

HUMANIZED IL-7 RODENTS

FIELD

[0001] Non-human animals (*e.g.*, mammals, *e.g.*, rodents such as mice, rats, and hamsters) that comprise a genetic modification comprising a replacement, at an endogenous locus, of a non-human IL-7 gene sequence with a human IL-7 gene sequence. Rodents and other non-human animals that express human IL-7 or humanized IL-7 from a locus under control of endogenous non-human regulatory sequences, or from an endogenous non-human IL-7 locus that comprises endogenous non-human regulatory sequences.

BACKGROUND

[0002] Transgenic mice that have randomly inserted transgenes that contain a human IL-7 sequence are known in the art. However, most if not all of these transgenic mice are not optimal in one aspect or another. For example, most mice transgenic for human IL-7 exhibit abnormal levels and/or ratios of certain cells, including T cells, that are likely due to a dysregulation of immune cell development, *e.g.*, T cell development.

[0003] There remains a need in the art for non-human animals that comprise human IL-7 encoding sequences, wherein the human IL-7 encoding sequences are at an endogenous non-human IL-7 locus, and for non-human animals that express human IL-7 under the control of endogenous non-human regulatory elements. There is a need in the art for non-human animals that express human IL-7 in a manner that is as physiologically relevant in the non-human animal as possible. There is a need in the art for non-human animals that express a human IL-7, wherein the non-human animals lack a significant abnormality in peripheral T cells, and/or in ratios of T cell subtypes.

SUMMARY

[0004] Genetically modified non-human animals, cells, tissues, and nucleic acids are provided that comprise a human IL-7 genomic sequence at an endogenous non-human IL-7 locus. The non-human animals express a humanized IL-7 protein from a modified locus regulated by one or more endogenous non-human regulatory sequences of the modified endogenous IL-7 locus. In various embodiments, the non-human animals are rodents, *e.g.*, mice, rats, hamsters, *etc.* In a specific embodiment, the rodent is a mouse or a rat.

[0005] In various embodiments and aspects, the non-human animals comprise a modified IL-7 gene in the germline of the non-human animal at a modified endogenous IL-7 locus, wherein the modified endogenous IL-7 locus comprises a humanization of at least a portion of the

endogenous IL-7 gene. In various embodiments, the mice are heterozygous or homozygous with respect to the modified IL-7 locus. In one embodiment, a non-human animal is provided that comprises a lack of a first endogenous IL-7 allele and a humanization of a second endogenous IL-7 allele. In various embodiments and aspects, the humanization is of one or more exons and/or introns. In various embodiments and aspects, non-human animals having a modified IL-7 locus are provided wherein one or both of an endogenous non-human 5'-untranslated region and an endogenous non-human 3'-untranslated region are retained in the modified animal.

[0006] In some aspects, non-human animals of the present invention comprise a 5'-untranslated region contained within SEQ ID NO: 1. In some aspects, non-human animals of the present invention comprise a 3'-untranslated region contained within SEQ ID NO: 2. In some embodiments, non-human animals of the present invention comprises a 5'-untranslated region contained within SEQ ID NO: 1 and a 3'-untranslated region contained within SEQ ID NO: 2.

[0007] In some aspects, non-human animals of the present invention comprise a 5'-untranslated region that is SEQ ID NO: 1. In some aspects, non-human animals of the present invention comprise a 3'-untranslated region that is SEQ ID NO: 2. In some aspects, non-human animals of the present invention comprise a 5'-untranslated region that is SEQ ID NO: 1 and a 3'-untranslated region that is SEQ ID NO: 2.

[0008] In some aspects, a humanized IL-7 gene of the present invention has a sequence that is at least 50% (e.g., 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more) identical to a continuous sequence comprising exons 2-6 of a human IL-7 gene. In some certain aspects, a human IL-7 gene of the present invention comprises SEQ ID NO: 3. In some aspects, a humanized IL-7 gene of the present invention has a sequence that reflects a humanization as set forth in Figure 1.

[0009] In one aspect, a genetically modified rodent is provided that comprises a replacement at an endogenous rodent IL-7 locus of an endogenous rodent IL-7 genomic sequence with a human IL-7 genomic sequence.

[00010] In one embodiment, the genetically modified rodent comprises a first rodent regulatory sequence upstream (with respect to the direction of transcription of the IL-7 gene) of the human IL-7 genomic sequence and a second rodent regulatory sequence downstream of the human IL-7 genomic sequence. In one embodiment, the first rodent regulatory sequence comprises a rodent promoter and/or enhancer, and the second rodent regulatory sequence comprises a 3'-UTR.

[00011] In one embodiment, the rodent is a mouse and comprises an endogenous mouse IL-7 gene locus having a mouse exon 1 and human exons 2, 3, 4, 5, and 6. In one embodiment, the endogenous mouse IL-7 gene locus comprises, from upstream to downstream with respect to

the direction of transcription, mouse exon 1, at least a portion of a first mouse intron, and a contiguous human genomic fragment comprising human exon 2 through human exon 6. In one embodiment, the mouse further comprises a contiguous sequence of endogenous mouse DNA comprising an complete endogenous mouse IL-7 upstream (with respect to the direction of transcription of the IL-7 gene) promoter and regulatory region, wherein the contiguous mouse DNA is upstream of the human genomic fragment; and further comprises a contiguous sequence of endogenous mouse DNA 3'-UTR downstream of the human genomic fragment.

[00012] In one embodiment, the mouse comprises a mouse sequence that is at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical with a sequence selected from SEQ ID NO:1, SEQ ID NO:2, and a combination thereof. In a specific embodiment, the mouse comprises a mouse sequence selected from SEQ ID NO:1 and SEQ ID NO:2.

[00013] In one aspect, a genetically modified mouse is provided that comprises a replacement at an endogenous mouse IL-7 locus of an endogenous mouse IL-7 genomic sequence with a human IL-7 genomic sequence to form a modified locus, wherein the human IL-7 genomic sequence comprises at least one human exon, and the modified locus comprises a mouse sequence selected from a sequence of SEQ ID NO:1, SEQ ID NO:2, and a combination thereof.

[00014] In one embodiment, the replacement comprises a human genomic fragment comprising exons 2 through 6, and the human genomic fragment is linked to mouse exon 1 to form a modified endogenous mouse IL-7 locus, wherein the modified mouse IL-7 locus comprises a mouse sequence selected from SEQ ID NO:1, SEQ ID NO:2, and a combination thereof.

[00015] In one aspect, a genetically modified rodent is provided that comprises an IL-7 gene that comprises a rodent exon 1 and at least a portion of a rodent intron 1, and a human IL-7 gene sequence of human IL-7 exons 2, 3, 4, 5, and 6, wherein the rodent comprises a sequence selected from a rodent upstream IL-7 regulatory sequence, a rodent IL-7 3'-UTR, and a combination thereof.

[00016] In one aspect, a genetically modified mouse is provided that comprises a sequence selected from SEQ ID NO:1, SEQ ID NO:2, and a combination thereof; wherein the mouse lacks an endogenous sequence encoding exons 2 through 5 of a mouse IL-7 protein, and the mouse comprises a nucleic acid sequence at an endogenous mouse IL-7 locus wherein the nucleic acid sequence encodes human IL-7 exons 2, 3, 4, 5, and 6.

[00017] In one aspect, a genetically modified rodent is provided that expresses a human or humanized IL-7 protein from an endogenous rodent IL-7 locus that is modified to express at

least one human IL-7 exon. In one embodiment, the rodent IL-7 locus is modified to express a human or humanized IL-7 protein encoded by a sequence comprising at least two human IL-7 exons. In one embodiment, the rodent IL-7 locus is modified to express a human or humanized IL-7 protein encoded by a sequence comprising at least three human IL-7 exons. In one embodiment, the rodent IL-7 locus is modified to express a human or humanized IL-7 protein encoded by a sequence comprising at least human IL-7 exons 2, 3, 4, 5, and 6 (*i.e.*, 2 through 6). In one embodiment, the rodent IL-7 locus is modified to express a human IL-7 protein. In some certain aspects, the rodent IL-7 locus is modified to express a human IL-7 protein whose sequence reflects a protein encoded by a locus as shown in Figure 1. In some certain aspects, the rodent IL-7 locus is modified to express a human IL-7 protein comprising a sequence encoded by exons 2-6 of a human IL-7 gene. In some certain aspects, the rodent IL-7 locus is modified to express a human IL-7 protein comprising a sequence encoded by exons 2-6 of a human IL-7 gene as set forth in SEQ ID NO: 3.

[00018] In one aspect, a genetically modified rodent is provided that expresses a human or humanized IL-7 protein from an endogenous rodent IL-7 locus that is modified to comprise at least human IL-7 exons 2 through 6 in place of rodent IL-7 exons 2 through 5.

[00019] In one aspect, a genetically modified rodent is provided that expresses a human or humanized IL-7 protein from a humanized endogenous rodent IL-7 locus comprising a humanized endogenous rodent IL-7 coding region, wherein the humanized endogenous rodent IL-7 locus comprises all endogenous rodent regulatory elements that are present in a wild-type rodent upstream of a wild-type rodent IL-7 coding region and that are downstream of the wild-type rodent IL-7 coding region.

[00020] In one aspect, a genetically modified rodent is provided that expresses a human or humanized IL-7 protein from a humanized rodent IL-7 locus that comprises rodent regulatory regions upstream and downstream of a nucleic acid sequence encoding the human or humanized IL-7 protein, wherein the human or humanized IL-7 protein is expressed in an expression pattern that is about the same as the expression pattern of a rodent IL-7 protein in a wild-type rodent. In one embodiment, the level of serum expression of the human or humanized IL-7 is about the same as the level of serum expression of a rodent IL-7 protein in a wild-type rodent.

[00021] In one aspect, a genetically modified rodent is provided that expresses a humanized IL-7 protein, wherein the lymphocyte population of the rodent is characterized by its B cell population that is about the same in number as a population of B cells in an age-matched wild-type mouse. In one embodiment, the modified rodent is characterized by a population of mature B cells that is about the same in number as a population of mature B cells in an age-matched wild-type mouse. In one embodiment, the humanized IL-7 protein is identical to a

human IL-7 protein. In one embodiment, the humanized IL-7 protein comprises human sequence encoded by at least exons 2 through 6 of a human IL-7 gene.

[00022] In one aspect, a genetically modified rodent is provided that expresses a humanized IL-7 protein, wherein the lymphocyte population of the rodent is characterized by a population of T cells that is about the same in number as a population of T cells in an age-matched wild-type mouse. In one embodiment, the modified rodent exhibits a population of mature T cells that is about the same in number as a population of mature T cells in an age-matched wild-type mouse. In one embodiment, the modified rodent exhibits a population of peripheral T cells that is about the same in number as the population of peripheral T cells in an age-matched wild-type mouse. In one embodiment, the humanized IL-7 protein is identical to a human IL-7 protein. In one embodiment, the humanized IL-7 protein comprises human sequence encoded by at least exons 2 through 6 of a human IL-7 gene.

[00023] In one aspect, a genetically modified rodent is provided that expresses a humanized IL-7 protein, wherein the lymphocyte population of the rodent is characterized by a T cell population that exhibits a CD4:CD8 ratio that is about the same as the CD4:CD8 ratio in the T cell population of an age-matched wild-type mouse. In one embodiment, the humanized IL-7 protein is identical to a human IL-7 protein. In one embodiment, the humanized IL-7 protein comprises human sequence encoded by at least exons 2 through 6 of a human IL-7 gene.

[00024] In one aspect, a genetically modified rodent is provided that expresses a humanized IL-7 protein, wherein the rodent comprises a characteristic selected from a lack of a propensity to develop a chronic colitis; lack of over-expression of IL-7 in colonic mucosal lymphocytes; normal, or wild-type, expression of IL-7 in colonic mucosal lymphocytes; lacks a severe dermatitis; lacks a dermatitis characterized by a massive dermal infiltration of mononuclear cells; exhibits a CD4:CD8 ratio in its T cell population that is about the same as the CD4:CD8 ratio of an age-matched wild-type mouse; exhibits an expression pattern of human IL-7 that is about the same as an expression pattern of mouse IL-7 in a wild-type mouse; and a combination thereof.

[00025] In one aspect, a genetically modified rodent is provided that expresses a humanized IL-7 protein, wherein the rodent lacks a propensity to develop a chronic colitis.

[00026] In one aspect, a genetically modified rodent is provided that expresses a humanized IL-7 protein, wherein the rodent does not exhibit over-expression of IL-7 in colonic mucosal lymphocytes.

[00027] In one aspect, a genetically modified rodent is provided that expresses a humanize IL-7 protein, wherein the rodent does not exhibit a dermatitis characterized by a massive dermal infiltration of mononuclear cells.

[00028] In one aspect, a genetically modified rodent is provided that expresses a humanized IL-7 protein, wherein the rodent does not exhibit a lymphoproliferation into dermis.

[00029] In one aspect, a genetically modified rodent is provided that expresses a humanized IL-7 protein, wherein the rodent does not exhibit B and/or T cell lymphomas at a higher frequency than an age-matched wild-type mouse.

[00030] In one aspect, a genetically modified mouse is provided that expresses a humanized IL-7 protein, or a human IL-7 protein, wherein the mouse is no more prone than a wild-type mouse to developing a pathology selected from colitis, chronic colitis, severe dermatitis, pathological and/or massive infiltration of the dermis by mononuclear cells, lymphoproliferation of the dermis, B cell lymphomas, T cell lymphomas, reduction in the number of mature B and/or T cells, reduction in the number of peripheral B and/or T cells, abnormal numbers of CD4⁺ T cells, abnormal numbers of CD8⁺ T cells, and a combination thereof.

[00031] In some aspects, a genetically modified mouse is provided that expresses a human IL-7 protein whose sequence reflects a replacement of a mouse IL-7 gene sequence with a human IL-7 gene sequence, wherein the human IL-7 gene sequence comprises exons 2-6 of a human IL-7 gene. In some certain aspects, the replacement is of a sequence comprising exons 2-5 of a mouse IL-7 gene. In some certain aspects, a human IL-7 gene comprises SEQ ID NO: 3. In some certain aspects, expression of the human IL-7 protein is under the control of mouse regulatory elements.

[00032] In some aspects, a genetically modified mouse is provided that does not detectably express a mouse IL-7 protein. In some certain aspects, the genome of a mouse as described herein comprises a deletion in whole or in part of a mouse IL-7 gene. In some certain aspects, the genome of a mouse as described herein comprises a deletion of an endogenous IL-7 gene sequence corresponding to exons 2-5.

[00033] In one aspect, a genetically modified non-human animal is provided, comprising, in its germline, a replacement of at least one non-human IL-7 exon with at least one human IL-7 exon to form a human or humanized IL-7-encoding gene, wherein the replacement is at an endogenous non-human IL-7 locus, wherein the human or humanized IL-7-encoding gene is under control of endogenous non-human regulatory elements.

[00034] In one embodiment, the genetically modified non-human animal is a rodent. In one embodiment, the rodent is selected from a rat and a mouse.

[00035] In one embodiment, the human or humanized IL-7-encoding gene comprises human exons selected from the group consisting of human exon 1, human exon 2, human exon 3, human exon 4, human exon 5, human exon 6, and a combination thereof. In one embodiment, the human or humanized IL-7-encoding gene comprises no more than five human exons.

[00036] In one embodiment, the genetically modified non-human animal is a rodent that is a mouse and the modified locus comprises a replacement of mouse exons 2, 3, 4, and 5 with a human genomic segment comprising human IL-7 exons 2, 3, 4, 5, and 6.

[00037] In one embodiment, the human or humanized IL-7-encoding gene comprises a cDNA encoding a human or humanized IL-7 protein.

[00038] In one aspect, a genetically modified non-human animal is provided, comprising, in its germline, a transgene comprising a nucleic acid sequence encoding a human or humanized IL-7 gene, wherein the human or humanized IL-7 gene is flanked upstream and downstream with endogenous non-human regulatory sequences.

[00039] In one embodiment, the genetically modified non-human animal is a rodent. In one embodiment, the rodent is selected from the group consisting of a mouse, a rat, and a hamster.

[00040] In one embodiment, the genetically modified non-human animal comprises a human exon selected from the group consisting of human exon 1, human exon 2, human exon 3, human exon 4, human exon 5, human exon 6, and a combination thereof. In one embodiment, the human or humanized IL-7 gene comprises at least five human exons.

[00041] In one aspect, a humanized IL-7 locus is provided, comprising, a non-human exon 1, a human exon 2, a human exon 3, a human exon 4, a human exon 5 and a human exon 6. In some certain aspects, the humanized IL-7 locus further comprises 5' and 3' non-human untranslated regions flanking non-human exon 1 and human exon 6. In some certain embodiments, the humanized IL-7 locus comprises a 3' human untranslated region, or portion thereof, that is contiguous with a non-human 3' untranslated region. In some certain aspects, the humanized IL-7 locus comprises a 5' non-human untranslated region, or portion thereof, and non-human exon 1 that is contiguous with a human exon 2. In some certain aspects, a humanized IL-7 locus comprises the structure set forth in Figure 1.

[00042] In one aspect, a humanized IL-7 locus is provided, comprising human exons 2-6 of a human IL-7 gene operably linked to non-human IL-7 regulatory sequences. In some certain aspects, a humanized IL-7 locus of the present invention comprises a non-human IL-7 exon 1. In some certain aspects, a humanized IL-7 locus of the present invention comprises a non-human IL-7 exon 1 and a non-human IL-7 intron 1. In some certain embodiments, a humanized IL-7 locus of the present invention comprises a 3' human IL-7 untranslated region, or portion thereof, that is contiguous with a non-human IL-7 3' untranslated region, or portion thereof. In some certain aspects, a humanized IL-7 locus of the present invention comprises a 5' non-human untranslated region, or portion thereof, and non-human exon 1 that is contiguous with a human IL-7 exon 2.

[00043] In one aspect, a humanized IL-7 locus is provided, comprising a sequence that encodes an IL-7 protein that is substantially human. In some certain aspects, a humanized IL-7 locus of the present invention comprises a sequence that is at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% identical to SEQ ID NO: 3. In some certain aspects, a humanized IL-7 locus of the present invention comprises SEQ ID NO: 3. In some certain aspects, an IL-7 protein of the present invention is encoded by a sequence that is at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% identical to SEQ ID NO: 3. In some certain aspects, an IL-7 protein of the present invention is encoded by SEQ ID NO: 3.

[00044] In one aspect, a method is provided for making a non-human animal with a human or humanized IL-7-encoding gene, comprising modifying the germline of the non-human animal to comprise a human or humanized IL-7-encoding gene flanked upstream and downstream with endogenous non-human IL-7 regulatory sequences.

[00045] In one embodiment of the method, the modification is at an endogenous non-human IL-7 locus.

[00046] In one embodiment of the method, the non-human animal is a rodent. In one embodiment, the rodent is selected from the group consisting of a mouse, a rat, and a hamster.

[00047] In one aspect, a genetically modified non-human animal is provided that is genetically modified to express human IL-7 in an expression pattern that is the same expression pattern as observed for a wild-type non-human animal of the same genus and species. In one embodiment, the non-human animal is a rodent. In a specific embodiment, the rodent is selected from a mouse and a rat.

[00048] In one embodiment, the level of human IL-7 expressed in the non-human animal is about the same as the level of non-human IL-7 in a corresponding wild-type mouse. In one embodiment, the non-human animal is a rodent. In a specific embodiment, the rodent is selected from a mouse and a rat.

[00049] In one aspect, a DNA construct is provided, comprising from 5' to 3' with respect to direction of transcription, a nucleic acid sequence homologous to a mouse IL-7 5' noncoding sequence, a human genomic fragment encoding a human IL-7 protein but not comprising a human regulatory sequence upstream or downstream of sequence encoding the human IL-7 protein, and a nucleic acid sequence homologous to a mouse IL-7 3' noncoding sequence.

[00050] In one aspect, a DNA construct is provided, comprising from 5' to 3' with respect to direction of transcription, a nucleic acid sequence that comprises a region of homology to a mouse IL-7 exon 1 sequence, a human genomic fragment encoding a human IL-7 protein but not

comprising a human regulatory sequence upstream or downstream of sequence encoding the human IL-7 protein, and a nucleic acid sequence homologous to a mouse IL-7 3' noncoding sequence.

[00051] In one aspect, a genetically modified rodent is provided, wherein the rodent comprises a DNA construct as described herein.

[00052] In one aspect, use of a DNA construct as described herein for making rodent or rodent cell that expresses a human IL-7 protein is provided. In some certain aspects, the rodent or rodent cell does not detectably express a rodent IL-7 protein.

[00053] In one aspect, a genetically modified rodent cell is provided, wherein the rodent cell comprises a replacement at an endogenous rodent IL-7 locus of a gene sequence encoding a rodent IL-7 with a human genomic sequence encoding a human IL-7. In some certain aspects, the replacement is made with DNA construct as described herein. In some certain aspects, the rodent cell is a rat cell. In some certain aspects, the rodent cell is a mouse cell.

[00054] In one embodiment, the human genomic sequence comprises a contiguous human nucleic acid sequence spanning human IL-7 exons 2 through human IL-7 exon 6.

[00055] In one embodiment, the genetically modified rodent comprises a mouse IL-7 promoter at the endogenous rodent IL-7 locus.

[00056] In one embodiment, the cell is selected from a pluripotent cell, an induced pluripotent cell, a totipotent cell, an ES cell, and an ovum.

[00057] In one embodiment, the cell secretes human IL-7. In one embodiment, the cell that secretes human IL-7 is selected from an epithelial cell (*e.g.*, an intestinal epithelial cell), a hepatocyte, a keratinocyte, a dendritic cell, and a follicular dendritic cell. In one embodiment, the rodent cell is a bone marrow dendritic cell. In one embodiment, the cell that secretes human IL-7 is a thymic stromal cell; in a specific embodiment, the thymic stromal cell is a cortical epithelial cell.

[00058] In one aspect, a rodent embryo is provided, wherein the embryo comprises at least one rodent donor cell (*e.g.*, an ES cell, a pluripotent cell, a totipotent cell, *etc.*) comprising a replacement of an endogenous rodent IL-7-encoding nucleic acid sequence with a nucleic acid sequence encoding a human IL-7 at the endogenous rodent IL-7 locus. In one embodiment, the donor cell is a mouse ES cell and the embryo is a host mouse embryo that is a pre-morula, a morula, or a blastocyst.

[00059] In one aspect, a rodent tissue that comprises a humanized IL-7 gene at an endogenous rodent IL-7 locus is provided, wherein the rodent tissue is selected from thymic, splenic, epidermal, and intestinal.

- [00060] In one aspect, a genetically modified mouse is provided that comprises a DNA sequence that encodes a human IL-7, wherein the mouse does not express a mouse IL-7, and wherein the mouse exhibits a T cell population that is about the same size as the T cell population of a wild-type mouse.
- [00061] In one embodiment, the mouse exhibits a peripheral T cell population that is about the same size as a peripheral T cell population of a wild-type mouse.
- [00062] In one embodiment, the T cell population is a mouse T cell population.
- [00063] In one embodiment, the mouse is not more prone than a wild-type mouse to develop a B cell tumor comprising a pro-B or a pre-B cell.
- [00064] In one embodiment, the mouse is not more prone than a wild-type mouse to develop a lymphoid tumor.
- [00065] In one embodiment, the mouse does not exhibit a lymphoproliferative disorder in the absence of a known lymphoproliferative causative agent.
- [00066] In one embodiment, the mouse does not exhibit a pathologic infiltration of T cell in a skin layer. In one embodiment, the mouse does not exhibit a symptom of alopecia.
- [00067] In one embodiment, the majority of T cells of the genetically modified mouse are about the same in size distribution as in an age-matched wild-type mouse. In a specific embodiment, the genetically modified mouse does not exhibit an enlargement of T cell
- [00068] In one aspect, a rodent is provided that expresses a humanized or human IL-7 protein from an endogenous modified rodent IL-7 locus, wherein the serum concentration of human IL-7 in the rodent is physiologically normal.
- [00069] In one aspect, a humanized rodent is provided that expresses a humanized IL-7 gene in the serum of the rodent at a physiologically normal concentration.
- [00070] In one embodiment, the rodent is selected from a mouse and a rat.
- [00071] In one embodiment, the physiologically normal serum concentration of human IL-7 is less than 10 picograms/mL. In one embodiment, the physiologically normal serum concentration of human IL-7 is less than 5 picograms/mL. In one embodiment, the physiologically normal serum concentration of human IL-7 in the rodent is about 2 picograms/mL to about 4 picograms/mL. In one embodiment, the physiologically normal serum concentration of human IL-7 in the rodent serum is about 2.4 picograms/mL to about 3.2 picograms/mL.
- [00072] In one aspect, a method for making a human IL-7 protein is provided, comprising inserting into the germline of the non-human animal a human or humanized IL-7 coding gene under control of endogenous non-human regulatory elements, allowing the non-human animal to

make the human or humanized IL-7, and isolating from the non-human animal (*e.g.*, a mammal, *e.g.*, a rodent such as, *e.g.*, a mouse or rat or hamster) human or humanized IL-7.

[00073] In one aspect, a method for making a human IL-7 protein is provided, comprising isolating from a non-human animal as described herein (*e.g.*, a mammal, *e.g.*, a rodent such as, *e.g.*, a mouse or rat or hamster).

[00074] In one aspect, a method is provided for making a non-human animal that comprises a human or humanized IL-7 gene in its germline, comprising inserting into the germline of the non-human animal a human or humanized IL-7-encoding nucleic acid sequence or fragment thereof, wherein the human or humanized IL-7-coding nucleic acid sequence or fragment thereof is under regulatory control of endogenous non-human regulatory elements. In one embodiment, the human or humanized IL-7 gene is at an endogenous non-human IL-7 locus (*i.e.*, inserted between upstream and downstream non-human regulatory elements at the endogenous non-human IL-7 locus, wherein the human or humanized IL-7-coding nucleic acid sequence replaces the wild-type existing non-human IL-7 coding sequence in whole or in part). In one embodiment, the non-human animal is a mammal, *e.g.*, rodent. In one embodiment, the rodent is selected from a mouse, a rat, and a hamster.

[00075] In one aspect, a method for making a non-human animal that comprises a human or humanized IL-7 gene is provided, comprising inserting a DNA construct comprising exons 2-6 of a human IL-7 gene into an endogenous non-human IL-7 gene of a non-human cell.

[00076] In one aspect, a method is provided for isolating from a non-human animal a T cell that has been exposed to a human or humanized IL-7 protein, comprising a step of isolating a T cell from a non-human animal as described herein. In one embodiment, the non-human animal is a mouse or a rat. In one embodiment, the T cell is a non-human T cell, *e.g.*, a rodent T cell, *e.g.*, a T cell of a mouse or a rat. In one embodiment, the T cell is selected from a T cell in the thymus and a peripheral T cell.

[00077] In one aspect, a method for identifying an agent that is an antagonist of human IL-7 is provided, comprising a step of administering an agent to a genetically modified rodent as described herein, determining an effect of the agent on a human IL-7-mediated function in the rodent, and identifying the agent as an IL-7 antagonist if it antagonizes the function of human IL-7 in the genetically modified rodent.

[00078] In one aspect, use of a genetically modified rodent as described herein for identifying an agent that is an antagonist of human IL-7 is provided, comprising of administering an agent to the genetically modified rodent, determining an effect of the agent on a human IL-7-mediated function in the rodent, and identifying the agent as an IL-7 antagonist if it antagonizes the function of human IL-7 in the genetically modified rodent.

[00079] In one embodiment, the agent comprises an immunoglobulin variable domain that binds IL-7. In one embodiment, the agent specifically binds human IL-7 but not rodent IL-7. In one embodiment, the agent is an antibody.

[00080] In one aspect, a method for determining whether an agent reduces IL-7-mediated peripheral T cell population is provided, comprising a step of administering to a genetically modified rodent as described herein an IL-7 antagonist for a period of time, measuring peripheral T cell population number of the rodent at one or more time periods following administration, and determining whether the IL-7 antagonist reduces the peripheral T cell population.

[00081] In one aspect, use of a genetically modified rodent as described herein for determining whether an agent reduces IL-7-mediated peripheral T cell population is provided, comprising administering to the genetically modified rodent an IL-7 antagonist for a period of time, measuring peripheral T cell population number of the rodent at one or more time periods following administration, and determining whether the IL-7 antagonist reduces the peripheral T cell population.

[00082] In one aspect, the genetically modified non-human animal is heterozygous for a human or humanized IL-7-encoding gene. In one embodiment, the non-human animal is unable to express an endogenous IL-7 protein. In a specific embodiment, the non-human animal comprises a knockout of both endogenous IL-7 alleles.

[00083] Each of the aspects and embodiments described above and below may be used together, unless otherwise stated and unless otherwise clear from the context.

BRIEF DESCRIPTION OF THE FIGURES

[00084] **Figure 1** depicts (not to scale) a schematic of a wild-type mouse IL7 gene locus (top) and a humanized endogenous mouse IL-7 locus (bottom). Open symbols indicate human sequence; closed symbols indicate mouse sequence; shaded items indicate untranslated regions; stippled region indicates other sequence.

[00085] **Figure 2** depicts human IL-7 concentration in serum of wild-type mice that has a genetic background of 75% C57B6 and 25% 129/SvJ (75/25 WT) and mice heterozygous for a humanized endogenous IL-7 locus as described herein (5148 Het).

DETAILED DESCRIPTION

[00086] In various embodiments, non-human animals are described that comprise the genetic modification(s) described herein. The genetically modified non-human animal may be selected from a group consisting of a mouse, rat, rabbit, pig, bovine (*e.g.*, cow, bull, buffalo),

deer, sheep, goat, chicken, cat, dog, ferret, primate (*e.g.*, marmoset, rhesus monkey). For the non-human animals where suitable genetically modifiable ES cells are not readily available, other methods are employed to make a non-human animal comprising the genetic modification. Such methods include, *e.g.*, modifying a non-ES cell genome (*e.g.*, a fibroblast or an induced pluripotent cell) and employing nuclear transfer to transfer the modified genome to a suitable cell, *e.g.*, an oocyte, and gestating the modified cell (*e.g.*, the modified oocyte) in a non-human animal under suitable conditions to form an embryo.

[00087] In one aspect, the non-human animal is a mammal. In one aspect, the non-human animal is a small mammal, *e.g.*, of the superfamily *Dipodoidea* or *Muroidea*. In one embodiment, the genetically modified animal is a rodent. In one embodiment, the rodent is selected from a mouse, a rat, and a hamster. In one embodiment, the rodent is selected from the superfamily *Muroidea*. In one embodiment, the genetically modified animal is from a family selected from *Calomyscidae* (*e.g.*, mouse-like hamsters), *Cricetidae* (*e.g.*, hamster, New World rats and mice, voles), *Muridae* (true mice and rats, gerbils, spiny mice, crested rats), *Nesomyidae* (climbing mice, rock mice, with-tailed rats, Malagasy rats and mice), *Platacanthomyidae* (*e.g.*, spiny dormice), and *Spalacidae* (*e.g.*, mole rates, bamboo rats, and zokors). In a specific embodiment, the genetically modified rodent is selected from a true mouse or rat (family *Muridae*), a gerbil, a spiny mouse, and a crested rat. In one embodiment, the genetically modified mouse is from a member of the family *Muridae*. In one embodiment, the animal is a rodent. In a specific embodiment, the rodent is selected from a mouse and a rat. In one embodiment, the non-human animal is a mouse.

[00088] In various embodiments, the non-human animal is a rodent that is a mouse of a C57BL strain selected from C57BL/A, C57BL/An, C57BL/GrFa, C57BL/KaLwN, C57BL/6, C57BL/6J, C57BL/6ByJ, C57BL/6NJ, C57BL/10, C57BL/10ScSn, C57BL/10Cr, and C57BL/Ola. In another embodiment, the mouse is a 129 strain selected from the group consisting of a strain that is 129P1, 129P2, 129P3, 129X1, 129S1 (*e.g.*, 129S1/SV, 129S1/SvIm), 129S2, 129S4, 129S5, 129S9/SvEvH, 129S6 (129/SvEvTac), 129S7, 129S8, 129T1, 129T2 (see, *e.g.*, Festing *et al.* (1999) Revised nomenclature for strain 129 mice, Mammalian Genome 10:836, *see also*, Auerbach *et al* (2000) Establishment and Chimera Analysis of 129/SvEv- and C57BL/6-Derived Mouse Embryonic Stem Cell Lines). In a specific embodiment, the genetically modified mouse is a mix of an aforementioned 129 strain and an aforementioned C57BL/6 strain. In another specific embodiment, the mouse is a mix of aforementioned 129 strains, or a mix of aforementioned BL/6 strains. In a specific embodiment, the 129 strain of the mix is a 129S6 (129/SvEvTac) strain. In another embodiment, the mouse is a BALB strain, *e.g.*,

BALB/c strain. In one embodiment, the mouse is a mix of a BALB strain and another aforementioned strain.

[00089] In one embodiment, the non-human animal is a rat. In one embodiment, the rat is selected from a Wistar rat, an LEA strain, a Sprague Dawley strain, a Fischer strain, F344, F6, and Dark Agouti. In one embodiment, the rat strain is a mix of two or more strains selected from the group consisting of Wistar, LEA, Sprague Dawley, Fischer, F344, F6, and Dark Agouti.

[00090] Genetically modified non-human animals that comprise a replacement of a non-human IL-7 gene sequence with a human IL-7 gene sequence are provided. Rodents that comprise a humanization of an IL-7 gene, at an endogenous rodent IL-7 locus, are provided. Methods for making rodents, *e.g.*, mice, that comprise a replacement of an endogenous IL-7 gene or fragment thereof (*e.g.*, a fragment comprising one or more exons) with a humanized IL-7 gene, or fragment thereof (*e.g.*, a fragment comprising one or more exons), at the endogenous IL-7 locus. Cells, tissues, and mice are provided that comprise the humanized gene are provided, as well as cells, tissues, and mice that express human IL-7 from an endogenous non-human IL-7 locus. Exemplary flanking genomic sequences of a humanized IL-7 gene of the present invention are provided in SEQ ID NO: 1 (5' flanking sequence) and SEQ ID NO: 2 (3' flanking sequence). An exemplary human IL-7 gene of the present invention is provided in SEQ ID NO: 3.

[00091] IL-7 is a cytokine that is essential for development of immature B and T cells and, to some degree, mature T cells; IL-7 knockout mice display a severe depletion of mature B and T cells (von Freeden-Jeffry U. *et al.* (1995) Lymphopenia in interleukin (IL)-7 gene-deleted mice identifies IL-7 as a nonredundant cytokine, *J. Exp. Med.* 181:1519-1526). The depletion is apparently due to a block between pro-B and pre-B cells, and a block in T cell proliferation (rather than a block in T cell differentiation; ratios of T cell types in IL-7 KO mice are about normal) that results in a depressed population of T cells and mature B cells (*Id.*). IL-7 is produced by epithelial cells in the thymus and intestine, in keratinocytes, liver, and dendritic cells—but not by normal lymphocytes (reviewed, *e.g.*, in Fry T.J. and Mackall, C.L. (2002) Interleukin-7: from bench to clinic, *Blood* 99(11):3892-3904).

[00092] Simply put, IL-7 increases T cell number and enhances T cell function (see, *e.g.*, Morrissey, J.J. (1991) Administration of IL-7 to normal mice stimulates B-lymphopoiesis and peripheral lymphadenopathy, *J. Immunol.* 147:561-568; Faltynek, C.R. *et al.* (1992) Administration of human recombinant IL-7 to normal and irradiated mice increases the numbers of lymphocytes and some immature cells of the myeloid lineage, *J. Immunol.* 149:1276-1282; Risdon, G.J. *et al.* (1994) Proliferative and cytotoxic responses of human cord blood T

lymphocytes following allogenic stimulation, *Cell. Immunol.* 154:14-24). Functional enhancement of T cells can be achieved by a short duration of IL-7 exposure, whereas increases in T cell number reflect a proliferative effect that is achieved with a longer duration exposure (Geiselhart, L.A. *et al.* (2001) IL-7 Administration Alters the CD4:CD8 Ratio Increases T Cell Numbers, and Increases T Cell Function in the Absence of Activation, *J. Immunol.* 166:3019-3027; see also, Tan J.T. *et al.* (2001) IL-7 is critical for homeostatic proliferation and survival of naïve T cells, *Proc. Natl. Acad. Sci. USA* 98(15):8732-8737).

[00093] IL-7 is necessary for both early and late stage T cell regulation. IL-7 is not expressed by T cells, which must encounter IL-7 that is released by non-thymic cells in the periphery and that is believed to be responsible for peripheral T cell proliferation and maintenance (reviewed, *e.g.*, in Guimond, M (2005) Cytokine Signals in T-Cell Homeostasis, *J. Immunother.* 28(4):289-294). IL-7 starvation results in severely impaired T cell development and survival of naïve T cells. IL-7 also appears to be necessary for the survival of mature T cells; mature T cells acquired through adoptive transfer into IL-7-deficient mice enter apoptosis where the mice lack an IL-7 gene, but not in mice that express IL-7 that lack an IL-7R gene (Schluns, K.S. *et al.* (2000) Interleukin-7 mediates the homeostasis of naïve and memory CD8 T cells *in vivo*, *Nat. Immunol.* 1(5):426-432. Loss of IL-7 function results in a SCID-like phenotype in mice (Puel, A. and Leonard, W.J. (2000) Mutations in the gene for the IL-7 receptor result in T(-)B(+)NK(+) severe combined immunodeficiency disease, *Curr. Opin. Immunol.* 12:468-473), presumably due to T cell atrophy and death caused by diminished growth rate likely mediated by glycolytic insufficiency in the absence of IL-7 stimulus (Jacobs, S.R. *et al.* (2010) IL-7 Is Essential for Homeostatic Control of T Cell Metabolism *In Vivo*, *J. Immunol.* 184:3461-3469).

[00094] The human IL-7 gene comprises 6 exons that extend over 33 kb and is located on chromosome 8 at 8q12-13. Mouse IL-7 comprises 5 exons (there is no counterpart in mouse to human exon 5) and is about 80% homologous to the human gene; analysis of non-coding sequences of the human and the mouse genes revealed a paucity of recognizable regulatory motifs responsible for transcription and regulation of gene expression (Lupton, S.D. *et al.* (1990) Characterization of the Human and Murine IL-7 Genes, *J. Immunol.* 144(9):3592-3601), suggesting that regulation of IL-7 expression may be complex. However, mouse BAC fragments comprising a reporter gene at the hIL-7 locus have been expressed in mice to successfully ascertain expression patterns of IL-7 in mice (see, *e.g.*, Avles, N.L. *et al.* (2009) Characterization of the thymic IL-7 niche *in vivo*, *Proc. Natl. Acad. Sci. USA* 106(5):1512-1517; Mazzucchelli, R.I. (2009) Visualization and Identification of IL-7 Producing Cells in Reporter Mice, *PLoS ONE* 4(11):e7637; Repas, J.F. *et al.* (2009) IL7-hCD25 and IL7-Cre BAC

transgenic mouse lines: new tools for analysis of IL-7 expressing cells, *Genesis* 47:281-287). In at least one case, a BAC-based replacement of an IL-7 exon with a reporter required the entire 43 kb IL-7 locus as well as 96 kb of 5' flanking sequence and 17 kb of 3' flanking sequence in the hope of faithfully recapitulating IL-7 expression of wild-type mice (Repass, J.F. *et al.* (2009)). In any case, data from the different studies on reporter expression driven by putative IL-7 regulatory elements vary somewhat from one another and from earlier observations, supporting an inference that IL-7 regulation might not have been faithfully recapitulated in these reporter mice (IL-7 reporter transgenic mice are reviewed in Kim, G.Y. *et al.* (2011) Seeing Is Believing: Illuminating the Source of *In Vivo* Interleukin-7, *Immune Network* 11(1):1-10). Human IL-7 is functional on mouse cells, but mouse IL-7 is not functional on human cells.

[00095] Transgenic mice that express abnormally or poorly regulated human IL-7 exhibit a panoply of pathologies or syndromes. Mice transgenic for a murine IL-7 cDNA under control of mouse Ig heavy chain enhancer, κ light chain enhancer, and light chain promoter) to target expression in the lymphoid compartment) exhibit significantly enhanced numbers of B cell precursors and an overall expansion of all subsets of thymocytes in the thymus and peripheral T cells (Samaridis, J. *et al.* (1991) Development of lymphocytes in interleukin 7-transgenic mice, *Eur. J. Immunol.* 21:453-460).

[00096] Transgenic mice that express IL-7 from a mouse cDNA under control of an SR α promoter develop a panoply of pathologies, including a chronic colitis that histopathologically mimics chronic colitis in humans, and is characterized by at least a transient over-expression of IL-7 in colonic mucosal lymphocytes (but not colonic epithelial cells) and its apparent accumulation in mucus of goblet cells of the colonic mucosa (Watanabe, M. *et al.* (1998) Interleukin 7 Transgenic Mice Develop Chronic Colitis with Decreased Interleukin 7 Protein Accumulation in the Colonic Mucosa, *J. Exp. Med.* 187(3):389-402; Takebe, Y. *et al.* (1988) sR α promoter: an efficient and versatile mammalian cDNA expression system composed of the simian virus 40 early promoter and the R-U5 segment of human T-cell leukemia virus type 1 long terminal repeat, *Mol. Cell Biol.* 8(1):466-472). Constitutive expression of mouse IL-7 driven by the same promoter in transgenic mice also develop a severe dermatitis characterized by gross deformities and a massive dermal infiltration of mononuclear cells that are mostly TCR $\gamma\delta$ cells (Uehira, M. *et al.* The development of dermatitis infiltrated by $\gamma\delta$ T cells in IL-7 transgenic mice, *Intl. Immunol.* 5(12):1619-1627). Transgenic mice expressing a murine IL-7 cDNA driven by a murine heavy chain promoter and enhancer also exhibited dermatitis and lymphoproliferation into the dermis, but reportedly of TCR $\alpha\beta$ cells and cells that express Thy-1, CD3, and CD5 but lack CD4 and CD8 (CD4⁺/CD8⁺ thymocytes are virtually absent from these transgenic mice); these mice also developed B and T cell lymphomas, presumably associated

with a prolonged lymphoproliferation observed in these mice (see, Rich, B.E. *et al.* (1993) Cutaneous lymphoproliferation and lymphomas in interleukin 7 transgenic mice, *J. Exp. Med.* 177:305-316).

[00097] Dysregulation of the IL-7 gene is associated with a variety of pathological states. Mice expressing transgenic mouse IL-7 under control of the MHC class II E α promoter are highly prone to lymphoid tumors (see, *e.g.*, Fisher, A.G. *et al.* (1995) Lymphoproliferative disorders in IL-7 transgenic mice: expansion of immature B cells which retain macrophage potential, *Int. Immunol.* 7(3):414-423; see, also, Ceredig, R. *et al.* (1999) Effect of deregulated IL-7 transgene expression on B lymphocyte development in mice expressing mutated pre-B cell receptors, *Eur. J. Immunol.* 29(9):2797-2807). T cell sizes are also larger in the transgenic mice, and a polyclonal T cell expansion is observed (predominantly CD8⁺, indicating a perturbed regulation in these mice) (Mertsching, E. *et al.* IL-7 transgenic mice: analysis of the role of IL-7 in the differentiation of thymocytes *in vivo* and *in vitro*, *Intl. Immunol.* 7(3):401-414). Other transgenic mice that over-express mIL-7 (by about 25-50-fold) through the MHC class II E α promoter appear grossly healthy (but for a low incidence of B cell tumors) and exhibit a 10-20-fold increase in T cell number over wild-type mice, characterized by large numbers of CD8⁺ cells that are also CD44^{hi} and CD122^{hi} (Kieper W.C. *et al.* (2002) Overexpression of Interleukin (IL)-7 Leads to IL-15-independent Generation of Memory Phenotype CD8⁺ T Cells, *J. Exp. Med.* 195(12):1533-1539).

[00098] Mice that constitutively express mouse IL-7 from a cDNA under control of the MHC class II E α promoter selectively expand IL-7-responsive early B cells, and are a good source of tumors comprising pro-B and pre-B cells. Mice that express IL-7 driven by a human K14 promoter develop a lymphoproliferative response that results in T cell infiltrates of skin that resemble alopecia.

[00099] Mice transgenic for IL-7R display large reductions in double negative (CD4-CD8-) precursor cells in thymus, presumably due to depletion of IL-7 by the large number of double positive thymocytes in the transgenic mice, suggesting that IL-7 levels must be exquisitely controlled to promote normal thymocyte development (see, *e.g.*, Malek, T.R. (2004) IL-7: a limited resource during thymopoiesis, *Blood*, 104(13):2842).

[000100] As early as the cloning of human IL-7, it has been known that human IL-7 can induce proliferation of murine pre-B cells (Goodwin, R.G. *et al.* (1989) Human interleukin 7: Molecular cloning and growth factor activity on human and murine B-lineage lines, *Proc. Natl. Acad. Sci. USA* 86:302-306). Although expressed in certain chronic lymphocytic leukemia cells, expression of mouse IL-7 in tumor cells implanted in mice induce inflammation and reduced tumorigenicity, yet paradoxically mice transgenic for IL-7 are prone to lymphomas

(reviewed in Foss, H.-D. *et al.* (1995) Frequent Expression of IL-7 Gene Transcripts in Tumor Cells of Classical Hodgkin's Disease, *Am. J. Pathol.* 146(1):33-39). Thus, it is desirable to obtain mice that express human IL-7 (but not mouse IL-7) from endogenous mouse IL-7 loci in a physiologically relevant fashion, in particular but not limited to mice that comprise human or mouse tumors, *e.g.*, lymphocytic tumors.

[000101] Mice that express human IL-7 in a physiologically relevant manner are also useful for evaluating anti-tumor properties of putative therapeutics (including human IL-7 and analogs thereof) in xenograft models of human solid tumors in mice. For example, SCID mice implanted with HT29 human colon adenocarcinoma and tested under a variety of conditions (*e.g.*, ablation of native T cells and addition of human T cells; addition of recombinant human IL-7, *etc.*) (see, Murphy, W.J. *et al.* (1993) Antitumor Effects of Interleukin-7 and Adoptive Immunotherapy on Human Colon Carcinoma Xenografts, *J. Clin. Invest.* 92:1918-1924). That study found that human IL-7 when administered with human T cells resulted in a significantly prolonged survival than in the absence of human IL-7 (*Id.*).

[000102] Thus, mice that express human IL-7, in particular mice that are capable of supporting a xenograft (*e.g.*, a human tumor), such as, *e.g.*, immunodeficient mice, have a specific and a well-established utility. IL-7 signaling has been shown to be necessary for development and survival of human T-cell acute lymphoblastic leukemias (T-ALL) *in vitro* and *in vivo*. (Touw, I. *et al.* (1990) Interleukin-7 is a growth factor of precursor B and T acute lymphoblastic leukemia. *Blood* 75, 2097–2101) T-ALL is an aggressive hematological cancer with poor prognosis; the understanding of mechanisms driving proliferation and survival of T-ALL cells remains relatively poor due to lack of xenograft models that can support the growth of patient derived tumors *in vivo*. Thus, an immunodeficient animal expressing human IL-7 can serve as an invaluable *in vivo* system for testing pharmaceutical compositions against such T-cell related malignancies, *e.g.*, testing the efficacy of a pharmaceutical composition to target IL-7-mediated signaling in a mouse that expresses human IL-7 and has an implanted T-cell derived tumor, wherein the tumor requires IL-7 signaling for development and survival.

EXAMPLES

Example 1. Humanizing the Mouse IL-7 Locus

[000103] Mouse ES cells were modified to replace mouse IL-7 gene sequences with human IL-7 gene sequences at the endogenous mouse IL-7 locus, under control of mouse IL-7 regulatory elements, using VELOCIGENE® genetic engineering technology, to produce a humanized locus as shown in FIG. 1.

[000104] Targeting Construct. Bacterial homologous recombination (BHR) is performed to construct a large targeting vector (LTVEC) containing the human IL-7 gene for targeting to the mouse IL-7 locus using standard BHR techniques (see, *e.g.*, Valenzuela *et al.* (2003) High-throughput engineering of the mouse genome coupled with high-resolution expression analysis, Nature Biotech. 21(6):652-659). Linear fragments are generated by ligating PCR-generated homology boxes to cloned cassettes followed by gel isolation of ligation products and electroporation into BHR-competent bacteria harboring the target bacterial artificial chromosome (BAC). Mouse BAC bMQ-271g18 is used as the source of mouse sequence; human BAC RP11-625K1 is used as the source of human sequence. Following a selection step, correctly recombined clones are identified by PCR across novel junctions, and by restriction analysis. A large targeting vector (LTVEC) containing the homology arms and human IL-7 gene sequences was made. Mouse ES cells were electroporated with the LTVEC constructs, grown on selection medium, and used as donor ES cells to make humanized IL-7 mice.

[000105] The mouse IL-7 gene (mouse Gene ID: 96561; Ref Seq transcript: NM_008371.4) is modified by deleting exons 2 through 5 (deletion coordinates NCBI37:chr3:7604650-7573021; minus strand) and replacing them with human IL-7 (Entrez Gene ID: 6023; Ref Seq transcript NM_000880.3) exons 2 through 6 (replacement coordinates GRCh37Lch*:79711168-79644608; minus strand). The human genomic IL-7 sequence is provided in SEQ ID NO: 3 (NC#166E2F2). The mouse genomic IL-7 locus is known and reported as a 41,351 nt sequence under accession number NC0000696 (hereby incorporated by reference); relevant 5' and 3' sequences of the mouse IL-7 genomic locus are provided in SEQ ID NO:1 (5' flanking) and SEQ ID NO:2 (3' flanking).

[000106] The LTVEC comprising the humanized IL-7 gene had a 48 kb upstream mouse targeting arm flanked upstream with a NotI site, and a 77 kb downstream mouse targeting arm flanked downstream with a NotI site. The LTVEC was linearized with NotI for electroporation.

[000107] Following construction of the LTVEC, nucleotide sequence of the LTVEC was obtained across the mouse/human 5' junction, which included, from 5' (mouse) to 3' (human), the following sequence with the mouse/human junction nucleotides in parenthesis: 5' - TGCAAGCACC AAAAAGGTGA CCACACTTCA CATTGGCGAT CGC(GG)GTTTC TATCTGAGGA TGTGAATTGA TTTACAGA - 3' (SEQ ID NO: 4).

[000108] Nucleotide sequence of the LTVEC across the junction of the human insertion and the 5' end of the cassette (see FIG. 1) was determined and included the following sequence having, from 5' to 3', human sequence/restriction site/loxP/cassette sequence with the human sequence/restriction site junction nucleotides in parenthesis: 5' - GTTATGTGCT GATGGGCTTT ATTTGATCTA CAGAAGATGC TCTGGTGACA CCCTCAGTGT

GTGTTGGTAA CACCTTCCTG (CC)TCGAGATA ACTTCGTATA ATGTATGCTA
TACGAAGTTA TATGCATGGC CTCCGCGCCG GGTTTTGGCG CC – 3' (SEQ ID NO: 5).

[000109] Nucleotide sequence of the LTVEC across the junction of the end of the cassette and the beginning of mouse sequence was determined and included the following sequence having, from 5' to 3', cassette sequence/restriction site/mouse sequence with the junction nucleotides in parenthesis: 5' – GTATGCTATA CGAAGTTATG CTAGTAACTA TAACGGTCCT AAGGTAGCGA GCTAG(CC)CAA TTGCGTACTT TGGATAGTGT CTCTTTTAA CCTAAATGAC CTTTATTAAC ACTGTCAGGT TCCCTTACTC TCGAGAGTGT TCATTGCTGC ACT – 3' (SEQ ID NO: 6).

[000110] Following electroporation of the ES cell, a loss of native allele assay (see, *e.g.*, Valenzuela *et al.* (2003)) is performed to detect loss of endogenous IL-7 sequence due to the targeting. Primer pairs, fragment sizes, and TAQMAN™ probes are as shown in Table 1. The C1 probe binds the mouse IL-7 genomic sequence (NC0000696) at nts 9,635-9,664; the C2 probe binds the mouse IL-7 genomic sequence (NC0000696) at nts 39,793-39,825. For a gain of allele assay, the C3 probe binds the human IL-7 genomic sequence (NC#166E2F2) at nts 29,214-29,242.

TABLE 1. LTVEC Primers and Probes

Primer		Sequence (5' to 3')	Size (bp)
Primer Pair C1 C1 TAQMAN™ probe	Forward	TTGCATTCTT TTCCAAATAA GTGG (SEQ ID NO: 7)	81
	Reverse	TTCCAGGATG AATAGGATAA ACAGG (SEQ ID NO: 8)	
		ATCCATCATC ACTCCCTGTG TTTGTTTCCC (SEQ ID NO: 9)	
Primer Pair C2 C2 TAQMAN™ probe	Forward	AGCTGACTGC TGCCGTCAG (SEQ ID NO: 10)	125
	Reverse	TAGACTTTGT AGTGTTAGAA ACATTTGGAA C (SEQ ID NO: 11)	
		ATTTTGTAA TGCAATCATG TCAACTGCAA TGC (SEQ ID NO: 12)	
Primer Pair C3 C3 TAQMAN™ probe	Forward	CTCACTCTAT CCCATCCAAG GG (SEQ ID NO: 13)	74
	Reverse	ATGGGCAGGT AGCATCCACA G (SEQ ID NO: 14)	
		TGAATCATCC CTTTGTCTAG CAGAACCGG (SEQ ID NO: 15)	

Example 2. Humanized IL-7 Mice

[000111] Generating humanized IL-7 mice. Donor mouse ES cells comprising a humanized IL-7 locus are introduced into early stage mouse embryos by the VELOCIMOUSE® method (Poueymirou *et al.* (2007) F0 generation mice fully derived from gene-targeted embryonic stem cells allowing immediate phenotypic analyses, *Nat Biotechnol* 25:91-99). Four F0 mice fully derived from donor ES cells were obtained that were heterozygous for humanization of the endogenous mouse IL-7 locus. F0 mice are bred to homozygosity with respect to the humanization. Homozygous mice are genotyped to confirm homozygosity. All

mouse studies were overseen and approved by Regeneron's Institutional Animal Care and Use Committee (IACUC).

Example 3. Expression of Human IL-7 in a Mouse

[000112] Mice humanized for the IL-7 gene and their non-humanized littermate controls were bled and serum concentrations of human IL-7 were measured using QuantikineHS Human IL-7 Immunoassay kit from R&D Systems, Inc. Data was analyzed using Microsoft Excel and plotted using Prism statistical analysis software. Mice heterozygous for the humanized IL-7 locus (designated MAID 5148 het) expressed human IL-7 in serum at a physiologically relevant concentration. This is in contrast to transgenic human IL-7 mice bearing lentivirally transduced human IL-7 in double knockout mice, which mice exhibit unphysiologically and potentially seriously detrimental high levels of human IL-7 in serum (10 to 100 pg/mL) (O'Connell, R.M. *et al.* (2010) Lentiviral Vector Delivery of Human Interleukin-7 (hIL-7) to Human Immune System (HIS) Mice Expands T Lymphocyte Populations, PLoS ONE 5(8):e12009). In contrast, mice heterozygous for a humanized endogenous IL-7 locus exhibited about 2.4 to about 3.2 pg/mL in serum (FIG. 2), reflecting normal, or physiologically appropriate, levels of IL-7.

I claim:

1. A mouse whose genome comprises a replacement of at least mouse IL-7 exons 2, 3, 4, and 5 with a human genomic segment comprising human IL-7 exons 2, 3, 4, 5, and 6 to form a human or humanized IL-7-encoding gene, wherein the replacement is at an endogenous mouse IL-7 locus, wherein the human or humanized IL-7-encoding gene is under control of endogenous mouse IL-7 regulatory elements, and wherein the mouse comprises human or humanized IL-7 in serum at a level that is about the same level of endogenous mouse IL-7 in serum of an age matched wild-type mouse.
2. The mouse of claim 1, wherein the level is 2.4 to 3.2 pg/mL.
3. The mouse of claim 1, wherein said replacement forms a human IL-7-encoding gene, and wherein the mouse comprises human IL-7 in serum at a level that is about the same level of endogenous mouse IL-7 in serum of an aged-matched wild-type mouse.
4. A method for making a mouse with a human or humanized IL-7-encoding gene, comprising modifying the genome of a mouse by replacing at the endogenous mouse IL-7 gene locus at least mouse exons 2, 3, 4 and 5 of the endogenous mouse IL-7-encoding gene with a human genomic segment comprising human IL-7 exons 2, 3, 4, 5, and 6 to form a human or humanized IL-7-encoding gene, wherein the human or humanized IL-7-encoding gene is under control of endogenous mouse IL-7 regulatory sequences, and wherein the mouse comprises human or humanized IL-7 in serum at a level that is about the same level of endogenous mouse IL-7 in serum of an aged-matched wild-type mouse.
5. The method of claim 4, wherein the level is 2.4 to 3.2 pg/mL.
6. The method of claim 4, wherein said human or humanized IL-7 gene encodes human IL-7, and wherein the mouse comprises human IL-7 in serum at a level that is about the same level of endogenous mouse IL-7 in serum of an aged-matched wild-type mouse.

SEQUENCE LISTING

<110> Regeneron Pharmaceuticals, Inc.

<120> Humanized IL-7 Rodents

<130> 2010794-0291

<150> US 61/660,976

<151> 2012-06-18

<150> US 61/740,074

<151> 2012-12-20

<150> US 13/795,765

<151> 2013-03-12

<160> 15

<170> PatentIn version 3.5

<210> 1

<211> 8777

<212> DNA

<213> Mus musculus

<220>

<221> misc_feature

<222> (1)..(8777)

<223> Mouse 5' genomic sequence present in humanized IL-7 mouse (from NC0000696)

<400> 1

ggcagatcct	acggaagtta	tggcaaagcc	agagcgccctg	ggtggccggt	gatgcatgcg	60
gccccctcttg	ggatggatgg	accaggcgtg	gcgtgggtga	gaggagtcag	ctgcctgaac	120
tgccctgccc	agcaccggtt	tgcggccacc	cggtggatga	ccggggtcct	gggagtgatt	180
atgggtggtg	agagccggtc	cctgctgcag	tcccagtcac	catgactaca	cccacctccc	240
gcagaccatg	ttccatggta	agcgctgctc	tctggtgcgc	acaagtaggt	gcgcctagcg	300
cgccggggac	tctgggacag	tccgggaggt	gccacccgcc	cccgcgcctc	cgcacgtccg	360
ggaatagccc	ggccttgac	tttggacagg	ctgagagctt	ggcctctccc	atggtcagcc	420
actaccgcgc	ctgagctcgc	ttgcccagaa	ccattggcac	ctgggcgtac	aaccctggcg	480
ggcggggagg	aacagttccc	gaggcggttt	tcagatcccc	agaccagag	cttcagtgcg	540
ggagcgcgca	cgcggtggcc	ccctgcagtc	aagactcagt	agtcagtggg	tttcagccac	600
tttgtcccta	gccagtacct	cttcaatgca	gcccttcctg	gcttcctggc	tgtgcagtta	660
ctcacaggct	gcctgggttc	agggcgttgc	tgggctctcg	cagctcagaa	cttcattggag	720
aatgaaagag	tcgctcccag	gatgcgcttt	taaaccctaa	aggacagatc	attggaaaac	780
cccctcttct	ccccgcagta	agtctgggag	tttccgatcc	aggctgtaag	ttgacttggt	840
tgctgggaac	ccaagtccctg	cggctgagat	tgcaaaaggc	cagattttat	tttccttcta	900
tatatattgct	acttaaggga	ggcagaactt	taagtaccca	tgagtacaaa	ttcttagctc	960
cctgatcaaa	tctaataaggc	ttgcattagt	tttaaataag	taaggattta	aagtggacaa	1020
gaacagaatt	gacagaggct	ggaatccatt	tgtagctaga	actaatagag	atgagaacag	1080
aatggagtgt	gaggaggtct	acctaaggga	atgcaggtgt	tttaaatact	tcctcaagca	1140
agagaacctta	tggaggtgca	ggatctagcc	taaggctctt	tccttttgca	acccattgca	1200
aaaccattgt	attggtttcc	ggccactgtt	tttaggtaca	attacttccc	ctctcttagg	1260
tactagcgaa	ccaaaacat	ttgaggaggt	acttatcaga	aaccaataaa	aagatgtgga	1320
gacctgagag	actgcccgaag	aaaatgatgg	aaggctgcca	aggtgccccct	gcaggagctc	1380
actgtacagc	tagagacacc	gcacccctgt	cttctttgca	atgccctggg	ttctgaaatt	1440
gcctttcact	ttaacctttg	gattacctac	aacctggaga	gataaaagga	caaaggaaaa	1500
gcaaagggtgt	aatttaaacy	aggaggcttt	tccatttgag	atacatccat	atcggacatg	1560
ccttatTTTT	ttagtaaaga	aaatatgaaa	atattaaact	cacgggagtt	aaagtaagtg	1620
gctTTTTTTT	tttctttcat	tttcgggtcca	aaatttacta	gaggcggtggg	taaactccat	1680
caaggctgtg	tgctgtgttt	ccactttgtt	atgtcgggac	accaagtaaa	caaggattca	1740

ctcgctgacg	ctcaattgtg	ctgcctcatt	atgaatcagc	atacatttta	tttgtatact	1800
aataaaagga	aacaatgaga	aacatagagc	cttggaata	tggaggaagc	ctgaagatct	1860
atctgtaaag	gagaattaga	aatttcatct	cagtgtgtat	acttcttgaa	caaaaatgga	1920
aagttctttt	ataaaaccaa	tctcatggcc	catgggtatg	aagtactggt	atcctgactc	1980
ttgacagata	attttgtttt	ttaattaatt	tatttttatt	ccttaatctt	tttttttaca	2040
gtacagactt	tatacctctc	ctgttctgcc	ccccccact	gctctctccc	ccatacctcc	2100
tccccagccc	ccacctccac	cctgactcca	agagaatgcc	ctcatccccc	atgccactag	2160
gcctccccac	tccctggggc	ttcaagtttc	tcaacagtta	ggtgcctctt	ctctcactga	2220
ggccagacca	ggcagtcctc	tgctctatat	gtgttgggga	cagacaactt	tataatatgt	2280
agaaatattt	actttttccc	ttgaaatagg	agcatacgct	gtagtttcag	agcttgacca	2340
agaagcccct	tcatgtagaa	gacaatgaat	atttgtactt	cctctcacta	tctgtgcatg	2400
cagttatggt	gtaggaagtg	taattcagta	gctaatagcg	gattccctag	acacctcaac	2460
ccgaacatca	aatgcagctc	ctgaatccct	agaaaaattg	ttttggagaa	ttgttctttg	2520
ggctccagat	tctctactgt	aaactgctag	tgacctgtat	atatatatat	atatatatat	2580
atatgtatca	tgaaatggct	ataaaattga	attatttggt	gaaatagact	tgggaaagga	2640
cattgaaaaga	acacttctca	aggaggatgg	gaaagtcctc	aagggtctcaa	ccctagacaa	2700
actgttcagg	ccacgaagaa	atgctgactg	acagtggaga	aatagacatc	cccagagagg	2760
agcatacaaa	ttgtttatcc	aaacagccag	ccctgaagac	atatgtgcaa	gtaaggttat	2820
acagactggg	caggttgact	ttatgtattt	agggagatag	atggatgata	gctagctagc	2880
tagctagagc	acaacactta	atgaaataaa	aggtcatgaa	tttgaaatag	agcaagaaag	2940
gatatatatg	agagtttagg	ggaagaaatt	gattgaggaa	ataaaataat	gatgttgtaa	3000
tctcaaaaaac	taaaagaaac	tgatagatga	caggatatga	tggactgagg	aatccaattt	3060
tattatgtcc	actttgacct	cataacttaa	gcagttgaag	attgtatgta	ttatttggct	3120
tacattttaa	accaacaaga	atttttagac	agctatcatt	ctggtttaac	caaattcccc	3180
actgaaaaca	aattctccag	tttcaaaccc	tgtaaagcgt	ttaaagacaa	tactacaagc	3240
caacacttgt	cttgaatgct	ttctacagtt	tgttttatct	gtgacctaat	gaaaagttca	3300
gtggaggctg	aggagtgagc	tataaatcaa	aagtaacaaa	atatggttaag	tgctgaattc	3360
ggatgccatt	gggacaaaag	tgttaaataa	actttcaaac	cagaaaaata	ttaacttggt	3420
acggtgcttg	tatgtggaag	aaataactgt	aaccacagaa	caaaggtcac	actcctgatg	3480
gtggagccag	aaaccatgg	gatcatacat	tatcatacat	atcatacatt	agagagcctg	3540
gaaggttttc	attttagaaa	tcagggccag	gaagctgaaa	tgaaactcag	ctatttagtc	3600
agttacacaa	aatcctaaat	tctctatgct	ctaaatctcc	ttgtttataa	tatatatact	3660
atttatatgt	attataaaat	attaagtata	tattataata	tattaaaata	tgtatggtag	3720
tgctctgggc	tgtcagcagc	tactttactt	gattgaaata	gtctacaaat	gaagggtggt	3780
attgtaaaaa	tagtatagaa	ttgaaaattt	cacgtaaacac	acacatgtat	tatcaaagca	3840
agtgtgaagc	aatgaaaaag	tgctgcccgg	tgagggtgta	ggtcacatca	ttctgggaag	3900
cacatatctc	agaagaaaac	tggaactctt	ggaaagtatg	gcaaatgaac	ttattgaaac	3960
aggaaatgga	ctttgaaatg	acttttagat	atagggtgcga	attaatctct	tttactaac	4020
catcataact	ttctcctttg	agttcaagtc	acattccctg	tctctttcat	ttgcctggtc	4080
cccccaaaaa	cataattttt	agggacctat	aaggcaaaaag	atgaaataaa	aagccagttt	4140
ctacaaaaaa	tgtagatggc	tataatccaa	ttgagtagta	attgatacct	gtgtatccca	4200
gtgaagggca	gtcataggag	aaggctgatg	aatggtagta	tgagaagggt	cctttcaaac	4260
agaatagcag	cagataaagat	gttatcaatt	gattatgggt	atttaaaaagt	gattgtcatt	4320
ttctccccct	cttgaagcag	atatagatca	gattaggcca	gattaaaagt	agataaaggc	4380
agttttgtta	ggaatccccct	ctctgggtgg	ttcatccatc	tcacagggtg	aagtcagtga	4440
agtcacacag	ccaggctaaa	gcatgggggt	tttatagagc	ttaagcaggg	agtagtgatg	4500
tgccagaagg	agctaggatg	gtgtccatac	gtggtcaaaa	actgagcccc	tgggtgggcac	4560
tctgggggtg	gttgaggaa	cccagggatg	agacatggcg	acttattggc	ctagagtttt	4620
ttgtttttgt	ttttgttttt	cccaagcagg	ggttccgggt	gcaggcaggg	ttggggaaaag	4680
gagggtagct	tccaagtggg	gtttccctgc	ttgttcagaa	tatgagcagg	agttccagcc	4740
taacaccccc	acctcttggg	gtatagatac	agccacactc	tgctgaagag	ggacgggaga	4800
gttgggagcg	ggtgggatca	tactcatctg	caggcatgct	gtaggaccat	tcgggtggtg	4860
gttacttaga	aacttttatg	aatccgtttc	tggtgaaga	gaaggtagca	aggtgctagg	4920
aagatgtgca	tgtgcaagg	gctaggaaga	ctgaggctag	ccatgtgaag	agtaacactg	4980
ctagagagaa	ttgaatgtgt	cttgggtgtg	ttgtgggaac	tcttttagaca	atttgcgagg	5040
tgactctgtc	caggtctcca	caaggccaga	ctcactgatg	taagagtggc	agggacatgc	5100
agatgccgcc	cttaccagtc	atgaggatac	ttttagggcc	attgaagcct	ataagaatct	5160
tattaagttt	acagagagag	agagagagag	agagagagag	acagacagac	agacagacag	5220
acagacacag	agacagacag	agacagagat	tttagacatg	ttagacagta	gacttatacc	5280
ttttgtcat	agtacaggct	tcggaaacat	taaaatttga	ttattattaa	agcttttgaa	5340
tttgaattct	taataataaca	gaaacatagc	taggggaaga	atctgaagca	tttttttaaa	5400
aaaatatatt	ttatgtcatt	ttttctcttt	tgtcttttaa	cctttataac	ttgcatttat	5460
taactttaaa	catcttttat	actatgaaag	aactttctta	catcctttga	atttaaaactt	5520

ttatatactc	agaccaccta	tgggtttttc	tctcttttta	tccagatatt	gaccatgact	5580
cgtaggtagc	tgatcattga	gagcagttat	tgcaaagtga	gttccttttag	ataaaggaat	5640
attgaaaatt	ttatattgaa	tttttcagtc	taataatgag	ataaattgta	tctagccaaa	5700
gtagtggcat	gtcttggaga	gtgtcgtttg	aggactgatt	tttacacatg	aagaggactg	5760
ggaaggtagc	tgaagtcttg	gatcctgatg	ttaaatgaat	cctcaaacc	accagagtcc	5820
tgagaaggat	caattttatc	tgagtaagga	gggaactgca	agagcaagca	gtttctgagt	5880
ctattaaaaa	tgacacagac	ttacaggact	cctggacag	tcagtcatcc	aggaattctc	5940
tgtggtcagt	ggggcatcca	ttttggctat	caggccaaga	aaatctggca	gactttgtgt	6000
gtgtgtgtga	atcaagacta	tgagaaaaag	actgccctac	cttgtctagg	caagtgaatc	6060
agtcaacttc	ccagtgtcct	acctgtccac	agtgtggccc	atgtgctgtc	aacagtgcga	6120
gcaaagggct	ctttatagcg	agcaagcttc	aggcagaagt	tcttctgggc	tgtgttcttt	6180
ggaggagatc	aggggtgctg	tcaagagctg	gtgtgtctct	gttatgaaaa	gctttttcat	6240
tagccatttt	aaatgccata	ttttatagac	ctctgaagcg	tctgaggacc	atttgtgtct	6300
ctacagtata	tctaaataga	caaacgtttg	ttttttggct	attcaatttt	tatttaactt	6360
tgaaaatata	gataggaggc	taagtaaaac	ttattttggt	aattaatcat	aattataagt	6420
gtagttatga	acatatataa	gaatgtgatt	atttttgagg	taactgataa	ctaacttgta	6480
tgttttaata	atgtttaaca	gcttataata	aatgctgtat	gttatattta	acctgaaggc	6540
agtgttagga	cagaaaaggc	ttaataagtt	ggaaaaatgt	ctcagtagcc	cttcatgggc	6600
ctaaggaaaa	agagtcgctg	tggcccaggc	ataggtttta	ggaagctgta	gttactggag	6660
gaaatggagt	gaccattaag	ttaaggggtg	tgggagaggc	tgatgtgctc	agtgtatgag	6720
caatgaggtc	tcctcacagg	acaggctgga	ctgtgcagag	tggatagggt	ggacatggga	6780
gtgagtgtag	ccttgcccca	ttggcgagga	gaaaagccag	gttaccagga	ggaagaggag	6840
gaggaggggg	gggggaagtg	gggggaggag	gagggctgct	gaagctttta	cagagtgcag	6900
gcgaactgaa	aggaaggaat	cctgcggggg	tacaagaacc	agagccatgt	ggaacacata	6960
gcaggctaaa	gaatcggact	tcagaattta	gaatcaaat	tccagacaag	taagtgtatc	7020
atacacactt	tgggaggatt	agcatggttt	ggagcaacca	ttgcagttac	aaaaggttga	7080
gtgtgtcaaa	gagaagaagt	gggaagagtc	tgggctctgt	caatacaggg	gtttgggggt	7140
tgggatccag	gtccttgag	gcaaggggtc	ttttggagtg	aacatccttg	ctagtaggac	7200
gtgagcctta	gaacattggc	tacagaggaa	gggacagggt	gtgggtccca	acaaacctgg	7260
ccagaaggga	ttcaggccat	ttgcccgc	accaaaagaa	atgttaagct	taagatccgt	7320
ggagaatttt	aacatcaaga	atgctctctt	gtggccgttt	actgaagcga	ggccatagaa	7380
caaagtctga	gacagtcccta	atlttgacaa	cttttgtagc	agtcacccca	ggaatgtctg	7440
aggatcagg	ttagactccg	tgttgcccat	ctcctagact	tgtggcgacc	tatgatacag	7500
tgtcccactt	ggtagcctgg	ggtaaaacag	tgaggagtaa	agaaaccttg	taaaggatat	7560
ctcagaatcc	aaatactagg	ccatggcttg	gcagaggatc	ttggtaagtt	caaagttgat	7620
ccttcagatg	aagagagaaa	gggagagaaa	ggagcagacc	ccatgcagcc	atggtccctg	7680
cccgttgggc	tgaggtctca	acttctcccg	cattttgaac	caagatgata	ggaattttct	7740
ctccatccat	gaagcagatc	tagggcagat	ttgatgagat	aaaaagtaga	tacaggcagg	7800
tttattagaa	gacaactctc	aagtgggttc	accgatctta	cacatggaag	tcagtcaagt	7860
cctatatctg	ggctaaaaag	caagggagg	tttatagagt	ttaggtgagg	aatgatgcca	7920
tgccagctag	gaactgggat	ggtgtgcata	catggtcaaa	aatgagaaa	aaaggagtga	7980
tagctctttc	ctgtgcttag	cacgatttag	ttgcctgtag	ttcttttgtc	tatagttgta	8040
gctctgtgag	attctgtaat	ttcgaccaag	catactttct	ttacatatat	atatatatac	8100
actcagctgc	taattttatg	tggattttata	aataaaattta	tttataaatt	tataatttat	8160
tgcccttttta	ataccatgta	taatagtatg	atatattgca	tcctatgata	tccttacatt	8220
ctttaagttg	tttccaatgt	caattccttg	ggttagaga	aatattgttt	agacttttaa	8280
atagagaaga	tgacataaaa	atgctgaaca	ctgggatttt	ataacgttaa	tttgggaaaa	8340
tcatggttaag	tatattttca	acataactga	gttcagggaa	aaatgaaagc	aagattcatg	8400
aagatatagg	tggcttaacg	tttttatgta	ccagaagttt	ccatcttaat	tatttactcc	8460
aagtgatgat	tccattttaa	atctccttcc	ttttaattaa	acagttcact	ctgattggca	8520
tgacttactt	gatgtagtca	taaacaccag	ctgagaggtc	tcgagtctat	tgtgtgaact	8580
ttgcctaaca	gggaagggaat	ttaaagagag	ctatgcttga	acagaatcta	ggtctttggg	8640
aaaatagata	cacaaaataa	tgacataagg	gaaagagttt	gcgaacatga	tttagggggc	8700
aaagtaaaac	tctgtaaaagt	ccatcacaaa	gaatcgccat	agtgcaagca	ccaaaaaggt	8760
gaccacactt	cacattg					8777

<210> 2
 <211> 944
 <212> DNA
 <213> Mus musculus

```

<220>
<221> misc_feature
<222> (1)..(944)
<223> Mouse IL-7 downstream (3') genomic sequence from the humanized
      IL_7 mouse (from NC00000696)

<400> 2
ccaattgcgt actttggata gtgtctcttt ttaacctaaa tgacctttat taacactgtc      60
aggttccctt actctcgaga gtgttcattg ctgcactgtc atttgatccc agttttattg      120
aacacatatc ctttaacaca ctcacgtcca gatttagcag gagactagga ccctataact      180
ttgttaagag agaaaacact aatttcttgt tttatagtag ggtcttattc gtatctaagg      240
caggctagga ttgcagacat gagccaatat gcttaattag aaacattctt tttatgttaa      300
actcatgtct tttacaagat gcctacatat atcctatgta tatgcctgtt taaatccttt      360
tttgtaaggt ctgctgtctt ccttcagttg taatggaaag aaacactatg ttgtagaggc      420
caaatttctg aaagtataaa ggggtttgctt gtactgaatt ctcatctccc ttgctttttc      480
cagccacgtg agcatctagc tatctatacg ctggatgtat ttgaccgatg cctgctccac      540
tggcacattg catgtgtggt agccatgcct tcttgcttct ccttttcccc aaccctata      600
atgctctact cagtgttaca gatagctggg attatcaca ttttgagaga aacaccaatt      660
gtttaaagtt tgtttcataa tcaccatttg cccagaaaac agttctctca acttgtttgc      720
aacatgtaat aatttaagaa actcaatttt gttaatggac ttctgataac ttccttagat      780
atcccacatc tcctacgtgt cagtcctttg tcctgaggaa ctggtaaaat gggtaagccc      840
ttagctagcg aactgaaggc attcgcatgt gtaagataat ctctatacct gcaaggctgt      900
ctggatggct ccctaccaat attgaacaat attctgattt tggc                                944

<210> 3
<211> 72752
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)..(72752)
<223> The human genomic IL-7 sequence (NC#166E2F2)

<400> 3
acatccgcgg caacgcctcc ttgggtgctg ccgcttccaa taaccagct tgcgtcctgc      60
acacttggtg cttccgtgca cacattaaca actcatgggt ctagctccca gtcgccaaagc      120
gttgccaagg cgttgagaga tcatctggga agtcttttac ccagaattgc tttgattcag      180
gccagctggg ttttctcgcg gtgattcgga aattcgcgaa ttctcttggt cctcatccag      240
gtgcgcggga agcaggtgcc caggagagag gggataatga agattccatg ctgatgatcc      300
caaagattga acctgcagac caagcgcaaa gtagaaactg aaagtacact gctggcggat      360
cctacggaag ttatggaaaa ggcaaagcgc agagccacgc cgtagtgtgt gccgcccccc      420
ttgggatgga tgaaactgca gtcgcggcgt gggtaagagg aaccagctgc agagatcacc      480
ctgcccacaa cagactcggc aactccgcgg aagaccaggg tcctgggagt gactatgggc      540
ggtgagagct tgctcctgct ccagttgcgg tcatcatgac tacgcccgcc tcccgcagac      600
catgttccat ggtaagcgct cttctccctt gcgcacaagt tcgcgcgccg gacgcgcggg      660
ggcaatccca gacgcgctgg gggccctgc tcctaggcaa gtccgggaat agcccggcct      720
tgcacttttg acctgcggag agcactggct ctcccatggg cagccaacag ccgcgcctga      780
gtatcctggc acatagccac ttgaacctgg ggcgctgct gccctggca ggctgcgagt      840
aacagtcccc aacgcctgct ttctgtcctg agaggggaac ctgcagcctc cgcgcgctc      900
agcgggtggc gccacagcc ggtctcagaa gcagccaaag gctctctgtc tggcgccctt      960
cccgctgctc tggccgcccc aagttactca cgcaggcggc ccgggttcgg cgagtagctg      1020
ggctcttgca gtcagaact ccctagagaa gtgaaagcga agctccacg ggacgcgctt      1080
ttaaaccta ggggaacagg tctccgaaa acccatttt tccccctga gtaagactgg      1140
gagtttccgg caagggctgt accttgcgcc tattgctggg aaaccagtcc tggggctggc      1200
gctgaggaag gccagcttct ggggtttttt gtttttgtt ttgtttttgt tgttattttt      1260
tcctacgggc gcttcttgat ggaggcagaa tgaaataggc gtgactctaa cttccagacc      1320
agtattgaga cctaataatat cttattttgt cagaatacgg atttagaatg gacagggaca      1380
gaattcagga gggttggatt cggatggcag tcatatatga ccaatgaaag agccaaaaaa      1440
cttactggaa ttaaaaaaga ggaaaaagga ttgtgagggg aaaagatctg cttaggaaaa      1500
ttggaatgct ttacagtaag tacttctca agcaagaaga cagctggggg gaggggtgcgg      1560

```

gaataggaaa	ctgactgctc	tttcttttga	tggctactcc	gtagatcaa	gacttctttc	1620
cactctcgtg	ggtaaagaat	caagaattga	cacaaccaag	gagtgccagc	tcagtaacaa	1680
aacaaagata	gagagagcgg	aaagaatagc	caacgtaatt	atggaggact	tctaaggaat	1740
gtcctcccgg	agcttaatac	aaaactaaaa	attgagcaca	accctatttt	ccttgcaatg	1800
cccatagttc	tgcagtttct	tcttctggat	cacccttggg	tctaatecct	gcaacacctc	1860
tgctctaaag	tagaaaagta	aactgagaaa	aggaagctag	cgtgtgcatt	tttcagaaaa	1920
agcctttact	tcctgaagca	cagttatatg	aatcatgggc	tataagtttt	cattagcaga	1980
caaaatatta	aaattctaata	aataatgatt	ataatgcatg	gcttcctgaa	gtttgtttca	2040
agaaatttca	ctagaagctt	gttccattaa	gagtgcacat	aatgttactc	tttacccttt	2100
gtctttgcca	tttcttttga	gagttgaagt	agttgaggat	ctactatgtg	gtctccaact	2160
gtcttatctg	gtttgggtaa	tttcatcata	tttgaggacc	aaaaagttga	atagcaataa	2220
aaatagactc	tactcgggag	gctgaggcag	gaggattgct	tgagcctgga	agtcaaggct	2280
gccgtgagcc	atgatcttac	cactgtcctc	cagcctaggc	aacagagtga	tgccctgtct	2340
caaaaaataa	taatagagaa	ctaataattag	aaaccctgaa	caagcataaa	ggagaattac	2400
aaactgcatc	acgttagtgt	ttgaatattt	ttttaaaaaa	tggaaaaggc	catttcatag	2460
aacgaactta	cgtgtcatat	tcacactcat	ctatgtgact	tttttttctg	cttttaaccc	2520
tgacacataa	cctactgtaa	caagaacaaa	tatttagtct	cttttttctga	aataaaagca	2580
tatgatgcag	tttcacagtt	tggccaggaa	gtaccttagt	gaggttcatg	cacaggaaga	2640
tgggttttta	tgcaatcccc	ttgactacac	atatatgggt	attttttaag	gaagcaatgt	2700
agttcagtg	ctaaaagctg	aggttctaga	ctcttcaatg	tgacagtctt	ggatttgaat	2760
tccatatcta	tattatgtac	aggaattttc	tgactaggca	tggtggctca	agcctgtaat	2820
cccaacactt	ggggaggtcg	aggtgggcag	atcaccttag	gtcaggagtt	cgagaccagg	2880
ctggccaaca	tggtgaaacc	tcgtctcaac	taaaaataca	aaaaaatttg	ccaggcggtg	2940
tgggtggcac	ctataatccc	agctactcag	gaggctgagg	gaggagaatc	acttgaacct	3000
gggaggctga	ggttgagtg	gaecgtgatc	gcaccattgc	actccagcct	agatgataga	3060
atgagactcc	atatcaaaaa	aaaaaaaaag	agagagaaaa	atacgaaagg	aattttccta	3120
catgactgtc	tttgtgcccc	agattctcca	tctataaatg	tgaataactt	gtagtactta	3180
cctacttctt	catgaagtgg	ttatggaatt	aaattatcag	tgaaaatagg	tctatgcaat	3240
ggacattcag	taaacactgg	ttttaagac	tgataaagac	tggagttgat	ggattgtaga	3300
aaactatttta	tgtaaacttt	gacccccata	acttaagcag	ctgaggattg	aatgtattat	3360
ttggcttaca	ttaaaaacca	acaagaattt	ttagacagac	ctccttctgg	tttaacccaa	3420
ttccctactg	aaaacaaatt	ctccaatttc	agcctcttca	ggggaagtaa	gggcaatccc	3480
acaagccacg	cttgccctgc	gttattccta	tggtttatct	tttcggtaac	ctaataaaaa	3540
gttcaggatg	gtggggagtg	tgggtgtgac	aaacaatgcca	aaagcactct	caaaccagcc	3600
attcttaata	tgttactctc	tatgtgatgt	aggagaaagg	tcttcaatta	tggaccaaac	3660
taccaagcta	catcattaat	gggagagctg	ggaacctatg	agatgtgggt	ccaaggccct	3720
aggatatgtt	gcagcattgt	ccgtgaggca	atttcagatc	taaagagttt	ctgcatttgg	3780
aggaccaggt	agattcctag	aataaggtgt	ctgcaagatg	aaaaagatca	tttagtctga	3840
agttttcatt	ttagaaatca	ggtaagtgtg	cttaagagat	gctgtgtcat	ttacacagtc	3900
acacaaacca	ttgtcttggc	aagtcaaaag	tctcaagttt	tgacttgact	actcagccta	3960
ggctcagtag	atcgtggctc	acggccatgg	cttacggcca	tggctcacgg	taagatcatg	4020
gctcatggca	gccttgactt	ccaggctcaa	acaactctcc	tgccctcagc	tcccaagtag	4080
agctctgttt	tattgctatt	caactttttg	gtcctcaaat	atgatgaaat	tacccaacc	4140
agataagaca	gttgagagacc	acatagtaga	tctcaacta	cttcaactct	caaaagaaat	4200
ggcatagaca	aagggttaaag	agtaacatta	tgtgcactct	taatggaaca	agcttctagt	4260
gaaatctctt	gaaacaaact	gcaggaagcc	atgcattata	attattatta	tgagaatttt	4320
aattccaaaa	cctctgtgct	ttatattgcc	atagtctgtc	tggggctaata	tattcaatga	4380
caacaatggc	aacagaaaac	actcttaaca	ggcaaggcaa	attatgtttt	aaaattgaga	4440
aagtacgtgt	aatatacaaa	aagactgaat	tttccagcaa	ccctcattgg	aaagaatgca	4500
caaaatgcc	tccggtgaat	aaataggttg	attttaaattt	gaggagcact	taactactga	4560
aaattgaggt	gaagaagaca	gctaagtctc	atagcaagta	aaacaacctc	atgtattaaa	4620
acaaaagggtg	gacctttgga	atattttatga	taatggtaaa	agtatccctt	tcactctagc	4680
atttaattat	tttattatat	tctcctttta	gtctatttca	agttatatgt	tatataattt	4740
ttcctctatc	atctactcct	cccgaagtat	accttttgga	cccctgtaag	atgacagaga	4800
aaataaaaaag	tatgatttca	tacaatctat	acaaatctga	ttacaagggtc	agaatctggg	4860
gaataattag	caattgatca	tccaaatgtc	catcagcaga	ggtttgata	aagaaaatgt	4920
ggtatggccg	ggcttgtaat	tacagcttgt	aattctgaca	cttaaggagg	ctgaggcagg	4980
aagattgctt	gagcccagga	gttcaagacc	agtctgtaca	aaagagtaag	agccgtctgc	5040
taaaaacaaa	ttttaaaaaa	ttagctgggc	atgggtgggc	accctgtagt	cctagctact	5100
cagaacgctg	aggtaggagg	atcgcttgaa	cctaggaatt	tgaggcttca	gtgagctatg	5160
atcatgccac	tgactccag	cctgggcagc	agagtgaaac	cctgtctcaa	aaagagaggg	5220
agaaaaaaaag	aaaatgtggg	atatgtatac	catggaatac	tactcagcca	taagagttaa	5280
gtcgtctttt	gcagcaaaat	ggatgaaact	tgaggccatt	atctaagtga	aatgactcag	5340

aaagtcacaat	gctgcactgtt	tttactttata	actgggagct	aaacagtgggt	acagatggac	5400
atacaggggtg	gaataatagg	cattggagac	tttgaaaggt	gggagagtag	gaggggggata	5460
aggattgaaa	aattacctat	tgggtaccat	gttccactatt	caggtgatag	atacactaaa	5520
gcccagactt	caccactgta	cagtatatta	aatatgtatt	agtaagaaat	ctgctctgggt	5580
cccccttaaa	tctatgagtg	tacatTTTTT	taattgccaa	aatatTTTTT	ttaaatttagc	5640
aattgatcac	tgaggatctt	taggttgaag	gaacaggagt	agaagagaga	ggcaaaaactt	5700
cattcagaag	acaaatgtga	ttacatgtta	tcaatagatt	atggccattt	ctaactcgaat	5760
cctggtaaa	caacaaattc	aggttagcat	ccaaactctgg	cactactatt	gtatgtgtta	5820
cagaaagact	aacttgcaga	actTTTTTga	tatttataaa	tcatatatat	atatatgaga	5880
ttttatatat	aaagtTctctg	acacatggta	gggtactcaac	taaaaggtaac	tagcatcatc	5940
atcattatct	gtctcctaag	ttaatTcatg	ctcatcatgc	atataggcac	ttagtggcag	6000
agttattaat	atatttTgat	aaataaaaatt	atcaattttt	gtttctctta	ctatgtttgtc	6060
acatatgcag	atgagaagtt	agatTTtatgt	ttgttttcat	aattgtctacc	cagaaaatttt	6120
tctctatTTTg	taacaacatg	ggtcacttTga	tttattggga	gggtgtattg	attgtttttat	6180
atgacagatc	atgatataat	agatgacaat	gttactggaa	actttatgat	atccctaaca	6240
gtcttccaggc	tgtcacaata	ttagtTcctt	gggtttgaag	gagtgttTgt	tgtactctta	6300
atcagagaag	gcacacaagt	gaaatatctt	gcattccaagt	acaaattgaag	ttcattttggg	6360
aaattcacag	gaaatacatt	gtcaacatgc	ctcagagtTt	acaaaagat	acaaataaga	6420
cactatggca	ggTTTTatgaa	gaaataggTc	cctgtatgat	cagatttttaa	tgTTTTgtggg	6480
aaccactggc	tttccatctt	tctgcctgaa	ataataccat	tatttccagtc	cttttgatta	6540
gacaattTgct	cctaattTggg	aagagTtatc	aaaaacagat	agaaatcatt	ggTTTTctatc	6600
tgaggatTgtg	aatttatTTta	cagagTtttt	ctaacatgac	aagaagctgg	atagcgctgt	6660
gtttgaaaag	aatctgggTc	tctggggact	cagagacaga	agatagtTgaa	aggataggag	6720
agtagtccca	aaatacaaac	ataaactTtTg	taagactTttt	gggaatgtaa	acccttcagg	6780
gttcattatt	aaaaagaaa	agtgcactta	cagtagTttac	agtTcaatcc	cagggagatt	6840
aaactccccac	agtgtTgcct	ccaagaagca	aatagacatg	gactaccatc	aaggtttTaca	6900
aaaatatata	attacTgtca	gtacatcata	aaatTccaac	aatatgtTaac	tcttTcgaact	6960
gtagtgcacc	tctttacctg	tatatgcctt	ttcttatggg	gatgtTcaac	ataaattTcaa	7020
attgattaac	acctTggagt	gtttttcaga	agcagtctat	gatttcatca	ccctTgtttt	7080
gcactttTcct	aaagagTaat	Tgcaaaaata	aaaagTgaaa	ggacgctata	ctccaaaatg	7140
ctgtTccact	ttggtTgtta	cataagTtca	actTTtgagg	ttcttctgt	agtatctcca	7200
aaccaagatg	tattttTaaa	attattagaa	attagtTgTc	cagTccattg	aaacccca	7260
atcaaatTgca	atacgatata	acattTtagct	cattcttatt	tactgtcaaa	tttagtttct	7320
tttaggtata	tctttTggact	tctctccctg	atcctTgtTc	TgtTgccagt	agcatcatct	7380
gattTgtata	TtgaagTtaa	agatTgcaaa	caatatgaga	gtgtTctaatt	ggTcagcatc	7440
gatcaattat	TggtatTgtga	TtatTTTgtT	Ttactcacat	tttcatgcatt	Tgggaaaatt	7500
TgaacctTTTt	TggtatTgcag	TTTTataatc	aagtattcat	ctttcttgac	aagaaagtga	7560
agtaactata	gaataaaaatt	Taatgagcta	ctaactgtat	atTTTtatag	ctgacataat	7620
Tatgtagctt	aaaaataaatt	ctttcctcga	ctctaagatt	ctcacaacta	TtcattTtcag	7680
TcctattTtcc	ctTTtagTaa	attTctTgtTa	agcataattc	agTatcactg	cctaaattTtc	7740
ctcacctccc	attTaccatg	TtagTccctg	Tagaagcatt	acattaaagag	Tgggaaaata	7800
acagagTaaa	TagtTaaagac	TtatTgTgTaa	TagatTgtTa	TTTtatTTTg	ctgtTgtTtag	7860
atgcataTgtt	atttatattga	TgttatTTTg	TatctatTgt	Taatcaataa	TTTgtTatga	7920
TttaaaattTt	ctattTTTgTa	TggtTaaagc	TTTtctaatt	aatagattTTt	atacctTtaga	7980
gccaactTtag	TTTTctagaa	aaTtTcagTca	gaaagTtagaa	aatTcccata	Tgctctctct	8040
ctctctgcac	TgtTtccctt	attatctTtac	atcagTatTg	cacattTtatt	acaattTgatg	8100
agccagcatt	gatacattac	ataagTgcatt	agTtaacatt	aggattcatt	ctttatTgtTt	8160
TatagTttTta	TgggtTttTga	TaaatTgtata	ccatcacata	Tccgtgatta	catatcatac	8220
aaatcatatg	Ttaaaaatct	cctatccacc	gactcatcct	TctctTtctt	cccctgaact	8280
cctagTaaacc	actgattTgt	TtatTgtctct	TtagTttTg	cttctTttaga	atgtcatata	8340
gtTgaatTca	Tgcggtctgt	atgtTgTcct	TttagactTg	attctTtTcac	TtagcaatTgt	8400
gaatcaaaagc	atcccccatg	attTTttTgt	gtTtTgatatt	TcattTTttTc	TtatTctTgg	8460
ataacagTct	attTaatTgga	Tataccacaa	ctTgtTttatt	TTTtTcactga	Ttgaaaaatg	8520
TgtcacagTt	gctTcaata	TTTggaaaatt	atgaataaaa	ctTctataaaa	catatacTgt	8580
cagggTttTt	TgtTgacata	agTttTcaac	TcaggTaaat	acctacaagc	atgactTgt	8640
gatcatatTg	TaagactTgt	TTtagctctg	Tacaaaactg	ccaaactTtTc	TtccaaagTg	8700
Tctgtaatat	TTTgcattct	Taccagcaat	gaatgagatc	ctaattgcctt	ccatctTtcgc</	

catcagagct	ttgttctttt	cagcatataa	atcctgtaaa	tattttatta	gacttatacc	9180
taaatatttc	atattttagt	gctattttta	atgggtgtgt	tctaatttca	aatttttagtt	9240
gtttatttgct	ggtacatagg	aaagcaattg	atttttgtat	attaacctat	gtcctgcaac	9300
cttactataa	tcacttgttt	gttctagaag	tctgttggtg	attattagga	attttctaca	9360
tagacaatca	tgtcatctgc	aagagttaat	tttttccaag	gtttcagagc	tgtatcaata	9420
caatgtgatt	gatttattgt	tttaacagat	aattagtctc	ttttcaatca	gattgaaact	9480
gaatagcaaa	ggaaaactct	ctcaaagtgt	cataagatgg	gagaaattgt	ctaactgtgc	9540
ccccgacttt	tactccactg	tctcttccac	atactcatac	tgaagtggca	tgatgccttg	9600
aggaatttag	tgttatacct	cttgtaggaa	tatggaaact	aaaaagagat	actgtgctac	9660
actgtacatt	gtaatccaga	ggttcctgat	tttgcccatt	gacaagaaaa	aaaatagtgc	9720
acagtaaattg	gcaattgtct	catttagatt	tcttgctaata	ttggacattg	catttgatga	9780
tgctactaaa	ttaatctttt	gagtcaagat	aatatttctc	atttaatttt	gttatctggg	9840
cagagaacaa	actagtgtca	gttcaacatt	tataaataac	tatatgtgta	taaaagtgc	9900
aaataatatg	ctattaaaaa	ttcagtaaaa	ggagagtttc	atccaacaga	ctcatgacac	9960
attttttttg	tgggagaata	tagaggagct	tatctcatta	acacacaaaa	caagaacaag	10020
tacatcagca	gcaataatta	tattattttc	aaaaaacaaa	acatggctac	tcttcttaag	10080
gagggttaatt	cacaagacat	ggaagagaac	acagctaata	agtccaactg	agtagttcca	10140
tagtaacctt	agaatgtttt	tctatacata	gaagggtgata	aatttgaggg	aaggagaaag	10200
aaagtctcaa	tgaattatta	atgtcaacat	gactggtaga	gcagatttag	ttactcattc	10260
attcagtggtg	gactagatgc	tttgacagaca	ttactgtggt	taagtcttgg	ggagaccata	10320
atactaataag	ttatgaagtg	cttggttatgt	tctcagtgct	ttccatgtgt	taactaattt	10380
aatccttaca	acagcccttg	agaaagacac	tcttactacc	tccgtttcac	aacagaagaa	10440
tctgaggccc	agggttatcc	agttttataag	tgaccgagcc	agaatctttg	tccatgctct	10500
ctaccccact	ctctcacctc	ccaaggacaa	tctctgtgat	agttttattca	atcagcaaac	10560
atttattttag	ggcctgatat	gtacaagtta	ctatgaaaaa	cccatttgtg	taggtctagt	10620
tgggttttggg	tgtggataga	atgatggacc	aagtacagat	cttttttcaa	gaagcttaca	10680
ttttgggtgag	tgttaaagat	tgggtggtgaa	taatgcaagt	tacagtttta	aaagtaggaa	10740
gagtgaacttc	ctgtttgtta	gatgtctgct	tatcatctaa	caaatagact	ggttgtaaaa	10800
caagctcaga	aacaaaaaga	tgtaaatggt	gttctggaag	tagtaaagaa	gcaatttttg	10860
cctgtgtaga	agtttcagca	agttatccag	aagggtctagc	taagatgatt	ggtaaaagtg	10920
gctacactaa	acaacagatt	tcaatgtaga	tgaaacatcc	ttctactgga	aacaggcgac	10980
atctagaact	ttcatagcta	agaagagaa	gtcaatgcct	ggcttcaaag	cttaagagga	11040
caaactaact	ctcttgttag	ggacaaatgc	agctgggtgac	tttaagtttt	agcaaaatat	11100
tactgtctcat	tgacaatgca	aaactagtca	cccaagagtg	ctgatggata	ttaatgtttt	11160
cataactgct	aatataacat	ctgttttttca	gcccgatga	caaagagtag	tttcaacctt	11220
caagccttat	tttttaagcc	atgtattttt	gaggctatgg	ctgccagaga	taatgattca	11280
tctaatagat	ctgggcaaag	aattgaaacc	ttgtgaacag	cattcattgt	tctgtagtag	11340
atgtccttaa	aaacatttgt	gattcatggg	aggaggtcaa	aatatccaca	ttaacaggag	11400
ttcggaagaa	gttgattcca	actgtcatag	atgactttga	ggggttcaag	acttcaatag	11460
agaaagtaaa	tgcagatatg	gtagaaatag	caagagaatt	agaattagaa	gtggagcctg	11520
aagatgtgac	tgaatgtctg	aaatctcagg	ataaaaactgg	aatggatgat	gagttgcttc	11580
tcaggcatga	gcaaagaaag	tgggttcttg	aaatgatattt	actttgagta	aagatgctgt	11640
gaacattgct	gaaatgacaa	gaaaaaattt	aggatattac	acaaaattag	ttgttaaagc	11700
aatggaagga	tttgagagga	ttgcctctaa	ttttaaaaga	agttctactg	tggataaaat	11760
gctttcaaac	agtatcacat	gctacagagg	aatcttttat	gaaagaaaga	gttaatctat	11820
gtggcacaact	tcattgttgc	ctcattttta	aaattactac	agccacccaa	ccttcagcaa	11880
ccaccactct	gatcagtcag	catccactaa	cgttgaagca	aggccctcca	ccagcaaaaa	11940
agttttacaac	accctgaagg	ctcagatgat	tgttagcatt	tttcagcaaa	aaattctttt	12000
taaattaaaa	tgtatacatt	gttatttttag	acataagact	attgtacaca	taatagacta	12060
cagtatagtg	taaacataac	ttttatatgc	tgggaaacca	aacaaaattg	tatgactcac	12120
tgtattgtga	tacttgcttt	actgcagtgg	aaccaaacc	acagtatctc	tgaggtatgc	12180
ctgcaataaaa	ttatgcaatc	attatcacta	tctaattcta	gaatattttc	atcattgcca	12240
aaagaaatat	tctacccatt	agcagtaact	ctttattccc	catcactagc	ctctggcagc	12300
cactattctg	cattctgctt	tctgtctcta	ggaatttgcc	tattctggac	atttcacatc	12360
tgtcttgtat	ataattcata	tggatgatat	gcagcttttt	gtattgatct	tgtttgcctt	12420
agtataaatgt	ttttaaaatt	aatccatatg	ataacaggag	ttagtatattc	atttctcttc	12480
atggctcaat	aaaattctgt	tgtatggata	tggcacattt	tgtttatcca	ttcatcaatt	12540
tctggacatt	tgggttttcc	attgtttggc	tatgcaagtt	tttatacaat	tgtcttgata	12600
tgttctctagt	agtcaaattg	ttggattata	tggctactct	gttaaacttt	ttgagaaact	12660
gcaaactggt	tctaaagagg	ctgcaccatt	tgcgtttcta	tcagcagtta	aggctctgat	12720
ttttctactt	tctcaccaaa	gcttgttatc	atctaacttt	ttattctagc	tatctctgtg	12780
ggtgtgaagt	agtatctcat	agtgatactg	attggcattt	ccttgatgac	taatgatgtc	12840
aagcatcttt	tcattattgg	ctgttattat	cagccatttt	atatactctc	ttttggagaa	12900

ttgtttattc	aaatctttca	cccactttta	aattggatta	tttgtctttt	cattttttata	12960
gttgtaagag	ttctttatat	gctctggatc	ttagaccttt	atcagatatt	atattttttc	13020
ctcccatcat	ttgtattggt	ttttattttc	ttgatagtgt	cctttgaagg	acatttttta	13080
cttttatgaa	gtccaattca	tttactcttg	ttgcccatgt	ttttgttttc	atatcaaaga	13140
aactattgct	taatccaaga	caacaaagat	ttacatctat	gttttattct	aagagcttta	13200
tagtttcagt	ctcacatggt	ggctcttgat	tcataattgag	ttaatttatg	tacgtgggtg	13260
gaggtagggg	tccaacttca	ttctttttca	tgtggctata	cagttgttcc	tgcactctgat	13320
attgaaaaatt	atattttccc	tcattgaatg	tctggacacc	cctgttgaaa	ataaaattgaa	13380
ctcaaatgta	tgggtttatt	tctgacctct	ccatggtaat	ccattgatat	ataatcccta	13440
tgccaggacc	agacagtctc	aattactgta	gcttggtggt	tagttttgaa	atcagttttg	13500
tctttcaatt	atgtttttat	tttcttaaaa	tcatttatac	tgatgaaatt	gctgatattt	13560
attttatgga	ttgactacct	ttttttaggg	attagtatat	taaatagctt	tataatttaa	13620
atgcaatcta	aatctctctg	gtgatgtcat	atctctgagc	aattactaaa	ccatgtgact	13680
ccatatacta	gtaagtatgg	tccagtgaag	ggcatggaca	gaagtaatga	cagactgtag	13740
agaagtgggtg	gggagcttaa	gagtattctc	ttccttatag	ctctcaagat	ccgttttcat	13800
tctcccatta	gattttgatg	atatgctcat	catttggtaa	gagcacatga	taatatatta	13860
agtataatgt	tattgattta	tttagagaca	gagtctcact	ccatcaccca	ggctggagtg	13920
cactgggtgtg	ttcttagctc	attgaaatct	ccacctccca	ggttcaagca	attcttgtgc	13980
ttctgcctac	caagtagcta	ggattacagg	catgtgccac	cacaccagc	taatttttgt	14040
attttttagta	gagatgggtt	tttgccatgt	tggccaggct	gttctcaaac	tcctgacctc	14100
aagtgatctg	cctgcttcag	cctctcgaag	tgtctgggatt	acaggcatga	gtcactgtgc	14160
ttggcctaag	tataactctg	taattgtcct	atctgtttta	aacatctttc	cattcataat	14220
tcccttattt	tcttactttt	gatataata	tttattttta	tgtagtga	tctatataat	14280
aaaatttcag	atggttcaat	ttgggcacca	aggtgggagg	gatcaggagc	tgggtgtgaa	14340
ttgatacaga	aatagttttc	ctataaagcc	acaaataagt	gatacttggg	gaagaaagaa	14400
cttgtctttc	ccccttgaat	aatcttggca	tcctcatcaa	acatcacttc	accagagatg	14460
tatgggttta	tttctggact	ctccaattcc	attttgttca	tctgtatata	tgtcctgggt	14520
cagtaccaa	ctgtctttat	tactctttct	ttggataagt	ttgaaatcgg	gaaatatgaa	14580
tcattttact	tttttttttt	ttgagattgt	tttggttcat	gcataaaact	atttgggacc	14640
atcattttcg	taataatggt	taaaaaatgct	tgtggtccat	gaacatggga	tttttgttcc	14700
atttatttgt	atctttttaa	ttttctttta	acaatatatt	atagttttca	gaatataggt	14760
tttacccttc	ttttgtttaa	tttatttcta	agtatcttat	gtctctttta	tgctattgca	14820
aatggaattt	tttctttatt	ttaaaattat	ctatgatttc	taactctcca	ctccttgtat	14880
acttaacctaa	gtatgtgtct	tatttccccg	tactagtcca	tatgtatatt	aaggacagat	14940
tttatgtttg	agtcactctt	gtatctcaca	gactatttag	ccagcatctt	acacgtagta	15000
gtttttcaaa	tgtttaatta	ataatttatg	gattgttaat	caacaccata	aattaatgaa	15060
aaccagagc	taattttgaa	taatctagga	agcctgtttt	tttaacatat	gttctttgga	15120
aatttggtat	gaattaaata	tcagggtact	tttgatatca	atatgaacta	gttttggtatg	15180
ttatacaata	ttttttatcc	ataaaaaatt	attttaccta	aatataactc	acatgggttg	15240
actacataac	tcttagtcac	cacagcaaag	gctgtttcaa	aatataaagg	ctgctagaaa	15300
tggccaaacg	ctttctagga	ataactcagt	ctaattgtag	gcaaatacag	ggctatccct	15360
ttatttttaag	ttgtaaaact	ataaatctaa	tgactaatcg	gttataatat	actttcccaa	15420
cttccaatat	ctttaaactgt	gactctattc	cagaggcttt	cacagattca	acttctgtct	15480
ttgcaactgac	agctctcata	tagcctgagg	tctacatttc	tcccattaac	tctaggacca	15540
tttaattcaa	atatctagta	gatatctcta	cccagatgta	ctatggcacc	tcatgcataa	15600
tagtcaacta	attgccatca	catttagcct	gttctgtgct	ctgtattctc	tatcttaggt	15660
aatttttagca	ttttcctagt	ctttcaattc	tgaagcccta	gaatcatctt	tgatggcctt	15720
catctcatcc	atcaccaa	tctatagttt	aatatatcat	cttaacacct	gtattatcca	15780
tctattctat	agacttctac	tactagtctt	agttcaagta	gttgtcagat	ctcacccggg	15840
ccacttctgc	agctgtcagt	gggcccgtgac	taaccttctc	gcctcccctg	tgcattctggc	15900
ctttttaatg	atgcttgagt	tatctgtccc	gattcaaa	tgttaccatt	tttcttcttt	15960
ttaaaaactc	tttaatgaag	tatctctccc	ccagcaccta	tcaggatttg	gtcttgcatt	16020
tgattgggtt	gctaacagaa	gtagccaaag	aaggatcaaa	ttctagccaa	atattgcttc	16080
aaaaatatgt	gtaaaataat	ggacaatggt	taaataattg	tagttaacaa	ataaggaaaa	16140
tgtaaattga	ttacaataaa	aattagtttt	ttaatatcaa	tttatgctag	agtaaaatat	16200
aaatttcctg	tttatatgac	tcagtagcat	gactaatcag	ttgcaattta	acaagagaca	16260
ttgcttttta	agaggcaagg	ctttttgttt	tatgaataac	ttttttctag	ttataaaaaat	16320
taaagaaaaa	tagactaatt	aaaagataga	gactgcctga	gtagatttta	aaaaccctac	16380
tttacgtttgc	ctaaaaagaa	cctactttta	atataaagat	acatatagat	tgaagtaaaa	16440
aggatggggg	atgatacact	atgttaacac	taatcaaaat	gggagtagct	atattcattt	16500
cagtcaaaagt	caacttcaga	gcaaggcgga	ctatcatgga	tataaagagg	gtgcattaca	16560
taataataaaa	gggccaatta	tccaagaaga	cataagaatc	cttgctctgt	acatatctaa	16620
aaacagcatc	aaactctgtg	aagcaaaaac	tgataaactg	caagaaatac	atgtatctat	16680

tattatagtt	ggaaacttca	cagccttctg	tcagtaattg	acagattcag	cagggaggaa	16740
atcagtaagg	ttacagatga	acttgaaagc	accataaatc	aactggatct	aattgacagt	16800
tataaaatac	ttcatcaaac	aacagcataa	tacacatttt	tctcagactc	acatggaata	16860
ttccccaaaa	ttgaacatgt	actgagccgt	aaaacacacc	ttaacaaatt	tttataaagt	16920
acaagtcatg	cacaacatgc	tctcaaccaa	aatgtaattg	aagtagaaat	caataaaaata	16980
agaaaaatag	gtggaaaatt	cccaaatttt	tggaatttaa	aaacacaatt	tttgataaca	17040
tatgggtcaa	acaaaatgtc	tcaaaagaaa	ttttaaaata	ttttgaatta	aatgaaaaga	17100
aaatagatat	ttgcatgata	cagtgaagagc	agtgccttagg	gtattaaatg	catagaaaaga	17160
aaagaaaaag	atataaaatc	aatagtctaa	tcttccacct	taggaaaaca	gaaatgagaa	17220
agaaaattaa	aactaaatta	atcagaagaa	aataaataat	gaaattagag	atgaaattga	17280
gaacaagaaa	ttagtagagg	aaaatcaatg	aaaccaaacc	tggttctttg	aaaagatcaa	17340
taaaattaat	aagcctccag	ccaggctgac	cacgaaaata	agaaacaaga	cacaaactac	17400
tactatcaga	agtgaaga	gagccatcac	tactgattcc	atggatatta	taaagataat	17460
gaggtaaaaag	tattttgatg	gttaattttta	tgcattaact	tatcttggcc	aaggaacacc	17520
aaggattgcc	agcagccacc	aaaatctagg	agaaagtcat	gaagtgggtt	caccacagag	17580
cctccaaaag	gaaccaaccc	tgccaacact	ttgatgtcag	acttatggct	tccagaactc	17640
tgagagacta	aatttctgtt	gttttaagcc	acctgttca	tggaattttg	ttatagaagc	17700
cctaggaaac	tcaataaat	ggtgacaaaa	gtggacaaca	tcctgaaaaa	aaattcacta	17760
acactccact	ttgaagagag	gccgtggaaa	tgtctactgg	ggaaaagcaa	gtgaattggg	17820
gaaatgacct	ctaaatatgg	tagtctctat	gaaaagcaaa	acacctcttt	ctcagttggg	17880
aggaaacttg	aagaccaaat	gagcactctt	tcctcatgca	ggccagctca	ccatacacca	17940
tgatgcactt	taacaaaagg	taaattgtta	aaaagagagc	acagtgttaa	taacagggaa	18000
ggctatgcat	gtgtggggac	agagagtatc	tgtgggaaaa	aaaacagttt	tcttattctc	18060
tccctcaaca	acaatcaaca	taggagactt	ctatgacca	atgtgtgaga	gtttttttcc	18120
tcattttcta	acaaaagaat	caattctgca	aaggacacaa	gctggctgtc	aattcaatta	18180
tgacactatc	tatctgaaga	cagcaccaca	tagcacaggt	tgaggctgtc	ttcatgactc	18240
ctccttcccc	ctccaccccc	atttcagatg	ccaatcacaa	accctaggat	gtctaacctg	18300
tgcttctgac	caactggctg	tacaatgggg	atcccacaac	ctgctccttg	ggtttaacta	18360
atttgctaga	gcagctctca	gaacttgggg	aaatacta	atattatcatt	tcttataaag	18420
gatattacaa	aggtacagat	gaagagattc	atgggcaaga	tatgggagaa	caggtctgga	18480
gctttcttgc	cttctctggg	catgccaccc	tccaaatacc	tccacatgtt	cagctatttg	18540
taagctctct	ggagagttag	gcatgactga	ttaaatacatt	ggccattggg	gatcaacata	18600
accttcagcc	ctctcctctc	cccagaagc	tgggggatgg	ggccgaaagt	cccaacctc	18660
tatttatgcc	ttgttatcct	aggggctggg	actggggctg	gagctggggg	ctgcctaggg	18720
gctgccagat	accagtcac	tcattagcac	agaaaaagac	attccttttg	aggtttcaag	18780
gattttatgg	gttgtgtgtc	aggaatctgg	gacaaagacc	aaacatacag	tcatacgaca	18840
caatgtttca	gtcaatgagg	gactgcatat	accatgatgg	cccataaga	ttataatgga	18900
gttgcaatat	tcatattgcc	tagtgacatc	atatctgtgg	taatgtctta	gaatgcatta	18960
ctcacatgtt	tgtgatgata	ctgatgtaaa	caaaccatt	gcactgccag	tcatataaag	19020
gtatagcaca	gtagtgttca	gtaatgtcct	aggccttcac	attcactcat	ggctcactca	19080
ctgactcatc	cagagcaact	tgcaagtctg	caagctccat	tcattggaag	tgccctatac	19140
aagtgtacta	ttttaatat	tttataccat	atttttactg	tacctgttct	atatttagat	19200
atgttttagac	acacaaatac	ttaccattgt	gttattatta	tctatttagt	gcattgctatg	19260
caggttttgta	gcctgagagc	aatagactat	accttatagc	ctagggtatgt	aataggctat	19320
accatttagg	tttgggttct	atgatgtttg	tgcatgatg	aatcatcta	atggcaccat	19380
tacaatgaca	catttctcat	aatatatccc	ctatcattaa	gtgacacata	actgtatttc	19440
acagtatcac	aatgtacatg	aggaatctct	ataccttctt	ctcatttttt	tgtggacctt	19500
aaattgctct	ataaaaatag	ctttaataaa	aagagagaaa	gaggacagtc	cctgtccacc	19560
aacaaaattg	accacaggtt	ttcccacttc	tcagtgcact	accattgcca	catacccttc	19620
cgcataatagc	tgtgttccca	ggctttccaa	gagcacacag	agcagataat	actgtggctt	19680
cacttagaaa	ttcaacagag	aagtgactgt	gataagtgag	aagaggatca	tgagatatgg	19740
agtcaaataa	atatcagcac	agagtgttcc	actttaaatt	taagatgaaa	ataacataca	19800
acgatacaga	aatgccacag	caaaataaaa	agactaaaag	aaacctagaa	tataagcatc	19860
cattctggaa	gggggcagac	acgaagaaac	agaataaaaa	ctttcatttg	tacttcacgc	19920
catagtttta	aagtacacat	gaattttaca	acagaatatc	aaagagtagt	tgataaaaga	19980
atagaatgag	atgaaaaaat	attatacaac	caaggaaata	cattgaaatc	caaaattatg	20040
cactccctcc	attttagatg	tgacaaaagt	gttagcaaca	acaagaagaa	tgaacaaaaa	20100
atatgaaata	gatttgttat	aatcaccata	aatgcacagt	aaaaatacaa	ataccaaaaca	20160
gttgctgaaa	caataaaaga	taagaagaga	tgatagtgat	ccattttatg	aataattggt	20220
cctaccaaaag	aaaattcatc	gaatggaaga	ataaaacaac	ctatgataga	ggaaaattttt	20280
tccacaaatt	gaggcaaaat	ggaatgaaca	gtgctaggta	gtatatcatg	tactataaaa	20340
attgattcaa	catgattgtt	actaagttat	atcttgga	agtgactgaa	tttcaagagc	20400
aaggaagaat	aattctaaag	gtggaaatgg	caagtcagtt	ggaggagaat	cagagtggct	20460

tcagatTTTT	cacatcTaaa	tgcaaaagat	aatggaataa	tgtctacaaa	attctgagag	20520
ataaaaaatgt	ggctcagaat	ttgataccta	gacaagatgt	tgttcaaata	taaagtgcac	20580
aggcagaaat	ttatgtatgt	cagaatTTtag	gcaatagaac	actcatgagc	cttttcaagg	20640
agaagatgga	gggggagggg	agctactgga	tataaaatcc	aaccaaccaa	gagaaaagtg	20700
aagacactgt	agtaaaaggt	caattgatag	cacaaaattc	acttccttgt	agaattagag	20760
tagcctcttc	aaaatatatt	atattctttt	attttcctca	tggttcttgc	tactgtctca	20820
aattatcata	tttttaggac	agagactctc	tgtcttgata	atccttgat	cccaccatc	20880
tagaatgtta	cctggtacag	acaagaccct	tcataaaatat	ttattgactg	actgagtga	20940
tgaacatagt	ttacattaaa	aaaaacttaa	atgttatTTT	aaagttataa	aattacagtg	21000
tagcataaaa	ttatatgtta	tatcgtgtat	atagtataat	tcaaaattat	gttgtaaaga	21060
tgttgatata	cataagtga	tgtgttagac	acttctggct	gccatatcaa	agaaccatgg	21120
actttggtac	tttggtggct	tataaacaag	agaaatTTtat	tcctcacagt	tctggaggct	21180
ggaagtccag	gattgggggtg	gcataatggtt	gggttcttgg	gaaggacctc	ttccagggtt	21240
tggactacca	gcttctcata	tcttcacgtg	gcagaatgtg	aaattttcag	atggctagag	21300
agctctctgg	tgtttcttta	taaggcacta	ccaccattca	ttagagggtc	accttcatga	21360
cttaattacc	ccccgaaggc	ctcactttct	aacgacaaca	cattgggggt	taggatttca	21420
acatatgaat	ttcgaaggaga	cacaaatggt	cagttcataa	cagtgcatt	ttaaaatcat	21480
tatatgactt	atagtcttca	ccatatTggc	tctatcagtg	acttctcact	attggtttat	21540
gtgctactca	tatatTTact	tgcagtttac	ctaattggctc	gcttatTTT	gcttaaccag	21600
gtgggtgttta	gagttatgct	ctcaaaacag	aacactctct	tctgacagtt	tggtttatca	21660
tacttggtctg	ctttgcttta	catatttctt	taataaatct	ttatctttga	tctgcctgtt	21720
accaccccac	ttcagctcac	tagaatcttc	gaatatatcc	atctcatact	tcatctctca	21780
aattgtctca	ttaatcacag	gttatatagt	tgaatttgat	atttaaagtt	caagtaaata	21840
gttataaagt	acagcatata	agcatttTgtg	attataaatt	tacagttgcc	acatatgtta	21900
attggttaatt	agatcgctgc	ttgtaggatg	gtataaacc	attactgcat	attaacctta	21960
agactaatga	gtgagagctg	ggccatgatg	gctgactaga	cacagttgca	gttgagggcc	22020
tccaccgaga	ataacaaaaa	cagcaagtga	atcctgtgct	ggcaactaag	gtatccaggt	22080
tctctcattt	ggactgacta	ggtggttgg	gcaactgaca	gaaagcaaag	aaatcagagt	22140
ggagtaatgg	cccactgca	gggggtaagt	gggactccca	tccccagcca	agggaggcag	22200
tgagtgattg	gccatcctgc	ccaggaaacc	atatttttcc	gtggatgggt	gcaacctgca	22260
aatcaggaga	ttcccatcat	aagcccacac	caaaagggcc	tggggttcca	agcacagagc	22320
agtgcataatt	ctctcagtg	ccactgggct	gggtctgctc	taagactaca	gagttcctag	22380
agggaaaggg	agccaccatc	gctatggcta	cctgtgctcc	aagatgactg	aacttagaaa	22440
aggggcagca	accatcactg	cagctccagt	ctgccttttc	ccctgctggt	gccagagata	22500
ttgggtgggt	cagatccagg	aggaattctc	cacagtgcac	cacagcagct	gtggcgagata	22560
atcaccagac	tgcctcttta	ggctgcaccc	ggaccatcc	atcttccactg	catgtggcct	22620
ccctctggga	atttcatcat	ctccagccag	gggtttacgg	acagagctct	gataccctg	22680
ggatggagct	tctgggggga	ggagcggctg	ttgtctctgt	ggatcagcag	acttagtctt	22740
ttccccgctg	gctctgagga	atccaggcag	ttcagacgag	tgggattcca	gccagagtgc	22800
ttcattaagt	gggtctttga	tctgtttctc	ctgactgggt	gagaccaccc	ccaacagggg	22860
tcaccagata	ccttatatag	agacattccc	actaacatga	agtcaataac	cctctgggat	22920
ggagctccca	gaggaaggag	cagtaagcca	tctttgctgt	tgcgcagcct	ccactgggtga	22980
cacccccagg	ggtgggagag	accaggcaa	atagggtctg	gagtgaaccc	ccagcaactg	23040
acaggagcct	tatggaagag	gggcctgact	gttaaaagaa	aagcaaacag	aaagcaacaa	23100
caacaacagc	atcaacaaaa	aggcaccac	agaaacccca	tccaaaggtc	agcagcctca	23160
aagatcaaag	gtagataacc	tcagcaagat	gagaaacagt	caatgaaaaa	acactgacaa	23220
ctcaaaagcc	agagtacctc	ttcttgaaat	gatcgcaaca	cctttccaac	aaggcacaga	23280
actgggctga	ggctgagatg	gataaaactg	cagaagtagg	cttcagaagg	tgggtaataa	23340
tgaacttcac	tgagccaaa	gagcatgtcc	taaccaatg	caaagaagtt	aagaaccatg	23400
ataaaacatt	atagaagctg	ttaaccagaa	taatgtttag	agagaaacat	aaatgacctg	23460
atggagctga	aaaatacaac	acaagaactt	ccaatgcaa	ccacaggtat	caatagctga	23520
atagatcaag	tggaggaaa	cacttcagaa	cttgaggact	atcttgctga	aataagacac	23580
aaaattagag	aaaaaaggca	tgaaaagaaa	tgaacagaa	ctgtgagaac	tatgggatta	23640
tgtaaaccca	caaaacctac	gcctgattgg	ggtacgtgaa	agagatgggg	agaattgaac	23700
taacttgga	aacatgcttt	aggatatcat	ccaggagaa	ttcctcaacc	tagcaagaca	23760
gggcaacagt	caaattcagg	aagtacagag	agccccagta	agatacgcca	tgagaagaac	23820
cactccaaga	cacatgatca	tcagattctc	caaggttgaa	atgaaggaaa	aaaatatata	23880
gggcagccag	agagaaaggc	caggtcacct	acaagggaaa	gccccatcga	ataacagcaa	23940
acctctcagc	agaaacccta	caagccagaa	gagattgggg	gccaatattc	aacactctta	24000
aaagaaaaat	gtttctaacc	agaatttcat	atccagtga	actaagcttc	ataaggcaag	24060
gagaaataaa	atcctttcca	gacaggcaaa	tgtgagggaa	atgtgtcatc	accaggcctg	24120
ccatgcaaga	gttactgaag	gaagcactaa	atatggaaa	gaaaaatgat	taccagccac	24180
tacaaaaaca	cactgaagta	cacagaccaa	tgatactatg	aagcaactac	atcaacaagt	24240

ctgtaaaata	accagctagc	atcatggtga	caagatcaac	tgcacacata	ggaatattaa	24300
ccttaaagt	aaatggccta	aatgccccaa	ttaaaaggca	cagagtggca	agctggataa	24360
agagtcaagg	tccactagt	agctgtat	aagagacaca	tctcatgtac	aaagacacat	24420
ataggctcaa	aatagtaaaa	tctaccgagc	aaatggaaaa	cagaaaaaat	caggggttgc	24480
aatcctagtt	tctgacaaaa	cagactttta	accaataaag	atcaaaaaag	ataaaggcat	24540
tacataattg	taaagggttc	aattcaacaa	gaagagctaa	catcctaaat	atatatgcac	24600
ccaatacagg	agcacctaga	ttcataaaac	atatctcttag	agacatacaa	agagacttag	24660
actcccacag	aataatagtg	agagaattta	acactgcact	gtcaatatta	gacagatcat	24720
tgaggcagaa	aattaacaag	gatattcagg	aattgaactc	agctctggat	caagtggacc	24780
tgatagatat	ctacagaact	ctccacccca	aaataacaga	atatacattc	ttcttggcac	24840
cacatggcac	ttactgtaaa	atcaaccaca	taattggatg	taaaacactc	ctcagcaa	24900
gccaaagaac	tgaaatcaca	acaacacagtc	tcttagacca	cagtgcac	aaattagaac	24960
tcaattttta	ggaactcact	caaaagcata	caattacatg	gaaattgaac	aacccgatcc	25020
tgaatgactc	ctcggtaaat	aatgaactta	aggcacaagt	caggaagttc	tttgaaatca	25080
atgaaaacaa	agaggcagtg	tgccagaatc	tctggaatgc	agctacagca	gtgttaagcg	25140
agaaatttat	aaaactaaat	gtccacatta	accatttttt	aagatctcta	gtcaacatcc	25200
taacatcaca	atgaaaagaa	ctagagaacc	aaggggcaaac	aaaccacaaa	gctagcagaa	25260
gacaagaaat	aaccaagatc	agaaaagaat	tgaagcagat	gtagacataa	aaaacccttc	25320
aaaatattaa	tgaatccaga	agctggtttt	tgaaaaaaat	taataaaaca	gactgctagt	25380
tagactaata	agaagaaaa	gggagaagaa	tcaaatatac	acaataaaac	gataagataa	25440
atatcatcac	tgacccacaca	gaaatacaaa	caaccatcag	agaataccat	aaacacctct	25500
atgcaaataa	attagaaaaat	ctagaagaaa	tggataaatt	cctggacaga	tatatactcc	25560
caagactgaa	ccaggaagaa	gttgaatcct	tgaataggcg	aataacaagt	tctgaaattg	25620
aggcagtaat	aaatagcctg	ccaaccaaga	aaacccgcga	ccagacagat	ttagagctga	25680
attctaccag	aggtacaaa	aggagctggt	accatttttt	ctgaaattat	tccaaacaat	25740
tgaaaaggag	ggactcctca	ctaactcatt	ttatgaagcc	agcatcattc	tcacacccaa	25800
acctggcaga	gatactacaa	aaaaagaaaa	cttcaggcca	acatctctga	tgaacgtcaa	25860
tacaaaaatc	ttcggtaaaa	tactgccaaa	ccaaatccag	gagcacatcg	aaaagcttat	25920
ccaccatgat	caagtggct	tcatctctgg	gatgtaaggc	tggtgcaaca	tacaaaaatc	25980
aataaatgta	attcatcaca	taaactgaac	taaagacaaa	aaccacttga	ttatctcaat	26040
agatgtagaa	aaggcctttg	ataaaattca	acatccccc	atgttaaaaa	ctctcaataa	26100
actagatatt	gatggaacat	acctcaaaat	aacaagagcc	atztatgaca	aacccacagc	26160
caatatcata	ctgaatggac	aaaagctgga	agcattcctc	tagaaaaacta	gcacaagaca	26220
aggatgcccc	ctctcaccac	tcctgttcaa	catagtattg	gaagttctgg	ccagggcaat	26280
caggcaaaaag	aaacaaataa	aggtaggcaa	atagggaagac	agggaagtcaa	actgtttgcc	26340
gatgatgtga	ttttatatct	agaaaacccc	attgtctcag	cccaaaagct	tcttaagctg	26400
ataagcaact	tcagcaaaat	ctcagaatac	aaaatcaatg	tgcaaaaatc	acaagcattc	26460
ctatacacca	acaatacaca	aggagaaagc	aaaatcatga	atgaactccc	atttacaatt	26520
gctaaaaaga	ggataaaata	cttaggaata	cagctaacaa	gggcaagtga	agacctctca	26580
gggagaaata	caaaccactg	ctcaagtata	tcagagagga	cacaaacaaa	tgaaaaaaca	26640
tgtcatgctc	atggatagga	agaatcaaca	ttgtgaaaat	ggccatactg	cccaaagtaa	26700
tttatagatc	caatgctact	ccatttaaat	taccattaac	attcttccca	gaattagaaa	26760
aaactaccat	aaaattcata	tggacccaga	aaagagccag	tattgtcaag	acaatcctaa	26820
gcaaaaagaa	caaagctgga	ggcaccatgc	tacccaactt	caaactacat	tctacaaggc	26880
tacagcaacc	aaaatagcac	agtactcata	caaaaacaga	cacgtagtcc	aatggaaaag	26940
aatagagacc	tcacaaagaa	gaccacatat	ctacagccat	ccgatctttg	acaaacctga	27000
caaaaacaag	caatggggaa	aggattccct	atttaataaa	tgtttcctta	atattccatt	27060
attttaaaaca	tttattaagc	atctgcta	agtaatctgt	caactcaaat	ctgaatgatg	27120
tattcccctc	ttcaagaact	ctagtgaact	agagtggaa	aacaatttta	atgggacttt	27180
gaagaatgta	tagttcttaa	ggaggcaaaa	atgaaaggga	atgccatttc	atcagagagg	27240
actatttgag	tcaaagcttc	gaatcctgcc	tttccatgca	attttgcatg	catttatgaa	27300
atggctgtta	aagattgtgt	gcaagctgtt	aaataatgag	cacaggtata	aaaaagacca	27360
gtttaccaga	ctatgaggtt	tagttttgaa	agagagctag	actcttaaat	aaagaattgc	27420
aatgcaatgg	gataatgctg	ataattacag	ttgaaaatgt	ttagggatac	caactaattt	27480
gacctggggg	cttggttaatt	agatttaagt	caatggcccc	atgtagctct	agaggagatt	27540
tggatgtaga	aaagttggaa	ggtagggtat	ggctagat	tgcaagacct	tacataccag	27600
gccgaagaat	gtgaacttga	tctttaggac	tatataataa	ggagcgatca	ggcttttaaa	27660
ctgcagcagt	gtagaattaa	atctgggatt	tagaaagata	attcatatgc	gccatataaa	27720
ataaatttgt	gatgaaaagc	attcagaaa	ataggttatt	tcagcattcg	tagttggcac	27780
tgttgagtat	ggcatgtttc	tttttaaaaa	ccatagtata	atttacagat	ggcagctgat	27840
gtcctctgaa	agtttgggag	tatgtgattg	atgatattgt	cattcaatca	gtaattttta	27900
ttacatgaaa	atacaatgga	aaactcaaag	attgataaaa	tatagttctt	gcattaggaa	27960
caagcaataa	aaaggcagta	gtgaatgcat	ggagtcctta	aaggtagttt	cccaaaagga	28020

agagtaaaac	tgaaatggcc	cccagcacct	ggagagaaaa	aggagaaact	gcaagttgga	28080
gcaatgagat	gaatgcta	gccacaacat	aattacaaa	tccgtcctag	tgaagaagga	28140
aggcactttc	agattgccct	tttttatagg	tgctgtgtgt	tgtcaaggcc	tggtctcata	28200
cctggccaga	cttccattaa	gtctgtgcat	tcaactttga	ggacaatgat	gcgtctata	28260
ctcccaggcc	tgaatagcta	ttttatgaaa	attactatat	tggtattttt	atttgttttg	28320
aaccacatc	tatgcctgca	ttagatatta	taaactttat	tatctagctt	ctttaccatg	28380
tcgagataga	ggtgaatctc	aactagacaa	ccgatgaaga	cattgtcgat	cacataatga	28440
taatatattgt	gcttcagttg	tttttctctt	aatgggtgctt	attatgcagg	ttattaattc	28500
aaagaccatc	attgggtattg	aggaatgtga	gagtaggaat	gtcattttata	gagatgaaaa	28560
gtttctattc	accatgaaga	tcacagatgt	tttcatctgc	cagggagtaa	tttatactgc	28620
atctacttat	gttatgacct	gtgtggacct	tggtgcaata	ttgaatctga	atatgccact	28680
tgctagctat	gtgacattgg	ataaattact	taatccttct	gtgccttagt	ttccttattt	28740
ctaaagtggg	gataaaatta	ggaccatac	ttcatagggg	tattttaaat	aaattaaatg	28800
ggctaata	tgtaaagctc	atggaaacagt	gcctggaa	taagcattca	acaagtcata	28860
gttcttgtca	tattattaat	gttagaaaata	atgtctgcaa	caatgctctc	taaatttctc	28920
atctcacatc	cttaagaaca	gatgcaaata	aaaacctgta	atatttgaaa	atggctagaa	28980
attgtgtgat	ttatgagagc	aaaattcaaa	catacacaat	atgattttgc	attcacttta	29040
gtccctctt	atccaacatt	tcagcttctg	tggtttcagt	tacccaaaaa	tcaatgaagg	29100
ttcaaaaatc	ttctatggaa	acttccagaa	ataattcgta	aattttaaat	tggtgcccgt	29160
tctgagtagc	atgatgaaat	cttgcaactgt	ctcactctat	cccatccaag	gggtgaatca	29220
tccctttgtc	tagcagaacc	gggctgtgga	tgctacctgc	ccattagtct	catagtagcc	29280
ttttagatta	tcagattggc	tgcaagagga	tctcagtgt	tatgttcaag	tcattcttac	29340
tttacttcat	aatggcccca	aaaagcaaga	gtagtgtatg	tagaatattg	tcataattgc	29400
tctatttcat	tattaggtat	tgttattaat	ctcttactgt	gcctaattta	taaattgaag	29460
ttttatcatt	ggtatgtatg	cataggaaga	aaagtaccgc	atatataggg	tctggtacca	29520
tgtatggtct	caggcatcca	ctggtggcct	tggaaagtat	cctccaagga	taaggggtac	29580
tactgtagag	aatgtagaag	tggtctattta	ataaccacta	aataatttatt	tagcatggaa	29640
gtgtttgaag	taaaatctta	cacagaggtc	cagtgaagtc	ccaagccctg	actatcctgt	29700
atcatcctta	cgcttacttc	taagcgcccc	cccagttacc	ttatgaaatc	ctaggactac	29760
atggaatatg	atctatgaaa	accactgccc	tagtccaatg	tactcatttt	gcttatgaga	29820
aaattcaagg	agaggttaca	gtaagtcagt	aaaacgctac	aggaagaaaa	aggactggaa	29880
atgaaatgct	ttggtcagag	tccccacttt	gccccttttg	ctatgagatg	ttggacaatt	29940
cagtttaactg	cttgaaagcc	tgatttttcc	aattagaatt	ttgattttca	taactctctga	30000
gatccatttc	tgctgtaaaa	ctattcaatg	tcagaaatgc	acacagtcac	ccacaaactc	30060
tagtttggtg	ttcttttcat	tgcaactgatg	tagaagtatc	gactacttag	gagaacccaa	30120
gaatgaatgc	cctggatgaa	ttccataata	acctttctgc	acatccagag	taggatattgt	30180
ataattttgt	gacgtatggc	actgtaccaa	gtacagggtga	atatgccgtc	aggttttcaa	30240
tagttatgca	gtgtgtgtat	ttaacatgaa	cactgatagc	taggcaaatc	tgccaattgt	30300
tgaatcatat	agttcctgga	acaccatttc	ttatccccaa	acttatataa	ccacacctgg	30360
attaaagtaa	attaataaaa	tactacgttg	tgtacctaa	gtgtgtttgt	aaagctggaa	30420
aaggcaactc	atgaataaaa	aatatatatt	acctccagaa	aaataaatgt	aatgcataca	30480
caactttaca	caagttaaag	aatgggttta	acaactaaga	tttgttcatt	accctttcat	30540
gagacattct	tttgttctgt	attcattaca	ttattagatt	ttctagttaa	tttcaccaat	30600
tgatttttct	taagttgagc	ttcatcagag	aaattctgta	gaggtatttt	cacaaatgaa	30660
aactcacaat	cacaagtttt	ctaactcttt	tgcataaaaa	agcactgagg	acactttcat	30720
gatgatatta	ttctgaaaca	ccatatttaa	gaatatagtc	atttttattc	tttgtttggt	30780
ctttatgtcc	taatgttctc	tacagtggat	tccatcaata	ttaattgtta	aaatattaac	30840
tttctatttc	tgccattggt	ttatgtacca	cagagacatg	tattagaaaa	cacgctatgt	30900
tatgggtgta	agttaaatga	gaagcacagt	gccaataaat	tgcacgagaa	ttgctttact	30960
tgggctattc	ttggtcatag	gaaggactgg	gaaattaata	tagtcacgtt	tttatagatg	31020
cagagctttt	attaattaac	atacagttgt	taattagtag	tatatgttca	cctttgttat	31080
taacataaaa	tttagtacaa	aacacttttg	ggatattaaa	ttttggtatt	aaatatgtcc	31140
tatttcatac	atgttagaat	ataattaata	tatacttatt	gtcatcacia	agaatcaatg	31200
ctaaagtcaa	aaaattccag	gtactttttt	tccttcttgt	taacctagca	atgttgggca	31260
ttagatgaag	aagaggcaag	gctacagggt	tagataagga	tctgcagtct	tagtctttgc	31320
aaatacttgg	tatctcttgc	cttctcaaaa	cttaggcatt	gaaaattatt	ataagtaatg	31380
aaatccaaaa	tgtagatag	ggtaaacaca	gttgaaactca	caaataatatg	tttttttttc	31440
ttttctctgc	tcttttggtg	gaaaatgtag	aacatgatta	ataaggttgg	agttttttct	31500
ttataatttt	tttcacagtg	gcgttccaaa	ctaaagaatg	cttggtttacc	taatatggcc	31560
aaattggagc	cagtaccttc	attcagctag	atttaccoca	gttgcatatt	tgcaatgagg	31620
cagaattcct	acagacagcc	ttccttctga	tttttctgcc	tttgttcctc	ctcacactgt	31680
gtttctccca	taattcacat	ctaccctcta	cctaattggc	ttctccagtc	aaagtggata	31740
agcatctcag	tcagaaatac	attatgagaa	cttcccaaac	atgtactaat	cgccacaaac	31800

caaggctcag	atcatgccat	atcgctgctc	aacaactttc	cttaggttac	cactcactgg	31860
ctattgcagg	actaatcct	tatgtgggca	ttggagaagg	aaaatctgtt	ctttacattt	31920
ctagcctact	tgccactctg	tattgcccct	tacacgcca	gcaccacaac	caaattggat	31980
tacttactgt	ttccaaaata	tgctccacat	ttttgtacct	cagtgccttt	gctgttttct	32040
cattgtggaa	ttttctactt	ccccgtgtct	gtccacaaaa	tcttcccgc	cccaaattta	32100
aagacagcag	gaattgaata	acatcctttg	ttcaataccg	ttcgttatga	cattgatgag	32160
aaaaaagtcc	atttctggcc	ctggaccact	gtctgtgtag	agtttagcaca	ttctcccgt	32220
gtctgtgtgg	gttttctctg	gggtactttg	tttcctccca	catcccaaag	acgtgcccac	32280
tgggtgaatg	gggatgtcga	catggtccta	gtctgagtgt	aggtgtgtgt	gaatgcaccc	32340
tgtgatcgag	gggtgcctat	ccaggactgg	tccgtgcttt	gtaatctgag	ctgctgagat	32400
agactccagc	cacctgaact	agaataagca	gtttggaaag	tgaccctgaa	ctagaataag	32460
cagtttgga	aatgaacaaa	tcaatcaatg	taaattattg	tcaaataaaa	atttggttaag	32520
taaatgggtca	ttatacaaat	acacaacaat	aaatgatgca	agacgaaggt	gctcatccag	32580
ctgtgagtca	gccttacttg	tttgtgattc	ttttttaact	gtgtgggtgga	agtgtcctcg	32640
acagttttag	ctttgcaaac	acttatttct	tgacttaatc	caccaccact	atgaccatcg	32700
acactcactg	atttacaata	acatgggtaa	ttatcttggt	tttggttaatc	tttcttaaat	32760
gtatgtgtag	ctcatattta	attcagtgtt	taatattaga	aatgtttggg	gtcttcattt	32820
agaaatttg	cgatgttttt	gtgatgagaa	atatgccaca	ggatcttaac	tcttttttat	32880
atcaattaac	ctacggtaaa	attggtttct	ttgtacaaca	gtttacttaa	agtcgcagtt	32940
tccaagaacc	tatccgtgat	gttagatgag	gacttactgt	gccatttaag	gtcaagttca	33000
ggttctactt	tattcataac	gcaagtcaaa	agtagtctta	ctgttgcaact	ttatcttgaa	33060
cactattaag	gaaggtatca	ttctatattt	tatgcataaa	atctgaatat	gcatatacat	33120
tcaatatttt	ttttaaaagta	gacatgtaaa	tgactaagca	aacaaaatgt	attacaggct	33180
atgtcatgtg	gtcagggctt	aggattcaga	aaataaatag	ttgtcttgaa	ttttgtctagc	33240
acttatattg	tcaactcttc	tattaaattc	tgttgattga	aaattttgaa	tcaagctcac	33300
attacttata	tgacaaattc	gggtaataga	aaaagcatgg	gctttgtaac	caggcaaac	33360
agtatttgca	tgctagccct	gccaatcatt	agtttttcca	cttagtggtt	ttgtgaatct	33420
ggtttctttg	ggattgtgga	gtgtaatgat	agtgcagtt	gttagatatt	gcttgcaactg	33480
tccattattc	taggaagaaa	gtttcctgga	ataggaaata	taactgattg	tttcccaca	33540
ggagaagaag	gcacttcctc	tcctctttgg	ggctagaaat	gacttacttt	aaaaatctca	33600
gttaagagag	gactaaagct	gttccaatgt	tatgattgta	ttcccctaac	tatgtgaagg	33660
tacagcagga	gcaagccttt	catttgtagc	agtggctgca	acagaaagg	gggcagtttt	33720
tagagcggcg	tggcacagg	tattagtttt	tgaatcctcc	aggctgaaga	atgtgtgctt	33780
cctcagcatg	tgtaagtatt	tgtgtcagta	tgctttcatg	tataattagt	agaaaactga	33840
acataaatgg	acttaaacat	taaagagtta	tttaatggcc	tgtataactg	aaaagacccc	33900
agttgaatgc	tttcaactgt	ggcttagaat	ttcaacttaa	tttctttgca	attttttgac	33960
tctgcgtttc	tccatgtggc	attaatcttc	atgttgtggc	ttaccagtag	ccaccagggt	34020
ttctttattc	ttccatatcc	agcagaatga	taattccttt	gcctataatt	aactaagttc	34080
ttagatgtac	tctgattgga	ttatctatga	aaaaatcctt	atgtcagcgg	aagacccagg	34140
tcttaactgc	cttagacctt	gtttaattga	gcaagttgct	ttggtcagag	agatgggata	34200
acctttattt	acttagtatc	taagtcttag	accaatcaaa	actcaagcca	gagctggaag	34260
tggatattac	tttcattaaa	aaaattactg	ctaaataatg	gagagagaga	aataggaatg	34320
atatgcaatg	aaaaccacaa	tgtctattgc	gttgaggagg	tttgagctc	caacagccag	34380
gaaacagcta	ggaaaacact	ttctgacata	ataagatctg	tcccctctcc	acaaatggag	34440
tgggaacatt	agtgattccc	actagagaag	tagctttacc	taggaaagtg	gtgatttcat	34500
gaagttcgtc	atttctatga	cagcaagttg	tggagaccaa	ggagaagaac	ctgaagagtt	34560
tattacagaa	cacacattag	ataacattat	gggaattttc	agaaattaca	tgggtgctttc	34620
agaggagttt	atctccatca	gataggaact	taaaggctta	aattataata	atgtgtgtat	34680
aaaaaaagaa	gagtgatttt	attatataat	cactggatag	acaaaactgt	aaagatctcc	34740
tataaagcaa	aaggaaataa	tttgtgtatc	tgtctacata	ctatcttcc	acctatctca	34800
cttgtgtgcg	tgtgcgtgtg	tatgtgtgtg	tgtgtgcgtg	tctttgcata	ttggctgtgtg	34860
tatgcatatg	tatatataat	taagagaaga	tgattgtatac	catagacaga	gcagagagct	34920
aatctataaa	taataagtgt	ttctgaagag	aaaatagccc	atcaaaacag	aagcaaaagt	34980
tcagaataaa	agagagatat	atttctgtat	taaaatctta	aacttggtga	ttatgactca	35040
agggtaagag	acaaacacta	ggatatatca	aggtgaattt	tttcaaggaa	gcacccctcc	35100
agtaagagag	gggaaacatg	tcgacaaaag	gatacaatta	ggtagcctc	tattttttta	35160
ccaatgttta	gctccaattg	accaagctct	actgaatttt	gtgataacta	ctaagttttg	35220
ttactgtggg	ttcacagtct	tagaccacag	caaattttat	tgaatgtacc	aagaataata	35280
aagacacaga	taggccagca	agggtaactg	ttctttattc	aataaaaacc	tgaccttaag	35340
attagtccat	ttggcttttg	ttgccactgc	ttttggtgtt	ttagacatga	agctcttgcc	35400
catgcctatg	tcctgaatgg	taaagcctag	gttttcttct	agggttttta	tggtttttagg	35460
cctaacattt	aagtctttta	tccatcttga	attatttttt	gtatcagggtg	taagggaagg	35520
atccagtttc	agctttctac	atatggctag	ccagttttcc	cagcaccatt	tattaaatag	35580

ggaatccttt	ccccattgct	tgtttttctc	aggtttgtea	aagatcagat	tgttgtagat	35640
gtgtggcatt	atttctgagg	cctctgttct	gttccattgg	tctatatctc	tgttttggta	35700
ccagtatcat	gttggttttg	ttactgtagc	cttgtagtat	agtttgaaat	caggtagtgt	35760
gatgcctcca	gctttgttct	tttggttagg	gtttgacttg	gcgatgtggg	ctcttttttg	35820
gttccatatg	aacttaaaa	tagttttttc	caattctgtg	aagaaagtca	ttggtagctt	35880
gatggggatg	gcattgaatc	tataaattac	cttgggcagt	atggccattt	tcatgatatt	35940
gattcttccct	acccatgagc	atggattgtt	cttccatttg	tttgtatcct	cttttatttc	36000
attgagcagt	gatttgtagt	tctccttgaa	gaggctcctc	acgtcccttg	taagttggat	36060
tcctaggtat	tttattctct	ttgaagcaat	tgtgaatggg	agttcactca	tgattttggc	36120
ctctgtttgt	ctgttatttg	tgtataaaaa	tgcttgtagt	ttttgtacat	tgattttgta	36180
tcctgagact	ttgctgaagt	tgccatcag	cttaaggaga	ttttgggctg	agacaatggg	36240
gttttctaga	tatacaatca	tgatcatctg	aaacagggac	aatttgactt	cctcttttcc	36300
taattgaata	ccctttat	ccttctcctg	cctaattgcc	ctggccagaa	cttccaacac	36360
tgtgttgaat	aggagtgttg	agagagggca	tccctgtcct	gtgccagttt	tcaaaggga	36420
tgcttccagt	ttttgcccat	tcagtatgat	attggctgtg	ggtttgcctc	agatagctct	36480
tatgattttg	agatacgtcc	catcaatacc	taagtatttg	agagttttta	gcatgaagg	36540
tggtgaattt	tgtcaaaagg	cttttctgca	tctattgaga	taatcatgtg	gtttttgtct	36600
ttggttctgt	ttatatgctg	gattacattt	attgatattg	gtatattgaa	ccagccttgc	36660
atcccaggga	tgaagccac	ttgatcaagg	tgataagct	tcttgacgtg	ctgctggatt	36720
cgggtttgcca	gtgacaaatg	ggatctaatt	aaactaaaga	gcttctgcac	agcaaaagaa	36780
actaccatca	gagtgaacag	gcaacataca	aaatgggaga	aaattttcgc	aacctactca	36840
tctgacaaa	ggctaataat	cagaatctac	aatgaactca	aacaaattta	caagaaaaaa	36900
acaaacaccc	ccatcaaaaa	gtgggcaaag	gacatgaaca	gacacttctc	aaaagaagac	36960
atttatgcag	ccaaaaaaca	catgaaaaaa	tgctcaccat	cactggccat	cagagaaatg	37020
caaatcaaaa	ccacaatgag	ataccatctc	acacaggtta	gaatggcaat	cattaaaaag	37080
tcaggaaaca	acaggtgctg	gagaggatgt	ggagaaatag	gaacactttt	acactgttgg	37140
tgggactgta	aactagttca	accattgtgg	aagtcagtgt	ggcgattcct	cagggatcta	37200
gaactagaaa	taccatttta	cccagccatc	ccattactgg	gtatataccc	aaagaactat	37260
aatcatgct	gctataaaga	cacatgcaca	cgtatgttta	ttgtggcact	attcacaata	37320
gcaaagactt	ggaaccaacc	caaatgtccg	tcaatgatag	actggattaa	gaaaatgtgg	37380
cacatatata	ccatggaata	ctatgcagcc	atacaaaaag	atgagttcat	gtccttttga	37440
gggacgtgga	tgaatttga	aatcatcatt	ctcagtaaac	tatcacaaga	acaaaaagcc	37500
aaacccgcga	tattctcact	cataggtggg	aattgaacaa	tgagaacaca	gggacacagg	37560
aaggggaaaca	tcacactctg	gggactgttg	tgaggtgggg	ggagggggag	ggatagcttt	37620
aggagatata	ccaaatgcta	aatgatgagt	taatgggtgc	agcacaccag	catggcacat	37680
gtatacttat	gtaactaacc	tgacacattg	gcacatgtac	cctaaaactt	aaagtataat	37740
aataataaaa	taaaaaagat	tactccattt	gaacaagata	ttaataaata	tcaataatag	37800
agaaatgggtg	atataaaaca	atcactatta	aatgctgcag	tatttggtga	tttctagata	37860
gctattgtaa	atattaaaac	acaaaaataa	cttgtttcac	ctaagcccta	agaatataaa	37920
aagtgcgtgg	ttatgggagg	actgagaaag	ctaaaaagat	gataaatccc	tccctttcat	37980
tagaatgatt	agtggatatg	tatactaatt	agattggtag	agaatataat	tttaataatt	38040
attggaaaac	actcttaaaa	gaattatagt	ctttcaaaatt	acaaagaaaa	aggaaaaatac	38100
aatgtagtca	cttaaatacc	aaaattatac	caaaattata	aaataaaagg	aaaggaaaca	38160
aaagaaatag	aatgactatc	tgacaataaa	tataaaattat	gttaaaactc	aaaattaacc	38220
tgattgttca	cactcacaca	cacacactca	cttgttcaca	ctgtatgcac	tatataagag	38280
ataaacacag	acacacacac	acactcactc	acactgtatg	cactatataa	gagataaacc	38340
taaagtaaaa	tatcaaaaat	ttttttaatc	ccttatataa	aattatcaac	tgatcattaa	38400
aagacaaaaa	acttataaga	aagtggataa	gaacagacta	ttcatagaaa	agaagatgca	38460
aattgttaat	taacatgaaa	tgatgttcat	cttcaagtag	ttacaaaaat	gcaaatgtaa	38520
gctataatga	ggcataattt	tttacttctc	aggattggta	aaaatggtaa	agactgatga	38580
catctgatcc	aaataagaat	gtaacagaat	ggcctccttt	atatgctggt	agaagcacaa	38640
attattttta	aaatacatat	accattttat	tcagcaaatc	tcacttttgg	gaactaagtc	38700
tacagaaatg	caagcattaa	tataaaatga	gataacaaac	acatacagat	acacatacaa	38760
agatgtctgt	tacagaattg	ttggtaggag	caaataattg	actattcatc	aataagtatt	38820
gaataatttg	tggaacacac	ttaatgtgga	atattacgca	gttataaaac	aattgttcta	38880
gtatgtttga	cctagaatga	cagtcatgat	ataaagtggg	aatgatacaa	aatcaaaagt	38940
gtaatgtata	cactgtgatc	ctatttttta	acaaaatgaa	aaaggaaaaat	accctcataa	39000
aaccctatat	atgcatgtat	atatgtgtat	tttctatgcc	tgacagacct	acacgcatag	39060
gcatagagatg	ctgagctgaa	agtatagagg	tctcatatac	tccttggtgc	cacagacaaa	39120
tttccccact	atcaaacagtt	gctatcacag	tggtacattt	attatgatca	atgactctac	39180
acatcattgt	cacccaaagt	ctatagttta	gattaagatt	cactcttggt	gttgtagata	39240
ctatgggttt	tgtcaaatgt	cttcaatcca	aattatatta	cagaatagtt	tcactctcct	39300
aacaacttca	ctgttcattc	tttgtgcctc	tcctattcat	ccacttgctc	cctcttaaat	39360

cttgacaaac	cacgaatctt	tttactgtct	ctagtttttac	cttttccaga	atgttacata	39420
gttgcaactca	aactgtatat	agcctttttc	agtttggtct	ctttcactta	ataatatgca	39480
tttaagatcc	ttccatgttt	tcttggtgct	ttatagctca	tttcatttta	gaactgaaaa	39540
aatattccat	tgtctggaag	caccacagtt	tacttattca	ttcacctact	gaaggacata	39600
ttcattccct	ccaagttttg	gtcattatga	ataaaagctgc	tataattatt	cacatggggg	39660
ttttgtgtgg	ccacaaat	tcaaattctt	tgggtatata	gcaaggattg	ctgcattatg	39720
tcgtaagaga	ttgttttagtt	ttgtagaaga	ccaccaaact	gtctttcaaa	gtggctgtac	39780
tgtttacctt	cccatcagca	atgaatgaga	attctttttg	ctttacatcc	ttgccagcat	39840
ttactgtggt	cagtgttttg	ggttttggcc	attctaataag	gggtgcatgg	tatctcattg	39900
ttgttttaat	ttgcattttc	ctgatggcat	atgctgttga	ataacgtttc	atatgcttat	39960
ttgctatctg	tgtatcttct	ttgctgaggt	gcttattcag	gttttttgcc	aattttttat	40020
tgggttgtaa	attgtcttat	tttagatttt	taagagttct	gtataaatatt	ttggataata	40080
ttattttacc	agatatgtct	tttgtaaata	ttttttccag	tctgtggctt	gtaatctcat	40140
tctcctgatg	ctgctttttg	caaagcagaa	gttctgaatt	ttaatggagc	tcagcttatc	40200
aatcacctct	ttcatagatc	atgccttttg	tattttat	aaaatgtcat	ctcaatgccc	40260
aagttcatca	agaattttct	ctatgtcatt	ctctaagatt	tttataatct	tgcattttac	40320
attgaagtct	atgatccatt	ttgagcta	ttttgtgaaa	ggttcaaggt	ctgtgtctag	40380
attaatgtta	ggggtgtgga	tgtgaatgtc	cagttgtctt	agcaccattt	gttgaaaaga	40440
gactgctcca	ttttattgcc	tttgcccgtt	tgtcaaaaat	caatggatta	tacttaggtg	40500
agtcgatctt	tcagctcata	ttctgggtcca	ttgatctatt	tgtctgtttt	ttcactaatg	40560
ctatagtgtc	ttgattactg	taagtttatg	gtagggtttg	aaattgagtg	gtgtcagtc	40620
tctaactttg	ctcttttctt	tcaatattga	atttactctc	ctgggtcttt	ttcctcttca	40680
cataaacttt	agaaccaatt	tgtcaatttc	tacaaaataa	cttctgggga	ttctgattgg	40740
aattgcattg	agtctgtcca	ttcattttgga	aagaactgac	atcatgacaa	tattgagctc	40800
ttctacccat	gacctggga	atctctccat	ttattttttt	ctttttttga	tattattttat	40860
cagagttttg	tagttttcct	catatgtatt	ttggacattt	tttttttagat	ttacacttaa	40920
gcatttttatt	tttagggctg	ctaacataaa	gtggcaatgg	gttttttaatt	tcaaatttca	40980
cttgtttcatt	gatggtacat	agaaaagtga	ttgacttatt	tctcttgat	cctgcaactt	41040
ttatataaatt	gcttattagt	tatcagagac	ttttttacca	atttaaaaaa	attttctaca	41100
tagacaatta	tatcatctgc	aaacaaagac	tgtattattt	tgttcttacc	aatctgtata	41160
catttttattt	ccttttttgt	cttactgcaa	tagctaagtt	ttgcagtaag	atgttgaaag	41220
ctgaagtga	gggagatagc	ttttttttta	ttatcaggaa	acctacaaat	ttcttattat	41280
taagtattgat	attagctata	ggacttttgt	agatgtcctt	taagttgagg	aagtcctctc	41340
ctattcctaa	tgtgttaaaa	ttttttatca	tgaatgggtg	ttgaatgttg	tcaaattgctt	41400
tttctgcata	tattgatattg	attgtgtgat	ttttcttcat	tggcctattg	atgtgatgga	41460
ttagattaaa	caatattcca	atgttaaaac	acctttgcat	acctgaaatt	aaatccactc	41520
aattgtgggtg	tagatgataa	gtgctatccc	caatagcaaa	ttgaatccaa	taatgtataa	41580
aagtatacag	ttttatgtgg	aggatttttg	aatctatggt	catgagaggt	acttgtctat	41640
agtttttattt	tcttgacgtg	tctttgat	ttgatattag	ggtaatgctg	gccttataga	41700
atgagttgag	aagtattcct	cctgctcctg	cttacacaca	ctgtcagata	gtgtggagca	41760
ttgatacaat	attgtcctta	actattttgat	agaattcagc	aataaactca	tctgggatta	41820
gtatttttttg	ttttgttaaca	tcattttttta	tttattttct	tgaatagata	tagtcttatt	41880
cagagtttct	atttctttttt	gtgtgagttt	tgttagattg	tgccttttga	gtaattgatg	41940
catttcata	aggttatcaa	atttgtggat	ttagagttgc	tcataatatt	tgtttattat	42000
ctgttttaattg	tctattggat	ctaaagtgat	gtctctgtat	cattttttata	tgaacaattt	42060
tcacttaata	ccaatctaaa	tctacttcca	aataacatta	taccacttta	taggaggtac	42120
aagtaatttta	tggtataaaa	atattactaa	ttctctccct	ctaacccttt	atcactgcta	42180
tcatttcattt	cacttataaa	taaacatata	agcataattg	aatacatggt	tgctatcatt	42240
atttgaaggt	attaactttt	atatcaatta	agaataagaa	aaacaggctg	ggggcggtgaa	42300
gattaaccac	cccatgtgcc	atcactggca	ccaacaaatg	ctgtccaggg	ggctgcata	42360
tggccaattc	tactaccac	tgacagtgtc	tgtgtgcagc	atctgggtgg	atgaggacag	42420
gtgcacctca	ccataatttt	cactaacaac	cagagcctaa	gccaatgaag	aactctcaga	42480
caatgctgac	attgatcgca	tccaaataga	acatacagag	acgacactac	tgtgctagcc	42540
cagaattaaa	gccaaaacat	cttccccaaa	caatactata	attacagcta	caggaaaagt	42600
ctttctctat	gaaagaagcc	aatccatgaa	attaaaagag	aaactgttaa	aatagatgca	42660
cagataaggt	aaggacatga	gaaatatgaa	aattcaagaa	aaaaatgaca	cctctgaagg	42720
aatacaatac	ttcttcagta	aaatatccca	aagaaatgta	aatatgttaa	aaagcctgaa	42780
aaagaattca	aaataatgtt	cttaagaaaa	tgcagcgaga	tacaagagga	cacagataca	42840
aatacaagag	gacacaatag	aaaaaaaaaa	atgcattggg	aaggcaattc	atgtcttcaa	42900
tgagaatttc	aagaaagaga	gacagatata	aaaaagaacc	cggcggttc	tagcccgc	42960
gccccctccc	cgcgcgtcgg	ccctgccgag	ccggccggcc	ggcctggctc	ccctccccgg	43020
ccccgcagg	cgggcggact	gccctgagga	ggcggggagg	ggagggctgg	accggccggc	43080
gggcgggcga	cgatgccgaa	cttctgcgct	gccgccaa	gcacgcggaa	gagcacgcag	43140

tccgacttga	cttggccttc	ttcagcttcc	cgcgggaccc	tgccagatgc	cagaagtggg	43200
tggagaactg	taggagagca	gacttagaag	ataaaacacc	tgatcagcta	aataaacatt	43260
atcgattatg	tgccaaacat	tttgagacct	ctatgatctg	tagaactggt	ccttatagga	43320
cagttcttcg	agataatgca	ataccaacaa	tatttgatct	taacagtcac	ttgaacaacc	43380
cacatagtag	acacagaaaa	cgaataaaa	aactgagtga	agatgaaatc	aggacactga	43440
aacagaaaaa	aattgatgaa	acttctgagc	aggaacaaaa	acataaagaa	accaacaata	43500
gcaatgctca	gaaccccagc	gaagaagagg	gtgaagggca	agatgaggac	attttacctc	43560
taacccttga	agagaaggaa	aacaaagaat	acctcaata	tctacttgaa	atcttgattc	43620
tgatgggaag	gcaaaacata	cctctggacg	gacatgagge	tgatgaaatc	ccagaaggtc	43680
tctttactcc	agataacttt	caggcactac	tggagtgtcg	gataaattct	ggtgaaggag	43740
ttctgagaaa	gcggtttgag	acaacagcag	ttaacacggt	gttttgttca	aaaacacagc	43800
agaggcagat	gctagagatc	tgtgagagct	gtattcgaga	agaaactctc	agggaagtga	43860
gagactcaca	cgtcttttcc	attatcactg	acgatgtagt	ggacatagca	ggggaagagc	43920
acctacctgt	gttggtgagg	tttggtgatg	aatctcataa	cctaagagag	gaatttatag	43980
gcttcttgcc	ttatgaagct	gatgcagaaa	ttttggctgt	gaaatttcac	actatgataa	44040
ctgagaagtg	gggattaaat	atggagtatt	gtcgtggcca	ggcttacatt	gtctctagtg	44100
gattttcttc	caaaatgaaa	gttggtgctt	ctagactttt	agagaaatat	ccccaagcta	44160
tctacacact	ctgctctttc	tgtgccttaa	atatgtgggt	ggcaaaatca	gtacctgtta	44220
tgggagtatc	tggtgcatta	ggaacaatcg	aggaagtttg	ttcttttttc	catcgatcac	44280
cacaactgct	tttagaactt	gacaacgtaa	tttctgttct	ttttcagaac	agtaaagaaa	44340
ggggtaaaga	actgaaggaa	atctgccatt	ctcagtggac	agggaggcat	gatgcttttg	44400
aaattttagt	ggaactcctg	caagcacttg	ttttatgttt	agatggtata	aatagtgaca	44460
caaataattag	atggaataac	tgtatagctg	gccgagcatt	tgtactctgc	agtgcagtaa	44520
cagatttttga	tttcattggt	actattgttg	ttcttaaaaa	tgtcctatct	tttacaagag	44580
cctttgggaa	aaacctccag	gggcaaacct	ctgatgtctt	ctttgcagcc	ggtagcttga	44640
ctgcagtagt	gcattcactc	aacgaagtga	tggaaaaatat	tgaagtttat	aatgaatttt	44700
ggtttgagga	agccacaaat	ttggcaacca	aacttgatat	tcaaatgaaa	ctccctggga	44760
aattccgcag	agctcaccag	ggtaacttgg	aatctcagct	aacctttgag	agttactata	44820
aagaaaccct	aagtgtccca	acagtggagc	acattattca	ggaacttaaa	gatataattct	44880
cagaacagca	cctcaaagct	cttaaatgct	tatctctggt	accctcagtc	atggggacaac	44940
tcaaattcaa	tactttggag	gaacaccatg	ctgacatgta	tagaagtgac	ttacccaatc	45000
ctgacacgct	gtcagctgag	cttcattggt	ggggaatcaa	atggaaacac	agggggaaaag	45060
atatagagct	tccgtccacc	atctatgaag	ccctccaact	gcctgacatc	aagttttttc	45120
ctaattgtga	tgcatgtctg	aaggtcctgt	gtattcttct	gtgatgaagg	ttgagaatga	45180
gcggtatgaa	aatggatgaa	agcgtcttaa	agcatatttg	aggaacactt	tgacagacca	45240
aagggtcaagt	aacttggtct	tgtttaacat	aaattttgat	ataaaacacg	acctggattt	45300
aatggtggac	acatatatta	aactctatac	aagtaagtca	gagcttccta	cagataattc	45360
cgaaactgtg	gaaaatacct	aagagacttt	taaaaacagg	ctttcttata	tttgataattt	45420
ggaagtaaaa	gccgtaaggt	gtatgtaggc	cacttaataca	ctaaatatct	ttgcctatag	45480
gactccattg	aatacattag	ccattgataa	tctacctgtt	taaatggccc	ctgtttgaac	45540
tctcaagctt	tgaagacctt	cctgttcttc	cagaagagaa	cgttgaaagt	tccatgtttc	45600
cttttgcgtg	atctctgttg	acggcactct	ggaattgttt	cagttaaagtc	attttagaca	45660
tagcattttat	tatcactgtg	gatctctact	tgttgggtgt	tatgaattct	ttgaaaaaat	45720
atattttgaa	gaggtgtggg	aggaaggaat	acattttata	aaatgttata	gttaagccca	45780
caattgacct	ttgactaata	ggagttttta	gtatgttaaa	aatctatact	ggacagttgc	45840
aagaaattac	cagagaaaag	cttgtgagct	caccaacaaa	ggatttcagt	gtagattttg	45900
tctttctcaa	acttaagaaa	acaaatgaca	aagtttgaat	ggaaaagcct	gctgttggtc	45960
cacatctcat	tgctgtttac	attcctttgt	ggagcctaca	tcttcctaag	cttttttagca	46020
ggtatatgtt	gaacacttct	gtttcatggt	tgagacagaa	tcagaggcca	tggatactga	46080
caactgattt	gtctggtttt	ttttttctgt	ctttttttcca	tgactcttat	ctactgcctc	46140
atcttgattt	ataagcaaaa	cctggaaaac	ctacaaaata	agtgttggtg	tttatctaga	46200
aaaatatgga	aaatattgct	gttatttttg	gtgaagaaaa	tcaattttgt	atagtttatt	46260
tcaatctaaa	taaaatgtga	gttttgttta	aagctaaaaa	aaaaaaagaa	cccagcagaa	46320
atcctggaaa	taaataattc	agtggatgaa	attaaaaatat	atatatacaa	tcaagagttc	46380
aacaatagac	taaatcaagc	agaagaattt	ttgaacttgg	tcttttaaaa	taacaaagcc	46440
agattaaaaa	aaaaggtggg	ggggggaata	aaagaataaa	agagaatgaa	gaaagcctaa	46500
tgacatatag	gacaccataa	agcaaacaaa	tatttgaaat	ttataagttc	cataagaata	46560
agaaaaatgga	aatgccatag	acaacctatt	tattgaaata	atatctgaaa	aattcttcct	46620
tcttgtgaag	gatatagaca	tctagatata	gaaagctaaa	atatctacta	gtagattcaa	46680
taaaaaatata	agtgttctcc	aaggcacatt	aaagttacac	tgtgaaaggt	tgaagacaga	46740
gggagaattt	taaaaaatagc	aagagaaaaa	catcaagtca	catgttgggg	gaaatcccat	46800
cagactagca	gcctattact	cagtaaaaaa	cttgcaggcc	aggagagcat	gagaaactat	46860
attcaaagtg	ctgagagaaa	aatgccaatg	aagaatacta	tgcccaggaa	agctatcctt	46920

taaaaaggat	ggagaaataa	catctttttc	agacaagtaa	aaactgaagg	aaattcatca	46980
ctactagatc	aaccatacaa	taaatgcttc	agggagtaca	acatctataa	gtaaaaggat	47040
gatgtctact	atthagaaag	cacaagaaag	aattaaactc	acgggtagag	cagatacact	47100
aatgaaagca	agaaagaaat	caaagcttgt	cactacagaa	aatgaccaa	ctgtaaagat	47160
aaatattaaa	agaggaaaaga	gaaacaaagg	atatacagaa	cattcagaaa	acagctatca	47220
aatgacagct	agtaagttct	cacctattat	taacaacatt	gaatgtaaat	ggtttaaatt	47280
ctacaattat	aaagtataga	ctggctgaat	gggtagaaaa	gaaaacacaa	aagacccaat	47340
tatatgctgc	caacaagaaa	ttcacatcat	gggtaaaagac	actatattag	tctgtcctca	47400
tgctgcta	aaagacatac	ctgagactgg	gtaacttata	aaggaaagag	gttaaattgga	47460
ctcacagttc	cacatgtctg	ggaaggtctc	acagtcatgg	tgtaaaacaa	gggaagaaca	47520
aagggatatc	ttacatgagg	gctggcaata	gaacttgtat	aaggaaattc	tcattttataa	47580
aaccatgaga	tctcatgaga	cttatttact	atcacaagaa	cagcatggga	aagacccaca	47640
atcatgagtc	aattacctcc	tactgggtcc	ctcccacaa	acatgggaat	tatgggagct	47700
acaattcaag	atgagatttg	ggtgaggaca	cagccaaacc	atatcagaca	caaatagact	47760
gaaagtgaag	tgacggaaac	catatcccat	gcataatgaa	gccaaaactt	tcaggagcta	47820
gctatactta	tatcgacaa	agtagactta	aagtcaaaaga	acataacaag	agataaagag	47880
gtctagtatg	taatgtgaa	gggatcaatt	cattaacagg	atataacaat	tgtaaataata	47940
tatggactca	acactggagc	actaagatat	ataaagcaaa	tattattaga	gctaaagaga	48000
gagatagact	ccaatacagt	aagagttgga	aatttcagca	ccccactttc	agcactgggg	48060
agatcatcta	gagagaaaat	caacaaagaa	atattggact	taatctgtgc	tatagaccaa	48120
gtggacctag	caggtattta	cgtaatat	tatccaacag	ctacagaata	cacattcttt	48180
tcaccagcac	atggaacgtt	cttcaggata	aaccatatgc	tagtccacaa	aacaagtctc	48240
aaaaaatttt	taaaaatcaa	aatcatgttg	agtaccttcc	cagagtacaa	tggataaaaa	48300
ctatagatca	ataataagag	aaattttgga	aactgtacaa	atacattgaa	ataaagcaat	48360
aggcttcaaa	gtgatcatta	gattaatgaa	aaaatgaaaga	tcaaaatgaa	aaaaaatctg	48420
aaacaaatga	aaatgtaaac	acaacatacc	caaacctatg	gaatatagta	aaagtagtgc	48480
taagagggaa	tgttatagca	atagccatct	acatcaaaaa	agtggaaaga	tttcaaataa	48540
acatcctaac	agtgaccac	aaggaactag	aaaagcaaga	gggatccaag	cccaaatta	48600
atacaaagaa	ggcaaaaata	aagagcagaa	aaaaggaaa	tagaaactaa	aagctaaact	48660
aaactaaata	ataaaaactat	taacaaaaca	aaattttatt	tcttgaaaag	ataaacataa	48720
accacttgga	aaataaaaata	aaaaataaat	cctagaaaaa	atttaaccaa	ggagatgaaa	48780
agataaaaaa	taaaccacta	gctggactaa	ctaataaaga	gagaagacc	aaataagtaa	48840
atcagaaaaa	aataaagcac	acattacaac	tgataccaca	gaaatataaa	ggactatcag	48900
agattatttt	gagcaactat	acactaacaa	atttgaaaac	ctagcggaaa	tgaatcaatt	48960
cctaaataca	tctaccctgt	caagacagaa	ccagaataaa	ataggaaaaca	tgaacagacc	49020
aataacgagt	aacaagactg	aatcaataat	aaaatttctc	caaaaaagaa	aagcccagga	49080
ccagatggct	ttattttctga	gttctaccaa	acttttaag	caagacaaat	gccatttctt	49140
ctcaagctat	tcttaagaa	aaaaacgaaa	aggagagaat	tcttcttaat	tcattctaca	49200
aagccagcat	taccttgata	gcaataccag	ataaagagac	aacccaaaaag	aaaactacaa	49260
gccaatatgc	aaagtttctc	aacaaaatac	taacaaactg	aatctaacaa	cacatctaaa	49320
aaataataga	acataataaa	gtgggattta	tcccaaggat	gcaaagaagg	ttcaacatac	49380
acaaatcaat	aaatgtgata	catcacttca	aaagagtga	gaacaaaaac	catatgatta	49440
tctcaactag	cacagaaaaa	aagcatttga	tataattcaa	gaactcttta	tgatgaaaac	49500
tcttaacaaa	ttggcataga	aacaaagtat	tgcaactcaa	taaaggccat	atattattaa	49560
cccacagcta	tcatcttaca	gaatgaggaa	aaactgaaag	tctttcttat	aataactgaa	49620
taagacaagg	atgccactt	ttaccactcc	tattcaacat	ctcactggaa	gccctagcca	49680
gagcaattag	gcaagagaaa	gaaataaaaag	atgtccaagt	tagaaaagaa	gaagtcaatt	49740
gtccctcttt	gcagatgaca	tgattataca	tagaaaaatc	taaatactcc	accaggaaac	49800
tcttagaact	gataaatgaa	ttcagtaaag	ttgccagata	caaaattaac	atacgagaat	49860
cagtagcatt	tttttatatc	ataatgaact	agctgaagga	gaaatcaaga	aagcaatctg	49920
atttacaatt	tttgccagga	aaataaaaata	aaaaataaaa	cctagaaaata	aatttaacca	49980
aggaggtgaa	gacctctaca	atgaaaacta	caaaacacta	atgaaagact	gaagagaata	50040
caaacaactg	taaagatata	atatgcctat	ggatttgaaa	aattaatatt	gttaaaatga	50100
ccatactaca	caaagcaatc	tacaacttta	atgcaatccc	tatcataata	ccaatgacat	50160
ttttcacaga	aagagaaaaa	acagtcctaa	aatttgatg	gaaatacaaa	ggacttgaat	50220
agcaaaagca	atactgctca	aaaagaacaa	agctggagggt	ctcatactat	ataatttcaa	50280
aatatactac	aaagctataa	ccaaaacaac	atagcactgg	tataaaaaaca	gacacataga	50340
ccaagggaa	ggaatagaga	agccagaaat	aaatcaatgt	atttacagcc	aacttatttt	50400
tggcaaatat	gaaagaacat	acatgggaaa	atgatggctc	ctttaataaa	tagtgctagg	50460
aaaactggat	gttcacaggc	agaagaagga	aactagacc	ctatctctca	ccatatataa	50520
gaatcaactt	gaaatggata	aaagacttaa	acatgaaacc	cagaaatata	aaaccactag	50580
aagagaatat	aggagaaatg	cttcagaaca	tttttaggga	aagatattgt	ggctgagatt	50640
tcaaaagcac	aagtagcaaa	aacaaaaaga	aacaaatgtg	actgtattaa	actaaaaact	50700

tctacacagc	aatggaaata	attaacagag	tggagagaca	acctatagaa	tgagacaaaa	50760
tatgtgcaaa	ttattcatcc	aacaagggat	taatttttcag	aatatataag	gaattcatac	50820
agctcaacag	caaaacaaaa	caacaacaaa	aacctgatta	aaaagtgagc	aaagccttgt	50880
agcatagttt	gaagtcaggt	agcgtgacgc	ctccagcttt	gttctttttg	cttaggattg	50940
tcttggctat	acgggctctt	ttttggttct	atgtgaaatt	taaagtagct	ttttctaact	51000
ctgtgaagaa	tttcagtgat	agcttgtttg	gaatagcatt	gaatctataa	attgctttgg	51060
gcagttatggc	cattttcacg	acattgattc	ttctttccat	gagcatggaa	tgtttttcca	51120
tttgcttggtg	tcctctctta	tttccttgag	cagtggtttg	tagttctcct	tcaagaggtc	51180
cttcacatcc	cttgtaagtt	gtattcctag	ttatttttatt	ctctttgtag	caattgtgaa	51240
ttggagtttt	ctcatgattt	ggctctctat	tatttggttta	tagggatgct	tgtgattttt	51300
gcacattgat	tttgtatcct	gagactttgc	tgaagttgct	tatcagctta	aggagttttg	51360
gggctgagac	gatgaggttt	tctaaatata	caatcacatc	atctgcaaac	agagataatt	51420
tcacatcctc	tcttcttatt	tgaatatcct	ttattttctt	ctcttgccctg	attgccctgg	51480
ccagaacttc	caatactatg	ttgaatagga	gtgggtgagag	agggcatcct	tgttttgtac	51540
cagttttcaa	aggaaatgta	accgaacagc	atggtaatgg	aacccaaaaca	aatatataga	51600
ccaattgaac	agaaccgagg	cctcagaaat	agcatcacac	atctacagcc	atctttgaca	51660
aacctgacaa	aaacaggaaa	tggggaaaag	ttcccttatt	taataaatgg	cgctgggaaa	51720
actggctagc	catatgcaga	aaactgaaac	tggaccctt	ccttatgcct	tagaacaaaa	51780
attaactcaa	gatggattaa	agacttaaac	atacgacct	aaaccataaa	aaccctagaa	51840
gaaaacctag	gcaataccat	tcacgacata	ggcatgggaa	gacttcatga	ctaaaacacc	51900
aaaagcaatg	gcaacaaagg	cccaaattga	caaatggtat	ctattttaa	taaagagctt	51960
ctgcacagca	aaagaaacta	taatcagagt	gaacaggtta	cctacagaat	gggagaaaa	52020
gtttgcaatt	tatccacctg	acaaagacct	aatatccaga	atctacaagg	aacttaaaaa	52080
aattttataag	aaaaaaataa	acaaacccat	caaaaagtgg	gcaaaggata	tgaacagaca	52140
cttttcaaat	ttatgcggcc	aacaaacata	tcaaaaaaag	ttcatcatca	ctggctatta	52200
gagaaatgca	aatcaaaaacc	acaaagagat	atcatctcac	accagttaga	atggcgatca	52260
ttaaaaagtc	aggaaacaac	agatgctgga	gaggatgtgg	agaaatagga	acgtttttgc	52320
actgtttgta	ggagtgtaaa	ttagttcaac	cattgtggaa	gacagtgtgg	tgattcctca	52380
aggatctaga	actataaata	ccatttgacc	caccaatccc	atataccag	aggattttta	52440
atcattctac	tataaagaca	cattcacata	tatgtttatt	gcagctattc	acaatagcaa	52500
agacttgga	ccaacccaaa	tgcccatcaa	tgttagactg	gataaagaaa	acgtggcaca	52560
tatacccat	ggaatactat	acagccataa	aaaataatga	gttcatgtcc	tttgacggga	52620
catggatgaa	gcaggaaacc	atcatttctc	gcaaactaac	acaggaacag	aaaaccaaag	52680
accgcacggt	ctcactccta	agtgggagtt	gaacaatgag	aacatattgg	cacagggagg	52740
ggaacatcac	acattggggc	ctgtcgcagg	gtgggggaca	aggggagaga	tagcattaag	52800
agagatacct	aatgtagatg	acgggttgac	gggtgcaaca	aaccaccatg	gcacatgtat	52860
acctatgtta	caagcctgca	cgttctgtat	cccagaactt	caagtataat	aataaaacaa	52920
aagttagcaa	aggatgtgaa	tagacattta	tgaactaaa	acatacaaat	ggccaataag	52980
tatgagaaaa	aatgctcaag	atcactaatc	actggaaaaa	aatgcaaatc	aataccacaa	53040
tgagctatca	cacctgtcag	aatggctatt	atcaaaaaaga	caaaagataa	gtgttgatga	53100
ggatgtggag	aaaaggaaac	cattggaatt	gttggtggga	atgtgaatta	gtacagccat	53160
tattgaaaaa	agtatgaagt	ttcctcacaa	aattaaaaat	ggaactagca	tgtgctcctg	53220
caatctcact	accaagcagt	tatccaaaag	aaaggaaaatc	agtctattaa	aggggacacct	53280
gtaacttaat	gtttattgca	gcagtattca	caatggctaa	gacatggaat	taacttaggt	53340
gtccatcaac	aaacaaatgg	atgaagaaaa	tgtagtatat	atacactcaa	tgaataaacc	53400
ttcagggtata	aaaaaagtat	gaaatcctgt	cactcacagc	aacacagatg	agcctggagg	53460
actttatatt	aagccaaatc	ggtcagtcac	agaagataa	acaccacatg	ctgtcattta	53520
tatgtgggag	ctaaaacata	attgagttca	tggaaagtaga	gaataaaaat	gtgggtatta	53580
aaggcacaaa	agggtaggag	ggaggggacg	atagggagaa	gttggttaac	agatgcaaaa	53640
ttataactag	ataggaggaa	ttagccctgg	cattctgcag	cactgcaggg	tgaacatagt	53700
ttaccataat	ttattgtata	tgctcagaaa	gctagaatag	aggatttgga	ttgttcataa	53760
cagaaagaaa	tgatgaaatg	tagaggggat	ggatatgcta	attaccctga	tttgatcatt	53820
acacattgta	tatcacatat	ggaaatata	cactgtgtca	tccataaata	tgtacgacta	53880
ttgtgtcaac	taaaaaataa	aggaaaaaaa	gtaaaaaata	gggaaagtat	ttattttacc	53940
ttcacttatt	ctctgatgtt	gttccttcct	ttatttagat	ccatgtttct	aacttatgta	54000
attttccttc	ttcctgaata	gcttctgcta	agatttcttg	caaggcaggt	ttacttgtaa	54060
caaattctct	caatttttgt	ttgtctgaga	aaggctttat	tcctccttca	cttttgaagg	54120
ctaaattcac	agagtacata	atttaaacac	tggtttttta	ctcttaacat	tttgaatatt	54180
tcattcctct	ctctttttgc	ttgcatgatt	tctgtggtga	atttgatgt	aattcttatt	54240
tttgctcttc	tataagtaag	ttgtttcttt	ttccactttt	gcattctttt	ctagatattt	54300
tcttcatccc	ttgatttttc	tttttctgtc	tcttctcctt	ttttatattc	ccattacatg	54360
tatgctactc	cttttgtagt	tgtccacag	ttcttagata	ttctgttctt	ttttatcagt	54420
tttttttttt	ttgaattttt	gcttctcagt	tttggaagtt	tctgttgtcc	tatcattaga	54480

ctccaagatt	ctttcctcag	ctatgtgaag	tctactaatg	agcccatcaa	aggcatat	54540
tctttctgtt	tttgatcttt	atcattttta	aattatttcc	tagaatttta	atctctctgc	54600
ttaaattttcc	tatctgttct	tgtctgttgt	ctaatttttt	cattacagct	ctgacagctc	54660
tgagcatatt	aatcatagac	tttattttatt	ttcttttttt	gagacggagt	ctcgctctgt	54720
tgcccaggct	ggagtgcagt	ggcacgatct	cggtccacag	aaacctccac	ctctcagggt	54780
cacgccattc	tcctgcctca	gcctcctgag	tagctgggac	tacaggtgcc	cgccaccatg	54840
tccagctaatt	tttttggtat	tttttagtaga	gacgggggtt	caccgtgtta	ggcaggatgg	54900
tctcgatctc	ctgacctcgt	gatctgcctg	ccttggcctc	tcaaagtgtc	gggattacag	54960
gcgtgagcca	ccacgcctgg	cctcaatcat	agacttttaa	aaagatttct	gttctgataa	55020
ttccaacctc	atggccatag	gtaagtctag	tccttatgct	tgctctggct	cttcaaactg	55080
tgtgtttttgc	cttctagtat	gccttgtaat	tttttttttc	atagctgatt	ataatgttct	55140
gagtaaaaga	aactgtgata	aacaggcctt	tagtgatgtc	acaatacggg	gtggaaaaag	55200
gggatgtgtt	ctataagcct	gtgattaggt	cttagtcttt	tggcgagcct	gtgacctgga	55260
ctgtgaactt	tcagtgtctg	tctttttttt	cccctcctta	ggtggtacag	ggcagccttc	55320
caacatgtga	aaaactagag	gacccttgag	ctgggtattt	ttttccccag	gcagatcaga	55380
ctctgataaa	acctcagaag	gttaggctct	ggtaaaatag	tcacccttga	gtttaggccc	55440
tttaaaggag	aacagactat	tcagcttttt	agaaattagt	attttttttt	tgagacaggg	55500
tcttactgtc	acccaggctg	gagtgcagtg	atataaatca	tggtcactg	cagccttgac	55560
ctcctgggtt	caagtgtatg	tcctatttca	acctgagtag	ctgggaccac	cagcatgtgc	55620
caccatgcat	ggctaatttt	tttgtaattg	tttgtaaaga	taggatctca	ctatgttgtc	55680
caggctgggtc	tcaaacttct	gggctcaagt	gatcctccca	cctctggctt	attttataat	55740
agttttttcc	cctcctccta	ccagaagcac	aagaggactt	tctcatctga	tacttactgt	55800
gaggacctag	tagttagagc	tcctaaagat	caaactcata	aaagtatata	gccccacaa	55860
ctatgactgg	gtacccttgg	agtttttaat	tctctaagtt	gtttcacact	gagccttcag	55920
caatttgcca	attacagttt	aattttttct	acccccacaa	tggttgctat	ggaggtttct	55980
gctcatggat	ctctgcttca	gtaagttgtg	gttctatctg	tttctcta	ttggggatcc	56040
tctcttttct	tccaacttta	gggcagtggt	ttgccctgtg	acctcacttc	tctgatctaa	56100
gaagagttgt	tgattttttt	ttaatgggtt	tagcttttta	cttttaagta	tggattggca	56160
acttctaagc	ttcttatatg	ccaaatggaa	aagtagaagt	tctcaaaaca	actattttat	56220
actaatat	tattgattta	tatagtatta	agtattataa	ttaaatgcta	agtataactt	56280
agtgttaagg	aattgactta	gtcaataagc	aactgaaatg	gtgggagaaa	atatacacga	56340
gtacataaga	aactaaacta	ctagtttgga	gtcttcattg	ttctctgggc	attagtgaat	56400
atgttttgac	agaaggaata	gaaactattg	atcatccaga	aagtcagtta	aatgacagtt	56460
aaacttctgg	tagataagtg	tgttcaagtg	tctacatatg	cattcacatt	taaatatagg	56520
cttctacata	gtaccttttt	ctcttaatgt	tttattatag	atttaccact	tgtttatgaa	56580
cattacctga	aaacaaatat	atctgcttaa	tattttat	tattttccat	catctatttt	56640
accattccat	tattagcttt	cttttctatt	ttagctgttt	tctttatgta	gataaatttt	56700
gaacaagact	caatttactt	gaccttttaa	ttggcattta	ctatggacca	ccacttctc	56760
aaaacaatcc	attctcttgg	ctttccttct	aactctctgg	ctttactatt	tgtctatattg	56820
acatctgttc	ctgaatcttt	gaaagtcagc	tcaaacgtca	tctgttttaa	acctaacaca	56880
taatttatac	actccacctc	ttcttctatt	tcctatctca	atggcaacac	aatactgatg	56940
gtaaccagct	taccatagtt	aggcttataa	tttttgaatt	tacaatgggc	ttattggaat	57000
gtaaacccat	tgtaagttta	ggagcatctg	actcttttgt	tgtactcacc	agacaactca	57060
agaatgatcc	ttgatatgtc	catcttgctt	aatttttatt	ttcaaatac	attaaatttg	57120
cttattttct	aaatctattc	atgtatttct	agattctctc	ttactatcaa	gtgcaataaa	57180
taattatgtt	aagcactgac	tatgtaatag	cctcataaag	attcacccat	atactttctt	57240
gaatctctcc	aaacctatctg	gcatatggct	gttaatatga	ccattgaaaa	aagtaaacta	57300
gaaaaactgt	tcccatgttt	gtaagtacaa	atacattaat	tattgctttt	aggattgata	57360
caaaaacttct	taaaatatcc	ttaaggccac	acataatttg	gtctcttcca	gctctggctt	57420
tatgtcaaac	cagttctgtc	tcttctctc	tcagccatat	tcctactttc	ccttgcctct	57480
ttctttctag	ccacatacag	gccatgatcc	ctctctcttc	aaagtagtca	cctatactat	57540
ttgctactga	atcccccttt	tccttaaggt	acttatgatt	gagatctctt	gtgaagtatc	57600
cttctccggg	aagtattcat	tgagggtttt	aagtaaaatc	ttcttgtata	ggcttcatgg	57660
cagcatatat	cttgatttca	taacagttct	caagttggga	attgattgct	gttattggat	57720
taatgttttt	gccaccaa	aataaacttc	ttgagggaag	gagccacgta	tgattttgat	57780
ccctgttgta	ttcctaatac	taaattggcac	atggtaaatg	ctcaaata	tgatcaaaga	57840
ataaatgact	ttaatttaaa	ctaagaatta	actaataagt	catactataa	tctgctaagc	57900
tacctgacaa	atggtaaaaa	ttgtagcaat	tgagatagaa	ttccagggaac	aatatacacc	57960
tttttcaaat	ttcatacaga	gtagattttc	taaaaaataa	gcagcgcatt	ttaaaaggcc	58020
ccctaaataa	ggcttcagat	ggcacaaggc	catggatagg	ttgtcatagt	gatgatcaga	58080
aatgaaaaat	atcttactct	tacttgaggt	aaggagtttg	aggacagcct	ggccaacatg	58140
gtgaaaccca	gtgtctacta	aaaatataaa	cattagctgg	ctttgggtgg	gcatgcctgg	58200
aatccagtta	cttaggaagc	tgaggcagga	gaattgcttg	aaccagagg	gcagagggtg	58260

cagtgagccg	agaccatgcc	actgcactcc	agcctgggca	acagacccca	tctcaaaaaa	58320
aaaaaaaaaa	aaaaagcaat	gaagtatat	tctatagggg	ccaactttat	ttatagcaag	58380
agacatgaga	ctgaatatat	tctatgccaa	aactttccaa	tccttagaat	cagccctaca	58440
aaaagaaaga	aaaaagaaca	gaaaggaagc	agcaatcagc	tatgagcaat	aattagacat	58500
tcgtttgcta	gctctagcac	atgtgaccat	gaagagtaac	tgtgaaccat	attgactttc	58560
tctcctgaaa	agaaaaatat	gaaaaaaatt	cagaagaaaa	ctgtcctatc	acaaagaata	58620
cagaaattgg	gtaagaatga	acagctgttt	catttcatta	cctttgccct	tttccacctt	58680
tatttttgga	caattagttg	atctaaaaag	caatagtctt	ctatcagtc	gtttttgcta	58740
caaacacata	cacacacaga	aagagagaaa	ggcatacagt	aatatgcatt	taccttaggt	58800
tcacaggtat	gcagtttggc	tgagttcgat	tacctccatg	tgtttcattc	taagtcataa	58860
gatggaagga	gcagctgtat	gggagtttta	acatatgcac	aaagatactc	caccttacaa	58920
gaggtacagc	ttaaattccc	tcctcttgag	tgtggattag	aattagtgac	tcactgcaag	58980
caactgaata	atgaggaaat	ggcagtggtg	gacttccatg	taataaaaga	catggcttcc	59040
tccttgcttt	ctcttacatt	gatacttggg	ggaaagtcag	caactatctt	ggaaggatat	59100
tgaagaaagc	ctgtggagaa	actcatgtgg	tgagaaattg	aggcattctg	ccaataacctg	59160
catgaatagg	tcactcttggg	aatagatcct	ctaatcctga	tggagtccag	atgactacag	59220
acatgaccaa	catcttgact	gcctcctcat	gaaagatgaa	ctagaagctc	ccggttaggc	59280
agcttccaaa	ttcttgatcc	acagaaactg	tactgaaagc	atcaatttct	taccacatgt	59340
cttttgga	aactcaacat	taatggacag	aggagcatac	ttctctatag	taggctaaat	59400
aatggccacc	cagataaaaa	aattctaata	tgaaaatgta	taaggtaaag	gaatctacag	59460
atgtgattga	attaagaatg	ttggtgtgat	aagtttatatt	tggattatct	tgggtggccc	59520
taaatgctat	cacaagttcc	ttctaagaga	aaagcaggag	aagacttgac	acccacacaa	59580
agaaggtgat	gtgaagatgg	aggcagagac	tggagccact	aggccacaag	ccaaggaaca	59640
ctaaggaatg	ctggcagaca	ccagaagata	gaagaggcaa	acaatgcatg	ctctcccaga	59700
gcctctagaa	atgtgagata	ataagttttt	attgttttga	gcctccaaat	ttttgtgaat	59760
ttgttacatc	agccatatgg	aatgaaaaca	tcctctcatt	tgttgagttt	agatgttaaa	59820
tactggctga	acaataatct	actctacttt	agcatctttt	caaaaataat	cacaaaattt	59880
aaaaggaaaa	ttatgcactg	gtactagcaa	aataaatgaa	caaatgaatt	aacacaaaat	59940
aggcaaaagg	aaaaatgaat	atctagacca	aagtttaatt	atccatgaaa	gcaatggaaa	60000
atgtgaagtc	tctaagaaac	caatgtaaaa	agagctaaaa	acaatatagt	atgaaagaaa	60060
ccagaaagaa	acaaatgttc	tttggatttt	ggagaaatac	agagactaaa	ataaaaaacca	60120
gaaatgaata	ctccattaaa	acaggcatac	gaaagacagg	atgggtaaaa	accacacaaa	60180
acgaaattgt	gtgtttgtgt	atatatacgt	gtgtacacac	atacacgaaa	agaaaaagtt	60240
caatagaaga	ttcatttttt	atgtaattag	tgtttctaaa	gaagataact	aaaatgtaat	60300
ttaaaaattc	aaagatagaa	gaaaactatg	ctgaaattaa	agaagatata	attctacaaa	60360
tgtaaagaac	attatgtatt	ttaagaactt	gaaagaaaag	gagtggggaa	gtggccaaga	60420
tggtccaacta	gaagcagctc	gtgtgagtg	ctctcacaaa	gagggacaaa	agggcgagta	60480
aatacagcac	cttccactga	aacatccaag	tactcgcact	gggactaatc	aaggaaacaa	60540
cttgacccat	ggagaacata	gaaaacaaag	gcaggacgac	agcccacctg	ggcacgacac	60600
ccagccaggt	gaacctcccc	tgcccagaga	atcggtgagt	gaatgtgtga	ccctggaaac	60660
cacactcttc	ccacgaatct	ttgcaacctc	gagttgggag	atccccctct	gaacccactc	60720
catcagggct	ttcagtcata	tacacagaga	tacgggagtc	ttggcagaga	agctgctcag	60780
gcacatggtg	gagaaccagg	aactgtagat	attccacctt	caggcttccc	ggcaaaaagta	60840
actgcaactc	cagaaaagca	ggagattaga	tccttgtgca	tacccttagg	aaagaggctg	60900
aatccagtg	gccaagcagc	gatgggtctg	aggccctact	tccatggtgc	ctcaaaggat	60960
aagacacatt	ggcttgaat	tccagccagc	caccagcagc	agtgttgtgc	ctacctggga	61020
cagagttccc	aggagagggg	gaaggccacc	atcttccactg	tttgggcaag	tcaccttttt	61080
cagcctgcag	actttgaaga	gtccaaaccg	atcgggcaga	agggatcccc	caacacagca	61140
caattgctct	accaacacgt	ggccagactg	cttctttaag	cagggtccctg	agccatccct	61200
ccttattggg	caggacctcc	caaccagggc	ctccagccat	ccccgctggt	gttctctggc	61260
ctacagagat	ttgaaaactc	cctgggacag	aggtctcaga	gggaggggtg	ggctgacatc	61320
tctgctat	gggtactgaa	cctgtccagc	ctgtgggctt	tggagagccc	aagccaacag	61380
gcggtgaagc	gttaccocag	cactgcgcag	ctgctctaca	aaagcatggc	cagactgctt	61440
ctataagtgg	gtccccaatc	ctcttctctc	tgactgggca	agacctccca	accaggatct	61500
ccagccacct	cctgcaggtg	cgttccacct	ggcaacaggt	tcatacctcc	ctgggccaga	61560
gctcttagaa	gaagtggcag	gctgccatct	ttgctgtttt	gcagccttca	ctggtgatac	61620
cttcagctac	cggaaaatcc	aaggcaacta	gggactggag	tagaccccca	gcaaaccaca	61680
gcagccctat	ggaaaattgg	ccaaattgtg	ccagggggaa	aaaaaaaggt	aggcaacgtc	61740
gaacattgaa	ggtagattag	ataagctcac	agaaatgaga	aagaatcaga	gcaagaatgc	61800
tgaaacctca	aaaagcctga	gtgccctctt	tcctccagct	gacctcatta	cctctccagc	61860
aagggttcaa	aatagccagt	atagagaagt	acttaatcct	cctgataggg	ctgaaaaaca	61920
cactacaaga	atctcgtaat	gcaatcacia	gtattaatag	tagaatagac	caaacagagg	61980
aaagaatttc	agagcttaat	gaaatatggc	aggcagacaa	atgtagagaa	aaaagaatga	62040

aaaggaatga	acaaaacctc	cgagaaatat	ggaataccat	atcacaccag	tcagaatggc	62100
tataattaaa	aagtcaaaaa	ataacatgct	ggcaagggtg	tgaagaaaaa	ggaatgctta	62160
tacactgttg	gtgggaatgt	aaatcagttc	agccattgtg	gaagatggta	tggcaatttc	62220
tcaaagacct	aaagacagat	atactattca	accagcagat	cccattactg	ggcatataac	62280
caagggaata	taaatcattc	tgttataaag	acacatgcac	atgtatgttc	attgcagcac	62340
tattcacaat	ggcaaagaca	tggaatcaaa	ctaaatggcc	atcaataatg	gactggataa	62400
agaaaatgtg	gtacgtatac	accatggaac	actatgcgac	cacaaaaaag	aatgagatca	62460
atgagatcat	gtccttttgc	gggacatgga	tggagctgga	ggccattatc	cttagcaaac	62520
taatgcagga	acagaaaacc	aaataccaca	tgttctcact	tataagtggc	agctaaatga	62580
tcagaacaca	tggacacata	caggggaaca	atacacactg	gggctttttg	gaggatggag	62640
ggtaggaaga	gggagaggat	caaaaaacaa	ttaatggata	ctaggcttaa	tacctgggtg	62700
atgaaataat	ctatacaaaa	aaaacccatg	acacaagtgt	acctatgtaa	caaacctgca	62760
cttgtacccc	tggacttaaa	ataaatgttt	aaaaaataga	gaaagaaaaa	gacactaaaa	62820
acatgaaaag	atatgaaaag	atataactca	ctgtaaagat	aaagcataaa	attcaccata	62880
aagataaaaa	atagtcaaat	tcagagggct	gtaatgaatt	tgtatgtaat	taagtgtata	62940
ctgtaattat	agtttataag	ttacttttcc	tctactataa	gagttaaaag	acaaaagtat	63000
taaaaaataa	cttcacctaa	aaaaaagaac	ttagccaatg	tcattgtttta	tactagaaaa	63060
tactgcagtt	cagtcttata	atcctggcct	ttctcttctg	attttccata	tttataaaat	63120
atttgaagaa	atttgtttct	tatgtacatc	ttgacatatg	tgatatatga	tttgtttctt	63180
tttatttttt	atttttttct	gagacagagt	cttgctctgt	tgcccaggct	ggagtgcagt	63240
ggcgtgatct	cagctcactg	caagctccgc	ctcccagggt	caagcgattc	tcctgcctca	63300
gcctcccaag	cagctgagat	tacaggcatg	tgccaccaca	cccggctaata	tttttttttt	63360
ttttttgtat	ttttagtaga	gatgggggtt	caccatgttg	gccaggctgg	tctcgaacta	63420
ctgacctcac	gatctaccca	ctttggcctc	ccaaagggtc	gggattacag	gcataaggca	63480
ccatgcctag	ctgtgatttg	tttcttattt	gcactctggac	atatgtgaca	tgtgaataag	63540
aaacaattat	tgggactttg	gtcaagtaat	tctattcttt	gttaaatcaa	aagatggcca	63600
tctaagtttc	ttttcaacac	catgtatcta	taattcttac	tctgagccat	tcttctgata	63660
gggcatgaat	gaaaagaatt	ttagaaagca	acagtaattg	gcaatcatat	agatctatat	63720
tagatgcatt	aataaaatgt	actaaggctg	atgaattaat	aactgtgacc	tctataggag	63780
tcaacctttt	aagggtatag	taacacatct	acattccata	tcaagcatta	ggtaaaaaat	63840
aatcaactgg	tataacatta	tctttctgtg	gatctgccaa	aaataagttt	tattaataac	63900
ctagaacagc	cacctaacca	atatggcttt	ttaaatatct	atgtgtcatg	caatttgcta	63960
acatgttgca	agaaattggc	attcattatg	tgacatattg	tctcatacga	tatttttggg	64020
gaatttggaag	ataacatata	gagtagctac	acgttttcacc	ttcttttttg	aaggatgaca	64080
tggtaaaaaa	taaatactct	atgtttttat	aaagaaaaaa	ttatgtatga	gttattgtcc	64140
ttgggggtat	gggaagtcaa	catgaaaatg	acttaatagg	caaataattaa	ttatccacta	64200
aatttttcagg	aatatgtaca	atggcaatgt	gaagatagtt	attgaaaatg	tatctttttac	64260
acttgagatg	tatgtattca	gacacttctt	gcagataaag	ctgatatgat	atacatttta	64320
aaatcagggt	aaacccagac	atcatcatgc	ttttcacagg	tgataagagt	aatgaatact	64380
tttctgagag	gcagatgagg	attcaaagcc	catgactaaa	tcctgccatt	gctccacttc	64440
ttatcctgtt	tctctggaga	cattacatag	gctaagattg	ctttcagtc	cagaagctct	64500
gatagcatgg	agttgttagt	ttgctggaca	gagctagtcc	aaacccggtg	ataagcaaat	64560
ctgaaacctt	aggaggtttt	tcctaataat	aactaaatta	ttgattttag	taactctctac	64620
cttctttctac	tacattcctt	gtaaatgaaa	aaaaaaatag	cgcacatatc	agtctgcttt	64680
ctcactccta	tgtttataat	acacacatat	aattacactg	tctcaggaaa	attctacctc	64740
aacctccca	gaaaattgga	ttgctaaaaa	tgttgtgaac	aaatttcaac	cttaattctc	64800
actgtcaatt	tcaaagtact	aatgcagatg	gttttatatt	ccttgccacat	ccaattaatt	64860
agttgtgact	gttgaaaata	ctatgttgat	tataagcctg	tagtctcagc	tcaactgaaa	64920
agagtgtaaa	acagacaact	gatatgaagg	ggtaaagggt	ttaggtatgt	tatacatttg	64980
tgattctttt	tcttatgtgt	tgagctttgt	atggatccct	tcattctaat	ataaattcct	65040
tttcttggtta	tttgttgatg	gcaggaaatt	tgactgaata	acctcttaag	ttcatctcaa	65100
cttaatgact	tcacatttta	taatactttg	tctataaagc	ataacttcta	aaatagggtac	65160
ttctattttc	ctagatgagc	cagattctct	tagagaatct	tgggattcaa	ttatgggatt	65220
tggggagggg	tctaaatatg	ggaggatttg	tgtatacact	tatttatcct	tcaactatag	65280
aaaatgattc	ctcatgctta	gtcagctgag	ccaggcaaaa	cttattttcc	ttaaaatgca	65340
catataaata	tcagatatta	taagattatt	attttttata	attacaagat	attagaaaag	65400
tactcagttt	taacctatatt	attttatgtt	atttattaca	ggacagcatg	aaagaaattg	65460
gtagcaattg	cctgaataat	gaatttaact	tttttaaaag	acatatctgt	gatgctaata	65520
aggtaatgat	aattattttg	agtttgtcat	tcaagcttga	ttttatagaa	gcttctattt	65580
tttgtgcctc	tgttagacaa	ttatatgaat	actatttaata	tttgcagcct	gatcacataa	65640
ttccatttga	ttaaatcata	ctatggccca	atttttatatt	tttgtttttac	aaatagtcct	65700
gtgcttatta	aataacaagt	tttttttgtt	tcaccattct	atttttttacc	ttgaaaatac	65760
tagaattgtc	gaattcaaag	acacacctat	ctcttatttt	ctttctttct	ttctttcttt	65820

gttttttttt	ttggaggcag	agtttcgctc	tgtcaccagg	ctggagtgtg	gtggcgcaat	65880
ctcagctcac	tgcaaaactcc	gcctcctggt	ttcaagcgat	tctcctgcct	cagtctcccg	65940
agtaactggg	tctacaggca	tgcaccacca	caccaacta	atttttgtat	tttttagtgga	66000
gacgggggtt	caccatgctg	gccaggatga	tctcgatctc	ctgacctcat	gatccgcctg	66060
cctccgcctc	ccaaagtgt	gggattacag	gcgtgagcca	cgggtgcctgg	cctctaaatt	66120
tcttatacag	aaaaatactt	gttaatgtga	atgcttgcac	acatacaaat	ataagtcatt	66180
ggtataat	agttggaagc	gtcctgaaaa	ttttcttttc	aataatttgct	tatctctaaa	66240
tgattaccac	atctagtgtg	tataatatta	cacttttaaaa	aacctaaaaa	gtttatatca	66300
tttctcccta	cagaaacaag	tgtgctat	catagtcttt	taaaaactca	cagtagctaa	66360
gttagcctca	tggcatctca	caaccataaa	ttcttttttt	taaatttctt	aatttaata	66420
tctgcaaaac	ttatgtttta	ggtgactaca	gtcctttatt	ttcttattat	cagctattct	66480
tccatagctc	aaaagatgca	agaaatacta	agaaaaaacc	acacatacct	cttataatac	66540
attgttgctt	ccagaagtct	tctccttcgg	ttatcatggt	taaaattgaa	taatcttcta	66600
atatgttcac	acataagcga	taagatcaca	taagcataat	agagaaaaca	aactttaaaa	66660
gtcaagataa	ttattaaacc	aagttctaag	aacttcatgc	tgtcacctag	gagccaaaca	66720
gttttagttc	tgttacttgt	caatcacatg	attaaactgga	atagaaaagct	ggggtggagg	66780
cggggcatta	cctagcaaca	tagctcaagc	tctaggctcc	ttaagaaagc	ttataatttc	66840
ttaatat	atgtgaacca	tggcccttct	gactttttcc	tataatagga	aggtatgttt	66900
ttattccgtg	ctgctcgcaa	gttgaggcaa	tttcttaaaa	tgaatagcac	tgggtgatttt	66960
gatctccact	tattaaaagt	ttcagaaggc	acaacaatac	tgttgaactg	cactggccag	67020
gtaagctaag	gactatttac	tttgaataaa	aataattaaat	actcctgtgc	caagatacca	67080
ctattctctg	atgatcacat	ccattatcat	agaatcctaa	gtgtttatta	tcatctaaag	67140
ttgaagtatg	tttactcaat	cctagaagag	gaaaggetca	gtttggaaat	acctattttat	67200
ctcttggcta	gagtgaattg	tttgtgaaag	gggagtaaaa	aataaataaa	taaattcttc	67260
attgcataaa	taacttccaa	ggatactagg	gtgatatatt	gggtggggaa	tggtaaat	67320
ctatatctaa	aacttattaa	tagctttaat	ccatatatgt	acacatttac	aagaactcct	67380
agtcaataaa	acaggaaatc	aaatgtat	aacaaatata	tttataggct	taaactagac	67440
ataaacatgt	ccaacaattt	tcccttcttt	aaataatttt	gatacaaata	gggctaatat	67500
tttctacttt	ttctactagt	ggttatgaac	taaaacaaca	aaaccaaata	tgggaagacat	67560
catctagaga	ctagacagca	gtttccttat	ctacaaaatg	cagaaaaaca	tatctacatt	67620
gtgggatttg	aaaggattaa	atggcataac	acatgtaaag	tgcttagtac	taaaaagttt	67680
tcaatattta	atacagtgtc	ttattttatt	tgtattattt	acctcttttt	ggattttacc	67740
agctgccaca	aaaaaccaaa	agtttatttt	atggttttta	atattttctt	aaataacatt	67800
tttatgactt	aaaaaagaat	tttgttttgt	ttgagcacta	gtagtttccc	atagaaggta	67860
aaatggtaag	attatctttg	aatcctattg	acagtgataa	aaatgtagat	tatctattat	67920
ataacttgga	tagcctcatt	tatcattgct	ttatgtactt	gatggaagca	agtctcctct	67980
tagtgtgtctg	gatttgccaa	acttatttcc	aaacttgcgt	ccttacgttt	gtcccctaga	68040
gagcattttct	actttttttt	tctataaatt	ggatctat	tgttctatgc	cttcaaggct	68100
cggctcaaga	ttcatgaaga	cttcctactc	tagtctacca	tttcttcatt	cctacttaac	68160
agcggtttca	aagtactgtc	taatgcagat	aggttttatg	ttgcttgcac	atccaattaa	68220
ttagttgtga	ctgttgaaaa	tactgtgttg	attataagcc	tccactcttg	gttcaactga	68280
aaagagtgtg	aaacggaaaa	ctgatatcac	ctcttggctc	actaagaggt	aaaggtctta	68340
ggtagt	atatttgtga	ttctttctct	tatgtattga	gctttatatg	gatcatcatg	68400
ttccaaaatt	aactgtagag	aaagaaaata	tgcaaaataa	ttaaatcttt	gaaattaaat	68460
tatattacat	tgattaaact	gatacaagtc	acctttttct	tgaataaaca	aggcaagatg	68520
ttaaagcagt	cagctacact	gaattttctt	catgagccag	gcacgctaca	agctttttac	68580
tattgtttta	tttcattttg	tttctgataa	gtgaagctta	ataaaatgta	tggccaggat	68640
ttacaatttt	cttgtaaact	ttatttttat	attgattaaa	attcaagttt	tatctctgct	68700
actataccct	actatgttaa	tttttcatac	ctcacagtag	ttaacacagt	actaggcaga	68760
cctacaaaaa	tatggattct	gggtattcag	aagactgaac	tatcttgctt	cttcctttac	68820
cctgatattc	catttctaaa	tcataattaat	attttacttt	cttaacaata	agaaatttaa	68880
agtagagtct	caaatagatt	agatgagctg	aaggcaatat	gaaaatttagc	aattacaaac	68940
aactggagga	gcaatgaaga	aataattcaat	attataaatg	tgactttgtt	tttaagggtta	69000
aaggaagaaa	accagctgcc	ctgggtgaag	cccaaccaac	aaagagtttg	gtgagaataa	69060
ttgtataatt	ttccttatgg	ttcatcaggt	ttttactcaa	cttaattcct	aatttttcat	69120
tttgaattgt	ttccttctta	tagctggttt	tgaataaatt	tattataaca	ttgataaaaag	69180
gagaagcgag	gtgccctca	aaaatttgat	tcctttaaat	tgcatttttta	aacccactat	69240
tttaaaaatag	aagctgttag	ggcaaatata	aaagcatgat	tttttttttt	tttagaagaa	69300
gcagcattaa	aatattgcag	ctagcacgta	aaagaaatga	acaaataatt	tatataggag	69360
aaaataaact	agatgacaaa	tacatgaaga	aaaaaagcca	tccctgttag	tttgtaaaaa	69420
aataaaaaatt	aaacaataag	gacttatctt	atatatacct	cttttattag	tgtagattgt	69480
acagtataaa	taatatataa	tagtatataa	acatatattt	atacatatac	tactagacat	69540
tattagataa	attatacaat	aatatggaaa	atatttatga	atgacttaat	aaggcagaat	69600

acttaaattgg	atctgactaa	acttttaaat	gatataggta	ctaattaagt	tgaggcatgg	69660
aaaaatgagc	acacctgggt	cataaaagt	atggattcct	cttttatatt	tccattat	69720
gaccaatagc	tacatggcaa	catggaaatt	ccttactcct	ttcagaaaag	caaagtgagc	69780
ctgtacactc	tgagatttag	gaaattctag	ggattctatg	caaagtggaa	catctgaagt	69840
gaatacagaa	gctaaaagca	atataatcac	cctgaaggct	tttactaag	agaatttggg	69900
aagtttagaa	aagaaaaggt	gggtgcggtg	gctcacgcct	gtaatcccag	cactttgggg	69960
gtccgaggtg	ggcggatcac	aaggtggaaa	gatcaagacc	atcctggcca	acatggtgaa	70020
accccgctct	tactaaaaat	acaaaaatta	gctgggcgtg	gtgcacgcct	gtagtcccag	70080
ctactcagga	ggctgaggca	ggagaatcac	ttgaacccag	gaggtggagg	ttgcagtga	70140
ccgagatcgc	gccactacac	tctagcctgg	gcaacagagt	gggactccgt	ctcaaaacaa	70200
aaaacaaaaa	acagagcaaa	aaaaaaaaaa	caaaaaaaa	aaaaaaagaa	aagaaaagat	70260
aactat	ccaggatgca	ggggtaaaac	caagattctc	tgTTTTTTac	TTTTtagtga	70320
atgcttattc	tcggtgtgca	aggaaaagta	tgaatttttc	acatctgtat	atttcaaate	70380
tgcttaggca	aatcaacttc	aacttgtact	taaaaaaatt	gtccaggacc	ccctattgaa	70440
aacaatatga	aaagtttgcc	tttatatttc	cctttgagat	ctggtgttta	atccttgaaa	70500
tgtattc	aaaaagtatg	tgctagtgtt	actaaatata	tgacaaaaag	agatctgaat	70560
ttgtggccaa	attaaaaata	ggacagagga	gctcaagatt	cagtcattat	atttacttga	70620
catatattta	tttacttgac	cttagcagct	tatttatcct	ctttgcggat	cagtttcttc	70680
atctgtgaaa	tgagttcaaa	tcatcaagtt	catatgatga	ttaagcaaat	aaaatgaagt	70740
aaattatgtt	aaacactgag	cacaatatat	gactgagaga	ataccaata	acttgttata	70800
taaattatct	agttacccaa	taactagtta	taatagt	tatatgtctt	gcacatccat	70860
ttacttgcta	gtgattgttg	aaaacactat	gttgatttta	accctgaagt	ctgggctcaa	70920
ctgtgaagag	tgtaaaacaa	acaactgata	tcacctcctg	gtctaggaag	gggtaaaagt	70980
cactggatag	ctttatat	gtgatcaact	agttgttata	taagtgaaga	attactctac	71040
cctgcactat	tcccattctc	acaggtcaga	ggactcagag	aaatataact	gagtcctata	71100
agagttactc	ctttatatgt	ctgttcatgc	caagtatctc	tttcttccta	cagggtgtac	71160
aggtagccct	ttttaagatt	cttgtcaggt	gctaaaacct	agcttatgag	gcaggcatct	71220
gacatactct	ggtgaaggtt	agttgttggg	ggagacctta	gggtacaagt	tccatcagct	71280
atatccttat	tatctttggc	aaaataatct	gagtattttc	aatgttgatt	attcttccca	71340
ctaaaaatac	atTTTTTctac	attaaagaaa	ctcaactgag	taacctacaa	ttacctttct	71400
catgaaattc	caaacagtgt	tattatgtcc	actgttaaac	tgtgaaaatg	gcggtcagct	71460
gatatagctc	tttggagaat	cctaagtcct	taatcacacc	aaccttgaat	tttctacatg	71520
tcagttatca	caaagatagt	tagaaatcat	cgtctttaaa	atgtcacaca	ggattctacc	71580
ttttcattgc	accagttttt	cagtataaag	taatatgatg	aaaaatagta	ttttaaaata	71640
tatatTTTTg	taaaaaatgtg	aagtttaaac	ttttaaaact	ctattctcta	ggaagaaaat	71700
aaatctttta	aggaacagaa	aaaactgaat	gacttgtgtt	tcctaaagag	actattacaa	71760
gagataaaaa	cttgtttggg	taaaattttg	atgggcacta	aagaacactg	aaaaatatgg	71820
agtggcaata	tagaaacacg	aacttttagct	gcatacctcca	agaatctatc	tgcttatgca	71880
gtttttcaga	gtggaatgct	tcctagaagt	tactgaatgc	accatggtca	aaacggatta	71940
gggcatttga	gaaatgcata	ttgtattact	agaagatgaa	tacaaacaat	ggaaactgaa	72000
tgctccagtc	aacaaactat	ttcttatata	tgtgaacatt	tatcaatcag	tataattctg	72060
tactgatttt	tgtaagacaa	tccatgtaag	gtatcagttg	caataatact	tctcaaacct	72120
gtttaaatat	ttcaagacat	taaactctatg	aagtatataa	tggtttcaaa	gattcaaaat	72180
tgacattgct	ttactgtcaa	aataattttta	tggctcacta	tgaatctatt	atactgtatt	72240
aagagtga	attgtcttct	tctgtgctgg	agatgtttta	gagttaacaa	tgatataatg	72300
ataatgccgg	tgagaataag	agagtcataa	accttaagta	agcaacagca	taacaaggtc	72360
caagatacct	aaaagagatt	tcaagagatt	taattaatca	tgaatgtgta	acacagtgcc	72420
ttcaataaat	ggtatagcaa	atgttttgac	atgaaaaaag	gacaatttca	aaaaataaaa	72480
ataaaataaa	aataaattca	cctagtcata	ggatgctaaa	ccttagtact	gagttacatt	72540
gtcattttata	tagattataa	cttgtctaaa	taagtttgca	atttgggaga	tatatTTTTa	72600
agataataat	atatgtttac	cttttaatta	atgaaatata	tgtatttaat	tttgacacta	72660
tatctgtata	taaaatattt	tcatacagca	ttacaaattg	cttactttgg	aatacatttc	72720
tcctttgata	aaataaatga	gctatgtatt	aa			72752

<210> 4
 <211> 78
 <212> DNA
 <213> Artificial

<220>
 <223> synthetic

<220>
 <221> synthetic
 <222> (1)..(78)

 <400> 4
 tgcaagcacc aaaaagggtga ccacacttca cattggcgat cgcggggttc tatctgagga 60
 tgtgaattta ttacaga 78

 <210> 5
 <211> 152
 <212> DNA
 <213> Artificial

 <220>
 <223> synthetic

 <220>
 <221> synthetic
 <222> (1)..(152)

 <400> 5
 gttatgtgct gatgggcttt atttgatcta cagaagatgc tctggtgaca ccctcagtgt 60
 gtgttggttaa caccttcctg cctcgagata acttcgtata atgtatgcta tacgaagtta 120
 tatgcatggc ctccgcgccg ggttttggcg cc 152

 <210> 6
 <211> 153
 <212> DNA
 <213> Artificial

 <220>
 <223> synthetic

 <220>
 <221> synthetic
 <222> (1)..(153)

 <400> 6
 gtatgctata cgaagttatg ctagtaacta taacggtcct aaggtagcga gctagcccaa 60
 ttgcgtactt tggatagtgt ctcttttttaa cctaaatgac ctttattaac actgtcaggt 120
 tcccttactc tcgagagtgt tcattgctgc act 153

 <210> 7
 <211> 24
 <212> DNA
 <213> Artificial

 <220>
 <223> synthetic

 <220>

<221> synthetic
 <222> (1)..(24)

 <400> 7
 ttgcattctt ttccaaataa gtgg 24

<210> 8
 <211> 25
 <212> DNA
 <213> Artificial

<220>
 <223> synthetic

<220>
 <221> synthetic
 <222> (1)..(25)

 <400> 8
 ttccaggatg aataggataa acagg 25

<210> 9
 <211> 30
 <212> DNA
 <213> Artificial

<220>
 <223> synthetic

<220>
 <221> synthetic
 <222> (1)..(30)

 <400> 9
 atccatcatc actccctgtg tttgtttccc 30

<210> 10
 <211> 19
 <212> DNA
 <213> Artificial

<220>
 <223> synthetic

<220>
 <221> synthetic
 <222> (1)..(19)

 <400> 10
 agctgactgc tgccgtcag 19

<210> 11
 <211> 31
 <212> DNA
 <213> Artificial

<220>
 <223> synthetic

<220>
 <221> synthetic
 <222> (1)..(31)

<400> 11
 tagactttgt agtggttagaa acatttgga c 31

<210> 12
 <211> 33
 <212> DNA
 <213> Artificial

<220>
 <223> synthetic

<220>
 <221> synthetic
 <222> (1)..(33)

<400> 12
 atttttgtaa tgcaatcatg tcaactgcaa tgc 33

<210> 13
 <211> 22
 <212> DNA
 <213> Artificial

<220>
 <223> synthetic

<220>
 <221> synthetic
 <222> (1)..(22)

<400> 13
 ctcaactctat cccatccaag gg 22

<210> 14
 <211> 21
 <212> DNA
 <213> Artificial

<220>
 <223> synthetic

<220>
 <221> synthetic
 <222> (1)..(21)

<400> 14
 atgggcaggt agcatccaca g 21

<210> 15
<211> 29
<212> DNA
<213> Artificial

<220>
<223> synthetic

<220>
<221> synthetic
<222> (1)..(29)

<400> 15
tgaatcatcc ctttgtctag cagaaccgg

29