGG CTGCTCTGTGGATAGCCTTA AGTTTGTAGCTTCGTGGAAA GGTCGGCTGCAAGAAGCAAA GCTGCAGATCAAGATGGGCG GCTTGCTTCTGGAAGGCTGC AGTTTTGACGGGAGCCGGCT CTCTGAAAACCACCACGATT CTCCAAGTGTGTCACCAGTT CTCCCTTGCTGTGTTGGCTG GATTCCCCAGGGTGCATATG GTCCCTATTCTCCTGACGAG TGCATATCTCTGCCCGTGTA CACGAGCGCTGAGAGGGAT CGTGTGGTAGCCAACATCGA CGTCCCGTGTGGGGGCANC CAAGACCAGTGGATTCAGTG TGGAGCCGCTCTGTTTCTAA AAAA |
| Dynactin | Cfa.1807.1.S1_at | 0.01 | PREDICTED: Canis familiaris similar to dynactin 3 isoform 2; transcript variant 1 (LOC474750); mRNA | 100 | AGGACGACAAGGCTCAGGAC GCAAAGTGTGAAACTGCCTT TGTAACAGGGCAGAAGCAGC TCTGTATTGGATTCACAACCT ACCTATCTGCATTCAGGTGG GGCTCGGAGGTCAGAGGTCT GGCTACTTGAGGTTTGCTGT TTGCAC |
| Kinesin | Cfa.10496.1.S1_s_at | 0.01 | PREDICTED: Canis familiaris similar to Kinesin-like protein KIF2 (Kinesin-2) (HK2); transcript variant 5 (LOC478071); mRNA | 99.73046 | AGCCACAGCATTTCCTTTTAA CTTGGTTCAATTTTTGTAGCA AGACTGAGCAGTTCTAAATC CTTTGCGTGCATGCATACCT CATCAGTGNACTGTACATAC CTTGCCCTCTCCCAGAGACA GCTGTGCTCACCTCTTCCTG CTTTGTGCCTTGACTAAGGC TTTTGACCCTAAATTTCTGAA GCACAGCCAAGATAAAGTAC ATTCCTTAATTGTCAGTGTAA ATTACCTTTATTGTGTGTACA TTTTTACTGTACTTGAGACAT TTTTTGTGTGTGACTAGTTAA TTTTGCAGGATGTGCCATATC ATTGAATGGAACTAAAGTCTG TGACAGTGGACATAGCTGCT GGACCATTCCATCTTACATGT A |

| Gene | Probe | P- value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Sequence |
|---|---|---|---|---|---|
| Heat Shock Protein 1 (HSP90) | CfaAffx.11022.1.S1_s_at | 0.01 | PREDICTED: Canis familiaris similar to Heat shock protein HSP 90-beta (HSP 84) (Tumor specific transplantation 84 kDa antigen) (TSTA) (LOC611252); mRNA | 100 | GGTGCTACTGTTTGAAACAG CTCTACTCTCCTCCGGCTTCT CACTGGAGGATCCCCAGACT CACTCCAACCGCATTTACCG CATGATAAAGCTAGGCCTGG GCATCGATGAAGATGAAGTG GCAGCGGAGGAACCCAGTG CTGCTGTTCCTGATGAGATC CCTCCACTTGAGGGTGATGA GGATGCCTCTCGCATGGAAG AAGTC |
| PPIase | CfaAffx.1740.1.S1_at | 0.01 | PREDICTED: Canis familiaris similar to Peptidyl-prolyl cis-trans isomerase C (PPIase) (Rotamase) (Cyclophilin C) (LOC481480); mRNA | 100 | GACATCACCAGTGGAGACGG CACCGGCGGTATAAGCATTT ATGGTGAGACGTTTCCAGAT GAAAACTTCAAACTGAAGCAT TATGGCATTGGTTGGGTCAG CATGGCCAACGCTGGGCCTG ACACCAACGGCTCTCAGTTC TTTATCACCTTGACCAAGCCC ACTTGGTTGGATGGCAAACA TGTGGTATTTGGAAAAGTCCT TGATGGAATGACTGTGGTCC ACTCCATAGAACTTCAGGCA ACCGATGGGCACG |
| Calcinuerin | Cfa.19761.1.S1_at | 0.001 | PREDICTED: Canis familiaris similar to protein phosphatase 3 (formerly 2B); catalytic subunit; beta isoform (calcineurin A beta); transcript variant 5 (LOC479248); mRNA | 98.83382 | GAATTAACAATCTGCTTGAGC CCCAAAACACTACTTATGCAC TTCACTTGCCAAAAGATTTGN GCAAGGTTTTGTACCCTGGT AAATGATGCCAAAGTTTGTTT TCTGTGGTGTTTGTCAAATGT TCTATGTATAATTGACTGTCT GTAACATGCTGTTTNCTTCCT CTGCAGATGTAGCTGCTTTC CTAAATCTGTCTGTCTTTCTT TAGGTTAGCTGTATGTCTGTA AAAGTATGTTAAATTAAATTA CTCTATCAGACGCTTGTCTGT CTTTTGATGTAGAAGCAACTT TGTAGCACCTTGTTTTGAGGT NNGCTGCATTTGTTGCTGTA CTTTGTGCAT |
| Protein kinase C | CfaAffx.408.1.S1_s_at | 0.01 | PREDICTED: Canis familiaris similar to myeloid-associated differentiation marker (LOC611521); mRNA | 99.64664 | TTCAGTTCCTGTCTCATGGC CGCTCCCGGGACCATGCCAT CGCCGCCACTGCCTTCTCCT GCATCGCTTGTGTGGCTTAT GCCACCGAAGTGGCCTGGA CCCGGGCCCGTCCCGGAGA GATCACCGGCTACATGGCCA NTGTGCCGGGCCTGCTCAAG GTGCTGGAGACCTTTGTGGC CTGCATCATCTTCGCCTTCAT CAGCAACCCCTCCCTGTACC AGCACCAGCCGGCCCTGGA GTGGTGTGTGGCCGTCTACT CCATCTGTTTCATCCTGGCG GCTGTGGCCATCCTACTGAA CCTGGGGGACTGCACCAACA TGCTGCCCATCTCCTTCCCC AGTTTCCTGTCGGGCCTGGC CCTGCTCTCCGTCCTGCTGT ATGCCACGGCTCTGGNTCTC TGGCCGCTCTACCAGTTCAA |

| Gene | Probe | P- value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Sequence |
|---|---|---|---|---|---|
| Protein Kinase C Binding Protein | Cfa.15485.1.A1_s_at | 0.01 | PREDICTED: Canis familiaris similar to protein kinase C binding protein 1 isoform b; transcript variant 11 (LOC477252); mRNA | 100 | CGAGAAGTATGGTGGCCAGC CCCGTCGGTCGAGGGATGTT AGCTGCGCCGACAGGCACA CCTACTACGTGTGTACCTGG GACCGCCGCCTGGCTGTGG CCATCCTGACAGCCATCAAC CTGCTGGCTTACGTGGCTGA CCTGGTGTAC GGAGCAGTCAGAACTAAGAC ATGGTCCGTTTTACTATATGA AGCAGCCACTCACCACAGAC CCTGTTGATGTTGTACCGCA GGATGGACGGAA |

**Table 10: Summary of genes affecting glucocorticoid receptors and nitric oxide production**

| Gene | Gene Expression Compared to Control | Role |
|---|---|---|
| Kinesin | ↓ | Transport of organelles from the (-) to (+) ends. Binds microtubules. ATPase activity |
| Capping Protein | ↓ | Part of dynactin-dynein hetero-complex |
| Calmodulin | ↓ | Directly influences calcium dependent dynein activity. Binds to nitric oxide synthase and up regulates the production of nitric oxide |
| Dynein | ↓ | Transport of organelles from the (+) to (-) ends. Binds microtubules. ATPase activity and force production |
| Dynactin | ↓ | Cytoplasmic dynein activator. Binds mirotubules and ↑average length of dyein movements. |
| Heat Shock Protein 1 beta (HSP90) | ↓ | Necessary for glucocorticoid receptor binding and fast transport of |

| Gene | Gene Expression Compared to Control | Role |
|---|---|---|
| | | dynein complex to nucleus. Calcinuerin activity. Enhances the nitric oxide production by binding to nitric oxide synthase |
| PPIase | ↓ | Necessary for dynein/glucocorticoid interaction and movement |
| Calcinuerin | ↓ | Part of dynactin-dynein hetero-complex. Catalyzes the conversion of arginine to citrulline and nitric oxide |
| Protein kinase C | ↓ | Calcium-activated, phospholipid-dependent, serine- and threonine-specific enzyme. |
| Protein Kinase C Binding Protein | ↓ | Associated with protein kinase C |

**Effect of nutrition on genes involved with DNA Damage/Protection and Neural Function**

**[00128]** Eleven genes are identified that are related to DNA damage/protection and neural function. With regard to the latter, the genes identified are important for rebound potentiation; they are believed to have a potential role in motor learning. Interestingly, of these genes, all were down regulated except for of gamma-aminobutyric acid (GABA) A receptor, gamma 2 which was up regulated. The compositions disclosed herein may be part of a therapeutic regimen to treat animals suffering from diseases or disorders associated with or relating to DNA damage/protection and neural function. The identity of these genes and their putative role in DNA damage/protection and neural function are described in Tables 11 and 12 below.

**Table 11: Genes involved in DNA damage/protection and neural function**

| Gene | Probe | P-value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Sequence |
|---|---|---|---|---|---|
| Gamma-aminobutyric acid (GABA) A receptor, | CfaAffx.26362.1.S1_at | < 0.01 | Homo sapiens gamma-aminobutyric acid (GABA) A receptor; | 100 | CCTCTTCTTCGGATGTTTTCCTTCAAGGCCCCTACCATTGAT |

| Gene | Probe | P-value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Sequence |
|---|---|---|---|---|---|
| gamma 2 | | | gamma 2 (GABRG2); transcript variant 1; mRNA | | |
| Calmodulin | Cfa.4168.1.S1_at | < 0.01 | PREDICTED: Canis familiaris similar to calmodulin 1; transcript variant 3 (LOC480416); mRNA | 52.54237 | CCACCCATGGTGACGAT GACACACATCCTGGTGG CATGCGTGTGTTGGTTT AGCGTTGTCTGCGTTGT ACTAGAGCGAAAATGGG TGTCAGGCTTGTCACCA TTCACACAGAAATTTAAA AAAAAAAAAAAAANNNN GANAAAAAACCTTTACC AAGGGAGCATCTTTGGA CTCTCTGTTTTTAAAACC TCCTGAACCATGACTTG GAGCCAGCAGATTAGGC TGTGGCTGTGGACTTCA GCACAACCATCAACATT GCTGATCAAGAAATTAC AATATACGTCCATTCCAA GTT |
| Calcinuerin | Cfa.19761.1.S1_at | < 0.001 | PREDICTED: Canis familiaris similar to protein phosphatase 3 (formerly 2B); catalytic subunit; beta isoform (calcineurin A beta); transcript variant 5 (LOC479248); mRNA | 98.83382 | GAATTAACAATCTGCTT GAGCCCCAAAACACTAC TTATGCACTTCACTTGC CAAAAGATTTGNGCAAG GTTTTGTACCCTGGTAA ATGATGCCAAAGTTTGT TTTCTGTGGTGTTTGTCA AATGTTCTATGTATAATT GACTGTCTGTAACATGC TGTTTNCTTCCTCTGCA GATGTAGCTGCTTTCCT AAATCTGTCTGTCTTTCT TTAGGTTAGCTGTATGT CTGTAAAAGTATGTTAAA TTAAATTACTCTATCAGA CGCTTGTCTGTCTTTTG ATGTAGAAGCAACTTTG TAGCACCTTGTTTTGAG GTNNGCTGCATTTGTTG CTGTACTTTGTGCAT |
| Calcium/calmodulin-dependent protein kinase II | Cfa.3884.1.S1_at | < 0.01 | Homo sapiens PTEN induced putative kinase 1 (PINK1); mRNA | 24.10714 | GGTGCTGTTCACCACAG TAAGTGGCCTCTCAGTG TTGCTGACCAAAGTGTG AAATCCTAGAGCTTCAG GGGAGAGGACGTGGGG GAAATCCGGGGCTTGAC TTTATAATAGGATTATAG AGATGAAAAGTACACCT TGCTTTAGGCAACAGTT GGGATTCCTAAGACGCA TGTGTAAGAGCATATGT GAAATCCCTTCCCCATT GTTGATCTCTACTCACA GAATTTTGTCTTTATTAT GGTGTAAGAATCACTCT TAAAGCCACATATTCAAT TCAAAGCAAATACGTGT TCTGCAGTTGCAAATGT GTATTTAATTCTTCACAA TTCCTGTAAG |

| Gene | Probe | P-value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Sequence |
|---|---|---|---|---|---|
| Adenylate cyclase-associated protein 1 | CfaAffx.5462.1.S1_s_at | < 0.01 | PREDICTED: Canis familiaris similar to Adenylyl cyclase-associated protein 1 (CAP 1); transcript variant 1 (LOC475317); mRNA | 100 | GAAACTCGGTCTGGTGT TCGATGACGTCGTGGGC ATTGTGGAGATAATCAA TAGTAGGGATGTCAAAG TTCAGGTAATGGGTAAA GTGCCAACCATTTCCAT CAACAAAACAGATGGCT GCCATGTTTACCTGAGC AAGAATTCCCTGGATTG CGAAATAGTCAGTGCCA AATCTTCTGAGATGAAT GTCCTCATTCCTACTGA AGGCGGTGACTATAATG AATTCCCAGTCCCTGAG CAGTTCAAGACCCTATG GAATGGGCAGAAGTTGG TCACCACAGTGACAGAA ATTGCTGGATAAGCGAA GTGCCACTGGGTTCTTT GCCCTCCCCCTCACACC ATGGGATAAATCTATCA GGACGGTTCTTTTCTAG ATTTCCTTTACCTTTCTG CTCTTAAACTGCTT |
| Protein Phosphatase I | Cfa.6174.1.A1_at | < 0.01 | PREDICTED: Canis familiaris similar to protein phosphatase 1A isoform 1; transcript variant 2 (LOC480344); mRNA | 100 | AAATCTTACGAAGCCCA ATATGCAGGGAGTTAAC TGAAAACTATCTTGGCA GTGAGGTTGGCACTGTT GATAAAGCTGGTCCCTT CCTTTAACTGTCTTTTAG GTTGTTCTTGCCTTGTT GCCAGGAGTATTGCAGG TAATACAGTATATTCATA AGAATATCAATCTTGGG GCTAAAATGCCTTGATT CTTTGCACCTCTTTTACA AGTCCTTACGTTGAATTA CTAATTGATAAGCAGCA GCTTCCTACATATAGTA GGAGACTGCCACGTTTT TGCTATCATGATTGGCT GGGCCTGCTGCTGTTCC TAGTAAGGTAT |
| Diazepam binding inhibitor | CfaAffx.14836.1.S1_s_at | < 0.01 | PREDICTED: Canis familiaris similar to peroxisomal D3;D2-enoyl-CoA isomerase isoform 1 (LOC478706); mRNA | 100 | AATGGTGCCATCTTACT GAGGGATTTTGTAGGCT GTTTTATAGATTTTCCTA AGCCTCTGGTTGCAGTG ATAAATGGTCCAGCCAT AGGAATCTCCGTCACCA TTCTCGGGCTATTCGAT CTTGTGTATGCTTCCGA CAGGGCAACATTTCACA CTCCTTTTACTCACCTG GGCCAAAGTCCAGAAG GATGTTCCTCCTATACTT TTCCCAAGATAATGGGC CAAGCCAAGGCAGCAG AGATGCTCATGTTTGGA AAGAAGTTAACAGCTAG AGAAGCCTGTGCTCAAG GACTTGTTACTGAAGTTT TTCCCGATAGCACTTTT CAGAAAGAAGTTTGGAC |

| Gene | Probe | P-value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Sequence |
|---|---|---|---|---|---|
| | | | | | CAGGCTGAAAGCATATT<br>CAAAACTCCCCCGAAAT<br>ACCTTGCATATTTCCAAA<br>CAGAGCATCAGAAATCT<br>TGAGAAAGAAAAGCTAC<br>ATGCTGTTAACGCAGAA<br>GAAAACAGCGTCCTCCA<br>GGAAAGGTGGCTGTCA<br>GACGAATGCATAAATGC<br>AGTCATGAGCTTCTTAT<br>CCCGGAAGGCCAA |
| Tumor protein p53 binding protein | Cfa.1611.1.A1_s_at | < 0.01 | PREDICTED: Canis familiaris similar to tumor protein p53 binding protein; 1; transcript variant 4 (LOC478274); mRNA | 97.90874 | ATGATAGTTGCCATGCC<br>AACCAGCTCCAGAATTA<br>CCGCAATTATTTGTTGC<br>CTGCAGGGTACAGCCTT<br>GAGGAGCAAAGAATTCT<br>GGATTGGCAACCCCGTG<br>AAAACCCTTTCCACAAT<br>CTGAAGGTACTCTTGGT<br>GTCAGACCAACAGCAGA<br>ACTTCCTGGAGCTCTGG<br>TCTGAGATCCTCATGAC<br>CGGGGGGGCAGCCTCT<br>GTGAAGCAGCACCATTC<br>AAGTGCCCATAACAAAG<br>ATATTGCTTTAGGGGTA<br>TTTGACGTGGTGGTGAC<br>GGATCCCTCATGCCCAG<br>CCTCGGTGCTGAAGTGT<br>GCTGAAGCATTGCAGCT<br>GCCTGTGGTGTCACAAG<br>AGTGGGTGATCCAGTGC<br>CTCATTGTTGGGGAGAG<br>AATTGGATTCAAGCAGC<br>ATCCAAAATACAAACAT<br>GATTATGTTTCTCACTAA<br>TACTTGGTCTTAACTGAT<br>TTTATTCCCTGCTGTTGT<br>GGAGATTGTGNTTNNNC<br>CAGGTTTTAAATGTGTCT<br>TGTGTGTAACTGGATTC<br>CTTGCATGGATCT |
| Ubiquitin conjugating enzyme E2D 3 | CfaAffx.275.1.S1_s_at | < 0.001 | PREDICTED: Pan troglodytes LOC461941 (LOC461941); mRNA | 97.19626 | GATTTGGCCCGTGACCC<br>TCCAGCACAATGTTCTG<br>CAGGTCCTGTTTGGGAT<br>GATATGTTTCATTGGCA<br>AGCCACAATTATAGGAC<br>CTAATGACAGCCCATAT<br>CAAGG |
| NEDD8 ultimate buster-1 | Cfa.12556.1.A1_s_at | < 0.001 | PREDICTED: Canis familiaris similar to NEDD8 ultimate buster-1 (NY-REN-18 antigen) (LOC475542); mRNA | 99.12473 | GGAATGGGCTACTCTAC<br>TCATGCAGNCAAGCAGG<br>NCCTGCATCAGGCCAGT<br>GGGAACCTGGACGAAG<br>CCCTGAAGATTCTTCTC<br>AGCAATCCTCAGATGTG<br>GTGGTTAAATGATTCAG<br>ATCCTGAAACGANCAAC<br>CAGCAAGAAAGTCCTTC<br>CCAGGAAAACATTGACC<br>AACTGGTGTACATGGGC<br>TTCGACGCTGTGGTGGC<br>TGATGCTGCCTTGAGAG |

| Gene | Probe | P-value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Sequence |
|---|---|---|---|---|---|
| | | | | | TGTTCAGGGGAAACGTG<br>CAGCTGGCAGCTCAGN<br>CCCTCGCCCACAACGGA<br>GGAACTCTTCCTCCTGA<br>CCTGCAGCTCTTGGTGG<br>AAGACTCTTCATCAACG<br>CCATCCACGTCCCCTTC<br>CGACTCCGCAGGTACCT<br>CTAGTGCCTCAACAGAT<br>GAAGATATGGAAACCGA<br>AGCTGTCAATGAAATAC<br>TGGAAGATATTCCAGAA<br>CATGAAGAAGATTATCTT<br>GACTCAACACTGGAAG |
| BCL2-associated X protein (BAX) | CfaAffx.6742.1.S1_s_at | < 0.01 | Canis familiaris BCL2-associated X protein (BAX); mRNA | 100 | GGCCCACCAGCTCTGA<br>GCAGATCATGAAGACAG<br>GGGCCCTTTTGCTTCAG<br>GGTTTCATCCAAGATCG<br>AGCAGGGCGAATGGGG<br>GGAGAGACACCTGAGCT<br>GCCCTTGGAGCAGGTG<br>CCCCAGGATGCATCCAC<br>CAAGAAGCTGAGCGAAT<br>GTCTCAAGCGCATCGGA<br>GATGAACTGGACAGTAA<br>CATGGAGTTGCAGAGGA<br>TGATCGCAGCTGTGGAC<br>ACAGACTCTCCCCGTGA<br>GGTCTTCTTCCGAGTGG<br>CAGCTGAGATGTTTTCT<br>GATGGCAACTTCAACTG<br>GGGCCGGGTTGTTGCC<br>CTCTTCTACTTTGCCAG<br>CAAACTGGTGCTCA |

**Table 12: Summary of genes important for rebound potentiation and DNA integrity**

| Gene | Gene Expression Compared to Control | Role |
|---|---|---|
| Gamma-aminobutyric acid (GABA) A receptor, gamma 2 | ↑ | Involved in single channel conductance (Cl- channel) |
| Calmodulin | ↓ | Influx of calcium results in calcium/calmodulin complex which activates CaMKII and calcineurin |
| Calcinuerin | ↓ | Involved in the pathway for RP suppression |
| Calcium/calmodulin-dependent protein kinase II | ↓ | Involved in induction and suppression of RP |
| Adenylate cyclase- | ↓ | Adenlyl cyclase is involved |

| Gene | Gene Expression Compared to Control | Role |
|---|---|---|
| associated protein 1 | | in suppression of RP |
| Protein Phosphatase I | ↓ | Dephosphorylates components in stress-activated pathways. Active PP-1 results in CaMKII inhibition and RP suppression |
| Diazepam binding inhibitor | ↓ | Displaces benzodiazepine Down regulates the effects of GABA |
| Tumor protein p53 binding protein | ↓ | Keep the cell from progressing through the cell cycle if there is damage to DNA present. |
| Ubiquitin conjugating enzyme E2D 3 (and NEDD8 ultimate buster-1) | ↓ | The regulated proteolysis of proteins by proteasomes removes denatured, damaged or improperly translated proteins from cells and regulates the level of proteins like cyclins or some transcription factors |
| BCL2-associated X protein | ↓ | Accelerates programmed cell death by binding to, and antagonizing the apoptosis repressor BCL2 |

**Effect of nutrition on genes involved with glucose metabolism**

**[00129]** Twenty four genes associated with glucose metabolism are down regulated in animals fed the super senior diet which would suggest that these animals are utilizing fat (fat oxidation) instead of glucose as a fuel source. The compositions disclosed herein may be part of a therapeutic regime in diabetic animals and/or for obesity prevention or treatment in an animal. These down regulated genes are identified and their putative role in glucose metabolism described in detail below in Tables 13 and 14.

**Table 13. Genes involved in Glucose Metabolism**

| Gene | Probe | P-Value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Seq. |
|---|---|---|---|---|---|
| Phosphorylase kinase | Cfa.10856.1.S1_at | < 0.01 | PREDICTED: Canis familiaris similar to phosphorylase kinase beta; transcript variant 2 (LOC478139); mRNA | 99.3392 | GAAAGTTCACCA<br>CTGCATGTTTTAT<br>GATCAGATAACT<br>CATTGAAATGAG<br>TCTTTGCTCTTTA<br>GACTAAATTCCC<br>ACCTAGTACTGC<br>CATTAAAATGAAT<br>TTGCCAGCTGGT<br>GTGCATACTGGA<br>AATGAAAAGATA<br>CTGAAAGAATGG<br>AACGAATGGTGA<br>GCTTAACTCAGT<br>GGCACTGTCATA<br>CTGGAAAAATAC<br>AGTAAAATCATAA<br>AAACAGATCTGC<br>CAGCTGATGTTT<br>TTATTCTCAGAAA<br>CAGCATTGTTGA<br>TAATATTTTAGTA<br>TACAGAGCTACT<br>GTACAATTTTTAC<br>CTTGNAAACATG<br>ACTGTGGTTTTG<br>TATTTGTGTTGAC<br>TTTAGGGGTTGG<br>GATAAAATNCAG<br>TATAATATATACC<br>TTATCAAACNTTT<br>TCTTTGAGCTCTT<br>ACTAAAAATATG<br>GCATGCATAAGA<br>TTGTTCAGAAGA<br>GTAGACTGTTAA<br>CCTAGTTTGTA |
| Phosphorylase | Cfa.10412.1.A1_s_at | < 0.01 | PREDICTED: Canis familiaris phosphorylase; glycogen; liver; transcript variant 1 (PYGL); mRNA | 99.36306 | CTTCCAGAGCTG<br>AAGCTGGCCATT<br>GATCNAAATTGA<br>CAATGGCTTCTT<br>CTCTCCCAAGCA<br>GCCTGNCCTCTT<br>CAAAGATTTAATC<br>AATATGCTATTTT<br>ATCATGACAGGT<br>TTAAAGTCTTCG<br>CAGACTATGAAG<br>CCTATGTCAAGT<br>GTCAAGAAAAAG<br>TCAGCCAGCTGT<br>ACATGAATCCAA<br>AGGCCTGGAACA<br>CAATGGTACTCA<br>AAAACATAGCTG<br>CCGCAGGGAAGT<br>TCTCTAGTGACC<br>GAACAATTAAGG<br>AATATGCCAGGG<br>ACATCTGGAACA<br>TGGAACCTTCAG<br>ATCTCAAGATTTC<br>CCTATCCAATG |

| Gene | Probe | P-Value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Seq. |
|---|---|---|---|---|---|
| Glycogen synthase kinase 3 | Cfa.913.1.A1_s_at | < 0.01 | PREDICTED: Canis familiaris similar to Glycogen synthase kinase-3 beta (GSK-3 beta); transcript variant 1 (LOC478575); mRNA | 99.49622 | GACTCCACCGGA GGCAATTGCACT GTGTAGCCGTCT GCTGGAGTATAC ACCAACTGCCCG ATTGACACCACT GGAAGCTTGTGC ACATTCATTTTTT GATGAATTAAGG GACCCAAATGTC AAACTACCAAAT GGGCGAGACACA CCTGCACTCTTC AACTTCACCACT CAAGAACTGTCA AGTAATCCACCT CTAGCTACCATC CTTATTCCTCCTC ATGCTCGGATTC AAGCAGCTGCTT CAACCCCTACAA ATGCCACAGCAG CCTCAGATGCTA ATGCCGGAGACC GTGGACAGACGA ACAATGCCNCTT CTGCATCAGCTT CTAACTCCACCT GAACAGTCCCGA GCAGCCAGCTGC ACAGGAAGAACC ACCAGTTACTTG AGTGTCACTCA |
| Calmodulin | Cfa.4168.1.S1_at | < 0.01 | PREDICTED: Canis familiaris similar to calmodulin 1; transcript variant 3 (LOC480416); mRNA | 52.54237 | CCACCCATGGTG ACGATGACACAC ATCCTGGTGGCA TGCGTGTGTTGG TTTAGCGTTGTCT GCGTTGTACTAG AGCGAAAATGGG TGTCAGGCTTGT CACCATTCACAC AGAAATTTAAAAA AAAAAAAAAAAN NNNGANAAAAAA CCTTTACCAAGG GAGCATCTTTGG ACTCTCTGTTTTT AAAACCTCCTGA ACCATGACTTGG AGCCAGCAGATT AGGCTGTGGCTG TGGACTTCAGCA CAACCATCAACA TTGCTGATCAAG AAATTACAATATA CGTCCATTCCAA GTT |
| Protein Kinase C | CfaAffx.408.1.S1_s_at | < 0.01 | PREDICTED: Canis familiaris similar to myeloid-associated differentiation marker (LOC611521); mRNA | 99.64664 | TTCAGTTCCTGT CTCATGGCCGCT CCCGGGACCATG CCATCGCCGCCA CTGCCTTCTCCT |

| Gene | Probe | P-Value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Seq. |
|---|---|---|---|---|---|
| | | | | | GCATCGCTTGTG<br>TGGCTTATGCCA<br>CCGAAGTGGCCT<br>GGACCCGGGCC<br>CGTCCCGGAGAG<br>ATCACCGGCTAC<br>ATGGCCANTGTG<br>CCGGGCCTGCTC<br>AAGGTGCTGGAG<br>ACCTTTGTGGCC<br>TGCATCATCTTC<br>GCCTTCATCAGC<br>AACCCCTCCCTG<br>TACCAGCACCAG<br>CCGGCCCTGGA<br>GTGGTGTGTGGC<br>CGTCTACTCCAT<br>CTGTTTCATCCT<br>GGCGGCTGTGG<br>CCATCCTACTGA<br>ACCTGGGGGACT<br>GCACCAACATGC<br>TGCCCATCTCCT<br>TCCCCAGTTTCC<br>TGTCGGGCCTGG<br>CCCTGCTCTCCG<br>TCCTGCTGTATG<br>CCACGGCTCTGG<br>NTCTCTGGCCGC<br>TCTACCAGTTCA<br>ACGAGAAGTATG<br>GTGGCCAGCCCC<br>GTCGGTCGAGG<br>GATGTTAGCTGC<br>GCCGACAGGCAC<br>ACCTACTACGTG<br>TGTACCTGGGAC<br>CGCCGCCTGGCT<br>GTGGCCATCCTG<br>ACAGCCATCAAC<br>CTGCTGGCTTAC<br>GTGGCTGACCTG<br>GTGTAC |
| Protein Kinase C Binding Protein | Cfa.15485.1.A1_s_at | < 0.01 | PREDICTED: Canis familiaris similar to protein kinase C binding protein 1 isoform b; transcript variant 11 (LOC477252); mRNA | 100 | GGAGCAGTCAGA<br>ACTAAGACATGG<br>TCCGTTTTACTAT<br>ATGAAGCAGCCA<br>CTCACCACAGAC<br>CCTGTTGATGTT<br>GTACCGCAGGAT<br>GGACGGAA |
| Hexokinase 3 | Cfa.19125.2.S1_at | < 0.01 | Macaca fascicularis testis cDNA; clone: QtsA-14856; similar to human receptor associated protein 80 (RAP80); mRNA; RefSeq: NM_016290.3 | 76.70683 | TAATGACTGCCA<br>ACTCACTGTTTGT<br>TGGAGTTATATG<br>CAGAAATAAAGN<br>CCAAGTCTTCAG<br>AAACAGGCTTCA<br>GGATGCCCTCAC<br>CAGGGATGGAAG<br>AGGCAGGCTGCA<br>GCAAAGAGATGC<br>AGAGTTCCCTTG<br>CACATCTCGACT |

| Gene | Probe | P-Value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Seq. |
|---|---|---|---|---|---|
| | | | | | TAAATGAGTCTC<br>CCATCAAGTCTTT<br>TGTTTCCATTTCA<br>GAAGCCACAGAT<br>TGCTTAGTGGAC<br>TTTAAAAAGCAAC<br>TTAACGTTCGGC<br>AAGGTAGTCGGA<br>CACGGACCAAAG<br>CAGGCAGAGGAA<br>GAAGGAGAAAAC<br>CCTGAATTTCTA<br>GGGTCCAGACAC<br>CCGACAAAACCA<br>TTAGCAATAGGG<br>GTGGGCCGTGTC<br>ATTAAGTCTTAGT<br>GGCTTCTGTTTC<br>ATTGTTGAACAA<br>GTTTTTTGGCCC<br>NGCAGTTTTCAC<br>CACCAGCACCAA<br>CTCAGCATTCTT<br>GTTTTGATGTTTT<br>CTATAAGCTATAC<br>AGACAATTGTGT<br>ATAGTATTCTGTT<br>TTATAACAGTCTG<br>GATTCACTT |
| Fructose 1,6 bisphosphatase | CfaAffx.26135.1.S1_s_at | < 0.01 | PREDICTED: Canis familiaris aldolase A; transcript variant 1 (LOC479787); mRNA | 100 | AGTGGCGCTGTG<br>TGCTGAAAATTG<br>GGGAACACACTC<br>CCTCAGCCCTTG<br>CGATCATGGAAA<br>ATGCCAACGTTC<br>TGGCCCGTTAT |
| Glyceraldehyde 3-phosphate dehydrogenase | AFFX-Cf_Gapdh_3_at | < 0.01 | Canis familiaris glyceraldehyde-3-phosphate dehydrogenase (GAPDH); mRNA | 100 | AGCTCACTGGCA<br>TGGCCTTCCGTG<br>TCCCCACCCCCA<br>ATGTATCAGTTGT<br>GGATCTGACCTG<br>CCGCCTGGAGAA<br>AGCTGCCAAATA<br>TGACGACATCAA<br>GAAGGTAGTGAA<br>GCAGGCATCGGA<br>GGGACCCCTCAA<br>AGGCATCCTGGG<br>CTACACTGAGGA<br>CCAGGTGGTCTC<br>CTGTGACTTCAA<br>CAGTGACACCCA<br>CTCTTCCACCTT<br>CGACGCCGGGG<br>CTGGCATTGCCC<br>TCAATGACCACT<br>TTGTCAAGCTCA<br>TTTCCTGGTATG<br>ACAATGAATTTG<br>GCTACAGCAACC<br>GGGTGGTGGAC<br>CTCATGGTCTAC<br>ATGG |

| Gene | Probe | P-Value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Seq. |
|---|---|---|---|---|---|
| Glucose 6-phosphate dehydrogenase | Cfa.19351.1.S1_at | < 0.01 | Homo sapiens cDNA FLJ30869 fis; clone FEBRA2004224 | 15.11194 | GAATGTGTTGGC<br>AGACTGAGGCCC<br>CCCATGTTTTTAA<br>TGCGCACTGGGG<br>ACAACCATCTAA<br>GGTCTAGAAACT<br>TTTGGACCATAG<br>GAAAGATAGGTT<br>TATGGTCCTCTT<br>CCAGATGCAGCC<br>CTAGGAGAGCAT<br>TCCCATGGGGTC<br>TCTGGATCCCTT<br>TCNTTGCTCTGT<br>GAGGCTCTGTGA<br>CCACCTTTTGNN<br>NTGNNGGGGGC<br>AGGGGGNCTTCC<br>TCAGCTCCGCCT<br>CCAGTGCCCCCA<br>GGTCCCCCACGG<br>CTCACAGTCCNT<br>GAAAATTCAGAG<br>CTGCCCTGTAAG<br>GATTTTGTCCACT<br>GGGCAATTCAGA<br>TATACTTCGATAT<br>CCCTGAGAAAGA<br>AGAGGCAGCAGC<br>AAACACTCCCNA<br>GGGCATCTGTCT<br>CAGNANTCTCTC<br>NTTGNATGAGAC<br>AGAAGCCTACTT<br>TTCAGAAANCTTA<br>TCANGGNTACTT<br>TATAAGAAACTTT<br>TTTTTTTTTNCTA<br>AAATCAGACAAA<br>AGGTGGCTTNTG<br>CATATTCTTNATT<br>AATAACTGTGTCT<br>TTGTCTCCTCTG<br>CTTAACTTTAGGA |
| Enolase | CfaAffx.30133.1.S1_s_at | < 0.01 | PREDICTED: Canis familiaris similar to T21B10.2b; transcript variant 1 (LOC479597); mRNA | 97.72257 | GGTACATCACGC<br>CTGATCAGCTGG<br>CTGACCTCTACA<br>AGTCCTTCATCA<br>GGGACTACCCAG<br>TGGTGTCTATCG<br>AAGACCCCTTCG<br>ACCAGGATGACT<br>GGGAAGCTTGGC<br>AGAAATTCACTG<br>CCAGCGCTGGAA<br>TCCAGGTGGNGG<br>GGGANGATCTCA<br>CCGTGACCAACC<br>CAAAGCGGATTT<br>CCAAGGCTGTGG<br>GCGAGAAATNGT |

| Gene | Probe | P-Value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Seq. |
|---|---|---|---|---|---|
| | | | | | GCAACTGCCTCC TGCTTAAAGTGA ACCAGATTGGCT CTGTGACCGAGT CTCTTCAGGCGT GCAAGCTGGCCC AGTCCAATGGGT GGGGCGTCATG GTGTCGCATCGC TCCGGGGAGACC GAAGATACCTTC ATCGCTGACCTG GTGGTGGGANTC TGCACTGGGCAG ATCAAGACGGGT GCACCATGCAGA TCTGAGCGCTTG GCCAAGTACAAC CAGATCCTCAGA ATTGAAGAGGAA CTGGGTAGCAAG GCCAAGTTCGCC GGCAGAAGCTTC AGAA |
| Lactate dehydrogenase | Cfa.300.1.S1_at | < 0.01 | PREDICTED: Canis familiaris similar to L-lactate dehydrogenase A chain (LDH-A) (LDH muscle subunit) (LDH-M) (Proliferation-inducing gene 19 protein); transcript variant 1 (LOC476882); mRNA | 97.99427 | ATCTGACCTGTT ACTCAAGTCGTA ATATTAAAATGGC CTAAGAAAAAAA CATCAGTTTCCTA AAGTTACACATA GGAATGGTTCAC AAAACCCTGCAG CTATGTCCTGAT GCTGGATGAGAC CTGTCTTGTGTA GTCCTAAATTGG TTAACGTAATATC GGAGGCACCACT GCCAATGTCATA TATGCTGCAGCT ACTCCTTAAACC AGATGTGTATTTA CTGTGTTTTGTAA CTTCTGATTCCTT CATCCCAACATC CAACATGCCTAG GCCATCTTTTCTT CTTCAGTCACAT CCTGGGATCCAA TGTATAAATTCAA TATTGCATGTATT GTGCATAACTCT TCTA |
| Citrate lyase | Cfa.10361.2.S1_at | < 0.01 | PREDICTED: Canis familiaris similar to citrate lyase beta like (LOC476974); mRNA | 98.49624 | AGTATGCCAGAT CGGAACCTTTTT CCCATTTACAGTT CATGTTAATCCAA TTTTTTTTATTAT CTCACTGGCCAG TTATTCCTTTAAA AATGAACTTCCTT CTTTTTGATTCCA AGCTTATGATTTT |

| Gene | Probe | P-Value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Seq. |
|---|---|---|---|---|---|
| | | | | | ACTGCTCATTAAT<br>GTGTTACAAATAT<br>GCACTTAATGATT<br>TCACAGGGAGAT<br>AAAATAGTGAAG<br>AGAGATGGGCTG<br>AGGGGCTGTTAG<br>GACTTTAATGAAA<br>CAGATCTTTCCC<br>GAATATTTCTCCC<br>TTCACATTTCTCA<br>CATTAGATGTTTC<br>CCACATTGTTCTA<br>CTCCACACTATA<br>AATAATTTTAAGG<br>CCAATCTTAAAAA<br>ATGGTAGTTAAG<br>TGAAGGGGTTGT<br>GTTTATTTCACTA<br>GAAATCTGATAA<br>AACGAGAGATGA<br>CATAGAAAAAGT<br>TATCATTTTTGTT<br>CATACAGATGGC<br>TTCTAAAAATAAA<br>TCTTCAAAACTGA<br>TTACTTTTAACCT<br>CCACCTCCCAAA<br>ATGAAACATCCC<br>TACATTTGAACTG<br>CTAGGTGAGAAC<br>TCTGAAAGCCCT<br>CATCC |
| Glycerol kinase | CfaAffx.21204.1.S1_s_at | < 0.01 | PREDICTED: Canis familiaris similar to glycerol kinase isoform 2; transcript variant 8 (LOC480872); mRNA | 100 | GGGTACATCCTA<br>TGGCTGCTATTT<br>CGTCCCCGCGTT<br>TTCAGGGTTATAT<br>GCACCTTACTGG<br>GAGCCCAGTGCA<br>AGAGGGATCATC<br>TGTGGGCTCACT<br>CAATTCACCAATA<br>AATGCCATATTG<br>CTTTTGCTGCATT<br>AGAAGCTGTTTG<br>TTTCCAAACCCG<br>GGAGATTTTGGA<br>TGCCATGAACCG<br>AGACTGCGGAAT<br>TCCACTCAGTCA<br>TTTGCAGGTAGA<br>TGGAGGAATGAC<br>CAACAACAAAATT<br>CTTATGCAACTA<br>CAAGCAGACATT<br>CTATATATCCCA<br>GTAGTGAAGCCC<br>TCGATGCCAGAA<br>ACAACTGCCCTG<br>GGAGCTGCCATG<br>GCAGCCGGGGC<br>TGCGGAGGGAGT<br>TGGTGTTTGGAG<br>TCTTGAACCCGA |

| Gene | Probe | P-Value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Seq. |
|---|---|---|---|---|---|
| | | | | | GGATCTGTCAGC<br>AGTCACGATGGA<br>GCGATTTGAACC<br>CCAGATCAATGC<br>TGAGGAAAGTGA<br>AATTCGTTACTCT<br>ACATGGAAGAAG<br>GCTGTGATGAAG<br>TCAGTGGGCTGG<br>GTTACAACTCA |
| Transketolase | CfaAffx.13684.1.S1_s_at | < 0.01 | Homo sapiens transketolase (Wernicke-Korsakoff syndrome); mRNA (cDNA clone MGC:15349 IMAGE:4310396); complete cds | 86.53846 | GAAGATCTGGCC<br>ATGTTTCGGTCC<br>ATCCCCACTGCT<br>ACGATCTTTTACC<br>CAAGTGACGGGG<br>TGTCAACAGAGA<br>AGGCGGTGGAAT<br>TAGCAGCCAATA<br>CAAAGGGCATCT<br>GCTTCATCCGGA<br>CCAGCCGCCCAG<br>AAAACGCCATCA<br>TCTATAACAACAA<br>TGAGGATTTCCA<br>AATCAAACAAGC<br>CAAGGTGGTCCT<br>GAAGAGCAAGGA<br>TGACCAGGTGAC<br>TGTGATTGGGGC<br>CGGAGTGACCCT<br>ACATGAGGCCTT<br>GGCTGCTGCTGA<br>ACTGCTGAAGAA<br>AGAGAAGATCAA<br>CATTCGTGTGTT<br>GGACCCCTTCAC<br>CATCAAGCCCCT<br>GGACAGAAATCT<br>CATTCTCGAAAG<br>CGCCCGTGCGAC<br>CAAGGGCAGGAT<br>CGTCACCGTGGA<br>GGACCATTACTA<br>TGAAGGTGGCAT<br>AGGTGAGGCAGT<br>GTCCTCTGCCTT<br>GGTGGGTGAGC<br>CTGGCATCACCG<br>TCTCCCGCCTTG<br>CAGTTGGTGAGG<br>TACCAAGAAGCG<br>GGAAGCCAGCTG<br>AGCTGCTGAAGA<br>TGTTTGGCATTG<br>ACAGGGACGCCA<br>TCGCACAAGCTG<br>TGAGGGACCTTG<br>TCGCCAA |
| Ribulose phosphate 3-epimerase | Cfa.13084.1.A1_s_at | < 0.01 | Homo sapiens SLIT-ROBO Rho GTPase activating protein 2 (SRGAP2); mRNA | 57.79468 | CCCCAAGGAGAT<br>GAGGAGCGATGA<br>CCCCAGCAACAG<br>GAANAACAGCCC<br>ACTGAAGGGCTG |

| Gene | Probe | P-Value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Seq. |
|---|---|---|---|---|---|
| | | | | | GTGTGTGTGTNC<br>TTCACGTGCCAG<br>AAGAGAAGTTTA<br>GATCCTCCCAGG<br>GGAATCGCAATG<br>TTGTGGCGTCCT<br>GACTTGTATGTC<br>ACGTTTTGTGTAA<br>AAATGGTATATTC<br>TTTAAAATAGTGT<br>TGATAACTGGAA<br>TATTGTATGTATG<br>CTTGGAGATGCT<br>TTGTGTGAACCT<br>AAGACTGTCACT<br>CAACAGATGTTG<br>GATTGGG |
| Ribose 5-phosphate isomerase | Cfa.335.2.S1_at | < 0.01 | PREDICTED: Canis familiaris similar to ribose 5-phosphate isomerase A (ribose 5-phosphate epimerase) (LOC475755); partial mRNA | 100 | AGCCTTTCTACT<br>GACCCTGCAAGA<br>GTGGAGCGTGTT<br>CACCTTGAACCC<br>CCAGCGTGCAGC<br>TGAGGTAGACAT<br>GCCTCTCCAGGA<br>GCCTTTGCCTTA<br>ATGCATCTGTGC<br>CAGACAGACGGC<br>TGG |
| Cytochrome c oxidase polypeptide VIIa-liver/heart, mitochondrial precursor | CfaAffx.4942.1.S1_s_at | < 0.01 | PREDICTED: Canis familiaris similar to cytochrome c oxidase; subunit 7a 3 (LOC611134); mRNA | 100 | GGCAGTTTGAAA<br>ATAAAGTTCCAG<br>AGAAACAAAAGC<br>TATTTCAGGAGG<br>ATAATGGAATTC<br>CAGTGCATCTAA<br>AGGGTGGAGTAG<br>CTGATGCCCTCC<br>TGTATAGAGCCA<br>CTATGATGCTTA<br>CAGTTGGTGGAA<br>CAGCATATGCCA<br>TGTATCAGCTAG<br>CTGTGGCTTCTT<br>TTCCCAAGAAGC<br>A |
| Cytochrome c oxidase subunit VIII liver form | Cfa.15065.1.S1_at | < 0.01 | PREDICTED: Canis familiaris similar to Cytochrome c oxidase polypeptide VIII-liver; mitochondrial precursor (Cytochrome c oxidase subunit 8-2) (LOC476040); mRNA | 99.75961 | GGTCCGCAGTCG<br>TTCTGTGCGGTC<br>ATGTCTGTGCTG<br>GTGCCGCAGCTG<br>CTGAGGGGCCTA<br>ACAGGCCTCACC<br>CGGCGGCTCCC<br>GGTGCATCGTGC<br>CCAGATCCATTC<br>CAAGCCGCCGC<br>GGGAGCAGCTC<br>GGGACCATGGAT<br>GTTGCCGTTGGG<br>CTCACCTNCTGC<br>TTCCTGTGTTTCC<br>TCCTGCCATCGG<br>GCTGGGTCCTGT<br>CACACCTGGAGA |

| Gene | Probe | P-Value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Seq. |
|---|---|---|---|---|---|
| | | | | | GCTACAAGAAGC<br>GGGAGTGAAGG<br>GGGCTGTCCTGT<br>CCCTCACCCTGT<br>GACCTGACCACC<br>CCTGGCCTGTCC<br>TGATCATGTCTG<br>CTGCATTCCTGG<br>CCGGCCTTCCAT<br>GGATCATGTCCT<br>TCAATTACAGTG<br>ACCTCTTCTACA<br>GTCATGACCTCT<br>TGATTTCTCCATG<br>GTGACATCCTGG<br>GACCAAACATAT<br>TGGTTTATAA |
| Ubiquinolùcytochrome c reductase | Cfa.1425.2.A1_at | < 0.01 | PREDICTED: Canis familiaris similar to Ubiquinol-cytochrome-c reductase complex core protein 2; mitochondrial precursor (Complex III subunit II); transcript variant 1 (LOC479815); mRNA | 27.18053 | CTTATGCATTCCT<br>TCCAAAATTGGA<br>TCATTTAGGTCAA<br>ATTATTTGATGTT<br>AAATCATAAGTTT<br>TCATTTGCTTACA<br>TTTACGATATCAG<br>CGTCAGCTACGG<br>AATCAATCTGCT<br>GAAGGACCGTGG<br>CTGGCGGCGTGT<br>ACGATCCAGCAA<br>CCAGCGCCTGG<br>GACCCGACTTCA<br>TCCAGGAACCCC<br>TCAGAAGACTCC<br>ACTGACATTAGG<br>AAGACTCATAAG<br>AACCTTACAAGA<br>AAAAGTATCAAC<br>CCCATCAAAACG<br>GCAGAAAAGAAA<br>CATATCTTGTTAT<br>TAGTAGCTGAAA<br>TTCCATTTTCTAC<br>ATGTTGCCATAC<br>CTTATAAAAACTA<br>CACTAAGCTACG<br>CTTAAGGAAATA<br>CATTTTCTTAAAT<br>AAATTAGAATTGA<br>AACCAATTTTTAA<br>GTAAATCTAGGG<br>NTTCAATTTATTC<br>TCATTGNGTNTT<br>GTTTCTGGTGCA<br>ATCATGAANAAC<br>AGCATNCTATTAA<br>CCAACCTTGGTC<br>CCATGTACATAA |
| ATP synthase | CfaAffx.3186.1.S1_s_at | < 0.01 | PREDICTED: Canis familiaris similar to ATP synthase; H+ transporting; mitochondrial F0 complex; subunit c | 98.57651 | AATTGGGACTGT<br>GTTTGGGAGCCT<br>CATCATTGGTTAT<br>NCCAGGAATCCC<br>TCTCTGAAGCAA<br>CAGCTCTTCTCC |

| Gene | Probe | P-Value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Seq. |
|---|---|---|---|---|---|
| | | | isoform 2a precursor (LOC477595); mRNA | | TACGCCATTCTG GGCTTTGCCCTC NCGGAGGCCATG GGGCTTTTTTGC CTGATNGTGGCC TTTCTCATCCTCT TNGCCATGTGAA GGAGTCGTCTCC ACCTCCCATAGG TCTTTCTCCCATG TCTTGTCTGCCC TGTATGCCCTGT ATGTTCCTTTTCC TATACCTCCCCA GGCAGCCTGGG GAAAGTGGTTGG CTCAGGGTTTGA CA |
| NADH-ubiquinone oxidoreductase | Cfa.4415.1.S1_at | < 0.01 | PREDICTED: Canis familiaris similar to NADH-ubiquinone oxidoreductase MLRQ subunit (Complex I-MLRQ) (CI-MLRQ) (LOC477682); mRNA | 98.20789 | GGTGACTTTGGA CGTCCGTTCCTG CTCTGTGGAGGC NNTGCTTCGTTC CGGGCCTTGCG GCAACTCGGTNT TTCCTTCCCCTG CGCGGGAGACCT CTGCCACAACCA TGTTACGCCAGA TCATCGGTCAGG CCAAGAAGCATC CGAGCTTGATCC CCCTCTTCATATT TATTGGGGCAGG AGGTACTGGAGC AGCGCTGTATGT ATTGCGCTTGGC ATTGTTCAATCCA GATGTTAGTTGG GATAGGAAGAAT AACCCAGAACCT TGGAACAAACTG GGTCCCAATGAT CAATACAAGTTCT ACTCAGTGAATG TAGATTACAGCA AACTGAAGAAAG AAGGTCCAGACT TCTAAATGAAATG TTTCACTATAAAG CTGCTTAGAATG AAGGTCTTCCAG AAGCCATCCGCA CAATTTTCCACTT ATCCAGGAAATA TTTCCCCTCTAAA TGCACGAAATCA TGTTGGTGTATT GTGTTGGGGTTT ACACTNNANNAN TAAATATCTGAAA CTTGANANGTGT CACTATTTAATGC TGAAAATTTGCTC TGAACTTTA |

| Gene | Probe | P-Value | Best current BLAST annotation | % match of probe sequence to BLAST hit | Probe Target Seq. |
|---|---|---|---|---|---|
| Facilitated glucose transporter/ Glucose transporter-like protein III (GLUT3) | Cfa.1370.1.A1_at | < 0.01 | Homo sapiens cDNA FLJ44038 fis; clone TESTI4028880; highly similar to Glucose transporter type 3; brain | 23.95833 | TTGGAAGGATGG ATGCTTGCCCCA GGTCATGGACAC CTCCACAAATCA TCTAGTTTCCCA GTATTTTTATAAA TGGAGATTGGGC TCCATGACACTTT ACTTGGTCTTCC TTCTTACATAGGT TTTTTGATTACCC TTTCTCTCCTTGG TGCTTATATACTT AAGACCCTTTAG CCAAACCCTTGC CAATGACAGTAT TTCAGTCACTAG TTCTCACTGTTTC CTCTGATCATTG AGCCTTTGGAAA AAAAATCTCACA GAGCTTATATGT AATGGGGCTTGG TTGAACAGATGA CTTCCTGTAACT GCACCTCTACTT TTGGCTTCTCAA AAACAGTGGGTT GGCAGTAATGCA GCGTGGAAGTTT TCCCATTTCTCA GTGAC |

**Table 14. Summary of Genes involved in Glucose Metabolism**

| Gene | Gene Expression Compared to Control | Role |
|---|---|---|
| Phosphorylase kinase | ↓ | Necessary for activation of glycogen synthase which stores glucose as glycogen |
| Phosphorylase | ↓ | Necessary for glycogen conversion to glucose 1-phosphate which feeds into glycolysis |
| Glycogen synthase kinase 3 | ↓ | Necessary for activation of glycogen synthase which stores glucose as glycogen |
| Calmodulin | ↓ | Necessary for activation of glycogen synthase which stores glucose as glycogen |

| Gene | Gene Expression Compared to Control | Role |
|---|---|---|
| Protein Kinase C | ↓ | Necessary for activation of glycogen synthase which stores glucose as glycogen |
| Protein Kinase C Binding Protein | ↓ | Necessary for activation of glycogen synthase which stores glucose as glycogen |
| Hexokinase 3 | ↓ | Necessary for glucose conversion to pyruvate to enter the TCA cycle |
| Fructose 1,6 bisphosphatase | ↓ | Necessary for glucose conversion to pyruvate to enter the TCA cycle |
| Glyceraldehyde 3-phosphate dehydrogenase | ↓ | Necessary for glucose conversion to pyruvate to enter the TCA cycle |
| Glucose 6-phosphate dehydrogenase | ↓ | Involved in pentose phosphate pathway |
| Enolase | ↓ | Necessary for glucose conversion to pyruvate to enter the TCA cycle |
| Lactate dehydrogenase | ↓ | Involved in converting private to lactate |
| Citrate lyase | ↓ | Necessary for citrate conversion to oxaloacetate which feeds acetyl-CoA into the fatty acid synthesis pathway |
| Glycerol kinase | ↓ | Necessary for changing glycerol into DHAP which feeds into glycolysis |
| Transketolase | ↓ | Involved in pentose phosphate pathway |
| Ribulose phosphate 3-epimerase | ↓ | Involved in pentose phosphate pathway |
| Ribose 5-phosphate isomerase | ↓ | Involved in pentose phosphate pathway |
| Cytochrome c oxidase polypeptide VIIa-liver/heart, mitochondrial precursor | ↓ | Associated with the production of ATP (energy source) in the electron transport chain which is associated with the TCA cycle |
| Cytochrome c oxidase | ↓ | Associated with the |

| Gene | Gene Expression Compared to Control | Role |
|---|---|---|
| subunit VIII liver form | | production of ATP (energy source) in the electron transport chain which is associated with the TCA cycle |
| Ubiquinol--cytochrome c reductase | ↓ | Associated with the production of ATP (energy source) in the electron transport chain which is associated with the TCA cycle |
| ATP synthase | ↓ | Associated with the production of ATP (energy source) in the electron transport chain which is associated with the TCA cycle |
| NADH-ubiquinone oxidoreductase | ↓ | Associated with the production of ATP (energy source) in the electron transport chain which is associated with the TCA cycle |
| Facilitated glucose transporter/ Glucose transporter-like protein-III (GLUT3) | ↓ | Involved in glucose uptake |

## Example 5

**Comparison of Gene Expression Profiles of Genes Associated with the Aging Process: Healthy Adult Dogs versus Senior Dogs in comparison to Control Diet versus Super Senior Diet**

**[00130]** A dog's gene expression profile changes as the dog ages from being an adult dog to becoming a geriatric (senior) dog. This is true for genes associated with numerous biological pathways such as, e.g., glucose metabolism, blood clotting and bone and muscle integrity but also with regard to genes that have been associated with the aging process, or senescence, in general. With regard to this class of "aging" associated genes, we have found that, by feeding senior dogs a super senior diet according to the present invention, the gene expression profile of

certain of these genes in lymphocytes tends to move towards the profile of an adult dog from that of a geriatric dog. Thus, geriatric dogs fed a super senior diet according to the present invention can have their genetic profile altered to resemble more closely the genetic profile of a healthy adult dog.

**[00131]** The results displayed below in Tables 15-20, show that genes normally altered with the aging process can be regulated through nutritional strategies targeted at common aging changes. Specifically, the results show that, when fed a super senior diet, generally the expression levels of the genes in lymphocytes move in the opposite direction as that of the expression level in a healthy adult animal compared to the expression level in a geriatric animal. That is, when the expression level in a healthy adult animal is high compared to a geriatric animal (i.e., "down regulated" in the geriatric animal), the super senior fed geriatric animals generally also have higher expression level (altered to be "up regulated" ) as compared to a geriatric animal fed the control diet. Similarly, when the expression level in a healthy adult animal is low compared to a geriatric animal ("up regulated" in the geriatric animal), the super senior fed geriatric animals generally also have lower expression level (altered to be "down regulated") as compared to a control diet fed geriatric animal. Thus, expression levels of aging related genes in geriatric dogs may be beneficially altered when the geriatric dog is fed a super senior diet of the present invention and thus the dogs may therefore lead lives of improved quality.

**Table 15. Aging Genes Associated With Inflammation**

| **Annotation** | **Probe ID.** | **Direction of Expression** | |
|---|---|---|---|
| | | **Adult v. Geriatric** | **Super Senior v. Control Diet** |
| C1q and tumor necrosis factor related protein 2 | CfaAffx.26423.1.S1_at | up | down |
| TNFRSF1A-associated via death domain isoform 1 | CfaAffx.31209.1.S1_s_at | down | down |
| T-cell surface antigen CD2 precursor | CfaAffx.15424.1.S1_at | down | down |

| Annotation | Probe ID. | Direction of Expression | |
|---|---|---|---|
| | | Adult v. Geriatric | Super Senior v. Control Diet |
| Delta-aminolevulinic acid dehydratase | Cfa.17192.1.S1_s_at | down | down |
| Attractin precursor | CfaAffx.10508.1.S1_at | up | up |
| Cytochrome C oxidase subunit III | Cfa.16058.1.A1_x_at | up | up |
| NEDD4-like ubiquitin-protein ligase 1 | Cfa.8453.1.A1_at | up | up |
| Ubiquitin specific peptidase 11 | CfaAffx.23104.1.S1_at | down | down |
| Cartilage intermediate layer protein | Cfa/15775.1.A1_at | up | up |

**Table 16. Genes Associated With DNA Repair/Cell Survival**

| Annotation | Probe | Direction of Expression | |
|---|---|---|---|
| | | Adult v. Geriatric | Super Senior v. Control Diet |
| Gemin 7 | CfaAffx.7805.1.S1_s_at | down | down |
| Iroquis-class homeodomain protein IRX-4 | CfaAffx..16317.1.S1_at | up | down |
| Chromobox homolog 4 | CfaAffx.9308.1.S1_at | down | down |
| Ubiquitin specific peptidase 11 | CfaAffx.23104,1,S1_at | down | down |
| ADP-ribosylation factor-like 10B | Cfa.13803.1.S1_s_at | down | down |
| Eukaryotic translation initiation factor 5B | CfaAffx.4294.1.S1_at | up | up |
| General | CfaAffx.1649.1.S1_s_at | down | down |

| Annotation | Probe | Direction of Expression | |
|---|---|---|---|
| | | Adult v. Geriatric | Super Senior v. Control Diet |
| transcription factoR 11 H. polypeptide 4 | | | |
| NEDD4-like ubiquitin-protein ligase 1 | Cfa,8453.1.A1_at | up | up |
| Poly(ADP-ribose)polymerase family, member 8 | Cfa.5341.1.A1_at | up | down |

**Table 17. Aging Genes Associated With Fat/Cholesterol Metabolism**

| | Annotation | Probe | Direction of Expression | |
|---|---|---|---|---|
| | | | Adult v. Geriatric | Super Senior v. Control Diet |
| Phophomevanonate kinase | | Cfa.1406.1.S1_s_at | down | down |
| 5-AMP-activated protein kinase, gamma-1 subunit | | CfaAffx.13848.1.S1_at | down | down |
| Apoliprotein A-II precursor | | Cfa.8770.1.S1_at | down | down |
| C1q and tumor necrosis factor related protein 2 | | CfaAffx.26423.1.S1_at | up | down |
| Attractin precursor | | CfaAffx.10508.1.S1_at | up | up |

**Table 18. Aging Genes Associated With Protein Synthesis**

| Annotation | Probe | Direction of Expression | |
|---|---|---|---|
| | | Adult v. Geriatric | Super Senior v. Control Diet |
| Branched chain keto acid | Cfa.17186.1_s_at | down | down |

| Annotation | Probe | Direction of Expression | |
|---|---|---|---|
| | | Adult v. Geriatric | Super Senior v. Control Diet |
| dehydrogenase E1, alpha polypeptide | | | |
| Seryl-tRNA synthesis | CfaAffx.9380.1.S1_s_at | down | down |
| Mitochondrial 28S ribosomal protein S33 | CfaAffx.200.1.S1_at | down | down |
| Ribosomal protein S3a | CfaAffx.416.1.S1_x_at | down | up |
| 60S ribosomal protein L21 | CfaAffx.802.1.S1_at | down | up |

**Table 19. Aging Genes Associated With Cell Growth/Death**

| Annotation | Probe | Direction of Expression | |
|---|---|---|---|
| | | Adult v. Geriatric | Super Senior v. Control Diet |
| Sorting nexin-9 | Cfa.1874.1.S1_at | up | up |
| Cell growth regulator with RING finger domain 1 | Cfa.3200.1.S1_s_at | down | down |
| Solute carrier family 39 (zinc transporter) | CfaAffx.14864.1.S1_at | up | up |
| Choline kinase alpha isoform a | Cfa.8353.1.A1_at | down | down |
| Kv Channel interacting protein 2 | Cfa.3460.1.S1_at | up | down |
| Ribosomal protein S3a | CfaAffx.416.1.S1_x_at | down | up |
| Ubiquin specific peptidase 11 | CfaAffx.23104.1.S1_at | down | down |

**Table 20. Genes Altered With Age and Super Senior Diet with Unknown Functions**

| Annotation | Probe | Direction of Expression | |
|---|---|---|---|
| | | Adult v. Geriatric | Super Senior v. Control Diet |
| Protein KIAA0406 | Cfa.13958.1.A1_at | up | up |
| Hypothetical LOC477905 | CfaAffx.12332.1.S1_at | up | up |
| Nitilase 1 | CfaAffx.19716.1.S1_s_at | down | down |
| CG5645-PA | CfaAffx.27184.1.S1_at | down | down |
| Transcribed locus | Cfa.12738.1.A1_at | up | up |
| Transcribed locus | Cfa.18839.1.S1_at | up | down |

SEQUENCE LISTING IN ELECTRONIC FORM

In accordance with Section 111(1) of the Patent Rules, this description contains a sequence listing in electronic form in ASCII text format (file: 75852-112 Seq 17-07-14 v1.txt).

A copy of the sequence listing in electronic form is available from the Canadian Intellectual Property Office.

The sequences in the sequence listing in electronic form are reproduced in the following table.

SEQUENCE TABLE

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Frantz, Nolan
Gao, Xiangming
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gacgaagccc tgaagattct tctcagcaat cctcagatgt ggtggttaaa tgattcagat 120
cctgaaacga ncaaccagca agaaagtcct tcccaggaaa acattgacca actggtgtac 180
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ctggcagctc agnccctcgc ccacaacgga ggaactcttc ctcctgacct gcagctcttg 300
gtggaagact cttcatcaac gccatccacg tccccttccg actccgcagg tacctctagt 360
gcctcaacag atgaagatat ggaaaccgaa gctgtcaatg aaatactgga agatattcca 420
gaacatgaag aagattatct tgactcaaca ctggaag 457

<210> 6
<211> 93
<212> DNA
<213> Canis familiaris

<400> 6
gagatggagt cctgagcacc tggtttctgt tttgttgatc ccacttcact gtgaggggaa 60
ggccttttca tgggaactct ccaaatatca ttc 93

<210> 7
<211> 374
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature
<222> (349)..(349)
<223> n is a, c, g, or t

<400> 7
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tcagtcggga gtactgtcct ccatggtgct tcccttcctc tccttaatgt ggggaagacc 120
atggggcaat gcatggcgca ggacctgcct cccccaaaag cagtctactt gctccacgga 180
gagagaactg ggtccacgtg ccagagtctt gcccctttggc ccagagtagc ctggtcttca 240
tggctgtatg ggagacaagt gccttctctg cttcttgttg taggtgatgc taatctcctt 300
aaccaaacct ttgtcccagc cgctaatctg ttctaactct ccctcctcnt gattctcctg 360
ctcaaagtct gttc 374

<210> 8
<211> 500
<212> DNA
<213> Canis familiaris

<400> 8
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ccgccctgga gagcgtctgc ggatacttgc acaggtccca gaaccgcagc gaggagtttc 120

tggtcgccgg aaacctgcgg gacggacact tgcagatcaa cacctgcagt ttcgtggccc 180
cgtggagcag cctgagtacc gctcagcgcc ggggcttcac caagacctat gctgctggct 240
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actgcttgtg gacggaccag ttcctcacag gctctgacaa gggtttccag agccgccacc 360
tggcctgcct gccaagagag ccagggatat gcacctggca gtccctgcgg ccccggatgg 420
cctaaatcct actccccgtg gaagccaaag cctgcacagt gttcacccca cttcccactc 480
ctgtctttct ttatccaaaa 500

<210> 9
<211> 300
<212> DNA
<213> Canis familiaris

<400> 9
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gggctggagg acgagcaaaa gatgctgacc gggtccggag atcccaagga ggatccccta 120
acaacagtga gagagcaatg cgagcagctg gagaaatgtg taaaggctcg ggagcggcta 180
gagctctgtg accagcgtgt atcctccagg tcacagacag aggaggattg cacagaggag 240
ctctttgact tcctgcatgc aagggaccac tgtgtggccc acaaactctt taacagcttg 300

<210> 10
<211> 560
<212> DNA
<213> Canis familiaris

<400> 10
tgtgggtccg agctaacagc tacgtggggc ctctgatggc aggacggcgg ccctctgccc 60
tgagcctggg tcgtgggcag gacctgctag gtacggtggg cgttaggtac tccagccaca 120
gcctctgagg cgacggtggg cagtttgggg accttgagag gctgtgatgg gccctcctat 180
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cttttctggg tcagaagcct cctctccgca ttgcatgtgc aacctcagtg aagcagcatg 300
ggcaggggag ccggacgggc cacccaacag agctccttat gctgcaggag gggttcacag 360
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agcgtgattc tcacgtgcag gtacctaagg gaactgggga agagatgcac caagacgaga 480
gccctcgtca tccctgggga gcccaagcct aggggttttc ttcctcttcc cgtttagcat 540
tttccaccat cgtatgttac 560

<210> 11
<211> 546
<212> DNA
<213> Canis familiaris

<400> 11
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gaacagtact gggccaattt ccccatcacc gcagtgactg ttgcccacag tgggatctac 120
cgatgctata gcttttccag caagttcccg tacctgtggt cagcccccag cgacccctg 180
gagcttgtgg taacaggtga gggagatgca gtccaagcct ttcttcttca gctcttgcat 240
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ccaaaggggt cagactctcc aactggtctt gctcaccagc actacaccaa gggcaatctg 360
gtccggatat gccttggagc tgtgattcta atactcctgg tgggaattct ggcagaagat 420
tggcacagca gaaagaaacc cctgttgctc cgggtcagag ctgtccacag gccactccca 480
cccctcccac agacccagaa accacacagt catcaggatg ggggtcgacc agatggccat 540
aaccat 546

<210> 12
<211> 406
<212> DNA
<213> Canis familiaris

<400> 12
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agaccatggg gctgtgggtg gactgcaggg ggcggggact caaggccctg cccgccctgc 120
cggtccacac ccgccacctc ctgctggcca ataacagcct ccgctccgtg ccccctggtg 180
ccttcgacca cctgcctggg ctgcagatcc tcgacgtgat gcacaacccc tggcactgtg 240
actgcagcct cacctacctg cgtctctggc tggaggacca cacgcccgag gccttgctgc 300
aggtccgctg tgccagcccc gcgctggcca ccacccggcc gctgggctgg ctgacgggct 360
acgagctggg cagctgcggc tggcagctac aggcaccctg gaccta 406

<210> 13
<211> 501
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature
<222> (403)..(403)
<223> n is a, c, g, or t

<400> 13
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catttgaagt gacactggag cccttgtctt tcaagagaga ggaggtgctg atcagagcgg 120
gcgagtacat gggccagctg ctagagcaag catacctgca cttctttgtc acagcgcgtg 180
tcaatgagtc caaggatatt ctggccaagc agaagtccac cgtgctgacg atcccccagc 240
tcatcatcaa ggtccgtggc gccaagatgg ttggttctga catggtggtg acagttgagt 300
tcaccaatcc cctgaaagaa actctgcgga atgtgtggat acacctggat ggtcctggag 360
tgataaagcc aatgaggaag atgttccgtg aaatccagcc cantgccacc atacaatggg 420
aagaagtgtg tcgaccctgg gtgtctggcc ctcggaagct gatagccagc atgacgagtg 480
actccctgag acacgtgtat g 501

<210> 14
<211> 294
<212> DNA
<213> Canis familiaris

<400> 14
ggcaacatgt cgtccatgga ggtcaacatc gacatgctgg agcagatgga cctgatggac 60
atctctgacc aggaggccct ggacgtcttc ctgaactccg gcgctgaaga caacacggtg 120
ccgtctccgg tctcagggcc tggctcgggg gacagtcggc aggaaatcac gctccgggtt 180
ccagatcccg ccgaatcgca agctgagcct cctccctcgc cgtgtgcctg tcctgagctg 240
gccgccccgg cccccggcga cggtgaggcc cccgtggtcc agtctgacga ggag 294

<210> 15
<211> 330
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature

<222> (69)..(69)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (103)..(103)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (248)..(248)
<223> n is a, c, g, or t

<400> 15
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ccctagacna accagctgct gttcttcctg gtggaggagg aanccggagg catggttgtg 120
ttgacagtga gaccccaaga gagaggcgcg gatcacaccc aggccatcgt gctgggctgt 180
gtaggggca tcgtggcagt ggggctgggg ctggtcctgg cttaccggct ctctgtggaa 240
atctacgncc gccgagaatt tagccgcttt gagaaggagc agaagcacct caactggaag 300
caggaaaaca atcctctcta cagaagcgcc 330

<210> 16
<211> 395
<212> DNA
<213> Canis familiaris

<400> 16
tgggcgcatg tatgcacctg cctgggtggc ccctgaagct ctgcagaaga agcctgaaga 60
tacaaacaga cgctcagcag atatgtggag ttttgcagtg cttctgtggg aactggtgac 120
gagggaggta ccctttgctg acctctccaa catggagatt ggaatgaagg tggcactgga 180
aggccttcgg cctactatcc caccaggcat ttccccccat gtgtgtaagc tcatgaagat 240
ctgcatgaat gaagaccctg ctaagcggcc caagtttgac atgattgtgc ctatcctgga 300
gaagatgcag gacaagtaga gctggaaagc ccttgcctaa actccagagg tgtcaggaca 360
cggttagggg agtgtgtctc cccaaagcag caggc 395

<210> 17
<211> 248
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature
<222> (182)..(186)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (200)..(205)
<223> n is a, c, g, or t

<400> 17
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ggtgttgcac cttctggaac cacgggctta agaaaacccc caggatcact cctccctgcc 120
ttttctctgc ttgcatatca ttgtggacac ctagaatacg ggacttgcct cgagaccatg 180

cnnnnntcca aatcagactn nnnnngtagc ctctgaacgc gaagagaatc ttccaagagc 240
atgaacag 248

<210> 18
<211> 453
<212> DNA
<213> Canis familiaris

<400> 18
gaagcccttg atggatactg tgaacgggaa caggctataa agacccacca ccactcctgt 60
tgccaccacc ctcctagccc tgcccgcgat gagtgctttg cccgtcaggc gccatacccc 120
aactatgacc gggacatcct gacccttgat ttcagccaag ttacccccaa cctcatgcaa 180
catctctgtg gaaatggaag acttctcacc aagcataaac agattcctgg gctgatccgg 240
aacatgactg cccactgctg tgacctgcca tttccagagc aggcctgctg tgctgaggag 300
gagaaatcgg ccttcattgc agacttgtgt ggttcccgac gtaacttctg gcgagactct 360
gccctctgct gtaacctgaa tcctggagat gaacagacca actgcttcaa cacttattat 420
ctgaggaatg tggctctagt ggctggagac aat 453

<210> 19
<211> 535
<212> DNA
<213> Canis familiaris

<400> 19
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ggctgctctt ggtagtcaca gaaatgccca cgcttcagtc ccctgggctt ccaatgcttc 120
tggacctctg aaccagcctg tgatgtccaa ggaaccccac gtcacgctcc aggctgctgc 180
tggtctgtct cccccacaag cttctcaaag tctggtagat tatgacagct ctgatgattc 240
tgaagtagaa gtcacagacc agcactcaac aaacagtaaa caaacatctt tacagcaaga 300
agcaaagaag aaatttcagg acacagttag aacaggtcca gatgaaaaag aacttagcat 360
ggagcctcaa tcaaggcctc tggttccaga acaatctaat attaatattc ccttctctgt 420
tgactgtgac atctccaaag taggaatatc ttacaggaca ctgaagtgct ttcaggagct 480
acagggtgcc atttaccgtt tgcagaaaaa aaatcttttc ccctataatg ccaca 535

<210> 20
<211> 264
<212> DNA
<213> Canis familiaris

<400> 20
gcggactgtg ttccaacccc ttcagccgac ttgccccctc cgtcccttct cttaagagac 60
ccatcccttg gccccccacc ccaccctcac ccagacctgc gggtccctca gaggggggtc 120
aggcctcttt ctctttcacc ttcatttgct ggcgtgagct gcgggggtgt gtgtttgtat 180
gtggggagta ggtgtttgag gttcccgttc tttcccttcc caagtctctg ggggtggaaa 240
ggaggaagag atattagtta caga 264

<210> 21
<211> 156
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature

<222> (72)..(77)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (79)..(83)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (85)..(89)
<223> n is a, c, g, or t

<400> 21
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aaacacccct gnnnnnnann nnnannnnnc accacgtttt gctatcagaa ctctccttgt 120
ttccagagcc cgtgtgcttt tgtttgcccc agcccc 156

<210> 22
<211> 295
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature
<222> (134)..(137)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (140)..(140)
<223> n is a, c, g, or t

<400> 22
ccacccatgg tgacgatgac acacatcctg gtggcatgcg tgtgttggtt tagcgttgtc 60
tgcgttgtac tagagcgaaa atgggtgtca ggcttgtcac cattcacaca gaaatttaaa 120
aaaaaaaaaa aaannnngan aaaaaacctt taccaaggga gcatctttgg actctctgtt 180
tttaaaacct cctgaaccat gacttggagc cagcagatta ggctgtggct gtggacttca 240
gcacaaccat caacattgct gatcaagaaa ttacaatata cgtccattcc aagtt 295

<210> 23
<211> 502
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature
<222> (51)..(51)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (457)..(457)
<223> n is a, c, g, or t

<400> 23
atacctcaga ggtctcgtag ctcgtgccct tgccatccag agctgggtgg nagagagctg 60
agaagcaggc tcttttctct gatacactcg acctgtcaga actcttccac ccagacacat 120
ttctcaatgc tcttcgccag gaaacagcaa gggtgatggg ctgctctgtg gatagcctta 180
agtttgtagc ttcgtggaaa ggtcggctgc aagaagcaaa gctgcagatc aagatgggcg 240
gcttgcttct ggaaggctgc agttttgacg ggagccggct ctctgaaaac caccacgatt 300
ctccaagtgt gtcaccagtt ctcccttgct gtgttggctg gattccccag ggtgcatatg 360
gtccctattc tcctgacgag tgcatatctc tgcccgtgta cacgagcgct gagagggatc 420
gtgtggtagc caacatcgac gtcccgtgtg ggggcancca agaccagtgg attcagtgtg 480
gagccgctct gtttctaaaa aa 502

<210> 24
<211> 147
<212> DNA
<213> Canis familiaris

<400> 24
aggacgacaa ggctcaggac gcaaagtgtg aaactgcctt tgtaacaggg cagaagcagc 60
tctgtattgg attcacaacc tacctatctg cattcaggtg gggctcggag gtcagaggtc 120
tggctacttg aggtttgctg tttgcac 147

<210> 25
<211> 371
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature
<222> (91)..(91)
<223> n is a, c, g, or t

<400> 25
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tcctttgcgt gcatgcatac ctcatcagtg nactgtacat accttgccct ctcccagaga 120
cagctgtgct cacctcttcc tgctttgtgc cttgactaag gcttttgacc ctaaatttct 180
gaagcacagc caagataaag tacattcctt aattgtcagt gtaaattacc tttattgtgt 240
gtacattttt actgtacttg agacattttt tgtgtgtgac tagttaattt tgcaggatgt 300
gccatatcat tgaatggaac taaagtctgt gacagtggac atagctgctg gaccattcca 360
tcttacatgt a 371

<210> 26
<211> 205
<212> DNA
<213> Canis familiaris

<400> 26
ggtgctactg tttgaaacag ctctactctc ctccggcttc tcactggagg atccccagac 60
tcactccaac cgcatttacc gcatgataaa gctaggcctg ggcatcgatg aagatgaagt 120
ggcagcggag gaacccagtg ctgctgttcc tgatgagatc cctccacttg agggtgatga 180
ggatgcctct cgcatggaag aagtc 205

<210> 27
<211> 256

<212> DNA
<213> Canis familiaris

<400> 27
gacatcacca gtggagacgg caccggcggt ataagcattt atggtgagac gtttccagat 60
gaaaacttca aactgaagca ttatggcatt ggttgggtca gcatggccaa cgctgggcct 120
gacaccaacg gctctcagtt ctttatcacc ttgaccaagc ccacttggtt ggatggcaaa 180
catgtggtat ttggaaaagt ccttgatgga atgactgtgg tccactccat agaacttcag 240
gcaaccgatg ggcacg 256

<210> 28
<211> 343
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature
<222> (63)..(63)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (161)..(161)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (314)..(315)
<223> n is a, c, g, or t

<400> 28
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aatgttctat gtataattga ctgtctgtaa catgctgttt ncttcctctg cagatgtagc 180
tgctttccta aatctgtctg tctttcttta ggttagctgt atgtctgtaa aagtatgtta 240
aattaaatta ctctatcaga cgcttgtctg tcttttgatg tagaagcaac tttgtagcac 300
cttgttttga ggtnngctgc atttgttgct gtactttgtg cat 343

<210> 29
<211> 566
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature
<222> (139)..(139)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (394)..(394)
<223> n is a, c, g, or t

<400> 29
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gcatcgcttg tgtggcttat gccaccgaag tggcctggac ccgggcccgt cccggagaga 120
tcaccggcta catggccant gtgccgggcc tgctcaaggt gctggagacc tttgtggcct 180
gcatcatctt cgccttcatc agcaacccct ccctgtacca gcaccagccg gccctggagt 240
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tgggggactg caccaacatg ctgcccatct ccttccccag tttcctgtcg ggcctggccc 360
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agaagtatgg tggccagccc cgtcggtcga gggatgttag ctgcgccgac aggcacacct 480
actacgtgtg tacctgggac cgccgcctgg ctgtggccat cctgacagcc atcaacctgc 540
tggcttacgt ggctgacctg gtgtac 566

<210> 30
<211> 93
<212> DNA
<213> Canis familiaris

<400> 30
ggagcagtca gaactaagac atggtccgtt ttactatatg aagcagccac tcaccacaga 60
ccctgttgat gttgtaccgc aggatggacg gaa 93

<210> 31
<211> 42
<212> DNA
<213> Canis familiaris

<400> 31
cctcttcttc ggatgttttc cttcaaggcc cctaccattg at 42

<210> 32
<211> 336
<212> DNA
<213> Canis familiaris

<400> 32
ggtgctgttc accacagtaa gtggcctctc agtgttgctg accaaagtgt gaaatcctag 60
agcttcaggg gagaggacgt gggggaaatc cggggcttga ctttataata ggattataga 120
gatgaaaagt acaccttgct ttaggcaaca gttgggattc ctaagacgca tgtgtaagag 180
catatgtgaa atcccttccc cattgttgat ctctactcac agaattttgt ctttattatg 240
gtgtaagaat cactcttaaa gccacatatt caattcaaag caaatacgtg ttctgcagtt 300
gcaaatgtgt atttaattct tcacaattcc tgtaag 336

<210> 33
<211> 406
<212> DNA
<213> Canis familiaris

<400> 33
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tgtcaaagtt caggtaatgg gtaaagtgcc aaccatttcc atcaacaaaa cagatggctg 120
ccatgtttac ctgagcaaga attccctgga ttgcgaaata gtcagtgcca aatcttctga 180
gatgaatgtc ctcattccta ctgaaggcgg tgactataat gaattcccag tccctgagca 240
gttcaagacc ctatggaatg ggcagaagtt ggtcaccaca gtgacagaaa ttgctggata 300
agcgaagtgc cactgggttc tttgccctcc ccctcacacc atgggataaa tctatcagga 360
cggttctttt ctagatttcc tttacctttc tgctcttaaa ctgctt 406

<210> 34
<211> 321
<212> DNA
<213> Canis familiaris

<400> 34
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gcactgttga taaagctggt cccttccttt aactgtcttt taggttgttc ttgccttgtt 120
gccaggagta ttgcaggtaa tacagtatat tcataagaat atcaatcttg gggctaaaat 180
gccttgattc tttgcacctc ttttacaagt ccttacgttg aattactaat tgataagcag 240
cagcttccta catatagtag gagactgcca cgtttttgct atcatgattg gctgggcctg 300
ctgctgttcc tagtaaggta t 321

<210> 35
<211> 524
<212> DNA
<213> Canis familiaris

<400> 35
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gttgcagtga taaatggtcc agccatagga atctccgtca ccattctcgg gctattcgat 120
cttgtgtatg cttccgacag ggcaacattt cacactcctt ttactcacct gggccaaagt 180
ccagaaggat gttcctccta tacttttccc aagataatgg gccaagccaa ggcagcagag 240
atgctcatgt ttggaaagaa gttaacagct agagaagcct gtgctcaagg acttgttact 300
gaagtttttc ccgatagcac ttttcagaaa gaagtttgga ccaggctgaa agcatattca 360
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aagctacatg ctgttaacgc agaagaaaac agcgtcctcc aggaaaggtg gctgtcagac 480
gaatgcataa atgcagtcat gagcttctta tcccggaagg ccaa 524

<210> 36
<211> 526
<212> DNA
<213> Canis familiaris

<220>
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<222> (472)..(472)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (475)..(477)
<223> n is a, c, g, or t

<400> 36
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acagccttga ggagcaaaga attctggatt ggcaaccccg tgaaaaccct ttccacaatc 120
tgaaggtact cttggtgtca gaccaacagc agaacttcct ggagctctgg tctgagatcc 180
tcatgaccgg gggggcagcc tctgtgaagc agcaccattc aagtgcccat aacaaagata 240
ttgctttagg ggtatttgac gtggtggtga cggatccctc atgcccagcc tcggtgctga 300
agtgtgctga agcattgcag ctgcctgtgg tgtcacaaga gtgggtgatc cagtgcctca 360
ttgttgggga gagaattgga ttcaagcagc atccaaaata caaacatgat tatgtttctc 420
actaatactt ggtcttaact gattttattc cctgctgttg tggagattgt gnttnnncca 480
ggttttaaat gtgtcttgtg tgtaactgga ttccttgcat ggatct 526

<210> 37
<211> 333
<212> DNA
<213> Canis familiaris

<400> 37
ggcccaccag ctctgagcag atcatgaaga caggggccct tttgcttcag ggtttcatcc 60
aagatcgagc agggcgaatg gggggagaga cacctgagct gcccttggag caggtgcccc 120
aggatgcatc caccaagaag ctgagcgaat gtctcaagcg catcggagat gaactggaca 180
gtaacatgga gttgcagagg atgatcgcag ctgtggacac agactctccc cgtgaggtct 240
tcttccgagt ggcagctgag atgttttctg atggcaactt caactggggc cgggttgttg 300
ccctcttcta ctttgccagc aaactggtgc tca 333

<210> 38
<211> 454
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature
<222> (300)..(300)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (353)..(353)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (379)..(379)
<223> n is a, c, g, or t

<400> 38
gaaagttcac cactgcatgt tttatgatca gataactcat tgaaatgagt ctttgctctt 60
tagactaaat tcccacctag tactgccatt aaaatgaatt tgccagctgg tgtgcatact 120
ggaaatgaaa agatactgaa agaatggaac gaatggtgag cttaactcag tggcactgtc 180
atactggaaa aatacagtaa aatcataaaa acagatctgc cagctgatgt ttttattctc 240
agaaacagca ttgttgataa tattttagta tacagagcta ctgtacaatt tttaccttgn 300
aaacatgact gtggttttgt atttgtgttg actttagggg ttgggataaa atncagtata 360
atatatacct tatcaaacnt tttctttgag ctcttactaa aaatatggca tgcataagat 420
tgttcagaag agtagactgt taacctagtt tgta 454

<210> 39
<211> 314
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature
<222> (29)..(29)
<223> n is a, c, g, or t

<220>
<221> misc_feature

<222> (66)..(66)
<223> n is a, c, g, or t

<400> 39
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gcctgncctc ttcaaagatt taatcaatat gctattttat catgacaggt ttaaagtctt 120
cgcagactat gaagcctatg tcaagtgtca agaaaaagtc agccagctgt acatgaatcc 180
aaaggcctgg aacacaatgg tactcaaaaa catagctgcc gcagggaagt tctctagtga 240
ccgaacaatt aaggaatatg ccagggacat ctggaacatg gaaccttcag atctcaagat 300
ttccctatcc aatg 314

<210> 40
<211> 397
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature
<222> (311)..(311)
<223> n is a, c, g, or t

<400> 40
gactccaccg gaggcaattg cactgtgtag ccgtctgctg gagtatacac caactgcccg 60
attgacacca ctggaagctt gtgcacattc atttttgat gaattaaggg acccaaatgt 120
caaactacca aatgggcgag acacacctgc actcttcaac ttcaccactc aagaactgtc 180
aagtaatcca cctctagcta ccatccttat tcctcctcat gctcggattc aagcagctgc 240
ttcaacccct acaaatgcca cagcagcctc agatgctaat gccggagacc gtggacagac 300
gaacaatgcc ncttctgcat cagcttctaa ctccacctga acagtcccga gcagccagct 360
gcacaggaag aaccaccagt tacttgagtg tcactca 397

<210> 41
<211> 498
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature
<222> (49)..(49)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (390)..(390)
<223> n is a, c, g, or t

<400> 41
taatgactgc caactcactg tttgttggag ttatatgcag aaataaagnc caagtcttca 60
gaaacaggct tcaggatgcc ctcaccaggg atggaagagg caggctgcag caaagagatg 120
cagagttccc ttgcacatct cgacttaaat gagtctccca tcaagtcttt tgtttccatt 180
tcagaagcca cagattgctt agtggacttt aaaaagcaac ttaacgttcg gcaaggtagt 240
cggacacgga ccaaagcagg cagaggaaga aggagaaaac cctgaatttc tagggtccag 300
acacccgaca aaaccattag caataggggt gggccgtgtc attaagtctt agtggcttct 360
gtttcattgt tgaacaagtt ttttggcccn gcagttttca ccaccagcac caactcagca 420
ttcttgtttt gatgttttct ataagctata cagacaattg tgtatagtat tctgttttat 480
aacagtctgg attcactt 498

<210> 42
<211> 83
<212> DNA
<213> Canis familiaris

<400> 42
agtggcgctg tgtgctgaaa attggggaac acactccctc agcccttgcg atcatggaaa 60
atgccaacgt tctggcccgt tat 83

<210> 43
<211> 315
<212> DNA
<213> Canis familiaris

<400> 43
agctcactgg catggccttc cgtgtcccca cccccaatgt atcagttgtg gatctgacct 60
gccgcctgga gaaagctgcc aaatatgacg acatcaagaa ggtagtgaag caggcatcgg 120
agggaccccc caaaggcatc ctgggctaca ctgaggacca ggtggtctcc tgtgacttca 180
acagtgacac ccactcttcc accttcgacg ccggggctgg cattgccctc aatgaccact 240
ttgtcaagct catttcctgg tatgacaatg aatttggcta cagcaaccgg gtggtggacc 300
tcatggtcta catgg 315

<210> 44
<211> 536
<212> DNA
<213> Canis familiaris

<220>
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<222> (160)..(160)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (192)..(194)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (197)..(198)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (211)..(211)
<223> n is a, c, g, or t

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<221> misc_feature
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<223> n is a, c, g, or t

<220>
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<222> (361)..(361)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (378)..(378)
<223> n is a, c, g, or t

<220>
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<223> n is a, c, g, or t

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<222> (387)..(387)
<223> n is a, c, g, or t

<220>
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<223> n is a, c, g, or t

<220>
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<222> (419)..(419)
<223> n is a, c, g, or t

<220>
<221> misc_feature
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<223> n is a, c, g, or t

<220>
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<223> n is a, c, g, or t

<220>
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<223> n is a, c, g, or t

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<222> (483)..(483)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (495)..(495)
<223> n is a, c, g, or t

<400> 44
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aggtctagaa acttttggac cataggaaag ataggtttat ggtcctcttc cagatgcagc 120
cctaggagag cattcccatg gggtctctgg atccctttcn ttgctctgtg aggctctgtg 180

accacctttt gnnntgnngg gggcaggggg ncttcctcag ctccgcctcc agtgccccca 240
ggtccccccac ggctcacagt ccntgaaaat tcagagctgc cctgtaagga ttttgtccac 300
tgggcaattc agatatactt cgatatccct gagaaagaag aggcagcagc aaacactccc 360
nagggcatct gtctcagnan tctctcnttg natgagacag aagcctactt ttcagaaanc 420
ttatcanggn tactttataa gaaacttttt ttttttnct aaaatcagac aaaaggtggc 480
ttntgcatat tcttnattaa taactgtgtc tttgtctcct ctgcttaact ttagga 536

<210> 45
<211> 483
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature
<222> (142)..(142)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (149)..(149)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (202)..(202)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (357)..(357)
<223> n is a, c, g, or t

<400> 45
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tggtgtctat cgaagacccc ttcgaccagg atgactggga agcttggcag aaattcactg 120
ccagcgctgg aatccaggtg gnggggggang atctcaccgt gaccaaccca aagcggattt 180
ccaaggctgt gggcgagaaa tngtgcaact gcctcctgct taaagtgaac cagattggct 240
ctgtgaccga gtctcttcag gcgtgcaagc tggcccagtc caatgggtgg ggcgtcatgg 300
tgtcgcatcg ctccggggag accgaagata ccttcatcgc tgacctggtg gtgggantct 360
gcactgggca gatcaagacg ggtgcaccat gcagatctga gcgcttggcc aagtacaacc 420
agatcctcag aattgaagag gaactgggta gcaaggccaa gttcgccggc agaagcttca 480
gaa 483

<210> 46
<211> 349
<212> DNA
<213> Canis familiaris

<400> 46
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taaagttaca cataggaatg gttcacaaaa ccctgcagct atgtcctgat gctggatgag 120
acctgtcttg tgtagtccta aattggttaa cgtaatatcg gaggcaccac tgccaatgtc 180
atatatgctg cagctactcc ttaaaccaga tgtgtattta ctgtgttttg taacttctga 240
ttccttcatc ccaacatcca acatgcctag gccatctttt cttcttcagt cacatcctgg 300
gatccaatgt ataaattcaa tattgcatgt attgtgcata actcttcta 349

<210> 47
<211> 532
<212> DNA
<213> Canis familiaris

<400> 47
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tatctcactg gccagttatt cctttaaaaa tgaacttcct tctttttgat tccaagctta 120
tgattttact gctcattaat gtgttacaaa tatgcactta atgatttcac agggagataa 180
aatagtgaag agagatgggc tgaggggctg ttaggacttt aatgaaacag atctttcccg 240
aatatttctc ccttcacatt tctcacatta gatgtttccc acattgttct actccacact 300
ataaataatt ttaaggccaa tcttaaaaaa tggtagttaa gtgaaggggt tgtgtttatt 360
tcactagaaa tctgataaaa cgagagatga catagaaaaa gttatcattt ttgttcatac 420
agatggcttc taaaaataaa tcttcaaaac tgattacttt taacctccac ctcccaaaat 480
gaaacatccc tacatttgaa ctgctaggtg agaactctga aagccctcat cc 532

<210> 48
<211> 495
<212> DNA
<213> Canis familiaris

<400> 48
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ggagcccagt gcaagaggga tcatctgtgg gctcactcaa ttcaccaata aatgccatat 120
tgcttttgct gcattagaag ctgtttgttt ccaaacccgg gagattttgg atgccatgaa 180
ccgagactgc ggaattccac tcagtcattt gcaggtagat ggaggaatga ccaacaacaa 240
aattcttatg caactacaag cagacattct atatatccca gtagtgaagc cctcgatgcc 300
agaaacaact gccctgggag ctgccatggc agccggggct gcggagggag ttggtgtttg 360
gagtcttgaa cccgaggatc tgtcagcagt cacgatggag cgatttgaac cccagatcaa 420
tgctgaggaa agtgaaattc gttactctac atggaagaag gctgtgatga agtcagtggg 480
ctgggttaca actca 495

<210> 49
<211> 572
<212> DNA
<213> Canis familiaris

<400> 49
gaagatctgg ccatgtttcg gtccatcccc actgctacga tcttttaccc aagtgacggg 60
gtgtcaacag agaaggcggt ggaattagca gccaatacaa agggcatctg cttcatccgg 120
accagccgcc cagaaaacgc catcatctat aacaacaatg aggatttcca aatcaaacaa 180
gccaaggtgg tcctgaagag caaggatgac caggtgactg tgattggggc cggagtgacc 240
ctacatgagg ccttggctgc tgctgaactg ctgaagaaag agaagatcaa cattcgtgtg 300
ttggaccccct tcaccatcaa gcccctggac agaaatctca ttctcgaaag cgcccgtgcg 360
accaagggca ggatcgtcac cgtggaggac cattactatg aaggtggcat aggtgaggca 420
gtgtcctctg ccttggtggg tgagcctggc atcaccgtct cccgccttgc agttggtgag 480
gtaccaagaa gcgggaagcc agctgagctg ctgaagatgt ttggcattga cagggacgcc 540
atcgcacaag ctgtgaggga ccttgtcgcc aa 572

<210> 50
<211> 263
<212> DNA
<213> Canis familiaris

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<222> (40)..(40)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (71)..(71)
<223> n is a, c, g, or t

<400> 50
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gtgtgtgtgt ncttcacgtg ccagaagaga agtttagatc ctcccagggg aatcgcaatg 120
ttgtggcgtc ctgacttgta tgtcacgttt tgtgtaaaaa tggtatattc tttaaaatag 180
tgttgataac tggaatattg tatgtatgct tggagatgct ttgtgtgaac ctaagactgt 240
cactcaacag atgttggatt ggg 263

<210> 51
<211> 123
<212> DNA
<213> Canis familiaris

<400> 51
agcctttcta ctgaccctgc aagagtggag cgtgttcacc ttgaaccccc agcgtgcagc 60
tgaggtagac atgcctctcc aggagccttt gccttaatgc atctgtgcca gacagacggc 120
tgg 123

<210> 52
<211> 181
<212> DNA
<213> Canis familiaris

<400> 52
ggcagtttga aaataaagtt ccagagaaac aaaagctatt tcaggaggat aatggaattc 60
cagtgcatct aaagggtgga gtagctgatg ccctcctgta tagagccact atgatgctta 120
cagttggtgg aacagcatat gccatgtatc agctagctgt ggcttctttt cccaagaagc 180
a 181

<210> 53
<211> 416
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature
<222> (161)..(161)
<223> n is a, c, g, or t

<400> 53
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acaggcctca cccggcggct cccggtgcat cgtgcccaga tccattccaa gccgccgcgg 120
gagcagctcg ggaccatgga tgttgccgtt gggctcacct nctgcttcct gtgtttcctc 180
ctgccatcgg gctgggtcct gtcacacctg gagagctaca agaagcggga gtgaaggggg 240
ctgtcctgtc cctcaccctg tgacctgacc acccctggcc tgtcctgatc atgtctgctg 300

cattcctggc cggccttcca tggatcatgt ccttcaatta cagtgacctc ttctacagtc 360
atgacctctt gatttctcca tggtgacatc ctgggaccaa acatattggt ttataa 416

<210> 54
<211> 493
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature
<222> (408)..(408)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (427)..(427)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (430)..(430)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (453)..(453)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (462)..(462)
<223> n is a, c, g, or t

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gttttcattt gcttacattt acgatatcag cgtcagctac ggaatcaatc tgctgaagga 120
ccgtggctgg cggcgtgtac gatccagcaa ccagcgcctg ggacccgact tcatccagga 180
acccctcaga agactccact gacattagga agactcataa gaaccttaca agaaaaagta 240
tcaaccccat caaaacggca gaaaagaaac atatcttgtt attagtagct gaaattccat 300
tttctacatg ttgccatacc ttataaaaac tacactaagc tacgcttaag gaaatacatt 360
ttcttaaata aattagaatt gaaaccaatt tttaagtaaa tctagggntt caatttattc 420
tcattgngtn ttgtttctgg tgcaatcatg aanaacagca tnctattaac caaccttggt 480
cccatgtaca taa 493

<210> 55
<211> 281
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature
<222> (38)..(38)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (98)..(98)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (127)..(127)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (148)..(148)
<223> n is a, c, g, or t

<400> 55
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acagctcttc tcctacgcca ttctgggctt tgccctcncg gaggccatgg ggctttttg 120
cctgatngtg gcctttctca tcctcttngc catgtgaagg agtcgtctcc acctcccata 180
ggtctttctc ccatgtcttg tctgccctgt atgccctgta tgttcctttt cctatacctc 240
cccaggcagc ctggggaaag tggttggctc agggtttgac a 281

<210> 56
<211> 558
<212> DNA
<213> Canis familiaris

<220>
<221> misc_feature
<222> (37)..(38)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (70)..(70)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (492)..(493)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (495)..(496)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (498)..(498)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (517)..(517)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (519)..(519)
<223> n is a, c, g, or t

<400> 56
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caactcggtn tttccttccc ctgcgcggga gacctctgcc acaaccatgt tacgccagat 120
catcggtcag gccaagaagc atccgagctt gatccccctc ttcatattta ttggggcagg 180
aggtactgga gcagcgctgt atgtattgcg cttggcattg ttcaatccag atgttagttg 240
ggataggaag aataacccag aaccttggaa caaactgggt cccaatgatc aatacaagtt 300
ctactcagtg aatgtagatt acagcaaact gaagaaagaa ggtccagact tctaaatgaa 360
atgtttcact ataaagctgc ttagaatgaa ggtcttccag aagccatccg cacaattttc 420
cacttatcca ggaaatattt cccctctaaa tgcacgaaat catgttggtg tattgtgttg 480
gggtttacac tnnannanta aatatctgaa acttganang tgtcactatt taatgctgaa 540
aatttgctct gaacttta 558

<210> 57
<211> 384
<212> DNA
<213> Canis familiaris

<400> 57
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gtatttttat aaatggagat tgggctccat gacactttac ttggtcttcc ttcttacata 120
ggtttttga ttacccttc tctccttggt gcttatatac ttaagaccct ttagccaaac 180
ccttgccaat gacagtattt cagtcactag ttctcactgt ttcctctgat cattgagcct 240
ttggaaaaaa aatctcacag agcttatatg taatggggct tggttgaaca gatgacttcc 300
tgtaactgca cctctacttt tggcttctca aaaacagtgg gttggcagta atgcagcgtg 360
gaagttttcc catttctcag tgac 384

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CLAIMS:

1. A composition comprising

a) 20.1% crude protein, 16.5% fat, 0.7% calcium, 0.6% phosphorus, 0.3% eicosapentaenoic acid (EPA), 0.2% docosahexaenoic acid (DHA), 4% linoleic acid, 1.3% total omega-3 fatty acids, 4% total omega-6 fatty acids, 1400 ppm taurine, 314 ppm carnitine, 1% methionine, 0.3% cystine, 87 ppm manganese, and 1492 IU/kg vitamin E, 127 ppm Vitamin C and 101 ppm lipoic acid, or

b) 19.3% crude protein, 16.9% fat, 0.7% calcium, 0.7% phosphorus, 0.3% eicosapentaenoic acid (EPA), 0.2% docosahexaenoic acid (DHA), 4% linoleic acid, 2.2% total omega-3 fatty acids, 4% total omega-6 fatty acids, 1525 ppm taurine, 337 ppm carnitine, 1.2% methionine, 0.2% cystine, 100 ppm manganese, and 1525 IU/kg vitamin E, 261 ppm Vitamin C and 135 ppm lipoic acid, or

c) 35.7% crude protein, 22.5% fat, 0.9% calcium, 0.8% phosphorus, 0.2% eicosapentaenoic acid (EPA), 0.3% docosahexaenoic acid (DHA), 5.1% linoleic acid, 1.1% total omega-3 fatty acids, 5.1% total omega-6 fatty acids, 2100 ppm taurine, 367 ppm carnitine, 1.3% methionine, 0.5% cystine, 104 ppm manganese, and 1292 IU/kg vitamin E, and 141 ppm Vitamin C,

for modulating biological functions associated with the aging process of a senior or super senior companion animal;

wherein the modulation of biological functions comprises one or more of:

improving blood clotting and platelet activation and aggregation, improving DNA damage and repair pathways, improving neural function, improving glucose metabolism, and improving an aging process, wherein

the improvement in the ageing process comprises an improvement in DNA repair, fat or cholesterol metabolism, and protein synthesis.

2. A composition according to claim 1, wherein the composition is suitable for consumption by a cat or a dog, and/or, wherein the composition is in the form of an animal treat, toy or a nutritional supplement.

3. A composition according to claim 2, wherein the composition further comprises at least one nutrient chosen from choline, beta-carotene, lysine, and mixtures thereof.

4. A composition according to claim 1, 2, or 3, wherein the composition is fed to the animal, and

wherein the animal consuming composition a) is a small/regular breed canine, wherein the animal consuming composition b) is a large breed canine and wherein the animal consuming composition c) is a feline.

5. A composition for use in modulating biological functions associated with the aging process of a senior or super senior companion animal wherein the composition comprises:

at least 9% by weight protein,

at least about 5% by weight fat, and

at least about 0.05% by weight of at least one omega-3 polyunsaturated fatty acid, wherein the modulation of biological functions comprises one or more of:

improving blood clotting and platelet activation and aggregation;

improving DNA damage and repair pathways, improving neural function, improving glucose metabolism, and improving an aging process, wherein

the improvement in the ageing process comprises an improvement in DNA repair, fat or cholesterol metabolism, and protein synthesis, and wherein

the composition is fed to the animal.

6. The composition for use according to claim 5 wherein the animal is chosen from a cat, a dog, and a horse.

7. The composition for use according to claim 5 or claim 6, wherein the at least one omega-3 polyunsaturated fatty acid is chosen from docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA).

8. The composition for use according to claim 7, wherein the at least one omega-3 polyunsaturated fatty acid is DHA and/or EPA in an amount of about 0.05% by weight to about 10% by weight as measured on a dry matter basis.

9. The composition for use according to claim 7 or 8, wherein the composition comprises EPA in an amount of at least 0.1% by weight, on a dry matter basis.

10. The composition for use according to claim 7, 8, or 9, wherein the composition comprises EPA in an amount of about 0.1% by weight to about 1% by weight as measured on a dry matter basis.

11. The composition for use according to any one of claims 5 to 10, wherein the composition further comprises an antioxidant chosen from vitamin E, vitamin C, taurine, beta-carotene, carnitine, lipoic acid and cystine or mixtures thereof, and at least one nutrient chosen from choline, manganese, methionine, cysteine, L-carnitine, lysine and mixtures thereof.

12. The composition for use according to claim 11, wherein the composition comprises at least about 500 IU/kg vitamin E, at least about 50 ppm vitamin C and at least about 600 ppm taurine, and further comprises at least about 1000 ppm choline.

13. The composition for use according to any one of claims 5 to 12 wherein the composition fed to the animal is an animal treat or an animal toy, and/or wherein the composition fed to the animal as a nutritional supplement.

14. The composition for use according to any one of claims 5 to 13, wherein the composition comprises:

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about 60% to about 70% by weight carbohydrate;

about 15% to about 25% by weight protein chosen from animal protein and vegetable protein;

about 5% to about 7% by weight fat chosen from animal fat and vegetable fat;

about 2.5% to about 4% by weight of at least one omega-3 polyunsaturated fatty acids;

about 1% to about 2% by weight fiber;

about 1% to about 2% by weight minerals; and

about 0.5 to about 1.5% by weight vitamins,

wherein the animal is a senior or super senior or regular breed canine.

15. The composition for use according to any one of claims 5 to 13, wherein the composition comprises:

about 60% to about 70% by weight carbohydrate;

about 15% to about 25% by weight protein chosen from animal protein and vegetable protein;

about 5% to about 7% by weight fat chosen from animal fat and vegetable fat;

about 3% to about 5% by weight of at least one omega-3 polyunsaturated fatty acids;

about 1% to about 1.5% by weight fiber;

about 0.5% to about 1% by weight minerals; and

about 0.75% to about 1.25% by weight vitamins,

wherein the animal is a senior or super senior or large breed dog.

16. The composition for use according to any one of claims 5 to 13, wherein the composition comprises

about 30% to about 35% by weight carbohydrate;

about 40% to about 50% by weight protein chosen from animal protein and vegetable protein;

about 12% to about 15% by weight fat chosen from animal fat and vegetable fat;

about 1% to about 2% by weight of at least one omega-3 polyunsaturated fatty acids;

about 3% to about 5% by weight fiber;

about 1% to about 2% by weight minerals; and

about 1% to about 2% by weight vitamins,

wherein the animal is a senior or super senior cat.