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(54) Title: SELECTIVE REDUCTION OF ALLELIC VARIANTS

(57) **Abrégé/Abstract:**

Disclosed herein are antisense compounds and methods for selectively of reducing expression of an allelic variant of a gene containing a single nucleotide polymorphism (SNP). Such methods, compounds, and composition are useful to treat, prevent, or ameliorate diseases, including neurodegenerative, such as Huntington's Disease (HD).



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(54) Title: SELECTIVE REDUCTION OF ALLELIC VARIANTS

(57) Abstract: Disclosed herein are antisense compounds and methods for selectively of reducing expression of an allelic variant of a gene containing a single nucleotide polymorphism (SNP). Such methods, compounds, and composition are useful to treat, prevent, or ameliorate diseases, including neurodegenerative, such as Huntington's Disease (HD).



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SELECTIVE REDUCTION OF ALLELIC VARIANTS

Sequence Listing

The present application is being filed along with a Sequence Listing in electronic format. The Sequence Listing is provided as a file entitled BIOL0124WOSEQ.txt created February 7, 2011, which is 322 Kb in size. The information in the electronic format of the sequence listing is incorporated herein by reference in its entirety.

Field of the Invention

Embodiments of the present invention provide methods, compounds, and compositions for selectively reducing expression of an allelic variant of a gene containing a single nucleotide polymorphism (SNP). Such methods, compounds, and compositions are useful to treat, prevent, or ameliorate diseases.

Background of the Invention

Genetic diseases are caused by abnormalities in genes or chromosomes. Such abnormalities may include insertions, deletions, and expansions. Huntington's Disease (HD) is one example of a genetic disease caused by an expansion. HD is a progressive neurodegenerative disorder that is inherited in a dominant fashion and results from a mutation that expands the polymorphic trinucleotide (CAG) tract in the huntingtin gene (*HTT*). The average CAG tract size in the general population is 17-26 repeats (wild type allele), however, in HD patients the CAG tract has expanded to 36 repeats or more (mutant allele) (Huntington's Disease Collaborative Research Group 1993. Cell 72(6):971-83). The *HTT* gene encodes the HTT protein and the expanded CAG tract results in a pathological increase in the polyglutamine repeats near the N-terminal of the protein. Individuals carry two copies of the *HTT* gene and one mutant allele is sufficient to result in HD.

HTT protein appears to have a role during development of the nervous system and a protective role in cells. In mouse models, constitutive knockout of the *HTT* gene is lethal during embryonic development (Nasir et al 1995. Cell 81(5):811-23), while adult inactivation of the *HTT* gene leads to progressive cell death in the brain and the testes (Dragatsis et al 2000. Nat. Genet 26:300-306). Reduction of huntingtin expression from the wild type allele may, therefore, have negative consequences.

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Like HD, there are disorders for which a strategy of selective reduction of a mutant allele would be beneficial. Thus, there remains an unmet need to selectively reduce expression of mutant allelic variants like that of *HTT*, which are causative of disease, over the wild type variant, which appears to be necessary for normal cellular processes.

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Brief Description of the Invention

Figure 1 provides the mRNA and genomic *HTT* sequence showing SNP positions.

Summary of the Invention

10 Provided herein are methods, compounds, and compositions for selectively reducing expression of an allelic variant of a gene containing a single nucleotide polymorphism (SNP). Such methods, compounds, and compositions are useful to treat, prevent, or ameliorate diseases. SNPs may be associated with a mutant allele, the expression of which causes disease. In certain embodiments, the expressed gene product of a mutant allele results in aggregation of the mutant
15 proteins causing disease. In certain embodiments, the expressed gene product of a mutant allele results in gain of function causing disease.

 In certain embodiments, selective reduction of mRNA and protein expression of a mutant allele is achieved by targeting a SNP located on the mutant allele with an antisense compound. In certain embodiments, the antisense compound is an antisense oligonucleotide

20 In certain embodiments, antisense compounds designed to selectively reduce an allelic variant of a gene containing a SNP are created based on potency and selectivity of the antisense compound as well as population genetics.

Detailed Description of the Invention

25 It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the invention, as claimed. Herein, the use of the singular includes the plural unless specifically stated otherwise. As used herein, the use of “or” means “and/or” unless stated otherwise. Furthermore, the use of the term “including” as well as other forms, such as “includes” and “included”, is not limiting. Also, terms
30 such as “element” or “component” encompass both elements and components comprising one unit and elements and components that comprise more than one subunit, unless specifically stated otherwise.

The section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described. All documents, or portions of documents, cited in this application, including, but not limited to, patents, patent applications, articles, books, and treatises, are hereby expressly incorporated by reference for the portions of the document discussed herein, as well as in their entirety.

Definitions

Unless specific definitions are provided, the nomenclature utilized in connection with, and the procedures and techniques of, analytical chemistry, synthetic organic chemistry, and medicinal and pharmaceutical chemistry described herein are those well known and commonly used in the art. Standard techniques may be used for chemical synthesis, and chemical analysis. Where permitted, all patents, applications, published applications and other publications, GENBANK Accession Numbers and associated sequence information obtainable through databases such as National Center for Biotechnology Information (NCBI) and other data referred to throughout in the disclosure herein are incorporated by reference for the portions of the document discussed herein, as well as in their entirety.

Unless otherwise indicated, the following terms have the following meanings:

“2'-O-methoxyethyl” (also 2'-MOE and 2'-O(CH₂)₂-OCH₃) refers to an O-methoxy-ethyl modification of the 2' position of a furosyl ring. A 2'-O-methoxyethyl modified sugar is a modified sugar.

“2'-O-methoxyethyl nucleotide” means a nucleotide comprising a 2'-O-methoxyethyl modified sugar moiety.

“5-methylcytosine” means a cytosine modified with a methyl group attached to the 5' position. A 5-methylcytosine is a modified nucleobase.

“Active pharmaceutical agent” means the substance or substances in a pharmaceutical composition that provide a therapeutic benefit when administered to an individual. For example, in certain embodiments an antisense oligonucleotide targeted to an allelic variant is an active pharmaceutical agent.

“Active target region” or “target region” means a region to which one or more active antisense compounds is targeted. “Active antisense compounds” means antisense compounds that reduce target nucleic acid levels or protein levels.

“Administered concomitantly” refers to the co-administration of two agents in any manner in which the pharmacological effects of both are manifest in the patient at the same time. Concomitant administration does not require that both agents be administered in a single pharmaceutical composition, in the same dosage form, or by the same route of administration. The effects of both agents need not manifest themselves at the same time. The effects need only be overlapping for a period of time and need not be coextensive.

“Administering” means providing a pharmaceutical agent to an individual, and includes, but is not limited to administering by a medical professional and self-administering.

“Allele” is one member of a pair of genes or one member of a series of different forms of a DNA sequences that can exist at a single locus or marker on a specific chromosome. For a diploid organism or cell or for autosomal chromosomes, each allelic pair will normally occupy corresponding positions (loci) on a pair of homologous chromosomes, one inherited from the mother and one inherited from the father. If these alleles are identical, the organism or cell is said to be ‘homozygous’ for that allele; if they differ, the organism or cell is said to be ‘heterozygous’ for that allele. “Major allele” refers to an allele containing the nucleotide present in a statistically significant proportion of individuals in the human population. “Minor allele” refers to an allele containing the nucleotide present in a relatively small proportion of individuals in the human population. “Wild type allele” refers to the genotype typically not associated with disease or dysfunction of the gene product. “Mutant allele” refers to the genotype associated with disease or dysfunction of the gene product.

“Allelic variant” refers to one of the pair of genes or DNA sequence existing at a single locus. For example, an allelic variant may refer to either the major allele or the minor allele.

“Amelioration” refers to a lessening of at least one indicator, sign, or symptom of an associated disease, disorder, or condition. The severity of indicators may be determined by subjective or objective measures, which are known to those skilled in the art.

“Animal” refers to a human or non-human animal, including, but not limited to, mice, rats, rabbits, dogs, cats, pigs, and non-human primates, including, but not limited to, monkeys and chimpanzees.

“Antibody” refers to a molecule characterized by reacting specifically with an antigen in some way, where the antibody and the antigen are each defined in terms of the other. Antibody may refer to a complete antibody molecule or any fragment or region thereof, such as the heavy chain, the light chain, Fab region, and Fc region.

“Antisense activity” means any detectable or measurable activity attributable to the hybridization of an antisense compound to its target nucleic acid. In certain embodiments, antisense activity is a decrease in the amount or expression of a target nucleic acid or protein encoded by such target nucleic acid.

“Antisense compound” means an oligomeric compound that is capable of undergoing hybridization to a target nucleic acid through hydrogen bonding.

“Antisense inhibition” means reduction of target nucleic acid levels or target protein levels in the presence of an antisense compound complementary to a target nucleic acid compared to target nucleic acid levels or target protein levels in the absence of the antisense compound.

“Antisense oligonucleotide” means a single-stranded oligonucleotide having a nucleobase sequence that permits hybridization to a corresponding region or segment of a target nucleic acid.

“Bicyclic sugar” means a furosyl ring modified by the bridging of two ring atoms. A bicyclic sugar is a modified sugar.

“Bicyclic nucleoside” means a nucleoside having a sugar moiety comprising a bridge connecting two carbon atoms of the sugar ring, thereby forming a bicyclic ring system. In certain embodiments, the bridge connects the 4'-carbon and the 2'-carbon of the sugar ring.

“Cap structure” or “terminal cap moiety” means chemical modifications, which have been incorporated at either terminus of an antisense compound.

“cEt” or “constrained ethyl” means a bicyclic nucleoside having a sugar moiety comprising a bridge connecting the 4'-carbon and the 2'-carbon, wherein the bridge has the formula: 4'-CH(CH₃)-O-2'.

“Chemically distinct region” refers to a region of an antisense compound that is in some way chemically different than another region of the same antisense compound. For example, a region having 2'-O-methoxyethyl nucleotides is chemically distinct from a region having nucleotides without 2'-O-methoxyethyl modifications.

“Chimeric antisense compound” means an antisense compound that has at least two chemically distinct regions.

“Co-administration” means administration of two or more pharmaceutical agents to an individual. The two or more pharmaceutical agents may be in a single pharmaceutical composition, or may be in separate pharmaceutical compositions. Each of the two or more pharmaceutical agents may be administered through the same or different routes of administration. Co-administration encompasses parallel or sequential administration.

“Complementarity” means the capacity for pairing between nucleobases of a first nucleic acid and a second nucleic acid.

“Contiguous nucleobases” means nucleobases immediately adjacent to each other.

“Differentiating polymorphism” means a variation in a nucleotide sequence that permits differentiation between a wild type and a mutant allele of a nucleic acid sequence. Differentiating polymorphisms may include insertions or deletions of one or a few nucleotides in a sequence, or changes in one or a few nucleotides in a sequence. A differentiating polymorphism or polymorphic allele can be in linkage disequilibrium with one or more other polymorphisms or polymorphic alleles.

“Diluent” means an ingredient in a composition that lacks pharmacological activity, but is pharmaceutically necessary or desirable. For example, the diluent in an injected composition may be a liquid, e.g. saline solution.

“Dose” means a specified quantity of a pharmaceutical agent provided in a single administration, or in a specified time period. In certain embodiments, a dose may be administered in one, two, or more boluses, tablets, or injections. For example, in certain embodiments where subcutaneous administration is desired, the desired dose requires a volume not easily accommodated by a single injection, therefore, two or more injections may be used to achieve the desired dose. In certain embodiments, the pharmaceutical agent is administered by infusion over an extended period of time or continuously. Doses may be stated as the amount of pharmaceutical agent per hour, day, week, or month.

“Effective amount” means the amount of active pharmaceutical agent sufficient to effectuate a desired physiological outcome in an individual in need of the agent. The effective amount may vary among individuals depending on the health and physical condition of the individual to be treated, the taxonomic group of the individuals to be treated, the formulation of the composition, assessment of the individual’s medical condition, and other relevant factors.

“Fully complementary” or “100% complementary” means each nucleobase of a first nucleic acid has a complementary nucleobase in a second nucleic acid. In certain embodiments, a first nucleic acid is an antisense compound and a target nucleic acid is a second nucleic acid.

“Gapmer” means a chimeric antisense compound in which an internal region having a plurality of nucleosides that support RNase H cleavage is positioned between external regions having one or more nucleosides, wherein the nucleosides comprising the internal region are

chemically distinct from the nucleoside or nucleosides comprising the external regions. The internal region may be referred to as the “gap” and the external regions may be referred to as the “wings.”

“Gap-widened” means a chimeric antisense compound having a gap segment of 12 or more contiguous 2'-deoxyribonucleosides positioned between and immediately adjacent to 5' and 3' wing segments having from one to six nucleosides.

“Gene product” refers to a biochemical material, such as RNA or protein, resulting from expression of a gene.

“Haplotype” means a set of alleles of closely linked loci on a chromosome that are generally inherited together. For example, a polymorphic allele at a first site in a nucleic acid sequence on the chromosome may be found to be associated with another polymorphic allele at a second site on the same chromosome, at a frequency other than would be expected for a random associate (e.g. “linkage equilibrium”). These two polymorphic alleles may be described as being in “linkage disequilibrium.” A haplotype may comprise two, three, four, or more alleles. The set of alleles in a haplotype along a given segment of a chromosome are generally transmitted to progeny together unless there has been a recombination event.

“High-affinity sugar modification” is a modified sugar moiety which when it is included in a nucleoside and said nucleoside is incorporated into an antisense oligonucleotide, the stability (as measured by T_m) of said antisense oligonucleotide: RNA duplex is increased as compared to the stability of a DNA:RNA duplex.

“High-affinity sugar-modified nucleoside” is a nucleoside comprising a modified sugar moiety that when said nucleoside is incorporated into an antisense compound, the binding affinity (as measured by T_m) of said antisense compound toward a complementary RNA molecule is increased. In certain embodiments of the invention at least one of said sugar-modified high-affinity nucleosides confers a ΔT_m of at least 1 to 4 degrees per nucleoside against a complementary RNA as determined in accordance with the methodology described in Freier et al., *Nucleic Acids Res.*, 1997, 25, 4429-4443, which is incorporated by reference in its entirety. In another aspect, at least one of the high-affinity sugar modifications confers about 2 or more, 3 or more, or 4 or more degrees per modification. In the context of the present invention, examples of sugar-modified high affinity nucleosides include, but are not limited to, (i) certain 2'-modified nucleosides, including 2'-substituted and 4' to 2' bicyclic nucleosides, and (ii) certain other non-ribofuranosyl nucleosides which provide a per modification increase in binding affinity such as modified tetrahydropyran and

tricycloDNA nucleosides. For other modifications that are sugar-modified high-affinity nucleosides see Freier et al., *Nucleic Acids Res.*, 1997, 25, 4429-4443.

“Hybridization” means the annealing of complementary nucleic acid molecules. In certain embodiments, complementary nucleic acid molecules include an antisense compound and a target nucleic acid.

“Immediately adjacent” means there are no intervening elements between the immediately adjacent elements.

“Individual” means a human or non-human animal selected for treatment or therapy.

“Internucleoside linkage” refers to the chemical bond between nucleosides.

“Linked nucleosides” means adjacent nucleosides which are bonded together.

“Mismatch” or “non-complementary nucleobase” refers to the case when a nucleobase of a first nucleic acid is not capable of pairing with the corresponding nucleobase of a second or target nucleic acid.

“Modified internucleoside linkage” refers to a substitution or any change from a naturally occurring internucleoside bond (i.e. a phosphodiester internucleoside bond).

“Modified nucleobase” refers to any nucleobase other than adenine, cytosine, guanine, thymidine, or uracil. An “unmodified nucleobase” means the purine bases adenine (A) and guanine (G), and the pyrimidine bases thymine (T), cytosine (C), and uracil (U).

“Modified nucleotide” means a nucleotide having, independently, a modified sugar moiety, modified internucleoside linkage, or modified nucleobase. A “modified nucleoside” means a nucleoside having, independently, a modified sugar moiety or modified nucleobase.

“Modified oligonucleotide” means an oligonucleotide comprising a modified internucleoside linkage, a modified sugar, or a modified nucleobase.

“Modified sugar” refers to a substitution or change from a natural sugar.

“Motif” means the pattern of chemically distinct regions in an antisense compound.

“Naturally occurring internucleoside linkage” means a 3' to 5' phosphodiester linkage.

“Natural sugar moiety” means a sugar found in DNA (2'-H) or RNA (2'-OH).

“Nuclease resistant modification” means a sugar modification or modified internucleoside linkage which, when incorporated into an oligonucleotide, makes said oligonucleotide more stable to degradation under cellular nucleases (e.g. exo- or endo-nucleases). Examples of nuclease resistant modifications include, but are not limited to, phosphorothioate internucleoside linkages, bicyclic sugar modifications, 2'-modified nucleotides, or neutral internucleoside linkages.

“Nucleic acid” refers to molecules composed of monomeric nucleotides. A nucleic acid includes ribonucleic acids (RNA), deoxyribonucleic acids (DNA), single-stranded nucleic acids, double-stranded nucleic acids, small interfering ribonucleic acids (siRNA), and microRNAs (miRNA).

“Nucleobase” means a heterocyclic moiety capable of pairing with a base of another nucleic acid.

“Nucleobase sequence” means the order of contiguous nucleobases independent of any sugar, linkage, or nucleobase modification.

“Nucleoside” means a nucleobase linked to a sugar.

“Nucleoside mimetic” includes those structures used to replace the sugar or the sugar and the base and not necessarily the linkage at one or more positions of an oligomeric compound such as for example nucleoside mimetics having morpholino, cyclohexenyl, cyclohexyl, tetrahydropyranyl, bicyclo or tricyclo sugar mimetics e.g. non furanose sugar units. Nucleotide mimetic includes those structures used to replace the nucleoside and the linkage at one or more positions of an oligomeric compound such as for example peptide nucleic acids or morpholinos (morpholinos linked by -N(H)-C(=O)-O- or other non-phosphodiester linkage). Sugar surrogate overlaps with the slightly broader term nucleoside mimetic but is intended to indicate replacement of the sugar unit (furanose ring) only. The tetrahydropyranyl rings provided herein are illustrative of an example of a sugar surrogate wherein the furanose sugar group has been replaced with a tetrahydropyranyl ring system.

“Nucleotide” means a nucleoside having a phosphate group covalently linked to the sugar portion of the nucleoside.

“Oligomeric compound” or “oligomer” means a polymer of linked monomeric subunits which is capable of hybridizing to at least a region of a nucleic acid molecule.

“Oligonucleotide” means a polymer of linked nucleosides each of which can be modified or unmodified, independent one from another.

“Parenteral administration” means administration through injection or infusion. Parenteral administration includes subcutaneous administration, intravenous administration, intramuscular administration, intraarterial administration, intraperitoneal administration, or intracranial administration, e.g. intrathecal or intracerebroventricular administration.

“Peptide” means a molecule formed by linking at least two amino acids by amide bonds. Peptide refers to polypeptides and proteins.

“Pharmaceutical composition” means a mixture of substances suitable for administering to an individual. For example, a pharmaceutical composition may comprise one or more active pharmaceutical agents and a sterile aqueous solution.

“Pharmaceutically acceptable salts” means physiologically and pharmaceutically acceptable salts of antisense compounds, i.e., salts that retain the desired biological activity of the parent oligonucleotide and do not impart undesired toxicological effects thereto.

“Phosphorothioate linkage” means a linkage between nucleosides where the phosphodiester bond is modified by replacing one of the non-bridging oxygen atoms with a sulfur atom. A phosphorothioate linkage (P=S) is a modified internucleoside linkage.

“Portion” means a defined number of contiguous (i.e. linked) nucleobases of a nucleic acid. In certain embodiments, a portion is a defined number of contiguous nucleobases of a target nucleic acid. In certain embodiments, a portion is a defined number of contiguous nucleobases of an antisense compound.

“Prevent” refers to delaying or forestalling the onset or development of a disease, disorder, or condition for a period of time from minutes to indefinitely. Prevent also means reducing risk of developing a disease, disorder, or condition.

“Prodrug” means a therapeutic agent that is prepared in an inactive form that is converted to an active form within the body or cells thereof by the action of endogenous enzymes or other chemicals or conditions.

“Selectively reducing expression of an allelic variant” means reducing expression of one allele more than the other, differing allele among a set of alleles. For example, a mutant allele containing a single nucleotide polymorphism (SNP) may be reduced more than a wild type allele not containing the SNP.

“Side effects” means physiological responses attributable to a treatment other than the desired effects. In certain embodiments, side effects include injection site reactions, liver function test abnormalities, renal function abnormalities, liver toxicity, renal toxicity, central nervous system abnormalities, myopathies, and malaise. For example, increased aminotransferase levels in serum may indicate liver toxicity or liver function abnormality. For example, increased bilirubin may indicate liver toxicity or liver function abnormality.

“Single nucleotide polymorphism” or “SNP” means a single nucleotide variation between the genomes of individuals of the same species. In some cases, a SNP may be a single nucleotide deletion or insertion. In general, SNPs occur relatively frequently in genomes and thus contribute to

genetic diversity. SNPs are thought to be mutationally more stable than other polymorphisms, lending their use in association studies in which linkage disequilibrium between markers and an unknown variant is used to map disease-causing mutations. The location of a SNP is generally flanked by highly conserved sequences. An individual may be homozygous or heterozygous for an allele at each SNP site. A heterozygous SNP allele can be a differentiating polymorphism. A SNP may be targeted with an antisense oligonucleotide, meaning that the SNP anneals to (or aligns with) position 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 of the antisense oligonucleotide. The remainder of the antisense oligonucleotide bases must have sufficient complementarity to the SNP site to facilitate hybridization.

“Single nucleotide polymorphism position” or “SNP position” refers to the nucleotide position of the SNP on a reference sequence.

“Single nucleotide polymorphism site” or “SNP site” refers to the nucleotides surrounding a SNP contained in a target nucleic acid to which an antisense compound is targeted.

“Single-stranded oligonucleotide” means an oligonucleotide which is not hybridized to a complementary strand.

“Specifically hybridizable” refers to an antisense compound having a sufficient degree of complementarity between an antisense oligonucleotide and a target nucleic acid to induce a desired effect, while exhibiting minimal or no effects on non-target nucleic acids under conditions in which specific binding is desired, i.e. under physiological conditions in the case of *in vivo* assays and therapeutic treatments.

“Targeting” or “targeted” means the process of design and selection of an antisense compound that will specifically hybridize to a target nucleic acid and induce a desired effect.

“Target nucleic acid,” “target RNA,” and “target RNA transcript” all refer to a nucleic acid capable of being targeted by antisense compounds.

“Target segment” means the sequence of nucleotides of a target nucleic acid to which an antisense compound is targeted. For example, for the purposes of this patent application, the target segment may be within the SNP site. “5’ target site” refers to the 5’-most nucleotide of a target segment. “3’ target site” refers to the 3’-most nucleotide of a target segment.

“Therapeutically effective amount” means an amount of a pharmaceutical agent that provides a therapeutic benefit to an individual.

“Treat” refers to administering a pharmaceutical composition to effect an alteration or improvement of a disease, disorder, or condition.

“Unmodified nucleotide” means a nucleotide composed of naturally occurring nucleobases, sugar moieties, and internucleoside linkages. In certain embodiments, an unmodified nucleotide is an RNA nucleotide (i.e. β -D-ribonucleosides) or a DNA nucleotide (i.e. β -D-deoxyribonucleoside).

Certain Embodiments

Embodiments of the present invention provide methods, compounds, and compositions for selectively inhibiting mRNA and protein expression of an allelic variant of a gene or DNA sequence. In certain embodiments, the allelic variant contains a single nucleotide polymorphism (SNP). In certain embodiments, the SNP is a differentiating polymorphism. In certain embodiments, a SNP is associated with a mutant allele. In certain embodiments, a SNP is in linkage disequilibrium with another polymorphism that is associated with or is causative of disease. In certain embodiments, a mutant allele is associated with disease. In certain embodiments, mRNA and protein expression of a mutant allele is associated with disease.

In certain embodiments, the expressed gene product of a mutant allele results in aggregation of the mutant proteins causing disease. In certain embodiments, the expressed gene product of a mutant allele results in gain of function causing disease. In certain embodiments, genes with an autosomal dominant mutation resulting in a toxic gain of function of the protein are the APP gene encoding amyloid precursor protein involved in Alzheimer's disease (Gene, 371: 68, 2006); the PrP gene encoding prion protein involved in Creutzfeldt-Jakob disease and in fatal familial insomnia (Nat. Med. 1997, 3: 1009); GFAP gene encoding glial fibrillary acidic protein involved in Alexander disease (J. Neurosci. 2006, 26:111623); alpha-synuclein gene encoding alpha-synuclein protein involved in Parkinson's disease (J. Clin. Invest. 2003, 111: 145); SOD-1 gene encoding the SOD-1 protein involved in amyotrophic lateral sclerosis (Science 1998, 281: 1851); atrophin-1 gene encoding atrophin-1 protein involved in dentato-rubral and pallido-luysian atrophy (DRPA) (Trends Mol. Med. 2001, 7: 479); SCA1 gene encoding ataxin-1 protein involved in spino-cerebellar ataxia-1 (SCA1) (Protein Sci. 2003, 12: 953); PLP gene encoding proteolipid protein involved in Pelizaeus-Merzbacher disease (NeuroMol Med. 2007, 4: 73); DYT1 gene encoding torsinA protein involved in Torsion dystonia (Brain Res. 2000, 877: 379); and alpha-B crystalline gene encoding alpha-B crystalline protein involved in protein aggregation diseases, including cardiomyopathy (Cell 2007, 130: 427); alpha1-antitrypsin gene encoding alpha1-antitrypsin protein involved in chronic obstructive pulmonary disease (COPD), liver disease and hepatocellular carcinoma (New Engl J Med. 2002, 346: 45); Ltk gene encoding leukocyte tyrosine kinase protein involved in systemic

lupus erythematosus (Hum. Mol. Gen. 2004, 13: 171); PCSK9 gene encoding PCSK9 protein involved in hypercholesterolemia (Hum Mutat. 2009, 30: 520); prolactin receptor gene encoding prolactin receptor protein involved in breast tumors (Proc. Natl. Assoc. Sci. 2008, 105: 4533); CCL5 gene encoding the chemokine CCL5 involved in COPD and asthma (Eur. Respir. J. 2008, 32: 327); PTPN22 gene encoding PTPN22 protein involved in Type 1 diabetes, Rheumatoid arthritis, Graves disease, and SLE (Proc. Natl. Assoc. Sci. 2007, 104: 19767); androgen receptor gene encoding the androgen receptor protein involved in spinal and bulbar muscular atrophy or Kennedy's disease (J Steroid Biochem. Mol. Biol. 2008, 108: 245); CHMP4B gene encoding chromatin modifying protein-4B involved in progressive childhood posterior subcapsular cataracts (Am. J. Hum. Genet 2007, 81: 596); FXR / NR1H4 gene encoding Farnesoid X receptor protein involved in cholesterol gallstone disease, atherosclerosis and diabetes (Mol. Endocrinol. 2007, 21: 1769); ABCA1 gene encoding ABCA1 protein involved in cardiovascular disease (Transl. Res. 2007, 149: 205); CaSR gene encoding the calcium sensing receptor protein involved in primary hypercalciuria (Kidney Int. 2007, 71: 1155); alpha-globin gene encoding alpha-globin protein involved in alpha-thalassemia (Science 2006, 312: 1215); httpr gene encoding HTTLPR protein involved in obsessive compulsive disorder (Am. J. Hum. Genet. 2006, 78: 815); AVP gene encoding arginine vasopressin protein in stress-related disorders such as anxiety disorders and comorbid depression (CNS Neurol. Disord. Drug Targets 2006, 5: 167); GNAS gene encoding G proteins involved in congenital visual defects, hypertension, metabolic syndrome (Trends Pharmacol. Sci. 2006, 27: 260); APAF1 gene encoding APAF1 protein involved in a predisposition to major depression (Mol. Psychiatry 2006, 11: 76); TGF-beta1 gene encoding TGF-beta1 protein involved in breast cancer and prostate cancer (Cancer Epidemiol. Biomarkers Prev. 2004, 13: 759); AChR gene encoding acetylcholine receptor involved in congenital myasthenic syndrome (Neurology 2004, 62: 1090); P2Y12 gene encoding adenosine diphosphate (ADP) receptor protein involved in risk of peripheral arterial disease (Circulation 2003, 108: 2971); LQT1 gene encoding LQT1 protein involved in atrial fibrillation (Cardiology 2003, 100: 109); RET protooncogene encoding RET protein involved in sporadic pheochromocytoma (J. Clin. Endocrinol. Metab. 2003, 88: 4911); filamin A gene encoding filamin A protein involved in various congenital malformations (Nat. Genet. 2003, 33: 487); TARDBP gene encoding TDP-43 protein involved in amyotrophic lateral sclerosis (Hum. Mol. Gene.t 2010, 19: 671); SCA3 gene encoding ataxin-3 protein involved in Machado-Joseph disease (PLoS One 2008, 3: e3341); SCA7 gene encoding ataxin-7 protein involved in spino-cerebellar ataxia-7 (PLoS One 2009, 4: e7232); and *HTT* gene encoding huntingtin protein involved in Huntington's disease (Neurobiol Dis. 1996,

3:183); and the CA4 gene encoding carbonic anhydrase 4 protein, CRX gene encoding cone-rod homeobox transcription factor protein, FSCN2 gene encoding retinal fascin homolog 2 protein, IMPDH1 gene encoding inosine monophosphate dehydrogenase 1 protein, NR2E3 gene encoding nuclear receptor subfamily 2 group E3 protein, NRL gene encoding neural retina leucine zipper protein, PRPF3 (RP18) gene encoding pre-mRNA splicing factor 3 protein, PRPF8 (RP13) gene encoding pre-mRNA splicing factor 8 protein, PRPF31 (RP11) gene encoding pre-mRNA splicing factor 31 protein, RDS gene encoding peripherin 2 protein, ROM1 gene encoding rod outer membrane protein 1 protein, RHO gene encoding rhodopsin protein, RP1 gene encoding RP1 protein, RPGR gene encoding retinitis pigmentosa GTPase regulator protein, all of which are involved in Autosomal Dominant Retinitis Pigmentosa disease (Adv Exp Med Biol. 2008, 613:203)

In certain embodiments, selective reduction of mRNA and protein expression of a mutant allele is achieved by targeting a SNP located on the mutant allele with an antisense compound. In certain embodiments, the antisense compound is an antisense oligonucleotide. In certain embodiments, the antisense compound is not a ribozyme, a double stranded siRNA, or an shRNA. In certain embodiments, the antisense oligonucleotide may have one or more modified sugar(s), nucleobase(s), or internucleoside linkage(s). In certain embodiments, the antisense oligonucleotide is complementary to the SNP site. In certain embodiments, the antisense oligonucleotide is at least 65%, 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% complementary to the SNP site. In certain embodiments, the antisense oligonucleotide is 100% complementary to the SNP site. In certain embodiments, the SNP site is 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleobases in length. In certain embodiments, the SNP anneals to position 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 of the antisense oligonucleotide.

In certain embodiments, antisense compounds designed to selectively reduce an allelic variant of a gene containing a SNP are created based on potency and selectivity of the antisense compound as well as population genetics.

In certain embodiments, selective reduction of mRNA and protein expression of an allelic variant of a gene containing a SNP occurs in a cell or tissue. In certain embodiments, the cell or tissue is in an animal. In certain embodiments, the animal is a human.

In certain embodiments, described herein are compounds comprising a modified antisense oligonucleotide consisting of 12 to 30 linked nucleosides targeted to a single nucleotide polymorphism site, wherein the modified oligonucleotide comprises a wing-gap-wing motif with a

5' wing region positioned at the 5' end of a deoxynucleoside gap, and a 3' wing region positioned at the 3' end of the deoxynucleoside gap, wherein position 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, or positions 1, 2, 3, 4, 5, 6, 7, 8, or 9 of the modified oligonucleotide, as counted from the 5' terminus of the gap, aligns with the single nucleotide polymorphism.

In certain embodiments, the single nucleotide polymorphism site is on a mutant allele that is associated with a disease. In certain embodiments, the single nucleotide polymorphism site contains a differentiating polymorphism.

In certain embodiments, the modified antisense oligonucleotide consists of 12 to 20 linked nucleosides. In certain embodiments, modified antisense oligonucleotide consists of 15 to 20 linked nucleosides. In certain embodiments, the modified antisense oligonucleotide consists of 15 to 19 linked nucleosides.

In certain embodiments, position 8, 9, or 10 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, or positions 4, 5, or 6 of the modified oligonucleotide, as counted from the 5' terminus of the gap, aligns with the single nucleotide polymorphism.

In certain embodiments, the gap region is 7-11 nucleosides in length, the 5' wing region is 1-6 nucleobases in length and the 3' wing region is 1-6 nucleobases in length.

In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 5-10-5, 2-9-6, 3-9-3, 3-9-4, 3-9-5, 4-7-4, 4-9-3, 4-9-4, 4-9-5, 4-10-5, 4-11-4, 4-11-5, 5-7-5, 5-8-6, 5-9-3, 5-9-5, 5-10-4, 5-10-5, 6-7-6, 6-8-5, and 6-9-2. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 2-9-6, 4-9-5, and 4-11-4.

In certain embodiments, at least one internucleoside linkage is a modified internucleoside linkage. In certain embodiments, each internucleoside linkage is a phosphorothioate internucleoside linkage.

In certain embodiments, at least one nucleoside comprises a modified nucleobase. In certain embodiments, the modified nucleobase is a 5'-methylcytosine.

In certain embodiments, at least one nucleoside of at least one of the wing regions comprises a modified sugar or sugar surrogate. In certain embodiments, each of the nucleosides of each wing region comprises a modified sugar or sugar surrogate. In certain embodiments, the sugar or sugar surrogate is a 2'-O-methoxyethyl modified sugar.

In certain embodiments, at least one of the wing regions comprises a 4' to 2' bicyclic nucleoside and at least one of the remaining wing nucleosides is a non-bicyclic 2'-modified nucleoside.

In certain embodiments, the non-bicyclic 2'-modified nucleoside is a 2'-O-methoxyethyl nucleoside.

In certain embodiments, the 4' to 2' bicyclic nucleoside is 4'-CH(CH₃)-O-2' bicyclic nucleoside.

In certain embodiments, the modified antisense oligonucleotide consisting of 17 linked nucleosides and wherein position 9 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with the differentiating polymorphism. In certain embodiments, the wing-gap-wing motif is 2-9-6.

In certain embodiments, described herein are compounds comprising a modified oligonucleotide consisting of 18 linked nucleosides and 90% complementary to a differentiating polymorphism, wherein the modified oligonucleotide comprises a wing-gap-wing motif, wherein position 9 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with the differentiating polymorphism; wherein each nucleoside of each wing segment comprises a 2'-O-methoxyethyl sugar; and wherein the wing-gap-wing motif is 4-9-5.

In certain embodiments, described herein are compounds comprising a modified oligonucleotide consisting of 19 linked nucleosides and 90% complementary to a differentiating polymorphism, wherein the modified oligonucleotide comprises a wing-gap-wing motif, wherein position 10 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with the differentiating polymorphism; wherein each nucleoside of each wing segment comprises a 2'-O-methoxyethyl sugar; and wherein the wing-gap-wing motif is 4-11-4.

In certain embodiments, described herein are compounds comprising a modified oligonucleotide consisting of 15 to 19 linked nucleosides and fully complementary to a differentiating polymorphism, wherein the modified oligonucleotide comprises a wing-gap-wing motif, wherein position 6, 7, 8, 9, 10, 11, 12, 13, or 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with the differentiating polymorphism; and at least one high-affinity sugar modification. In certain embodiments, the modified oligonucleotide is 100% complementary to the single nucleotide polymorphism site.

In certain embodiments, at least one of the wing regions comprises a high-affinity sugar modification. In certain embodiments, the high-affinity sugar modification is a bicyclic sugar. In certain embodiments, the bicyclic sugar comprises a 4'-CH(CH₃)-O-2' bridge.

In certain embodiments, at least one of positions 2, 3, 6, 9, 10, 11, 13, or 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, comprises the at least one high-affinity sugar modification.

In certain embodiments, at least one of positions 2, 3, 13, and 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, comprises the at least one high-affinity sugar modification.

In certain embodiments, each of nucleoside positions 2, 3, 13, and 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, comprise the at least one high-affinity sugar modification.

In certain embodiments, the high-affinity sugar modification is a bicyclic sugar. In certain embodiments, the bicyclic sugar comprises a 4'-CH(CH₃)-O-2' bridge.

In certain embodiments, the wing-gap-wing motif is any of the group consisting of 3-9-3, 4-9-4, and 5-9-5.

In certain embodiments, described herein are compounds comprising a modified oligonucleotide consisting of 15, 17, or 19 linked nucleosides and fully complementary to a differentiating polymorphism, wherein the modified oligonucleotide comprises a wing-gap-wing motif, wherein position 6, 8, 10, or 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with the differentiating polymorphism; and at least one high-affinity sugar modification.

In certain embodiments, at least one of positions 2, 3, 6, 9, 10, 11, 13, or 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, comprises the at least one high-affinity sugar modification.

In certain embodiments, the high-affinity sugar modification is a bicyclic sugar. In certain embodiments, the bicyclic sugar comprises a 4'-CH(CH₃)-O-2' bridge.

In certain embodiments, the wing-gap-wing motif is any of the group consisting of 3-9-3, 4-9-4, and 5-9-5.

In certain embodiments, described herein are compounds comprising a modified oligonucleotide consisting of 15 linked nucleosides and 90% complementary to a differentiating polymorphism, wherein the modified oligonucleotide comprises a wing-gap-wing motif, wherein position 8 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with the differentiating polymorphism; and at least one high-affinity sugar

modification. In certain embodiments, the modified oligonucleotide is 100% complementary to the differentiating polymorphism.

In certain embodiments, each of nucleoside positions 2, 3, 13, and 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, comprise the at least one high-affinity sugar modification.

In certain embodiments, the high-affinity sugar modification is a bicyclic sugar. In certain embodiments, the bicyclic sugar comprises a 4'-CH(CH₃)-O-2' bridge.

In certain embodiments, the wing-gap-wing motif is 3-9-3.

In certain embodiments, described herein are methods of selectively reducing expression of an allelic variant of a gene containing a single nucleotide polymorphism in a cell, tissue, or animal, comprising administering to the cell, tissue, or animal a compound comprising a modified oligonucleotide complementary to a differentiating polymorphism, wherein the modified oligonucleotide comprises a wing-gap-wing motif and wherein position 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with the differentiating polymorphism. In certain embodiments, the modified oligonucleotide is 90% complementary to the single differentiating polymorphism. In certain embodiments, the modified oligonucleotide is 95% complementary to the single nucleotide polymorphism site. In certain embodiments, the modified oligonucleotide is 100% complementary to the single nucleotide polymorphism site.

In certain embodiments, the single nucleotide polymorphism site is from 12 to 30 nucleobases in length. In certain embodiments, the single nucleotide polymorphism site is from 15 to 25 nucleobases in length. In certain embodiments, the single nucleotide polymorphism site is from 17 to 22 nucleobases in length. In certain embodiments, the single nucleotide polymorphism site is 17 nucleobases in length. In certain embodiments, the single nucleotide polymorphism site is 18 nucleobases in length. In certain embodiments, the single nucleotide polymorphism site is 19 nucleobases in length. In certain embodiments, the single nucleotide polymorphism site is 20 nucleobases in length.

In certain embodiments, the allelic variant is associated with disease. In certain embodiments, the disease is Huntington's Disease.

In certain embodiments, the modified oligonucleotide is a single-stranded oligonucleotide.

In certain embodiments, at least one internucleoside linkage is a modified internucleoside linkage. In certain embodiments, each internucleoside linkage is a phosphorothioate internucleoside linkage.

In certain embodiments, at least one nucleoside comprises a modified nucleobase. In certain embodiments, the at least one modified nucleobase is a 5'-methylcytosine.

In certain embodiments, at least one nucleoside comprises a modified sugar. In certain embodiments, the modified sugar is a high-affinity sugar modification. In certain embodiments, the high-affinity sugar is a bicyclic sugar. In certain embodiments, each bicyclic sugar comprises a 4'-CH(CH₃)-O-2' bridge.

In certain embodiments, at least one of nucleoside positions 2, 3, 13, and 14 of the modified oligonucleotide, counting from the 5' terminus of the modified oligonucleotide, comprises a nucleoside having a bicyclic sugar wherein the bicyclic sugar comprises a 4'-CH(CH₃)-O-2' bridge.

In certain embodiments, each of nucleoside positions 2, 3, 13, and 14 of the modified oligonucleotide, counting from the 5' terminus of the modified oligonucleotide, comprises a bicyclic sugar wherein the bicyclic sugar comprises a 4'-CH(CH₃)-O-2' bridge.

In certain embodiments, the at least one modified sugar comprises a 2'-O-methoxyethyl. In certain embodiments, each nucleoside positioned in a wing segment of the modified oligonucleotide comprises a 2'-O-methoxyethyl modification.

In certain embodiments, the wing-gap-wing motif is any of the group consisting of 2-9-6, 3-9-3, 3-9-4, 3-9-5, 4-7-4, 4-9-4, 4-9-5, 4-10-5, 4-11-4, 4-11-5, 5-7-5, 5-8-6, 5-9-3, 5-9-5, 5-10-4, 5-10-5, 6-7-6, 6-8-5, and 6-9-2.

In certain embodiments, the modified oligonucleotide is not a ribozyme, a double stranded siRNA, or an shRNA.

In certain embodiments, the single nucleotide polymorphism site is on a mutant allele that is associated with disease. In certain embodiments, the single nucleotide polymorphism site contains a differentiating polymorphism.

In certain embodiments, the modified antisense oligonucleotide consists of 12 to 20 linked nucleosides. In certain embodiments, the modified antisense oligonucleotide consists of 15 to 19 linked nucleosides.

In certain embodiments, the gap region is 7 to 11 nucleosides in length, the 5' wing region is 1 to 6 nucleobases in length and 3' wing region is 1 to 6 nucleobases in length.

In certain embodiments, wherein at least one nucleoside of at least one of the wing regions comprises a modified sugar or sugar surrogate.

In certain embodiments, each of the nucleosides of each wing region comprises a modified sugar or sugar surrogate. In certain embodiments, the sugar or sugar surrogate is a 2'-O-methoxyethyl modified sugar.

In certain embodiments, at least one of the wing regions comprises a 4' to 2' bicyclic nucleoside and at least one of the remaining wing nucleosides is a non-bicyclic 2'-modified nucleoside.

In certain embodiments, the non-bicyclic 2'-modified nucleoside is a 2'-O-methoxyethyl nucleoside.

In certain embodiments, 4' to 2' bicyclic nucleoside is a 4'-CH(CH₃)-O-2' bicyclic nucleoside.

In certain embodiments, described herein are methods of selectively reducing expression of an allelic variant of a gene containing a single nucleotide polymorphism in a cell, tissue, or animal, comprising administering to the cell, tissue, or animal a compound comprising a modified oligonucleotide complementary to a differentiating polymorphism, wherein the modified oligonucleotide comprises a wing-gap-wing motif and wherein position 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with the differentiating polymorphism.

In certain embodiments, described herein are methods of selectively reducing expression of an allelic variant of a gene containing a single nucleotide polymorphism in a cell, tissue, or animal, comprising administering to the cell, tissue, or animal a compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides and complementary to a differentiating polymorphism, wherein the modified oligonucleotide comprises a wing-gap-wing motif and wherein position 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide aligns with the differentiating polymorphism; and wherein the allelic variant is a mutant allele.

In certain embodiments, the mutant allele is associated with any disease from the group consisting of Alzheimer's disease, Creutzfeldt-Jakob disease, fatal familial insomnia, Alexander disease, Parkinson's disease, amyotrophic lateral sclerosis, dentato-rubral and pallido-luysian atrophy DRPA, spino-cerebellar ataxia, Torsion dystonia, cardiomyopathy, chronic obstructive pulmonary disease (COPD), liver disease, hepatocellular carcinoma, systemic lupus erythematosus,

hypercholesterolemia, breast cancer, asthma, Type 1 diabetes, Rheumatoid arthritis, Graves disease, SLE, spinal and bulbar muscular atrophy, Kennedy's disease, progressive childhood posterior subcapsular cataracts, cholesterol gallstone disease, arthrosclerosis, cardiovascular disease, primary hypercalciuria, alpha-thalassemia, obsessive compulsive disorder, Anxiety, comorbid depression, congenital visual defects, hypertension, metabolic syndrome, prostate cancer, congenital myasthenic syndrome, peripheral arterial disease, atrial fibrillation, sporadic pheochromocytoma, congenital malformations, Machado-Joseph disease, Huntington's disease, and Autosomal Dominant Retinitis Pigmentosa disease.

In certain embodiments, described herein are methods of treating Huntington's Disease, comprising selectively reducing expression of an allelic variant of a gene containing a single nucleotide polymorphism in a cell, tissue, or animal, comprising administering to the cell, tissue, or animal a compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides and complementary to differentiating polymorphism, wherein the modified oligonucleotide comprises a wing-gap-wing motif and wherein position 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with differentiating polymorphism; and wherein the allelic variant is associated with Huntington's Disease.

In certain embodiments, position 8, 9, or 10 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, or positions 4, 5, or 6 of the modified oligonucleotide, as counted from the 5' terminus of the gap, aligns with the single nucleotide polymorphism.

Single Nucleotide Polymorphisms (SNPs)

Single-nucleotide polymorphisms (SNPs) are single base-pair alterations in the DNA sequence that represent a major source of genetic heterogeneity (Gene. 1999, 234:177). SNP genotyping is an important tool with which to investigate these genetic variants (Genome Res. 2000, 10:895; Trends Biotechnol. 2000, 18:77). In certain embodiments, antisense compounds designed to selectively reduce an allelic variant of a gene containing an SNP were selected based on potency, selectivity and population genetics coverage.

Potency

In certain embodiments, antisense compounds designed to selectively reduce an allelic variant of a gene containing a SNP are created based on potency of the antisense compound. Potency generally refers to how amenable the targeted sequence area is to antisense inhibition. In certain embodiments, specific SNP sites may be particularly amenable to antisense inhibition. Certain such highly amenable SNP sites may be targeted by antisense compounds for selectively reducing an allelic variant of a gene. Potency is demonstrated by the percent inhibition of mutant mRNA achieved by the antisense oligonucleotides targeting a SNP compared to the percent inhibition of mutant mRNA achieved by the benchmark oligonucleotide.

Selectivity

In certain embodiments, antisense compounds designed to selectively reduce an allelic variant of a gene containing a SNP are created based on selectivity of the antisense compound. Selectivity generally refers to antisense compounds comprising a particular sequence, motif, and chemical modification(s) that preferentially target the one or more differentiating polymorphisms (SNPs) in the RNA encoding a mutant HTT protein compared to the RNA encoding a wild type HTT protein. In certain embodiments, specific sequences, motifs, and chemical modification(s) are particularly selective in reducing an allelic variant of a gene containing a SNP. Certain such sequences, motifs, and chemical modification(s) are utilized to selectively reduce an allelic variant of a gene. Selectivity is demonstrated by the ability of the antisense oligonucleotide targeting a SNP to inhibit expression of the major allele or mutant allele preferentially compared to the minor allele or wild type allele.

Population Genetics

In certain embodiments, antisense compounds designed to selectively reduce an allelic variant of a gene containing an SNP are created based on the population genetics of a population afflicted with disease. Population genetics means the frequency at which the SNP appears in the disease chromosome of patients afflicted with a particular disease. In certain embodiments, the disease is Huntington disease. Where potency and selectivity amongst antisense compounds is equal, SNP targets that have higher population genetics coverage are favored over SNPs that have a weaker association with disease chromosomes.

Antisense Compounds

Oligomeric compounds may include, but are not limited to, oligonucleotides, oligonucleosides, oligonucleotide analogs, oligonucleotide mimetics, antisense compounds, antisense oligonucleotides, and siRNAs. An oligomeric compound may be “antisense” to a target nucleic acid, meaning that it is capable of undergoing hybridization to a target nucleic acid through hydrogen bonding.

In certain embodiments, an antisense compound is an antisense oligonucleotide. In certain embodiments, the antisense compound is not a ribozyme, a double stranded siRNA, or an shRNA.

In certain embodiments, an antisense compound has a nucleobase sequence that, when written in the 5' to 3' direction, comprises the reverse complement of the target segment of a target nucleic acid to which it is targeted. In certain such embodiments, an antisense oligonucleotide has a nucleobase sequence that, when written in the 5' to 3' direction, comprises the reverse complement of the target segment of a target nucleic acid to which it is targeted.

In certain embodiments, antisense compounds are 12 to 30 subunits in length. In other words, such antisense compounds are from 12 to 30 linked subunits. In other embodiments, the antisense compound is 8 to 80, 12 to 50, 15 to 30, 18 to 24, 19 to 22, or 20 linked subunits. In certain such embodiments, the antisense compounds are 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, or 80 linked subunits in length, or a range defined by any two of the above values. In some embodiments the antisense compound is an antisense oligonucleotide, and the linked subunits are nucleosides.

In certain embodiments antisense oligonucleotides targeted to a nucleic acid may be shortened or truncated. For example, a single subunit may be deleted from the 5' end (5' truncation), or alternatively from the 3' end (3' truncation). A shortened or truncated antisense compound targeted to a nucleic acid may have two subunits deleted from the 5' end, or alternatively may have two subunits deleted from the 3' end, of the antisense compound. Alternatively, the deleted nucleosides may be dispersed throughout the antisense compound, for example, in an antisense compound having one nucleoside deleted from the 5' end and one nucleoside deleted from the 3' end.

When a single additional subunit is present in a lengthened antisense compound, the additional subunit may be located at the 5' or 3' end of the antisense compound. When two or more additional subunits are present, the added subunits may be adjacent to each other, for example, in an

antisense compound having two subunits added to the 5' end (5' addition), or alternatively to the 3' end (3' addition), of the antisense compound. Alternatively, the added subunits may be dispersed throughout the antisense compound, for example, in an antisense compound having one subunit added to the 5' end and one subunit added to the 3' end.

It is possible to increase or decrease the length of an antisense compound, such as an antisense oligonucleotide, and/or introduce mismatch bases without eliminating activity. For example, in Woolf et al. (Proc. Natl. Acad. Sci. USA 89:7305-7309, 1992), a series of antisense oligonucleotides 13-25 nucleobases in length were tested for their ability to induce cleavage of a target RNA in an oocyte injection model. Antisense oligonucleotides 25 nucleobases in length with 8 or 11 mismatch bases near the ends of the antisense oligonucleotides were able to direct specific cleavage of the target mRNA, albeit to a lesser extent than the antisense oligonucleotides that contained no mismatches. Similarly, target specific cleavage was achieved using 13 nucleobase antisense oligonucleotides, including those with 1 or 3 mismatches.

Gautschi et al (J. Natl. Cancer Inst. 93:463-471, March 2001) demonstrated the ability of an oligonucleotide having 100% complementarity to the bcl-2 mRNA and having 3 mismatches to the bcl-xL mRNA to reduce the expression of both bcl-2 and bcl-xL *in vitro* and *in vivo*. Furthermore, this oligonucleotide demonstrated potent anti-tumor activity *in vivo*.

Maher and Dolnick (Nuc. Acid. Res. 16:3341-3358, 1988) tested a series of tandem 14 nucleobase antisense oligonucleotides, and a 28 and 42 nucleobase antisense oligonucleotides comprised of the sequence of two or three of the tandem antisense oligonucleotides, respectively, for their ability to arrest translation of human DHFR in a rabbit reticulocyte assay. Each of the three 14 nucleobase antisense oligonucleotides alone was able to inhibit translation, albeit at a more modest level than the 28 or 42 nucleobase antisense oligonucleotides.

However, selective reduction of expression of an allelic variant is optimized when the SNP contained in the target nucleic anneals to a complementary base in the antisense compound and not a mismatched base. Moreover, selectivity in general is increased when there are fewer mismatches between the SNP site and the antisense compound. However, a certain number of mismatches may be tolerated.

Antisense Compound Motifs

In certain embodiments, antisense compounds targeted to a nucleic acid have chemically modified subunits arranged in patterns, or motifs, to confer to the antisense compounds properties

such as enhanced the inhibitory activity, increased binding affinity for a target nucleic acid, or resistance to degradation by *in vivo* nucleases.

Chimeric antisense compounds typically contain at least one region modified so as to confer increased resistance to nuclease degradation, increased cellular uptake, increased binding affinity for the target nucleic acid, and/or increased inhibitory activity. A second region of a chimeric antisense compound may optionally serve as a substrate for the cellular endonuclease RNase H, which cleaves the RNA strand of an RNA:DNA duplex.

Antisense compounds having a gapmer motif are considered chimeric antisense compounds. In a gapmer an internal region having a plurality of nucleotides that supports RNaseH cleavage is positioned between external regions having a plurality of nucleotides that are chemically distinct from the nucleosides of the internal region. In the case of an antisense oligonucleotide having a gapmer motif, the gap segment generally serves as the substrate for endonuclease cleavage, while the wing segments comprise modified nucleosides. In the case of an antisense oligonucleotide for selectively reducing expression of an allelic variant of a gene containing a SNP, the SNP anneals to a nucleobase within the gap segment.

In certain embodiments, the SNP anneals or is complementary to a nucleobase at position 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 of the antisense oligonucleotide, wherein position refers to the orientation of a nucleobase within the antisense oligonucleotide counting from the 5' terminus of the antisense oligonucleotide. For example, the 5' most nucleobase within the antisense oligonucleotide is in the first position of the antisense oligonucleotide. In certain embodiments, the SNP anneals or is complementary to a nucleobase at position 6, 7, 8, 9, or 10 of the antisense oligonucleotide (counting from the 5' terminus). In certain embodiments, the SNP anneals or is complementary to a nucleobase at position 9 or 10 of the antisense oligonucleotide (counting from the 5' terminus).

In certain embodiments, the SNP anneals to a nucleobase at position 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 of the gap segment, wherein position refers to the orientation of a nucleobase within the gap segment counting from the 5' terminus of the gap segment. For example, the 5' most nucleobase within the gap segment is in the first position of the gap segment. In certain embodiments, the SNP anneals to a nucleobase at position 4, 5, 6, or 7 counting from the 5' terminus of the gap segment. In certain embodiments, the SNP anneals to a nucleobase at position 4 or 5 beginning from the 5' terminus of the gap segment.

In certain embodiments, the regions of a gapmer are differentiated by the types of sugar moieties comprising each distinct region. The types of sugar moieties that are used to differentiate

the regions of a gapmer may in some embodiments include β -D-ribonucleosides, β -D-deoxyribonucleosides, 2'-modified nucleosides (such 2'-modified nucleosides may include 2'-MOE, and 2'-O-CH₃, among others), and bicyclic sugar modified nucleosides (such bicyclic sugar modified nucleosides may include those having a 4'-(CH₂)_n-O-2' bridge, where n=1 or n=2). The bicyclic moiety may be a cEt having the formula 4'-CH(CH₃)-O-2.'

The wing-gap-wing motif is frequently described as "X-Y-Z", where "X" represents the length of the 5' wing region, "Y" represents the length of the gap region, and "Z" represents the length of the 3' wing region. As used herein, a gapmer described as "X-Y-Z" has a configuration such that the gap segment is positioned immediately adjacent to each of the 5' wing segment and the 3' wing segment. Thus, no intervening nucleotides exist between the 5' wing segment and gap segment, or the gap segment and the 3' wing segment. Any of the antisense compounds described herein can have a gapmer motif. In some embodiments, X and Z are the same, in other embodiments they are different. In certain embodiments, Y is between 8 and 15 nucleotides. In certain embodiments, Y is comprised of deoxynucleotides. X, Y or Z can be any of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30 or more nucleotides. Thus, gapmers of the present invention include, but are not limited to, for example 1-10-1, 1-18-1, 2-8-2, 2-9-6, 2-10-2, 2-13-5, 2-16-2, 3-9-3, 3-9-5, 3-10-3, 3-14-3, 4-8-4, 4-9-5, 4-10-5, 4-11-4, 4-12-3, 4-12-4, 5-8-5, 5-9-5, 5-10-4, 5-10-5, or 6-8-6.

In certain embodiments, the antisense compound has a "wingmer" motif, having a wing-gap or gap-wing configuration, i.e. an X-Y or Y-Z configuration as described above for the gapmer configuration. Thus, wingmer configurations of the present invention include, but are not limited to, for example 5-10, 8-4, 4-12, 12-4, 3-14, 16-2, 18-1, 10-3, 2-10, 1-10, 8-2, 2-13, 5-13, 5-8, or 6-8.

In certain embodiments, antisense compounds targeted to a nucleic acid possess a 2-9-6 gapmer motif or a 6-9-2 gapmer motif.

In certain embodiments, antisense compounds targeted to a nucleic acid possess a 3-9-3 gapmer motif.

In certain embodiments, antisense compounds targeted to a nucleic acid possess a 3-9-5 gapmer motif or 5-9-3 gapmer motif.

In certain embodiments, antisense compounds targeted to a nucleic acid possess a 4-9-5 gapmer motif or 5-9-4 gapmer motif.

In certain embodiments, antisense compounds targeted to a nucleic acid possess a 4-10-5 gapmer motif or 5-10-4 gapmer motif.

In certain embodiments, antisense compounds targeted to a nucleic acid possess a 4-11-4 gapmer motif.

In certain embodiments, antisense compounds targeted to a nucleic acid possess a 5-9-5 gapmer motif.

In certain embodiments, antisense compounds targeted to a nucleic acid possess a 5-8-6 gapmer motif or a 6-8-5 gapmer motif.

In certain embodiments, antisense compounds targeted to a nucleic acid possess a 6-7-6 gapmer motif.

In certain embodiments, antisense compounds targeted to a nucleic acid possess a 6-8-5 gapmer motif or a 5-8-6 gapmer motif.

In certain embodiments, antisense compounds targeted to a nucleic acid possess a 3-9-4 gapmer motif or a 4-9-3 gapmer motif.

In certain embodiments, antisense compounds targeted to a nucleic acid possess a 5-7-5 gapmer motif.

In certain embodiments, antisense compounds targeted to a nucleic acid possess a 4-7-4 gapmer motif.

In certain embodiments, antisense compounds targeted to a nucleic acid possess a 5-10-5 gapmer motif.

In certain embodiments, an antisense compound targeted to a nucleic acid has a gap-widened motif.

Certain Mixed Wings

In certain embodiments, the invention provides gapmer compounds wherein at least one nucleoside of one wing is differently modified compared to at least one other nucleoside of the same wing. Such antisense compounds are referred to as mixed wing antisense compounds (see WO 2008/049085). In certain embodiments, the modifications (or no modification) of one or more nucleosides of the 3' wing are different from those of one or more other nucleosides of the 3' wing. Such antisense compounds may be referred to as 3' mixed wing gapmers. In certain embodiments, the modifications (or no modification) of one or more nucleosides of the 5' wing are different from those of one or more other nucleosides of the 5' wing. Such antisense compounds may be referred to as 5' mixed wing gapmers. In certain embodiments, the modifications (or no modification) of one or more nucleosides of the 3' wing are different from those of one or more other nucleosides of

the 3' wing and the modifications (or no modification) of one or more nucleosides of the 5' wing are different from those of one or more other nucleosides of the 5' wing. Such antisense compounds may be referred to as 3', 5' mixed wing gapmers. In such embodiment, the modifications and combination of modifications at the 3' wing and at the 5' wing may be the same or they may be different.

In certain embodiments, mixed wing compounds have desirable properties. Certain nucleoside modifications confer on the antisense compound a desirable property, for example increased affinity for a target or nuclease resistance, but also confer an undesirable property, for example increased toxicity. Incorporation of certain other nucleoside modifications results in antisense compounds with different profiles of properties. In certain embodiments, one may combine modifications in one or both wings to optimize desirable characteristics and/or minimize undesirable characteristics. In certain embodiments, the wings of a mixed wing antisense compound comprise one or more nucleoside comprising a first modification that increases affinity of the antisense compound for a target nucleic acid compared to an antisense compound comprising unmodified nucleosides; and one or more nucleoside comprising a second modification that results in reduced toxicity compared to an antisense compound with wings comprising nucleosides that all comprise the first modification.

In certain embodiments, an antisense compound comprises at least one wing comprising at least one MOE substituted nucleoside and at least one high affinity modification. In certain such embodiments, the at least one MOE substituted nucleoside and the at least one high affinity are in the 3' wing. In certain such embodiments, the at least one MOE substituted nucleoside and the at least one high affinity are in the 5' wing.

In certain embodiments, an antisense compound comprises 1, 2 or 3 high affinity modifications in the 5' and/or 3' wings.

Target Nucleic Acids, Target Regions and Nucleotide Sequences

In certain embodiments, an allelic variant of huntingtin is selectively reduced. Nucleotide sequences that encode huntingtin include, without limitation, the following: GENBANK Accession No. NT_006081.18, truncated from nucleotides 1566000 to 1768000 (replaced by GENBANK Accession No. NT_006051), incorporated herein as SEQ ID NO: 1, and NM_002111.6, incorporated herein as SEQ ID NO: 2.

It is understood that the sequence set forth in each SEQ ID NO in the Examples contained herein is independent of any modification to a sugar moiety, an internucleoside linkage, or a nucleobase. As such, antisense compounds defined by a SEQ ID NO may comprise, independently, one or more modifications to a sugar moiety, an internucleoside linkage, or a nucleobase. Antisense compounds described by Isis Number (Isis No) indicate a combination of nucleobase sequence and motif.

In certain embodiments, a target region is a structurally defined region of the target nucleic acid. For example, a target region may encompass a 3' UTR, a 5' UTR, an exon, an intron, an exon/intron junction, a coding region, a translation initiation region, translation termination region, or other defined nucleic acid region. The structurally defined regions for huntingtin can be obtained by accession number from sequence databases such as NCBI and such information is incorporated herein by reference. In certain embodiments, a target region may encompass the sequence from a 5' target site of one target segment within the target region to a 3' target site of another target segment within the same target region.

Targeting includes determination of at least one target segment to which an antisense compound hybridizes, such that a desired effect occurs. In certain embodiments, the desired effect is a reduction in mRNA target nucleic acid levels of a particular allelic variant. In certain embodiments, the desired effect is reduction of levels of the protein encoded by the target nucleic acid or a phenotypic change associated with a particular allelic variant.

A target region may contain one or more target segments. Multiple target segments within a target region may be overlapping. Alternatively, they may be non-overlapping. In certain embodiments, target segments within a target region are separated by no more than about 300 nucleotides. In certain embodiments, target segments within a target region are separated by a number of nucleotides that is, is about, is no more than, is no more than about, 250, 200, 150, 100, 90, 80, 70, 60, 50, 40, 30, 20, or 10 nucleotides on the target nucleic acid, or is a range defined by any two of the preceding values. In certain embodiments, target segments within a target region are separated by no more than, or no more than about, 5 nucleotides on the target nucleic acid. In certain embodiments, target segments are contiguous. Contemplated are target regions defined by a range having a starting nucleic acid that is any of the 5' target sites or 3' target sites listed herein.

Suitable target segments may be found within a 5' UTR, a coding region, a 3' UTR, an intron, an exon, or an exon/intron junction. Target segments containing a start codon or a stop

codon are also suitable target segments. A suitable target segment may specifically exclude a certain structurally defined region such as the start codon or stop codon.

The determination of suitable target segments may include a comparison of the sequence of a target nucleic acid to other sequences throughout the genome. For example, the BLAST algorithm may be used to identify regions of similarity amongst different nucleic acids. This comparison can prevent the selection of antisense compound sequences that may hybridize in a non-specific manner to sequences other than a selected target nucleic acid (i.e., non-target or off-target sequences).

Cell Lines

In certain embodiments, the GM04281, GM02171, and GM02173B cell lines are used in experiments described herein below. The GM04281 cell line has a wild-type *HTT* allele that contains 17 repeats and a mutant *HTT* allele that contains 69 repeats. The cell line was derived from a patient both of whose parents were also affected by the disease. The GM02171 cell line was chosen as a counter screen control to the GM04281. This cell line was derived from the daughter of parents, only one of whom had the disease. The daughter had not developed HD but was considered to be at risk. The GM02173B cell line was also patient-derived and was used as a haplotype test control.

Table 1 provides SNPs found in the GM04281, GM02171, and GM02173B cell lines. Also provided are the allelic variants found at each SNP position, the genotype for each of the cell lines, and the percentage of HD patients having a particular allelic variant. For example, the two allelic variants for SNP rs6446723 are T and C. The GM02171 cell line is homozygous CC, the GM02173 cell line is heterozygous TC, and the GM04281 cell line is homozygous TT. Fifty percent of HD patients have a T at SNP position rs6446723.

Table 1

Allelic Variations for SNPs Associated with HD

SNP	Variation	GM02171	GM02173	GM04281	TargetPOP	allele
rs6446723	T/C	CC	TC	TT	0.50	T
rs3856973	A/G	AA	AG	GG	0.50	G
rs2285086	A/G	GG	AG	AA	0.50	A
rs363092	A/C	AA	AC	CC	0.49	C
rs916171	C/G	GG	GC	CC	0.49	C
rs6844859	T/C	CC	TC	TT	0.49	T
rs7691627	A/G	AA	AG	GG	0.49	G
rs4690073	A/G	AA	AG	GG	0.49	G

rs2024115	A/G	GG	AG	AA	0.48	A
rs11731237	T/C	CC	TC	TT	0.43	T
rs362296	A/C	AC	AC	AC	0.42	C
rs10015979	A/G	AA	AG	GG	0.42	G
rs7659144	C/G	CG	CG	CC	0.41	C
rs363096	T/C	CC	TC	TT	0.40	T
rs362273	A/G	AG	AG	AA	0.39	A
rs16843804	T/C	TC	TC	CC	0.38	C
rs362271	A/G	AG	AG	GG	0.38	G
rs362275	T/C	TC	TC	CC	0.38	C
rs3121419	T/C	TC	TC	CC	0.38	C
rs362272	A/G	--	AG	GG	0.38	G
rs3775061	A/G	AG	AG	AA	0.38	A
rs34315806	T/C	TC	TC	CC	0.38	C
rs363099	T/C	TC	TC	CC	0.38	C
rs2298967	T/C	TC	TC	TT	0.38	T
rs363088	A/T	TA	TA	AA	0.38	A
rs363064	T/C	TC	TC	CC	0.35	C
rs363102	A/G	AA	AA	AA	0.23	G
rs2798235	A/G	GG	GG	GG	0.21	A
rs363080	T/C	CC	CC	CC	0.21	T
rs363072	A/T	TA	AA	AA	0.13	A
rs363125	A/C	AC	CC	CC	0.12	C
rs362303	T/C	TC	CC	CC	0.12	C
rs362310	T/C	TC	CC	CC	0.12	C
rs10488840	A/G	AG	GG	GG	0.12	G
rs362325	T/C	TC	TT	TT	0.11	T
rs35892913	A/G	GG	GG	GG	0.10	A
rs363102	A/G	AA	AA	AA	0.09	A
rs363096	T/C	CC	TC	TT	0.09	C
rs11731237	T/C	CC	TC	TT	0.09	C
rs10015979	A/G	AA	AG	GG	0.08	A
rs363080	T/C	CC	CC	CC	0.07	C
rs2798235	A/G	GG	GG	GG	0.07	G
rs1936032	C/G	CC	CC	CC	0.06	C
rs2276881	A/G	GG	GG	GG	0.06	G
rs363070	A/G	AA	AA	AA	0.06	A
rs35892913	A/G	GG	GG	GG	0.04	G
rs12502045	T/C	CC	CC	CC	0.04	C
rs6446723	T/C	CC	TC	TT	0.04	C
rs7685686	A/G	GG	AG	AA	0.04	G
rs3733217	T/C	CC	CC	CC	0.03	C

rs6844859	T/C	CC	TC	TT	0.03	C
rs362331	T/C	CC	TC	TT	0.03	C

Hybridization

In some embodiments, hybridization occurs between an antisense compound disclosed herein and a SNP site. The most common mechanism of hybridization involves hydrogen bonding (e.g., Watson-Crick, Hoogsteen or reversed Hoogsteen hydrogen bonding) between complementary nucleobases of the nucleic acid molecules.

Hybridization can occur under varying conditions. Stringent conditions are sequence-dependent and are determined by the nature and composition of the nucleic acid molecules to be hybridized.

In certain embodiments, the antisense compounds provided herein are specifically hybridizable with the nucleic acid of a particular allelic variant.

Complementarity

An antisense compound and a target nucleic acid are complementary to each other when a sufficient number of nucleobases of the antisense compound can hydrogen bond with the corresponding nucleobases of the target nucleic acid, such that a desired effect will occur (e.g., selective reduction of a gene product of an allelic variant).

Non-complementary nucleobases between an antisense compound and a target nucleic acid may be tolerated provided that the antisense compound remains able to specifically hybridize to a target nucleic acid. Moreover, an antisense compound may hybridize over one or more segments of a target nucleic acid such that intervening or adjacent segments are not involved in the hybridization event (e.g., a loop structure, mismatch or hairpin structure).

In certain embodiments, the antisense compounds provided herein, or a specified portion thereof, are, or are at least, 70%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% complementary to a target nucleic acid, a target region, target segment, SNP site, or specified portion thereof. Percent complementarity of an antisense compound with a target nucleic acid can be determined using routine methods.

For example, an antisense compound in which 18 of 20 nucleobases of the antisense compound are complementary to a target region, and would therefore specifically hybridize, would represent 90 percent complementarity. In this example, the remaining noncomplementary nucleobases may be

clustered or interspersed with complementary nucleobases and need not be contiguous to each other or to complementary nucleobases. As such, an antisense compound which is 18 nucleobases in length having 4 (four) noncomplementary nucleobases which are flanked by two regions of complete complementarity with the target nucleic acid would have 77.8% overall complementarity with the target nucleic acid and would thus fall within the scope of the present invention. Percent complementarity of an antisense compound with a region of a target nucleic acid can be determined routinely using BLAST programs (basic local alignment search tools) and PowerBLAST programs known in the art (Altschul et al., J. Mol. Biol., 1990, 215, 403 410; Zhang and Madden, Genome Res., 1997, 7, 649 656). Percent homology, sequence identity or complementarity, can be determined by, for example, the Gap program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, Madison Wis.), using default settings, which uses the algorithm of Smith and Waterman (Adv. Appl. Math., 1981, 2, 482 489).

In certain embodiments, the antisense compounds provided herein, or specified portions thereof, are fully complementary (i.e. 100% complementary) to a target nucleic acid, a SNP site, target region, target segment, or specified portion thereof. As used herein, "fully complementary" means each nucleobase of an antisense compound is capable of precise base pairing with the corresponding nucleobases of a target nucleic acid. For example, a 20 nucleobase antisense compound is fully complementary to a target sequence that is 400 nucleobases long, so long as there is a corresponding 20 nucleobase portion of the target nucleic acid that is fully complementary to the antisense compound. Fully complementary can also be used in reference to a specified portion of the first and /or the second nucleic acid. For example, a 20 nucleobase portion of a 30 nucleobase antisense compound can be "fully complementary" to a target sequence that is 400 nucleobases long. The 20 nucleobase portion of the 30 nucleobase oligonucleotide is fully complementary to the target sequence if the target sequence has a corresponding 20 nucleobase portion wherein each nucleobase is complementary to the 20 nucleobase portion of the antisense compound. At the same time, the entire 30 nucleobase antisense compound may or may not be fully complementary to the target sequence, depending on whether the remaining 10 nucleobases of the antisense compound are also complementary to the target sequence.

The location of a non-complementary nucleobase may be at the 5' end or 3' end of the antisense compound. Alternatively, the non-complementary nucleobase or nucleobases may be at an internal position of the antisense compound. When two or more non-complementary nucleobases

are present, they may be contiguous (i.e. linked) or non-contiguous. In one embodiment, a non-complementary nucleobase is located in the wing segment of a gapmer antisense oligonucleotide.

In certain embodiments, antisense compounds that are, or are up to 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleobases in length comprise no more than 6, no more than 5, no more than 4, no more than 3, no more than 2, or no more than 1 non-complementary nucleobase(s) relative to a target nucleic acid, SNP site, or specified portion thereof.

In certain embodiments, antisense oligonucleotides that are, or are up to 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 nucleobases in length comprise no more than 6, no more than 5, no more than 4, no more than 3, no more than 2, or no more than 1 non-complementary nucleobase(s) relative to a target nucleic acid, SNP site, or specified portion thereof.

The antisense compounds provided herein also include those which are complementary to a portion of a target nucleic acid. As used herein, "portion" refers to a defined number of contiguous (i.e. linked) nucleobases within a region or segment of a target nucleic acid. A "portion" can also refer to a defined number of contiguous nucleobases of an antisense compound. In certain embodiments, the antisense compounds, are complementary to at least an 8 nucleobase portion of a target segment. In certain embodiments, the antisense compounds are complementary to at least a 12 nucleobase portion of a target segment. In certain embodiments, the antisense compounds are complementary to at least a 15 nucleobase portion of a target segment. Also contemplated are antisense compounds that are complementary to at least a 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more nucleobase portion of a target segment, or a range defined by any two of these values.

Identity

The antisense compounds provided herein may also have a defined percent identity to a particular nucleotide sequence, SEQ ID NO, or compound represented by a specific Isis number, or portion thereof. As used herein, an antisense compound is identical to the sequence disclosed herein if it has the same nucleobase pairing ability. For example, a RNA which contains uracil in place of thymidine in a disclosed DNA sequence would be considered identical to the DNA sequence since both uracil and thymidine pair with adenine. Shortened and lengthened versions of the antisense compounds described herein as well as compounds having non-identical bases relative to the antisense compounds provided herein also are contemplated. The non-identical bases may be adjacent to each other or dispersed throughout the antisense compound. Percent identity of an

antisense compound is calculated according to the number of bases that have identical base pairing relative to the sequence to which it is being compared.

In certain embodiments, the antisense compounds, or portions thereof, are at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to one or more of the antisense compounds or SEQ ID NOs, or a portion thereof, disclosed herein.

In certain embodiments, a portion of the antisense compound is compared to an equal length portion of the target nucleic acid. In certain embodiments, an 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 nucleobase portion is compared to an equal length portion of the target nucleic acid.

In certain embodiments, a portion of the antisense oligonucleotide is compared to an equal length portion of the target nucleic acid. In certain embodiments, an 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 nucleobase portion is compared to an equal length portion of the target nucleic acid.

Modifications

A nucleoside is a base-sugar combination. The nucleobase (also known as base) portion of the nucleoside is normally a heterocyclic base moiety. Nucleotides are nucleosides that further include a phosphate group covalently linked to the sugar portion of the nucleoside. For those nucleosides that include a pentofuranosyl sugar, the phosphate group can be linked to the 2', 3' or 5' hydroxyl moiety of the sugar. Oligonucleotides are formed through the covalent linkage of adjacent nucleosides to one another, to form a linear polymeric oligonucleotide. Within the oligonucleotide structure, the phosphate groups are commonly referred to as forming the internucleoside linkages of the oligonucleotide.

Modifications to antisense compounds encompass substitutions or changes to internucleoside linkages, sugar moieties, or nucleobases. Modified antisense compounds are often preferred over native forms because of desirable properties such as, for example, enhanced cellular uptake, enhanced affinity for nucleic acid target, increased stability in the presence of nucleases, or increased inhibitory activity.

Chemically modified nucleosides may also be employed to increase the binding affinity of a shortened or truncated antisense oligonucleotide for its target nucleic acid. Consequently, comparable results can often be obtained with shorter antisense compounds that have such chemically modified nucleosides.

Chemically modified nucleosides may also be employed to increase selectivity in reducing expression the gene product of an allelic variant.

Modified Internucleoside Linkages

The naturally occurring internucleoside linkage of RNA and DNA is a 3' to 5' phosphodiester linkage. Antisense compounds having one or more modified, i.e. non-naturally occurring, internucleoside linkages are often selected over antisense compounds having naturally occurring internucleoside linkages because of desirable properties such as, for example, enhanced cellular uptake, enhanced affinity for target nucleic acids, and increased stability in the presence of nucleases.

Oligonucleotides having modified internucleoside linkages include internucleoside linkages that retain a phosphorus atom as well as internucleoside linkages that do not have a phosphorus atom. Representative phosphorus containing internucleoside linkages include, but are not limited to, phosphodiesters, phosphotriesters, methylphosphonates, phosphoramidate, and phosphorothioate. Methods of preparation of phosphorous-containing and non-phosphorous-containing linkages are well known.

In certain embodiments, antisense compounds comprise one or more modified internucleoside linkages. In certain embodiments, the modified internucleoside linkages are phosphorothioate linkages. In certain embodiments, each internucleoside linkage of an antisense compound is a phosphorothioate internucleoside linkage.

Modified Sugar Moieties

Antisense compounds of the invention can optionally contain one or more nucleosides wherein the sugar group has been modified. Such sugar modified nucleosides may impart enhanced nuclease stability, increased binding affinity, increased selectivity for an allelic variant, or some other beneficial biological property to the antisense compounds. In certain embodiments, nucleosides comprise a chemically modified ribofuranose ring moieties. Examples of chemically modified ribofuranose rings include without limitation, addition of substituent groups (including 5' and 2' substituent groups, bridging of non-geminal ring atoms to form bicyclic nucleic acids (BNA), replacement of the ribosyl ring oxygen atom with S, N(R), or C(R1)(R)2 (R = H, C1-C12 alkyl or a protecting group) and combinations thereof. Examples of chemically modified sugars include 2'-F-5'-methyl substituted nucleoside (see PCT International Application WO 2008/101157 Published on

8/21/08 for other disclosed 5',2'-bis substituted nucleosides) or replacement of the ribosyl ring oxygen atom with S with further substitution at the 2'-position (see published U.S. Patent Application US2005-0130923, published on June 16, 2005) or alternatively 5'-substitution of a BNA (see PCT International Application WO 2007/134181 Published on 11/22/07 wherein LNA is substituted with for example a 5'-methyl or a 5'-vinyl group).

Examples of nucleosides having modified sugar moieties include without limitation nucleosides comprising 5'-vinyl, 5'-methyl (R or S), 4'-S, 2'-F, 2'-OCH₃ and 2'-O(CH₂)₂OCH₃ substituent groups. The substituent at the 2' position can also be selected from allyl, amino, azido, thio, O-allyl, O-C₁-C₁₀ alkyl, OCF₃, O(CH₂)₂SCH₃, O(CH₂)₂-O-N(R_m)(R_n), and O-CH₂-C(=O)-N(R_m)(R_n), where each R_m and R_n is, independently, H or substituted or unsubstituted C₁-C₁₀ alkyl.

As used herein, "bicyclic nucleosides" refer to modified nucleosides comprising a bicyclic sugar moiety. Examples of bicyclic nucleosides include without limitation nucleosides comprising a bridge between the 4' and the 2' ribosyl ring atoms. In certain embodiments, antisense compounds provided herein include one or more bicyclic nucleosides wherein the bridge comprises a 4' to 2' bicyclic nucleoside. Examples of such 4' to 2' bicyclic nucleosides, include but are not limited to one of the formulae: 4'-(CH₂)-O-2' (LNA); 4'-(CH₂)-S-2'; 4'-(CH₂)₂-O-2' (ENA); 4'-CH(CH₃)-O-2' and 4'-CH(CH₂OCH₃)-O-2' (and analogs thereof see U.S. Patent 7,399,845, issued on July 15, 2008); 4'-C(CH₃)(CH₃)-O-2' (and analogs thereof see published International Application WO/2009/006478, published January 8, 2009); 4'-CH₂-N(OCH₃)-2' (and analogs thereof see published International Application WO/2008/150729, published December 11, 2008); 4'-CH₂-O-N(CH₃)-2' (see published U.S. Patent Application US2004-0171570, published September 2, 2004); 4'-CH₂-N(R)-O-2', wherein R is H, C₁-C₁₂ alkyl, or a protecting group (see U.S. Patent 7,427,672, issued on September 23, 2008); 4'-CH₂-C(H)(CH₃)-2' (see Chattopadhyaya, *et al.*, *J. Org. Chem.*, 2009, 74, 118-134); and 4'-CH₂-C(=CH₂)-2' (and analogs thereof see published International Application WO 2008/154401, published on December 8, 2008). See, for example: Singh et al., *Chem. Commun.*, 1998, 4, 455-456; Koshkin et al., *Tetrahedron*, 1998, 54, 3607-3630; Wahlestedt et al., *Proc. Natl. Acad. Sci. U. S. A.*, 2000, 97, 5633-5638; Kumar et al., *Bioorg. Med. Chem. Lett.*, 1998, 8, 2219-2222; Singh et al., *J. Org. Chem.*, 1998, 63, 10035-10039; Srivastava et al., *J. Am. Chem. Soc.*, 129(26) 8362-8379 (Jul. 4, 2007); U.S. Patent Nos. 7,053,207; 6,268,490; 6,770,748; 6,794,499; 7,034,133; and 6,525,191; Elayadi *et al.*, *Curr. Opinion Invens. Drugs*, 2001, 2, 558-561; Braasch *et al.*, *Chem. Biol.*, 2001, 8, 1-7; and Orum *et al.*, *Curr. Opinion Mol. Ther.*, 2001, 3,

239-243; and U.S. 6,670,461; International applications WO 2004/106356; WO 94/14226; WO 2005/021570; U.S. Patent Publication Nos. US2004-0171570; US2007-0287831; US2008-0039618; U.S. Patent Nos. 7,399,845; U.S. Patent Serial Nos. 12/129,154; 60/989,574; 61/026,995; 61/026,998; 61/056,564; 61/086,231; 61/097,787; 61/099,844; PCT International Applications Nos. PCT/US2008/064591; PCT/US2008/066154; PCT/US2008/068922; and Published PCT International Applications WO 2007/134181. Each of the foregoing bicyclic nucleosides can be prepared having one or more stereochemical sugar configurations including for example α -L-ribofuranose and β -D-ribofuranose (see PCT international application PCT/DK98/00393, published on March 25, 1999 as WO 99/14226).

In certain embodiments, bicyclic sugar moieties of BNA nucleosides include, but are not limited to, compounds having at least one bridge between the 4' and the 2' position of the pentofuranosyl sugar moiety wherein such bridges independently comprises 1 or from 2 to 4 linked groups independently selected from $-[C(R_a)(R_b)]_n-$, $-C(R_a)=C(R_b)-$, $-C(R_a)=N-$, $-C(=NR_a)-$, $-C(=O)-$, $-C(=S)-$, $-O-$, $-Si(R_a)_2-$, $-S(=O)_x-$, and $-N(R_a)-$;

wherein:

x is 0, 1, or 2;

n is 1, 2, 3, or 4;

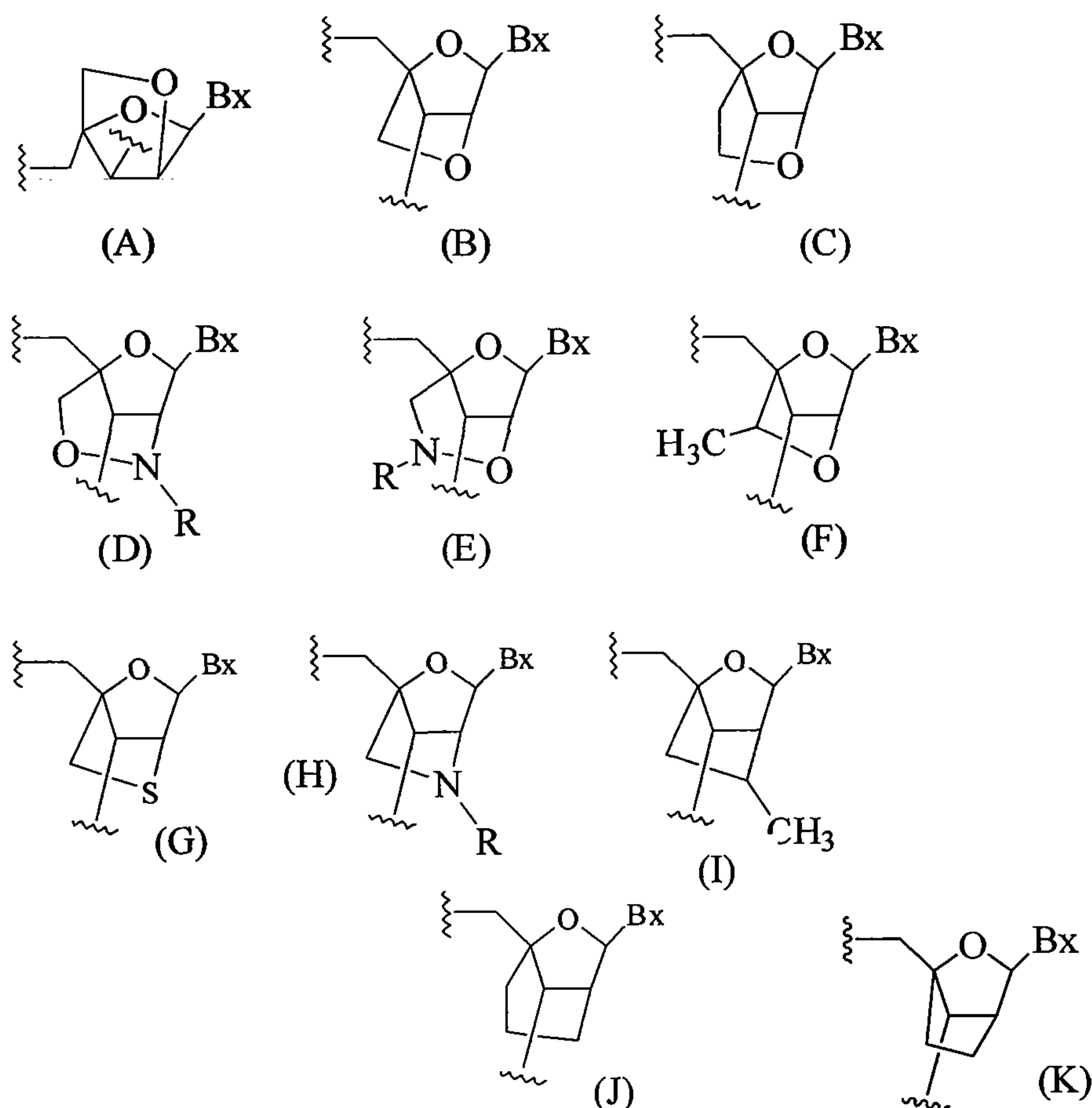
each R_a and R_b is, independently, H, a protecting group, hydroxyl, C_1 - C_{12} alkyl, substituted C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, substituted C_2 - C_{12} alkenyl, C_2 - C_{12} alkynyl, substituted C_2 - C_{12} alkynyl, C_5 - C_{20} aryl, substituted C_5 - C_{20} aryl, heterocycle radical, substituted heterocycle radical, heteroaryl, substituted heteroaryl, C_5 - C_7 alicyclic radical, substituted C_5 - C_7 alicyclic radical, halogen, OJ_1 , NJ_1J_2 , SJ_1 , N_3 , $COOJ_1$, acyl ($C(=O)-H$), substituted acyl, CN, sulfonyl ($S(=O)_2-J_1$), or sulfoxyl ($S(=O)-J_1$); and

each J_1 and J_2 is, independently, H, C_1 - C_{12} alkyl, substituted C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, substituted C_2 - C_{12} alkenyl, C_2 - C_{12} alkynyl, substituted C_2 - C_{12} alkynyl, C_5 - C_{20} aryl, substituted C_5 - C_{20} aryl, acyl ($C(=O)-H$), substituted acyl, a heterocycle radical, a substituted heterocycle radical, C_1 - C_{12} aminoalkyl, substituted C_1 - C_{12} aminoalkyl or a protecting group.

In certain embodiments, the bridge of a bicyclic sugar moiety is $-[C(R_a)(R_b)]_n-$, $-[C(R_a)(R_b)]_n-O-$, $-C(R_aR_b)-N(R)-O-$ or $-C(R_aR_b)-O-N(R)-$. In certain embodiments, the bridge is 4'-CH₂-2', 4'-(CH₂)₂-2', 4'-(CH₂)₃-2', 4'-CH₂-O-2', 4'-(CH₂)₂-O-2', 4'-CH₂-O-N(R)-2' and 4'-CH₂-N(R)-O-2' wherein each R is, independently, H, a protecting group or C_1 - C_{12} alkyl.

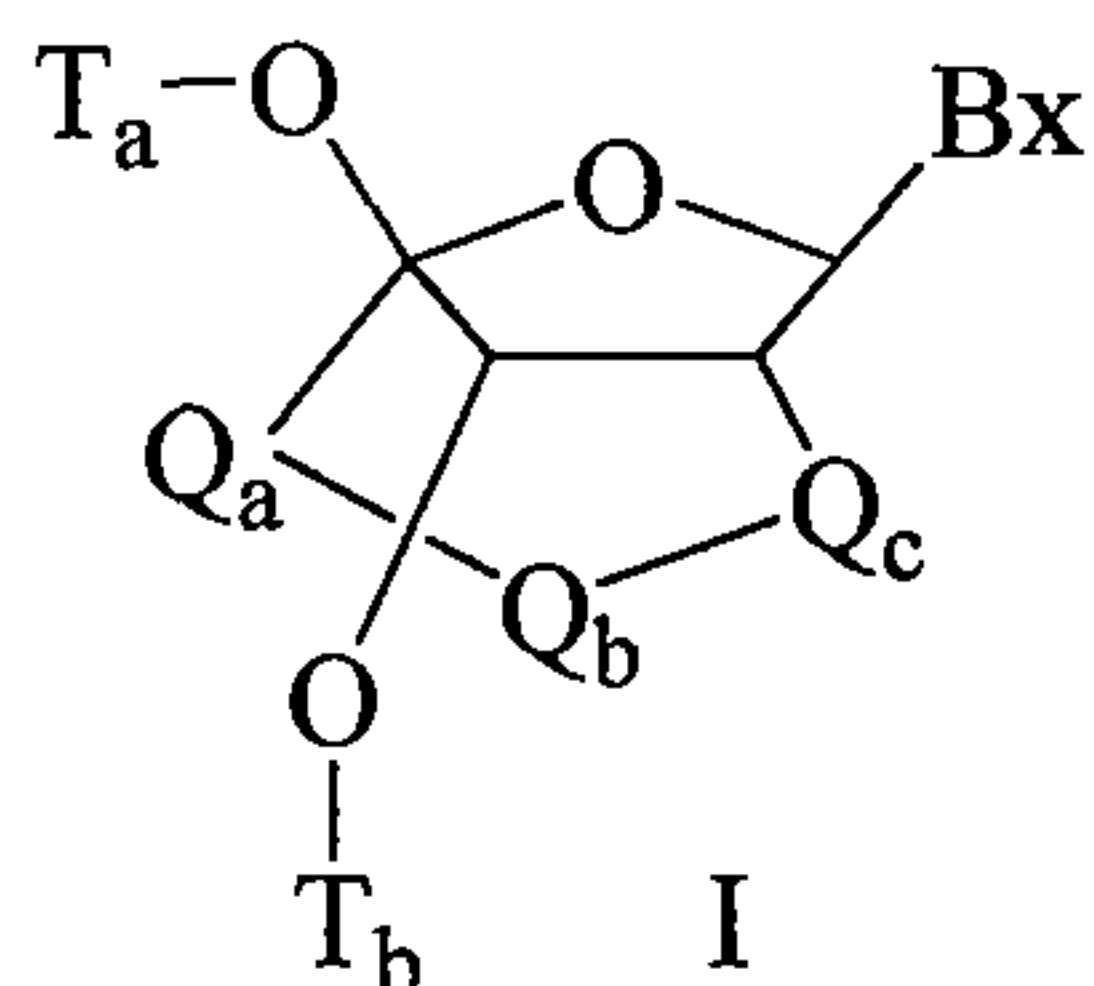
In certain embodiments, bicyclic nucleosides are further defined by isomeric configuration. For example, a nucleoside comprising a 4'-2' methylene-oxy bridge, may be in the α -L configuration or in the β -D configuration. Previously, α -L-methyleneoxy (4'-CH₂-O-2') BNA's have been incorporated into antisense oligonucleotides that showed antisense activity (Frieden *et al.*, *Nucleic Acids Research*, 2003, 21, 6365-6372).

In certain embodiments, bicyclic nucleosides include, but are not limited to, (A) α -L-Methyleneoxy (4'-CH₂-O-2') BNA, (B) β -D-Methyleneoxy (4'-CH₂-O-2') BNA, (C) Ethyleneoxy (4'-(CH₂)₂-O-2') BNA, (D) Aminooxy (4'-CH₂-O-N(R)-2') BNA, (E) Oxyamino (4'-CH₂-N(R)-O-2') BNA, and (F) Methyl(methyleneoxy) (4'-CH(CH₃)-O-2') BNA, (G) methylene-thio (4'-CH₂-S-2') BNA, (H) methylene-amino (4'-CH₂-N(R)-2') BNA, (I) methyl carbocyclic (4'-CH₂-CH(CH₃)-2') BNA, (J) propylene carbocyclic (4'-(CH₂)₃-2') BNA, and (K) ethylene carbocyclic (4'-CH₂-CH₂-2') (carba LNA or "cLNA") as depicted below.



wherein Bx is the base moiety and R is independently H, a protecting group or C₁-C₁₂ alkyl.

In certain embodiments, bicyclic nucleoside having Formula I:



wherein:

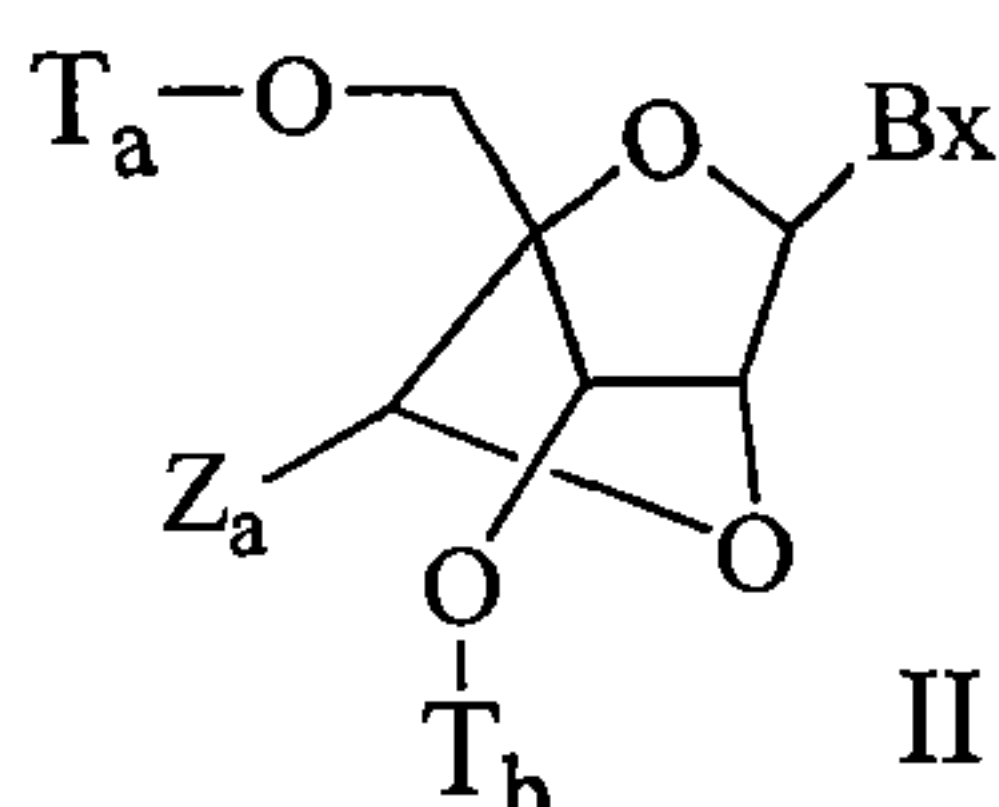
Bx is a heterocyclic base moiety;

-Q_a-Q_b-Q_c- is -CH₂-N(R_c)-CH₂-, -C(=O)-N(R_c)-CH₂-, -CH₂-O-N(R_c)-, -CH₂-N(R_c)-O- or -N(R_c)-O-CH₂;

R_c is C₁-C₁₂ alkyl or an amino protecting group; and

T_a and T_b are each, independently H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety or a covalent attachment to a support medium.

In certain embodiments, bicyclic nucleoside having Formula II:



wherein:

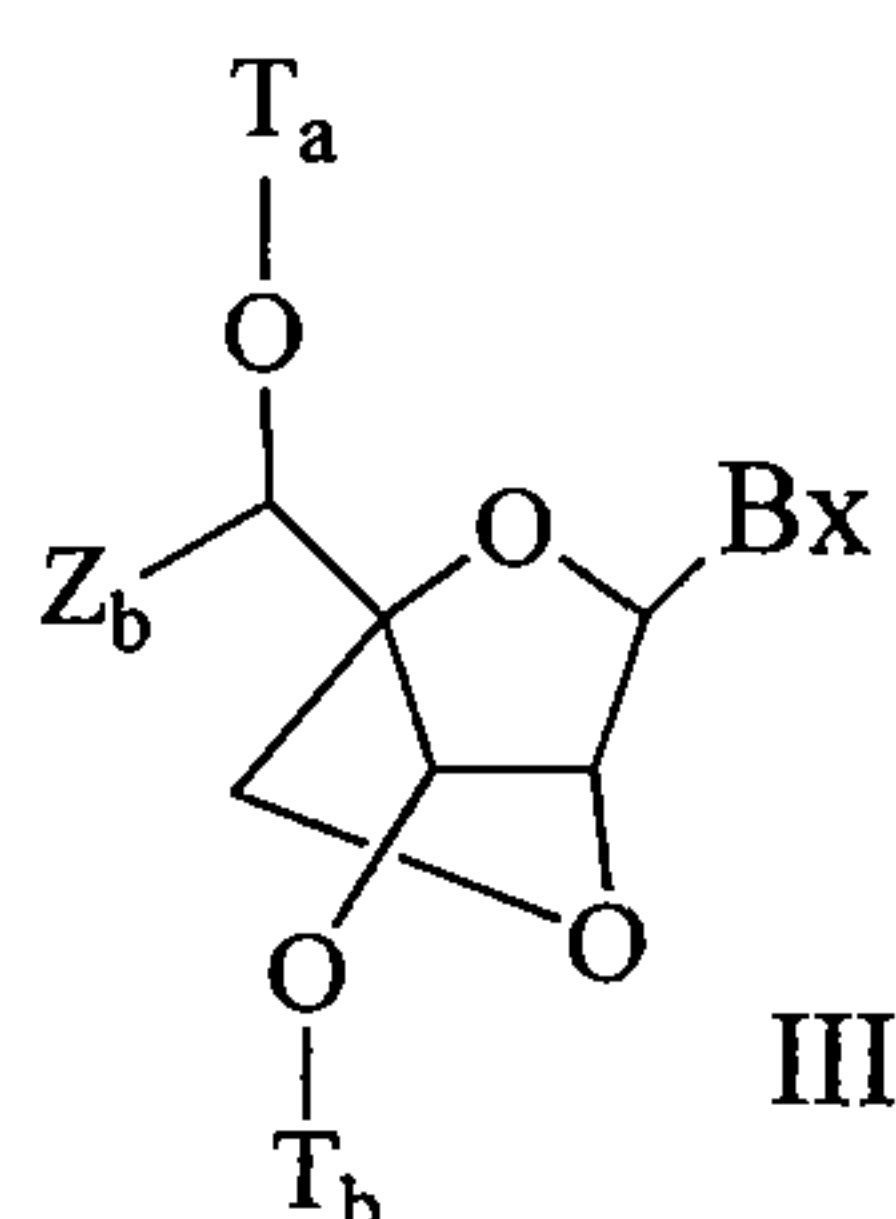
Bx is a heterocyclic base moiety;

T_a and T_b are each, independently H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety or a covalent attachment to a support medium;

Z_a is C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, substituted C₁-C₆ alkyl, substituted C₂-C₆ alkenyl, substituted C₂-C₆ alkynyl, acyl, substituted acyl, substituted amide, thiol or substituted thio.

In one embodiment, each of the substituted groups, is, independently, mono or poly substituted with substituent groups independently selected from halogen, oxo, hydroxyl, OJ_c, NJ_cJ_d, SJ_c, N₃, OC(=X)J_c, and NJ_cC(=X)NJ_cJ_d, wherein each J_c, J_d and J_e is, independently, H, C₁-C₆ alkyl, or substituted C₁-C₆ alkyl and X is O or NJ_c.

In certain embodiments, bicyclic nucleoside having Formula III:



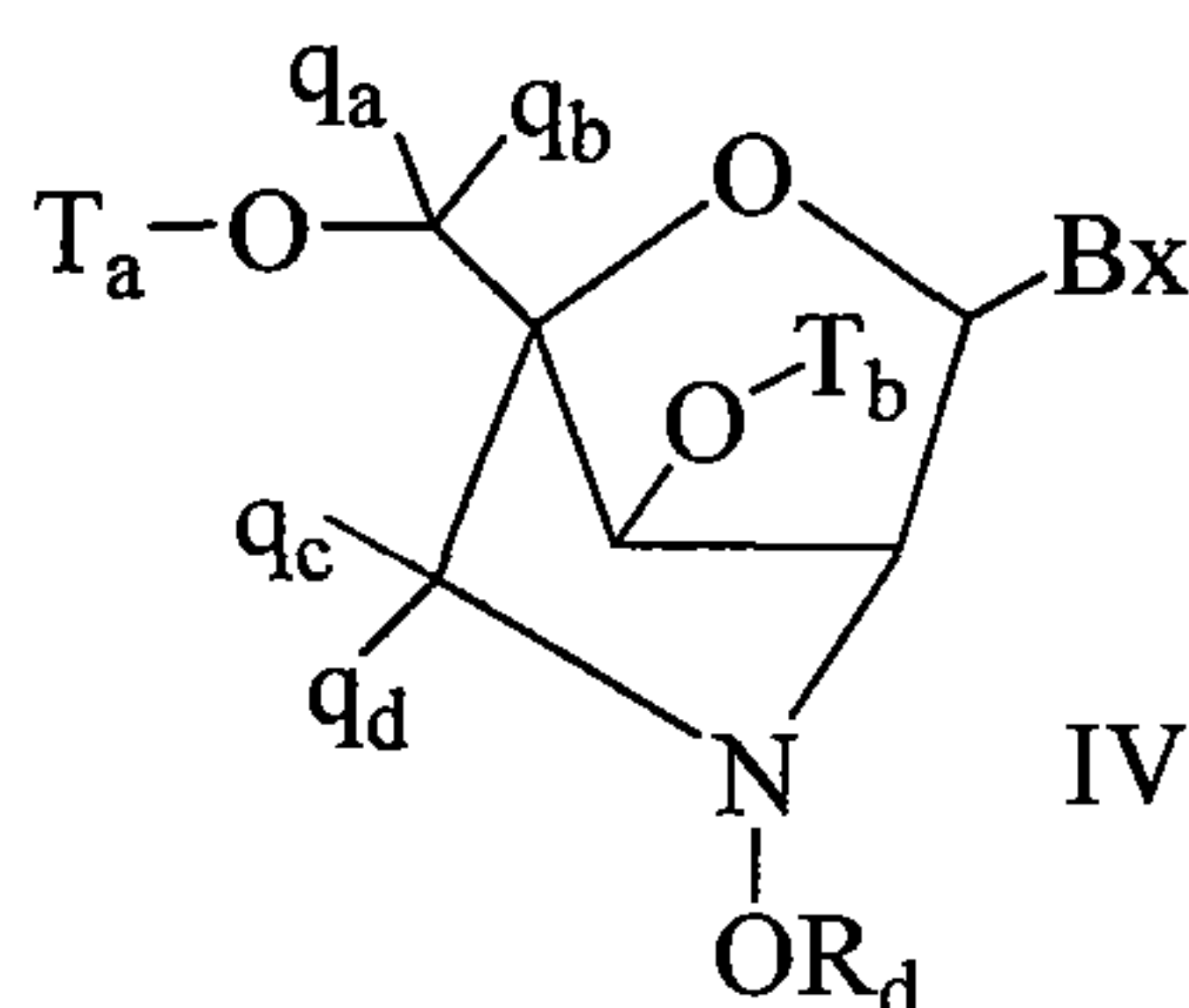
wherein:

Bx is a heterocyclic base moiety;

T_a and T_b are each, independently H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety or a covalent attachment to a support medium;

Z_b is C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, substituted C₁-C₆ alkyl, substituted C₂-C₆ alkenyl, substituted C₂-C₆ alkynyl or substituted acyl (C(=O)-).

In certain embodiments, bicyclic nucleoside having Formula IV:



wherein:

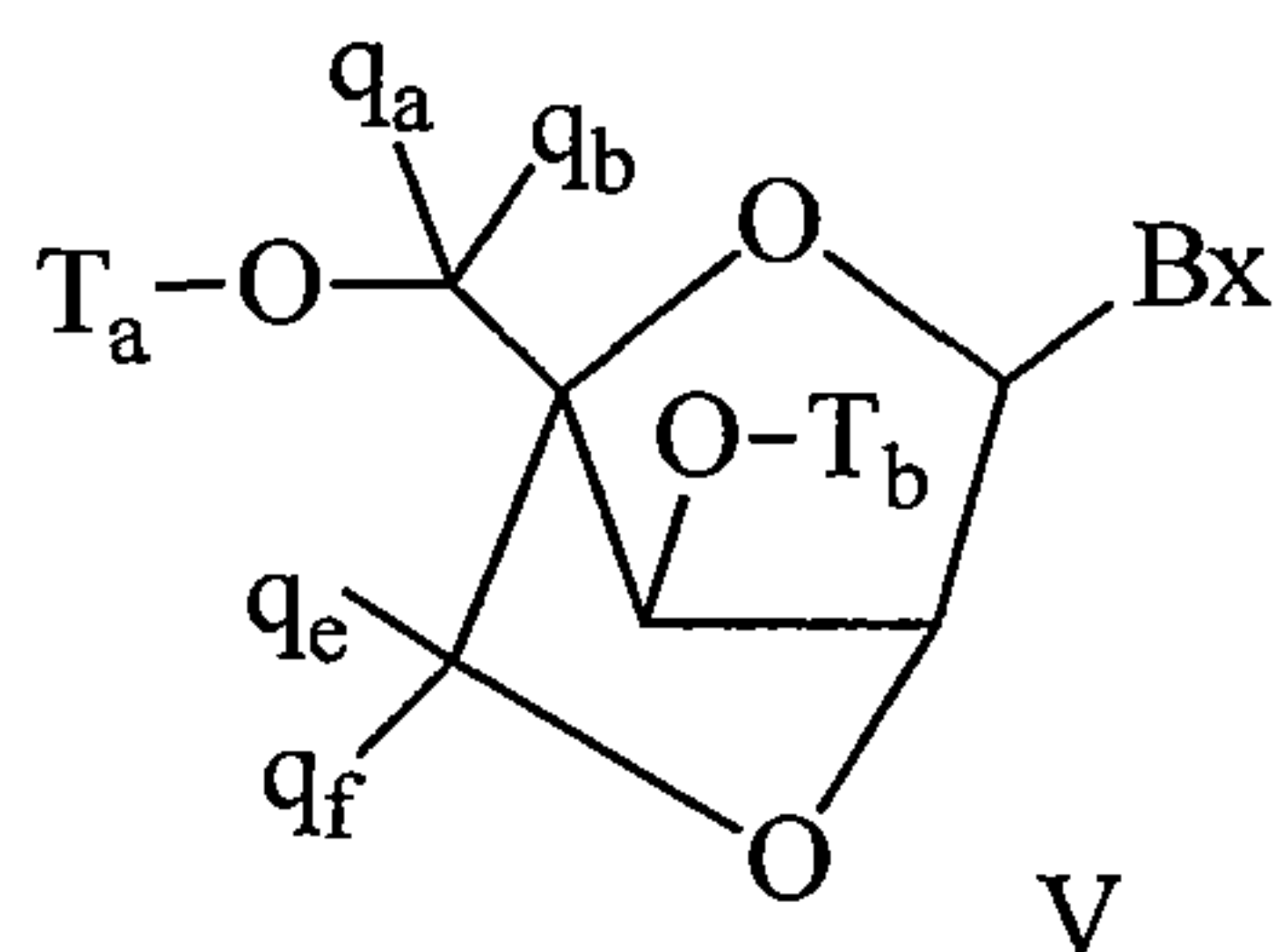
Bx is a heterocyclic base moiety;

T_a and T_b are each, independently H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety or a covalent attachment to a support medium;

R_d is C₁-C₆ alkyl, substituted C₁-C₆ alkyl, C₂-C₆ alkenyl, substituted C₂-C₆ alkenyl, C₂-C₆ alkynyl or substituted C₂-C₆ alkynyl;

each q_a, q_b, q_c and q_d is, independently, H, halogen, C₁-C₆ alkyl, substituted C₁-C₆ alkyl, C₂-C₆ alkenyl, substituted C₂-C₆ alkenyl, C₂-C₆ alkynyl or substituted C₂-C₆ alkynyl, C₁-C₆ alkoxy, substituted C₁-C₆ alkoxy, acyl, substituted acyl, C₁-C₆ aminoalkyl or substituted C₁-C₆ aminoalkyl;

In certain embodiments, bicyclic nucleoside having Formula V:



wherein:

Bx is a heterocyclic base moiety;

T_a and T_b are each, independently H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety or a covalent attachment to a support medium;

q_a, q_b, q_e and q_f are each, independently, hydrogen, halogen, C₁-C₁₂ alkyl, substituted C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, substituted C₂-C₁₂ alkenyl, C₂-C₁₂ alkynyl, substituted C₂-C₁₂ alkynyl, C₁-C₁₂ alkoxy, substituted C₁-C₁₂ alkoxy, OJ_j, SJ_j, SOJ_j, SO₂J_j, NJ_jJ_k, N₃, CN, C(=O)OJ_j, C(=O)NJ_jJ_k, C(=O)J_j, O-C(=O)NJ_jJ_k, N(H)C(=NH)NJ_jJ_k, N(H)C(=O)NJ_jJ_k or N(H)C(=S)NJ_jJ_k;

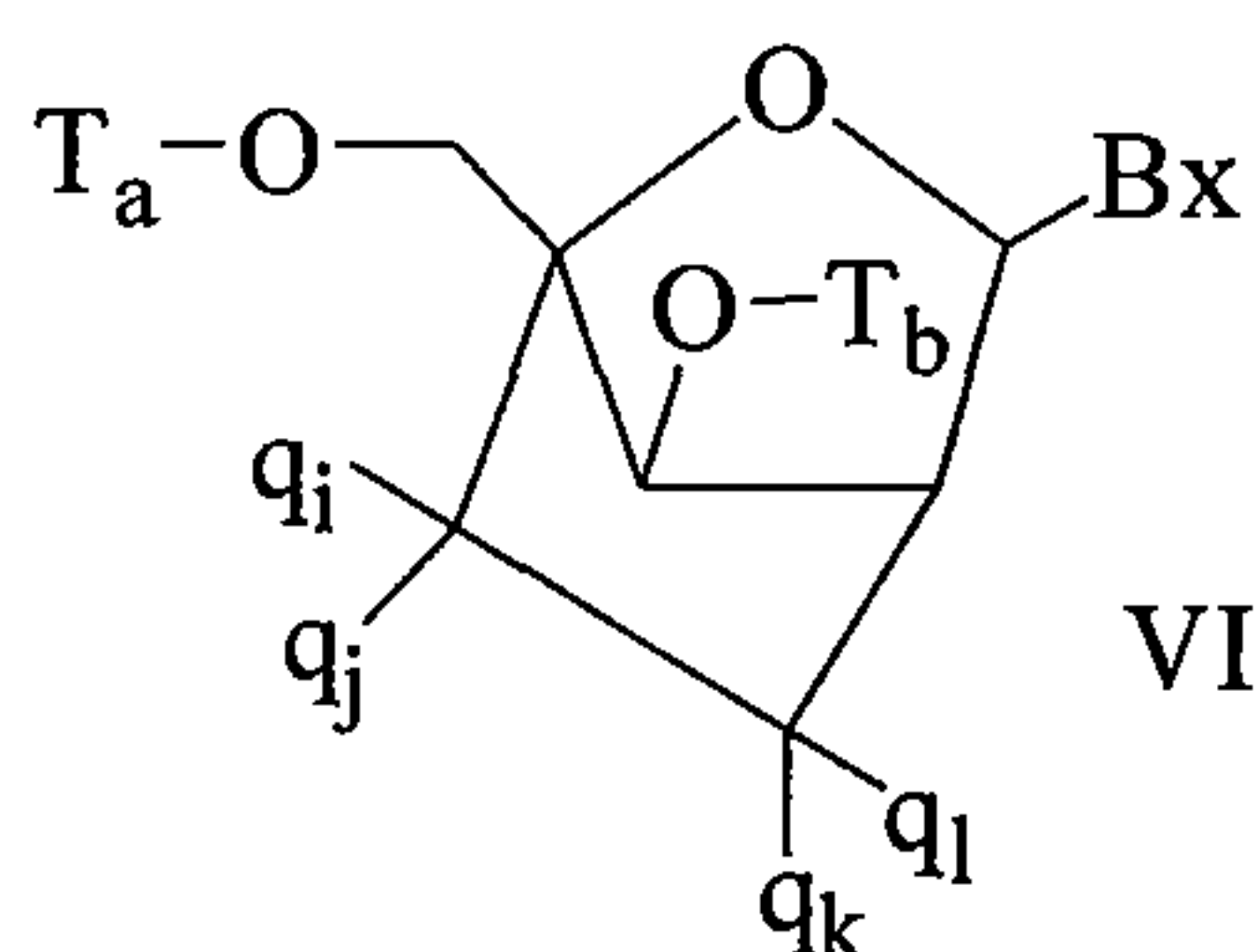
or q_e and q_f together are =C(q_g)(q_h);

q_g and q_h are each, independently, H, halogen, C₁-C₁₂ alkyl or substituted C₁-C₁₂ alkyl.

The synthesis and preparation of the methyleneoxy (4'-CH₂-O-2') BNA monomers adenine, cytosine, guanine, 5-methyl-cytosine, thymine and uracil, along with their oligomerization, and nucleic acid recognition properties have been described (Koshkin et al., *Tetrahedron*, 1998, 54, 3607-3630). BNAs and preparation thereof are also described in WO 98/39352 and WO 99/14226.

Analogues of methyleneoxy (4'-CH₂-O-2') BNA, methyleneoxy (4'-CH₂-O-2') BNA and 2'-thio-BNAs, have also been prepared (Kumar et al., *Bioorg. Med. Chem. Lett.*, 1998, 8, 2219-2222). Preparation of locked nucleoside analogs comprising oligodeoxyribonucleotide duplexes as substrates for nucleic acid polymerases has also been described (Wengel et al., WO 99/14226). Furthermore, synthesis of 2'-amino-BNA, a novel conformationally restricted high-affinity oligonucleotide analog has been described in the art (Singh et al., *J. Org. Chem.*, 1998, 63, 10035-10039). In addition, 2'-Amino- and 2'-methylamino-BNA's have been prepared and the thermal stability of their duplexes with complementary RNA and DNA strands has been previously reported.

In certain embodiments, bicyclic nucleoside having Formula VI:



wherein:

Bx is a heterocyclic base moiety;

T_a and T_b are each, independently H, a hydroxyl protecting group, a conjugate group, a reactive phosphorus group, a phosphorus moiety or a covalent attachment to a support medium;

each q_i, q_j, q_k and q_l is, independently, H, halogen, C₁-C₁₂ alkyl, substituted C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, substituted C₂-C₁₂ alkenyl, C₂-C₁₂ alkynyl, substituted C₂-C₁₂ alkynyl, C₁-C₁₂ alkoxy, substituted C₁-C₁₂ alkoxy, OJ_j, SJ_j, SOJ_j, SO₂J_j, NJ_jJ_k, N₃, CN, C(=O)OJ_j, C(=O)NJ_jJ_k, C(=O)J_j, O-C(=O)NJ_jJ_k, N(H)C(=NH)NJ_jJ_k, N(H)C(=O)NJ_jJ_k or N(H)C(=S)NJ_jJ_k; and

q_i and q_j or q_l and q_k together are =C(q_g)(q_h), wherein q_g and q_h are each, independently, H, halogen, C₁-C₁₂ alkyl or substituted C₁-C₁₂ alkyl.

One carbocyclic bicyclic nucleoside having a 4'-(CH₂)₃-2' bridge and the alkenyl analog bridge 4'-CH=CH-CH₂-2' have been described (Frier *et al.*, *Nucleic Acids Research*, 1997, 25(22), 4429-4443 and Albaek *et al.*, *J. Org. Chem.*, 2006, 71, 7731-7740). The synthesis and preparation of carbocyclic bicyclic nucleosides along with their oligomerization and biochemical studies have also been described (Srivastava *et al.*, *J. Am. Chem. Soc.* 2007, 129(26), 8362-8379).

As used herein, "4'-2' bicyclic nucleoside" or "4' to 2' bicyclic nucleoside" refers to a bicyclic nucleoside comprising a furanose ring comprising a bridge connecting two carbon atoms of the furanose ring connects the 2' carbon atom and the 4' carbon atom of the sugar ring.

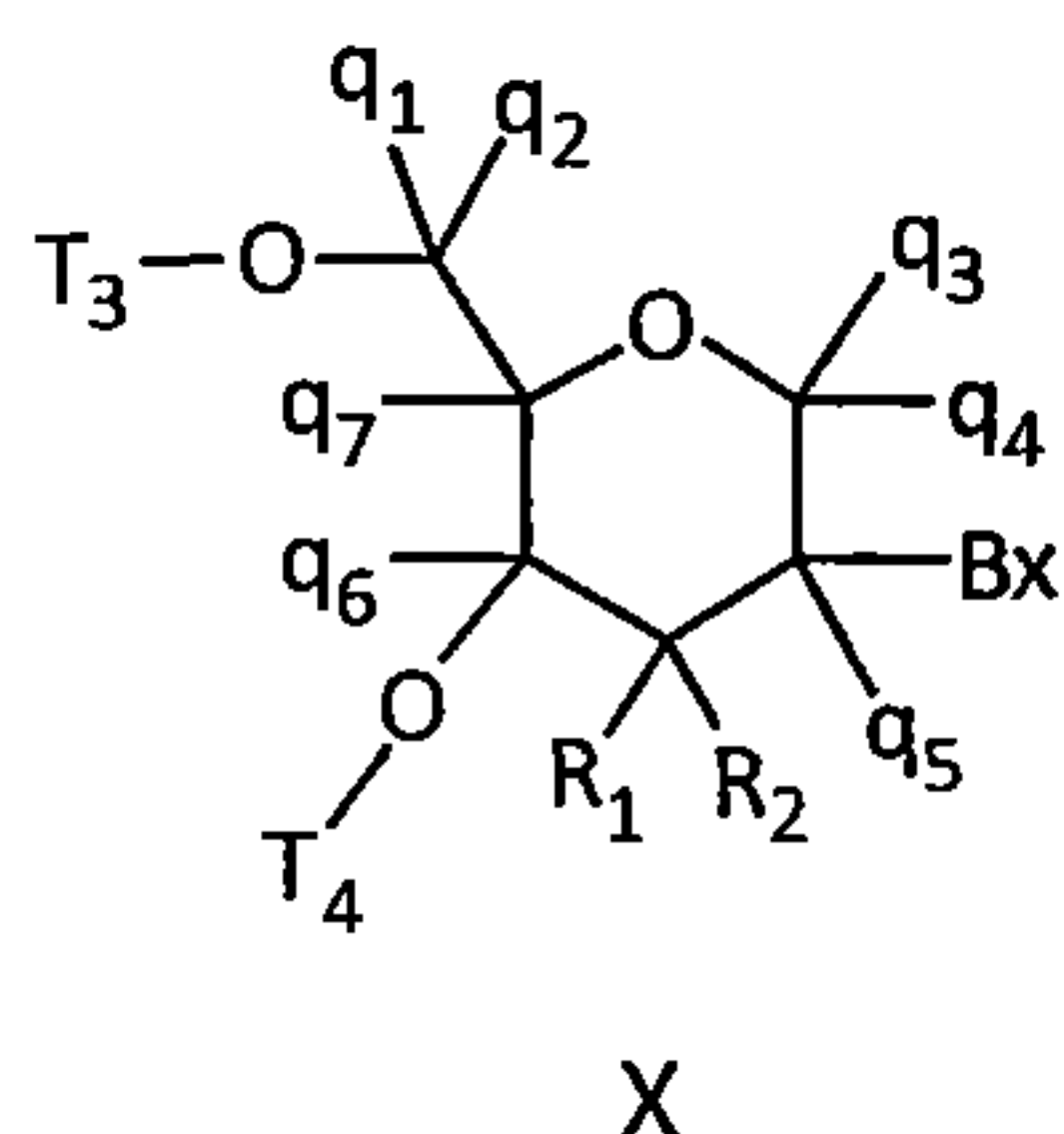
As used herein, "monocyclic nucleosides" refer to nucleosides comprising modified sugar moieties that are not bicyclic sugar moieties. In certain embodiments, the sugar moiety, or sugar moiety analogue, of a nucleoside may be modified or substituted at any position.

As used herein, "2'-modified sugar" means a furanosyl sugar modified at the 2' position. In certain embodiments, such modifications include substituents selected from: a halide, including, but not limited to substituted and unsubstituted alkoxy, substituted and unsubstituted thioalkyl, substituted and unsubstituted amino alkyl, substituted and unsubstituted alkyl, substituted and unsubstituted allyl, and substituted and unsubstituted alkynyl. In certain embodiments, 2'

modifications are selected from substituents including, but not limited to: $O[(CH_2)_nO]_mCH_3$, $O(CH_2)_nNH_2$, $O(CH_2)_nCH_3$, $O(CH_2)_nONH_2$, $OCH_2C(=O)N(H)CH_3$, and $O(CH_2)_nON[(CH_2)_nCH_3]_2$, where n and m are from 1 to about 10. Other 2'-substituent groups can also be selected from: C_1 - C_{12} alkyl, substituted alkyl, alkenyl, alkynyl, alkaryl, aralkyl, O-alkaryl or O-aralkyl, SH, SCH₃, OCN, Cl, Br, CN, CF₃, OCF₃, SOCH₃, SO₂CH₃, ONO₂, NO₂, N₃, NH₂, heterocycloalkyl, heterocycloalkaryl, aminoalkylamino, polyalkylamino, substituted silyl, an RNA cleaving group, a reporter group, an intercalator, a group for improving pharmacokinetic properties, or a group for improving the pharmacodynamic properties of an antisense compound, and other substituents having similar properties. In certain embodiments, modified nucleosides comprise a 2'-MOE side chain (Baker et al., *J. Biol. Chem.*, 1997, 272, 11944-12000). Such 2'-MOE substitution have been described as having improved binding affinity compared to unmodified nucleosides and to other modified nucleosides, such as 2'-O-methyl, O-propyl, and O-aminopropyl. Oligonucleotides having the 2'-MOE substituent also have been shown to be antisense inhibitors of gene expression with promising features for *in vivo* use (Martin, P., *Helv. Chim. Acta*, 1995, 78, 486-504; Altmann et al., *Chimia*, 1996, 50, 168-176; Altmann et al., *Biochem. Soc. Trans.*, 1996, 24, 630-637; and Altmann et al., *Nucleosides Nucleotides*, 1997, 16, 917-926).

As used herein, a "modified tetrahydropyran nucleoside" or "modified THP nucleoside" means a nucleoside having a six-membered tetrahydropyran "sugar" substituted in for the pentofuranosyl residue in normal nucleosides (a sugar surrogate). Modified THP nucleosides include, but are not limited to, what is referred to in the art as hexitol nucleic acid (HNA), anitol nucleic acid (ANA), manitol nucleic acid (MNA) (*see* Leumann, *CJ. Bioorg. & Med. Chem.* (2002) 10:841-854), fluoro HNA (F-HNA) or those compounds having Formula X:

Formula X:



wherein independently for each of said at least one tetrahydropyran nucleoside analog of Formula X:

Bx is a heterocyclic base moiety;

T_3 and T_4 are each, independently, an internucleoside linking group linking the tetrahydropyran nucleoside analog to the antisense compound or one of T_3 and T_4 is an internucleoside linking group linking the tetrahydropyran nucleoside analog to the antisense compound and the other of T_3 and T_4 is H, a hydroxyl protecting group, a linked conjugate group or a 5' or 3'-terminal group;

$q_1, q_2, q_3, q_4, q_5, q_6$ and q_7 are each independently, H, C_1 - C_6 alkyl, substituted C_1 - C_6 alkyl, C_2 - C_6 alkenyl, substituted C_2 - C_6 alkenyl, C_2 - C_6 alkynyl or substituted C_2 - C_6 alkynyl; and

one of R_1 and R_2 is hydrogen and the other is selected from halogen, substituted or unsubstituted alkoxy, NJ_1J_2 , SJ_1 , N_3 , $OC(=X)J_1$, $OC(=X)NJ_1J_2$, $NJ_3C(=X)NJ_1J_2$ and CN, wherein X is O, S or NJ_1 and each J_1, J_2 and J_3 is, independently, H or C_1 - C_6 alkyl.

In certain embodiments, the modified THP nucleosides of Formula X are provided wherein $q_m, q_n, q_p, q_r, q_s, q_t$ and q_u are each H. In certain embodiments, at least one of $q_m, q_n, q_p, q_r, q_s, q_t$ and q_u is other than H. In certain embodiments, at least one of $q_m, q_n, q_p, q_r, q_s, q_t$ and q_u is methyl. In certain embodiments, THP nucleosides of Formula X are provided wherein one of R_1 and R_2 is F. In certain embodiments, R_1 is fluoro and R_2 is H; R_1 is methoxy and R_2 is H, and R_1 is methoxyethoxy and R_2 is H.

As used herein, "2'-modified" or "2'-substituted" refers to a nucleoside comprising a sugar comprising a substituent at the 2' position other than H or OH. 2'-modified nucleosides, include, but are not limited to, bicyclic nucleosides wherein the bridge connecting two carbon atoms of the sugar ring connects the 2' carbon and another carbon of the sugar ring; and nucleosides with non-bridging 2'substituents, such as allyl, amino, azido, thio, O-allyl, O- C_1 - C_{10} alkyl, $-OCF_3$, O- $(CH_2)_2$ -O- CH_3 , 2'-O $(CH_2)_2SCH_3$, O- $(CH_2)_2$ -O-N(R_m)(R_n), or O- CH_2 -C(=O)-N(R_m)(R_n), where each R_m and R_n is, independently, H or substituted or unsubstituted C_1 - C_{10} alkyl. 2'-modified nucleosides may further comprise other modifications, for example at other positions of the sugar and/or at the nucleobase.

As used herein, "2'-F" refers to a nucleoside comprising a sugar comprising a fluoro group at the 2' position.

As used herein, "2'-OMe" or "2'-OCH₃" or "2'-O-methyl" each refers to a nucleoside comprising a sugar comprising an -OCH₃ group at the 2' position of the sugar ring.

As used herein, "MOE" or "2'-MOE" or "2'-OCH₂CH₂OCH₃" or "2'-O-methoxyethyl" each refers to a nucleoside comprising a sugar comprising a -OCH₂CH₂OCH₃ group at the 2' position of the sugar ring.

As used herein, "oligonucleotide" refers to a compound comprising a plurality of linked nucleosides. In certain embodiments, one or more of the plurality of nucleosides is modified. In certain embodiments, an oligonucleotide comprises one or more ribonucleosides (RNA) and/or deoxyribonucleosides (DNA).

Many other bicyclo and tricyclo sugar surrogate ring systems are also known in the art that can be used to modify nucleosides for incorporation into antisense compounds (see for example review article: Leumann, J. C, *Bioorganic & Medicinal Chemistry*, **2002**, *10*, 841-854).

Such ring systems can undergo various additional substitutions to enhance activity.

Methods for the preparations of modified sugars are well known to those skilled in the art.

In nucleotides having modified sugar moieties, the nucleobase moieties (natural, modified or a combination thereof) are maintained for hybridization with an appropriate nucleic acid target.

In certain embodiments, antisense compounds comprise one or more nucleotides having modified sugar moieties. In certain embodiments, the modified sugar moiety is 2'-MOE. In certain embodiments, the 2'-MOE modified nucleotides are arranged in a gapmer motif. In certain embodiments, the modified sugar moiety is a cEt. In certain embodiments, the cEt modified nucleotides are arranged throughout the wings of a gapmer motif.

Modified Nucleobases

Nucleobase (or base) modifications or substitutions are structurally distinguishable from, yet functionally interchangeable with, naturally occurring or synthetic unmodified nucleobases. Both natural and modified nucleobases are capable of participating in hydrogen bonding. Such nucleobase modifications may impart nuclease stability, binding affinity, increased selectivity for an allelic variant, or some other beneficial biological property to antisense compounds. Modified nucleobases include synthetic and natural nucleobases such as, for example, 5-methylcytosine (5-me-C). Certain nucleobase substitutions, including 5-methylcytosine substitutions, are particularly useful for increasing the binding affinity of an antisense compound for a target nucleic acid. For example, 5-methylcytosine substitutions have been shown to increase nucleic acid duplex stability by 0.6-1.2°C (Sanghvi, Y.S., Crooke, S.T. and Lebleu, B., eds., *Antisense Research and Applications*, CRC Press, Boca Raton, **1993**, pp. 276-278).

Additional modified nucleobases include 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-methyl and other alkyl derivatives of adenine and guanine, 2-propyl and other alkyl derivatives of adenine and guanine, 2-thiouracil, 2-thiothymine and 2-

thiocytosine, 5-halouracil and cytosine, 5-propynyl ($-C\equiv C-CH_3$) uracil and cytosine and other alkynyl derivatives of pyrimidine bases, 6-azo uracil, cytosine and thymine, 5-uracil (pseudouracil), 4-thiouracil, 8-halo, 8-amino, 8-thiol, 8-thioalkyl, 8-hydroxyl and other 8-substituted adenines and guanines, 5-halo particularly 5-bromo, 5-trifluoromethyl and other 5-substituted uracils and cytosines, 7-methylguanine and 7-methyladenine, 2-F-adenine, 2-amino-adenine, 8-azaguanine and 8-azaadenine, 7-deazaguanine and 7-deazaadenine and 3-deazaguanine and 3-deazaadenine.

Heterocyclic base moieties may also include those in which the purine or pyrimidine base is replaced with other heterocycles, for example 7-deaza-adenine, 7-deazaguanosine, 2-aminopyridine and 2-pyridone. Nucleobases that are particularly useful for increasing the binding affinity of antisense compounds include 5-substituted pyrimidines, 6-azapyrimidines and N-2, N-6 and O-6 substituted purines, including 2 aminopropyladenine, 5-propynyluracil and 5-propynylcytosine.

In certain embodiments, antisense compounds comprise one or more modified nucleobases. In certain embodiments, gap-widened antisense oligonucleotides comprise one or more modified nucleobases. In certain embodiments, the modified nucleobase is 5-methylcytosine. In certain embodiments, each cytosine is a 5-methylcytosine.

Compositions and Methods for Formulating Pharmaceutical Compositions

Antisense oligonucleotides may be admixed with pharmaceutically acceptable active or inert substances for the preparation of pharmaceutical compositions or formulations. Compositions and methods for the formulation of pharmaceutical compositions are dependent upon a number of criteria, including, but not limited to, route of administration, extent of disease, or dose to be administered.

An antisense compound can be utilized in pharmaceutical compositions by combining the antisense compound with a suitable pharmaceutically acceptable diluent or carrier. A pharmaceutically acceptable diluent includes phosphate-buffered saline (PBS). PBS is a diluent suitable for use in compositions to be delivered parenterally. Accordingly, in one embodiment, employed in the methods described herein is a pharmaceutical composition comprising an antisense compound and a pharmaceutically acceptable diluent. In certain embodiments, the pharmaceutically acceptable diluent is PBS. In certain embodiments, the antisense compound is an antisense oligonucleotide.

Pharmaceutical compositions comprising antisense compounds encompass any pharmaceutically acceptable salts, esters, or salts of such esters, or any other oligonucleotide which, upon administration to an animal, including a human, is capable of providing (directly or indirectly) the biologically active metabolite or residue thereof. Accordingly, for example, the disclosure is also drawn to pharmaceutically acceptable salts of antisense compounds, prodrugs, pharmaceutically acceptable salts of such prodrugs, and other bioequivalents. Suitable pharmaceutically acceptable salts include, but are not limited to, sodium and potassium salts.

A prodrug can include the incorporation of additional nucleosides at one or both ends of an antisense compound which are cleaved by endogenous nucleases within the body, to form the active antisense compound.

Conjugated Antisense Compounds

Antisense compounds may be covalently linked to one or more moieties or conjugates which enhance the activity, cellular distribution, increased selectivity for an allelic variant, or cellular uptake of the resulting antisense oligonucleotides. Typical conjugate groups include cholesterol moieties and lipid moieties. Additional conjugate groups include carbohydrates, phospholipids, biotin, phenazine, folate, phenanthridine, anthraquinone, acridine, fluoresceins, rhodamines, coumarins, and dyes.

Antisense compounds can also be modified to have one or more stabilizing groups that are generally attached to one or both termini of antisense compounds to enhance properties such as, for example, nuclease stability. Included in stabilizing groups are cap structures. These terminal modifications protect the antisense compound having terminal nucleic acid from exonuclease degradation, and can help in delivery and/or localization within a cell. The cap can be present at the 5'-terminus (5'-cap), or at the 3'-terminus (3'-cap), or can be present on both termini. Cap structures are well known in the art and include, for example, inverted deoxy abasic caps. Further 3' and 5'-stabilizing groups that can be used to cap one or both ends of an antisense compound to impart nuclease stability include those disclosed in WO 03/004602 published on January 16, 2003.

Cell culture and antisense compounds treatment

The effects of antisense compounds on the level, activity or expression target nucleic acids can be tested *in vitro* in a variety of cell types. Cell types used for such analyses are available from commercial vendors (e.g. American Type Culture Collection, Manassus, VA; Zen-Bio, Inc.,

Research Triangle Park, NC; Clonetics Corporation, Walkersville, MD) and are cultured according to the vendor's instructions using commercially available reagents (e.g. Invitrogen Life Technologies, Carlsbad, CA). Illustrative cell types include, but are not limited to, HepG2 cells, Hep3B cells, and primary hepatocytes. Illustrative cell lines include GM04281, GM02171, and GM02173B cells.

In vitro testing of antisense oligonucleotides

Described herein are methods for treatment of cells with antisense oligonucleotides, which can be modified appropriately for treatment with other antisense compounds.

In general, cells are treated with antisense oligonucleotides when the cells reach approximately 60-80% confluency in culture.

One reagent commonly used to introduce antisense oligonucleotides into cultured cells includes the cationic lipid transfection reagent LIPOFECTIN (Invitrogen, Carlsbad, CA). Antisense oligonucleotides are mixed with LIPOFECTIN in OPTI-MEM 1 (Invitrogen, Carlsbad, CA) to achieve the desired final concentration of antisense oligonucleotide and a LIPOFECTIN concentration that typically ranges 2 to 12 ug/mL per 100 nM antisense oligonucleotide.

Another reagent used to introduce antisense oligonucleotides into cultured cells includes LIPOFECTAMINE (Invitrogen, Carlsbad, CA). Antisense oligonucleotide is mixed with LIPOFECTAMINE in OPTI-MEM 1 reduced serum medium (Invitrogen, Carlsbad, CA) to achieve the desired concentration of antisense oligonucleotide and a LIPOFECTAMINE concentration that typically ranges 2 to 12 ug/mL per 100 nM antisense oligonucleotide.

Another technique used to introduce antisense oligonucleotides into cultured cells includes electroporation.

Cells are treated with antisense oligonucleotides by routine methods. Cells are typically harvested 16-24 hours after antisense oligonucleotide treatment, at which time RNA or protein levels of target nucleic acids are measured by methods known in the art and described herein. In general, when treatments are performed in multiple replicates, the data are presented as the average of the replicate treatments.

The concentration of antisense oligonucleotide used varies from cell line to cell line. Methods to determine the optimal antisense oligonucleotide concentration for a particular cell line are well known in the art. Antisense oligonucleotides are typically used at concentrations ranging from 1 nM to 300 nM when transfected with LIPOFECTAMINE. Antisense oligonucleotides are

used at higher concentrations ranging from 625 to 20,000 nM when transfected using electroporation.

RNA Isolation

RNA analysis can be performed on total cellular RNA or poly(A)+ mRNA. Methods of RNA isolation are well known in the art. RNA is prepared using methods well known in the art, for example, using the TRIZOL Reagent (Invitrogen, Carlsbad, CA) according to the manufacturer's recommended protocols.

Analysis of inhibition of target levels or expression

Reduction, inhibition, or expression of a target nucleic acid can be assayed in a variety of ways known in the art. For example, target nucleic acid levels can be quantitated by, e.g., Northern blot analysis, competitive polymerase chain reaction (PCR), or quantitative real-time PCR. RNA analysis can be performed on total cellular RNA or poly(A)+ mRNA. Methods of RNA isolation are well known in the art. Northern blot analysis is also routine in the art. Quantitative real-time PCR can be conveniently accomplished using the commercially available ABI PRISM 7600, 7700, or 7900 Sequence Detection System, available from PE-Applied Biosystems, Foster City, CA and used according to manufacturer's instructions.

Quantitative Real-Time PCR Analysis of Target RNA Levels

Quantitation of target RNA levels may be accomplished by quantitative real-time PCR using the ABI PRISM 7600, 7700, or 7900 Sequence Detection System (PE-Applied Biosystems, Foster City, CA) according to manufacturer's instructions. Methods of quantitative real-time PCR are well known in the art.

Prior to real-time PCR, the isolated RNA is subjected to a reverse transcriptase (RT) reaction, which produces complementary DNA (cDNA) that is then used as the substrate for the real-time PCR amplification. The RT and real-time PCR reactions are performed sequentially in the same sample well. RT and real-time PCR reagents are obtained from Invitrogen (Carlsbad, CA). RT real-time-PCR reactions are carried out by methods well known to those skilled in the art.

Gene (or RNA) target quantities obtained by real time PCR are normalized using either the expression level of a gene whose expression is constant, such as cyclophilin A, or by quantifying total RNA using RIBOGREEN (Invitrogen, Inc. Carlsbad, CA). Cyclophilin A expression is

quantified by real time PCR, by being run simultaneously with the target, multiplexing, or separately. Total RNA is quantified using RIBOGREEN RNA quantification reagent (Invetrogen, Inc. Eugene, OR). Methods of RNA quantification by RIBOGREEN are taught in Jones, L.J., et al, (Analytical Biochemistry, 1998, 265, 368-374). A CYTOFLUOR 4000 instrument (PE Applied Biosystems) is used to measure RIBOGREEN fluorescence.

Probes and primers are designed to hybridize to target nucleic acids. Methods for designing real-time PCR probes and primers are well known in the art, and may include the use of software such as PRIMER EXPRESS Software (Applied Biosystems, Foster City, CA).

Analysis of Protein Levels

Reduction, inhibition, or expression of target nucleic acids can be assessed by measuring target protein levels. Target protein levels can be evaluated or quantitated in a variety of ways well known in the art, such as immunoprecipitation, Western blot analysis (immunoblotting), enzyme-linked immunosorbent assay (ELISA), quantitative protein assays, protein activity assays (for example, caspase activity assays), immunohistochemistry, immunocytochemistry or fluorescence-activated cell sorting (FACS). Antibodies directed to a target can be identified and obtained from a variety of sources, such as the MSRS catalog of antibodies (Aerie Corporation, Birmingham, MI), or can be prepared via conventional monoclonal or polyclonal antibody generation methods well known in the art. Antibodies useful for the detection of mouse, rat, monkey, and human proteins are commercially available.

In vivo testing of antisense compounds

Antisense compounds, for example, antisense oligonucleotides, are tested in animals to assess their ability to selectively reduce or inhibit expression of target gene product and produce phenotypic changes, such as, amelioration of a disease symptom. Testing may be performed in normal animals, or in experimental disease models. For administration to animals, antisense oligonucleotides are formulated in a pharmaceutically acceptable diluent, such as phosphate-buffered saline. Administration includes parenteral routes of administration, such as intraperitoneal, intravenous, and subcutaneous. Calculation of antisense oligonucleotide dosage and dosing frequency is within the abilities of those skilled in the art, and depends upon factors such as route of administration and animal body weight. Following a period of treatment with antisense

oligonucleotides, RNA or protein is isolated from tissue and changes in target nucleic acid or protein expression are measured.

Administration

In certain embodiments, the compounds and compositions described herein may be administered in a number of ways depending upon whether local or systemic treatment is desired and upon the area to be treated. Administration may be topical (including ophthalmic, vaginal, rectal, intranasal), oral, pulmonary (including by inhalation or insufflation of powders or aerosols, including by nebulizer; intratracheal, intranasal, epidermal and transdermal) or parenteral, for example, by intravenous drip, intravenous injection or subcutaneous, intraperitoneal, intraocular, intravitreal, or intramuscular injection.

In certain embodiments, the compounds and compositions as described herein are administered parenterally.

In certain embodiments, parenteral administration is by infusion. Infusion can be chronic or continuous or short or intermittent. In certain embodiments, infused pharmaceutical agents are delivered with a pump. In certain embodiments, parenteral administration is by injection.

In certain embodiments, compounds and compositions are delivered to the CNS. In certain embodiments, compounds and compositions are delivered to the cerebrospinal fluid. In certain embodiments, compounds and compositions are administered to the brain parenchyma. In certain embodiments, compounds and compositions are delivered to an animal by intrathecal administration, or intracerebroventricular administration. Broad distribution of compounds and compositions, described herein, within the central nervous system may be achieved with intraparenchymal administration, intrathecal administration, or intracerebroventricular administration.

In certain embodiments, parenteral administration is by injection. The injection may be delivered with a syringe or a pump. In certain embodiments, the injection is a bolus injection. In certain embodiments, the injection is administered directly to a tissue, such as striatum, caudate, cortex, hippocampus and cerebellum.

In certain embodiments, methods of specifically localizing a pharmaceutical agent, such as by bolus injection, decreases median effective concentration (EC₅₀) by a factor of 20, 25, 30, 35, 40, 45 or 50. In certain embodiments, the pharmaceutical agent is an antisense compound as further described herein. In certain embodiments, the targeted tissue is brain tissue. In certain

embodiments the targeted tissue is striatal tissue. In certain embodiments, decreasing EC50 is desirable because it reduces the dose required to achieve a pharmacological result in a patient in need thereof.

In certain embodiments, an antisense oligonucleotide is delivered by injection or infusion once every month, every two months, every 90 days, every 3 months, every 6 months, twice a year or once a year.

Certain Compounds and Indications

Provided herein are compounds and methods that provide potent inhibition and increased selectivity for a mutant allele. Potency is demonstrated by the percent inhibition of mutant mRNA achieved by the antisense oligonucleotides targeting a SNP compared to the percent inhibition of mutant mRNA achieved by the benchmark oligonucleotide. Selectivity is demonstrated by the ability of the antisense oligonucleotide targeting a SNP to inhibit expression of the major allele or mutant allele preferentially compared to the minor allele or wild type allele. The usage of three cell lines with different genotypes at each SNP position have facilitated the determination of design rules that provide for potent and selective SNP targeting antisense oligonucleotides.

In certain embodiments, the compounds are antisense oligonucleotides as further described herein. The antisense oligonucleotides preferentially target a SNP or differentiating polymorphism. Oligonucleotides of various lengths were tested and certain lengths were determined to be beneficial for the targeting of SNPs.

In certain embodiments, the antisense oligonucleotides have a sequence that is 12-30 nucleobases in length. In certain embodiments, the antisense oligonucleotides have a sequence that is 12-25 nucleobases in length. In certain embodiments, the antisense oligonucleotides have a sequence that is 12-21 nucleobases in length. In certain embodiments, the antisense oligonucleotides have a sequence that is 12-20 nucleobases in length. In certain embodiments, the antisense oligonucleotides have a sequence that is 13-20 nucleobases in length. In certain embodiments, the antisense oligonucleotides have a sequence that is 14-20 nucleobases in length. In certain embodiments, the antisense oligonucleotides have a sequence that is 15-20 nucleobases in length. In certain embodiments, the antisense oligonucleotides have a sequence that is 12-19 nucleobases in length. In certain embodiments, the antisense oligonucleotides have a sequence that is 13-19 nucleobases in length. In certain embodiments, the antisense oligonucleotides have a sequence that is 14-19 nucleobases in length. In certain embodiments, the antisense

oligonucleotides have a sequence that is 15-19, nucleobases in length. In certain embodiments, the antisense oligonucleotides have a sequence that is 16-19 nucleobases in length. In certain embodiments, the antisense oligonucleotides have a sequence that is 17-19 nucleobases in length. In certain embodiments, the antisense oligonucleotides have a sequence that is 12, 13, 14, 15, 16, 17, 18, 19, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30 nucleobases in length.

For oligonucleotides of various lengths, the position of the nucleoside complementary to the SNP position was shifted within the gap and the wings and the effect was tested. Certain positions within the antisense oligonucleotide are shown to be beneficial for targeting SNPs.

In certain embodiments, the antisense oligonucleotide is at least 12, at least 13, at least 14, at least 15, at least 16, at least 17 at least 18 or at least 19 nucleobases in length and the SNP is complementary to positions 6-15 counting from the 5' terminus of the antisense oligonucleotide and/or positions 1-9 counting from the 5' end of the gap. In certain embodiments, the antisense oligonucleotide is at least 12, at least 13, at least 14, at least 15, at least 16, at least 17 at least 18 or at least 19 nucleobases in length and the SNP is complementary to positions 8-14 counting from the 5' terminus of the antisense oligonucleotide and/or positions 1-9 counting from the 5' end of the gap. In certain embodiments, the antisense oligonucleotide is at least 12, at least 13, at least 14, at least 15, at least 16, at least 17 at least 18 or at least 19 nucleobases in length and the SNP is complementary to positions 8-14 counting from the 5' terminus of the antisense oligonucleotide and/or positions 4-7 counting from the 5' end of the gap. In certain embodiments, the antisense oligonucleotide is at least 12, at least 13, at least 14, at least 15, at least 16, at least 17 at least 18 or at least 19 nucleobases in length and the SNP is complementary to positions 8-10 counting from the 5' terminus of the antisense oligonucleotide and/or positions 4-6 counting from the 5' end of the gap.

In certain embodiments, the SNP is complementary to position 8, 9, or 10 counting from the 5' terminus of the oligonucleotide or position 4, 5, or 6, counting from the 5' end of the gap. For oligonucleotides of various lengths, the effect of the length of the gap, 5' wing, and 3' wing was tested.

Certain wing-gap-wing combinations were shown to be beneficial for a SNP targeting antisense oligonucleotide. In certain embodiments the gap is 7-11 nucleobases in length and each wing is independently 1-6 nucleobases in length. In certain embodiments the gap is 7-11 nucleobases in length and each wing is independently 2-6 nucleobases in length. In certain embodiments the gap is 8-11 nucleobases in length and each wing is independently 2-6 nucleobases in length. In certain embodiments the gap is 9-11 nucleobases in length and each wing is

independently 2-6 nucleobases in length. In certain embodiments the gap is 9 nucleobases in length and each wing is independently 2-6 nucleobases in length. In certain embodiments the gap is 10 nucleobases in length and each wing is independently 2-6 or 4-5 nucleobases in length. In certain embodiments the gap is 11 nucleobases in length and each wing is independently 2-6, or 4-5 nucleobases in length. In certain embodiments, the wing-gap-wing configuration is one of 4-7-4, 5-8-6, 6-8-5, 6-7-6, 5-7-5, 6-8-5, 5-8-6, 3-9-4, 4-9-3, 2-9-6, 6,9,2,3-9-3, 3-9-5, 5-9-3, 5-9-4, 4-9-5, 5-9-5, 4-11-4, 4-10-5 and 5-10-4.

For oligonucleotides of various lengths, the effect of certain chemistries was tested. Certain chemistry modifications were shown to be beneficial for a SNP targeting antisense oligonucleotide. In certain embodiments, each nucleoside of each wing of the modified antisense oligonucleotide has a 2'-MOE modification. In certain embodiments, each nucleoside of each wing of the modified antisense oligonucleotide has a high affinity modification. In certain embodiments, the antisense oligonucleotide is a mixed wing gapmer. In such embodiment, the modifications and combination of modifications at the 3' wing and at the 5' wing may be the same or they may be different. In certain embodiments, the antisense oligonucleotide has one or more 2'-MOE modifications in the wings and/or one or more high affinity modifications in the wings. In certain embodiments, the high affinity modification is a cEt modification. In certain embodiments, the antisense oligonucleotide has a high affinity modification at positions 2, 3, 13, and 14 of the antisense oligonucleotide (counting from the 5' terminus). In certain embodiments, the antisense oligonucleotide has one, two, three, or four high affinity modifications in at least one of the wings. In certain embodiments, the antisense oligonucleotide has one, two, three, or four high affinity modifications in each of the 5' and 3' wings independently. In certain embodiments, the antisense oligonucleotide has a high affinity modification at positions 2 and 3 in one or both of the 5' and 3' wings (counting from the 5' terminus of the 5' wing and the 3' terminus of the 3' wing). In certain embodiments, the antisense oligonucleotide has a high affinity modification at positions 2, 3 and 4 in one or both of the 5' and 3' wings (counting from the 5' terminus of the 5' wing and the 3' terminus of the 3' wing). In certain embodiments, the antisense oligonucleotide has a high affinity modification at positions 1 of the 5' and/or 3' wings (counting from the 5' terminus of the 5' wing and the 3' terminus of the 3' wing). In certain embodiments, the antisense oligonucleotide has a high affinity modification at positions 1 of the 5' and 3' wings (counting from the 5' terminus of the 5' wing and the 3' terminus of the 3' wing) and at least one other position in the wing. In certain

embodiments, the antisense oligonucleotide has alternating 2'-MOE and high affinity modification in at least one of the 5' and 3' wings.

In certain embodiments, the compound comprises an antisense oligonucleotide incorporating one or more of the design rules provided above.

In certain embodiments, the compound comprises a modified antisense oligonucleotide consisting of 12 to 30 linked nucleosides, fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein the single nucleotide polymorphism aligns with any one of positions 6-15 beginning from the 5' terminus of the antisense oligonucleotide or positions 1-9 beginning from the 5' end of the gap of the modified antisense oligonucleotide; and wherein each nucleoside of each wing has a modified sugar or sugar surrogate. In certain embodiments the single nucleotide polymorphism site contains a differentiating polymorphism. In certain embodiments, the single nucleotide polymorphism site is on a mutant allele. In certain embodiments, the mutant allele is associated with disease. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 4-7-4, 5-8-6, 6-8-5, 6-7-6, 5-7-5, 6-8-5, 5-8-6, 3-9-4, 4-9-3, 2-9-6, 6,9,2,3-9-3, 3-9-5,5-9-3, 5-9-4, 4-9-5, 5-9-5, 4-11-4,4-10-5 and 5-10-4.

In certain embodiments, the compound comprises a modified antisense oligonucleotide consisting of 12 to 20 linked nucleosides, fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein the single nucleotide polymorphism aligns with any one of positions 6-15 beginning from the 5' terminus of the antisense oligonucleotide or positions 1-9 beginning from the 5' end of the gap of the modified antisense oligonucleotide; and wherein each nucleoside of each wing has a modified sugar or sugar surrogate. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 4-7-4, 5-8-6, 6-8-5, 6-7-6, 5-7-5, 6-8-5, 5-8-6, 3-9-4, 4-9-3, 2-9-6, 6,9,2,3-9-3, 3-9-5,5-9-3, 5-9-4, 4-9-5, 5-9-5, 4-11-4,4-10-5 and 5-10-4.

In certain embodiments, the compound comprises a modified antisense oligonucleotide consisting of 12 to 20 linked nucleosides, fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein the single nucleotide polymorphism aligns with any one of positions 8-14 beginning from the 5' terminus of the antisense oligonucleotide or positions 1-9 beginning from the 5' end of the gap of the modified antisense oligonucleotide; and wherein each nucleoside of each wing has a modified sugar or sugar surrogate. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 4-

7-4, 5-8-6, 6-8-5, 6-7-6, 5-7-5. 6-8-5, 5-8-6, 3-9-4, 4-9-3, 2-9-6, 6,9,2,3-9-3, 3-9-5,5-9-3, 5-9-4, 4-9-5, 5-9-5, 4-11-4,4-10-5 and 5-10-4.

In certain embodiments, the compound comprises a modified antisense oligonucleotide consisting of 12 to 20 linked nucleosides, fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein the single nucleotide polymorphism aligns with any one of positions 8-14 beginning from the 5' terminus of the antisense oligonucleotide or positions 4-7 beginning from the 5' end of the gap of the modified antisense oligonucleotide; and wherein each nucleoside of each wing has a modified sugar or sugar surrogate. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 4-7-4, 5-8-6, 6-8-5, 6-7-6, 5-7-5. 6-8-5, 5-8-6, 3-9-4, 4-9-3, 2-9-6, 6,9,2,3-9-3, 3-9-5,5-9-3, 5-9-4, 4-9-5, 5-9-5, 4-11-4,4-10-5 and 5-10-4.

In certain embodiments, the compound comprises a modified antisense oligonucleotide consisting of 12 to 20 linked nucleosides, fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein the single nucleotide polymorphism aligns with any one of positions 8-10 beginning from the 5' terminus of the antisense oligonucleotide or positions 4-6 beginning from the 5' end of the gap of the modified antisense oligonucleotide; and wherein each nucleoside of each wing has a modified sugar or sugar surrogate. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 4-7-4, 5-8-6, 6-8-5, 6-7-6, 5-7-5. 6-8-5, 5-8-6, 3-9-4, 4-9-3, 2-9-6, 6,9,2,3-9-3, 3-9-5,5-9-3, 5-9-4, 4-9-5, 5-9-5, 4-11-4,4-10-5 and 5-10-4.

In certain embodiments, the compound comprises a modified antisense oligonucleotide consisting of 12 to 19 linked nucleosides, fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein the single nucleotide polymorphism aligns with any one of positions 8-10 beginning from the 5' terminus of the antisense oligonucleotide or positions 4-6 beginning from the 5' end of the gap of the modified antisense oligonucleotide; and wherein each nucleoside of each wing has a modified sugar or sugar surrogate. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 4-7-4, 5-8-6, 6-8-5, 6-7-6, 5-7-5. 6-8-5, 5-8-6, 3-9-4, 4-9-3, 2-9-6, 6,9,2,3-9-3, 3-9-5,5-9-3, 5-9-4, 4-9-5, 5-9-5, 4-11-4,4-10-5 and 5-10-4.

In certain embodiments, the compound comprises a modified antisense oligonucleotide consisting of 13 to 19 linked nucleosides, fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein the

single nucleotide polymorphism aligns with any one of positions 8-10 beginning from the 5' terminus of the antisense oligonucleotide or positions 4-6 beginning from the 5' end of the gap of the modified antisense oligonucleotide; and wherein each nucleoside of each wing has a modified sugar or sugar surrogate. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 4-7-4, 5-8-6, 6-8-5, 6-7-6, 5-7-5, 6-8-5, 5-8-6, 3-9-4, 4-9-3, 2-9-6, 6,9,2,3-9-3, 3-9-5,5-9-3, 5-9-4, 4-9-5, 5-9-5, 4-11-4,4-10-5 and 5-10-4.

In certain embodiments, the compound comprises a modified antisense oligonucleotide consisting of 14 to 19 linked nucleosides, fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein the single nucleotide polymorphism aligns with any one of positions 8-10 beginning from the 5' terminus of the antisense oligonucleotide or positions 4-6 beginning from the 5' end of the gap of the modified antisense oligonucleotide; and wherein each nucleoside of each wing has a modified sugar or sugar surrogate. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 4-7-4, 5-8-6, 6-8-5, 6-7-6, 5-7-5, 6-8-5, 5-8-6, 3-9-4, 4-9-3, 2-9-6, 6,9,2,3-9-3, 3-9-5,5-9-3, 5-9-4, 4-9-5, 5-9-5, 4-11-4,4-10-5 and 5-10-4.

In certain embodiments, the compound comprises a modified antisense oligonucleotide consisting of 15 to 19 linked nucleosides, fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein the single nucleotide polymorphism aligns with any one of positions 6-15 beginning from the 5' terminus of the antisense oligonucleotide or positions 1-9 beginning from the 5' end of the gap of the modified antisense oligonucleotide; and wherein each nucleoside of each wing has a modified sugar or sugar surrogate. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 4-7-4, 5-8-6, 6-8-5, 6-7-6, 5-7-5, 6-8-5, 5-8-6, 3-9-4, 4-9-3, 2-9-6, 6,9,2,3-9-3, 3-9-5,5-9-3, 5-9-4, 4-9-5, 5-9-5, 4-11-4,4-10-5 and 5-10-4.

In certain embodiments, the compound comprises a modified antisense oligonucleotide consisting of 15 to 19 linked nucleosides, fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein the single nucleotide polymorphism aligns with any one of positions 8-10 beginning from the 5' terminus of the antisense oligonucleotide or positions 4-6 beginning from the 5' end of the gap of the modified antisense oligonucleotide; and wherein each nucleoside of each wing has a modified sugar or sugar surrogate. In certain embodiments, the wing-gap-wing motif is any one of the group

consisting of 4-7-4, 5-8-6, 6-8-5, 6-7-6, 5-7-5, 6-8-5, 5-8-6, 3-9-4, 4-9-3, 2-9-6, 6,9,2,3-9-3, 3-9-5,5-9-3, 5-9-4, 4-9-5, 5-9-5, 4-11-4,4-10-5 and 5-10-4.

In certain embodiments, the compound comprises a modified antisense oligonucleotide consisting of 15 to 19 linked nucleosides, fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein position 6, 8, 9, 10, 11, or 14 beginning from the 5' terminus of the modified antisense oligonucleotide aligns with the single nucleotide polymorphism; and wherein each nucleoside of each wing segment modified sugar or sugar surrogate. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 2-9-6, 3-9-3, 3-9-5, 4-9-5, 4-11-4, and 5-10-4.

In certain embodiments, the compound comprises a modified antisense oligonucleotide consisting of 15 to 19 linked nucleosides, fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein position 1, 4, 5, 6, 7, or 9 of the gap segment aligns with the single nucleotide polymorphism; and wherein each nucleoside of each wing segment has a modified sugar or sugar surrogate. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 2-9-6, 3-9-3, 3-9-5, 4-9-5, 4-11-4, and 5-10-4.

In certain embodiments, the compound comprises a modified antisense oligonucleotide consisting of 15 to 19 linked nucleosides, fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein position 6, 7, 8, 9, 10, 11, or 12 of the modified antisense oligonucleotide aligns with the single nucleotide polymorphism; and positions 2 and 3 of the 5' and 3' wing segments comprise a 4'-CH(CH₃)-O-2' bridge. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 2-9-6, 3-9-3, 3-9-5, 4-9-5, 4-11-4, and 5-10-4.

In certain embodiments, the compound comprises a modified antisense oligonucleotide consisting of 15 to 19 linked nucleosides and fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein position 3, 4, 5, 6, 7, 8 or 9 of the gap segment aligns with the single nucleotide polymorphism; and positions 2 and 3 of the 5' and 3' wing segments comprise a 4'-CH(CH₃)-O-2' bridge. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 2-9-6, 3-9-3, 3-9-5, 4-9-5, 4-11-4, and 5-10-4.

A compound comprising a modified antisense oligonucleotide consisting of 15 to 19 linked nucleosides and fully complementary to a single nucleotide polymorphism site, wherein the

modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein position 6, 7, 8, 9, 10, 11, or 12 of the modified antisense oligonucleotide aligns with the single nucleotide polymorphism; and positions 2, 3, 13, and 14 of the antisense oligonucleotide comprise a 4'-CH(CH₃)-O-2' bridge.. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 2-9-6, 3-9-3, 3-9-5, 4-9-5, 4-11-4, and 5-10-4.

A compound comprising a modified antisense oligonucleotide consisting of 15 to 19 linked nucleosides and fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein position 3, 4, 5, 6, 7, 8, or 9 of the gap segment aligns with the single nucleotide polymorphism; and positions 2, 3, 13, and 14 of the antisense oligonucleotide comprise a 4'-CH(CH₃)-O-2' bridge. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 2-9-6, 3-9-3, 3-9-5, 4-9-5, 4-11-4, and 5-10-4.

In certain embodiments, the compound comprise a modified antisense oligonucleotide consisting of 17 to 19 linked nucleosides, fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein position 8, 9, or 10 of the modified antisense oligonucleotide aligns with the single nucleotide polymorphism; and wherein each nucleoside of each wing segment comprises a 2'-O-methoxyethyl sugar. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 2-9-6, 3-9-3, 3-9-5, 4-9-5, 4-11-4, and 5-10-4.

In certain embodiments, the compound comprises a modified antisense oligonucleotide consisting of 17 to 19 linked nucleosides, fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein position 5, 6, or 7 of the gap segment aligns with the single nucleotide polymorphism; and wherein each nucleoside of each wing segment comprises a 2'-O-methoxyethyl sugar. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 2-9-6, 3-9-3, 3-9-5, 4-9-5, 4-11-4, and 5-10-4.

In certain embodiments, the compound comprises a modified antisense oligonucleotide consisting of 17 to 19 linked nucleosides, fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein position 8, 9, or 10 of the modified antisense oligonucleotide aligns with the single nucleotide polymorphism; and positions 2 and 3 of the 5' and 3' wing segments comprise a 4'-CH(CH₃)-O-2'

bridge. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 2-9-6, 3-9-3, 3-9-5, 4-9-5, 4-11-4, and 5-10-4.

In certain embodiments, the compound comprises a modified antisense oligonucleotide consisting of 17 to 19 linked nucleosides and fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein position 5, 6, or 7 of the gap segment aligns with the single nucleotide polymorphism; and positions 2 and 3 of the 5' and 3' wing segments comprise a 4'-CH(CH₃)-O-2' bridge. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 2-9-6, 3-9-3, 3-9-5, 4-9-5, 4-11-4, and 5-10-4.

A compound comprising a modified antisense oligonucleotide consisting of 17 to 19 linked nucleosides and fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein position 8, 9, or 10 of the modified oligonucleotide aligns with the single nucleotide polymorphism; and positions 2, 3, 13, and 14 of the antisense oligonucleotide comprise a 4'-CH(CH₃)-O-2' bridge.. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 2-9-6, 3-9-3, 3-9-5, 4-9-5, 4-11-4, and 5-10-4.

A compound comprising a modified antisense oligonucleotide consisting of 17 to 19 linked nucleosides and fully complementary to a single nucleotide polymorphism site, wherein the modified antisense oligonucleotide comprises a wing-gap-wing motif, wherein position 5, 6, or 7 of the gap segment aligns with the single nucleotide polymorphism; and positions 2, 3, 13, and 14 of the antisense oligonucleotide comprise a 4'-CH(CH₃)-O-2' bridge. In certain embodiments, the wing-gap-wing motif is any one of the group consisting of 2-9-6, 3-9-3, 3-9-5, 4-9-5, 4-11-4, and 5-10-4.

In a certain embodiment, the antisense oligonucleotide is 11 to 20 linked nucleosides in length and has, independently, 2 to 5 linked nucleosides in the 5' and 3' wings and 7 to 11 linked nucleosides in the gap. The SNP is complementary to position 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 of the antisense oligonucleotide (counting from the 5' terminus of the antisense oligonucleotide) or position 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 counting from the 5' terminus of the gap segment.

In a certain embodiment, the antisense oligonucleotide is 15 to 19 linked nucleosides in length and has, independently, 2 to 5 linked nucleosides in the 5' and 3' wings and 7 to 11 linked nucleosides in the gap. The SNP is complementary to position 6, 7, 8, 9, or 10 of the antisense

oligonucleotide (counting from the 5' terminus of the antisense oligonucleotide) or position 4, 5, 6, or 7 counting from the 5' terminus of the gap segment.

In a certain embodiment, the antisense oligonucleotide is 17 linked nucleosides in length and has, independently, 2 to 5 linked nucleosides in the 5' and 3' wing segments and 9 to 11 linked nucleosides in the gap segment. The SNP is complementary to position 8, 9, or 10 of the antisense oligonucleotide (counting from the 5' terminus of the antisense oligonucleotide) or position 5, 6, or 7 (counting from the 5' terminus of the gap segment).

In a certain embodiment, the antisense oligonucleotide is 18 linked nucleosides in length and has, independently, 2 to 5 linked nucleosides in the 5' and 3' wing segments and 9 to 11 linked nucleosides in the gap segment. The SNP is complementary to position 8, 9, or 10 of the antisense oligonucleotide (counting from the 5' terminus of the antisense oligonucleotide) or position 5, 6, or 7 (counting from the 5' terminus of the gap segment).

In a certain embodiment, the antisense oligonucleotide is 19 linked nucleosides in length and has, independently, 2 to 5 linked nucleosides in the 5' and 3' wing segments and 9 to 11 linked nucleosides in the gap segment. The SNP is complementary to position 8, 9, or 10 of the antisense oligonucleotide (counting from the 5' terminus of the antisense oligonucleotide) or position 5, 6, or 7 (counting from the 5' terminus of the gap segment).

In certain embodiments, the invention provides methods of treating an individual comprising administering one or more pharmaceutical compositions described herein. In certain embodiments, the individual has an allelic variant associated with a disease or disorder. The pharmaceutical compositions provided herein preferentially target a SNP. In certain embodiments, the SNP is a differentiating polymorphism.

Methods have been described for determining whether a SNP is specific to a disease associated allele and more specifically whether a SNP variant of an allele of a heterozygous patient is on the same allele as a disease-causing mutation that is at a remote region of the gene's mRNA (WO 2008/147930 and WO 2008/143774).

Diseases associated with SNPs have been described for certain genes. In certain embodiments, the gene and associated disease are any of the following: APP gene encoding amyloid precursor protein involved in Alzheimer's disease (Gene, 371: 68, 2006); the PrP gene encoding prion protein involved in Creutzfeldt-Jakob disease and in fatal familial insomnia (Nat. Med. 1997, 3: 1009); GFAP gene encoding glial fibrillary acidic protein involved in Alexander disease (J. Neurosci. 2006, 26:111623); alpha-synuclein gene encoding alpha-synuclein protein involved in

Parkinson's disease (J. Clin. Invest. 2003, 111: 145); SOD-1 gene encoding the SOD-1 protein involved in amyotrophic lateral sclerosis (Science 1998, 281: 1851); atrophin-1 gene encoding atrophin-1 protein involved in dentato-rubral and pallido-luysian atrophy (DRPA) (Trends Mol. Med. 2001, 7: 479); SCA1 gene encoding ataxin-1 protein involved in spino-cerebellar ataxia-1 (SCA1) (Protein Sci. 2003, 12: 953); PLP gene encoding proteolipid protein involved in Pelizaeus-Merzbacher disease (NeuroMol Med. 2007, 4: 73); DYT1 gene encoding torsinA protein involved in Torsion dystonia (Brain Res. 2000, 877: 379); and alpha-B crystalline gene encoding alpha-B crystalline protein involved in protein aggregation diseases, including cardiomyopathy (Cell 2007, 130: 427); alpha1-antitrypsin gene encoding alpha1-antitrypsin protein involved in chronic obstructive pulmonary disease (COPD), liver disease and hepatocellular carcinoma (New Engl J Med. 2002, 346: 45); Ltk gene encoding leukocyte tyrosine kinase protein involved in systemic lupus erythematosus (Hum. Mol. Gen. 2004, 13: 171); PCSK9 gene encoding PCSK9 protein involved in hypercholesterolemia (Hum Mutat. 2009, 30: 520); prolactin receptor gene encoding prolactin receptor protein involved in breast tumors (Proc. Natl. Assoc. Sci. 2008, 105: 4533); CCL5 gene encoding the chemokine CCL5 involved in COPD and asthma (Eur. Respir. J. 2008, 32: 327); PTPN22 gene encoding PTPN22 protein involved in Type 1 diabetes, Rheumatoid arthritis, Graves disease, and SLE (Proc. Natl. Assoc. Sci. 2007, 104: 19767); androgen receptor gene encoding the androgen receptor protein involved in spinal and bulbar muscular atrophy or Kennedy's disease (J Steroid Biochem. Mol. Biol. 2008, 108: 245); CHMP4B gene encoding chromatin modifying protein-4B involved in progressive childhood posterior subcapsular cataracts (Am. J. Hum. Genet 2007, 81: 596); FXR / NR1H4 gene encoding Farnesoid X receptor protein involved in cholesterol gallstone disease, atherosclerosis and diabetes (Mol. Endocrinol. 2007, 21: 1769); ABCA1 gene encoding ABCA1 protein involved in cardiovascular disease (Transl. Res. 2007, 149: 205); CaSR gene encoding the calcium sensing receptor protein involved in primary hypercalciuria (Kidney Int. 2007, 71: 1155); alpha-globin gene encoding alpha-globin protein involved in alpha-thalassemia (Science 2006, 312: 1215); httlpr gene encoding HTTLPR protein involved in obsessive compulsive disorder (Am. J. Hum. Genet. 2006, 78: 815); AVP gene encoding arginine vasopressin protein in stress-related disorders such as anxiety disorders and comorbid depression (CNS Neurol. Disord. Drug Targets 2006, 5: 167); GNAS gene encoding G proteins involved in congenital visual defects, hypertension, metabolic syndrome (Trends Pharmacol. Sci. 2006, 27: 260); APAF1 gene encoding APAF1 protein involved in a predisposition to major depression (Mol. Psychiatry 2006, 11: 76); TGF-beta1 gene encoding TGF-beta1 protein involved in breast cancer and prostate cancer (Cancer

Epidemiol. Biomarkers Prev. 2004, 13: 759); AChR gene encoding acetylcholine receptor involved in congenital myasthenic syndrome (Neurology 2004, 62: 1090); P2Y12 gene encoding adenosine diphosphate (ADP) receptor protein involved in risk of peripheral arterial disease (Circulation 2003, 108: 2971); LQT1 gene encoding LQT1 protein involved in atrial fibrillation (Cardiology 2003, 100: 109); RET protooncogene encoding RET protein involved in sporadic pheochromocytoma (J. Clin. Endocrinol. Metab. 2003, 88: 4911); filamin A gene encoding filamin A protein involved in various congenital malformations (Nat. Genet. 2003, 33: 487); TARDBP gene encoding TDP-43 protein involved in amyotrophic lateral sclerosis (Hum. Mol. Gene.t 2010, 19: 671); SCA3 gene encoding ataxin-3 protein involved in Machado-Joseph disease (PLoS One 2008, 3: e3341); SCA7 gene encoding ataxin-7 protein involved in spino-cerebellar ataxia-7 (PLoS One 2009, 4: e7232); *HTT* gene encoding huntingtin protein involved in Huntington's disease (Neurobiol Dis. 1996, 3:183); and the CA4 gene encoding carbonic anhydrase 4 protein, CRX gene encoding cone-rod homeobox transcription factor protein, FSCN2 gene encoding retinal fascin homolog 2 protein, IMPDH1 gene encoding inosine monophosphate dehydrogenase 1 protein, NR2E3 gene encoding nuclear receptor subfamily 2 group E3 protein, NRL gene encoding neural retina leucine zipper protein, PRPF3 (RP18) gene encoding pre-mRNA splicing factor 3 protein, PRPF8 (RP13) gene encoding pre-mRNA splicing factor 8 protein, PRPF31 (RP11) gene encoding pre-mRNA splicing factor 31 protein, RDS gene encoding peripherin 2 protein, ROM1 gene encoding rod outer membrane protein 1 protein, RHO gene encoding rhodopsin protein, RP1 gene encoding RP1 protein, RPGR gene encoding retinitis pigmentosa GTPase regulator protein, all of which are involved in Autosomal Dominant Retinitis Pigmentosa disease (Adv Exp Med Biol. 2008, 613:203)

In certain embodiments, the disease is a neurodegenerative disorder. In certain embodiments, the neurodegenerative disorder is Huntington's Disease. In certain embodiments, the targeted SNP is one or more of: rs6446723, rs3856973, rs2285086, rs363092, rs916171, rs6844859, rs7691627, rs4690073, rs2024115, rs11731237, rs362296, rs10015979, rs7659144, rs363096, rs362273, rs16843804, rs362271, rs362275, rs3121419, rs362272, rs3775061, rs34315806, rs363099, rs2298967, rs363088, rs363064, rs363102, rs2798235, rs363080, rs363072, rs363125, rs362303, rs362310, rs10488840, rs362325, rs35892913, rs363102, rs363096, rs11731237, rs10015979, rs363080, rs2798235, rs1936032, rs2276881, rs363070, rs35892913, rs12502045, rs6446723, rs7685686, rs3733217, rs6844859, rs362331, rs1143646, rs2285086, rs2298969, rs4690072, rs916171, rs3025849, rs7691627, rs4690073, rs3856973, rs363092, rs362310, rs362325, rs363144, rs362303, rs34315806, rs363099, rs363081, rs3775061, rs2024115, rs10488840,

rs363125, rs362296, rs2298967, rs363088, rs363064, rs362275, rs3121419, rs3025849, rs363070, rs362273, rs362272, rs362306, rs362271, rs363072, rs16843804, rs7659144, rs363120, and rs12502045. In certain embodiments the compounds are ISIS460065, ISIS 459978, ISIS 460028, ISIS 460209, ISIS 460208, and ISIS 460206.

Therapeutically Effective Dosages

In certain embodiments, administration of a therapeutically effective amount of an antisense compound targeted to the mutant huntingtin allele is accompanied by monitoring of expression of a gene product in an individual, to determine an individual's response to administration of the antisense compound. In certain embodiments, the gene product is huntingtin mRNA or protein. An individual's response to administration of the antisense compound is used by a physician to determine the amount and duration of therapeutic intervention.

In certain embodiments, administration of an antisense compound targeted to a mutant nucleic acid results in reduction of mRNA or protein expression by at least 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95 or 99%, or a range defined by any two of these values. In certain embodiments, the mutant nucleic acid is huntingtin nucleic acid, the mRNA is huntingtin mRNA, and the protein is huntingtin protein.

In certain embodiments, pharmaceutical compositions comprising an antisense compound targeted to a mutant allele are used for the preparation of a medicament for treating a patient suffering or susceptible to any of Huntington's Disease, Alzheimer's Disease, Crutzfeldt-Jakob Disease, Fatal Familial Insomnia, Huntington's Disease, Alexander Disease, Parkinson's Disease, Amyotrophic Lateral Sclerosis (ALS), Dentato-Rubral and Pallido-Luysian Atrophy, Spino-Cerebellar Ataxia 1, Pelizaeus-Merzbacher Disease, Torsion Dystonia, Cardiomyopathy, Chronic Obstructive Pulmonary Disease (COPD), liver disease and hepatocellular carcinoma, SLE, Hypercholesterolemia, breast tumors, Asthma, Type 1 Diabetes, Rheumatoid Arthritis, Graves Disease, Spinal and Bulbar Muscular Atrophy, Kennedy's Disease, progressive childhood posterior subcapsular cataracts, Cholesterol Gallstone Disease, Arthrosclerosis, cardiovascular disease, primary hypercalciuria, alpha-thalassemia, OCD, stress-related disorders (including anxiety disorders and comorbid depression), congenital visual defects, hypertension, metabolic syndrome, major depression, breast cancer, prostate cancer, congenital myasthenic syndrome, peripheral arterial syndrome, atrial fibrillation, sporadic pheochromocytoma, congenital malformations, NJD, SCA7, and autosomal dominant retinitis pigmentosa adRP.

Certain Combination Therapies

In certain embodiments, one or more pharmaceutical compositions of the present invention are co-administered with one or more other pharmaceutical agents. In certain embodiments, such one or more other pharmaceutical agents are designed to treat the same disease, disorder, or condition as the one or more pharmaceutical compositions of the present invention. In certain embodiments, such one or more other pharmaceutical agents are designed to treat a different disease, disorder, or condition as the one or more pharmaceutical compositions of the present invention. In certain embodiments, such one or more other pharmaceutical agents are designed to treat an undesired side effect of one or more pharmaceutical compositions of the present invention. In certain embodiments, one or more pharmaceutical compositions of the present invention are co-administered with another pharmaceutical agent to treat an undesired effect of that other pharmaceutical agent. In certain embodiments, one or more pharmaceutical compositions of the present invention are co-administered with another pharmaceutical agent to produce a combinational effect. In certain embodiments, one or more pharmaceutical compositions of the present invention are co-administered with another pharmaceutical agent to produce a synergistic effect.

In certain embodiments, one or more pharmaceutical compositions of the present invention and one or more other pharmaceutical agents are administered at the same time. In certain embodiments, one or more pharmaceutical compositions of the present invention and one or more other pharmaceutical agents are administered at different times. In certain embodiments, one or more pharmaceutical compositions of the present invention and one or more other pharmaceutical agents are prepared together in a single formulation. In certain embodiments, one or more pharmaceutical compositions of the present invention and one or more other pharmaceutical agents are prepared separately.

EXAMPLES*Non-limiting disclosure and incorporation by reference*

While certain compounds, compositions and methods described herein have been described with specificity in accordance with certain embodiments, the following examples serve only to illustrate the compounds described herein and are not intended to limit the same. Each of the

patents, applications, printed publications, and other published documents mentioned or referred to in this specification are herein incorporated by reference in their entirety.

Example 1: Single nucleotide polymorphisms (SNPs) in the huntingtin (*HTT*) gene sequence

The *HTT* genomic sequence, designated herein as SEQ ID NO: 1 (NT_006081.18 truncated from nucleotides 1566000 to 1768000) was aligned with the *HTT* mRNA, designated herein as SEQ ID NO: 2 (NM_002111.6), using the EMBL-EBI sequence database (ClustalW2, <http://www.ebi.ac.uk/Tools/clustalw2/index.html>), and the output is presented in Figure 1. SNP positions (identified by Hayden et al, WO/2009/135322) associated with the *HTT* gene were mapped to the two sequences and have been demarcated in Figure 1 by their reference SNP ID number from the Entrez SNP database at the National Center for Biotechnology Information (NCBI, <http://www.ncbi.nlm.nih.gov/sites/entrez?db=snp>), incorporated herein by reference. Table 2 furnishes further details on each SNP. The 'Reference SNP ID number' or 'RS number' is the number designated to each SNP from the Entrez SNP database at NCBI, incorporated herein by reference. 'SNP position' refers to the nucleotide position of the SNP on SEQ ID NO: 1. 'Polymorphism' indicates the nucleotide variants at that SNP position. 'Major allele' indicates the nucleotide associated with the major allele, or the nucleotide present in a statistically significant proportion of individuals in the human population. 'Minor allele' indicates the nucleotide associated with the minor allele, or the nucleotide present in a relatively small proportion of individuals in the human population.

Table 2
Single Nuclear Polymorphisms (SNPs) and their positions on SEQ ID NO: 1

RS No.	SNP position	Polymorphism	Major allele	Minor allele
rs2857936	1963	C/T	C	T
rs12506200	3707	A/G	G	A
rs762855	14449	A/G	G	A
rs3856973	19826	G/A	G	A
rs2285086	28912	G/A	A	G
rs7659144	37974	C/G	C	G
rs16843804	44043	C/T	C	T
rs2024115	44221	G/A	A	G
rs10015979	49095	A/G	A	G
rs7691627	51063	A/G	G	A

rs2798235	54485	G/A	G	A
rs4690072	62160	G/T	T	G
rs6446723	66466	C/T	T	C
rs363081	73280	G/A	G	A
rs363080	73564	T/C	C	T
rs363075	77327	G/A	G	A
rs363064	81063	T/C	C	T
rs3025849	83420	A/G	A	G
rs6855981	87929	A/G	G	A
rs363102	88669	G/A	A	G
rs11731237	91466	C/T	C	T
rs4690073	99803	A/G	G	A
rs363144	100948	T/G	T	G
rs3025838	101099	C/T	C	T
rs34315806	101687	A/G	G	A
rs363099	101709	T/C	C	T
rs363096	119674	T/C	T	C
rs2298967	125400	C/T	T	C
rs2298969	125897	A/G	G	A
rs6844859	130139	C/T	T	C
rs363092	135682	C/A	C	A
rs7685686	146795	A/G	A	G
rs363088	149983	A/T	A	T
rs362331	155488	C/T	T	C
rs916171	156468	G/C	C	G
rs362322	161018	A/G	A	G
rs362275	164255	T/C	C	T
rs362273	167080	A/G	A	G
rs2276881	171314	G/A	G	A
rs3121419	171910	T/C	C	T
rs362272	174633	G/A	G	A
rs362271	175171	G/A	G	A
rs3775061	178407	C/T	C	T
rs362310	179429	A/G	G	A
rs362307	181498	T/C	C	T
rs362306	181753	G/A	G	A
rs362303	181960	T/C	C	T
rs362296	186660	C/A	C	A
rs1006798	198026	A/G	A	G

Example 2: Design of antisense oligonucleotides targeting huntingtin gene SNPs and inhibition of *HTT* mRNA in Coriell fibroblast cell lines (GM04281, GM02171, and GM02173B)

Antisense oligonucleotides targeting nucleotides overlapping SNP positions presented in Table 1 were designed and tested for potency in three huntingtin patient-derived Coriell fibroblast cell lines, GM04281, GM02171, and GM02173B (from the Coriell Institute for Medical Research).

Cultured GM04281 cells or GM02171 cells or GM02173B cells at a density of 20,000 cells per well were transfected using electroporation with 10,000 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and *HTT* mRNA levels were measured by quantitative real time PCR using primer probe set RTS2617 (forward sequence CTCCGTCCGGTAGACATGCT, designated herein as SEQ ID NO: 3; reverse sequence GGAAATCAGAACCCTCAAAATGG, designated herein as SEQ ID NO: 4; probe sequence TGAGCACTGTTCAACTGTGGATATCGGGAX, designated herein as SEQ ID NO: 5). *HTT* mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN. Results are presented as percent inhibition of *HTT* mRNA, relative to untreated control cells.

ISIS 387916 (TCTCTATTGCACATTCCAAG, 5-10-5 MOE (SEQ ID NO: 6)) and ISIS 388816 (GCCGTAGCCTGGGACCCGCC, 5-10-5 MOE (SEQ ID NO: 7)) were included in each study as benchmark oligonucleotides against which the potency of the antisense oligonucleotides targeting nucleotides overlapping each SNP position could be compared.

The chimeric antisense oligonucleotides in Tables 3 and 4 were designed as 5-9-5 MOE gapmers. The gapmers are 19 nucleotides in length, wherein the central gap segment is comprised of nine 2'-deoxynucleotides and is flanked on both sides (in the 5' and 3' directions) by wings comprising five nucleotides each. Each nucleotide in the 5' wing segment and each nucleotide in the 3' wing segment has a 2'-MOE modification. The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine nucleobases throughout each gapmer are 5-methylcytosines.

The oligonucleotides are further described in Table 3. The percent inhibition of *HTT* mRNA by the antisense oligonucleotides in each cell line is shown in Table 4. 'Target allele' indicates whether the gapmer is targeted to the major or the minor allele at the SNP position. The number in parentheses indicates the nucleotide position in the gapmer opposite to the SNP position, starting from the 5'-terminus of the oligonucleotide. 'Start site' indicates the 5'-most nucleotide to which the gapmer is targeted. "Stop site" indicates the 3'-most nucleotide to which the gapmer is targeted. Each gapmer listed in Tables 3 and 4 is targeted to human *HTT* pre-mRNA, which is SEQ ID NO: 1.

Table 3
Chimeric oligonucleotides targeting SNP positions on the *HTT* gene

ISIS No	SNP RS No.	Target allele	Sequence	Start Site	Stop Site	SEQ ID NO
387916	n/a	n/a	TCTCTATTGCACATTCCAAG	145466	145485	6
388816	n/a	n/a	GCCGTAGCCTGGGACCCGCC	16501	16520	7
435330	rs3856973	Major (8)	TAACACTCGATTAAACCCTG	19815	19833	8
435348	rs3856973	Minor (8)	TAACACTTGATTAAACCCTG	19815	19833	9
435294	rs3856973	Major (10)	GTTAACACTCGATTAAACCC	19817	19835	10
435312	rs3856973	Minor (10)	GTTAACACTTGATTAAACCC	19817	19835	11
435864	rs2285086	Major (10)	GCTAGTTCATCCCAGTGAG	28903	28921	12
435889	rs2285086	Minor (10)	GCTAGTTCACCCCAGTGAG	28903	28921	13
435878	rs7659144	Major (10)	TGGAAATGGGTTTTTCCAC	37965	37983	14
435903	rs7659144	Minor (10)	TGGAAATGGCTTTTTTCCAC	37965	37983	15
435863	rs16843804	Major (10)	TTTAACCGTGGCATGGGCA	44034	44052	16
435888	rs16843804	Minor (10)	TTTAACCGTAGCATGGGCA	44034	44052	17
435331	rs2024115	Major (8)	TTCAAGCTAGTAACGATGC	44210	44228	18
435349	rs2024115	Minor (8)	TTCAAGCCAGTAACGATGC	44210	44228	19
435295	rs2024115	Major (10)	ACTTCAAGCTAGTAACGAT	44212	44230	20
435313	rs2024115	Minor (10)	ACTTCAAGCCAGTAACGAT	44212	44230	21
435862	rs10015979	Major (10)	GCAGCTAGGTTAAAGAGTC	49086	49104	22
435887	rs10015979	Minor (10)	GCAGCTAGGCTAAAGAGTC	49086	49104	23
435880	rs7691627	Major (10)	AATAAGAAACACAATCAAA	51054	51072	24
435905	rs7691627	Minor (10)	AATAAGAAATACAATCAAA	51054	51072	25
435885	rs2798235	Major (10)	CAGAGGAGGCATACTGTAT	54476	54494	26
435910	rs2798235	Minor (10)	CAGAGGAGGTATACTGTAT	54476	54494	27
435874	rs4690072	Major (10)	CACAGTGCTACCCAACCTT	62151	62169	28
435899	rs4690072	Minor (10)	CACAGTGCTCCCCAACCTT	62151	62169	29
435875	rs6446723	Major (10)	TAATTTTCTAGACTTTATG	66457	66475	30
435900	rs6446723	Minor (10)	TAATTTTCTGGACTTTATG	66457	66475	31
435332	rs363081	Major (8)	GCTACAACGCAGGTCAAAT	73269	73287	32
435350	rs363081	Minor (8)	GCTACAATGCAGGTCAAAT	73269	73287	33
435296	rs363081	Major (10)	GAGCTACAACGCAGGTCAA	73271	73289	34
435314	rs363081	Minor (10)	GAGCTACAATGCAGGTCAA	73271	73289	35
435886	rs363080	Major (10)	AGAGAGAACGAGAAGGCTC	73555	73573	36
435911	rs363080	Minor (10)	AGAGAGACAAGAAGGCTC	73555	73573	37
435914	rs363075	Major (6)	AGCCCCTCTGTGTAAGTTT	77314	77332	38
435926	rs363075	Minor (6)	AGCCCTTCTGTGTAAGTTT	77314	77332	39
435916	rs363075	Major (7)	GAGCCCCTCTGTGTAAGTT	77315	77333	40
435928	rs363075	Minor (7)	GAGCCCTTCTGTGTAAGTT	77315	77333	41
435333	rs363075	Major (8)	TGAGCCCCTCTGTGTAAGT	77316	77334	42

435351	rs363075	Minor (8)	TGAGCCCTTCTGTGTAAGT	77316	77334	43
435918	rs363075	Major (9)	ATGAGCCCCTCTGTGTAAG	77317	77335	44
435930	rs363075	Minor (9)	ATGAGCCCTTCTGTGTAAG	77317	77335	45
435297	rs363075	Major (10)	GATGAGCCCCTCTGTGTAA	77318	77336	46
435315	rs363075	Minor (10)	GATGAGCCCTTCTGTGTAA	77318	77336	47
435920	rs363075	Major (11)	TGATGAGCCCCTCTGTGTA	77319	77337	48
435932	rs363075	Minor (11)	TGATGAGCCCTTCTGTGTA	77319	77337	49
435366	rs363075	Major (12)	ATGATGAGCCCCTCTGTGT	77320	77338	50
435924	rs363075	Minor (12)	ATGATGAGCCCTTCTGTGT	77320	77338	51
435922	rs363075	Major (14)	TAATGATGAGCCCCTCTGT	77322	77340	52
435934	rs363075	Minor (14)	TAATGATGAGCCCTTCTGT	77322	77340	53
435334	rs363064	Major (8)	AGAATACGGGTAACATTTT	81052	81070	54
435352	rs363064	Minor (8)	AGAATACAGGTAACATTTT	81052	81070	55
435298	rs363064	Major (10)	GGAGAATACGGGTAACATT	81054	81072	56
435316	rs363064	Minor (10)	GGAGAATACAGGTAACATT	81054	81072	57
435335	rs3025849	Major (8)	TTAGTAATCAATTTTAATG	83409	83427	58
435353	rs3025849	Minor (8)	TTAGTAACCAATTTTAATG	83409	83427	59
435299	rs3025849	Major (10)	AGTTAGTAATCAATTTTAA	83411	83429	60
435317	rs3025849	Minor (10)	AGTTAGTAACCAATTTTAA	83411	83429	61
435877	rs6855981	Major (10)	GAAGGAATGCTTTTACTAG	87920	87938	62
435902	rs6855981	Minor (10)	GAAGGAATGTTTTTACTAG	87920	87938	63
435336	rs363102	Major (8)	CTAAAACTAACTTGAGAAT	88658	88676	64
435354	rs363102	Minor (8)	CTAAACCAACTTGAGAAT	88658	88676	65
435300	rs363102	Major (10)	ATCTAAAACTAACTTGAGA	88660	88678	66
435318	rs363102	Minor (10)	ATCTAAACCAACTTGAGA	88660	88678	67
435884	rs11731237	Major (10)	GGTGGGCAGGAAGGACTGA	91457	91475	68
435909	rs11731237	Minor (10)	GGTGGGCAGAAAGGACTGA	91457	91475	69
435337	rs4690073	Major (8)	CCTAAATCAATCTACAAGT	99792	99810	70
435355	rs4690073	Minor (8)	CCTAAATTAATCTACAAGT	99792	99810	71
435301	rs4690073	Major (10)	TCCCTAAATCAATCTACAA	99794	99812	72
435319	rs4690073	Minor (10)	TCCCTAAATTAATCTACAA	99794	99812	73
435883	rs363144	Major (10)	GAAAATGTGAGTGGATCTA	100939	100957	74
435908	rs363144	Minor (10)	GAAAATGTGCGTGGATCTA	100939	100957	75
435338	rs3025838	Major (8)	GTAAGGCGAGACTGACTAG	101088	101106	76
435356	rs3025838	Minor (8)	GTAAGGCAAGACTGACTAG	101088	101106	77
435302	rs3025838	Major (10)	AGGTAAGGCGAGACTGACT	101090	101108	78
435320	rs3025838	Minor (10)	AGGTAAGGCAAGACTGACT	101090	101108	79
435339	rs363099	Major (8)	CTGAGCGGAGAAACCCTCC	101698	101716	80
435357	rs363099	Minor (8)	CTGAGCGAAGAAACCCTCC	101698	101716	81
435303	rs363099	Major (10)	GGCTGAGCGGAGAAACCCT	101700	101718	82
435321	rs363099	Minor (10)	GGCTGAGCGAAGAAACCCT	101700	101718	83
435367	rs363099	Major (12)	AAGGCTGAGCGGAGAAACC	101702	101720	84

435340	rs363096	Major (8)	TTCCCTAAAAACAAAAACA	119663	119681	85
435358	rs363096	Minor (8)	TTCCCTAGAAACAAAAACA	119663	119681	86
435304	rs363096	Major (10)	GATTCCTAAAAACAAAAA	119665	119683	87
435322	rs363096	Minor (10)	GATTCCTAGAAACAAAAA	119665	119683	88
435341	rs2298967	Major (8)	CTTTTCTATTGTCTGTCCC	125389	125407	89
435359	rs2298967	Minor (8)	CTTTTCTGTTGTCTGTCCC	125389	125407	90
435305	rs2298967	Major (10)	TGCTTTTCTATTGTCTGTC	125391	125409	91
435323	rs2298967	Minor (10)	TGCTTTTCTGTTGTCTGTC	125391	125409	92
435865	rs2298969	Major (10)	AAGGGATGCCGACTTGGGC	125888	125906	93
435890	rs2298969	Minor (10)	AAGGGATGCTGACTTGGGC	125888	125906	94
435876	rs6844859	Major (10)	ACCTTCCTCACTGAGGATG	130130	130148	95
435901	rs6844859	Minor (10)	ACCTTCCTCGCTGAGGATG	130130	130148	96
435872	rs363092	Major (10)	CAAACCACTGTGGGATGAA	135673	135691	97
435897	rs363092	Minor (10)	CAAACCACTTTGGGATGAA	135673	135691	98
435879	rs7685686	Major (10)	AATAAATTGTCATCACCAG	146786	146804	99
435904	rs7685686	Minor (10)	AATAAATTGCCATCACCAG	146786	146804	100
435871	rs363088	Major (10)	TCACAGCTATCTTCTCATC	149974	149992	101
435896	rs363088	Minor (10)	TCACAGCTAACTTCTCATC	149974	149992	102
435870	rs362331	Major (10)	GCACACAGTAGATGAGGGA	155479	155497	103
435895	rs362331	Minor (10)	GCACACAGTGGATGAGGGA	155479	155497	104
435881	rs916171	Major (10)	CAGAACAAAGAGAAGAATT	156459	156477	105
435906	rs916171	Minor (10)	CAGAACAAACAGAAGAATT	156459	156477	106
435342	rs362322	Major (8)	GCTTACATGCCTTCAGTGA	161007	161025	107
435360	rs362322	Minor (8)	GCTTACACGCCTTCAGTGA	161007	161025	108
435306	rs362322	Major (10)	CAGCTTACATGCCTTCAGT	161009	161027	109
435324	rs362322	Minor (10)	CAGCTTACACGCCTTCAGT	161009	161027	110
435868	rs362275	Major (10)	AAGAAGCCTGATAAAATCT	164246	164264	111
435893	rs362275	Minor (10)	AAGAAGCCTAATAAAATCT	164246	164264	112
435343	rs2276881	Major (8)	CATACATCAGCTCAAACCTG	171303	171321	113
435361	rs2276881	Minor (8)	CATACATTAGCTCAAACCTG	171303	171321	114
435307	rs2276881	Major (10)	CACATACATCAGCTCAAAC	171305	171323	115
435325	rs2276881	Minor (10)	CACATACATTAGCTCAAAC	171305	171323	116
435368	rs2276881	Major (12)	GTCACATACATCAGCTCAA	171307	171325	117
435866	rs3121419	Major (10)	GAGACTATAGCACCCAGAT	171901	171919	118
435891	rs3121419	Minor (10)	GAGACTATAACACCCAGAT	171901	171919	119
435344	rs362272	Major (8)	TAGAGGACGCCGTGCAGGG	174622	174640	120
435362	rs362272	Minor (8)	TAGAGGATGCCGTGCAGGG	174622	174640	121
435308	rs362272	Major (10)	CATAGAGGACGCCGTGCAG	174624	174642	122
435326	rs362272	Minor (10)	CATAGAGGATGCCGTGCAG	174624	174642	123
435369	rs362272	Major (12)	CACATAGAGGACGCCGTGC	174626	174644	124
435867	rs362271	Major (10)	ACGTGTGTACAGAACCTGC	175162	175180	125
435892	rs362271	Minor (10)	ACGTGTGTATAGAACCTGC	175162	175180	126

435873	rs3775061	Major (10)	TGTTTCAGAAATGCCTCATCT	178398	178416	127
435898	rs3775061	Minor (10)	TGTTTCAGAACGCCTCATCT	178398	178416	128
435345	rs362310	Major (8)	AAACGGCGCAGCGGGAAGG	179418	179436	129
435363	rs362310	Minor (8)	AAACGGCACAGCGGGAAGG	179418	179436	130
435309	rs362310	Major (10)	AGAAACGGCGCAGCGGGAA	179420	179438	131
435327	rs362310	Minor (10)	AGAAACGGCACAGCGGGAA	179420	179438	132
435915	rs362307	Major (6)	AGGGCGCAGACTTCCAAAG	181485	181503	133
435927	rs362307	Minor (6)	AGGGCACAGACTTCCAAAG	181485	181503	134
435917	rs362307	Major (7)	AAGGGCGCAGACTTCCAAA	181486	181504	135
435929	rs362307	Minor (7)	AAGGGCACAGACTTCCAAA	181486	181504	136
435346	rs362307	Major (8)	CAAGGGCGCAGACTTCCAA	181487	181505	137
435364	rs362307	Minor (8)	CAAGGGCACAGACTTCCAA	181487	181505	138
435919	rs362307	Major (9)	ACAAGGGCGCAGACTTCCA	181488	181506	139
435931	rs362307	Minor (9)	ACAAGGGCACAGACTTCCA	181488	181506	140
435310	rs362307	Major (10)	CACAAGGGCGCAGACTTCC	181489	181507	141
435328	rs362307	Minor (10)	CACAAGGGCACAGACTTCC	181489	181507	142
435921	rs362307	Major (11)	GCACAAGGGCGCAGACTTC	181490	181508	143
435933	rs362307	Minor (11)	GCACAAGGGCACAGACTTC	181490	181508	144
435370	rs362307	Major (12)	GGCACAAGGGCGCAGACTT	181491	181509	145
435925	rs362307	Minor (12)	GGCACAAGGGCACAGACTT	181491	181509	146
435923	rs362307	Major (14)	AGGGCACAAGGGCGCAGAC	181493	181511	147
435935	rs362307	Minor (14)	AGGGCACAAGGGCACAGAC	181493	181511	148
435869	rs362306	Major (10)	GAGCAGCTGCAACCTGGCA	181744	181762	149
435894	rs362306	Minor (10)	GAGCAGCTGTAACCTGGCA	181744	181762	150
435347	rs362303	Major (8)	TGGTGCCGGGTGTCTAGCA	181949	181967	151
435365	rs362303	Minor (8)	TGGTGCCAGGTGTCTAGCA	181949	181967	152
435311	rs362303	Major (10)	AATGGTGCCGGGTGTCTAG	181951	181969	153
435329	rs362303	Minor (10)	AATGGTGCCAGGTGTCTAG	181951	181969	154
435882	rs362296	Major (10)	GGGGACAGGGTGTGCTCTC	186651	186669	155
435907	rs362296	Minor (10)	GGGGACAGGTTGTGCTCTC	186651	186669	156

Table 4

Comparison of inhibition of *HTT* mRNA levels by ISIS 387916 and ISIS 388816 with that by chimeric oligonucleotides targeting SNP positions on the *HTT* gene (SEQ ID NO: 1)

ISIS No	SNP RS No.	Target allele	% inhibition			SEQ ID NO
			GM04281	GM02171	GM02173B	
387916	n/a	n/a	96	96	98	6
388816	n/a	n/a	76	88	85	7
435330	rs3856973	Major (8)	64	51	36	8
435348	rs3856973	Minor (8)	50	88	80	9
435294	rs3856973	Major (10)	54	46	54	10
435312	rs3856973	Minor (10)	20	82	58	11

435864	rs2285086	Major (10)	54	28	26	12
435889	rs2285086	Minor (10)	17	43	41	13
435878	rs7659144	Major (10)	43	32	39	14
435903	rs7659144	Minor (10)	16	37	29	15
435863	rs16843804	Major (10)	63	78	81	16
435888	rs16843804	Minor (10)	58	75	77	17
435331	rs2024115	Major (8)	56	27	56	18
435349	rs2024115	Minor (8)	26	91	66	19
435295	rs2024115	Major (10)	53	57	62	20
435313	rs2024115	Minor (10)	25	87	53	21
435862	rs10015979	Major (10)	8	51	40	22
435887	rs10015979	Minor (10)	40	22	28	23
435880	rs7691627	Major (10)	43	17	21	24
435905	rs7691627	Minor (10)	13	27	15	25
435885	rs2798235	Major (10)	38	39	30	26
435910	rs2798235	Minor (10)	17	30	16	27
435874	rs4690072	Major (10)	61	34	48	28
435899	rs4690072	Minor (10)	50	41	45	29
435875	rs6446723	Major (10)	28	13	35	30
435900	rs6446723	Minor (10)	24	56	37	31
435332	rs363081	Major (8)	76	95	88	32
435350	rs363081	Minor (8)	27	61	43	33
435296	rs363081	Major (10)	59	77	66	34
435314	rs363081	Minor (10)	38	66	40	35
435886	rs363080	Major (10)	74	72	79	36
435911	rs363080	Minor (10)	57	58	54	37
435914	rs363075	Major (6)	95	92	95	38
435926	rs363075	Minor (6)	88	81	79	39
435916	rs363075	Major (7)	90	92	94	40
435928	rs363075	Minor (7)	83	79	85	41
435333	rs363075	Major (8)	86	97	91	42
435351	rs363075	Minor (8)	59	80	58	43
435918	rs363075	Major (9)	83	90	91	44
435930	rs363075	Minor (9)	29	49	49	45
435297	rs363075	Major (10)	74	84	83	46
435315	rs363075	Minor (10)	47	63	45	47
435920	rs363075	Major (11)	78	66	83	48
435932	rs363075	Minor (11)	39	20	19	49
435366	rs363075	Major (12)	80	91	85	50
435924	rs363075	Minor (12)	37	49	58	51
435922	rs363075	Major (14)	80	90	91	52
435934	rs363075	Minor (14)	63	70	80	53

435334	rs363064	Major (8)	50	59	44	54
435352	rs363064	Minor (8)	12	37	48	55
435298	rs363064	Major (10)	81	92	87	56
435316	rs363064	Minor (10)	69	90	80	57
435335	rs3025849	Major (8)	0	40	37	58
435353	rs3025849	Minor (8)	0	29	18	59
435299	rs3025849	Major (10)	0	34	67	60
435317	rs3025849	Minor (10)	0	38	34	61
435877	rs6855981	Major (10)	31	59	58	62
435902	rs6855981	Minor (10)	0	43	27	63
435336	rs363102	Major (8)	0	21	19	64
435354	rs363102	Minor (8)	0	36	33	65
435300	rs363102	Major (10)	0	34	24	66
435318	rs363102	Minor (10)	0	30	20	67
435884	rs11731237	Major (10)	7	46	51	68
435909	rs11731237	Minor (10)	30	47	41	69
435337	rs4690073	Major (8)	12	0	12	70
435355	rs4690073	Minor (8)	0	26	33	71
435301	rs4690073	Major (10)	23	0	10	72
435319	rs4690073	Minor (10)	0	45	53	73
435883	rs363144	Major (10)	24	23	39	74
435908	rs363144	Minor (10)	27	20	22	75
435338	rs3025838	Major (8)	31	46	69	76
435356	rs3025838	Minor (8)	3	25	17	77
435302	rs3025838	Major (10)	39	73	67	78
435320	rs3025838	Minor (10)	21	49	32	79
435339	rs363099	Major (8)	84	87	76	80
435357	rs363099	Minor (8)	71	91	90	81
435303	rs363099	Major (10)	83	92	85	82
435321	rs363099	Minor (10)	84	95	89	83
435367	rs363099	Major (12)	76	82	72	84
435340	rs363096	Major (8)	0	47	52	85
435358	rs363096	Minor (8)	0	25	35	86
435304	rs363096	Major (10)	5	33	36	87
435322	rs363096	Minor (10)	2	30	32	88
435341	rs2298967	Major (8)	54	72	56	89
435359	rs2298967	Minor (8)	25	59	63	90
435305	rs2298967	Major (10)	66	80	78	91
435323	rs2298967	Minor (10)	36	79	66	92
435865	rs2298969	Major (10)	53	72	79	93
435890	rs2298969	Minor (10)	65	46	54	94
435876	rs6844859	Major (10)	70	67	77	95

435901	rs6844859	Minor (10)	39	83	80	96
435872	rs363092	Major (10)	46	41	54	97
435897	rs363092	Minor (10)	37	69	57	98
435879	rs7685686	Major (10)	83	31	70	99
435904	rs7685686	Minor (10)	30	92	72	100
435871	rs363088	Major (10)	70	55	70	101
435896	rs363088	Minor (10)	66	74	80	102
435870	rs362331	Major (10)	88	74	88	103
435895	rs362331	Minor (10)	78	92	86	104
435881	rs916171	Major (10)	0	57	51	105
435906	rs916171	Minor (10)	14	26	17	106
435342	rs362322	Major (8)	47	74	67	107
435360	rs362322	Minor (8)	17	58	52	108
435306	rs362322	Major (10)	50	77	65	109
435324	rs362322	Minor (10)	42	61	64	110
435868	rs362275	Major (10)	54	35	43	111
435893	rs362275	Minor (10)	3	27	33	112
435343	rs2276881	Major (8)	59	76	65	113
435361	rs2276881	Minor (8)	58	44	20	114
435307	rs2276881	Major (10)	69	82	81	115
435325	rs2276881	Minor (10)	17	47	43	116
435368	rs2276881	Major (12)	84	96	92	117
435866	rs3121419	Major (10)	67	61	64	118
435891	rs3121419	Minor (10)	53	76	73	119
435344	rs362272	Major (8)	35	46	36	120
435362	rs362272	Minor (8)	34	68	57	121
435308	rs362272	Major (10)	26	30	35	122
435326	rs362272	Minor (10)	29	50	39	123
435369	rs362272	Major (12)	66	74	65	124
435867	rs362271	Major (10)	73	74	75	125
435892	rs362271	Minor (10)	52	74	79	126
435873	rs3775061	Major (10)	40	32	47	127
435898	rs3775061	Minor (10)	13	20	24	128
435345	rs362310	Major (8)	38	55	52	129
435363	rs362310	Minor (8)	45	67	60	130
435309	rs362310	Major (10)	33	44	56	131
435327	rs362310	Minor (10)	33	71	61	132
435915	rs362307	Major (6)	61	54	58	133
435927	rs362307	Minor (6)	31	35	44	134
435917	rs362307	Major (7)	67	76	66	135
435929	rs362307	Minor (7)	33	34	55	136
435346	rs362307	Major (8)	67	89	66	137

435364	rs362307	Minor (8)	46	72	66	138
435919	rs362307	Major (9)	84	79	70	139
435931	rs362307	Minor (9)	74	74	86	140
435310	rs362307	Major (10)	74	81	71	141
435328	rs362307	Minor (10)	47	69	75	142
435921	rs362307	Major (11)	74	77	69	143
435933	rs362307	Minor (11)	38	47	74	144
435370	rs362307	Major (12)	64	74	38	145
435925	rs362307	Minor (12)	60	66	80	146
435923	rs362307	Major (14)	73	66	71	147
435935	rs362307	Minor (14)	68	75	87	148
435869	rs362306	Major (10)	82	77	81	149
435894	rs362306	Minor (10)	28	79	72	150
435347	rs362303	Major (8)	68	74	71	151
435365	rs362303	Minor (8)	69	83	76	152
435311	rs362303	Major (10)	46	56	72	153
435329	rs362303	Minor (10)	49	62	39	154
435882	rs362296	Major (10)	29	48	56	155
435907	rs362296	Minor (10)	42	56	52	156

Example 3: Dose-dependent antisense inhibition of human huntingtin mRNA levels in Coriell fibroblast cell lines

Gapmers from the study described in Example 2 were selected and tested at various doses in GM04281, GM02171, and GM02173B cell lines. Each cell line was plated at a density of 25,000 cells per well and transfected using electroporation with 750 nM, 1,500 nM, 3,000 nM, 6,000 nM, and 12,000 nM concentrations of antisense oligonucleotide, as specified in Table 5, 6, and 7. After a treatment period of approximately 16 hours, RNA was isolated from the cells and *HTT* mRNA levels were measured by quantitative real-time PCR. Human *HTT* primer probe set RTS2617 was used to measure mRNA levels. *HTT* mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN. Results are presented as percent inhibition of *HTT* mRNA, relative to untreated control cells. IC₅₀ values are also provided in Tables 5, 6, and 7.

Table 5
Dose-dependent antisense inhibition of human *HTT* in GM04281 cells

ISIS No.	750 nM	1,500 nM	3,000 nM	6,000 nM	12,000 nM	IC ₅₀ (μM)
387916	51	81	80	91	97	0.6

435330	24	49	50	73	85	2.5
435331	23	38	64	72	74	2.4
435868	3	17	7	29	63	6.7
435870	53	73	77	86	93	0.6
435871	28	51	52	78	89	1.7
435874	14	21	28	64	82	3.3
435879	42	57	57	81	91	1.1
435890	48	56	62	76	91	0.9
435929	10	0	5	12	48	13.8
435931	20	17	53	62	81	2.9
435933	0	7	24	43	49	10.7
435935	0	38	38	62	29	4.2

Table 6
Dose-dependent antisense inhibition of human *HTT* in GM02171 cells

ISIS No.	750 nM	1,500 nM	3,000 nM	6,000 nM	12,000 nM	IC ₅₀ (μM)
387916	57	73	81	93	98	0.4
435330	27	37	0	44	63	4.4
435331	35	34	19	41	63	3.5
435868	21	21	39	24	12	>12.0
435870	50	53	57	70	79	0.9
435871	32	46	45	58	62	3.9
435874	1	0	4	11	6	>12.0
435879	32	14	17	45	38	>12.0
435890	34	33	40	51	62	5.4
435929	25	22	31	5	29	>12.0
435931	15	28	27	60	79	3.7
435933	13	36	21	43	48	12.2
435935	25	42	27	61	68	3.2

Table 7
Dose-dependent antisense inhibition of human *HTT* in GM02173B cells

ISIS No.	750 nM	1,500 nM	3,000 nM	6,000 nM	12,000 nM	IC ₅₀ (μM)
387916	43	67	80	86	97	1.1
435330	22	21	0	52	62	5.3
435331	19	17	32	50	55	9.4
435868	17	25	41	13	26	>12.0
435870	24	57	70	78	75	1.8
435871	8	30	42	50	48	5.0
435874	31	35	28	35	42	>12.0

435879	39	44	42	60	64	2.5
435890	38	36	50	65	73	3.1
435929	19	17	19	42	35	7.7
435931	40	19	31	48	71	5.8
435933	35	24	47	52	59	4.4
435935	25	23	40	73	77	3.7

Example 4: Dose-dependent antisense inhibition of human huntingtin mRNA levels in Coriell fibroblast cell lines

Gapmers from the study described in Example 2 were selected and tested at various doses in GM04281, GM02171, and GM02173B cell lines. Each cell line was plated at a density of 25,000 cells per well and transfected using electroporation with 750 nM, 1,500 nM, 3,000 nM, 6,000 nM, and 12,000 nM concentrations of antisense oligonucleotide, as specified in Table 8, 9, and 10. After a treatment period of approximately 16 hours, RNA was isolated from the cells and *HTT* mRNA levels were measured by quantitative real-time PCR. Human *HTT* primer probe set RTS2617 was used to measure mRNA levels. *HTT* mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN. Results are presented as percent inhibition of *HTT* mRNA relative to untreated control cells. IC₅₀ values are also provided in Tables 8, 9, and 10.

Table 8
Dose-dependent antisense inhibition of human *HTT* in GM04281 cells

ISIS No.	750 nM	1,500 nM	3,000 nM	6,000 nM	12,000 nM	IC ₅₀ (μM)
387916	61	78	90	94	97	<0.8
435303	33	39	69	79	91	1.5
435328	0	12	16	51	75	5.3
435331	27	48	48	70	82	2.1
435339	46	37	61	73	89	2.3
435869	17	35	44	66	80	3.3
435870	44	60	64	84	84	1.1
435871	41	50	71	78	87	1.2
435874	24	36	35	65	73	3.1
435879	46	52	78	81	92	0.9
435890	41	53	63	80	86	1.3
435925	0	14	39	60	87	4.2
435926	20	28	67	81	89	2.0
435928	32	49	73	86	86	1.8

435931	22	24	40	59	90	3.8

Table 9
Dose-dependent antisense inhibition of human *HTT* in GM02171 cells

ISIS No.	750 nM	1,500 nM	3,000 nM	6,000 nM	□□□□ nM	IC ₅₀ (μM)
387916	50	64	90	95	96	0.7
435303	14	32	68	79	85	2.8
435328	0	12	20	38	55	10.3
435331	0	13	5	30	36	>12.0
435339	30	40	58	63	49	2.5
435869	13	25	31	47	87	4.0
435870	18	31	44	66	74	3.5
435871	1	20	29	49	64	6.5
435874	3	6	12	17	31	>12.0
435879	0	2	12	35	44	>12.0
435890	15	16	30	48	72	5.8
435925	0	0	22	48	29	6.3
435926	25	28	58	74	85	2.3
435928	18	53	61	86	83	2.5
435931	0	4	25	46	68	6.7

Table 10
Dose-dependent antisense inhibition of human *HTT* in GM02173B cells

ISIS No.	750 nM	1,500 nM	3,000 nM	6,000 nM	12,000 nM	IC ₅₀ (μM)
387916	27	65	84	81	96	1.9
435303	23	48	52	76	76	2.9
435328	8	14	19	34	50	15.7
435331	10	17	16	27	32	>12.0
435339	28	26	38	67	82	3.8
435869	12	24	37	45	79	4.2
435870	20	26	58	53	78	2.7
435871	15	16	32	45	71	6.0
435874	13	8	28	36	31	>12.0
435879	22	20	36	53	60	6.0
435890	21	28	34	54	71	4.3
435925	2	10	28	43	78	5.9
435926	7	25	37	73	79	3.5
435928	15	39	60	73	87	2.5
435931	13	13	32	61	62	6.7

Example 5: Antisense inhibition of human *HTT* in GM04281 cells

Additional antisense oligonucleotides were designed based on the gapmers selected from studies described in Example 4. These oligonucleotides were designed by creating gapmers shifted slightly upstream and downstream (i.e. “microwalk”) of the original gapmers from Tables 8, 9, and 10. Antisense oligonucleotides were also created with uniform MOE, as well as with various motifs, 2-9-6 MOE, 3-9-3 MOE, 3-9-4 MOE, 3-9-5 MOE, 4-10-5 MOE, 4-11-4 MOE, 4-7-4 MOE, 4-9-4 MOE, 4-9-5 MOE, 5-10-4 MOE, 5-7-5 MOE, 5-8-6 MOE, 5-9-3 MOE, 5-9-5 MOE, 6-7-6 MOE, 6-9-2 MOE, and 6-8-5 MOE.

In addition, antisense oligonucleotides were designed targeting SNP RS Nos. rs2857936, rs12506200, rs762855, and rs1006798 (refer to Table 2). The oligonucleotides were designed targeting either the major allele or the minor allele, and with the SNP position opposite either position 8 or position 10 of the gapmer.

These gapmers were tested *in vitro*. Cultured GM04281 cells at a density of 25,000 cells per well were transfected using electroporation with 10,000 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and *HTT* mRNA levels were measured by quantitative real-time PCR. *HTT* mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN. Results are presented in Tables 11-19 as percent inhibition of *HTT* mRNA, relative to untreated control cells.

The gapmers, ISIS 435869, ISIS 435870, ISIS 435874, ISIS 435879, and ISIS 435890, from which some of the newly designed gapmers were derived are marked with an asterisk (*) in the table. ISIS 387916 was included in the study as a benchmark oligonucleotide against which the potency of the antisense oligonucleotides targeting nucleotides overlapping each SNP position could be compared.

The uniform MOE oligonucleotides are 15 nucleotides in length.

The 2-9-6 gapmers are 17 nucleotides in length, wherein the central gap segment is comprised of nine 2'-deoxynucleotides and is flanked on the 5' direction by a wing comprising 2 nucleotides and on the 3' direction by a wing comprising 6 nucleotides.

The 3-9-3 gapmers are 15 nucleotides in length, wherein the central gap segment is comprised of nine 2'-deoxynucleotides and is flanked on both 5' and 3' directions by wings comprising 3 nucleotides each.

The 3-9-4 gapmers are 16 nucleotides in length, wherein the central gap segment is comprised of nine 2'-deoxynucleotides and is flanked on the 5' direction by a wing comprising 3 nucleotides and on the 3' direction by a wing comprising 4 nucleotides.

The 3-9-5 gapmers are 17 nucleotides in length, wherein the central gap segment is comprised of nine 2'-deoxynucleotides and is flanked on the 5' direction by a wing comprising 3 nucleotides and on the 3' direction by a wing comprising 5 nucleotides.

The 4-10-5 gapmers are 19 nucleotides in length, wherein the central gap segment is comprised of ten 2'-deoxynucleotides and is flanked on the 5' direction by a wing comprising 4 nucleotides and on the 3' direction by a wing comprising 5 nucleotides.

The 4-11-4 gapmers are 19 nucleotides in length, wherein the central gap segment is comprised of eleven 2'-deoxynucleotides and is flanked on both 5' and 3' directions by wings comprising 4 nucleotides each.

The 4-7-4 gapmers are 15 nucleotides in length, wherein the central gap segment is comprised of seven 2'-deoxynucleotides and is flanked on both 5' and 3' directions by wings comprising 4 nucleotides each.

The 4-9-4 gapmers are 17 nucleotides in length, wherein the central gap segment is comprised of nine 2'-deoxynucleotides and is flanked on both 5' and 3' directions by wings comprising 4 nucleotides each.

The 4-9-5 gapmers are 18 nucleotides in length, wherein the central gap segment is comprised of nine 2'-deoxynucleotides and is flanked on the 5' direction by a wing comprising 4 nucleotides and on the 3' direction by a wing comprising 5 nucleotides.

The 5-10-4 gapmers are 19 nucleotides in length, wherein the central gap segment is comprised of ten 2'-deoxynucleotides and is flanked on the 5' direction by a wing comprising 5 nucleotides and on the 3' direction by a wing comprising 4 nucleotides.

The 5-7-5 gapmers are 17 nucleotides in length, wherein the central gap segment is comprised of seven 2'-deoxynucleotides and is flanked on both 5' and 3' directions by wings comprising 5 nucleotides each.

The 5-8-6 gapmers are 19 nucleotides in length, wherein the central gap segment is comprised of eight 2'-deoxynucleotides and is flanked on the 5' direction by a wing comprising 5 nucleotides and on the 3' direction by a wing comprising 6 nucleotides.

The 5-9-3 gapmers are 17 nucleotides in length, wherein the central gap segment is comprised of nine 2'-deoxynucleotides and is flanked on the 5' direction by a wing comprising 5 nucleotides and on the 3' direction by a wing comprising 3 nucleotides.

The 5-9-5 gapmers are 19 nucleotides in length, wherein the central gap segment is comprised of nine 2'-deoxynucleotides and is flanked on both 5' and 3' directions by wings comprising 5 nucleotides each.

The 6-7-6 gapmers are 19 nucleotides in length, wherein the central gap segment is comprised of seven 2'-deoxynucleotides and is flanked on both 5' and 3' directions by wings comprising 6 nucleotides each.

The 6-9-2 gapmers are 17 nucleotides in length, wherein the central gap segment is comprised of nine 2'-deoxynucleotides and is flanked on the 5' direction by a wing comprising 6 nucleotides and on the 3' direction by a wing comprising 2 nucleotides.

The 6-8-5 gapmers are 19 nucleotides in length, wherein the central gap segment is comprised of eight 2'-deoxynucleotides and is flanked on the 5' direction by a wing comprising 6 nucleotides and on the 3' direction by a wing comprising 5 nucleotides.

For each of the motifs, each nucleotide in the 5' wing segment and each nucleotide in the 3' wing segment has a 2'-MOE modification. The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine nucleobases throughout each gapmer are 5-methylcytosines.

The oligonucleotides are organized in tables according to the SNP they target. "Start site" indicates the 5'-most nucleotide to which the gapmer is targeted. "Stop site" indicates the 3'-most nucleotide to which the gapmer is targeted. "Target allele" indicates whether the gapmer is targeted

to the major or the minor allele. The number in parentheses indicates the position on the oligonucleotide opposite to the SNP position.

Table 11

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs2857936 (nucleobases 1952 to 1972 of SEQ ID NO: 1)

Start Site	Stop Site	Target allele	ISIS No.	Sequence	Motif	% inhibition	SEQ ID NO
145466	145485	n/a	387916	TCTCTATTGCACATTCCAAG	5-10-5	98	6
1952	1970	Minor (8)	459908	GCTTTTCATTGAAAAGAAA	5-9-5	26	157
1952	1970	Major (8)	459916	GCTTTTCGTTGAAAAGAAA	5-9-5	8	158
1954	1972	Minor (10)	459904	CTGCTTTTCATTGAAAAGA	5-9-5	23	159
1954	1972	Major (10)	459912	CTGCTTTTCGTTGAAAAGA	5-9-5	8	160

Table 12

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs12506200 (nucleobases 3695 to 3715 of SEQ ID NO: 1)

Start Site	Stop Site	Target allele	ISIS No.	Sequence	Motif	% inhibition	SEQ ID NO
145466	145485	n/a	387916	TCTCTATTGCACATTCCAAG	5-10-5	98	6
3695	3713	Major (8)	459909	ACTAGGCCGGGCATGCTGG	5-9-5	48	161
3695	3713	Minor (8)	459917	ACTAGGCTGGGCATGCTGG	5-9-5	35	162
3697	3715	Major (10)	459905	AGACTAGGCCGGGCATGCT	5-9-5	33	163
3697	3715	Minor (10)	459913	AGACTAGGCTGGGCATGCT	5-9-5	45	164

Table 13

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs762855 (nucleobases 14437 to 14457 of SEQ ID NO: 1)

Start Site	Stop Site	Target allele	ISIS No.	Sequence	Motif	% inhibition	SEQ ID NO
145466	145485	n/a	387916	TCTCTATTGCACATTCCAAG	5-10-5	98	6
14437	14455	Minor (8)	459910	AAACAGCTGTAGTTCCCA	5-9-5	27	165
14437	14455	Major (8)	459918	AAACAGCCGTAGTTCCCA	5-9-5	39	166
14439	14457	Minor (10)	459906	AGAAACAGCTGTAGTTCC	5-9-5	24	167
14439	14457	Major (10)	459914	AGAAACAGCCGTAGTTCC	5-9-5	28	168

Table 14

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs4690072 (nucleobases 62147 to 62173 of SEQ ID NO: 1)

Start Site	Stop Site	Target allele	ISIS No.	Sequence	Motif	% inhibition	SEQ ID NO
145466	145485	n/a	387916	TCTCTATTGCACATTCCAAG	5-10-5	98	6
62147	62165	Major (6)	460145	GTGCTACCCAACCTTTCTG	5-9-5	62	169
62148	62166	Major (7)	460144	AGTGCTACCCAACCTTTCT	5-9-5	61	170
62149	62167	Major (8)	460143	CAGTGCTACCCAACCTTTC	5-9-5	65	171
62150	62168	Major (9)	460142	ACAGTGCTACCCAACCTTT	5-9-5	83	172
62151	62169	Major (10)	*435874	CACAGTGCTACCCAACCTT	5-9-5	76	28
62151	62169	Major (10)	460022	CACAGTGCTACCCAACCTT	4-10-5	75	28
62151	62169	Major (10)	460033	CACAGTGCTACCCAACCTT	4-11-4	89	28
62151	62168	Major (9)	460063	ACAGTGCTACCCAACCTT	4-9-5	77	173
62151	62169	Major (10)	460073	CACAGTGCTACCCAACCTT	5-10-4	86	28
62151	62169	Major (10)	460093	CACAGTGCTACCCAACCTT	5-8-6	61	28
62151	62169	Major (10)	460169	CACAGTGCTACCCAACCTT	6-7-6	16	28
62151	62169	Major (10)	460188	CACAGTGCTACCCAACCTT	6-8-5	53	28
62152	62168	Major (9)	459978	ACAGTGCTACCCAACCT	2-9-6	87	174
62152	62167	Major (8)	459999	CAGTGCTACCCAACCT	3-9-4	48	175
62152	62168	Major (9)	460012	ACAGTGCTACCCAACCT	3-9-5	84	174
62152	62168	Major (9)	460052	ACAGTGCTACCCAACCT	4-9-4	51	174
62152	62168	Major (9)	460083	ACAGTGCTACCCAACCT	5-7-5	37	174
62152	62168	Major (9)	460103	ACAGTGCTACCCAACCT	5-9-3	80	174
62152	62170	Major (11)	460137	TCACAGTGCTACCCAACCT	5-9-5	65	176
62152	62168	Major (9)	460179	ACAGTGCTACCCAACCT	6-9-2	67	174
62153	62167	Major (8)	459989	CAGTGCTACCCAACC	3-9-3	60	177
62153	62167	Major (8)	460043	CAGTGCTACCCAACC	4-7-4	24	177
62153	62171	Major (12)	460138	ATCACAGTGCTACCCAACC	5-9-5	76	178
62154	62172	Major (13)	460139	TATCACAGTGCTACCCAAC	5-9-5	68	179
62155	62173	Major (14)	460140	ATATCACAGTGCTACCCAA	5-9-5	79	180

Table 15

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs2298969 (nucleobases 125883 to 125911 of SEQ ID NO: 1)

Start Site	Stop Site	Target allele	ISIS No.	Sequence	Motif	% inhibition	SEQ ID NO
145466	145485	n/a	387916	TCTCTATTGCACATTCCAAG	5-10-5	98	6
125883	125901	Minor (5)	460166	ATGCTGACTTGGGCCATTC	5-9-5	83	181
125884	125902	Minor (6)	460165	GATGCTGACTTGGGCCATT	5-9-5	88	182
125885	125903	Minor (7)	460164	GGATGCTGACTTGGGCCAT	5-9-5	68	183

125886	125904	Minor (8)	460163	GGGATGCTGACTTGGGCCA	5-9-5	73	184
125887	125905	Minor (9)	460162	AGGGATGCTGACTTGGGCC	5-9-5	88	185
125888	125906	Minor (10)	*435890	AAGGGATGCTGACTTGGGC	5-9-5	83	94
125888	125906	Minor (10)	460026	AAGGGATGCTGACTTGGGC	4-10-5	90	94
125888	125906	Minor (10)	460037	AAGGGATGCTGACTTGGGC	4-11-4	86	94
125888	125905	Minor (9)	460068	AGGGATGCTGACTTGGGC	4-9-5	90	186
125888	125906	Minor (10)	460076	AAGGGATGCTGACTTGGGC	5-10-4	90	94
125888	125906	Minor (10)	460096	AAGGGATGCTGACTTGGGC	5-8-6	88	94
125888	125906	Minor (10)	460171	AAGGGATGCTGACTTGGGC	6-7-6	87	94
125888	125906	Minor (10)	460190	AAGGGATGCTGACTTGGGC	6-8-5	69	94
125889	125905	Minor (9)	459983	AGGGATGCTGACTTGGG	2-9-6	80	187
125889	125904	Minor (8)	460005	GGGATGCTGACTTGGG	3-9-4	80	284
125889	125905	Minor (9)	460016	AGGGATGCTGACTTGGG	3-9-5	90	187
125889	125905	Minor (9)	460057	AGGGATGCTGACTTGGG	4-9-4	86	187
125889	125905	Minor (9)	460087	AGGGATGCTGACTTGGG	5-7-5	86	187
125889	125905	Minor (9)	460107	AGGGATGCTGACTTGGG	5-9-3	79	187
125889	125907	Major (11)	460157	CAAGGGATGCTGACTTGGG	5-9-5	88	188
125889	125905	Minor (9)	460181	AGGGATGCTGACTTGGG	6-9-2	62	187
125890	125904	Minor (8)	459972	GGGATGCTGACTTGG	Uniform	18	189
125890	125904	Minor (8)	459992	GGGATGCTGACTTGG	3-9-3	90	189
125890	125904	Minor (8)	460046	GGGATGCTGACTTGG	4-7-4	59	189
125890	125908	Major (12)	460158	CCAAGGGATGCTGACTTGG	5-9-5	79	190
125891	125909	Major (13)	460159	GCCAAGGGATGCTGACTTG	5-9-5	82	191
125892	125910	Major (14)	460160	TGCCAAGGGATGCTGACTT	5-9-5	87	192
125893	125911	Major (15)	460161	CTGCCAAGGGATGCTGACT	5-9-5	78	193

Table 16

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs7685686 (nucleobases 146781 to 146809 of SEQ ID NO: 1)

Start Site	Stop Site	Target allele	ISIS No.	Sequence	Motif	% inhibition	SEQ ID NO
145466	145485	n/a	387916	TCTCTATTGCACATTCCAAG	5-10-5	98	6
146781	146799	Major (5)	460156	ATTGTCATCACCAGAAAAA	5-9-5	88	194
146782	146800	Major (6)	460155	AATTGTCATCACCAGAAAA	5-9-5	89	195
146783	146801	Major (7)	460154	AAATTGTCATCACCAGAAA	5-9-5	89	196
146784	146802	Major (8)	460153	TAAATTGTCATCACCAGAA	5-9-5	93	197
146785	146803	Major (9)	460152	ATAAATTGTCATCACCAGA	5-9-5	95	198
146786	146804	Major (10)	*435879	AATAAATTGTCATCACCAG	5-9-5	94	99
146786	146804	Major (10)	460024	AATAAATTGTCATCACCAG	4-10-5	88	99
146786	146804	Major (10)	460035	AATAAATTGTCATCACCAG	4-11-4	91	99
146786	146803	Major (9)	460065	ATAAATTGTCATCACCAG	4-9-5	96	199
146786	146804	Major (10)	460074	AATAAATTGTCATCACCAG	5-10-4	94	99

146786	146804	Major (10)	460095	AATAAATTGTCATCACCAG	5-8-6	92	99
146786	146804	Major (10)	460170	AATAAATTGTCATCACCAG	6-7-6	91	99
146786	146804	Major (10)	460189	AATAAATTGTCATCACCAG	6-8-5	94	99
146787	146803	Major (9)	459981	ATAAATTGTCATCACCA	2-9-6	85	200
146787	146802	Major (8)	460002	TAAATTGTCATCACCA	3-9-4	86	201
146787	146803	Major (9)	460014	ATAAATTGTCATCACCA	3-9-5	91	200
146787	146803	Major (9)	460055	ATAAATTGTCATCACCA	4-9-4	90	200
146787	146803	Major (9)	460085	ATAAATTGTCATCACCA	5-7-5	94	200
146787	146803	Major (9)	460104	ATAAATTGTCATCACCA	5-9-3	93	200
146787	146805	Major (11)	460147	TAATAAATTGTCATCACCA	5-9-5	91	202
146787	146803	Major (9)	460180	ATAAATTGTCATCACCA	6-9-2	91	200
146788	146802	Major (8)	459970	TAAATTGTCATCACC	Uniform	9	203
146788	146802	Major (8)	459990	TAAATTGTCATCACC	3-9-3	67	203
146788	146802	Major (8)	460045	TAAATTGTCATCACC	4-7-4	84	203
146788	146806	Major (12)	460148	TTAATAAATTGTCATCACC	5-9-5	88	204
146789	146807	Major (13)	460149	ATTAATAAATTGTCATCAC	5-9-5	32	205
146790	146808	Major (14)	460150	TATTAATAAATTGTCATCA	5-9-5	29	206
146791	146809	Major (15)	460151	CTATTAATAAATTGTCATC	5-9-5	33	207

Table 17

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs362331 (nucleobases 155474 to 155502 of SEQ ID NO: 1)

Start Site	Stop Site	Target allele	ISIS No.	Sequence	Motif	% inhibition	SEQ ID NO
145466	145485	n/a	387916	TCTCTATTGCACATTCCAAG	5-10-5	98	6
155474	155492	Major (5)	460136	CAGTAGATGAGGGAGCAGG	5-9-5	81	208
155475	155493	Major (6)	460135	ACAGTAGATGAGGGAGCAG	5-9-5	84	209
155476	155494	Major (7)	460134	CACAGTAGATGAGGGAGCA	5-9-5	87	210
155477	155495	Major (8)	460133	ACACAGTAGATGAGGGAGC	5-9-5	85	211
155478	155496	Major (9)	460132	CACACAGTAGATGAGGGAG	5-9-5	86	212
155479	155497	Major (10)	*435870	GCACACAGTAGATGAGGGA	5-9-5	91	103
155479	155497	Major (10)	460019	GCACACAGTAGATGAGGGA	4-10-5	92	103
155479	155497	Major (10)	460031	GCACACAGTAGATGAGGGA	4-11-4	95	103
155479	155496	Major (9)	460061	CACACAGTAGATGAGGGA	4-9-5	87	213
155479	155497	Major (10)	460071	GCACACAGTAGATGAGGGA	5-10-4	94	103
155479	155497	Major (10)	460090	GCACACAGTAGATGAGGGA	5-8-6	86	103
155479	155497	Major (10)	460168	GCACACAGTAGATGAGGGA	6-7-6	84	103
155479	155497	Major (10)	460187	GCACACAGTAGATGAGGGA	6-8-5	89	103
155480	155496	Major (9)	459977	CACACAGTAGATGAGGG	2-9-6	90	214
155480	155495	Major (8)	459996	ACACAGTAGATGAGGG	3-9-4	37	215
155480	155496	Major (9)	460009	CACACAGTAGATGAGGG	3-9-5	90	214
155480	155496	Major (9)	460051	CACACAGTAGATGAGGG	4-9-4	73	214

155480	155496	Major (9)	460081	CACACAGTAGATGAGGG	5-7-5	77	214
155480	155496	Major (9)	460101	CACACAGTAGATGAGGG	5-9-3	84	214
155480	155498	Major (11)	460127	TGCACACAGTAGATGAGGG	5-9-5	89	216
155480	155496	Major (9)	460178	CACACAGTAGATGAGGG	6-9-2	92	214
155481	155495	Major (8)	459967	ACACAGTAGATGAGG	Uniform	81	217
155481	155495	Major (8)	459987	ACACAGTAGATGAGG	3-9-3	18	217
155481	155495	Major (8)	460041	ACACAGTAGATGAGG	4-7-4	54	217
155481	155499	Major (12)	460128	GTGCACACAGTAGATGAGG	5-9-5	73	218
155482	155500	Major (13)	460129	AGTGCACACAGTAGATGAG	5-9-5	86	219
155483	155501	Major (14)	460130	AAGTGCACACAGTAGATGA	5-9-5	60	220
155484	155502	Major (15)	460131	GAAGTGCACACAGTAGATG	5-9-5	73	221

Table 18

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs362306 (nucleobases 181739 to 181767 of SEQ ID NO: 1)

Start Site	Stop Site	Target allele	ISIS No.	Sequence	Motif	% inhibition	SEQ ID NO
145466	145485	n/a	387916	TCTCTATTGCACATTCCAAG	5-10-5	98	6
181739	181757	Major (5)	460126	GCTGCAACCTGGCAACAAC	5-9-5	87	222
181740	181758	Major (6)	460125	AGCTGCAACCTGGCAACAA	5-9-5	70	223
181741	181759	Major (7)	460123	CAGCTGCAACCTGGCAACA	5-9-5	83	224
181742	181760	Major (8)	460121	GCAGCTGCAACCTGGCAAC	5-9-5	47	225
181743	181761	Major (9)	460118	AGCAGCTGCAACCTGGCAA	5-9-5	75	226
181744	181762	Major (10)	*435869	GAGCAGCTGCAACCTGGCA	5-9-5	91	149
181744	181762	Major (10)	460018	GAGCAGCTGCAACCTGGCA	4-10-5	86	149
181744	181762	Major (10)	460028	GAGCAGCTGCAACCTGGCA	4-11-4	89	149
181744	181761	Major (9)	460058	AGCAGCTGCAACCTGGCA	4-9-5	85	227
181744	181762	Major (10)	460069	GAGCAGCTGCAACCTGGCA	5-10-4	91	149
181744	181762	Major (10)	460089	GAGCAGCTGCAACCTGGCA	5-8-6	54	149
181744	181762	Major (10)	460167	GAGCAGCTGCAACCTGGCA	6-7-6	85	149
181744	181762	Major (10)	460186	GAGCAGCTGCAACCTGGCA	6-8-5	84	149
181745	181761	Major (9)	459975	AGCAGCTGCAACCTGGC	2-9-6	86	228
181745	181760	Major (8)	459995	GCAGCTGCAACCTGGC	3-9-4	87	229
181745	181761	Major (9)	460008	AGCAGCTGCAACCTGGC	3-9-5	83	228
181745	181761	Major (9)	460049	AGCAGCTGCAACCTGGC	4-9-4	88	228
181745	181761	Major (9)	460079	AGCAGCTGCAACCTGGC	5-7-5	46	228
181745	181761	Major (9)	460099	AGCAGCTGCAACCTGGC	5-9-3	44	228
181745	181763	Major (11)	460108	AGAGCAGCTGCAACCTGGC	5-9-5	50	230
181745	181761	Major (9)	460177	AGCAGCTGCAACCTGGC	6-9-2	67	228
181746	181760	Major (8)	459966	GCAGCTGCAACCTGG	Uniform	26	231
181746	181760	Major (8)	459985	GCAGCTGCAACCTGG	3-9-3	69	231
181746	181760	Major (8)	460039	GCAGCTGCAACCTGG	4-7-4	56	231

181746	181764	Major (12)	460110	AAGAGCAGCTGCAACCTGG	5-9-5	75	232
181747	181765	Major (13)	460113	CAAGAGCAGCTGCAACCTG	5-9-5	36	233
181748	181766	Major (14)	460115	GCAAGAGCAGCTGCAACCT	5-9-5	78	234
181749	181767	Major (15)	460117	TGCAAGAGCAGCTGCAACC	5-9-5	73	235

Table 19

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs1006798 (nucleobases 198015 to 198035 of SEQ ID NO: 1)

Start Site	Stop Site	Target allele	ISIS No.	Sequence	Motif	% inhibition	SEQ ID NO
145466	145485	n/a	387916	TCTCTATTGCACATTCCAAG	5-10-5	98	6
198015	198033	Minor (8)	459911	ACCATGATATCTCCAGCAC	5-9-5	33	236
198015	198033	Minor (8)	459919	ACCATGACATCTCCAGCAC	5-9-5	26	237
198017	198035	Major (10)	459907	CCACCATGATATCTCCAGC	5-9-5	32	238
198017	198035	Minor (10)	459915	CCACCATGACATCTCCAGC	5-9-5	51	239

Example 6: Dose-dependent antisense inhibition of human huntingtin mRNA levels in Coriell fibroblast cell lines

Gapmers from the studies described in Example 5 were selected and tested at various doses in GM04281, GM02171, and GM02173B cell lines. Each cell line was plated at a density of 25,000 cells per well and transfected using electroporation with 750 nM, 1,500 nM, 3,000 nM, 6,000 nM, and 12,000 nM concentrations of antisense oligonucleotide, as specified in Tables 20, 21, and 22. After a treatment period of approximately 16 hours, RNA was isolated from the cells and *HTT* mRNA levels were measured by quantitative real-time PCR. Human *HTT* primer probe set RTS2617 was used to measure mRNA levels. *HTT* mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN. Results are presented as percent inhibition of *HTT* mRNA, relative to untreated control cells. IC₅₀ values are also provided in Tables 20, 21, and 22.

Table 20

Dose-dependent antisense inhibition of human *HTT* in GM04281 cells

ISIS No.	750 nM	1,500 nM	3,000 nM	6,000 nM	12,000 nM	IC ₅₀ (μM)
387916	56	81	89	96	98	0.6
435869	38	49	66	86	91	1.4
435874	33	27	37	49	62	8.4
435879	42	55	73	86	96	1.1
435890	39	51	74	83	89	1.3

459978	29	33	51	69	86	2.5
459992	14	27	51	54	84	3.2
460012	15	24	54	70	81	3.1
460016	3	36	48	71	77	3.3
460019	54	59	74	87	94	0.7
460026	48	47	71	79	88	0.8
460028	39	38	73	77	87	1.4
460031	44	62	72	87	92	0.9
460033	11	38	52	64	87	3.0
460065	43	54	74	89	96	1.1
460068	47	28	63	76	90	2.6
460069	38	50	65	77	91	1.4
460071	53	61	80	89	93	0.6
460073	16	39	42	58	75	4.0
460076	26	47	54	70	86	2.1
460085	48	60	79	89	94	0.8
460140	6	24	44	44	64	6.6
460142	2	38	46	46	68	4.8
460152	35	61	76	92	94	1.2
460157	51	36	53	74	89	2.6
460162	64	41	71	76	85	2.1
460165	41	50	56	76	84	1.5

Table 21
Dose-dependent antisense inhibition of human *HTT* in GM02171 cells

ISIS No.	750 nM	1,500 nM	3,000 nM	6,000 nM	12,000 nM	IC ₅₀ (μM)
387916	53	66	88	96	98	0.7
435869	4	20	36	63	86	3.9
435870	25	39	48	62	83	2.8
435874	12	20	18	27	37	>12.0
435879	10	7	11	42	51	10.6
435890	10	23	29	29	55	9.2
459978	15	7	6	29	52	12.7
459992	11	19	26	39	62	8.7
460012	3	3	10	19	41	>12.0
460016	0	14	12	22	48	>12.0
460019	27	21	41	60	73	4.4
460026	9	25	30	46	58	7.8
460028	24	8	32	54	77	5.3
460031	8	25	42	60	83	3.8
460033	11	25	30	40	75	4.1

460065	11	16	11	31	53	10.3
460068	15	13	39	44	53	8.8
460069	17	28	37	60	79	3.9
460071	16	36	58	70	88	2.6
460073	5	19	24	33	56	8.7
460076	19	29	44	54	83	3.3
460085	10	15	17	28	31	>12.0
460140	8	22	22	28	47	>12.0
460142	11	24	28	36	38	>12.0
460152	14	21	8	25	44	22
460157	22	21	29	44	66	6.7
460162	24	55	52	62	82	2.8
460165	14	34	50	69	81	3.1

Table 22
Dose-dependent antisense inhibition of human *HTT* in GM02173B cells

ISIS No.	750 nM	1,500 nM	3,000 nM	6,000 nM	12,000 nM	IC ₅₀ (μM)
387916	37	63	86	88	98	1.0
435869	10	20	43	70	85	3.5
435870	24	24	56	72	87	2.3
435874	0	11	12	30	44	>12.0
435879	4	17	43	64	74	4.3
435890	31	29	54	57	69	4.4
459978	7	13	17	35	64	8.4
459992	18	15	30	51	71	5.7
460012	0	10	24	37	72	7.1
460016	15	5	30	38	59	9.5
460019	10	32	51	65	87	3.1
460026	0	34	21	55	65	6.4
460028	0	14	31	51	77	5.2
460031	0	31	53	71	88	3.2
460033	11	8	6	52	84	5.0
460065	19	37	53	58	74	3.6
460068	17	11	31	59	69	5.5
460069	11	21	37	55	75	4.6
460071	6	42	61	83	88	2.6
460073	7	13	19	49	66	6.3
460076	27	31	49	43	81	2.9
460085	17	34	51	54	68	4.4
460140	0	2	28	18	46	>12.0
460142	2	32	37	42	59	7.6

460152	17	32	35	51	66	5.5
460157	9	34	38	52	74	4.5
460162	22	45	57	65	79	2.5
460165	5	45	52	72	84	3.2

Example 7: Antisense inhibition of human *HTT* in GM04281 cells and GM02171 cells

Additional antisense oligonucleotides were designed based on the gapmers selected from studies described in Example 2. These oligonucleotides were designed by creating gapmers shifted slightly upstream and downstream (i.e. “microwalk”) of the original gapmers from Table 4.

The gapmers were tested in the GM04281 and the GM02171 cell lines. Cultured GM04281 or GM02171 cells at a density of 25,000 cells per well were transfected using electroporation with 10,000 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and *HTT* mRNA levels were measured by quantitative real-time PCR using primer probe set RTS2617. *HTT* mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN. Results are presented as percent inhibition of *HTT* mRNA, relative to untreated control cells.

The gapmers, from which the newly designed oligonucleotides were derived, were also included in the assay. These parent gapmers, ISIS 435294, ISIS 435295, ISIS 435301, ISIS 435303, ISIS 435304, ISIS 435305, ISIS 435308, ISIS 435330, ISIS 435331, ISIS 435337, ISIS 435339, ISIS 435340, ISIS 435341, ISIS 435344, ISIS 435862, ISIS 435863, ISIS 435864, ISIS 435866, ISIS 435867, ISIS 435868, ISIS 435871, ISIS 435873, ISIS 435875, ISIS 435876, ISIS 435878, ISIS 435880, ISIS 435881, ISIS 435882, ISIS 435884, ISIS 435890, and ISIS 435897 are marked with an asterisk (*) in the table. ISIS 387916 was included in the study as a benchmark oligonucleotide against which the potency of the antisense oligonucleotides targeting nucleotides overlapping each SNP position could be compared.

The chimeric antisense oligonucleotides in Tables 23-48 were designed as 5-9-5 MOE gapmers. The 5-9-5 gapmers are 19 nucleotides in length, wherein the central gap segment is comprised of nine 2'-deoxynucleotides and is flanked on both 5' and 3' directions by wings comprising 5 nucleotides each. Each nucleotide in the 5' wing segment and each nucleotide in the 3' wing segment has a 2'-MOE modification. The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine nucleobases throughout each gapmer are 5-methylcytosines.

The gapmers are organized in Tables 23-48, according to the SNP site they target. “Start site” indicates the 5’-most nucleotide to which the gapmer is targeted. “Stop site” indicates the 3’-most nucleotide to which the gapmer is targeted. ‘Target allele’ indicates whether the gapmer is targeted to the major or the minor allele. The number in parentheses indicates the position on the oligonucleotide opposite to the SNP position.

Table 23

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs3856973 (nucleobases 19815 to 19835 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
19815	19833	*435330	Major (8)	TAACACTCGATTAACCCTG	88	31	8
19816	19834	476441	Major (9)	TTAACACTCGATTAACCCT	88	0	240
19817	19835	*435294	Major (10)	GTTAACACTCGATTAACCC	72	30	10

Table 24

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs2285086 (nucleobases 28901 to 28921 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
28901	28919	463570	Major (8)	TAGTTCATCCCAGTGAGAA	66	12	241
28902	28920	463573	Major (9)	CTAGTTCATCCCAGTGAGA	66	36	242
28903	28921	*435864	Major (10)	GCTAGTTCATCCCAGTGAG	40	18	12

Table 25

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs7659144 (nucleobases 37963 to 37983 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
37963	37981	476462	Major (8)	GAAATGGGTTTTTCCACAT	38	0	243
37964	37982	476439	Major (9)	GGAAATGGGTTTTTCCACA	80	45	244
37965	37983	*435878	Major (10)	TGGAAATGGGTTTTTCCAC	76	3	14

Table 26

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs16843804 (nucleobases 44032 to 44052 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
44032	44050	476471	Major (8)	TAACCGTGGCATGGGCAGT	82	53	245
44033	44051	476452	Major (9)	TTAACCGTGGCATGGGCAG	84	44	246
44034	44052	*435863	Major (10)	TTTAACCGTGGCATGGGCA	89	89	16

Table 27

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs2024115 (nucleobases 44210 to 44230 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
44210	44228	*435331	Major (8)	TTCAAGCTAGTAACGATGC	84	20	18
44211	44229	476447	Major (9)	CTTCAAGCTAGTAACGATG	87	57	247
44212	44230	*435295	Major (10)	ACTTCAAGCTAGTAACGAT	85	67	20

Table 28

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs10015979 (nucleobases 49084 to 49104 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
49084	49102	476470	Major (8)	AGCTAGGTTAAAGAGTCAC	55	74	248
49085	49103	476450	Major (9)	CAGCTAGGTTAAAGAGTCA	44	5	249
49086	49104	*435862	Major (10)	GCAGCTAGGTTAAAGAGTC	56	49	22

Table 29

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs7691627 (nucleobases 51052 to 51072 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
51052	51070	476467	Major (8)	TAAGAAACACAATCAAAGA	45	21	250

51053	51071	476445	Major (9)	ATAAGAAACACAATCAAAG	34	1	251
51054	51072	*435880	Major (10)	AATAAGAAACACAATCAAA	68	7	24

Table 30

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs6446723 (nucleobases 66455 to 66475 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
66455	66473	476463	Major (8)	ATTTTCTAGACTTTATGAT	37	7	252
66456	66474	476440	Major (9)	AATTTTCTAGACTTTATGA	57	0	253
66457	66475	*435875	Major (10)	TAATTTTCTAGACTTTATG	42	0	30

Table 31

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and a chimeric antisense oligonucleotide targeted to SNP rs363064 (nucleobases 81053 to 81071 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
81053	81071	476461	Major (9)	GAGAATACGGGTAACATTT	87	62	254

Table 32

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs11731237 (nucleobases 91455 to 91475 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
91455	91473	476468	Major (8)	TGGGCAGGAAGGACTGAAC	58	56	255
91456	91474	476448	Major (9)	GTGGGCAGGAAGGACTGAA	61	69	256
91457	91475	*435884	Major (10)	GGTGGGCAGGAAGGACTGA	59	49	68

Table 33

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs4690073 (nucleobases 99792 to 99812 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6

99792	99810	*435337	Major (8)	CCTAAATCAATCTACAAGT	69	7	70
99793	99811	476446	Major (9)	CCCTAAATCAATCTACAAG	61	0	257
99794	99812	*435301	Major (10)	TCCCTAAATCAATCTACAA	63	1	72

Table 34

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs34315806 (nucleobases 101676 to 101696 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
101676	101694	463569	Major (8)	CTTTTCCGTGCTGTTCTGA	96	95	258
101677	101695	463572	Major (9)	ACTTTTCCGTGCTGTTCTG	93	91	259
101678	101696	463567	Major (10)	AACTTTTCCGTGCTGTTCT	98	97	260

Table 35

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs363099 (nucleobases 101698 to 101718 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
101698	101716	*435339	Major (8)	CTGAGCGGAGAAACCCTCC	94	85	80
101699	101717	476458	Major (9)	GCTGAGCGGAGAAACCCTC	92	79	261
101700	101718	*435303	Major (10)	GGCTGAGCGGAGAAACCCT	96	93	82

Table 36

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs363096 (nucleobases 119663 to 119683 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
119663	119681	*435340	Major (8)	TTCCCTAAAAACAAAAACA	42	21	85
119664	119682	476451	Major (9)	ATTCCCTAAAAACAAAAAC	0	0	262
119665	119683	*435304	Major (10)	GATTCCCTAAAAACAAAAA	41	27	87

Table 37

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs2298967 (nucleobases 125389 to 125409 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
125389	125407	*435341	Major (8)	CTTTTCTATTGTCTGTCCC	83	65	89
125390	125408	476459	Major (9)	GCTTTTCTATTGTCTGTCC	89	82	263
125391	125409	*435305	Major (10)	TGCTTTTCTATTGTCTGTC	92	85	91

Table 38

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and a chimeric antisense oligonucleotide targeted to SNP rs2298969 (nucleobases 125888 to 125906 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
125888	125906	*435890	Minor (10)	AAGGGATGCTGACTTGGGC	91	64	94

Table 39

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs6844859 (nucleobases 130128 to 130148 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
130128	130146	476466	Major (8)	CTTCCTCACTGAGGATGAA	87	64	264
130129	130147	476444	Major (9)	CCTTCCTCACTGAGGATGA	92	77	265
130130	130148	*435876	Major (10)	ACCTTCCTCACTGAGGATG	94	87	95

Table 40

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs363092 (nucleobases 135671 to 135691 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
135671	135689	476464	Major (8)	AACCACTTTGGGATGAATA	51	71	266
135672	135690	476442	Major (9)	AAACCACTTTGGGATGAAT	58	59	267
135673	135691	*435897	Minor (10)	CAAACCACTTTGGGATGAA	48	78	98

Table 41

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs363088 (nucleobases 149972 to 149992 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
149972	149990	476476	Major (8)	ACAGCTATCTTCTCATCAA	90	65	268
149973	149991	476460	Major (9)	CACAGCTATCTTCTCATCA	86	39	269
149974	149992	*435871	Major (10)	TCACAGCTATCTTCTCATC	91	54	101

Table 42

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs916171 (nucleobases 156457 to 156477 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
156457	156475	476465	Major (8)	GAACAAAGAGAAGAATTTC	38	0	270
156458	156476	476443	Major (9)	AGAACAAAGAGAAGAATTT	58	0	271
156459	156477	*435881	Major (10)	CAGAACAAAGAGAAGAATT	59	16	105

Table 43

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs362275 (nucleobases 164244 to 164264 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
164244	164262	476473	Major (8)	GAAGCCTGATAAAATCTCT	83	51	272
164245	164263	476454	Major (9)	AGAAGCCTGATAAAATCTC	79	61	273
164246	164264	*435868	Major (10)	AAGAAGCCTGATAAAATCT	69	56	111

Table 44

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs362273 (nucleobases 167061 to 167081 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
167061	167079	463568	Major (8)	TGATCTGTAGCAGCAGCTT	96	78	274

167062	167080	463571	Major (9)	TTGATCTGTAGCAGCAGCT	95	86	275
167063	167081	463566	Major (10)	GTTGATCTGTAGCAGCAGC	94	78	276

Table 45

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs362272 (nucleobases 174622 to 174642 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
174622	174640	*435344	Major (8)	TAGAGGACGCCGTGCAGGG	78	63	120
174623	174641	476456	Major (9)	ATAGAGGACGCCGTGCAGG	87	60	277
174624	174642	*435308	Major (10)	CATAGAGGACGCCGTGCAG	76	48	122

Table 46

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs362271 (nucleobases 175160 to 175180 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
175160	175178	476472	Major (8)	GTGTGTACAGAACCTGCCG	85	52	278
175161	175179	476453	Major (9)	CGTGTGTACAGAACCTGCC	88	69	279
175162	175180	*435867	Major (10)	ACGTGTGTACAGAACCTGC	91	80	125

Table 47

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs3775061 (nucleobases 178396 to 178416 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
178396	178414	476475	Major (8)	TTCAGAATGCCTCATCTGG	61	1	280
178397	178415	476457	Major (9)	G TTCAGAATGCCTCATCTG	80	50	281
178398	178416	*435873	Major (10)	TG TTCAGAATGCCTCATCT	80	43	127

Table 48

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs362296 (nucleobases 186649 to 1786669 of SEQ ID NO: 1)

Start Site	Stop Site	ISIS No	Target allele	Sequence	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO

145466	145485	387916	n/a	TCTCTATTGCACATTCCAAG	100	99	6
186649	186667	476469	Major (8)	GGACAGGGTGTGCTCTCCG	80	58	282
186650	186668	476449	Major (9)	GGGACAGGGTGTGCTCTCC	80	64	283
186651	186669	*435882	Major (10)	GGGGACAGGGTGTGCTCTC	61	61	155

Example 8: Dose-dependent antisense inhibition of human huntingtin mRNA levels in Coriell fibroblast cell lines

Gapmers from the studies described in Example 7 were selected and tested at various doses in GM04281, GM02171, and GM02173B cell lines. Each cell line was plated at a density of 25,000 cells per well and transfected using electroporation with 750 nM, 1,500 nM, 3,000 nM, 6,000 nM, and 12,000 nM concentrations of antisense oligonucleotide, as specified in Tables 49, 50, and 51. After a treatment period of approximately 16 hours, RNA was isolated from the cells and *HTT* mRNA levels were measured by quantitative real-time PCR. Human *HTT* primer probe set RTS2617 was used to measure mRNA levels. *HTT* mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN. Results are presented as percent inhibition of *HTT* mRNA, relative to untreated control cells. IC₅₀ values are also provided in Tables 49, 50, and 51.

Table 49
Dose-dependent antisense inhibition of human *HTT* in GM04281 cells

ISIS No.	750 nM	1500 nM	3000 nM	6000 nM	12000 nM	IC ₅₀ (μM)
387916	67	88	95	97	99	<0.8
463566	25	65	79	88	95	1.5
463567	34	73	90	93	98	1.1
463568	33	56	75	87	92	1.3
463571	32	21	70	90	93	1.4
476441	11	27	50	70	87	3.1
476444	20	31	68	49	93	2.3
476449	4	28	34	47	77	4.9
476453	21	21	48	73	85	2.7
476455	5	19	34	56	80	4.6
476458	36	72	83	93	96	1.1
476459	23	59	75	85	91	1.5
476469	17	27	47	47	67	5.5
476473	0	6	32	50	68	6.2
476476	3	7	32	53	86	4.9

Table 50
Dose-dependent antisense inhibition of human *HTT* in GM02171 cells

ISIS No.	750 nM	1500 nM	3000 nM	6000 nM	12000 nM	IC ₅₀ (μM)
387916	59	79	93	98	98	<0.8
463566	4	33	42	62	79	3.8
463567	38	41	69	85	94	1.5
463568	21	26	41	58	64	4.8
463571	8	23	56	63	75	3.7
476441	0	13	7	0	12	>12.0
476444	11	0	0	67	59	8.8
476449	4	27	37	51	63	5.8
476453	6	40	40	51	73	4.9
476455	32	15	18	47	61	7.8
476458	42	54	71	86	84	1.2
476459	22	38	70	44	73	4.3
476469	7	24	30	56	58	7.8
476473	4	10	15	33	43	>12.0
476476	5	16	18	23	41	>12.0

Table 51
Dose-dependent antisense inhibition of human *HTT* in GM02171 cells

ISIS No.	750 nM	1500 nM	3000 nM	6000 nM	12000 nM	IC ₅₀ (μM)
387916	66	89	95	97	99	<0.8
463566	32	55	76	77	93	1.3
463567	51	61	87	94	97	0.7
463568	26	23	72	87	94	1.6
463571	32	34	60	86	94	1.9
476441	18	18	27	47	44	>12.0
476444	15	0	31	51	58	7.1
476449	27	33	56	80	81	2.6
476453	24	28	55	75	83	2.7
476455	24	26	52	55	73	3.7
476458	63	77	87	89	94	0.2
476459	37	55	56	62	86	1.5
476469	22	41	40	63	76	2.9
476473	7	28	33	51	73	5.0
476476	11	29	26	55	69	4.6

Example 9: Antisense inhibition of human *HTT* in GM04281 cells by oligonucleotides designed by microwalk

Additional gapmers were designed based on the gapmers selected from studies described in Example 4. These gapmers were designed by creating gapmers shifted slightly upstream and downstream (i.e. “microwalk”) of the original gapmers from Tables 8, 9, and 10. Gapmers were also created with 3-9-3 or 5-9-5 motifs, and with constrained 6(S)-CH₃-bicyclic nucleic acid (BNA) molecules at various nucleoside positions.

These gapmers were tested *in vitro*. Cultured GM04281 cells at a density of 25,000 cells per well were transfected using electroporation with 5,000 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and *HTT* mRNA levels were measured by quantitative real-time PCR. *HTT* mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN. Results are presented as percent inhibition of *HTT* mRNA, relative to untreated control cells.

The chimeric antisense oligonucleotides in Tables 52-56 were designed as 3-9-3 or 5-9-5 gapmers. The parent gapmers, ISIS 435869, ISIS 435870, ISIS 435874, ISIS 435879, and ISIS 435890, from which the newly designed gapmers were derived are marked with an asterisk (*) in the table. ISIS 387916 was included in the study as a benchmark oligonucleotide against which the potency of the antisense oligonucleotides targeting nucleotides overlapping each SNP position could be compared.

The 3-9-3 gapmers are 15 nucleotides in length, wherein the central gap segment is comprised of nine 2'- deoxynucleosides and is flanked on both 5' and 3' directions by wings comprising 3 sugar modified nucleosides each.

The 5-9-5 gapmers are 19 nucleotides in length, wherein the central gap segment is comprised of nine 2'- deoxynucleosides and is flanked on both 5' and 3' directions by wings comprising 5 sugar modified nucleosides each.

The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine nucleobases throughout each gapmer are 5-methylcytosines. Bolded and underlined nucleotides in Tables 52-56 indicate the positions of the 6(S)-CH₃-BNA molecules (e.g. cEt molecules) in each gapmer. Italicized nucleotides are MOE subunits.

“Start site” indicates the 5’-most nucleotide to which the gapmer is targeted. “Stop site” indicates the 3’-most nucleotide to which the gapmer is targeted. ‘Target allele’ indicates whether the gapmer is targeted to the major or the minor allele. The number in parentheses indicates the position on the oligonucleotide opposite to the SNP position.

Table 52

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs4690072 (nucleobases 62147 to 62173 of SEQ ID NO: 1)

Start Site	Stop Site	Target allele	ISIS No.	Sequence	Motif	% inhibition	SEQ ID NO
145466	145485	n/a	387916	<i>TCTCTATTGCACATTCCAAG</i>	5-10-5	97	6
62147	62165	Major (6)	460266	<i>GTGCT<u>A</u>CCCAACCTTTCTG</i>	5-9-5	63	169
62151	62169	Major (10)	*435874	<i>CACAGTGCTACCCAACCTT</i>	5-9-5	50	28
62151	62169	Major (10)	460213	<i>CACAGTGCT<u>A</u>CCCAACCTT</i>	5-9-5	22	28
62151	62169	Major (10)	460220	<i>CACAGTGCT<u>T</u>ACCCAACCTT</i>	5-9-5	24	28
62151	62169	Major (10)	460221	<i>CACAGTGCTA<u>C</u>CCAACCTT</i>	5-9-5	28	28
62153	62167	Major (8)	460208	<i><u>C</u>AGTGCTACCCA<u>A</u>CC</i>	3-9-3	81	177
62155	62173	Major (14)	460267	<i>ATATCACAGTGCT<u>A</u>CCCAA</i>	5-9-5	37	180

Table 53

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs2298969 (nucleobases 125884 to 125910 of SEQ ID NO: 1)

Start Site	Stop Site	Target allele	ISIS No.	Sequence	Motif	% inhibition	SEQ ID NO
145466	145485	n/a	387916	<i>TCTCTATTGCACATTCCAAG</i>	5-10-5	97	6
125884	125902	Minor (6)	460233	<i>GATGCT<u>T</u>GACTTGGGCCATT</i>	5-9-5	76	182
125888	125906	Minor (10)	*435890	<i>AAGGGATGCTGACTTGGGC</i>	5-9-5	75	94
125888	125906	Minor (10)	460215	<i>AAGGGATGCT<u>T</u>GACTTGGGC</i>	5-9-5	26	94
125888	125906	Minor (10)	460224	<i>AAGGGATG<u>C</u>TGACTTGGGC</i>	5-9-5	38	94
125888	125906	Minor (10)	460225	<i>AAGGGATGCTG<u>A</u>CTTGGGC</i>	5-9-5	49	94
125890	125904	Minor (8)	460210	<i><u>G</u>GGATGCTGACT<u>T</u>GG</i>	3-9-3	97	189
125892	125910	Minor (14)	460229	<i>TGCCAAGGGATGCT<u>T</u>GACTT</i>	5-9-5	60	192

Table 54

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs7685686 (nucleobases 146782 to 146808 of SEQ ID NO: 1)

Start Site	Stop Site	Target allele	ISIS No.	Sequence	Motif	% inhibition	SEQ ID NO
145466	145485	n/a	387916	<i>TCTCTATTGCACATTCCAAG</i>	5-10-5	97	6
146782	146800	Major (6)	460232	<i>AATTGTCATCACCAGAAAA</i>	5-9-5	82	195
146786	146804	Major (10)	*435879	<i>AATAAATTGTCATCACCAG</i>	5-9-5	84	99
146786	146804	Major (10)	460214	<i>AATAAATTGTCATCACCAG</i>	5-9-5	33	99
146786	146804	Major (10)	460222	<i>AATAAATTGTCATCACCAG</i>	5-9-5	87	99
146786	146804	Major (10)	460223	<i>AATAAATTGTCATCACCAG</i>	5-9-5	75	99
146788	146802	Major (8)	460209	<i>TAAATTGTCATCACC</i>	3-9-3	96	203
146790	146808	Major (14)	460228	<i>TATTAATAAATTGTCATCA</i>	5-9-5	0	206

Table 55

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs362331 (nucleobases 155475 to 155501 of SEQ ID NO: 1)

Start Site	Stop Site	Target allele	ISIS No.	Sequence	Motif	% inhibition	SEQ ID NO
145466	145485	n/a	387916	<i>TCTCTATTGCACATTCCAAG</i>	5-10-5	97	6
155475	155493	Major (6)	460231	<i>ACAGTAGATGAGGGAGCAG</i>	5-9-5	88	209
155479	155497	Major (10)	*435870	<i>GCACACAGTAGATGAGGGA</i>	5-9-5	86	103
155479	155497	Major (10)	460212	<i>GCACACAGTAGATGAGGGA</i>	5-9-5	89	103
155479	155497	Major (10)	460218	<i>GCACACAGTAGATGAGGGA</i>	5-9-5	90	103
155479	155497	Major (10)	460219	<i>GCACACAGTAGATGAGGGA</i>	5-9-5	88	103
155481	155495	Major (8)	460207	<i>ACACAGTAGATGAGG</i>	3-9-3	89	217
155483	155501	Major (14)	460227	<i>AAGTGCACACAGTAGATGA</i>	5-9-5	45	220

Table 56

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs362306 (nucleobases 181740 to 181766 of SEQ ID NO: 1)

Start Site	Stop Site	Target allele	ISIS No.	Sequence	Motif	% inhibition	SEQ ID NO
145466	145485	n/a	387916	<i>TCTCTATTGCACATTCCAAG</i>	5-10-5	97	6
181740	181758	Major (6)	460230	<i>AGCTGCAACCTGGCAACAA</i>	5-9-5	66	223
181744	181762	Major (10)	*435869	<i>GAGCAGCTGCAACCTGGCA</i>	5-9-5	69	149
181744	181762	Major (10)	460211	<i>GAGCAGCTGCAACCTGGCA</i>	5-9-5	22	149
181744	181762	Major (10)	460216	<i>GAGCAGCTGCAACCTGGCA</i>	5-9-5	18	149
181744	181762	Major (10)	460217	<i>GAGCAGCTGCAACCTGGCA</i>	5-9-5	56	149

181746	181760	Major (8)	460206	<u>GC</u> AGCTGCAACCT <u>TGG</u>	3-9-3	83	231
181748	181766	Major (14)	460226	GCAAGAGCAGCTG <u>CA</u> ACCT	5-9-5	51	234

Example 10: Dose-dependent antisense inhibition of human huntingtin mRNA levels in Coriell fibroblast cell lines

Gapmers from studies described in Example 9 were selected and tested at various doses in GM04281, GM02171 and GM02173B cell lines. Each cell line was plated at a density of 25,000 cells per well and transfected using electroporation with 312.5 nM, 625 nM, 1,250 nM, 2,500 nM, 5,000 nM and 10,000 nM concentrations of antisense oligonucleotide, as specified in Tables 75, 58, and 59. After a treatment period of approximately 16 hours, RNA was isolated from the cells and *HTT* mRNA levels were measured by quantitative real-time PCR. Human *HTT* primer probe set RTS2617 was used to measure mRNA levels. *HTT* mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN. Results are presented as percent inhibition of *HTT* mRNA, relative to untreated control cells. IC₅₀ values are also provided in Tables 57, 58, and 59.

Table 57
Dose-dependent antisense inhibition of human *HTT* in GM04281 cells

ISIS No.	312.5 nM	625 nM	1,250 nM	2,500 nM	5,000 nM	10,000 nM	IC ₅₀ (μM)
387916	26	49	68	86	94	97	0.7
435869	0	0	23	48	62	82	3.2
435870	15	38	50	65	85	88	1.3
435874	14	22	32	49	65	73	2.7
435879	0	17	40	61	83	94	1.8
435890	5	13	37	56	70	82	2.3
460206	10	18	37	52	66	85	2.3
460207	20	27	50	65	80	91	1.4
460208	21	34	51	63	70	79	1.5
460209	52	74	89	94	94	95	0.2
460210	34	61	84	91	97	98	0.5
460212	13	31	50	62	75	82	1.6
460218	14	27	50	63	78	86	1.8
460219	9	32	42	64	77	87	1.6
460222	19	21	42	57	73	78	1.7
460231	12	24	41	57	71	84	1.9
460233	16	28	59	66	72	74	1.8
460266	4	17	32	48	60	75	2.9

Table 58
Dose-dependent antisense inhibition of human *HTT* in GM02171 cells

ISIS No.	312.5 nM	625 nM	1,250 nM	2,500 nM	5,000 nM	10,000 nM	IC ₅₀ (μ M)
387916	32	56	77	89	95	97	0.7
435869	0	6	22	40	69	84	2.9
435870	15	19	32	51	68	77	2.4
435874	0	5	1	17	17	30	>10.0
435879	0	8	0	16	36	47	15.3
435890	14	16	19	19	39	57	9.3
460206	5	13	33	41	68	80	2.7
460207	13	10	22	22	33	39	45.6
460208	13	15	11	11	15	53	10.8
460209	8	27	46	70	80	86	1.6
460210	19	37	55	75	88	96	1.1
460212	8	23	30	43	57	74	2.2
460218	15	26	27	36	52	78	3.2
460219	16	17	32	44	69	76	2.5
460222	14	3	0	0	13	0	>10.0
460231	6	8	13	16	33	56	10.4
460233	27	30	39	46	61	73	2.4
460266	0	15	20	15	18	34	>10.0

Table 59
Dose-dependent antisense inhibition of human *HTT* in GM02173B cells

ISIS No.	312.5 nM	625 nM	1,250 nM	2,500 nM	5,000 nM	10,000 nM	IC ₅₀ (μ M)
387916	22	47	76	88	96	98	0.7
435869	10	0	16	38	59	76	3.9
435870	22	36	44	58	69	81	2.0
435874	11	6	25	23	32	42	>10.0
435879	0	9	21	30	52	68	4.8
435890	12	16	30	31	48	66	4.5
460206	11	13	18	35	59	74	3.5
460207	15	25	30	37	42	66	4.3
460208	5	14	27	32	52	51	9.0
460209	27	49	61	79	81	74	0.8
460210	19	40	61	77	89	95	1.0
460212	0	19	32	32	61	78	2.9
460218	4	17	26	38	64	82	3.0
460219	5	6	26	47	68	84	2.9

460222	13	19	23	30	35	50	16.1
460231	7	33	25	35	54	77	3.7
460233	11	20	37	52	68	69	2.3
460266	12	6	10	21	25	47	>10.0

Example 11: Dose-dependent antisense inhibition of human *HTT* in GM04281 and GM02171 cells by oligonucleotides designed by microwalk

Additional gapmers were designed based on the gapmers selected from studies described in Example 10. These gapmers were designed by creating gapmers shifted slightly upstream and downstream (i.e. “microwalk”) of the original gapmers from Tables 57, 58, and 59. Gapmers were also created with 4-9-4 MOE or 5-9-5 MOE motifs, and with constrained 6(S)-CH₃-bicyclic nucleic acid (BNA) molecules at various nucleotide positions.

These gapmers were tested in the GM04281 and GM02171 cell lines. Cultured GM04281 or GM02171 cells at a density of 25,000 cells per well were transfected using electroporation with 2,500 nM or 5,000 nM antisense oligonucleotide. After a treatment period of approximately 24 hours, RNA was isolated from the cells and *HTT* mRNA levels were measured by quantitative real-time PCR. *HTT* mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN. Results are presented as percent inhibition of *HTT* mRNA, relative to untreated control cells.

The chimeric antisense oligonucleotides in Tables 60, 61, and 62 were designed as 3-9-3, 4-9-4, or 5-9-5 MOE gapmers. The parent gapmers, ISIS 435890, ISIS 460210, ISIS 435879, ISIS 460209, ISIS 435870, and ISIS 460207, from which the newly designed gapmers were derived are marked with an asterisk (*) in the table. ISIS 387916 was included in the study as a benchmark oligonucleotide against which the potency of the antisense oligonucleotides targeting nucleotides overlapping each SNP position could be compared.

The 3-9-3 gapmers are 15 nucleotides in length, wherein the central gap segment is comprised of nine 2'-deoxynucleotides and is flanked on both 5' and 3' directions by wings comprising 3 nucleotides each.

The 4-9-4 gapmers are 17 nucleotides in length, wherein the central gap segment is comprised of nine 2'-deoxynucleotides and is flanked on both 5' and 3' directions by wings comprising 4 nucleotides each.

The 5-9-5 gapmers are 19 nucleotides in length, wherein the central gap segment is comprised of nine 2'-deoxynucleotides and is flanked on both 5' and 3' directions by wings comprising 5 nucleotides each.

The internucleoside linkages throughout each gapmer are phosphorothioate (P=S) linkages. All cytosine nucleobases throughout each gapmer are 5-methylcytosines. Bolded and underlined nucleotides in Tables 60, 61, and 62 indicate the positions of the 6(S)-CH₃-BNA (e.g. cEt molecules)molecules in each gapmer. Italicized nucleotides are MOE subunits.

The gapmers are organized in Tables 60, 61, and 62, according to the SNP site they target. "Start site" indicates the 5'-most nucleotide to which the gapmer is targeted. "Stop site" indicates the 3'-most nucleotide to which the gapmer is targeted. 'Target allele' indicates whether the gapmer is targeted to the major or the minor allele. The number in parentheses indicates the position on the oligonucleotide opposite to the SNP position.

Table 60
Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs2298969 (nucleobases 125888 to 125907 of SEQ ID NO: 1)

Start position	Stop position	ISIS No.	Sequence	Motif	Concentration (nM)	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	TCTCTATTGCA CATTCCAAG	5-10-5	5000	57	24	6
125888	125907	*435890	<u>AAGGG</u> ATGCTG ACTTGGGC	5-9-5	2500	22	0	94
					5000	41	23	
125890	125904	*460210	<u>GGG</u> ATGCTGAC TTGG	3-9-3	2500	59	24	189
					5000	81	33	
125889	125905	474870	<u>AGGG</u> ATGCTG ACTTGGG	4-9-4	2500	23	3	187
					5000	44	34	
125889	125905	474890	<u>AGGG</u> ATGCTG ACTTGGG	4-9-4	2500	38	6	187
					5000	49	25	
125889	125905	474910	<u>AGGG</u> ATGCTGA CTTGGG	4-9-4	2500	34	8	187
					5000	49	41	
125889	125905	474914	<u>AGGG</u> ATGCTGA CTTGGG	4-9-4	2500	44	14	187
					5000	44	21	
125888	125907	474918	<u>AAGGG</u> ATGCT GACTTGGGC	5-9-5	2500	31	0	94
					5000	26	25	
125888	125907	474922	<u>AAGGG</u> ATGCT GACTTGGGC	5-9-5	2500	33	14	94
					5000	65	24	
125889	125905	476332	<u>AGGG</u> ATGCTG	4-9-4	2500	23	13	187

			ACTTGGG		5000	51	42	
125888	125907	476336	AAGGGATGCTG ACTTGGGC	5-9-5	2500	5	0	94
					5000	43	9	

Table 61

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs7685686 (nucleobases 146786 to 146805 of SEQ ID NO: 1)

Start position	Stop position	ISIS No.	Sequence	Motif	Concentration (nM)	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	TCTCTATTGCA CATTCCAAG	5-10-5	5000	57	24	6
146786	146805	*435879	AATAAATTGTC ATCACCAG	5-9-5	2500	39	0	99
					5000	59	19	
146788	146802	*460209	TAAATTGTCAT CACC	3-9-3	2500	3	0	203
					5000	13	5	
146787	146803	474871	ATAAATTGTCA TCACCA	4-9-4	2500	82	32	200
					5000	83	58	
146787	146803	474891	ATAAATTGTCA TCACCA	4-9-4	2500	84	29	200
					5000	89	56	
146787	146803	474911	ATAAATTGTCA TCACCA	4-9-4	2500	70	18	200
					5000	83	40	
146787	146803	474915	ATAAATTGTCA TCACCA	4-9-4	2500	38	9	200
					5000	74	14	
146786	146805	474919	AATAAATTGTC ATCACCAG	5-9-5	2500	80	7	99
					5000	84	37	
146786	146805	474923	AATAAATTGTC ATCACCAG	5-9-5	2500	74	32	99
					5000	83	51	
146787	146803	476333	ATAAATTGTCA TCACCA	4-9-4	2500	75	28	200
					5000	86	21	
146786	146805	476337	AATAAATTGTC ATCACCAG	5-9-5	2500	71	6	99
					5000	83	31	

Table 62

Comparison of inhibition of human *HTT* mRNA levels by ISIS 387916 and chimeric antisense oligonucleotides targeted to SNP rs362331 (nucleobases 155478 to 155498 of SEQ ID NO: 1)

Start position	Stop position	ISIS No.	Sequence	Motif	Concentration (nM)	% inhibition in GM04281	% inhibition in GM02171	SEQ ID NO
145466	145485	387916	TCTCTATTGCAC ATTCCAAG	5-10-5	5000	57	24	6
155479	155498	*435870	GCACACAGTAG ATGAGGGA	5-9-5	2500	19	1	103
					5000	49	34	

155481	155495	*460207	<u>A</u> CACAGTAGAT GAGG	3-9-3	2500	0	0	217
					5000	7	8	
155480	155496	474872	<u>CACAC</u> AGTAGA TGAGGG	4-9-4	2500	35	9	214
					5000	63	37	
155480	155496	474892	<u>CACAC</u> AGTAGA TGAGGG	4-9-4	2500	43	16	214
					5000	69	31	
155480	155496	474912	<u>CACAC</u> AGTAGA TGAGGG	4-9-4	2500	16	9	214
					5000	36	6	
155480	155496	474916	<u>CACAC</u> AGTAGA TGAGGG	4-9-4	2500	22	5	214
					5000	47	7	
155479	155498	474920	<u>GCACAC</u> AGTAG ATGAGGGA	5-9-5	2500	19	0	103
					5000	43	23	
155479	155498	474924	<u>GCACAC</u> AGTAG ATGAGGGA	5-9-5	2500	29	8	103
					5000	48	22	
155480	155496	476334	<u>CACAC</u> AGTAGA TGAGGG	4-9-4	2500	35	7	214
					5000	62	32	
155479	155498	476338	<u>GCACAC</u> AGTAG ATGAGGGA	5-9-5	2500	26	9	103
					5000	40	4	
155479	155495	474873	<u>A</u> CACAGTAGAT GAGGGA	4-9-4	2500	53	9	285
					5000	61	29	
155479	155495	474893	<u>A</u> CACAGTAGAT GAGGGA	4-9-4	2500	47	5	285
					5000	59	30	
155479	155495	474913	<u>A</u> CACAGTAGAT GAGGGA	4-9-4	2500	30	16	285
					5000	29	17	
155479	155495	474917	<u>A</u> CACAGTAGAT GAGGGA	4-9-4	2500	23	12	285
					5000	40	5	
155478	155497	474921	<u>CACAC</u> AGTAGA TGAGGGAG	5-9-5	2500	28	0	212
					5000	43	23	
155478	155497	474925	<u>CACAC</u> AGTAGA TGAGGGAG	5-9-5	2500	30	9	212
					5000	61	34	
155479	155495	476335	<u>A</u> CACAGTAGAT GAGGGA	4-9-4	2500	35	2	285
					5000	53	31	
155478	155497	476339	<u>CACAC</u> AGTAGA TGAGGGAG	5-9-5	2500	15	0	212
					5000	34	13	

Example 12: Dose-dependent antisense inhibition of human huntingtin mRNA levels in Coriell fibroblast cell lines

Gapmers from the studies described in Example 11 were selected and tested at various doses in GM04281, GM02171 and GM02173B cell lines. Each cell line was plated at a density of 25,000 cells per well and transfected using electroporation with 625 nM, 1,250 nM, 2,500 nM, 5,000 nM

and 10,000 nM concentrations of antisense oligonucleotide, as specified in Tables 63, 64, and 65. After a treatment period of approximately 16 hours, RNA was isolated from the cells and *HTT* mRNA levels were measured by quantitative real-time PCR. Human *HTT* primer probe set RTS2617 was used to measure mRNA levels. *HTT* mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN. Results are presented as percent inhibition of *HTT* mRNA, relative to untreated control cells. IC₅₀ values are also provided in Tables 63, 64, and 65.

Table 63
Dose-dependent antisense inhibition of human *HTT* in GM04281 cells

ISIS No	625 nM	1250 nM	2500 nM	5000 nM	10000 nM	IC ₅₀ (μM)
387916	70	83	94	96	98	<0.6
460207	51	63	83	91	93	0.5
460209	83	93	96	97	97	<0.6
460210	70	89	94	97	98	0.6
474871	94	97	96	96	95	<0.6
474873	51	73	89	94	95	0.5
474891	93	95	97	96	95	<0.6
474892	48	72	89	93	95	0.6
474911	85	92	96	95	94	<0.6
474919	89	94	95	94	96	<0.6
474922	21	47	73	86	96	1.5
474923	86	94	96	95	94	<0.6
476333	92	94	95	95	96	<0.6
476334	45	70	87	92	95	0.6
476337	83	92	95	96	96	<0.6

Table 64
Dose-dependent antisense inhibition of human *HTT* in GM02171 cells

ISIS No	625 nM	1250 nM	2500 nM	5000 nM	10000 nM	IC ₅₀ (μM)
387916	28	38	63	82	99	1.6
460207	16	0	20	22	55	10.0
460209	27	50	61	87	94	9.9
460210	34	60	80	86	97	0.9
474871	62	74	84	87	90	0.1
474873	13	29	61	77	89	2.2
474891	57	72	80	83	88	0.2
474892	23	26	51	68	81	2.5
474911	47	58	68	72	82	0.7

474919	44	48	65	71	83	1.1
474922	15	27	49	74	79	2.6
474923	27	53	74	79	84	1.5
476333	42	53	75	76	84	1.0
476334	20	23	58	71	87	2.3
476337	23	34	60	62	75	2.7

Table 65
Dose-dependent antisense inhibition of human *HTT* in GM02173B cells

ISIS No	625 nM	1250 nM	2500 nM	5000 nM	10000 nM	IC ₅₀ (μ M)
387916	38	75	89	95	99	0.9
460207	13	27	52	46	63	6.5
460209	79	68	84	90	92	<0.6
460210	37	62	79	92	97	0.9
474871	74	83	87	92	89	<0.6
474873	22	32	67	72	92	1.9
474891	69	78	84	89	89	<0.6
474892	26	50	75	83	91	1.3
474911	50	66	76	86	86	0.6
474919	57	67	74	87	82	<0.6
474922	15	32	61	71	90	2.2
474923	49	67	78	83	85	0.5
476333	58	71	78	87	89	<0.6
476334	20	42	63	76	91	1.8
476337	48	63	71	79	80	0.6

Example 13: Strategy for selection of antisense oligonucleotides based on potency and selectivity

Gapmers from each of the studies described above were selected for further analysis based on potency and selectivity.

Potency was based on the percent inhibition of *HTT* mRNA achieved by the antisense oligonucleotides targeting a SNP compared to the percent inhibition of *HTT* mRNA achieved by the benchmark oligonucleotide, ISIS 387916.

Selectivity was based on the ability of the antisense oligonucleotides targeting a SNP to inhibit expression of the major allele and not of the minor allele. The usage of the three cell lines with different genotypes at each SNP position facilitated this process.

ISIS 460065 (5'-ATAAATTGTCATCACCAG-3' (SEQ ID NO: 199)) is a 4-9-5 MOE gapmer targeted to SNP rs7685686 (major allele A, minor allele G) at position 9 of the oligonucleotide. The GM04281 cell line is homozygous AA at SNP position rs7685686. The GM02173B cell line is heterozygous AG at SNP position rs7685686. The GM02171 cell line is homozygous GG at SNP position rs7685686. Therefore, selectivity is shown if ISIS 460065 causes potent inhibition of *HTT* mRNA in GM04281, less potent inhibition of *HTT* mRNA in GM02173, and little to no significant inhibition of *HTT* mRNA in GM02171. IC₅₀ values taken from Table 20, 21, and 22, and presented below in Table 66, confirm varying degrees of inhibition in the three cell lines, wherein expression was most reduced in the homozygous AA cell line, moderately reduced in the heterozygous AG cell line, and less reduced in the homozygous GG cell line. IC₅₀ is the concentration of antisense oligonucleotide required for 50 percent inhibition *HTT* mRNA. IC₅₀ values are in μ M.

Table 66
Genotype of the Coriell cell lines for SNP rs7685686 and comparison of inhibition of *HTT* mRNA by ISIS 460065 in each cell line

	GM04281	GM02173B	GM02171
Genotype	AA	AG	GG
IC ₅₀ with ISIS 460065	1.1	3.6	10.3

ISIS 459978 (5'-ACAGTGCTACCCAACCT-3' (SEQ ID NO: 174)) is a 2-9-6 MOE gapmer targeted to SNP rs4690072 (major allele T, minor allele G) at position 9 of the oligonucleotide. The GM04281 cell line is homozygous TT at SNP position rs4690072. The GM02173B cell line is heterozygous TG at SNP position rs4690072. The GM02171 cell line is homozygous GG at SNP position rs4690072. Therefore, selectivity is shown if ISIS 459978 causes potent inhibition of *HTT* mRNA in GM04281, less potent inhibition of *HTT* mRNA in GM02173, and little to no significant inhibition of *HTT* mRNA in GM02171. IC₅₀ values taken from Table 20, 21, and 22, and presented below in Table 67, confirm varying degrees of inhibition in the three cell lines, wherein expression was most reduced in the homozygous TT cell line, moderately reduced in the heterozygous TG cell line, and less reduced in the homozygous GG cell line. IC₅₀ is the concentration of antisense oligonucleotide required for 50 percent inhibition *HTT* mRNA. IC₅₀ values are in μ M.

Table 67
Genotype of the Coriell cell lines for SNP rs4690072 and comparison of inhibition of *HTT* mRNA by ISIS 459978 in each cell line

	GM04281	GM02173B	GM02171
Genotype	TT	TG	GG
IC ₅₀ with ISIS 459978	2.5	8.4	12.7

ISIS 460028 (5'-GAGCAGCTGCAACCTGGCA -3' (SEQ ID NO: 149)) is a 4-11-4 MOE gapmer targeted to SNP rs362306 (major allele G, minor allele A) at position 10 of the oligonucleotide. The GM04281 cell line is homozygous GG at SNP position rs362306. The GM02173B and GM02171 cell lines are heterozygous GA at SNP position rs362306. Therefore, selectivity is shown if ISIS 460028 causes potent inhibition of *HTT* mRNA in GM04281 and less potent inhibition of *HTT* mRNA in GM02173 and GM02171. IC₅₀ values taken from Table 20, 21, and 22, and presented below in Table 68, confirm varying degrees of inhibition between the GM04281 cell line and the GM02173B and GM02171 cell lines, wherein expression was most reduced in the homozygous GG cell line and less reduced in the heterozygous AG cell line. IC₅₀ is the concentration of antisense oligonucleotide required for 50 percent inhibition *HTT* mRNA. IC₅₀ values are in μ M.

Table 68
Genotype of the Coriell cell lines for SNP rs362306 and comparison of inhibition of *HTT* mRNA by ISIS 460028 in each cell line

	GM04281	GM02173B	GM02171
Genotype	GG	AG	AG
IC ₅₀ with ISIS 460028	1.4	5.2	5.3

Example 14: Strategy for selection of antisense oligonucleotides with cEt motifs based on potency and selectivity

Gapmers from each of the studies described above were selected for further analysis based on potency and selectivity.

Potency was based on the percent inhibition of *HTT* mRNA achieved by the antisense oligonucleotides targeting a SNP compared to the percent inhibition of *HTT* mRNA achieved by the benchmark oligonucleotide, ISIS 387916.

Selectivity was based on the ability of the antisense oligonucleotides targeting a SNP to inhibit expression of the major allele and not of the minor allele. The usage of the three cell lines with different genotypes at each SNP position facilitated this process.

ISIS 460209 (5'- TAAATTGTCATCACC -3' (SEQ ID NO: 203)) is a 3-9-3 gapmer with cEt subunits at positions 2, 3, 13, and 14, targeted to SNP rs7685686 (major allele A, minor allele G) at position 8 of the oligonucleotide. The GM04281 cell line is homozygous AA at SNP position rs7685686. The GM02173B cell line is heterozygous AG at SNP position rs7685686. The GM02171 cell line is homozygous GG at SNP position rs7685686. Therefore, selectivity is shown if ISIS 460209 causes potent inhibition of *HTT* mRNA in GM04281, less potent inhibition of *HTT* mRNA in GM02173, and little to no significant inhibition of *HTT* mRNA in GM02171. IC₅₀ values taken from Table 57, 58, and 59, and presented below in Table 69, confirm varying degrees of inhibition in the three cell lines, wherein expression was most reduced in the homozygous AA cell line, moderately reduced in the heterozygous AG cell line, and less reduced in the homozygous GG cell line. IC₅₀ is the concentration of antisense oligonucleotide required for 50 percent inhibition *HTT* mRNA. IC₅₀ values are in μ M.

Table 69
Genotype of the Coriell cell lines for SNP rs7685686 and comparison of inhibition of *HTT* mRNA by ISIS 460209 in each cell line

	GM04281	GM02173B	GM02171
Genotype	AA	AG	GG
IC ₅₀ with ISIS 460209	0.2	0.8	1.6

ISIS 460208 (5'- CAGTGCTACCCAACC -3' (SEQ ID NO: 177)) is a 3-9-3 gapmer with cEt subunits at positions 2, 3, 13, and 14, targeted to SNP rs4690072 (major allele T, minor allele G) at position 8 of the oligonucleotide. The GM04281 cell line is homozygous TT at SNP position rs4690072. The GM02173B cell line is heterozygous TG at SNP position rs4690072. The GM02171 cell line is homozygous GG at SNP position rs4690072. Therefore, selectivity is shown if ISIS 460208 causes potent inhibition of *HTT* mRNA in GM04281, less potent inhibition of *HTT*

mRNA in GM02173, and little to no significant inhibition of HTT mRNA in GM02171. IC₅₀ values taken from Table 57, 58, and 59, and presented below in Table 70, confirm varying degrees of inhibition in the three cell lines, wherein expression was most reduced in the homozygous TT cell line, moderately reduced in the heterozygous TG cell line, and less reduced in the homozygous GG cell line. IC₅₀ is the concentration of antisense oligonucleotide required for 50 percent inhibition HTT mRNA. IC₅₀ values are in μ M.

Table 70
Genotype of the Coriell cell lines for SNP rs4690072 and comparison of inhibition of HTT mRNA by ISIS 460208 in each cell line

	GM04281	GM02173B	GM02171
Genotype	TT	TG	GG
IC ₅₀ with ISIS 460208	1.5	9.0	10.8

ISIS 460206 (5'- GCAGCTGCAACCTGG -3' (SEQ ID NO: 231)) is a 3-9-3 gapmer with cEt subunits at positions 2, 3, 13, and 14, targeted to SNP rs362306 (major allele G, minor allele A) at position 8 of the oligonucleotide. The GM04281 cell line is homozygous GG at SNP position rs362306. The GM02173B and GM02171 cell lines are heterozygous GA at SNP position rs362306. Therefore, selectivity is shown if ISIS 460206 causes potent inhibition of HTT mRNA in GM04281 and less potent inhibition of HTT mRNA in GM02173 and GM02171. IC₅₀ values taken from Table 57, 58, and 59, and presented below in Table 71, confirm varying degrees of inhibition between the GM04281 cell line and the GM02173B and GM02171 cell lines, wherein expression was most reduced in the homozygous GG cell line and less reduced in the heterozygous AG cell line. IC₅₀ is the concentration of antisense oligonucleotide required for 50 percent inhibition HTT mRNA. IC₅₀ values are in μ M.

Table 71
Genotype of the Coriell cell lines for SNP rs362306 and comparison of inhibition of HTT mRNA by ISIS 460206 in each cell line

	GM04281	GM02173B	GM02171
Genotype	GG	AG	AG
IC ₅₀ with ISIS 460206	2.3	2.7	2.7

Example 15: Comparison of SNPs in various cell lines and mouse models associated with Huntington's disease

The genotype at various SNP positions associated with Huntington's disease was compared amongst the three Coriell cell lines, used in the above Examples, as well as with the GM04022 fibroblast, the BACHD mouse model and the YAC18 mouse model.

The donor patient of the GM04022 fibroblast cell line was heterozygous at SNP position rs363125 (NCBI Entrez SNP database), harboring an A allele (adenine) and a C allele (cytosine) at nucleotide 5310 of SEQ ID NO: 2 (van Bilsen, P.H.J. et al., Human Gene Therapy.19: 710-718, 2008). YAC18 mice were developed with a YAC transgene containing human huntingtin gene (Hodgson, et al. Hum. Mol. Genet. 5: 1875-85, 1996). BACHD mice were developed expressing a full-length mutant huntingtin gene with 97 glutamine repeats under the control of a bacterial artificial chromosome (Gray, M. et al., J. Neurosci. 28: 6182-95, 2008). The comparative genotype at the indicated SNP positions in all four cell lines and mouse models is presented in Table 72.

Table 72
Genotypes of the Coriell cell lines and Huntington mouse models

SNP	GM02171	GM02173	GM04281	GM04022	BACHD	YAC18
rs3856973	AA	AG	GG	AG	GG	AA
rs2285086	GG	AG	AA	AG	AA	GG
rs7659144	CG	CG	CC	CG	CC	GG
rs16843804	TC	TC	CC	CC	CC	TT
rs2024115	GG	AG	AA	AG	AA	GG
rs3733217	CC	CC	CC	CC	CC	CC
rs10015979	AA	AG	GG	AA	AA	AA
rs7691627	AA	AG	GG	AG	GG	AA
rs2798235	GG	GG	GG	AG	GG	GG
rs4690072	GG	TG	TT	TG	TT	GG
rs6446723	CC	TC	TT	TC	TT	CC
rs363081	GG	GG	GG	GG	GG	GG
rs363080	CC	CC	CC	TC	CC	CC
rs363075	GG	GG	GG	GG	GG	GG
rs363064	TC	TC	CC	CC	CC	TT
rs3025849	AA	AA	AA	AA	AA	AA
rs363102	AA	AA	AA	AG	AA	AA

rs11731237	CC	TC	TT	CC	CC	CC
rs4690073	AA	AG	GG	AG	GG	AA
rs363144	TT	TT	TT	TT	TT	TT
rs3025838	CC	CC	CC	CC	CC	CC
rs34315806	TC	TC	CC	CC	CC	TT
rs363099	TC	TC	CC	CC	CC	TT
rs363096	CC	TC	TT	CC	TT	CC
rs2298967	TC	TC	TT	TT	TT	CC
rs2298969	GG	AG	AA	AG	AA	GG
rs6844859	CC	TC	TT	TC	TT	CC
rs363092	AA	AC	CC	AC	AA	AA
rs7685686	GG	AG	AA	AG	AA	GG
rs363088	TA	TA	AA	AA	AA	TT
rs362331	CC	TC	TT	TC	TT	CC
rs916171	GG	GC	CC	GC	CC	GG
rs362322	AA	AA	AA	AA	AA	AA
rs362275	TC	TC	CC	CC	CC	TT
rs362273	AG	AG	AA	AA	AA	GG
rs2276881	GG	GG	GG	GG	GG	GG
rs3121419	TC	TC	CC	CC	CC	TT
rs362272	--	AG	GG	GG	GG	AA
rs362271	AG	AG	GG	GG	GG	AA
rs3775061	AG	AG	AA	AA	AA	GG
rs362310	TC	CC	CC	TC	CC	CC
rs362307	CC	TC	CC	CC	CC	CC
rs362306	AG	AG	GG	GG	GG	AA
rs362303	TC	CC	CC	TC	CC	CC
rs362296	AC	AC	AC	CC	CC	AA

Example 16: Allele-specific inhibition measured in BacHD cortical neurons

Antisense oligonucleotides, ISIS 460209 (5'-TAAATTGTCATCACC-3' (SEQ ID NO: 203)), targeting SNP rs7685686 of human *HTT*, and ISIS 387916 (TCTCTATTGCACATTCCAAG (SEQ ID NO: 6)), and with no human or murine SNP target site, were tested for their effect on Htt protein levels *in vitro*. ISIS 387916 is cross-reactive with murine Htt mRNA (GENBANK Accession No. NM_010414.1, designated herein as SEQ ID NO: 286) at target start site 5763 with one mismatch. ISIS 460209 is cross-reactive with murine Htt mRNA at target start site 6866 with three mismatches.

Primary BACHD cortical neurons, which express human Htt and murine Htt, were isolated in the following way: Embryos were dissected from E15.5-E17.5 pregnant females. Cortices were dissected into ice-cold divalent-free Hank's Balanced Salt Solution (Invitrogen, 14025-134). The cortices were chopped into pieces and digested with 0.05% Trypsin-EDTA (Invitrogen, 25300-120) at 37°C for 8 minutes. The digestion was halted by addition of complete neurobasal media (Invitrogen, 10888-022). Cells were resuspended in media and treated with DNase I (Invitrogen, 18047-019). After titration through a 100ul pipette tip, cells are resuspended in neurobasal media with B27 supplement (Invitrogen, 17504-044), and counted. 1.7×10^5 cells/well were plated in 24-well plates precoated with poly-D-lysine (BD Biosciences, 354210). Neurons were fed with 200 μ l neurobasal media with B27 on the second day in vitro.

ISIS 460209 or ISIS 387916 was added to the supplementary media fed to neurons on division 2 at 0.7 μ M, 1.4 μ M or 1.5 μ M final concentrations. Cells were harvested after 8 days with into 1 mL of media using a cell scraper. Cells were centrifuged at 2,500 rpm for 5 min at 4°C and the pellets were resuspended in a buffer of 50 mM Tris, pH = 8.0, 150 mM NaCl, 1% Igepal, 40 mM β -glycerophosphate, 10mM NaF, 1 x Roche complete protease inhibitor, 1mM Sodium Orthovanadate and 800 μ M PMSF. The lysates were centrifuged after 15 min incubation and protein concentration was measured with the DC assay (BioRad).

Protein lysates were run on low-bis gels to separate huntingtin alleles (resolving gel – 2001:Acrylamide:BIS (10% acrylamide, 0.5% BIS, 375mMTris pH 8.8; stacking gel – 4%Acrylamide-BIS(29:1), 156 mM Tris pH6.8; Running buffer – 25mM Tris, 190mM Glycine, 0.1% SDS + 10 μ M beta-mercaptoethanol added fresh). After electrophoresis, proteins in the gel were transferred to a nitrocellulose membrane (Hybond-C Extra; GE Healthcare Bio-Sciences) at 90V for 40' to allow samples to penetrate the stacking gel and then at 190V for 2.5h to resolve proteins.

Primary antibodies specific for human Htt and murine calnexin protein were used at 1:10,000 dilutions. HRP-conjugated anti-mouse secondary antibody (1:10,000, Jackson ImmunoResearch Laboratories) was used for visualizing proteins using SuperSignal West Pico Chemiluminescent Substrate (Thermo Scientific). Protein bands were quantified using ImageJ software and normalized to calnexin levels. Protein bands were quantified using ImageJ software. Table 73 provides an estimate of the percentage inhibition relative to the negative control sample.

The comparative percent inhibitions of the human Htt protein and the murine Htt protein are presented.

Table 73
Effect of antisense inhibition on mutant human and wild-type murine Htt protein (percent inhibition normalized to PBS control)

	Dose (μ M)	Human	Murine
ISIS 387916	0.7	54	38
	1.4	75	58
	1.5	92	88
ISIS 460209	0.2	71	35
	0.4	82	41
	1.5	94	56

Example 17: Dose-dependent antisense inhibition of human huntingtin mRNA levels in Coriell fibroblast cell lines

Gapmers from the studies described in Examples, 3, 4, 10, and 12 were selected and tested at various doses in GM04281, GM02171 and GM02173B cell lines. Each cell line was plated at a density of 25,000 cells per well and transfected using electroporation with 0.4747 nM, 1.5011 nM, 4.7463 nM, 15.0079 nM 45.455 nM, 150.0527 nM, 474.4673 nM, 1,500.27 nM, 4,743.833 nM, and 15,000 nM concentrations of antisense oligonucleotide, as specified in Tables 72, 73, and 74. After a treatment period of approximately 16 hours, RNA was isolated from the cells and *HTT* mRNA levels were measured by quantitative real-time PCR. Human *HTT* primer probe set RTS2617 was used to measure mRNA levels. *HTT* mRNA levels were adjusted according to total RNA content, as measured by RIBOGREEN. Results are presented as percent inhibition of *HTT* mRNA, relative to untreated control cells. IC₅₀ values are also provided in Tables 72, 73, and 74.

Table 74
Dose-dependent antisense inhibition of human *HTT* in GM04281 cells

ISIS No	0.4747 nM	1.5011 nM	4.7463 nM	15.0079 nM	47.455 nM	150.0527 nM	474.4673 nM	1500.27 nM	4743.833 nM	15000.0 nM	IC ₅₀ (μ M)
387916	15	12	4	5	7	26	70	89	98	99	0.33
435879	0	8	19	13	24	23	45	53	84	93	0.25
435890	16	1	8	12	25	23	32	52	61	91	0.82

460209	2	9	21	17	36	46	80	89	94	93	0.09
460210	4	7	5	19	20	35	69	85	98	98	0.21
476333	7	10	8	11	42	65	86	93	93	95	0.05

Table 75
Dose-dependent antisense inhibition of human *HTT* in GM02171 cells

ISIS No	0.4747 nM	1.5011 nM	4.7463 nM	15.007 9 nM	47.455 nM	150.05 27 nM	474.46 73 nM	1500.2 7 nM	4743.8 33 nM	15000. 0 nM	IC ₅₀ (μM)
387916	22	8	0	9	0	32	60	90	96	97	0.27
435879	0	1	6	2	0	0	8	9	46	57	7.62
435890	0	0	0	6	0	0	0	31	27	71	4.37
460209	11	5	15	0	0	7	30	69	82	88	0.96
460210	0	0	0	2	17	18	38	70	93	95	0.56
476333	0	0	0	0	13	18	44	69	72	91	0.75

Table 76
Dose-dependent antisense inhibition of human *HTT* in GM02173B cells

ISIS No	0.4747 nM	1.5011 nM	4.7463 nM	15.007 9 nM	47.455 nM	150.05 27 nM	474.46 73 nM	1500.2 7 nM	4743.8 33 nM	15000. 0 nM	IC ₅₀ (μM)
387916	3	17	7	25	27	33	65	88	98	99	0.19
435879	0	6	0	8	3	10	16	24	50	68	3.72
435890	0	13	0	1	2	12	16	23	49	82	4.60
460209	0	7	29	2	9	32	52	71	82	86	0.27
460210	0	13	0	5	16	18	49	74	93	97	0.27
476333	11	13	20	7	23	36	63	75	83	90	0.13

Example 18: Validation of the specificity of ISIS oligonucleotides targeting SNPs of human huntingtin by the Molecular Beacon assay

Some of the gapmers from the study described in Example 17 were tested in GM04022 fibroblasts (from the Coriell Institute for Medical Research).

To verify allele-specific suppression of *HTT* mRNA in GM04022 fibroblasts by ISIS 435879, ISIS 460209, and ISIS 476333, the Molecular Beacon assay, as described in the van Bilsen et al publication (van Bilsen, P.H.J. et al., Human Gene Therapy.19: 710-718, 2008), was conducted using 'molecular beacon' synthetic oligonucleotides linked with a fluorophore and quencher. GM04022 fibroblasts were transfected by electroporation with ISIS 435879, ISIS 460209, or ISIS 476333 at 0.06 μM, 0.19 μM, 0.56 μM, 1.67 μM, 5 μM and 15 μM concentrations of antisense oligonucleotide, as specified in Tables 75-77. ISIS 387916 was included in the assay as a benchmark

oligonucleotide. The qRT-PCR assay for molecular beacon for the A allele was conducted with the annealing temperature at 56.5°C. The qRT-PCR assay for molecular beacon for the C allele was conducted with the annealing temperature at 62.0°C. Primer probe set RTS2617 was used to measure the total *HTT* mRNA reduction. The results of the assay are presented in Tables 77-79 as percent inhibition over the PBS control. The results demonstrate that the SNP-specific ISIS oligonucleotides specifically target the C allele of rs7685686 compared to the A allele (Table 80).

Table 77**Dose-dependent antisense inhibition of the A allele of rs7685686 in GM04022 fibroblasts**

ISIS No	0.06 μM	0.19 μM	0.56 μM	1.67 μM	5.00 μM	15.00 μM	IC ₅₀ (μM)
387916	33	40	53	90	99	98	0.56
435879	0	0	50	29	38	47	10.8
460209	14	4	54	73	81	95	0.53
476333	2	44	41	77	91	86	0.64

Table 78**Dose-dependent antisense inhibition of the C allele of rs7685686 in GM04022 fibroblasts**

ISIS No	0.06 μM	0.19 μM	0.56 μM	1.67 μM	5.00 μM	15.00 μM	IC ₅₀ (μM)
387916	41	42	46	86	95	92	0.54
435879	0	0	75	60	68	81	2.9
460209	35	48	76	84	88	92	0.19
476333	22	60	75	84	90	93	0.15

Table 79**Dose-dependent antisense inhibition of total HTT mRNA in GM04022 fibroblasts**

ISIS No	0.06 μM	0.19 μM	0.56 μM	1.67 μM	5.00 μM	15.00 μM
387916	32	59	49	89	98	99
435879	0	0	42	25	41	62
460209	26	27	54	75	84	96
476333	25	51	58	82	92	90

Table 80**IC₅₀ ratio (A/C) in GM04022 fibroblasts**

ISIS No	Ratio
387916	1.0
435879	4.2
460209	2.8
476333	4.3

Example 19: Allele-specific inhibition measured in cortical neurons from BACHD and YAC18 mice.

In order to identify potential SNPs for screening of human allele-specific ISIS oligonucleotides, the *HTT* mRNA of YAC18 and BACHD mice were sequenced by the Goldengate 96SNP assay. It was determined that the BAC and YAC mice carried different alleles at several key SNP positions (Table 72) and could therefore be used as a screening tool for allele-specific knockdown. Each of the SNP positions chosen for targeting in the mouse strains were also compared to human HD chromosomes. For each target, approximately 50% of the human HD population is heterozygous for the target expressed in the BACHD mice, but not the YAC18 mice.

In order to verify the allele-specificity of the ISIS oligonucleotides (described in Examples 2, 9, 17 and 18), the antisense oligonucleotides, ISIS 460207, targeting SNP rs362331; ISIS 460209, targeting SNP rs7685686; ISIS 435879, targeting SNP rs7685686; ISIS 476333, targeting SNP rs7685686; ISIS 460210, targeting SNP rs2298969; ISIS 435874, targeting SNP rs4690072; ISIS 460208, targeting SNP rs4690072; ISIS 435331, targeting SNP rs2024115; and ISIS 435871, targeting SNP rs363088, were tested for their effect on HTT protein levels in BACHD and YAC18 cortical neurons. ISIS 387916, which has no human or murine SNP target site, was used as the benchmark. ISIS 387916 is cross-reactive with murine *HTT* mRNA (GENBANK Accession No. NM_010414.1, designated herein as SEQ ID NO: 286) at target start site 5763 with one mismatch. It was expected that treatment with the allele-specific antisense oligonucleotides would cause significant inhibition of *HTT* mRNA in the BACHD neurons and not in the YAC18 neurons. It was also expected that treatment with ISIS 387916 would cause inhibition of *HTT* mRNA in both sets of neurons.

YAC18 cultures were prepared from E16.5 pregnant female YAC18 (line 60, +/+) mice who had been bred with YAC18 (line 60, +/+) males. All progeny are thus homozygous YAC18 (line 60), facilitating pooled cortical cultures. BACHD E16.5 embryos were isolated from pregnant BACHD (+/-) mice who had been bred with pregnant BACHD (+/-) male mice, necessitating single pup cultures and genotyping. Single cortices were isolated, using caution to prevent cross-contamination of samples. Each dissociated cortex was used to seed 5 wells of a 6-well plate. After genotyping, only BACHD (+/-) cultures were used for ASO treatment. The antisense oligonucleotides were added to the supplementary media fed to the neurons on division 2. Cells

were harvested after 8 days with into 1 mL of media using a cell scraper. Cells were centrifuged at 2,500 rpm for 5 min at 4°C and the pellets were resuspended in a buffer of 50 mM Tris, pH = 8.0, 150 mM NaCl, 1% Igepal, 40 mM β -glycerophosphate, 10mM NaF, 1 x Roche complete protease inhibitor, 1mM Sodium Orthovanadate and 800 μ M PMSF. The lysates were centrifuged after 15 min incubation and protein concentration was measured with the DC assay (BioRad).

Protein lysates were run on low-bis gels to separate huntingtin alleles (resolving gel – 2001:Acrylamide:BIS (10% acrylamide, 0.5% BIS, 375mMTris pH 8.8; stacking gel – 4%Acrylamide-BIS(29:1), 156 mM Tris pH6.8; Running buffer – 25mM Tris, 190mM Glycine, 0.1% SDS + 10 μ M beta-mercaptoethanol added fresh). After electrophoresis, proteins in the gel were transferred to a nitrocellulose membrane (Hybond-C Extra; GE Healthcare Bio-Sciences) at 90V for 40' to allow samples to penetrate the stacking gel and then at 190V for 2.5h to resolve proteins.

Primary antibodies specific for human HTT and murine calnexin protein were used at 1:10,000 dilutions. HRP-conjugated anti-mouse secondary antibody (1:10,000, Jackson ImmunoResearch Laboratories) was used for visualizing proteins using SuperSignal West Pico Chemiluminescent Substrate (Thermo Scientific). Protein bands were quantified using ImageJ software and normalized to calnexin levels. Tables 81-91 provide the percentage inhibition relative to the untreated control sample. The percentage inhibition of human HTT protein levels in BACHD and YAC18 neurons are presented.

Table 81
HTT SNPs in BACHD and YAC18 mice and correlation with human HTT SNPs

SNP	Allele present in YAC18 Mice	Allele present in BACHD Mice	Allele present in human patients with high CAG repeats	% of human patients heterozgous at the SNP position
rs2024115	G	A	A	48
rs2298969	G	A	A	52
rs362331	C	T	T	49
rs363088	G	T	T	38
rs4690072	T	A	A	49
rs7685686	G	A	A	49

Table 82**Effect of antisense inhibition by ISIS 387916 in BACHD and YAC18 neurons**

	500 nM	1500 nM
YAC18	69	81
BACHD	84	90

Table 83**Effect of antisense inhibition by ISIS 435331, targeting rs2024115 in BACHD and YAC18 neurons**

	500 nM	1500 nM
YAC18	0	0
BACHD	39	43

Table 84**Effect of antisense inhibition by ISIS 460210, targeting rs2298969 in BACHD and YAC18 neurons**

	500 nM	1500 nM
YAC18	31	51
BACHD	79	89

Table 85**Effect of antisense inhibition by ISIS 460207, targeting rs362331 in BACHD and YAC18 neurons**

	500 nM	1500 nM
YAC18	0	0
BACHD	29	44

Table 86**Effect of antisense inhibition by ISIS 435871, targeting rs363088 in BACHD and YAC18 neurons**

	500 nM	1500 nM
YAC18	0	0
BACHD	51	68

Table 87**Effect of antisense inhibition by ISIS 435874, targeting rs4690072 in BACHD and YAC18 neurons**

	500 nM	1500 nM
YAC18	9	5
BACHD	30	44

Table 88

Effect of antisense inhibition by ISIS 460208, targeting rs4690072 in BACHD and YAC18 neurons

	500 nM	1500 nM
YAC18	1	8
BACHD	54	68

Table 89

Effect of antisense inhibition by ISIS 460209, targeting rs7685686 in BACHD and YAC18 neurons

	500 nM	1500 nM
YAC18	12	32
BACHD	72	83

Table 90

Effect of antisense inhibition by ISIS 435879, targeting rs7685686 in BACHD and YAC18 neurons

	500 nM	1500 nM
YAC18	0	7
BACHD	36	58

Table 91

Effect of antisense inhibition by ISIS 476333, targeting rs7685686 in BACHD and YAC18 neurons

	500 nM	1500 nM
YAC18	46	61
BACHD	89	91

CLAIMS

What is claimed is:

1. A compound comprising a modified antisense oligonucleotide consisting of 12 to 30 linked nucleosides targeted to a single nucleotide polymorphism site, wherein the modified oligonucleotide comprises a wing-gap-wing motif with a 5' wing region positioned at the 5' end of a deoxynucleoside gap, and a 3' wing region positioned at the 3' end of the deoxynucleoside gap, wherein position 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, or positions 1, 2, 3, 4, 5, 6, 7, 8, or 9 of the modified oligonucleotide, as counted from the 5' terminus of the gap, aligns with the single nucleotide polymorphism.
2. The compound of claim 1, wherein the single nucleotide polymorphism site is on a mutant allele that is associated with a disease.
3. The compound of claim 1, wherein the single nucleotide polymorphism site contains a differentiating polymorphism.
4. The compound of claim 1, wherein the modified antisense oligonucleotide consists of 12 to 20 linked nucleosides.
5. The compound of claim 1, wherein the modified antisense oligonucleotide consists of 15 to 20 linked nucleosides.
6. The compound of claim 1, wherein the modified antisense oligonucleotide consists of 15 to 19 linked nucleosides.
7. The compound of any one of claim 1, 4, 5, and 6, wherein position 8, 9, or 10 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, or

positions 4, 5, or 6 of the modified oligonucleotide, as counted from the 5' terminus of the gap, aligns with the single nucleotide polymorphism.

8. The compound of claim 7, wherein the gap region is 7-11 nucleosides in length, the 5' wing region is 1-6 nucleobases in length and the 3' wing region is 1-6 nucleobases in length.

9. The compound of claim 8, wherein the wing-gap-wing motif is any one of the group consisting of 5-10-5, 2-9-6, 3-9-3, 3-9-4, 3-9-5, 4-7-4, 4-9-3, 4-9-4, 4-9-5, 4-10-5, 4-11-4, 4-11-5, 5-7-5, 5-8-6, 5-9-3, 5-9-5, 5-10-4, 5-10-5, 6-7-6, 6-8-5, and 6-9-2.

10. The compound of claim 9, wherein the wing-gap-wing motif is any one of the group consisting of 2-9-6, 4-9-5, and 4-11-4.

11. The compound of claim 1, wherein at least one internucleoside linkage is a modified internucleoside linkage.

12. The compound of claim 2, wherein each internucleoside linkage is a phosphorothioate internucleoside linkage.

13. The compound of claim 1, wherein at least one nucleoside comprises a modified nucleobase.

14. The compound of claim 5, wherein the modified nucleobase is a 5'-methylcytosine.

15. The compound of claim 1, wherein at least one nucleoside of at least one of the wing regions comprises a modified sugar or sugar surrogate.

16. The compound of claim 1, wherein each of the nucleosides of each wing region comprises a modified sugar or sugar surrogate.

17. The compound of claim 16, wherein the sugar or sugar surrogate is a 2'-O-methoxyethyl modified sugar.
18. The compound of claim 1, wherein at least one of the wing regions comprises a 4' to 2' bicyclic nucleoside and at least one of the remaining wing nucleosides is a non-bicyclic 2'-modified nucleoside.
19. The compound of claim 16, wherein the non-bicyclic 2'-modified nucleoside is a 2'-O-methoxyethyl nucleoside.
20. The compound of claim 1, wherein the 4' to 2' bicyclic nucleoside is 4'-CH(CH₃)-O-2' bicyclic nucleoside.
21. The compound of claim 1, wherein the modified antisense oligonucleotide consists of 17 linked nucleosides and wherein position 9 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with the differentiating polymorphism.
22. The compound of claim 21, wherein the wing-gap-wing motif is 2-9-6.
23. A compound comprising a modified oligonucleotide consisting of 18 linked nucleosides and 90% complementary to a differentiating polymorphism site, wherein the modified oligonucleotide comprises a wing-gap-wing motif, wherein position 9 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with the differentiating polymorphism; wherein each nucleoside of each wing segment comprises a 2'-O-methoxyethyl sugar; and wherein the wing-gap-wing motif is 4-9-5.
24. A compound comprising a modified oligonucleotide consisting of 19 linked nucleosides and 90% complementary to a differentiating polymorphism site, wherein the modified oligonucleotide comprises a wing-gap-wing motif, wherein position 10 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with the differentiating polymorphism; wherein each nucleoside of each wing segment comprises a 2'-O-methoxyethyl sugar; and wherein the wing-gap-wing motif is 4-11-4.

25. A compound comprising:
a modified oligonucleotide consisting of 15 to 19 linked nucleosides and complementary to a differentiating polymorphism site, wherein the modified oligonucleotide comprises a wing-gap-wing motif, wherein position 6, 7, 8, 9, 10, 11, 12, 13, or 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with the differentiating polymorphism;
and at least one high-affinity sugar modification.
26. The compound of claim 1, wherein the modified oligonucleotide is 100% complementary to the single nucleotide polymorphism site.
27. The compound of claim 1, wherein at least one of the wing regions comprises a high-affinity sugar modification.
28. The compound of claim 27, wherein the high-affinity sugar modification is a bicyclic sugar.
29. The compound of claim 28, wherein the bicyclic sugar comprises a 4'-CH(CH₃)-O-2' bridge.
30. The compound of claim 25, wherein at least one of positions 2, 3, 6, 9, 10, 11, 13, or 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, comprises the at least one high-affinity sugar modification.
31. The compound of claim 25, wherein at least one of positions 2, 3, 13, and 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, comprises the at least one high-affinity sugar modification.

32. The compound of claim 31, wherein each of nucleoside positions 2, 3, 13, and 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, comprise the at least one high-affinity sugar modification.
33. The compound of claim 32, wherein the high-affinity sugar modification is a bicyclic sugar.
34. The compound of claim 33, wherein the bicyclic sugar comprises a 4'-CH(CH₃)-O-2' bridge.
35. The compound of claim 25, wherein the wing-gap-wing motif is any of the group consisting of 3-9-3, 4-9-4, and 5-9-5.
36. A compound comprising:
a modified oligonucleotide consisting of 15, 17, or 19 linked nucleosides and fully complementary to a differentiating polymorphism site, wherein the modified oligonucleotide comprises a wing-gap-wing motif, wherein position 6, 8, 10, or 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with the differentiating polymorphism;
and at least one high-affinity sugar modification.
37. The compound of claim 36, wherein at least one of positions 2, 3, 6, 9, 10, 11, 13, or 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, comprises the at least one high-affinity sugar modification.
38. The compound of claim 37, wherein the high-affinity sugar modification is a bicyclic sugar.
39. The compound of claim 38, wherein the bicyclic sugar comprises a 4'-CH(CH₃)-O-2' bridge.

40. The compound of claim 36, wherein the wing-gap-wing motif is any of the group consisting of 3-9-3, 4-9-4, and 5-9-5.
41. A compound comprising:
a modified oligonucleotide consisting of 15 linked nucleosides and 90% complementary to a differentiating polymorphism, wherein the modified oligonucleotide comprises a wing-gap-wing motif, wherein position 8 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with the differentiating polymorphism;
and at least one high-affinity sugar modification.
42. The compound of claim 41, wherein the modified oligonucleotide is 100% complementary to the differentiating polymorphism.
43. The compound of claim 41, wherein each of nucleoside positions 2, 3, 13, and 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, comprise the at least one high-affinity sugar modification.
44. The compound of claim 43, wherein the high-affinity sugar modification is a bicyclic sugar.
45. The compound of claim 44, wherein the bicyclic sugar comprises a 4'-CH(CH₃)-O-2' bridge.
46. The compound of claim 41, wherein the wing-gap-wing motif is 3-9-3.
47. A method of selectively reducing expression of an allelic variant of a gene containing a single nucleotide polymorphism in a cell, tissue, or animal, comprising administering to the cell, tissue, or animal a compound comprising a modified oligonucleotide complementary to a differentiating polymorphism site, wherein the modified oligonucleotide comprises a wing-gap-wing motif and wherein position 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 of the modified

oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with the differentiating polymorphism.

48. The method of claim 47, wherein the modified oligonucleotide is 90% complementary to the single differentiating polymorphism.

49. The method of claims 47, wherein the modified oligonucleotide is 95% complementary to the single nucleotide polymorphism site.

50. The method of claim 47, wherein the modified oligonucleotide is 100% complementary to the single nucleotide polymorphism site.

51. The method of claim 47, wherein the single nucleotide polymorphism site is from 12 to 30 nucleobases in length.

52. The method of claim 47, wherein the single nucleotide polymorphism site is from 15 to 25 nucleobases in length.

53. The method of claim 47, wherein the single nucleotide polymorphism site is from 17 to 22 nucleobases in length.

54. The method of claim 47, wherein the single nucleotide polymorphism site is 17 nucleobases in length.

55. The method of claim 47, wherein the single nucleotide polymorphism site is 18 nucleobases in length.

56. The method of claim 47, wherein the single nucleotide polymorphism site is 19 nucleobases in length.

57. The method of claim 47, wherein the single nucleotide polymorphism site is 20 nucleobases in length.
58. The method of claim 47, wherein the allelic variant is associated with disease.
59. The method of claim 58, wherein the disease is Huntington's Disease.
60. The method of claim 47, wherein the modified oligonucleotide is a single-stranded oligonucleotide.
61. The method of claim 60, wherein at least one internucleoside linkage is a modified internucleoside linkage.
62. The method of claim 61, wherein each internucleoside linkage is a phosphorothioate internucleoside linkage.
63. The method of claim 60, wherein at least one nucleoside comprises a modified nucleobase.
64. The method of claim 63, wherein the at least one modified nucleobase is a 5'-methylcytosine.
65. The method of claim 60, wherein at least one nucleoside comprises a modified sugar.
66. The method of claim 65, wherein the modified sugar is a high-affinity sugar modification.
67. The method of claim 66, wherein the high-affinity sugar is a bicyclic sugar.
68. The method of claim 67, wherein each bicyclic sugar comprises a 4'-CH(CH₃)-O-2' bridge.

69. The method of claim 60, wherein at least one of nucleoside positions 2, 3, 13, and 14 of the modified oligonucleotide, counting from the 5' terminus of the modified oligonucleotide, comprises a nucleoside having a bicyclic sugar wherein the bicyclic sugar comprises a 4'-CH(CH₃)-O-2' bridge.
70. The method of claim 69, wherein each of nucleoside positions 2, 3, 13, and 14 of the modified oligonucleotide, counting from the 5' terminus of the modified oligonucleotide, comprises a bicyclic sugar wherein the bicyclic sugar comprises a 4'-CH(CH₃)-O-2' bridge.
71. The method of claim 65, wherein the at least one modified sugar comprises a 2'-O-methoxyethyl.
72. The method of claim 71, wherein each nucleoside positioned in a wing segment of the modified oligonucleotide comprises a 2'-O-methoxyethyl modification.
73. The method of claim 47, wherein the wing-gap-wing motif is any of the group consisting of 2-9-6, 3-9-3, 3-9-4, 3-9-5, 4-7-4, 4-9-4, 4-9-5, 4-10-5, 4-11-4, 4-11-5, 5-7-5, 5-8-6, 5-9-3, 5-9-5, 5-10-4, 5-10-5, 6-7-6, 6-8-5, and 6-9-2.
74. The method of claim 47, wherein the modified oligonucleotide is not a ribozyme, a double stranded siRNA, or an shRNA.
75. The method of claim 47, wherein the single nucleotide polymorphism site is on a mutant allele that is associated with disease.
76. The method of claim 47, wherein the single nucleotide polymorphism site contains a differentiating polymorphism.
77. The method of claim 47, wherein the modified antisense oligonucleotide consists of 12 to 20 linked nucleosides.

78. The method of claim 47, wherein the modified antisense oligonucleotide consists of 15 to 19 linked nucleosides.
79. The method of claim 47, wherein the gap region is 7 to 11 nucleosides in length, the 5' wing region is 1 to 6 nucleobases in length and 3' wing region is 1 to 6 nucleobases in length.
80. The method of claim 47, wherein at least one nucleoside of at least one of the wing regions comprises a modified sugar or sugar surrogate.
81. The method of claim 47, wherein each of the nucleosides of each wing region comprises a modified sugar or sugar surrogate.
82. The method of claim 81, wherein the sugar or sugar surrogate is a 2'-O-methoxyethyl modified sugar.
83. The method of claim 47, wherein at least one of the wing regions comprises a 4' to 2' bicyclic nucleoside and at least one of the remaining wing nucleosides is a non-bicyclic 2'-modified nucleoside.
84. The method of claim 81, wherein the non-bicyclic 2'-modified nucleoside is a 2'-O-methoxyethyl nucleoside.
85. The method of claim 47, wherein the 4' to 2' bicyclic nucleoside is a 4'-CH(CH₃)-O-2' bicyclic nucleoside.
86. A method of selectively reducing expression of an allelic variant of a gene containing a single nucleotide polymorphism in a cell, tissue, or animal, comprising administering to the cell, tissue, or animal a compound comprising a modified oligonucleotide complementary to a differentiating polymorphism, wherein the modified oligonucleotide comprises a wing-gap-wing motif and wherein position 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 of the modified oligonucleotide,

as counted from the 5' terminus of the modified oligonucleotide, aligns with the differentiating polymorphism.

87. A method of selectively reducing expression of an allelic variant of a gene containing a single nucleotide polymorphism in a cell, tissue, or animal, comprising administering to the cell, tissue, or animal a compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides and complementary to a differentiating polymorphism, wherein the modified oligonucleotide comprises a wing-gap-wing motif and wherein position 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide aligns with the differentiating polymorphism; and wherein the allelic variant is a mutant allele.

88. The method of claim 81, wherein the mutant allele is associated with any disease from the group consisting of Alzheimer's disease, Creutzfeldt-Jakob disease, fatal familial insomnia, Alexander disease, Parkinson's disease, amyotrophic lateral sclerosis, dentato-rubral and pallidoluysian atrophy DRPA, spino-cerebellar ataxia, Torsion dystonia, cardiomyopathy, chronic obstructive pulmonary disease (COPD), liver disease, hepatocellular carcinoma, systemic lupus erythematosus, hypercholesterolemia, breast cancer, asthma, Type 1 diabetes, Rheumatoid arthritis, Graves disease, SLE, spinal and bulbar muscular atrophy, Kennedy's disease, progressive childhood posterior subcapsular cataracts, cholesterol gallstone disease, arteriosclerosis, cardiovascular disease, primary hypercalciuria, alpha-thalassemia, obsessive compulsive disorder, Anxiety, comorbid depression, congenital visual defects, hypertension, metabolic syndrome, prostate cancer, congenital myasthenic syndrome, peripheral arterial disease, atrial fibrillation, sporadic pheochromocytoma, congenital malformations, Machado-Joseph disease, Huntington's disease, and Autosomal Dominant Retinitis Pigmentosa disease.

89. A method of treating Huntington's Disease, comprising selectively reducing expression of an allelic variant of a gene containing a single nucleotide polymorphism in a cell, tissue, or animal, comprising administering to the cell, tissue, or animal a compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides and complementary to differentiating polymorphism, wherein the modified oligonucleotide comprises a wing-gap-wing

motif and wherein position 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or 15 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with differentiating polymorphism; and wherein the allelic variant is associated with Huntington's Disease.

90. The method of any one of claims 47, 86, 87, and 89, wherein position 8, 9, or 10 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, or positions 4, 5, or 6 of the modified oligonucleotide, as counted from the 5' terminus of the gap, aligns with the single nucleotide polymorphism.

91. A compound comprising:

a modified oligonucleotide consisting of 15 to 19 linked nucleosides and complementary to a differentiating polymorphism site, wherein the nucleoside at position 6, 7, 8, 9, 10, 11, 12, 13, or 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, aligns with the differentiating polymorphism;

and wherein the nucleoside at at least one of positions 2, 3, 6, 9, 10, 11, 13, or 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, comprises a high-affinity sugar modification.

92. The compound of claim 91, wherein the nucleoside that aligns with the differentiating polymorphism comprises a high-affinity sugar modification.

93. The compound of claim 91 or 92, wherein the nucleoside immediately adjacent to and at the 5'-side of the nucleoside that aligns with the differentiating polymorphism comprises a high-affinity sugar modification.

94. The compound of any one of claims 91-93, wherein the nucleoside immediately adjacent to and at the 3'-side of the nucleoside that aligns with the differentiating polymorphism comprises a high-affinity sugar modification.

95. The compound of claim 91, wherein the modified oligonucleotide is 100% complementary to the single nucleotide polymorphism site.
96. The compound of claim 91, wherein the high-affinity sugar modification is a bicyclic sugar.
97. The compound of claim 96, wherein the bicyclic sugar comprises a 4'-CH(CH₃)-O-2' bridge.
98. The compound of claim 91, wherein the nucleoside at at least one of positions 2, 3, 13, and 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, comprises a high-affinity sugar modification.
99. The compound of claim 98, wherein each of nucleosides at positions 2, 3, 13, and 14 of the modified oligonucleotide, as counted from the 5' terminus of the modified oligonucleotide, comprises a high-affinity sugar modification.
100. The compound of claim 99, wherein the high-affinity sugar modification is a bicyclic sugar.
101. The compound of claim 100, wherein the bicyclic sugar comprises a 4'-CH(CH₃)-O-2' bridge.
102. A method of selectively reducing expression of an allelic variant of a gene containing a single nucleotide polymorphism in a cell, tissue, or animal, comprising administering to the cell, tissue, or animal a compound according to any of claims 91-101.

Figure 1

CLUSTAL 2.0.12 multiple sequence alignment

genome mRNA	GCCCAGCAGGTGTCAGCCTCATTTTACCCCGCCCCTATTCAAGATGAAGTTGTTCTGGTT -----	60
genome mRNA	CCAACGCCTCTGACATATTAGCTGCATCATTTTACATTTCTTTTTTTTTTTTCCTTTTAA -----	120
genome mRNA	ATGGGGTCTTGCTCTGTCACCCAGGCTGGAGTGCTGTGGTATGATCTCGGCTCACTGCAA -----	180
genome mRNA	TCTCCACCTCCGAGGTTCAGCGATTCTCTTGCCCTCAGCCTCCCGAGTAGCTGGGACTAC -----	240
genome mRNA	AGGCACCCACCATCATACTGGGCTAATTTTTGTGTTTTTAGTAGAGATGGGGTTTCCCCA -----	300
genome mRNA	TGTTGCCCAGGCTGATCTCAAACCTCTGGGCTTAAGCAATACAGCCGCGTTGGCCTCCCA -----	360
genome mRNA	AAGTGTTGGGATTACAAGCATGAGCTACCCACCCAGCTCATTTTACATTTCCACTTGTT -----	420
genome mRNA	AAACTGAAACTGGCCCGAGAAAGCTTCTGTACTGCCATCCTTGCGTCCTTGCAGATGAA -----	480
genome mRNA	TCGTAACCTAGCATAGTAGGTAGGCAGACTGAAAACCTAACTTAGCAGTAGGCTTCTGTA -----	540
genome mRNA	ACAACAGCTGTGTCTCAGCCAGTTCTGCAGCCAGACTTCAACCACTCACAGGCCGCAAA -----	600
genome mRNA	CTGTTCAAACCTGTGTTCTGGAGAAGGCGAATTCATCTGGCTGTTAACGTGCCTCACTTCTG -----	660
genome mRNA	CTTTCTGTGGCCACTTTCCTTTTCTGTCCATAAATTTGCTTTGACCACACAGCATCCCT -----	720
genome mRNA	AGAGTCTCCCTGAATCTGCTGTGATTCTGGGACCTGCACCATTGTGAATTGTTTTTTTT -----	780
genome mRNA	TTCCTTGATCAGCTAAACTCTGTTCAATTCAATTTGTTGGAAGTTTTTAACATACCAATG -----	840
genome mRNA	GTGCACCAAGGTTCCAATTTCTCCACTTCCTCATAAATAAGTCATTTTAAATGGCTTTTC -----	900
genome mRNA	AGTATTCCAATATTTGGAAGTATTAATGTTTCTACCAATTTTCTATTTTGGACATTGAG -----	960
genome mRNA	GTTGTTTCATTTTTTTTTTTCTTTTTTTGAGACAGAGTCTCGCTCCGTCACCCAGGCTGGA -----	1020
genome mRNA	GTGCAGTGGCCTGATCCCGGCCCACTGCAACCTCCACCTCCCTCCTCAGCCTCCTGAGTA -----	1080
genome mRNA	GCTGGGATTACAGGTGCATGCACCACCACACCCAGCTAATTTTTGTATTTTGTAGTAGAGA -----	1140
genome mRNA	TGGGGTTTCACCATGTTGGTCAGGCTGGTCTCAAACCTCCTGACCTCAGGTGGTCCACCTG -----	1200
genome	CCTTGGCCTCCCAAAATGCTGGGATTACAGGCCTGAGCCACTGCGCCTGGCCTCATCTTC -----	1260

Figure 1

mRNA	-----	
genome mRNA	TTGATATTAATGTTGCTTTAACATCTTTGTCCCTGTGTTTTTTGTTTTTTTTTTTGAGAC	1320
genome mRNA	-----	
genome mRNA	GGAGTCTCATTTCATTCTGTCACCCAGGCTGGAGTTCAGTGGCGTGATCTCAGCTCACTGC	1380
genome mRNA	-----	
genome mRNA	AACCTCTGTCTCCTGGGTTCAGTGATTCTCCTGCGTCGGTCTCCTGAGTAGCTGTGTTC	1440
genome mRNA	-----	
genome mRNA	CTGGGTCTTTCGATGGTTATTTAATACTTCCCTACAGTAATGCCCTGTGCGTACATGCTA	1500
genome mRNA	-----	
genome mRNA	AGTGTGATGAAATGGTTGGCACAGTTAAATCTTTTGAAAGACATTGCCAAGTCACTCTTC	1560
genome mRNA	-----	
genome mRNA	AGAAAAGTGATAGGAGGTCATAGCAATTTTAAGAAGTCCTCATTTCTACATTTCCTTACT	1620
genome mRNA	-----	
genome mRNA	AATCTCGGTTGGTGTCTCTTCAATCTTTCCTCACACTTTTCTTGGGTTTTTCCTGAATCA	1680
genome mRNA	-----	
genome mRNA	TGAGTCTACTACATTTACACATTTTAAAGCATCTTTAGAAACAGGATCTCATTTTGTTGC	1740
genome mRNA	-----	
genome mRNA	CCAGGCTAGAGTTTGGTGGCATGATTATAGCTCCTCATACTCCTGGGCTCAAGTGATCCT	1800
genome mRNA	-----	
genome mRNA	TCCACCTCTGAAACCCCAAATTTGAGAAAGGTCTCATTTAATTTAGAAAGTTTATTTTG	1860
genome mRNA	-----	
genome mRNA	CCAAGGTTGAGGGTGACACCTGTGATGATATACGAGTTAAAAAGAAATTATTTAGGCAG	1920
genome mRNA	-----	
genome mRNA	ATACTGAGGGTAAGAAAGTCCTCGGTAAGGTTTTCTTTTCAAT	rs2857936
genome mRNA	-----	
genome mRNA	ATACTGAGGGTAAGAAAGTCCTCGGTAAGGTTTTCTTTTCAAT	1980
genome mRNA	-----	
genome mRNA	CATTTTCTTTTCTAACAAAGAGCAGCCTGTAAAATCGAGCTGCAGACATACACAAGCAAG	2040
genome mRNA	-----	
genome mRNA	CTGGAAGCTTGCACAGGTGAATGCTGGCAGCTGTGCCAATAAGAAAAGGCTACCTGGGGC	2100
genome mRNA	-----	
genome mRNA	CAGGCAGATCCAACATGGCGGCTCCATCTTCCCTTTCCTTGTCAACCATGTGCACAGTAA	2160
genome mRNA	-----	
genome mRNA	GGAGCAGGCAACATAGTGTCCCCGAGTAGAGACCAATTTGCATAATAAAAGGTGAGGGT	2220
genome mRNA	-----	
genome mRNA	AGGGTGGGCAGCTTCTTTGCATGCTATGTAAACATTATGCCTGGTCCAACCAATCTTTGG	2280
genome mRNA	-----	
genome mRNA	GCCCTGTGTAAATTAGACACCACCTCCTCAAGCCTGTCTATAAAACCCTGTCCATTCTGC	2340
genome mRNA	-----	
genome mRNA	CGCAGGCTGGAAGACCCACTGGGGCACCCCTCTCTCTCTATAGGAGACAGCTATTCATTT	2400
genome mRNA	-----	
genome mRNA	TTCTCTTTCTTTTACCTATTAAAGCTCCACTCTTAACCCCACTCCGTGTGTATCTATGTT	2460
genome mRNA	-----	
genome	CTTGATTTTCCTTGGCATGAGGCAATGAACCTTGGGTATTACCCCAGAACCTTGGGTATTA	2520

Figure 1

mRNA	-----	
genome mRNA	TGCCACTTCAGTGACACAGCCTCAGGAAATCCTGATGACATGTTCCCAAGATGGTCGGGG	2580
genome mRNA	-----	
genome mRNA	CACAGCTTGGTTTTATACATTTTAGGGAGACATGAGACGTCAATTCATATATGTAAGAAG	2640
genome mRNA	-----	
genome mRNA	TACATTGGTTCGGTCCAGAAAGGCGGGGACAACTTGAGGCAGGGAGAGAGCTTCTAGGTC	2700
genome mRNA	-----	
genome mRNA	ACAGGTAGACAAATGGTTGCATTCTTTTGAATCTCCGATAAGCCTTCCAAAGGAGGCAA	2760
genome mRNA	-----	
genome mRNA	TCAGAAATATGCGTCTATTGACTGGGCGCAGTGGCTCATGCCTGTAATGCCAGCACTTTGG	2820
genome mRNA	-----	
genome mRNA	GAGGCGGAGGTGGGTGGATCACCTGAGGTCAGGAGTTTGAGAGCAGCCCGGCCAACATGG	2880
genome mRNA	-----	
genome mRNA	TGAAACCCTGTCTCTACTAAAAATACAAAAAATTAGCTGGGCGTGGTGGCGGGCGCCTGT	2940
genome mRNA	-----	
genome mRNA	AATCCCAGCTACTCGGGAGGCTGAGGCAGGAGAATAGCTTGAACCCAGAAGGAAGAGGTT	3000
genome mRNA	-----	
genome mRNA	GCAGTGAGCTGAGATGGTGCCATTGCACTCCAGCCTGGGCAACAAGAGTGAAACTCCATC	3060
genome mRNA	-----	
genome mRNA	TCAGAAAAAAAAAAAAAAAAAGGCCTGGGCAAAGTGGCTCACGCCTGTAATCCCAGCACTTTG	3120
genome mRNA	-----	
genome mRNA	GGAAGCCGAGGCGGGCAGGTCACAAAGTCAGGAGATTGAGACCATCCTGGCTAACATGAT	3180
genome mRNA	-----	
genome mRNA	GAAACCCCATCTCTACTAAAAAATACAAAAAACTAGCTGGGTGTGGTGGCGAGCACCTGT	3240
genome mRNA	-----	
genome mRNA	AGTCCCAGCTACTCGGCAGGCTGAGGCAGGAGAATGGCGTGAACCGGGGAGGCGGAGCTT	3300
genome mRNA	-----	
genome mRNA	GCAGTGAGCCGAGATCACACCACTGCACTCCAGCCCGGACGACAGGGCAAGACTCTATCT	3360
genome mRNA	-----	
genome mRNA	CAAATTAAAAAAAAAAAAAAAAAAAAAAAAAAGAGAGAGAGAATATGCATCTATCTCAG	3420
genome mRNA	-----	
genome mRNA	TGAGCAGAAGGATGACTTTGAATGGAATGGGAGCAGTTCCTAGCTTGAACCTCCCCTTTA	3480
genome mRNA	-----	
genome mRNA	GCTTCAGTGATTTGGGGGCTCAAGGTATGTTCTTTTACATACCTCAGCCTCCCAAGTAG	3540
genome mRNA	-----	
genome mRNA	CTGGGACCACAAGTGCATGCCACCACACGTGGCTAATGTTTTATTTTTTTGTAGGAATA	3600
genome mRNA	-----	
genome mRNA	GGGTCTCACTATGTGTCCAGGCTGGTCTAAAACCCCTGAGCTCAAATGGTCCTCCCGCCT	3660
genome mRNA	-----	
genome mRNA	CAGCCTCCCGAAATGCTGGGATTACAGGCATGAGCCAGCATGCCCGGCCTAGTCTACATT	3720
genome mRNA	-----	

rs12506200

Figure 1

genome mRNA	TTTATAAATTGCTAATTCAAAGTTCCCTCTCCAAAACCTCATGGTTTTCCCTGTTCTCAT	3780
genome mRNA	CCCCTGACCCCTCCCTTCCCCTGGAGTACTCACCTGGCCTTGGAGGTCTGGTGTGAGCCC	3840
genome mRNA	GGACTTCGATTCTAGGCACAGCATGTGATGAGCGCCCCCAGGTCAAACACCTCCCCTCTG	3900
genome mRNA	CGGCCTGTGCTTCACCGCCTTGACAGTGAGAAAGGTCTCCCTTCGGCTCATTCTCGAAGT	3960
genome mRNA	CTCAAACCTTCACTTCTCCTGTGCGCTGATTCTGAATTCAGCCCCCGTCCAAGGTCCTGGC	4020
genome mRNA	CCCTTTCTCTTCTGCTTGGCGTGTTGTTTCATCACCCTGTGCACTGCTGAGGGTAAGTGC	4080
genome mRNA	GGTTCTCTGGACCTCTGCTTTATCATTAGAACAGACTCTTGCGGTTTCCCACGACATTCC	4140
genome mRNA	TTTCACTTCTCACTTGAAGATGAGCCGTGAGGAAATCCTGTGTTGTGTGGTATGTGGGC	4200
genome mRNA	TGTGCTTCTGCTTGACTTGAGGGCCAAGCAGCATTGCAAGCCATGGTTTTAAATAAGAAA	4260
genome mRNA	GAACATTTCTAACCTTCATCTTCTAGTAAGGAAACAAGTGGGCTTTAGAGTTCTTGCTCA	4320
genome mRNA	GGAAAGACCTATGTCCCAGTCCAACCGGACCTTTTACTAAAGAGATCTTCCTGATCCTCC	4380
genome mRNA	TCCCCAGGCCAGGGGAGGGGTCTCCCTGGGGTTGGAGCCTTTAGTAGGGGGTCGGAGAC	4440
genome mRNA	ACGACGTAGCCTTCATGACATTCATAGTCTAGTTACACGATCCCTGTAAGGGTCAGTTGA	4500
genome mRNA	AGTAAGTGCTACAAAGGAAGGGAGGTGCTCAGTGGAGAGGGCTCTCTTTTATGTATTATA	4560
genome mRNA	TTTCTTTTCATGGGGAGGGATATGGATCAGGGATCAGCAGAGGTGTTTCAGTCCCGAGGGA	4620
genome mRNA	AAGAAAGTCAGCGTGGCTTGGGAGTTGGGAGCAGCAAGACAGTGGCTCAAGATATCTTAA	4680
genome mRNA	GACTAGTGGAGTACACCTTGCATGTTAAAAGCCTTGCTCAGGGCTGCCTGGTTCTTGTA	4740
genome mRNA	GACGACAGAGATGGCCTAGCTCTGCATACTGCACCCCCAGGGGCTCAGAACAGTGCAAAT	4800
genome mRNA	GTCAGTCTATCTGTTCAGTGGCAGAGCCAGCCTTGGAGCAGGGGTGCAAGGAGGTCTCTGC	4860
genome mRNA	ACTGGCCAGGCATGCAGAACATTCTGTTTCAGTAGCACTGGACAGAAGGCCCCATCTAGAT	4920
genome mRNA	GAGACAGAGCTGGTGGGGCAGGACAAAGACTCCTGGCAGCTCAAACGGCCTGGCAGATGC	4980

Figure 1

genome mRNA	TTGGAGAGAGGGGGCTTCTTGAGACAGCACCATTTCTGGGAAGAGAGTCACCTGGGAGGG	5040

genome mRNA	ATGAGGCCACGCTCCGGCTTGAGGTGAAGAGAGGGGCTGCTGCAAGAAAGAATTAGAGA	5100

genome mRNA	CATGCCAGCCTTTGCTGTGTTGCCAGGCTGGTCATGAACTCTTGGCCTCAAGCAATCTT	5160

genome mRNA	CCCACCTCAGCCTCCCCAAGCGCTGGGATTATAGACATGAGCCCCCATGCTGGCCAATAA	5220

genome mRNA	AAGATGATTTTATGGAGGGGATGGTGGTGAAGGTTGTGGGTGGTATGAAATAGTAAGAAA	5280

genome mRNA	TATATATTGGTCTGCACCCAGTTCCTGCCACAGAGCTCCTAAAATCCTGAGAACTTCCTG	5340

genome mRNA	GGTGAGCATCTTTTGTCTAATGAGGTGACTCTTGGTGGCTCCTGGATAGGAGTGAATCA	5400

genome mRNA	CCAGAAAGATCAAGCCAGAGTTAGAAGCAGAAAGTGCTGGCTATAACACAGGAAAGCTGT	5460

genome mRNA	AACACAAATAATAAAGTTTTTTTTTTTTTTTTTGGAGATGGAGCCTCACTCTGTTGCCAG	5520

genome mRNA	GCTGGAGTGCAATGGTGCAATCTCAGCTCACTACAAGCTCTGCCTCCCAGGTTCAAGTGA	5580

genome mRNA	TTCTCCTGCCTCAGCCTCCTGAGCAGTTGGGACTACAGGTGTGTGCCACCACATCTGGCT	5640

genome mRNA	AATTTTGTATTTTATAGCAGAGACGGGGTTTACCATATTAACCAGGCTGGCCTCAAAC	5700

genome mRNA	CCTTACCTTGTGATCCGCCTGCCTCAGCCTCCCAAAGTGCTGGGATTACAGGCATGAGCC	5760

genome mRNA	ACCGTGCCTGGCCAAAAGACATTGTTCTTAAAAGAATCAACTAACTAACCAAATAAATAA	5820

genome mRNA	AAATCTAACCTAATTAAGAACTAAAAATACACAAAAATTAATTTCAAGGGGAGAAAAAT	5880

genome mRNA	CATGTAAAGAGAGAAAGATAATGAATACTTTGCAGAAATTTATGAACATAAACATAAAAC	5940

genome mRNA	TTGGATGAAATGCATTTCTAGGAAAACATAATTTATCAAACTAACCACAAGTAAAATAG	6000

genome mRNA	AAGCCTAAATAGGATATTTTCAAGAGAAGAAGTAAAGTTGTCAAAGTGCTACCCTTCAA	6060

genome mRNA	AAAACACCAGGCTCAAACAATCTGACATGGGAATGTTAGCACACCTTAGAGAGCAAATAA	6120

genome mRNA	AACTTTGAATGGGCTTGAAATATTCCAGACTCTAGAAAAACAAACTTCCCAATTCTTTT	6180

genome mRNA	TATAAAGCAAGTATAAATTGATACCAAATCTTATAAAGACCTTATACAAACTTCATAC	6240

Figure 1

genome mRNA	CAATCTCTTTTATGAATACAAAACCCTTAATAAAGTATTACCAGACAGAACCCAACAATA	6300

genome mRNA	CATAAAAATGTCACATCATAACATAGTGGGGTTTATTTCAATAATGCATGGATGGTTCAA	6360

genome mRNA	TACAAGGAAATT CAGTAACACAATATAATAGATCATGTGAATATACCCAAAGAAAAAATA	6420

genome mRNA	GATTATTTTCATAGATGCTGTAAAGGCATTTGACCAAATTC AACACCTACTTTTTAGGTG	6480

genome mRNA	GTCAATAAAATAAATTAGTTACTCCTTCTTTAGCATGATAAAATATATTTATCAGCCCAG	6540

genome mRNA	AAGGCATCATTTTACCCGATAAGGGCACACGCTGGAGGGAATAATGTTAAATTAGGAAT	6600

genome mRNA	AAGAGGATAGCTAGTTTCTTTCTTCTTTTTTTTTTTTGAGACGGAGTCTTGCTCTGTTGC	6660

genome mRNA	CAGGCTGGAGTGCAGTGGTGCAATGTTGGCTCACTGCACGCCCCCGCCTCCCAGGTTCA	6720

genome mRNA	AGCGATTCTCCTGCCTCAGCCTCCCGAGTAGCTGGGACTACAGGCGCGCACCACCATGCC	6780

genome mRNA	CGGCTAATTTTTTTTTTGTATTTTAGTAGAGATGGGGTTTCACCATGTTGGTCAGGCTGGT	6840

genome mRNA	CTTGAAC TCCCAACCTCACGTACTGGGATTACCGGTGTGAGCCACCACGCCAGCCCAACT	6900

genome mRNA	ACTTTCAACATTATCCTTAATACTGATGCTTATTGACTTACTATGGGGTTACCTCTAGAT	6960

genome mRNA	AAATCCATAATAAGTTGAAAATATAAGTAAAAAATGCCCTTAATACACCTAACCTACCAA	7020

genome mRNA	ACATCATAGCTGAGCCCAGCCTGCCTTAGCTATGCTCAGACACTGACGTCAGCCTACAAT	7080

genome mRNA	TGGCAAAATCACACAGCAGCACAGTCTACTGCAGAGCATCTGCTGTTTGCCCTTGTGACT	7140

genome mRNA	GCGTGGCTGCCTGGGAGCTTCCCAGCTTCACAAGACAGTATTACGTAGCACATCACTAGC	7200

genome mRNA	CTGGGGAAAGATCAAAGTTGAAAATTTGAAGTGTGGTTTCCATTGAATGTGTACTGCTTT	7260

genome mRNA	TGCACCATCATCAAGTCAAAAAATTTTAGTTGAACCAGCCTAAGTTTGGGACCATCTTTA	7320

genome mRNA	TTTTCAGGAGGAACTTCCATGTACATTGATGACGGACGATAGAATCCGTTTCTATCATCC	7380

genome mRNA	TAATGAACATAATGAATAAATCCAGACAAACATAAACATTAAACAGAGTAAGCAGCTTTTCG	7440

genome mRNA	GGGCTGGAAGCCAGAAGAGGGTGGGAGCGCAGAGAGAGAGGCCAAACACCAGGGCTGCTT	7500

Figure 1

genome mRNA	CTGCTTTGCGGGTATTTGCTGATCTGGACAAGGTATCTGGAAGGCTGAGCTAAGCCTCCT	7560
genome mRNA	TTTTTTTGGAGGTGGCGTCTCACTCTGTTGCCAGGCTGGAGTGCAATGGTGCGATCTCAG	7620
genome mRNA	CTCACTGCAACCTCCACCTCCCTGGTTCAAGCGATTCTCCTGCCTCAGCCTCCCGAGTAG	7680
genome mRNA	CTGGGATTACAGGCTCCCGCCACTACACCCAGCTGATTTTTTGTAAATTTAGTAGAGACGG	7740
genome mRNA	GGTTTCACCATGTTGGCCAGGATGGTCTCGATCTCTTGACGTCATGATCTGTCCACCTCG	7800
genome mRNA	GCCTCCCAAAGTGCTGGGATTATAGGCGTGACCCACCGTGCCCCGTCTGAGCTAAGCCTC	7860
genome mRNA	TTGAGCATAGGGGACTAAAAATGAAATCTAGCGCATGCCAAGTTTAGGGTCCCAGGCAAT	7920
genome mRNA	TCCTTTCCACTTTGGGGTCCACTTTGGGGTCCACCCACCCAAGAAGAAGGATGACTTGG	7980
genome mRNA	AAGTAAACCAGCTCTGAAATATGGATGGTCTCTGGGACCATACCAATCCCTTCATATCA	8040
genome mRNA	ACCACATCCAGTTCCTCAAACTGGAACCTGGATTAAAGATGGCCTAGGACTTCTAGTGTC	8100
genome mRNA	CCAGGAGCCTGGCATTGCAAAACAAAATCCTCTCCGGAAGAAGATAATACCTTAAGCTTC	8160
genome mRNA	AAATGACTCTCTAATAAATTTCAAATACAATGTCCAGCACACAAACACAAATTACCAGGA	8220
genome mRNA	ACGTGATATGAGGCCTGATGGATGGGAATTAGCAGAACTTCAGGCATGAGAAACATACC	8280
genome mRNA	CTCAGAGGCCTAGAATCTATCTAGTGTCTAGATAATGGAGATATGAAATACAGACACTTA	8340
genome mRNA	AACAACATATGTTTCCCATGTTCAAAGAGGAAATTTGCAAACTTGAAAGTGTTGGCAGGA	8400
genome mRNA	AATCAGAACTATAAAATGTGACAACAGCATACTTTAGAGTCAGTATAAATTACGGTCCC	8460
genome mRNA	GAAAACTGCAGAATTCCAGAACTTAATGGTAAAGCAAGGGTTTAAACAGCAGAATAGAAAT	8520
genome mRNA	AGCCAGAGAGAACTAGGAAGTAAGTCAGATGACACTACCCAGAATAAGGCACTGAGAGGC	8580
genome mRNA	CAAGGAATGGAAAATGCAGAAGAAAGGATATGGTGAGAGGATCTAATATACATTTATTTG	8640
genome mRNA	GAGTACCAGGGAGAGAGAGAAGGAGAAGAACAGAAGCCGTGTTTCAAGGACGGTGACTGA	8700
genome mRNA	GAGGCTTCGAAACTGATGAAAGCCATCAGTTCACAAATTCAAAGCCCAGTGAATTCCAAG	8760

Figure 1

genome mRNA	GAGAAAAAAGAAATCCATACTGTGAAAGCAAGTCCAGACAATGACAAACACCATCAACA	8820
genome mRNA	ATACACAGGACAGGCATAAGATGCATTTAATGGGGACACTCAGAGGCAGAGGGTTATCAG	8880
genome mRNA	AAGGAGGCACTTCTCTCCCAAGTTCTCATCATCCCAGGGCCAGGGACAGCTGGTCACACC	8940
genome mRNA	TTAGGGAGTTCAGTAGGAGAGGGATCTGGCTTCTTGTCATTCTGGGTATTTGTAGGGAAA	9000
genome mRNA	TTGGAAGGGAACCGAGAGCACCTAGCCAATCGCATAGCAATGGGAGATTTTCAGGCTGTGG	9060
genome mRNA	GGAATGTCTTTGCTGGTGAAAAGAACATCCTGACCTTAGAAATCTTTCACCGAGGGGGAT	9120
genome mRNA	CTGCGTTCCAGAACTTCTGGAGCTGGTATAGGTAAGGCTTTGAGCTTTCCTACTGAGCCA	9180
genome mRNA	GCCTGTTGCTAGGTTACCAAAGGGGACCTCGAGGGCCATCTGGCCAACAAGCAGACTTGT	9240
genome mRNA	CTCTCCTTACACCCCCAGACGTATCACTGCAAAACTACAGAAAACCAAAGACAGAGAAAA	9300
genome mRNA	TCTTAAAAGCAGCCAGATTTAAAAAATGGCATATTAGTTTCAAAGCAGCAGCCATGAAAT	9360
genome mRNA	TGACAGCTGATGTCTCAACAGCAAGAATGAAAAGTGGAAGACAGGCCAGGTGTGGTGGCT	9420
genome mRNA	CAGGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGTGGATCACGAGGTCAGGAGAC	9480
genome mRNA	CAAGACCATCCTGGCTAACATGGTGAAACCCCGTCTCTACTAAAAATACAAAAAATTAG	9540
genome mRNA	TCGGGCATGGTGGTGGGTGCCTGTAGTCCCAGCTACTCGGGAGGCTGAGGCAGGAGAATG	9600
genome mRNA	GCGTGAACCCGGGAGGCGGAGCTTGCAGTGAGCCGAGATTGTGCCACTGCACTCCAGCCT	9660
genome mRNA	GGGTGACAGAGCAAGACTCTGTCTCAAAAAAAAAAAAAAAAAAAAAAAAAAAGGGTGAC	9720
genome mRNA	GAAGCTTCAATCTCCTGAAAGGAAGCAACTGCCGCCTTTGATTGATACCCACCAAATC	9780
genome mRNA	CGTGAAGAAGGAAGGCAAAATAAAAACACTTCCTGATTGAACTGGAAAGATTCCGCAAT	9840
genome mRNA	AGAAGACCCACTGTCCAAGGAATTCTAAAGGATGCTTTCAGGCAGAAGAAAATGACCCC	9900
genome mRNA	AGAGGAAGATCAGAGATTCAGGAAAGAAATGGAGAGTGATAAAAATGGAAAATTCGGGGG	9960
genome mRNA	CCAATTTAAACAAAAGCTGACTGCTCTACAACCTGTTGTGTCTCTATCTTTTGTAACATAT	10020
genome	ATGTGTGTGTAGCTTTTTTTTTTTTTTTTTTGTCAAGATGGATTCTCACTCTGTCGCCCAGG	10080

Figure 1

mRNA	-----	
genome mRNA	CTACAGTGAAATGGCACGGTCTCGGCTCACTGCAACCTCTGCCCCTTGGGCTCAAATGAT	10140
genome mRNA	-----	
genome mRNA	TCTCTTGCCTCAGCCTCCTGAGTAGCTGAGATTACAGGTGCCTGGCACAATGCCTGGCTA	10200
genome mRNA	-----	
genome mRNA	ATTTTTGTATTTTACTAGAGATGGGATTTCTCCATGTTGGCCAGGCTGGTCTTGAACAC	10260
genome mRNA	-----	
genome mRNA	CTGACCTCAGGTGATCCACCTGCCTGGGCCTCCCAAAGTGCTAGGATTACAGGCGCGAGC	10320
genome mRNA	-----	
genome mRNA	CACTGCATCTGGCCTATGTGTGTGTTTATATGGAATTAAACACATGGCAATAATACCCT	10380
genome mRNA	-----	
genome mRNA	CCAAATTGGGAGAAACCAAAAATAGCATTTAAATGTTGTAAGCTCCCTGCATAATCAAGA	10440
genome mRNA	-----	
genome mRNA	AGAGAATAGATTTACGTTAGATTTTGATACCTGGAGGATGAATGTTGTAATTTCTAGGGT	10500
genome mRNA	-----	
genome mRNA	GACCATGAAAAGAGGAGACAACGGTGTATGTTTTTTTTTTTTTGGAGATGGAGTCTCACTT	10560
genome mRNA	-----	
genome mRNA	TGTCACCCAGGCTGGAGTGTTGTGGTGTGATCTTGGCTCACTGCAACCTCCTCCTCTTGG	10620
genome mRNA	-----	
genome mRNA	G TTCAGGCCATCCTCCCACCTAGGCCTCCAGAGTAGGTGGGATCACAGGCACCTGCCACC	10680
genome mRNA	-----	
genome mRNA	ACACCTGGCTAATTTTTTTTTTTTTTTTAAATATTTAGTAGAGATGGGGTTTCACCATGTT	10740
genome mRNA	-----	
genome mRNA	GGCCAGGCTGGTCTTGAACTCCTGACCTCAGGCGATCTGCCTACCTCTGCCTCTCAAAGT	10800
genome mRNA	-----	
genome mRNA	GCTGGGATTACAGGTGTGAGCCATCGCGCCCGGCCAACAGTGATCACTTCAAACCTAACA	10860
genome mRNA	-----	
genome mRNA	GAGGTTCAAAAATAAAATCAGACTTAACCAAAAACCAGGTAACAGAGCTGGTAGGATATA	10920
genome mRNA	-----	
genome mRNA	CAGAAAGACTGACCTCACGTATATCAACGATTACAGTTAATATTAATGAAGGAAATGCTC	10980
genome mRNA	-----	
genome mRNA	TAGTTTAAAAACGAGGGTGTCAAAGACCCACATAAGAAGCTCCTTACCAGCGGTGCAC	11040
genome mRNA	-----	
genome mRNA	CTAGAACCTAAGGAAACAGGACAGATGAAGGAGGACGCGCCCCGCGCTGTCCTGCGCC	11100
genome mRNA	-----	
genome mRNA	TCAGCCATCCTATGAGACGGGAAAGGTTTCTGTCTGCAGCTGGGCCCCGTGCTCTTTACCA	11160
genome mRNA	-----	
genome mRNA	GCTCCTGGCTTTCTTCTCTGGAAGGTTCTGCCTGTTTTGCCCTCACACCTGCTCCTCTC	11220
genome mRNA	-----	
genome mRNA	TCAGCCCTCTCAGGGGTGGGGCTGGAGGCCACCAAAGAGCCTCCTCTGCTCTCCAGTTGC	11280
genome mRNA	-----	
genome mRNA	TCGACTGCTCCTCATTTCCCCCTGGGGTCTGCGTCAGGGTTTCCTTCTTTTCCAGCCCCA	11340

Figure 1

mRNA	-----	
genome mRNA	CCCCGCGTGCATCCCACCTGGTCTCGGGTCGGGGCTGCTCCCGCTTACTGCCCCCTGCCC	11400
genome mRNA	-----	
genome mRNA	AGGCTGGTGTGCACCCCCCTCTGGCTGCTTTCAAGGCCTCTTCTCTCTTCTCGGCAGGACA	11460
genome mRNA	-----	
genome mRNA	GGCACAGGCAGGTGGCCAGGTGTCATGCTTAGCTCCCCGCCAGTGAGATTCTTTCATTT	11520
genome mRNA	-----	
genome mRNA	AACAATCTTCCCCTGAATAGTTCATGTTTCATTGCTGAAAATTTGAAAAATATGGAAAAGC	11580
genome mRNA	-----	
genome mRNA	ACAAAGATTAAGATATAAACCGCCCTCAATTCCCCTGCCAGAGAGAGTCACTGCTATGA	11640
genome mRNA	-----	
genome mRNA	CTTGGTGACTAGGAACCTTATTTCTCTCTCGCTCTTTTTTTTTTTTTTTGAGACAGAGTCT	11700
genome mRNA	-----	
genome mRNA	TGCTCTGTCACCCAGGCTGGAGTGCAGTGGCTCGATCTCAGCTCACTGCAACCTCCGCCT	11760
genome mRNA	-----	
genome mRNA	CCTGGGTTCAGCGATTCTCCTGCCTCAGCCTCTTGAGTAGCTGGGATTACAGGCACCTG	11820
genome mRNA	-----	
genome mRNA	CCACCATGCCCGGCTAATTTTTGTATTTTGTAGTTGAGAGAGGGTTTCATCTTGTTGGTCA	11880
genome mRNA	-----	
genome mRNA	GGCGGACTTGAACTCCTGACCTCAGGTGATCAGCCACCTCGGCCTCCCAAAGTGCTGGG	11940
genome mRNA	-----	
genome mRNA	ATTACAGGTGTGAGCCACTGCGCCTTCATCTCTCTTCTGTGTATGTGTACGCTGTTTTTT	12000
genome mRNA	-----	
genome mRNA	CTTTAGAATGGGGGACGTTATCAGGCTCTACATGGTGTGTAGTCGGCTAGCATGTTGTAA	12060
genome mRNA	-----	
genome mRNA	GCCTTTCCTGTGTCACAAGTGCTCATCTGGAACAGGATTCTAATGACTGCCTGTGGCTA	12120
genome mRNA	-----	
genome mRNA	TGTTGGGATTCTTTAACTCAGCTCCTTCTGCCCAGCATCTATCTTTTTTCCATCTTTTG	12180
genome mRNA	-----	
genome mRNA	TCCTAAGTGTTGCTATAATAAATCATTGATCACACATGCCTGACTGTTTGCATAGGATAA	12240
genome mRNA	-----	
genome mRNA	ATTACGGGAAATGTTTTTGCTGTTTCAGGGACTGTGCCCATTTTTAGGCCTCAGAGACACC	12300
genome mRNA	-----	
genome mRNA	ATGCCAGACTGCCAGTATTGATCTTTACTCTTTTGTAGATGATGCCAACTTTTCTGTGA	12360
genome mRNA	-----	
genome mRNA	ACTTTAAAAACCTGTGTCTTGACAGTCCATTTCTGTAAGTCTTTCACATTAGATTTCTG	12420
genome mRNA	-----	
genome mRNA	TCAGGATGATAGTCAATTCTAGGCAGATGATGTTTTCTCAGCCATGGCTGAAGCAGTTGT	12480
genome mRNA	-----	
genome mRNA	GATTTGTTGTGGCCATGTAAAGTCCCGATGATCCATTGCCTCCCTGGATGGGTGGAATA	12540
genome mRNA	-----	
genome	ATTTGGTTTGGGAGCATATAACAGAATGACCTGGAGTCACAGCAGCTCAGACGGAAGTGT	12600

Figure 1

mRNA	-----	
genome mRNA	ATTTCTCCCTTACAGATGAAAGAATTCCAGGCCAGGCTGGAATGACAACTGCACACAGTC	12660
genome mRNA	-----	
genome mRNA	ATCTGGGCCCCCTCCTTCCAGCTCCCATCACCCAGGATGTGGCTTTTATGCAGATGATC	12720
genome mRNA	-----	
genome mRNA	CAAAATGGCTGCTCAAGTCCCAGCCAACACATCCCATTCCAGGGAGCAGGAAAAAGGTGT	12780
genome mRNA	-----	
genome mRNA	GTCTTTCCCTTCATTTTATGTGATTCTTTCTAGAAGTACTACTCATTACTTCTGCTTGC	12840
genome mRNA	-----	
genome mRNA	ATCTCCCTGGCTAGCACTTACTTAGTTATATGGCCATAGCTAGCTGAAGGAAGGACAGGG	12900
genome mRNA	-----	
genome mRNA	ACTGTCATACACTAGCTAAGAGGCCAACTGCTTAGATAAAAAGGTCTCTAAAGAAGGTCA	12960
genome mRNA	-----	
genome mRNA	GAGCGGCTGCTAGGGTGCAACTCTATTACTTATTGTTATGGGACGAACTGTGTCCCTCAT	13020
genome mRNA	-----	
genome mRNA	TCAGGTTGATGTCCTAAGCCCCAGAACCTCAGAATGGGATTGTATTTGGAGACAGGTTCT	13080
genome mRNA	-----	
genome mRNA	TTAAGGAGGTAAGGAGGCTAAAATGAGATCATTAGGGTGGGCCATAATCCGACTGATGTC	13140
genome mRNA	-----	
genome mRNA	TTACAAGAAGAGATTAGGACACGGACATGCTCAGAGGGACGGCCACGTGAGGACACCAAG	13200
genome mRNA	-----	
genome mRNA	AAAGGCAGCTGTCTGCAAGTCAAGGACAGGGCTCAGGGGAAACCAACCTTGCCAACACCT	13260
genome mRNA	-----	
genome mRNA	TCATCTCGGACTTCTAGCCTCTAGGACCATGAGAAGATACATTTCTGTTGTTTAAGCTGC	13320
genome mRNA	-----	
genome mRNA	CCGGTCTGTGGTACTTTGTTATGGCAGCCCAAGTAAACAAATACAGTCATCTGCTGCTGG	13380
genome mRNA	-----	
genome mRNA	AACAAATCACCCCAGCACTGTGGCTTGGCAGCACACATGTCTAGTCATAGAGTTATATGT	13440
genome mRNA	-----	
genome mRNA	AGTTACGTGTAGAGCCATATGTATCGTCACACGTTCTGTGGGTCAGGAATTTGGACCCAG	13500
genome mRNA	-----	
genome mRNA	CTTAACCAGCTCCACTTCTCGCCAGGGTTCAGTCAAATACCAGCTGCCTCCCACCTGAGA	13560
genome mRNA	-----	
genome mRNA	GCTCAGCCGGGGAAGGGTCCCTTTCCAATCTCACGTGGTGTGGCAGGATCCAGTTCCTC	13620
genome mRNA	-----	
genome mRNA	ATGGCCTGCTGGACTGAGAACCTCAGTTCTCACTGCCTGTTGGCCAGAGGCCGCCTTTAT	13680
genome mRNA	-----	
genome mRNA	GTCCTCGCCATGTGGGCCTCTCCAACATGGCAGCTGACTTCATCAGAGCATCCATGCCAA	13740
genome mRNA	-----	
genome mRNA	GAAGGCAACAGAGAGGGCCAGGGAGACTGAAGTCATACCCTTTTGCGACCTAGTCATGGG	13800
genome	-----	
genome	GTGACATTCCATCACCTTTGCCCATTTGGTTAGAAGCAGGCCACCAGGTACAGCCCAAGCT	13860

Figure 1

mRNA	-----	
genome mRNA	CACGGGGAGGGGTCATACAAGGGTGTCAATACCAGGAGGTGAGGGGTGCTGGGGCCATCT	13920
genome mRNA	-----	
genome mRNA	TATGAGTCTGCCCAGTGAAGTAACTAACAACCTTGAGGCCTGACACAGTGGACAAAGGCC	13980
genome mRNA	-----	
genome mRNA	CTTATTAAACAGCAGAGAACTGGGAACCTTATTTATTTATTTATTTTGGAGACAGAGTCTC	14040
genome mRNA	-----	
genome mRNA	ACTCTTGTCACCCAGGCTGGAGTGCAATGGCATGATCTTGGCTCACTGCAACCTCCACCT	14100
genome mRNA	-----	
genome mRNA	CCCAGGTTCAAGCAATTCTGCCTCAGCCTCCGGAATAGCTGGGACTACAGGCATGCACCA	14160
genome mRNA	-----	
genome mRNA	CTACACCCGGCTAATTTTTGTATTTTGTAGTAGAGACAGGGTTTCGCCATGTTGGCCAGGC	14220
genome mRNA	-----	
genome mRNA	TGGTCTCGAACTCCTGACCTCTGGTGATCTGCCTGCCTTGGCCTCCCAAAGTGCTGGGAT	14280
genome mRNA	-----	
genome mRNA	TACAGGCGTGAGCCACCGCACCTCGCTGGAACCTAATTTTTTTAGAGACAGTGTGCTCT	14340
genome mRNA	-----	
genome mRNA	ATCACCCAAGCTGGAGTGCAGTGGTGCAATCCTAGCTCACTTGCAGCCTCAAATCCTGG	14400
genome mRNA	-----	
genome mRNA	G TTCAGGTGATCCTCCCACATCAGCCTCCCAAGAACTGGGAAC TAAC rs762855 AGCTGTTTCTCTG	14460
genome mRNA	-----	
genome mRNA	CTGTCCTTCTCAAGAAAAGGGAGGCTACTGCTACCCCACTGGGGACAATGCTGGGTTTCC	14520
genome mRNA	-----	
genome mRNA	CTTTAGGACAGGCTCTGAGACAAGGCGGAGGTGCTGTTTGTGGCCACAGAGCAGGGGACT	14580
genome mRNA	-----	
genome mRNA	CTGGGTTGCAGGTGTGGCCTGGCTAAAGTAGGCTTTACTGGGCTCCTCTCTGCCTGCATC	14640
genome mRNA	-----	
genome mRNA	ACCCCCCGGCTGGGCGGTTGTCTCTGAGGCCAACCTTACTCCCTGCTGGGCAGGCTGGAC	14700
genome mRNA	-----	
genome mRNA	AGCTGCCCTCTCCGTTTGCCCTCTACCACCCAAAAGGCAGGAGGCTCTGGAGACCAGGA	14760
genome mRNA	-----	
genome mRNA	CCCTGCCCCGCCACGGCCTGTGTCCCAGGCGTGAGGGGGTGCCCCACAGACCTCTGCTGAG	14820
genome mRNA	-----	
genome mRNA	CTGCTGCTGAATGACGCCCCCTTGGGGGTCTGCCGGAAGGTCAGAGCAGGGGTGCACTCC	14880
genome mRNA	-----	
genome mRNA	CATAAAGAAACGCCCCCAGGTCGGGACTCATTCCTGTGGGCGGCATCTTGTGGCCATAGC	14940
genome mRNA	-----	
genome mRNA	TGCTTCTCGCTGCACTAATCACAGTGCTCTGTGGGCAGCAGGCGCTGACCACCCAGGCC	15000
genome mRNA	-----	
genome mRNA	TGCCCCAGACCCTCTCCTCCCTTCCGGGGCGCTGCGCTGGGACCGATGGGGGGCGCCAGG	15060
genome	-----	
genome	CCTGTGGACACCGCCCTGCAGGGGCCTCTCCAGCTCACTGGGGGTGGGGTGGGGTGCACA	15120

Figure 1

mRNA	-----	
genome	CTTGGGGTCCTCAGGTCGTGCCGACCACGCGCATTCTCTGCGCTCTGCGCAGGAGCTCGC	15180
mRNA	-----	
genome	CCACCCTCTCCCCGTGCAGAGAGCCCCGCAGCTGGCTCCCCGCAGGGCTGTCCGGGTGAG	15240
mRNA	-----	
genome	TATGGCTCTGGCCACGGGCCAGTGTGGCGGGAGGGCAAACCCCAAGGCCACCTCGGCTCA	15300
mRNA	-----	
genome	GAGTCCACGGCCGGCTGTCGCCCCGCTCCAGGCGTCGGCGGGGGATCCTTTCCGCATGGG	15360
mRNA	-----	
genome	CCTGCGCCCGCGCTCGGCGCCCCCTCCACGGCCCCGCCCCGTCCATGGCCCCGTCTTCA	15420
mRNA	-----	
genome	TGGGCGAGCCCCTCCATGGCCCTGCCCCCTCCGCGCCCCACCCCTCCCTCGCCCCACCTCT	15480
mRNA	-----	
genome	CACCTTCCTGCCCCGCCCCCAGCCTCCCCACCCCTCACCGGCCAGTCCCCTCCCCTATCC	15540
mRNA	-----	
genome	CGCTCCGCCCCCTCAGCCGCCCCGCCCCCTCAGCCGGCCTGCCTAATGTCCCCGTCCCCAGC	15600
mRNA	-----	
genome	ATCGCCCCGCCCCGCCCCCGTCTCGCCCCGCCCCCTCAGGCGGCCTCCCTGCTGTGCCCCG	15660
mRNA	-----	
genome	CCCCGGCCTCGCCACGCCCCCTACCTCACCACGCCCCCGCATCGCCACGCCCCCGCATC	15720
mRNA	-----	
genome	GCCACGCCTCCCTTACCATGCAGTCCCGCCCCGTCCCTTCCTCGTCCCGCCTCGCCGCGA	15780
mRNA	-----	
genome	CACTTCACACACAGCTTCGCCTCACCCCATTAACAGTCTCACCACGCCCCGTCCCCTCTCC	15840
mRNA	-----	
genome	GTTGAGCCCCGCGCCTTCGCCCCGGGTGGGGCGCTGCGCTGTCAGCGGCCTTGCTGTGTGA	15900
mRNA	-----	
genome	GGCAGAACCTGCGGGGGCAGGGGCGGGCTGGTTCCCTGGCCAGCCATTGGCAGAGTCCGC	15960
mRNA	-----	
genome	AGGCTAGGGCTGTCAATCATGCTGGCCGGCGTGGCCCCGCCTCCGCCGGCGCGGGCCCCGC	16020
mRNA	-----	
genome	CTCCGCCGGCGCAGCGTCTGGGACGCAAGGCGCCGTGGGGGCTGCCGGGACGGGTCCAAG	16080
mRNA	-----	
genome	ATGGACGGCCGCTCAGGTTCTGCTTTTACCTGCGGCCAGAGCCCCATTCATTGCCCCGG	16140
mRNA	-----	
genome	TGCTGAGCGGCGCCGCGAGTCGGCCCCGAGGCCTCCGGGGACTGCCGTGCCGGGCGGGAGA	16200
mRNA	-----	
genome	CCGCCATGGCGACCCTGGAAAAGCTGATGAAGGCCTTCGAGTCCCTCAAGTCCTTCCAGC	16260
mRNA	-----	
genome	AGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGCAGC	16320
mRNA	-----	
genome	CGCCACCGCCGCGCCGCGCCGCGCCGCTCCTCAGCTTCCTCAGCCGCGCCGCGCAGGCAC	16380

Figure 1

mRNA	-----	
genome mRNA	AGCCGCTGCTGCCTCAGCCGCAGCCGCCCCCGCCGCCGCCCCCGCCGCCACCCGGCCCGG	16440
genome mRNA	-----	
genome mRNA	CTGTGGCTGAGGAGCCGCTGCACCGACCGTGAGTTTGGGCCCCGCTGCAGCTCCCTGTCCC	16500
genome mRNA	-----	
genome mRNA	GGCGGGTCCCAGGCTACGGCGGGGATGGCGGTAACCCTGCAGCCTGCGGGCCGGCGACAC	16560
genome mRNA	-----	
genome mRNA	GAACCCCGGCCCCGCAGAGACAGAGTGACCCAGCAACCCAGAGCCCATGAGGGACACCC	16620
genome mRNA	-----	
genome mRNA	GCCCCCTCCTGGGGCGAGGCCTTCCCCCACTTCAGCCCCGCTCCCTCACTTGGGTCTTCC	16680
genome mRNA	-----	
genome mRNA	CTTGTCCTCTCGCGAGGGGAGGCAGAGCCTTGTTGGGGCCTGTCCTGAATTCACCGAGGG	16740
genome mRNA	-----	
genome mRNA	GAGTCACGGCCTCAGCCCTCTCGCCCTTCGCAGGATGCGAAGAGTTGGGGCGAGAACTTG	16800
genome mRNA	-----	
genome mRNA	TTTCTTTTATTTGCGAGAAACCAGGGCGGGGGTTCTTTTAACTGCGTTGTGAAGAGAAC	16860
genome mRNA	-----	
genome mRNA	TTGGAGGAGCCGAGATTTGCTCAGTGCCACTTCCCTCTTCTAGTCTGAGAGGGAAGAGGG	16920
genome mRNA	-----	
genome mRNA	CTGGGGGCGCGGGACACTTCGAGAGGAGGCGGGGTTTGGAGCTGGAGAGATGTGGGGGCA	16980
genome mRNA	-----	
genome mRNA	GTGGATGACATAATGCTTTTAGGACGCCTCGGCGGGAGTGGCGGGGCAGGGGGGGGGCGG	17040
genome mRNA	-----	
genome mRNA	GGAGTGAGGGCGCGTCCAATGGGAGATTTCTTTTCCTAGTGGCACTTAAAACAGCCTGAG	17100
genome mRNA	-----	
genome mRNA	ATTTGAGGCTCTTCCTACATTGTCAGGACATTTCAATTTAGTTTCATGATCACGGTGGTAGT	17160
genome mRNA	-----	
genome mRNA	AACACGATTTTAAGCACCACTAAGAGATCTGCTCATCTAAGCCTAAGTTGGTCTGCAGG	17220
genome mRNA	-----	
genome mRNA	CGTTTGAATGAGTTGTGGTTGCCAAGTAAAGTGGTGAACCTTACGTGGTGATTAATGAAAT	17280
genome mRNA	-----	
genome mRNA	TATCTTAAATATTAGGAAGAGTTGATTGAAGTTTTTTGCCTATGTGTGTTGGGAATAAAA	17340
genome mRNA	-----	
genome mRNA	CCAACACGTTGCTGATGGGGAGGTTAATTGCCGAGGGATGAATGAGGTGTACATTTTACC	17400
genome mRNA	-----	
genome mRNA	AGTATTCCAGTCAGGCTTGCCAGAATACGGGGGGTCCGCAGACTCCGTGGGCATCTCAGA	17460
genome mRNA	-----	
genome mRNA	TGTGCCAGTGAAAGGGTTTCTGTTTGCTTCATTGCTGACAGCTTGTTACTTTTTGGAAGC	17520
genome mRNA	-----	
genome mRNA	TAGGGGTTTCTGTTGCTTGTTCTTGGGGAGAATTTTTGAAACAGGAAAAGAGAGACCATT	17580
genome mRNA	-----	
genome mRNA	AAAACATCTAGCGGAACCCAGGACTTCCCTGGAAGTCTGTGTGTCGAGTGTACAGTAG	17640

Figure 1

mRNA	-----	
genome mRNA	GAGTTAGGAAGTACTCTGGTGCAGTTCAGGCCTTTCTCTTACCTCTCAGTATTCTATTTTC	17700
genome mRNA	-----	
genome mRNA	CGATCTGGATGTGTCCCAGATGGCATTGTTGGTAAGAATATCTCTGTTAAGACTGATTAATT	17760
genome mRNA	-----	
genome mRNA	TTTAGTAATATTTCTTGTCTTTGTTTCTGTTATGATCCTTGTCTCGTCTTCAAAGTTTA	17820
genome mRNA	-----	
genome mRNA	ATTAGAAAATGATTCGGAGAGCAGTGTTAGCTTATTTGTTGGAATAAAATTTAGGAATAA	17880
genome mRNA	-----	
genome mRNA	ATTATTCTAAAGGATGGAAAACTTTTTGGATATTTGGAGAAATTTTAAAACAATTTGGC	17940
genome mRNA	-----	
genome mRNA	TTATCTCTTCAGTAAGTAATTTCTCATCCAGAAATTTACTGTAGTGCTTTTCTAGGAGGT	18000
genome mRNA	-----	
genome mRNA	AGGTGTCATAAAAGTTCACACATTGCATGTATCTTGTGTAAACACTAAACAGGGCTCCTG	18060
genome mRNA	-----	
genome mRNA	ATGGGAAGGAAGACCTTTCTGCTGGGCTGCTTCAGACACTTGATCATTCTAAAAATATGC	18120
genome mRNA	-----	
genome mRNA	CTTCTCTTCTTATGCTGATTTGACAGAACCTGCATTTGCTTATCTTCAAATATGGGTA	18180
genome mRNA	-----	
genome mRNA	TCAAGAAATTTCTTTGCTGCCTTGACAAAGGAGATAGATTTTGTTCATTACTTTAAGG	18240
genome mRNA	-----	
genome mRNA	TAATATATGATTACCTTATTTAAAAAATTTAATCAGGACTGGCAAGGTGGCTTACACCTT	18300
genome mRNA	-----	
genome mRNA	TAATCCGAGCACTTTGGGAGGCCTAGGTGGACGAATCACCTGAGGTCAGGAGTTTGAGAC	18360
genome mRNA	-----	
genome mRNA	CAGCCTGGCTAACATGGTGAAACCCTGTCTCTACTAAAAATACAAAAATTAGCTGGTCAT	18420
genome mRNA	-----	
genome mRNA	GGTGGCACGTGCCTGTAATCCAAGCTACCTGGGAGGCTGAGGCAGGAAAATCGCTTGAAC	18480
genome mRNA	-----	
genome mRNA	CCGGGAGGCAGAGTCTGCAGTGAGTTGAGATCACGCCACTGCACTCCAGCCTGGGTGACA	18540
genome mRNA	-----	
genome mRNA	GAGCGAGACTCTATCTCAAAAAAATTTTTTTTAATGTATTATTTTGCATAAGTAATAC	18600
genome mRNA	-----	
genome mRNA	ATTGACATGATACAAATTCTGTAATTACAAAAGGGCAATAATTAAAATATCTTCCTTCCA	18660
genome mRNA	-----	
genome mRNA	CCCCTTTCCTCTGAGTACCTAACTTTGTCCCCAAGAACAAGCACTATTTTCAGTTCCTCAT	18720
genome mRNA	-----	
genome mRNA	GTATCCTGCCAGATATAACCTGTTTCATATTGTAAGATAGATTTAAAATGCTCTAAAAACA	18780
genome mRNA	-----	
genome mRNA	AAAGTAGTTTAGAATAATATATATCTATATATTTTTTGAGATGTAGTCTCACATTGTCAC	18840
genome mRNA	-----	
genome	CCAGGCTGGAGTGCAGTGATACAATCTCGGCTCACTGCAGTCTCTGCCTCCCAGGTTCAA	18900

mRNA	-----	
genome	ATGCTTCTCCTGCCTCAGCCTTCTGAGTAGCTGGGATTACAGGCGCCCACCACCATGTCC	18960
mRNA	-----	
genome	AGCTAATTTTGTATTTTGTAGTAGAGATGGGGTTTCACCATGTTGGCCAGGCTGGTCTTG	19020
mRNA	-----	
genome	AACTCCTGACCTTGTGATCTGTCCACCTCGGCCTCCCAAAGTGCTGGGATTACAGGTGTG	19080
mRNA	-----	
genome	AGCCACCATGCCTGGCTAGAAATAATAACTTTTAAAGGTTCTTAGCATGCTCTGAAATCAA	19140
mRNA	-----	
genome	CTGCATTAGGTTTATTTATAGTTTTATAGTTATTTTAAATAAAATGCATATTTGTCATAT	19200
mRNA	-----	
genome	TTCTCTGTATTTTGCTGTTGAGAAAGGAGGTATTCACCTAATTTTGAGTAACAAACACTGC	19260
mRNA	-----	
genome	TCACAAAGTTTGGATTTTGGCAGTTCTGTTTACGTGCTTCAGCCAAAAAATCCTCTTCTC	19320
mRNA	-----	
genome	AAAGTAAGATTGATGAAAGCAATTTAGAAAGTATCTGTTCTGTTTTTATGGCTCTTGCTC	19380
mRNA	-----	
genome	TTTGGTGTGGAAGTGTGGTGTACGCCATGCATGGGCCTCAGTTTATGAGTGTTTGTGCT	19440
mRNA	-----	
genome	CTGCTCAGCATAACAGGATGCAGGAGTTCCTTATGGGGCTGGCTGCAGGCTCAGCAAATCT	19500
mRNA	-----	
genome	AGCATGCTTGGGAGGGTCCTCACAGTAATTAGGAGGCAATTAATACTTGCTTCTGGCAGT	19560
mRNA	-----	
genome	TTCTTATTCTCCTTCAGATTCCTATCTGGTGTTCCTGACTTTATTCATTCATCAGTAA	19620
mRNA	-----	
genome	ATATTTACTAAACATGTACTATGTGCCTGGCACTGTTATAGGTGCAGGGCTCAGCAGTGA	19680
mRNA	-----	
genome	GCAGACAAAGCTCTGCCCTCGTGAAGCTTTCATTCTAATGAAGGACATAGACAGTAAGCA	19740
mRNA	-----	
genome	AGATAGATAAGTAAAATATACAGTACGTTAATACGTGGAGGAACTTCAAAGCAGGGAAGG	19800
mRNA	-----	
genome	GGATAGGGAAATGTCAGGGTTAATC G AGTGTTAACTTATTTTATTTTAAAAAAATTGT	19860
mRNA	-----	
genome	TAAGGGCTTTCCAGCAAAACCCAGAAAGCCTGCTAGACAAATTCCAAAAGAGCTGTAGCA	19920
mRNA	-----	
genome	CTAAGTGTTGACATTTTTATTTTATTTTGTTTTGTTTTGTTTTTTTTGGAGACAGTTCTTG	19980
mRNA	-----	
genome	CTCTATCAGCCAGGCTGGAGTGCCTAGTGTGATCTTGGCTCACTGCAACCTCTGCCTCT	20040
mRNA	-----	
genome	TGGGTTCAAGTGATTCTCATGCCTCAGCCTCCTGTTTAGCTGGGATTATAGACATGCACT	20100
mRNA	-----	
genome	GCCATGCCTGGGTAAATTTTTTTTTTTTTCCCCCGAGACGGAGTCTTGCTCTGTGCGCCAGG	20160

Figure 1

mRNA	-----	
genome	CTGGAGTGCAGTGGCGCGATCTCAGCTCACTGCAAGCTCCGCTTCCCGAGTTCACGCCAT	20220
mRNA	-----	
genome	TCTCCTGCCTCAGTCTCCCAAGTAGCTGGGACTACAGGCGCCTGCCACCACGTCCAGCTA	20280
mRNA	-----	
genome	ATTTTTTTGTATTTTAAATAGAGACGGGGTTTCACCGTGTTAGCCAGGATGATCTTGATC	20340
mRNA	-----	
genome	TCCTGACCTCGTCATCCGCCGACCTTGTGATCCGCCACCTCGGCCTCCCAAAGTGCTGG	20400
mRNA	-----	
genome	GATTACAGGCATGAGCCACTGTGCCCCGCCACGCCTGGGTAATTTTTGTATTTTAGTAG	20460
mRNA	-----	
genome	AGATGGGGTTTTGCCATGATGAGCAGGCTGGTCTCGAACTCCCGGCCTCATGTGATCTGC	20520
mRNA	-----	
genome	CTGCCTTGGCCTCCCAAAGTGCTAGGATTACAGGCATGAGCCACCATACTGGCCAGTGT	20580
mRNA	-----	
genome	TGATATTTTAAATACGGTGTTCAAGGAAGGTCCACTGAGAAGACAGCTTTTTTTTTTTTT	20640
mRNA	-----	
genome	TTTTTTGGGGTTGGGGGGCAAGGTCTTGCTCTTTAACCCAGGCTGGAATGCAGTATCACT	20700
mRNA	-----	
genome	ATCGTAGCTCACTTCAGCCTTGAACCTCCTGGGCTCAAGTGATCCTCCCACCTCAACCTCA	20760
mRNA	-----	
genome	CAATGTGTTGGGACTATAGGTGTGAGCCATCACACCTGGCCAGATGATGGCTTTTGAGTA	20820
mRNA	-----	
genome	AAGACCTCAAGCGAGTTAAGAGTCTAGTGTAAGGGTGTATGAAGTAGTGGTATTCCAGAT	20880
mRNA	-----	
genome	GGGGGGAACAGGTCCAAAATCTTCCTGTTTCAGGAATAGCAAGGATGTCATTTTAGTTGG	20940
mRNA	-----	
genome	GTGAATTGAGTGAGGGGGACATTTGTAGTAAGAAGTAAGGTCCAAGAGGTCAAGGGAGTG	21000
mRNA	-----	
genome	CCATATCAGACCAATACTACTTGCCTTGTAGATGGAATAAAGATATTGGCATTATGTGA	21060
mRNA	-----	
genome	GTGAGATGGGATGTCACCTGGAGGATTAGAGCAGAGGAGTAGCATGATCTGAATTTCAATC	21120
mRNA	-----	
genome	TTAAGTGAACCTCTGGCTGACAACAGAGTGAAGGGGAACACCGGCAAAGCAGAAACCAGT	21180
mRNA	-----	
genome	TAGGAAGCCACTGCAGTGCTCAGATAAGCATGGTGGGTCTGTCAGGGTACCGGCTGTCG	21240
mRNA	-----	
genome	GCTGTGGGCAGTGTGAGGAATGACTGACTGGATTTTGAATGCGGAACCAACTGCACTTGT	21300
mRNA	-----	
genome	TGAACTCTGCTAAGTATAACAATTTAGCAGTAGCTTGCGTTATCAGGTTTGTATTCAGCT	21360
mRNA	-----	
genome	GCAAGTAACAGAAAATCCTGCTGCAATAGCTTAAACTGGTAACAAGCAAGAGCTTATCAG	21420

Figure 1

mRNA	-----	
genome mRNA	AAGACAAAAATAAGTCTGGGGAAATTCAACAATAAGTTAAGGAACCCAGGCTCTTTCTTT	21480

genome mRNA	TTTTTTTTTTTGAACGGAGTTTCGCTCTTGTCACCCGGGCTGGAGTGCAATGATGTGAT	21540

genome mRNA	CTCAGCTCACTAAAACCTCTACCTCCTGGGTTCAAGTGATTCTTCTGCCTCAGCCTCCCA	21600

genome mRNA	AGTAACTGGGATTACAGGCGTATACCACCATGCCAGCTAATTTTTGTGTTTTTAGTAGA	21660

genome mRNA	GATGGGGTTTCACCATGTTGGCCAGGCTGGTCTCGAACTTCTGACCTCAGGTGATCCACT	21720

genome mRNA	CGCCTCAGCCTGCCAAAGTGCTGGGATTACAGGTTTGGGCCACTGCACCCGGTCAGAACC	21780

genome mRNA	CAGGCTCTTCTTATACTTACCTTGCAAACCTTGTTCTCATTTTTTCCCTTTGTATTTT	21840

genome mRNA	TATTGTTGAATTGTAATAGTTCTTTATATATTCTGGATACTGGATTCTTATCAGATAGAT	21900

genome mRNA	GATTTGTAAAACTCTCCCTTCCTTTGGATTGTCTTTTTACTTTCTTGATAGTGTCTTTT	21960

genome mRNA	GAAGTGTAAGTTTAAATTTTATGATGAAGTCGAGTTTATCTATTTTGTCTTTGGTTGCT	22020

genome mRNA	GTGCTTCAAGTGTCATATCTAAGAAATCATTGTCTAATCCAAAGTCAAAAAGGTTTACTC	22080

genome mRNA	CTATGTTTTCTTCTAAGAATTTTAGAGTTTACATTTAAGTCTGATCCATTTTGAGTTAA	22140

genome mRNA	TTTTTATATATGGTTCAGGTAGAAGTCCAACCTTATTCTTTTCCATGTGGTTATTCAGTT	22200

genome mRNA	GTCCCAGCACTGTTTGTTGAAGAGACTATTCTTTCCCATGGAATTATCTTAGTACCCTT	22260

genome mRNA	GTTGAAAATTAATCGTCCTTAATTGTATAAATTTATTTCTAGACTGTCAGTTCTACCTGT	22320

genome mRNA	TGGTCTTTATGTCGATCCTGTGCCAGTACCATACAGTCTTGATTACTGAAGTTTGTGTCA	22380

genome mRNA	CAGTTTAAATTCATGAAATGTGAGTTCTCCAACCTTTGTTCTTTTCAAGATTGATTTGGC	22440

genome mRNA	CATGCTGGGTCCCTTGCAATTTCCGTACGAATTGTAGGATCAGCTTGTGAGTTTCAACAAA	22500

genome mRNA	GAAGCCAAGTAGGATTCTGAGAGGGATTGTGTTGAATCTGTAGATCAACTTGGGGAGTAT	22560

genome mRNA	TCGCATCTTAACAATATTGTCTTCCACCTATGAACATGGGCAAACCTTTGTGTAAATGGTC	22620

genome	AGATTGTAAGTATTTCTGGGCTGTGTGGGCACAGTGTCTCTGTACAGCTACGCGGCTCTG	22680

Figure 1

mRNA	-----	
genome	CCATTGTAGCATGAAAGTAGCCATAAGCAATATGTATGAGTGTCTGTGTTCCAATAGAAT	22740
mRNA	-----	
genome	TTTATTAATGACAAGGAAGTTTGAATTCATATAATTTTCACCTGTCATGAGATAGTATT	22800
mRNA	-----	
genome	TGATTATTTTGGTCAACCATTTAAAAATGTAAAAACATTTCTTAGCTTGTGAACTAGCCA	22860
mRNA	-----	
genome	AAAATATGCAGGTTATAGTTTTCCCACTCCTAGGTTAAAATATGATAGGACCACATTTGG	22920
mRNA	-----	
genome	AAAGCATTTCTTTTTTTTTTTTTTTTTTTTTTTTTTTTGAGACGGAGTTTCACTCTTGTTGCC	22980
mRNA	-----	
genome	CAGGCTGGAGTGCAGTGGCGCGATCTCGGCTCACTGCAACCTCTGCCTCCCAGGTTCAAG	23040
mRNA	-----	
genome	ACATTCTCCTGCACGGCCTCCCTAGTAGCTGGGATTACAGGCATGCGCCACCACACCCAG	23100
mRNA	-----	
genome	CTAATTTTGTATTTTGTAGTAGAGACGGGGTTTCTCCATGTTGGTCAGGCTGGTCTTGAAC	23160
mRNA	-----	
genome	TCCTGACCTCAGGTGATCCACCCGCCTCAGCCTCCCAAAGTGCTGGGATTACAGGGTGTG	23220
mRNA	-----	
genome	AGCCACCACACCCTGCTGGAAAGCATTTCTTTTTTGGCTGTTTTTGTTTTTTTTTTTAAAC	23280
mRNA	-----	
genome	TAGTTTTGAAAATTATAAAAGTTACACATATACATTATAAAAATATCTTCAAGCAGCACA	23340
mRNA	-----	
genome	GATGAAAAACAAAGCCCTTCTTGCAAGTCTGTCATCTTTGTCTAACTTCCTAAGAACAAA	23400
mRNA	-----	
genome	AGTGTTTCTTGTGTCTTCTTCCCAGATTTTAATATGCATATACAAGCATTTAAATGTGTC	23460
mRNA	-----	
genome	ATTTTTTGTGTTGCTTGACTGAGATCACATTACATATGTATTTTTTTACTTAACAATGTGT	23520
mRNA	-----	
genome	CATAGATATTGTTCCATAGCAGTACCTGTAATTCTTATTAATTGCTATGTAATATTTTAG	23580
mRNA	-----	
genome	AATTTCTTTTTTAAAAGAGGACTTTTGGAGATGTAAAGGCAAAGGTCTCACATTTTGTGG	23640
mRNA	-----	
genome	CTGTAGAATGTGCTGGTGACATATTCTCTCTACCTTGAGAAGTCCCCATCCCCATCACCT	23700
mRNA	-----	
genome	CCATTTCTGTAAATAAGTCAACCACTTGATAAACTACCTTTGAATGGATCCCACTCAA	23760
mRNA	-----	
genome	AACATTTAGTCTTATTCAGACAACAAGGAGGAAAAATAAAATACCTTATAAAGCACTGTT	23820
mRNA	-----	
genome	TAATATTGTATTAAATTGGATCAATTTGGGGGCTAGAATGTATGTTAGAGACATGATATG	23880
mRNA	-----	
genome	TCCATAGGTCCTTGCTATCACAGTGAGGTCTCAGGGACAGTCGTTTGGTATCATTTGGGA	23940

Figure 1

mRNA	-----	
genome mRNA	TCTCATAAGCAGACTCTCTCTGCTTGACCTGACAAATCAGAGTCTGTGTTTTAACAGGTT	24000
genome mRNA	-----	
genome mRNA	CAGTGAGTGACTTACATGCACATTGGAGTTTGGGAAGCTCCACTGTAGGTGCTTAGACCT	24060
genome mRNA	-----	
genome mRNA	TACCTTTGTTGTTGCTAATAACAATGCAAGCATTGTTGGGAGGAAGACCTGTGTTGCTCATA	24120
genome mRNA	-----	
genome mRNA	TGTGTCCAGGTGTAGCTGAGGTGGCCTTGCTTATCTGCTGTAGGGCCGTTGAGCATTTCT	24180
genome mRNA	-----	
genome mRNA	GTAGCTGTGATGAGTGAGCTGAGGTGAGCCTGCGGAGAGCTCCCAGCCATTGGTAGTGGG	24240
genome mRNA	-----	
genome mRNA	ACTCGCTTAGATGAACTGGAAGGACCCTTTCATCTGAGCAGCCACTATGGAGAAAAACAA	24300
genome mRNA	-----	
genome mRNA	CCGAATGAGGGGAGAGACAATGTGCAATTTTATTAGGGCACAAAGGAGAGCTGTGGTTA	24360
genome mRNA	-----	
genome mRNA	GAAGGTGACATTTGAGTGGAAGGGGGCAAGCCATGTGTATAGCGGGAGAAGAGAGGTCC	24420
genome mRNA	-----	
genome mRNA	AGGCAGAGTTAACAGAAGGCAGAAATGCTTTCATGTTTGAGAACCAGTAAGGAGGCCAG	24480
genome mRNA	-----	
genome mRNA	TGGCTGAAGTAAGGTGAAGGGCAGAAATAAGGATGAGGCTGCGAGAGATGAGAGGTTAGA	24540
genome mRNA	-----	
genome mRNA	GACGAGCGTCTTGTGCACCAAGATAAGCTTGTGTGGTCAAAACAAGTAGTTTAATTTATG	24600
genome mRNA	-----	
genome mRNA	TTTTTAAAAGATCATTTTGGCTGGGCACAATGGTTCATGCCTGTAATACCAGTAGTTTGA	24660
genome mRNA	-----	
genome mRNA	GACGGTGTGGTGGGAGGATTGCCTGAGGCCAGACGACCAGCATAGCCAACATAGCAGCAC	24720
genome mRNA	-----	
genome mRNA	CTATAAGGTCTCTACAAAAAAGCTTTAAAAAATTAGCTGGGCATAGTGGTGTGTGCCTGTA	24780
genome mRNA	-----	
genome mRNA	GTCCCAGCTACTCAGGAGGCTGAGGAGGCTGGAGGATTGCTTGAGTCCAGGAGTTTGAGG	24840
genome mRNA	-----	
genome mRNA	CTGCAGTGAGCTATGATTATGCCACTACACTACAACCTGGGCAAGAGAGTGAGACCCTGT	24900
genome mRNA	-----	
genome mRNA	CTCTAAATATACACACACACACACACACACACACACACACACACACACACACACACAC	24960
genome mRNA	-----	
genome mRNA	ACACACATATATATGTATATATATGCATTTAGATGAAAAGATCACTTTGACAATACCACA	25020
genome mRNA	-----	
genome mRNA	TGCTGGTGAGGATTTAGAAAACTAGGTCACCTTATGCTGGTGGGAATATAATATAGTAC	25080
genome mRNA	-----	
genome mRNA	GGCCACTCTGGAAAACAGTTTGGCAGTTTGTTCATAAACTGAACATACCGTTAGTATACA	25140
genome mRNA	-----	
genome	GCCCAGCAGCAACTACAATCCTGGGCATTAATCCTAGAGAAATGAAACCTTAATGTTTAC	25200

Figure 1

mRNA	-----	
genome	ATAAAAACCTATACTCAAGTATGCATAGCAGCTTTACCCATAATATCTAAGAACTGGAAT	25260
mRNA	-----	
genome	CAGCTCAGATGTCCTTCAACAGGTGAATGGTTAACTACTCAGTAATAAAAAGGAATGAG	25320
mRNA	-----	
genome	CTACTGATAGCATGCAACAGTTTAGGTGAAGTTATGCTAATGAAAAAGCCAATCCCAAA	25380
mRNA	-----	
genome	AGGTTATACATACTGTATGATTCTATGTTTTTTTGGCAATGGCACAGTTTTAGGGATGGAG	25440
mRNA	-----	
genome	AATAGATTAGTGGTTGCCTGGGGTTAGAGATGGGGTAGTAGAGTAGGTTAGTGGTGGCAG	25500
mRNA	-----	
genome	AGGAGAGAAAAGAGAGGGAGGTGAATGTGGTTATAAAAGGACAACACAGGGGAATACTTG	25560
mRNA	-----	
genome	TAATGGAAATGCTTTGTCTTTTTTTTTTTTTTTTTTTTTTTGGCGACAGAGTCTTGCTCT	25620
mRNA	-----	
genome	GTTGCCCAGGCTGGAGTGCAGTGGCATGATCTTTTCTCACTGCAACCTCTGCCTCCTGGG	25680
mRNA	-----	
genome	TTCAAGTGATACTTGTGTCTCAGTCTCCCATGTTTCAGAGTGAAACAAACCAGAGGTAATG	25740
mRNA	-----	
genome	TTCATCCAAATAATCCAACACACATGACATTAAACATCAAGATCAGGTCGGACGTGGTG	25800
mRNA	-----	
genome	GCTCATGCCTGTAATCCCAGCACTTTTGGGAGGCCAAGGTGGGCAGATCACTTGAGGTCA	25860
mRNA	-----	
genome	GGAGTTCGAGACCAGCCGGGCCAACATGATGAAACCCCATCTTGACTAAAAATACAAAAA	25920
mRNA	-----	
genome	TTAGCCGGGCATGGTGGTGTGCACCTGTAGTCCCAGCTACTTGGGAGGCTGAGGCAAGAG	25980
mRNA	-----	
genome	AACTGCTTGAACCCGAGGGGCAGAGGTTGCAGTGAGCTGAGAGTGCGCCATTGCACTTCA	26040
mRNA	-----	
genome	GCCTGTGTGACAGAGTAAGACTCCATCTCCAAAAAAAAAAAAACCAAGATCAATTAAAATA	26100
mRNA	-----	
genome	CAGCATTACTGGGCCGGGTGTGGTGGCTCACACCTGTAATCCCAGCACTTTGGGAGGCCG	26160
mRNA	-----	
genome	AGATGGGCAGATCACGAGGTCAGGAGATCCAGACCATCCCGGCTAACACGGTGAAACCCC	26220
mRNA	-----	
genome	GTCTCTACTAAAAAATACAAAAAATTAGCCGGGTATAGTGGTGGGTGCCTGTAGTCCCAG	26280
mRNA	-----	
genome	CTACTTGGGAGGCTGAAGCAGGAGAATGGTGTGAACCCGGGAGGCAGAGCTGGCAGTGAG	26340
mRNA	-----	
genome	CTGAGATCGCGCCACTGCACTCCAGCCTGGGCGACAGAGCAAGACTCCGTCTCGGGGGAA	26400
mRNA	-----	
genome	AAAAAAAAATAAATAAATAGAATGCTGTAGTGTCTTGAGTTTACATGCCCTCCTTACG	26460

Figure 1

mRNA	-----	
genome	CTTGTGTGCCCCGTGCAGATTGCTTGATTACACAATTAGAGGAGGCTGGCGGAGGATTGTT	26520
mRNA	-----	
genome	TTAATTTTTTTTTTTTTTTGAGACAGTCTGGCTCTGTTCCCCAGGCTAGAGTGCAATGGCGC	26580
mRNA	-----	
genome	AATCTTGGTGCACTGCAACCTCTGCCTCCTGGGTTC AAGCAGTTCTTCTGCCGCAGCCTC	26640
mRNA	-----	
genome	CCGAGTAGCTGGGATTATAGGCGCCCGCCACCACGCCCAACTATTTTTTGTATTTT TAGT	26700
mRNA	-----	
genome	AGAGCAGCGTTTCACCATGCTGGCCAGGCTGGTCTCGAACTCCTGACCTCAGATGATCTG	26760
mRNA	-----	
genome	CTGCCCCAGCCTCCCAAAGTGCTGGGATTACAGGCGTGAGCCACACCTGGCCGTTTGTTT	26820
mRNA	-----	
genome	TAATTTTGAAGGTGAAGTGAAAGTGACTACATTTACCAAAAGTGATTGAAAAGCCAGGAC	26880
mRNA	-----	
genome	TGTTCTTACCCTGTTTTTCCAGTTCTTGCTCAGAGCAAGGTGGTTTCTTTTTCACTTAAT	26940
mRNA	-----	
genome	CACCATACTTACTTTTTCATGTAGAACAAGTCAGTTTGAGTTATCAGTTCATCATCTTAAC	27000
mRNA	-----	
genome	TAAATTCCATGGGGGAAGGAATTAGTTTTAGTTTCTTAAACTTCCAGGTTTGCTTATTGG	27060
mRNA	-----	
genome	ACAAAATGAGATAGCAAGGCAGTGTTTTTAAGTTAGATTTTTTATTTCTTTGGTAATACA	27120
mRNA	-----	
genome	ATTTTCTCAGAAACTTAGTAGTCTTTTAGTTTAGTTGTTTTTAGTTGGTCCTATGTTTTG	27180
mRNA	-----	
genome	GATCACCCCTCTCTACTTTATTTTGATAGTGCCAACTGTGAAGACATCTGAAGCCATAGG	27240
mRNA	-----	
genome	TTTGGATGGGAAGGAGGCATCTTTAGCCTGATCATCTTCGCCAGGCTGTTTATCTCCTTT	27300
mRNA	-----	
genome	TGCTTGGCTGAGAAGTCTTAATAGGAGGCTTATTC CAGCTATTGGGGACATAGAAGCA	27360
mRNA	-----	
genome	GTTAGCCATTGCTTATATTTTACTGAGGTCTGTGTGGTATGTTGATTGTAGTCAGTTAAC	27420
mRNA	-----	
genome	GATTTTGAGAACTGAAGGCAGCCTGGTATATATAGAGTAGGTATTAGACTGTGTTTCTTC	27480
mRNA	-----	
genome	TAATTGAATTTCCCATCTCTTGTAATCTATGCCATCATCTTCTGTACTGCTGAGAAAGAA	27540
mRNA	-----	
genome	AGAAAGTTTCTAATCAAAC TATACCACTGGTTGTAAGATGCAGTTTGGCTTTAGTGATGT	27600
mRNA	-----	
genome	TAACACATGATTCAAACGTGAAATTGATTGAGTATTGGTGAAATACAGAGGAGATTTAAA	27660
mRNA	-----	
genome	GCCAGAAGACCTGGGTTTAAATGCTGGCTGTATGACTTCATATCTGTGTGATCTTGGGCA	27720

Figure 1

mRNA	-----	
genome mRNA	TGTCATGGTTGGCACTTCAATTTCTTCTCTCTATAATGGGGGAAGTGAGGCCAGTCATGG	27780
genome mRNA	-----	
genome mRNA	TGGCTCATACCTATAATCCCAGTGCTTTGGGAGGCCAAGATGGGAAGATCGCTTGAGGCC	27840
genome mRNA	-----	
genome mRNA	AGGAGTTTGAGCAATTGGGCAACATCGTGAGGCCCCGTCTCTACAAAATATTTTGAAAAA	27900
genome mRNA	-----	
genome mRNA	ATTAGCCAGGCCCAGTGGTGCGTGCCTGTGGTCCGCGCCACTCAGGAGGCTGAGACGGGA	27960
genome mRNA	-----	
genome mRNA	GGATCCTTTCAGCCTAGGAGTTTAAGGCTAAAGTGAGCCATGATTGTGCTATCGTACTCC	28020
genome mRNA	-----	
genome mRNA	AGCCTGGGCAGCAGAGCAAGATCCTGACTCTAAAAAAAAGTAAAATAAAGTAAAATGGGG	28080
genome mRNA	-----	
genome mRNA	GAAATGAACTGCTTTAGTAACATCATCTGTTTTTTCTGTGAGCAGCGTAGCTTGACAGCC	28140
genome mRNA	-----	
genome mRNA	ATTGGTGAACTCGTGCCCTGTGCTTCCCTGTCCAGATCCCCATTCTGCCCACAACATGGA	28200
genome mRNA	-----	
genome mRNA	GTATAACGGTTTATTTCATAGTAGTCGAGAAACACTCACTGAATGAATGAATGAGGTGTAG	28260
genome mRNA	-----	
genome mRNA	AACTAAGTGGAGTGGGTAATTCAACACATATTAATTTCTTCTTTTTTTTATTTTGTAGAA	28320
genome mRNA	-----	
genome mRNA	AGAAAGAACTTTCAGCTACCAAGAAAGACCGTGTGAATCATTGTCTGACAATATGTGAAA	28380
genome mRNA	-----	
genome mRNA	ACATAGTGGCACAGTCTGTCAGGTAATTGCACTTTGAACTGTCTAGAGAAAATAAGAACT	28440
genome mRNA	-----	
genome mRNA	TTGTATATTTTCAGTCTTAATGGGCTAGAATATTCTTTGTGTCCCAGCTATTTTAAATGG	28500
genome mRNA	-----	
genome mRNA	ATTCAGAAATCCATTTAAGATGAAGAAGGACCCTTTTCCCATATTTCTGGCTATATACAA	28560
genome mRNA	-----	
genome mRNA	GGATATCCAGACACTGAAATGAATAATGTTCCCTTTTGTAACTCTTTTATGCAAAAATTA	28620
genome mRNA	-----	
genome mRNA	AAACCATTATGGTAATTGAACAACATGTTTATGTTTAGTTAACACCCTTAGCAACTATAG	28680
genome mRNA	-----	
genome mRNA	TTATTTTAAAACCATCTATGGTTTGATATTTTGCATTTGTTGCAATAGTAGGAACAGCA	28740
genome mRNA	-----	
genome mRNA	CAAGACAGTTCAGTTTGTCTCTCTTATTTGCTTTTTCTTGGCAGTTTGCTGTCCTATTGT	28800
genome mRNA	-----	
genome mRNA	ACCTCTGCTCCTAGCAGTGGCTGGAGCCCACTCCTCTGTGCTTCGGGATTAGTGGGGATC	28860
genome mRNA	-----	
genome mRNA	GTGGGGCATTGACTGTAGGTCAGCTTTCCTTGCTTGATCTTCTCACTGGGATGAAGTAG	28920
genome	-----	
genome	CAGCACCTTCTTTTGTAGCTGCTTTGCTTTTGACTATCTTCTGACCGTTGTTCCCTAGTA	28980

rs2285086

Figure 1

mRNA	-----	
genome	GCTGTAGATGGTAAATATATTTAGGCCTGTTTCCAATGGCTCAGTAGGAGACATATTCAC	29040
mRNA	-----	
genome	CTATGATATCTGAATTCTGTTACCCACATGGGCATGCGTGAAATAGTTGCCTTGCCTTAC	29100
mRNA	-----	
genome	TTTCCCTTGGAATAAATAATTCATGTTATTCTCCTGGTAGAAGCTAGAAAAAGCCTTTAT	29160
mRNA	-----	
genome	AGTCAGTCAGAAAAAATTTTTAGACAAATAATCTTGATTTTAGTACTGACAAAAACGTG	29220
mRNA	-----	
genome	TGGTGATTCTTTTTTTAATTTTTTTTTTGAGACGGAGTTTCACTCTTGTTGCCCAGGCTGG	29280
mRNA	-----	
genome	AGTGCAATGGCGTGATCTCGGCTCACTGCAACCTCTGCCTCCTGGGTTCAAGTGATTCTC	29340
mRNA	-----	
genome	CTGCCTCAGCCTCCCAAGTAGCTGGAGTTACAGGCATGTGCTACTGTGCCCAGCTAATTT	29400
mRNA	-----	
genome	TGTATTTTGTAGTAGAGATGTTGGTCAGGCTGATCTCGAACTCCCAACCTTAGGTGATCTG	29460
mRNA	-----	
genome	CCCGCCTCAGCCTCCCAAAGTGCTGGGATTACAGGCGTGAGCCAGGGCGCCCGGTGATTC	29520
mRNA	-----	
genome	ATTTGTTTTTTTCAAAAAATTTCTCTTGGCCATTGCTTTTCACTTTTGTTTTTTTTTTTT	29580
mRNA	-----	
genome	TTTTGAGACGGAGTCACGATCTGTCACCCAGGCTGGAGTGCAGTGGCATGATCTTGGCTT	29640
mRNA	-----	
genome	ACTGCAAGCTCTGCCTCCCAGGTTACGCCATTCTCCTGCTTCAGCCTGGCGAGTAGCTG	29700
mRNA	-----	
genome	GGACTACAGGTGCTCGCCACCACACCCGGCTAATTTTTTGTATTTTGTAGTAGAGATGGGG	29760
mRNA	-----	
genome	TTTCACCGTGGTCTTGATCTCCTGACCTCATGACCCGCTCAACTCAGCCTCCCAAAGTGC	29820
mRNA	-----	
genome	TGGGATTACAGGCGTGAGCCACCGCGCCCGGCCCTCTCTTGTCTTTTTTATTGTGGTAAAA	29880
mRNA	-----	
genome	TGCACATAAAATTGACTGTCTTAACCATTTTTAGGGGTACAGTTCAGTATATATATTCGT	29940
mRNA	-----	
genome	AATGTTGTACAGCCATCACTGCCATCTACTTCATAAGTTTTTCTTCTGTCAAACTGAAC	30000
mRNA	-----	
genome	ATCTGTCTTCATTAAACTCCCTATCATCCATTCTTTCCTGTAGTCCCTTTCTACTTTCTG	30060
mRNA	-----	
genome	TCTGTATGAGTGTAAGTCTGCTCTGGAGACCTCATGTAAGTGGATTCCCTACAGGATTTGTGT	30120
mRNA	-----	
genome	TTTTTTTTTGGTGATCTGCTTATTTTTAATGCCTCTGTGCATTTGTATTATATACTTTCA	30180
mRNA	-----	
genome	AAGTGATTTACAAAACCGTTTCATTTTAGGTTAACTCATTTCTGTTGTTTGTGAAATAC	30240

Figure 1

mRNA	-----	
genome mRNA	TGTGTATGATTCTGTTCTGTTTCTGTCTAATTTGTGGAAATGTTGTGGGAAGAAAATGAA	30300
genome mRNA	ATAACAAATGAGCATATGTCCTGAAAATAAAAATATAAAAATTCTAAGTTAGCATGCTAT	30360
genome mRNA	TGTAGAATACAACGCTATGATAAAAGTAGGAAAAAAAAAGGTTTGAATTCTATCTCTGCT	30420
genome mRNA	ACCTGTGTAAGCTGGGTGACTTTAGATAAGCTGTAACGTGTTTGAGCCTTACTGGCTCAT	30480
genome mRNA	TTTTGAAATGTAATCCCTAGTTACACAGTTCTTGTGGGATCAGATGGTACATGTGAAACA	30540
genome mRNA	CTGTGAAAAAGCAACTGCATAGATATGTTCAATTAGCCACCTGAGCGGGAAGCGTATCCCA	30600
genome mRNA	TTGCGATGCCCATCATCCAAAGCTATATGTTATCTTTACTTTTTTTTTTTTGTGAGACAGAG	30660
genome mRNA	TCTTGCTCTGTTGCCAGGCTAGAGTGCAGTGGTGCAATCTCAGCTCACTGCAAGCTCCA	30720
genome mRNA	CCTCCCGGGTTCACGCTATTCTCCTGCCCCAGCCTCCCAAGTAGCTGGGACTACAGGCAC	30780
genome mRNA	CCGCCACCATGCCTGGCTAAATTTTTGTATTTTGTAGTAGAGATGGGGTTTCACCGTGTTA	30840
genome mRNA	GCCAGGATGGTCTTGATCTCCTGACCTCGTGATCCGCCCCGCTCGGCCTCCCAAAGTGCT	30900
genome mRNA	GGGATTACAGGCGTGAGCCACTGCCCCCTGGCCATCTTTACTTTTTTTGTGAAATGACTTT	30960
genome mRNA	AAATACTTGGCAAACATTTGGTCATTGTTTCATCTGATCTCCACCATCCAGGTCTCAGAGA	31020
genome mRNA	ACATAATTTCTCTCTGAAAGCTTATTGACCCAGGAAATAAGATCTCTTTCAATCTGAGTG	31080
genome mRNA	CGTCAGGCTTTATTCTTGTCATTTTGTCTTTTGATAATTTTCAAATGGAATTCATGGAAT	31140
genome mRNA	GTTGGCTTATATTCATATATTAGTAAAGTATGTTGAGACATCTTAAGATTGATTTGTGGT	31200
genome mRNA	TCTATATGCCATATTAAATCAAATAATAGCTGTTAATGGTTTTTCACATTAGTCTGTCTC	31260
genome mRNA	TTGTTTTTATGGAGTAATGCTGAGAGTTCATTATGCTTGTTCTACAGAAGAGCATGTTAA	31320
genome mRNA	AAGGAGTTTTTGGAGTCAGAGAGGTTATTCTTGGTTTTCATAGGATACACTCTATACTTTT	31380
genome mRNA	TAGGGATTTTCAGAGTATATAGCTGAAGGTGATATTTTATGTAAATATGTTTTATGGAAAC	31440
genome	TTATTGCTCATCGCTGTTTCCTGTAACTCTCCTAAAATATAATTAACTTTTGGAACCTT	31500

Figure 1

mRNA	-----	
genome mRNA	TTTTATAGCTTTTGTGCTAGACTAATTTTGTCTCTAATGAGGTTATATAAATGGCAGCT	31560
genome mRNA	-----	
genome mRNA	TCTGACGTTTTCATGTAGGAAGTCATTTAAACTTCATGTATATTGTGAAAATGTAGTC	31620
genome mRNA	-----	
genome mRNA	TGCTTTAAGCTCTCTAAAGTGGTCTAAGTTACTGGTTCCTAAGTATGGATGAGCATCAAA	31680
genome mRNA	-----	
genome mRNA	ATCATCTGGAAAATTTGTTAAAAATACAGTAATGAAGGCACCTCACTGTCCTTTTCCCA	31740
genome mRNA	-----	
genome mRNA	AACATACTTCTGCATTCTGTTTGAGTAGGTAGGGACTACACATTTTTCACAAGTATCCTC	31800
genome mRNA	-----	
genome mRNA	TTGGGAATACCCAGGAATGCTTACTTGAGCAACCTCTTACTAATATGTACCTTGATAAGG	31860
genome mRNA	-----	
genome mRNA	TGGCTAGGTAAACATAAATATACAAAAATCCATAGATCTCCCATATATTAGCATAAATCA	31920
genome mRNA	-----	
genome mRNA	GCTAGAAAATATAACGTTTAAAGATCTAGTTCACAGTAGCACCAATATATCGAACTCTAA	31980
genome mRNA	-----	
genome mRNA	GGAATCGATAAATATGCAAAAACCTTTATAAAAACCTTCTGTTAATGTTTCTGAAAGATATA	32040
genome mRNA	-----	
genome mRNA	GGTGACCACTTTCTAGATAGGAAGATTTTATATTACTAAGTTGAATTTTCTCTAAATTAA	32100
genome mRNA	-----	
genome mRNA	CACAGAAATTTAAAATAATCTTGATCAAAATTCTAGTAGAGGTATTTTGAACCTGTTCA	32160
genome mRNA	-----	
genome mRNA	CTGCAAGAATAAATACATAATTGCAAAGAATATCTCAAAATCATCACCAGGCCTGGTGTG	32220
genome mRNA	-----	
genome mRNA	GTGGCCCATGCCTGTAATCCCAGCACTTTGGGAGGCTGAGGCAGGCAGATCACCTGAGGT	32280
genome mRNA	-----	
genome mRNA	CAAGAGTTTGAGACCAGCTGGACCAGTGCGGTGAAACACTGCCTCTACTAAAAATACAAA	32340
genome mRNA	-----	
genome mRNA	AATTAGCTGGGTGTGGTGGTGCATGCCTGTAGTCCCAGCTACTTGGGAGGCTGAGGCAGG	32400
genome mRNA	-----	
genome mRNA	AGAATTGCTTGAACCCAGGAGGTACAGGTGCGGTGAGCCTAGATCGCACCCTGCATTC	32460
genome mRNA	-----	
genome mRNA	CAGCCTGGGCGACAAGAGCAAAATTCTGTCTCAAGAAAAAGAGAAAAAGAAAAAGAAA	32520
genome mRNA	-----	
genome mRNA	TCAACACTAATATGGTGAGACTTAATGTATGTGACATTAAATAGTGATTGGATGTTAAA	32580
genome mRNA	-----	
genome mRNA	ACAGGTATAGAACAGAAAGAAGAGTGTATGTGTGTATCTGTATGAATTTATGATGGGTGT	32640
genome mRNA	-----	
genome mRNA	AACATATATGTATTAGGGAAATGAGGGAAATGATACATTTCTCTGACTTTGGGAGAACAT	32700
genome	-----	
genome	TATATCTCTACCTCATATTGCAAACAAACATAAAGTTCAGATTAATTACCTAAATGTGAA	32760

Figure 1

mRNA	-----	
genome mRNA	AAAATGAAATAATTTCTTTAAAAAATGTAATCTTAGTTTGAGGAAGGTAAACATTATAAA	32820
genome mRNA	GGAAAAAAGTGTGTTGAGTGGAATATAGTTCAATATGTCAAATCCACCTTCAACAAAAT	32880
genome mRNA	TGAAAGTAAATTGAACTTGGGGAAAGTATTGACAGCATATAGATCAAAGGTTACTAGCCT	32940
genome mRNA	GTGTAAAGAGCAGTTATAAATATCGTTAAGAAAAACACTGTCGACCTGTCGGCACCTTGT	33000
genome mRNA	TCTCCGACTCCCAGCCTCCAGAACTGTGACGAGTAAGTGCTTATTGTTTAAACCACCCAG	33060
genome mRNA	TCTGTATGTGGTATTTTGTATAGAACTCAAGCTGATTAGGACACTAGTAATCAGTAGA	33120
genome mRNA	CTGAAACTGAAACAAAAATAAGAACCTTTTTTACCTGTCAAATTGGCAAACATTAAGAAT	33180
genome mRNA	ATTCAGATTTTGTGTCAGAGGTGATACAACCTTCTAAGAAGGCAATTTGGGAAAATATAAA	33240
genome mRNA	GCTTTAGATTATTATATGTCTGACCTAGCAGTTTTACCTCTAGGGTGCTTACCCCTAGGA	33300
genome mRNA	AAGTGTGTAATGATATTGGTGCAGTGCCCTTCATCCCATTAGAAAATTAAAAATAACCTT	33360
genome mRNA	AATGGCCTACCACTAAAAGGGGATTGAAAATTTAAGATATATTTATTTATGTGTTTATTG	33420
genome mRNA	AGATGGAGTCTTGCACTGTCCGCCTGGGCCAGAGTGCAATGGTGCGATCTCGGCTCACTG	33480
genome mRNA	CAACCTCTGCTTCCCGGGTTCATGTGATTCTCCTGCCTCAGCCTCCTGAGTAGCTGGGAT	33540
genome mRNA	TACAGGCTCACACCACCGCACCCGGCTAATTTTTTGTATTTTATAGTAGAGATGGGGTTTC	33600
genome mRNA	ACTGTGTTGGCCAGACTGGTCTCGAACTCCTGACCTCATGATCCGCGCCCCCTCGGCCTCC	33660
genome mRNA	CAGTGTTGGGATTACAGGTGTGAGCCACTGCGCCTGGCCAGATACATTTATACAAGAGAA	33720
genome mRNA	TGTTAGTTAACATTCATAGATATTTATATTTTGTGTTACTTTTTATTAAAAAATTTTTTT	33780
genome mRNA	TAGAGACAGGATCTTACTCTGTCACCCAGGCAGGATGCAGTTGCACAATCATAGCCCACT	33840
genome mRNA	GCAGCCTGAACTCCTGGGCTTAAGTGATCCTTCTGCCTCAGCCTTTTGAGTACCTGGGGG	33900
genome mRNA	ACTTTAGGCAGTGCTACTATACCTGGCTAATTTTTTAAATGTTTTATAGATGAGATCTTGC	33960
genome	TGTATTGCCAGGCTGGTCTAGAATTCCTGGGCCCAAGTGATCCTCCACCTTGGCCTCC	34020

Figure 1

mRNA	-----	
genome mRNA	CAAAGCGCTGAGATTACAGGCATGAGCCACCACTTCTGACCAATAGATATTTATATTTGT	34080
genome mRNA	-----	
genome mRNA	GACTGGAAAATATATTAACAATGTGTTAAAAAATTCAGTTAAAAAATAATGAAAGATTTT	34140
genome mRNA	-----	
genome mRNA	TGCTTCTGGCTAAGATAGAATAACAAGGACAGCATTTATCTTCTTGCCTTGAAATAGTTG	34200
genome mRNA	-----	
genome mRNA	AAAACGGAAGAAATATATGTAACAGTGGTTTTCAAGTTATTGGGCATCAGGCAAAGAAGA	34260
genome mRNA	-----	
genome mRNA	ATAGTTATCCCAGGAAAATGAATGTGGAGAGCCCTACAATTCCTTACATTACTGCCTGG	34320
genome mRNA	-----	
genome mRNA	TCATGGCAAGAGGAAAACTGAGAGGAGACTGAGGCTGAGCCAGTGGTTTGCTGGGTTGA	34380
genome mRNA	-----	
genome mRNA	GGAGGCAGAGCTGGGAGTGCAGAGATGCAAGGTGGTGAGAGCCCATATGGAAGAATACCA	34440
genome mRNA	-----	
genome mRNA	GGGAAGAGAGCTGCAGAGGGAGCTCCGGAGACCTGCACCCTGCCCTCTCAGTACCCTGTC	34500
genome mRNA	-----	
genome mRNA	ATGTGTGTAGCTGAGTACTGACGAGCACTTGCTTGTGCGGAAATGACCCAGGGCTGGAGG	34560
genome mRNA	-----	
genome mRNA	TAGAGCCACCTGAAAGGATTAGAAGGAACAGTTGCTGAAAGTCACACAGGGCCAGGAAGA	34620
genome mRNA	-----	
genome mRNA	ATTTCTAATCACACCAGTTGGAGTGGAAAACCTCAGCTCTCATAGAGCAGGTAGGGTACT	34680
genome mRNA	-----	
genome mRNA	CAGAAGGGTTTGCCACCTAGCCCCAGACTAAGTTTCGTTACTCTGACCCTACCTAATAT	34740
genome mRNA	-----	
genome mRNA	TAAAAAGAGATTAATTAAATTGTTGCAACAAAAATAATATATTTTCAGTGTTTGTAACAC	34800
genome mRNA	-----	
genome mRNA	GTAGAAGTGAATTGTATGACAATAGCATAAAGGCTGGAAGAGCAGAAATTGACATGTATT	34860
genome mRNA	-----	
genome mRNA	TGCGCTGGGCAGAATAATGCTCCCCTCTTTCCCCAAAAGATATCAAGTCCTAATCCCTGG	34920
genome mRNA	-----	
genome mRNA	AGCCTGTAAATATTACTTTATATGGAAAATTGTTTTATGATGTGATTAAATTCAGGATCT	34980
genome mRNA	-----	
genome mRNA	TGAGATGAGGGGGCTATCTTGGATGATCTGGGTAGGCACTAAATGCAATCACATATATAT	35040
genome mRNA	-----	
genome mRNA	AAAAAGGAGGCAGAGGGAGATTTTACACACAGAGAGAAGGCCCTGTGAAGATGGAACAGA	35100
genome mRNA	-----	
genome mRNA	AAGATTTGAAGGTGCTGGCCTTGAAAATTGGAGTGATGAAGCTATAAGCCAAGGAATGCA	35160
genome mRNA	-----	
genome mRNA	GCAGCCACCAAAGCTGGAAGAGGCACGGAGCAGTTCTCATTTAGAGCCTACTCCAGAGGG	35220
genome mRNA	-----	
genome mRNA	AATGTGGTGCTGCCAATTCCTTTTTTTTTTTTTTTTTTTTAAAGATATCATTTACCCCTTTAA	35280

Figure 1

mRNA	-----	
genome mRNA	GTTGGTTTTTTTTTTTTTTTTTTTTTTTTTTTAGTATTTATTGATCATTCTTGGGTGTTTCTT	35340
genome mRNA	-----	
genome mRNA	GGAGAGGGGGATTTGGCAGGGTCATAGGACAATAGTGGAGGGAAGGTCAGCAGATAAACA	35400
genome mRNA	-----	
genome mRNA	TGTAAACAAAGGTCTCTGGTTTTCTAGGCAGAGGGCCCTGCCACGTTCTGCAGTGTTTG	35460
genome mRNA	-----	
genome mRNA	TGTCCCTGGGTACTTGAGATTAGGGAGTGGTGATGACTCTTAACGAGTATGCTGCCTTCA	35520
genome mRNA	-----	
genome mRNA	AGCATCTGTTTAACAAAGCACATCTTGACCGCCCTTAATCCATTTAACCCCTTAGTGGAC	35580
genome mRNA	-----	
genome mRNA	ACAGCACATGTTTCAGAGAGCACGGGGTTGGGGGTAAGGTTATAGATTAAACAGCATCCCA	35640
genome mRNA	-----	
genome mRNA	AGGCAGAAGAATTTTTCTTAGTACAGAACAAAATGGAGTGTCTATGTCTACTTCTTTCT	35700
genome mRNA	-----	
genome mRNA	ACGCAGACACAGTAACAATCTGATCTCTCTTTCTTTTCCCACATTTCTCCTTTTCTATT	35760
genome mRNA	-----	
genome mRNA	CGACAAAACCTGCCACCGTCATCATGGACTGTTCTCAATGAGCTATTGGGTACACCTCCCA	35820
genome mRNA	-----	
genome mRNA	GATGGGGTGGCGGCCGGGCAGAGGGGCTCCTCACTTCCCAGATGGGGCGGCCGGGCAGAG	35880
genome mRNA	-----	
genome mRNA	GCGCCCCCAACCTCCCAGACGGGGCGGCGGCTGGGCGGGGGCTGCCCCCACCTCCCGG	35940
genome mRNA	-----	
genome mRNA	ACGGGGCGGGTGGCCGGGCGGGGGCTGCCCACCACCTCCCGGACGGGGCGGCTGGCCGGG	36000
genome mRNA	-----	
genome mRNA	CGGGGGCTGCCCCCACCTCCCGGACGGGGCGGGTGGCCGGGCGGGGGCTGCCCCCACCT	36060
genome mRNA	-----	
genome mRNA	TCCCGGACGGGGCGGCTGGCCGGGCGGGGGCTGCCCCCACCTCCCGGACGGAGCGGCTG	36120
genome mRNA	-----	
genome mRNA	CCGGGCGGAGGGGCTCCTCACTTCCCGGACGGGGCGGCTGCTGGGCGGAGGGGCTCCTCA	36180
genome mRNA	-----	
genome mRNA	CTTCTCAGACGGGGCGGCTGGTCAGAGACGCTCCTCACCTCCCAGACGGGGTGGCAGTGG	36240
genome mRNA	-----	
genome mRNA	GGCAGAGACATTCTTAAGTTCCCAGACGGAGTCACGGCCGGGCAGAGGTGCTCTTCACAT	36300
genome mRNA	-----	
genome mRNA	CTCAGACGGGGCGGCGGGGCAGAGGTGCTCCCCACTTCCCAGACGATGGGCGGCCGGGCA	36360
genome mRNA	-----	
genome mRNA	GAGATGCTCCTCACTTCCTAGATGGGATGACAGCCGGGAAGAGGCGCTCCTCACTTCCCA	36420
genome mRNA	-----	
genome mRNA	GACTGGGCAGCCAGGCAGAGGGGCTCCTCACATCCCAGACGATGGGCGGCCAGGCAGAAA	36480
genome mRNA	-----	
genome mRNA	CGCTCCTCACTTCCTAGACGGGGTGGCGGCTGGGCAGAGGCCGCAATCTTGGCACTTTGG	36540

Figure 1

mRNA	-----	
genome mRNA	GAGGCCAAGGCAGGCGGCTGGGAGGTGAAGGTTGTAGTGACCCGAGATCACGCCACTGCA	36600
genome mRNA	-----	
genome mRNA	CTCCAGCCTGGGCAACACTGAGCACTGAGTGAGCGAGACTCCGTCTGCAATCCCGGCACC	36660
genome mRNA	-----	
genome mRNA	TCGGGAGGCCGAGGCTGGCAGATCACTTGCAGTCAGGAGCTGGAGACCAGCCCGGCCAAC	36720
genome mRNA	-----	
genome mRNA	ACGGCGAAACCCCGTCTCCACCAAAAAACACGAAAACCAGTCAGACATGGCGGTGCGTGC	36780
genome mRNA	-----	
genome mRNA	CTGCAATCCCAGGCACTTGGCAGGCTGAGGCAGGAGAATCAGGTAGGGAGGTTGCAGTGA	36840
genome mRNA	-----	
genome mRNA	GTAGAGATGGTGGCAGTACAGTCCAGCCTTGGCTCGGCATCAGAGGGAGACTGTGCGAGG	36900
genome mRNA	-----	
genome mRNA	GCGAGGGCGAGGGCGAGGGAATTCCTTAATTTTCAGTTTAGTGATACTAATTTTGGACTCT	36960
genome mRNA	-----	
genome mRNA	GGCCTCTAAAACTGTGAAAGAAAAAATTTTTTGTGTTGTTTCTTTTAAGCCACATAG	37020
genome mRNA	-----	
genome mRNA	TTTGTGGTAATTTGTTACAGCAGCTGCAGGAACTAATTTATGCTGCATGTGAAATGGTG	37080
genome mRNA	-----	
genome mRNA	TAATAAGGTAGATTGTGATGAAGATACATAGTATAACAATTAAGCAACAACATAAAAGCA	37140
genome mRNA	-----	
genome mRNA	CAACAAGGAATTATAGCTAATGAACCAAAAAAGGAGATTAGAATAATAAAAATGGTGAAT	37200
genome mRNA	-----	
genome mRNA	CCCAAAGAAGCCAGAAATAGGGGAAGAGGCAAATAAAGGAAAGAAAGAGCTTGATGGTAG	37260
genome mRNA	-----	
genome mRNA	ATTTCAACCTAACTATGTCAAAAAGGACATTACATGTAAAAGGCAGCGATTTTTCAGATT	37320
genome mRNA	-----	
genome mRNA	GAATGGAAAAGTAAGACTCGGTATATGCTGCTGCCTGCAAGAAACACATTCTAAATATAA	37380
genome mRNA	-----	
genome mRNA	AGGCAAAAATAACCTACAGGTAACAGAACGGAAAGAAGTTCACTGTGCTTACAAGAATTA	37440
genome mRNA	-----	
genome mRNA	GATGCAAGCTAGACTGGTTCTGTTAATATCAGACAAAGTGGATTTCAAAGCAAAGGCTCT	37500
genome mRNA	-----	
genome mRNA	TGCCCAGGATGAGATGGTCATTTTATAATGATGAAGGGGATTCGTTTCATCAGCCTGGCAT	37560
genome mRNA	-----	
genome mRNA	AGCAAGCTGAAATGTTTATGCACCGGACTACAGAGCTAAAATACATGAAGCAAAGCCTGA	37620
genome mRNA	-----	
genome mRNA	CAGAACTACAAGTAGAAACAGACAAATCCACAGTGATAGAGATTTTCAGTAGCCGCTCTCA	37680
genome mRNA	-----	
genome mRNA	ATGATTTGTAGAACACGTAGCCATAATATCTGGATCTAGAACACTTGACCAACACTGTCC	37740
genome mRNA	-----	
genome	CCTGTGCAACCTCATTGGCATTTCACAGGACACTCCACCCAGCACCAGCAGAAGAGACACT	37800

Figure 1

mRNA	-----	
genome	CTCTCAAGTGCTCACAGAATGTTTGCCAAGATAGAGCAGATGCTGGGCCATAAAACAAGT	37860
mRNA	-----	
genome	CTCTAAATTAAAAGCATTCAAATTATTCAGAGTATGTTTTCTGACCTCAGTATCATTAAG	37920
mRNA	-----	
genome	TTGGAATATATTATAGGAAGATAACCTGGAAAAGCCTCAGATATGTGGAAAAA	37980
mRNA	-----	
genome	CCACATGGCCCATGGGTCAGAAGTGAAGTCAAAGGGAAATTTGAAAGTCTTTTGGATTG	38040
mRNA	-----	
genome	ACTGATATAAAAACAATAGATTTCTAACTTGTGGGGTGCTGTTACAGCATAGTAAATGG	38100
mRNA	-----	
genome	AAATTTCTAGCATTAAATGCCTGTTTTAGGAAAGAAAGATTTCAAATCAATGACCTCAGC	38160
mRNA	-----	
genome	TTCTACCTTTGGAAACTTGAAAATGACAAGCAAATGGAATCCAGAGTTACCAGAAGGGCC	38220
mRNA	-----	
genome	AGGTACGGTGGCTTATGCCTGCAGTTCTGCCACTTTGGGAGGCCGAGGCAGGTGGATTGT	38280
mRNA	-----	
genome	TTGAGACTGGCAGTTGAAGACCAGCCTGGGCAGCCTAGGGAGACCCCATATCTACAAAAA	38340
mRNA	-----	
genome	ACAAAAAATTAGCCAGGTGTGGTGGCATGTGCCTGTAGTCCCAGCTAACCAGGAGTCTA	38400
mRNA	-----	
genome	AGGTGGGAGGATTGCTTGAGTCTGGGAGGTTGAGGCTGCAGTGAAGTGTGATTGTGCCAC	38460
mRNA	-----	
genome	TGTGTTCCATCCTGGGCAACAGAATGAGACCCTGTCTCAAAAACAAAAACAGTTACTAGA	38520
mRNA	-----	
genome	AGAATGGACATCATAAAGATAGGAGCAGAAGTCAGTAAAATAGAAAACAAAAATACATAG	38580
mRNA	-----	
genome	GAAATCAATAAAACCAAAAGCTGGTTCATCAAGAACATCAATAAATTGGTAAAGCTGATA	38640
mRNA	-----	
genome	GGAAAAACAGTGAAGTCACAAATTAGCAATATCAGGAATGAGGGAGATGACAGTAGTATA	38700
mRNA	-----	
genome	GATTATATAGATATTAAAAGGACTGTATGAGGCAGGTGTGGTGGTTCACGCCTGTAATCC	38760
mRNA	-----	
genome	CAGCACCTTGGGAGGCCGAGGTGGACAGATCACCTGAGGTCAGGAGTTTGGGACCAGCCT	38820
mRNA	-----	
genome	GGCCAACATGGTGAAACTCTGTCTCTACTAAAAATACAAAAATTAGTTGGTCGTGGTGCT	38880
mRNA	-----	
genome	GTGTGCCTGTAATCCCAGCTACTTGGGAGGCTGAGGCAGGAGAATTGCTTGAACCTGGGA	38940
mRNA	-----	
genome	GGCGGAGGTTGCAGTGAGCTGAGATTGTGCCGTTGCACTCCAGCCTGGGTGACAGAGCAA	39000
mRNA	-----	
genome	GACTCCATCTCAAAACAAATAAATAAATAAAAAGGACTATATGGTAATATTATGAACAAC	39060

Figure 1

mRNA	-----	
genome mRNA	TTTATGCCAATAAAATTTGACAACTTATAGATGAAATGGATGAGTTCCTTGAAAGACACAG	39120

genome mRNA	AAACTATTAAAGCTCTCTCAAGAAGATATAGATAAGCTGATTAGCCCTATATCTATTTTA	39180

genome mRNA	TTGAATTTAAATGTAAAAATCAATATTTAGTTACTGGAAAACCTTTAAGTGTGGTTGGAA	39240

genome mRNA	ATGGTATACGAACTTTTTCAACTGAATTTTATGAAGTCTAATCACAGGTAAAGGTTTTCT	39300

genome mRNA	GATGAAAATTTAGTGTCTGAATTGAGATATACTGTAAAAAATGTTATATATCTTAATTAT	39360

genome mRNA	TTCTTCACATTAATTACATGTTGAAATAATACTTTGGGTGTATTGGGTAAATTAAATAT	39420

genome mRNA	TATGAAAATCTTGCCTGTTTTCTTTTTACTTTTGATGCGTCAGCTAGGAAATATAAAAGT	39480

genome mRNA	GTAGCTCACATTCTGTTTCTGTTGACAGTACTGCTTTGGAGCACAGTGGTTGAATGATCT	39540

genome mRNA	ATCATTTCAAAGACCTTTCCTCAGTTCGTTATTCATGGCTGTCTGTATTCCACATAGATA	39600

genome mRNA	AGGTCTGAAATACTGCTAAGTGGCATGTTTTGTTTTATGCTTTTATAAGTTTGTTGATCA	39660

genome mRNA	TTACTGATGTGGACTTTTGGTGCCTCTTAGGCTCATTGCTATCTTCCAACCATTTGTTGC	39720

genome mRNA	AATTTTTACCTAGAGATAAAGAGAAAGAGACATTTGGTTTCAGAGTAGTTAGATTGGGAT	39780

genome mRNA	CATGAAAGAGCAACCTCATTTTGATGCTTCAAAAATAGCACATCCCCCGTATTACTGGGA	39840

genome mRNA	TTTGCTATTCTTGGGATTACTTCAAGAACATCCTTGTGTTACTGGTTTGGATGCTTCTGA	39900

genome mRNA	ATGCTGTGAAGTCAGTTTCATGTACATGGCTCATCAGTTTAGCTCTCTCTTGGCTTTGTT	39960

genome mRNA	TAGACAGTTGGAGCATGATGGCCTAAACAGCTTCTTTCAATTAAACATTTTAAAATAGTT	40020

genome mRNA	TACAAATAGTAAACAAACTCCAGTTTTTGTGACTCTTGTCTCGCACAACAAAACACAA	40080

genome mRNA	TCTGACCATGATCATCTGGCATCTTAGGGTGAAATATGGTTATACTTTGGCCCATACCGA	40140

genome mRNA	AAGCAAGATTAAAAAGGGGCAGGAGAGATAGACTGCTGAACTGATTTTCAAGGTTCCAAG	40200

genome mRNA	AATATTGTAGGTTAAGAGTAAAAGTAACTTTTGGTAGAAAGCAGTGGGTTGTCTAGGAT	40260

genome	TGAAGTATCTGAAGTTTTTAAACGAAAATTTAAAAAGAAAATGAGAATTGCCTTACAAG	40320

Figure 1

mRNA	-----	
genome mRNA	TACAATCTCTTCTTTTTTAAAAAATAAACTTTATTTTGAAATAGTTTGTAGATTTATAGAA	40380
genome mRNA	-----	
genome mRNA	AAAAATTAGATAGGGTAGGAAGTTTTCATATACCCTACATCCAGTTACCCCAGTTATTAT	40440
genome mRNA	-----	
genome mRNA	CATCCTAATTTAGTGTGAGACATTTTCATGTTTAATGAATCAATATTGATATGCTATTAA	40500
genome mRNA	-----	
genome mRNA	CTTAAGTCCAGACTTTATTTCAGATTTTCTTAATTTCTATGTAATGTCCTTTTTCTGTTCC	40560
genome mRNA	-----	
genome mRNA	AGAATTCCATGCAGGACACCGGATACCTCATTACATTTTCATTGTCATGTCACCTTAGGCT	40620
genome mRNA	-----	
genome mRNA	CCTCTTGACAGTTTCTCTTCTTTTTTTGCTTAGAAATTCTCCAGAATTCAGAACTTCT	40680
genome mRNA	-----	
genome mRNA	GGGCATCGCTATGGAACTTTTTCTGCTGTGCAGTGATGACGCAGAGTCAGATGTCAGGAT	40740
genome mRNA	-----	
genome mRNA	GGTGGCTGACGAATGCCTCAACAAAGTTATCAAAGTAAGAACCGTGTGGATGATGTTCTC	40800
genome mRNA	-----	
genome mRNA	CTCAGAGCTATCATTGTTGTAGGCTGAGAGAAGAAGCGATCATTGAGTGTTCTTCTGTTT	40860
genome mRNA	-----	
genome mRNA	TGAGTCCCTGAGGATGTCTGCACTTTTTTCCTTTCTGATGTATGGTTTGGAGGTGCTCTG	40920
genome mRNA	-----	
genome mRNA	TTGTATGGTTTGGAGGTGCTCTGTTGTATGGTTTGGAGGTGCTCTATTGTATGGTTTGGGA	40980
genome mRNA	-----	
genome mRNA	GGTGCTCTGTTGTATGGTTTGGAGGTGCTCTTGTATGGTTTGGAGGTGCTCTTGTATGGT	41040
genome mRNA	-----	
genome mRNA	TTGGAGGTGCTCTGTTGTATGGTTTGGAGGTGGTCTTGTATGGTTTGCAGGTGCTCTATT	41100
genome mRNA	-----	
genome mRNA	GCATGGTTTGCAGGTGCTCTATTGTATGGTTTGGGAAGTGCTCTTGTATGGTTTGGAGGTG	41160
genome mRNA	-----	
genome mRNA	CTCTTGTATGGTTTGGAGATGCTCTATTGTATGGTTTGCAGGTGCTCTATTGTATGGTTT	41220
genome mRNA	-----	
genome mRNA	GGAAGTGCTCTTGTATGGTTTGGAGGTGCTCTTGTATGGTTTGGAGGTGCTCTGTTGTAT	41280
genome mRNA	-----	
genome mRNA	GGTTTGGAGGTGCTCTGTTGTATGGTTTGGAGGTGCTCTTGTATGGTTTGGAGGTGCTCT	41340
genome mRNA	-----	
genome mRNA	ATTGTATGGTTTGGAGATGCTCTGGTATCTGCCTGCATTGCTTGCCACACCTGCCCGGTC	41400
genome mRNA	-----	
genome mRNA	AGAAGGCGCTATGTTGACAATTGTGCCTGCACGGTGCCTAGGTCAATGAAGGGAACCGAT	41460
genome mRNA	-----	
genome mRNA	GGTAGCCACTGGATGCTCCTGGGAAAATGTCACTACAGGCACCAGAGAAGCCAGAGCTAT	41520
genome mRNA	-----	
genome	GCCCAAATTTCTATGAGTCTCAGTTTTCTTAACCATAAAATGGGATCAATGTTTTTGTGG	41580

Figure 1

mRNA	-----	
genome mRNA	CATGTGTATGAGTGTGTGTCTGTGTATGTGTGAGGATTAAATTGTGTATGTGTGAGGACT	41640
genome mRNA	-----	
genome mRNA	AATTGCCACTACTGGATCCTCAAAGTGGTAAGAAGTGTTCTTATTAATAATGACATCCTT	41700
genome mRNA	-----	
genome mRNA	ACACTCTTACCCAGCAAGATTGATGGGTGTGGCACTGCTTCTCTTTTTCCATCACATGGT	41760
genome mRNA	-----	
genome mRNA	TTCCATGGTATCCTTTTGCCAGGGAATCTTTGCTTTGTGGCTAGCACTTTGTTGTTTGG	41820
genome mRNA	-----	
genome mRNA	CTAATCACGCTTTCTGTGGTCAGGACGCTGGCTTCTCTGGAGCCATGGGATTCTAGCTCC	41880
genome mRNA	-----	
genome mRNA	CTGTCTTGTCCTTAGAGTGGTCACTGTCTTCTCTCTCCGCTTGCAATTCCTGCTTTGCTC	41940
genome mRNA	-----	
genome mRNA	GCATCTCACTTATGCAGTGACGTATATCAGTTTCACCTTGTTCTCCGTGCCTGCTGATCA	42000
genome mRNA	-----	
genome mRNA	TTGGCACCACCTTGCATGGTGCCATTTAGGGCCTGCTTCCAGTTAAGCTTGCTTCTCCACA	42060
genome mRNA	-----	
genome mRNA	GGCCTAAATATCCTTGCTTGCTTCTTTTATTCTCACTGGCAGGACCAGGGCGGTCTGTCT	42120
genome mRNA	-----	
genome mRNA	TTGCATGAGACAGGGTCTCGCTCAGTCACCCAGGCTGGAGTGCAGTGGCTGATCACGGCT	42180
genome mRNA	-----	
genome mRNA	CATTGCAGCCTTGAGCTACCGGGCTCAAGCTATCCTCCTGGCTTGCCCCCTTGAGTAGCT	42240
genome mRNA	-----	
genome mRNA	GGGACTACAGGCGTGCACCACCATGCCCAGCTAATTTTTTAAAATTATTTGTAGAGATGGG	42300
genome mRNA	-----	
genome mRNA	ATCTCGCCAGGTTGCCAGGCTGGTCTTGAACGCCTGGGCTCAAGTGATCCTCCCTCCTT	42360
genome mRNA	-----	
genome mRNA	GGTTTCCCAAAGTGCTGGGATCACAGGTGTGAGCCACTGTGCCTGGCCCCTTGATGTTTCA	42420
genome mRNA	-----	
genome mRNA	GTTCCTTGATATTTTGATCCTCAGAGTCAGAAAATCTAAAAAGAGGGCTATCCCAGGTTGCC	42480
genome mRNA	-----	
genome mRNA	TTGGTTCATGGCAAATGGGACGTTAAGAGGGCAGAGAGAATATGAACAGAACTGTTCTA	42540
genome mRNA	-----	
genome mRNA	ATATTGGTCATTTAATGTGTAAGTATTGTTCTTTTTTAAACCTCCTTCATTTTTTTTCCA	42600
genome mRNA	-----	
genome mRNA	GGAATTGCTGGACACAGTGGCTTGGTGTGTGTCTGAGGACTGTAGGCCATGGCCCTAGGT	42660
genome mRNA	-----	
genome mRNA	TGTGGTTTTAGGTCTCAGGTGCTCTTCCCTGGCTGTCTCCTTGCTTCTTTCCCATGTCCTC	42720
genome mRNA	-----	
genome mRNA	TTCTTTGTTTCCAGCCATTTCTCCCTTATGCTTAAGTTTGGTGCAGCAGGGTTTGGCTGC	42780
genome mRNA	-----	
genome	TCTCAGATTCCTGCTTCCTCAGATGCTGTAGTTGTCAGGCCAGCGGGCTGGCAGCGGGA	42840

Figure 1

mRNA	-----	
genome mRNA	TCAGGATCTGGCTAGGTTTGCTCTCACTGTGGCAGAGTAGGGGGAGGCGTGGGAGAGCAC	42900
genome mRNA	-----	
genome mRNA	GTGTGACCCCAGGCCAGCTGTAGGGAGCATAGGCATGGTCACGTAGCCTTCAGGTCCTAG	42960
genome mRNA	-----	
genome mRNA	ACTTTGTCTTCTCATGAGTATGGCTGTGTGTGTATGGTGAAAAGTAGGTTCTACTTAGCC	43020
genome mRNA	-----	
genome mRNA	CAAGAAAATGGGCACATTTTGCATGTGGTTTCTGTAGAGAAATGCACTGGGTATCTGACA	43080
genome mRNA	-----	
genome mRNA	TAGCCTGGCAGCATGCCTCCCTCAGGTAGGTTAGTCTCAGGCGGTGAAGCACGTGTGTCC	43140
genome mRNA	-----	
genome mRNA	AGCAAGAACTTCATATGTGGCATAAAGTCTCCGTTCTGTGAGGTGCTGGCAAATCACCAC	43200
genome mRNA	-----	
genome mRNA	CACCGTCAAGAGGCTGAAGTGATTTTGTCTAGGGAGGCAGGAAAGGCTTCCTGGAGTCA	43260
genome mRNA	-----	
genome mRNA	GCAGCCAGTAGGTGAAAGAGTAGATTGGAGACCTTCTTAATCATCACCGCCTCTTGTCTC	43320
genome mRNA	-----	
genome mRNA	AAGGGGTGCCAGGAAGCTGTGGAGGCTGAACCCATCTTATGCTGCCAGAGAGTGGGACAC	43380
genome mRNA	-----	
genome mRNA	CATGAGGGTCAGGTCAAGGGGTGTACCTTGTTTGGTAGAGAATTAGGGGCTCTTGAAGA	43440
genome mRNA	-----	
genome mRNA	CTTTGGATGTGGTCAGGGGAGTGTATCATTTAGGAAGAGTGACCCGGTGAGGACGTGGGG	43500
genome mRNA	-----	
genome mRNA	TAGAGGAGGACAGGTGGGAGGGAGTCCAGGTGGGAGTGAGTAGACCCAGCAGGAGTGCAG	43560
genome mRNA	-----	
genome mRNA	GGCCTCGAGCCAGGATGGTGGCAGGGCTGTGAGGAGAGGCAGCCACCTGTGTGTCTGCGG	43620
genome mRNA	-----	
genome mRNA	AAGCAGGGGCAAGAGGGAAGAGGCCAGCAGCGTGCTGCCATCACCCAGCGACTGGCGTAG	43680
genome mRNA	-----	
genome mRNA	ATTGTGAGAGACCATTCCCTGCTCTTAGGAGGGGCTGAGTTTTAGTTTTCTCTTGTTATA	43740
genome mRNA	-----	
genome mRNA	CAATAAGCTTGGTATTTGTTTACAAAACATTTGTAAAGCTAAATCAAGGTTTGATAAGGC	43800
genome mRNA	-----	
genome mRNA	TTCTAGTTTTATTTAAGAAGTAATGTTGAAATAAATGTTTGTCCAATTCGCTTTGCTCAT	43860
genome mRNA	-----	
genome mRNA	TTAAGGACTTTCAGTACAACTGCAACAACAGGATTAGGATTTAAACGTTTCTGAGATGT	43920
genome mRNA	-----	
genome mRNA	TTTTACTCCTCAGAATTTCCCAGAATGTGATCTGGTTTTGATTTTCAAGCTTGCTGACCC	43980
genome mRNA	-----	
genome mRNA	AATAGGTTAACCCACAAGTTTACGAAGACCATCTCAGTCCACTTACATCAACTGCCCAT	44040
genome	-----	
genome	rs16843804 GCCACGGTTAAAGAGATCATCGACTGATGTTTGGCACAGCTTCCTCCCTCTTGGGTGGGC	44100

Figure 1

mRNA	-----	
genome	AAGCATTTGGAAGAGAAGGCTCCTATGGGTGAGAGTGGGGCACCAAAGTCTTCCCTGTCC	44160
mRNA	-----	
genome	CATCCCCTAGCTTGAGAAGCCCTTCTCTAATGTGGACTTTGTGCCGTTAGCATCGTTACT	44220
mRNA	-----	
	rs2024115	
genome	A GCTTGAAGTTGACCATCTGGACGTACTTTCTGGTTTAGCCTCACAAAGTGAGCAAGGAGG	44280
mRNA	-----	
genome	GTTGAGAGATGTGCTGTGAGGAATGTGGGGCCCCAGCTGGCAGCAGGCTCTGGGTCAGGG	44340
mRNA	-----	
genome	GGGCAGGGACCACGGGCATACCTGACAGTGAGGAGGGGCCACACCTGCAGAAAAGGATGC	44400
mRNA	-----	
genome	AGGACTCCGCCTTGGAAGTGTTCTAGGCCAGAGCGAGGGTCTGTGGTTTATAAGTACAC	44460
mRNA	-----	
genome	CCACAGTGCTCGGGACCCTGCAGATGTCCAGGGTGCCGTCTGAGCCCGTATCATCCAACA	44520
mRNA	-----	
genome	GAATGTTCTGCTAGTGAAGATTAAAGATTTACTCCAGGGGCTTTAGGATTTATTATATAT	44580
mRNA	-----	
genome	ATATAAATCCTATATATATAATTTTTTTTTTTTTTTTTTTTTTTGAGATGGAGTTTCGCTCTT	44640
mRNA	-----	
genome	GTTGCCCAGGCTGGAGTGCAATGGCGTGATCTTGGCTCACTGCAACCTCCGCCTCCCGGG	44700
mRNA	-----	
genome	TTCAAAC TATTCTCCTGCCTCAGCCTCTCGAGTAGCTGGGATTACAGGCGCCCACCACCA	44760
mRNA	-----	
genome	CACCCGGCTAATTTTTGTATTTTTTTAGTAGAGACGGAGTTTCTCCATGTTGGTCAGGCTG	44820
mRNA	-----	
genome	GTCTTGAAC TCTGACCTCAGGTGATCTGCCCCGCTTGGCCTCCCAAAGTGCTGGGATTA	44880
mRNA	-----	
genome	CAGGCATGAGCCACCCACCTGGCCAGGATTTATTGTATTTGAACCATCTACCATTTTAA	44940
mRNA	-----	
genome	TTTTGATGTTATGTAGTATTTGATGATAATGAAAGTTAAATTGTTTTTCTTTCCATTTTT	45000
mRNA	-----	
genome	CTGTTTAAGTGAATGACCTGTATCTAGTTTATTTCAGTAACTTCCTGCATATATTGTTTC	45060
mRNA	-----	
genome	TTTCATTCTTAATGAATATATTCTTAATTTAGTTGCTATTATGTTTTGCTTTGCCCCAAA	45120
mRNA	-----	
genome	ATTGAAATCTTAGTTTCCTTTTAGCTCGTTTTAGAACTAGTGATGGGATGTGTCCTCCAT	45180
mRNA	-----	
genome	AAATCTCTTG TGATTTGTTGTAGGCTTTGATGGATTCTAATCTTCCAAGGTTACAGCTCG	45240
mRNA	-----	
genome	AGCTCTATAAGGAAATTAAAAAGGTGGGCCTTGCTTTTCTTTTTTAAAAATGTTTTAAAT	45300
mRNA	-----	
genome	TTTAAATTTTTATAGGTACACGTATTTTGTAGGTACATGTAAATGTATATATTTATGGGG	45360

Figure 1

mRNA	-----	
genome mRNA	TACATGAGATATTTTGATACAGGTATACAATACATAATAATCACACCATGGAAAGTTGGA	45420
genome mRNA	-----	
genome mRNA	TATCCATGCCCTCAAGCATTTATCCTTTGTGTTACAAACAATCCAGTTACATGCTTTACT	45480
genome mRNA	-----	
genome mRNA	TATTTTATTTTATTTTGTGAGACAGAGTCTTGCTTTCACCCATGCTAGAGTACAGTGGCAT	45540
genome mRNA	-----	
genome mRNA	GACCTTGGCTCACTGCAACCTCCGCCTCCCGGGTTCAACCGAACTTTGGGCTGGTCTCAA	45600
genome mRNA	-----	
genome mRNA	ACTCCTGACCTCAGGTGATCCGCCCCGCTCGGCCTCCCAAAGTGTTGGGATTACAGGCGT	45660
genome mRNA	-----	
genome mRNA	GAGCCACTGTGCCGGGCCTGATTGTACATTTTAAAATAACTAAAACAGTCAGGGCACAGT	45720
genome mRNA	-----	
genome mRNA	GGCTCATGCCTGTAATCCCAGCATTTTGGGAGGCTGAGGCAGGTGATCACCTGAGATCAG	45780
genome mRNA	-----	
genome mRNA	GAGTTCGAGACCAGCCTGGCCAACATGGAGAAACCCTGTCTCTACTAAAAATACAAAAT	45840
genome mRNA	-----	
genome mRNA	TAGCCAAGTGTGGTGGCGGGCGCCTGTAATCCTGGCTACTCGGGAGGCTGAGGTAGGGGA	45900
genome mRNA	-----	
genome mRNA	ATCGCTTGAACCTGGGGGTGGAGGTTGCAGTGAGCCGAGATCACGCCACTGCATTCCAGC	45960
genome mRNA	-----	
genome mRNA	CTGAGCGACAGAGTGAGACTTTGTCTCAAAAAATAAAAATGAAATAAAATTGGGCCGGGT	46020
genome mRNA	-----	
genome mRNA	GTGGTGGCTCACACCTTAGTCCCAGCACTTTGGGAACCTGAGGCAGGTGGATGCTTGAGA	46080
genome mRNA	-----	
genome mRNA	CCAGGAGTTTGAGACCAGCATGGGCAACATGGCAAAACGCTGTCTGTACAGAAATTAGCT	46140
genome mRNA	-----	
genome mRNA	GGGTGTGGTGGTGCACAACTATAGTCTCAGCTACTTGGGAGATTGAGGTGGGAGGATTAA	46200
genome mRNA	-----	
genome mRNA	TTGAGCCTGGAAGGTTGAATCTATAGGTAGCTGAGATTGTGCCACTGCCCTTCAGCCTGG	46260
genome mRNA	-----	
genome mRNA	GCGACCAAGTGAGACCCTGTCTCAAAAGAAAAACAAAAAACAAAAACAAACCACTATT	46320
genome mRNA	-----	
genome mRNA	ATCGACTATATATTATTGTCTATGATCCCTCTGCTGTGCTGTGCGAATACCAGGTCTTGGG	46380
genome mRNA	-----	
genome mRNA	CCCTTATTTCCATCACTGAGCAAACCTCACTCTGTTAAGCAGCAGGTGTGGGATTTTCATC	46440
genome mRNA	-----	
genome mRNA	GTTATTCAGTAATTCACAATGTTAGAAGGAAATGCTGTTTGGTAGACGATTGCTTTACTT	46500
genome mRNA	-----	
genome mRNA	TTCTTCAAAGGTTACTCTTTATTAGATGAGATGAGAATTAAAAATGGTAACTTACTTTA	46560
genome	-----	
genome	TATCTTTATAATTGAAGCCCACTAGACCTTAAAGTAGTTACCAGATGTTTTATGCATTTA	46620

Figure 1

mRNA	-----	
genome mRNA	AATGGCCTTTTCTCTAAAATTAGAAAGTAACAAGGAAAGAAAATGCTTCGTTTCTATGCA	4 6680

genome mRNA	ACCCTCTTGGTGACTAGTATGTGACTCTTAATGCAACCCTCATTCACCCCCCTCAGAATG	4 6740

genome mRNA	GTGCCCCCTCGGAGTTTGCGTGCTGCCCTGTGGAGGTTTGCTGAGCTGGCTCACCTGGTTC	4 6800

genome mRNA	GGCCTCAGAAATGCAGGTAAGTTGTACACTCTGGATGTTGGTTTTTGTGCGGGGCCAGCT	4 6860

genome mRNA	GCTACTGATCCTTTATGTCTCAGCTCAGATGTCATTTCAAAGTCTGCTCTGCCCTCTCC	4 6920

genome mRNA	AAATTGCAGTCGACCTTGCCCTGTTTATGTTTCCCTCATAGCACTAATCCATGTCAGAAA	4 6980

genome mRNA	TTGTCACGTACAGTCTATCTGTGTGCTTGTTTATTTTCTATCCCACCCTTCCGCAAGAGA	4 7040

genome mRNA	CTTATGGGATGTGTGCCCCAGGACAGCAGGGGTCTTACTGTCTTATGCTCTGTTGCAGCC	4 7100

genome mRNA	CAGCAGCGATAACAGTGTCTGCACATAGTACTTGCTTAAAAGATACTTGCCAAATTGTTG	4 7160

genome mRNA	AAGGTTGAGGTACCAATTTTATTATTGCTGACTATAGGAGTTATAGCAAAATATCCATTT	4 7220

genome mRNA	GTCTGTTACATGAGTTAAAAATATGGTTGTTGCACTGTGAATAGTTTGGTTTAGTCAAAA	4 7280

genome mRNA	CAGTTGTATCTTAACGGATTGAGAAACAAAAGCAGGACCACTTTTCATCAGCTCCCTCCT	4 7340

genome mRNA	TCTCCTTAACCAGCAATACATGCTGATGCTGATATCCCATAGACCCTCAGCTCCATCCTG	4 7400

genome mRNA	AGTCACTGGGAATGTGGTCTAAACCCTCACTATTAATATGAACTGAGTTTCAATAAGAAT	4 7460

genome mRNA	CTTATATGGGTGCGGCATAGTGGCTCATACCTTTGATCCCAGCACTTCAGGAGGCCAAGG	4 7520

genome mRNA	CAGGTGGATTGCTTGACCCAGACTAGGCAACATGGTGAAACGCCGCCTCTACAAAAAATA	4 7580

genome mRNA	CAAACTTAGCCAGGCATGGTGGTGCCTGTGGTCACAGCCACTCGAGAGGCTGAGG	4 7640

genome mRNA	TGGGAGGATCACTTGAGCCTGGGAGGTGGAGGTCGTGTTGAGCCAAGATCGCACCCTGC	4 7700

genome mRNA	ACTCCAGCCTGGGCAACAGAGTGAGACCTGTCTCAAAAAACCAAAATCCAGAAAAGAAC	4 7760

genome mRNA	TTATATGGCTGCAGAGGTATAATCACTAAGGAAATTTCTTTTGTATAATCTTTTTTCTT	4 7820

genome	TTACTATCATTTAAAAAATGTGTTATATTTCTGAAGCAACACATCCAGGTTCTGCACAT	4 7880

Figure 1

mRNA	-----	
genome mRNA	AGCAGCCAAAGTGACCTTAAAGAATATAACTGGGTCTTGTCATTCCCTTATTTAAACTCT	47940
genome mRNA	-----	
genome mRNA	TGTACCCATTTCCCAGTGCCGTTTAGATAGAGATTCCAGACTCGTCAATGGCTCTGTCAC	48000
genome mRNA	-----	
genome mRNA	CTCAGACACCCTGCATTGACTCATTAGTCTGATTAGAGTCAGGTTTTTCTTCCTCCTGAT	48060
genome mRNA	-----	
genome mRNA	GGTTTTTTTTTCCCCCTTAGTTCTCAGCGGAACAGTCACTTCCTTAGGGAGGTTTCCCCA	48120
genome mRNA	-----	
genome mRNA	GCCACCCTCTGAGGCCGTGCTTGTTGCCAGACTCTGCCACTAGAGGGCAGGGCTGCACCA	48180
genome mRNA	-----	
genome mRNA	CTCCTGGCACCTCGCACCCGGCCTGCCCTGTCACTCTGTGTGTTGGGTGAATTCCTGTGA	48240
genome mRNA	-----	
genome mRNA	TCTGTGACTCACTGCTCTGTGTCCTACACATTCGGCTTTTCTTCTCTCCCCACAACCCCA	48300
genome mRNA	-----	
genome mRNA	TTTTATAATTCTCCTTTTTCAGGAAAGCTTTATTCCCATTAAAAAATTTTTGTTTTTAAA	48360
genome mRNA	-----	
genome mRNA	ATGGTATTTTCTTACACTTATTTTCTAATTAAAAATGAGTGTTTTAAGAAGTATTATGAT	48420
genome mRNA	-----	
genome mRNA	TTACTGCAAATAATTTTAAACCCAGCCTTTTAGATCCTCTGTGATCATAAGAGAAATGA	48480
genome mRNA	-----	
genome mRNA	AGGATGTCTCCCAACACTTGAGCTTCATCCACATTTTCATCCTCCTGTTCTTTCAGCTGAG	48540
genome mRNA	-----	
genome mRNA	TTTTCCCCATCCCATTAGGGACTGTTGGAATATAAAACTGGCTTTTCCCTAACAGGGAAT	48600
genome mRNA	-----	
genome mRNA	GAATTGCTTCTGTTTCTCCTGAAGGAGAGCTGGAAGAATGACTTGCGTTCTTTTGCATAC	48660
genome mRNA	-----	
genome mRNA	ACAGGCCTTACCTGGTGAACCTTCTGCCGTGCCTGACTCGAACAAGCAAGAGACCCGAAG	48720
genome mRNA	-----	
genome mRNA	AATCAGTCCAGGAGACCTTGGCTGCAGCTGTTCCCAAATTATGGCTTCTTTTGGCAATT	48780
genome mRNA	-----	
genome mRNA	TTGCAAATGACAATGAAATTAAGGTATGATTGTTGCCTCAGGTCACAAACATGCGAGTGA	48840
genome mRNA	-----	
genome mRNA	TGCTGTGAGTGAGTCTGTGGAGGGTGAGGGCTTCTGAACAGGGAGTCCTGTGGGAGTGCT	48900
genome mRNA	-----	
genome mRNA	TCTTGGGGTATGTTGTATGTCGTAATTTAGACTACCATCATTTGTGTTATTTTGGAGCA	48960
genome mRNA	-----	
genome mRNA	CCTAAGGACTTCTTTCCACTTCTCATTTCTTACTGTGGGGTGAAGAGTTGAATTGGGAGA	49020
genome mRNA	-----	
genome mRNA	TGGTTTCTAGATGCAAATTGAAAAGGCATTTTCCAGAGCAGATTTGTTTTCGGCGTACT	49080
genome mRNA	-----	
genome	AGAGTGACTCTTTA[rs10015979]CCTAGCTGCGGGAAGATGACTGTGCCAAGACTGCAGGTAGGAGAA	49140

Figure 1

mRNA	-----	
genome mRNA	AGCTCACTGACGAGGCCTTGTGGGTCTGAACGTCCTGCAGCTATCAGAGCCTGTTGGCTT	49200
genome mRNA	-----	
genome mRNA	CCTGTTGTGCATTCCAACAAATCATCTTCAAACCCACTTTAGTGTTTTGTTTATAATGTC	49260
genome mRNA	-----	
genome mRNA	CAGAAATAGTGACCCTGTCACATGCTCTACAGATTACAGGATTCTTAGCCTCTTCCTTTT	49320
genome mRNA	-----	
genome mRNA	TGGTAGGTCAGTCCTGGGTTTGAGCCCAAGTGACCCTCCTGGGAGGTGATGATACACACT	49380
genome mRNA	-----	
genome mRNA	GGGTAGAGTGGAATCAGATGGACTTGGATTAGAATTCTGTCCTCTTTACTAGTTATTTTC	49440
genome mRNA	-----	
genome mRNA	CTCTAGGCCAACTGCCCAACAGCTCTAAGCTATTTCTTCGTATTCTGAAAAATAAGCCT	49500
genome mRNA	-----	
genome mRNA	TAATGGGACCCATATAGGGCAACTCTGAGAGTAAATAAAGGAATATGTGTTAGAGTGTA	49560
genome mRNA	-----	
genome mRNA	GCATAGTCACCCACGGGAAGGGCTTAGATGTTAGCTGCTACTGCTCTTATTAGCTGAATG	49620
genome mRNA	-----	
genome mRNA	ATTTGGAATAAACTGTTAGCCTCTCTCATGTTTTTCTCTTGAGCTTCGAAGTTTCTTG	49680
genome mRNA	-----	
genome mRNA	TTAATACTAAGGAGATATTCAAACCTAGTCATGGGGTTTGGGAATGACGAAGGGAGATGAT	49740
genome mRNA	-----	
genome mRNA	GAATCTAAAGAATTTAGTGTAATATTTCTTCATGCTCAGTAAATGGTAGTTTCTGCTGCT	49800
genome mRNA	-----	
genome mRNA	GTTATTTTTATTACCATCTCTTTGGAATGGGAGTAGGTGCTCCTTTGTGGTCAGAGGCTG	49860
genome mRNA	-----	
genome mRNA	TGAGAGCTCCACAGCGCCAGTTTGCCCATCTGTACACTGGGGTCTGTTGAAGGCAGTCCC	49920
genome mRNA	-----	
genome mRNA	CTCTGTGATATCTCTGGCTGTCAGAGCTCAGATGATAGATGGTATTTTTGTACTCTTAGT	49980
genome mRNA	-----	
genome mRNA	TCTCATCATTTTCATGATTTTCGATCACCATTTGAGTATGATGATGCTAACACTTTGTTGA	50040
genome mRNA	-----	
genome mRNA	ACGTAGAATCCGTTAATTACTTCCTTCCTGAACCTTTGGCATTAAAAAAATCTATTCTG	50100
genome mRNA	-----	
genome mRNA	CTACCTCTCTGCTCATTTATGGTTATTCAAATTTATTATCAAGAGCCTGGTACAGTGGCT	50160
genome mRNA	-----	
genome mRNA	TGTGCCTATAATTGTAGCTACTTGGGAGGCTGAGGTAGGAGGATTGCTTGAGGCCAGGAG	50220
genome mRNA	-----	
genome mRNA	TTTGAGACCAGCCTGGGCAAGATAGTGAGACCCTATCTCTAAAAAACTGAAAAAAATT	50280
genome mRNA	-----	
genome mRNA	AGCTGGACATGATGGCATGTGCCTGTGGTCCTAGCTACTCAGGAGGCTGAGACAGGAGGC	50340
genome mRNA	-----	
genome	TCGGTTGAGCCCAGGAGTTGGAGTTCGAGGCTACACTGAGCTGTGATTGTGCCACCACAC	50400

Figure 1

mRNA	-----	
genome	TCCAGCATGGGTGGTAAAACAAGATGCCATTTCTTAAAAAAAAAAAAATATATATATATAT	50460
mRNA	-----	
genome	ATTATCAATGAAATTCAGTAGTACCAACAGGATTATAAACAAAGATAGTAGTTCCTTCC	50520
mRNA	-----	
genome	TACTTTTCTCTTAATCCTTGTGTCTCACAGGCAAACATAACTCTTAGTATTTCTTCCAA	50580
mRNA	-----	
genome	TATTTACTTTCATGTTTCTTTCTTTCTTTCTTTTCTTTGAGATGGAGTTTGGCTC	50640
mRNA	-----	
genome	TTGTTGCCAAGGCTGGAGTGCAATGACGCAATCTTGGCTCACCACAACCTCTGTCTCCCG	50700
mRNA	-----	
genome	GGTTCAAGCGATTCTCCTGCCTCAGCCTCCTAGTAGCTGGGATTACAGGCATGCATCACC	50760
mRNA	-----	
genome	ACGCTCGGCTAATTTTGTACTTTTAGTAGAGATGGGGTTTCTCCGGGTGGTCAGGCTGG	50820
mRNA	-----	
genome	TCTCGAACTCCTGACCTCAGGTGATCCTCCACCTCAGCCTCCCAAAGTGCTGGGATTAC	50880
mRNA	-----	
genome	AGGCGTGAGCCACTGCGCCCAGCAACTTCCACATTTCTAAATAACATGCTTCTACTGCTA	50940
mRNA	-----	
genome	TTTTTTTTTTCAATTTTAGACATTTTTTTACTTTCACTATAGTTCTATCAGAATTCAGTG	51000
mRNA	-----	
genome	TGTACGTTATTATGCCTAAGTAAATAGTCATGGTTGCTTACGTATTATATTTCTTTGATT	51060
mRNA	-----	
	rs7691627	
genome	GTCTTTCTTATTTGATGAGAAAGCTGTGTTTTTTGCTCTGGGTGAAACTGGAGAGAGGA	51120
mRNA	-----	
genome	CCTGGGGAGGAGGAGGAGGACAGATGAAGTTGGTGACTGTACCTTCATGGCCATAGCTGG	51180
mRNA	-----	
genome	GTTCTCAGCACCCGGGGATCTGCTGATCACCTACTCATAGGCCAGGCCCTATCGAAGTT	51240
mRNA	-----	
genome	CTAGGTGACCCAGTGCTGGGGACGGGGGGGCCACCTGCAAGGTCTAATCATGGAGGTGGG	51300
mRNA	-----	
genome	GGCTACAGTGTTGGCTTGTGCTGGGGCCAGCATCCTTAGGAAGGCATCTTGGAGGTGGAG	51360
mRNA	-----	
genome	GAGACAGCCGCCCACTTCTTGATTGGGGCCTTCAGCAGCACCAGCTTCTTGGGCAGGCTG	51420
mRNA	-----	
genome	GTGCTGGCTTTCATCACCATGTCGTGTTCAATCTTCTTCCAGATCCTGACTTCTAGGTTT	51480
mRNA	-----	
genome	AGCTTTCCTCAGACCCTGGTTCCTTTCAGAGGCCATTGCTGCTGCCTTGCTCTTTGCTGG	51540
mRNA	-----	
genome	CTTGTGCCTTGATTATATGTCTTTGTACAACTTTTTGTTTTCTGGAGTTAATCTTCACA	51600
mRNA	-----	
genome	TCTGTTTTCTTGGAGTTAATCGTTACCTCTATATCGCTTGCTTATTATTTCTTTGGCCTTT	51660

Figure 1

mRNA	-----	
genome mRNA	TTGTCTTCTCACACCTTCCAACTTCTTTGTAATATGTGTTTAGTACAATTTTTCATGACA	51720

genome mRNA	GGTAGTTTACTGAATCAGTTTTTCCCCAGTGTGGTCATCCAACTTGAGTTATCCAGCTCT	51780

genome mRNA	CTGCCCCAGTCTGGGCAGGTTGATCTTCAGGTCTGTAGTACACTTGTATCCTAGGACTTC	51840

genome mRNA	TCTTTGCCATTAGCCTGGAATTTCCCTTGCAGTCTCCCGTTGGATGCCAGTTCCTAGA	51900

genome mRNA	TGCCATATGTTTTTCTATCGTCTAGTAGCTTCCTGAGAGAAGATGAATGGGAGGGAAATT	51960

genome mRNA	GTATGAGGTTTTGCATTCATAAAAATGCCATTTTTTTTCTGTACACTTGGCTGGGTATG	52020

genome mRNA	GTGTTCTGGGGTAGAAATCATTTTCCCTCAGAAATGCAAAGTCTTGGCCCTGTTGTCTTA	52080

genome mRNA	AAATCTCCAACGTGACCCGATTCCTTAACCTATGAATGTACTTTTCTTTGGAAGCTTTCC	52140

genome mRNA	ATTTTTGGGGAGGTGAAGTGCTAGGTACTTAGTAGGCCTTTTAATTTGGAAACTTACATC	52200

genome mRNA	CCTTCAGTTCTGGGAAAATTTTCTTAACATTTCTCTGAGAAGTCTTGCCTTTTATTTTC	52260

genome mRNA	TGTGTTCTCTCCTGAAATGGTTAGTTGGATGTTGGTCCTCCTAGATTGACTCACATCTT	52320

genome mRNA	ACCTTTTTCTTTTCTTTTCTGGTACTTTTTAGATATCCATCTCAAACCTTTCTATTTCAT	52380

genome mRNA	TGTTATGTTTTTAACCTCTTTCTTTTCTTTGTCTCTTGATGGGGTCTTGCCCTGTTGCCC	52440

genome mRNA	AGGTTGTGGTGCAGTGGTGCGATCATAGCTCACTGCAGCCTCAAATTCCTGGGCTCAAGC	52500

genome mRNA	AGCTGTTCTGCCTCACCCCTCCCAAGTAGTTGGGACTACAGGTATGCACCACCACGTCCAG	52560

genome mRNA	CTATTTTCTTTACTTTTTTTTTTTTTTTTTTTTGGAGATGGAGTCCTACTCTGTGCGCCAGGC	52620

genome mRNA	TAGAGTGCGGTGGTGGGATTTTGGCTCACTTAAGCCTCTGCCTCCCAGGTTCAAGCAGTT	52680

genome mRNA	CTCCTGCCTCAGCCTCTCAAGTAGCTGGGATTACAGGTGTGCACCACCATGCCCCGGCTAA	52740

genome mRNA	TTTTTGTATTTTLAGTAGAGCCAGAGTTTCACCATGTTGGCCAGGCTGGTCTCGAACGCC	52800

genome mRNA	TGACCTCAGGTGATCCGCCTGCCTTGGCCTCCGAAAGTGCCGGGATTACAGGCGTGAGCC	52860

genome	CATCATTAGATCTTTAAATACCAGTATCTATAAGTCTTTTCTCTTGAGTCAGCTAGTAT	52920

Figure 1

mRNA	-----	
genome mRNA	CCCTGGAAGGAAATTACTCATTTTCCTGCTTGGAGGCTATAAGCTTGGCTATGTTTATCC	52980
genome mRNA	-----	
genome mRNA	TGCAACCGGGGACTGGAAGGGAGGGGACTGACAGTGTTGCTGGTCAGGGTGCCCTCTTAC	53040
genome mRNA	-----	
genome mRNA	TTTTTGTTTTCTGTGTGCATCTCACGTCTGTCCTCAGCCTATGTAAACACCTCTTGAGAT	53100
genome mRNA	-----	
genome mRNA	TATCCCTCTCAATCTTTGCCGGAGGTGGGGGAGGGGCTGCTTCCTGGGCTGCCTTGGATT	53160
genome mRNA	-----	
genome mRNA	GGAGGGAAGACCTCAGGTGAGTGGGTGGGAATTTGCCCAAGGAGCCATGAGACCAGCCAC	53220
genome mRNA	-----	
genome mRNA	TATTTACCCCTCTCCATCCCTCCACTTTCAGATGTATGTGGCGCCTCCAAAGCCCGAGCT	53280
genome mRNA	-----	
genome mRNA	CTTCTTGGCGTCTGTGGCTTCAATAAGCTTGCTTTTGTGCTGGTATCCCTCCTACCCTCCC	53340
genome mRNA	-----	
genome mRNA	CTGTCCCCAGCAAAGCTTGCATTTGAACTTCTTCCTACGGGCTAACAAATCAGTCAGTTA	53400
genome mRNA	-----	
genome mRNA	TGTAGCTCTTGTTACTTTTTAGCTTCCGAAGTTTTGTTGACACCCGTAGTCTGCTAATGT	53460
genome mRNA	-----	
genome mRNA	CCCTGTTCTGTTCTTTCTGTTTCGTGTAAATATATGCTTTATACAACTTCTTTACATGATT	53520
genome mRNA	-----	
genome mRNA	TTTGTGGGGTTTCTGGGTAGCAGAGCTTCACAAAGTTCAATCCAGCGTGTTGGATTAGAAA	53580
genome mRNA	-----	
genome mRNA	TCTCCCACCCTCTGGTTTATTCTTATTCTCAAAATTACCTGCCAAACACTGATACTCCCT	53640
genome mRNA	-----	
genome mRNA	TGTTTTTCCTTTTCCTGACAGGAAATGTACATACCATACAGGACAGAAATCATTAGTGTA	53700
genome mRNA	-----	
genome mRNA	TCCCTTGGTGAATAACCACAAAGTGAACCTTAACCCTTGTAACCGCCACCCAGGTCAAGAC	53760
genome mRNA	-----	
genome mRNA	AGAATATTACCAAGCACTCAGAAGCCTCTCCCCTATTCCCCCGTCACTGCTCCTGCCTTC	53820
genome mRNA	-----	
genome mRNA	CTCCCCAAGGTCATGACTGCTGGCTTCTAATTCCAGAGTCTGTTTTTAAATTCTGTGTAC	53880
genome mRNA	-----	
genome mRNA	ATAGACCATGGATTAAGTGTTCTTTTTGTCTGGTTTATTTTGGTCGACATTAAGTTCATG	53940
genome mRNA	-----	
genome mRNA	AGAGTCTTCTATATTATCGTGTGTATTAGTATTCCTGTAGTTTTAGGAGCTTCATAGCAT	54000
genome mRNA	-----	
genome mRNA	TCCATTGTAGGGATATACCACAGTTTATTCATTGTATTATCACTGGGTTGTTTCTAGTTC	54060
genome mRNA	-----	
genome mRNA	TTGGCTATTGCGAGCAGTGCTACTGTGACCACTCTTAGGTGTGTCTTTTGGAGTACATGT	54120
genome mRNA	-----	
genome	GCAGGTTTCCATCTTGCACAGCTAGAGGTGGAGTTGTTGGGTGATAGGGTGTGTGCATCT	54180

Figure 1

mRNA	-----	
genome	CAGCTGCAGTAGAACTGCCAAATAGCTTTCCTTGAGTGCTTGTACCAGCTCACCCCTTTT	54240
mRNA	-----	
genome	GCCACTGTGTATGGGGATTCCAGGAGCTCTGGTCCTCGCTAGCACTTGGGAATTGCTGATG	54300
mRNA	-----	
genome	CTTTTACTCTTAGCCTTCCTGATGGGTGTTTTCTGGAATCACATTATGATTTTAATTTCC	54360
mRNA	-----	
genome	ATTCCTTAAAGTACCCTTGGCTCTGAAGTTTAATGATTCATGCATCTCTCCCTTTTGAA	54420
mRNA	-----	
genome	GTACTCTTACAGGTATGTTGTGCATGTGTTGAAAAGTGGCACTATCTATTCTAAAATACA	54480
mRNA	-----	
genome	rs2798235 GTATGCTCCTCTGTGTTTGAACAGTTGTAGCGTGGCCTTGGGGCCTCCTGTTAGCTGGC	54540
mRNA	-----	
genome	TTGGAGAAGGGATTCTTGGGATTGTAGAGATTAGACCTGAGGAGGCCCTTGGAGCTCTC	54600
mRNA	-----	
genome	TGACTAAATTTTATTCTTTATTATTCCAAACTATTTAAGCTCACCGTGTGCTGACTCATC	54660
mRNA	-----	
genome	ATAATAATGAGTAGCTCTCATTGTGCTTGTCTATTTGGACTCATACAATGATTTTTTTTTT	54720
mRNA	-----	
genome	TTTCTTTGAGACAGAGTCTTGCTCTGTTGCCTAGGCTGGAGTGCAGTGGCACAATCTCGG	54780
mRNA	-----	
genome	CTCACTGCAGCCTCCACCTCCCAGGTTCAAGTGATTCTTGTGCCTCAGCTTCTCAAGTAG	54840
mRNA	-----	
genome	CTGAGACTGCAGGTGCGTACCACCATGCCTGGCTAATGTTTGTATTTTGTAGTAGAGACGG	54900
mRNA	-----	
genome	GGTTTCACCATGTTGGCCAGGTTGGTCTCAAACCTCCTGACCTCAAGTGATCTGCCTTCTT	54960
mRNA	-----	
genome	CAGCCTCCCAAAGTGCTGGGATTACAGGTGTGAGCCACTGAGCTTGGCCAAAGTAGTTTTT	55020
mRNA	-----	
genome	TTAAGATGTTAGTATCTTTTCTTGCAGCTAAAAAAGTTTGTGAGAGATGATTCTACTTTG	55080
mRNA	-----	
genome	TTCTCCAGGTGTTTTCTCAGGGAGAAATTGGAGGCAGTAAGCCACTGGGGGAGTCCTGTG	55140
mRNA	-----	
genome	GCTGGGGGGTGGGGTAGTCCTGTGGCTCCTTGTGAGGGAGTCCTGTGGCTGGCAAGGAGA	55200
mRNA	-----	
genome	GAAGTCCTGTGGCTGGGTGGGAGGGAGTCCTGTGGCTGGGGTCTCATCCTGTGCCTAAC	55260
mRNA	-----	
genome	AGTGTCCAGAGGTGCCGAGACCAGCTCAGTCGGGGAGACCCTAACCCAGCAGCGCTAGAG	55320
mRNA	-----	
genome	GAATTAAAGACACACACAGAAATATAGAGGTGTGAAGTGGGAAATCAGGGGTCTCACA	55380
mRNA	-----	
genome	GCCTTTAGAGCTGAGAGCCCTGAACAGAGATTTACCCACATATTTATTAATAGCAAACCA	55440

Figure 1

mRNA	-----	
genome mRNA	GTCATTAGCATTTGTTTCTATAGATGTAAATTAATAAAAGTATCCCTTATGGGAAACGA	55500
genome mRNA	-----	
genome mRNA	GGGGATGGGCCGAATTAAAGAAGAGGTTGGGCTAGTTAACCGCAGCAGGAGCATGTCCT	55560
genome mRNA	-----	
genome mRNA	TAAGGCACAGATCGCTCATGCTATTGTTTGTGGCTTAAGAATGCCTTTAAGCGGTTTTCC	55620
genome mRNA	-----	
genome mRNA	ACCCTGGGTGGGCCAGGTGTTTCCTTGCCCTCATTCCTGTCAACCCACAACCTTCCAGTGT	55680
genome mRNA	-----	
genome mRNA	GGGCATTAGGGCCATTATGAACATGTTACAGTGCTTCAGAGATTTTGTTTATGGCCAGTT	55740
genome mRNA	-----	
genome mRNA	TTGGGGCCAGTTTATGGCCAGATTTTGGGGGGCCTGCTCCCAATACAGAGGTCTCGTGTA	55800
genome mRNA	-----	
genome mRNA	AATTCCTGGGAGGCGATAAGCCTCTGAGAAACAGACTATGCTAACCACGCCATGAAAGA	55860
genome mRNA	-----	
genome mRNA	GAAACTTATTTATAAATCAGATGCCAGTTACTAGTTTACTGCTTATTTGCCCAGGCGTAG	55920
genome mRNA	-----	
genome mRNA	CTCTGACAGAGTCCCCGACTCATAGTGCTTGCTCAGTGCATGCTGAACAATGATTGGAAT	55980
genome mRNA	-----	
genome mRNA	CAAGTCATGGCTCAGAGCATAGTTTGAATAATGGGAAATGGATGTTCTTAAGTAACATA	56040
genome mRNA	-----	
genome mRNA	GTCACCAAGATAATGCGACTAGCTGGGTCACCCCTTTTCAATTTTAGGATATTTTATCA	56100
genome mRNA	-----	
genome mRNA	AGATTTAAATGGCCATCATTAGAGTTATAGCACTTCTCCTTTGGATTGTCCTAGAGGCC	56160
genome mRNA	-----	
genome mRNA	CATGAGAAAGTATTCCTAATTTCTTAGGAGAACAGTTTGTGGGTAGTATGCGGTCATGT	56220
genome mRNA	-----	
genome mRNA	CCAGTTAAATTGCAGATATTTCCGATCGAAGATGTTCCAGTCCTGAGAACTTCGTGACAT	56280
genome mRNA	-----	
genome mRNA	TAGCAGGACTTCTACAAGCCATCTCTTAGGGTGGGGCATTTACTGCAGTTGGCTAGTACT	56340
genome mRNA	-----	
genome mRNA	CTTTTCTCCTTAACTTTGTCATTTGTTGATTTTTTTTTTAACTGTCCCCAAATACTGTGGG	56400
genome mRNA	-----	
genome mRNA	CAGAGTGTATCTAGAATTGAGGCCTCCACCATTGCGGAGAGGACATGGATGCTGAGCAGT	56460
genome mRNA	-----	
genome mRNA	CCCCTGAGTGAAGGTTATAAAGAAGCAAATAGACTACACATGTCTGTAAACTGCTCTTGA	56520
genome mRNA	-----	
genome mRNA	GTGTCCCAAATTTGGGGTACTTCAGTTCAGCTGTAGGAAAAGCCTCAAACGTGTTTATACT	56580
genome mRNA	-----	
genome mRNA	TTGCAAGAATTGGAAACTTCTAATTCACGTTAAGTTTTATGTAATACATGATAAGCTTCA	56640
genome mRNA	-----	
genome mRNA	TAGGAGCTTCATCTTTTATCTACTTGGACTTTTGCTTCCGTAGGTTTTGTAAAGGCCTT	56700

Figure 1

mRNA	-----	
genome mRNA	CATAGCGAACCTGAAGTCAAGCTCCCCACCATTCGGCGGACAGCGGCTGGATCAGCAGT	56760

genome mRNA	GAGCATCTGCCAGCACTCAAGAAGGACACAATATTTCTATAGTTGGCTACTAAATGTGCT	56820

genome mRNA	CTTAGGTAAGGTGGAGGCATATGAGTGGAAGAGTCTCCAGCATGTACTCAAGATAGACCT	56880

genome mRNA	TTGAAATAAATAAAACCAGATGATCCCTCAGCTTCTAGACCAGGCTATTTGGCACTGGTT	56940

genome mRNA	GATTGAATGTGAACTGCACTGGGGCTGCTGTGAGCCCGCATGGGTCTCTGTGACCCTGCA	57000

genome mRNA	GATGCAGCCGTGCCCAGGGACTGGGCAGTGGGTGTGGGCTGGTGTGAGCCCTGTCTGCCA	57060

genome mRNA	CCCAGGGCCTGGCCCTCTGTCTGTGTCGGCCATGACTATGGTGAGTCTTGTAGGCTTGAG	57120

genome mRNA	ACTGTGCCTCGGGTTCCTGCGGGTCTCTGTAGGTCAGTTGACAGTTTCTCCTGTTGTTT	57180

genome mRNA	GGGTAACGTGTGGAAACGAACACTGGCAAGTGCTGAAGCGAGCATGTGGACGTGCGATATG	57240

genome mRNA	AAATAACGACCTGGCTTTCAAAGGCAGTGAGGCTCTCTGGAAAGGACCTTGCTGAGCTAG	57300

genome mRNA	GGATGTGGGTGTGTAGCCATTCCCAGTGGGCCTCATGGCGTACTCGTTCATGATCATGTT	57360

genome mRNA	TGTGCCATCTTGATCTCTCAGGATCTCTTCTTTTTTAACAGATTAAGCCGGAATCTCCA	57420

genome mRNA	AACAGTGAGTCAGATGTTAAGATGTCTTGCTTCCACCCCCACAGGCTTACTCGTTCCTGT	57480

genome mRNA	CGAGGATGAACACTCCACTCTGCTGATTCTTGGCGTGCTGCTCACCTGAGGTATTTGGT	57540

genome mRNA	GCCCTTGCTGCAGCAGCAGGTCAAGGACACAAGCCTGAAAGGCAGCTTCGGAGTGACAAG	57600

genome mRNA	GAAAGAAATGGAAGTCTCTCCTTCTGCAGAGCAGCTTGTCCAGGTAGGAGCACAGGGTTT	57660

genome mRNA	ACTCTAGGCCCTGCATGTGAATGACTGACATTCAAAGAACCGATTAATTTGGAAGAGAAG	57720

genome mRNA	CGGCAGAACCGAGAGTTAGAGGTGTGGACTCTGGAGCTGCGCTGCTCGTTTCCAACCCTA	57780

genome mRNA	GGTGCTGACCTCTAGCTGTCTTCCCTCTGTATGTCCCTGTCACCGTGAGTCAAATGCGGG	57840

genome mRNA	TGATGCCTCCTCAGGTGCCGTGTTACCTAAGCCTCTCAGAGACCACTGCTACCCTGTTTC	57900

genome	TAAAACCAGAGGTCACGATATGTGTTTCATCCACCCAGTAAATACTGATTGAGCACCCACT	57960

Figure 1

mRNA	-----	
genome mRNA	GTGTGCTAGGCTCTGGGATAGGGGCTGGGTATACAATGGTGAGTATTCAGCTGCAGCTT	58020

genome mRNA	CTGCCCCGTGGAGGCTGTGGCCTAGCACACTGGTCTAGGCACGGTGGTATATGCTCACTC	58080

genome mRNA	AAGGAGATAGGGACGTGGTCGTTTGGGGTGTCCGAACAAAATGTCGGAACCTTCTCTTTCC	58140

genome mRNA	AATGCAGAGAAACCTTGCAGTAATTCTAATGTACTGTGATTGGCAGTTGACTTCAGTTCT	58200

genome mRNA	TTGTAGCACGCTTACTCAGGTTATTTCACTAACTATGTAACCATGCAGCCTCATTTTAAG	58260

genome mRNA	CAATTGGATTTTTTTGAACTTTACTTAAAATGTTATGTCAGGGTTTTTTATTGTGCTTAATG	58320

genome mRNA	TGTGCCATTTAGCTAAGTTTTGTAGGATACGAAATTGTAAGTGGCTTAAAATGATTCTTA	58380

genome mRNA	ATAGAATCATGAATTGAAGATAATGCTAATAATTTAAGCACTGAGTTAGGTAGTGTGTTGT	58440

genome mRNA	AAAATGCTTAGAATGCTTCCTGGCACATGTTAAGGCCATGTAAGTGCTGCGTGTTGATAA	58500

genome mRNA	ACAGCTGAGCAAAAGTGGACTCTTAAGAAAGTATTGGGGCTGAGAGTTCTGTTCCAACCA	58560

genome mRNA	GCTGCCCTTTGGTTATTTTTTCAGAATAAAAGCAGAGTCTCATGGGATATGACATTTATAT	58620

genome mRNA	TTCCTTCACAAAAAACACTGCTGAGTGTTTTGTTGAGTAAAAAGGGTGTAGCCATGGTAA	58680

genome mRNA	TAATACATTTAAAATATAGTTTATTTTCATCTTTACCTTGCCTTGTTTTTTTTTTAAGCTA	58740

genome mRNA	GCTTTTTTATTGAGAATTCCACACATACAAAAGTATCAACTCATGACCAGTTATATTTTCAT	58800

genome mRNA	TTATAATCCTACTTCTCCCTTTTTTTTATTATTTGAAAGCAAACCCCAATTATCCTCTTAT	58860

genome mRNA	TTCATCTATAAGTATTTTCAGTATCTCTATAGATGAGGACTCTTCTTTATTTTTTAAACTT	58920

genome mRNA	TATTTTTTAAATGATGGTCAGATGCAGTGTTTCATGCCTGTAATCCCAGAACTTTGGGAGG	58980

genome mRNA	CCAAGCTGGGCGGATCACTTGAACCTGGGAGTTTGAGACCAGCCCGGGAACATGGCGAA	59040

genome mRNA	ACCCCATGTCTTAAAGAAAAAATCAGCCAAGTGTGGTGATGCATGCCTGTAGTCCCAGC	59100

genome mRNA	TACTTGGGAGGCTGAGATGGGAGGGTCACATGAGCCTGGAAGATCAAGGCTGCAGTGATC	59160

Figure 1

genome mRNA	CATGATTGTACCACTGCACTCCATCCTGGGTGATGGAGCAAGATTCTGTCTCAAAAAAAC	59220

genome mRNA	AAAACTGCAAAACAACGTCACAAAACAGTGCCATTGTTAGACCTGAAAATATTAAACATT	59280

genome mRNA	TCCTACATCAAATACCCACCAACTCATTATCAATTTTTCTCTCTACTCTTTTGGAAATCAG	59340

genome mRNA	CATCTAAATAAAATTGGTCGATAAGGATTGTAAATCTCTTTGATGAACTGGTTCCCCTCC	59400

genome mRNA	ATCCCAGTTTTTTTTCCCTTAGAGTTCATTTATTGAGAAACCAGATTGTTTGTCTTCTAAG	59460

genome mRNA	TTTTCCTGTGGTCTGATATACTGCTTCCATCTCCACTGTGTAAATTAACACCTTTTTCTC	59520

genome mRNA	TTCTCTGTATTTCTGTAAATCAATAATTGGAGGAAAAGCCTTGTCAGATTTAGTGTATA	59580

genome mRNA	TTTTATATCTGAGTCCAGTATTTCTTATATAATATTTTAAGATAAGTGTACTCTTTTAAA	59640

genome mRNA	AAGTATTGAACTATATGCTCAATTTTTTTTTAACTGATGCTTTTAAGAAGGCTGCTTGAT	59700

genome mRNA	CATAAAAGTTTAGAGATCATTGGTCTGATGGGAAAAGCAAATAATTACTAAACCGTTTAG	59760

genome mRNA	CAAGGTTGAGGTGCACATGGTGGGGCCTGGAGAAGTTCAGTCATGAGCCGTCCTTATGG	59820

genome mRNA	GCACGTGGAATCTGACCCGGCACAGAGTTGGGAGAAGACAGGAGCTTTATAGACAGAAAA	59880

genome mRNA	TGTGGTCTTTGCTAAGTCCCAGGAGTGAAAGGGTGAGACAGTGCTCACAGCACACGAGTG	59940

genome mRNA	TGGGTGCGTAGACAGAGCAAGGGTGGGTCTGAAAAGGCCTGCAGGCTTTCTCATAGATT	60000

genome mRNA	AGCAAGAGTGCTGGTTACGGAGGTTTCTAACATTTGTGAACAGATCGAAACTGTGTTAAA	60060

genome mRNA	TTGGGATTGCAGTAATCCTGGAAGGACAGGGATAGAGGGTGAAGGGGAAAAAAGGGTATG	60120

genome mRNA	GATGTGAGACTTAATTGCTGATTTTCTTAAGACCTTTCTCCAAAGTAAATAAATGATGTG	60180

genome mRNA	GCACATTTTGAACCTGGCAAATTCTAAACTCTAGATATGATTATCTCTATAACATATCTT	60240

genome mRNA	ACTCCATCTTCTTTTGAATAAAACTGTTCTTAATTAAATTACCATGAGACGTTCAATTC	60300

genome mRNA	AGCAAATGTAGTTTGGCTAACCATATTTAATTAGAATTTAATATAATCCTAGGCCTGGCC	60360

genome mRNA	AAACTATTAAGCAAGTGTGGGCAAAATATTGATAATTTTAGATATGCAGGAACTTAGTTT	60420

Figure 1

genome mRNA	GCTTTCCATGTGTGCTTTTCGAAAAAGGAATAAATTGAAAAATAGAGGAAGCCCTGAAAT	60480

genome mRNA	CCAAGAAGCAAACCTCTCTCACCTAGGCATGCAGTAAAAGCAATTCTAGGATGATTGCTGT	60540

genome mRNA	TTGGCGCGTAGTTCGTATTAGAAACCATTCTTCTTGAATAAATAGTATGTTTAAGAAGCT	60600

genome mRNA	GGGCAGAGGGAAGGCATATGCATATATTATCAACAAGGAGGGAGAAAAAGGCAATTAGTA	60660

genome mRNA	ACCATCCATAGGAGGGTCAGCAAGATTTATAAAGGAAATTTGTGATCCAAGTATGAAGCA	60720

genome mRNA	AAATAAGGTGCAGAATAAATTTTAAGCAAGTAATAGATTAGAGTAAGAGAACCCATTTGA	60780

genome mRNA	CCATTAACCTTGGGACATTCTCTTTCAAATGACATGGAGTAGTACTGAAATCTTCTTTC	60840

genome mRNA	TTTCTGAGTCTAGGTTATTGTGACTGGACTCAGAAAGAAATATTTTCATTATTGCAGTGAA	60900

genome mRNA	TAACATTTGTGAACATTATTGTTTCATAAATTATGCAGTGAATAACATTTATGAACACGTG	60960

genome mRNA	ATGTGTAAGATACATACTGTTTATTTTTAGTTAAGTTTTTTGGCTCAACTTCTAGGCAGA	61020

genome mRNA	GAACATTAAATGTAAATAGTGTTACCTAGGAGCATGTAAATGGAAATCTCCATAGTATGA	61080

genome mRNA	AAGCAGTGCTGTTGCTAACAGAATTTAGGAGGGGGCAGATGAGGTGAAGGAAATGTGGGT	61140

genome mRNA	GCTGATTTTCCTTATTACATTGAGAGGAGCCAGGAGATTCTTTGTTCAAAATGGATGGCTT	61200

genome mRNA	AAGAAGTCAAAGTATAAGCTGATTACGTAGAGCAGGTACCCAAAAATGTTTTGTGTAAGG	61260

genome mRNA	GGCCAGATAGTAAATATTTTCAGTCTTGCAGGCCATCCCAAGTCTGTGGCAGCTACTCAA	61320

genome mRNA	CACTACCTTTGTAGCATGAAAGCAGCCACAGGCAGCCCATAAATGTGGCTCTGTTCCGGT	61380

genome mRNA	GAAACTTTAGGTACAAAAGCAGGTGCAGGCCAGACCTGACCTGTGCACTGTGGTTTGCTG	61440

genome mRNA	ACCTGGGATTCAGGGGTATAGAAGTTACCATCAGAAGAGCTAAAAGTGAGACTTTTTACT	61500

genome mRNA	TTATACTCTTCTACACTGTCTGATTTTGAAAAAAGAAACATGTATTTTATAATATTAAA	61560

genome mRNA	GATAGGGTTGGCAAATAGCAAATAAAAATACAGAATACCAGTGAAATTTGAACTTCAGAT	61620

genome mRNA	ACATTATGAGTAATTTTATGGTGTAAGTATATTCCAAATCATGTGGGACATACTTACACT	61680

Figure 1

genome mRNA	ACAAAATTATTTGTTGTTTGTTCACAGTTTAAATTTGAGTGCCTTGTATTTTATCTGGCA	61740
genome mRNA	ACTGTAATTAAAGGGAAAAAGAATAAATTCATTATGTTTCATATAATGTGATATAGCAGGG	61800
genome mRNA	GTCCCCAACCCCCAGGCTGCAGAGTGGTACTGGTCCATGGGTCCCCAACCCCCAGGCTGC	61860
genome mRNA	AGAGCGGTATTGGTCCATGGCCTGTTAGGAACCAGGCTGCCAGCAGGAAGTGAGCAGCA	61920
genome mRNA	GGTGAGCTGGCATTCCCACCTGAGCACCGCCTCCTGTCAGATCAGTGGCAGCATTAGATT	61980
genome mRNA	CCCATAGGAGTGCAAACCCATTGTGAACTGCACATGTGAGGGGTCTAGGTTGTGCGCTC	62040
genome mRNA	CTTATGAGAATCTAATGCCTGATGATCTGAGGTGGAACAGTCTCGTCTTGAAACCATCCC	62100
genome mRNA	CTGGCCCTGTGGAAAAATTGTCTCCCATGAAACCAGTCTCTGGTGCCAGAAAGGTGGG	62160
genome mRNA	AGCACTGTGATATAGTATTAAAAGTGCTAATAAATATGGCATACTGCCTTTAAATGTCT	62220
genome mRNA	GGTAGCTCTTTCTCAGTGGCACTCATAATAGTGTTTTTTGATTTTAAATGTGTGTCAAG	62280
genome mRNA	CTGACTCTCCCCTCCGTGTATGCTGGGCTTTATTTTCCCTTTCCCTAGTCACCAGTTTTGG	62340
genome mRNA	GAAATAGAGATCTTCATTCTCATGCTGCTCCTCTAGTGCAAGTGCTCCATTTATTTTAA	62400
genome mRNA	GGAATTAATATAACAAAAAATCATGGGAATTTAGAAAACAACATGGAAGCTAATGATCAC	62460
genome mRNA	ATTGGTGGAAGTGATAGGGAAATATTTAGGGGGAGAAGTTAAGGTATAAACTTTGTCAAT	62520
genome mRNA	GAAGTCCTATTAAAAACAACAAAAAGTGAAGCTTAGGATGCATTTTATAAACTCTGACC	62580
genome mRNA	AGAACACCTGTGTTTCTCTGTTTCTAGGTTTATGAACTGACGTTACATCATAACAGCAC	62640
genome mRNA	CAAGACCACAATGTTGTGACCGGAGCCCTGGAGCTGTTGCAGCAGCTCTTCAGAACGCCT	62700
genome mRNA	CCACCCGAGCTTCTGCAAACCCTGACCGCAGTCGGGGGCATTGGGCAGCTCACCGCTGCT	62760
genome mRNA	AAGGAGGAGTCTGGTGGCCGAAGCCGTAGTGGGAGTATTGTGGAACCTTATAGGCAAGTTA	62820
genome mRNA	TTAGCAAGGTCTACTCTTACAATTAACCTTGCAGTAATACTAGTTACACTCTATTGATTA	62880
genome mRNA	TGGGCCTGCCCTGTGCTAAGCAGTCTGCATTCCATCTTCCTTGCCAAACTTATAATACA	62940

Figure 1

genome mRNA	AATTCATCTTTATTTTATAAATAGGGGAGTTGGGCTGGGTGTGGTGGCTCACGCCTGTA	63000

genome mRNA	ATTCAGCACTTTGGAAGGATCGCTTCAGCCCAGGAGTTTGAGACAACCTGGCCAAGTGA	63060

genome mRNA	GACCCTGTCTCTACAAAAAAAAAAAAAAAAAAAAAAAAAATTAGCTGGGCATGGTGGCACATGC	63120

genome mRNA	CTGTAGTCCCAGCTGCTTTGGAGGCTGAGGTGGTAGGATTGCTTAAGCCCAAGAGGTTGA	63180

genome mRNA	GGCTGCAGTGAATCTTGATGGCAGCTGCACTGAGCCTGGTGACAGAGCAAGATGCTGTCT	63240

genome mRNA	CAAAATAAATTTAAAAATAAAATAAGAGAATTAAAGTTTAGCAGGTTGGGTGGCAAATG	63300

genome mRNA	AGGCCACACATTTAAAGCCCCCTCCTCCTGATTCTTTTCTCTGCCTTGGCTGCCTCCTGTG	63360

genome mRNA	GCATTTTAGGTGCTGAGAAATGAAACAGTAGGGAAAATAGTTCCAGGATCCTCATGTTA	63420

genome mRNA	ATTTGCCAGAAATGGCATCTTCAAGTCGTCAGAGGGATCTGAGAGTTCCTTCCTGGCCTG	63480

genome mRNA	ACTTGAGAAAATCCGTCTGTCCCCAGCTCTGCGTCTGCCTCCACTGCCAGTCACCTCCT	63540

genome mRNA	CTCCATGCTCTTGGGGCTGGGCCCTACCCACCATGCAGTGCTGCCCTGGAGCAGTGAGC	63600

genome mRNA	TTGGTGGGTCTGTCTGGCATGAGAGCTGCCTTTGGGAGCTGGATCCCAGCCTCTACCAC	63660

genome mRNA	TGGGTCTGGTGCCTAGCAGGCTATGGATAAACTTCTGCTGACTCCGGCCTCTCCTAAGCC	63720

genome mRNA	ACTGCAACGTGGTCCGTGTAGTGCACAGTGTGTGTGCAGCGTGGCCTTACTCACAGCCTC	63780

genome mRNA	CACATTAGAGAGAATCTGACTGAAGTCTTACTGCTGCCTCGTGTGAACATAAATGTTTGC	63840

genome mRNA	CAGAACCATGAGCAGGAAATGTTAATCTGCCTTGTTTCCTGTCCTTTACACGGAAGAATT	63900

genome mRNA	TTTTTCTGTATGGAATGCGTGCCTTACAAATAATGAGTGGAATACCCATCGCTAATGAA	63960

genome mRNA	AAGTTATACTTGACTGTTAGTCAGCTAAATAATCTGAGATTTCTAATACTTTTAATTTGG	64020

genome mRNA	CTTTTACAATGCAATTTATCTTAGCTTTTTTGATTTCTTAGGTCATATCTTTAGAACTAT	64080

genome mRNA	ATATTTGAATGTTAATGTAATTTTCATATTGAAATTAAATGTTGAACTGCGATGTTAAG	64140

genome mRNA	TGTTTCCTGTGGAAAAACGTTACATTTTCTCTAGTTTTTAAAGTTGAATCAAGCTGTTTG	64200

Figure 1

genome mRNA	AAGATTTTCACATTTCTTCTAGATTTTATCAGCTTGTTACTTTATCTGTCACTTTCTGTG	64260

genome mRNA	ATTTGCAGCTGGAGGGGGTTCCTCATGCAGCCCTGTCCTTCAAGAAAACAAAAGGTGA	64320

genome mRNA	TTATTTTCAGAAATCAGAGTCTTGTGTTGAATCTTACTGATTTTCTTGTATTTCTGTAATG	64380

genome mRNA	TAATGTATCTTGTATTTCTTGTAAATACTGTATTGGACTCTGTGTATATCTCTTCTCAGAT	64440

genome mRNA	GAGTGATTATATGTGTGAATGTTGCTGGAATCTGATAACCAGGCCTGAATAGTTTGTAG	64500

genome mRNA	GGTGGCTTTTAAAAATTACTTTCATATCAGAATTGCTTGTGCATAAATTTGAACGCATC	64560

genome mRNA	ATAAATTTCTAATGTTTCGGGGTCAGCAGACTTTTTTTGTAAAGGGACAGAGTGTAACAT	64620

genome mRNA	CTTAGCTTTATGGGCCATATGGTCTCTTTTGCAACATTCAGCTCTGCCCTGTGACAGGAA	64680

genome mRNA	TGCAGTTGTAAAGACATGAGCTACTGGCCAGCTATGTTCCAGTAGAACTTTACTTACAGA	64740

genome mRNA	AACAGACAGGCTGTAGTTTGCCAATACCTGCCTTAGGGAATGTGTTGTTATATTTTGTGA	64800

genome mRNA	GTTACCTTCTCAGTAAATTTTATTTAGTATTAGTCAGGAATATTATTAAGTAGCTTCTTT	64860

genome mRNA	TCCAGCCTGGTCAACATAGTGAGACCCGGTCTCTACCAAAACAAAACAAAACAAAAAAC	64920

genome mRNA	AGCCACGCATGTGGCATGTGCCTGTAGCCTCAGCTGCTGCTCAGGGGGCTGAGGCAAGAG	64980

genome mRNA	GATTGTTTGAGCCCAGGAGTTTGAGGTCACAGTGAGCTGTAGTCATGCCACTGCACTCCA	65040

genome mRNA	GCCTAGGCAACAGAATGAGACCTTGTGTCTTAAAAAAAAAAGTTTCCTTTGTTGGGTTA	65100

genome mRNA	TTTTAATTTGGACCTGGTTATCATTTTTTCAGCCATATTTAACTTTGTACATATCAGAATG	65160

genome mRNA	TTCTGATAAACTTAACTTTTATTAAAGTGTTTGTGATATAATCTGCTAGTTTTTGGTACA	65220

genome mRNA	CATTATCTTTTGCAATGCCAGTTATTTTCTTTTCCAGTGTTGGGTTGCATAGGAAAAGAA	65280

genome mRNA	TTGCTGTCACTTTCTATTTTGAAATCTTAAAGACTGATCCTTTTTTGTGTCATGATTTG	65340

genome mRNA	AGTATTTAATTGAGAGCCTAATGCCTAATATTATTTGCAGTATTAAATGGGATCTTAACA	65400

genome mRNA	GGAATAGCATTTCTAGCCTTCATTGAATTAAGTAAACATTTCTTAAGAGAACTTGGAATCT	65460

Figure 1

genome mRNA	ATAATATTTGCGTCATCATAGTATGAGATACTTAATCAAGTTTGAGATTTTAGTGAAACA	65520

genome mRNA	TTGTTTAGAAGCCAAAAGGATTCTAGGAAAAATTAATGTCTATATTCTTGAATTAGGAGA	65580

genome mRNA	GATTTTGGGACGTGTGACTAAGTTACGCTGACACTTGTTTGTTTCTTAGTCGCTTTTTCC	65640

genome mRNA	AGTGGCGGTGAGAACGAAGATGACTGATTCACATTGCTCAGATGAGTTTATCCTCTTCTG	65700

genome mRNA	GCTGGGACATGGGATATATCCTGTCTCTTTTAAGCCTTTTTGGTATTTTCCCCATTGA	65760

genome mRNA	GAGCTGTGTCTTCAAACCTCTTCTGTTATAGCTGGAAAATCCTTTTTAAGTGAAATCTGCC	65820

genome mRNA	CAAATTATAAGACAGATGAAGGTAGAGTTGTGTTGGATATAGGATTAGGGTGAAAGTAGT	65880

genome mRNA	GGGGGTGTCCTGGAGCCTCTCTTCTGGTGGCAGCCTAGCTCTTGTGCCTTTGAGGAAATT	65940

genome mRNA	ACCCTGGGGACGGCTCTGTGGAACATATTTGCAAACCACTGATTTGGAAGATAGAGATGG	66000

genome mRNA	CTTTTGTTAAGATCTGAATTCACCTTTTTGGCATTTTATTTGATTTCTCAAGGTAAAGAA	66060

genome mRNA	CTTATTTTGTAATAAAGTTTCCTATTATTTAGTAGATAGGCCAAGTTGCTGTGTTAATTC	66120

genome mRNA	CATGTAGATTTTGGGTTTCCTTTGCTCATTTTTTCACTCTTAATCTCACATCATTGTAAG	66180

genome mRNA	TTTATGGAAGTTATCATACTTCTGACTTTTTCTTTGAAGAGCAGAAATTAGAAATCCCA	66240

genome mRNA	ATAATTATTTTGATAGTGTCATTTAATGACACTCACATGTGATGTAGCCACAAAGATTTA	66300

genome mRNA	ATGAGTTCAGTTTTTAAATCATATTAAGACTGTTGGTTTCATTTGTTCTCATTAATGTAAT	66360

genome mRNA	TCTGAAGATGAACAATAAAATGTATTTTGAAGACTTTCAAATGAAATATTATTTTCATCCT	66420

genome mRNA	TCCAGATCATATAATGCTTAAGTTCTGATTGTTAATCATAAAGTC	rs6446723

genome mRNA	TAATAAAATGAAAGTGACTTTTAGGTATTAGAGTTTATTATAAAATCTGGTGTGTCATT	66540

genome mRNA	GGAGCTATGACATGAATATTTCAAAGGCCAATAGCATTGGATCTTTACAGTTATAACTTA	66600

genome mRNA	CCATTTTAAAGTTTAAAGTAGTAATATAGATTATTTAATAATCAAAATCAATAAATATTAA	66660

genome mRNA	TTATTAAATGTTTTGTGGTATAGTTTGAGAATCATTGCTTTTAACTTTTCCATATAGG	66720

Figure 1

genome mRNA	TTTATTGACTTTAATAGCATTCTAAACATAACATCTCTACATTCTTTGTGTTTAATACTG	66780

genome mRNA	TGGAGGTATAAAAATACTTATATATGATGATAAACTATATTAGAGTAAATTAAATATTCT	66840

genome mRNA	TATGAGTTTCATTTTAGAGTGCATTTACTTAATTTTGAAGTCCTTATTTTTAGCAAATA	66900

genome mRNA	AAAGGAATGTTGGTACATTATTTACTAGGCAAAGTGCTCTTAGGAGAAGAAGAAGCCTTG	66960

genome mRNA	GAGGATGACTCTGAATCGAGATCGGATGTCAGCAGCTCTGCCTTAACAGGTAGTTCTCAC	67020

genome mRNA	TAGTTAGCCGCTGGTGTGGACCTTCACTGTCTGCCTTCCACCCCTTGCCCTTCCTGCTCG	67080

genome mRNA	TCCCCCTGCACCTGGTGGACAGCACGACTGGGGGCAGCAGTGGAGCCAGGTTGCTTAAAT	67140

genome mRNA	GGGGCATATTCGGGCTTCTTTTATAATACTTACTCTGAAGCTTGTGTGTCTGTGGTGT	67200

genome mRNA	GCATCATATATTTGTTGTTTTCCATGGTTTAGGCTGTTTTAAAATTAGGTTTATGGCTTG	67260

genome mRNA	AGCATAGGGCTTTGTGAGTAGGGGATGGCAGGTCGAAACATCTCATGAGTTGGATGGGT	67320

genome mRNA	ATGCTGGGGGTTGGGAAATGGGATGAAAAATTATGGGATGAAAAATTGCCTATGGATAGT	67380

genome mRNA	TTAACTTGAAAGAATCTGCCTTTGTTTACAGATAGTTATCTTTTTCTTTTTTGAGATAG	67440

genome mRNA	AGTCTCACACTGTCACCCAGTGCAGATACCCAGTGTCACTGGAGTGCAGTGGTGTGCTCT	67500

genome mRNA	TGGTGCACTGCAGCCTCCGCCTTCTGGGTTCAGCGATTCTCCTGCCTCAGCCTCCCAAG	67560

genome mRNA	TAGCTGGGACTACAGGTGCCCCGCCACCACGCTTGGCTAATTTTTGTATTTTTTTGTGGAG	67620

genome mRNA	ACGGGTTTTTGCCATGTTGGTCAGGCTGGTCTTGAACCTCCTGACCTCAAGTGATCTGCCT	67680

genome mRNA	GCCTCAGCCTCCCACAGTGCCGGGATTACAGGAGTGAGCCACTGTGCCCCGCCAGTTACA	67740

genome mRNA	GATACTTATCTAATGAAATTCTCTGTGTACTTTATAAAAGATGAGGATTAAGTGAAGGTA	67800

genome mRNA	CTAATAACTGGATTATATGAGGGTGGTTTTGGTTGTATAATCCTATCTAAAAGAATATTT	67860

genome mRNA	TAGCTATAACTGAAAGTAAGACTTAAATATTTAGAGAGGAAAATCTGAATAATTCTAGTA	67920

genome mRNA	GTAATTATTTATTTACAAAATAAAAATAGATTTTTTTTTTGATTACACAAATTAAACAACA	67980

Figure 1

genome mRNA	ATAAAACATCACAGCAATCCGGATACTATAAAGCTCACATGCTTACCGACCCAACTGCCC	68040

genome mRNA	CAGGAGTGACCACTGCCAACAGCTTCATGTCGACCTTTTTGCCATAATTTTATATAGCC	68100

genome mRNA	TTTTTTGTTTTTAAATGGTAATTTAGAAAGTCAACTAGGAAAATGTGTTACAGGTTTATC	68160

genome mRNA	TTCCAGGAGAATAGGACTGGAGTCGAGATCTTGAATGTGGCTTGGAAGAAGGCAAGCCCA	68220

genome mRNA	CCCCAGAGAGATGAGTTGACAGTTGTTTCTGACCACTGCTTGCTTAGAGGGCCTGCGTGT	68280

genome mRNA	CTGTGACCGCCTAGCTTTGCGCCCCTGACTAGGCTGCCCCTTAATTACAAATGTCTTTAT	68340

genome mRNA	ATATTGCTCCAGCTAAGGCTTGGAGTAGTCGGTTAAGAACTTGAACCTCGGTTTTTGCAG	68400

genome mRNA	TGAAACAGCATTGAGAATATCACCTTCTGATAAGCCTTATTTTATAAGGTGGGTACTGT	68460

genome mRNA	AGTGGGAGGCAGTGTGAGAGATGCTTGAAGGATGCACTGCTGTCCTGCATTTTCAGCATCT	68520

genome mRNA	TCAGGATGCTGTGCAGCTGAAACATTTGATAACGGTGGAAGTGTTCGTTATTTTGCAAGC	68580

genome mRNA	CTGTGATTCCCTATTGAATGTTTTCTCTCGCCATTTGACAAATGAGTGTTTCTCTGTCTT	68640

genome mRNA	CAGCCTCAGTGAAGGATGAGATCAGTGGAGAGCTGGCTGCTTCTTCAGGGGTTTCCACTC	68700

genome mRNA	CAGGGTCAGCAGGTCATGACATCATCACAGAACAGCCACGGTCACAGCACACACTGCAGG	68760

genome mRNA	CGGACTCAGTGGATCTGGCCAGCTGTGACTTGACAAGCTCTGCCACTGATGGGGATGAGG	68820

genome mRNA	AGGATATCTTGAGCCACAGCTCCAGCCAGGTCAGCGCCGTCCCATCTGACCCTGCCATGG	68880

genome mRNA	ACCTGAATGATGGGACCCAGGCCTCGTCGCCCATCAGCGACAGCTCCCAGACCACCACCG	68940

genome mRNA	AAGGGCCTGATTCAGCTGTTACCCCTTCAGACAGTTCTGAAATTGTAAGTGGGCAGAGGG	69000

genome mRNA	GCCTGACATCTTTTTTTTTTATTTTTTATTTGAGACAGAGTCTCACTCCATAGTGCAGTGG	69060

genome mRNA	AGGCCGGGCACAGGGGCTCATGCCTGTAATCCCAGCACTTTGGGAGACTGAGGCAGGCGG	69120

genome mRNA	ATCACTTGAGGTCAGGAGTTCGAGACCAGCCTGGCCAACATGGTGAAACCCTGTCTCTAC	69180

genome mRNA	TAAAAATACAAAATTAGTTGGGCGTGGTGGCACATGTCTGTAGTCCCAGCTGTTAGGGA	69240

Figure 1

genome mRNA	GGCTGAGGCAGGAGAATTGCTTGAGCCTGGGAGGCAGAGGTTGCAATGAGCCGAGATCGT	69300

genome mRNA	GACACTGCACTCCAGCCCGGGCAACAGAGCAAGACTCCATTTCAAAAAAATAAAAAAAT	69360

genome mRNA	AAAGTGCAGTGGCTCGTTCTCAGCCCACTGCAACTTCTGCCTCCCAGGCTCGAGCGATTTC	69420

genome mRNA	TCCCGCCTCAGCCTCCTGAGTAGGTGGGATTACAGGTGGGCACCACCACACTCAGCTAAT	69480

genome mRNA	GTTTGTATTTTCAGTAGAGACAGGGTTTCACCATGTTGGCCAGGCTGGTCTCAAACCTCCT	69540

genome mRNA	GACCTTAGATGATCCACCCACCTTGGCCTCCTAAAGTATTGGGATTATAGTTGTGAGCCA	69600

genome mRNA	CCATGCCCCGGCCCTGCCACCTGCCATCTTTTGAGTTCTTCCCTGGAGACCTAGACCTGAA	69660

genome mRNA	CCCTCCTGCTTGTTCTTGTATCTAATACCCCTATTGACAGCGCAGCTTAGATCATTA	69720

genome mRNA	ATGGAGAGCTTGACCTCATCTGATACCTTCACTGAAGGAAACAACCTTAGTGTCTTTTGTG	69780

genome mRNA	TTGAACACTGAGGTAAAAAATTGGAATAGTTGATTATATGAACTCTGCTAAAATTGAGTG	69840

genome mRNA	CATTTTACATTTTTTAAGGCCTTGTTGGGCCCTGGTTAAATAATTATTTTAAAAATCCT	69900

genome mRNA	TAAGGAGCCTATTATAAACAGATCTGTGGTCTTAATGAAATGTGATTAATACTGTGCATT	69960

genome mRNA	ATTTTAAGAACTTTTGACTTTTCAAAAACTTTTACAACATTTCCCATTTGATAGCGGCA	70020

genome mRNA	TAGGTTTAAGCACTTCTCATCTCTAAGTTAGTGGACAAAAAACCTCATGGATAGTCTAA	70080

genome mRNA	TAATGTTTGCTACAAGTCCATGTTGAGTTTATACTCCATTTTATTTTCAGTTTAAAAA	70140

genome mRNA	CTGTGGTTAAATATGTGTAACATAAAATTTATGTTCTTAACCATTTTTTGCGTATACAGT	70200

genome mRNA	TCGCTGGTATTAAATACATTTAAATAATGTCATGGAATCATTGCTACCACCCATCTCTGT	70260

genome mRNA	AACCTTTTGATCATGTAACACTGAAGCTCTGTTCCCATTGAACCTATTCTCCTTTTCCC	70320

genome mRNA	GCCAAGTCCCTGGCAACCACGATTCTTCTTTCTGTCTTCTGAATTTGACTACTTTGGGTT	70380

genome mRNA	CTCATATACTTTAGGAGTCACACAGTATTTGTTTTACTTAGCATAATGTCCCCAAAGCTC	70440

genome mRNA	ATGCATGTTGTAGCCTATGTTAGAACTTCCTAATGTTTCAGGCCAAATACTATTCCATTG	70500

Figure 1

genome mRNA	TATGGATAGGCCACATTTTGCCTTTCCATTCCTCTGTCCATGGACACTTGTATTGCTTCA	70560

genome mRNA	TGTTTTAGCCATTGTGAATCATGCTGTTATGAACGTGGGTGTACAGATAGCTCCTGGAGA	70620

genome mRNA	CTCTGCTTTCCATTTTTTTGGCTAAATACCCAGAAATGGAGTTGCTTTTACATTCCAATT	70680

genome mRNA	TTAATTTAAACATTCATATCATTGAGTGTTTTACTTAATAGTATAGTAGTTAACAACT	70740

genome mRNA	TAATAAAATAGTATTTTGGTAATAATTTGCTGGTAGTCCATTGTTTCAGTTTTTTTAGGTA	70800

genome mRNA	AATTACACAGGACATTTCAAGTGGACATGAAACATCTTGTGATGTGGAATCATGCCCCAA	70860

genome mRNA	GCTGATGGCTAAACATATGAAATACCATAACCCTAAATTTAGTAGATTTAGTCTTTGCAAT	70920

genome mRNA	TTAGGAGATAACCTGTTATATTGTTAGGTTTTTGTGCGAAAAGCTTTGTCCTCATATTTCC	70980

genome mRNA	AACTTGCTGTAAAATTTGTTTGTGAAGACAAATATTTTGTATGGGTTTTTTCTTTTCA	71040

genome mRNA	TATTAAAAAGAAATGTCCACATTGGAATTTTTTTGGAGTTTTTAGAGCTAATAGAGCTTT	71100

genome mRNA	TCATAATGTAGTGGGAATGAGTGATCAGTAAGCTCTTAGCAGTTTCCATGCGTGCAATTC	71160

genome mRNA	TGTGCCTTGAAATAAATGACAGATGAGTACATTTGTGTTCTGTGTGTAATAATGTGCTCTT	71220

genome mRNA	TCCTCATTGCACTTCCATGTTGGAGGGCTTGTCTCTTGGTGATCACACTTCAAATTCCTC	71280

genome mRNA	ACAGCCCCCCTTGAACCGTTTAGGTGTTAGACGGTACCGACAACCAGTATTTGGGCCTGC	71340

genome mRNA	AGATTGGACAGCCCCAGGATGAAGATGAGGAAGCCACAGGTATTCTTCCTGATGAAGCCT	71400

genome mRNA	CGGAGGCCTTCAGGAACTCTTCCATGGGTATGTGGACTACAGGTGATGCGCTACAAAGTG	71460

genome mRNA	GTTTGTATTCAGACCTGGACATCTTAATTATATCTTTGCTTCCAAGAAGAAGTCCTTTGA	71520

genome mRNA	TACTGTTTTCTGAGTTCTGAATAGCTGATGAAAATGACCAATTGAGGAATAATCATACTT	71580

genome mRNA	TTTCTTGATCTAAATCTTATACTTTTGAGTTATCTTAGCATAAATGTATAATTGTATTTT	71640

genome mRNA	AAGTGGAAATTTGTCACTTAATCTTGATTTCTCTGTTTTTAAAGCCCTTCAACAGGCACA	71700

genome mRNA	TTTATTGAAAAACATGAGTCACTGCAGGCAGCCTTCTGACAGCAGTGTTGATAAATTTGT	71760

Figure 1

genome mRNA	GTTGAGAGATGAAGCTACTGAACCGGGTGATCAAGAAAACAAGGTGAGGGACATAGGCTT	71820

genome mRNA	GAGACGACTTGGTGTTTCTGAGCTTGTGTGAGGATTTAAAATCGCCCTGGCTACTGTCTA	71880

genome mRNA	CTTTATTGCTTTCCCATCCCTGGGCCTTTAAATTTCCCCTTTAAATACCAGCTCTTCCCA	71940

genome mRNA	GGCCTGTTGTTTTCTGCCTTTCCAGGTACTACCCACAGCCTTGAGAATTGCCTGAGTTCT	72000

genome mRNA	GCCTCCTTTGAGAGTGTGCCCCAGACAAATCTATTCTGTACTGAATGTTTCCTTGTCTGA	72060

genome mRNA	TTTCTTGGATCATTCATTTGATGGTTGCGTATGGCCTGCAACGTTTCTTGTTTTGGTTCT	72120

genome mRNA	ACTGAACTGTTCTAAAAGTCTCTCTTCATATTATCTTTTACATGTAAATGTAAGTGTCT	72180

genome mRNA	TCACTTTTAATTCCTCAAGGACAAGGAATAGCGTTTCACAGTTCGTCCCATCAATCAGAA	72240

genome mRNA	TTATAGCCTTTGGCATCTCCCTATCTACCAGGCCCACTTCCTCTTAGATTGTTGGCTTCCC	72300

genome mRNA	CAGGCTGTTGCCTTTCCCCAAGTAGCTTCTGCTTGTCCTGTAGAAGACCTTTCATGCTTT	72360

genome mRNA	GCTTCTGCAGCAGCCGTTCTGAATGCCTAGTGTCAACTGCCTTCTTACCACGCCCCACCC	72420

genome mRNA	TCCCTGCATGCTGCATTTATCCCCTGCCACAGCCCTGTGACCCTGTGTCCTGCTGCCTCT	72480

genome mRNA	GACTTGTCTGTTTCTGCTTGGCCATGGTCTCTGTGAGGTCAGGTGTGCATATGGGCACAA	72540

genome mRNA	ACCAGGGCATCTCTTTATCCCCAGCACCTGGCTTAAGTGCTGCTCTGGAAGTATCTGTTG	72600

genome mRNA	AATGAACTAATGCATGAATGTATTGTTGAGTATGAGACAAACAAGTGTCATTGTCTCCTT	72660

genome mRNA	TCTAGCCTTGCCGCATCAAAGGTGACATTGGACAGTCCACTGATGATGACTCTGCACCTC	72720

genome mRNA	TTGTCCATTGTGTCCGCCTTTTATCTGCTTCGTTTTTGCTAACAGGGGGAAAAAATGGTG	72780

genome mRNA	AGTACAAAAGGGGATGTGCACAGTTGAAGGAAATAACTAGGTTTCAGAGGTCAGCTTGGT	72840

genome mRNA	GGCCTGTTTTTGCCTTGCCTGTCAGCAGAGGAAGTAGAATCTGAGGATGAGTTTGGTTTTT	72900

genome mRNA	ACTAGCCGAGGGGAGGGAGGAAATGATGGGAGCAGGTAGGTTATTGGGTCTGGTTTTTGT	72960

genome mRNA	CATTTGAAAACAATCTGTTGTTTGAGGCTGAAGGTGGCTTGGGTGATTTCTTGGCAGTGC	73020

Figure 1

genome mRNA	TGGTTCCGGACAGGGATGTGAGGGTCAGCGTGAAGGCCCTGGCCCTCAGCTGTGTGGGAG	73080
genome mRNA	CAGCTGTGGCCCTCCACCCGGAATCTTTCTTCAGCAAACCTCTATAAAGTTCCTCTTGACA	73140
genome mRNA	CCACGGAATACCCTGGTATGTTAAAAGTTCACATCTTATTTTCTCAGATTTAATCATTAT	73200
genome mRNA	TGTAAAACTATTTTCAGTATTGACTATTTTAGTTTTAGAGCAGTAAGTGTTTTGAGTTCA	73260
genome mRNA	TTTGGGATATTTGACCTGCGTTGTAGCTCTTCAGAAAACACATGAATAGTGAAGTTCTTT	73320
genome mRNA	GTTTCATGGGTTCCTTTAGATGAAACCCATAGAGGAGAAAAGTAGAAACCTCAGCACGT	73380
genome mRNA	AAGAGCCAACATATATACACATCGGATTTAAACCTAAAGCACAAATTGTGCCTGGTCGCA	73440
genome mRNA	GTGGCGCTGAGTCGCACTCAGCCAGGCCAGGCATTCACACTCAGGGTGAGTGGGAACCAG	73500
genome mRNA	GACTGGCTGAGGCAGCAGTGGACCCAAGTCTCCATCGCGCCCATGCTTACTATGGAGCCT	73560
genome mRNA	TCTCGTTCTCTCTTTTCTTTGGGTGAGAGGGTACACTTGTGTTTTTGAATTTATATGAG	73620
genome mRNA	GTAAGTGTGTAATAGGGTTTTTCTAATCTTTTTTAAGTGAATCTGGAATTTTAATCAG	73680
genome mRNA	ATTTATTATCTGACAACCTAGAATTATAATCCAGAAAGTCTGTGGTATTGAGGACATATT	73740
genome mRNA	GGCAATATGATGAATCTCTAATTCTTAAATCCTGAACTTTTTTTTTTTAATCACTTAG	73800
genome mRNA	GGTTATTATAGTGAAGTCATTTCTGAATTTGGATCTTCTCTTCACACCTCTTTTCTCTT	73860
genome mRNA	TCCTGAGAATTAAGCTTTTGTTCGAGTTAGAAAGTTGATAGTAGGGAATTGTTCCATGG	73920
genome mRNA	CTGAGCAATTTATCTCCACAGAGGAACAGTATGTCTCAGACATCTTGAACCTACATCGATC	73980
genome mRNA	ATGGAGACCCACAGGTTTCGAGGAGCCACTGCCATCTCTGTGGGACCCTCATCTGCTCCA	74040
genome mRNA	TCCTCAGCAGGTCCCGCTTCCACGTGGGAGATTGGATGGGCACCATTAGAACCCTCACAG	74100
genome mRNA	GTAACGGCCAGTTTTTCAGCTGTGTTTTTCTAGTTATGCTTACTAAGGTTTAAGTTTAG	74160
genome mRNA	ATGATGATGTTTGTTGCTTGTTCTTCTGGTTAGGAAATACATTTTCTTTGGCGGATTGCA	74220
genome mRNA	TTCTTTTGCTGCGGAAAACACTGAAGGATGAGTCTTCTGTTACTTGCAAGTTAGCTTGTA	74280

Figure 1

genome mRNA	CAGCTGTGAGGGTGAGCATAATCTTCTGTGGAACCATTTCTTCACTTAGTGGACATTTTA	74340

genome mRNA	TCATTGCTACAATTAAAATTGGAGCTTAATAGGAAATATTTCCATGCACTCTAAAGCTGT	74400

genome mRNA	AACCAGTAATACCCACCATGTATCCATCTCTCAGCTTTAGAAAGAAAACGTTGCCAGTAA	74460

genome mRNA	AGTTAATGCTTCATAAACTTCAGTTTAAGTTCTAATTCTCAGAATATTTGTTTGAAATAG	74520

genome mRNA	ACCTCTTCCTAAAGGATATATTTAGAAATAACCTATCATTAAAGTGTAAGTCTGTTGAAT	74580

genome mRNA	ATGCTGGGCACGGTGACTCACACCTGTAATCTGACCACTTTGGGAGGCCAAGGTGGAAGG	74640

genome mRNA	ATTGCTTGAGCCCAGGAGTTCAAGACTATGGGCAACATAGTTGACCCTGTCCCTACAGAA	74700

genome mRNA	AATTAAAAAAAAAAAAAAAAAAGTAGCTGGGTATGGTGGTGCATACCTGTAGTCTCAGC	74760

genome mRNA	TACTCGGGAAGCTGAGGTGGAGGGGGGATTGCTTGAGCCCCAGAGATCAAGGCTGCAGTA	74820

genome mRNA	AGGCGTGGTTACACCACTGCCCTCTAGCCTGGGCAACAGAGTGAGACTGTCTCAAAAATA	74880

genome mRNA	ATAGTAATAATAATCAGTTGAATTAATAAAAAAAAAAAAAAAAAAACCCTGTGCTAGGCCCA	74940

genome mRNA	TAGTATGGTAAGAGTTAAAGTGAGCCTTAGGGATTATTTACTCAACCTCTGTTTCTGTAT	75000

genome mRNA	AAAGTGGAATAGGCTCAATTCTTTAAGTGATAGCATGTTGAACCTTTCCATACCAACTGG	75060

genome mRNA	CTCATAAGTCACAACCTGGCCAGTCAACAAGAGTAAAAATTAAGTGGTAAAAATCAAAGCA	75120

genome mRNA	AAAAACCTACAATTGTCAAATTTGTGGGATAACTCCCCCTTTTAAAATGTCATGCCTGAC	75180

genome mRNA	AGTAATTTCTCTCTAGTTTCCAGGTTTTTCAGTCAGTTGTGTCTTTTTTGAGCAGAAGGAA	75240

genome mRNA	GCATGCTAAGAGCTCAATCTTGTGGCTAGCTGGGGGTCTTTGTGTCAGCCATGCATGTGA	75300

genome mRNA	TGGTGCCCCTGGGTGCTTGGGGCTGCAGGGGAGGGGTACAGCAGTAGGGGCCTGTTCTGT	75360

genome mRNA	TCTCTCGTGCTGTGGAGTACATAGTGACATAGTGGGGTGGTCCTTGGTGTAGGTCCCTTG	75420

genome mRNA	TTCTTACCCCTGGGTCTGAGATTTATTTAGAAGTGGTGTGGGGCTGTGCGGCAGGCCCC	75480

genome mRNA	TCTGTAAGTATCAATGTTTGTGAAGTTGCTGTTTGAGAGTTGAAACCATGACATAAGCA	75540

Figure 1

genome mRNA	GAAATGGAAGGAAGAAAGAACCAGTTATGTGAAAGGGACACATTTACTTTTAAGCTTGTA	75600

genome mRNA	TTTACTGAGATAAAGTATTCTTAATCAATGTTCTTGAGAGGTGTGGGAAAAATGCAACAT	75660

genome mRNA	CCTGGTTGCAGTTAAACCCAGAACATTGTGTGTTGAAGAGTGACGGTTCTCAAACCGTCA	75720

genome mRNA	AGACGCGGGTACTGAGTGGGACTAACCTGCTGTCCTCTTGCCTTGGACCTTGTGTTCCAG	75780

genome mRNA	AACTGTGTCATGAGTCTCTGCAGCAGCAGCTACAGTGAGTTAGGACTGCAGCTGATCATC	75840

genome mRNA	GATGTGCTGACTCTGAGGAACAGTTCCTATTGGCTGGTGAGGACAGAGCTTCTGGAAACC	75900

genome mRNA	CTTGCAGAGATTGACTTCAGGTAAGTGAGTCACATCCATTAGATTTTCATGAACTAAGCTC	75960

genome mRNA	AATTGAAAGTTCTGGGATCACTTGATGCAAGGAATGATGTTATCAAGTACCCTGTCCATC	76020

genome mRNA	AGAAATCCGAGTGGTTTAGGTAGATGACAGTGATTTTCTCCTCCCAGTGGCTTTTGTCTG	76080

genome mRNA	AACTTTGCCCTATGCTTGGAATTTTATTTTATTTTATTATTTATTTAGAGACAAGATCTT	76140

genome mRNA	GCTCTGTCGCCCAGGCTTGAATGCAGTAGCACAATCATAGCTCACTGAAGCTTTGAACTC	76200

genome mRNA	TAGGACTCAAGTGGTCCTCCTGCCTCAGCCTCCCGATTAGCTAGGAGAATAGGTGTGTGC	76260

genome mRNA	CGTCACACTGGCTAATATTTTTTTGTAGAAATGGGGTCTTGCTATGTTGCCAGGCTGGTC	76320

genome mRNA	TCAAACCTCCTGGGCTTGATTGATCCTCCATCTTGGCCTCCCAAAGTGCTGGGATTACAGG	76380

genome mRNA	CATGAGCCACTGTGCCTGGCCTAGAATTTTAAAATATAAGTAGAAGAGTAGATTTTTTTTT	76440

genome mRNA	TTTGGTAGTCCTCGTCATTTAAGTATTCTGGATAGTGGGAATAAAAGAGCTTAGAATTTT	76500

genome mRNA	TCATCTTTGTCTTAACTTTTAAAAAAATGTAGCTTATATTAATTCTGCTTGTTTAAAAA	76560

genome mRNA	GAATATACTCTTCATTATACTGAACCTAGGTAAGACAGCTGGTTTATATTTTGTTGCAAT	76620

genome mRNA	TAAAAAACGTGAGCTGTGGTTGCAGTGAGCCAAGATTGTGGCCATTGCACTTCAGCCTGG	76680

genome mRNA	CAACAGAGTGAGACTTGGCCTCAAAAAAAAAAAAAATAACATGAGCTGTGTTGGCACTTTC	76740

genome mRNA	ATTTTCTAAGAGTAGTTTTGGCTGGAGAAGTTTTCTTTCAGTACTTTCTTTTAGAAGGGA	76800

Figure 1

genome mRNA	AATTTTCCTTTATAATTTAGGGTTTGT	76860
genome mRNA	CTTGTGGGTATTTCAATTAATCCTTAGAATGTTTATAAATCTGGGCTTGTTCTCGGCTC	76920
genome mRNA	CACCCACAGATAGGGACGCTGAGCGTGCATGAGTGGGCAGCAAGATAGCAGGTTATGGAG	76980
genome mRNA	GGCCCAGCTCACCCCTTCTGTGGCTTGAGCCAATTTTATAGGGCACTTACAGAGTCTTTT	77040
genome mRNA	GAAATAGTATTTATTTTGAAGAAAAAGAAAAACAGTTTACTGAGTACTGTCTTATTGAGT	77100
genome mRNA	CTGGAATTGTGAGAGGAATGCCACCTCTATTTATTTAAAGCCATTGGCCTTTTTTGTGT	77160
genome mRNA	TTTGAGTAAGTGCTGCCCAAGGTCCTTCCAGGGCACCTGGATGAGCCTGCTCTGGAGCAA	77220
genome mRNA	GCTGGCGGTAAGTGTTTACTGAGTAACTAAATGATTTCAATTGTTAAATGTGCTCTTTTGT	77280
genome mRNA	TAGGCTGGTGAGCTTTTTGGAGGCAAAGCAGAAACTTACACAGAGGGGCTCATCATTA	77340
genome mRNA	TACAGGGGTAAGCGGTTTATTTTTGTGAGATGCTGTTTTACCTTCAAGAAGGTGAAAGTG	77400
genome mRNA	AGGCTTTCCTTGTGGAATTTCTCTAAATGCATTCGTCATGTTTTAGATGTTTATTTTACA	77460
genome mRNA	GTTTATATCATGAAAGTTATAATCTTGTCATATGGATTTAAGTCTAGTAATGTTGAGTTC	77520
genome mRNA	TTTCTCACTAGCTTTCCTAAATATCTTACCTAAATTTAGTCAAATACAAGATTATGTTT	77580
genome mRNA	ATTTTTATTATCCTTCTCTCTAAAGCTTTTAAACTGCAAGAACGAGTGCTCAATAATGT	77640
genome mRNA	TGTCATCCATTTGCTTGGAGATGAAGACCCAGGGTGCGACATGTTGCCGCAGCATCACT	77700
genome mRNA	AATTAGGTATTTACCAATATTTTATCTCTTTTCCTTTTTTGGTTGAAGTACTAAAAGATA	77760
genome mRNA	CGAGAATGGAAAGAGAGGGAAGAATTCAAAGGATGTAGAGCAGTATTCCTGAATCTGAGC	77820
genome mRNA	TCATTTCAAGCCATTCTATTCTTAACTATAATGAAAAAAAAATCCAAAAAGTCTAAAT	77880
genome mRNA	TATAATTAAAAACAACAAATACTAACTGTCCATTGTAAAAAGTAATGCACTTTCATT	77940
genome mRNA	GTAAAAATTTTGGACTATAGAGAATAGTACTAAGAAGAAAAAAAAAATCACCTTCAATTC	78000
genome mRNA	TGCTGCCACCTGGAGGTAATCACTGTTAATATTTTGTCTATACTCTATGAGTTTCTTGT	78060

Figure 1

genome mRNA	TCAAAATCAGGTCAAATTACATGCAATTTTGTAACTCTGACAATTTCCACTTAATATTTT	78120

genome mRNA	ATTAGCATTTTCCTGTTATGAAACAGTAATTTTAGTTATGGGTCGTTGTTTTGCTATGCG	78180

genome mRNA	GTTGGGATAAAATTTTATATACTTTTTTTGGCAATTACTTATTATACATAAAATGTTTGTG	78240

genome mRNA	TATAGTTTTCTTTTTCTGAGAATTCCTGGAAGTTGAGTTACCAGGCCCGGCTTTGAATTT	78300

genome mRNA	TTTTTTTTATTTTTTTTTTTGAGACAGAGTCCTGCTCTATTGTCCAGGTGCTATCTCGGCT	78360

genome mRNA	CACTGCAACCTCTGTCTCCCTGGTTCAAGCGATTCTCCTGCCTCAGCCTCCCGAGTAGCT	78420

genome mRNA	GGGATTACAGGGGCACACCACCACGCCCAATTAATTTTTGTATTTTGTAGTAGAGACAGGG	78480

genome mRNA	TTTCACGATATTGGCCAGGCTGGTCTCGAACTTCTGACCCCGTGATCCACCTGCATTGGC	78540

genome mRNA	CTCCCAAAGTGCTGGGATTACAGGCGTGAGCCATGGCGCCTGGCCAGGCTTTAAATTTAA	78600

genome mRNA	AACAAATCTTCTAATAGCTTTATGGAGGTTATAATTTACATTTCTTGAAATGTACTCACT	78660

genome mRNA	TTGAGTGTATAGTAAACTCCAATTTTATCACATTTCTGTCACCCCAAATGTATCCTTGTG	78720

genome mRNA	CCCATTGCTGTAACTCCGGTTCCTGCCCCAACTCCTAGGCAGCCACTCATCTATTTTC	78780

genome mRNA	TGTCCCTTAAGATTTGTGTTTTCGCCAGGCGCTCATGCCTGTAATCCCAGCACTTTGGGA	78840

genome mRNA	GGCCGAGGTTGGTGGATCACTTGAGGTCAGGAGTTCGAGACCAGCCTGGCCAACATGGTG	78900

genome mRNA	AAACCTTGTCTCTACTAAAAATACAAAAATTAGTCGGATGTGGTGGCACACGCCTGTAAT	78960

genome mRNA	CCCAGCTACTCGGGAGGCTGAGGCAGGAGAATCACTTGAACCTGGGAGGCGGAGGTTGCA	79020

genome mRNA	GTGAGCAGAGATCGCGCCACTGCCTTCCAACCTGGGCAACAGAGAGAGACTGTCTCAAAA	79080

genome mRNA	CAAACAAAGATTTGTATTTTCTGGACATTTTATAGTACTGGGGTCATAGTATAGATGGAC	79140

genome mRNA	TTTTGCATTTGGCTTCTTTTACTTAATTGTGAGATTGGTTCTTGTTGTAGCATGTATCAG	79200

genome mRNA	TAGTTTGTTTCATTTTTTATTGGCGAAAGTATTCTATTATATGAATAATACCATATTTTATC	79260

genome mRNA	TATCCATCAGATGGATATTATAGAGTTCATGTTTTGGCTAATTTATGAATTATGGTACTG	79320

genome mRNA	TGAACATTTGCCTGCAAGATTTTGTGTAGACATGTCTTCATTTCTCTTGAGTAGATCACC	79380

genome mRNA	TAGAAGTGGATTTTAAATAATTTGGTACTTACTGTGAAACTGCTCTTCAAAAACATAC	79440

genome mRNA	CATTGFTCCTTCCTTCCTTCCTTCCTTCCTTCCTTCCTTCCTTCCTTCCTTCCTCC	79500

genome mRNA	CTCCCTTCCTACTTCCTCTCCCTTTCCTTTCCTTCCCCTTTTCCCTTCCCCTTCCC	79560

genome mRNA	GCCTGCCTGCCTGCCTGCCTTCCTTCCTTCCTTCCTTCGTTTCTTTCTACATATACACAT	79620

genome mRNA	TTTTTTAAATTTCAATGGTTTTTGGGGTACAAGTGGTTTTTGGTTACATGGCTGAATTTT	79680

genome mRNA	GGTTACATGGTGAAGTCTGAGATTTTAGTACACCTGTCACCCGAGTAGTGTACCTTGTAC	79740

genome mRNA	CCAATATGTAGTTTTTTGTCCCTCACCTTCAGCCTTCGCCTTGTGAGTCTCCAATGTC	79800

genome mRNA	CATTATACCACACTGTATGCCCTTGCGTACCCACAGCTCAGCTCCCACCTTCTGAGAACAT	79860

genome mRNA	ATAGCAGAAACATGCCAAAGTATACTCCCACTACCAGAATGTGATTGTGCCTGATTCTTC	79920

genome mRNA	TCACCAGTACAAATATTTCAAAAAAAGTTAAATATGTATCAGTTTTTTGGGCAGAAGTTG	79980

genome mRNA	ATACTTCTCTTTATTTATTTATTTTTTTTTGAGATAGGGTCTCATTCTATGATGCCCAGGC	80040

genome mRNA	TGGAGTGTGGTGGTGGGATCTCGGCTCACTGCAGTCTCTGCCTCCCAGGTTCAAGTGATT	80100

genome mRNA	CCCACGTCAGCCTCCCAGGAAGCTGGAATTACAGGCGAGGGCCACCACTGCCAGCTAATT	80160

genome mRNA	TTTGTATTTTTTTGGTAGAGATGGGGTTTCACCATGTTGGCCAGACTGGTCTCAAGCTCCT	80220

genome mRNA	GACCTCAAGTGATCCACCTGCCTTGGCCTTCCAAAGTGCTGGGATTACAGGCGTGAGCTA	80280

genome mRNA	CCACACCCGGCTGATATTTCTTTTTAAATAACTTACCTTCTTTTGAAAGTAATACATGT	80340

genome mRNA	TTAATGAACAGAATTTAAGGAAAATATAAAAAAACGAAATAATCTTTGTAATCAAACCTAC	80400

genome mRNA	TGAAAAGAAAACCAAAGTTACATTTTGGTGCATATTCTTTTTCATTTTCATCATTGTAAT	80460

genome mRNA	TTGCATTTCTTTGATTACTTGTGAGACACTCCTTTCATTTACTTAATAGGTTTATATGAC	80520

genome mRNA	TTGCCTATTCAGAGATTTTGCAGCTTTACCATTTTCTGCAAATGATAGCAACTTCTTTTT	80580

Figure 1

genome mRNA	GTTTGTTTGTGGAGACAGAGTCTCGCTCTGTCACTCAGGCAGGAATGCAGTGGTGG	80640

genome mRNA	AATCTTGGCTCATTGCAACTATTGCCTCCTGGGTTCAAGCGATTTTCCTGCCTCAGCCTC	80700

genome mRNA	CCAAGTAGCTGGGATTACAGGAGTGTGCCACCATGCCCCGGCTAATTTTTGTATCTTTAGT	80760

genome mRNA	AGAGATGGGGTTTTGCCATGTTGGCCGGGCTGATCTTGAACCTCCTGGCCTCAAGCGGTCC	80820

genome mRNA	CCCTGTCTCGGCCTCCCAAAGTGCTGGGATTACAGGCGTGAGCCACCGTACCCAGCCAGT	80880

genome mRNA	AGTTACTTCTTATATTCTAGAAAAAATTCTACTCATGATCAAGTCTCCATGAGGAAAGAG	80940

genome mRNA	ACTTTAATTGAAGATCATGGGGCTTGCAGACCAATATGATAAAATAGTTCATTGTTTCTA	81000

genome mRNA	AAAGTATTACTGAGTGTTGATGGCAGATATGAACCCTTTTGTTTTGTAGGAAAATGTTA	81060

	rs363064	
genome mRNA	CCCGTATTCTCCATTTGAATTCAGTTTAGATTTGTTAGGAATCGCAGCTTAAGCTTTGCC	81120

genome mRNA	ATCTGGGAGTGTTTGGGACAGTTTGCAGACAAAATTGCAAAAGTGCCTAAGGAATGCAG	81180

genome mRNA	CTGGCATTTCAGACCTGCTCTGTGCTCAGTACTCTGTGGACAGACACTGTTTCAGCACTTGT	81240

genome mRNA	TGATCAGAAGGTTTAGAAAGAGAACTTTCAAAGTTGGTTTTTAATTAAAGCATTTAATAG	81300

genome mRNA	TGTAAATAGAAAGGGATTAAATTTTATGACAGACAAAAGAAAGTACAGCACCCAGCTGGG	81360

genome mRNA	CGTGGGGGCTCACGCCTGTAATCCAGCACTATGGGGGGCTGAGGTGGGTGGATCACGAGG	81420

genome mRNA	TCAGGAGTTCAAGAGTTCAAGAACAGCCTGGCCAAGGTGATGAAACCCTGTCTCTACTAA	81480

genome mRNA	AACTACAAAAATTAGCCGGGCGCGGTGGCAGGCGCCTGTAATCCCAGCTACTCAGGAGGC	81540

genome mRNA	TGAGGCAGGAGAATCACTTGAACCTGGACGGCAGAGGTTGCAGTGAGCCAAGATTGCACC	81600

genome mRNA	ATTGTACTCCGGCCTGGGCCACAGAGTGACATTCTGTCTCAAAAAAAAAAAAAAAAAAGAAA	81660

genome mRNA	AAAAGAAAGTACAGCACCCAGTTATGTCCGAGTGGGTGCATGAGAGTGACCCTGAGATTG	81720

genome mRNA	GAGACAACGCTGTCACGTGCTTGAAGAACGCCACCTGAGAAAGGGGGCGAGAAGTGGTGT	81780

genome mRNA	CCGCTGGTAACCAGAGGTGTTGGCTTAGCCATCTGCAGGGAGGAGGGTGGTCTATCACAG	81840

Figure 1

genome mRNA	GTGAGTTTCATCTACTTTCTTAAGCAAATTAACCTTACTTTTGTGTTAGGCTTGTCCCAA	81900

genome mRNA	AGCTGTTTTATAAATGTGACCAAGGACAAGCTGATCCAGTAGTGGCCGTGGCAAGAGATC	81960

genome mRNA	AAAGCAGTGTTTACCTGAAACTTCTCATGCATGAGACGCAGCCTCCATCTCATTTCTCCG	82020

genome mRNA	TCAGCACAATAACCAGGTATGCTGACCCAGTGGCATCTTCACATTGTCGGGAAAATGCCC	82080

genome mRNA	TTTCCTGATGCCTTTCTTTAGGCTTTAATTGAAAACATTTTATTTTCTAGAAAAAGCTT	82140

genome mRNA	CAGCTCAGGATGTTTGAGTGTAGGTCAGTCCTTTGATAGGATATTATCATTTTGAGGATT	82200

genome mRNA	GACCACACCACCTCTGTATTTAAGCTCTGCCACAATCACTCAGCTGTGACACTGTAAATC	82260

genome mRNA	TCTTAATAGTTTATTACATTCCATGTGCTGACAGTTGTATTTTTGTTTGTGACACTTACG	82320

genome mRNA	TATTATCTGTTAAACATTTTCACTTTAGTTGTGTTACCTTTAAAGAGGATTGTATTCTA	82380

genome mRNA	TCATGCCTGTTGATTTTTTGGTGAGCGGGCTATTAAAGTCAGTGTTATTTAGGGTTATCC	82440

genome mRNA	ACTAGTTCAGTGATTTGCGAGATTATCATTCACATTTATTGTGGAGCTTTTGAATATCGT	82500

genome mRNA	GTCAAATGGCCACATATATCCCATTCTTATCTGCTTCTTAGGTGAGTGGGACACAGTGCT	82560

genome mRNA	TTAATGAAGCTATAATCTTCAGAACTCTAGCTTGCAGAGAAGATTGCAGAAGTGATAAGA	82620

genome mRNA	CTTGTGCTTTTTTAATTTTGTCTTTTAAATGTTATTTTAAAAATTGGCTTTATATGATACT	82680

genome mRNA	CTTTTTTTCTGCTGAGTAACAGTGTTTTACAAAACCTTGGACTAAATGACTTCTAAGCTTA	82740

genome mRNA	AATGATCACTTGATGCTTTTTTTCTGAATTAGGAACTCAGCTTATCAAATATCAAAGTCA	82800

genome mRNA	TAATTCCTGAATAAATAACGTCTTTTTTTCATGTAAAGACTGCTTTAAAAAACACATGGAA	82860

genome mRNA	GGCTGGGTGCGGTGGCTCACGCCTGTAATCCTAACACTTTGGGAGGCCCAGGTGGGCAGG	82920

genome mRNA	TCGCTTGAGCTCAGGGGTTCAAGACCACCCAGGGCAACATGGCAAAACCCACCTCTACTC	82980

genome mRNA	AAATACAAAAAATTAGCCAGGCGTGGTGGCGGGCCCCTGTAATCCCAGCTACTCGGGAGG	83040

genome mRNA	CTGAGGGATGAGAATCACTTGAGCCCCGGAGGCAGAGGTTGCAGTGAGCCAAGATTGTGC	83100

Figure 1

genome mRNA	CATTGCACTCCCAGCTTGGGCTACAGAGTGAGACTCTGTCTCAAAAAAGACACACACAC	83160

genome mRNA	AAACAAAAAAACATGGAGACATTTTTTTGGCCACCTTAATATTTCCCCTCAGATAATTT	83220

genome mRNA	CCTTTGTTTAAACTCAGAACTGGCATTCTCTCTTGGAGAAGATTCAGGACAAATACTC	83280

genome mRNA	CTTTAAGATAAGTAGAAGCAGTGAAAGAGGATTTGATTATCAGGAATTTGATAAGCTTAG	83340

genome mRNA	AATAAATTGTTGCTTCTTAATGTCATTTCAGAAGATGAATATTTATTAATAGATGCCAAC	83400

	rs3025849	
genome mRNA	TGAGATATCATTAATAATTGATTACTAATACTACTTGGAAAAGTCTCCCAGTTCCAAACT	83460

genome mRNA	TCAGCAGGCCTCTTGACAATTCAGCTGTGGTCAATTGGGTCTTGCCTGATAGATACAATG	83520

genome mRNA	ACCAATTGTGCAGCAGAGTGTGCTGCTTAGCTGCCTATTCTGTTAGCATTTCATGTGTAA	83580

genome mRNA	CTTAAAATCATAATCTCCTTAGTTTTGTTGAGTGTCTCCGTGGACAAGACACTGTGAGGG	83640

genome mRNA	ATACAAAATCAGATTGGCTTTATTCAAACCACTGGGGTATTATAATTCATTTATAATTTA	83700

genome mRNA	TTTTATTTTTTGCCTTTTTTCCATGTGTTCTAAAGGAATTAGAGTTTGTATATAACTATA	83760

genome mRNA	ATGGGGGATAGAAATTGACATGTGCCATGAAGGGAATGCAAAAAGTGCCGTGGGAGATG	83820

genome mRNA	AGAAGTGGAGAAAGGAATTTCTTTTTCTTGGAAGCAGGAATAACTTCATGAAGCATGTA	83880

genome mRNA	TTTCAACTTAAACAGATAGTAGGCAACGCTGTAAGGGGAGTATGGCTGCAGCAAAAGTGT	83940

genome mRNA	TCGGGGCAGACTGGGAGGAAGGGAGGGAATAAATTCAGCCATTGTTATGGAATAATGATC	84000

genome mRNA	AAAATTTATTTTCAGCCCGTTTCACTTAAAAGTTGAGACTGCTTAACTTTTTTTAATCTT	84060

genome mRNA	TAATCTTAACTTTTAAATGCCATTTGATCTTTAAAAATATATGTTTTAATAGTGTATTT	84120

genome mRNA	TAAGTCTCTATATTTTTGTTATTAGAATATATAGAGGCTATAACCTACTACCAAGCATAA	84180

genome mRNA	CAGACGTCCTATGGAAAATAACCTTTCAAGAGTTATTGCAGCAGTTTCTCATGAACTAA	84240

genome mRNA	TCACATCAACCACCAGAGCACTCACAGTAAGTCTCTTTCTTGATCGGTCTTACTGACATT	84300

genome mRNA	GTAATAGTTTTTGGTAGCTTGTATGGCCAGTTAGTTGTATGGTCATCTTACGGTGAGGTG	84360

Figure 1

genome mRNA	CTTGTCTTACAGCTCTTACTTATCCATGAGGCTTGCTAAGAAATTGTGCTTCTGTGAAAA	84420
genome mRNA	GAATCTCAGCTTACTCCAGGAATGTAAATGACTATGTTTTTTCTGATTATTAAAGTAATA	84480
genome mRNA	CACGCCCAAATAAAAAAATTCAGCCAATTTAGGAAGACACAACAATTAAAATAAGCCAG	84540
genome mRNA	GCATGGTGGCTCATGCCTGTAATCCCAGCACTTTGGGAGGCCAAGGTTGGGGGCTCACTT	84600
genome mRNA	GAGGTCAGGAGTCGGATACCAGCCTGGCCAACGTGGTGAAACCCCATCTCTACTAAAAAT	84660
genome mRNA	ACAAAAATTAGCTGGGCGTGGTGGCGGGCGCCTGTAATCCCAGCTACTCAGGAGGCTGAG	84720
genome mRNA	GCAGGAGAATCGCTTGAACCTGGGAGGTAGAGGTTGCAGTGAGCTGAGGTCAAGCCACTG	84780
genome mRNA	CACTCCAGCCTGTGCAATAGAGCGAGACTCTGTCTCAAAAAAAAAAAAAAAAAAAGAAAA	84840
genome mRNA	GAAAAAAGTAACTACTGTCACCTGCATTGGTAATGTATCAGAAGTTTAAATGTCTAGA	84900
genome mRNA	TTATAATTAACCTCAGTGACCTGGTAATATATACTAAGGGAAAAATATTTATAATTTACAT	84960
genome mRNA	TTTTACATTTTTATTTTTTTAATTTTATTATTTTTTTTTTTGAGACAGAGTTTTGCTCTTG	85020
genome mRNA	TTGCCCAGGCTGGAGTGCAATGGCATGATCTCAGCTCACCACAACCTCCACCTCCCGGGT	85080
genome mRNA	TCAAGCAATTCTCCTGCCTCAGCCTCCTGAGTAGCTGGGATTACAGGCATGCACCACCAT	85140
genome mRNA	GCCCCGCTAATTTTGTATTTTATAGTAGAGACAGGGTTTCTCCATGTTGGTCAGGCTGGTC	85200
genome mRNA	TCAAACCTCCCAACCTCAGGTGATCCGCCCTCCTCGACCCCCCAAAGTGCTGGGATTACAG	85260
genome mRNA	GTGTGAGCCACCATGCCTGGCCTTACATTTTTTATAATAAGAATTTATGTTGCTGACATTA	85320
genome mRNA	GAAAAGAACCATAATATCCAAGAATCCAAGAATAATTAAATTATGTACATATGCTAGTAT	85380
genome mRNA	ATAGTGTGATGCTTTGGAGAATTTTAAACAATATGGAGATGTATAATCTGGATTGTAATA	85440
genome mRNA	TTGAGTGAAAAAAGGCAGAATACAAACCTGGTGGGGGTATAGTCGGATTTTCAGTTAAGAA	85500
genome mRNA	AAATAATATTTACATATATACATTTCTCACACTGGCAGATAATCACCAAGATAAATTTTG	85560
genome mRNA	GGATTGTGGATGATTTTTTTCTTCTTTATATTTTTCAGATATTCTCAAATTTTCTAAAAT	85620

Figure 1

genome mRNA	GAGCAAGTATAACTTTTGTTCATCAGAAAAAATAATATACAAAAGTAATGTTAATTTGCT	85680

genome mRNA	GGTGACCAGGTAAACCTTTTTATTTTATTTTGTGAGATGGAATCTCACTCTGTTGCCC	85740

genome mRNA	AGGCTAGAGCACAGTGGCATGATCTTGGCTCACTGCAGCCTCCGCTTCCTGGGTCAAAT	85800

genome mRNA	GATTCTCTGGCCCCAGCCTCCTGAGTGGCTGGAATTACAGGCGTGTGGCACCACACCTGG	85860

genome mRNA	CTAATTTTGTATTTTGTAGTAGAGGTAGGGTTTCACCAGGTTGGTCAGGCTGGTCTCGAA	85920

genome mRNA	CTCCTGACCTCGTGATCCACCCACCTCGGCCTCCCAAAGTGCTGGGATTACAGGCGTGAG	85980

genome mRNA	CTACTGCGCCCAGCCAGACCTTTTTATTTTATTTGACAAAAGAAATACTTCCATGTTATA	86040

genome mRNA	GAAGACTAAATATTGTTTGGGCTGTCTGCAGTATGGTCTTCCCTTGATTGTTCAAAATA	86100

genome mRNA	TCGTAAACTTTGCTTATTTATTTTATTGTGGCCGACTGTGTCGGGCACTGTTGTAGGCT	86160

genome mRNA	TGGGATGGAAAAACAGGATTCCTGCCCTTAGGGTTTCTGCAGGCTGGTCAGGGAGACGAT	86220

genome mRNA	GTGGTAAGCTGGAGCTCAGCTCCTAAGGATGTGCAGGGGCAGTTGAGAGGCGGAAGGGTG	86280

genome mRNA	GGAGATCATTCAGGGTGTGGGCAGCACAGGAACCTCTCTTCATTGGGATATAATTGCCA	86340

genome mRNA	TTCTGATAACACGTGTTTGTAGGTGTCTAAAGTAGGAAGTTGTACCATGGTGGGACAGATA	86400

genome mRNA	TCCTGTGGTTATCATAACAGATCTCAGTTTTCTTCTCATTTGTTTGTACTTTTTATAAAG	86460

genome mRNA	GGTAACAGGAGATATAATTCAATAAACCTTTGTGGTGTGTTGGGTGTGATTTTATTGTTTC	86520

genome mRNA	TTTCTTCTCAGTTTGGATGCTGTGAAGCTTTGTGTCTTCTTTCCACTGCCTTCCCAGTTT	86580

genome mRNA	GCATTTGGAGTTTAGGTTGGCACTGTGGGTATGTATTTTCTCAGTATATATTAATAGTT	86640

genome mRNA	GTCTACAACAGTATGACATAAACATAGTTATTAGGATGCCCTTTTTCTTCTTTTAAAGT	86700

genome mRNA	CTTTTATCAATTTGGCTTTTGGAAAAATATCTGATGGAATACTTGTCTGCTATATTA	86760

genome mRNA	GCTGTGTGAGACTAGTGACAGGAGCTGTGGGAAATGAATGCCAAATGTTCTTAGGCATTG	86820

genome mRNA	ATGGGAATTTCAAGGTGTGGTCTTCAAGTTCATTTAAGGGAATTTTCATATGCTGGCAA	86880

Figure 1

genome mRNA	AGGCTTTTCTCATTAGCTTGACTCTTTCCAAAATTATTTGCTGTGAATTAGAAGTTTAGG	86940

genome mRNA	AACCTTTTTTTCACCTTAATTGTGACCTAGCATACGAAATGGTGATGATTTAGGAACTACTG	87000

genome mRNA	TTCTTGTATTAAACAGCTTTTATTTAAAAATGATTTTCCTCCAGTAGATGGCCCTACTAGC	87060

genome mRNA	ATCTGGGAAATAATTTCAAGTCTTCTCCAGCATTGAGGAATAGGCTTTCATTTTGTGTAT	87120

genome mRNA	CAATTACTGAGAATGATTTTGGTGACTCACATCACATTTGAGAAGTAAACCTGCAGATTT	87180

genome mRNA	CTTGTGTGTGTCAGCAAATGACCAACTGATATTTGCTTGAAGTGGATTACATTATCTGCT	87240

genome mRNA	CTAGAATGATTGCTTTCCACCTTCCTCACATACAGACTGAGCAGCTACGGTTTCTAATC	87300

genome mRNA	ATAGGTCTGGCACTAGACTTCACTTCTGGGCAACTTTGGCATTGGAGTAAAATGTATTAA	87360

genome mRNA	TTTAAAGAAAGTTAAAAATCCGTTCAAGTAAACATACAGTTCTAATACTTTTTACAATTT	87420

genome mRNA	AAAATATAGATTTAAATGATAAAATAAAAAAGAAAATATGGGTAGACACCATAATCCTCG	87480

genome mRNA	TTTCTGCATCTGTTTACAAGGGGTGATATTTATGAGTTCTATTCTCCATATCCATTCTA	87540

genome mRNA	TGTTCTCTTAATGCTCAGTCAGCACCTCAGGTGGTTGGAGTTCAATGCTTGGTAGTTTGA	87600

genome mRNA	CTTACACTGTCTTTTCTAGGGGATTGAGCCCTGGGTAGTCCTGCTTATTTGAGGTTGCAA	87660

genome mRNA	TTTGTCTTTCAATAACTTTTACTACAAGATATGGCGTGTTAAAGGATACCATTGGGGAAC	87720

genome mRNA	CAACATAATAATATCAGGAAAATAACCACGTCAGACCTGCCCCATTGTGTATCAAGTAC	87780

genome mRNA	ACTATTTTTCATAGTAATAAAGAGTTCACCCCAGCCAATTCTCTTTTATTTTGTGCCTG	87840

genome mRNA	TTTACTCAATGGCATTAAACATGCCCAAATGTCTGGGTAGCTGTCTCATCTCCAGTTCAGC	87900

genome mRNA	AGAACCATTGTCATATGCCCTAGTAAAGCATTTCCTTCATTGGACACTTAGGCCCAATA	87960

genome mRNA	CTTTCATTGAGATCTACTACCTGATTTTCATTTCTCAAATGATTTTATGGAGCTCTGATT	88020

genome mRNA	TATAGGAAAGATGTTAGTTGATTAAAAATAAAACAATTTCTGAGCTGGTATAAAATGTAT	88080

genome mRNA	TGTGACATGCCTTCCTCTTGGAATTGCAAGAGAAAGGAAGACTGTTGTTTGCTTAAAAAT	88140

rs6855981

Figure 1

genome mRNA	TGTCTATAATTTGACTTTGCAAATGTCTGCTTCCAGAGTGCCTCCACTGAGTGCCTCAGA	88200

genome mRNA	TGAGTCTAGGAAGAGCTGTACCGTTGGGATGGCCACAATGATTCTGACCCTGCTCTCGTC	88260

genome mRNA	AGCTTGGTTCCCATTGGATCTCTCAGCCCATCAAGATGCTTTGATTTTGGCCGGAACTT	88320

genome mRNA	GCTTGCAGGTACTGGTACTGAGTTGAAACAGGGACTCCAGGACTTGGATTTTGATTTTCCT	88380

genome mRNA	TAGGGGGAATGGGGGTGGTGAGCATATGAGGGGAAAATACTATAAGGTCATTGCCAGTGA	88440

genome mRNA	TGGCTTGTCCTTTAGTCAAATTTGAGATGTTACCTATATGCATAAACACATGCAGTTGG	88500

genome mRNA	CAGCTGTTCTGTGCTGAGTATTTTAAAGTAGCCTCTTCCCAATATAGCCCCTCAGTTAAC	88560

genome mRNA	TACAAGTAACTCATTTTGAATTTTCAATTTAATGGGCACCATATGCCAGTACTCCCTCGG	88620

genome mRNA	GCACTGGGATGTTAAGAAAGTATAATGTATGGACTTCATTCTCAAGTTAAGTTTATAGATTA	88680

genome mRNA	GAGGGGGATACACGTAAACAAAAGTGCAGTGGTCACACAGAGTGGCCCTAATCACTCTCC	88740

genome mRNA	TTGGGCAGATTTATGGGCTGGTAGGAAAGAGCACAAACACGGAGAGGGTGTAGCACCTTGG	88800

genome mRNA	CGATGATAATGGAGGATGTGGCCAGCAAGGAAGACGGAGTCCATTGAAATTGATTTTGGG	88860

genome mRNA	AGAAGTTGCCAATCTCCATGAAAGAATTGGGGCCTGTGCTATTTGCTTCAGGGGGCTATA	88920

genome mRNA	GGAGAGTTTCGTGAAAGGGACTAAAAGATGAGTATTTTAATAAGATCATTCATCCAACCTT	88980

genome mRNA	GAACATGGGCTGGAGGAGAAGGTAGGGAGACTCAGGAGATTAATGTTGATGCTAAGGCAA	89040

genome mRNA	GATAATGGCTTTGGGACTGTAGGGAAGACACTGATTGTAAGAGAATGAAGGAGGCAGAAT	89100

genome mRNA	TGCCAGGCCTGGTTACCAACTGAACTTCGGTTGTGAAGACAAAGAAACCTGGGATGACT	89160

genome mRNA	TCACATCCTGGGCAGGTGTGTGGTGGTGACAGTCATGGAAATTGGGAACACAGATTTGTG	89220

genome mRNA	CGGGAAACATCAGTTTCAGTTTGAGTTTGGCTTATCAGTTGAATATCAGGCACAGATGTC	89280

genome mRNA	TGGCCAACTCTCAACATAGGGTCTTAAATGACTTCAGTTCCCCAAGCAATTTGTCCTTCC	89340

genome mRNA	CATGCTATTGGGGTGGAGAGGTAATGTCTGTGCCCATATCACAGCCAGTGCTCCCAAATC	89400

Figure 1

genome mRNA	TCTGAGAAGTTCATGGGCCTCTGAAGAAGAAGCCAACCCAGCAGCCACCAAGCAAGAGGA	89460

genome mRNA	GGTCTGGCCAGCCCTGGGGGACCGGGCCCTGGTGCCCATGGTGGAGCAGCTCTTCTCTCA	89520

genome mRNA	CCTGCTGAAGGTGATTAAACATTTGTGCCCACGTCCTGGATGACGTGGCTCCTGGACCCGC	89580

genome mRNA	AATAAAGGTAATGTCCCACTTGGGTGCTGGATTACATACAGCCTTAATGACTATGGGTTTC	89640

genome mRNA	CAGACTACCTTTGTTTAGTAATCTGTCCCTTCTTTATTCTCTTTTGCTTTAAATGAACA	89700

genome mRNA	AAATTGCTCAGATTGTGACACTAAATTTAACATCAAAATGTGACCATGTGGATGGGTGCA	89760

genome mRNA	GTGGCTCGTGCCTGTTATTCCAGCACTTTGGGAGACTGAGGCAAGTGGATCACTTGAGGC	89820

genome mRNA	CAAGAGTTCGAGACCAGCCTGGGCAACATCACGAAACCCCTCTCTACTAAAAATACAAA	89880

genome mRNA	AAATTAGATGGGTGTTGGGCCGGCGTGGTGGCTCAAGCCTGTAATCCCAGCACTTTGGGAG	89940

genome mRNA	GCCGAGGTGGGCGGATCACGAGGTCAAGAGATCAAGACCATCCTGGCTAACACAGTGAAA	90000

genome mRNA	CCCCGTCTCTACTAAAAATACAAAAAATTATCTGAGCATGGTGGCGGGCGCCTGTAGTC	90060

genome mRNA	CCAGCTGCTCGGGAGGCTGAGGCAGGAGAATGGCGTGAATCCGGGAGGCGGAGCTTGCAG	90120

genome mRNA	TGAGCCGAGATCGTGCCACTGCACTCCAGCCTGGGTGACAGAGCGAGACTCCGTCTCAAA	90180

genome mRNA	AAAAAAATTAGATGGGCATGGTGGTGCGTGCCTGTAATCCCAGCTACTTGGGAGGCTGAG	90240

genome mRNA	GCAAGAGAGTTGCTTGAACCTGGGAGGCGGAGTTTGCAGTAAGCCTTGATTGTGCCGCTG	90300

genome mRNA	CACTCCAGCCTGGGTGACAGAGTCAGACTCTTTCCAAAAGAAGAAAAAATGTGACCATG	90360

genome mRNA	TGTTTTATAGCTCTTTTAGTATCATCAGTCACTGTTATCCCTAAGAGGGAAATACCTAGC	90420

genome mRNA	TTTAGTTTTAGGTTTCCAGCATTAGCCAAGAAAGCTCAGAATTGATGTTTCCTGGCCAAGT	90480

genome mRNA	ACCTCATTGCTGTCTCCTTAAATCTTGGTTAATGGCTACTGTCCTGGCTAGCATAGTTAT	90540

genome mRNA	GGAGCATTTCCATGGTTGTAGAATGTTCTGCCAATCTCAGGGACAGTTTTGCTTTTCTGT	90600

genome mRNA	GAAGCAATAAAATCAACTTCAAAACAAATGTTAACTATTTGTACAATGGATTTAAGATAG	90660

Figure 1

genome mRNA	ACCAGTTCACATACTTTTTTTTTTTTTTTTTTTTTTTTGAGATGGAGTTTCATTCTTGTTGCCT	90720

genome mRNA	GGGCTGGAGTGCAATGGTGTGATCTCAGCTCACTGCAACTTCTGCCTCCTGGGTCAAAC	90780

genome mRNA	GATTCTTCTGCCTCAGCCTCTCGAGGCAGATTACAGCTGGGATTACAGGCATGCACCACC	90840

genome mRNA	ACACCCAGCTAATTTTTTTGTAGTTTTAGTAGAGACGGGGTTTCACCATGTTGGTCAGGT	90900

genome mRNA	TGGTCTCAAACCTCCTGACCTGAAGTGATCTATCCGCTTCGGCCTCCCAAAGTGTTGGGAT	90960

genome mRNA	TACGGGCATGAGCCACCACGCCAGCCTAAGATAGACCAGTTCACCTACTGTTTATATCT	91020

genome mRNA	GATTACTCTCTCTTTGCCTTGTCTTCTACCTTTAAAAATCTCCCTACTAACTTCCCATTCT	91080

genome mRNA	TCCTTTAGCTGCCATCAGTCTTCTCCCTTCTCTGCAAACATCTCTGGAGAGTCCCAGCCT	91140

genome mRNA	CAGCCCACAGAGCTTCCCAGTCTGCTCTGAGGTGGACCTTGTTTGCAAGGCTTCTTTGGCTC	91200

genome mRNA	TCTTGGCCTGGACCCTGTCTACTACTTCAGCCATCCTTCCTTAACCCCTGCTGGTGGTTT	91260

genome mRNA	CTGTTGCCACACTCCATAGCAGCGTTTCCCGCCCAGATCATGTCTTTACATCTCTGGGCA	91320

genome mRNA	CTGCTCTGGTCCTGCCTGCCTTTCCTCTTTGTATCCTGCAGGCTGCTACCCCCATCTTG	91380

genome mRNA	AGTGTCTCTTTCAGTTGGCTTTCAGAGGGCCTCCTGGGTGTTCCCTTACCCACTTGCCAC	91440

genome mRNA	rs11731237 TCCCCAGTCACTGGGTTCAGTCCTTCTGCCCCACCAGCACATGCTTTCTAGGCTCTGTCC	91500

genome mRNA	TAGGCCGTCTTCTCTCTTTGTAGTCTCTGGGCCAGTGCTGTTCTAGAGAGTGGCAGAATT	91560

genome mRNA	TTCTATAACCATGGCAGTGCTCCATAGCTATGCCAGGCAAGACAGTAGCCACTAAACACA	91620

genome mRNA	TATAGCTGTTGAGCCCTTGAAATGCAGCTAGTGTGACTGAAGAACTGAACCCCGATTTCGG	91680

genome mRNA	TTTAATTTTCATTAAATTTAAATTTAAATAACCTTATGTGGGTAGTGGCTCCAGTATTGG	91740

genome mRNA	GCAGGGCAGCCTGAGAGTCGGGGCTGTTCTCCTGTCTTCAGTGTCTAGATGAGGGACCTC	91800

genome mRNA	AGAGGACCTGTCTCTGGAGCTGCAGTTCAATGTAGCCAGCTGCCCCGTGACACTTACATA	91860

genome mRNA	TAGCTGATTTGTGGATATGTCAGACACGGTGTGATGAGCTCAGCTTTCTGTCCTCCTCCC	91920

Figure 1

genome mRNA	CACATCTGCCCCTGCCCCATTTACCCCACTTTGTGTCTTATCAAGCTAGAAACAGGTCAC	91980

genome mRNA	CACAAGTCTTCATTTCCACTCACCAAGTCTTTTGTTCCTTAAATATTTTGCGAGA	92040

genome mRNA	AGAAAGTGTGTACCTTTGTATTACATACATGTACATGCACATATACATGCACATATGCA	92100

genome mRNA	GGGGTCCCCAACCTCTGTTAAAAACCGGACTGCAGGCCGTGCGTGGTGGCTCACGCCTGT	92160

genome mRNA	AATTCAGAACTTTGGGAGGCCGAGACCAGTGCATCACAAGGTCAGGAGATCGAGACCAT	92220

genome mRNA	TCCGGCTCACACGGTGAAACCCCGTCTCTACTAAAAATACAAAAAAAAAATTAGCCGGGTG	92280

genome mRNA	TGGTGGCGGGCGCCCATAGTCCCAGCTACCTGGGAGGCTGATGCAGGAGAACGGCGTGAA	92340

genome mRNA	CCTGGGAGGCGGAGCTTGCACTGAGCCGAGATTGTGCCATTGCACTCCAGCCTGGGCGAC	92400

genome mRNA	AGAGCGAGACTCTGTCTCAAAAACAAAACAAAACAAAAAAAAAAAAACCAGGCTGCACA	92460

genome mRNA	GGAAGAAGTGAGCAAGCATTACCATCTGAGCTCTATCTCCTCTCAGGCCAGTGGTGGCAT	92520

genome mRNA	TAGATTCTCATAGGAGCGTGTATGAGTTCGTTCTCACACTTCTGTAAAGACATACCTGAG	92580

genome mRNA	ACATATAAAGAAAAGAGGTTTAATTGGCTCACAGTTCTGCAGGCTGTACAGGCTTCTGTT	92640

genome mRNA	TCTGGGAAGGCCTCAGGAACTTGCACTCATGGCAGAAGGTGAAGGGGAAGTAGGCACAT	92700

genome mRNA	CTTCACATGGCCACAGGAAAAAGAGAGAAGGAGAGAGAGAGAGACAGAGAGAGAGAGAG	92760

genome mRNA	AGAAAAAGAAAGATTGAGAGGGAGAGAGAGGAGGGAGAAAGGAGAGTGCCTGTAGGGGGAGT	92820

genome mRNA	TGCTACACAAAGGAGCACCAGGGGGATGGTGCTCAACCATTAGAACTACCCCATGATC	92880

genome mRNA	CAATCACCTCCCACCAGGCCCCACCTCCGACACTGGAGATTACAATTCAGCATGAGATTT	92940

genome mRNA	GGGTGGGGACACAGAGCCAAACCATATCAGAGCATGAACCCTATTGTGAACTGCACATTT	93000

genome mRNA	GAGGGATCTAGGTTGCATGCTCCTTATGAGAATCTAATGCCTGATGATGATTTGAGGTGG	93060

genome mRNA	AACAGTTTCATCCCGAAACCATCCCCCGCCAACCCTGGTTTGTGGAAAAATTGTCTTCCA	93120

genome mRNA	CAGAACCGGTCCCTGGTGCCAAAAAGTTTGGGGACCTCTGCACATATGCATGCACCTGTA	93180

Figure 1

genome mRNA	CATGGACACATAATACATGTACATATGCATACTTTATATTCTCTGCCACTTCTGGTCCAG	93240

genome mRNA	ACTGATATACTATCTCATTTGGATTACTGCACTAGCCTTTTGTGTTTGGAAACAGCATTTT	93300

genome mRNA	TTAAAAAATTTAATTTAATTTTTTTTGAGATAGGGTGTCATTCTGTTGCCAGCTTGGAGT	93360

genome mRNA	GCAGTGTCATGATCATAGCTCACTGCGGCCTCGATCTCCCAGGCTCAAGTGATCCTTCTG	93420

genome mRNA	CCTCAGCCTTCTCAGTAGTTGGGACTACAGGCATACCCACCATGCCAGCTAATTTTTTTG	93480

genome mRNA	ATTTTTTTTTTTTTTTTGAGACAGAGTCTCAGCCTGTCGCCCAGGCTGGAGTGGGTGGCG	93540

genome mRNA	CGATCTCAGCTCACTGCAACTTCTGCCTCCCAGGTTCAAGTGATTCTCCTGCCTCAGCCT	93600

genome mRNA	CCCGAGTAGTTGGGATTACAGGCGCTGCCACCACACCCAGCTAACTTTTGTATTTT	93660

genome mRNA	GTAGAGACGGGGTTTCACCATGTTGGCCAGGCTGGTCTCGAACTTGTGACCTCGTGATTA	93720

genome mRNA	GCCCGCCTCGGCCTCCCAAAGTGCTGGGATTACAGGCGTGAGCTACCGCTCCCAGCCAGG	93780

genome mRNA	AAACAGCATTCTTGAGATAATTCATATAATTCACCCATTTAAAGTATATAATTCATTCTC	93840

genome mRNA	TTTAGTATGCCACAGAGTTGTACAGCCATCACCAGAATCAGTTTTAGAACCCATAAAGG	93900

genome mRNA	AACTCTGTACTCTTTACCCAAAACCTCCATGCCTCCAGCTGCAGGCAGCCACTAACCTGC	93960

genome mRNA	CTTCTGTCTCTGTGACTCTACGTCTTCTGGACATTACTGTGGATGGGCTCATACAGTCAG	94020

genome mRNA	TGAGCTTGTGACTGGTGCCTTCTACCAAGCAGGGTTTTAGTGTAGCAGCCTCTCTGTTT	94080

genome mRNA	TTCTTTTTTTTTTAAATTGTGACGGAATTCTGCCTCCCGGGTTCAAGCGATTCTCCTGC	94140

genome mRNA	CTCAGCCTCCCGAGTGGCTGGGACTACAGGCCCATGTCACCATGCCTGGCTAATTTTTTTT	94200

genome mRNA	TTTTTTTTTTTTTTAGTAGAGATGGGTTTCAACATGTTAGCCAGGGTGGTCTCGATCTCCT	94260

genome mRNA	GACTTCATGATCCGCCTGCCTCGGCCTCCCAAAGTGCTGGGATTACAGGCGTGAGCCACC	94320

genome mRNA	ATGCCCGGCTAACCTTTCATTTACTGTCTGCATTTCTTCCCTGATGCCTTCCAGTCCATG	94380

genome mRNA	CACCCGATTGTAGCCATTATCCTATTATGGTTTAAGGTGACTGTCTTAGTCAGCATGGG	94440

Figure 1

genome mRNA	TTGCCATAACAAAATACCATAGCCTGGGTGGCTTCAACAACAGAATTTACTTCTCACACT	94500

genome mRNA	TCTGGAGGTTGGGAAGTCCAAGATCCAGGACTTTCGCCTTGCCCTCATGTGGTGAGGGGG	94560

genome mRNA	TGAGGAAGCTCTGTGGGGCCTCTTATATATGGATGCTAATCTCATTCATGAGGGGTCTGC	94620

genome mRNA	CCTCATGACCCAGTCACCTCCCAAAGGCCCCACCTCCTAATACCATCACCTGGTAATTA	94680

genome mRNA	AGTTTCAGTGTATAAATTTGGGGGACTATAGACATTGAAACCATAACAAGCACTTTTCTA	94740

genome mRNA	AGATCAGGGAGTGAGTAAGTAGCAGAGCTAGGACCTCAATTCACATGTCAGTCATCTTG	94800

genome mRNA	CCTTCACTCTGCTCCATGATGGCTGCCTCCTAGAGCATTGGGAGTCTCGATGTTCTATAT	94860

genome mRNA	GCTCTCATGTGTTGTGTATTGGAGATAGTTGAGGCTTTATGAATACATCTGGATTGTGTTG	94920

genome mRNA	ACTTCTAGCTTTGCTGGTAACCAGCTGTGACCTTGAATAAGTTACTTCATCTCTGAGCCT	94980

genome mRNA	GTTTCCTCTTTTAGAAACAGGAGTTTAAAATGCTGCTTTGGGTGGGCACGGTGGCTCAT	95040

genome mRNA	GCCTGTAATTCAGCACTTTGGGAGGCTGAGATGGGAGGATCACTGGAGCTTGGAGTTCG	95100

genome mRNA	AGACCAGCCTGGGCATCATAGTGTGAGATCCTGTCTCCTCAAGAAATTAAAAAATTAGCT	95160

genome mRNA	GGGTGATGTGGCGTGTGCCTGTGGTCCCATCTACTCTGGAGGCTGAGGTGGGAGGATTGC	95220

genome mRNA	TTGAGCCCAGGAGGTTGAGGCTACAATGAAATATGATTGCACCCCATCCTGGGTGACGAG	95280

genome mRNA	TGAGACCCTGTCTCAAAAAGAAAAAAAAAATGCTGCTTTGTACCCCTTTCATGTCATGG	95340

genome mRNA	CGTCATGGCCAACATAGAATGCCCTGGTTGTTTGCTGTTGGAGGGCATGGGCCTGGGGGC	95400

genome mRNA	TCCCTGAGGGCTCCTTCCATCTTCAACTCATCTCTGTGCACCTGTTAGGAAGTTGTGGG	95460

genome mRNA	CCAGTCCCTACCATGTATCATTGTGTGGGTAAAAGTAAATAAAATGTGTACAGTGTCTGA	95520

genome mRNA	ACTGTACATATCAGGGTCCAAGAACAAAATGAGTGACATGGGTAGCTCTTTTAAATAAA	95580

genome mRNA	TGGTAAAACCAAATATTCTAATTTTCAGTTTTGTTATACTTCCATCACATGTTTTTGT	95640

genome mRNA	TTTTGTTTTTTGTTTTTGTCTTTTCTATTTTAGGCAGCCTTGCCTTCTCTAACAAACCCCC	95700

Figure 1

genome mRNA	CTTCTCTAAGTCCCATCCGACGAAAGGGGAAGGAGAAAGAACCAGGAGAACAAGCATCTG	95760

genome mRNA	TACCGTTGAGTCCCAAGAAAGGCAGTGAGGCCAGTGCAGGTAGGAAACAGCGTGGGGAAG	95820

genome mRNA	GGAGGGACATGAGTGCAGCATCTGTCATGTAGAAACATAGGATTTAAGTAACTTGGTGTT	95880

genome mRNA	TTAGAGAAATAAATATAATACACATCAGTAAAGTGAGAGAAAGTTTCTCCAGGTGCGGTT	95940

genome mRNA	CAAGATATTAGAAACTAATGACTGATGTACACAGACCACCTTTTGGTCTGAAGCATTCT	96000

genome mRNA	AAGTGCCACTGGCTGACATGCAGCCCCTACAGCCTCCAGGCTTCCAGCCCTAGCATGGAG	96060

genome mRNA	CATCACTCTCCTATGCTTCCCTGGTTGCAGGTGATGGCTGGAGAGGCCTCCTGATTTTCA	96120

genome mRNA	GTAAGGGAAGTGGTGTAGATGCTTAGGAATAGATGTAGTGAGTGAAAAAACTGATTCTGA	96180

genome mRNA	TATGTCAAAAATTCTGATTGGAAATGGAATATTTACATTTGGAAGAGCTAAAGGCGAGAG	96240

genome mRNA	AAAGTGGGGATAAAGTCATCTGAGTTGGAGGAGCTTAAACCATTACAAAGTTTGGAGGAC	96300

genome mRNA	CTTTTTTTACCCATGAAAAGGTCAGAACAGAAGGGGCTAGGATTTAGGTGTGACTGCAGT	96360

genome mRNA	TTATTGAATTCCCATCCATACTGCTCTCGGTGGGCAGTGGCAGGGGCAGGAGAGGAGCCT	96420

genome mRNA	GGCAAAGCATGAAGTGACTGCTGCTGCCTCTGCTATCTGGGACGCCTGGCCACCTGTCTG	96480

genome mRNA	TACAGTCTCCCTCCAGACCCATTCTCACGCTGTCTCTTGGCACCCAGGGGCCAGTGATGG	96540

genome mRNA	TTCTCCCATTTGTTTTGTGTATATAGCATTTATATCAAGGCTATTTATTTATTTATTTAT	96600

genome mRNA	TTTATTTATTTATTTTTTTTGGAGACAGAGTCTCACTCTGTCACCCAGGCTGGAGTGCAGTG	96660

genome mRNA	GTGCAATCTCGGCTCAGTGCAAGCTCTGCCTCCTGGGTTCAAGCAATTCTCCTGCCTCAG	96720

genome mRNA	CCTCCTGAGTAGCTGGGACTACAGGTGTGCACCACCACACCTGGCTAATTTTTTGTATTT	96780

genome mRNA	TTTATTAGTGGAGACGGGGTTTCACCTTGTTGGCCAGGATGGTCTTGATCTCCTGACCTC	96840

genome mRNA	GTGATCCGTCCACCTCAGCCTCTCAAAGTGCTGGGATTACAGGCATGAGTCACTGTACCC	96900

genome mRNA	GGCCTATTTATTTATTTTTTAATTGACAAAATTGTATATATCTGTAATATACAACATGATG	96960

Figure 1

genome	TTTGAAATATGTGTACATTGGCCAGGCGTGGTGGCTCACACCTGTAATCCCAGCACTTTG	97020
mRNA	-----	
genome	GGAGGCTGAGGTGGGCGGATCACGAGGTCGGGAGTTCAAGACCAAAGTGGCCAGCATGGT	97080
mRNA	-----	
genome	GAAATCCTGTCTCTACTAAAAATACCACAAAAAAAAAAAAAAAAAAAAAAAAAGCCGGGCAT	97140
mRNA	-----	
genome	GGTGGCTCGCGCCAGTCGTCCCAGCTACTTGGGAGGCTGAGGCAGGAGAATTGCTTGAAT	97200
mRNA	-----	
genome	CTGGCAGGTGGAGGTTGCAGTGAGCTGAGTTCATGCCACTGCACTCTAGCCTGGGCGATA	97260
mRNA	-----	
genome	GAGCGAGACTCCGTCTCAAAAAAAAAAAAAAAAAAGAAGAAATACATATGCATTGTGGAATG	97320
mRNA	-----	
genome	GCTAATTAACCTGTGCATCACCTCACGTATCATTTGTTTTGTGGTGAGAACTTAAAATC	97380
mRNA	-----	
genome	TACTCTTTCAGTGATTTTCTTGTCATATGGTACATTGCTATTAAGTGCAGTCACCATGCTA	97440
mRNA	-----	
genome	TACAGTAGATCTCTTGAAGTCATTCCTCCTGTCTATAAATGAAATTTTGTATCCTTGACC	97500
mRNA	-----	
genome	AACACATTCAAGGTTTTTTTTTGAGATGGAGTCTTCTTCACCCAGGCTGGAGTACCATGGC	97560
mRNA	-----	
genome	ACGATCTCATCTCACTGCAACCTCCGCCTCCCAGGTTCAAGCAATTCTCCTGCCTCAGCC	97620
mRNA	-----	
genome	TCCTGAGTAGCTGGGATTACAGGCACATGCTACTGCACCTGGCTAATTTTGTATTTTTA	97680
mRNA	-----	
genome	GTAGAAGTGGAGTTTCACCATGTTGGCCAGGCTGGTCTCGAACTCCTGACCTCAAGTGAT	97740
mRNA	-----	
genome	CCGCCTGCCTTGGCCTGCCAAAGTGCTGGGATTACAGGTGTGAGCCACTGCACCCGGCCT	97800
mRNA	-----	
genome	CAAGCGTTTTAAAGATGCTCTTTTCTAAGGATTGACTGTAGTACAGGAGGAAGATTGAC	97860
mRNA	-----	
genome	CTGTTGAAAAGCCTCAGCCTTTACAAGTGTAATAATTATCAGTATATTACTATCATCTTTC	97920
mRNA	-----	
genome	TGATGAATTAAATAAACTAAGGACTCCAAGTCAAAAGTCTTCAAAGTGAAGTAGAATAGT	97980
mRNA	-----	
genome	TGTATATAGTGCTTGGCACTTTAATATTTAGTATCGGTTTAATGATAATGTTTGTGCCTT	98040
mRNA	-----	
genome	TGCCGTCTTTAAACATTTTTACATCATCCCTGTTTGATTACTTGGTGTGCTCATGAAGT	98100
mRNA	-----	
genome	TGTTGGCCACTAAGGAATCTTAGGCTCAGAGAGGTTCTGGAATTGGCCAGTGGTCCTTGA	98160
mRNA	-----	
genome	ATCAGCTGCTCCTATGATTCTCTAACTGATTTCTCACAAAGCAAACAAGCAATCATAACA	98220
mRNA	-----	

Figure 1

genome mRNA	AAACAACTGTGCACACTGCTCTTCTTATTTTGTATTTTAAAAAGTACTTAGGCTCTACTT	98280

genome mRNA	ATGTTTGTTAGTCAATTTCTCATTACTTCTAGTTAATCAAAAGGTCAGAGGAAATACTTG	98340

genome mRNA	AATATTTTCATACTAGAACTTTTAAAAAATCATGATTTCCAGTAATCTCTTTAAACTT	98400

genome mRNA	GGCAAGTTATTTTGATCTAAAAGTTTATCTTTTGTGTGCATATTTTAAAGCTTCTAGAC	98460

genome mRNA	AATCTGATACCTCAGGTCCTGTTACAACAAGTAAATCCTCATCACTGGGGAGTTTCTATC	98520

genome mRNA	ATCTTCCTTCATACCTCAAAGTGCATGATGTCCTGAAAGCTACACACGCTAACTACAAGG	98580

genome mRNA	TATGGGCCTCTGCATCTTTTAAAAATATATATGCACACATACTTACGTCTAATGGATAGT	98640

genome mRNA	TGATGTTTTTCTTATGATTTGTAGGATGTATAAGCCCTTTGAGATATGAGTTACATTTAG	98700

genome mRNA	TTTTTTCAAGTTTGTGTCTTTCAGCTTTGTTTATGATAGCTTCTATCATACAGGTGTT	98760

genome mRNA	TTGGATTTTTCATATTGTTTGTACTCACAGCTAAGATTGATTACAGTGACAGAGCTAGGAT	98820

genome mRNA	GTGCAGCCAGGTTATAGGGGGAAGTGGCCCTGGTGGAGTCTGGAGGGATCCGTGTACAGG	98880

genome mRNA	CTTCCTTCCCTCCCGTGAGGCTCACACAAAAATACAGCAACATGCTGGTCCTGCAGGTAC	98940

genome mRNA	CCTCTGCCTAACATGAGCCACAATTCCAGACTCACAGAAGAAAAGCAGGTGTTTCGGCATA	99000

genome mRNA	AACCATGTGTTTCAAATAGTCTGGGCATGGTGAGCCACTTGTTATCAGCTAGGGAAAGTT	99060

genome mRNA	TATGTCAGCGTAAGAAACTGTTACCAGATACCCCCAAGAGCCAGCCTTTCTGTCTAGGG	99120

genome mRNA	ATGTTTTAGTTTTTTAGTTCATTTTTTTTTTTAACTTTAAAATTTTCTGTTTCATCTGCAA	99180

genome mRNA	TTTGTTAGATATGAAGTATGTGTCTAATTTAATTTTGTGTTTTGGTTGTCCCCAATAATG	99240

genome mRNA	TTTACAGAAGAATTTTCTGCACTAATTGGCTTGAGTTACTTACATTCTCATAGTTCTCT	99300

genome mRNA	AGTTTCAGTAGTTTCATTTATTATTTTGTATATCAATCTATCTGTCTGCTCATCTATTA	99360

genome mRNA	GAAGCATCCTTGTTTTTTTTTTTTCTTTTTTAGACAGAGTCTTGCTCTGTCCCCAGGTTG	99420

genome mRNA	GAGTGCAGTGGTGCAACCATGCCTCCCTGCAGTCTCAGGGCTCAAGTGATCCTCCCACCT	99480

Figure 1

genome mRNA	CAGCTCCTGAGTACCTGGGACTACCGGCATGTGCCACCACACCCAGCTAATTTTACATT	99540

genome mRNA	TTTTGTAGAGACAGGGTCTCCCTAAGTTGCCTGGGCTGGTCTCAAGCTCCTGGCTTAAGT	99600

genome mRNA	AATCCTCCCTCCTTGGCCTCCCAAAGTGCTGGGATTACAGGTGTGAGCAACTGCACCCGG	99660

genome mRNA	CTACAAGTATACTTCTTAATTATTGTAGCTTAATGGTATTTATGAGGGGATCAGTTCCCC	99720

genome mRNA	TGTTGTTCTTTAGAATTTTCTGGATATTCTTCTTTATTGATTTTGGGATGTGAACAATAG	99780

genome mRNA	AATCAACTTCTACTTGTAGATTGATTTAGGGAGAACTTATACCTCAGATGTTAAGTCACC	99840

genome mRNA	CTGTCCAGAATGTGGGATGCTTTCCTATTTGTTTCAAGAACTTTTAAATTACCTCAGAAGC	99900

genome mRNA	ACATGAAATTTAAAGGATTTTAAAAAAACTTAAAGATTATTTACATAGCTCTTGCACA	99960

genome mRNA	TTTCTTGATAAATGAATCCTCAGGTATTCCTCTGTTTTTGTACTAATAGTTACTTCTTA	100020

genome mRNA	TGGGTTTTTTTTCCCTGAAAATCATTTATCAAACGTATGTGGCTTATTTTCTGAAGGAT	100080

genome mRNA	GTTTGATAATTTTGAAGATATGAAAGTCTTCATATTTTACAAGGTTTGAGGTCTCTTTA	100140

genome mRNA	AGCTGCATGGTTCTCATGTCAGCTCCCAAAGCAGAAGACGGCATGTTGAAAAATGCCGTA	100200

genome mRNA	GAGAAGATACTTCTTTTCCACCTGTTTTCAACTCATATCATCTTGAATTTCAAGGCACCT	100260

genome mRNA	TTCCATGCTCCTAGTGCTTGCTATCTGTTTATTATTTTCTTCCTGAATACCCTGAACTC	100320

genome mRNA	CAGCATGTTCTGCTGTAATTCTGGCCTCCCTGGCATCTTGGACTCCTGTTTCCTTTGCTC	100380

genome mRNA	TGTCATCCCCGCGGTCAGCTCCTGCTGCGCAGCTTCTCAGCTGAAGTGCGTTTGGAGTGC	100440

genome mRNA	CTGGCGTGTCTTGCTGGATCTTTGAGTATTGCCTCTGGTTTCCTTGGTTCCTTCTGCTGA	100500

genome mRNA	GTTGCTCAGCGTCTCCACTCCCCATTTCTTGTGTGGCCCTTCCTGCACTCCTCTGATTCC	100560

genome mRNA	TTTTGTCTTCCCTGGTTTCTTGCTTTGGTTTCGAGTCTCCACAGAACTTTTGCAGCTCTT	100620

genome mRNA	CTGAAGACCTGGAAGCTTTTTCATCTTAATTCTCATCTCATGACCTCTTTTCCCTTCTTT	100680

genome mRNA	GAGAGCTAGAACTTCCCATGGTGAACCTCTCTTTCCAGAATTCCATGCCTTCTTTTCCCT	100740

Figure 1

genome mRNA	CCCACCTTACCTGTTGTCCAGGAGAGGTCAGATTGCTGTGCATATTGGAGGAGAACCCTTT	100800

genome mRNA	CTTCCCTGGGCTCTTCATCTCACATGACATCACCACATCACCTCGTTCCTTGGACCCTCA	100860

genome mRNA	GTGGTGTCACCTGCTGGATTTTTCTTTCCTTTGGCTGGCCTTAGGGCACACCCAGGTTGAC	100920

	rs363144	
genome mRNA	TAGCGTAGTCATGGTATTTAGATCCACTCACATTTTCAGTTTCTGTGTCTGTCTCTTGCC	100980

genome mRNA	TGCTTCTGACTTCGCCCAGAGAAAGCTTCTCTTTCACAAGGGTTCTTAGATTTATGTTCA	101040

	rs3025838	
genome mRNA	CTGAGCACCTTCTTTTCTGAGGCAGTGTTTTACCAATATTTATTTTCCTAGTCAGTCTCG	101100

genome mRNA	CCTTACCTTTCTTGTTATGCATGTCTTTGGTCCTGACCCATTCTCTGAGTCTGTAAAATA	101160

genome mRNA	GAATTGCTGTATAATTTAATTACATGAAATCCTTTAGAATCTTAACACATCTTACACCTG	101220

genome mRNA	ATTTAATATTTTATTGTATCCAAATTGAACCAACCCTATGTGAATTTGACAGTGATTTCT	101280

genome mRNA	CCCAGGGATCCTAGTGTATAAGGAATAGGACTTAGTATTTTCTATTTTTTGATATACCAC	101340

genome mRNA	ATACCAGATACTGATTATGATGGACATTTAACCCTTTTTTCTCATTATGAAAGAAAGTTA	101400

genome mRNA	GGAATTATTTCTTCCAGTAGCGCCAGTGTAACCTGAAAGCCTTTGAAAGAGTAGTTTTTG	101460

genome mRNA	TATAGCTATCTGAAAGGAATTTCTTTCAAAATATTTTTCCAGTGCTGACAACAAACACG	101520

genome mRNA	CAGACACACCCTGCAAGGTGAGTGACGGCGCCGCACAGTGGAGGCATCTGCTGCAGCCG	101580

genome mRNA	TCGATGTTTGTGTCTTTGGTTGTACATTATGAGATCGTGACAGGGCCAGTAACCGTGTGT	101640

	rs34315806	
genome mRNA	TCTCTCCTTCACCTTCCCAAGGTCACGCTGGATCTTCAGAACAGCAGGAAAGTTTGGA	101700

	rs363099	
genome mRNA	GGGTTTCTCGCTCAGCCTTGGATGTTCTTCTCAGATACTAGAGCTGGCCACACTGCAG	101760

genome mRNA	GACATTGGGAAGGTTTGTGTCTTGTTTTTCTCCTTGGGTTGTGGCTGGCACACTTGATG	101820

genome mRNA	TGCGTCTTCTGGGCTGAGTTCATCTAGGATGGAGCCTGGTTCTCCAGGGTGCCTCCGGGA	101880

genome mRNA	GACTCCTCCCTGCCCCACGTGCTTGC GTCACAGGACCCAAGTCTGACTCTGCCTTAGCCA	101940

Figure 1

genome mRNA	TGAAGTTTAGGGGGAAGTTTCTATTTGTATTCTATTTTGTCTGTTATCATGTATTAGCT	102000

genome mRNA	TAGACCCAGTTTAGTTTGGAAAATCAGTGGGTTTCAAAATGTGTTTGTAGAGTCCTTTAT	102060

genome mRNA	TTCTTAACTTGACCTTTTCAAGTGGAAAGGGGCAAAACAGACGGGTAAAGGGGGCGGGGCG	102120

genome mRNA	GGAGGTGTGACTTGCTCTTTTGTGCCTGAGGAAGTAACAGAGCTGGGGTTGACAGTCATA	102180

genome mRNA	TTCTCTGACACAGATAGTCTCTGACTTATCTCACAGAAAGTCAGCGGCAGAGCCTGAGTT	102240

genome mRNA	AAAAGTCTCGTAGATTTTCTTTTCTTTTTTTTGGTGGCTAATTCAGTTTTATTATAT	102300

genome mRNA	TTGTTTATTTATTTATTATACTTTAAGTTCTGGGTTACATGTGCAGAATGTGCAGTTTTG	102360

genome mRNA	TTACATAGGTATACACGTGCCATGATGGTTTGCTGCACCCATCAACCCATCACCTACATT	102420

genome mRNA	AGGTATTTCTCCTAATGTTATCCCTCCCCCAGTCCCCTCACTCCCCATGGGCCCCGGTGT	102480

genome mRNA	GTGATGTTCTCCTCCCTGTGCCCATGTGTTCTCATTGTTCAATTTCCACTTGTGAGTGAG	102540

genome mRNA	AACATGCGGTGTTTGGTTTTCTGATCTTGTGATAGTTTGCTGAGAATGATGGTTTCCAGC	102600

genome mRNA	ATCATCCATGTGCCTGCAAAGGACATGAACTCATCCTTTTTTTATGGCTGTATAGTATTCC	102660

genome mRNA	ATGGTGTATATGTGCCACATTTTCTTAATCCAGTCTATCATTGATGGACATTCGGGTTGG	102720

genome mRNA	TTCCAAGTCTTTGCTATTGTGACTAGTGCCACAATAAACATACATGTGCATGTGTCTTTA	102780

genome mRNA	TCGTAGAATGATTTATAATCCTTTGGGTATATGCCCAGTAATGGGATTGCTGGGTCAAAT	102840

genome mRNA	GGTATTTCTAGTTCTAGACCTTTGAGGAATCGCCAGACTGTCTTCCACAATAGTTGAACT	102900

genome mRNA	AATTTACACTCCCACCAACAGTGTAAGTGTTCCTATTTTTCCACAACCTCTCCAGCAT	102960

genome mRNA	CTGTTGTTTCGTGACTTTTTAACGATCGCCATCCTAACTGGCGTGAGATGGTATCTCATT	103020

genome mRNA	GTGATTTTGATCTGCATTTCTCTAATGACCAGTGGTGATGAGCATTTTTTCGTATGTCTG	103080

genome mRNA	TTGGCTGCATAAATGTCTTCTTTTGCGAAGTGTCTGTTTCATATCCTTTGTCCATTTTTTG	103140

genome mRNA	ATGGGGTTGTTTGCTTTTTTTTCGTAAATTTGTTTAAGTTCTTTGTAGATTCTGGATGTT	103200

Figure 1

genome mRNA	AATCTTTTGTGTCAGATGGGTAGATTGCAAAAATTTTATCCCATTCTGTAGGTTGCCTGTTC	103260

genome mRNA	ACTCTGATGATAGTTTCTTTTGCTATGCAGAAGCTCTTTAGTTTAATTAGATCCCGTTTG	103320

genome mRNA	TCAATTTTGGCTTTTGTGTCATTGCTTTTGGTGTTTGTAGACATGAAGTCTTGCCTATG	103380

genome mRNA	CCTATGTCCTGAATGTTATGGCCCAGGTTTCTTCTAGGATTTTATGGTCCTAGGTCTT	103440

genome mRNA	ATGTTTAAGTCTTTGATCCATCTTGAGTTGATTTTGTGTAAGGTATAAGGAAGGGGTCC	103500

genome mRNA	AGTTTCAGTTTCTGTCATGTGGCTAGCCAGTTTCCCAACACCATTATTAATAGGGAA	103560

genome mRNA	TCTTTTCCCCATTGCTTATGTGTGTCAGGTTTGTCAAAGATCAGATGATTGTAGATGTGT	103620

genome mRNA	GGTGGTATTTCTGAGGCCTCTGTTCTGTTCCATTGGTCTATATATCTGTTTTGGTACCAG	103680

genome mRNA	TACCATGCAGTTTGGTTACTGTAGTGTGTAGTATAGTTTGAAGTCAGGTAGTGTGATG	103740

genome mRNA	CCTCCAGCTTTGTTCTTCTAGCCCAGGATTGTCTTGGCTATGCAGGCTCTTTTTTGGTTC	103800

genome mRNA	CATATGAAGTTTAAAATAGTTTTTCCAATTCTGTGAAGAAAGTCAGTGATAGCTTGATG	103860

genome mRNA	GGGGGATAGCATTGAATCTATAAATTACTTTGGGCAGCAAGGCCATTTTCACGATATTGA	103920

genome mRNA	TTCGTCCTATCCATGAACATGGAATGTTTTCTATTTGTTTGTGTCTCTCTTATTTCT	103980

genome mRNA	TGAGCAGTGGTTTGTAGTTCTCCTTGAAGAGGTCCTTCACATCCCTTGTAAGTTGTCTTC	104040

genome mRNA	CTAGGTGTTTCATTCCCTTAGTAGCATTGTGAATGGGAGTTCACTCATGATTTGGCTCT	104100

genome mRNA	CTGTTTGTCTGTTATTGGTGTATAGGAATGCTTGTGATTTTGCACATTGATTTTGTATC	104160

genome mRNA	CTGAGACTTTGCTGAAGTTGCTAATCAGCTTAAGGAGATTTTGAGCTGAACCAATAGGGT	104220

genome mRNA	TTTCTAAATATAACAATCATGTCATCTGCAAACAGGGACAGTTTTACTTCCTCTCTCCTA	104280

genome mRNA	TTTGAATACCCTTTATTGCTTTCTCTTGCCTGATTGCGCTGGCCAGAACTTCCAATACTA	104340

genome mRNA	TGTTGAATAGGAGTGGTGAGAGAGGGCATCCTTGTCTTGTGCCGGTTTTTGAAGGGAATG	104400

genome mRNA	CTTCCAGTTTTTGGCCATTGAGTATGATATTAGCTGTGGGTTTGTGATAAATAGCTCTTA	104460

Figure 1

genome mRNA	CTATGTTGAGATACGTTCCATCGATACCTAGTTTATTGAGAGTTTTTAGCATGAAAGGCT	104520

genome mRNA	GTTGAATTTTGTCAAAGGCCCTTTTCTGCATCTGTTGAGATAATCATATGGTTTTTGTGT	104580

genome mRNA	TGGTTCTGTTTATGTGATGGATTACGTTTATTGATTTGCGTATGTTGAACCAGCCTTGCA	104640

genome mRNA	TTCCAGGGATGAAGCTGACTTGATTGTGGTGGATAAGCTTTTTGATGTGCTGCTGGATTC	104700

genome mRNA	AGTTTGCCAGTATTTTATTGAGGATTTTCACATCGATGTTTCATCAGGGATATTGGCCTAA	104760

genome mRNA	AATTCTCTTTTTTTGTGTGTCTCTGCCAGGCTTTGGTATCAGGATGATGCTGGCCTCAT	104820

genome mRNA	AAAATGAGTTAGGGAGGATTCTCTCTTTTTCTATTGATTGGAATAGTTTCAGAAGGAATG	104880

genome mRNA	GTACCATCTCCTCTTTGTACCTCTGGTAGAATTCGGCTGTGAATCCATCCTGGACTTTTT	104940

genome mRNA	TTGGTTAGTAGGCTATTAACCTATTGCCTCAAGTTTAGAACCTGTTATCAGTCTATTCAGA	105000

genome mRNA	GATTCAGCTTTTTTCTGGTTTAGTCTTGGGAGGGTGTATGTGTCCAGGAATTTATCCATT	105060

genome mRNA	TCTTCTAGATTTTCTAGTTTATTTGGGTAGAGATGTTTATAGTATTCTCTGATGGTAGTT	105120

genome mRNA	TGTATTTCTGTGGGATCGGTGGTGATATCCCCTTTATCGTTTTTATTGAGTCTATTTGAT	105180

genome mRNA	TCTTCTCTCTTTTCTTCTTTATTAGTCTTGCTAGCGGTCTACCTATTTTATTGATCTTTT	105240

genome mRNA	CAAAAACCAGCACCTGGATTCATTGATTTTTTTTGGAGGGTTTTTTTTTCGTGTCTCTAT	105300

genome mRNA	CTCCTTCAGTTCTGCTCTGATCTTAGTTATTTTTTGTCTTCTGCTAGCTTTTGAATTTGT	105360

genome mRNA	TTGCTCTTGCTTTTCTAGTTCTTTTAATTGTGATGTTAGGGTGTTAATTTTAGATCTTTT	105420

genome mRNA	CTGCTTTCTCTTGTGGGCATTTAGTGCTATAAATTTCCCTCTACACACTGCTTTAAATGT	105480

genome mRNA	GTCCCAGAGATTCTGGTATGTTGTGTCTTCGTTCTCATTGGTTTCCAAGAAAATTTTAT	105540

genome mRNA	TTCTGCCTTCATTTTCGTTATTTACCCAGTAGTCATTCAAGAGCAGGTTGTTTCAGTTTCCA	105600

genome mRNA	TGTAGTTGTGTGGTTTTGAGTGAGATTCTCAATCCTGAGTTCTAATTTGATTGCACTGTG	105660

genome mRNA	GTCTGACAGACAGTTTGTTGTGATTTCTGTTCTTTTACATTTGCTGAGGAGTGTTTTACT	105720

Figure 1

genome mRNA	TCCAACATATGTGGTCAGTTTTAGATAAGTGCAATGTGGTGCTGAGAAGAATGTATGTTC	105780

genome mRNA	TGTTGATTTGGGGTGCAGAGTTCTGTAGATGTCTATTAGGTCCGCTTGGTCCAGTGCTGA	105840

genome mRNA	GTTCAAGTCCTGGATATCCTTGTTAATTTCTGGCTCATTGATCTGCCTAATATTGACAG	105900

genome mRNA	TGGGGTGTTAAAGTCTCCCACTATTACCGGGTGGGAGTCTCTTTGTAGGTCTCTAAGAAC	105960

genome mRNA	TTGCTTCATGAATCTGGGTGCTCCTGTATTGGGGGCGTGTATATTTAGGATAGTTAGCTC	106020

genome mRNA	TTCTTGTTGAATTGATCCCTTTACCATTATGTAATGGCCTTCTTTGTCTCCTTTGAACTT	106080

genome mRNA	TGTTGATTTAAAGTCTGTTTTATCAGAGACTAGGATTGCAATCCCTGCTTTTTTTTTTGCT	106140

genome mRNA	TTCCATTTGCTTGTTAGATCTTCCTCCATCCCTTTATTTTGAGCCAATGAGTGTCTTTGC	106200

genome mRNA	ATGTGAGATGGGTCTCCTGAATACAGCACACCAATGGGTCTTGACTCTTTATCCAATTTG	106260

genome mRNA	CCAGTCTGTGTCTTTTAATTGGGGCATTTAGCCCATTTACATTTAAGGTTAATATTGCTA	106320

genome mRNA	TGTGTGAATTTGATCCTGTCATTATGATCCTAGTTGGTTATTTTGCCCGTTAACTGATGC	106380

genome mRNA	AGTTTCTTCATAGCGTCAGTAGTCTTTACAATTTGGCATGTTTTTGCACTGGCTGGTACT	106440

genome mRNA	GGTTGTTCCCTTTCCATGTTTAGTGCTTCCTTCAGGAGCTCTTGTAAGGCAGGCCTGGTGG	106500

genome mRNA	TGACAAAATCTCTGCATTTGCTTGTCTGTAAAGGATTTTATTTCTCGTTCACTTATGAAG	106560

genome mRNA	CTTAGTTTGGCTGGATATGAAATCTGGGTTGAAAATACTTTTTTTAAAGAATGTTGAAT	106620

genome mRNA	ATTGGCTCCCACTCTTTTCTGGCTTGTAGGATTTCTGCAGAGAGATCTGCTGTTAGTCTG	106680

genome mRNA	ATGGGCTTCCCTTTGTGGGTAACCCGACCTTTCTCTCTGGCTGCCCTTTCCTTCATTTCA	106740

genome mRNA	ATCTTGGTGGATCTGATGATTATGTGTCTTGGGGTTGCTCTTCTCGAGGAGTATCTTTGT	106800

genome mRNA	GGTGTCTCTGTATTTCTGAATTTGAATGTTGGTCTGCCTTGCTAGGTTGGGGAAGTTC	106860

genome mRNA	TCCTGGATAATATCCTGAAGAGTGTCTTCTAACTTGGTTCTATTCTCCCCATCACTTTCA	106920

genome mRNA	GGTACACCAATCAAACGTAGATTTGGTCTTTTCACATAGTCCCATATTTCTTGGAGGCTT	106980

Figure 1

genome mRNA	GGTTCATTTCTTTTCACTCTTTTTTCTCTAATCTTGTCTTCTCGCTTTATTTCAATTAATT	107040

genome mRNA	TGATCTTCAATCACTGATATCCTTTCTTCTGCTTGATTGAATCGGCTGTCGAAGCTTGTG	107100

genome mRNA	TATACTTCACAAAATTCTCGTTCTGTGGTTTTTAGCTCCATCAGGTCATTTAAGCTCTTC	107160

genome mRNA	TCTACACTGGTTATTCTAGCCATTAGTCTAACATTTTTTTCAAGGTTTTTAGCTTCCTTG	107220

genome mRNA	TGATGGGTTAGAACATGCTCCTTTAGCTCGGAGAAGTTTGTTATTACCGACCTTCTGAAG	107280

genome mRNA	CCTACTTCTGTCAATTCATCAAACCTCATTCTCCATCCAGTTTTGTTCCCTTGCTGGTGAG	107340

genome mRNA	GAGTTGTGATCCTTTGGAGGAGAAGAGGTGTTCTGGTTTTTGGAATTTTCAGCCTTTCTG	107400

genome mRNA	CTATGGTTTCTCCCCATCATTGTGGTTTTATCTACCTTTGGTCTTTGATGTTGGTGACCT	107460

genome mRNA	ACGGATGGGGTTTTGGTGTGGGTGTCCTTTTTGTTGATGTTGATGCTATTCCTTTCTGTT	107520

genome mRNA	TGTTAGTTTTCTCTCTAACAGACAGGCCCTCAGCTGCAGGTCTGTTGGAGTTTGCTGGA	107580

genome mRNA	GGTCCACTCCAGGCCCTGTTTGCCTGGGCATCACCAGCAGAGGCTGCAGAACAGCAAATA	107640

genome mRNA	TTGCTGCCTGATCCTTCCTCTGGAAACATCGTCCCAGAGCACGAAGGTGTCTGCCTGTAT	107700

genome mRNA	GAGGTGTTTGTTGGCCCCCTACTGGGAGGTGTCTCCAGTCAGGCTACATGGGGGTCAGGG	107760

genome mRNA	ACCCACTTGAGGCAGTCTGTTTCATTATCGGAGCTTGAATGCCGTACCGGGAGAACCACTG	107820

genome mRNA	CTCTCTTCAGAGCTGTCAGGCACGTATGTTTAAATCTGGAGAAGCTGTCTGCTGCCTTTT	107880

genome mRNA	GTTTCAGATGTGCCCTTCCCCCAGAGGTGGAATCTAGAGAGGCAGTAGGCCTTGCTGAGCT	107940

genome mRNA	GCAGTGGGCTCTGCCCAGTTCGAGCTTCCCTGCTGCTTTGTTTAACTGTGAGCATAGAA	108000

genome mRNA	CCACCTACTCTAGCCTCAGCAGTGGTGGACACCCCTCCCCCAGCCAAGCTCCTGCATCCC	108060

genome mRNA	AGGTCGATTTTCAGAGTGCTGCGCTAGCAGTGAGCAAGGCCCATGGGCGTGGGACCCGCT	108120

genome mRNA	GAGCCAGGCACAGGAGAGAATCTCCTGGTCTGCTGGTTGTGAAGACTGTGGGAAAAGTGC	108180

genome mRNA	AGTATTTGGGCAGGAGTGTAAGTCTCCTTCAGGTACAGTCACTCATGGCTTCCTTTGGCT	108240

Figure 1

genome mRNA	TGGAAAGGGAAGTCCCCGACCCCTTGTGCTTCCCAGGTGAGGCAACACCCCGCCCTGCT	108300

genome mRNA	TCGGCTTGCCCTCCGTGGGCTGCACCCACTGTCCAGCAAGTCCCAGTGAGATGAACTAGG	108360

genome mRNA	TACCTCAGTTGGAAATGCAGAAATCACCTGTCTTCTGTGTCGATCTCACTGGGAGCTGTA	108420

genome mRNA	GACTGGAGCTGTTCTTATTCGGCCATTTTGGAAAGCATCCCTTGTTTTTTGAGGTGGAGTC	108480

genome mRNA	TTGCTCTGTCGCCCAGGCTGACGTGCATCGGCACAATCTCGGCCCACTGCAACCTTTGCC	108540

genome mRNA	TCCTGGTTTCAAGCGATTCTCCTACCTCAGCCTCCGGAGTAGCTGGGATTACAGGCACCT	108600

genome mRNA	GCCACCATGCCTGGCTAATTTTTTGTATTTTTAGTGGAGATGGGGTTTCACCACATTGGC	108660

genome mRNA	CAGGCTAGTCTCGAACTCCTGACCTTGTGATCCACCCACCTCAGCCTCCTAGAGTGCTGG	108720

genome mRNA	GATCACAGGTGTCAGCCACCACGCCCAGCCATATTTTCAGATCTCCCTCTCTTTGCCCTA	108780

genome mRNA	AACCACTGTGCTTAATAAGTAGTTTTTGTAGTGGCCAGCAGTCTCCATGTATAACACATTTT	108840

genome mRNA	AGCAAAATGGAAAATACTATATGTTTTTAAATTTGAACGTGAGATTATACTGAAATAAAAA	108900

genome mRNA	TCATCTAACTGGGATTCTTTAAATAGTAAGATTTTCTTTTTTGTATGTGGGTTTTTTTTT	108960

genome mRNA	AACCTTATTATTATGACTGTCATATATAGAAATGGCTGTTTTTTCAGTTACAGTCAGTGAA	109020

genome mRNA	TGTATCAAATGCTGCCTTATCCAAATAATAAAAGTAAATTATTAATAAGTCACAATTTAA	109080

genome mRNA	TGAAGATTGATGTTAGTTGATCTTTATATTCTTGAAATCAGCCATATGGTTGTGTGTGTA	109140

genome mRNA	TGTATATATTTTTAAAGGTACATAAAGATAATAAGCTCATCTCTGAAAATTTTTACATTT	109200

genome mRNA	GGCATAAGAATAACTGGATAATTAAGCATCTTATTCTCTGGCCTGTGTCTTTACAGTTAA	109260

genome mRNA	AGGTAGATTTACTCACCTCTCCTTTTTTGTTTTTCTAAGTTCATCTTTTTTGCTGTTTCA	109320

genome mRNA	AGACAGAGGCCCATTTTAGCTTTCTCGCATATCCTTTTGTGTTGTACTTTGGAAGCCTCAC	109380

genome mRNA	CTGCTTAATTGTTGAGTTTTTATCCGTGGTCTTTTAGAGGGGGATATGTAGGGTAGAAGC	109440

genome mRNA	TTTCACAGGTTCTTGTTTGCACCTGGCCCCCTGACTGTTTTGAGGAATCTCCCTCACTGAC	109500

Figure 1

genome mRNA	TCACAGCATGGCAAGGTTTCAGATCTCTTTCTGCCACACAGCAGTTCTGAGGCAGCTGGA	109560

genome mRNA	AAGATATCCAGATGCTTAGATTGTCAGGCCAGGCTTGAGATATACAAACTATTGAGCCTT	109620

genome mRNA	ATCTGTGACCTTGCTTAGGTGAAGGCATCAGAGCCCCTGCACCAACATGCATAGGCCTCT	109680

genome mRNA	GCATGTGTGCGGGGCTGGGTGTTGAGGTCTGAGCACAAGTGTAGCTGGAGAGGTGAGCTT	109740

genome mRNA	GATGTGGCGACGGGTATGAGCAGGTTTTCTTCAGACTTCTGTGAGTTTACCTAGTTCCAG	109800

genome mRNA	GATTTAAAGGCACAGAGACTTTAGAATTAAAATAGAATCATTTTCTTTTCTAAATAGCA	109860

genome mRNA	ACACTAGGAATAAAAAATAATAATTCACATTCTTGACAGGTAATGTTTTTCTTGTCTT	109920

genome mRNA	CTAATCCTTATTTATTCATACTCATTTTTATACATAATTGAAATGTATTATGCATTGGA	109980

genome mRNA	TTTTTCTTTTGCATTATATTATAGACGATTTTTCATGTAACCTTACTGTTCCATTTTA	110040

genome mRNA	TATGTTTTGTCTGGTTTAAGACTTTATCTGCAAACCGGGAAACTGTCTCTACAAAAGAA	110100

genome mRNA	AAACAAAATAGTTGGCCGAGTGGCATGCGTCTGTGGTCCCAGCTACTCGGGGCTGAGG	110160

genome mRNA	TGGGAGGATTGCTTGAGCCTTGGGAGGTTGAGGCTGCAAAGAGCCATGATCATGCCATTG	110220

genome mRNA	CACTCCAGCATGGGTGACAGACTTTATACTGTCTGTTTTGGGTGATTTGATAATGATATG	110280

genome mRNA	CCCTGATGTAGTTTTTTTATATCTTGTGTTTCTTGTGCCTGGGTTTATTGAGGTGGGTC	110340

genome mRNA	TGTGGCTTCATAGTATTTTTTAAAGTTTGAAAATTTTAGGCCATTCTTTCTTTCTTTCTT	110400

genome mRNA	TCTTTTTTTTTTTTTTGGAGACAGTGTCTCGCTCTGTGCGCTGCGTTGGAGTGCAGTGACA	110460

genome mRNA	CTATCTTGGCTCACTGCAAGCTCTGCCTCCTGGGTTACGCCATTCTCCTGCCTCAGCCT	110520

genome mRNA	CCTGAGTAGCTGGGACTACAGGCGCCTGCCACCACGCCTGGCTAATTTTTTGTATTTTAA	110580

genome mRNA	GTAGAGACGAGGTTTCACTGTGTTAGCCAGGATGGTCTCAATCTCCTGACCTCGTGATCT	110640

genome mRNA	GCCCGCCTGGGCCTCCCAAAGTGCTGGGATTACAGGCGTGAGCCACTGCACCCAGCTAGG	110700

genome mRNA	CCATTATTTCTTCAAAGATTTTTTTTCTGCCCTGCCTCCCTCCTTTTTTCCCTCTCTTAA	110760

Figure 1

genome mRNA	AGGGGCTGTGATTTCTGAATGATTGCTTAGTGTTGTCCCATAGCTTACTGATGCTCTTT	110820

genome mRNA	TCAGTGTTTGATTGTTTTATGTGTTTTCTGTTTTGTATAGTTTCTATTATTGTGTTTTCA	110880

genome mRNA	AGTTCTCTGATCTTTTCTTCTACAGTGTCTACTCTGTTGTTAATCTGTTAATCTGTTGTT	110940

genome mRNA	AATCCTGTCCAGCGTATTTTTTTTTTTTGTGTTTTGAAACAGTCTCACTCTGTTGCCCAGGC	111000

genome mRNA	TGGAGTTTAGTGGTGCGATATCAGCTCACTGCAACCTCCACCTCCCAGGCTCAAGCAATT	111060

genome mRNA	CTTCTGCCTCAGCCTCCCGAGTAGCTGGGACTATAGGCACGTGCCACCACACCTGGCTAA	111120

genome mRNA	TTTGTGTATTTTTATTAGAGATGGGGTTTCACCATGTTGGCCAAACTGGCCTTGAAGTCC	111180

genome mRNA	TGACCTCAGGTGATTCATCCGCCTCGGTCTCCCAAAGTGTGTTGGGATTATAGGCATGAGCC	111240

genome mRNA	ACCGTGTCTGGCCCCTGTTTCAGTGTATATCACTAATTTTGTGTTTTATCTCTAGAAGTTTG	111300

genome mRNA	ATTTAGGTCTTTTAAAAATGTCTCCCTGTGTTTCTGTTTAGCTTTGTGAACACAATTGTA	111360

genome mRNA	ATAACTGTTTTAATATCCTTCTCTGCTAGTTCTAAGATCTTCTAATAACTTCCCAGTTCT	111420

genome mRNA	TGGTGTTTCTCATTGGTTGATTGATACTCCTCGTTTTGGGTTGTATTTTCCTGCCTCTTT	111480

genome mRNA	GTATGGCTGCCAATTTTTTATTGGATGCCCAACCTTGTGAATTTTACTTTGTTGGATGCT	111540

genome mRNA	ATATATTTTTGTGTTCCCATAGATCTTCTTGAGCTTTGTTCTGAGGTTAGTTGAGTTACA	111600

genome mRNA	TATAGATGGTTTACTCTTTTGGGTCTTGCTTTATAATTTGTCAGATGGGTTGGAGCAGTG	111660

genome mRNA	CTTAGTTTAGGACTAATTTTTTTTTTTGGACTAATTATTCCTCTTTAGGAATAATTAGGTA	111720

genome mRNA	CCATGCTTAGGAGGCAAGACCATCCTGAGTACTCTACCTAATGAACCAGAAAGTTTGGGT	111780

genome mRNA	TTTCCAGTCCGCCTGCTGAGAACAGTGACTTTCTAGCCCTGTGTGAGCGCTGAGCTCTGC	111840

genome mRNA	TCCTTCTAATCCTTTCCAATGCTTCTTTCCCTGGCCTCAGGGAGTTTTCTCACACACATA	111900

genome mRNA	TCTCTGCTGAGTACTCGAGAGGGACCTTCCCCAGATCTCCAGAGCTCTCTCTGTCTTGTT	111960

genome mRNA	TTCTCTTCTCTGGTGCTCTGTCTTATGAACTGTGGCTGTCTTGGTCTCCTTAGATTCTCA	112020

Figure 1

genome mRNA	GCACCTCTTCAATTCAGAGGGTTGCCTGTCCCTCCTCCTTGTGCCACAGCCTAGGAACTC	112080

genome mRNA	TCTCAAAGCAGCGAGTTGGGGCAGCCATAGGGCTGACTTAGTCTCTCGTCTCCCAGGGAT	112140

genome mRNA	CACTGTCCTTCATTGCTCATGTCCAGTGTCTTGAGGACTCTGGGTTTTGTCTGTTTTGTT	112200

genome mRNA	TTTTGGTTTGCTTTGGTTGTCTCAGGCAGGAGGGTAAACCCAGTCCCTCACCTCATTGT	112260

genome mRNA	GCTCAGTAGTGGAAGTCTCACTCTATTACATTAGATATTAGTATTTGTAGCAGAGCCCTG	112320

genome mRNA	GTTCCCTGGTACTTGGGGAGCTCTTGAAAGGCCAGAAACAGCATGCTTCTCACCTTTTC	112380

genome mRNA	CAGGGCTTCAGTTTCTGGTGACATCAAGCATTCCATACACATTTGTTAAAGTCCTTTGT	112440

genome mRNA	TAGACAAGTAGTGATTACAGGTTCTATTTGTAATTTTTTCAGTTAACATGTATTGGGTA	112500

genome mRNA	TCTGCTGGGAGCTAGTAAAAACAAAAGTGGTGTGTGACAAATTCAATTCTGACAAGAAC	112560

genome mRNA	AACCTTAAACACTTAGAATATACTTTGAGCATATCAGAATTTTAAAAATGTGTGGCCCTT	112620

genome mRNA	GAGTATTTGAAACCAACAAGAATCTATTGCTTATTAGTAGAGGATATTTTGTAAACAAG	112680

genome mRNA	TGGAGAGAGAGGCATTTTCAGTCTAATTGGTGTGGCTTTTAGCAGCTGATGGAAACCAG	112740

genome mRNA	TTCGTGATTAGCCAGGCAGTGGTGAAACAGGCTGTGCATTCTGAATGCCTAGGTATCTAG	112800

genome mRNA	GCATTCAGAATGGTGGCGCTCTTTGAGTTAGCATCTTCTTCTTTCTTGATTCTTTTTTTT	112860

genome mRNA	TTTTTTTTGAGATGGACTTTCGCTCTTGTTGCCCAGGTAACTCCAGTGCAATGGCGC	112920

genome mRNA	CATCTCGGCTCACTGTAACTCTGCCTCCCTGGTTCAAGCGATTCTCCTGCCTCAGCCTC	112980

genome mRNA	TCAAGTAGCTGGGATTACAGGTGTGCGCCACCACGCCTGGCTAATTTTGTATTTTGGTA	113040

genome mRNA	GAGATGGGGTTTCACTATATTGGTCAGGCTGGTCTTGAACCTCCTGACCTCAAGTGATGCA	113100

genome mRNA	CCTGCCTCGATCTCCCAAATGCTGGGATTACAGGCGTGAGCCACCACTCCCAGCCCCTT	113160

genome mRNA	CTTGATTCTTGAAAAGGACATTGGGTGCTGTACATCTCGTTATAGATGTTGATAAAAATG	113220

genome mRNA	CTTGTGAGAAGAGTAACATTAAGGTAGTTATTTGGTCATTTTGCAGATTATTTTAAGAC	113280

Figure 1

genome mRNA	AATTCTAGGACTGATTTGTGGTAAATCACACATTGCTGTATCATAGTTGTGTTCACTGAA	113340

genome mRNA	CATATTCAGGGGCTCTACAGATGCAGGGCTCTTAGCTGCTTTGCACACTTCTGAATTCCT	113400

genome mRNA	GCCCTGCGAACAGGACTGGATACCTAATAGACAACAGGTACTTGATAACAGTTTATTGAA	113460

genome mRNA	TTAATGAGTGAATGAACAGATACATAAATGCATGAAAGAATGGTTGTAATGTATATAACT	113520

genome mRNA	TGGATTTCAAGACTTTTTACTGACTGTTCAAATAAGAAATTGAAAACCTTCCTCTGATT	113580

genome mRNA	TTCTCTACTATTTACACAATTTAAATGGAAGTTATCTTGACCTTCAATTTCTGTCTAG	113640

genome mRNA	GATTCGTACAATAACGGGTCATCTCTGAGTCGCTTAATGTCTCACTTGTCTTTCTACAGT	113700

genome mRNA	GTGTTGAAGAGATCCTAGGATACCTGAAATCCTGCTTTAGTCGAGAACCAATGATGGCAA	113760

genome mRNA	CTGTTTGTGTTCAACAAGTAAGAGCTTCATTCTTTTCCTCTTCTGTTAAGACGTTTCGGGT	113820

genome mRNA	ATGACAGCAAAACGCTGCTACTCCTTAAGAGGCAGGCGCTGTTGGCATAATCAGCTGGGA	113880

genome mRNA	GGATTGTGGGGTCCAGCGCAGCACTTTTTGGCTCAGTCCATGATTGAGCCAAGAGGCCAT	113940

genome mRNA	CCTTCCCTTCACTCCCCAGGAGGACGAGGTCTGTCACTGTGGAGGGCAGAGGACACCAGA	114000

genome mRNA	AGCTCCTCTGCAACCTCGCTAGTTAACTTCCAGTCCCTCGGAGTTTCTGTTTAGAATGCT	114060

genome mRNA	CAATCTCATTTAGAATTGCAAGGAAACCCAAAACGCCTATTTAAGGTACAAACAGCACTT	114120

genome mRNA	CATACAATATCTCATGAGGTATTAATAGTGATTACAGGAAGAATTTACGCTGTGAGTC	114180

genome mRNA	TTTGCTAACATATCCAGTTATTTACAGATGGATTTGATATTTGTGTGGGAGATTCTTAA	114240

genome mRNA	AGTGTTGTTACGCCACATTGTTGATGCCTCATTTTTTTCACTGTAGTTGTTGAAGACTC	114300

genome mRNA	TCTTTGGCACAACTTGGCCTCCCAGTTTGATGGCTTATCTTCCAACCCCAGCAAGTCAC	114360

genome mRNA	AAGGCCGAGCACAGCGCCTTGGCTCCTCCAGTGTGAGGCCAGGCTTGTACCACTACTGCT	114420

genome mRNA	TCATGGCCCCGTACACCCACTTCACCCAGGCCCTCGCTGACGCCAGCCTGAGGAACATGG	114480

genome mRNA	TGCAGGCGGAGCAGGAGAACGACACCTCGGGGTAACAGTTGTGGCAAGAATGCTGTCGTT	114540

Figure 1

genome mRNA	GGTGGAAGCACGAAAGAGCAAGCAGGAAATACTTTGTAAAAGAATAAAAACGAAAAATGT	114600

genome mRNA	TAGCGAACATCTTCTAATAGTCTGCTGTATTCAGAGAACTCTAGGAGATATATATGGTTG	114660

genome mRNA	ATGCAAAGATGATTTAAGGCATAGCCCGGCCTTCCAAGAAGTGTGTGGCCAGTGAGTGAG	114720

genome mRNA	ATGGGCTTGGGACTTACACATCTCAGAGGTGGGGGTAGAGGAGGAGGAACACTGAGTGGG	114780

genome mRNA	CTGAGAAGCAGCCAGCTCTCATTGCCAAAGTGTGTCAGCAAACCAGAATGCAGTTCATAA	114840

genome mRNA	TGTCCCCACCCATTCAAAGCACAGGACCTGTAGAGTGGTGTGGCATGTGTTGGTGGCACT	114900

genome mRNA	TTTCAGGCCTGTAACAAGGATGAAAGAACAGCTTCATAGCAGCACAGTAGTGCTGGTGT	114960

genome mRNA	CAGAGGTGTGTGAAGGCCATAGAAGCATCTTGGATATATTACCTTGTGTTTTGTCAGCTT	115020

genome mRNA	TATGACTAGAAGTCTCTTTTCACTTAAATTTGTTTTTTTTTTTTTTGAGACGGAGTCTTG	115080

genome mRNA	CTCTGTCGCCCAGGCTGGAGTGCAGTGGTGAATCTCAGCTCACTGCAAGCTCTGCATCC	115140

genome mRNA	TGGGTTTCATGCCATTCTCCTGCCTCAGCCTCCCGAGTAGCTGGGACTACAGGCGCCTGCC	115200

genome mRNA	ATCACGCCTGGCTAACTTTTTTTTGTATTTTGTAGTAGAGACGGGGTTTCACCATGTTAGC	115260

genome mRNA	CAGGATGGTCTCGATCTCCTGACCTCGTGATCTGCCCCGTCCCGGCCTCCCAAAGTGCTGG	115320

genome mRNA	GATTACAGGCGTGAGCCACCGCGCCCGGCCTCTTTTCACTTAAATTTATGTTTGTGTTTT	115380

genome mRNA	TAATGCCTAGTATACAGGACTTCTTAAATTGCCTTAAGTATGAACAGGTATTTGAGTTGC	115440

genome mRNA	TAATCTGTATAGTAGCAATAATAGAATCCCTTGTTTTTCCTTTTATAAATTTAGCGATTA	115500

genome mRNA	AATAGCTACAATTAAAACACTAGAGTCAGGAGTCAAGGAAAATACCCATGTTCCAGGCTG	115560

genome mRNA	TATGTTAGTGATGTACTTACTATATATTGGAGTTTCAGGAGTAAGTCTGTTTCAATGCTT	115620

genome mRNA	TCTGTAACCATTTGGGGTATTAATAAGCATGTGAGTGTGTGCATGTTTGGGTAAATTTCA	115680

genome mRNA	TATATGTTTCTTAGAAGGGATATCATTGATGTAAATATTTTAAAGGCTTGTCTCCAAAA	115740

genome mRNA	AAATCATGTAATTTCTTCTAAATTACTGATCTTTTAAATGACCTTCACCTTTCTCTCAA	115800

Figure 1

genome mRNA	TCTCACTTAAGACTGGGCTGAGTAGTCAGTTTCCTGTAGCAGAAAAAGCTCAGACTTGA	115860

genome mRNA	GTAGCCTTCTGCGAGTGAGGAGACTTGATGGCTGTCAGGCAGCTGTAAACTCTAAATAGA	115920

genome mRNA	GTGTCATTATCTGAAGAGGGCGATGCTGCCACACTGAGTGGCCTTTCAAGTTGTTTCTCA	115980

genome mRNA	ATCTGACACGTTCTGATCGTGTGAATGTGAAATTGGTTTGAGCAGGAGTATATCTGAGTG	116040

genome mRNA	CAGAGGAGATTATTTAAAGATATTCTCATTCTCTGCTTCCCTTTTATTCCCATTGCGCAG	116100

genome mRNA	ATGGTTTGATGTCCTCCAGAAAGTGTCTACCCAGTTGAAGACAAACCTCACGAGTGTCAC	116160

genome mRNA	AAAGAACCGTGCAGATAAGGTAAATGGTGCCGTTTGTGGCATGTGAACTCAGGCGTGTCA	116220

genome mRNA	GTGCTAGAGAGGAAACTGGAGCTGAGACTTTCAGGTATTTTGCTTGAAGCTTTTAGTTG	116280

genome mRNA	AAGGCTTACTTATGGATTCTTCTTTCTTTTTTCTTTTTTATAGAATGCTATTCATAAT	116340

genome mRNA	CACATTCGTTTGTTTGAACCTCTTGTTATAAAAGCTTTAAACAGTACACGACTACAACA	116400

genome mRNA	TGTGTGCAGTTACAGAAGCAGGTTTTAGATTTGCTGGCGCAGCTGGTTCAGTTACGGGTT	116460

genome mRNA	AATTACTGTCTTCTGGATTCTAGATCAGGTTTGTCACTTTTATCTTTCATCCATCATACCT	116520

genome mRNA	GTCCTAATTTAGTACAAATTACCCTAAAAGACACTGAAATCTACTTTAAAGAAATGTGG	116580

genome mRNA	TCTGCATGTTTCCCTCATCAGTTGCTGCTGCTTATCTTTTTTCATGCACCTAGCTGGTGCA	116640

genome mRNA	GAAGGCCTGGGGCATAGCCAGCCTCAGCAAGTCAGCATCCTTGCCCCAGCTCCCTGGACT	116700

genome mRNA	CAAGGCTAACCTGGGGTTGGCTGTTAGGGATTTCCAAAGGTTTGTCCCATCCACTTGCCT	116760

genome mRNA	CCCCTCCAAAATAAGTTTGAATTTAAATTGTGAGATACAATTAAGATTTATTGTTTGGGG	116820

genome mRNA	AACATTTTTCGAAAATCTAGAGTTAGTTTAAACAGATTATCAATTATTACCATAATTGAT	116880

genome mRNA	CATCTGCAGTTTCAAGCTATCTAACAGGTTCACTTACCTCTTTAAAAGGAATGGAATTT	116940

genome mRNA	AGCAGGACAGTAACTGAGACCCGTGCTCCTGGAGTCCATGTGGGAGCTGTGTGGCTCTGC	117000

genome mRNA	ACAAGCATTTGCACGCTTCCCCTCTTGACTGCATTACCTTCCTCCTATAGTTGCTGTGGG	117060

Figure 1

genome mRNA	CACCAGATTCTGGCTAGTCCTGTCCCTTCATGATGCACATTTTCCTCAAGATTCGTCCCA	117120

genome mRNA	GTTAAATCACTGCAGATGAAACTGCCTTTTCATCGTCAAAATTTAACTGTCATTTTGTAG	117180

genome mRNA	CCGTGATCTTGGGCTACTTTCTTATGTGGGGTAGGAATATTTGTGAGTTAGAAATATTAC	117240

genome mRNA	ACTTCTCTATTTCCCTTCTAGACGTAAATCTGTTAATCCTGTCAGCACTGTTACTCACCTG	117300

genome mRNA	AAAGGGTCTGTTTCCCTAGGAGAACTGAGGGCACTCGGTCAACACTGATTTTCCACAGTG	117360

genome mRNA	GGTATTGGGGTGGTATCTGCTTGTTTTTTTTGTTGTTGTTGTTTGTTTTTTTTTGTTTTT	117420

genome mRNA	TTTTTGAGATGGAGTCTCGCTCTGTCACCCAGGCTGGAGTGCAGGGGTGCGATCTCGGCT	117480

genome mRNA	CACTGCCAGCTCCGCCTCAGAGGTTACGCCATTCTCCTGCCTCAGCCTCCCGAGTAGCT	117540

genome mRNA	GGGACTACAGGCACCCACCACTACGCCAGGCTAATTTTTTGTATTTTGTAGAGACGAG	117600

genome mRNA	GTTTCACTGTGTTAGCCAGGATGGTCTCCATCTCCTGACCTCGTGATCTGCCCCGCCTCGG	117660

genome mRNA	CCTCCCAAAGTGCTGGGATGACAGGCGTGAGCCACCGCGCCCGGCCTGGGGTCTGCTTTT	117720

genome mRNA	AATGAAGGAGGCATCAAGGGGTGGGCTTTGCGTTGGCCTGATGCTTTCATCTTTCTTTCA	117780

genome mRNA	CAAAACCTGTCCGAAGAAAATCCGTCTAAATGGGCCATTGCTCTCCTCAGGAAATAGTCA	117840

genome mRNA	TTGGGAACTTCTTTTCCTTTCTTTGACACTAGGAGGCTGACTGGGGAGAAGCCCTGGTC	117900

genome mRNA	TATGGCTGTGGGCAGCAGGGGCTGAGAGGAGCAGGCTCTCAGGGGGGCACGGGTACCCCA	117960

genome mRNA	AGGGAAGCCAGAGCCCTGATTTGTTCCATTCTAGTAAGAACAAGACTGCTCTGGTTTCA	118020

genome mRNA	TGTTTGTTCTGATTGCCTTTCATCAACCGGTCCCCTTTCTCCAGTTCTTAAGATTCAGT	118080

genome mRNA	ACAGTGACAGTTTTATGAACAAGAATAGAACACTAGAACAGACAAACCATTTGAACCTCTAT	118140

genome mRNA	GCTGATAAAGATTTATTGAGCTCCTGCTGTATGTTTGCATTCTGCCCAGAGGCTCTGAGA	118200

genome mRNA	AAACCAGGCCATATGCTCCATGCTTTATCCATGGAAGCTCCCCGTCAGGTTGGGAAAGCT	118260

genome mRNA	GACAGCTGCAGGGAATACAGTGTGACACAAAACCTGGCTCCCATGCAGCCCTTACGTGTCTG	118320

Figure 1

genome mRNA	CCTCTCAGATGGTTGGGGGACGAAGGTCGACTCCTTTGGGTATCTTATTACTAAACCAGT	118380

genome mRNA	TTCAGGGAATCTGTGCCACCCTATCTGCCATTAACGTGAACAGATGAGTCCCCAAGGTGT	118440

genome mRNA	AATTTTGGGTATTGTCTGATGTCTCTTGAATTTATTATTTGTTTTTCCAATGAGATTTTC	118500

genome mRNA	ACCTCAGGGTATAGTAAAGTTGTTGAGGGGATTCCTGGATGTGTTCTGCAATTATCTAGG	118560

genome mRNA	CTGATTTTCAGAATAGAGTTATGCTTATAGTCAAATTTATCAGCTGTCAAGAATTTTATTT	118620

genome mRNA	AAAATTTATGCAGATAAGCAGGAGGAAAAGAAGCCTGGTTTTTACATTTTAATCCTATTA	118680

genome mRNA	TTGATGTGAAATTTTATTTTCCTTCCTGTAGGTGTTTATTGGCTTTGTATTGAAACAGTT	118740

genome mRNA	TGAATACATTGAAGTGGGCCAGTTCAGGTAATAGCATTTTATTATTTTAGATTTTTTTCT	118800

genome mRNA	TCTTCTTGTGTACTTACATGTAATTTAGGTTATTAAGTGAATGTTTAAACTACTGTTAGG	118860

genome mRNA	CATTTTGTCTGTTTTCTTTAAATGGAAATCTGACTAACATACTGTGCATTTTGTCTCTC	118920

genome mRNA	TTAAAAATTAATGTATATCTCAAGACTTGTTTGGAAGTAGTTATGTATCTGAAAATTCCA	118980

genome mRNA	TATGTTGTCAGTATTCATTGCACATTTCAAAGCATTTAATTGTGTTGACAGATGGTGGAA	119040

genome mRNA	TGAAATCTTGTGGTGGAGCACTAGTTTTTAAATCTTCTTAGAGAAAGCAGTTTTATATAA	119100

genome mRNA	TGTTGTCTTTAGTAATTATTATGCATTTGTATTCTCTGCAGCTTTTTCTTGCTAGATGTT	119160

genome mRNA	GAGGTTTTAATACTTCTTGCTAGTCCATTACAGGTTTATAATTATTAAAAGTTAAAATTC	119220

genome mRNA	TTTGTAGTACCTAAAATGCTTAATAAACATTGTAATTAGGAAAATTTAGTGCAGAAGGAAA	119280

genome mRNA	GTGTTCCCAGATTCCCTGGGGTCTGGAAACATAGTGTTTATTCTAATTACATGACACCTC	119340

genome mRNA	CACTGTGTTTTGGGGCAAGTTACTGTTTCTCTTTTGAGTTTCAATTTCTTCAAGAGCAAA	119400

genome mRNA	GAGGCAGAGGAGAGCTAGGAAGATCGTAGCTGCTGTGCCCCTGTGCCGTGCGGTGCCTTC	119460

genome mRNA	TACCTGCTGCCTCCGAACCTTTACACATGTCCCTGCTCTGCGGAGGGCACAGATGGGAT	119520

genome mRNA	GCACTGTGGCAGGGGTGGGGTTAGAGTAGATCACGGACACCTGTTAGCTTGATGTGTGCT	119580

Figure 1

genome mRNA	TGCTGTCAAGGTTGAATCATGAATTATTTTATGTTGCTTATATTGATATGTATCTTAATT	119640

	rs363096	
genome mRNA	TTAAAAGAAAGGTCTAAATGGATGTTTTTGTTTTAGGGAATCAGAGGCAATCATTCCAA	119700

genome mRNA	ACATCTTTTCTTCTTGGTATTACTATCTTATGAACGCTATCATTCAAAACAGATCATTG	119760

genome mRNA	GAATTCCTAAAATCATTTCAGCTCTGTGATGGCATCATGGCCAGTGGAAAGGAAGGCTGTGA	119820

genome mRNA	CACATGGTAACGGGACACACCTTTCCTGTCGTCTTCGGTGTCTGATGTGCTTGGCAGT	119880

genome mRNA	GTTTCGTTTTTCATATACCCACTTTGAACGTTGTCAGTGGCAGCCATGTGCTTCTCAGGCTC	119940

genome mRNA	TGCATGTGTGTCTGTGTATGTGAAGGTACTGGTTAGAGACGTTTCAAAGAGAAGAGAGC	120000

genome mRNA	ATATTCCTTACTCTCAGCAATTTGTAATCTTCTCAGGGAAAAAAATTCAAGAAACAGTAA	120060

genome mRNA	GATAACCTAAGGTACAGATAGATTCTGAATATAAAGTTCCTGTTTCATTACATGAAACGC	120120

genome mRNA	TAAAAGTTCTTCACTTGATCTTAGCCAAAAGGCCAAGAAGCGATGCAACACTAAAATTC	120180

genome mRNA	TTAAATCGAACTTGCCGTGAATTAAATTTTGATCTCTCATCCAGTGGTATTGGAGATATA	120240

genome mRNA	GTTTGACTTGGGTTCAGGGCTTTCTGTTTTGCCTGATGATTTTGCTGGAGCTTAAATAAG	120300

genome mRNA	GAACCCAGGAGATGGCCAGCTGTGCAAGCCCCCAGCCTGTGGAAGGAGCTAGTGTGGTTT	120360

genome mRNA	TATGAATGAGTTGCAAATCTTCTTTGAGCTTTTTGAACTGATCTTCCAGCATTGCCCTA	120420

genome mRNA	TTGACCCCTCCCTGACTCCTTTGCTGGAATCTGTAGGCTTTTGAACTTTGACAGGGACAC	120480

genome mRNA	ATCCTAAGACCCTTGCAAACCTCCAGATGTGAGAATGGCACTACTACTTAGAGTCTTTTC	120540

genome mRNA	GACTCAGCGTGTGTGCAGAAGAGCATCAACCGGGCTGTGTTGCGAGGCAGGGCCTTGGCT	120600

genome mRNA	GACCTCTCAGTGTTTACATAGCTAAGCCAGTTAGTGTTTGCCACGGCCTCACAAGGGCTT	120660

genome mRNA	CAGATTCACACAGCCAAAGTATAGATTATTAAAGGCATAGGTGTTTGGTTTCCTGGACTT	120720

genome mRNA	GGAGGGTCTTTGGACAGAAAATCAGTAGGCAACCACACCCAGTACTTTGTGCTGGGAAGC	120780

genome mRNA	TTGGTCATCTGTGAGAGGGTCAGAGAGTATACCCATGCGTGCATGCCACCGAAGGGTCAG	120840

Figure 1

genome mRNA	TGAGTATTCCTGTGTGTGCATGTCTCAGGGCCGGAGAGAGTATGTGTCACTGAGAGGTCA	120900

genome mRNA	GAGTGTTTGTGTGTGTGTCAAAGAGGGTTGCATTGTGCCCTTCACTGAGGGGTCAGAGGG	120960

genome mRNA	TGCCTCGCGTGTGTGTGTGTGTACGTGTGTGTGTGTCACTGAGGGGTCAGAGTGTGCCTG	121020

genome mRNA	TGTGTGTGCTTGTGTGTGCGTACATGTCACTGAGGGGTCAGAGTGTGCCTCTGTGTGTGT	121080

genome mRNA	GCTCATGTGTGTGCATACGTGTCACTGAGGGGTCAGAGTGTGCCTCTGTGTGTGCTCATT	121140

genome mRNA	TGTGAGCGTATGTGTCACTGAGGGGTCAGAGTGTGCCTCTGTGTGTGTGCTCATGTGTG	121200

genome mRNA	AGCGTATGTGTCACTGAGGGGTCAGAGTGTGCCTCTGTGTGTGTGCTCATGTGTGAGCG	121260

genome mRNA	TATGTGTCACTGAGGGGTCAGTGTTCCCTATGTGCTCATGACATTGAGGGTCAGAGTGTGC	121320

genome mRNA	CTGTGTGCCAATGAAAGGCATTTCTTATATTTTTTTTATATGTGGTCATAGTAGACCAGTT	121380

genome mRNA	AATTTATTTTGACTCCTGTGTAGACCAAAATAAGACTTGGGGGAAAGTCCCTTATCTAT	121440

genome mRNA	CTAATGACAGAGTGAGTTTACTTAAAAAAGCATAATAATCCAGTGGCTTTGACTAAATGT	121500

genome mRNA	ATTATGTGGAAGTCTTTATTGTCTTTTCAGATGAATCAAGTAGATTATTCTTGAGACCAG	121560

genome mRNA	GAATGTTGCTGTTTTGGTTATTTGGAAAGTTTATCATTTTCAAATTGACTTTTGAATTT	121620

genome mRNA	GAGTCACCTTTTTTTCAGAAGTGGTGTAAATTATAGGAGCCCTAGGTTTTTTTTCTTTTT	121680

genome mRNA	TTAGAAGTCATCACAAAATGATCAGTGTTTCAAGGAAGAGCTTTGACCTTCCACATGGTA	121740

genome mRNA	TAATGATTGATAACCTTAATTCATCTCTTACCATAAACCAAGTATGTGTAAGGGTTTTCT	121800

genome mRNA	TTATTTCTTGAAAGCATTTTGTAGATGTTGAGAGCAGTTTTTCCAAATGTAATTTCCATGA	121860

genome mRNA	AATGCCTGATAAGGGTACCCTTTTGTCCCCACAGCCATACCGGCTCTGCAGCCCATAGTC	121920

genome mRNA	CACGACCTCTTTGTATTAAGAGGAACAAATAAAGCTGATGCAGGAAAAGAGCTTGAAACC	121980

genome mRNA	CAAAAAGAGGTGGTGGTGTCAATGTTACTGAGACTCATCCAGTACCATCAGGTAAGAGGA	122040

genome mRNA	ATGTATGTTGGAAGTGTGCGTGGATACTTTATTGACCCGTGCAGATGGAAGGAAGTGCCAT	122100

Figure 1

genome mRNA	GTGGTAACGCTCACTGTAACTGTGTTACTTTGAACCAGGTTTGGGCTTTCTGGGGCCTG	122160

genome mRNA	GGTAGATGCCGGTGCAGGGGGATGGGGAGGGAGGCGGGGGGTGGGGGGGTGTGGTGGAGT	122220

genome mRNA	TGGGGAGGTGCAGTGGCAGGAGGTGTTGTTGGTGTGTATCCTTTTTTTTTTTTTTGAGATG	122280

genome mRNA	GAGTCTCTCTCCGTCGCCCAGGCTGGAGTGTGGTGGCACGATCTTGGCTCATTGCAAGCT	122340

genome mRNA	CCACCTCCCGGGTTTAAGCAATTCTCCTGCCTCCACCTCCCGAGTAGCTGGGATTACAGG	122400

genome mRNA	CATGCACCACCATGCCCAGCAAATTTTTTTTTTTGTATTTTAGTAGAGATGGGGTTTCA	122460

genome mRNA	CCATGATGGCCAAGCTGTTTCGAACTCCTGACCTCAAGTGATCCTCCTGCCTTGGCCTCC	122520

genome mRNA	CAAAGTGCTAGGATTACAGGCGTGAGCCACCATGCCCAGCCTGGTGTATTATCTTTAAAGT	122580

genome mRNA	GGGCACAGCCACAGGAGTTCACCTGACTCCTGGTCTGAGAGTCACGAGATCGTTCAAGAT	122640

genome mRNA	AGTGAGGCCCTCTTTTCCAAAACGAGGACCAAAAATCAATTGACAGTGTTGGTCAAGATG	122700

genome mRNA	GTAGAAACCTTAAAATGATAGAAATCTCAACTCTGAAATAAAAACCTTTATTTGTATATTT	122760

genome mRNA	ATTTACCACTATTTTGACATAGGGCTAAGGTCTTTTTCTTTGAGCTGATTTCTGGTTTTG	122820

genome mRNA	TTTTCTTAAAGTGGCATAAGAATTCAAAGACATTTTGAGGAAGGCTGAGTGCAGAAATCT	122880

genome mRNA	CTCTTTTTTAAATGACTTCTCCTTTCTTTTAACTTGCACTGTTGTCTAGCCCTCACTTATT	122940

genome mRNA	TTGTCAATTCTTTTGTAGCTGTTTGTCTTTGAATCTTCATAAAGCCATAGCTTTTCTCATA	123000

genome mRNA	AGAAGCAGCACTTTCTTTGTTTCATTCATATTTTAATGAACCCCTGTAGTATTTAATTAAA	123060

genome mRNA	TACTTAATGCCTAATTAAATCACATAATTGCAATGCAAAAGTACATGTATCATAAAGAGG	123120

genome mRNA	TCTGAAAATGAGCAACTGGCAAGCAGGTGGTGGCAGGCAGAGCTGCTTGGGTGGGTGGGT	123180

genome mRNA	GTCATGGAGAGGAGTTCATCAGCCACATGTTTCAGTGAGCTCTGGATATGTCTGTTTAGAA	123240

genome mRNA	ATGATCACTAATAAACTTGTGCTCAACCATGTATACCTCTGGGAAGCAGGTGCTCTTCAG	123300

genome mRNA	TAGATTGCCTCTGCAGAGAACACAGAATTGAAGTGAATGTCCACAAAGGCAATGAGCCAC	123360

Figure 1

genome mRNA	CTGCAGAATAGTTTAGTCAAGGCTGTGTTTGAAGTTTGCCAAAGATTAATATACATTTGA	123420

genome mRNA	TTTTCATGTTGTGCCTTTTCTCTGATTGTGAAATATTACAAATTCTATACAAATAACAAT	123480

genome mRNA	GATGGCAAATCCTCCTGAGCAAAGTGTGCACCTTGTATGTGCCCTAGAGGAACCTTGTGTT	123540

genome mRNA	TCGTTCTGATTCCCCTACATTTCTCATGT CATAGAGTGGGGTTCATTAGTGTCCCCCT	123600

genome mRNA	GTCCTCGCTGGGATCACATCTGTTTGGATCCTAGAGTCTTCCAGCTGAACTGGGACAAGT	123660

genome mRNA	ATAACAGACGGACACGTAGGGGTGGAAAGGCGTCTCTTGGCAGCAGACTTTCTAATTGTG	123720

genome mRNA	CACGCTCTTATAGGTGTTGGAGATGTTCAATTCTTGTCTGCAGCAGTGCCACAAGGAGAA	123780

genome mRNA	TGAAGACAAGTGGAAGCGACTGTCTCGACAGATAGCTGACATCATCCTCCCAATGTTAGC	123840

genome mRNA	CAAACAGCAGGTTTGTCCCCGCAGCCTTGGCTTGTTGTTGCATAGTGATGGTAGCTTAAG	123900

genome mRNA	GTCCTTGTGAAAGGTGGGTGGCTGGAATCAGCTCTTCCTTCAGTCCTAATCTGTGCCTTG	123960

genome mRNA	ATAGCAGTTCTCCGTGCTAGTCATGGGACAGCTGACTTCATTTCTTCTCACAATGCCATC	124020

genome mRNA	TCAGGTGGTATTGCCACCTACTTTACAGGGGGGATCCACAGCTCCGAGAGGTTATGG	124080

genome mRNA	AGGTGATCAGGCAGCACACAGCTTTAGAGTGCTGGGGTGAGGGCGGGCCAAGGCTAACTC	124140

genome mRNA	TAAAGCCCGAACCCTTACCTCCTACACTGCCTCCTGCATTCTGGTCAACCCAGTGTTTTA	124200

genome mRNA	TTTGGTGGTTAGATTTTTGTTTTTGTACCTTACTGCTTGTAATTTAGCAGTTTTCTTTT	124260

genome mRNA	CCTTTCCTTCCTTTTCTTTCCGACAGGGTCTCACTCTGTCACCCAGGCTAGAGTGCAGT	124320

genome mRNA	CGTGTAATCTCACTGCAACAACCTCTGCCTCCCAGGTCAACCAATTCTCCACCTCAGC	124380

genome mRNA	CTCCTGAGTAGCAAGGACCACAGGTGTGCACCACTACGCCTGGCTAGTTTTTTGTATTTT	124440

genome mRNA	TAGTAGAGATGAGGTCTCGCTGTGTTGCCAGGCTGGTTTTTAACTCCTGGGCGCAAGTG	124500

genome mRNA	ATCCACCAACCTTGGCCTGCCAAAGTGCTGGCATTACAGGTGTGAGCCACCTCGCCTGGC	124560

genome mRNA	CTATTCATCACTAATCAGAATTTCTATGATCAAATGACATGAATCATTTGTTTCCACAAC	124620

Figure 1

genome mRNA	GCAGTGGAAGGAAATGGCCTGGCAGTGCCAGTTTCAGAAGCAGCCTGCCCCCAGTCAGGC	124680
genome mRNA	ACAGGCCACTGTGCCCCCAGTGTAGCAGCACCTCTGTAGCTCACAGAGAAGGGTGGTGGG	124740
genome mRNA	GACCTCCTTGAGGCAGCTCTGCCAGAAAATCTCATGAGCTGCCTGGCACAGCTTGAGGTT	124800
genome mRNA	GCCTTTTAAGTGGACTCAGCAAATACATGTTTGTTCATCTTGATTATACACAATAAACAA	124860
genome mRNA	CTACTCTGTATAGTACGAGTAGTCCGTGGTTTTTGGCATTTCGATTTAACTTAGAGGCAT	124920
genome mRNA	GTGATATTGATGTTACTGCCTTCATGACTGCACCCCCATTCTGATTTCATAATGGAATGT	124980
genome mRNA	TATCTTGAGACCAGTTAGACAACAGGACAGGGATCTTGGCTTCTGGTGAGATTGACAGCA	125040
genome mRNA	GTTTTAGTGTGGTCAGGGTCTCCCTGCCTACAGATGGTTTTAGAAATGGTGCCCTGGAAGC	125100
genome mRNA	TTTATCCCATTCTTTTCTGTGCGTAATCTGAGTAGAGTGGAGATCGAAGGCCTGAATACA	125160
genome mRNA	TAGTAAATACCTGACTTAATATCTGCCGCAATGGAAATTGTGTGATACAACATTTATGAA	125220
genome mRNA	ACGCTTAGTGCAGCACCTGCCAGGTAGCTCACCACAGGTGCATGTTGCATTTCAGAAGTAG	125280
genome mRNA	TGCTAGATACTATCCTGTTACTGGCAGTGCATACATCAGTGATCAAAGCAGATTAAAGAA	125340
genome mRNA	AGACCCCCTGCCTTCTTGGAGTGAAGATTTTGTGTTGGGATGCGGGTAAGGGGACAGACAAT	125400
genome mRNA	AGAAAAGCAAGTGAGTGAAGTCTATACCATGGCGGCTGATCAGGAACACCGTACAGAAGA	125460
genome mRNA	ATCCAGGAGGGAAGAGAGTTAGGTGGTGTCTGCGGTGGGAGTGGCATTGTTTCAGCTGGTG	125520
genome mRNA	ATGAGAAGAAGCTTTGGTGATCTGGTGACATTTGAGTGAATTTGCAGAAAGGAAAGATAC	125580
genome mRNA	AAGCCTAGGAGATACCTGGGGAAGGAACATTCAGGCAGAGCAAATAGCAGTGCAAAGGC	125640
genome mRNA	CCTGGCGGGGGGCGGACATGCTGTTAGGGTACAAGCAATGAGGGTGGAGGAGTGGGGCAG	125700
genome mRNA	CCATGGGGAGGGAAGGGAGTGAGGCCTGGTGGGGTGAGGCCAGTGTGGAGGAGCCTTGAG	125760
genome mRNA	AGGGTTTGCGCTGATGTGGTGTAGGTTTTAGCAGGATCATTCCTTATTCCTGAGTTGAGAA	125820
genome mRNA	TAGCCTTGAGGGGGAGGTGAGGGCAGAGCAGGGCCACCCATGTGAGACCCGGCACTGGAG	125880

rs2298967

Figure 1

	rs2298969	
genome	TGGAATGGCCCAAGTCAAGCATCCCTTGGCAGCATGAAAGCAAAACCAGCAAGGTTTGCTG	125940
mRNA	-----	
genome	GTGGCTTAGATGTGGCATGTGAGAGAGAGCAGGGCTTTGGGGGTGATTTTCAGGGTGAGGA	126000
mRNA	-----	
genome	CAGGGTGGCTGTGGACAAGGTAGGGCAGACATTGGGGGCAGCAGGAGGTCAGAGCCTGTC	126060
mRNA	-----	
genome	TGGATGTAGCAGTTGAGACCCCATAGGTGCCTAATGAGGTGAGGCCAGCATCAGGTGTAT	126120
mRNA	-----	
genome	GAGCCTGGAGTTGTGAGAGACTGTGGGGCAGGGGGTCAGCATCTGAGATGTCCACTCAC	126180
mRNA	-----	
genome	AGTGGACCCAGACTGGCTGGAGAGGAGGAGGAGCTTGAATACCGAGCCTGCTGAGTCCCA	126240
mRNA	-----	
genome	GCTCCAAGGTCAGGTAGGTGAGGGGAGCCAGTGCTGGGGCAGGGGGAGTAGGCAGGTGTG	126300
mRNA	-----	
genome	GGGTTCCCTAAAGCCAAGATTTTTTTTAAGGCATTTTGTGCAGGAGGGCGACATCTGCTGT	126360
mRNA	-----	
genome	CAGCACCTTGGGAACCTGGCCCAGGTTTGGCAGCACCGAGGGCACTGATGAGTGCTTTTG	126420
mRNA	-----	
genome	GAGGAGCAAAGGGAGCCAAACCCTAATGGGAATGTGTTCTGAAAGGACAGGAGAGAGAC	126480
mRNA	-----	
genome	TTGGGAAAAGGTTTTACTTGAAGAGGGAACGGAGAAATAGGGCAGTAGCCAGAGGAGGAG	126540
mRNA	-----	
genome	AGGAGTCGGCAATGGGTTAAGTTGGCAGAAATGAAGGCCTGTTTACGCACTGAGGGCAGA	126600
mRNA	-----	
genome	AGCAACAGGGAGGATCAGTTCATGACACAGGAGACACAAATCGCCGTTGTGGTGTTCACA	126660
mRNA	-----	
genome	GACATGGGTTAGGATTGGCTGCATGGATGACAGAGCACTGTGGGTTCTCCCAGAGTTGCT	126720
mRNA	-----	
genome	GGGGAGGAGGCAGAGTTGGTGAGCACAGGCGAGGGTCCAGGATGCAGGAATCCTGGAGCT	126780
mRNA	-----	
genome	CAAGTCAGTTGTTCCCTTGTTGTAAGATGTGGCCAGTGTTGTGAGCTTCACATCTGTGCC	126840
mRNA	-----	
genome	TTGAAAAACACCACATCTGTTTGCAGAGTTGTTTACTATGTATACACACTCAGTAGAAAC	126900
mRNA	-----	
genome	AAAAATTGGAAACAGTCAGTGCCCACCATCAATAAGTAATGGTTGAACACACTGTGGTAT	126960
mRNA	-----	
genome	AAGCTTAGACTATTTTAGCTTGGGCTATTTTGCATGATTAAAAATGTTCTGGCCAGGTGT	127020
mRNA	-----	
genome	GGTGGCTCATGCCTGTAATCCCAGCACTTTGGGAGGCCAAGGCAGGCAGATTGCTTGAGC	127080
mRNA	-----	
genome	TCAGGAGTTTGAGACCAGCCTGGGCAACATGGTGAAACCCTGTCTCTACTAGAAATACAA	127140
mRNA	-----	

:

Figure 1

genome mRNA	AAAGTAGCTGGGTGTGGTGGTGTGCGCCTGTAGTCCTGGCTAACTCAGGAGGCTGAGGTG	127200
genome mRNA	GGAGGATCACTTGAGCCCATTCGTGCGCCACTGCACTCCTGGGGCACAGAGTGAGACTCT	127260
genome mRNA	GTTAGAAAGAGAGAGAGAGAGAAAGAAGAGAGAGGGAGGGAGGAAGGAAGGAAGGAAATAAA	127320
genome mRNA	TGGAAGAAATGGAAGGGAGGAAGGGGAGGGAGGAAGGAAGAAAGGAAGTTCAGCCAGTTG	127380
genome mRNA	CCTTGGGAGTTCTCCATTGCACTGGGTTAAGTGAGAAGAGCAGAGACGTTTATGATTTTTT	127440
genome mRNA	CAAAACAACATAAAACAAACCTCTGTGGGTGAGGGGGCAAGGATATGGCTATAGGAACAT	127500
genome mRNA	GGGGCAGATTAAGAAAGGGATATACACACACCACTTAGCATTTGTTACAACCTGTTGTGGG	127560
genome mRNA	AGGGATGGAGTGCAGAAAAAGAAAAAAAAAAGTGACACCATCCCATGTATGTGTATACA	127620
genome mRNA	AAGGGACGCTTGAAGACTGGTCCCCAAAATGTTGGTAATGATTGTGTCAGGGTGCTGCA	127680
genome mRNA	GTGCTAGTTGATTTTTTTTTCACACTTTTGTATATTTGAGTCTTTTACAGAAAGCATTTAT	127740
genome mRNA	TATTTATGTAATAAAAATCTAAATGACAAGATTTCTGTTATGGGAAAAATGTAGCTATAC	127800
genome mRNA	AGTGTTGTTGTAAAAATGTTTGCTTGGTTCACCACTGAACTTAAAATGCTTTTAAATGAG	127860
genome mRNA	GGAAGGTGACGATGAGATGATTATGATGATTTGCCCTTGAGTTACATAGCTGGTGTACAG	127920
genome mRNA	GAAGCTGTCGTTTCTTTTGGCTTACGTAGAAATGTTTGTGGTGTCTAATTCCACAGATGC	127980
genome mRNA	ACATTGACTCTCATGAAGCCCTTGGAGTGTTAAATACATTATTTGAGATTTTGGCCCCTT	128040
genome mRNA	CCTCCCTCCGTCCGGTAGACATGCTTTTACGGAGTATGTTTCGTCACTCCAAACACAATGG	128100
genome mRNA	TGAGTCTCTCGCCTGGCTCAGCAGATGAATCTGGACGGCTTGTTTCAGGCTCTGATTACTG	128160
genome mRNA	GGACCACCCCCAGAATGTCTGAGTCAGTCAGTTTGGGTAGGGCTTCTTGAGAGTTTGCTT	128220
genome mRNA	TTTTTTTTTTTTTTTTTTTTTGGTGTGGGGGTGGTGCAGAACAGAGTCTCACTCTGTCGCC	128280
genome mRNA	CAGGCTGGAGTACAGTGTGATGATCTCGGCTCACTGCAAGCTCTGCCTTCCAGCTTCACA	128340
genome mRNA	CCATTCTCCTGCCTCAGCCTCCCGAGTTGCTGGGACTACAAGCGCCCAACCACGCCCCG	128400

Figure 1

genome mRNA	GCTAATTTTTTTGTATTTTTAGTAGAGATGGGGTTTCACCGTGTTAGCCAGGATGGTCTT	128460

genome mRNA	GATCTCCTGACCTCGTGACCCGCCCATCTCAGCCTCCCAAAGTGCTGGGATTACAGGCGT	128520

genome mRNA	GAGCCACCGCACCCGGCCTTTTTATTTTTTTTGGAGATGGAGCCTTGCTCTGTCACCCAG	128580

genome mRNA	GCTGGAGTACAGTGGCGCTACCTCGACTCACTGCAACCTCCGCCTCCCGGGTTCAAGCAA	128640

genome mRNA	TTTTCTGCTCAGCCTCCCGAGTAGCTGGGACTACAGGTGCGTGCCACTGTGCCCGGCT	128700

genome mRNA	AATTTTTTGTATTTTTAGTAGAGACGGGGTTTCACTGTGTTAGCCAGGATGGTCGCGATC	128760

genome mRNA	TCCTGACCTTGTGATCCGCCCGCCTCGGCCTCCCAAAGTGTTGGGATTACAGGTGGCTCT	128820

genome mRNA	CGCACCAAGCCAAGAGTTTGCATTTTTAGCAAATTCACAGGTGAACTAATGCCTGCTTT	128880

genome mRNA	TCTGGGAGCACACTTTGGGACTCAGTGATAGAGAGGTTTATTGGTAGGATAGTAAAATAG	128940

genome mRNA	GAGTTATTTTCTTTCACAAAATTGGCAATTGGGGGAAATTTAATCTTCCTTTTTTCTTCA	129000

genome mRNA	GCTGTGACTTATGTATTATGTTTATTTTAGGCGTCCGTGAGCACTGTTCAACTGTGGATA	129060

genome mRNA	TCGGGAATTCTGGCCATTTTGAGGGTTCTGATTTCCAGTCAACTGAAGATATTGTTCTT	129120

genome mRNA	TCTCGTATTCAGGAGCTCTCCTTCTCTCCGTATTTAATCTCCTGTACAGTAATTAATAGG	129180

genome mRNA	TTAAGAGATGGGGACAGTACTTCAACGCTAGAAGAACACAGTGAAGGGAAACAAATAAAG	129240

genome mRNA	AATTTGCCAGAAGAAACATTTTCAAGGTATGCTTTCTATCTGAGCCTATAACTAACCCAT	129300

genome mRNA	GCCTTTTGGGAAGTCACGTGATGTTTCACAGTCAGTAAGTCTGGAATAATACCTGGTCTT	129360

genome mRNA	GCTTCACTTCTGAGTTGGGTAAAGAAGTCTGTATCAGTGTAATTTTCTAATCCGTCCTGC	129420

genome mRNA	ATTATCTATGGCTCTTGGTTCATACCTGTCTTGAAGTTCTGTCATGTTCTGTCTCTTGTC	129480

genome mRNA	CTCAGTAGAGATGCTACAGCAGTGGCTCGCCTCAGGCAGGGCAGGGCAGTGGGGTGGCTG	129540

genome mRNA	TCCTGGGGGCAGGCAGTAGGGGCACGCTGACGTGAGGGAAGTTGAAACCCAAGAGAAGCC	129600

genome mRNA	AGTAAAAGTGAGTCTCAGATTGTCACCATGTGCTGGCAGTTTTACACGCTGTCAGTAATA	129660

Figure 1

genome mRNA	AAAGTCTTCTCCCTGCAGGGCAGCCTGCCTCCAATAAATACGTGTAGTATCAAATCCTGT	129720
genome mRNA	CTTCCCTCATAAATTGTTTGGAAGCTCCCCAAGGACAGTGATGAGGCACTCGTAAGTGCT	129780
genome mRNA	TGCTGCCTAGATGGGTCCCTCTCCACCTTTGCTAGATTCTGAGCATTCACTGAGTTAGAG	129840
genome mRNA	CTGCTTCTGCAAATGTGCTGCTTCTGCTAAGTGGCTGTGACTTCATGCAGCCTTCACTTG	129900
genome mRNA	GTTTGTCATCAGTGGAGATGCCCTGTGTTGTGCGAAGGAGATAAGCCCAGTAAGCCTGCTG	129960
genome mRNA	GGCACCTTTTGGTTTGCAGGTTCAGCAGGCAGCCCATGGCTTTCCCTGTGTGCGATTGAA	130020
genome mRNA	GCAGCTGGCTAAAATTGATGATACATTAAATTCCTGTGACAGATGATCAGCTTGTATTTG	130080
genome mRNA	TGTAATGGTGTACAGTTCACAAAGCTTAAAAAAATGCTACCTGCCATTTTCATCCTCAGT	130140
genome mRNA	AGGAAGGTGATACACAGAGAGACCAAGTGACTGTGTCCACGGCGACGGCGCTCTGCATTT	130200
genome mRNA	CACTTTAGCGGTTAATGTACTCTACCTATATTTTTACTTTATATTTACCATATATCTTTT	130260
genome mRNA	CATGTATACTTGGCGTAAGTGCTTTATAGTAGTCACCTAATTCAGTGTGATCTTTTTTGT	130320
genome mRNA	TTCTTGGAAGGTTTCTATTACAACTGGTTGGTATTCTTTTAGAAGACATTGTTACAAAAC	130380
genome mRNA	AGCTGAAGGTGGAAATGAGTGAGCAGCAACATACTTTCTATTGCCAGGAAGTAGGCACAC	130440
genome mRNA	TGCTAATGTGTCTGATCCACATCTTCAAGTCTGGTAGGTGAATCACATTAGTCTTCCTGG	130500
genome mRNA	AGTGTCTCGTTCCCCATTCTGCACTATACACTCTCAGAGTGTAGGAGCTGTGCTGCCCGG	130560
genome mRNA	TAGAAACTCTGCCTTGCCCCAGTGTGCCAGTTGAAAATATTTGTTGCTGTAAGAGTACACC	130620
genome mRNA	TGATACCATGTGACCCAGCAGTTCCACTCTTGGGTATATACCCAAAAGAATGGAAAGCAG	130680
genome mRNA	GGTGGTGAAAAGATATTTGCATGCCAGCATTATAGCAGCATTATTCACGATAGCTAAAA	130740
genome mRNA	TGTGGAACCAACTGAAGTGTCCCTCGATGGATGAATGGATAAGCAAATCTGGTGTATAT	130800
genome mRNA	TTACAGTGGAATATTATTCAGCCTTAAAAAAGGACATTCTGACACATGCTACAACATGG	130860
genome mRNA	GTGACCCTTAAGGACATTATGCTAAATGAAATAAGCCAGTCACAAAAGGACAAATACTAT	130920

Figure 1

genome mRNA	GTGATTCCACTTACATGAGGGACCTGGAGTAGTTAATTCATAGATATAGAAAGTAGAATG	130980

genome mRNA	GTGGTTGCCAGGGGCTGCAGGGGAGGGGAGTTATTTTACAAGATGAAGAGAGTTATTCT	131040

genome mRNA	AGAAATGAATGGTGGTGATGGTTGTATAACATTATGAATGTACTTAATGCTACTGAACTG	131100

genome mRNA	TACAGTTAAAAATAGTTAAGAGGACCAGGTGTCATGGCTCATGCCTGAAATCCAAGCACT	131160

genome mRNA	TTGAGAGGCCAAGGCAGGAGGATTGCTTGAGCCAAGGAGTTTGAGACCAGCCTCAGCAAC	131220

genome mRNA	ATGGTAGGACCCCATCTGTACAAACAACTAGCCGGGGATAGTGGTGTGCATGTGGTCCC	131280

genome mRNA	AGCTACTCAGGAGACTGAGGCTGGAGGATCGCTTGAGCCCAGGAGGTTAAGTCTCTAGTG	131340

genome mRNA	AGATGTGTTTCATGCCACTGCACTCCAGCCTCGGCTATAGAGTAAGACCCTGCCTCAAAAA	131400

genome mRNA	AACAAAACAAAACAAGACAAGAGCCAAAAATGGTTAAGATGGGCCAATCACAGTGGCTTA	131460

genome mRNA	TGCCTGTAATCCCAACACTTTGGGAGGTCAAGGTAAAAGGATCACTTGAAGCCAGGAGCT	131520

genome mRNA	TGGGACCAGCCTGAGCAACATATCGAGACCCCTATCTCTACAAAGAAAATCAAAAACCTAG	131580

genome mRNA	CTAGATATGGTGGGCACATGCCTGTAGTCCCAGCTACTTGGGAGGCTGAGGTGGGAGGAT	131640

genome mRNA	CTCTTGAGCTCAGGAGTTCGAGGCTGCAGGGAGCTATTATTGCACTCCAGCCTGGGCTAC	131700

genome mRNA	AGAATGATACCCTGCCTCTTATTAAAAAAAATCCAAAAAAAAGTAAACCTGAG	131760

genome mRNA	AGCTTCCTCCTCCTGTGTAAATTTGGAGGCCAAGATGTTTTTGTACTTTTACAAATGA	131820

genome mRNA	TCAAGGACGGTGAAGGTTGGGCATGGTAGCTCACACCTGAAATCCCAGCACTTTGGGAGG	131880

genome mRNA	CTGAGGCGGGGTGATCGCTTGAGCTTGAGACCAGCCTGGACAACATAGCAAGAGACCCCA	131940

genome mRNA	TCTCCACAAAAATAAAAAAATAAAAAAATAGCCAGGAGTAGTGGCATGAGCCTGAGCC	132000

genome mRNA	CAGGAGGTCAAGCTGTAGTGAGCCATGATCATGCCACTGCACTCCAGCCTGGGCGAGATC	132060

genome mRNA	GAGACCATGTCTCTAGAGAAAGAAAATGACAAGGACAGTGAACCCAAGAAAGTCATAAGA	132120

genome mRNA	TGCCAGCTGTGCAGCAAGCATGGAAAGCAGCCAGTCCAAATTAGGACAGTGTGTTTTCCA	132180

Figure 1

genome mRNA	AGAAGAACGATCGTTTGTAATGAGAATGCTTTGCTTTAAATAAATGACTAAATAGCTAGA	132240
genome mRNA	AGCCTAGTTCTAGGGGATAGGCACGTCTTTCTTCTCTCAAGAAAATAGAAAGGCAATTCT	132300
genome mRNA	AATTTCTAGTAACAGCAAACAGCATTAAAGTCATGGTCCAAATATGAGGCAAACCAAATG	132360
genome mRNA	TGGCTTGATTGTTTCAGCAGTTGATCTGTTGGAAGCCCTTGATATTAAAAAGGTTCTCCTT	132420
genome mRNA	TAAGCGGCTTAGGAGTCACGATCAAAGACCTATAGAAAGAGATGCCATCCTTCTAGGATC	132480
genome mRNA	CTTGGCTCTCTTGGGAACTAGATTCAGATAGTCATAATGTAAATACTGCTTGAGCTTTCT	132540
genome mRNA	TTCTTTCTTTCTTTCTTTCTTTCTTTTGGAGACAGAGTTTCACTCTTGTTGCCCATCC	132600
genome mRNA	TGGAGTGCAATGGTGCCATCTCGGCTCACCGCAACCTCTGCCTCCCAGGTTCAAGCAATT	132660
genome mRNA	CTCCTGCCTCAGCCTCCCGAGTAGCTGGGATTACGGGCATGCACCACCACGCCTGGCTAA	132720
genome mRNA	TTTTTTGTATTTTGTAGTAGAGACAGGGTTTCTCCATGTTGAGGCTGGTCTCGAACTCCTG	132780
genome mRNA	ACCTCAGGTGATCCACCCGCCTCGGCCTCCCAAAGTGCTGGGATTACAGGTGTGAGCCAC	132840
genome mRNA	CGCACCCGGCCCGAGCTTTCATTTTGAATCAATGTATGACTGAAACACTGAAGACTTA	132900
genome mRNA	CTGACTTAATTATGGTTTCAGAACAGAATGAAAATGTCTTCGGTTCTGATGAATATAAAA	132960
genome mRNA	GGAAACTAACCAAGTTAATTTGGCAAGTAGATGGTAGAGATAGAGGTGGGGAGTGGAAG	133020
genome mRNA	GGGAACTAAAATCTTCACCTAGCATTTGTTGGGATTATATGGTTACATCATCTGAAGTTGA	133080
genome mRNA	CAGACCAAATATAGAGGCTTCAGAGGTCTCCAAATAGAACTAAACATGTAATTCAGATT	133140
genome mRNA	GTTAGGAGGTAGTATAAATGAGCTAAATCTCATCTTTATTACGGTAGAGTTAATGGGTGA	133200
genome mRNA	TGTCTAAAGTTGTCTGAAGTCTATAAATCATGACAAATTATGATGTGGTGATTGTATTCA	133260
genome mRNA	ACAGTCTTTCAGTTGCAGGGATAAAACCCAGTTTAACTAGAGTAAGAGAAAGAATGTG	133320
genome mRNA	TTGGTTTAAGCTCCTGGAAAGTGCAGGCAAGGGTAGTTGGTAGGACTGCATCTAGTGTTG	133380
genome mRNA	TAATTCTGTGGTCTGCATTGTATATTTATGCATCTCAGCTCTGCTTTCTTCTTTTCATTT	133440

Figure 1

genome mRNA	ATATAATTTTAAATTTTATTTTAAAGATAGGGTCTCACTTTGTGCGCCTAGGCTGAAGTG	133500

genome mRNA	CAGTGGCATGAAGTGCAGTGCAGGCTCACTCTAGCCTCGAACTCCTGGGCTCTAGAGTT	133560

genome mRNA	CTTCCTGCCTCAGCCTTCTAAGTAGCTGAGACAATAGGCATGTACCAACATGCCTGGATA	133620

genome mRNA	GGTTTTAAATTTTTTTGTAGAAATGGAAGTCTTGCTGTGTTGCCAGGCGGGTCTTTAA	133680

genome mRNA	CTCTTAGCTTCAGGCGATCCTCCTGCCTCTGCCTCCCAAATGCTGAGGTTATAGGTGTC	133740

genome mRNA	ACCCACCACGCCCAGTCTCATCTCTGCTTCCTGTGTTAGTTTTGTTCTCTGGTGGGCTGT	133800

genome mRNA	TTTCACATGACCGAAGATGACCTCTAGCAGGCTGTGTTCTCAGCCCCCTCAAGTAGGCCTA	133860

genome mRNA	TGTGATTGGCCTTGCATGAGTAATATGGGTGACCATAAACCCCTGAATGCTCTGGTCCAC	133920

genome mRNA	ATGGGCCAAATGGGAGACTGGACAGCATTCCATTGATGAGGAGGTGGGGCTGGTCTCCGG	133980

genome mRNA	GAGTAAGGGAGAGGAGCACATGCAGTAACTGATGGTCTGCTGCAAGGGATAGCAGCACAG	134040

genome mRNA	CAGTTAGAATTTTGGAGGTAACCTACCAGAACTGAAAACAGAAATGATAACAAGTAGTTGC	134100

genome mRNA	CTTAAAAAGGGATGGGAGCAGGGTGCTTTTGTGATCAAAGCTCCTTTCTCTTACTGGATT	134160

genome mRNA	TTTGTACACATTTTGCATACATATCTTAGAGTAAAAGATAGCATTTCAGCCTTGGTCCA	134220

genome mRNA	TTTGAGGATACTCTTGGCGTGGCCCGCCTCCATGCTAGCAGGCTCTGGTTGTGCCAAGTT	134280

genome mRNA	CAGTTGAGCATCCTGGCTCTTGCCCTGCACGGAACCTCCAGTCAGTGCGTCAGTATCACAA	134340

genome mRNA	GTCTTGATATTTCCCTATGAAGAAGAACAGTAGTGACAGACGAAATGGGTGGGCAG	134400

genome mRNA	GCAGAGGCAGGATTTCTGAGGGAGAGAAGTAGCTAGCTTTTTGCAGAGAAGAGTTCCGGC	134460

genome mRNA	ACCCAAGAGAGCAGCTGAGAGTACAGGCAGGCAGGCAGGATGCCGGTAGGGCCCGGCCGC	134520

genome mRNA	ACGGCGCCACAGAATCCTGGAGAAAGGGGCCTCTTCATGGCCTCTGCATTTCAGCTGCTGT	134580

genome mRNA	CACCCTCCGCACAGGCCATGGCCAAAATTTAATTTTCATAGTGGACTCTAGTTTTTGAGC	134640

genome mRNA	CTTACTTGCTATTATTGAAATAATTTTCTTGTTTCTTTTTAAAGATCTTCGGATTATGCT	134700

Figure 1

genome mRNA	TCACTGACCACTGTAATAAGTTTAAAGTTGAGAAAATATGGCTTGTTAATGAATGATAGG	134760

genome mRNA	TCAATTTTAGTATGTTGGTCATTTTAATATTTTGCCACCAGTTGGTTTGGATTTGATGCC	134820

genome mRNA	AGGAGGAGACAGCCTCATTCTAAGGACTAGTCTTGCCTTTGTGGGATAAGGGTGGTGTG	134880

genome mRNA	TTCTGTGTCCTTCTACATGTCCGAGCGATCTCTGTGCAGCTCAAATGTGGTCACTGTCTT	134940

genome mRNA	ATTGCGCTGATTTCCCTCTCCTTCCATCTCACAATTGAGGCAAAATATTGTTACTGTTGAA	135000

genome mRNA	GTGTTGTCCAATAGGACTTCCAGCAGAGACAGGATGTCTGCACTGTCTAATTTAGTTGCC	135060

genome mRNA	TTTAGCCACATGTGGTGTCTGTACCTGAAATGTGGCTGGTCTGATTGGATAGCTTAATT	135120

genome mRNA	TATAATTTTATTTAATTTTAATTAACCTTAAATTTAAACAGCTCTGTGTGGATAGTGGCTC	135180

genome mRNA	CTGTATGAGACAGTGCAGGTCTGTTGAGAAGCAGCTTTACTGGTGGGAGTGGAGGGCTTG	135240

genome mRNA	GAGAGGGCACGTGGGTTTCCTGCTGGTATCTTTTGACCTTATTTAATCTGCCCAACATTT	135300

genome mRNA	GCAAGTAAGTTGTGTGTGTGTATATATAAATGTGTGTTTCTGTCTTCTTGTTCCTTT	135360

genome mRNA	GACTGCATTTATTTGAAAGACACTAGGTGGCAGAATTACTGTATTTGATTGGTTTCAAGA	135420

genome mRNA	TAAGAGTTGAAATAATTCATCTCGTGTTTTTATATAAGTAAGGTGTGTTTAGCATGTAAA	135480

genome mRNA	ATTGGTAATATGTATTCACGTACTGCTTAAACAAAGGCTATGAATTCCACCCATAAACCG	135540

genome mRNA	AAAATGAAGACCTTTAAATTTGTCCATTTCAAGCGTGGGTACTTCTTAAATAATACCTGG	135600

genome mRNA	TTCAGGAAGTAGTCAGAATGGCACCCTTGACTTTTTGTTTCCTGCTTTTCCTCTTGTGG	135660

	rs363092	
genome mRNA	GAGAGGAGGGTATTCATCCCAAGTGGTTTGCCTATTTACATTCATCTAGGATAAGCA	135720

genome mRNA	GAATAGCCAAGAAAGATAGCTGTCCTCCTGTTTACAACATTTGGGGTAACCAGCATCCCT	135780

genome mRNA	CTCTTTTGGTCCAAGATAGACTGGTTTAGAAACAGATGATGGCACCAGAGGCCAGGAGG	135840

genome mRNA	TGGAAACATCAGCTTTGTTTGTGTCCATGTGGCTGAATTAGAGCTGTCTGGCCTTGTAG	135900

genome mRNA	CCTCAACACGGCCTTCCAGCTTTGCTCACCGTGATTTTCAAGGACACATCTTGTGCTCTT	135960

Figure 1

genome mRNA	CCCTGCCTGCCATCCAGACTATACCCAGTCAGGGTGGCAGGAGCTGCTGCCCCCTTCCTCC	136020
genome mRNA	CTGAGTCCTGGTCGTGGGTGGTGGAGATGTGCCATGACGCTCACGGAGGCATGCTCACCC	136080
genome mRNA	CTTCCTCTGTGGCAGAGGGGATGGCTGCACGACAGCTCTTCCCTGTCCTTTCCAAAGCGT	136140
genome mRNA	CTGTGGTTCCACTTTTTGGGGCAAAGCAGGAATACTGGAAGAGAGAGAAAGTGGTCCTTT	136200
genome mRNA	CTATAGTAATAAAGTTGACATTGATTCAAGTTCATGCTTGGGGAAAGGACAGGGCTACTA	136260
genome mRNA	ACAATTATAATGCTGGGAGCAATGGAATTTTCTCATGGGTATGTGGTAGGTTTAATTTTA	136320
genome mRNA	ATTATCCCAGTTAATTCTTAGAACTGCTCTGTGAAGTATTTCCCGCTTTGTGCTTAAGTT	136380
genome mRNA	CTAAAAGATCCTGTGCCAAAACCAAGAATGAAAACCCAAGCATTCTTTCTTGCCCATCGA	136440
genome mRNA	TCTTTCTCTCATCAGGCCACTTCTTGGGTGATAGTGGTGAGTGAGCCGCTGCCACTTT	136500
genome mRNA	CAGAATACCCACCATGGGCCCCAGTCACTGTGTGGCGTGGAGAAGAGATGGTTCTCTCTG	136560
genome mRNA	TGTCATAGCTGAACAAGCCCAGCCCAGAGAGGTTTCTGCCCTAGGAGCTCTCGATGGTGG	136620
genome mRNA	AATTGGGATGCGATCCCACATCCTGCCTGTTTTGAAAACAGCATTCTTTATTTCCAATTC	136680
genome mRNA	CTGCTTCCATTGTTTCCTTTTAATATTTCTTTGTTTAGCTCACAAAAACACGGCTTGCGGA	136740
genome mRNA	GCTGCTGCGTGCAGCTGTAGCTGTTTCTCTGGGTGCAGCCTGCATCCGCCTTCCTGCCCCG	136800
genome mRNA	CCTCCTTTCTGCACTGCCATCGTGGTCTCCGGGCACTTGGTCCCTTTCTCTTCCCCTGA	136860
genome mRNA	GTCCCTTTGGCTCCCCTGTGCCACCCTTGTGATCCACAGGCTCTGCCTTCTTTCTGTCTC	136920
genome mRNA	AGACTGCTGCTCATCACTACTCGGGACCCTAGGAAGGGAGGTTCCACCGAGAAGCATCTT	136980
genome mRNA	CTCATCTCAGCCACGTTCTCAGTGCCACTGTTGTCTTTGTTAGGTAATGGTAGCTACTGT	137040
genome mRNA	AACAAATAAACCAACATTTCCATGGCTTCACACCAGAGAAGGTTGTTTCTTGGTTTTATG	137100
genome mRNA	ACAATGTATTGAGGGTGTTCTTGGTTCACGGATGGTTTTCTCCATGTGGGAATTCGGGG	137160
genome mRNA	ACCCAGGCTCCTTTCTTCTTTTGGTTCTGTTCTCCAGGCCTTCACATCCTCTGTGTCTG	137220

Figure 1

genome mRNA	GTTGGGGACAAGGAGAGGGAAGGTAAAGAAGGCTTTGTGGCCTTGGATAAGTGACAGGCA	137280

genome mRNA	TGCCTTTGCTGGTGTCTCTCGTGGTGACAGGTCACAGCCCCACCCTGTAAAAGGGGACT	137340

genome mRNA	GAGAGACGTCGTCCTGCTGCTTCCCAGCAGCAGCACTGTGGTCTCTGATGTGTTTTCTGT	137400

genome mRNA	GAGGATAAAAACAGGTGATTCCAGGATGAGGAAAGTCAGGGAAACCCTTGAAGGAGGGG	137460

genome mRNA	ACCAGGCGGGTGTCACCATGGGATTAGTGGTGGCTTCAGAATGAGCTGCAGCGAGTGCCA	137520

genome mRNA	TGCCTTCTAAAGCTTTTGCTATTCTGATATGCCACACCATGCCCAGCAGGTGTCTGCCT	137580

genome mRNA	TGCTCTCCGCAGAGAGAGTGATGAATCCTTCTCATGAGCCTCTGTCCAGTTGTTCCCTCCC	137640

genome mRNA	TCCACCTGGAAGGGACCCTGGGTTCCTCATAACATCCCAGCGGAACAGGGGACCTTCTAT	137700

genome mRNA	CCTGTCCCAAGTTCATCCTCATCCTCCTGCCGGCTTCCTGGCCCCTCTTATGTCTGCTT	137760

genome mRNA	CCTGACGCCACATCCTTCTGGATTCTCTGGAATTGAATTTGCCTTTGATGCTTATTTAA	137820

genome mRNA	AAATATCCATTGCAGGCCAGGTGTGGTGGCTCACACCTGTAATCCTGTGCACTTTGGGAA	137880

genome mRNA	GCCAAGGTGGGCAGATTGCTTGAGCCCAGGAGTTTGAGATTAGCCTGAGCAACATGTTGA	137940

genome mRNA	AATCCTGTTTCTATAGAAAATACAAAATTAGCTGGGCATGGTGGCGCACACCTATACTC	138000

genome mRNA	CCAGCTACTCAGGAACCTGAGACAGGAGGATCAATTGAGCCCCGGAGGCCAAAGCTACAG	138060

genome mRNA	TGGGCTGTGATCGTGCCACTGTACTCCAGTCTGGTCAAACAGAGTGAGACCCTGTCTGAA	138120

genome mRNA	AAAAAAAAAAAAATCCATTGCATACTTCACCGTAGCGAAACATGTATGTCTTACCTTTCC	138180

genome mRNA	TTTCCTGCCTGTAGCTGCTCTTTTACACTTAACAGCCACACTAAGCCAGCCTTAAATGAA	138240

genome mRNA	AAACAAACCAGCACTTCCTGTGCCCTCCTGCTTCCTTCATGAGGGGTCCCTCCCTCTGTG	138300

genome mRNA	TACACTCCATTCTCATTGCCCATGGTGGTTTGTTCCTCTTGTTTCTCAAGCCATGGCA	138360

genome mRNA	GCCTGCCTCTTGCCCTCTTTACTAAAAAGGCCTTTGCAGAGGCTGCCTGTGTTCTTTCTT	138420

genome mRNA	TCTAGGTCTCTCTCATCCTAGGCCCTCCAGCTTGATTCTGTGGAGCTGCCCTCTTGTCAC	138480

Figure 1

genome mRNA	TCAGTAGCTTGTGGGGTCTTCTCTGTCTAGCCACTTAATTGATTGTGTTCCCTCGAGTTGC	138540

genome mRNA	TGTCCATGGTCTCTCGTTACTGTTTTCTCTGTGTTTCTGCCTCTCTCCTTGGCCTTGGTA	138600

genome mRNA	GGTCCATCCCCTTTGTGACCTTGGCTGTTGCTCTCATGGACAACTTTCTCTTGCTGGTCC	138660

genome mRNA	TTGTAGTCCTGGCATCCAGCTTCTCGACACGGGACTTGTCCCTGCCAGTACCTCAGACTTG	138720

genome mRNA	CACTTAAAATTGAACTAGCACCCTGTCACTCTCCAGGGCCTCTTCTTGTTAATTAGATC	138780

genome mRNA	ATTAGGGATGTTTCAGAATCCCAGCATCATAGTATGTTCCCTCCTCCCGCTACCCAGGAAC	138840

genome mRNA	CCTAACCTTACCTCCTCCTCTCTATCTACTAGGAGGTGGCCCTCAGAGTCCGTCTCATCT	138900

genome mRNA	TCCACCTGAACTTCCCTAATAGGCTCCAGCAGCTGCCACCCCGGGGGCTGAGTACTTCCT	138960

genome mRNA	CCATGCCTTGTGCAGTGCTGAGCCCTTTACCTGGGTTCTCCTGTTTGCTCCTTATTACAG	139020

genome mRNA	CCCTGCGAACAGATACTGCTCTTAATTCCATCTTACACCTAAGGAAGCTGAGGCCCCAGG	139080

genome mRNA	TAAGGTGCATCCAAGGTCACCCAGGTAGTAGACAGTAGAGCCACGATCTGAACCAGGCAG	139140

genome mRNA	TCTGATTGAGAGCCTGTGTTGACACTCAGCCACCTAGAACACAGCTTGGATTGTGGGTTT	139200

genome mRNA	CTATTACCTGTTCAAAACCCCTACATCCCGGGTCTGTCCCTGCACGTGCTCTGTGGCCTG	139260

genome mRNA	GCTGCATCTTCCTTGAAGGCAGTGCATGCCTCTTCACTCAGGGGGCCCATGCAGGAACAG	139320

genome mRNA	AGGGCCCCACAGAAGGATGAGGCCAGTGCAGAATGGGCTGGAGGGGACAATGCTGACCAG	139380

genome mRNA	GAAGCAAGTGTAGAGAAATCCCAGGAAACCTGGAGGAGCCAGAGACAAGGCATTAGAACT	139440

genome mRNA	CCTCGTCGTGACCTGGTCTGCATTCTCTGAGTGTGCTGCTTCTGTTAGCTCGCTTCCTTG	139500

genome mRNA	GTCTCAGGTTATAGTTTAAGGCATTGTGGAGCCCTAAAAAGCCTGTACTCTGTTTTTACC	139560

genome mRNA	TGTTTTAGGACCCTTTCACCTTGGGGATGTGTTGATTTTTTTTTTTTTTTTTTTTTTTT	139620

genome mRNA	TTTGAGATAGAGTCTCGCTCCATTGCCAGGCTAGAGTGCAGTGGCACGATCTTGGCCAC	139680

genome mRNA	TGCTGCCCCCTGCCTCCTGGGTTCAAGCAATTCTTGTGCTCCCGCCTCCCAAATACCTGGG	139740

Figure 1

genome mRNA	ATTACAGGCACCCGCCACCACACTCGGCCAATTTTTGTATTTTATAGTGGAGACAGGGTTT	139800

genome mRNA	TACCATGTTGGTCAGGCTGGTCTCGAACTCCTGACCTCAAGTGATCTGCCCACCTTGGCC	139860

genome mRNA	TCCCAAAGTGCTGTGATTATAGGCGTGAGCCACCACACCCGGCCTGAAATTTAAATCAGA	139920

genome mRNA	AATAAAATTTTGATCCCAACAGTGATGCCAGGCAGCCCAGATCTGGGGGAGAGGGTGGCC	139980

genome mRNA	TTGGCCAGCTGGGCCTTTCTCTGTTTCCCAAGTCTTGCTGCCTCTCCCTGCTGGGCTTTG	140040

genome mRNA	CAGCCTGTGCATGTCTCTGTGCCTTTGACCTTGTTTATCCAAAGGAGAGGATAGAATGAA	140100

genome mRNA	GTCATGATTCCCTGGAGCCCTGAGAAGGATGCTGTGGAGAAATTTGCCGGTAGAATCTAGC	140160

genome mRNA	TGAGTGTGTTGCTGAGGTGCCAGCATTCTGTGTGGGGAGGCTGACCGCTTGGCCTGCCTA	140220

genome mRNA	GGCCCAGGATGCTCCATGGCCGGGCACAGAGGCCACTTGGCTGTCAGGTGTCAGGAGCCT	140280

genome mRNA	GCAGAGGGCACACAGAGCCTGGACCGCAGGGGGGTCCTGCTTTCTCACCTGGCCTCCTTC	140340

genome mRNA	AGCATTTCTGTCCCTCAGTCCTTAGCAAGCCCAGGAGCTGTTGAGTTTGGCAGGTGCCGA	140400

genome mRNA	GTGCTGTTCCCTGCCTGTGTAGCTGTGGCTCAGTCCTGTGGGGGCCCCGCTGTGGCCCCGAG	140460

genome mRNA	TGCAGTGATTGAGGCGCTGAGTGTTCCCTGACTCCTTCTCCAGGAGCTGTGTTTCAGACT	140520

genome mRNA	TTCGCAGCTCTTGGCTTGGAGCTCCTGGAGGGCTTGGCATTGCCGACCAATGTGGAGGTC	140580

genome mRNA	GACAGTGAGAGAGGAGGAATGCTAGCTTTCTTGACCAGTCCATTAAATAAGTGGGATATT	140640

genome mRNA	GGCCAGGCACGGCGGCTCACGCCTTAATCCCAGCACCTTGGGAGGCTGAGGCGGGTGGAT	140700

genome mRNA	CACGAGCTCAGGAGTTCAAGACCAGCCTGGCCAACATGGTGAAACCCCCTCTATACTAAA	140760

genome mRNA	AATACAAATATTAGCTGGGCGTGGTGGCAGGCGCCTGTAATCCTAGCTACTTGGGAGGCT	140820

genome mRNA	GAGGCAGGAGAACAGCTTGAAACCGGAAGGTGGAGTTTGCAGTGAGCCAAGATTGCGCCA	140880

genome mRNA	CTGCACTCCAACCTGGGCAACAAGAGCAAACTCTATCTCAAAAAAAAAAAAAAAAAAGTAG	140940

genome mRNA	GATATCTGTTTCTGCTTAGAAAAATCAGAATTTTCTAAATGCCAGGTGTTCTGAATACGT	141000

Figure 1

genome mRNA	AAGTATGGGAGACGACTCAGCCTGTTTCATTTTTATGTAAAATCTTCGCGTAGCCATGTG	141060

genome mRNA	GCACTGGACCGAGATGAAAGCAAAGACATTTCTCCTTAACCTTGTTTCTAGGAATGTTCC	141120

genome mRNA	GGAGAATCACAGCAGCTGCCACTAGGCTGTTCCGCAGTGATGGCTGTGGCGGCAGTTTCT	141180

genome mRNA	ACACCCCTGGACAGCTTGAACCTGCGGGCTCGTTCCATGATCACCACCCACCCGGCCCTGG	141240

genome mRNA	TGCTGCTCTGGTGTGAGATACTGCTGCTTGTCAACCACACCGACTACCGCTGGTGGGCAG	141300

genome mRNA	AAGTGCAGCAGACCCCGAAGTAGGTTCATAATGCCCCACAGCCCAGGGCGCCAGCCCAGC	141360

genome mRNA	ACCCTGTCCTGAGACTCCCAGTAACCTGAGCTTTGGCCACCGTTAAAGCATTTCATTTT	141420

genome mRNA	CCATTTTTTTGTGAGGGCTTGTGAAATTTCTGCTGCATATTAATATTCCTTTCATGGACAG	141480

genome mRNA	CATATTATTGGGACAAACATGCGGTCCAGCTAAAGGCATTCAAAATAGCAGTTGCTTTCT	141540

genome mRNA	AAATGCGATTTTCTTTGGCAGGTTCTTTGACACCATTGCATCTTGTGGGATATGCTTGTC	141600

genome mRNA	ATGCTCTGTGGCTCCTACTAAGTTCTAGTCCTTAAATTGGTTCCATAGCCAGACATGTTG	141660

genome mRNA	CAATGTCTTAACCTCATTATAAAGTAAATGTGGTTCTGGTTATCCTTAGATAATGAAGTA	141720

genome mRNA	ACAGTGTAGCAAATTTCAAAACCTCTTGAAATGTTATTTTACCATTCAAAAAGGCTTAC	141780

genome mRNA	TAAGGTTCTCGTTATGGGTGGCCCTCTTTTGCAAAAGGTTTTTCAGGCTTAAGCTCCATT	141840

genome mRNA	TCTAGGTGCTCCAACACTCCATTATTTGTATATGTATGGAAATAAAAGCTGTGACCACCC	141900

genome mRNA	CCAACCCTGGCCCCCGCCAGCTGAATCCTCAGCACAGTATTTCTGGAAGGCTCAAGATC	141960

genome mRNA	CCACGCTGGGGAAAAGAAGTTCTGGAGACAAAAGAGGGCAGGTGCTGCCGTGCCCTCTCTG	142020

genome mRNA	CTCAGTATGGATACTGGACCTTGTGCTGCCAGGGCTCCCAGTAGGGCCAGTTCATGGCAC	142080

genome mRNA	TCAGCTGGAAAGTCCACTGTTGGGAGGCATTCTTAACCATCCACTCTGTGCCGTATGTAG	142140

genome mRNA	TGGGGTCTGGTCATTCTGTTGGAGGAGACAGACCAAGTGACGACATTTGAAATGCTTGGTG	142200

genome mRNA	GATGTCTTAGGCCTGTTACGATGACTGAGCACTGTGGGGGCAGGAGACAGAAAGTCAGTG	142260

Figure 1

genome mRNA	TCTCCTAGTTCTGTGCTGCTTTAACGTGCATAGAAATCAGCTGCGGATTCAGCAGATCAC	142320
genome mRNA	TCCTTTTCTGACAGATGGGCCTGCTTACTCTGATGTTATATCAGAAAGCTCTGAATCTGG	142380
genome mRNA	GAATTGTGTCCCCTGAATTGGAGTAACAGAAATGCTTAGATGATGAGTGTTTAAAAGAAA	142440
genome mRNA	TAAACCAAAGGTAAATTTAGTTTGAATTCAGCAAGCGTCTTCATTGAGCCCTCTGAGGG	142500
genome mRNA	CAAACCTACAGCTTTTTGTAAATGTAGGTAAATTCTGTGACTGTTTCGTGACCCCTCTGA	142560
genome mRNA	TCCAGTTTTCTTTTATAACCTTCTGTATTGTTCTTCTATTATCCTGAAATAACATTAAT	142620
genome mRNA	AGATTAGGCTGGGCGTGGTGGCTCATGCCTATAATCCCAGCACCTTGGGAAGCCAAGGCG	142680
genome mRNA	GGCAGATCACCTGAGGCCAGGACTTCGAGACCAGCCTGGCCAACATGATGAAATGCTGTC	142740
genome mRNA	TCTACTGAAAATAACAAAAATTAGCCGAGCATGGTGACAGGTGCCTGTAGTCCCTGCTAC	142800
genome mRNA	TCAGAAGGCTGAGGCGGGAGAATCGCTTGAACCTAGGAGGAAAAGGTTGCAGTGAGCTGA	142860
genome mRNA	GATCGCGCCACTGCACTCTAGCCTGGGTGACAGAGTGAGACTCCATCTCAAAAAAAAAAA	142920
genome mRNA	AAAAAAAAAAAAAATTAATGGATCAATGGATTTTTTAACCTAATAATTAAATTTCAAAAAAT	142980
genome mRNA	ATCGTTCTTTAATGGTAATGTAAAGGTAAAATTAAGATAATATGTAACAAGCATGTGAGT	143040
genome mRNA	GTCTAAGGTGTCCCCGTGGTGGGAAGGAAAAATAAATCCCCATAAGTGTCCAAGATGCCC	143100
genome mRNA	ATAGAGAGCAGAGCTGTTCTGGTTTAAACCCCTGCTCTTAGCACTGTGTTTTTCCAGCTG	143160
genome mRNA	TGGGTGGTGGGGGATGAGTATCTTTTTATTTCCATGAGATGAGAAAAATGAATTACTAGA	143220
genome mRNA	AGTGTGAAATACAAAACACAGCTGCTCTTTTTTTAGCCATAGACTCAGCAGCCATAAAAT	143280
genome mRNA	TGCTGTATCCAGTTGCAGAAATTCCTGCTGCTTACTCTTGACCCTCTCTCGGTTTGTGTG	143340
genome mRNA	CATCTCCTCTCAGGCTGGCTCCCAGATGGGAGCTGGCTCCAGGCGACACTGGGTGCTCTG	143400
genome mRNA	CTCCAGGAGGTCCTTATGTGGGTCCCTGCCCTAGCCTAGCCCCCTCTCTTATGGACTCTGTC	143460
genome mRNA	ACTGTGGGTTTATGATTCACCTCTCAATCTGTCTTACCTCTTGGTGAACCTGTTAGAGTCCT	143520

Figure 1

genome mRNA	GCCTATACTTTGGCGCTTGTGGGTGTGTTGTGGTACACATGATGTGTTGGTCACTTCCCA	143580
genome mRNA	GCTCATCTTGTTCTGAGTCACCCTAGATTTGGGACATTCATTCGCCACCAGTACCGGGCG	143640
genome mRNA	GTGTATGGCCTGAGATTTGGGGGGGCTTGTGCTGCTACAAATTGGGGCTGAATTTGAGTT	143700
genome mRNA	GACAGTGGACCTTCTTTATGTCTACTGCTCATATTTGAATTGCAAATACTGCCTCTTCTC	143760
genome mRNA	TTTCAGAGGCTCATTACCCTATAGCTGTATTATTGCAAAGTGACAATTACAGCTTGAGT	143820
genome mRNA	GTAAGTCACACTGCGCTGGCAGGACGGCCCACTGAGAAAGGGCACGTTTCCTGTTTCGTTA	143880
genome mRNA	GTTTTTCACATTGACACATAATTTACAATACAGTAAAATGTACTTTTCTATCAACTGTAGT	143940
genome mRNA	CAGTAACAGCCCCCTCCCCCAACCACATCAAGATATAGAGGAGTGCTGTCACTTCAAAC	144000
genome mRNA	AGTTCCCTCTTCCTCTGCCACATCCTGCCCCCTCCCAGGTCTAACCACCAATCCGTGCTC	144060
genome mRNA	TGTCCCTCTGTTTCAGCCCATTGCAGAAGGCCATAGAAATAGAATCTATAGGCTAGGTGTG	144120
genome mRNA	GTGGCTCATGCCTGTAATCCCAGTATTTTGAGAGGCTGAAGTGGGAGGATGACTTGAGGC	144180
genome mRNA	TGGGAGTTCAAGACTAGCCTGGGCTGCCTAGCAAGACCCCATCTCCAGAAAAAAAAAATT	144240
genome mRNA	TAAAAATTACAATCACGTCCCTGTAGTTCAGCTGCTTGGGAGGCTGAGGCAGGAGGATCA	144300
genome mRNA	CTTGAGCTCAGGAGTTAGAGGTTACAGTGAGCTATGATCGTGCCACTGTGCTCCAGCCTA	144360
genome mRNA	GGTGACACAGCAAGACGTTGTCTCTGGGGAAAAAAGAAAGAAACGGAACCACGCGGTGTG	144420
genome mRNA	CAGCCTTCTGAGTCTGGCCCCCTTTCGGTGAGCAGTGTCTAAAGTTCTGTCGCGTGTGCC	144480
genome mRNA	CACGCGTCGGTGGCTCGCTCCTTGCAACTGCTGAGCATTGTATGGCTAGGCTGTAGTTTG	144540
genome mRNA	TTTTCACTTCACCAGTTGGGAAACAGAGAAAAGGCACTTTTTAAAAAGTTTAAATCTGTA	144600
genome mRNA	GAATTTTGGTTTTTACCAGTTCTCTTCTAAATCCTGAGGGATTACAGGAAAAGTTGTTGT	144660
genome mRNA	ATTCAGAATATTCTTAGCTTGATGTGACCTCTGTCCCCGTTAAGGCCCTTTGCCGCAAT	144720
genome mRNA	GGGAAGGACGTCGCTCGGTCAGACCCTGAAGGTCAGAGGGGCAGTTTGGGAGTGTGTCAA	144780

Figure 1

genome mRNA	CATTTTAACTGTATGGACTAGAGCCAAGAGTCTCAAGGTTTATAATTCCCACGTATTCAA	144840

genome mRNA	AAAGAAAAAACAATAAAGTGAGAAGTCAGTGTAGAGTGAAATAACCTGTGTTAGTGGGG	144900

genome mRNA	AAGAAGTGTTTTTAAACAGGATTTCCATAACGTATAACATCAACATGTTTAGAGTGGTGA	144960

genome mRNA	TGTTTCATTGGGAAACGAACAGTAAACATGAAAGCAGGGAGGTTTTTCATTCTGGCAGTT	145020

genome mRNA	GGCAACTTTCACGGCAGATGGAGAATTTCAAAGCAATTGCTCAATTATCAAACATAGCC	145080

genome mRNA	AGTGTGAGTTCTGAAATAAAGGTGCTGATTGAATGTGCAGCTTTATGGTGGATTTTGCTA	145140

genome mRNA	TTCAGGCAAGCATTTTAAATTTTCTGCCTGTAAATTTCTGTTTTCTTTAGTTTTTCATATG	145200

genome mRNA	TGGTTTATTGTAGCTTAGGAATAGATAACTGAGAGTATATATTACACATACAACATTCTG	145260

genome mRNA	ATATGGCAATATTTAAAACAACTTGTCTGTTTTAGAACTAGAATTAAACATAATCATCTT	145320

genome mRNA	CAGTATTTTGCAAATAAGCTCACTGCCATCCAGAAACATTGTCAATGCATCTGTTGCTCC	145380

genome mRNA	TTCTAGAAGACACAGTCTGTCCAGCACAAAGTTACTTAGTCCCCAGATGTCTGGAGAAGA	145440

genome mRNA	GGAGGATTCTGACTTGGCAGCCAACTTGGAATGTGCAATAGAGAAATAGTACGAAGAGG	145500

genome mRNA	GGCTCTCATTCTCTTCTGTGATTATGTCGTAAGTTTGAAATGCCTGTAAACGGGGTTGAG	145560

genome mRNA	GGAGGTGGGGACCAGGAGAACATCCTGTGTAGATGACACTTGCATGGACCCTCTGGAACC	145620

genome mRNA	CAGACCGCCCGGTGTCCTGCCAAGCTCCATCGAAACTAAATCTAGAATGAATGTTTACTT	145680

genome mRNA	CTGCTGTGACATATAATTGGAGACCAGGCCTGGCCTTCCAGTCACTGGATTCTAAGTTGG	145740

genome mRNA	ACTGTGAGAGTTTTTGCAGCTGACTCATTTATCAAATGCCCCGGCTATTGGCTCACGCCTA	145800

genome mRNA	CATGATGCTGGGTATGTTTGTTAATTTGAGGGAAGCAATGGAATAATAATAACTAATGAT	145860

genome mRNA	TTAAAAACAAAGTAAGTGCATTGACTGTAGTGGGGTTCTGATTTTAAATTTTTTTAAAA	145920

genome mRNA	ATTAATACCAGGAGCAGTGGCTTATGCCTAAATTCCAGCAACTCGAGAGGCTGAGGTAGG	145980

genome mRNA	AAGATCACTTGAGCCCAGGAGTTTGAGACAAGCCTGGGCTATGGTGTGAGACACCCATCT	146040

Figure 1

genome mRNA	CTAAAAAATAAAAAATAAAAAATTATCCAAGTGTGGTGGCTCGTGCCTGTAATCACAGC	146100
genome mRNA	TCTTTGAGAAGCTGAGGGCGGAGGATGGCTTGAGCCTGGGAGTTCGAGACCAGCCTGGCA	146160
genome mRNA	ACACAGAGAAACCCTGCCTCTACCAAAAAAAGAAAGAGAGGAAGAAAGAAAAATTAGCCT	146220
genome mRNA	GGCGTGGTGGTGCATGCCTGTGGTCCCAGCCACCTGAGAGACTGAGAAGGGAGGATTGCT	146280
genome mRNA	TGAGCCCAGAAGTTTGAGGCTGCAGTGAGCTGTGACTGTGTCACCTCCGGCCTGGG	146340
genome mRNA	TGACAAGGCGAGACCCCTGCTCTAAAATAATTTTTTTAAGTTAATTTGTAGAAAAGGTGT	146400
genome mRNA	TAGATGTTCTTTGTCACATTTTATGATGGATTCCCTGTTTAAATGCCGTTCTCTTTAAAGA	146460
genome mRNA	AAAAAAATAACTTGTGGGAGTTTTTAACCATAAACTAGCATCACATATTTACCATGGA	146520
genome mRNA	GAATTTACAAAAAACAAATAAACGGAGGAAAATAAACCTCCTGTAATCATACTACTCA	146580
genome mRNA	GAGATAACTTGCTGTTAGATTTTGGTCTAGATTTAATACTTTTTCTATATTTATATTTAAA	146640
genome mRNA	AATATTTAAACATATGCATTTCTTTGTCACAAACATGGTATCTTATAGATACTACTGTC	146700
genome mRNA	ACATAGCAAAACAGTGTTAAATATCTGAATCAGAAAAGGAAGCCGACTCTCCAACCTGAA	146760
genome mRNA	AGAGGTGTTATCCTAGAGACTTTTTCTGGTGTGATGA ^{rs7685686} CAATTTATTAATAGTCACTTTTTGC	146820
genome mRNA	TTTACTTTCTCTATTGAAGTAGTTTTTCTATTTTGTCTACTTTTAAGGATAATATAATT	146880
genome mRNA	TATAATGCTGTTTTTTCACAGAAATATAAGAAAAAGATACTAATTTTATAAGTTAATAAA	146940
genome mRNA	GTTTGATCATCCCAAATCCAAAAATCTGAAATCCAAAATGCTCCAAATTCTGAAGCTTTT	147000
genome mRNA	TGAGTGCTGACATTATGTTCAAAGGAAATGTTTCATTGGAAGGTTTCAGATTTTCGGATTT	147060
genome mRNA	AGGGAGCTCAACAAATAAGTATAATGCACATATTTCAAACCTGAAAAAATCCTAAATT	147120
genome mRNA	CAGAATACTTCTGATCCCAAACATTTTCAGATAAGGGTTATTCAACCTGTACTGTCAGATG	147180
genome mRNA	ATCCCAAATGAAAAATATTAATCGTTAACCAAATATCAAGGAATTGATCACATTTTACAG	147240
genome mRNA	TTTCTGCCTAGGATTATGAATCAAGATGAAAAGGCTCTGCATGTTTAAAAATATATATTT	147300

Figure 1

genome mRNA	TTATTTTCTTATAAATCTTAAATATCTACACTTAAGATTTATTTGATATGTGGGATCCAT	147360

genome mRNA	TCATATTTTGGATTCAACAGTTCTGTCAAACTGTGGCAGTGATAGGGGATTCTTTTTTTT	147420

genome mRNA	CCCACTGAACATATCACAAAATTGGAAAAAGAGTAATTGGAGAACCCCACTGGCTTAGCCG	147480

genome mRNA	GCCCGAAGCCCGGGAGAGGGCAGGCAGTGCTGTGGATGGGGTCATCCCAGCGCAACGCTG	147540

genome mRNA	CCCCTGCTACCTGCGGATCTCGCTGAGGCCTGCCTTTGTCCTTTGACCCTTGGCCATTTG	147600

genome mRNA	TTAGTGTCTCTGAGAGCTGGACTGCTGTACCCTACTTCCCCAGGGGGCCTAACTTCACAC	147660

genome mRNA	AGCCTCTGCCGCAGTGCGTGGTTGGAGGTGACGGCCTTGGTAAATCGAGTTTCCTACCTC	147720

genome mRNA	CTCAATTATTTGTGCTCATACTGTATATTTTTTAGTGAGGTTTATATTTGGGATGTGTT	147780

genome mRNA	TTCTCCTTCTTACCCTTTCTGGCCTTTCTATGGCATTAAACCTGGTCTCTTCTTGTGTA	147840

genome mRNA	CTTGAAAATGAATCTCTCATCATATTTTTCCTTAGTGTCAGAACCTCCATGACTCCGAGC	147900

genome mRNA	ACTTAACGTGGCTCATTTGTAAATCACATTCAAGATCTGATCAGCCTTTCCCACGAGCCTC	147960

genome mRNA	CAGTACAGGACTTCATCAGTGCCGTTTCATCGGAACTCTGCTGCCAGCGGCCTGTTCATCC	148020

genome mRNA	AGGCAATTCAGTCTCGTTGTGAAAACCTTTCAACTGTACGTCTTCATCCTGCCGACTATT	148080

genome mRNA	GCCAGTTGCAGTTTTCCCTGCCTTAAAAATGGAGTATTGAAATTTTAACTTTAATTTCT	148140

genome mRNA	GATTTGCAAAATAGTCATCTTTTGTTCTTTTCCTTCTTGCTGTTAGCCAACCATGCTGAA	148200

genome mRNA	GAAAACCTTTCAGTGCTTGGAGGGGATCCAFCTCAGCCAGTCGGGAGCTGTGCTCACGCT	148260

genome mRNA	GTATGTGGACAGGCTTCTGTGCACCCCTTTCCGTGTGCTGGCTCGCATGGTCGACATCCT	148320

genome mRNA	TGCTTGTCGCCGGGTAGAAATGCTTCTGGCTGCAAATTTACAGGTATTGGGAAGAGAAAC	148380

genome mRNA	CCTGATATTGATTTATATTGAAAATTTAGCAGGCCAAGCAAACAGGTGGCTGGCTTTTTT	148440

genome mRNA	CCTCCGTAAGTATGGTCTTGACATGGTCACCGATAGAAACATGGAAACATCTGCAAACCTT	148500

genome mRNA	GCCGTTACTCGTGTGTCCGATCTGACTGTTTCTTGATTTTTTTTCTAGTCTGCCCTTACT	148560

Figure 1

genome mRNA	AGGATGAACTGTACACATCAGTTCATCCTTTTTTAAATGAGCATGAGGTTATTTTGGGTTG	148620
genome mRNA	TTAGGTGTTACAAACACACTAATGTGTTTTTGTCTATTAGAGCAGCATGGCCCAGTTGCC	148680
genome mRNA	AATGGAAGAACTCAACAGAATCCAGGAATACCTTCAGAGCAGCGGGCTCGCTCAGAGGTA	148740
genome mRNA	ATGCTGGAAACACAGGTCGTCCTTGTGTTAGGACAACCCAGGATATAAAGGATATAGATT	148800
genome mRNA	TGTACGGGAATAAATTACAGGACAAGAAATCGATGTGCCTTATAGGTGGGTTTACTGCA	148860
genome mRNA	GAAGTGCCATAATAGAACCTTCCTACTTTTAAAACAACCAGATCTCACTTTCTAAAGAGT	148920
genome mRNA	AAAGGATGACCGGCAGGATCACGTCTGTGACGTGAGTGGAGGCAGTTTGCACTCCTGGTG	148980
genome mRNA	GCTGTTTGAGAGGTAGCATTTAGAATGCCTGTATTCAGTGTCTGTGATGAGTGGGAAAA	149040
genome mRNA	TAGGTTATCAGGTTTATCTTAGCAAAATCAAAGCATGTCATCTAATTGCTAAACAAGAGT	149100
genome mRNA	TGGCAAATCTGAGAGACATTACTCAATCCTTGGCATGCAGGACTTACATCTGCATCCTGT	149160
genome mRNA	TGCCATTTTATGTCTTCAAAGCATTTAATCATTTAGTTGTGTTTGCAAAGTCTTTGAGAA	149220
genome mRNA	GCCTTTGTCAGAAATCCCTACATCTCCTATGTGAGTGTATTTCCATGACTGCAGAATAAG	149280
genome mRNA	TTAAACTTTTACCTTTTTCCTTCCCTTGCGGGGCGGGGTGGGGGGCAGGGATTGTGTGTG	149340
genome mRNA	TGAGAGGGAGAGAGAGACAGCAGAGAAGGAGAATATAATTATCATGCTGTGTACTTTGAG	149400
genome mRNA	CTGAAACTGCAAAAAAGGAAAAACACACAAAAATTATTATGCTTTTCAGTCTTTAGAGTA	149460
genome mRNA	CCTTGTCTATTATGCTTTTCAGTCTTTAGAGTACCTTGTTGATGGTGTTTTTAAATGGGA	149520
genome mRNA	TTGGGCACAATTAGGTGGACAGTTTGGGATGATTTTTCAGTCTGTAGGGCCAAGCTCTTT	149580
genome mRNA	TGTAATTTGCATTATGAAGTTGTCACTCTCATAGCAGATGGCGGGAGATAAACTATTATT	149640
genome mRNA	ACTTTTGTGACCCTAGACTTAGTCTTCAGTCCAGATGAGGGAGATTAAAAGATTATAAATA	149700
genome mRNA	TCTTGTGCCAGATGAGGTGATTTTATTTTGAAATGACCATGAATTCCTATCAGTTGTCTT	149760
genome mRNA	ACTGGGATATTTGATAGTGGAATTTGTGCATTTGAGTCTTAGATGATCTGTTTTACATTT	149820

Figure 1

genome mRNA	ATTAAGAAAGCCTTTATTAGCTTTTATACTGTGTATTGCCTGTTGCAGTGTTTGAGTATA	149880
genome mRNA	AATGAAATTTCTGGAAAATATTAATGGAGTACAACTGTGATACTTAAAAGTAACTAGG	149940
genome mRNA	GCCTGCATTTGTATCATGACCTGTTTGAGTATTGATGAGAAGTAGCTGTGAAGAAAAAG	150000
genome mRNA	GTTTAAACAAGTGTATTTTCCTTTAAGAAGCCACTAATAGTGCATCTCCTTAGAGTGTAT	150060
genome mRNA	ATTTCTAGAATCCTAGTGTGCAGAGTTTAGACTAAGACTAAAAAAAAAAAAACAAATT	150120
genome mRNA	ATACTGTAATTTTCATTTTTATTTGTATTTTAGACACCAAAGGCTCTATTCCCTGCTGGAC	150180
genome mRNA	AGGTTTCGTCTCTCCACCATGCAAGACTCACTTAGTCCCTCTCCTCCAGTCTCTTCCCAC	150240
genome mRNA	CCGCTGGACGGGGATGGGCACGTGTCACTGGAAACAGTGAGTCCGGACAAAGTAAGTGTC	150300
genome mRNA	CAGCGTGTCTGCATGGGAGGCACAGGGCGCTGAGTGCCTCTGTACCTGTGGCAGATACA	150360
genome mRNA	GAGAGTGCAGAGGAGGTGCCGTGGACCCAAGGAGTTCTGGCGCTCGGCTCGGCTCAGTGA	150420
genome mRNA	AGCTGTGGTTAGAGACGTGGGGGGCCATCAAGGTCTGAGGGAGCCAAGCAGTGCTGATGT	150480
genome mRNA	GGGACCCTTTTGGTAGGAGTGTGGGGTGAGTAGTTAGTGGGTGAATCAAGGAATAGTCGG	150540
genome mRNA	CCGTGGCCTGCAGGCCCTGACTGCACAGGCCTTCAAGCACATGTCAATGCCGTTAGCCT	150600
genome mRNA	CCCTCCATCTCCTCATACCTTCTGGCCACCTGTGAGTTGCACTGCCACTGCCAGCCATTC	150660
genome mRNA	TGGTATGTTGTCAGCACCTCCACTGCTCATACCTCATGGTTAGGGACCACCTGGAGCCTT	150720
genome mRNA	GGTAGAGCCTTGGTAGAGCCTTGGTACTCTACTTTCCTGGACAAAGTTCAGCTTATGAAT	150780
genome mRNA	ATGAATTTAGATTTCAAAAACCAGCAGCCCAAGTATAAGAAAGCGAAGGTTTCAGTCCTGC	150840
genome mRNA	CTTCTTAGGCTCTATTGCTAAGCACCTGCCCTGCCCTGGTTGCTGGGGAGAGATGAGTA	150900
genome mRNA	AAGCAGACAACCCAGGAGAGGATGGCAAAGGGGGCGCTAACCTTAGTGGTTTAGCTATA	150960
genome mRNA	TTTGGAAGGCCTATTGGAAGTTCACCAGGTGAAGGGGGAGGCTGTGAGGGTGCCCAGGCA	151020
genome mRNA	GGTAACAGAAGTCCAAAGGGGAAAACCTGTGGTGTGGTGAGCCGTATAGCCACAGCCTGC	151080

Figure 1

genome mRNA	CGGCCGGCAGCCCTCTCAGCCTAGTGCGGTGTTCCCAAGCACTGGCCTAGGCCTGTAGCT	151140

genome mRNA	CCAGGGATGTGAAGTCCCCTTGAACGCCGCCCATCATGTTCCCCTTATCCATTTTTTTCT	151200

genome mRNA	TCCCAGGACTGGTACGTTTCATCTTGTCAAATCCCAGTGTTGGACCAGGTCAGATTCTGCA	151260

genome mRNA	CTGCTGGAAGGTGCAGAGCTGGTGAATCGGATTCCTGCTGAAGATATGAATGCCTTCATG	151320

genome mRNA	ATGAACTCGGTACGGGGGGAGCAGTGGAGGCAAGGAATCCTCAGCTTTTCTTGTGACTTC	151380

genome mRNA	CAAGTGGGATTTGTCTCATCATCATGTGACCCACTTGTTGACAACACATGTTGGGGACTC	151440

genome mRNA	CAGTCTGGGCAGGGACGGGATGTCGGAGAGACTCCACTCTGAATGGGGCCGGGAAGTGGG	151500

genome mRNA	GAGGACTCCATTTTCAGATGGGGTCGGGACATGGGGGTATGCTGATCGAGACAGAAAAGC	151560

genome mRNA	ACATTGTTTCAGCCACATTAGAATCCACGGAGGTGTTGTTTTGAAATCCAGCTGGCCCCA	151620

genome mRNA	AGGCTGGGTGTATGGTTTGGGATGAGAACTATCTGGCCTCCACTGGAGGAACAAACACAG	151680

genome mRNA	GATGTTATCATCTAAGCTCCATGGCCAAGACAGAATGGAAGTCAAGGTTGCGTATTTGCC	151740

genome mRNA	GTAGACTTCAACACAGTGTCGTAATGCGTGACGTCAATAACTTGTTTCTAGTGTCTTGGA	151800

genome mRNA	AGTTGATCTTTAGTCGTAAAAGAGACCCTTGGATGCAGCGAGATTTCTCTACTCACACC	151860

genome mRNA	TCTGTTAGATGTAGTGAGGTTCTTCACCCCCCAACCCAGATGTCAGAGGGCACCCCTGCG	151920

genome mRNA	CAGAGCTAGGAGGCCATGCAAAGCCTTGGTGTCCCTGTCCCTCACCCGTGGGCAGGTCCT	151980

genome mRNA	GTGAGCAGTGGGGGGGCCACCTCTTGGGTATGGTGCAGCCATGGCCCAAGCAGGGCTTCT	152040

genome mRNA	TCTCAGACCTACTAGGACGGGAGAAACCTCCTGGTGCTTTAGCCCTGCGTTGATATGCAG	152100

genome mRNA	CAAATGGGAGGGAAGTGGGCACCTGGGAGGACAAATGCCTGTAGAGGCCGGGAGTGACGG	152160

genome mRNA	CAGGTGTTTCATGAAAAGAGACCTTGTGGGGAGGGCAACACAACAGTGTGTTCTGATGTAC	152220

genome mRNA	TGAAGAGCTCAACTGAAAACAACAGGAGAATTAGCCCCAAATCCATTTACTAAAATTGTT	152280

genome mRNA	TATCTTTTTTTTTTTTTTTTGGAGACAAAGTCTCGCTGTTGTCCCCCAGGCTGGAGTGCAAT	152340

Figure 1

genome mRNA	GGCGCTATCTTGGCTCACTGCAACCTCCGCCTCCTGGGTTCATACGATTCTCCTGCCTCA	152400
genome mRNA	GCCTCCCAAATAGCTGGTATTAACAGGCATGCACCACCACGCCCCGGCTAATTTTTGTATT	152460
genome mRNA	TTTAGTAGAGACGGGATTTACCATGTTGGCCAGGCTGGTCTCAAACCTCCTGACCTCAGG	152520
genome mRNA	TGATCCGCCCACCTCGGCCTCCCAAAGTGCTGGGATTATAGGCCTGAGCCACCACGCCCCG	152580
genome mRNA	GCCTAAAATTGTTTATCTTAAGATTCATGCAGTGAAAGCTAACTTACTGAGTGATAAATT	152640
genome mRNA	TGCTTAGTGATCTGTTTATTAGGTTTTCCAAATTTGCTAATTGGGCTTTGAACAGCTGTA	152700
genome mRNA	AAAGTTCTGACTGTAAAAGAAAGCTTCAACTTTTGGCATTTCATGATGCTTTTCTGAGTAT	152760
genome mRNA	TAAACTAAGATAGATGTTTTACCTGAAGGATCGGCCACCAATCTTTAAATGGCTAAACAA	152820
genome mRNA	AAGGGTTGCTAAACATAATCCAAATTGACATAAGAAATACCATTTTTCCAACCAAATTT	152880
genome mRNA	TTGGCATTTCATATGGCTACTTTTACGTATTTTCAGCTGCATTTGAACATCTTTTTCAAAC	152940
genome mRNA	TTAGGGTGGTTGGTGTATCACTGAGGTCTTGGATGACACTTTAGCTTTGATTTTGTTTTT	153000
genome mRNA	ATGAATTAAAATTGTCATACCAAATTTTTATTTCAAGCAAATCCAAGAGCATAAAAAAT	153060
genome mRNA	TAAAATATTACTTAAAATACTAAGAGAGAACAGATATATATTTTACTAAGCATATGTTGA	153120
genome mRNA	ATGAAATTGTTCAAATATTTATAACAGGCATAGAGTAGAATTTTCTTAAAAATATTTTTG	153180
genome mRNA	ATGGTATACCAATTTGTATTTTCTCAGAAACATTTGCCTTATTCTTTTTTCTGTTGTGTT	153240
genome mRNA	TTTCTTACCTGATTGAAAGCTCATAATCTGTTGTTATTGTTTGTTAACCTTTAATGCTCT	153300
genome mRNA	GATTCAGGAGTTCAACCTAAGCCTGCTAGCTCCATGCTTAAGCCTAGGGATGAGTGAAA	153360
genome mRNA	TTTCTGGTGGCCAGAAGAGTGCCCTTTTTGAAGCAGCCCGTGAGGTGACTCTGGCCCGTG	153420
genome mRNA	TGAGCGGCACCGTGCAGCAGCTCCCTGCTGTCCATCATGTCTCCAGCCCGAGCTGCCTG	153480
genome mRNA	CAGAGCCGGCGGCCTACTGGAGCAAGTTGAATGATCTGTTTGGTAATTAAAATTAAAATT	153540
genome mRNA	TATCTTATTTTTTAAAAAGCATTCCAGGGCCAGTATAGTACTTTGCACCAAGTAAATGTAC	153600

Figure 1

genome mRNA	AATAAAGGCAGTGGATCTAATACATTGAAAGCGTTTACAGAGGTAGCTAAAGAGCAGCAC	153660

genome mRNA	GGGTGTCCTCGGCTCAGAATTTCTTCCTGTGTGTTTGCCACTTTGCCATTCATTGACATG	153720

genome mRNA	GTCATGGACATAGGGCTCTAAGCCCTTGAGGAAGGCTGGGCCAGACCTCAGGGGAGATGC	153780

genome mRNA	AGCCCCAAACCACGTGCAGTCCTGTGGACGGATGTGTAGATGTGCCACTGAGGAACAATG	153840

genome mRNA	TCTTGAGCTTTCATCAGATTCTCAGAGAATTGCTTGACTGCCTTTCGAAGTTGATGCATC	153900

genome mRNA	TGTGCTCACGTTTGCACCCACCCACGAGGTCCTTCTGTTTCAGGGGATGCTGCACTGTAT	153960

genome mRNA	CAGTCCCTGCCCCACTCTGGCCCGGGCCCTGGCACAGTACCTGGTGGTGGTCTCCAAACTG	154020

genome mRNA	CCCAGTCATTTGCACCTTCCTCCTGAGAAAGAGAAGGACATTGTGAAATTCGTGGTGGCA	154080

genome mRNA	ACCCTTGAGGTAAGAGGCAGCTCGGGAGCTCAGTGTTGCTGTGGGGAGGGGGCATGGGGC	154140

genome mRNA	TGACACTGAAGAGGGTAAAGCAGTTTTATTTGAAAAGCAAGATCTCTGACCAGTCCAGTC	154200

genome mRNA	ACTTTTCCATCTCAGCCTGGCAGTAAGTCTTGTCACCGTCAAGTTATTGTAGCCATCCTT	154260

genome mRNA	CACCCTCACCTCGCCACTCCTCATGGTGGCCTGTGAGGTCAGCCAGGTCCCCTTCTCATC	154320

genome mRNA	TGCACCTACCATGTTAGGTGGATCCTAATTTTAGAGACATGAAAAATAATCATCTGGAAG	154380

genome mRNA	TACTTTATGTCTTAAGTTGGCCTGGACATGTCAGCCAAGGAATACTTACTTGGTTTGTGT	154440

genome mRNA	TAGTGCTTGTAATTCGCCCCCAGAATGTGTACACGTTCTGGATGCATTAAAGTCTGGCCT	154500

genome mRNA	GTATCCTTAAAGGGCCATCGCTGTGCTGCCTGCCCTCAGCAAGGACACACTTTGCAGACC	154560

genome mRNA	CACAGAGGCTCCGCCTCCACCTCACACCAAAGAAAGGGAGGAGTCCAAAGGGCATCAGTG	154620

genome mRNA	CCATTACTCACAAAATGATAAATACACCCTTATTCTGAACCACGTGGAGTCATATGGTTT	154680

genome mRNA	GTGATCCCTGTCCTTCAGGTTTCAGCTTAGTGGGGAAGTGGGAAAGTCAGCGTGTGATCA	154740

genome mRNA	CAGCACAGGGTGATTGCTGCTGATTATATTATGTGCCTGCTGTATGCAGGATGAAATACT	154800

genome mRNA	TTATATGCGTCATCTTATTTGACTCTCACAAACCCCTGTGAGATAGGCTCTGTTACTCCC	154860

Figure 1

genome	ATTGACAGGTGAGGAAAGCAAGGCTTAGAGAATTTAGTGACTTGCCCAGGTCCTCTGA	154920
mRNA	-----	
genome	GCTAGGAAGTAGCCATTCTGGCATTGGAACCCAAGGCCTGCTATCCCTAGAACCCACGCT	154980
mRNA	-----	
genome	CTCAAATTCAACCTATGACAGAGGCAAGCCCTGGTGCTGTGGGAGCCCCAAGGAAGAGCC	155040
mRNA	-----	
genome	TCTGGCCTGGTGGCCACGTAGCCCAGGAGAGATTTCTACAGGAGCCCACAGCGCTGAAGG	155100
mRNA	-----	
genome	AGAGAGAGGCAGCAGAGTAAGGGGGCTTTGTGGCAGAGAGGGGACTGGCACTTTGGGGAA	155160
mRNA	-----	
genome	TAGGTGGGTCAGGACTGAATGTAATGGAGCCATGTCAGAGCTGTCCTTCTGGAAGGGCAA	155220
mRNA	-----	
genome	GGGCACCTGGACGCGCTGCCCCCTCAGTGCTTTGGACGGTTCACAACCTGTGATTCACACG	155280
mRNA	-----	
genome	GCTTCCCCAAACGAAGGTACACGAGTGGGCATTCTGTGACTCGGTACTTCCCTTTAGGCC	155340
mRNA	-----	
genome	CTGTCCTGGCATTGATCCATGAGCAGATCCCGCTGAGTCTGGATCTCCAGGCAGGGCTG	155400
mRNA	-----	
genome	GACTGCTGCTGCCTGGCCCTGCAGCTGCCTGGCCTCTGGAGCGTGGTCTCCTCCACAGAG	155460
mRNA	-----	
	rs362331	
genome	TTTGTGACCCACGCCTGCTCCCTCATCTACTGTGTGCACTTCATCCTGGAGGCCGGTGAG	155520
mRNA	-----	
genome	TCCCCGTCCATGAACGGTGGGTTCCCTATCATAGTTCCTGTCTGCTTCACCATGTTTTTAT	155580
mRNA	-----	
genome	TTTGTGCTGCCTGTTTGCCAGGTACTAAGCTAGGAATTGGGGATGGAGAGGTAGATAAAA	155640
mRNA	-----	
genome	TATGCATCAGGAAGGGCTGGGCCCCATCTCTTACTCTCCAATATATTGGAGTCTACACTG	155700
mRNA	-----	
genome	GAATTTAACTGGAATTTGCTTTTTTAGTCATTTTATTTAGATTTTGAAGTTTCAGCTTTC	155760
mRNA	-----	
genome	ATCAAAAATACCTCTAAACTTTATGTCTCTGTGATCTTGGTCTTAGCTGTTTTATGTAT	155820
mRNA	-----	
genome	TTAGTCTTATATGATCATAAGATTAATAACATTACATTGAGAAGATTATTTGTTTTCTGT	155880
mRNA	-----	
genome	CAGAGTTAAAATGTTTGTGTTTTTATACTGCATTGTAATATTAACGTACTGTAAAATAAAG	155940
mRNA	-----	
genome	TGGCTTGTTCTTTTCAAGGAACAGTATCCTCAACAAGGGTCATTAGCCACAATTTTAA	156000
mRNA	-----	
genome	AAATTGGACGTCATAGTTTACATGTTAGAGGGCGTTTTGAAGCTTTGTATTTTTAAATTA	156060
mRNA	-----	
genome	AATGTTATAGAGTGATGTTTTTCATGTTTCATAATTGTTTTTCATCTGTGCATTTGTAGCCA	156120
mRNA	-----	

Figure 1

genome mRNA	ACTTGAAAACAAAGATCCAGGGATTACTACTTAAAAGCCAGACTTCTTGGAGGTTATAGT	156180
genome mRNA	GATGATTTTGATAGTATCTTGAGCCGTCTCATAATAACCTCAGGGTGAGAGATGGCCAAC	156240
genome mRNA	AGGAGACAGTCGAGGGACTTAGAAATCTGAATGAAATCTGAAGTTCAAATCTTCAGACAT	156300
genome mRNA	ATACCACTAACCAAGAGATTGGTACCTCAGTCTAGTATTGTCTGTTTGTCTAAAATTGGT	156360
genome mRNA	TCTAAGGAATCTAGGCTAGTCTGTCTATCCCTTCAACTTTTGTGAGGCTGCACAAATGT	156420
genome mRNA	AAAATGTTGAATAAAAAGCACTGATGGAAGTGTGTAGAAATTCTTCTCTTTTGTCTGTTG	156480
genome mRNA	TAATTTTAGTTGCAGTGCAGCCTGGAGAGCAGCTTCTTAGTCCAGAAAGAAGGACAAATA	156540
genome mRNA	CCCCAAAAGCCATCAGCGAGGAGGAGGAGGAAGTAGATCCAAACACACAGAGTAAGTCTC	156600
genome mRNA	AGGACCCATTTTTTTCTTACATGTTGTTCTCCAGGACTTAAAAATCATTCACAGAGACG	156660
genome mRNA	TGCACCGCGGTGAGTGTGGACTCCTGGAAGCGCACCGTAGCTCCGCTGTGTCTCTGCTGCT	156720
genome mRNA	CCTCCCTAGCTGTCAGGGAGGCTGTAGTCCATTGCTTTGCCAGCTCTTTTGTTCCTCGAGT	156780
genome mRNA	GAACACCTTATCCGTACACATGCGGCTGTCTCTGACCCTACAGACCAGCTGGGATGCCAC	156840
genome mRNA	TGGGGGAGCGCTCCCTTCCCCCGCACTTCCCACACTCTGCAGTTATTCTGAGATCCTTG	156900
genome mRNA	AGGGCAGGGAACAGGTTTGTCTTCTTTGTGTTCTCAGAAATTAATGCTCGGCCTCTGGTC	156960
genome mRNA	AGCAAGCAACAACCTTTTGTGAGTGATAATGAATAAATAAATGTTTCCCACATGAGTAT	157020
genome mRNA	TCAGTAACCTCAGTGTGAGTTTCTGTTTGGTGGATATTTAAAAGAAAATTCC	157080
genome mRNA	GCTTTTCCTACAGAAAAAAAAAAAAATCCAAATCCCAGTGATTTAAGCCAGTTATAGACT	157140
genome mRNA	TAGACATATACTACGGCTTTTCATGCACTTTCCTCCCAATTCTAGAGTAGGTATTTTACT	157200
genome mRNA	AGGAAAATGGTGGCAGTGCCTGTTGGGAGGAAGATTCTTTGGCCAAGTGTCTTTTGTCTCT	157260
genome mRNA	TGCCAGGGCCCCTAGGCTGCTGGGGTGCTTCAGCTTCTTTAGCCCAGTGTCTGGTGGGGA	157320
genome mRNA	ATGGCCCCTGTTGCCTGTCCCACAGAGGTGGGGGTGCCTCACCTGGAGCCTGTCCACACA	157380

Figure 1

genome mRNA	TTTTACACAGCACGCTTACCTGGAGCATCAGGCATCTTTTCCATGCTCTGTGGCTCAGGA	157440
genome mRNA	AACACGCCTTTTCAATCATGAGTGCACCAGTGCTTTTGGGCTTTTCTCCCCGCTTTTGT	157500
genome mRNA	GCAATCCTGGTTGTGGATGGAGTTTTCTGTCTTTAGTCTTCTGCATAGTACTTTTCTCT	157560
genome mRNA	TCTGGTTCCCGGTTCAAGGTTTTGTAATTAGAGAATGACCCAGAAGCAATGGCATTTTAA	157620
genome mRNA	TGCACAGCCAAGGACTTCTCTGAATTTGTATCTCAAACCTCTGTGGGTCCTTCAGGCTTC	157680
genome mRNA	AGTTTGTGATTTTCATGATTTCTTGTTGCTACCTAAGGAATATGAAAACACCCACCTCCCT	157740
genome mRNA	ACTCTGCATCTTCCAGCCGAGTGGCACCTCAGGCTGTGGATCCTGTGCTTCTGTGGTGAG	157800
genome mRNA	GATAAGAATAGTGCCAACCGTGTGGATTGAAATCAATCAGTTAATCCCTCCATGTAAAGC	157860
genome mRNA	ACCTGGAACGGATGACAGTCTTGTTATGAATACTCAACAAATGCTATCATGATTTTGTAGT	157920
genome mRNA	TAGATTTCCATTGCTTTAAACAGTTGAGACATCTTGGCGGTTTGAGTTAGAGCAACGGG	157980
genome mRNA	CCCTGAAGTGGGTTCTGTTTGGGTGAAGATGATTATGCTTATTCCCCATGGCCCTCTTTA	158040
genome mRNA	GGCAAGAGTGGGAAGCTTTCTTTGTTTTTTTAATCACCTCGATAGGACGTTACTTCTTAA	158100
genome mRNA	AGGTCATCCAATAAATATTAATAGGCCGGGCGCGGTGGCTCACGCCTGTAATCCCAGCAC	158160
genome mRNA	TTTGGGAGGCCGAGGCGGGCGGATCACGAGGTCAGGAGATCGAGACCATCCCAGCTAAAA	158220
genome mRNA	CGGTGAAACCCCGTCTCTACTAAAAATACAAAAAATTAGCCGGGCGTAGTGGCGGGCGCC	158280
genome mRNA	TGTAGTCCCAGCTACTTGGGAGGCTGAGGCAGGAGAATGGCGTGAACCCGGGAGGCGGAG	158340
genome mRNA	CTTGCAGTGAGCCGAGATCCCGCCACTGCACTCCAGCCTGGGCGACAGAGCAAGACTCCG	158400
genome mRNA	TCTCAAAAAAAAAAAAAAAAAAATATTAATAAAGCCAACTCGTTAGCGTGGGGCTTAATTGCTT	158460
genome mRNA	AAGTCCAATGAGAAGTCCTTCTCTATCCTAGGAAGTTGCCCAAACGTAGAATCTCGTGG	158520
genome mRNA	CCTGTGGGTAATAGCCACGTAATACACACTCACTGCCTCAACAAATCATATTTTAGTAGG	158580
genome mRNA	TATGATATTCTAGACTCAAGACACCATTCTGTGGATCTTCCCAAGGGTGTGAAGTGTCCA	158640

Figure 1

genome mRNA	CAGCGTCTGCCTTGGGAGTTTCCATGCCCACCAGAACCATGCCCCAAGCCCCCTCAAGCAC	158700
genome mRNA	TCTGACCTAGGAAAGCCAGTGAAGCAAGGATGACAACATGGCCCTTTGATACTAGCTGAG	158760
genome mRNA	GGACAGACACAGGTCCTGGGAGACCAGAGAAAGACGAGGGGCAGAGGAGGTGTCCTAAAG	158820
genome mRNA	GAAGTCTGAGGCTGAGGAGCCACAGGATGGCTTCCAGCTGTCACAGGCTGCTGCTGGCCT	158880
genome mRNA	TATCACAGAGAGTGGGCCAGAGGGCTGGGAACCAAGGCCAGAGCTCAGGTTTACAGACCAT	158940
genome mRNA	TCCAGCAATCCCAGCAGAAAAATGGGGAGAATTGTATGGTATAGGCGGATATGAAGGTAGA	159000
genome mRNA	ATCTGCAGGCCTTCAGTGGCCAACTCAGAGTCTAAGTGGATTCCACAGTTACAGCTTGAG	159060
genome mRNA	CAGCTGGTTGTAGGTCATGCTTTCTACACTGGGCATATAGGATGTGTTTTTTAAAAAGTC	159120
genome mRNA	CTCTCTTAACCGTTGCTTGTTTAGATCCTAAGTATATCACTGCAGCCTGTGAGATGGTGG	159180
genome mRNA	CAGAAATGGTGGAGTCTCTGCAGTCGGTGTGGCCTTGGGTCTATAAAAGGAATAGCGGCG	159240
genome mRNA	TGCCGGCGTTTCTCACGCCATTGCTAAGGAACATCATCATCAGCCTGGCCCGCCTGCCCC	159300
genome mRNA	TTGTCAACAGCTACACACGTGTGCCCCCACTGGTGAGTCTGCTCGTTCCTTGCAGAAGAC	159360
genome mRNA	CAAGTACGGTGAAAGGCACCGGTAGGCCCTGGGCTGGGCACACGTGAGAGGGCGGGACAG	159420
genome mRNA	AATCCCCGCAGCCCAGAGGCTGCCTGCTGTGGTTCTGGTGCCCACTGTGGTTCTGGTGCC	159480
genome mRNA	AGGCTGCTTTCCTCAGGCACCACGTGTGGAGGTCGCTAGTAGAAATACTGGGTTTTCTAA	159540
genome mRNA	AATGAACTGAGGCCCTACATCCCTAAGAGATTAGTGTTAGACCTGATTCTAGAGCAACTA	159600
genome mRNA	GACCACTTTGCTTAATAGCAGACCAGAAACCACACCCCCTCGAGTGAGTGAGATTTTCCT	159660
genome mRNA	TTGGAGATAATTCATGTTTTTCTACACAGTTTTGCAGTTGTCTTCAGAATTGGTTTAAAG	159720
genome mRNA	TAGGTGTTATTGCCAGGCGCAGTAGCTCATGCCTGTAATCCCAGCACTTTGGGAAGCCAA	159780
genome mRNA	GGTGGGCGGATCACTTGAGGTCAGGATTTTCGAGACCAGCCTGGCCAACATGGTGAAACCC	159840
genome mRNA	CATCTCTACTAAAAATATAAAAATTAGCCAGGTGTGGTGGTGTACGCCTGTAATCCCAGC	159900

Figure 1

genome mRNA	TACTCAGGAGACTGAGACAGGAGAATCGCTTGAACCCAGGAGGCCGAAGGTTGCAGTAAGC	159960

genome mRNA	CGAGATCGCGCCACTGCACTCTAGCCTGGGCAACAGAGCAAGACTCCGTCTCAAAAAAAAA	160020

genome mRNA	AAAAGGTAGGTGTTATTGATCAGAACCCTTGTTTCAGATAACATGAGGAGCTTAGCTTGA	160080

genome mRNA	GGAGAGTGAGGGTTGATGGAGGGGGACTGACTTCTGCCCAGTGAAATGGCATCATCTCCC	160140

genome mRNA	ACCAGCCCGCTGAAATAAGATGATGGGGCCTGTTCCCTTAGGGCCTGCAGCATCCTCAGGC	160200

genome mRNA	AGGAAAGAAAGGCCGACCTGGCAGGGTGTGAGCCAGCAGGTGTAGGTCAGGGAGAATGGA	160260

genome mRNA	GCCAGGTCCCAGGGAAGAGGCTTGTGGCTGCCTGAGAAGGGTGCGTGCCTGCCTGTGTGT	160320

genome mRNA	GTGTGTGCACGTGTGTGTATGTATGCTGGAGAGTCTAGGGAGGCTTGCTCCAAGGACGCA	160380

genome mRNA	GTATTGTTTGATCCTGAGAGATAAGGATTCTGCCGCAGGGAATGAAGGTATTCCAGATGG	160440

genome mRNA	CGGGCTTATTCCGAAGAAGAGGCCAGTGCCTGGCGGTGCTGGAAGCAGTTGCAGAACAGG	160500

genome mRNA	GAGTTGTAGGCTTTCCTGGGAAGAGAGCAGCAGGGGTGCTGGAGAAGCAGGCCACACTTG	160560

genome mRNA	CTGCATGGGGTTGCTCTCGGCCCCACTCTTGGTGCACAGCGAGTCACTGTGGGTTCATTA	160620

genome mRNA	GCATCTGGTTATGAGACAGTAACTGCTCCTTTGGAGGGGCTCGTGGAGACCATGCAGGAG	160680

genome mRNA	GGCACGGTCTTGAGGTCATGCCGTCCAGAGCACACCTGAGGATAGGCCAGGACGGGCTGC	160740

genome mRNA	ACGCTGTAGGTAAAATTCCCTCCAGCAAGCTCTTCACTGGCATTGAGGAGTTCCTGAGTG	160800

genome mRNA	CGGTCATCTGGAAGGCAGCTGTAACAGGCACTGCAGTCTCTCCCTGGGTGGGTACCAGAG	160860

genome mRNA	AGGAGCATAGGGGAGCATAACCGATTTAAAGAGAGGGCTTTCCTGTGGTGAGGTAAGAGA	160920

genome mRNA	TTAGCTGGTCATTATCATAGAGCCCCCTCTGCCTTTGTGCAGATGGGCTGTGGGAATCCT	160980

genome mRNA	GGGGTTCCGTTGGGTCTTTGTACCTCACTGAAGGC ^{rs362322} ATGTAAGCTGAGCTGGCCAGACC	161040

genome mRNA	GTGAGCTGATCCTGCCACTTGAACAGCATCAAGCCTGCCTCTGGATTCTTCTGTGCATGG	161100

genome mRNA	CACTTGTCTGAGCACCTCACGCACAGAGAACTGGACTTCAGAGTTTACAGAAATAAGCTG	161160

Figure 1

genome mRNA	TATGGTTCATTTTCATGCCTGCTTGCCAATAAACATATCTGAGCTGAACCTCATTGAACG	161220
genome mRNA	CCTGCCTTTATTCTAGCACAGCACCTGCTGTTTGTGGGCGAGGGGTGCTGTCTCTAACTC	161280
genome mRNA	CTGCCTGCTTCTCCCAGCACTCCCTGAGTGGGGTGTGCCAGCAGCCTCAGGATGAGGACA	161340
genome mRNA	GGAAGTGGGAGGGCAGAGCAGATTTGGGAGGGCCACTTGATGGGGAAGGAAGTCCCAGGA	161400
genome mRNA	AGCAGTTGGAGCTGTTTTCTGGGGGAGAAGGTGCCAGCTCTGGGACAGTGTTGGGGTAGT	161460
genome mRNA	GAGGAGGGAGCCCAGTGGAGAGAAGTCGGGCTTCCTGCTTCCTCACAGTATGTCTGTCCT	161520
genome mRNA	GACTCAACTCGGATGATGTCACCTTCCTTTTCATCTTCTCAGGTGTGGAAGCTTGGATGGT	161580
genome mRNA	CACCCAAACCGGGAGGGGATTTTGGCACAGCATTCCCTGAGATCCCCGTGGAGTTCCTCC	161640
genome mRNA	AGGAAAAGGAAGTCTTTAAGGAGTTCATCTACCGCATCAACACACTAGGTACTCTTGGGG	161700
genome mRNA	CCTCTCCTTCAGGTCACCATTGTCGGACATCTACCGGGAGGAAATCCAGAGCCCCCAGTA	161760
genome mRNA	CTGGGATCTTCTCATTTGACTCCAGAAAAGATTTAAGCATGATAATAACAAACCTATG	161820
genome mRNA	TGAATACATTTTGCAGTGTTGGCAAACTCCTTTTATACTGAGAAAATAGATCCCAGTTC	161880
genome mRNA	CTGTGTTTTGTGGCTTGAATCCCAGCTTTGTGTATTCCGGGCTTGTTTGAAGTCAGGAAA	161940
genome mRNA	GGTTCATGTGTAGTGGACAACGTGAGACCAAATCTGCCTTAGATTTTGCATTTAGGCTA	162000
genome mRNA	AACAGTGGCAGCACTTGTCTCAGAATGTTTTCTTGTGTTCAACAGTCTGATCCTGTTGTG	162060
genome mRNA	TCTCAGTGGTCCATTTTCTCATATGGGAACAAGCAGACGGGAGCAGATGGAGTCAGGTTT	162120
genome mRNA	CTTGGCACTCGCCTTCCCCAGAGCCTAGAGGCAGCATGGGGAGAAAGCAGGCTTGGGGCT	162180
genome mRNA	CAGACAGTCCTGGTCTGCTTCCAGCCCTCCTACCTGAGCAGCGCAGGGCAAGTCCGTCTA	162240
genome mRNA	ACCTCTAGAGACCCTCAGTTTTGTCATATGTAAAATGGGGGTCGTGTCTATTTCATAGAA	162300
genome mRNA	TTGTTGCAGATTTAGAAATTACATTTCTAAACAAATGTTACCCCTTATTTCTAAATAAGT	162360
genome mRNA	GTCTAAATGAATAAGTCACCACTTTTGCCCCCTATTTGATGGCAAGAGGTGTGATCTTGTG	162420

Figure 1

genome mRNA	GTGGGACTGTAATCAGTCAGTTCTCAGTGACTGTGCCCTGCTGTGGTGTTCCTGGAATG	162480

genome mRNA	TTCCTGTCTTGTCCTAGAAAGTCTGGCAGGGGCACCCTGACTCCACTGTCCAGTCCTCTC	162540

genome mRNA	CCCAGTCCCTCGGGCTTCTGCAGATTTGAGGCTTGTTTGGATCCCAGAAGGTTGTGGCAG	162600

genome mRNA	GAGACACCTTGCCTCTACTTTCCCCTTTATAATTCAATGTCCAAAGAGAGCCCTGAGCAG	162660

genome mRNA	GTACCTCACGCCAGCTGCCTCACGGAGCTCCTCCTCTTCCCTGGCTGTGAGGATCGGTATC	162720

genome mRNA	AGTGGCCTCCTGCTCTCTCCCCCTTGCCTAACACGAGCACCTTTGCTTACTTGGGTGCCC	162780

genome mRNA	TTGCTCTTGAAGTGCCCATCGGACGTGCGTGACCCAAGACTGTGCCGCAGTCCTTGCCTT	162840

genome mRNA	GTCTGTGCTCATTTTCTTTGTTTCATTTTTTTCCCTGTAACGTAAATTGTTATATTTGTCT	162900

genome mRNA	GTATCTGTGTCTGAATCAGTCCTGCACGCTCTCCTTCTCTCTGTCTCTTGTTCCTTCTTT	162960

genome mRNA	ACCCCGTTTATCACGGGGACCCCGATGTCCATTGCTCTAGTTCTCCTGTCCTAAGCACCC	163020

genome mRNA	CATCCCGTCTCTCTGGCCTTACCACAAGTGGCGTGGCTGCCTCAGACATCATGATGGGGA	163080

genome mRNA	CATGAAGCACAGCTGTCAGAAACAAGTGTTCGTTAGATACTCGAATGCAGCTCATCAA	163140

genome mRNA	TAGGGATGGAGGGTCTGTCGGATGTATTTTCACTGAATCCCCGTTCCCTACCTTGATACAC	163200

genome mRNA	TCTTTTAAATCTATTCTTCTAGACAGGTGAGAGGAACCATTAAGTTTGAAGTTTAAATTTT	163260

genome mRNA	TAGCAGCTTTATTGAGGTAGAATTCACATACTACAGATTTACCCACTCTAAGCGGACAG	163320

genome mRNA	CTTGGTGGCCATTAGTTTTATCCACAGAGTTGTGCAGCCAGCTGCACAGTCTCAGGGCTG	163380

genome mRNA	GACTCCAGGGAAGATTTTAGCCCATTTAGTGAGTGGGGCAGAAGTGGCCCTGGCCCTGCA	163440

genome mRNA	CGAGGTTGCCTGCATGGGCGTCCCTGCCCTGTCCCTGTGTCTGCTCCACTGGGGGTTGAC	163500

genome mRNA	CAGGCTGCCAGGGCCGACTTGGGCCTGTGCCACCTGCCTCTCATGTGTCTCGGACAGTGC	163560

genome mRNA	AGCCGATGTCTATACTTCGGTTTCCTCAATGATGAAATGGAGGGGATAGTGTTCCTCCGCA	163620

genome mRNA	TCATAGAACTGTGTGAGGTTTAAAGGGACTCACTGCCCTTGGCGTGGAGCCTTCTCCAGGG	163680

Figure 1

genome mRNA	GCCGTGCTGTGTCGGCGTAGCTGTCAGCTCTCCGTTACAGGCTTGAGAAGGGTTGACACT	163740
genome mRNA	CTCTCATGTAACATTTATATTTCTAGGCTGGACCAGTCGTACTCAGTTTGAAGAACTTG	163800
genome mRNA	GGCCACCCTCCTTGGTGTCTGGTGACGCAGCCCCTCGTGATGGAGCAGGAGGAGAGCCC	163860
genome mRNA	ACCAGAAGTAAGGCCACACCCTGTGCTGGTTGGCACATGGGCAGTTATGGCCGCTTGCAG	163920
genome mRNA	GCCTTTGGTGGGGAATAAAATAAGGCAGCAAGCTGGTGTTCTTTTTTCTCTTACCTTAT	163980
genome mRNA	TTTGTAAAGAGTAGCTGAATGGTGTCTTGACTGATATTCCAGAGCAGGGACAAAGCCTGC	164040
genome mRNA	TGAGGTCTGGGGGCTGCGATTACCAATGGCTGGAATGCATTTTATTACGGTGCATTCCAT	164100
genome mRNA	GTTAAGGATCAATACGATTGTGCCCTTCTGGAAAATATCTTTTAGTTTATCAATATTCA	164160
genome mRNA	GAGGAGTGTAGGTTGAATTAAATGAAAAGGCACCTTTATAAAGGCCATGAGTAGTACCTG	164220
genome mRNA	GTTTCATTTTTCTAATGTCTTGCAGAGATTTTATCAGGCTTCTTGAAGTGTTACGTACA	164280
genome mRNA	TTACGCTAACACGATATTAATAATAACTGTGCTCTGGTACAGCGGAGCCAGCAGAATGGG	164340
genome mRNA	AAGTTGTGGAATGCAGGCCCTTGATTCTGATAGAAGGTGTGGTTTGAACCTCACAGAAATG	164400
genome mRNA	ACAGTTTGGAGGGTAGACATATGTCACAAGTCATCAAGATTGTCTTTAAATTCATGCATA	164460
genome mRNA	GAAGCTAACAGGGTGTCTATAAGCAAGGCCTGTAAAATGTATGAGGGAATTCAAAGATAAT	164520
genome mRNA	TTATTAAAAAGTAATTCATGTTTGGAGTTTGTGCCCAAAGGAGTCCTTGATTTGAAAAA	164580
genome mRNA	TGGGCTTTTGCCCATCAGATTGTTTCAGGGCCCGTGTGTGCGGAGGCCCTGCCTTGTGCC	164640
genome mRNA	CCGTGAGCTCAGCCTGACAGAAATCCTTTGGTAGCACTTAAGGCTCCTCTTCCTCCCATT	164700
genome mRNA	GAGGCAGGGAAGACTCTGGGTCTGCAGGCAGAGGTGGTTGTGGGTGTCTTGCTGCTCTT	164760
genome mRNA	GTTGACATGTGGGCTCTCCTTCCAGGAAGACACAGAGAGGACCCAGATCAACGTCCTGGC	164820
genome mRNA	CGTGCAGGCCATCACCTCACTGGTGCTCAGTGCAATGACTGTGCCTGTGGCCGGCAACCC	164880
genome mRNA	AGCTGTAAGCTGCTTGGAGCAGCAGCCCCGGAACAAGCCTCTGAAAGCTCTCGACACCAG	164940

Figure 1

genome mRNA	GTTTGCTTGAGTTCCCACGTGTCTCTGGGACATAGCAGGTGCTGGGGACAGTGGGTTC	165000
genome mRNA	CGCTGAAGCGTCCAGCAGCTTCAACCAGGCCGTTTTCTTCATTGCTAGAATTGAAAACA	165060
genome mRNA	CCGTCCGTGTGGCCTGTGCAGGAGATGCAGACCCAAAGGTGGCCTCCTGGTCAGTGAGAA	165120
genome mRNA	GCTGGAAACCTGACAGCAACTCACCTGGGGTTATTGAGCATTTAGGGGAAGACGTTAGCA	165180
genome mRNA	GAGCAGGAATGAGCAGGCAACTAGTAGAACACCCACTTAAGGGCTCACGGACAGGTGCTC	165240
genome mRNA	ACTTAGGAAGTGAGTTTCATTTGGTATTACACCAGGTTCTTTAGGCAAAGCGGAGGGAA	165300
genome mRNA	AGTTCTGGTGTTTTTCACTTGTAAGATTTTGAAGGAAACAAAACACTCTTTACCTTTTTT	165360
genome mRNA	CTAAAATGTAGGTTTGGGAGGAAGCTGAGCATTATCAGAGGGATTGTGGAGCAAGAGATT	165420
genome mRNA	CAAGCAATGGTTTCAAAGAGAGAGAATATTGCCACCCATCATTTATATCAGGCATGGGAT	165480
genome mRNA	CCTGTCCCTTCTCTGTCTCCGGCTACTACAGGTACCTGAGGGAAAGGGTGCGGGGAGCG	165540
genome mRNA	GTTGTACTTGGGCTAGAATGAGAGAAGACTGGCATGCTCACCACACCAGTGATGCGGGAA	165600
genome mRNA	GACCTGAGTGTGGTCTGAGTTGGAGGCTGTGGTGCTAAATACGCTGCCCCCTTTCATAAGC	165660
genome mRNA	AGGAGTCTTAGTCAGGCCAGGGAGGAAGTAAATCTGGAAATGAATGAGAAGCATTCTC	165720
genome mRNA	TCCTGCCAGTCAAGAAATGAGAAGCGAAAGAATTCTCACGGGCTGTAAGACCAGCAGGAT	165780
genome mRNA	TTAAAAGTTGAATTAGTTGCTTATGTTAAGAACTCAACCAAGTTCATCTACACAAGCTGA	165840
genome mRNA	ATCTCCAGCTTTTCTAAGAAACCATGTGTGGCAGTGGCTGCAGGGCAGGGCACAGCTGG	165900
genome mRNA	GCCTGAGCACCCCGCTCCCTGCACCTCTCCCCTCCCTGGGCCCTGCCTGTCACTGCCAC	165960
genome mRNA	TCTCCACCAAGCCTTCCGGTTGTGTGCCTGCCCTATCACAGGCATCGGAGCTTGTACCC	166020
genome mRNA	TGGTTTAAAAGAAGAGAGTTGTGTGGGGATTTGGGATGCACGTTTTTCACTCAAAAGTAT	166080
genome mRNA	TTTAGCGTAGAGCTCTGTGATTCCGTAGCTATTTAGGAGTTTAAGCACCTTGAAGGCTTT	166140
genome mRNA	AATTGCAGAAAGTTCTATGTGGACGTGCAATGTGTTATACGCAGTGTCTATGAGACTCAA	166200

Figure 1

genome mRNA	ATGTTTATTAGGGCGTTGAAGTAACTGAGCACTTGGAGGGCCATGGATCCAGCCTTCAA	166260

genome mRNA	GGAGCTCATAAGTCAGGAGGACCCAGGAGCAATGACCTGTCATAGAAGGCAGAAAAGAGG	166320

genome mRNA	GGCACAGAGGTGGGTGGGAGGCATACACAGGCAGCTCCTGGAGCTCCAAGGGGAGCAAGT	166380

genome mRNA	GCTTCCAGGGAAGGGGGCGTGGAGGCCCTTTGGAGGAGGCAAGTTGATCTGGGGTCTGG	166440

genome mRNA	CAGAGGGTTAGCTGGGGACATTTAGCGGGAGGCTGGTGCCCGGGAATTGGGGGGATGCCC	166500

genome mRNA	AGCAGAAAGACATGAGGAGGCTGGCCTGGGGCGTGGGGGGGTGTGAAAGGTTAAGTGGGG	166560

genome mRNA	GCATTATCCTGCTCCCGCTCCTGCCGGCTGTATCTGGTCAGCCTGGGCACCGAGGTGGGG	166620

genome mRNA	TTCTGGAAGGCACTGTTACCAAAAATGCTTATCTGGGTCCCCCAGAGAGCTTGCCTGCCT	166680

genome mRNA	GGACTGTCGGCTCGCCTGCAACTGCTGACTCCTAAGCTTTTGCAGCTCAGCCCACAACCA	166740

genome mRNA	G TTCCTATTCACAGAGGTGGGAGCTGAGGGGTGACAAGTGA CTGCTGCAGTCTTATTTGT	166800

genome mRNA	CATAGAGAAAAAGTGACAGAGTCCAGCTTGCCCACTGGCCCTGCCAGCTTAACTGGTTAT	166860

genome mRNA	AAAGTGACAAATCCCCAAGACCCACAGGGCTCTGCACAACCTGGGCCCTCCTGCCAGTGG	166920

genome mRNA	CGGCGAGGGCAGGTGGCTCACGGCTGGGTGCCTGTCTGGGCAGGAGCTGGGCTGGTATGG	166980

genome mRNA	GGTGGGCCTGCGGCCCTGCCCCCCTGTGCAGATCAAGACTCAGGGTGCTGGTGTTCACAG	167040

genome mRNA	GTGCCCTCATCAGCCACGAGAAGCTGCTGCTA CAGATCAACCCCGAGCGGGAGCTGGGGA	167100

genome mRNA	GCATGAGCTACAAACTCGGCCAGGTCAGTCTCGCGCCCCCGCCGCCTGGCCTCTGTCCGT	167160

genome mRNA	TTCTGTCCTCAGACTTTGGCGCTTGACACACCCAGGAGAAAAGCTCAGTGCACTTTTTAA	167220

genome mRNA	ATGAAAGGAAGTTTTTCCTTTTTTTTAAAAAAAATTTAATGTTTCATTGTTTTATCTGTT	167280

genome mRNA	TTATTCCTAGGTCCCGCAAGCAGAGGAAGCATTAGTTTTGTTTTTATTTATGTTCTGTAT	167340

genome mRNA	TCCAGAAAGTAGTTAAGAGACCTCACATGTAGCGATAGAGATGTGTGTAAGAGACAGTGA	167400

genome mRNA	GAGGGCGTGACTTGGACTTAAGCAAGGACCGTGAGACACAAAAAGGGGGGTGAGGACAGA	167460

Figure 1

genome mRNA	GTGGAGTCAGCTGAAATGCTCAGGAGGAAGTAGACGCCATGAAGGGCCATGGTATGGGGG	167520

genome mRNA	GCCGCAGGCGTGGCCGTGAGTGTCCCTGGGGCCAGCTCTTGGGGGGCTCCCTGAGTGTCC	167580

genome mRNA	CTGTCCCTGTGGCCAGTTCTGGGTGGGAGCCCCGTGTGCAGGCAGACAGCTCGGCCACTT	167640

genome mRNA	CCTAGCAGGTCACATTGGTCTGTGCTTCTGTTTCCTCCTCAGATAAGTGAAGGGATTCAA	167700

genome mRNA	GGGTCTGGGTGTGGTGGCTAACACCTGTAATCTATAACATTTTAGGAGGCTGAGGCAGGA	167760

genome mRNA	GGCTTACCTGAGCTCAGGAGGTTGAGGCTGCAGTGAGCCATGATTGCACCACTGCACTCC	167820

genome mRNA	AGCCTGGGCAACAGACCAGTACTCTGTCCCTTAAAAAAAAAATGTAAACAGAAACGTAGGG	167880

genome mRNA	CCATTTGCATATGATGGCACATGGCGTGGAGCCCTACAGGTGTATGCTGGGCGGGGCCCCG	167940

genome mRNA	GCTGTGCTGGCCGACTTGACACCTTCCCTCCACCCCGGTGCTGTGTCTTTCGCTCACCGG	168000

genome mRNA	G TTCCTGATTTAGTGAAAGCAGTTGTGCAGGACAGTTCTCTTTGTAGCTTTTGTCTGT	168060

genome mRNA	GGAAATGGGTCAGAATATGGTGTTTAGAAACACTTATGAGCTCTGAGAGTTTCCTCTTCT	168120

genome mRNA	GAGTTCCTGGCCTGCAGCCTTCACAGCAGAAACCCTGTGATGTCACAAGCCTGTTTCTGT	168180

genome mRNA	TCCCTGCTCTCTGCCTGTACTGTCCTGTTTTGTGCCTGCCGGTTTCAGTGACAGGAAGCA	168240

genome mRNA	GGGAGCTACTGGACCAGCCTGTATTTTTCTAGACATAGTTGGAAAAAGAAGTCCCACTCT	168300

genome mRNA	TCTGTCCTTTCACCTTTGACAGATGTTTCCACCCCAAGATAAGTGAAAATGACCAATAGG	168360

genome mRNA	ATGCACTGTATTTTTTCATGAAAGTGTTTCTGAAGGGCAGGCTGAGAGTGAGAGGCCTGGG	168420

genome mRNA	GCTCACTGGGTGCCTCTGGCCTTGTCCTGGGCCCAGGGACACTGGTCTGTGCCCGAGGTA	168480

genome mRNA	TTCCCTATCCCCCAACCCCGCTGCATTGGCCACATCCTTCAATGTTTGC GTTGTGTCC	168540

genome mRNA	AGCGTCCGCAAACCAACTGTCATGGGATCATACTGGGGCTGAAGTACGGTCCCACCCCTG	168600

genome mRNA	CCCTGTCTGGGGCTGAAGTACAGTGCCACCCCTGCCCTGTCTGGGGCTGAAGGACAGTGC	168660

genome mRNA	CACCCCTGCCCTGTCTGGGGCTGAAGTACAGTGCCACCCCTGCCCTGTCTGGGGCTGAAG	168720

Figure 1

genome mRNA	GACAGTGCCACCCCTTCCCTGTCTGGGGCTGAAGGACAGTGCCACCCCTGCCCTGTCTGG	168780

genome mRNA	GGCTGAAGGACAGTGCCACCCCTGCCCTGTCTGGGGCTGAAGGACAGTGCCACCCCTGCC	168840

genome mRNA	CTGTCTGGGGCTGAAGGACAGTGCCACCCCTGCCCTGTCTGGGGCTGAAGGACAGTGCCA	168900

genome mRNA	CCCCTGCCCTGTCTGGGGCTGAAGGACAGTGCCACCCCTGCCCTGTCTGGGGCTGAAGGA	168960

genome mRNA	CAGTGCCACCCCTGCCCTGTCTGGGGCTGAAGGACAGTGCCACCCCTGCCCTGTCTGGGG	169020

genome mRNA	CTGAAGGACAGTGCCACCCCTGCCCTGTCTGGGGCTGAAGGACAGTGCCACCCCTGCCCT	169080

genome mRNA	GTCTGGGGCTGAAGGACAGTGCCACCCCTGCCCTGTCTGGGGCTGAAGGACAGTGCCACC	169140

genome mRNA	CCTGCCCTGTCTGGGGCTGAAGGACAGTGCCACCCCTGCCCTGTCTGGGGCTGAAGGACA	169200

genome mRNA	GTGCCACCCCTGCCCTGTCTGGGATGTTTAGCCCCCTAGATGCCACTGGACTGAGCCGCTA	169260

genome mRNA	CTTGCTTTTGGGAAAGAGGGGTGGGGTTAGGGGTCTGGGCGAGGGGAGTGCAGGGGCTC	169320

genome mRNA	CTCCTTGGCCTGAGAGCTGTTACATACAGACTCCTCGCCCACTCCCTGCAGGGTGCTGGGT	169380

genome mRNA	CCCAGGGGGGAAATGGCCCTTGGTGCCAAGAACGTGAGTTGGGGCTAGTGCCAGTGATGA	169440

genome mRNA	TGGAGAACAGCTTTTTATGGGCACACAGCCCACAGCACTGTGCCAAGTGCTCGAGGCTTC	169500

genome mRNA	CCGAGAACCAGGCAGAAAGGAGGACAGTCGAGGTGTGCTGACTGCGTGGTGGCTGCGTGA	169560

genome mRNA	TCTAGAGCGCGGGTCACAAAGGCGGAGGGAGCTCTGGCCTTGGGTTTACCGCAATGACT	169620

genome mRNA	GCCAGTGCGGGAGACTGGAAAAGGAATCTCACGTATTGGTTCCGTGTTTTGGGGACTCCA	169680

genome mRNA	TTCAGATGTCACTTAGGAGTGAAAGCATCCCTTCGTAGAGCCTCTTTCTGTGTCACCCTC	169740

genome mRNA	CTCAGCTGCTCCTGGGGTTGACTGGCCCCCTGATTCATGCCTTTAGCATGTGCTGGAGCTT	169800

genome mRNA	CCCAGCAGCTGTCCAGCCCCTGCCCCACCCTCTCTGTGGGCTCCCTTGCCCGTAACCTGG	169860

genome mRNA	GGTGTCTGAACGACCCTTGCTAAGGGGCAGACTGTTAGACGGTAGGCATGTGCTGAGTCC	169920

genome mRNA	CAGTGGCCACACCCACCCACCAGGAGCCTGGCACTGTGGCCGCAGCACTGAGCAGTGCCC	169980

Figure 1

genome	CGTTTCTGTGGCAGGTGTCCATACTCCGTGTGGCTGGGGAACAGCATCACACCCCTGA	170040
mRNA	-----	
genome	GGGAGGAGGAATGGGACGAGGAAGAGGAGGAGGAGGCCGACGCCCCTGCACCTTCGTCAC	170100
mRNA	-----	
genome	CACCCACGTCTCCAGTCAACTCCAGGTTTTCCAATGGCCTTTTTCTTTTAAACAGAAATT	170160
mRNA	-----	
genome	TGAAATTTCTTATCAGTCATTTGATTTGTTTGAGGTGCTTCTTGAAATGAGCCTCTCATC	170220
mRNA	-----	
genome	TCATGTACTTGGAAAATACCCATCTCGCATATTCCACAGGAAACACCGGGCTGGAGTTGA	170280
mRNA	-----	
genome	CATCCACTCCTGTTTCGAGTTTTTGCTTGAGTTGTACAGCCGCTGGATCCTGCCGTCCAG	170340
mRNA	-----	
genome	CTCAGCCAGGAGGACCCCGGCCATCCTGATCAGTGAGGTGGTCAGATCCGTAAGTGAGCC	170400
mRNA	-----	
genome	TTCCCATTTCCCTCACACCTGCACGTGCCACACGCACCACACACGCCACACACCCACAC	170460
mRNA	-----	
genome	ACACACACCGCCACACACATGCCACTTGCACACACACCCCTCATGCATGCAACACACAC	170520
mRNA	-----	
genome	ACAGGCCACACGCACCATAGACACCACACACACATGCCACATGCACACACATACACGGCA	170580
mRNA	-----	
genome	TGCACCATACACACAACACACACAGCACACATGCCACACACACAGCCACACCACATGCA	170640
mRNA	-----	
genome	CCACACACATGCCACATGCACACACACTCCACATGCATGCACCACACACACACACACACA	170700
mRNA	-----	
genome	CCACACACACCACATGCACCACACCACACAGGTTACATGCACACAACACACACATGCCAC	170760
mRNA	-----	
genome	GTGCACACACCCACACACCACATGTATGTGCCACACACAGCACACAACCACACACATGC	170820
mRNA	-----	
genome	ACCACACACATGCCACATGTGCATGCACCAGACACATGGCACACACTACACACACGCCAC	170880
mRNA	-----	
genome	GTGCACACACCCACACACATGTACGCACCACACACATGCCACACACACATGCACCACAC	170940
mRNA	-----	
genome	ACATGCCACATGTACACACATGTATATACACACCCACACCACACACACACCACTTGCAC	171000
mRNA	-----	
genome	ACCACGCACACACACCACATGCGCACACACACACCACATACGCCACATGTACACACCATA	171060
mRNA	-----GCTGCCGGGACGGGTCCAAGATGGA	25
	* ** ** ** *	
genome	CACACACCATACATGCACCACGTGTACCACGCACCCACACAGACACAGCACACGCATACA	171120
mRNA	CG---GCCGCTCAGGTTCTGCTTTTACC-TGCGGCC-CAGAGCCCCA-TTCATTGCCCCG	79
	* ** ** * * * * * ** ** ** ** *	
genome	CCACACACACACGCACACATGCGTCCCGCACAGTAATGTCTCTTGGGTGTAAGAACACGA	171180
mRNA	GTGCTGAGCGGCGCCGCGAGTCGGCCCGAGGCCTCCGGGGACTGCCGTGCCGGGCGGGAG	139
	* * *** * * * * * * * ** *** *	
genome	CTTGCCAGTAGTAGCGTTCTGGATGCGTTGCCTGGATTCTAACAGCGCGATTCTCCCCTT	171240
mRNA	ACCGCCA-TGGCGAC--CCTGGAAAAGCTGATGAAGGCCT-----TCGAGTC-CCTCAA	189

Figure 1

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          *****
genome      GCCCTCCTGGTTTTCCACATCTCCAGCTTCTAGTGGTCTCAGACTTGTTACCGAGCGCA 171300
mRNA        GTCCTTCCAGCAG-CAGCAGCAGCAGCAGC-AGCAGCAGCAGCAGCAGCAGC--AGCAGC 245
          * * * * *
          rs2276881
genome      ACCAGTTTGAGCTGATGTATGTGACGCTGACAGAACTGCGAAGGGTGCACCCTTCAGAAG 171360
mRNA        AGCAGCAGCAGCAGCAACAGCCGCCACCGCCGCCGCCGCCGCCGCCG-CTCCTCAGCTT 304
          * * * * *
genome      ACGAGATCCTCGCTCAGTACCTGGTGCCTGCCACCTGCAAGGCAGCTGCCGTCCTTGGA 171420
mRNA        CCTCAGCCGCCGCCGCGAGGCACAGCCGCTGCTGCCTCAGCCGAGCCGCCGCCGCCGCCGCCG 364
          * * * * *
genome      TGGTAAGTGACAGGTGGCACAGAGGTTTCTGTGCTGAAGCCACGGGGGCCCATCTGCCTT 171480
mRNA        CCCCCGCCGCCACCCGGCCCGGCTGTGGCTGAG---GAGCCGCTGCA-CCGACCAAAGAA 420
          * * * * *
genome      GGGACCTGGTGTGGCCAGAGGTGCCGGGTGCGGCTGCCTCCTTCCAAGAGTTGACCCGA 171540
mRNA        AGAACTTTCAGCTACCAAGAAAGACCGTGTG-AATCATTTGTCTGACAATATGTGA---AA 476
          * * * * *
genome      ACCGGACTCCACGGCCACGTGAG---CTGCAGTGCTTCTCAGATGGAGGGGGTTTCAGCG 171597
mRNA        ACATAGTGGCACAGTCTGTGAGAAATTTCTCCAGAATTTTCAGAAACTTCTGGGCATC-GCT 535
          * * * * *
genome      ACGGTCAGTGCCATTCACAGGTCACTG-TGATGTGGGTTGTGGCGGCCAAGCCATGGTTT 171656
mRNA        ATGG--AACTTTTTCTGCTGTGCAGTGATGACGCAGAGTCAGATGTCAGGATGGTGGCTG 593
          * * * * *
genome      GGGGTCCTGATCCCTGGGCTTATGACATCATTTGTAGTAGCCCATCCCCACAGAACCACG 171716
mRNA        ACGAAT--GCCTCAACAAAGTTATCAAAGCTTTGATGGATTCTAATCTTCCAAGGTTACA 651
          * * * * *
genome      GTGTGTGGTGGCGCTGAGGCATCGTAGATGGTGGAAATGCTACTGGCTTCCCCATGCTCT 171776
mRNA        GCTCG-AGCTCTATAAGGAAATTAAGAAAGAAATGGTGCCCTCGGAGTTTGC---GTGCT 706
          * * * * *
genome      GCCCTGAGGCCTGACTGCCTCACTCCCCTTCTCAGTTATGTTCCAGGCCCCCGAGCTTC 171836
mRNA        GCCCTGTGGAG-GTTTGCTGAGCTGGCTCACCTGGTTCGGCCTCAGAAATGCAGGCCTTA 765
          * * * * *
genome      CTGGCTGGACAGCTTCTCTCCTGGGGGCCGTTTGTGTCACAGTGACCCTGTGTTTCTAGTC 171896
mRNA        CCTGGTGAACCTTCTGCCGTGCCTGACTCGAACAAGCA-AGAGACCCGAAGAATC-AGTC 823
          * * * * *
          rs3121419
genome      CCAAATCTGGGTGCTATAGTCTCTTTTATAGCGTGGTGGTTGTCTTAGTCTTTTTTGGCTG 171956
mRNA        CAGGAGACCTTGGCTGCAG-CTGTTCCCAAATTTATGGCT-----TCTTTTGGCAA 873
          * * * * *
genome      CTACCACAAGTTACCTTAGACTGGGTAATTTATAAACAGTGGAATTTACTTCTCACCCT 172016
mRNA        TT-TTGCAAATGACAATGAAATTAAGGTTTGTAAAGGC-----CTTCATAGCGA 923
          * * * * *
genome      TCTGGGGGCTGGAAGTTTTTCATGGTCAAGGTGCCAGCAGATTTGGTGTGTGATGAGGGCT 172076
mRNA        ACCTGAAGTCAAGCTCCCCCACCATTGGCGGACAGC-GGCTGGATCAGCAGTGAGCATC 982
          * * * * *
genome      GCTCTCTGCTTCATAGATGGCATCTTCTGGCTGGGTCTCAGGTGGAAGGAGTGAACAA 172136
mRNA        TGCCAGCACT-CAAGAAGGACACAATATTTCTATAGT-TGGCTACTAAATGTGCTCTTAG 1040
          * * * * *
genome      GCTCCCTCAGGCCTTTTAGAAGGGCCCCAATCCACAAGGGCTCTCCCATCATGACCTCAT 172196
mRNA        GCTTACTC-GTTCCTGTCGAGGATGAACACTCCACTCTG-CTGATTCTTGGCGTGCTGCT 1098
          * * * * *
genome      CACCTCCCAAGGCCCCACCTTCTTGTACTGTGGCACTGCAAATTAGGTGTGAGTGTAGGA 172256
mRNA        CACC--CTGAGGTATTTGGTGCCCTTGCTGCAGCA--GCAGGTCA-----AGGACACAA 1148
          * * * * *
genome      GTTTCAGGAGGGATAGAAACATTCAGACCATCCAGCGGTCAAGTGTTCATCCTCTTGAG 172316
mRNA        GCCT---GAAAGGCAGCTTCGGAGTGACAAGGAAAGAAATGGAAGTCTCTCCTTCTGCAG 1205
          * * * * *
genome      TTCCTCCTTATTCTGCTTCTGGTTTATCAGGATTCAGCCAGTGCAGCAT-GGTACCTGTA 172375
mRNA        AGCAGCTTGTCCAGGTTTATGAACTGAC--GTTACATCATACACAGACCAAGACCACAA 1263
          * * * * *
genome      TTCTGTGGCACATCACCACATGGTATTTGC--CAAGTATCCATCACCTGCACACGTGAA 172433
mRNA        TGTGTGAC-CGAGCCCTGGAGCTGTTGCAGCAGCTCTCAGAACGCCTCCACCCGAGC 1322

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Figure 1

genome	* * * * *	TCATTGCCCCGTGGGTCCCGACATCTGGCGAAGCATATTCAAGGATGGCAGAACTGTCAGA	172493
mRNA	T-----	TCTGCAAACCCTGACCGCAGTCGGGG-GCAT-T-GGGCAGCTCACCGCTGCTAAG	1375
genome	* * * * *	GCTGGCACCTCTGGTTCCTTGTCAT-GTGGCATTACCTAGTAATCCATTTTATGATAGCA	172552
mRNA	GAGGAGTCTGGTGGC-	CGAAGCCGTAGTGGGAGTATTGTGGAAC-----TTATAGCTGGA	1429
genome	* * * * *	ATGGAAACTCATTTCTTCAACAAACACCTGAGTGGCTGCCGTGTGCCAGCCGTCTGGGGC	172612
mRNA	GGGGG-----	TTCTCATGCAGC-CCTGTCCTTTCAAGAAAACAAAAGGCAAAGTGC	1481
genome	* * * * *	CCTTGGTGAGAATGGCATGGTGGTGCCCATCAGGGCCTGCCTAGCCCGTGCTCTGG-ACG	172671
mRNA	TCTTAG-GAGAA-----	GAAGAAGCCTTGGAGGATGACTCTGAATCGAGATCGGATGTC	1534
genome	* * * * *	GGCTCCTGTGTGTCAGGAACGACAATGCTGTGTCATGACGGTGAATGATTTTTTTTTTTGCC	172731
mRNA	AGCAGCTCTGCCTTAACAGCCTCAGTGAAG-	ATGA-GATCAGTGGAGAGCTG----GCT	1588
genome	* * * * *	ATCACTCCAGCCGCTAACATTTGCGGAGCTCTTCCCTCCCGCACCCCCACCTGACAAGGCC	172791
mRNA	GCTTCTTCAGGGGTTTCCACT--	CCAGGGTCAGCAGGTCATGACATCATCACAGAACAGC	1646
genome	* * * * *	AAGGGTGACCTTGGCCCCACCCTAGGCGGCCAAGGTCAGAGGTTAGCTGGCTTGTCTGGG	172851
mRNA	CACGGTCACAGCA--	CACACTGCAGGCGGAC----TCAGTGGAT--CTGGCCAGCTGTGA	1698
genome	* * * * *	TCACACAAAATGCAGCAGAGGTTGAGGTGAGCACATGTCCGTGACCTGGAGCCTGACTCC	172911
mRNA	CTTGACAAGCTCTGCCACTGATGGGGATGAGGAGGATATCTTGAGCCACAGCTCCAG-CC		1757
genome	* * * * *	CTCTCTGCGA-GTCTTGACTGCTCTTGCCCTAGACTCTGTCCTCCCCGAGCCCAAACGCCA	172970
mRNA	AGGTCAGCGCCGTCCCATCTGACCCTGCCATGGACCTGAA-	TGATGGGACCCAGGCC---	1813
genome	* * * * *	GTCATCTTCCCTTGTGGGTGTCCTTCAGCCTGGTGCCATGCTGG-TGACTCAGCAG----	173025
mRNA	-TCGTCGCCCATCAGCGACAGCTCCCAGACCACCACCGAAGGGCCTGATTCAGCTGTTAC		1872
genome	* * * * *	CCGTCCAGGGAGTGGAACAATTGAGTGTGTGGGTTCCTGTGTGGGCATCTC--TCTTC	173083
mRNA	CCCTTCAGACAGTTCTGA-AATTGTGTTAGACGGTACCGACAACCAGTATTTGGGCCTGC		1931
genome	* * * * *	ACGGCGAACACCCTCTGGGTGTTGCCACACGATGTCAAAGCGGCTCTTGAAGGGGTCC	173143
mRNA	AGATTGGACAGCCCCAGGATGAAGATGAGGAAGCCACAGGTATTCTTCCTGATGAAGCCT		1991
genome	* * * * *	TTCTCCTTTGTGGGAAGTTTCAGCTGCTGGGCTAACTTGAATTGTAAGTGTGGTTTTGTG	173203
mRNA	CGGAGGCCTTCAGGAAGTCT----	TCCATGGCC--CTTCAACAGGCACA-----TTTATT	2040
genome	* * * * *	CTCAGGCCAGATCCCCCTAGGCAAGTGTGTGCCATCAGTAATCAAATGAGAAATAATC	173263
mRNA	GAAAAACATGAGTCACTGCAGGCA-GCCTTCTGACAGCAGTGTT-----	GATAAATTTGT	2094
genome	* * * * *	ATTTTGAAAAGCAGATCCTAAGGCAGGATGGTCATGGACACTCACTCCCAGCTCTTTGTG	173323
mRNA	GTTGAGAGATGAAGCTACTGAA-CCGGGTGATCAAGAAAAC-----	AAGCCTTGCCG	2145
genome	* * * * *	CACTCATGCTTTCTGGAAGATGGCCATCCTCTG-TGAAGGTTTTAGCGCGTCATGCTTG	173382
mRNA	CATCAAAGGT----	GACATTGGACAGTCCACTGATGACTCTGCACCTCTTGTCATT	2201
genome	* * * * *	GTACCCACGTATCCAGAGCATGTCGTTTTGAGGTATTTGCCACCGTTGTGAAATCCGTG	173442
mRNA	GTGTCCGCCTTTT-----	ATCTGCTTC---GTTTTTGCTAACAGGGGGAAAAAATGTG	2251
genome	* * * * *	CCACCCGAGAGCAGGTCTGATGTGGGGCTTTTCAGAAGTGGGACCTGGGGCCGTACGCAG	173502
mRNA	CTGGTTCCGGACAGG----	GATGTGAGGGT--CAGCGTAAGGCCCTGGCCCT----CAG	2301
genome	* * * * *	TCCTTAGGGAGGGGGCCGTGTGGCGTTGTGCGTGTGAGGGGATAGCACAGGGTGAGGTGGG	173562
mRNA	CTGTGTGGGAGCAGC--	TGTGGCCCTCCACCCGAATCTTTCTTCAGCAAACCTCTATAAA	2359
genome	* * * * *	GGCCC----AAGAAGGAAGTGACCCACAAAGAACAGCCTCCTCTTTTGGTCCTTGTTCT	173618
mRNA	GTTCTCTTGACACCACGAATACCCTGAGGAACAGTATG-TCTCAGACATCTTGAAC-T		2417
genome	* * * * *	GGGATGGCTGGGAGTGGCTTCTGTGTCGTCGGCCATTTCCCCTG-CGGAGAGGCTCCTA	173677
mRNA	ACATCGATCATGGAGACCCACAGGTTTCGAGGAGCCACTGCCATTCTGTGGGACCCTCA		2477

Figure 1

genome	CCACTGCCGAGAACCTCATCATTCACAAAAACAAGAGGCCGCTGGCCATCCAGCGCTC	173737
mRNA	TCTGCTCC---ATCCTCAGCAGGTCCCGCTTCCACGTGGGAGATTGGAT-----GGGCAC	2529
genome	CATGGGAATTCTGTGTCCCCATAGTCTTGGGCTGAAGGAGGGTGA-CATTCCTTGCTGA-	173795
mRNA	CATTAGAACCCTCACAGGAAATACATTTTCTTTGGCGGATTGCATTCCTTTGCTGCGGAA	2589
genome	----CTTCTGCAGGGGTCTCCTCACTGTTAAAGAGCAGATTGAAA----GTGAAGAAC-G	173846
mRNA	AACACTGAAGGATGAGTCTTCTGTTACTTGCAAGTTAGCTTGTACAGCTGTGAGGAACTG	2649
genome	TGGGCTAAGTGTTTAGGTTCGATATTTAACCCTGCTAGGTTTTGGATACTAAGTGAAATTG	173906
mRNA	TGTCATGAGTCTCTGCAGCAGCAGCTA---CAGTGAG--TTAGGACTGCAGCTGA--TCA	2702
genome	AGGCCATTTTGGTTGAAGTTGACAGAAACCACTATCAGGGATCCCCAAGACTACCCAGG	173966
mRNA	TCGATGTGCTGACTCTGAGGAACAGTTCCTATTGGCTGGTGAGGACAGAGCTTCTGGAAA	2762
genome	CTTTTCTAGAAA--GACTCTCAGCTAAGATGTGTTATGGTAAAAGCACACAAAACAAAAT	174024
mRNA	CCCTTGCAAGAGATTGACTTCAGGCTGGTGAGCTTTTTTG-----AGGCAAAAG	2810
genome	CAGCAAAGAAAATTAGCAAGGGCAGAGGGCCCATGGGGCGATGTCCCGAGGACACCAGGCT	174084
mRNA	C-----AGAAAACCTTACACAG--AGGGGCTCAT----CATTATAC--AGGGCTTT----T	2853
genome	TGAGCTTCCAGAATCCTCTCCCAGCGGGGTCGTGCAGGACGCACTTAACCTCCCGCACAG	174144
mRNA	AAAAGTGAAGAACGAGTGCTCAATAATGTTGTATCCATTGCTTGAGATGAAGACCC	2913
genome	TGAGCCGTGACAGCGCGTGTGCAGTGTGTCGCCAGGAAAGCACACTAGAGACTCGGTGC	174204
mRNA	CAGGGTGCGACA--TGT-TGCCGCGCATCACTAATTAGGCTTGTCCCAAAGCTGTT-T	2968
genome	CAGGGTTTTTACTGGGGGCTGGGCACATGGGCACCCTCTGCCTGCCTCGTGCCAGACTC	174264
mRNA	TATAAATGTGACCAAGGACAAGCTGATCCAGTAGTGGCCG--TGGCAAGAGATCAAAGCA	3026
genome	TGGACTCCCGAGGGGAAGGCAAGTTCTCA-GCACCAACCCTGGTGCCCA-CACAAGCAGC	174322
mRNA	GTGTTTACCTGA-----AACTTCTCATGCATGAGACGCAGCCTCCATCTCATTTCTC	3078
genome	TGAGCACAGGGAGCCCCCTCCTCAGTGAGGATGGTGGGCACCGTCCCAACACCAGCCAGGG	174382
mRNA	CGTCAGCACATAAACCAGAAATATATAGAGGCTATAACCTACTACCAAGCATAA--CAGAC	3136
genome	GCCAGCCTTGACACAGGCCTCTCAGGATGGTCTCCGGCCTGCTGTGTAGTCTCTTCTGC	174442
mRNA	GTCACATATGGAATAACCTTTCAAGAGTTATTGCAGCAGTTTCTCATGAACATAATC-AC	3195
genome	ACACAAGCGTGAGGGCAGCGCCCCCGCCTCGGCTGTGGGGAGGAGCCACTGGGACGTGAG	174502
mRNA	AT-CAACCACCAGAGCA----CTCACATTTGGATGCTGTGAAG---CTTTGTGTC-TTCT	3246
genome	CTCTGGTGGCATGCAGCAGCTTTTGTCTGTGTGTGCCTAGGACAAGGCCGTGGCGGAGCC	174562
mRNA	TTCCACTGCCTTCC--CAGTTTGCATTTG---GAGTTTAGGTTGGCACTGTG---GAGTG	3298
genome	TGTCAGCCGCTGCTGGAGAGCAGCTCAGGAGCAGCCACCTGCCAGCAGGGTTGGAGC	174622
mRNA	CCTCCACTGAGTGCCTCAGATGA-GTCTAGGAAGAGCTGTACCGTTGGGATGGCCACAAT	3357
genome	CCTGCACGGCCTCCTCTATGTGCTGGAGTGCAGCCTGCTGGACGACACTGCCAAGCAGCT	174682
mRNA	GATTCTGACCCTGCTCT--CGTCAGCTTGGTTCCCATTTGGATCTCTCAGCCCATCAAGA	3414
genome	CATCCCGGTCATCAGCGACTATCTCCTCTCCAACCTGAAAGGGATCGCCAGTGAGTGGG	174742
mRNA	TGCTTTGATT-TTGGCCGGAAACTTGCTTGACAGCC---AGTGCTC-CCAAATCTCTGAG	3468
genome	AGCCTGGCTGGGG-CTGGGGCGGGGGTC---TCAGAATGAGCTGTGAAGGAAGCAGCATC	174798
mRNA	AAGTTCATGGGCCTCTGAAGAAGAAGCCAACCCAGCAGCCACCAAGCAAGAGGAGGTCTG	3528
genome	ACCCTCTCCAAGTGCCCAGGCTCCTGGCCAGATGGCAGGCCAGGTATCAGTGGGAACCC-	174857
mRNA	GCCAGCCCTGGGGGACCGGGCCCTGGTGCCCATGGTGGAGCAGCTCTTCTCTCACCTGCT	3588
genome	--AGGTGGGTGCCAT---GGCTGAGGTGAGTGAGACGAAGAGCACAGGTGCGTCCTAG	174911

Figure 1

mRNA	GAAGGTGATTAAACATTTGTGCCACGTCCTGGATGACGTG-GCTCCTGGACCCGCAATAA	3647
	***** * *** * * * * * * * * * * * * *	
genome	AGGCTTCCTCGGGCACCTCCAGCGAGCTGGAGCTCTCGCCTCTGCTGCTGTCTCATGTGG	174971
mRNA	AGGCAGCCTTGC-CTTCTCTAACAAACC----CCCCTTCTCTAAGTCCCATCCGACGAAA	3702
	***** * * * * * * * * * * * * * * * *	
genome	CGCTTAGCACACTCTCCACGTCGCCATTCCTGACTCTGCTCTCGAGGCCATCGGCTCTC	175031
mRNA	GGGGAAGGAGAAAGAACCAGGAGAACAAGCAT--CTGTACCGTTGAGTCCCAAGAAAGGC	3760
	* ** * * * * * * * * * * * * * * * *	
genome	ATTCTCTGCTCCAGAACCTGTTATTACCCAGGCTAGCCTCCTCTCTGCACCTTCCCCG	175091
mRNA	AGT----GAGGCCAGTGCA--GCTTCTAGACAATCTGATAC---CTCAGGTCCTGTTAC-	3810
	* * * * * * * * * * * * * * * * * * * *	
genome	CCCTGGCCCAGTACCTCCCTCTTGTTCCTGTTTCCACTGTGATTCCGACCTCACCTTAT-CTTAA	175150
mRNA	-----AACAAGTAAATCCTCATCACTGGGGA-GTTTCTATCATCTTCCTTCATACCTCAA	3864
	* ***** * * * * * * * * * * * * * * *	
rs362271		
genome	GCTGCTGGACGGCAGGTTCTGATACACACGTGTCCTTGACAAAGCACGGCTGGTGCCGCAA	175210
mRNA	ACTGCATGATGTCCTGAAAGCTACACACGCTAACT--ACAAGGTCACGCTGGATCTTCAG	3922
	***** * * * * * * * * * * * * * * * *	
genome	CCCCTCAGCGAGCAAGTCA-AGCTCTTCACAGCGATGTCTTACAAGCGCAGAGGGCTCTG	175269
mRNA	AACAGCACGGAAAGTTTGGAGGGTTTCTCCGCTCAGCCTTGGATGTTT-----TTTC	3975
	* ** * * * * * * * * * * * * * * * *	
genome	TGACACCCTGGTCTCACCGCCACTCTTCCAAA-GTCGCAGAGGCTTTAGCAGAGATGGGC	175328
mRNA	TCAGATACTAGAGCTG--GCCACACTGCAGGACATTGGGAAGTGTTGAAGAGAT---C	4030
	* * * * * * * * * * * * * * * * * * * *	
genome	CCAGCCTCTCTGAGTCATAGGCTTCTGCACACGGGAGCTGTCTTTAGAGGGAGGGTGGAA	175388
mRNA	CTAGGATACCTGAA----ATCCTGCTTTAGTCGAGAACCAG--TGATGGCAACTGTTTGT	4084
	* * * * * * * * * * * * * * * * * * * *	
genome	TTTCATCAGCCACCCACATGGGGGAGTTGAGGGCAAGAATTAGGAGCAAAGATGGGAAGG	175448
mRNA	GTTCAACAATT-----GTTGAAGACTCTCTTT-GGCACAACTTGGCCTCC	4129
	***** * * * * * * * * * * * * * * *	
genome	GGTCTGGGAGGAATGGCCAGTGATCCCCTTTGACAAGTGGGCAGGAAACGGGGGCTAGGT	175508
mRNA	CAGTTTGATGGCTTATCTTCCAACCCAGCAAGTCACAAGGCCGAGCACAGCGCCTTGGC	4189
	* * * * * * * * * * * * * * * * * * * *	
genome	CAAAGTTGAGTGGAAGACCTGGAGGGAGACGGGAAGGTCTCTGTAGGCACAGTTCAGACA	175568
mRNA	TCC--TCCAGTGTGAGGCCAGGCTTGTACCACTACTGCTTCA--TGGCCCCGTACACCCA	4245
	* ***** * * * * * * * * * * * * * * *	
genome	GGAGGGAGGTGTGAGCCAGGGCACATGCCGGTGGCCGTCTGGCAGGATTTGGGACATGCT	175628
mRNA	C-----TTCACCCAGGCCCTCGCTGACGCCAGCCTGA-GGAACATGGTGAGGC-	4293
	* ** * * * * * * * * * * * * * * * *	
genome	GGAGCAGGGACAGCGGCTCATCAGGGGCCATTGCCCTCATCCAGGCCAGAGTGTCAACAG	175688
mRNA	GGAGCAGGAG-AACGACACCTCGGGATGGTTTGATGTCTCCAG---AAAGTGTCT---A	4346
	***** * * * * * * * * * * * * * * *	
genome	CCCGTGGGGAGGCCCTTCTCGCCTGTCTCCTTGCTGGGCAGTGGGTCTGTGCTAGCAG	175748
mRNA	CCCAGTTGAAGACAAACCTCACGAGT-----GTCACAAAGAACCCTGC-----A	4390
	*** * * * * * * * * * * * * * * * *	
genome	GACAGGCGGACGGCTGGCAACTGTCTCTGCATCCCTGGAGCCTGGCATAGGGCCAAGTCA	175808
mRNA	GATAAGAATGCTATTTCATAATCACATTCGT-TTGTTTGAACCTCTTGTTATAAAAGCTTT	4449
	* * * * * * * * * * * * * * * * * * * *	
genome	CACGGGGCACAGGCCTGCAAATCAGGCACATATGTTGGTGCAGTGACGTGATTTTGGGGG	175868
mRNA	AAAACAGTACACGACTACAA-----CATGTGTGAGTTACAGAAGCAGGTTTGTAGATTT	4503
	* * * * * * * * * * * * * * * * * * * *	
genome	GCAGCCCCAGAACAGGCCCCAGACACAGGCCAAAGCCCTGCCTGTGCTGGTGTGTTGGGC	175928
mRNA	GCTGGCGCAG--CTGGTTC-AGTTACGGGTTAAT-TACTGTCTTCTGGATTGAGATCAGG	4559
	* * * * * * * * * * * * * * * * * * * *	
genome	TGTTCTATGGCTCTTGTGTGGGCATGGAGGACTCAGGGAAGGAGAGTTGAGGTGGTCCA	175988
mRNA	TGTTTATTGGCTTT-----GTATTGAAA---CAGTTTGAATACATTGAAGTGGGCCA	4608
	***** * * * * * * * * * * * * * * *	
genome	GGAGTTGCGTTTGGGATGCAGAGAGCTTGTGGCATCCAGGTAGAAATGGTGCGTGGGGCT	176048
mRNA	G-----TTCAGGGAATCAGAGGCAATCATTCACAA-----CATCTTTTT	4647
	* * * * * * * * * * * * * * * * * * * *	
genome	GACCTCAGCACCATGGGCAGAGGGGCCGTGTACGTGCCTCCGAGGTGGAGGTGGGACCA	176108
mRNA	CTTCTTGGTATTACTATCTTATGAACGCTATCAT-----TCAAAACAGATCATTGAATT	4702
	* * * * * * * * * * * * * * * * * * * *	

Figure 1

genome	CGTGGTGACAGATATACGCATCACTGGGCACGTTTTTGTGGGTGTTGGGGGGCATCGTAT	176168
mRNA	CCT-----AAAATCATTCAGCTCTGTG-ATGGCATCATGGCCAGTGGAAGGAA-----	4749
	* * * * *	
genome	TGGCTCCTCTGTTACAGTGGCCACTCATTAGTCCCTGGCTACCAGGTCCTCACTGTGC	176228
mRNA	-GGCTGTGACACATGCCATACCGGCTC-TGCAGCCCATAGT--CCACGACCTCTTTGTAT	4805
	**** * * * * *	
genome	CATGGGGAAGGCCGGCGCTGTCGGGGGATCACAGAAGGCAGCACGTCATGATGGCATGTG	176288
mRNA	TAAGAGGAA-----CAAATAAAGCTG-----	4826
	* * * * *	
genome	CCATGAAGGAAAAGCACAGGGCACTCAGGAAGTAGAGGGGACTGGCCTGGGGTGTGGGAA	176348
mRNA	--ATGCAGGAAAAGAGCTTGAACCCAAAAAG-AGGTGGTGGTGTCAATGTTACTGAGAC	4883
	* * * * *	
genome	TC-TAGGGCCTCGTTGAGGGACAGAGAGAGGAAGTGTGTGGTGGCCAGCATGGAGGTGGC	176407
mRNA	TCATCCAGTACCATCAGGTGTTGGAGATGTTTCTCT---TGTCCTGCA--GCAGTG-C	4936
	* * * * *	
genome	CACAGGGGAGGCTGAGTTAGGCCGAGAGGGCAGGGCGTTGGGGAGGTAGACGGGCTCAGC	176467
mRNA	CACAAGGAGAATGAAGACAAGTGAAGCGACTG---TCTCGACAGATAGCTGACATCATC	4993
	**** * * * * *	
genome	CACTCAGGGAGTGGTCAAGCAGAGGCTGAAGGGTCAGGCCAGGTTGCAGGGGCCTGGGGG	176527
mRNA	CTCCAATGT-TAGCCAAACAGCAGATGCACATTGACTC----TCATGAAGCCCTTGGAG	5048
	* * * * *	
genome	AGCCACTCAGGGTAGGCGCTCCCGGGAGCCCGCCTGGCCCATAGCTCTACACTCCGCGT	176587
mRNA	TGTTAAATACATTA-----TTTGAGATTT---TGCCCCCTTCCTC---CCTCCGTCC	5094
	* * * * *	
genome	GGGGCCGGACATGCTGTGAAGCCCTCTCCACGTTGGATGGGGGTGGCTGAGCCTGGATGC	176647
mRNA	GG---TAGACATGCT-----TTTACGGAGTATGTTCTGTCCTC--CAACACAA	5138
	* * * * *	
genome	TGTCTCCCGTTTTTCAGCTGCGTGAACATTCACAGCCAGCAGCACGTACTGGTCATGTGTG	176707
mRNA	TGGCGTCCGTGAGCA-CTGTTCACTGTGGATATCGGGAATTCTGGCC--ATTTTGAGGG	5195
	* * * * *	
genome	CCACTGCGTTTTTACCTCATTGAGAACTATCCTCTGGACGTAGGGCCGGAATTTTCAGCAT	176767
mRNA	TTCTGATTTCCAGTCAACTGAAGATATTGTTCTTTCTCGTATTCAGGAGCTCTCCTTCT	5255
	* * * * *	
genome	CAATAATACAGGTGAGTGGGCCCTGGCTGTCTTCTCTGCACACGGGGAGTGGGCTTCCC	176827
mRNA	C-----TCCGTATTTAATCTCCTGTACAGTAATTAATAGGTTAAGAGATGGGGACAGTAC	5310
	* * * * *	
genome	TTCTCTTTTCTTGCAGGATCATAACAGTGGGCCAGTTTTGACTTGGTCGGGAGGAGGCA	176887
mRNA	TTCA----ACGCTAGAAGAACACAGTGAAGGGAAACAAATAAAGAATTTGCCAGAAGA--	5364
	*** * * * *	
genome	TGAACACCTGAGACTGTGCAGCGATTCTTTGACACAGAGGCCTTTCTCCCTGTGCAGATG	176947
mRNA	--AACATTTT-----CAAGGTTTCTATTACAAGTGGTGGTATTCTTTTAGAAGACA	5414
	**** * * * * *	
genome	TGTGGGGTGATGCTGTCTGGAAGTGAGGAGTCCACCCCTCCATCATTTACCACTGTGCC	177007
mRNA	T-TGTTACAAAACAG-CTGAAGGTG-GAAATGAGTGAGCAGCAACATA--CTTTCTATT	5468
	* * * * *	
genome	CTCAGAGGCCTGGAGCGCCTCCTGC-TCTCTGAGCAGCTCTCCCGCCTGGATGCAGAATC	177066
mRNA	GCCAGGAAGTGGACACTGCTAATGTGTCTGATCCACATCTTCA----AGTCTGGAAT-	5523
	*** * * * *	
genome	GCTGGTCAAGCTGAGTGTGGACAGAGTGAACGTGCACAGCCCGCACCG--GGCCATGGCG	177124
mRNA	----GTTCCGGAGAATCACAGCAGCTGCCACTAGGCTGTTCCGCAGTGATGGCTGTGGCG	5579
	* * * * *	
genome	GCTCTGGGCCTGATGCTCACCTGCATGTACACAGGTGAGCATGTACACGGTGCCCATAG	177184
mRNA	GCAGTTT-CTACACCCTGGACAGCTTGAAGTTGCGGGCTCGT-TCCATGATCACCACCA	5637
	* * * * *	
genome	GCCAGCCCAAGTCCTGTTCAAGGGAGGCAGGAGCATGCTCACTCAAGGGACCTCGACTAG	177244
mRNA	CCCGGCCCTGGTGCTGCTC--TGGTGTGAGATACTGCTGCTTGTCAACCACACCGACTA-	5694
	* * * * *	
genome	GTGCCCTCTGATTT-CACACTTCTGGTGTGCCCCAAGCCGGCCCCATC-ACCTTGCAAG	177302
mRNA	----CCGCTGGTGGGCAGAGTGCAGCAG-ACCCGAAAAGACACAGTCTGTCCAGCACA	5749
	* * * * *	
genome	AAAGGCTCTGGAGCCCCCAGGGCTGGAGTACCTGGTCAAGGTTGACCGTCCCTGTGGTCA	177362
mRNA	AAGTTACTTAGTCCCCAGATGTCTGGAGAA---GAGGAGGATT--CTGACTTGGCAGCCA	5804
	* * * * *	

Figure 1

genome	CTCATCCCATGTGGCTGAGCTGGGCTGGGTCTGGGCAAGCAAGGGGCTGATATCACCTG	177422
mRNA	AACTTGGAATGTGC---AATAGAG--AAATAGTACGAAGAGGGGCTCTCATTCTCTTCTG	5859
	* * * * *	
genome	CTTTCAGATCTCCAGGGACTCACTGGACCCCTGTGTACAAAGCACTGTCTACAGAGCCTA	177482
mRNA	TGATTATGTCTGTGAGAACCTCCATGACTCC--GAGCACTTAACGTGGCTCATTGTAAATC	5918
	* * * * *	
genome	TTGGGTTGTATAGAGGTAACCTTCGTACTGAACACTTTTGTACAGGAAAGGAGAAAGTC	177542
mRNA	ACATTCAAGATCTGATCAGCCTTCCCACGAGC-----CTCCAGTACAGGACTTCATC	5971
	* * * * *	
genome	AGTCCGGGTAGAACTTCAGACCCTAATCCTGCAGCCCCCGACAGCGAGTCAGTG-ATTGT	177601
mRNA	AGTGCCGTTCA---TCGGAACCTCTGCTGCCAGCGGCCTGTTTCATCCAGGCAATTCAGTCT	6028
	* * * * *	
genome	TGCTATGGAGCGGGTATCTGTTCTTTTGTATAGGTAAGAAGCGAAGCCC-CATCCCTCAG	177660
mRNA	CGTTGTGAAA-----ACCTTTCAACTCCAACCATGCTGAAGAAAACCTCTCAGTGCTTGG	6083
	* * * * *	
genome	CCGTTAGCTTCCCTAGAACTTTGGCCTGAAGCTGTGCTTTTG-TGTGTGTCTGCTGATCC	177719
mRNA	AGGGGATCCATCTCAG----CCAGTCGGGAGCTGTGCTCACGCTGTATGTGGACAGGCTT	6139
	* * * * *	
genome	CCTGGCGCTGTTGCTGGAGTCCTGCCAGTGATTCCCCACCACAGCCTGACCATGGGCTGC	177779
mRNA	CTGTGCACCCCTTCCGTGTGCTGGC-----TCGCATGGTC---GACATC	6181
	* * * * *	
genome	CTTGGCTCAGGGTCCACTGGCGAGCTGGTGGTCCTTGGACCCCAGCACTCAGGTGTAGC	177839
mRNA	CTTGCTT-----GTCGCCGGGTAGAAATGCTTCTGGCTGCAAATTTACAGAGCAGC	6232
	* * * * *	
genome	GTTGACCAGTTCCAAGGTTGTCCCAGTGCCTGCCATCTCTCCTGAGGGCTCAGGGACAG	177899
mRNA	ATGGCCCAGTTGC-----CAATG---GAAGAACTCAAC--AGAATCCAGGAATAC	6277
	* * * * *	
genome	TACCTGGCAGTTGGGGGTGTGGCAGGGGGCAGGAATGACCAGCCTCTGGGAGGGTGGGGC	177959
mRNA	--CTTCAGAGCAGCGGGCTCGCTCAGAGACACCAAAGGCTCTATTCCCTGCTGGACAGGT	6335
	* * * * *	
genome	AGAAGCCTGTACAGTGAGGAGGAGCTGGCTCAGCCTGGCTGCCTATCGTGAGAGGGGAGC	178019
mRNA	TTC-GTCTCTCCACCATGCAAGA-CTCACTTAGTC-----CCTCTCCTCCAGTCTCTTC	6387
	* * * * *	
genome	CCACGGGGCTGTGGGAGGGGGGCCGTGGTGCCTGTGAGCAGGGTGAGGAGCAGCGGCAGG	178079
mRNA	CCAC---CCGCTGGACGGGGATGG--GCACGTGTCACTGGA-----AACAGTGA-GTC	6434
	* * * * *	
genome	AGGATGAAGGTGGAACCCACACATGCATCTT-TGAGACCCGTGTGGTCACTGGCTTCTGC	178138
mRNA	CGGACAAAG-----ACTGGTACGTTCATCTTGTCAAATCCCAGTGTGGACCAGGTCAG-	6488
	* * * * *	
genome	CCCCCACCACCCCTGCTGTGCGTGCATAGAATTGGCTTCCCTCACCTGCTCTGGAA	178198
mRNA	-----ATTCTGCACTGCTG-GAAGGTGCAGAGCTGGTGAATCGGATTCCTGCTGAAG	6539
	* * * * *	
genome	GTGGGTTAGGAGCTTGGTAGGGCTTTTTCTCAAGGACAAGGGCCCCTGATTTGCTCTCAG	178258
mRNA	AT--ATGAATGCCTTCATGATGAA---CTCGGAGTTCAA--CCTAAGCCTGCT---A	6586
	* * * * *	
genome	GCCTCAGTCCTGGCGACATGGTGGATCTGGAGCCTTGTGCACTGCCTTGCCTGTGCTCT	178318
mRNA	GCTCCATGCTTAAGCCTAGGGATGAGTGAAATTTCTGGTG---GCCAGAAGAGTGCCCT	6642
	* * * * *	
genome	CCAATCAGGGTGGCCAGTGGGGAGCCATTTGGCTTTTCTCAAGAGCATACT-CAGGTGGA	178377
mRNA	TT--TTGAAGCAGCCCGTGAGGTGAC-TCTGGCCCGTGTGAGCGGCACCGTGCAGCAGCT	6699
	* * * * *	
	rs3775061	
genome	CCTTGCT--CCACTGT-TTGACCAGATGAGGCAATTCTGAACAGCCAAGCCTGTGCTGGTC	178434
mRNA	CCCTGCTGTCCATCATGTCTTCCAGCCCGAGCTGCCTGCAGAGCCGGCGGCCTACTGG--	6757
	* * * * *	
genome	TGTTTTTCATGTTGATTTTTTTTTTCTTTTCTTTTGTAGATGGAGTTTTTCCCTTGTCAC	178494
mRNA	----AGCAAGTTGAATGATCTGTTTGGGGATGCT---GCACTGTATCAGTCCCTGCCAC	6810
	* * * * *	
genome	CCAGGCTGGAGTGCAATGGTGTGATCTCGGCTCACTGCAACCTCCGCCTCCCGGGTTCAA	178554
mRNA	TCTGGCCCGGGCCC--TGGCACAGTACC---TGGTGGTGGTCTCCAAACTGCCAGTCAT	6865
	* * * * *	
genome	GTGATTCTCCTGCCTCAGCCTCCCTAGTAGCTGGGATTACAGGCACACACCACCATGCCC	178614
mRNA	TTGCACCTTCCTCCTGAGA-----AAGAGAAGGACATTGTGAAATTCGTGGTGGCAACC	6919

Figure 1

mRNA	GGAACAGCATCACACCCCTGAGGGAGGAGGAATGGGACGAGGAAGAGGAGGAGGAGGCCG	8084
	* *	
genome	CCAGGATCCTGCCCCAGTTTCTAG--ACGACTTCTTCCCACCCAGGACATCATGAACAA	179922
mRNA	ACGCCCCCTGCACCTTCGTCAACACCCACGTCTCCAGTCAACTCCAGGAAAC-----ACCG	8139
	* *	
genome	AGTCATCGGAGAGTTTCTGTCCAACCAGCAGCCATACCCCCAGTT-CATGGCCACCGTGG	179981
mRNA	GGCTGGAGTTGACATCCACTCCTGTTTCGAGTTTTTGTCTTGAGTTGTACAGCCGCTGGAT	8199
	* *	
genome	TGTATAAGGTGAGGTTGCATGTGGGATGGGGATGGAGTGGGAAAGCCTGGAGGTGGAGTT	180041
mRNA	CCTGCCGTCCAGCTCAGCCAGGAGGACCCCGGCCATCCTGATCAGTGAGGTGGTCAGATC	8259
	* *	
genome	GCCTCCGACTTCCCAGCAGATTCGCCAGCAGAGCCCAGCTCCTCCGCTTTAAAGCA-GCA	180100
mRNA	CCTTCTAGTGGTCT--CAGACTTGTTACCGAGCGCAACCAGTTTGAGCTGATGTATGTG	8317
	* *	
genome	ATGCCTCTGGCCCCACCCACCCCGCCACCCAGGCGCAGCAGGTGCTTCCCGTCCCCC	180160
mRNA	ACGCTGACAGAACT-GCGAAGGGTGCACCCTTCAGAAGACGAGATCCTCGCTCAGTACCT	8376
	* *	
genome	CAGCCCTGACACTCAGGCACCTGCTTGCTCCTTGCAAGGTGTTTCAGACTCTGCACAGCAC	180220
mRNA	GGTGCCTGCCACCTGCAAGGCAGCTGCCGTCTTGGGATGGACAAGGCCGTG-GCGGAGC	8435
	* *	
genome	CGGGCAGTCGTCCATGGTCCGGGACTGGGTGCTGCTCCCTCTCCAACCTTCACGCAGAG	180280
mRNA	CTGTGAGCCGCC--TGCTGGAGAGCAGCTCAGGAGCAGCCACCTGCCAGCAGGGTTGG	8493
	* *	
genome	GGCCCCGGTCGCCATGGCC-ACGTGGAGCCTCTCCTGCTTCTTTGTGAGCGC-GTCCACC	180338
mRNA	AGCCCTGCACGGCGTCTCTATGTGCTGGAG-TGCGACCTGCTGGACGACACTGCCAAGC	8552
	* *	
genome	AGCCCGTG--GGTCG-CGGCGA-TGTATCCTCTCTGGGTCCCTGGTGCTGGCCCCGTTTC	180394
mRNA	AGCTCATCCCGGTCATCAGCGACTATCTCCTCTCCAA---CCTGAAA--GGGATCGCCCCA	8607
	* *	
genome	CCTTGTCAACACCGA-GGCTCATGTTTCATGATAAGGTTTGAAC-CTAACCTTTGCAA	180452
mRNA	CTGCGTGAACATTACAGCCAGCAGCACGTACTGGTCATGTGTGCCACTGCGTTTACCT	8667
	* *	
genome	AAACCCACAGATGCCAGGGTGACAGGCCCTCAGCCCCAGGGAAGTAAAATGCTGACAGG	180512
mRNA	CATTGAGAACTATCCTCTGGACGTAGGGCCGGAATTTTCAGCATCAATAAT---ACAGA	8723
	* *	
genome	GGTACAGAAAGGAGCACGTCCAGACATTTGCTGACCAGGGCCTCTCAGAGGGGCGGCTGT	180572
mRNA	TGTGTGGGGTGATGC-TGTCTGGAAGTGAGGAGTCCACCCCTCCATCATTTACCACTGT	8782
	* *	
genome	ATGGCAGGAGGGTCGAGCTGAGGGGCCTTTCTGTGGAGGGCCTGGGTGAGGGGAGCGAG	180632
mRNA	GCCCTCAGAGGCCTGGAGCGCCTCCTGCTCTCTGAGCAGCTCTCCCGCCTGGATGCAGAA	8842
	* *	
genome	GGTGGGCGGTGGTCTCTGCAGACGTCCCGCCCACTCGCGGGCTCTGTGTGGCTGGGCTTC	180692
mRNA	-----TCGCTG-----GTCAAGCTGA---GTGTGGACAGAGTGAACGTGCACA	8882
	* *	
genome	TCCTGACACTGCTTCTCATTAGCTTTGGTTCATTGTGCCTCGATCGCCCTCTCGGGGAAAG	180752
mRNA	GCCCG-CACCGGGCCATGGCGGCTCTGGGCCTGATGC-----TCACCTGCATGTACACAG	8936
	* *	
genome	GCTTAAGTAAAGATCCAGTTCACACCCCCAGATGCTGGCTGCCAGGAGTTTCCCTTTCCA	180812
mRNA	GA--AAGGAGAAAGTCAGT-----CCGGGTA--GAACTTCAGA---CCCTAATCCTG	8981
	* *	
genome	CAGCCCTTCCCCAAGACAGACCACAAGAGCCTCCAAGCAGCACAGTTGTCCTGGTGCTGA	180872
mRNA	CAGCCCCCGAC--AGCGAGTCAGTGATTGTTGCTATGGAGCGGGTATCTGTTCTTTTGA	9039
	* *	
genome	CAGCACAGCCTTGCCCGGCGTGCTGGCAGGGCTCTGCCCTCACTGCATTGGAGCAGGGC	180932
mRNA	TAG---GATCAGGAAAGGCTTTCCTTGTGAAGC-----CAGAGTGGTGGCCAGGATC	9088
	* *	
genome	TAGTGGAGGCCAGCGGAAGCACCGGCCACCAGCGCTGCACAGGAGCCAGGCCAGGTGAGT	180992
mRNA	CTGCCCCAGTTTCTAGACG-ACTTCTTCCCACCCAGGACATCA--TGAACAAAGTCA--	9143
	* *	
genome	GCTGCCGAGTGGGTGCCCTGCCTGCAGGGCATCCAGCCAGCCAAGGGTTGCAGGAATGGA	181052
mRNA	-TCGGAGAGTTTCTGTCCAACCAGCAGC-CATACCCCAAGTTTCATGGCCACCGTGGTGTA	9201
	* *	
genome	GGTGGAGGCGCTGATGCAGCTGGAGGCATCCAGGTGGCCCTTCCGGGGCTCTG-CTCGCT	181111

Figure 1

mRNA	TAAGGTGTTTCAGACTCTGC--ACAGCA-CCGGGCAGTCGTCCATGGTCCGGGACTGGGT	9258
	* * * * *	
genome	C-TCCAGGCTCCCTGGACCCCTTTGTAGACTGTTTCAGGAGAGGAACTCCCAGGTGAGGA	181170
mRNA	CATGCTGTCCCTCTCCAACCTCACGCAGAGGGCCCCGGTCGCC--ATGGCCACGTGGAGC	9316
	* * * * *	
genome	CAGGGAGGCAGCATTCCC--CTCATTGCGCGCCTTTTTCCTTAACTCCTGCACCAGCCT	181228
mRNA	CTCTCCTGCTTCTTTGTTCAGCGCGTCCACCAGCC-----CGTGGGTCGCG-GCGATCCT	9369
	* * * * *	
genome	CCCACATGTCATCAGCAGGATGGGCAAGCTGGAGCAGGTGGACGTGAACCTTTTCTGCCT	181288
mRNA	CCCACATGTCATCAGCAGGATGGGCAAGCTGGAGCAGGTGGACGTGAACCTTTTCTGCCT	9429

genome	GGTCGCCACAGACTTCTACAGACACCAGATAGAGGAGGAGCTCGACCGCAGGGCCTTCCA	181348
mRNA	GGTCGCCACAGACTTCTACAGACACCAGATAGAGGAGGAGCTCGACCGCAGGGCCTTCCA	9489

genome	GTCTGTGCTTGAGGTGGTTGCAGCCCCAGGAAGCCCATATCACCGGCTGCTGACTTGTTT	181408
mRNA	GTCTGTGCTTGAGGTGGTTGCAGCCCCAGGAAGCCCATATCACCGGCTGCTGACTTGTTT	9549

genome	ACGAAATGTCCACAAGGTCACCACCTGCTGAGCGCCATGGTGGGAGAGACTGTGAGGCGG	181468
mRNA	ACGAAATGTCCACAAGGTCACCACCTGCTGAGCGCCATGGTGGGAGAGACTGTGAGGCGG	9609

	rs362307	
genome	CAGCTGGGGCCGGAGCCTTTGGAAGTCTGCGCCCTTGTCCTCCACCGAGCCAGC	181528
mRNA	CAGCTGGGGCCGGAGCCTTTGGAAGTCTGCGCCCTTGTCCTCCACCGAGCCAGC	9669

genome	TTGGTCCCTATGGGCTTCCGCACATGCCGCGGGCGGCCAGGCAACGTGCGTGTCTCTGCC	181588
mRNA	TTGGTCCCTATGGGCTTCCGCACATGCCGCGGGCGGCCAGGCAACGTGCGTGTCTCTGCC	9729

genome	ATGTGGCAGAAGTGCTCTTTGTGGCAGTGGCCAGGCAGGGAGTGTCTGCAGTCCTGGTGG	181648
mRNA	ATGTGGCAGAAGTGCTCTTTGTGGCAGTGGCCAGGCAGGGAGTGTCTGCAGTCCTGGTGG	9789

genome	GGCTGAGCCTGAGGCCTTCCAGAAAGCAGGAGCAGCTGTGCTGCACCCCATGTGGGTGAC	181708
mRNA	GGCTGAGCCTGAGGCCTTCCAGAAAGCAGGAGCAGCTGTGCTGCACCCCATGTGGGTGAC	9849

	rs362306	
genome	CAGGTCCTTTCTCCTGATAGTCACCTGCTGGTTGTTGCCAGGTTGCAGCTGCTCTTGCA	181768
mRNA	CAGGTCCTTTCTCCTGATAGTCACCTGCTGGTTGTTGCCAGGTTGCAGCTGCTCTTGCA	9909

genome	CTGGGCCAGAAAGTCCCTCCCTCCTGCAGGCTGGCTGTTGGCCCCCTCTGCTGTCTGCAGTA	181828
mRNA	CTGGGCCAGAAAGTCCCTCCCTCCTGCAGGCTGGCTGTTGGCCCCCTCTGCTGTCTGCAGTA	9969

genome	GAAGGTGCCGTGAGCAGGCTTTGGGAACACTGGCCTGGGTCTCCCTGGTGGGGTGTGCAT	181888
mRNA	GAAGGTGCCGTGAGCAGGCTTTGGGAACACTGGCCTGGGTCTCCCTGGTGGGGTGTGCAT	10029

genome	GCCACGCCCCGTGTCTGGATGCACAGATGCCATGGCCTGTGCTGGGCCAGTGGCTGGGGG	181948
mRNA	GCCACGCCCCGTGTCTGGATGCACAGATGCCATGGCCTGTGCTGGGCCAGTGGCTGGGGG	10089

	rs362303	
genome	TGCTAGACACCCGGCACCATTCTCCCTTCTCTCTTTTCTTCTCAGGATTTAAAATTTAAT	182008
mRNA	TGCTAGACACCCGGCACCATTCTCCCTTCTCTCTTTTCTTCTCAGGATTTAAAATTTAAT	10149

genome	TATATCAGTAAAGAGATTAATTTTAACGTAACCTCTTCTATGCCCGTGTAAGTATGTGA	182068
mRNA	TATATCAGTAAAGAGATTAATTTTAACGTAACCTCTTCTATGCCCGTGTAAGTATGTGA	10209

genome	ATCGCAAGGCCTGTGCTGCATGCGACAGCGTCCGGGGTGGTGGACAGGGCCCCCGGCCAC	182128
mRNA	ATCGCAAGGCCTGTGCTGCATGCGACAGCGTCCGGGGTGGTGGACAGGGCCCCCGGCCAC	10269

genome	GCTCCCTCTCCTGTAGCCACTGGCATAGCCCTCCTGAGCACCCGCTGACATTTCCGTTGT	182188
mRNA	GCTCCCTCTCCTGTAGCCACTGGCATAGCCCTCCTGAGCACCCGCTGACATTTCCGTTGT	10329

genome	ACATGTTCTCTGTTTATGCATTACAAGGTGACTGGGATGTAGAGAGGCGTTAGTGGGCAG	182248
mRNA	ACATGTTCTCTGTTTATGCATTACAAGGTGACTGGGATGTAGAGAGGCGTTAGTGGGCAG	10389

Figure 1

genome	GTGGCCACAGCAGGACTGAGGACAGGCCCCCATTATCCTAGGGGTGCGCTCACCTGCAGC	182308
mRNA	GTGGCCACAGCAGGACTGAGGACAGGCCCCCATTATCCTAGGGGTGCGCTCACCTGCAGC	10449

genome	CCCTCCTCCTCGGGCACAGACGACTGTCGTTCTCCACCCACCAGTCAGGGACAGCAGCCT	182368
mRNA	CCCTCCTCCTCGGGCACAGACGACTGTCGTTCTCCACCCACCAGTCAGGGACAGCAGCCT	10509

genome	CCCTGTCACTCAGCTGAGAAGGCCAGCCCTCCCTGGCTGTGAGCAGCCTCCACTGTGTCC	182428
mRNA	CCCTGTCACTCAGCTGAGAAGGCCAGCCCTCCCTGGCTGTGAGCAGCCTCCACTGTGTCC	10569

genome	AGAGACATGGGCCTCCCACTCCTGTTCTTGTAGCCCTGGGGTGGCGTCTGCCTAGGAG	182488
mRNA	AGAGACATGGGCCTCCCACTCCTGTTCTTGTAGCCCTGGGGTGGCGTCTGCCTAGGAG	10629

genome	CTGGCTGGCAGGTGTTGGGACCTGCTGCTCCATGGATGCATGCCCTAAGAGTGTCACTGA	182548
mRNA	CTGGCTGGCAGGTGTTGGGACCTGCTGCTCCATGGATGCATGCCCTAAGAGTGTCACTGA	10689

genome	GCTGTGTTTTGTCTGAGCCTCTCTCGGTCAACAGCAAAGCTTGGTGTCTTGGCACTGTTA	182608
mRNA	GCTGTGTTTTGTCTGAGCCTCTCTCGGTCAACAGCAAAGCTTGGTGTCTTGGCACTGTTA	10749

genome	GTGACAGAGCCCAGCATCCCTTCTGCCCCGTTCCAGCTGACATCTTGACGGTGACCCC	182668
mRNA	GTGACAGAGCCCAGCATCCCTTCTGCCCCGTTCCAGCTGACATCTTGACGGTGACCCC	10809

genome	TTTGTAGTCAGGAGAGTGCAGATCTGTGCTCATCGGAGACTGCCCCACGGCCCTGTCAGAG	182728
mRNA	TTTGTAGTCAGGAGAGTGCAGATCTGTGCTCATCGGAGACTGCCCCACGGCCCTGTCAGAG	10869

genome	CCGCCACTCCTATCCCCAGGCCAGGTCCCTGGACCAGCCTCCTGTTTGCAGGCCAGAGG	182788
mRNA	CCGCCACTCCTATCCCCAGGCCAGGTCCCTGGACCAGCCTCCTGTTTGCAGGCCAGAGG	10929

genome	AGCCAAGTCATTAAAATGGAAGTGGATTCTGGATGGCCGGGCTGCTGCTGATGTAGGAGC	182848
mRNA	AGCCAAGTCATTAAAATGGAAGTGGATTCTGGATGGCCGGGCTGCTGCTGATGTAGGAGC	10989

genome	TGGATTTGGGAGCTCTGCTTGCCGACTGGCTGTGAGACGAGGCAGGGGCTCTGCTTCCTC	182908
mRNA	TGGATTTGGGAGCTCTGCTTGCCGACTGGCTGTGAGACGAGGCAGGGGCTCTGCTTCCTC	11049

genome	AGCCCTAGAGGCGAGCCAGGCAAGGTTGGCGACTGTGATGTGGCTTGGTTTGGTCATGCC	182968
mRNA	AGCCCTAGAGGCGAGCCAGGCAAGGTTGGCGACTGTGATGTGGCTTGGTTTGGTCATGCC	11109

genome	CGTCGATGTTTTGGGTATTGAATGTGGTAAGTGGAGGAAATGTTGGAACCTCTGTGCAGGT	183028
mRNA	CGTCGATGTTTTGGGTATTGAATGTGGTAAGTGGAGGAAATGTTGGAACCTCTGTGCAGGT	11169

genome	GCTGCCTTGAGACCCCCAAGCTTCCACCTGTCCCTCTCCTATGTGGCAGCTGGGGAGCAG	183088
mRNA	GCTGCCTTGAGACCCCCAAGCTTCCACCTGTCCCTCTCCTATGTGGCAGCTGGGGAGCAG	11229

genome	CTGAGATGTGGACTTGTATGCTGCCCACATACGTGAGGGGGAGCTGAAAGGGAGCCCCTC	183148
mRNA	CTGAGATGTGGACTTGTATGCTGCCCACATACGTGAGGGGGAGCTGAAAGGGAGCCCCTC	11289

genome	CTCTGAGCAGCCTCTGCCAGGCCTGTATGAGGCTTTTCCCACCAGCTCCCAACAGAGGCC	183208
mRNA	CTCTGAGCAGCCTCTGCCAGGCCTGTATGAGGCTTTTCCCACCAGCTCCCAACAGAGGCC	11349

genome	TCCCCCAGCCAGGACCACCTCGTCCTCGTGGCGGGGAGCAGGAGCGGTAGAAAGGGGTC	183268
mRNA	TCCCCCAGCCAGGACCACCTCGTCCTCGTGGCGGGGAGCAGGAGCGGTAGAAAGGGGTC	11409

genome	CGATGTTTGAGGAGGCCCTTAAGGGAAGCTACTGAATTATAACACGTAAGAAAATCACCA	183328
mRNA	CGATGTTTGAGGAGGCCCTTAAGGGAAGCTACTGAATTATAACACGTAAGAAAATCACCA	11469

genome	TTCCGTATTGGTTGGGGGCTCCTGTTTCTCATCCTAGCTTTTTCCTGGAAAGCCCGCTAG	183388
mRNA	TTCCGTATTGGTTGGGGGCTCCTGTTTCTCATCCTAGCTTTTTCCTGGAAAGCCCGCTAG	11529

genome	AAGGTTTGGAACGAGGGGAAAGTTCTCAGAACTGTTGGCTGCTCCCCACCCGCCTCCCG	183448
mRNA	AAGGTTTGGAACGAGGGGAAAGTTCTCAGAACTGTTGGCTGCTCCCCACCCGCCTCCCG	11589

genome	CCTCCCCCGCAGGTTATGTCAGCAGCTCTGAGACAGCAGTATCACAGGCCAGATGTTGTT	183508
mRNA	CCTCCCCCGCAGGTTATGTCAGCAGCTCTGAGACAGCAGTATCACAGGCCAGATGTTGTT	11649

Figure 1

genome	CCTGGCTAGATGTTTACATTTGTAAGAAATAACACTGTGAATGTAAACAGAGCCATTCC	183568
mRNA	CCTGGCTAGATGTTTACATTTGTAAGAAATAACACTGTGAATGTAAACAGAGCCATTCC	11709
genome	CTTGGGAATGCATATCGCTGGGCTCAACATAGAGTTTGTCTTCCTCTTGTTTACGACGTGA	183628
mRNA	CTTGGGAATGCATATCGCTGGGCTCAACATAGAGTTTGTCTTCCTCTTGTTTACGACGTGA	11769
genome	TCTAAACCAGTCCTTAGCAAGGGGCTCAGAACACCCCGCTCTGGCAGTAGGTGTCCCCCA	183688
mRNA	TCTAAACCAGTCCTTAGCAAGGGGCTCAGAACACCCCGCTCTGGCAGTAGGTGTCCCCCA	11829
genome	CCCCCAAAGACCTGCCTGTGTGCTCCGGAGATGAATATGAGCTCATTAGTAAAAATGACT	183748
mRNA	CCCCCAAAGACCTGCCTGTGTGCTCCGGAGATGAATATGAGCTCATTAGTAAAAATGACT	11889
genome	TCACCCACGCATATACATAAAGTATCCATGCATGTGCATATAGACACATCTATAATTTTA	183808
mRNA	TCACCCACGCATATACATAAAGTATCCATGCATGTGCATATAGACACATCTATAATTTTA	11949
genome	CACACACACCTCTCAAGACGGAGATGCATGGCCTCTAAGAGTGCCCGTGTGCGTTCTTCC	183868
mRNA	CACACACACCTCTCAAGACGGAGATGCATGGCCTCTAAGAGTGCCCGTGTGCGTTCTTCC	12009
genome	TGGAAGTTGACTTTCCTTAGACCCGCCAGGTCAAGTTAGCCGCGTGACGGACATCCAGGC	183928
mRNA	TGGAAGTTGACTTTCCTTAGACCCGCCAGGTCAAGTTAGCCGCGTGACGGACATCCAGGC	12069
genome	GTGGGACGTGGTCAGGGCAGGGCTCATTCATTGCCCACTAGGATCCCACTGGCGAAGATG	183988
mRNA	GTGGGACGTGGTCAGGGCAGGGCTCATTCATTGCCCACTAGGATCCCACTGGCGAAGATG	12129
genome	GTCTCCATATCAGCTCTCTGCAGAAGGGAGGAAGACTTTATCATGTTCTTAAAAATCTGT	184048
mRNA	GTCTCCATATCAGCTCTCTGCAGAAGGGAGGAAGACTTTATCATGTTCTTAAAAATCTGT	12189
genome	GGCAAGCACCCATCGTATTATCCAAATTTTGTGCAATGTGATTAATTTGGTTGTCAAG	184108
mRNA	GGCAAGCACCCATCGTATTATCCAAATTTTGTGCAATGTGATTAATTTGGTTGTCAAG	12249
genome	TTTTGGGGGTGGGCTGTGGGGAGATTGCTTTTGTTCCTGCTGGTAATATCGGGAAAGA	184168
mRNA	TTTTGGGGGTGGGCTGTGGGGAGATTGCTTTTGTTCCTGCTGGTAATATCGGGAAAGA	12309
genome	TTTAAATGAAACCAGGGTAGAATTGTTTGGCAATGCACTGAAGCGTGTTTCTTCCCAA	184228
mRNA	TTTAAATGAAACCAGGGTAGAATTGTTTGGCAATGCACTGAAGCGTGTTTCTTCCCAA	12369
genome	ATGTGCCTCCCTTCCGCTGCGGGCCCAGCTGAGTCTATGTAGGTGATGTTTCCAGCTGCC	184288
mRNA	ATGTGCCTCCCTTCCGCTGCGGGCCCAGCTGAGTCTATGTAGGTGATGTTTCCAGCTGCC	12429
genome	AAGTGCTCTTTGTTACTGTCCACCCTCATTTCTGCCAGCGCATGTGTCCTTTCAAGGGGA	184348
mRNA	AAGTGCTCTTTGTTACTGTCCACCCTCATTTCTGCCAGCGCATGTGTCCTTTCAAGGGGA	12489
genome	AAATGTGAAGCTGAACCCCTCCAGACACCCAGAATGTAGCATCTGAGAAGGCCCTGTGC	184408
mRNA	AAATGTGAAGCTGAACCCCTCCAGACACCCAGAATGTAGCATCTGAGAAGGCCCTGTGC	12549
genome	CCTAAAGGACACCCCTCGCCCCCATCTTCATGGAGGGGGTCAATTCAGAGCCCTCGGAGC	184468
mRNA	CCTAAAGGACACCCCTCGCCCCCATCTTCATGGAGGGGGTCAATTCAGAGCCCTCGGAGC	12609
genome	CAATGAACAGCTCCTCCTCTTGAGCTGAGATGAGCCCCACGTGGAGCTCGGGACGGATA	184528
mRNA	CAATGAACAGCTCCTCCTCTTGAGCTGAGATGAGCCCCACGTGGAGCTCGGGACGGATA	12669
genome	GTAGACAGCAATAACTCGGTGTGTGGCCGCTGGCAGGTGGAACCTCCTCCCGTTGCGGG	184588
mRNA	GTAGACAGCAATAACTCGGTGTGTGGCCGCTGGCAGGTGGAACCTCCTCCCGTTGCGGG	12729
genome	GTGGAGTGAGGTTAGTTCTGTGTGTCTGGTGGGTGGAGTCAGGCTTCTCTTGCTACCTGT	184648
mRNA	GTGGAGTGAGGTTAGTTCTGTGTGTCTGGTGGGTGGAGTCAGGCTTCTCTTGCTACCTGT	12789
genome	GAGCATCCTTCCCAGCAGACATCCTCATCGGGCTTTGTCCCTCCCCCGCTTCTCCCTCT	184708
mRNA	GAGCATCCTTCCCAGCAGACATCCTCATCGGGCTTTGTCCCTCCCCCGCTTCTCCCTCT	12849
genome	GCGGGGAGGACCCGGGACCACAGCTGCTGGCCAGGGTAGACTTGAGCTGTCCTCCAGAG	184768
mRNA	GCGGGGAGGACCCGGGACCACAGCTGCTGGCCAGGGTAGACTTGAGCTGTCCTCCAGAG	12909

Figure 1

genome	GGGTCACGTGTAGGAGTGAGAAGAAGGAAGATCTTGAGAGCTGCTGAGGGACCTTGGAGA	184828
mRNA	GGGTCACGTGTAGGAGTGAGAAGAAGGAAGATCTTGAGAGCTGCTGAGGGACCTTGGAGA	12969

genome	GCTCAGGATGGCTCAGACGAGGACACTCGCTTGCCGGGCCTGGGCCTCCTGGGAAGGAGG	184888
mRNA	GCTCAGGATGGCTCAGACGAGGACACTCGCTTGCCGGGCCTGGGCCTCCTGGGAAGGAGG	13029

genome	GAGCTGCTCAGAATGCCGCATGACAACTGAAGGCAACCTGGAAGGTTGAGGGCCGCTCT	184948
mRNA	GAGCTGCTCAGAATGCCGCATGACAACTGAAGGCAACCTGGAAGGTTGAGGGCCGCTCT	13089

genome	TCCCCCATGTGCCTGTGACGCTCTGGTGCAGTCAAAGGAACGCCTTCCCCTCAGTTGTTT	185008
mRNA	TCCCCCATGTGCCTGTGACGCTCTGGTGCAGTCAAAGGAACGCCTTCCCCTCAGTTGTTT	13149

genome	CTAAGAGCAGAGTCTCCCGCTGCAATCTGGGTGGTAACTGCCAGCCTTGGAGGATCGTGG	185068
mRNA	CTAAGAGCAGAGTCTCCCGCTGCAATCTGGGTGGTAACTGCCAGCCTTGGAGGATCGTGG	13209

genome	CCAACGTGGACCTGCCTACGGAGGGTGGGCTCTGACCCAAGTGGGGCCTCCTTGTCCAGG	185128
mRNA	CCAACGTGGACCTGCCTACGGAGGGTGGGCTCTGACCCAAGTGGGGCCTCCTTGTCCAGG	13269

genome	TCTCACTGCTTTGCACCGTGGTCAGAGGGACTGTCAGCTGAGCTTGAGCTCCCCTGGAGC	185188
mRNA	TCTCACTGCTTTGCACCGTGGTCAGAGGGACTGTCAGCTGAGCTTGAGCTCCCCTGGAGC	13329

genome	CAGCAGGGCTGTGATGGGCGAGTCCCGGAGCCCCACCCAGACCTGAATGCTTCTGAGAGC	185248
mRNA	CAGCAGGGCTGTGATGGGCGAGTCCCGGAGCCCCACCCAGACCTGAATGCTTCTGAGAGC	13389

genome	AAAGGGAAGGACTGACGAGAGATGTATATTTAATTTTTTAACTGCTGCAAACATTGTACA	185308
mRNA	AAAGGGAAGGACTGACGAGAGATGTATATTTAATTTTTTAACTGCTGCAAACATTGTACA	13449

genome	TCCAAATTAAAGGAAAAAATGGAAACCATCAGTTGTTGCTGTGTGAGGCTTGCTTTGCT	185368
mRNA	TCCAAATTAAAGGAAAAAATGGAAACCATCA-----	13481

genome	TCATGAGAACCTAGACCTTGCTGAGCTGGAGTCTTAGGAAGCAGTCTCCTAAGTGCTTCT	185428
mRNA	-----	
genome	CCAGCAGGGGCAGAACTGTCCCACCAGCTAACATCTGGCATTATGGAGGGTCCCCCAGG	185488
mRNA	-----	
genome	CAGCTGCCAGCAGGGACAGGCCCCGTGTTTTCTGTAGCCAGGGATGAGGAAGTGGCCCCA	185548
mRNA	-----	
genome	GGGCATGGGCCTGGCTGGGTGCTTCTGCAAGGGCCTTCCCAAACACAGTACAGGTGGTC	185608
mRNA	-----	
genome	TTCTGCCCCTGCAGATGGGAGCTGTGGGAGCTGCTGGAGCTGCTGGAGCCTTCATGGTCA	185668
mRNA	-----	
genome	AGTGACATCATAAGCTTATATGACATACACAAGCCTCAGGACTTGGCCCATGGCACTGAA	185728
mRNA	-----	
genome	GCAGGTCATCAGGCCCAGCACAGAGACTAGAGCTGTGTTCTCACAGGGCCCACCACCTT	185788
mRNA	-----	
genome	CCACCTCCTTGGCCATTGACACCTGCGTCCCTGGCCCAGCTGCTCCCAGGTAACCCCCAA	185848
mRNA	-----	
genome	AGCAGCTGGCACATCCCACCTCTGGTGTGGCCGGGGCTGCTGTGTGTCCGCAGGGCCTGC	185908
mRNA	-----	
genome	CCCGTCTATTCTAGCTTGTTTGTCTGTCTGAACCAGCGCCTACTCCAAGAAGCCTCTGC	185968
mRNA	-----	
genome	TCAGCCCAGCGGGGATGCTTCTAAGCTCCGGACGAGCCTCTCGGAAGCCTTGGTGATTGG	186028
mRNA	-----	

Figure 1

genome mRNA	TGGTGTAGTCATCTTGGGATGCAGATGTCTTACCAACCTGCAAGAACAAAAACCCTGTGG	186088
genome mRNA	CTTCCTCTGGTGCAGGGTATTTAGTCAATGTTTGCTGAGGTCCCGTCTGGTTCTGGCTAA	186148
genome mRNA	TTGGCAGGGGTCGTCCACCCATTCTTTCCCTGCTCTGCTGTCTGTGCCAGGAGAGACGGG	186208
genome mRNA	GGCCAGTCGGCCAAGGGGCCAGCTCCTGCTGCCTGCTCCTCTTGGGCACGTGCGGGGGCC	186268
genome mRNA	CCCTTTCTCTGAGCAGGGATAGGGATCAGTCTGCCGGAGGGATGTGGTGGACAGGCCTAA	186328
genome mRNA	AGCATTTGGGGCGGGGCATGCCACTTGAGCTCCCTAAATCTGTCTCCTCATAGGTGACAC	186388
genome mRNA	CGCTCCAGGGCCCCCAGTGGCCTCTCCTTTCAGAGCTACCTAAATTCTGGTCACTTCAG	186448
genome mRNA	AGAAATGGAGCACCCCCTTCTCCCTGGTCCAGGTGTGGACAGCCTGGCACACTGAGCACA	186508
genome mRNA	CCTGGCATGGCTGGTAATTTAGAAAGAAGAGGGGCGGGGTCCAGTGGGAAGCAGCGGT	186568
genome mRNA	GAACCCCTCGTGAGTGGGCTTTGCAGTCCCTCCCCATGCCACGGCAGAGCTGCCCTCAAC	186628
genome mRNA	ACAGCCTTCCTCTTCCTCATCGGAGAGCACACCTGTCCCCTTGCCGAGCTGTGCCCTGT	186688
genome mRNA	GCCTTCGGTGGTATTTGATTTTGGCTGCTACTGGCTTTGTTGGGATCTGGAAGTCGCTTC	186748
genome mRNA	CCCTGCGTGGTGCCTGGAGCACTGTAAGTCAGATGAGGGAAGTAGCCAGGGTGAGGTGAG	186808
genome mRNA	TACCGGGTGGAGCCGCCACTGAAGGGACTGGGTAGGGGGGCCTTGCCTCTACATGATGTG	186868
genome mRNA	ACACAGCCAACCGAGGACAGAGGAAGCCCCGTTCTTGGGGGTGTGGGGTGACCCCTCAG	186928
genome mRNA	GGAAGCCTGCAGTGGGGCCTGAGGAAAGGCATCCTCCGCGAGCCCACGAGTCTGGTCCAT	186988
genome mRNA	GAGCACCGTGACAGTGTCTGTGGGTAGAGGTGGACCCGGCCTTGTGTCATCACCAGGACC	187048
genome mRNA	TCTTTTGGGAAACCATGTGGACATCGCTTGCGGGTCCCCCAGGCTCTGCAGCCCCAGCAG	187108
genome mRNA	CCTGGCTGCCTTTTGGGCAAGTGGCTTGAGCCACAGAGGACCCAGTCCTGTTGCAGCCAC	187168
genome mRNA	ATCCTCTGGGGGGGCCCCGAGTGTGGCCGGCTTTCTCCACCCCTACACCAGGCCTCCAGG	187228
genome mRNA	TGTCCTGGTCGGGGGTGTCTGGGCCCTGGGTGGGCCCTGTGGACCTGTGAGGTCAGGGTC	187288

Figure 1

genome mRNA	AGGGCATCACTGGAGGCAGAGGGCTGAAGTTGTGGGTCTGGGTTCCTTGTGTGCACAG	187348
genome mRNA	-----	
genome mRNA	GCCCCTGCCCTCCATGCTTGGTCAGGCAGCTACCCCCAAAAGTCTAGGACAGGCTGGTC	187408
genome mRNA	-----	
genome mRNA	CTGAGGTGGATCCTGGCCCCCTGTACCCTCTGGACAGCCCACCCGCCAACCTTCTACCCT	187468
genome mRNA	-----	
genome mRNA	GCCCCAGCGGCGGCAGTGTGGCCACATCCTTCCCCTCCTGGCCCCAATTGCTCTGGGGA	187528
genome mRNA	-----	
genome mRNA	AGTCCAGGCTCCGGAGCCTGCCAGGGGCCCCCGTGATTTGGGCCCAGGACTCCACGTG	187588
genome mRNA	-----	
genome mRNA	GTTCTCTGCCTTCACCCAAGCCCTGAACTCCTCAGCTGCCAAATCCCCACCCATCTGCAC	187648
genome mRNA	-----	
genome mRNA	AGGCTGTGCTCACCCTGCTGCTCCTGGAAGGTGCCCTCAGTGGGACGCCACCTCCTC	187708
genome mRNA	-----	
genome mRNA	TCTGGGCTTCTGTGTTTGGGAGCCCTGCTGCCCCACCCCTTGGTCAGTCCCCATGTCCTG	187768
genome mRNA	-----	
genome mRNA	CTGGCCTGTCAGGCAGGGCAGAAAATCCACCCAGAAATGCTGAGCAGGATGAGAGTCTAG	187828
genome mRNA	-----	
genome mRNA	TTGGGCCCAGCCTCATTATTTAGAAGGGATGGAGGCCTAGGGAGCATGCTTCTAGCCTGA	187888
genome mRNA	-----	
genome mRNA	GCCCAGCAGGGCCCCGCCCATGTCCCAGGTCTGCACCAGGGACAGCTCCTGCCGAGGCCT	187948
genome mRNA	-----	
genome mRNA	GACCTGCCCCCTTCTCCCTCAGGTGCTGCTGGTTGACCAGCCTCTGGCCCTAGGAGACCCC	188008
genome mRNA	-----	
genome mRNA	GTAGCGACTGAGGGTCCCAGCAGGCCATGCAGCTTTGCCAAGGTACGAGCCCCTCCCCAG	188068
genome mRNA	-----	
genome mRNA	CAGGGGACAGATGTGGGGACCCTCCCAGGCAGGAGCAGCTGGGTGCCTGGTGCTGCCATC	188128
genome mRNA	-----	
genome mRNA	TGCTGCCTGCCTGGTTCTTGTCTCACATTGGAGGTGAGTGTGAGGGCTCTGCCTCGGGA	188188
genome mRNA	-----	
genome mRNA	AAGGCCATGGAGCTTGCCCTGTCCAGGGCCTCCCATGTGCACTGAGCCTGGGAAGAGAGG	188248
genome mRNA	-----	
genome mRNA	GTTGGAGTTGAGCCTTTTACCCTGGGAATGCTGCCTGGAGGATGGTGCGGGTGTGGGGTG	188308
genome mRNA	-----	
genome mRNA	GCACCCTGCCAGGCAGGGCCCTGCCTCCCTGCGCCCACTGGAACTCGGGCAGGCAGGGGT	188368
genome mRNA	-----	
genome mRNA	GTAGGTGCCTCCTCTAGAGCCGTCCGGTGGGGGCCCCCGGCAGTGGTGGTGGTGTCCACT	188428
genome mRNA	-----	
genome mRNA	GGCCAGCAGCTGCCCCTTCAGCCAGGACAGTAGGCCTGACGCTGTCCCCAGCAGCTCCAA	188488
genome mRNA	-----	
genome mRNA	GGTGGATTTGTGGAAGGGGGTAGAGGGCACGTAGAGGCCCATGACCTCCCCAGGGTTCT	188548
genome mRNA	-----	

Figure 1

genome mRNA	GGGAGGGCTGTGCCCCCTTAGCCAGCACCATGCTGGGTGATATAGTCAGATCCTGTTACC	188608
genome mRNA	CCTGTTGTGGAGGTGAGGAAACAGGTTAGTGGGGAGGACATGACTAAGGTCCATGCTGAG	188668
genome mRNA	TCGCTAGAGCTGCACCCAGAACCACTGCTGGGACCCCATGCCTTTCTGCTTACCCCTTGT	188728
genome mRNA	GCCGGGAGATGCCAAGAGATGCTGGGAGCCAGCCCCACCTCTGCCCTTGGAGTCATGGCT	188788
genome mRNA	ACGGAAAGGGCATTCGGACCGGTCCCTGACCTCACCGGGGAGGGCCGAACCCTGTTCTTG	188848
genome mRNA	AGGAGCCAGGGCTTCCTAGAGGAGGTAGGCCTTCTAGTCACTCCTTCATCTGCAGGCACT	188908
genome mRNA	CCACAGAGCTCTCTGTGCCAGCCCCCAGCACGGAGGGCTGACCTTAGTCGAGTGGAGATG	188968
genome mRNA	CCCCAGTGCCAGGCAGTAGGGATGATGTCTCCTGAGGCCCAGATGGAAGGGACTGGACTA	189028
genome mRNA	GTCTCATGGGGCTGATGGTGGGGCCAGGCCTTGACCAGGGACCCAGTGTAGGGGGTGCAG	189088
genome mRNA	AGACCCCTCTGAGTTCCTCACACATCCCTGGGGCCCTCCCCATACACTTCCTATCCTGAC	189148
genome mRNA	TGCGGGCAAGAGGGAGCCCCAGTTCGCCTTCCCTATGCTGGGCACCCACAGTGGGGCTGG	189208
genome mRNA	GCACCCCGCCATGCCCTGCCCCTGTCTTCCCCTGAGAGCCTCGGTCCCACCTCCAAGG	189268
genome mRNA	TGCCTCAGAGGACAGCAGGGGCAGCGGGCAGAGGCCGAGATGCCTCCTCATTCAGGCTC	189328
genome mRNA	AGCTGCCCTTCTTGGGGCAGCCCACACCTGAGAGTCTCCTGCAGTTGGTCAGGCCTGAGG	189388
genome mRNA	AGGGCAGGGGGGTGCCTGCTGTCCCTCTGCTGACCACAGTGGCATTTAGCCTGGGCACCG	189448
genome mRNA	CGCCCAGCACAGTCCATGCTGCACAGGTGCCGTGGGCTCCACAGAGCCCTGCCTGACATG	189508
genome mRNA	CATGTGTTACGTTTCGGGTGCCGATGCCCTTGGGCGGCACCTTCTCCGGGCAGAACCCCCA	189568
genome mRNA	GGCCACCGCTCCGGTTCCGGTTCCGCTGCATCTGGGGCTCTCGGCAGGCTGTGGTCCTCC	189628
genome mRNA	GGCCAGCCTGGGGGCATCTCAGTCCCTCAGCCCCACAGGGGCCTGCCCCGCAGCCTGGGC	189688
genome mRNA	CTCGAGCCCCGTCTCCGCACGCTGTGCCGAATCTGGCTGCCCATCAGCTCCCTGCGTACC	189748
genome mRNA	CAGACTGTGCCCTGCCATGCCCGTGGCTCTTCCCAGGAGTGCCCTGTGGCCTCCCCCTGG	189808

Figure 1

genome mRNA	CTTGCTGGGCTGATTCCCTCCTGTGTCTCAAACAGAGCTCACCTTTGCCATCACTGCTGT	189868
genome mRNA	CCTCACCGGCCGGTGCCAGAGGCCCGTGTCTGTGTACCCTGTGTCTGCACCTCTGGGCAG	189928
genome mRNA	GGCCTGGCTCTGACCAACCCGGGCTTCCAGTGTCCACAGACCTAAGGCCCAGGGCGCCTG	189988
genome mRNA	GGGGCTGGAGCAAGAGAAGCAAAAGGAGCCAAGGGTGGGGGTTTGGGGTTCTTGTGAGGG	190048
genome mRNA	CCCAGCCCCAGGACCCCAGGACCAGGACACCCAGGAGCCCCAGGGCCCAGCCCCAGTTCA	190108
genome mRNA	GAAGGCAGGGGCCTTCTGAGGGAGCTTAAGGGTCCCACAGCCCAGGACCCCCACCAGGGC	190168
genome mRNA	CAGTGGCCAGCGTTGGGGGACTCAGCCTCCTCGTCGCTCGTCCTCTCTGTTTCTCCCACC	190228
genome mRNA	TTTTGCCCCCTTTCTCCTTGCCGTGTTCCACCCGAGGCCCCCTCTTGGCCTGCGTGAGCC	190288
genome mRNA	GGGGCGGCACTGAACTGGGGGCCGATCCGCCTGGGCGGCGGTGAGAGGCAGGGCCGGGAG	190348
genome mRNA	CCGGGCCGCTGGGTTTGGGCCTGGCCCGCTCGCCGCAATATTGATGGCCCGTCAGTGCAG	190408
genome mRNA	CCCTGATTCCTGTGCTTTCAGTTAAAAGGTTTCTGTTGTTGTAGCTTATGCAGTTGCTCT	190468
genome mRNA	GTTGCTATGGAAACGTGACATCAAAATGACGTTTCCCGTTTAAAAGCTTTTAACTAAATT	190528
genome mRNA	CCTGCCTGTCAGATGTAGGCCCCATTTTGAGCGTGGAGCTGCCTTCGAGCGAGCGTGAGC	190588
genome mRNA	GGCGCCTCCCGCCCATGGTGCGTGGGGCCGGGCCGGGGCCCTCGCTGAGCGCGCTCTCTC	190648
genome mRNA	ACCCACAGGCGCCTCCGGCATGGCGGCGGGCCGAGGGGCCCGGCTACCTCGTGTCTCCCC	190708
genome mRNA	AGGCGGAGAAGCACCGGCGGGCCCGCAACTGGACGGACGCCGAGATGCGCGGCCTCATGC	190768
genome mRNA	TGGTCTGGGAGGAGTTCTTCGACGAGCTCAAGCAGACCAAGCGCAACGCCAAGGTGTACG	190828
genome mRNA	AGAAGATGGCCAGCAAGCTCTTCGAGATGACCGGCGAGCGCAGGCTGGGCGAGGAGATCA	190888
genome mRNA	AGATCAAGATCACCAACATGACCTTCCAGTACAGGTGGGCGAGCGGGCAGTGTGGGCCCC	190948
genome mRNA	ACCAGGACGGGCGGGCCCGGGCGTGGCGGGCCGCTCCTGACTTTCTTGGAGCTCTGAGTC	191008
genome mRNA	GGGACGATGTGTGGGTGCTGGCCTGCCTGTGCGTCTCCTCTGGCCGGGTATGGGCAGAAC	191068

Figure 1

genome mRNA	CCCACGGGGTGAGACGGGGCCCCACGGAAACCGTGTGTGCAGCCTTCCATTGGGGAAGTGG	191128
genome mRNA	GGAAACTGAGGCCCAGCAAGGGCAGGAAACCAGTCTAAGAGCTGAGGGGTAGCAGGGGTG	191188
genome mRNA	GGGCTGGTGCTGGGCAGAGGCCAGGATGGCTCCCAGGACGTATGGGCGGTCTGGGCACTG	191248
genome mRNA	TCCCTCGGAGGCAGCAACACTCATGGTGGTGCCCACTGACCTCACACCCTGCTCCCCCAT	191308
genome mRNA	AGGGAGGCGGCGGCTGCCAGTGCCCTCCCCACCACCAAGCTCCCAAGCTCAGCAGGGGTT	191368
genome mRNA	TCAGGGGCCTACTGCGTCATTGGGGAAATTGAGACTGCAAGTGAGAAGGAGGCTCAGTGC	191428
genome mRNA	TCTGCGACTTGGAGCATCCACTGAGCCTCTGCCATGAGCCGGTGAGCCCCACTGGGGCTG	191488
genome mRNA	GCCCTAGGGTCACGGTGGGGTATTTCCAGAAATCACCAGGTGAGGTGCAGGACCAGCCAG	191548
genome mRNA	CGCATGGGTGGGGCTTACGGTGCGAAGAAGAAAGAGGTGGAGGCCTGCCCTGGCCCAGGA	191608
genome mRNA	CTCCCAGCGTGGGGGCTCCCGGCCTGGCCCCACCTCTGCTCCTGCTACATGGCAGGTGGG	191668
genome mRNA	CCCTTCCTGCCCTGGCAACCTGCAGGGAAGGCCGGAGGGGACCACCCAGCCAGGGAGATG	191728
genome mRNA	TTGGCGTCTAGGAGGGGACAGGTGTGGTCCCACACACCCAGCATCTTAAAGTGCGTGGGT	191788
genome mRNA	CCCCAGCCCATTAGGACAGGGTCCCGGGTGGGCAGGGGTGATGGTGGGGTGAAGGTCTCA	191848
genome mRNA	GGCACAGGCAAGGTCACAGGTGCGGTGAGGGTCTTGACAGGGTGTGAAGGTCATAGGTGTG	191908
genome mRNA	CGGTGAAGGTCACAGGTGTGGGGTGATGGTTTTGGGTGTGGGGAGGGTCTTGACGGAGC	191968
genome mRNA	GAGGGTGGCAGCAAGAGCTGGAAGCTGCAGGGGGAGAATGGCAGCAGAGAGCACCCGGCC	192028
genome mRNA	CTGTGGGCGGCCTGGACAGGGCTGGGCCTGGGGCTGCCGGAGAGCCTGTCAGCTTCCAGG	192088
genome mRNA	ATGGGAGTGGCCTCACTCAGCTGCTCCACCTCCGGGTGAGGCAGGTGAGCCTGGGGCAGA	192148
genome mRNA	GAGGCTGAGAGCACCTGAGCCACTTGTGGGAGAGGCCACCCCCACTGCCCCCCTCAGGCG	192208
genome mRNA	AGGAGCCGGCCTCCAGCACAGCAGAAGGGAACCCCCAGTCCCCAGCCCTAGTGGGAGTGG	192268
genome mRNA	GGAAGAGGCCCAGCAAGGCCCGGACAGACCGCCAGCCTGTGAGGTCTCCGCTTTCAGTT	192328

Figure 1

genome mRNA	GCGTTGATTTGATTTTTTCTGAGCCTTGAAGGAGGGGTCCGGGGCCTGGCCCTGCCCAA 192388
genome mRNA	GGCCCCTAGGCAGGCCCCAAAGCCGGGACCTAGGGTGCTGAGCATGACGGATGTTGGGTT 192448
genome mRNA	TGAGCGGCTGGCTTGCGACGTGAGGGCTGAGGTGTGAGCCTGGGTATCTTCAGAGGTTTCG 192508
genome mRNA	GTGGACACAGGCAGCTGCCCCGGGCCCCACTGTTCCCGTGGCCTCCTAGTCCTGCTCAGG 192568
genome mRNA	CACCTGGTGAGGAAGGGACGCAGAGGGCAGTGGGAGGTGGCCACGACTGTTCCAGCAGGC 192628
genome mRNA	TCCCCCTCTGACTCAGGAATTCACGGGCACCACTCCCTGGCTGGCTCTGGTTGGTGTCTG 192688
genome mRNA	GCCAGGTTATTCATTATTTATGCTGAAAGCCTCTTCAGAGTCCCAGGGGAGGGTTTCTGT 192748
genome mRNA	CTCCATTCTCTGGAGGCTGAGAGATGAGGGTGCAGCAGAGTGGGGGCCTCCACTCCAGACC 192808
genome mRNA	CTGCAGTCTGGGCTGGCCAAGGGCTGCACCGGTGCACTGCACGTCATGGCTGATGAAGCA 192868
genome mRNA	CTTCCACACCGCAGCCCCCTCAGAGCTGCCACAGTCAGCCTTAGTTACCCGAGGGGGAAGC 192928
genome mRNA	TGAGGCCCAGAGCATGAGAGGGACTTGCCCAGGGCCACATAGTCCTTAGCAGAGGAAGCT 192988
genome mRNA	GTGGCTGGGTGACTCGATCTTTGTCCTTTTCTTTTATACCCGCAGTCTCCCCATAGCAGA 193048
genome mRNA	GGCTTTTCTTTTTTTTTTCTTTTTCTTTTTTTTTTTTTTACAAGAACTCTTTATATATTA 193108
genome mRNA	AGGCTGTTGGGCTGAAGAAGCCTGAGAGGGTGGCTGGTTCTGTGGAGCATGGTTTGTGTA 193168
genome mRNA	AGTACAGTTTGGGGGCCTCCTACACTGAGAATAGGCCTTTTCTCGTTTCTCCAAAGAGTG 193228
genome mRNA	GGCTGGCTCAAGTAGGGCAGAGAGAGAAGCCTGGGGCAGAGGTTAGGGATGGGCACCCAG 193288
genome mRNA	CGCCTGCCCTCACACGCTCTGTGCTGGTGTCTTCACAGCCACGTGCCACCCTGGGCAGCA 193348
genome mRNA	TCCCCTGCTCACCATCTGGCTGTGCCTGTTTGCTGGGGGCACCTCATTGAGAATCCAGCT 193408
genome mRNA	TATTGTTTCCAACGGCCAATGGCCACACCCTGGCAGGTAGCAAGAGTAGGAGAGAGGAGA 193468
genome mRNA	CACCCACTCCGAGCACAGGTTGGGTTTGGAGCCCGGCCTTGGGGCACTCTGTCACTCAAA 193528
genome mRNA	GGCAGAGTGGGGAGTGGGCACTGGGCCTTAGGAGGTACTGGGTCCAGTGAGGCAGAGATG 193588

Figure 1

genome mRNA	CCCCTGCCCCACCCCCACCTTGTGGCTTCTTCCCTGGCCTGGCCAGAGCTGTCTGGCCGC	193648
genome mRNA	CATGGGGCCCTGTGTCTCCTGCCTTGACCTCCCAGAGGGCAGCCGAGGCCAGGGGAGGC	193708
genome mRNA	CTGGGGACTTAGCCTCTCAGGGCAGGACCTGTCTGCAGGAGTAGGTGGGTGCTGGGGGTC	193768
genome mRNA	CCAGTGGTAATGAGGCATCAGGCAGTGTGGGAAGGGGCCCATCCGGCCCACCCAGGGCC	193828
genome mRNA	TCTGGGCAGGTTGCAGGTTGTAGCGCTGGATCTAGGCTCCTGCCCAGACTGTAGGTTCAA	193888
genome mRNA	CCAAGAATGGCATGGGAGCCCAGCCTGCTGTTTGCTTTATTAAATCTGCCCTGTAGCTGG	193948
genome mRNA	GGGAGGGGCTTACTTTGATCATCACTATGTCATTGATATAAAAATAGAGGCTCAGAGAGG	194008
genome mRNA	TGAATGAACCTGCCCAAAGTCACACAGCAAAGTGTGGAGATGAGATACTGACTCAGGGCT	194068
genome mRNA	GTGGACACTGAAGCCTGTGCTCTAACGCCAGTGGCTGTCGCTCCCTGAGGCATTCTCTCC	194128
genome mRNA	CGAACAACACAGTTATTATATTACAAAATATTATCACTATATTTATATATCTTATAATAC	194188
genome mRNA	CTTATTATTACAATAAAACCTTATTACTCTACCTTTCAAATGAATTATTTAAAAAGCAG	194248
genome mRNA	TATTTGCTCATTGCAGAGAGTCTAGAACTATAGAAAAGCAAGGGAAAAGCAATAGGACC	194308
genome mRNA	AGCCCCAAGGTCCCAGCATGCACAGATAACCTTAGTAATACTGGGACGTGTGCTTCCTTT	194368
genome mRNA	TTAACATCTGAGCCCGTGTAGGTCCTGAAGCCCAGCTTCTTTCTAAGTCCATTGTCATCT	194428
genome mRNA	TGACCCTGGAGCCTGGCCGATTTTGCTGGGGAGGCCCTTGCCAGCCGAGAGCGGCTCCTG	194488
genome mRNA	CCTGTGCCGGCGTGGCGCGCCCCTCTGCTGAGGCTGGGCAGGACAGGGGCTGGGCCAGCT	194548
genome mRNA	CTGTTTCTCACCTTGGCTCTTGTGTCTCTCGTTTCAGGAAATTAAAATGCATGACAGAT	194608
genome mRNA	AGCGAGTCCGCCCCGCCCCGACTGGCCCTATTACCTAGCCATTGATGGGATTCTGGCCAAG	194668
genome mRNA	GTCCCCGAGTCCTGTGATGGCAAACCTGCCGGACAGCCAGCCGCCGGGGCCCTCCACGTCC	194728
genome mRNA	CAGACCGAGGCGTCCCTGTCGCCGCCCCGCTAAGTCCACCCCTCTGTACTTCCCGTATAAC	194788
genome mRNA	CAGTGCTCCTACGAAGGCCGCTTCGAGGATGATCGCTCCGACAGCTCCTCCAGCTTACTG	194848

Figure 1

genome mRNA	TCCCTTAAGTTCAGGTAGTGTGTCTGCTTGTCCCTTCCCCTGCCCTGGGGTATCTCAGCCC	194908

genome mRNA	CCACCATTTAGAGAAAGGGACTGGGAGTGGCAAGGCCGGCGGCGGCCACAGTGGTTG	194968

genome mRNA	CAGAGGCCGTGGCTGCGGGCAGCGCCTCCAGGGACAGGCGGCCTCAGACCAGGGAGGGCT	195028

genome mRNA	TTAGTGTCCACAGGCAGACCGAGTTTGTCTCCCAGCTCCATCACTTTTGAGCTGCACGGA	195088

genome mRNA	AAGTTCCTTGACTTCTCTGGCCTCAGTCTCCCTCCTATAAAATGGGGGTAAATCAGTACC	195148

genome mRNA	TTTCTCAGAGGGTGGCTGGGAGCATCACAGGAGAGAAGACGCAGCATGGGGCCCGGCACA	195208

genome mRNA	CGGAGGGAGACCAAGCCCCAGACCCCAGAATGCGCCCCCTGGCCTCCCTTAGCCACACA	195268

genome mRNA	GACCCACCCCTCACAGGCTAGCTGCCCTCTCAGCACTGGGGAGGGTGTGCGGCTGCACCT	195328

genome mRNA	CATCACGTGTTGCCGTGGGCATGACCCGTCCCCTCTGCCATCCATCCACACCTCAGACC	195388

genome mRNA	CGTCCCGTGCTGGCCACGTGACTGTGCCTGCAAGATGCTCACAGGGCAGCCGGGAGCCAG	195448

genome mRNA	GCAGCATGCAGGACAGACACCTGCGGGGTGGGCCTGGGGAGCCCAGAGAAGGTGCTTTTG	195508

genome mRNA	AGGAGGGGACATTTGGGGTGGGCTTTCAAGGTAAAATAGAAGTTGGCCATTTGGAGGCAA	195568

genome mRNA	GAACAGGAAGATTGTGGATTTGAGTCACAGCTTCTCCCCTGCCCTGGTCTTCAAGTCTTT	195628

genome mRNA	CTGACAGGAGGTGTCAGAAAAGTATCTTTAGTAGAGAAGGCGTCTCCGAGGAGGGTCCCT	195688

genome mRNA	CTCATGCCGGGGGCCGCTGCTTGACTCAGGATTTCTCATTGAAGACCTGAGACAAAAACG	195748

genome mRNA	CTTTTGCTGGCAGCTAGAAGGAACCAGCAGGAGGCCTGAGATTTGTGGCTGTTGTTCCCG	195808

genome mRNA	TGGACTGAGCCCAGTTCTCAGACTCAGCTGCCTGGGGCCTTGACAGGACTGGGGCGTGG	195868

genome mRNA	GGGCTGCCCTCCCTGATCAGGCCCAAAGCGCGGATCTCACGCCCTGAGGTTGGCTGTAC	195928

genome mRNA	CCTCTCAGCTCAGAGCAGAGTGTGGGCCAGGGATGAGCAGGCACTGGAGCAGGGCCCTGG	195988

genome mRNA	GGTCTGTGGGTTTTTGGCAGCTCCCTGCCCTTCAGGGAGGTCTGCTGAGACCACGGGTGGC	196048

genome mRNA	CCCTACCCCAGCAGCAGAGCTCTCAGGAGGCGCCACAGGGCTGGACTGCCTTTACTCAC	196108

Figure 1

genome	GGGCCGGGCGGCTGGTGGTACTGCTCAGGCCACCCAGGGCAGGCCACTCAGGCCAGGCGG	197428
mRNA	-----	
genome	GCAAGGGGGCCGCCCCGCGAGCGGAGACCGCCTTCCACCTGGCCTCTGGCAGGATGTCCC	197488
mRNA	-----	
genome	TTCTGAGGGGTATTTTGAGGAACCCCCAGGCCCTGGGGACCGTGAGGCTCCAGTCTCCAG	197548
mRNA	-----	
genome	CATGAATGCCCTTCCTCGGACACAGGCCAGGGCCTCTGGGGTTCACTCCGAGTAAGAACG	197608
mRNA	-----	
genome	TCCTAGAGCCACTCTCCAGTGTGCTTACTATCAATGATACTTGACGTGGCTTTGATATTA	197668
mRNA	-----	
genome	AACGTATACTTTTTTCATTCTTGCCTGGAACGCACAGTTTGCTGTTGCTGGCTTGGTGAGG	197728
mRNA	-----	
genome	ATGCCCTGATTGATGGATCCCGAAAATGAAAGCAGATGGAAACGGGTTGGGGCAGGCTGG	197788
mRNA	-----	
genome	AGCTGGGGGAGCTCTCTCCTGAAGGGAACCCTGTGTCCTCCCTCACCAGGACCTCTGCGT	197848
mRNA	-----	
genome	CTCTCCTTAAATGGCCTCTGACGCCTGATGAAAACCCAGCGACCTTCCAGGAGGCTTTT	197908
mRNA	-----	
genome	ATTCAGCTCTGTTTGGAGCATCAGGTGTTTCCACTGCCTCCTTAGCAATGACACTAATAA	197968
mRNA	-----	
genome	AAGTCGTAACACCTGTTTACATGCACAGCCCTGTTGAGTGTTCTGGGTGCTGGAGATATC	198028
mRNA	-----	
genome	ATGGTGGATGACACAAAGGCCCTGGCCTCTTGGAGCTTATGCTCCCATGCGGGGAAGACA	198088
mRNA	-----	
genome	CATGGGTCAGTAGAGAAATGGTTGCAGGTGTGATAAGTGCTGGAAGGGAGGGGTTGGCC	198148
mRNA	-----	
genome	TGAGGACACGGAGGCAGACATACGTGGAGCTGGGAACAGTGGCCACACAGGGAACGGCCA	198208
mRNA	-----	
genome	GTGCGAAGGCCCAGAGGCAGAGGACACTGGAGCAAGCCCAGGAGCAGCTAGGAGGCTGGT	198268
mRNA	-----	
genome	GGCCAGCAGCCAGGCCACGGAAGCCCGTGCAGCCCGTGGGGAGGAGTGTTTCATGCTTTTC	198328
mRNA	-----	
genome	AAGCTTAGTGGGAGTCTTTTGGCCAGTGCAGCTCTGGGTCTGACATCGGTGGGGGACAGA	198388
mRNA	-----	
genome	GGGGTGGTGGAGCGGCCACAGCTGCAAGCTCACCTCACTGCCGGCCCTTCCACCAGTTTC	198448
mRNA	-----	
genome	AAACTCTTTCTAGAAGCTCCAGCTTTCCCAAAGCTGAATTCTCTATGAGCCTCCTTGGCC	198508
mRNA	-----	
genome	GGGACTCGGGCGTCTGGTTGCCCTGGCTGCAAAGGAGGCTGGGGCCAGGTGTGTTTGAGT	198568
mRNA	-----	
genome	CACCTCCTGGAATTAGGCAAGTTGCTGCCCAAATAGAAGGTTGTTGGCAGGTGGGTCAGC	198628
mRNA	-----	

rs1006798

Figure 1

genome mRNA	AGGTGAACAGCATGGTTTGA CT CAGGGTTCAGAAAAATCTCCCTCTGGCTGCCAAGCGAG	198688
genome mRNA	CAGGCCGTGGAGACAGGTGCAGAGGCAGGTGTGGCAGCAGGCATCCTGCCAGGCAGTGCT	198748
genome mRNA	GCAGTCATCCTGCGACAAGCAGCAGCAGCTCATCCTACCCTCTAGGGGGTCTTGAGGTCA	198808
genome mRNA	GCCAGGCAAGAGAGCAGCTTGGACTCCACTGGGTGTGGGACCAGCCTGTGGACCATGGTG	198868
genome mRNA	GTGTGGAGGGTGGCCTCGGCCTGCCTGTGTGAAGGAGAGGCCGGCGTGTTCGTGGAGCC	198928
genome mRNA	CAAAGGGGAGCTGGGCAAGCAGGATTCACCTTCACTCTGAGGGTCCTGGAGCTCCCACCCT	198988
genome mRNA	CCTCAGCCATCTCCCCAGAGCCTGTGTGCCGAGGACTCGGCCCATGTTGCTGTGGGATGA	199048
genome mRNA	GAGGCAGAGTGTTCGTGAGGGTGTAAAGGAGCGGCGGCAGTGGTGGGAGGAGGGAGCAGCAG	199108
genome mRNA	CCAGCGCTACGGTGCCAGTTTCCAGCTGCCAGATGACGCCGCTGACCCTGTGGTTGAGAA	199168
genome mRNA	GAGATGCACAGAGCCAGCTCTTGCAAGCCAGTGTGGCTGCCATAGCACCTGCCGAGAAGC	199228
genome mRNA	AGAAGGAAGGGTGGCCCCAGGAGGACAGAGGATGCGGGCACATCTGATGCGGGCCTGAGT	199288
genome mRNA	TTTGGGAGCTTTTGCTCTAGCCAGTTTCCAGCTCCGGGACCCACCCGCCTCGTAGGCAAG	199348
genome mRNA	ACACCACCCAAGAAATCATTTGCTTAACAAACACACTGGGCTCCAAGTGGACACCTGTGC	199408
genome mRNA	CACCCTAGATGCTGGGAACCCAGCCATGACACAGGCACCTGCCCCCAGCTGCTGACCACT	199468
genome mRNA	GAGGCTGGCTAGCAGCTCCCATGGGGCCAGTGTGGGGTTCCCCAGCCTCCTAACAGGGAG	199528
genome mRNA	CCAGTCACAAGCCCTCGAGAGGGAAGGGTGGCCGCGGCCCTGGCAGGAAGGTTAGGCTGG	199588
genome mRNA	ACGCTCCCACAAGACATAACAGATGGAGGTTCTAAATGATGTAGCAACTTCTTCACCCTG	199648
genome mRNA	AAACTGCTGTAGAGTCAGCCATGACGCACCGGTACTTCAGTAACTGCCAGGCATCCGGGA	199708
genome mRNA	CAGCACACCGCGAGTCGCTGCTGTGCTTGGGTTAGAAGTGGTTTGGTCTGTCTTTCTTCTC	199768
genome mRNA	GCCCTCTCTAATCAGAGTCAGTGATTCATGCCCTTCCATCACCTTAGAGAAGGGGCAGGC	199828
genome mRNA	GCTGCCCCGACCTTCTCCAGGCTGGAGCAGCATCGCCTCATGTCAGCAGAACTCAGCTGTA	199888

Figure 1

genome mRNA	GAATATCGTGGGGTTGGTGCCTTTCATCAGCAGCATGTCCTTAACAACCTTCTGATTTCT	199948
genome mRNA	TCCTTAGTTGTTGGTCCATTAAGGAGAAAAAAATGATCTCAGCCATTGCTAAAATATTT	200008
genome mRNA	GATAAGATTGAGCAAAGCAGCATGTTAACATTGAAAAGTAGAATCAGGAGCCAGGCAGAT	200068
genome mRNA	GTGCTTGCTTTTCACCTGTAGTATTTTCATGTTGTTTGGACGTTTTTAGCTAATGCATTAA	200128
genome mRNA	GATAAATAAACAAAAGCCGGGCACGGTGGTTCACGCCTGTAATCCCAGCACTTTGGGAGG	200188
genome mRNA	CTGAGGCGGGAGGATCCTCTGAGGTCAGGAGTTCAAGACCAGCCTGACCAACATGGAGAA	200248
genome mRNA	ACCTCGTCATTACTAAAAATACAAAATTAGCTGGGCGTGGTGGTGCATGCCTGTAATCCC	200308
genome mRNA	AGCTACTTGGGAGGCTGAGGCAGGAGAATCGCTTGAACCCGGGAGGCGGAGGTTGCAGTG	200368
genome mRNA	AGCTGAGATTGCACCACTGCACTCCAGCCTGGGTGACAGTGAAACTCGGTCTCAAAAAAA	200428
genome mRNA	AAAAAAAATTAAAAAAGATAAAATAAAATAAGCAGGATAAGAAATGAAGAAAGTAGAGTT	200488
genome mRNA	ACCTTTGTTTTTCAGATTTTCATTTTTGTATACCCAGAAAGCCAAATGTACAAAAGACTGGG	200548
genome mRNA	AGCTCTTTAAACCAGCTTAAACTTGTTGAAAATGAGGATGAAGAAATATCCCATTGAGAG	200608
genome mRNA	TTGGAATGAATTTAACCCAGAAGGAACAGGACCTCTACTGAAGAGAACTATGCAGTCTTA	200668
genome mRNA	CTGAAAAATCTAAATAATACCTGAGCGCTGGAGAACTTCGCACACTCCTGAAAGCTCCA	200728
genome mRNA	AAGTCAATGTCATCATTTTTATTAATGTCATTCCAAACATAGTCTCAATAATATCACTTCT	200788
genome mRNA	TGGTTTTGACATGGACGCGATGATGTTTAAATTTCATATGAAAAAAGAACGGGGCCAAAAG	200848
genome mRNA	TCCAAGGCCAGTCAGCGTGAGAAGACCGCTCGGCCTCCCTCGGAGTCGGGGAGTTGGAAC	200908
genome mRNA	CGCAGACTGAGATCATGTGGCTGCTGGAGGCCAGGACGAACGTCGGGAAATGGAGACTCC	200968
genome mRNA	TGCGTTGCTGGTGGGATGTGGTGCAGCCGCTTCCAGGAGCAATTTGGTGTCCCGTCCTAA	201028
genome mRNA	AGCTGAAGAAACGCATTTCCCTCTGGTCAGTGCCACTCCTAGACAGGCCACCCTGCGGCAG	201088
genome mRNA	CCGTCCTCAAACCTGGTCTGAGGACCCCTCAACGCTCTTAAAAATCATTAAGTGGGCCA	201148

Figure 1

genome mRNA	GGTGCGGTGGCTCACACCTGTAATCCCAGCACTTTGGGAGGCCAAGACAGGCGGATCACG	201208

genome mRNA	AGGTCAGGACATTGAGATCATCCTGGCTAACACGGTGAAACCCCGTCTCTACTAAAAATA	201268

genome mRNA	CAAAAAATTAGCCGGGCGTGGTGGCGGGCGCCTGTAGTCCCAGCTACTTGGGAGGCTGAG	201328

genome mRNA	CCAGGAGAATGGCGTGAACCCAGGAGGTGGAGCTTGCAGTGAGCTGAGATCACTCCACTG	201388

genome mRNA	CACTCCAGCCTGGGCAGCAGAGCGAGACTCTGTCTCAAAAAAAAAATAATAATAATAAA	201448

genome mRNA	TAAAAATAAAATAAAATAAAATTCATTAAGTGCCAAAGAACTTTTGCTTATGTGAGTT	201508

genome mRNA	CTAATGACCAATATTAATACACATTAGAATATCTTATTAGAAATTAAACCTGAGACCTTT	201568

genome mRNA	AGAAAACATGTATTTCATTTCAAATAGCAATAAACCCATGACATATTAACATAAATAACA	201628

genome mRNA	ATTGTATGAAAAATATATTTTCCAAAACAAAAAGTTTTCGGGAGAAGTGTGGCATAGTTT	201688

genome mRNA	TACATGGTCGTAAATCTCTGGCTTAAGAGAAGCCCACTGGCCTCTCAGCAGGCTCTGGGT	201748

genome mRNA	CCGTCCACTTTGGGGGTGTTTTGGTTGTGAAGTATAGGAGTGAATGGAGAAGCTCATTCT	201808

genome mRNA	TACCCAGATGTGTATTTGAAAAGAAAAGGAACATTTTAATAACCTTTGCAAATAATCGGT	201868

genome mRNA	ATATTCTTCCGTGATCCTATTCCAACACTGGACAGGTGGTGGTTTGTTTTTTTTTTTTGG	201928

genome mRNA	AGACGGAGTCCCGCTCTGTCACTCAGGCTGGAGTGCAGTGGCGCGATTTCAGCTCACTGC	201988

genome mRNA	AAGCTCCGCCTCC	202001
